



School of Chemical Biology & Biotechnology, Peking University

# Review Report

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**Supervisor :** Prof. Dr. Yong Huang

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# Review Report

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ELSEVIER

## Tetrahedron

journal homepage: [www.elsevier.com/locate/tet](http://www.elsevier.com/locate/tet)



Tetrahedron report number 1010

### The Claisen rearrangement in the syntheses of bioactive natural products<sup>☆</sup>



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*Department of Chemistry, University of Kalyani, Kalyani 741235, West Bengal, India*



L. Claisen





- Background of Claisen Rearrangement
  - Aromatic Claisen Rearrangement
  - Aliphatic Claisen Rearrangement
  - Stereochemistry
  - The Factors
- Applications of Claisen Rearrangement
  - Aromatic Claisen Rearrangement
  - Aliphatic Claisen Rearrangement
  - Tandem Reaction
  - Aza-Claisen Rearrangement
  - Thio-Claisen Rearrangement
  - Retro-Claisen Rearrangement
- Conclusion



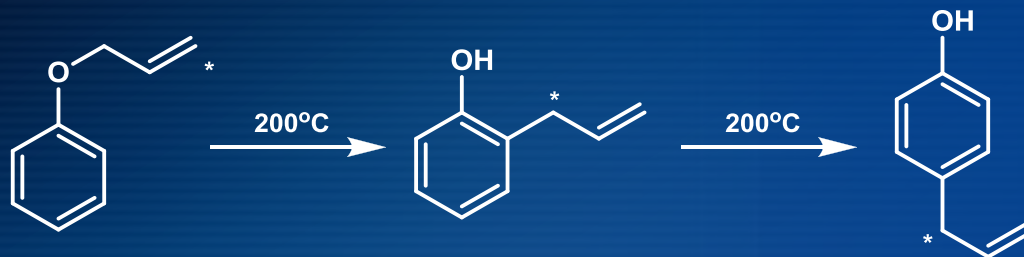


- **Background of Claisen Rearrangement**
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- **Conclusion**

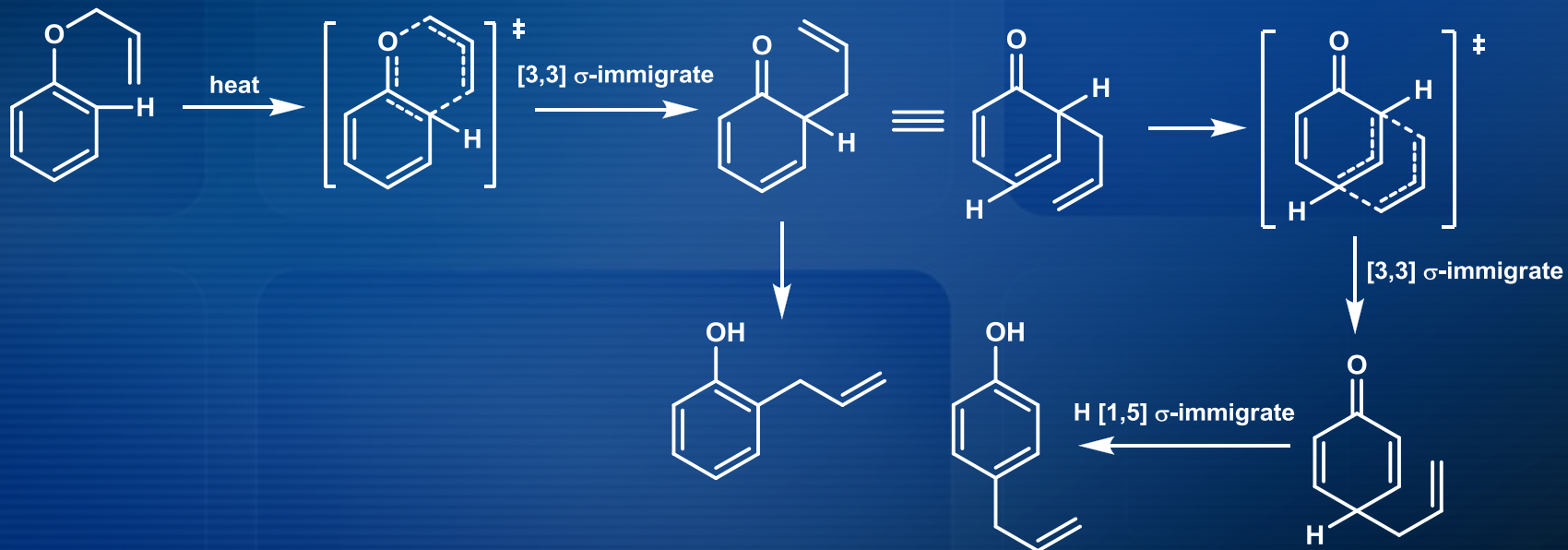


# Background

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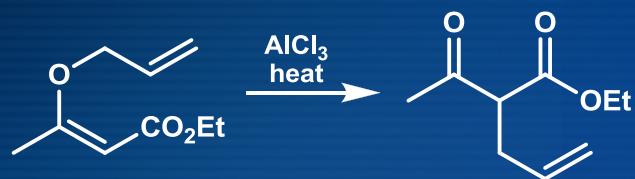
(L. Claisen *Chem. Ber.* 1912, 45, 3157-3166.)



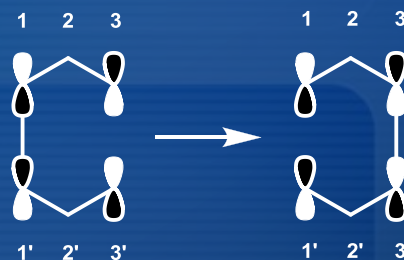


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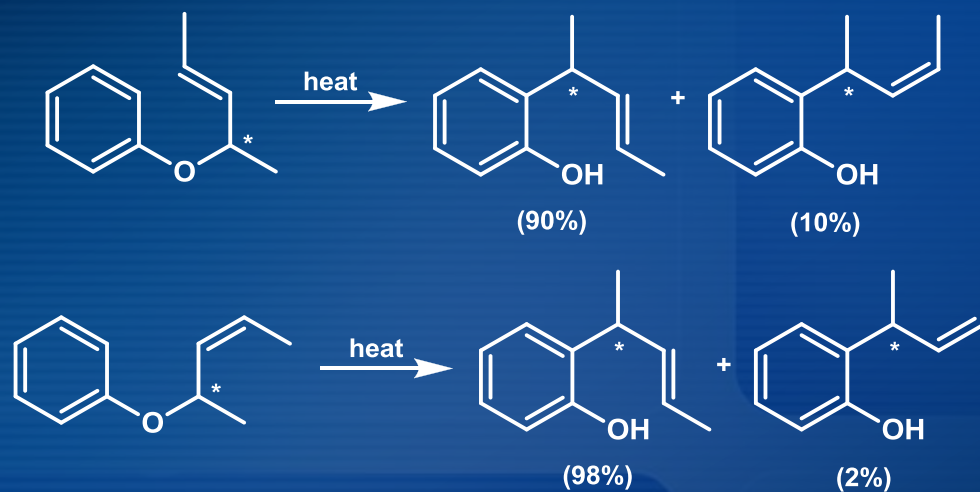
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(L. Claisen *Chem. Ber.* 1912, 45, 3157-3166.)



(Dewar & Houk)



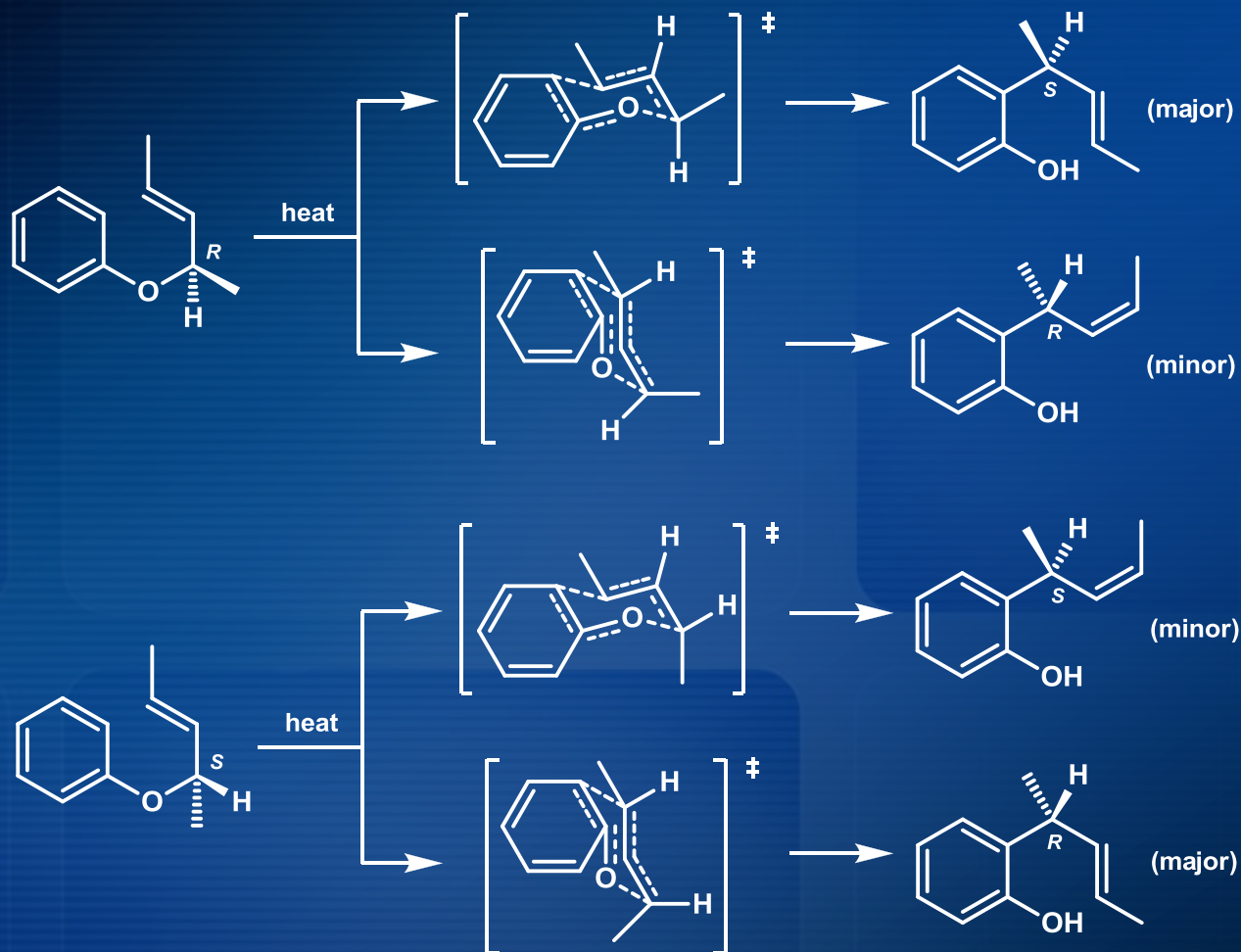




# Stereochemistry

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### Background



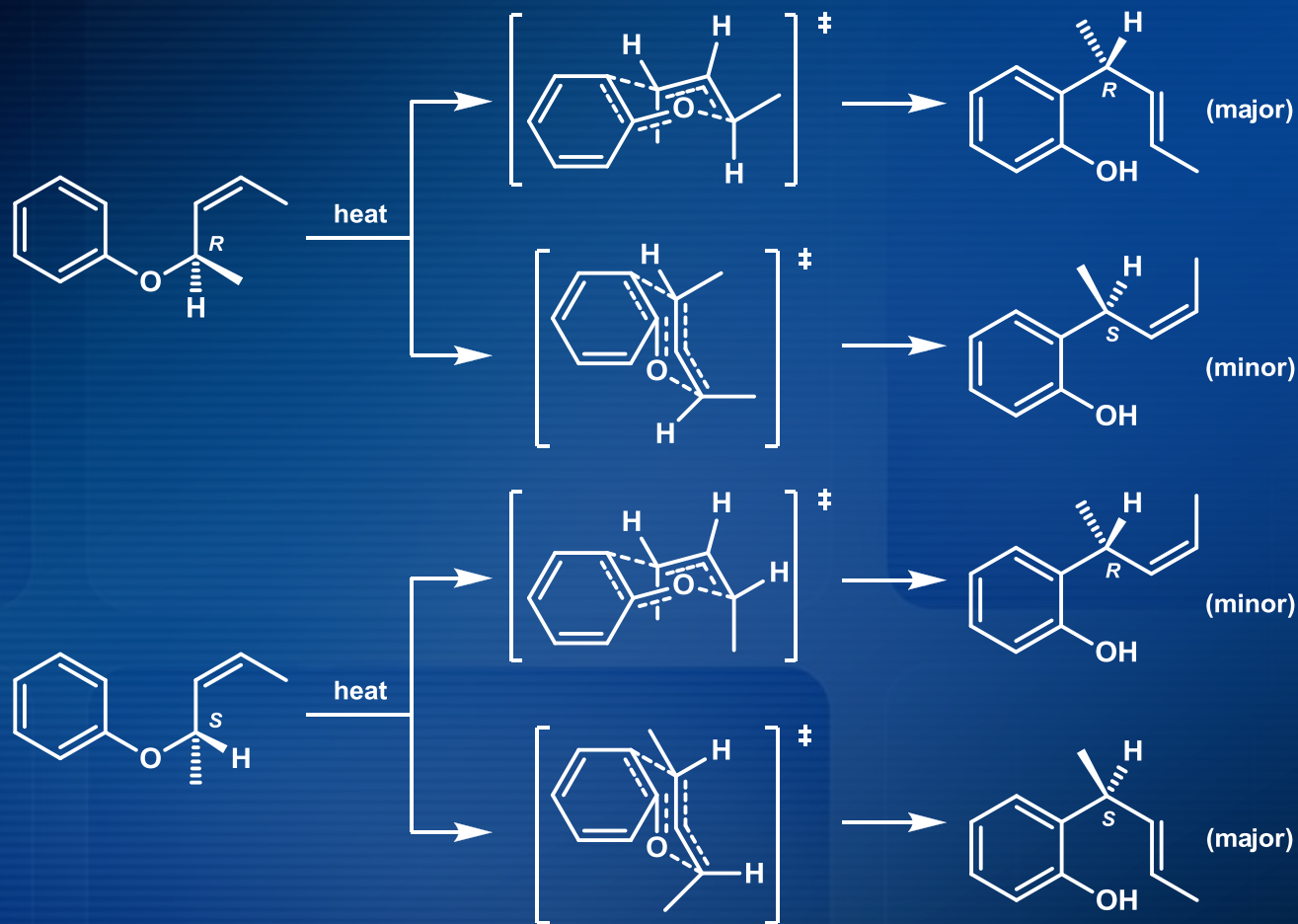




# Stereochemistry

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### Background

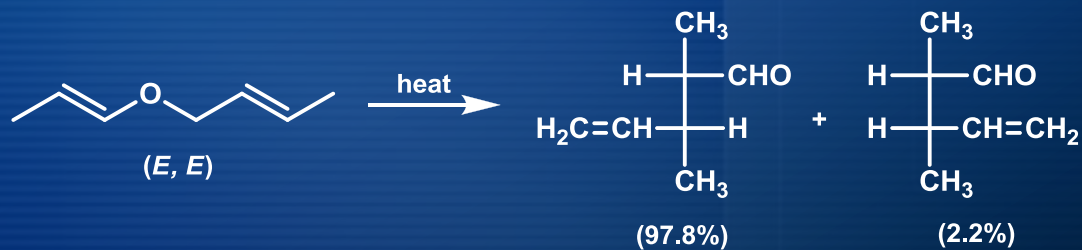
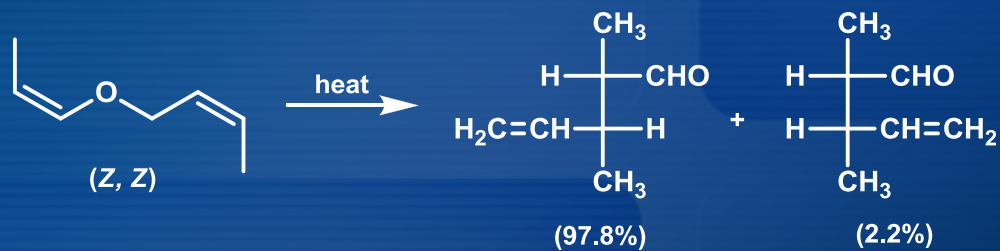
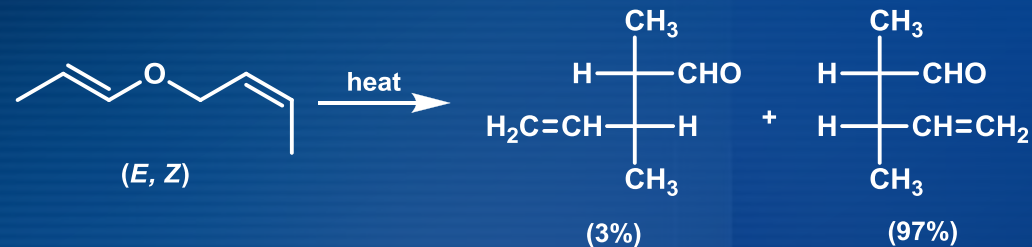
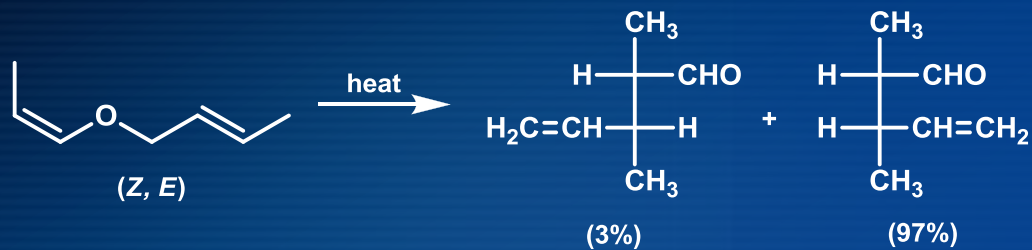




# Stereochemistry

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### Background

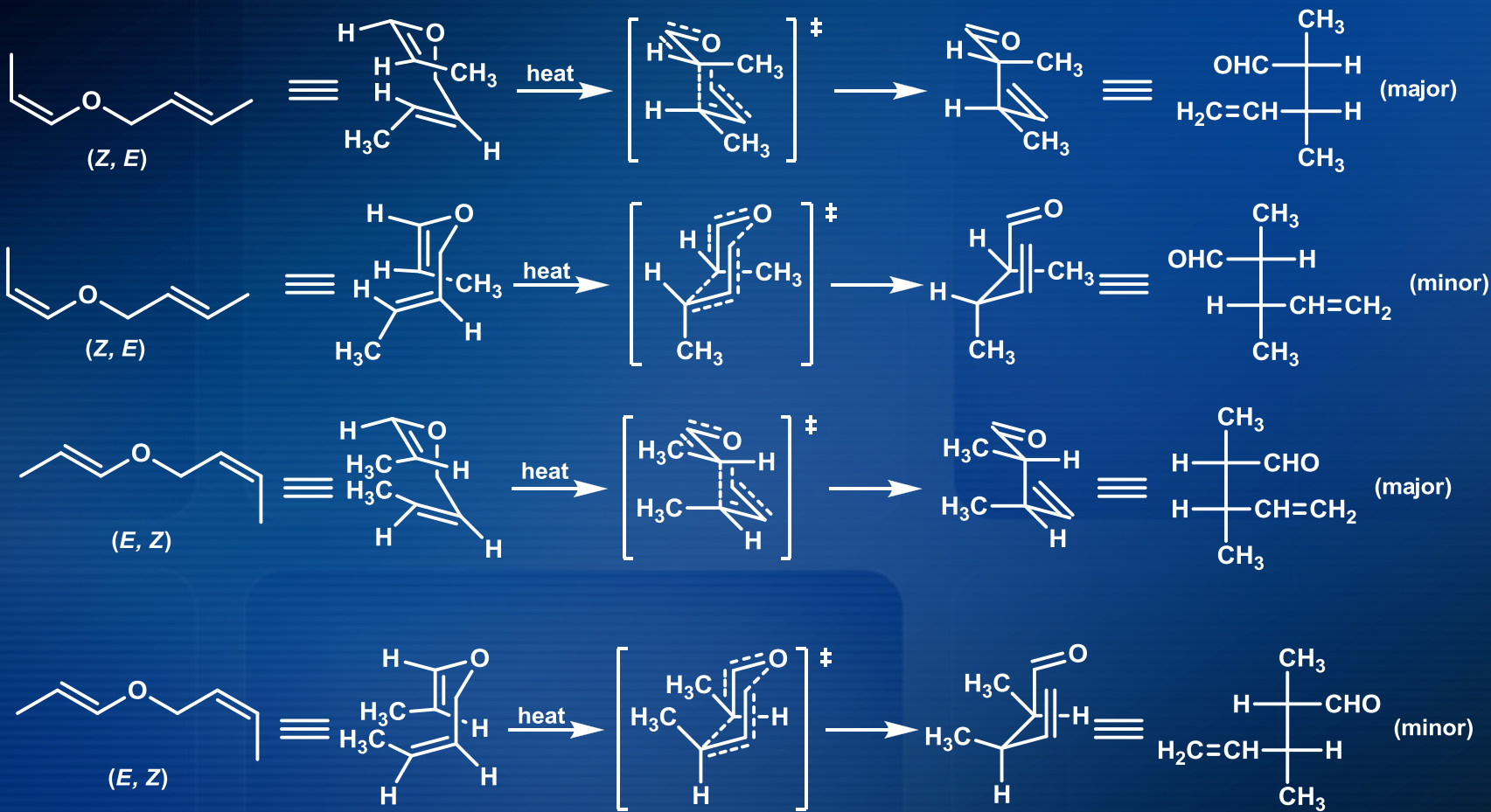




# Stereochemistry

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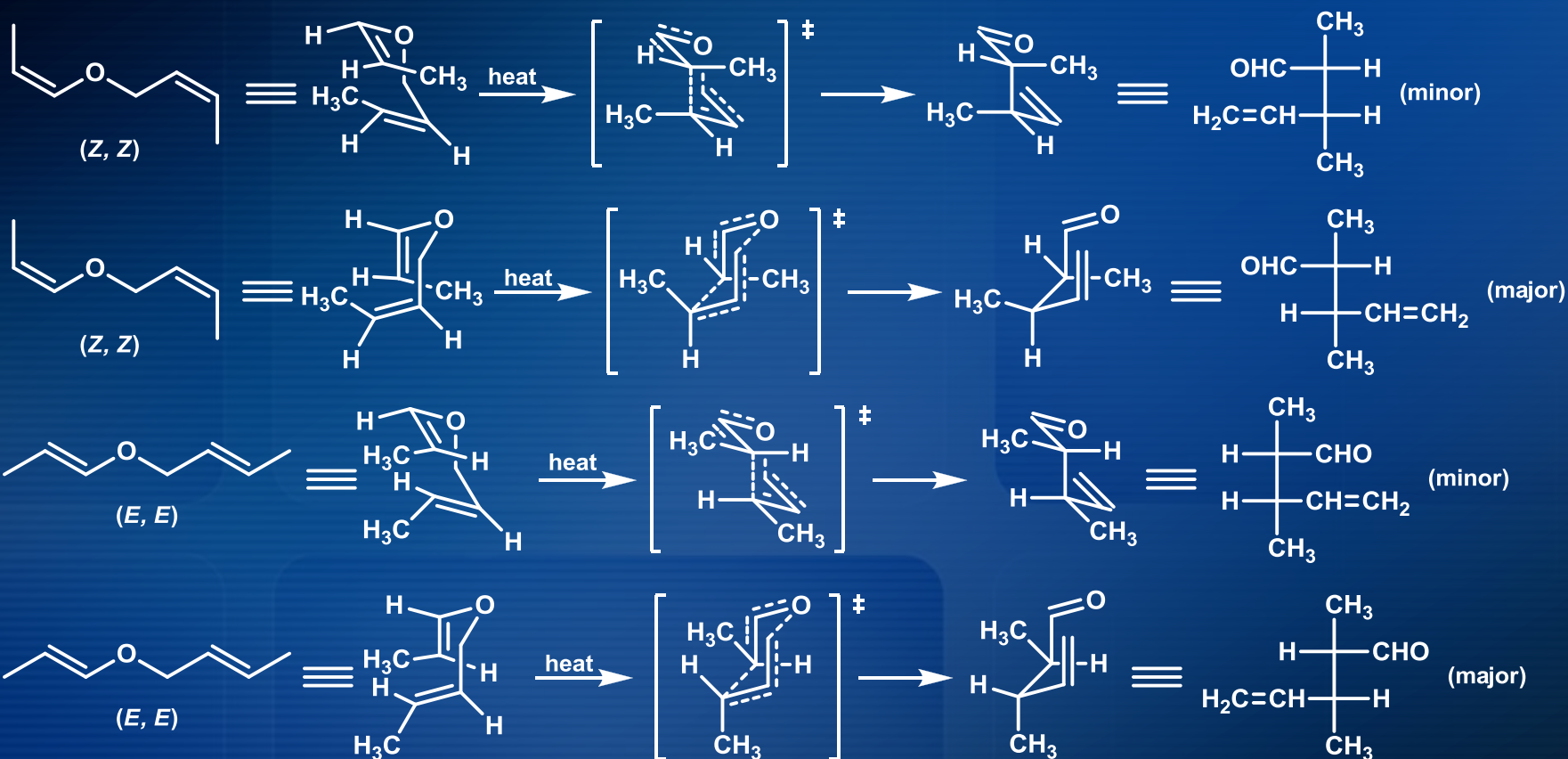




# Stereochemistry

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### Background

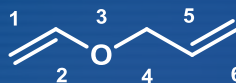




### ■ The Factors

- Pressure: high pressure can accelerate the reaction
- Solvent
  - Aromatic ether: EtOH/H<sub>2</sub>O > carbitol > tetradecane
  - Aliphatic ether: H<sub>2</sub>O > TFA > MeOH > EtOH > *i*PrOH > MeCN > acetone ≈ benzene > cyclohexane

### ■ Substitute



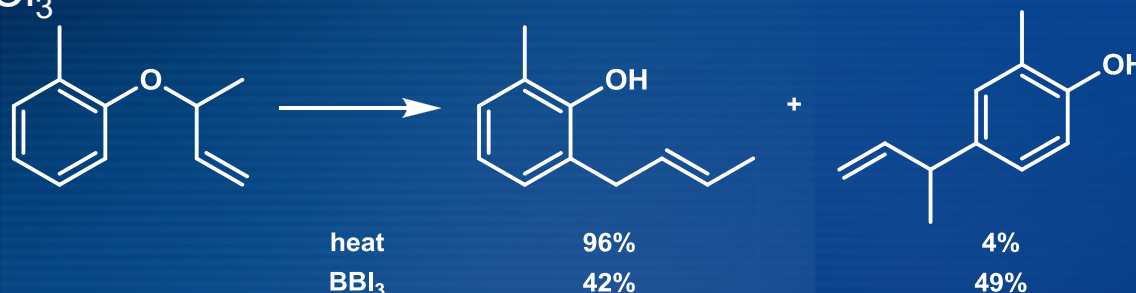
	improve the rate		decrease the rate	
	electronic	electrophilic	electronic	electrophilic
1	O, NH <sub>2</sub> , F, Me	--	--	CN, CO <sub>2</sub> CF <sub>3</sub>
2	OTMS, Me, F	CN, CO <sub>2</sub> <sup>-</sup> , CO <sub>2</sub> Me, CF <sub>3</sub>	--	--
4	Me, OMe	CN, CF <sub>3</sub>	--	--
5	--	CN	Me, OMe	--
6	Me, OMe	--	--	CN



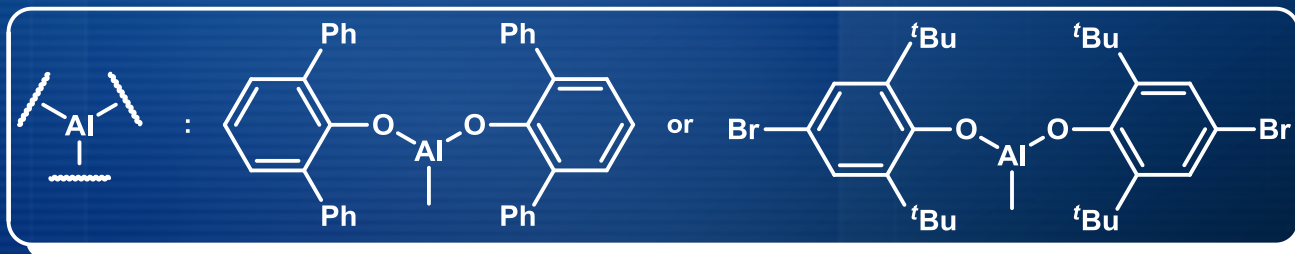
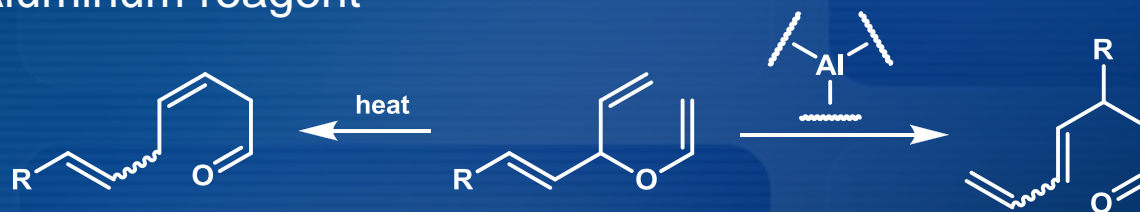
### ■ The Factors

#### ■ Lewis acid

- $\text{BCl}_3$



- Aluminum reagent



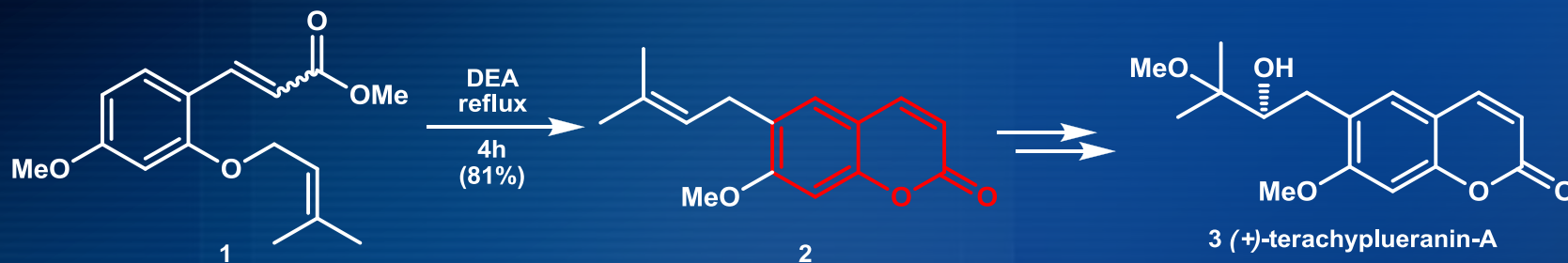




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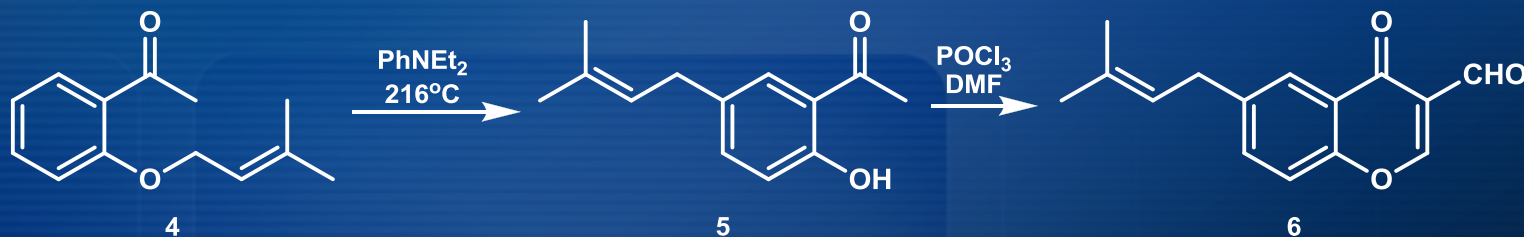


#### ■ In the Synthesis of Coumarin



Stermitz, F.R.; et al. *Tetrahedron Lett.* **2001**, 42, 6491-6494.

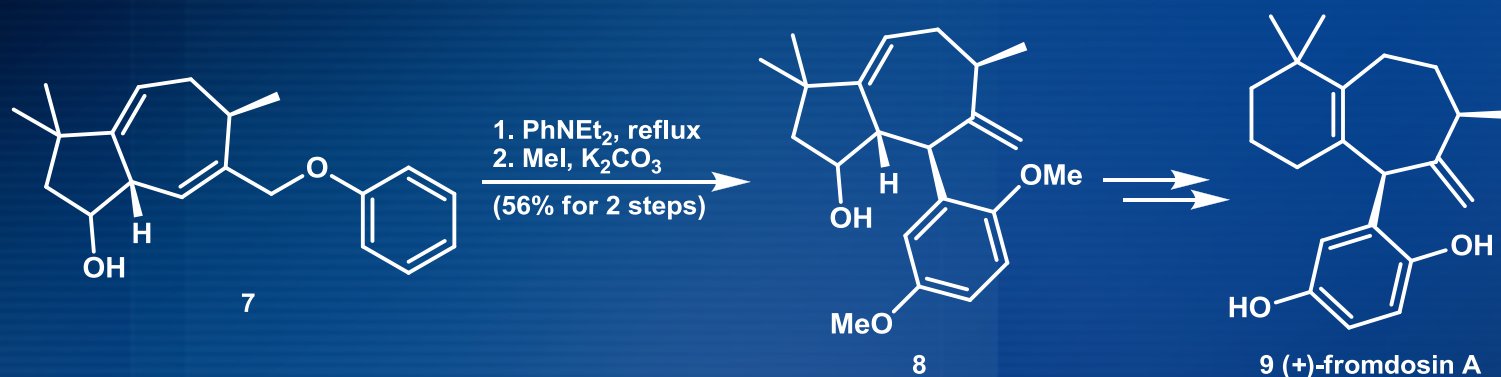
#### ■ In the Synthesis of Chromanone



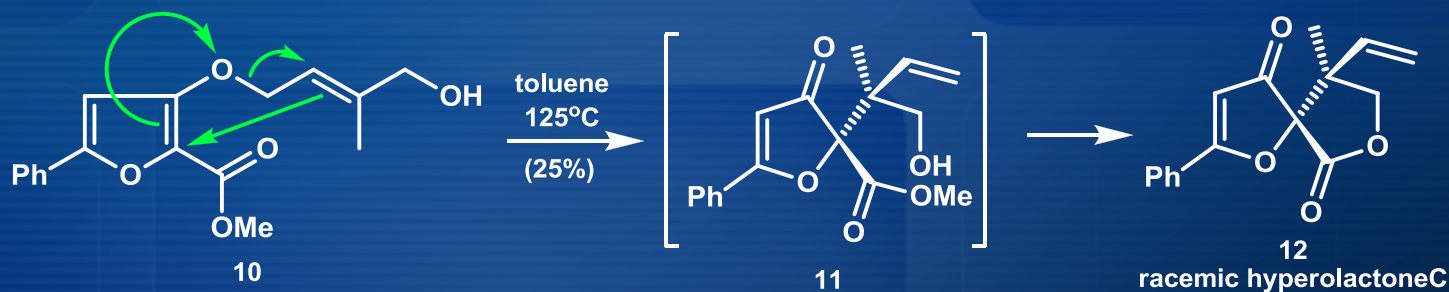
Krol, W.; et al. *Int. J. Oncol.* **2011**, 38, 941-953.



## ■ In the Synthesis of Mix-sourced Lignans



Trost, B. M.; *et al. J. Am. Chem. Soc.* **2007**, *129*, 11781-11790.



Kraus, G. A.; *et al. J. Nat. Prod.* **2004**, *67*, 1039-1040.

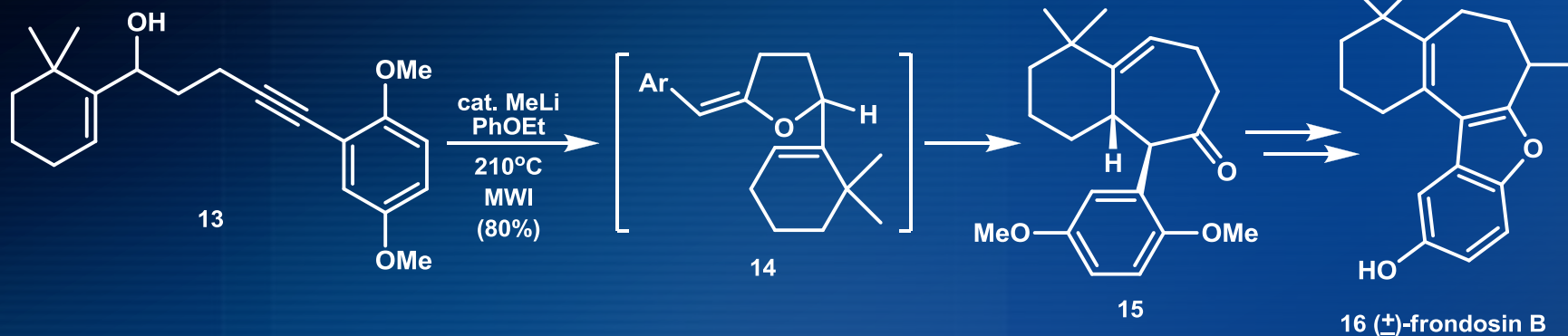




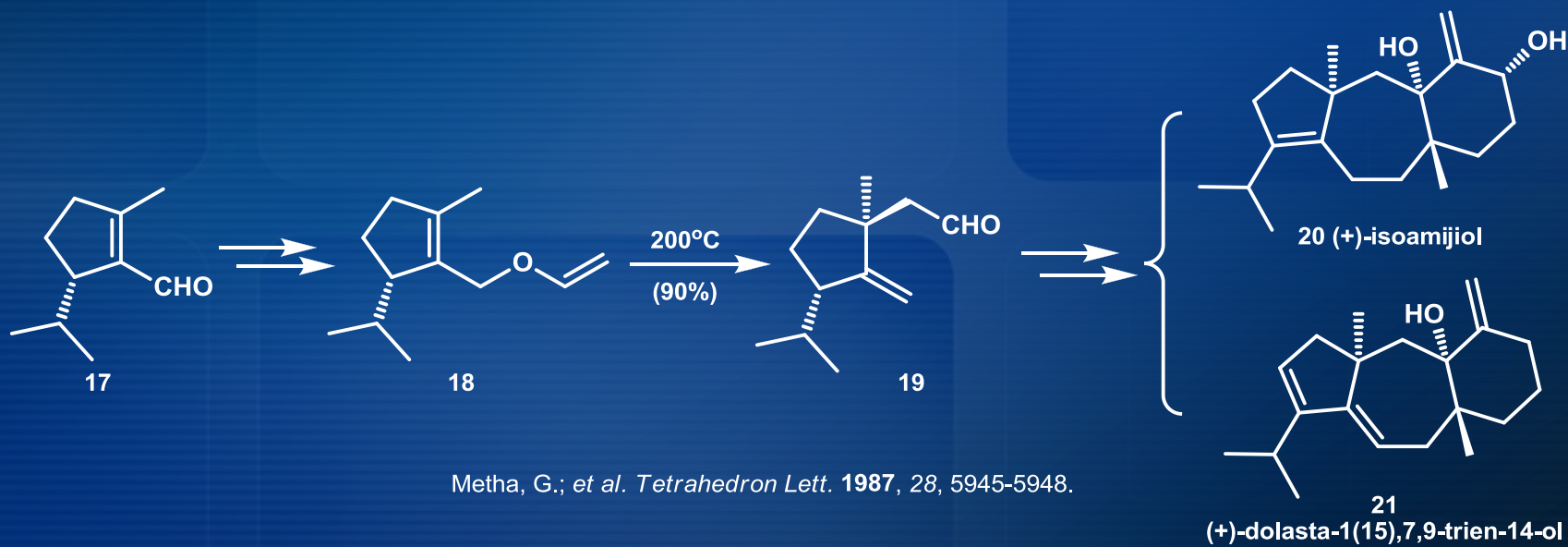
# Aliphatic Substrates

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### Application



Ovaska, T. V.; et al. *Org. Lett.* **2007**, 9, 3837-3840.



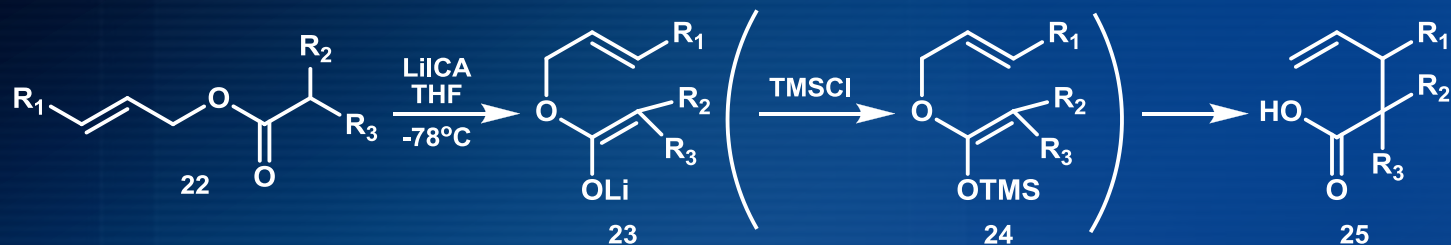
Metha, G.; et al. *Tetrahedron Lett.* **1987**, 28, 5945-5948.



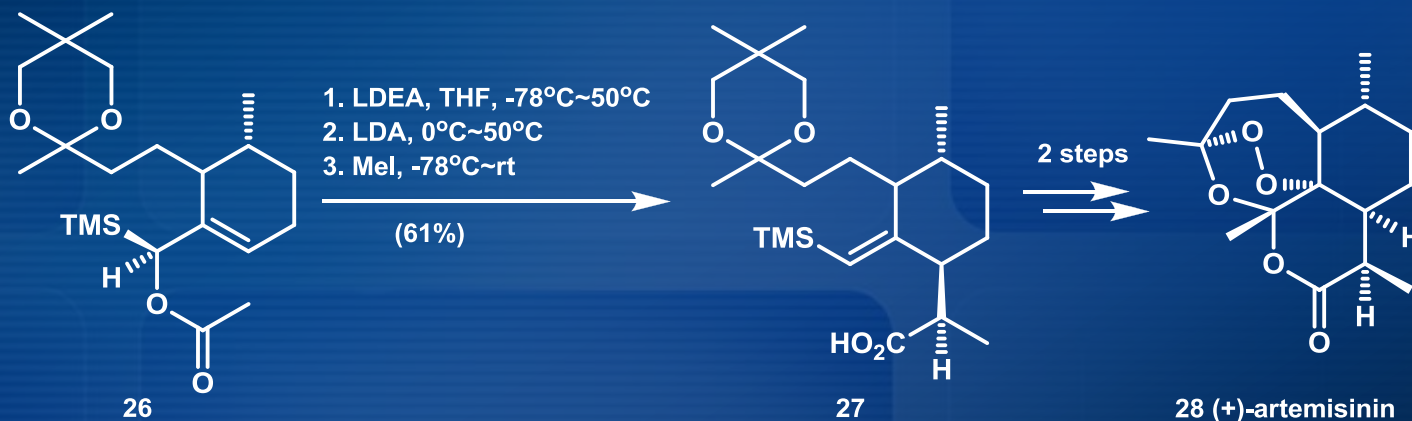
# Ireland-Claisen Rearrangement

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### Application



Ireland, R. E.; *et al. J. Am. Chem. Soc.* **1972**, *94*, 5897-5898.



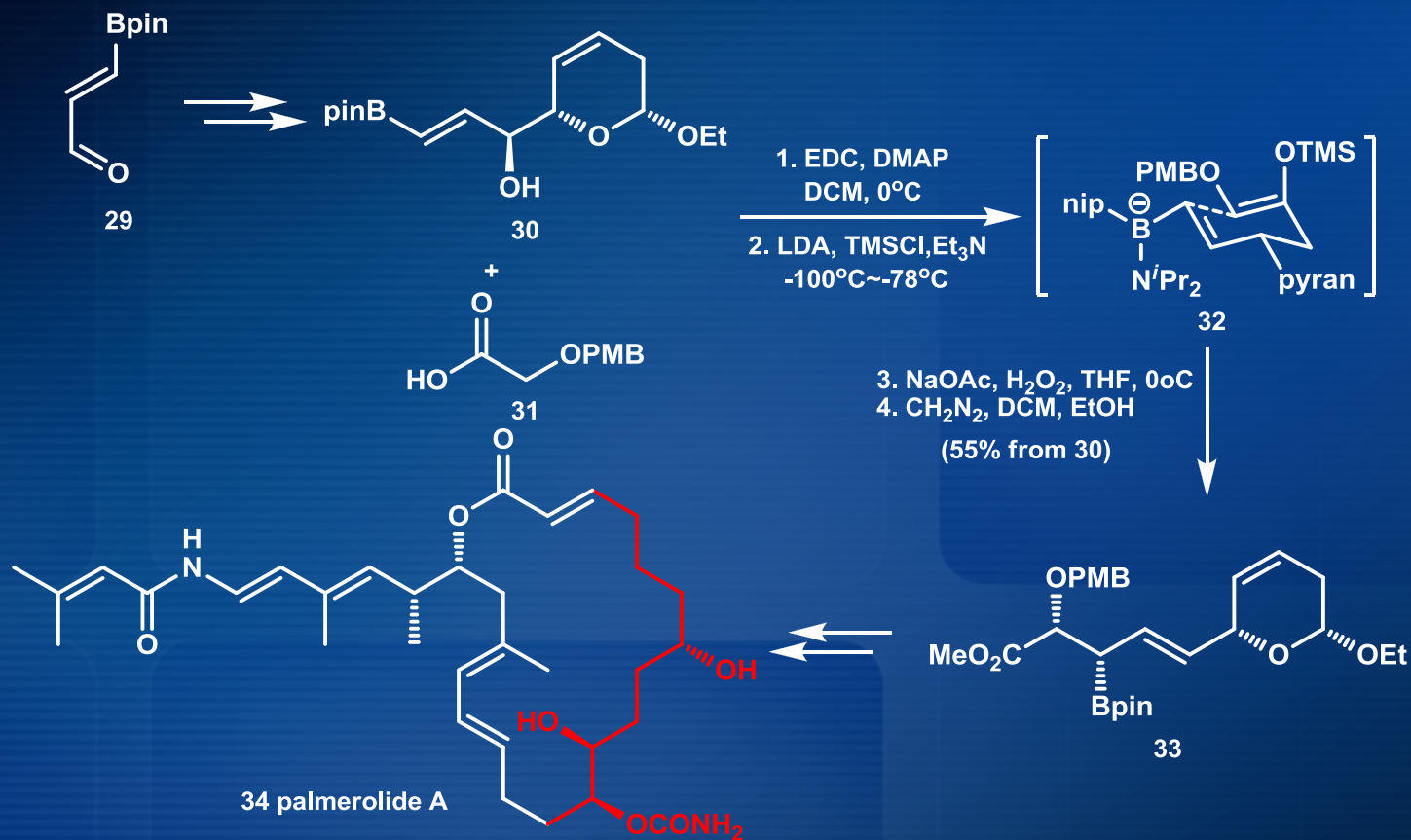
Avery, M. A.; *et al. J. Am. Chem. Soc.* **1992**, *114*, 974-979.



# Ireland-Claisen Rearrangement

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### Application



Hall, D. G.; *et al.* *J. Am. Chem. Soc.* **2009**, *131*, 14216-14217.

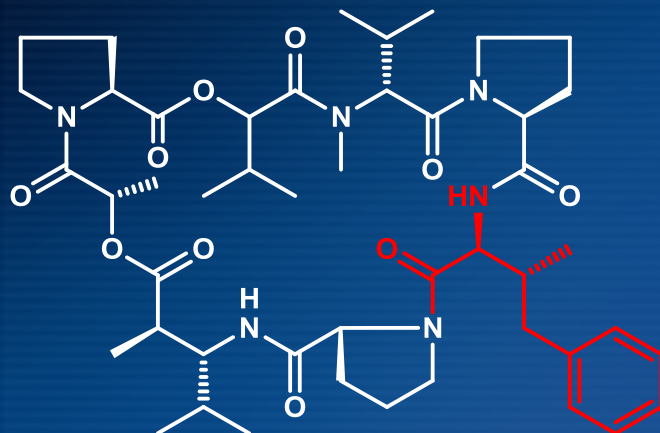




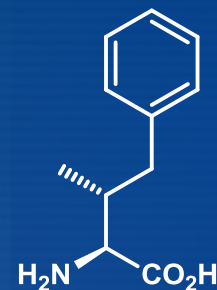
# Ireland-Claisen Rearrangement

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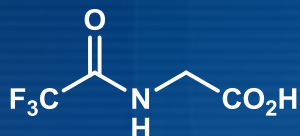
### Application



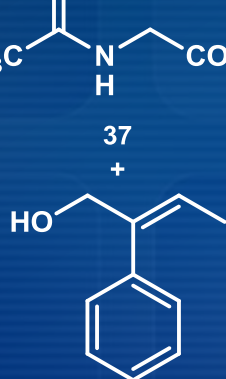
35 dolastatin 16



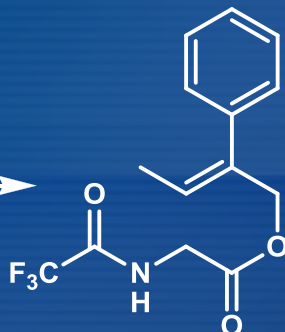
36 dolaphenvaline (Dpv)



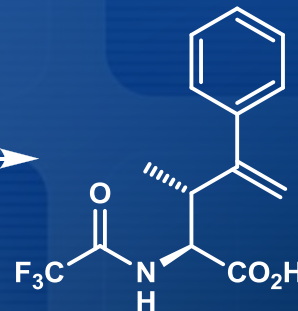
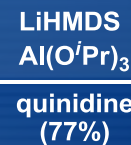
37



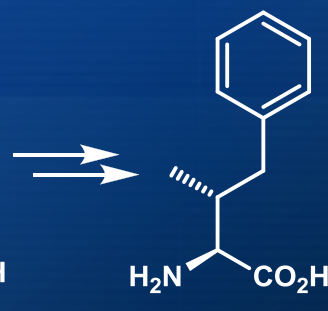
38



39



40



36

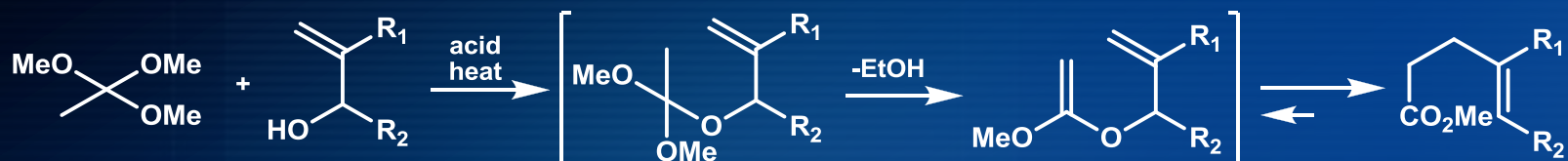
Pettit, G. R.; *et al.* *J. Nat. Prod.* **2011**, *74*, 1003-1008.



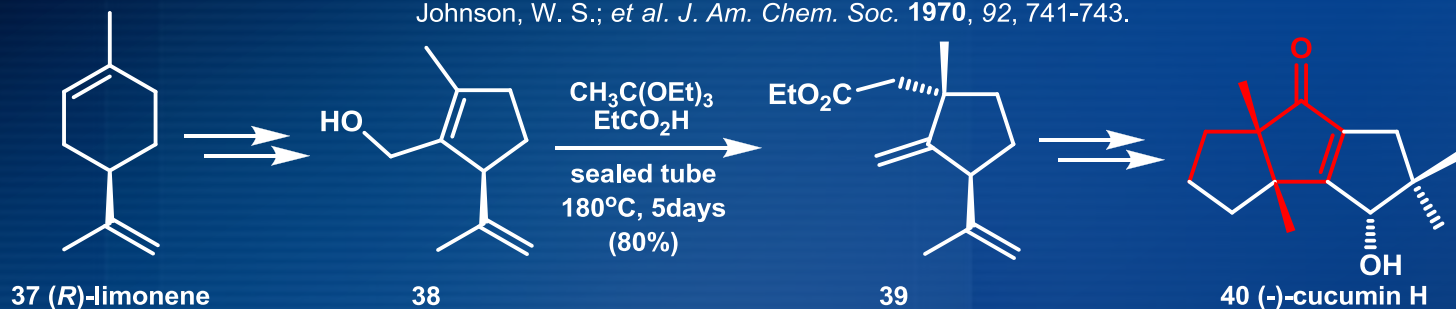
# Johnson-Claisen Rearrangement

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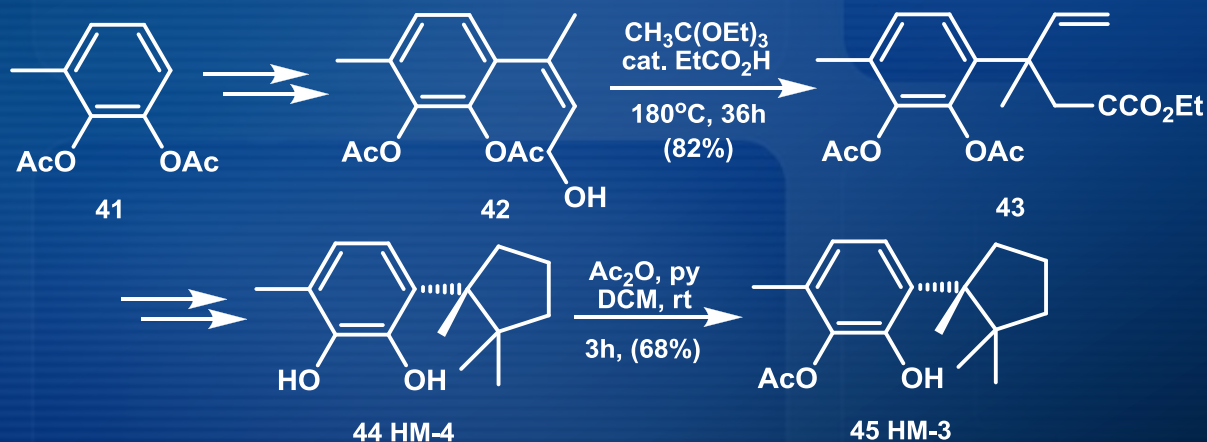
## Application



Johnson, W. S.; *et al.* *J. Am. Chem. Soc.* **1970**, *92*, 741-743.



Srikrishna, A.; *et al.* *Org. Lett.* **2003**, *5*, 2295-2298.



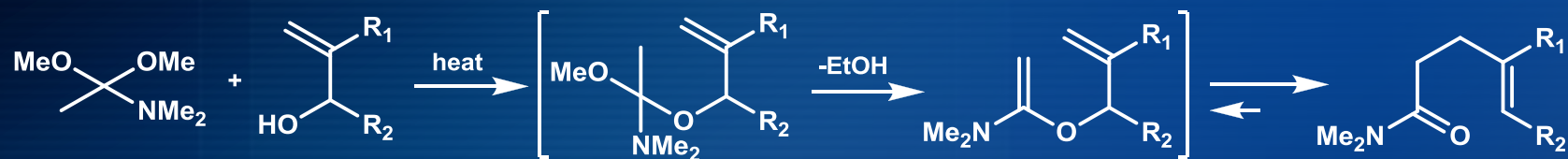
Srikrishna, A.; *et al.* *Tetrahedron* **2006**, *62*, 9393-9402.



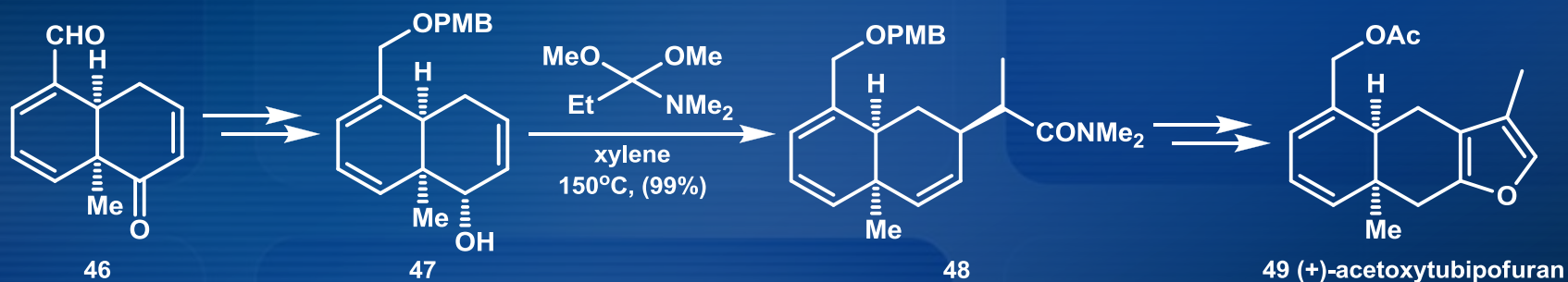
# Eschenmoser-Claisen Rearrangement

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## Application



Eschenmoser, A.; et al. *Helv. Chim. Acta* **1964**, *47*, 2425-2429.



Kundig, E. P.; et al. *J. Am. Chem. Soc.* **2003**, *125*, 5642-5643.

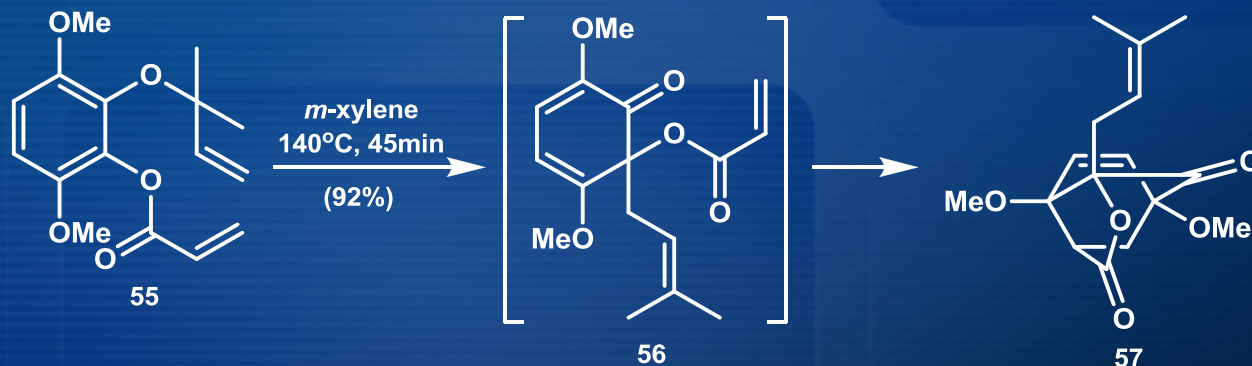
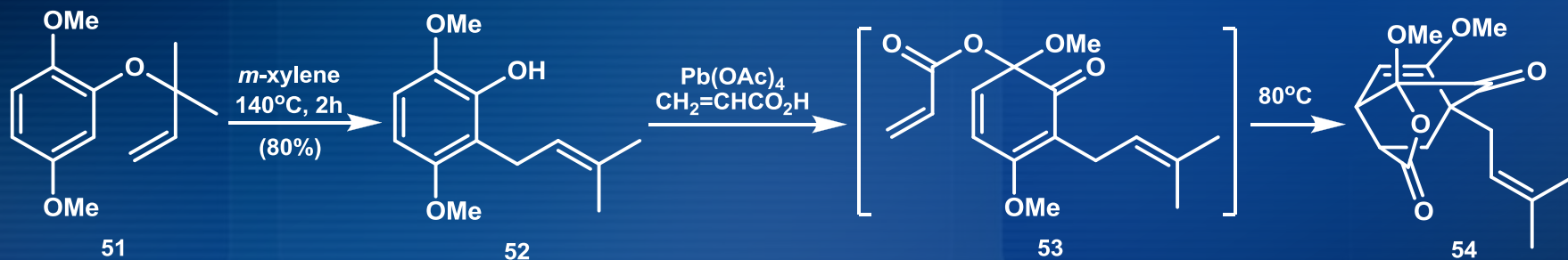
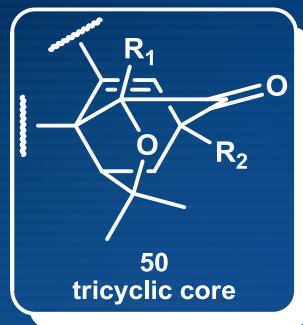




# Tandem Reaction

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### Application



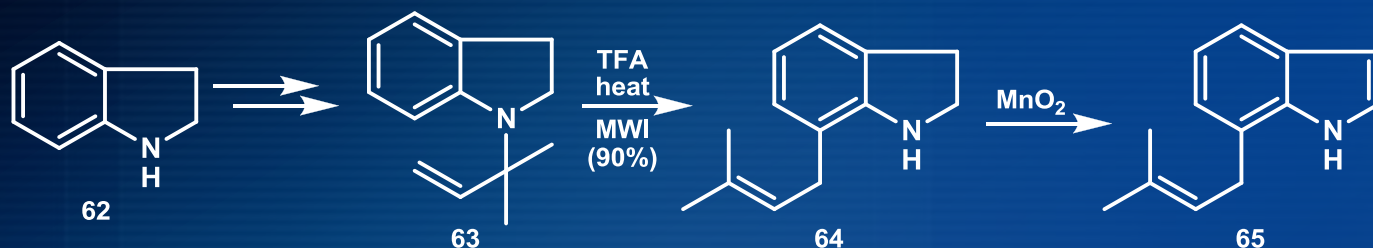
Theodorakis, E. A.; et al. *Org. Lett.* **2002**, *4*, 909-912.



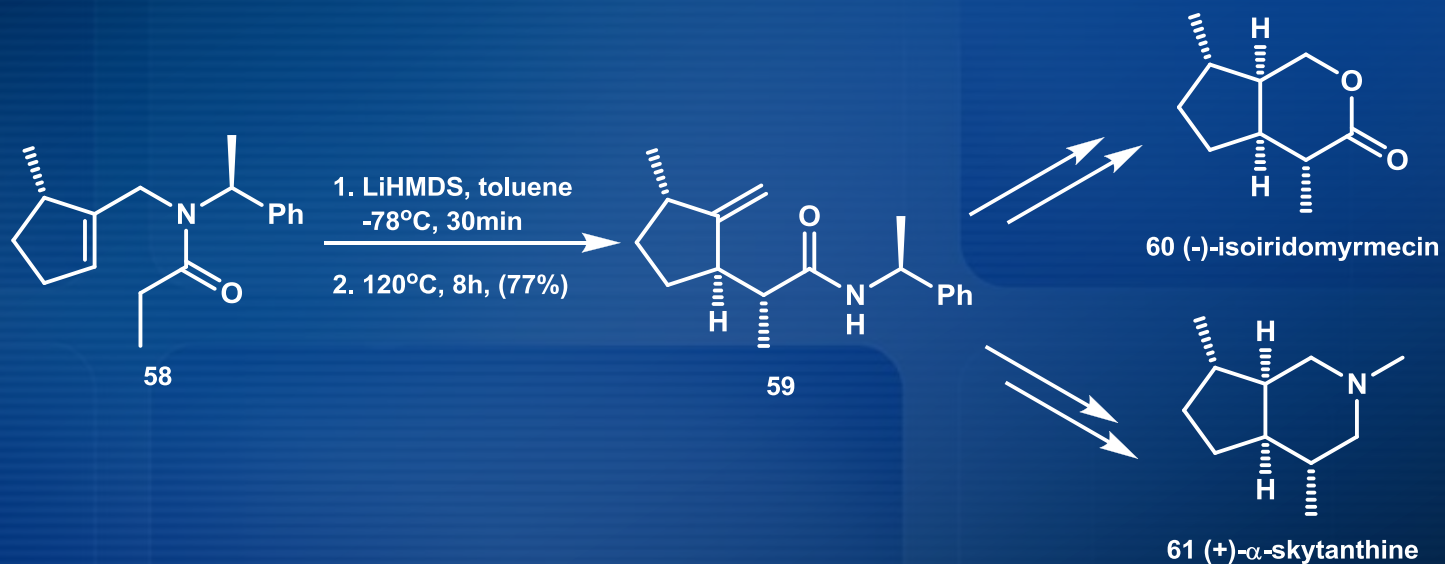
# Aza-Claisen Rearrangement

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### Application



Pirrung, M. C.; *et al. J. Org. Chem.* **2007**, 72, 5832-5834.



Tsunoda, T.; *et al. Pure Appl. Chem.* **1994**, 66, 2071-2074.

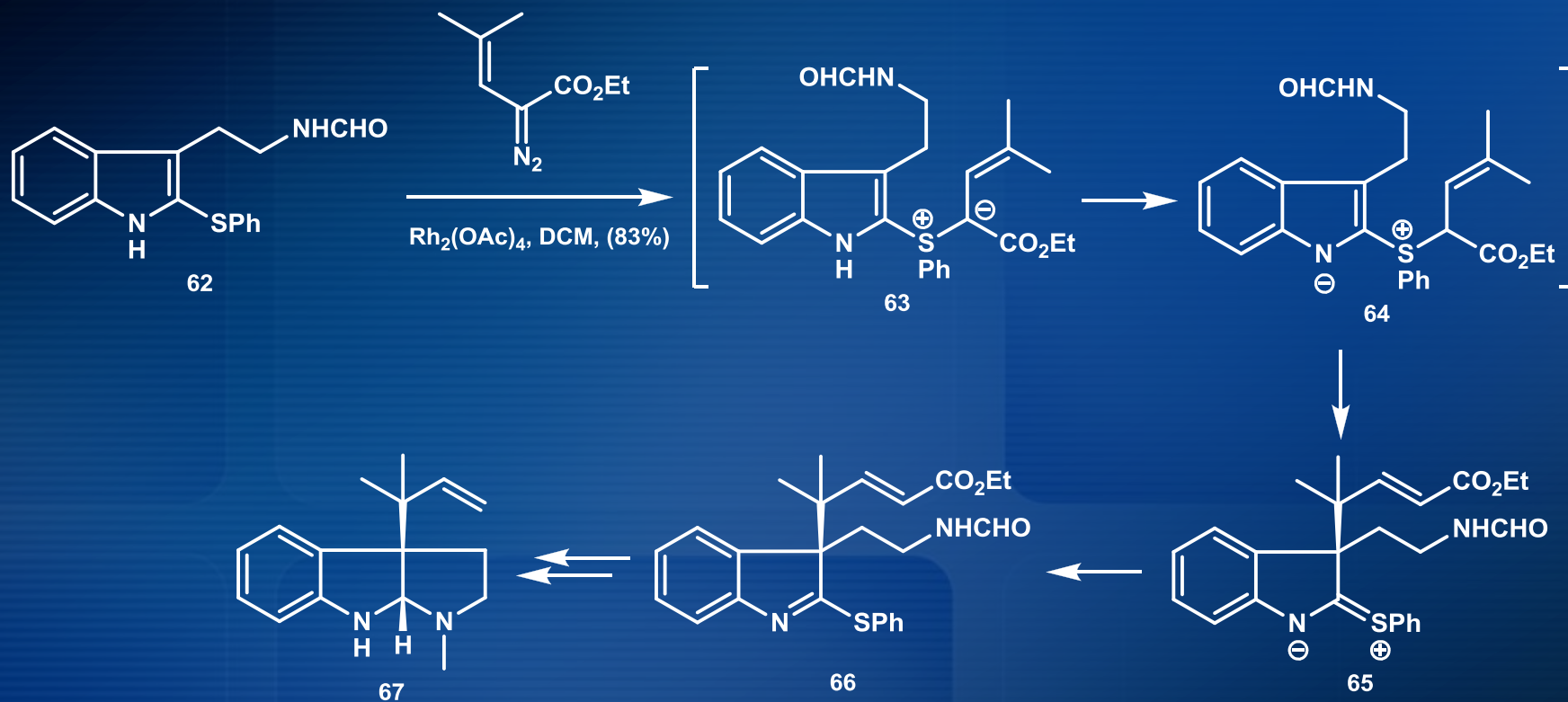
Tsunoda, T.; *et al. Tetrahedron Lett.* **1996**, 37, 2463-2466.



# Thio-Claisen Rearrangement

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### Application



Rainier, J. D.; *et al. Arkivoc* **2010**, 8, 116-125.

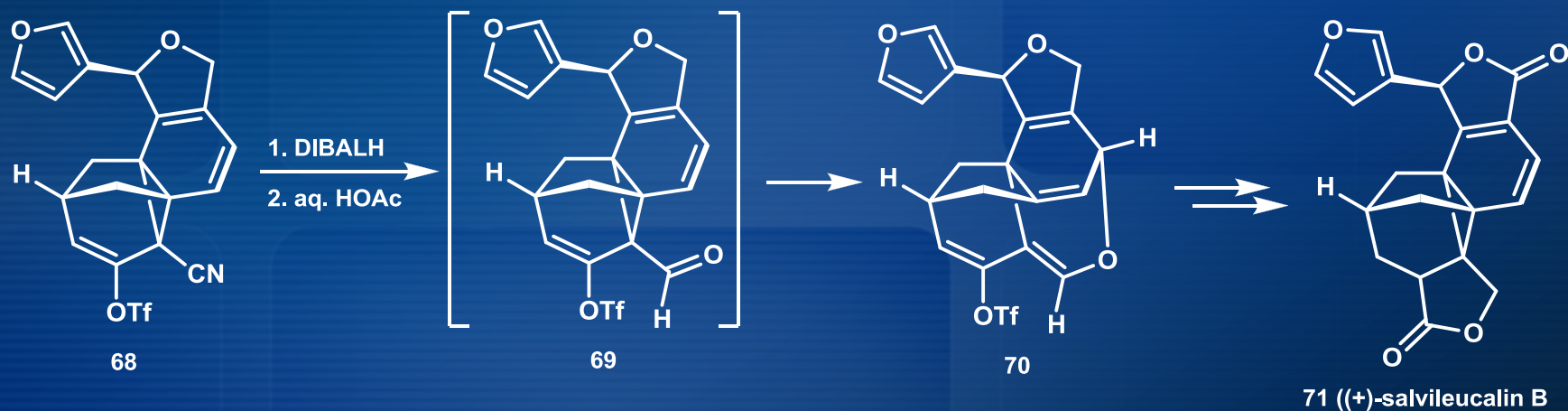
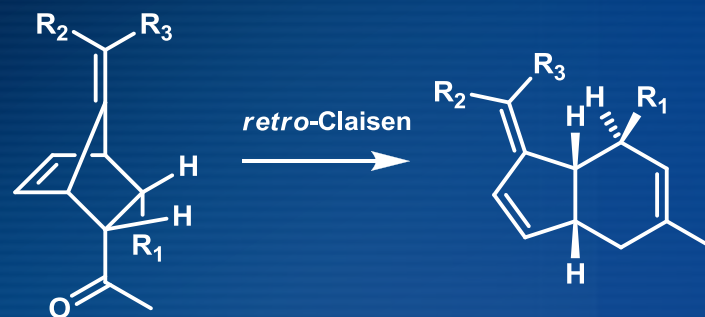




# Retro-Claisen Rearrangement

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### Application



Reisman, S. E.; *et al.* *J. Am. Chem. Soc.* **2011**, *133*, 774-776.



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- Conclusion



- **Claisen**重排反应作为一个经典的C-C键生成反应被广泛用于多种骨架的天然产物合成中。
- 由于可预测六元环过渡态的稳定结构，因此可以控制**Claisen**重排产物的立体构型。
- 虽然**Claisen**重排常被用于天然产物的全合成中，但是由于该反应需要高温条件，限制了它的应用。用**Lewis**酸催化，可降低重排反应温度，拓宽了**Claisen**重排的应用范围。
- 与其它反应串联的**Claisen**重排，可被用来合成结构复杂的多环骨架。





# Review Report

# Thank You !

Dr. Hao Jiang  
Aug. 26<sup>th</sup>, 2013

