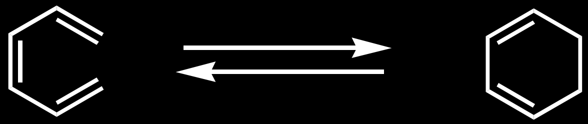
Electrocyclic Reactions

Lecture Notes

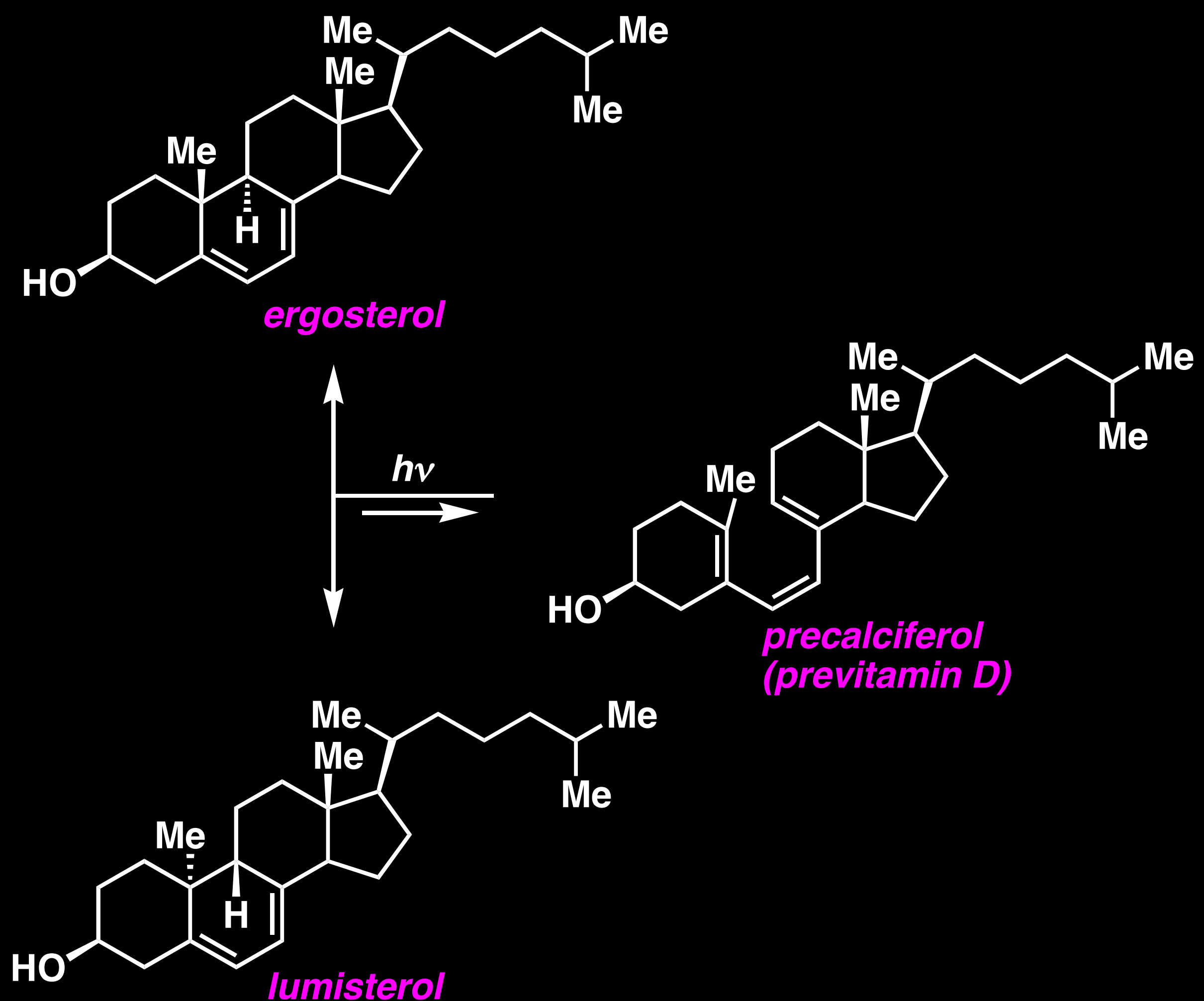


Key Reviews:

Electrocyclic Reactions:
Comprehensive Organic Synthesis, Vol. 5, p. 699

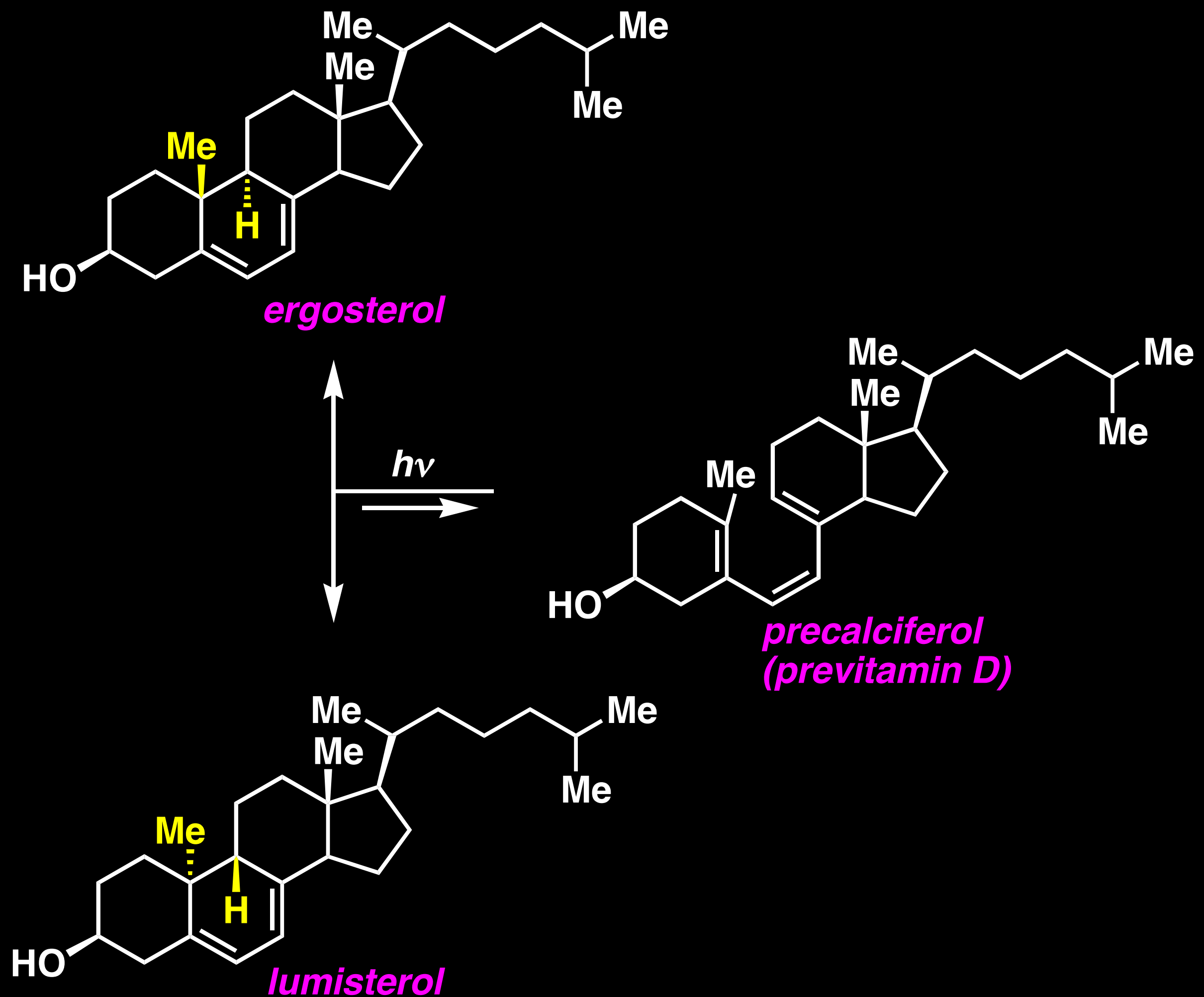
Nazarov Cyclization (4π-electrocyclization):
S. E. Denmark, Org. React. 1994, 45, 1-158.

A Series of Observations: The Birth of the Woodward-Hoffmann Rules and Electrocyclizations



E. Havinga and co-workers, Tetrahedron 1960, 11, 276.
E. Havinga and co-workers, Tetrahedron 1961, 12, 146.

A Series of Observations:
The Birth of the Woodward-Hoffmann Rules and Electrocyclizations



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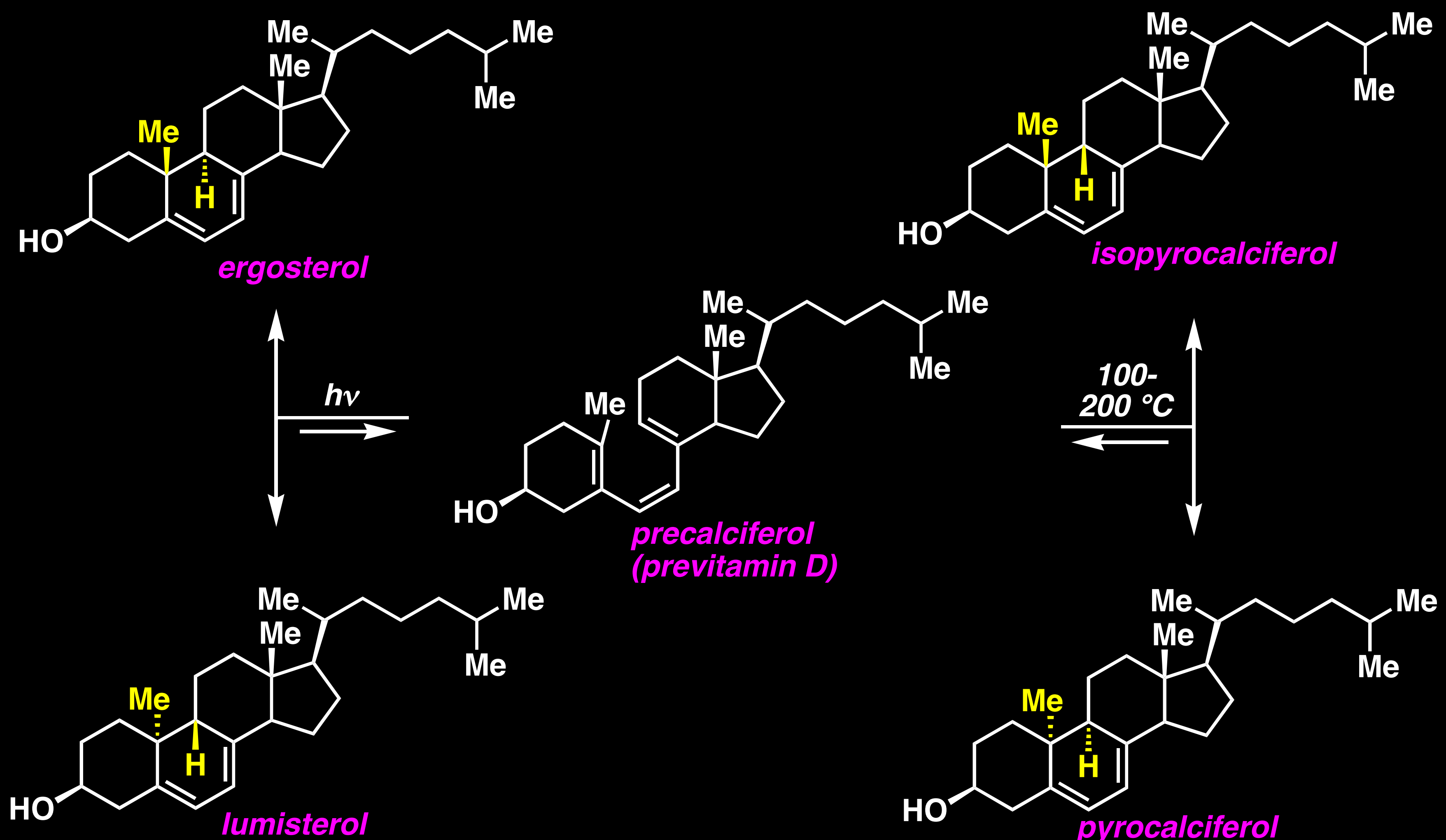
A Series of Observations:
The Birth of the Woodward-Hoffmann Rules and Electrocyclizations



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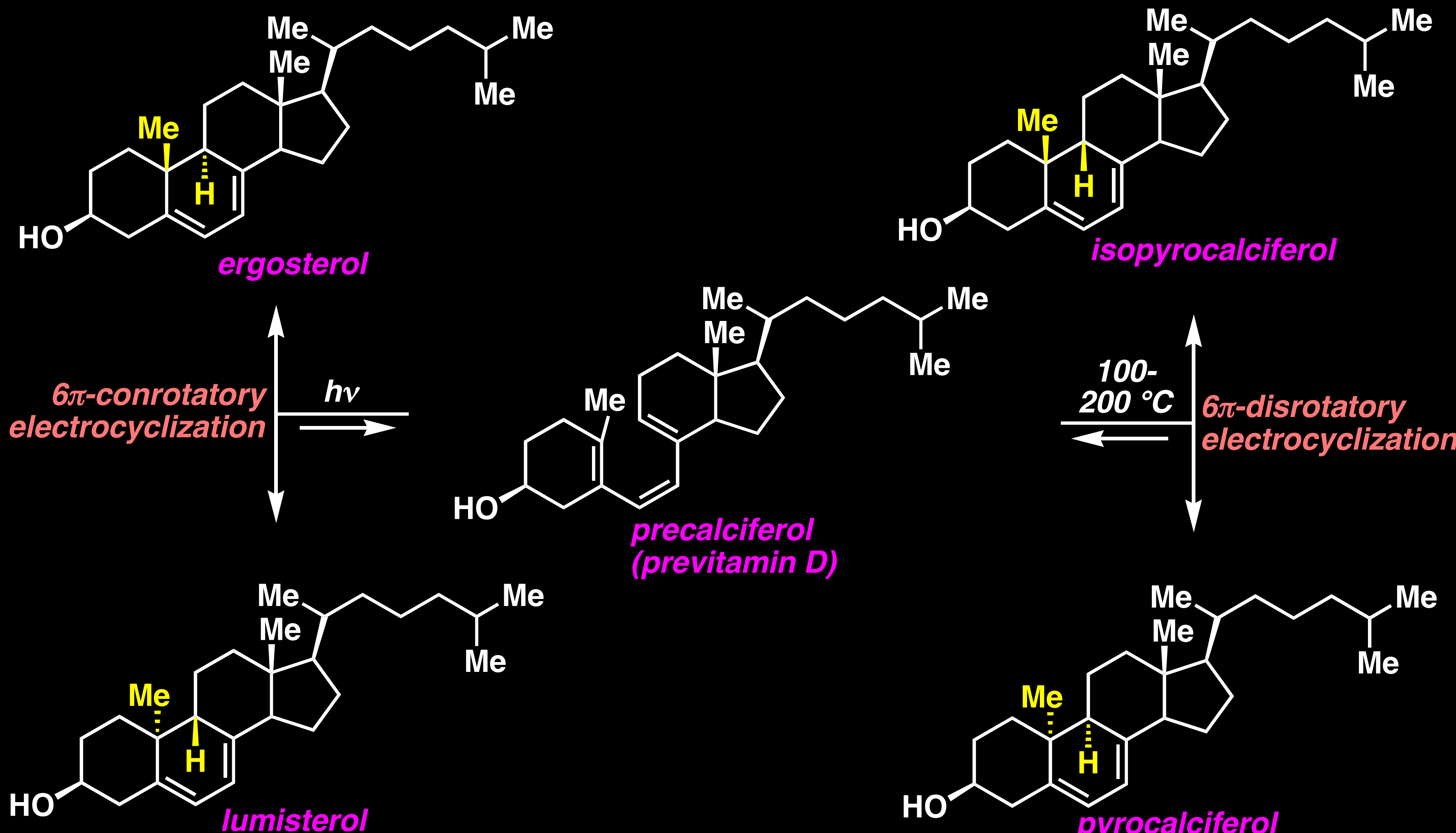
A Series of Observations: The Birth of the Woodward-Hoffmann Rules and Electrocyclizations



E. Havinga and co-workers, Tetrahedron 1960, 11, 276.
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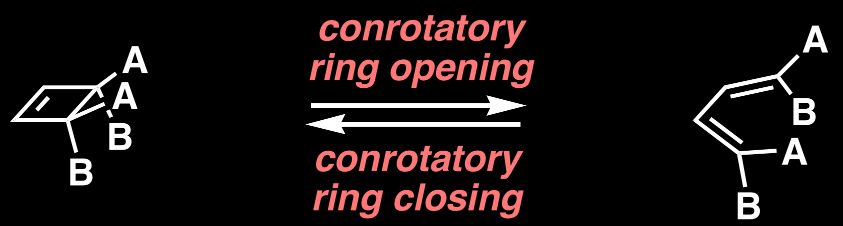
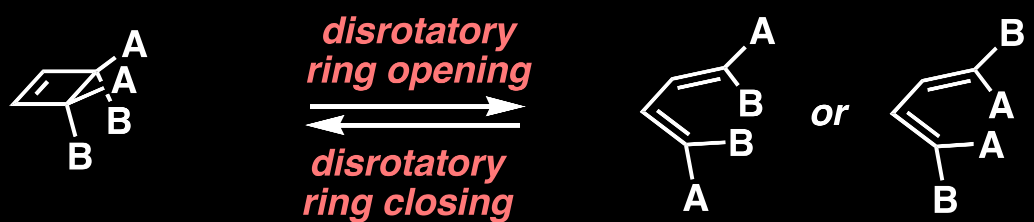
Electrocyclic Reactions:
Background and Basic Principles

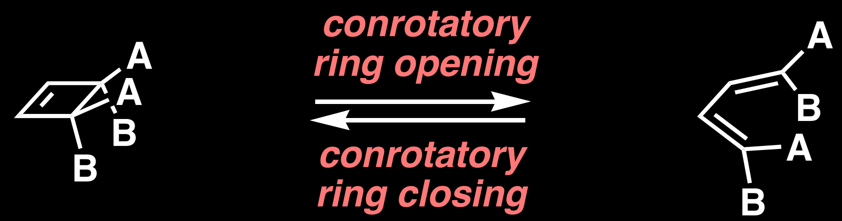
Conrotatory versus disrotatory cyclization: how can I differentiate them?

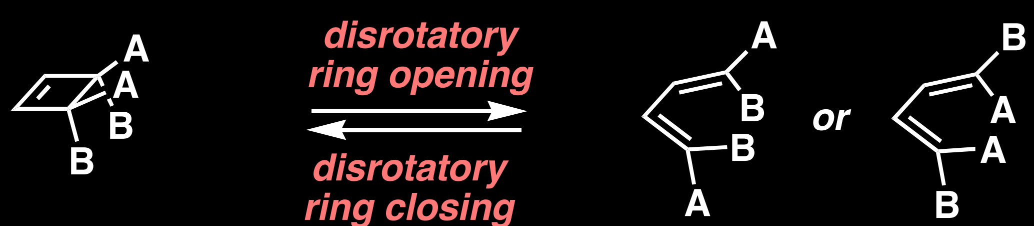


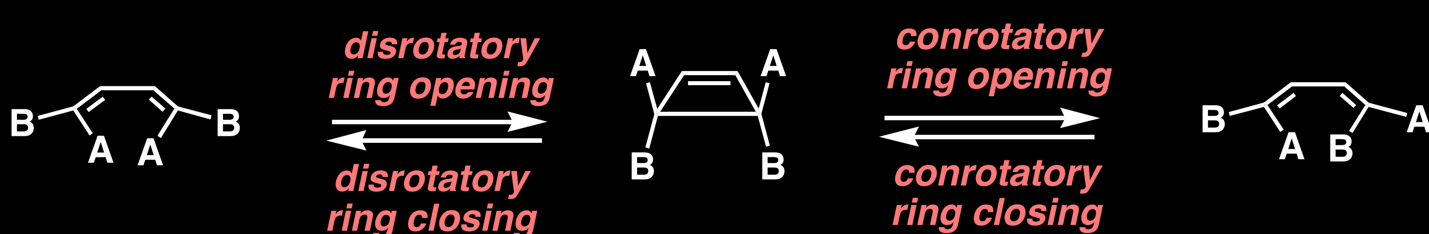


Electrocyclic Reactions:
Background and Basic Principles

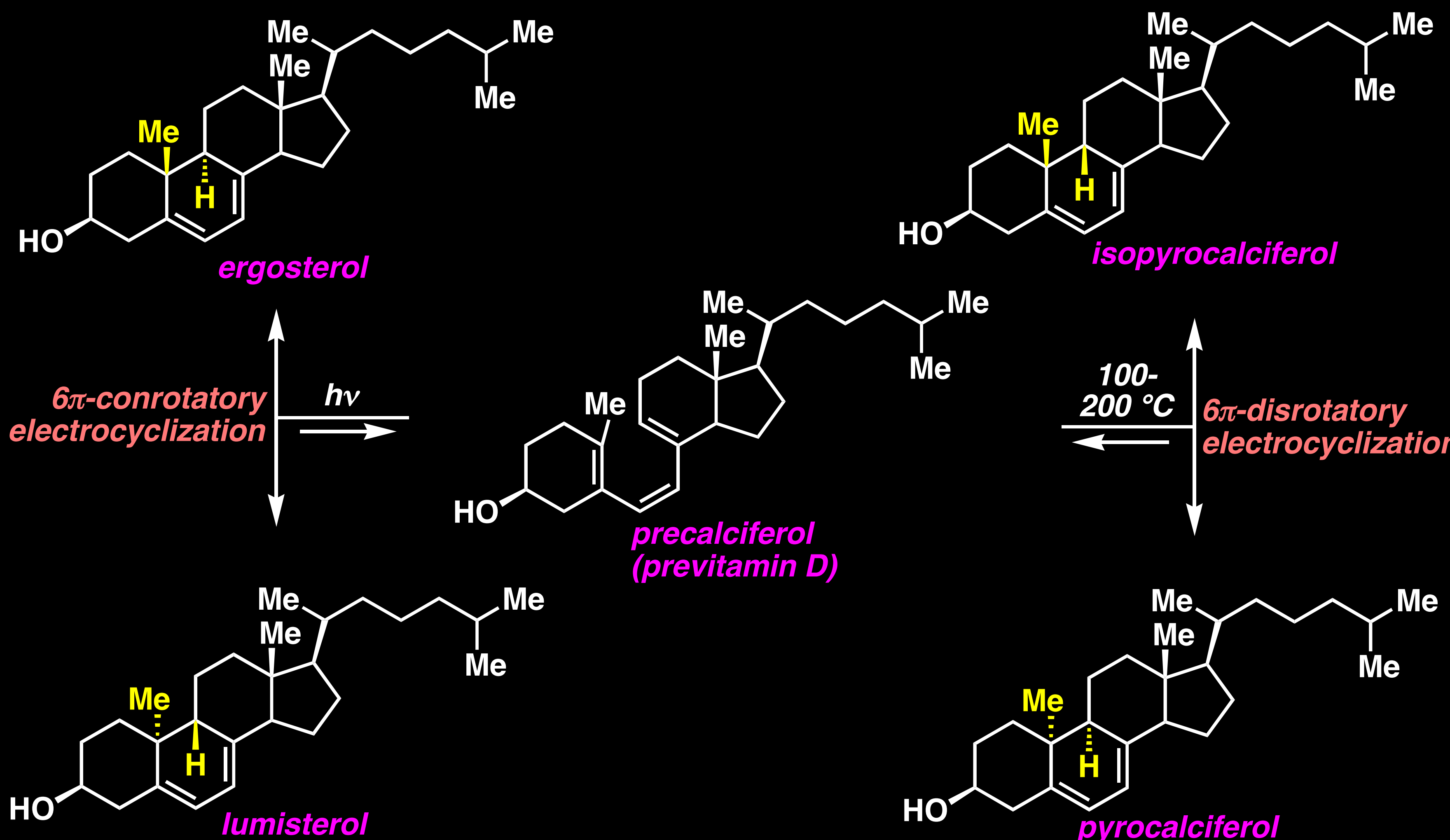
Conrotatory versus disrotatory cyclization: how can I differentiate them?







A Series of Observations: The Birth of the Woodward-Hoffmann Rules and Electrocyclizations

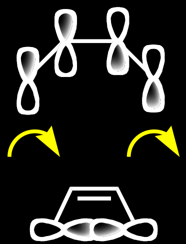


E. Havinga and co-workers, *Tetrahedron* 1960, *11*, 276.
E. Havinga and co-workers, *Tetrahedron* 1961, *12*, 146.

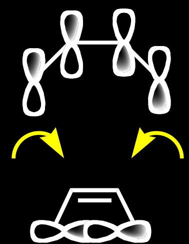
Electrocyclic Reactions: Background and Basic Principles

Thermal reaction

butadiene HOMO (Ψ^2)
(4π-electron system)



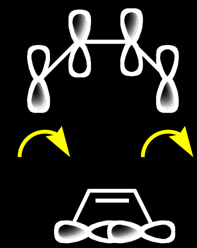
allowed



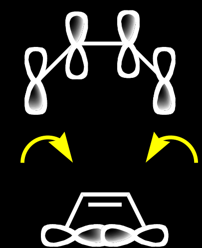
disallowed

Photochemical reaction

butadiene HOMO (Ψ^3)
(4π-electron system)



disallowed



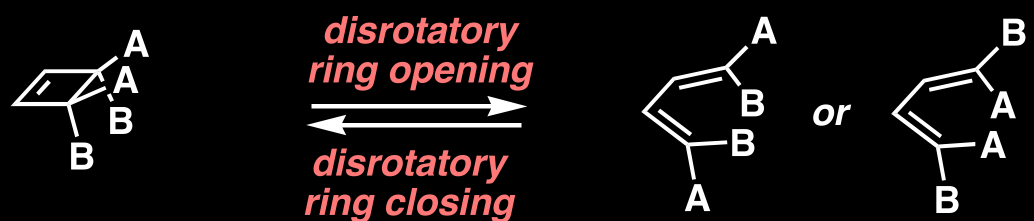
allowed

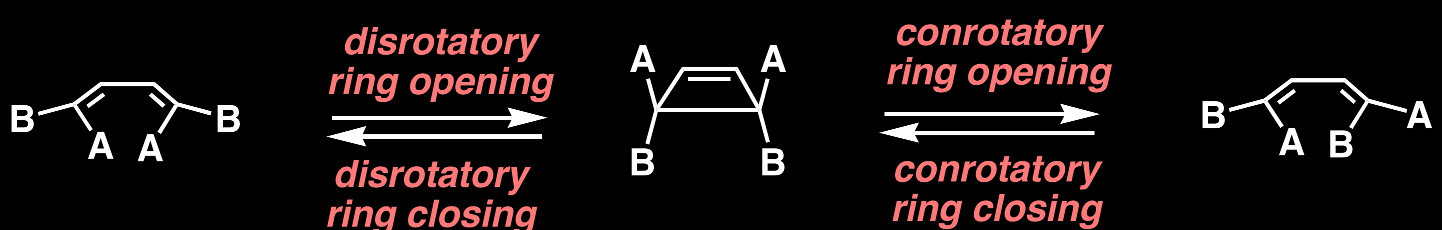
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

The Woodward-Hoffmann rules predict that photochemical reactions will be precisely complementary to thermal reactions. Thus, what is allowed photochemically is forbidden thermally, and vice versa. This prediction is true.

Electrocyclic Reactions: Background and Basic Principles

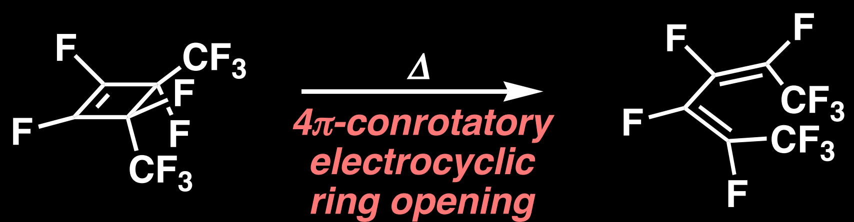
Conrotatory versus disrotatory cyclization: how can I differentiate them?



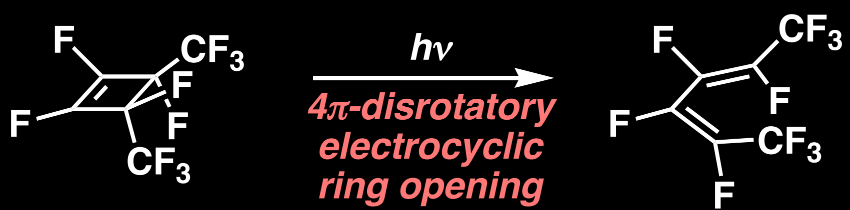


Electrocyclic Reactions: Background and Basic Principles

What happens when the rotating groups are different? Will one product predominate?

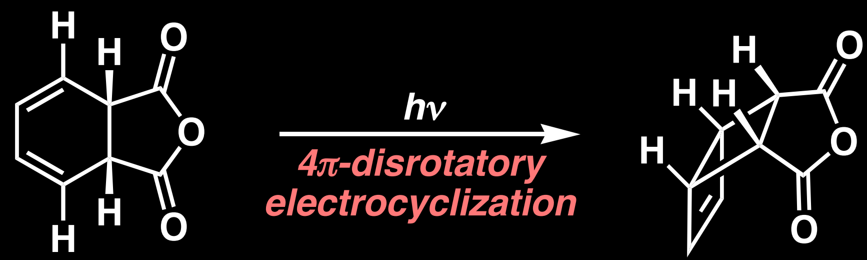


Guiding Principle:
Electron donors go outward; electron withdrawers go inward.



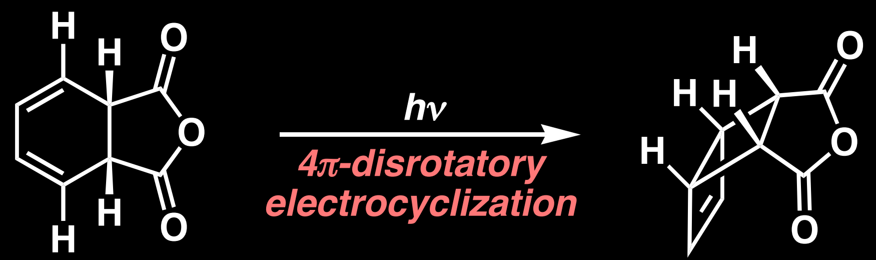
Here, the products are degenerate; i.e., the same

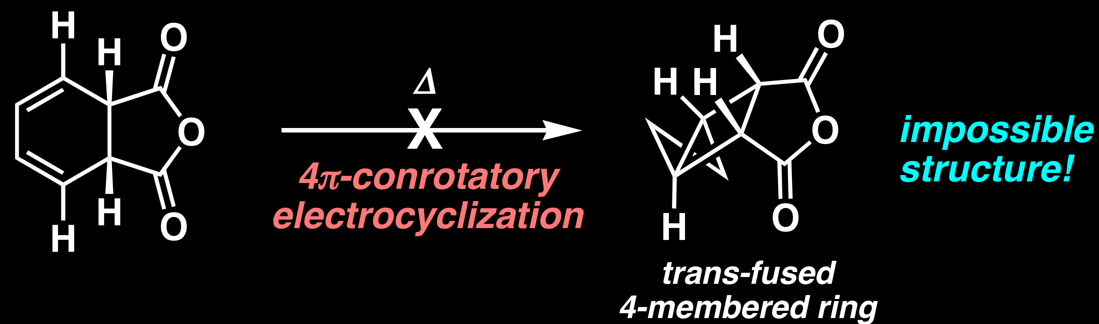
Electrocyclic Reactions: Background and Basic Principles



$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles



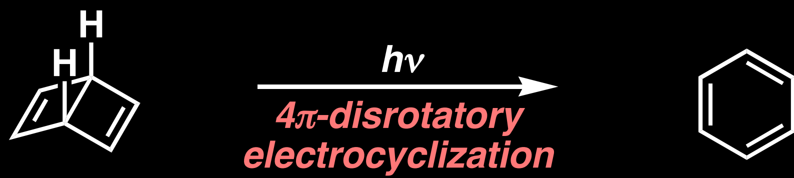


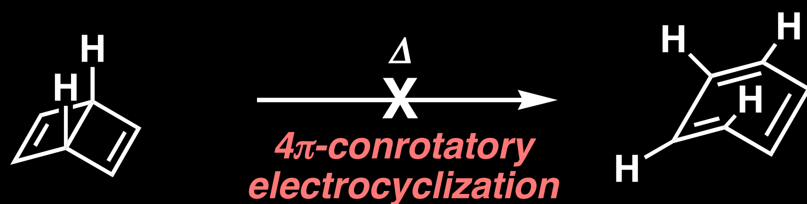
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles

$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles

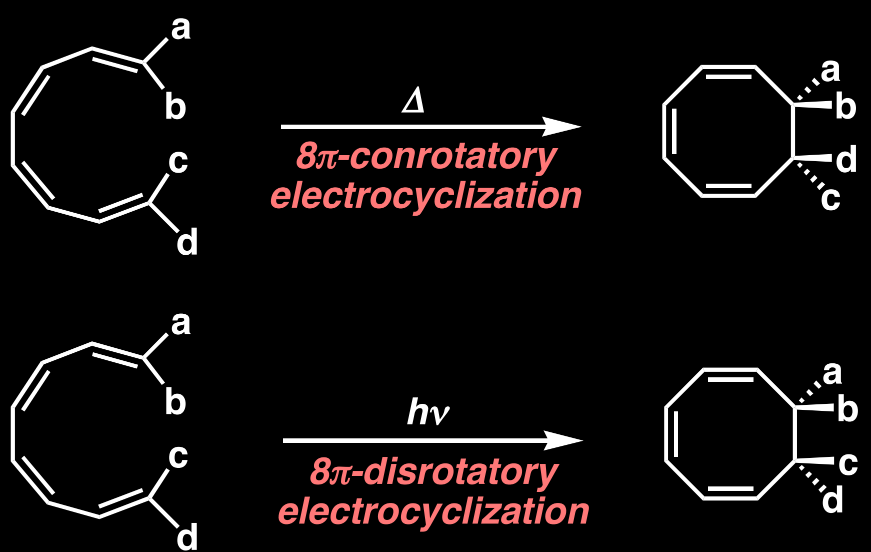




impossible structure!

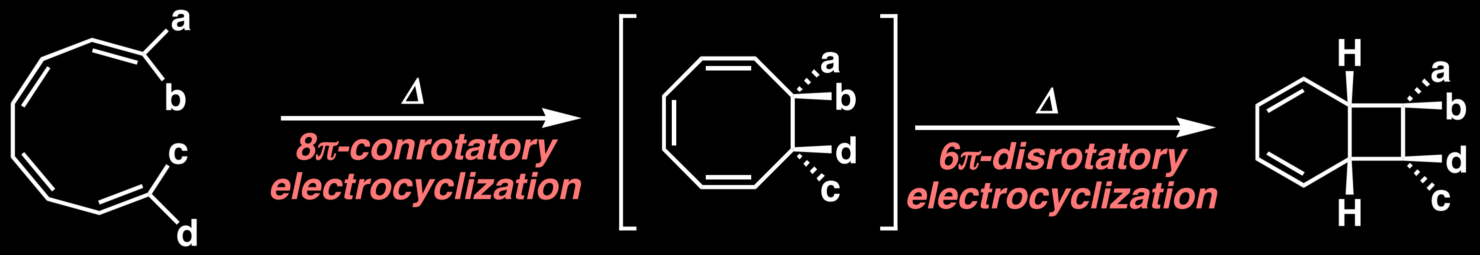
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

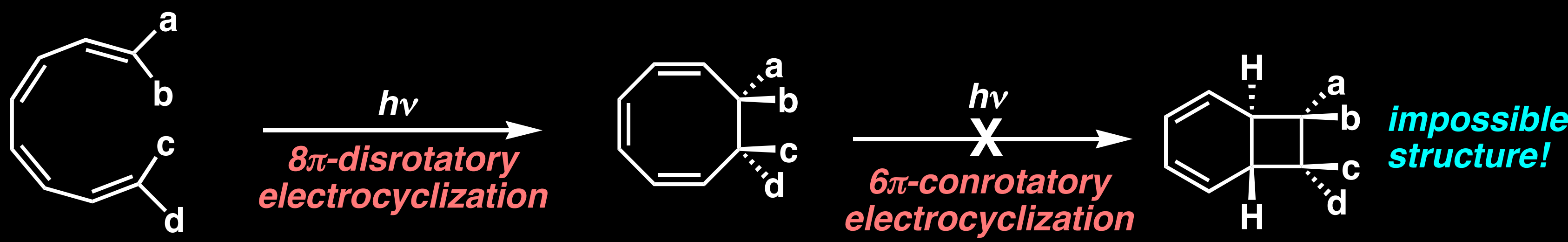
Electrocyclic Reactions: Background and Basic Principles



$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles

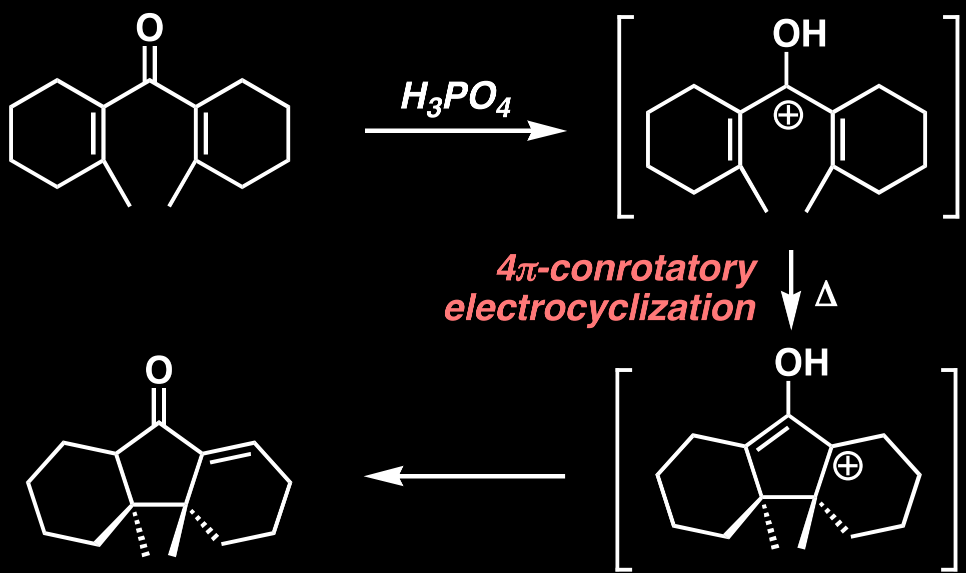




$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles

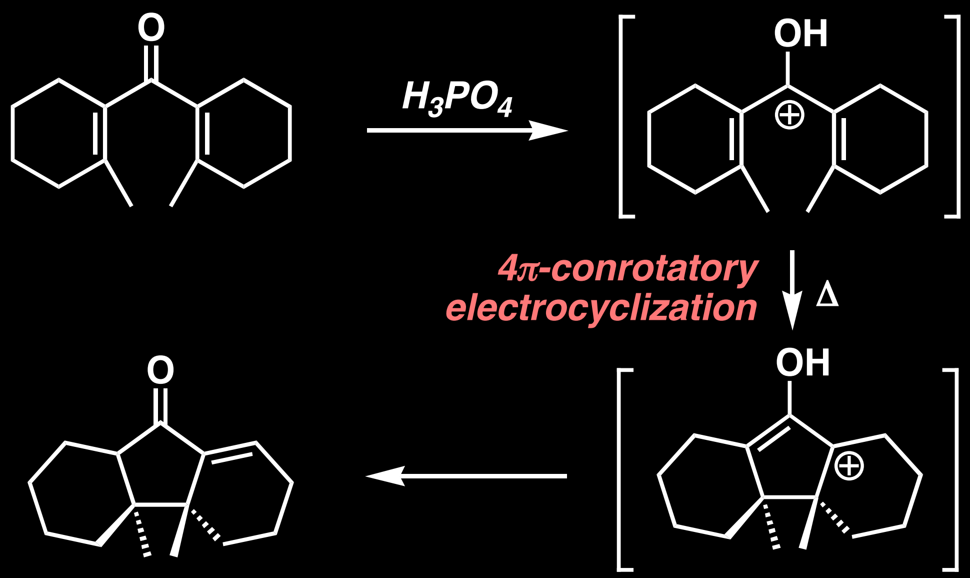
Note: Electrocyclic reactions can involve both cationic and anionic intermediates



$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Background and Basic Principles

Note: Electrocyclic reactions can involve both cationic and anionic intermediates

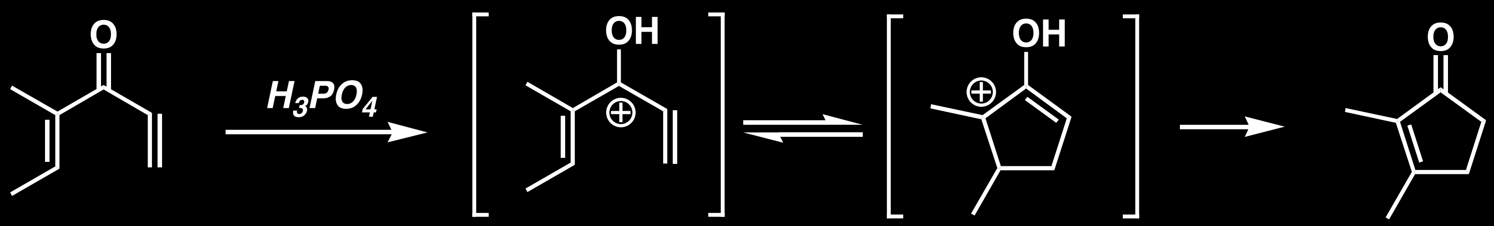


This reaction is known as the Nazarov cyclization and was first discovered in 1948

$e^{\ominus}$	thermal	photochemical
2	disrotatory	conrotatory
4	conrotatory	disrotatory
6	disrotatory	conrotatory
8	conrotatory	disrotatory

Electrocyclic Reactions: Background and Basic Principles

The Nazarov reaction is highly regioselective based on carbocation stability

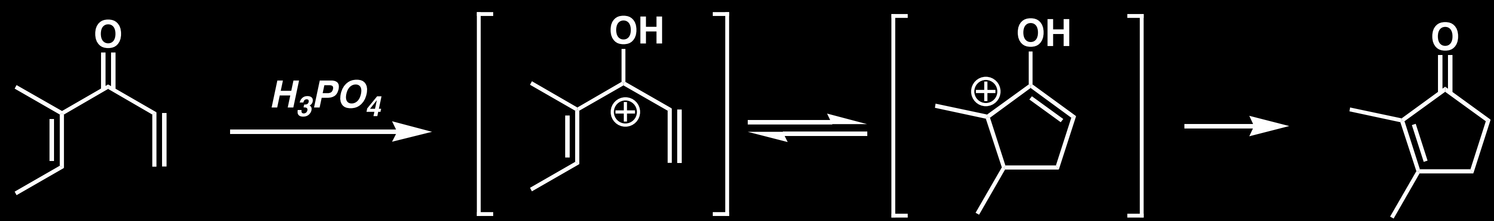


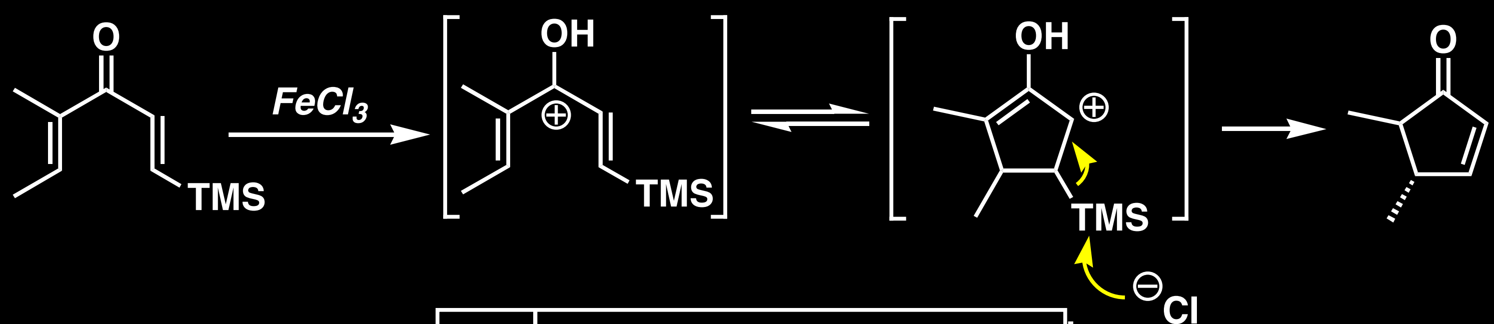
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

S. E. Denmark and co-workers, J. Am. Chem. Soc. 1982, 104, 2642.

Electrocyclic Reactions:
Background and Basic Principles

The Nazarov reaction is highly regioselective based on carbocation stability





$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

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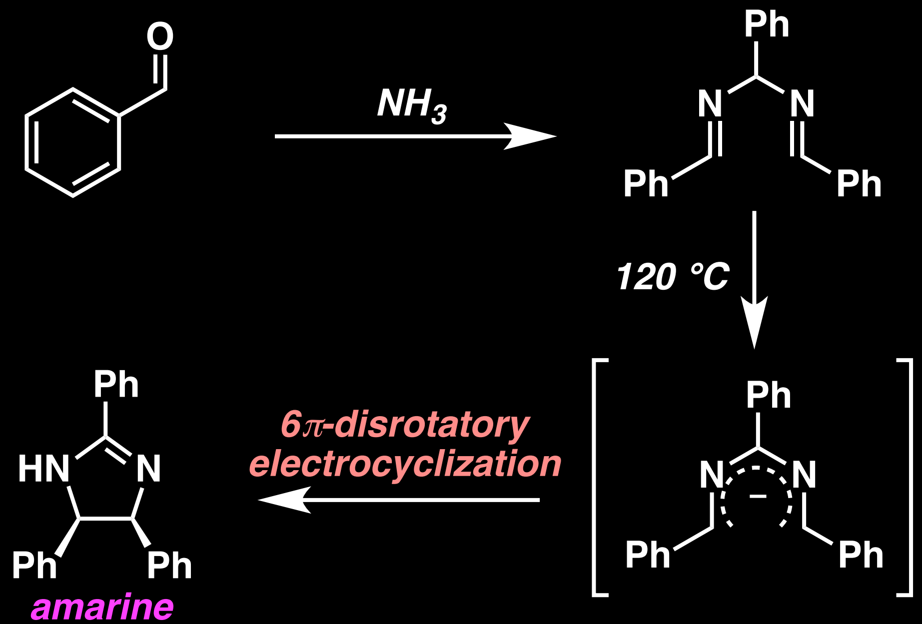
Electrocyclic Reactions:
First Discovery of an Electrocyclic Reaction

Alexander Borodin
(1833-1887)



Piece you heard was from the Prince Igor opera: Polovetsian Dances

For discussion, see: E. J. Corey, F. N. M. Kuhnle, Tetrahedron Lett. 1997, 38, 8631.

Electrocyclic Reactions: First Discovery of an Electrocyclic Reaction

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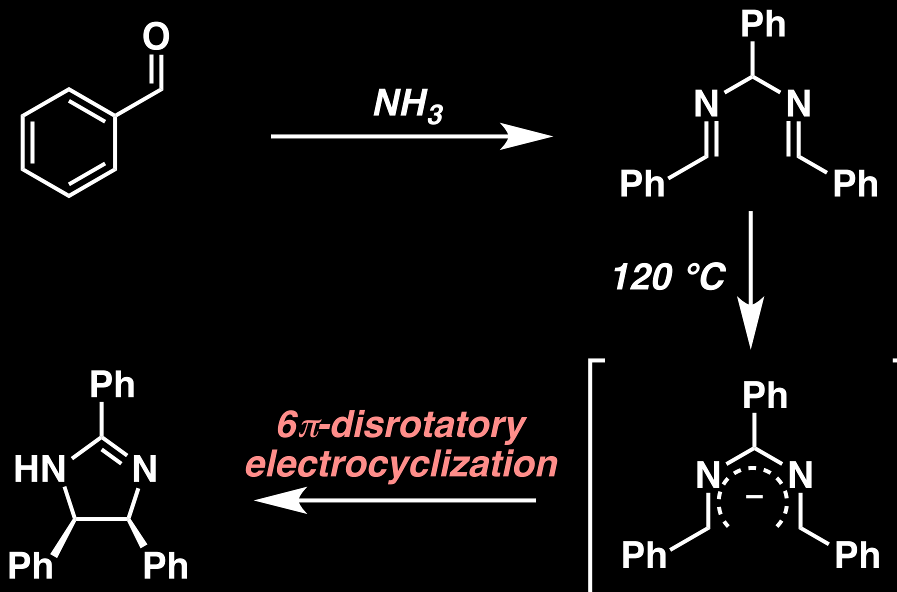
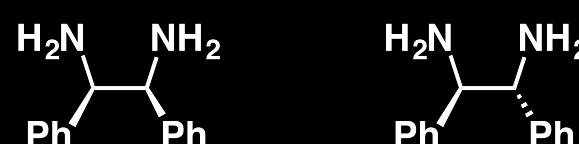


amarine

Piece you heard was from the Prince Igor opera: Polovetsian Dances

Process is still used today . . .



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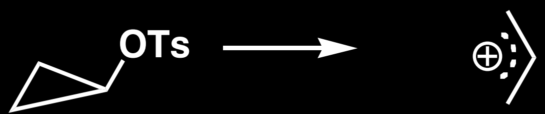
Electrocyclic Reactions: Background and Basic Principles

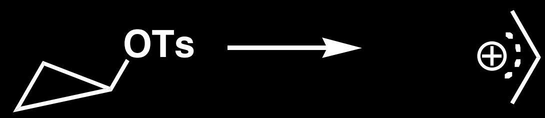


e⊖	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

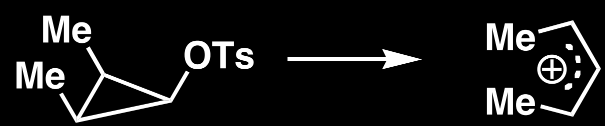
Electrocyclic Reactions:
Background and Basic Principles

k_{rel}

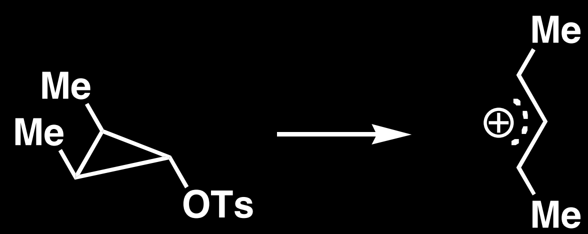
1



4

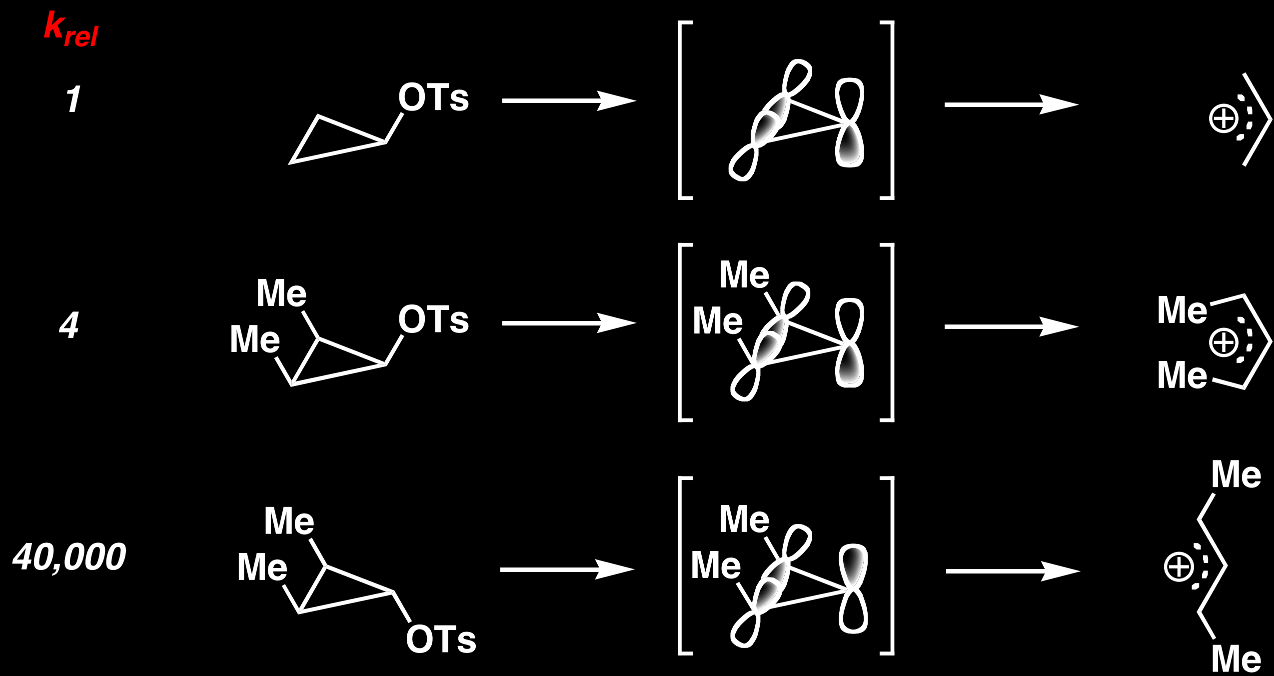


40,000



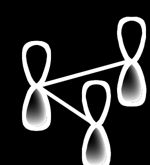
$e^{\ominus}$	thermal	photochemical
2	disrotatory	conrotatory
4	conrotatory	disrotatory
6	disrotatory	conrotatory
8	conrotatory	disrotatory

Electrocyclic Reactions: Background and Basic Principles



$e^{\ominus}$	thermal	photochemical
2	disrotatory	conrotatory
4	conrotatory	disrotatory
6	disrotatory	conrotatory
8	conrotatory	disrotatory

Rule: groups opposite leaving group migrate outwards



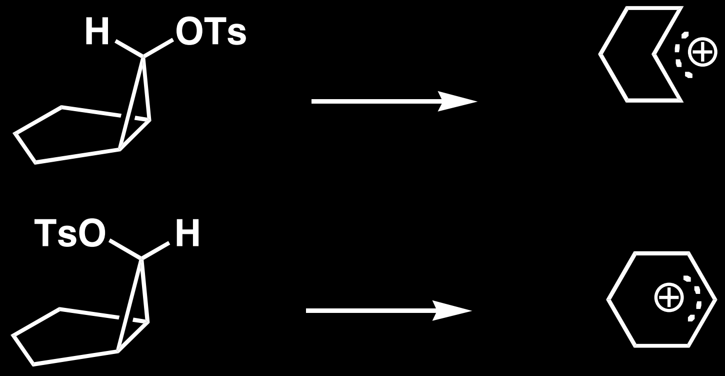
lobe system required after opening for cation

Electrocyclic Reactions:
Background and Basic Principles

k_{rel}

1

1,000,000



Essentially an impossible structure!

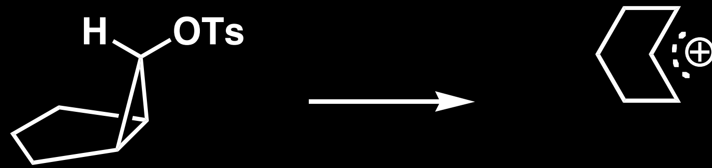
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Rule: groups opposite leaving group migrate outwards

Electrocyclic Reactions:
Background and Basic Principles

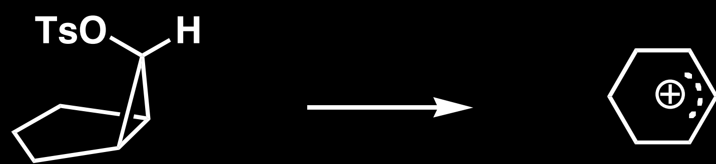
k_{rel}

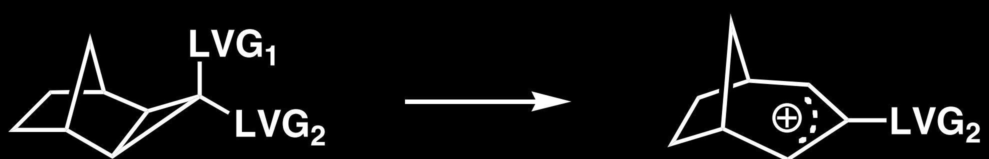
1



Essentially an impossible structure!

1,000,000



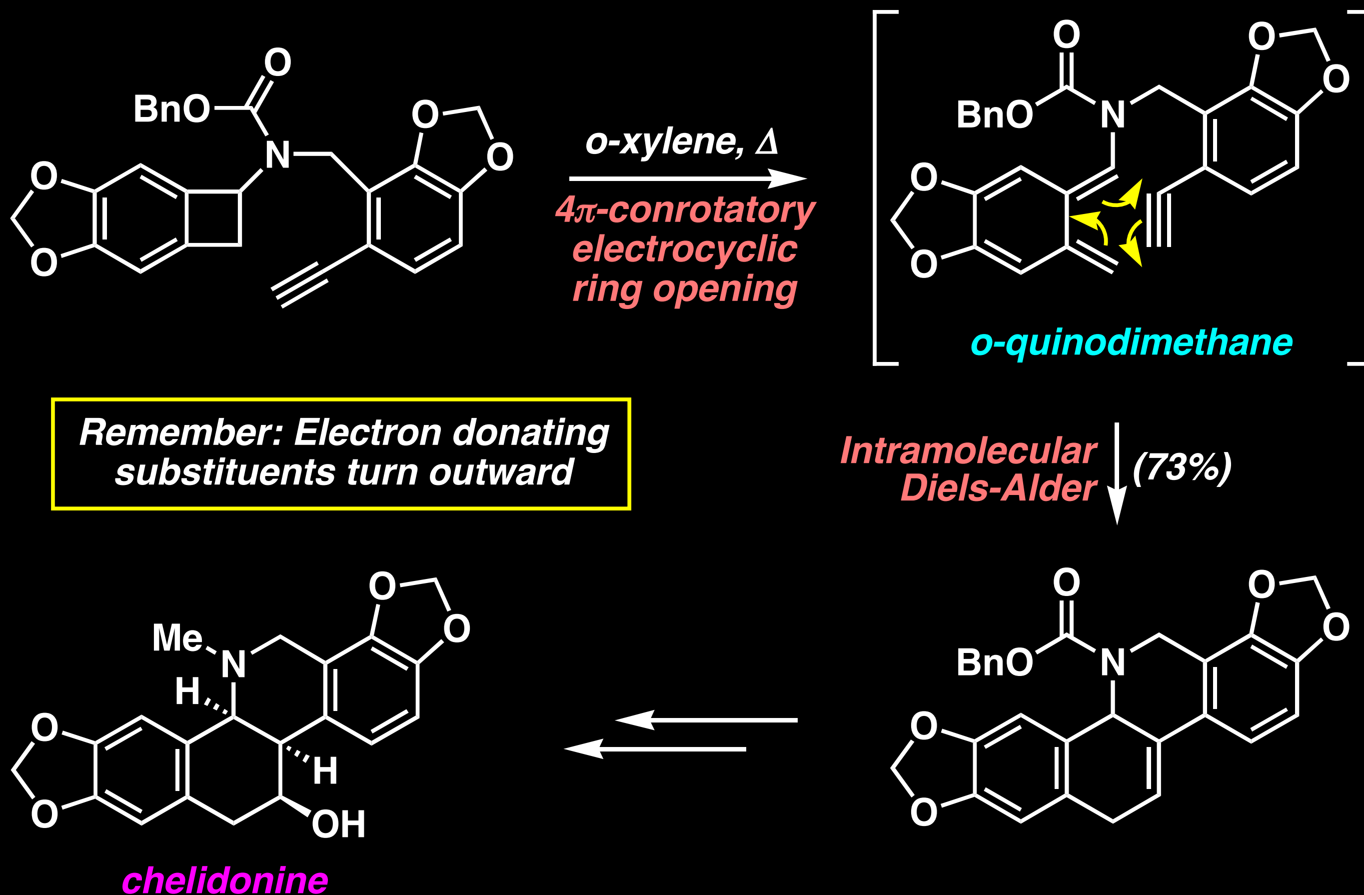


Can predict easily which of the two groups will depart

Rule: groups opposite leaving group migrate outwards

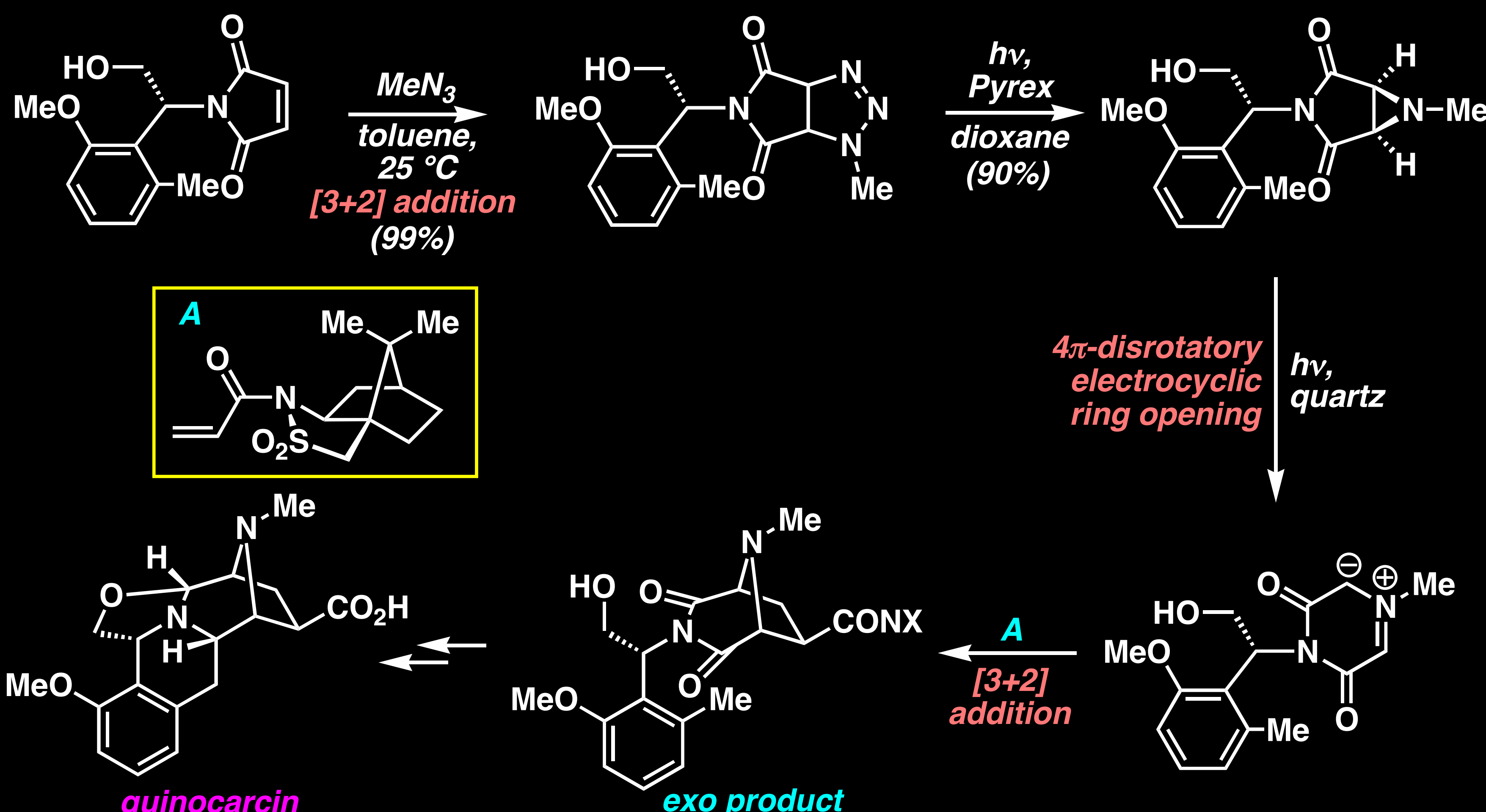
$e^{\ominus}$	thermal	photochemical
2	*disrotatory*	*conrotatory*
4	*conrotatory*	*disrotatory*
6	*disrotatory*	*conrotatory*
8	*conrotatory*	*disrotatory*

Electrocyclic Reactions: Examples You Have Already Seen



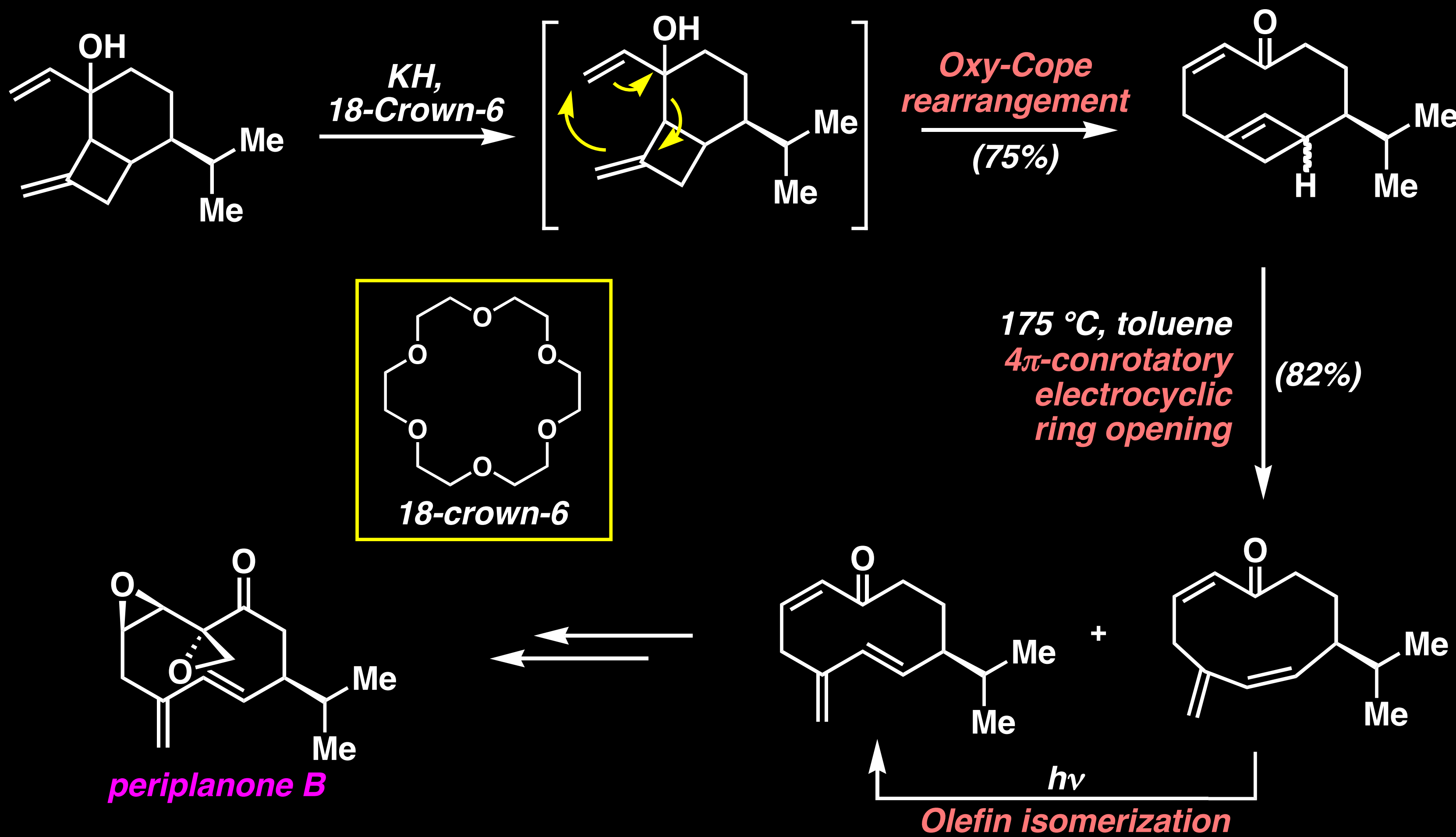
W. Oppolzer, C. Robbiani, Helv. Chim. Acta 1983, 66, 1119.

Electrocyclic Reactions:
Examples You Have Already Seen



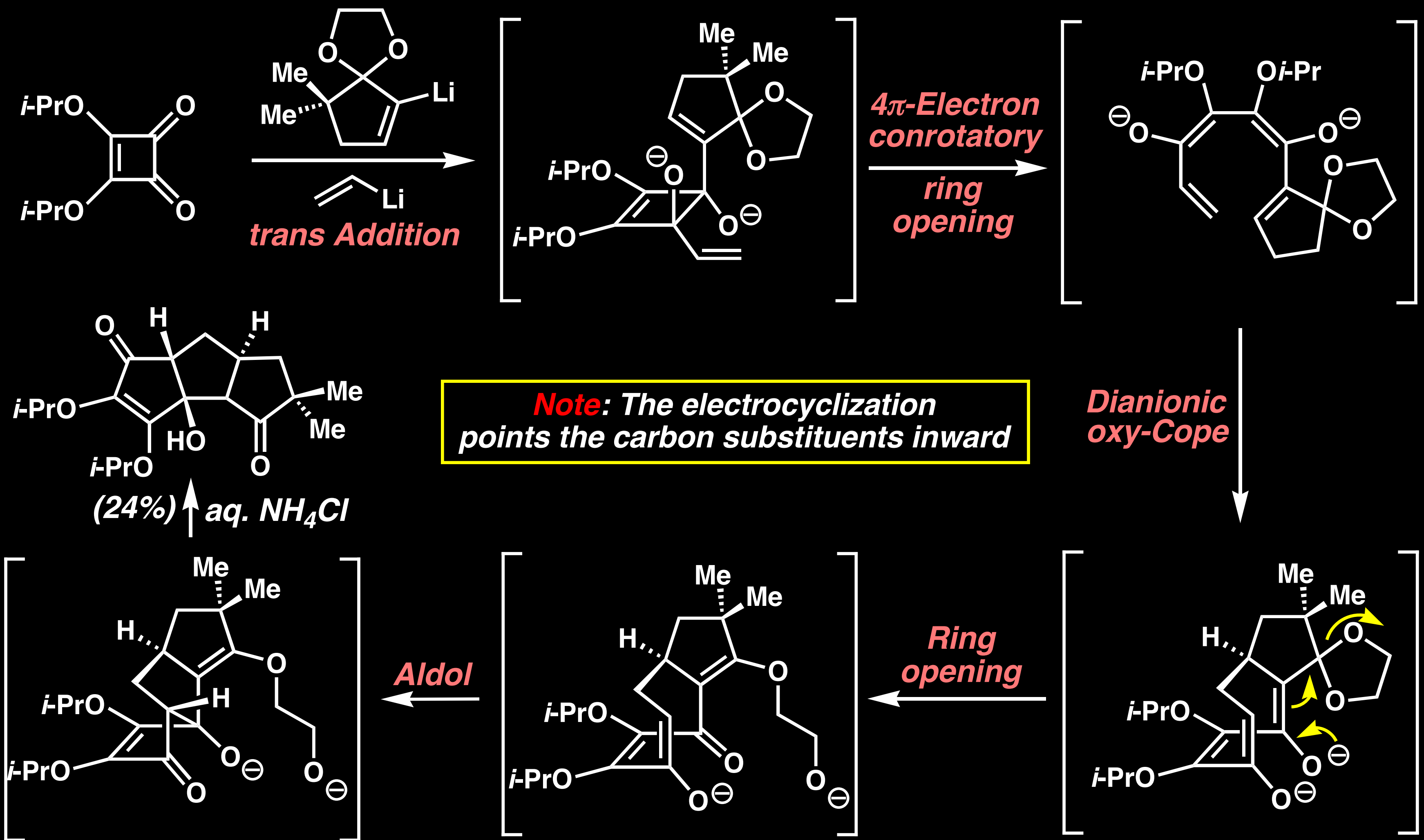
P. Garner, W.B. Ho, H. Shin, J. Am. Chem. Soc. 1993, 115, 10742.

4π-Electrocyclic Reactions: Part of a Total Synthesis of Periplanone B



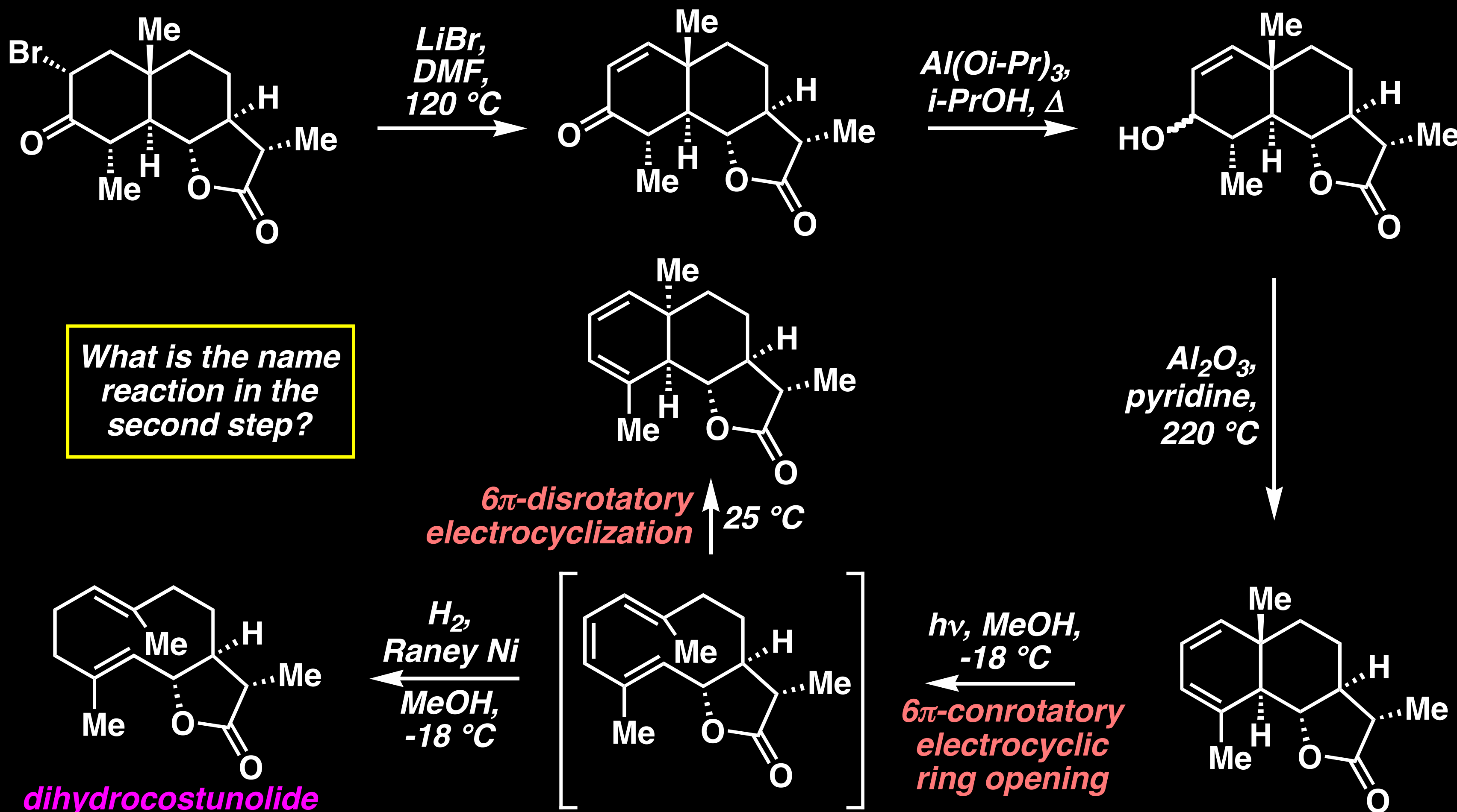
S. L. Schreiber, C. Santini, J. Am. Chem. Soc. 1984, 106, 4038.
For a review, see: Classics in Total Synthesis I, Chapter 21

4π-Electrocyclic Reactions: Part of a Cascade Sequence to Coriolin



L. A. Paquette and co-workers, J. Am. Chem. Soc. 2002, 124, 9199.
For a review, see: L. A. Paquette, Eur. J. Org. Chem. 1998, 1709.

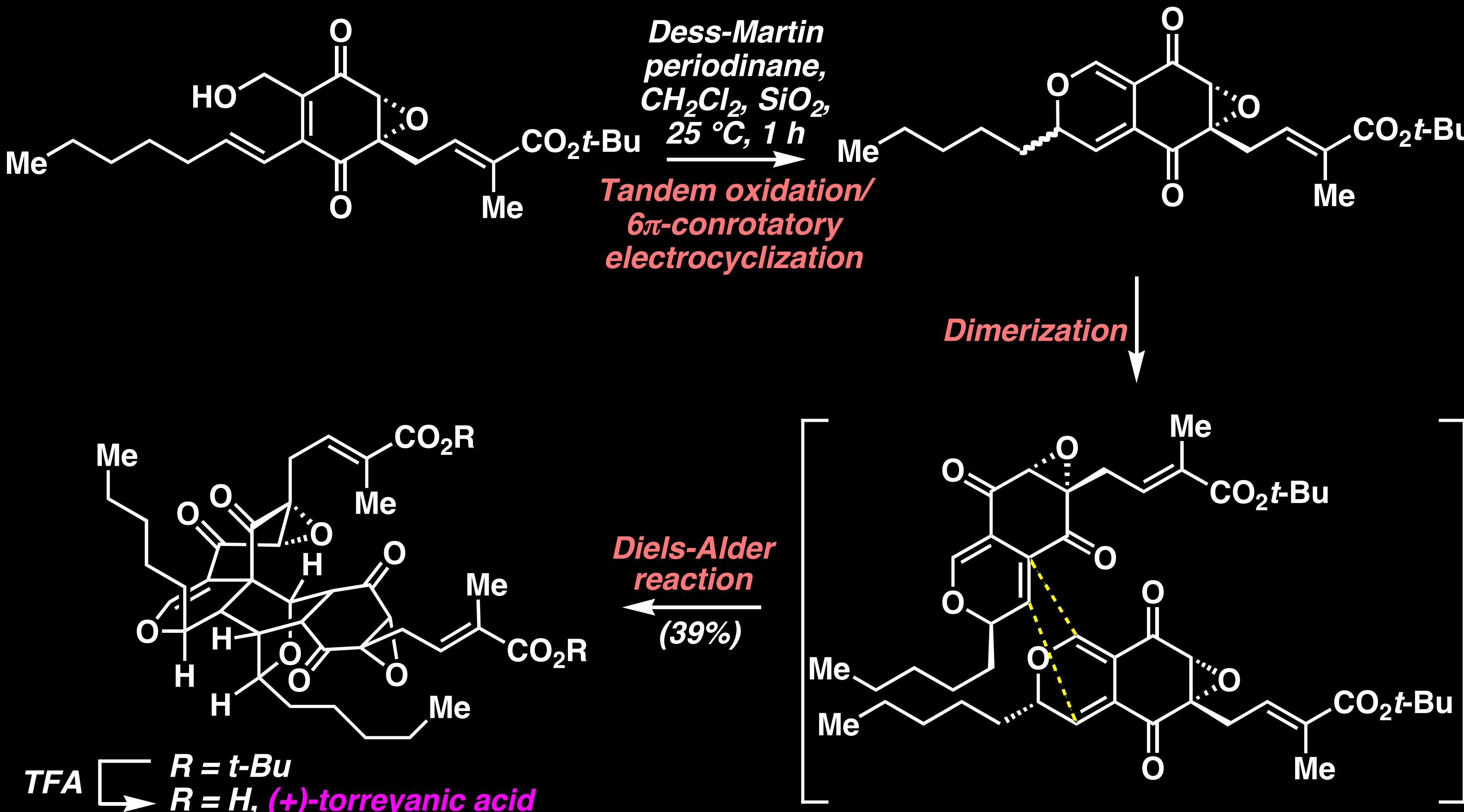
6π-Electrocyclic Reactions: Erasure of the Ring-Opened Product



What is the name reaction in the second step?

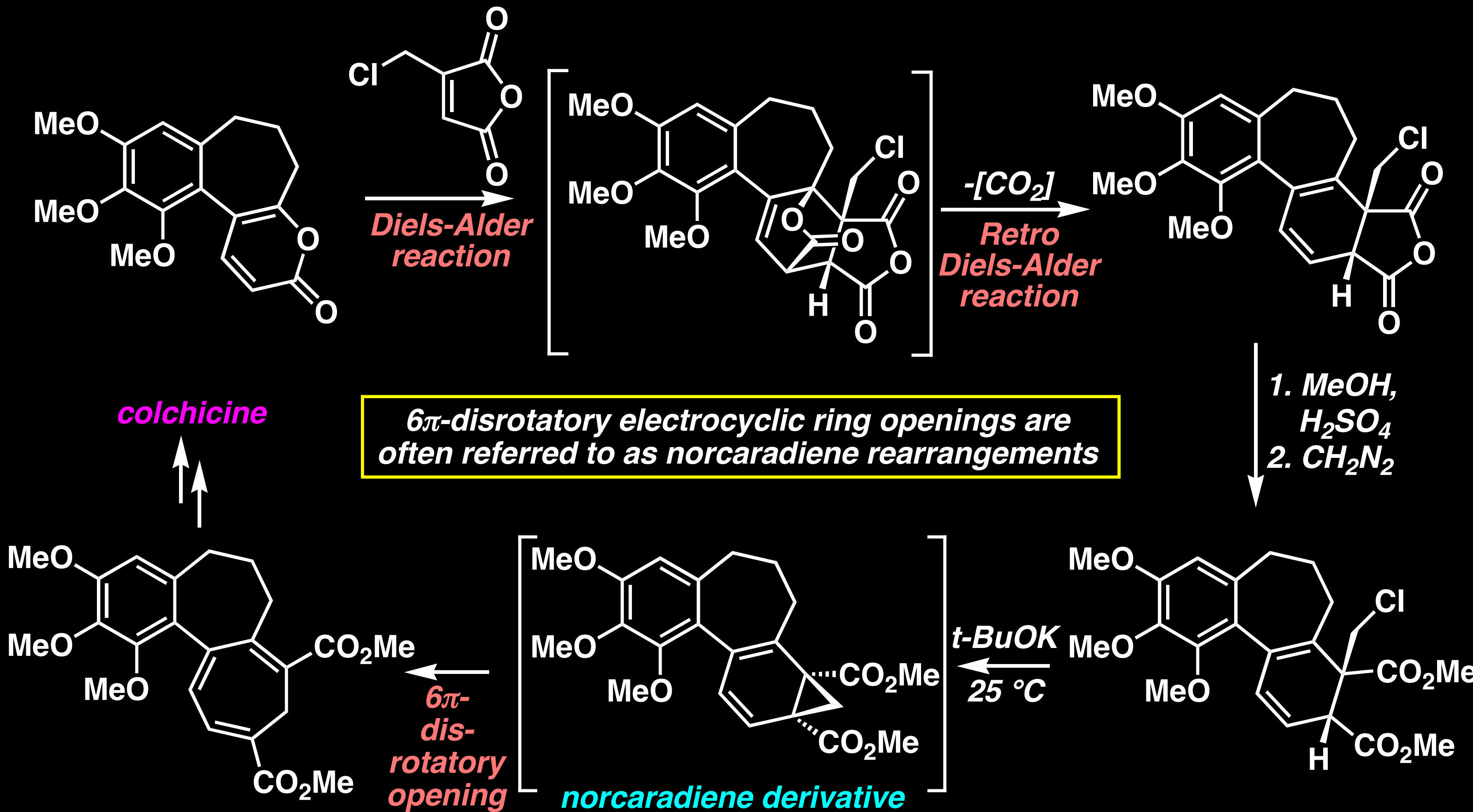
E. J. Corey, A. G. Hortmann, *J. Am. Chem. Soc.* **1965**, *87*, 5736.

6π-Electrocyclic Reactions: Total Synthesis of Torreyanic Acid



J. A. Porco and co-workers, J. Am. Chem. Soc. 2000, 122, 10484.

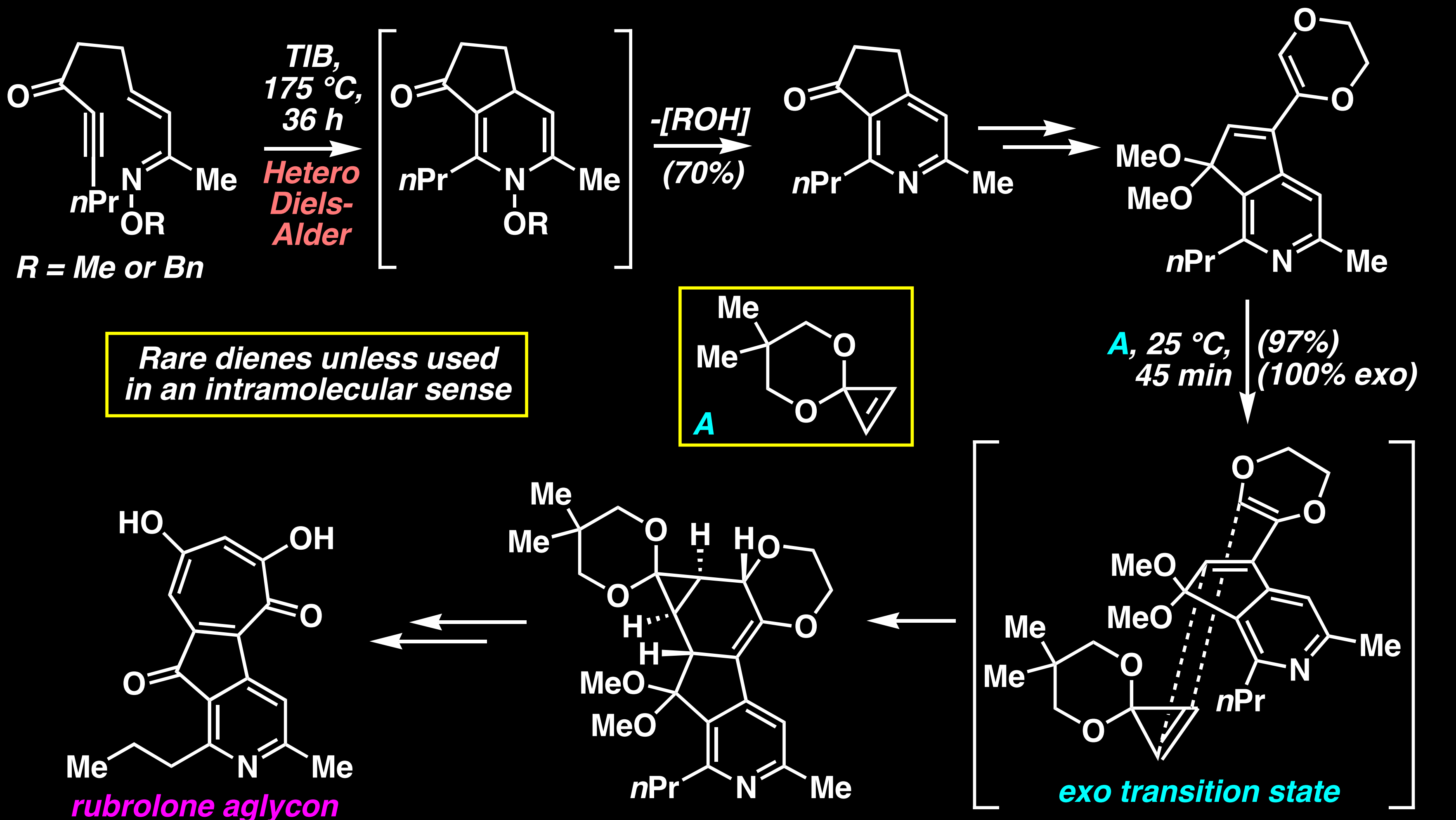
6π-Electrocyclic Reactions:
One of Three Pericyclic Reactions in a Colchicine Total Synthesis



6π-disrotatory electrocyclic ring openings are often referred to as norcaradiene rearrangements

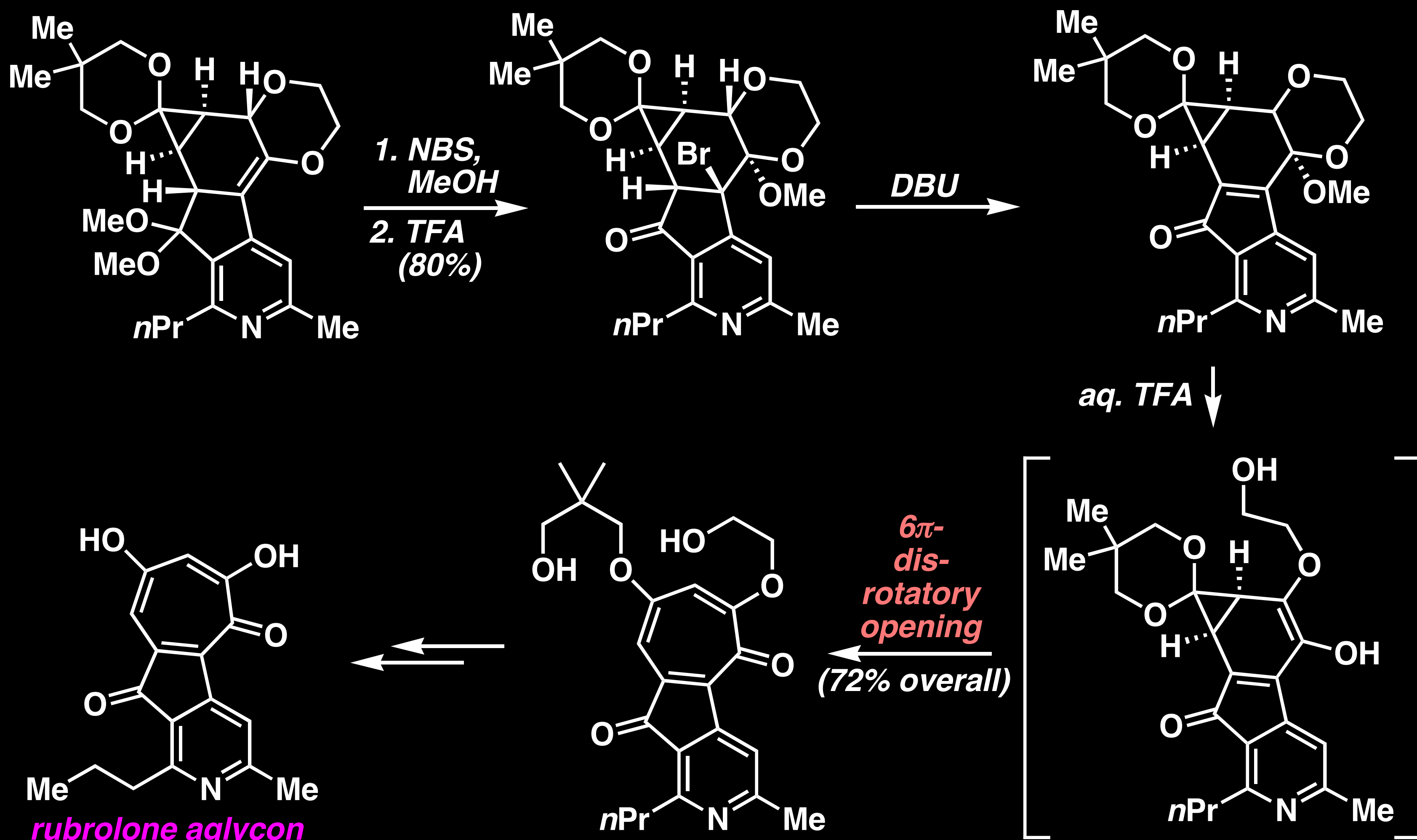
A. Eschenmoser and co-workers, Helv. Chim. Acta 1961, 44, 540.

Hetero Diels-Alder Reactions: Oxime Ethers as Diene Components



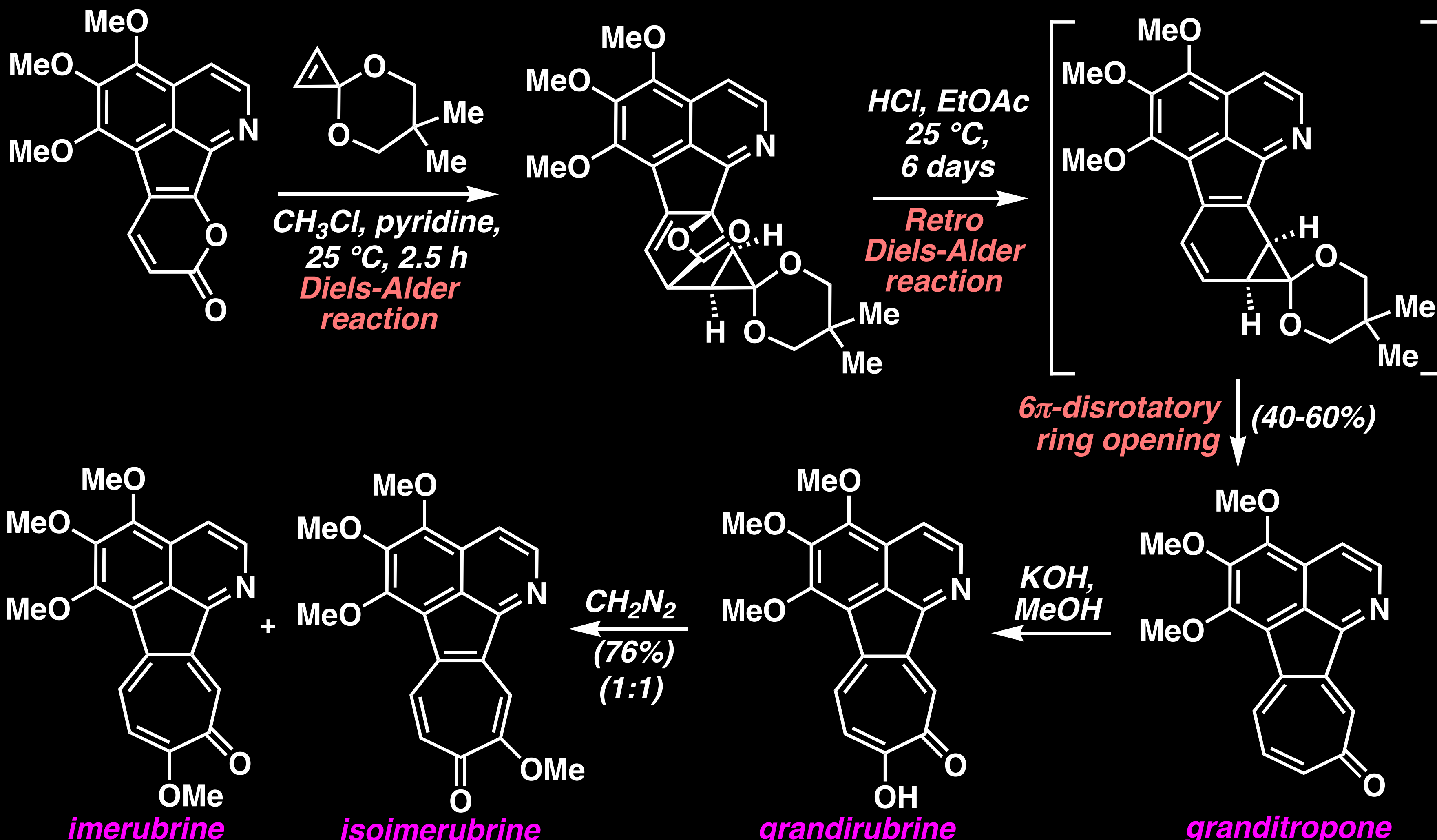
D. L. Boger, S. Ichikawa, H. Jiang, J. Am. Chem. Soc. 2000, 122, 12169.

6π-Electrocyclic Reactions: A Pericyclic Reaction in a Rubrolone Total Synthesis



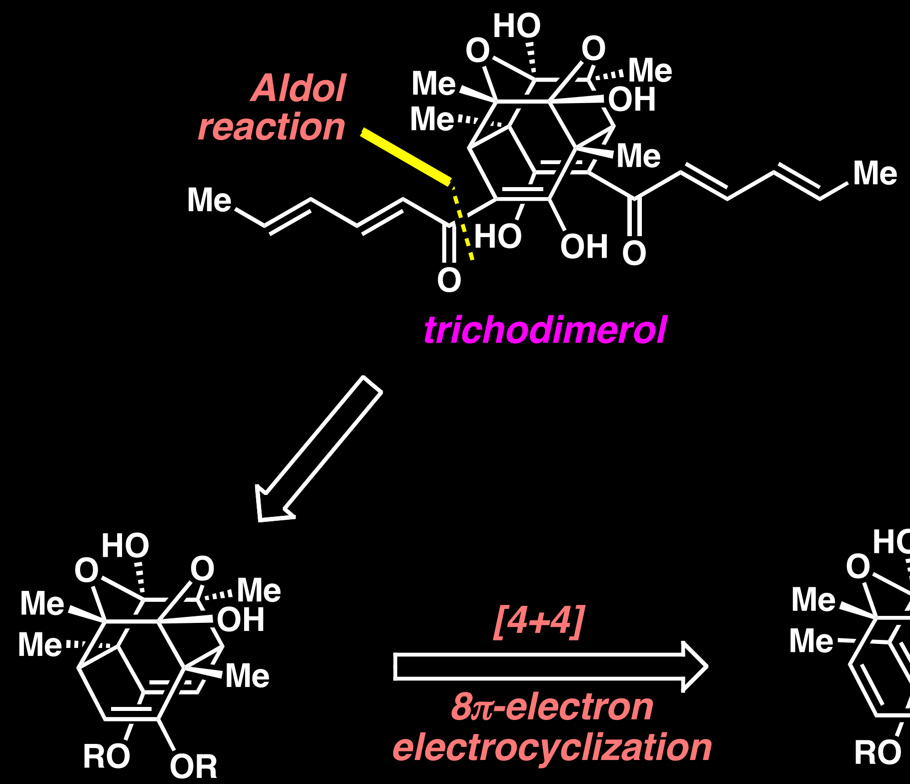
D. L. Boger, S. Ichikawa, H. Jiang, J. Am. Chem. Soc. 2000, 122, 12169.

6π-Electrocyclic Reactions: A Pericyclic Reaction in the Synthesis of Tropoisoquinolines



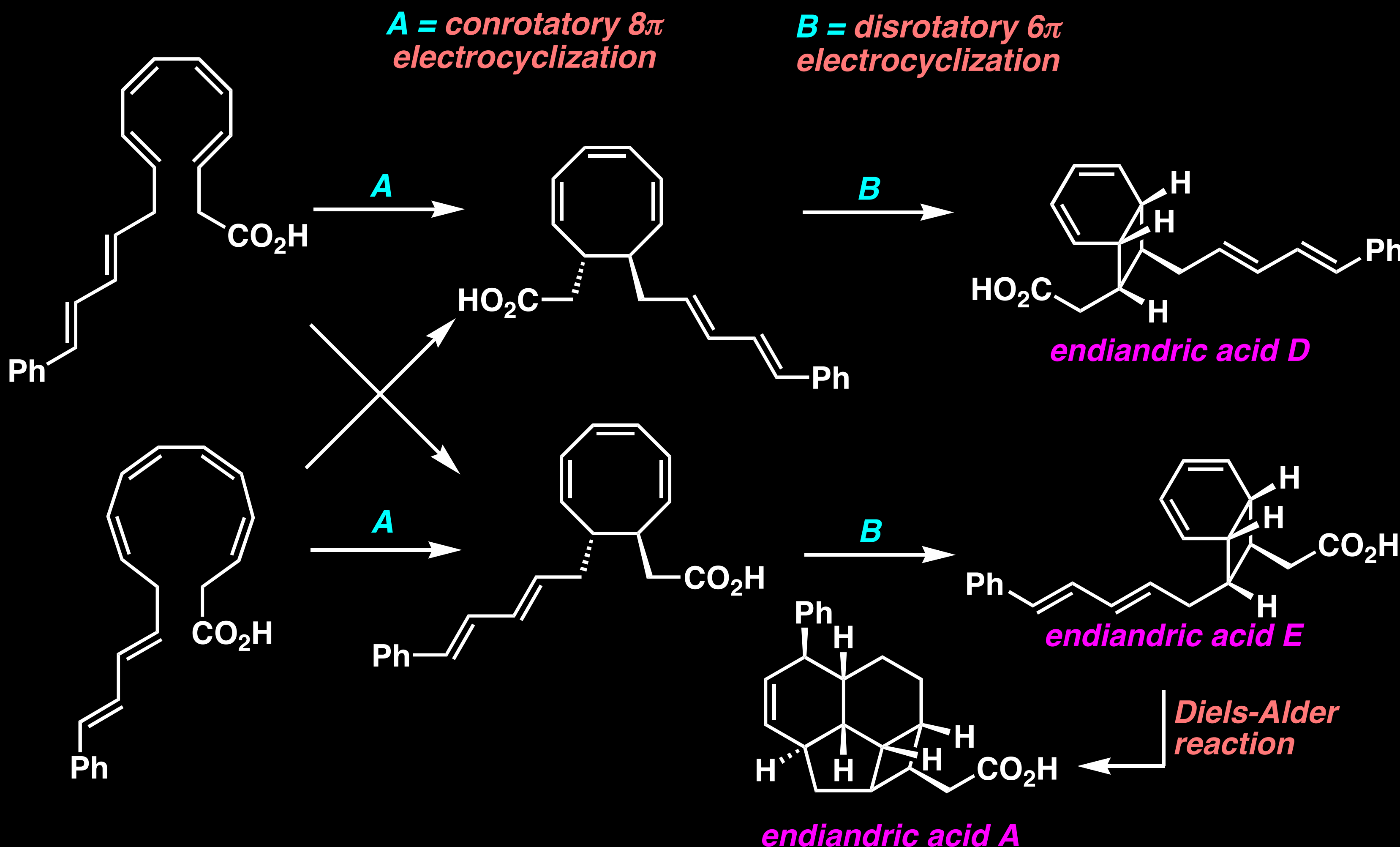
D. L. Boger, K. Takahashi, *J. Am. Chem. Soc.* 1995, 117, 12452.

8π-Electrocyclic Reactions:
Possible Role in the Biosynthesis of Trichodimerol



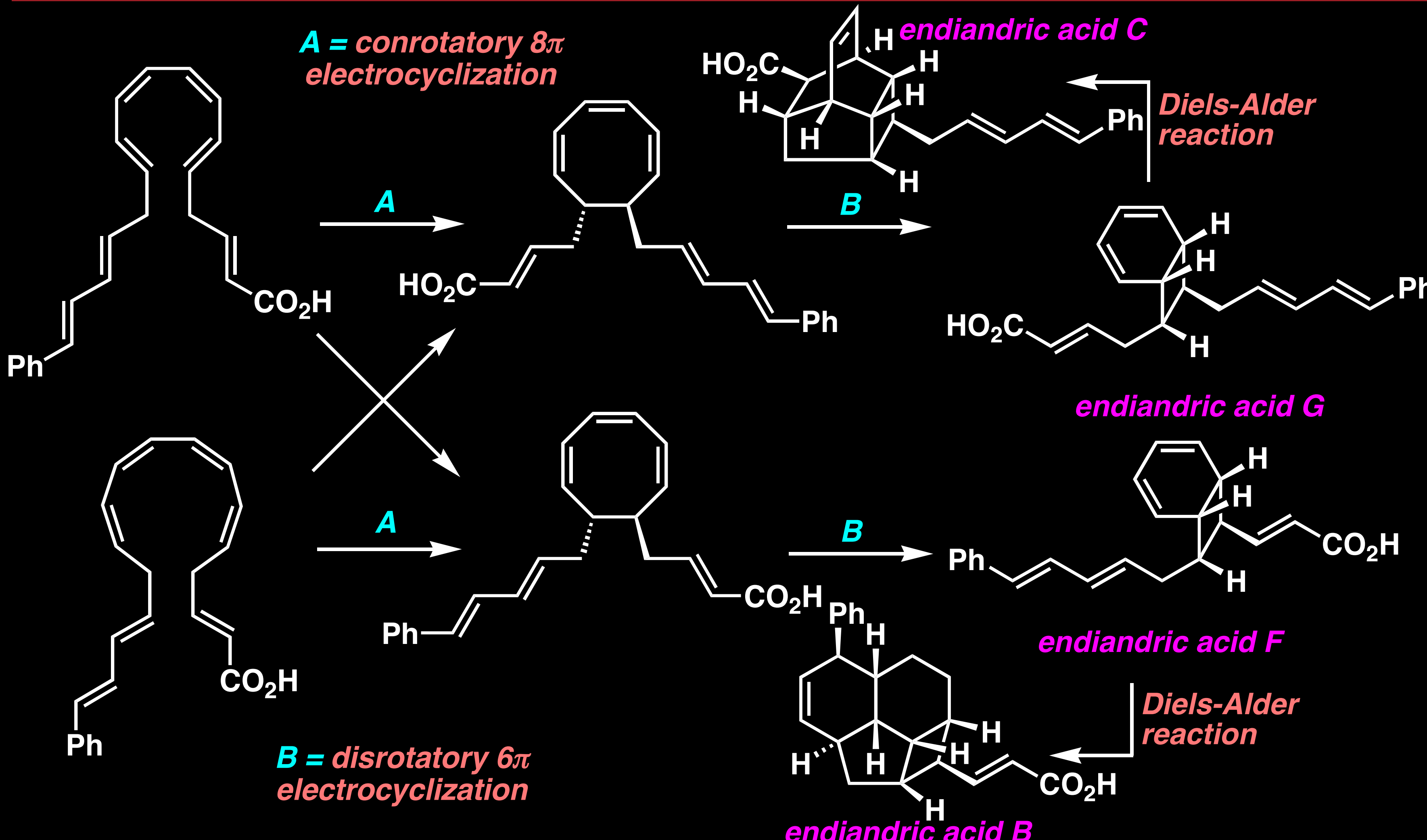
K. C. Nicolaou and co-workers, *Chem. Eur. J.* 1999, *5*, 3651.

Electrocyclization Cascades:
Black's Hypothesis for the Biosynthesis of the Endiandric Acids



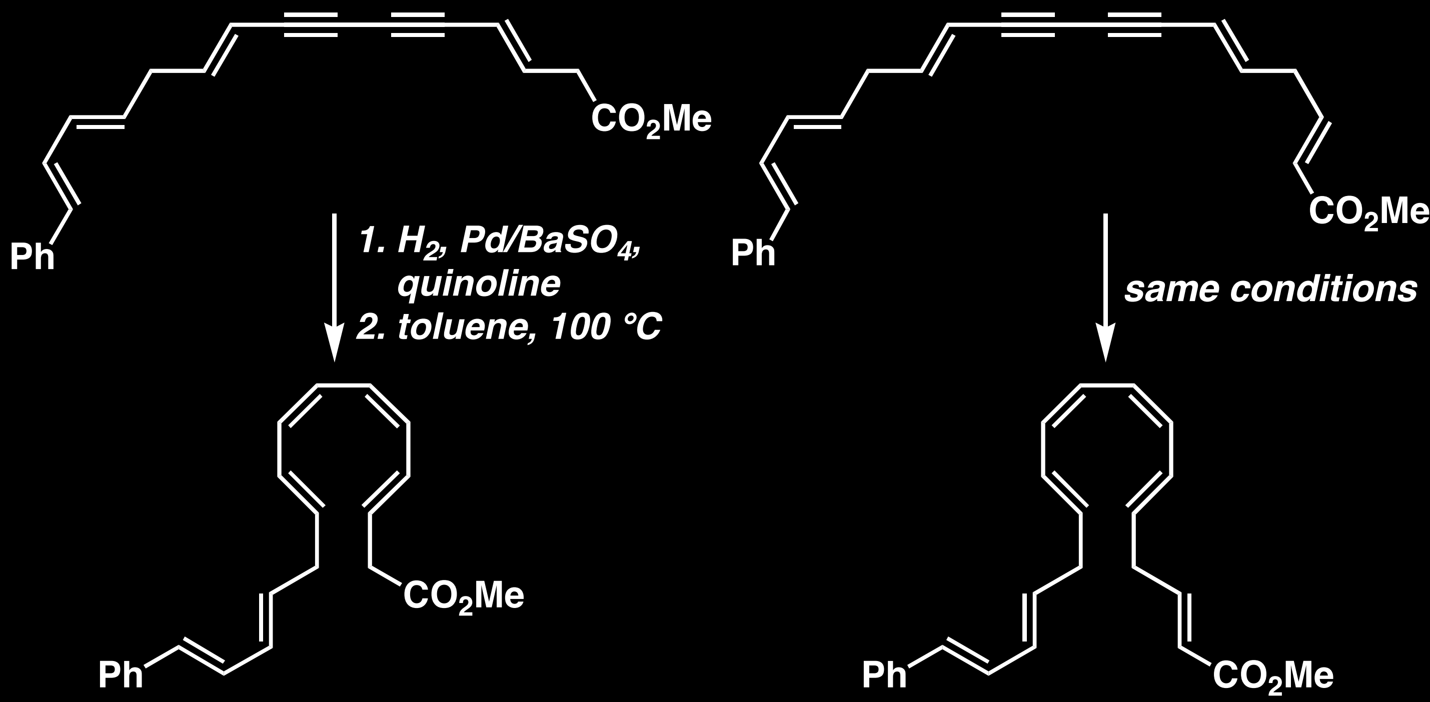
D. St. C. Black and co-workers, *Aust. J. Chem.* 1982, 35, 2247.

Electrocyclization Cascades:
Black's Hypothesis for the Biosynthesis of the Endiandric Acids



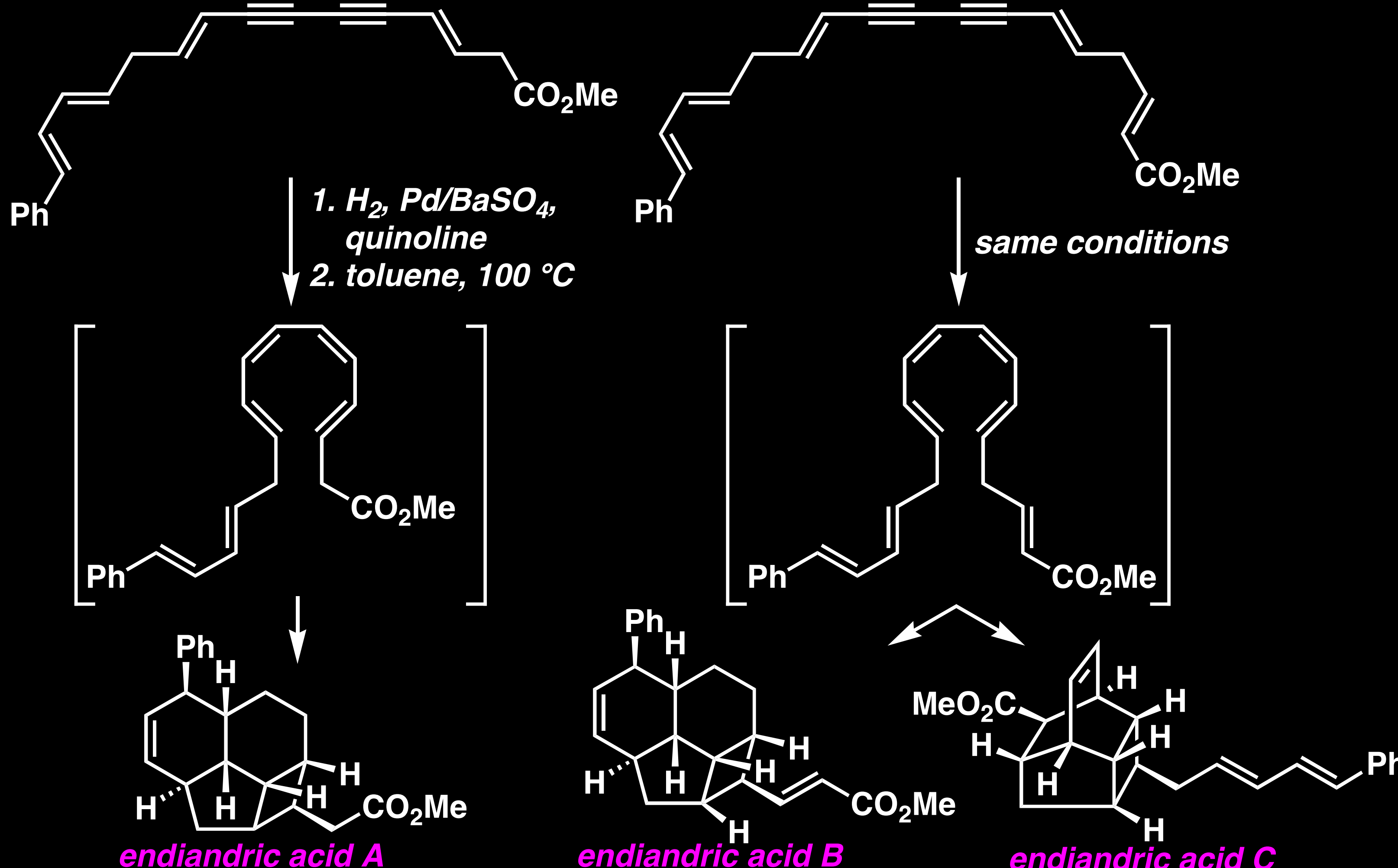
D. St. C. Black and co-workers, *Aust. J. Chem.* 1982, *35*, 2247.

Electrocyclization Cascades: Total Synthesis of the Endiandric Acids



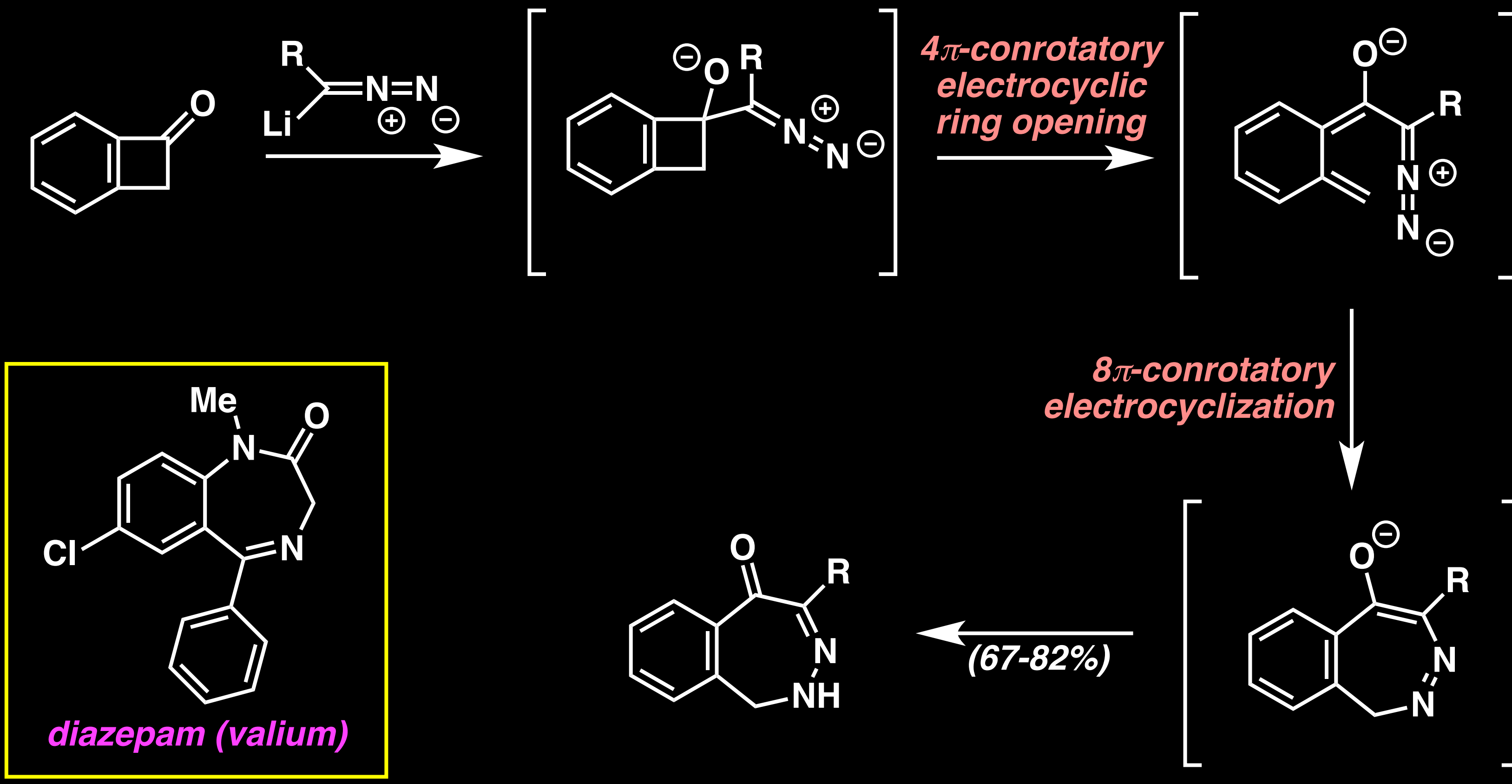
K. C. Nicolaou and co-workers, J. Am. Chem. Soc. 1982, 104, 5555.
For a review, see Classics in Total Synthesis I.

Electrocyclization Cascades: Total Synthesis of the Endiandric Acids



K. C. Nicolaou and co-workers, J. Am. Chem. Soc. 1982, 104, 5555.
For a review, see Classics in Total Synthesis I.

Current Frontiers in Electrocyclic Reactions: Access to Benzodiazepine Derivatives



H. Nemoto and co-workers, J. Am. Chem. Soc. 2006, 128, 13072.