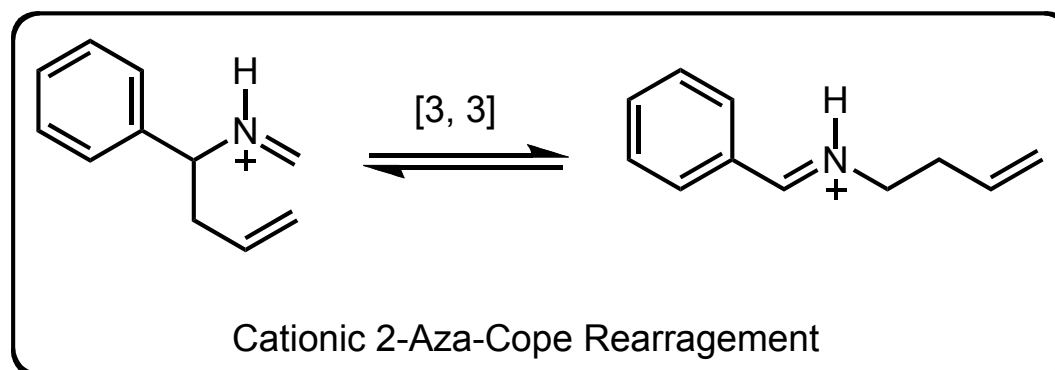
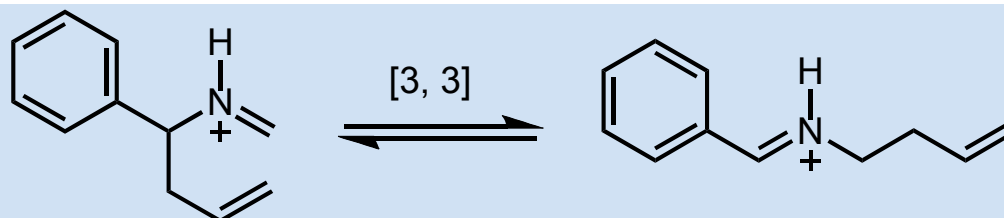


Aza-Cope Rearrangement



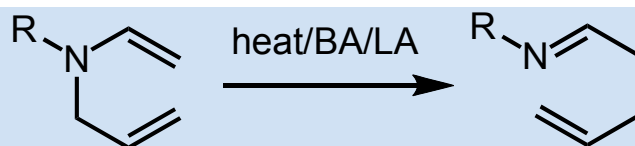
Hong Ren
The Wulff Group
04-10-09

Introduction to Aza-Cope Rearrangement



Cationic 2-Aza-Cope Rearrangement

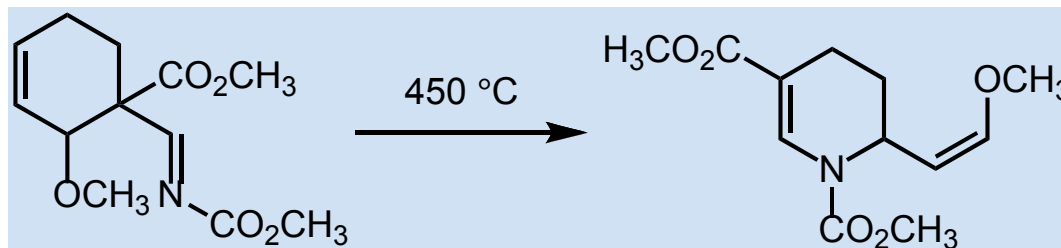
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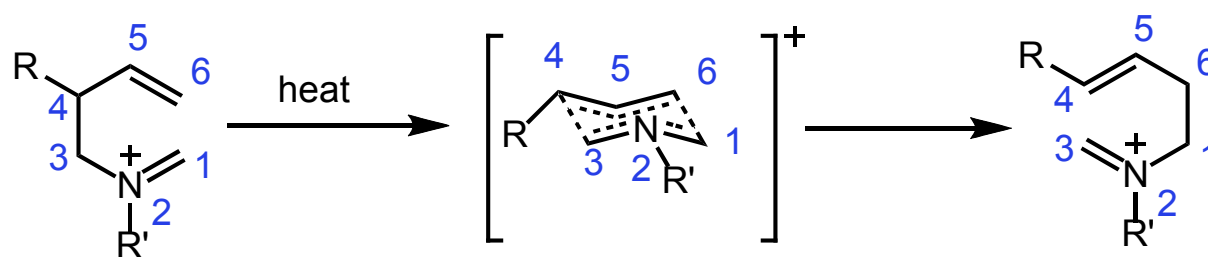
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1-Aza-Cope Rearrangement

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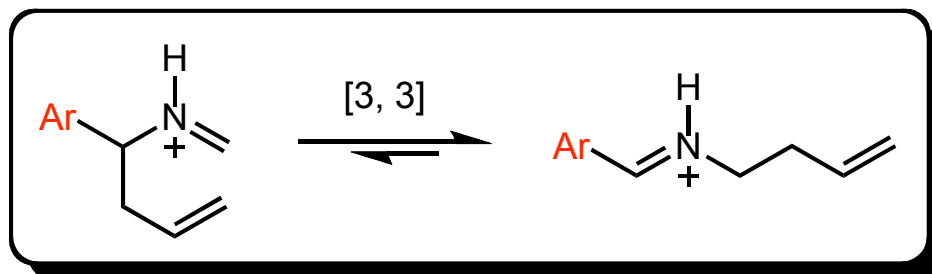
Mechanism of 2-Aza-Cope Rearrangement



- Highly Polarized System
- Lower Free Energy of Activation
- Distorted Concerted Mechanism
- Milder Reaction Conditions

Protocols for Driving Aza-Cope Rearrangement to a Single Product

→ By Aryl conjugation of the iminium ion

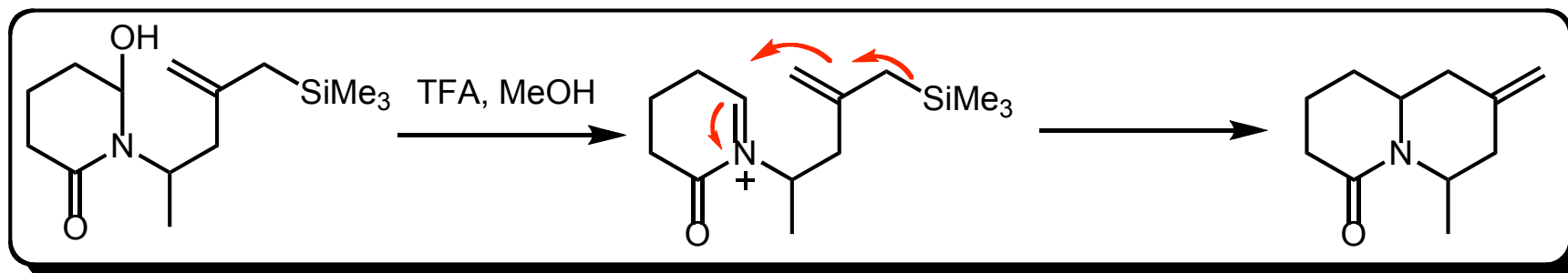


Geisel, M.; Grob, C. A.; Wohl, R. A. *Helv. Chim. Acta.* **1969**, 52, 2206.

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Grob, C. A.; Kunz, W.; Marbet, P. R. *Tetrahedron Lett.* **1975**, 2613.

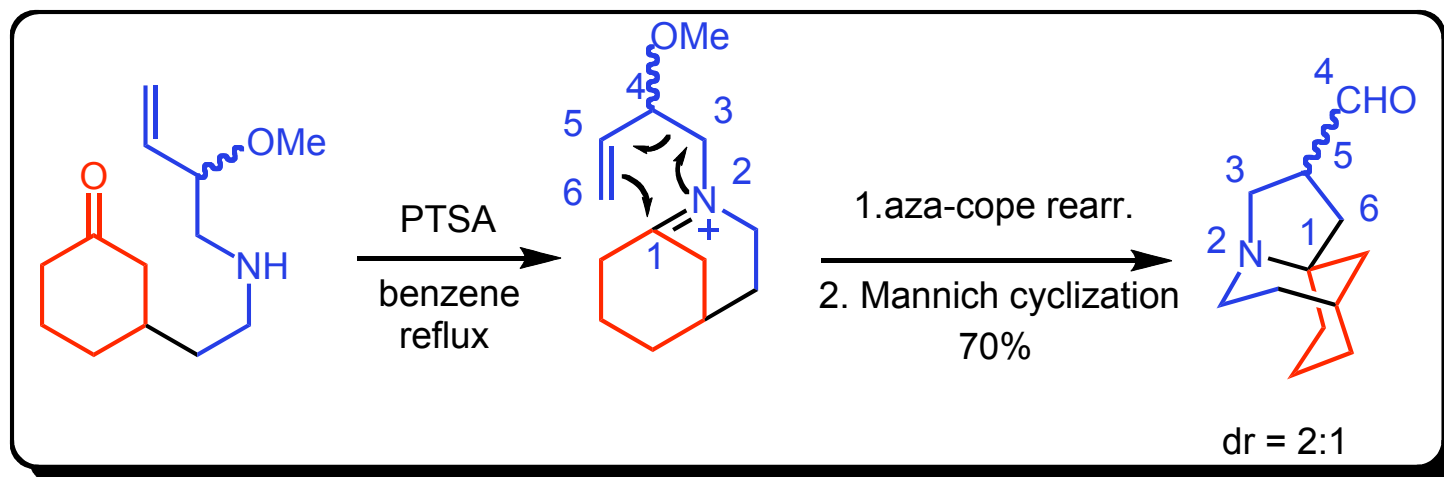
→ By Intramolecular trapping of the iminium ion with an incorporated nucleophile



Gelas-Mialhe, Y.; Gramain, J.-C.; Louvet, A.; Remuson, R. *Tetrahedron Lett.* **1992**, 33, 73.

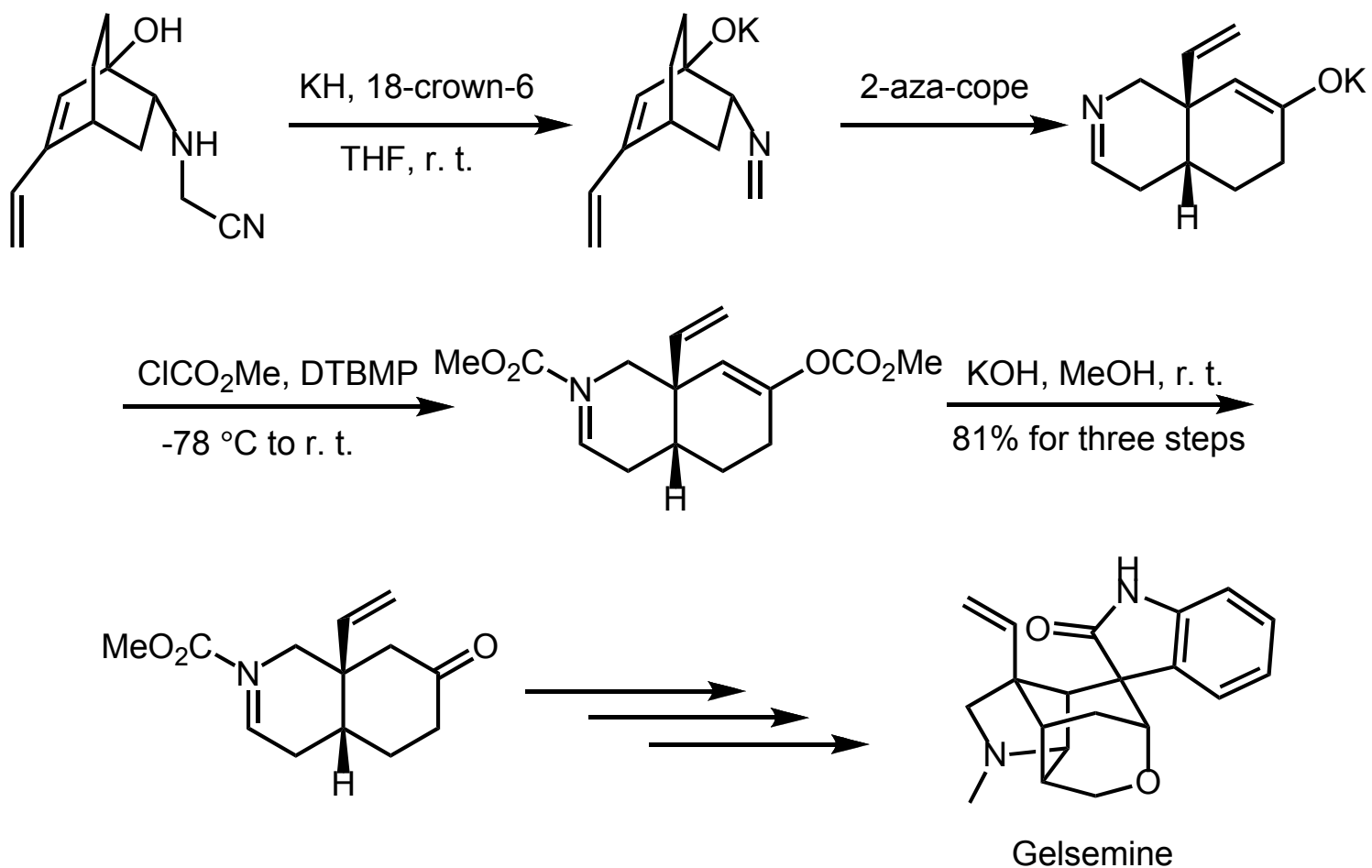
Protocols for Driving Aza-Cope Rearrangement to a Single Product

→ By trapping one iminium ion with Mannich reaction

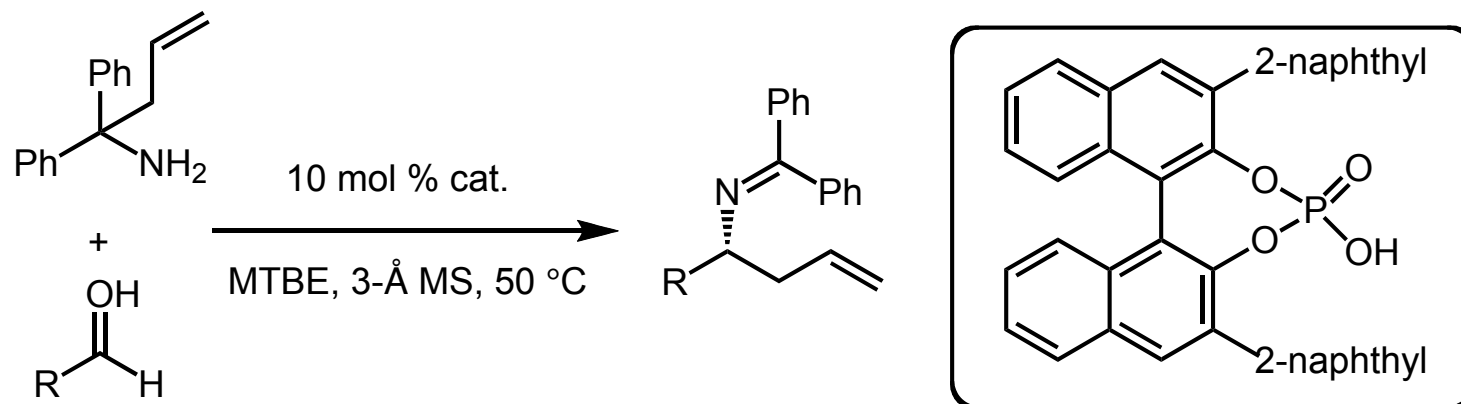


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Synthetic Applications of 2-Aza-Cope Rearrangement



The First Bronsted Acid Catalyzed Asymmetric 2-Aza-Cope Rearrangement



11 examples, 80-94% ee

