Erick M. Carreira

Gaich Group Seminar

Birte Schröder

13.01.14

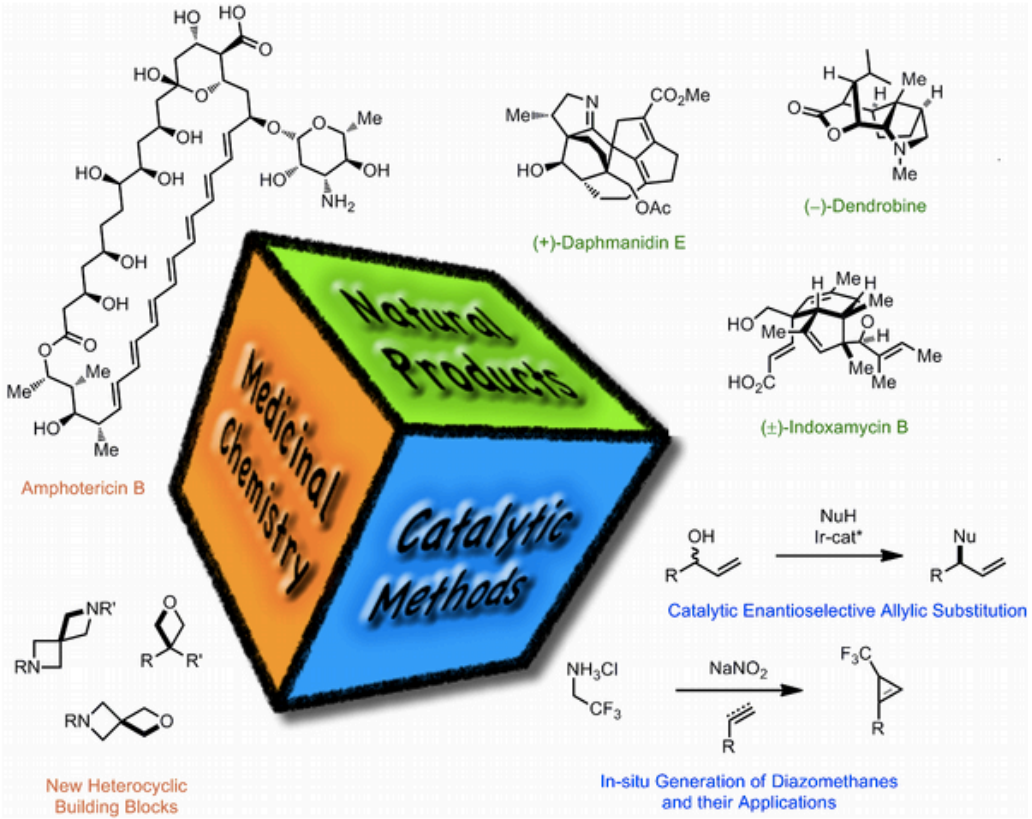
Leibniz Universität Hannover

Prof. Erick M. Carreira

- Born in Havana, Cuba (1963)
- Education;
  - **B. Sc.:** University of Illinois at Urbana Champaign (1984)
    under supervision of *Prof. Scott E. Denmark*
  - **PhD.:** Harvard University (1990)
    under supervision of Prof. David A. Evans
  - **PostDoc:** California Institute of Technology
    under supervision of Prof. Peter Dervan
  - **Associate professor:** California Institute of Technology (1996)
  - **Full professor:** California Institute of Technology (1997)
    ETH Zürich (1998-now)
- **Former member:** Justin Du Bois, Teshik P. Yoon, Karl Gademann, Nicolai Cramer, Tobias Ritter, Corey Stephenson

Research Interest:

- **Asymmetric synthesis by organometallic chemistry**
- Total synthesis
- Medicinal chemistry



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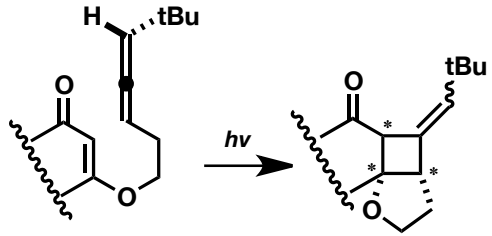
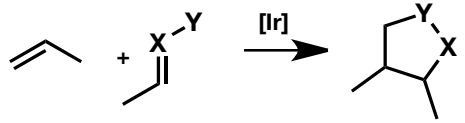
Methodology

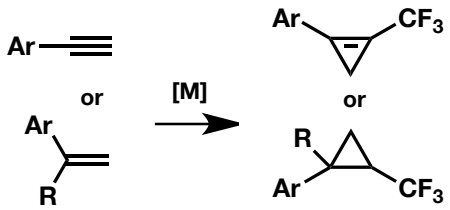
Photochemistry



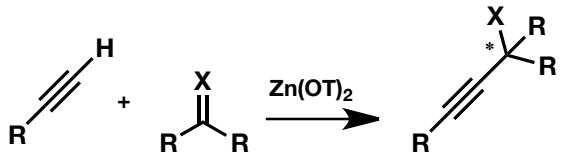
Nitrile oxide cycloaddition



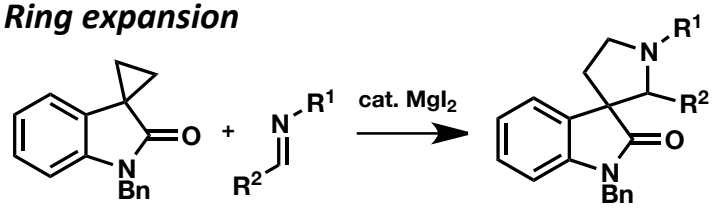
Cyclopropanation



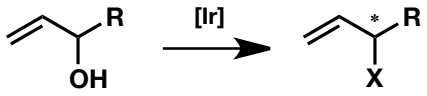
Terminal alkyne addition



Ring expansion



Branched allylic alcohol substitution



X = OR; NH_2; NHR; SR; ...

... and many others...

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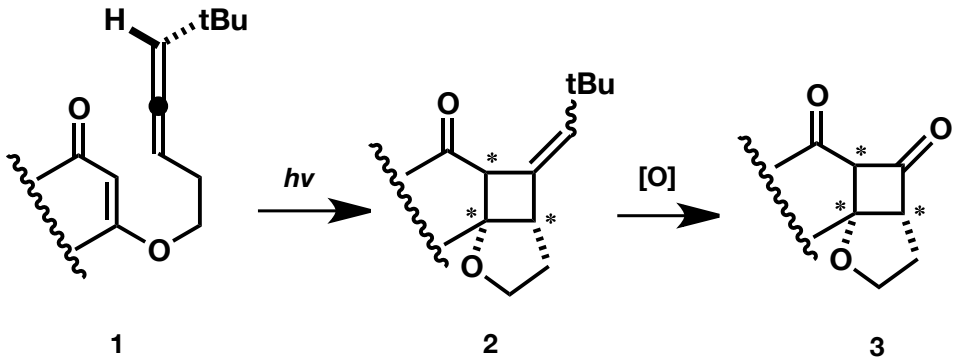
Methodology - Photochemistry

a. Intramolecular [2+2] cycloaddition of 1,2-disubstituted allenes with enones and enoates



- use of optically active allenes (89-92%ee)
- asymmetric induction through the allene fragment (83-100%)

Carreira *et al.* JACS 1994, 116, 6622-6630

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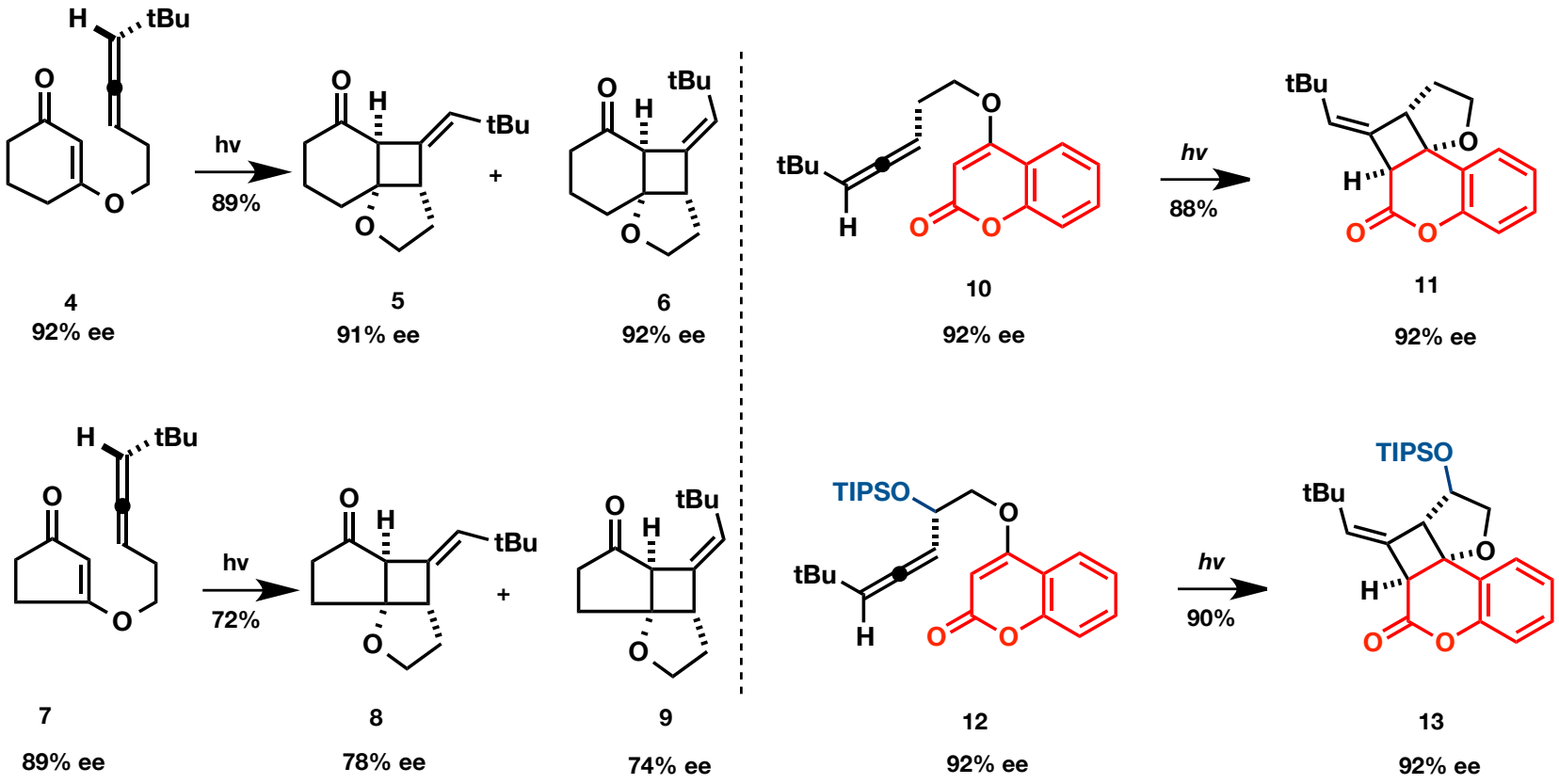
Methodology - Photochemistry

a. Intramolecular [2+2] Photocycloaddition of 1,2-Disubstituted Allenes with Enones and Enoates



Carreira *et al.* JACS 1994, 116, 6622-6630

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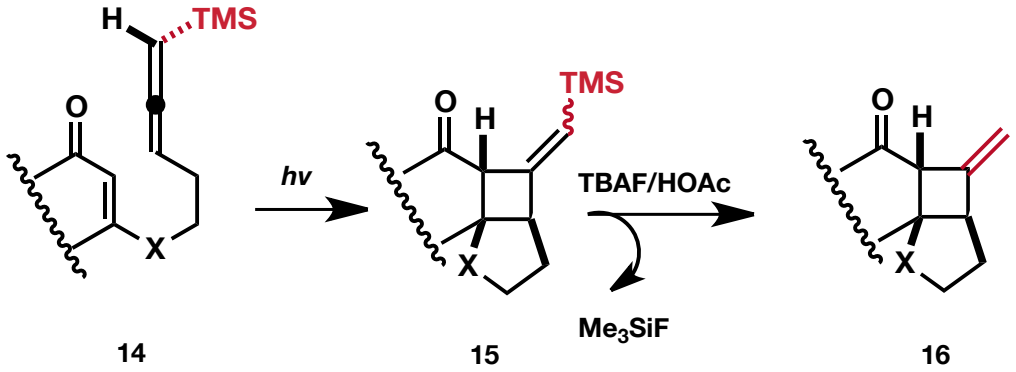
Methodology - Photochemistry

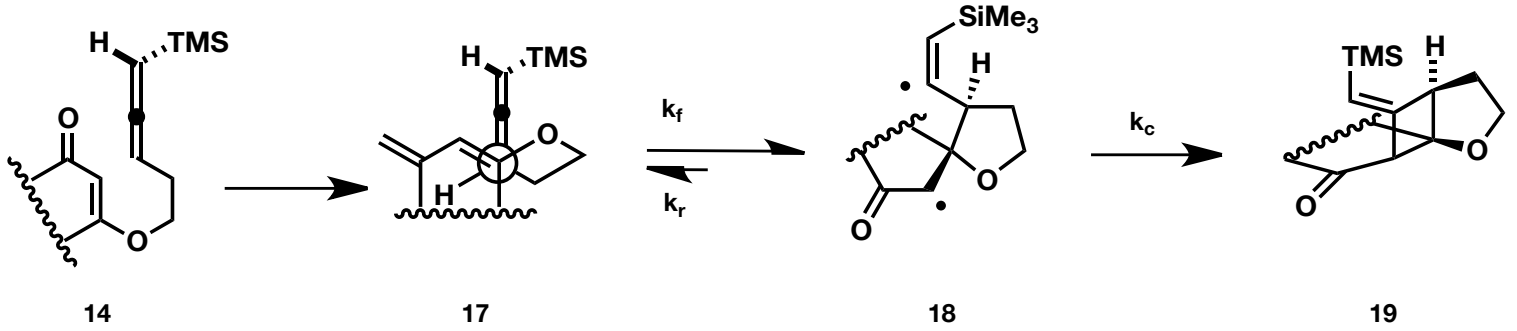
b. Asymmetric [2+2] Photocycloaddition with an Allenylsilane



Scope:

- X = O, NBoc
- 5- and 6-membered rings
- Coumarin derivates (X= O, S)

- TMS group is used as a removable stereochemical controlling group



Carreira *et al.* JACS 1997, 119, 2597-2605

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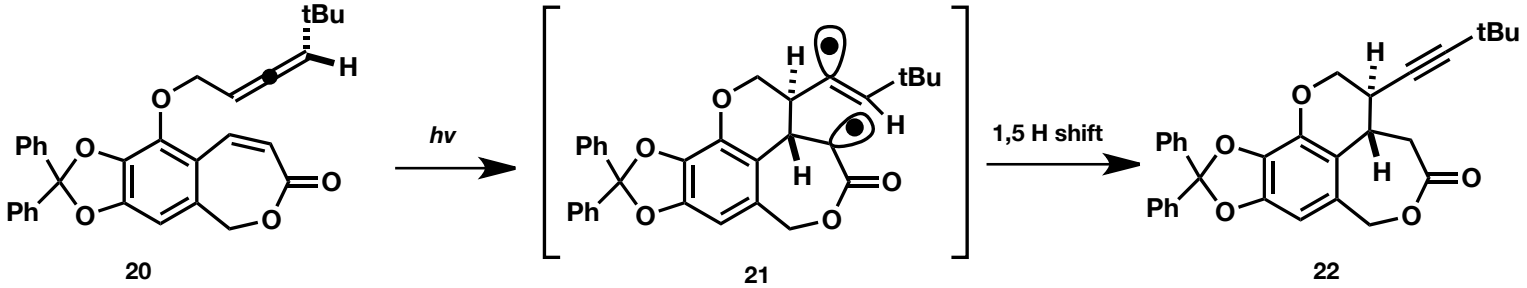
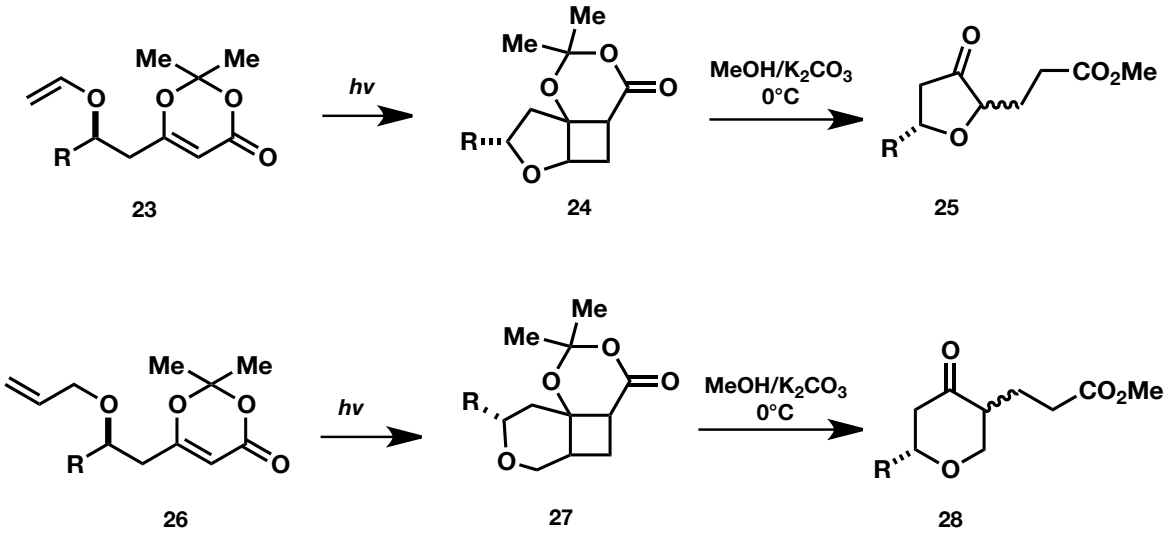
Methodology - Photochemistry

c. Stereospecific 1,5-Hydrogen-Atom Transfer



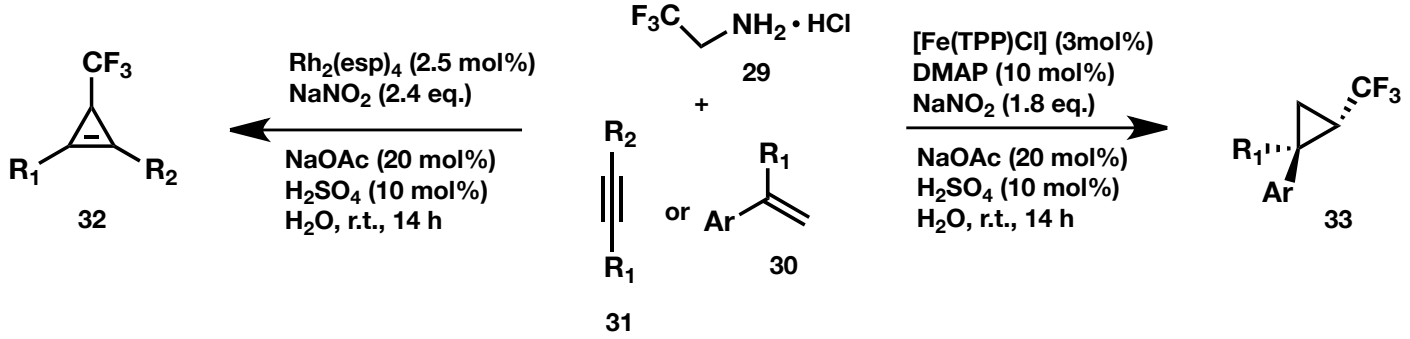
d. Photocycloaddition/Fragmentation Reaction of Dioxinones



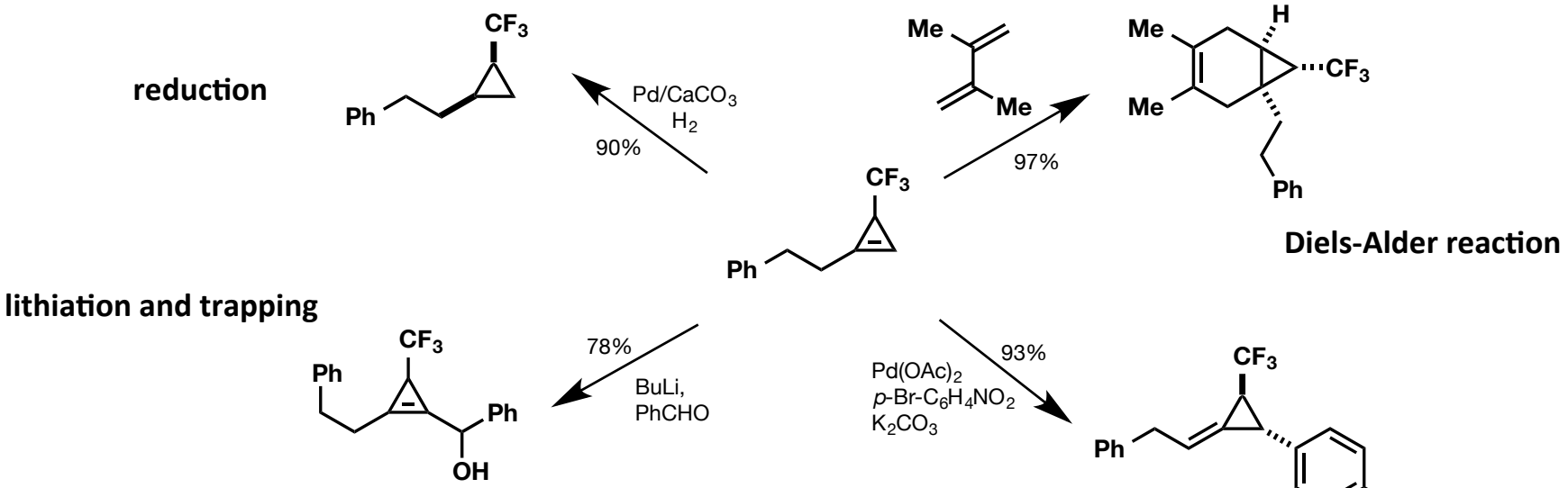
c. Carreira *et al.* JACS **1997**, *119*, 2597-2605 d. Tet. Lett**. 1997**, *38*, 5579-5582

Methodology – Cyclopropanes

a. Trifluoromethyl-substituted Cyclopropanes and Cyclopropenes



Reactivity of Cyclopropenes



Carreira *et al.* Angew. Chem. Int. Ed. **2010**, *49*, 938
Carreira *et al.* Angew. Chem. Int. Ed**. 2010**, *49*, 4294

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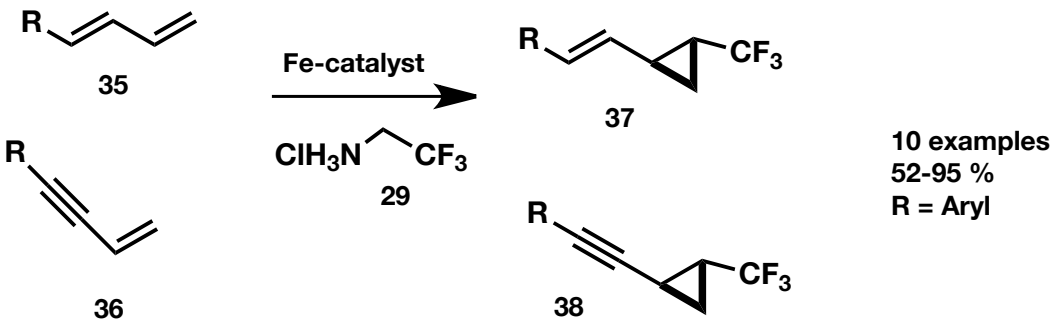
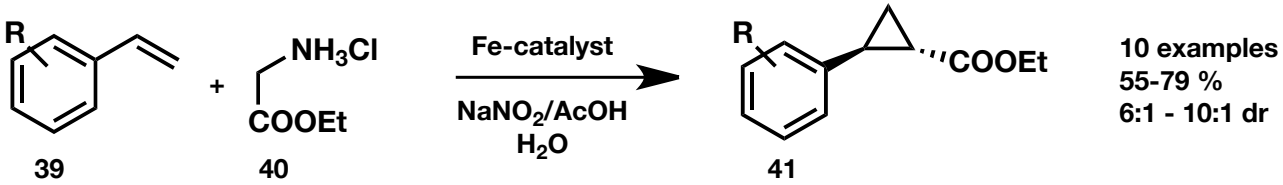
Methodology – Cyclopropanes

b. Iron-catalyzed Preparation of Vinyl-and Alkynylcyclopropanes



Carreira *et al.* Org. Lett. **2011**, *13*, 3080-3081.

c. Iron-catalyzed Cyclopropanations



Carreira *et al.* Org. Lett. **2012**, *14*, 2162-2183.

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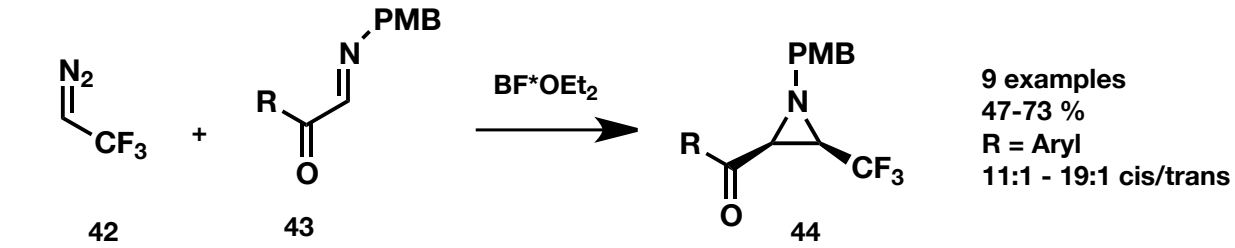
Methodology - Cyclopropanes

d. Preparation of Trifluoromethyl-substituted Aziridines



42 43 44

in situ generated

- Good yields, good diastereoselectivity
- *cis*-substituted aziridine is major product
- Deprotection w/ CAN gives the free aziridine

Carreira *et al.* Org. Lett. **2012**, *14*, 1900-1901

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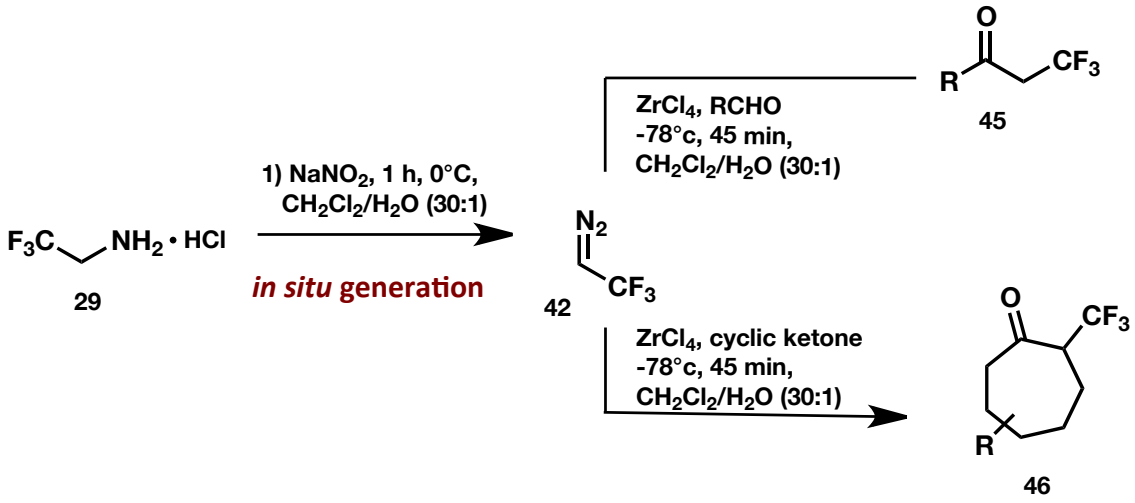
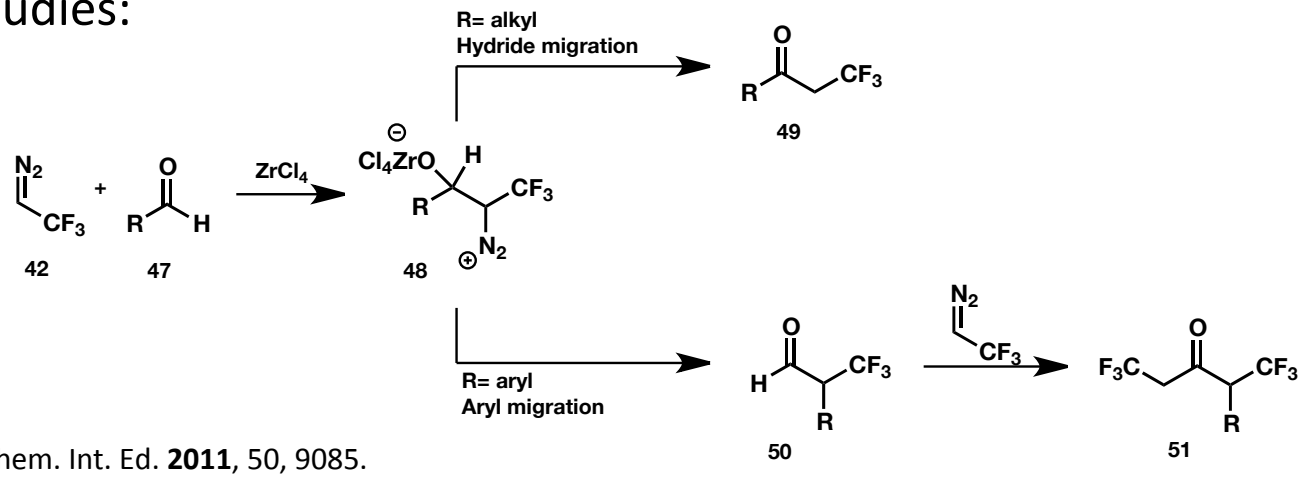
Methodology – Cyclopropanes

e. Trifluoroethyl-substituted Ketones from Aldehydes and Cyclohexanones



Mechanistic studies:



Carreira *et al.* Angew. Chem. Int. Ed. **2011**, 50, 9085.

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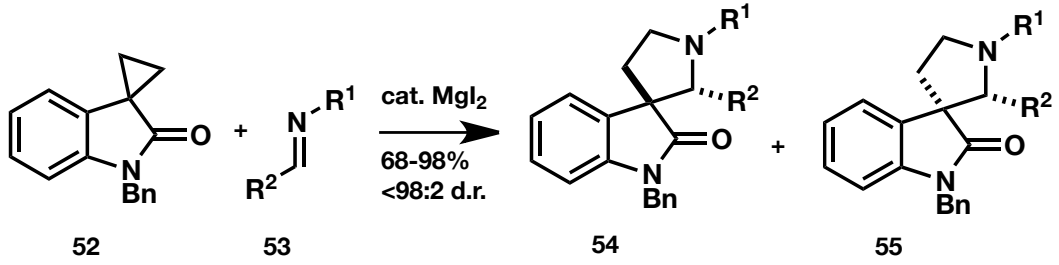
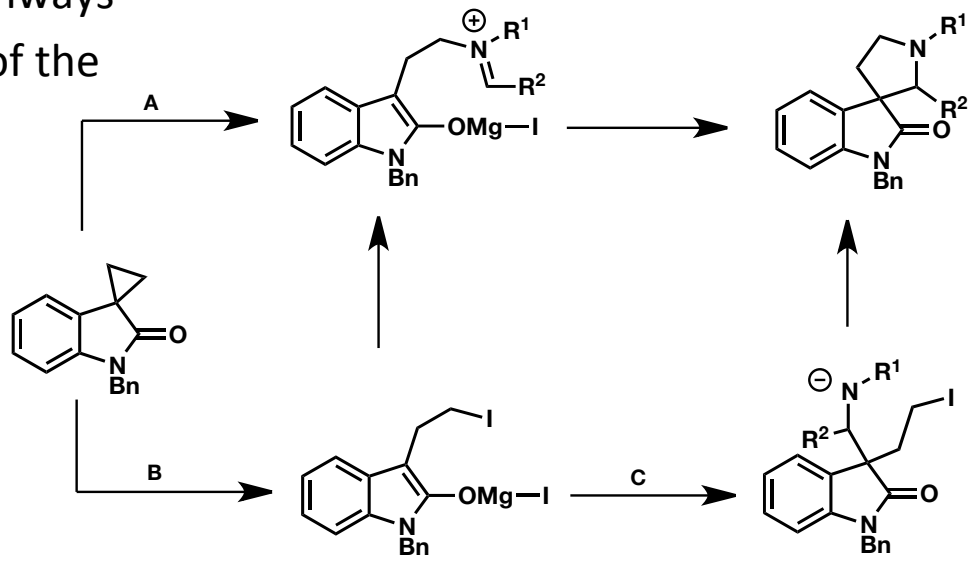
Methodology – Ring expansion

Ring expansion of Cyclopropanes by Aldimines



Potential mechanistic pathways leading to the formation of the pyrrolidine ring:



Carreira *et al.* Angew. Chem. Int. Ed. **1999**, *38*, 3186

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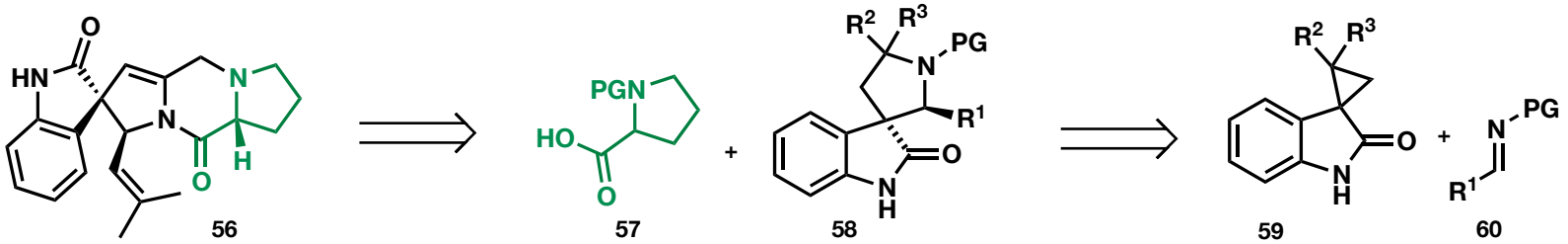
Methodology – Ring expansion

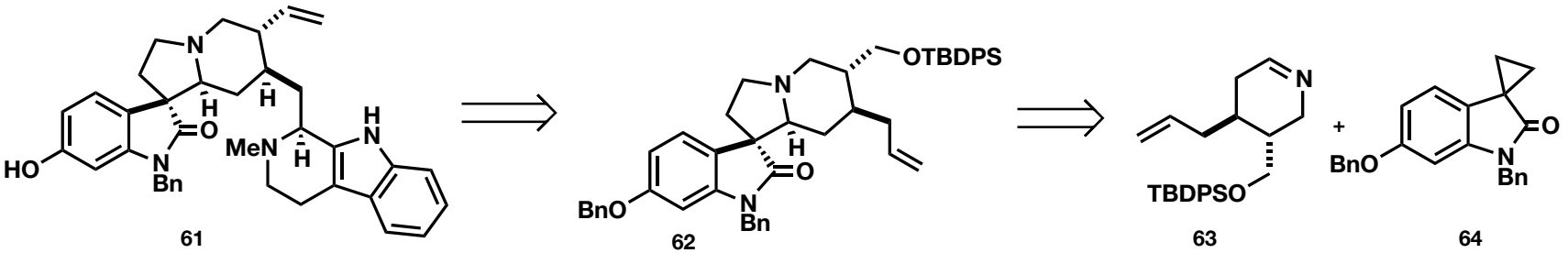
Applications in Total Synthesis

1) (+)-Spirotryprostatin B



(+)-Spirotryprostatin B

2) Strychnofoline

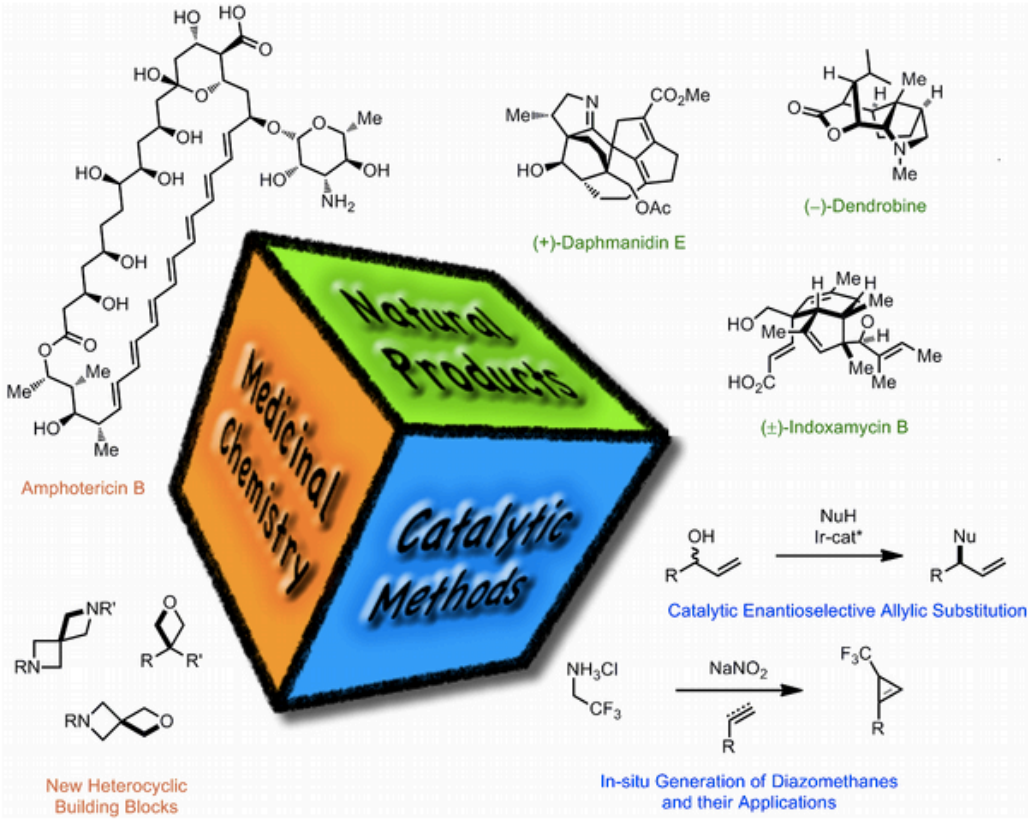


Strychnofoline

Carreira *et al.* Angew. Chem. Int. Ed. **1999**, *38*, 3186.
Carreira *et al*. J. Am. Chem. Soc. **2005**, *127*, 11505.
Carreira *et al.* Angew. Chem. Int. Ed. **2003**, *42*, 694.

Research Interest:

- Asymmetric synthesis by organometallic chemistry
- **Total synthesis**
- Medicinal chemistry



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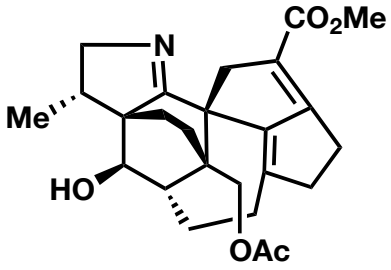
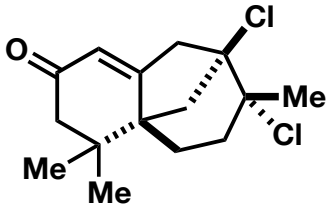
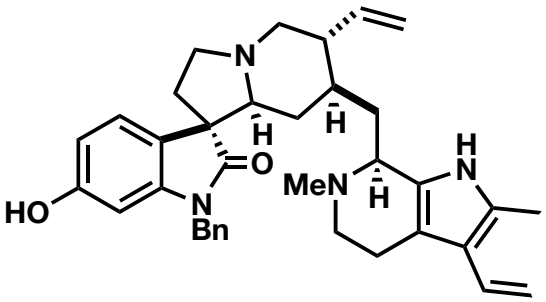
Total Synthesis



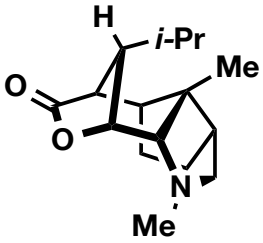
(+)-daphmanidin E



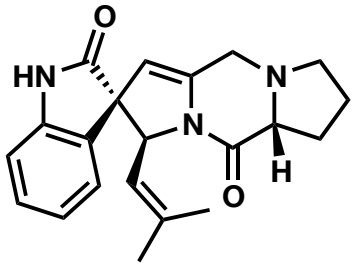
Gomerone C



Strychnofoline

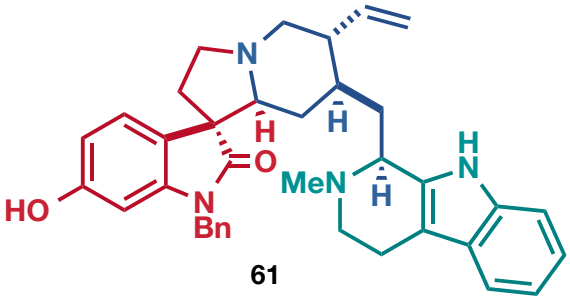


(-) Dendrobine



(+)-Spirotryprostatin B

Total Synthesis of Strychnofoline

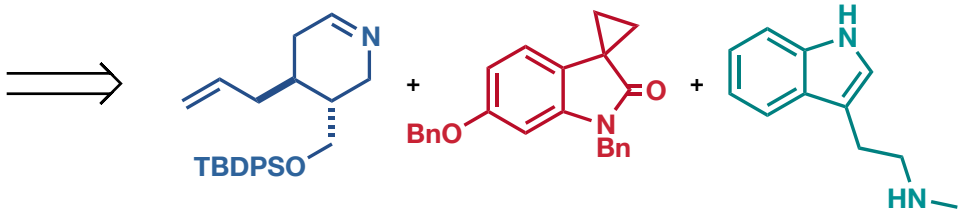


61

Strychnofoline

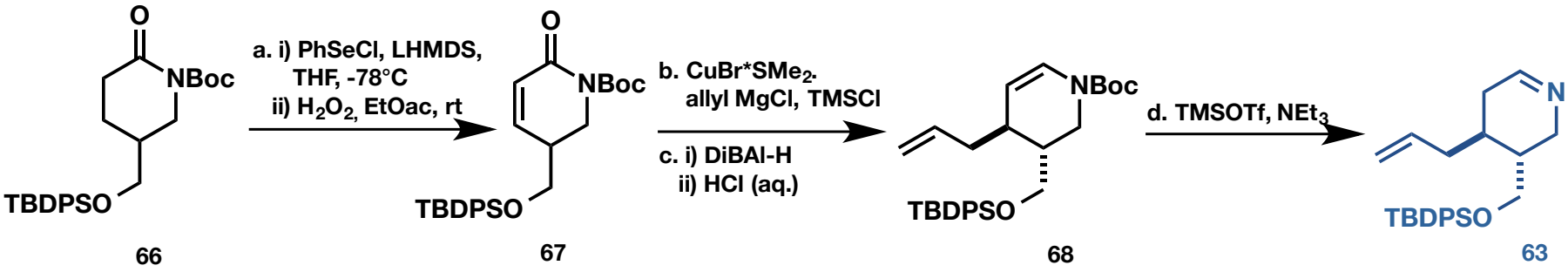
Key features:

- Ring expansion of a spiro-[cyclopropan-1,3'-oxindole] and a cyclic imine



63 64 65

Synthetic Approach:



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Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 3436-3439

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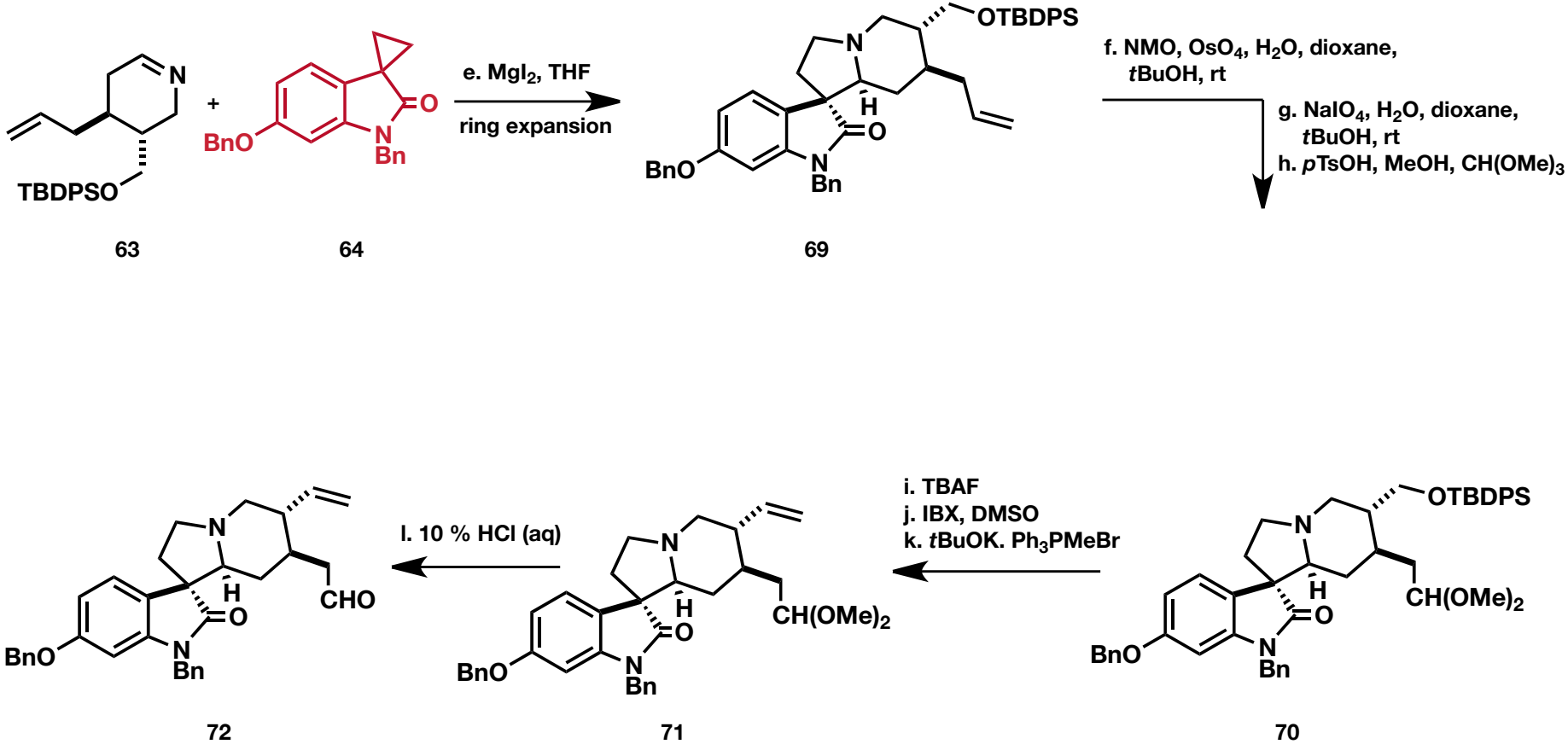
Strychnofoline



Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 3436-3439

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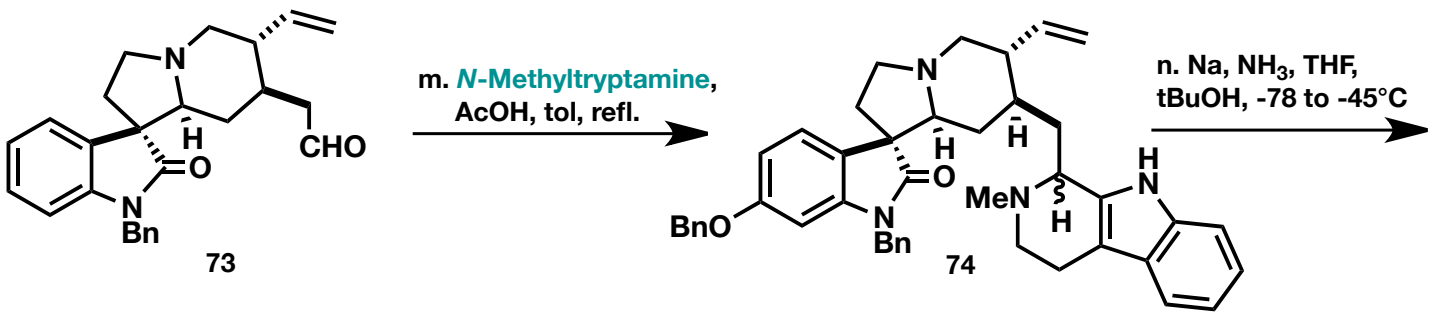
Strychnofoline



Strychnofoline 61

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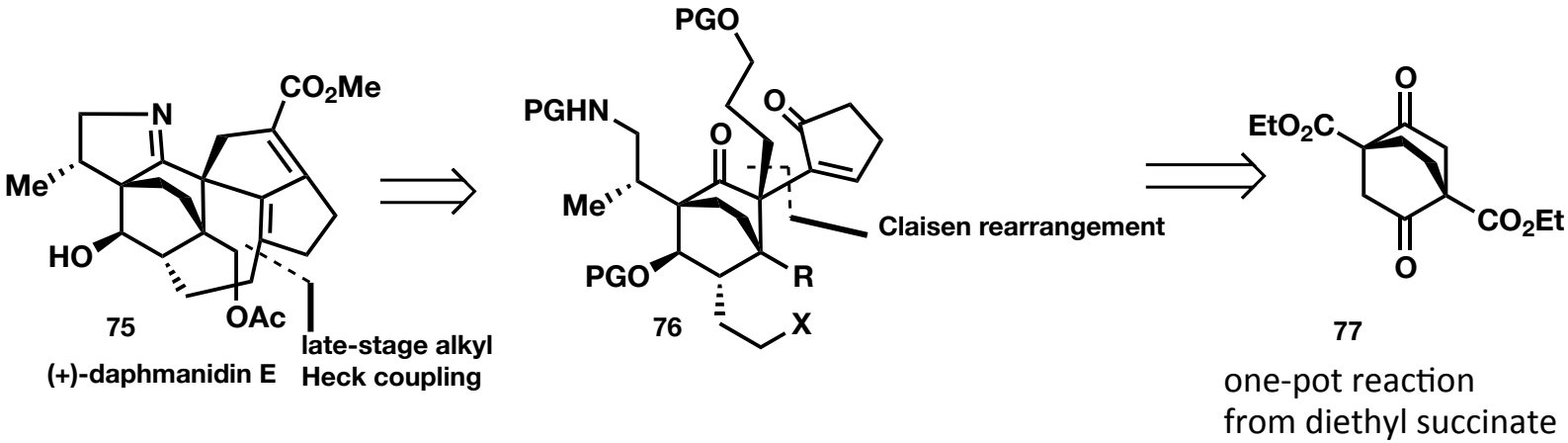
Total Synthesis of (+)-Daphmanidin E

Retrosynthetic plan



Key features:

- Readily available building block which features two quaternary centers and the bicyclo[2.2.2]octane skeleton
- Two Claisen rearrangements
- Late-stage cobalt-catalyzed Heck coupling

Carreira *et al.* Angew. Chem. Int. Ed. **2011**, *50*, 11501-11505

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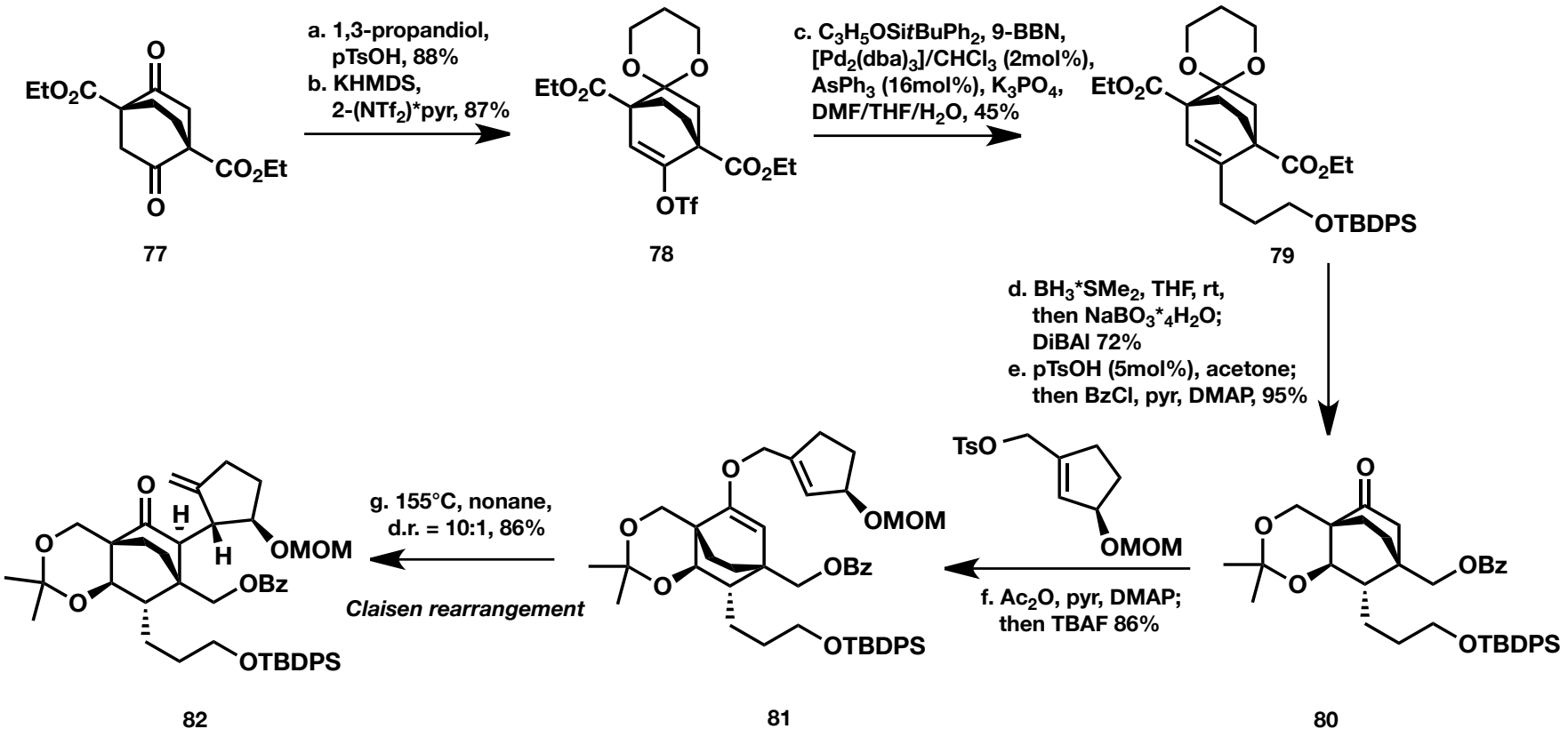
(+)- Daphmanidin E



Carreira *et al.* Angew. Chem. Int. Ed. **2011**, *50*, 11501-11505

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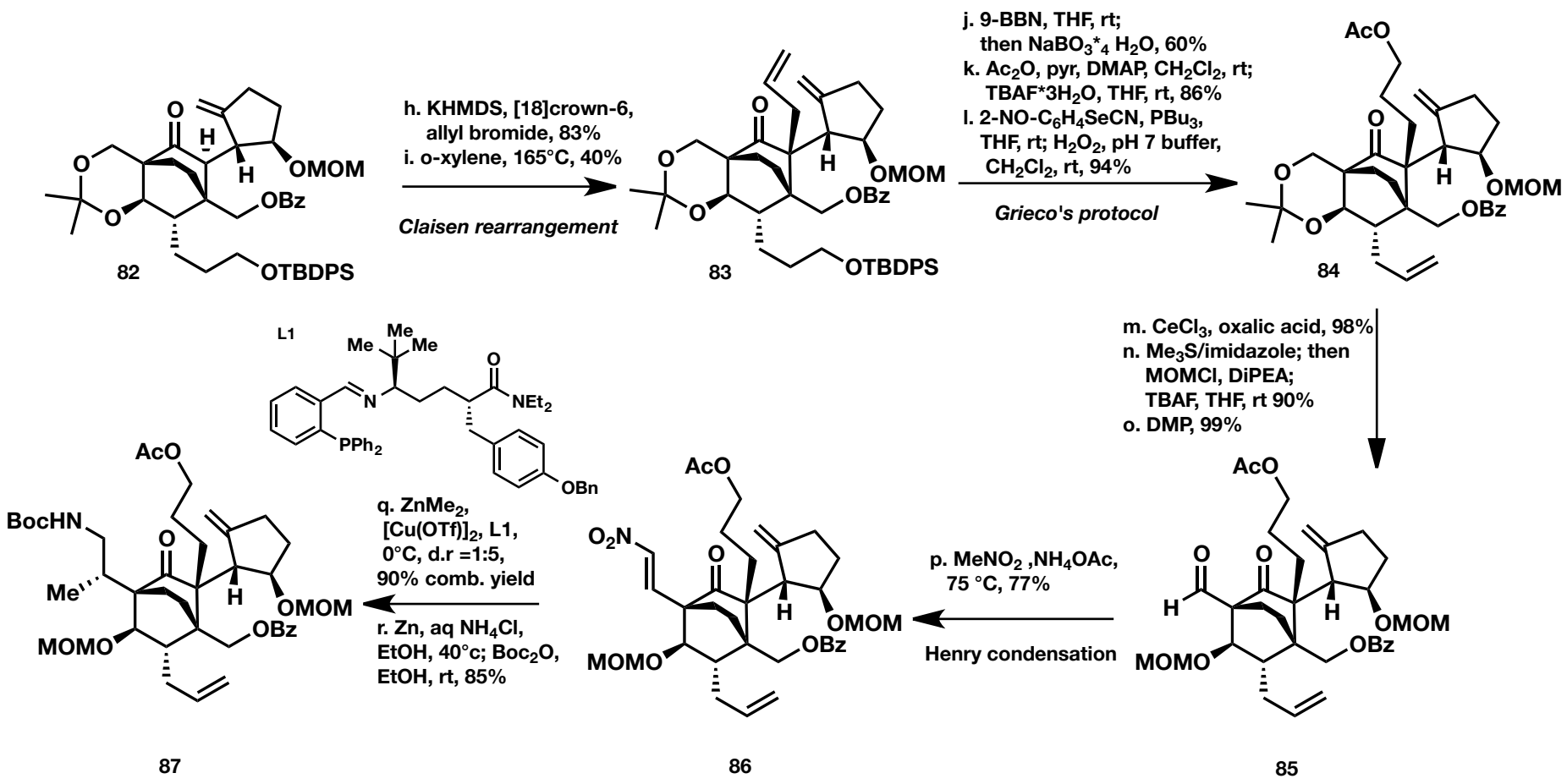
(+)- Daphmanidin E



Carreira *et al.* Angew. Chem. Int. Ed. **2011**, *50*, 11501-11505

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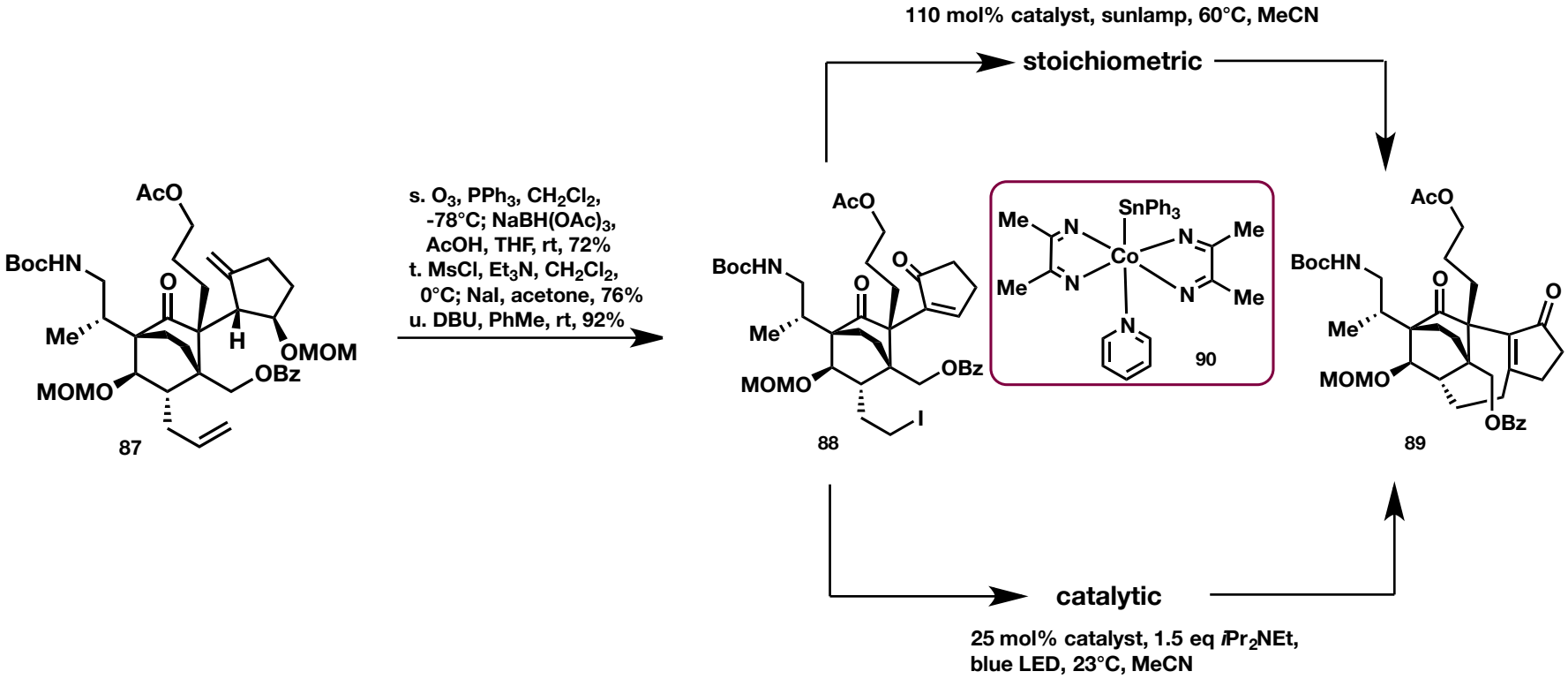
(+)- Daphmanidin E

Key step: Late-stage cobalt-catalyzed alkyl-Heck cyclization



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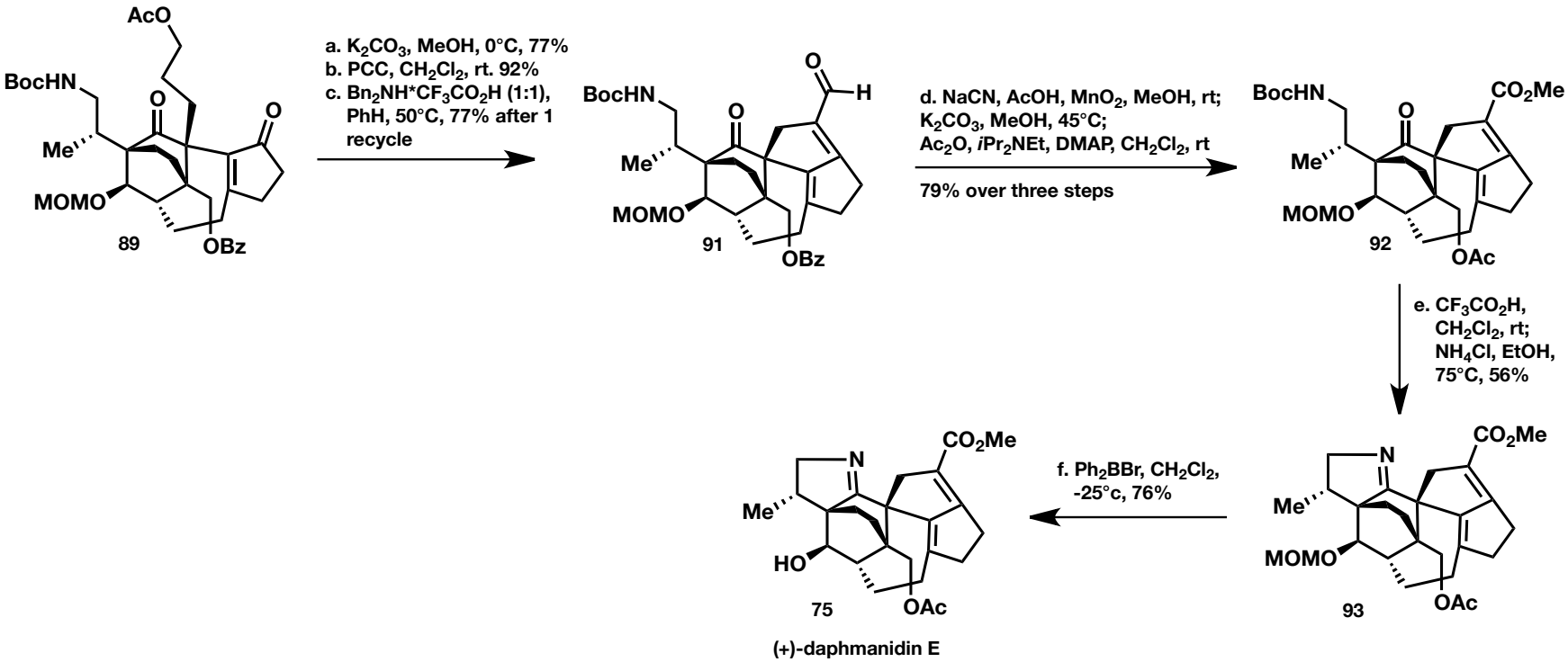
(+)- Daphmanidin E

Endgame



Carreira *et al.* Angew. Chem. Int. Ed. **2011**, *50*, 11501-11505

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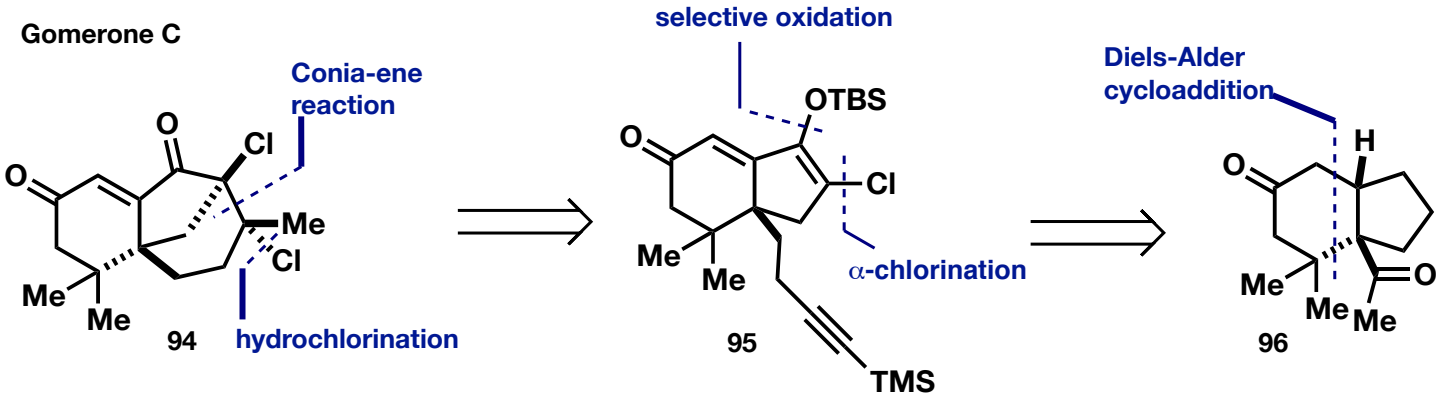
Total Synthesis of Gomerone C

Retrosynthetic plan



Key features:

- Diels-Alder cycloaddition
- γ-Selective oxidation
- α−Chlorination
- Hydrochlorination
- Late-stage Conia-ene reaction

Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 13066-13069

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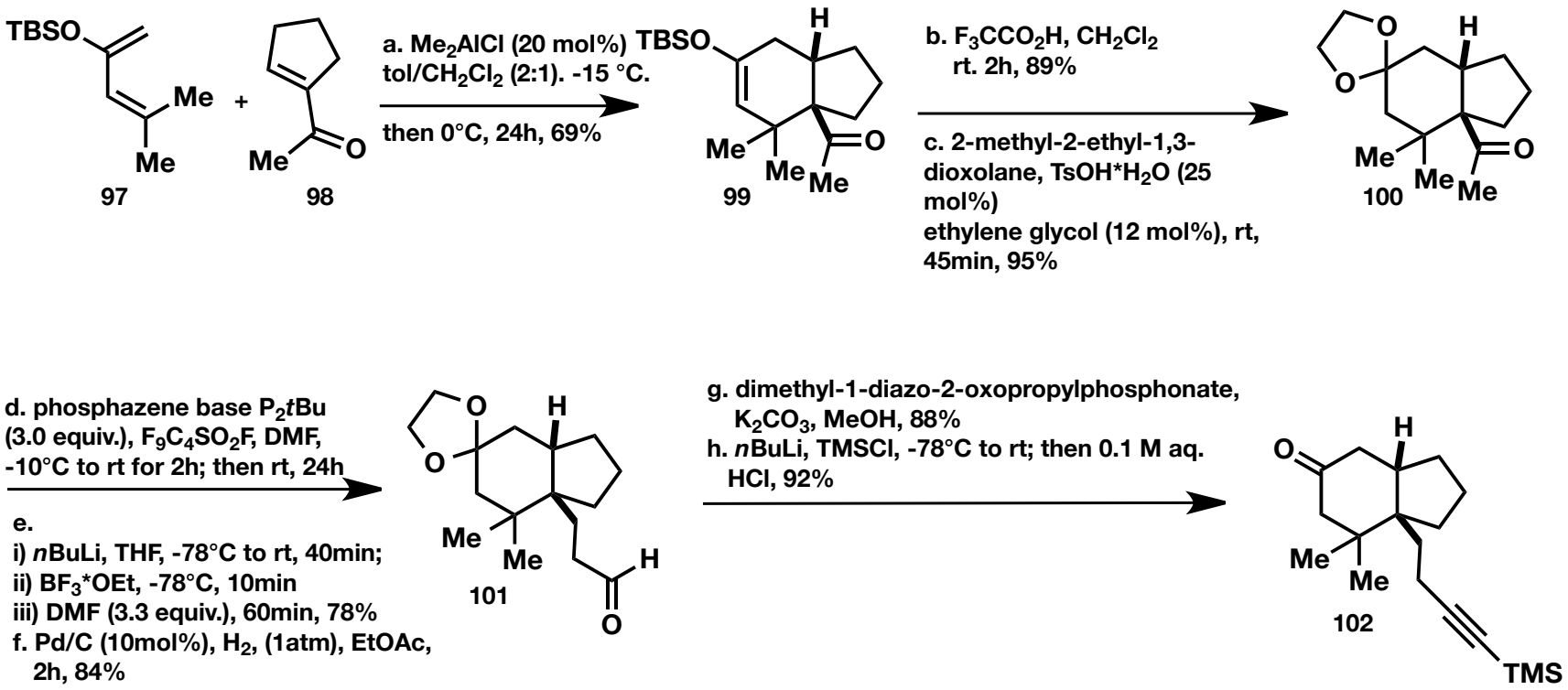
Gomerone C



Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 13066-13069

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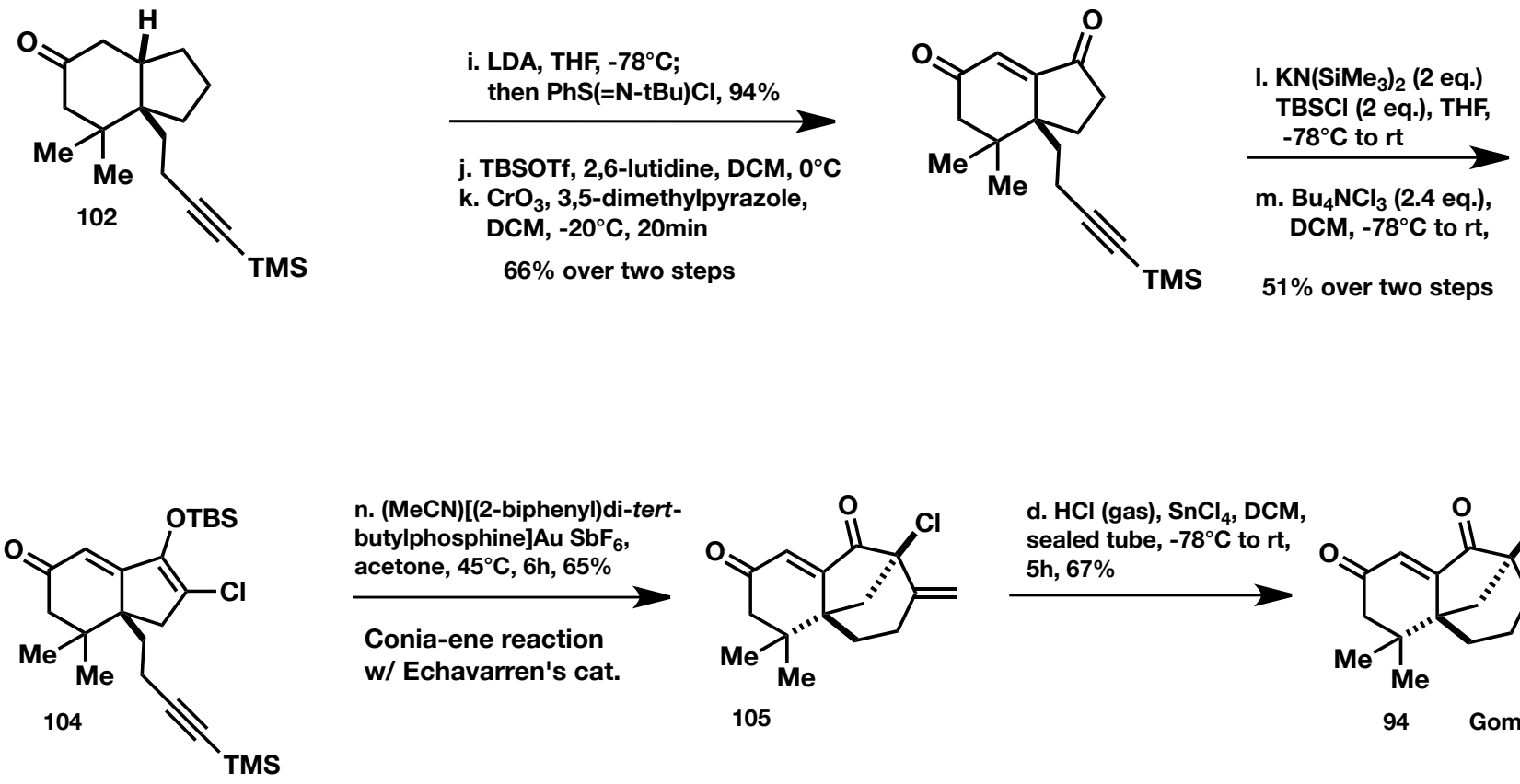
Gomerone C



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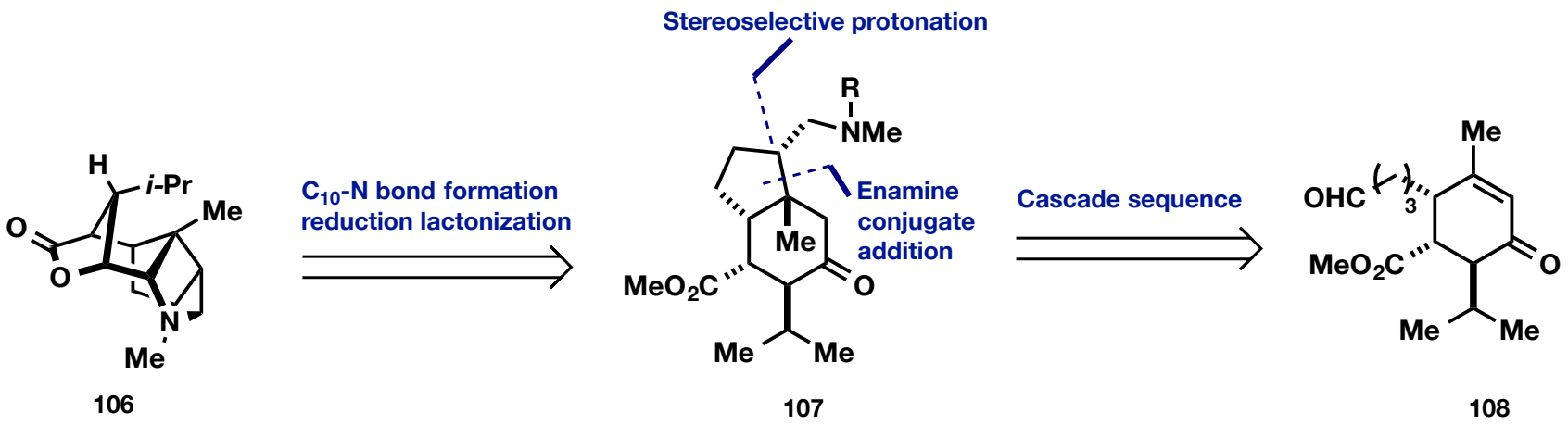
Total Synthesis of (-)-Dendrobine

Strategy for the construction of the core of (-)-dendrobine



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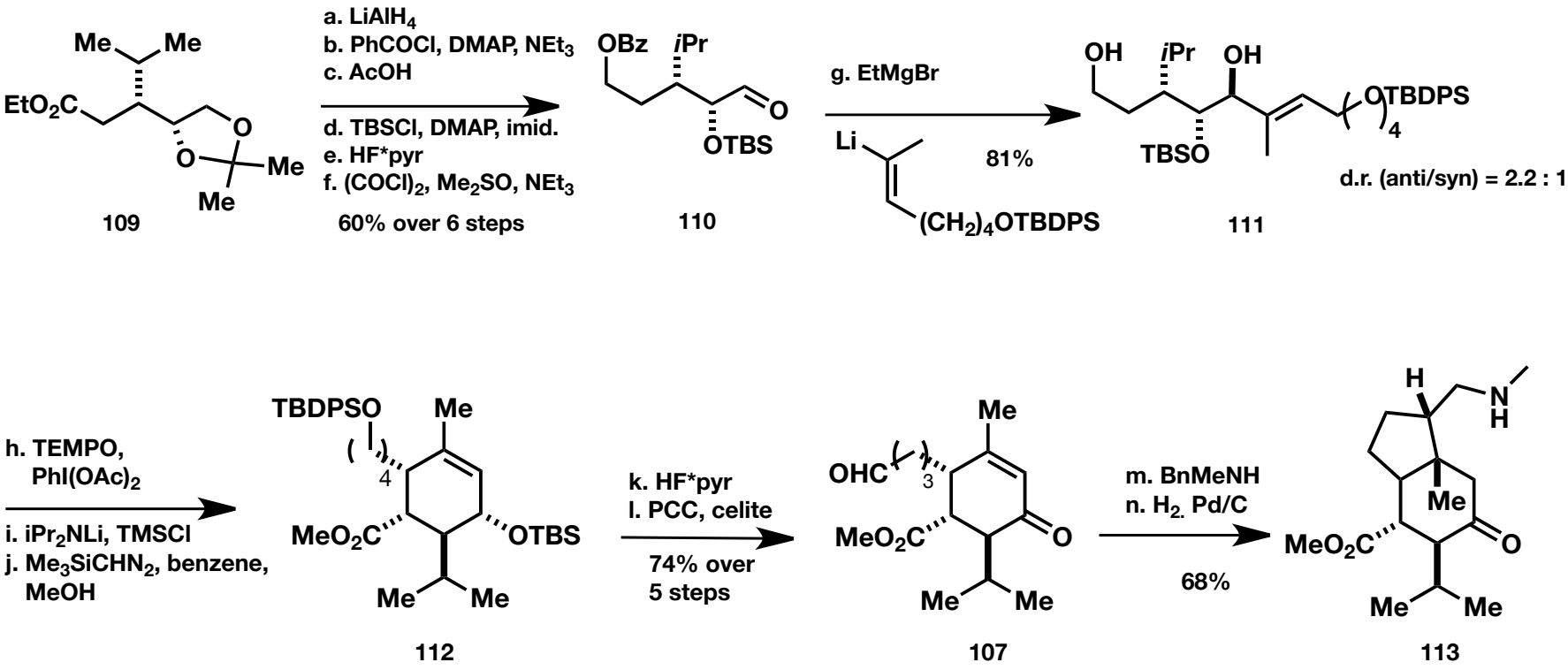
(-)-Dendrobine

Synthetic Approach



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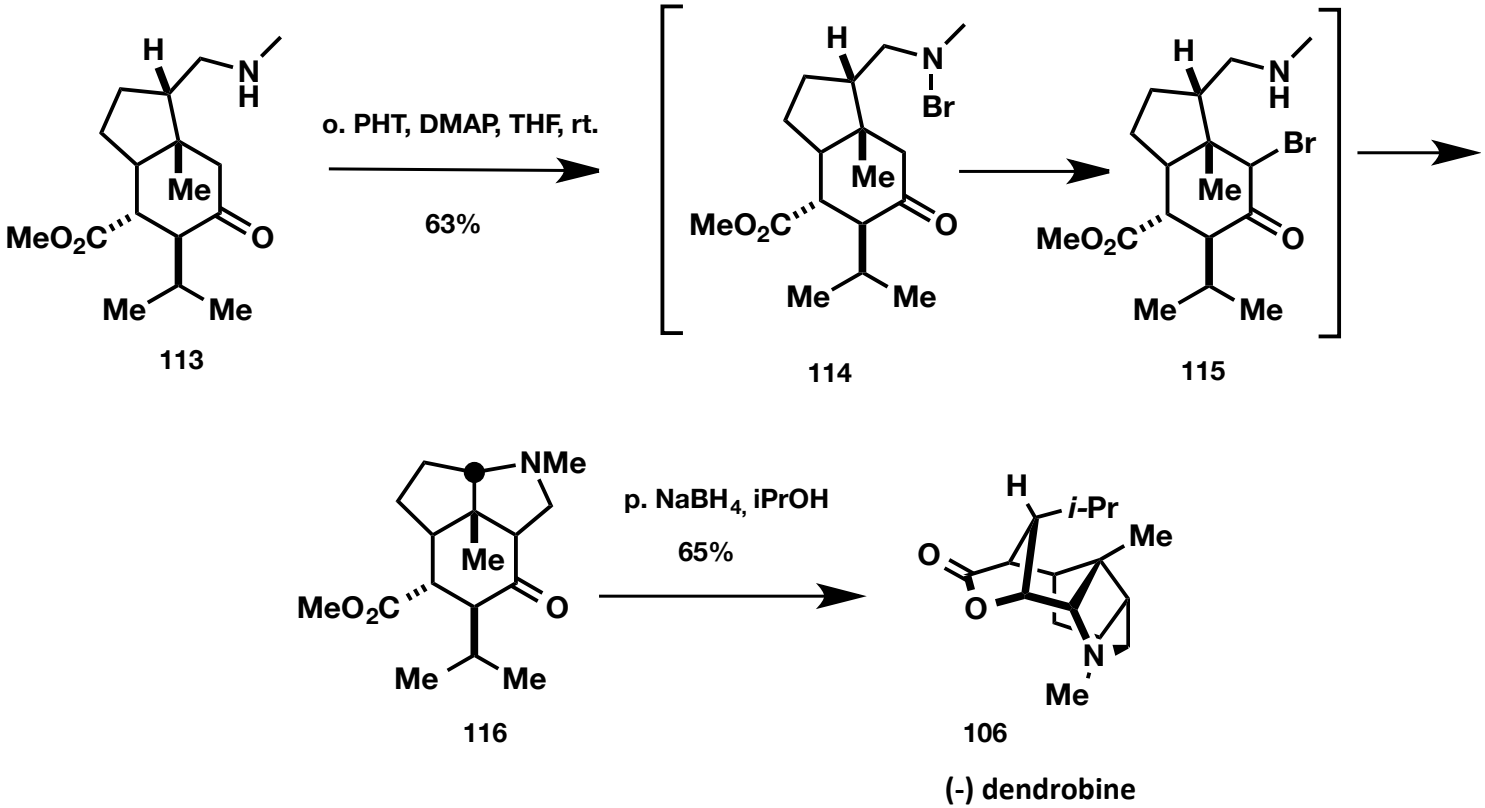
(-)-Dendrobine



Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 3436-3439

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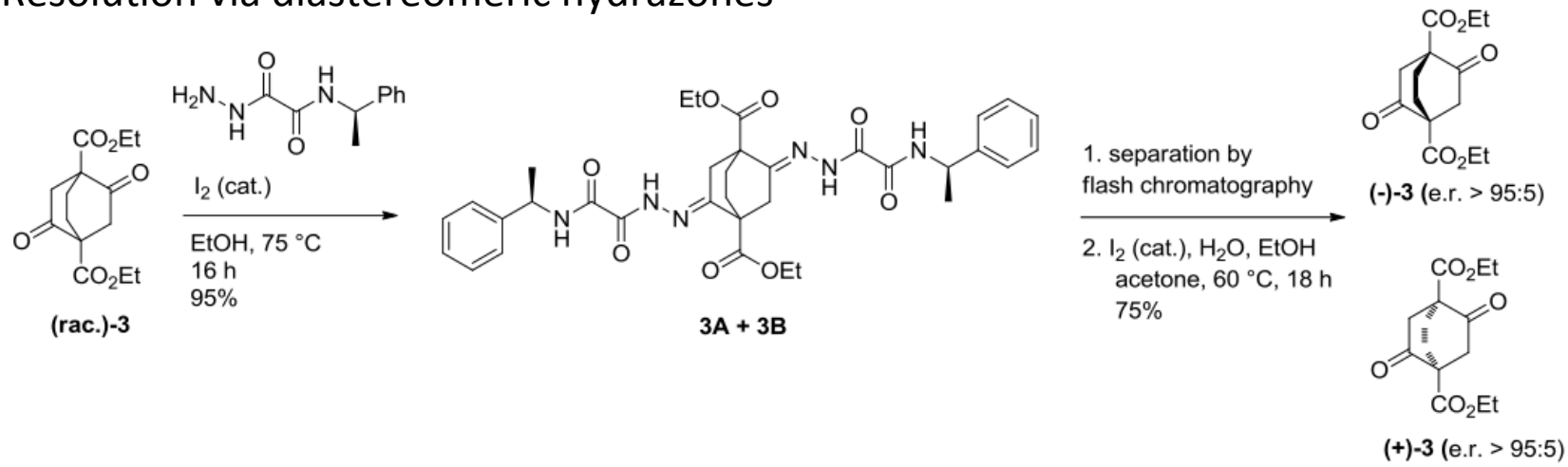
Supplementary Slides

Daphmanidin

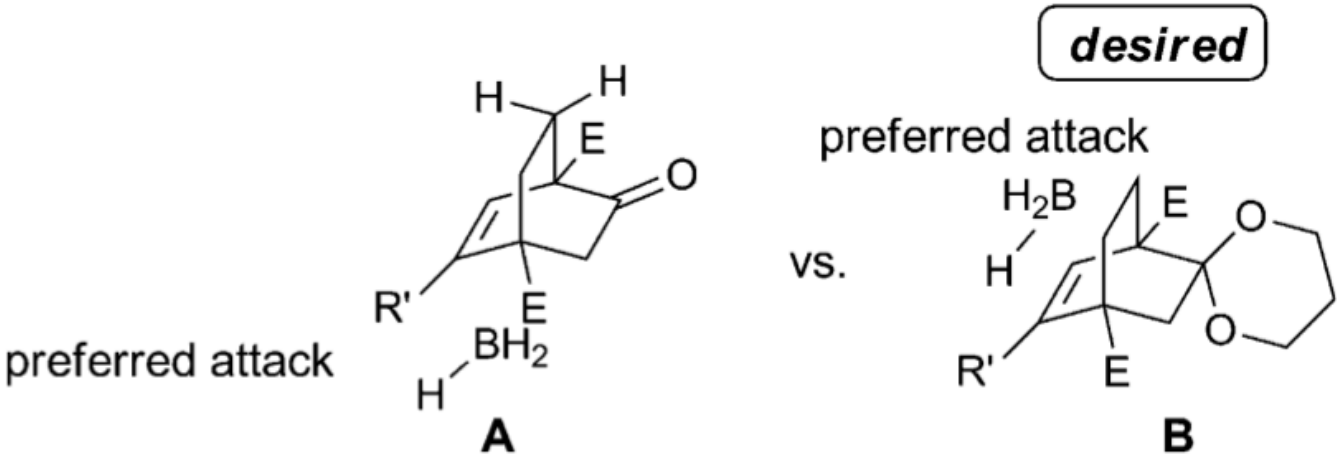
Resolution via diastereomeric hydrazones



Leibniz Universität Hannover

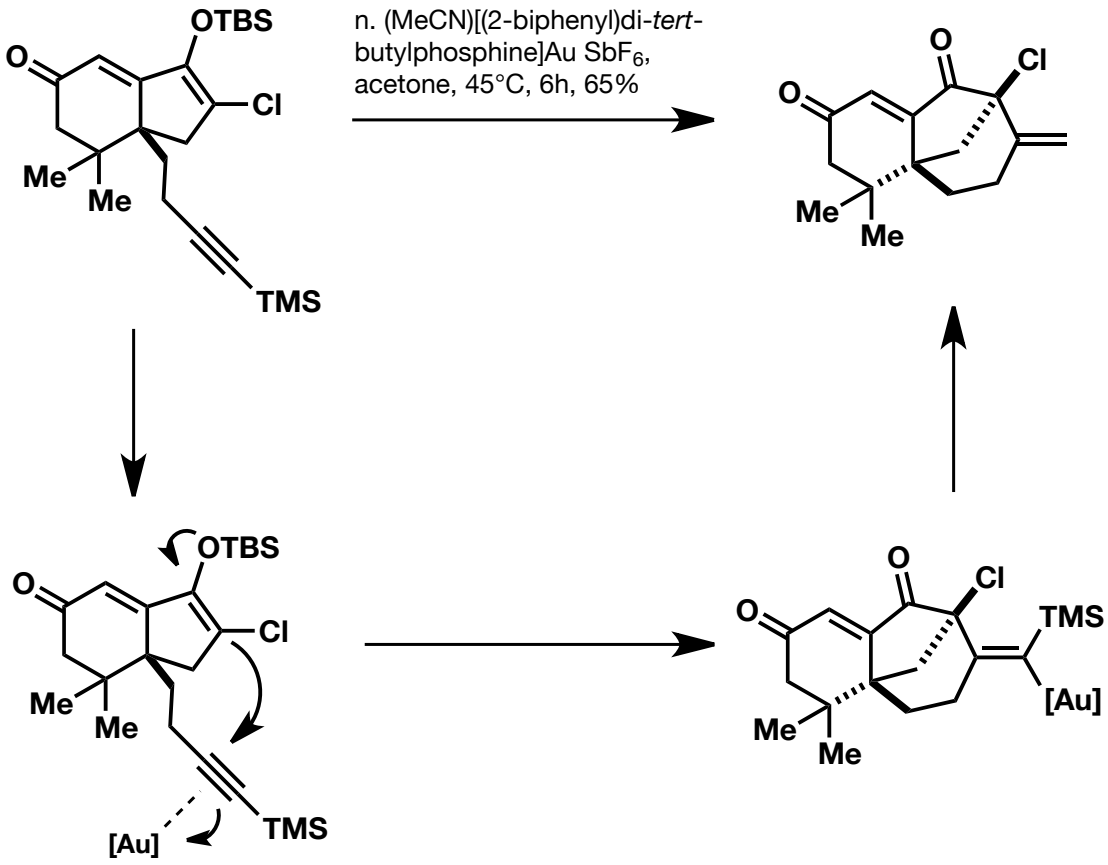
Supplementary Slides

Daphmanidin
Comins reagent

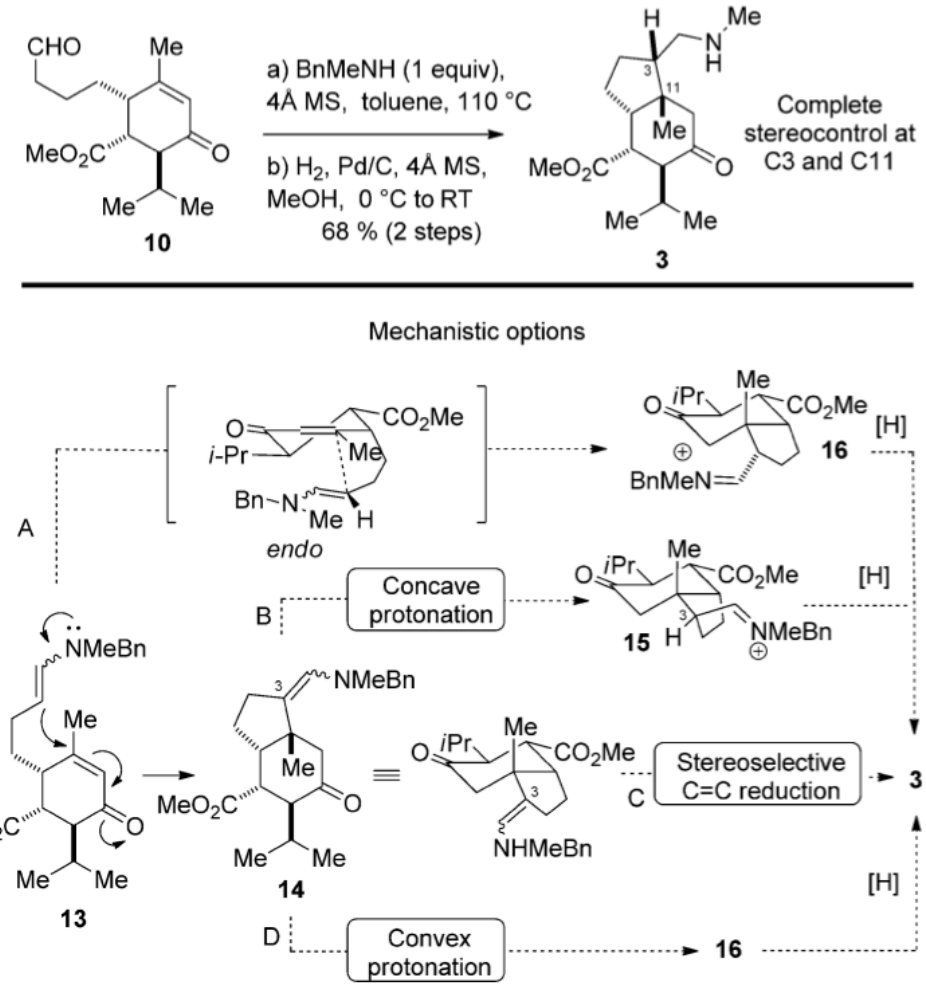


Gomerone C

Mechanism of Conia-ene reaction:



(-)-Dendrobine



Carreira *et al.* Angew. Chem. Int. Ed. **2012**, *51*, 3436-3439