

CU Synthesis Lit Group Presents

Career in Review:

Stephen F. Martin



September 7, 2007
Kristy Tran – Leighton Group



Career Snapshot

1968 BS, University of Mexico (Prof. R. N. Castle)

1970 MA, Princeton University (Prof. E. C. Taylor)

1972 Ph. D, Princeton University (Prof. E. C. Taylor)

1972-73 Post-Doc, University of Munich (R. Gompper)

1973-74 Post-Doc, MIT, (G. Buchi)

1974-1980 Assistant Professor, University of Texas

1980-1986 Associate Professor, University of Texas

1986-Present Professor, University of Texas

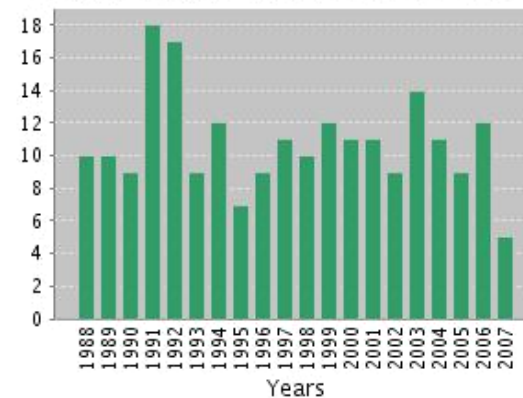
2000-Present M. June and J. Virgil Waggoner Regents Chair in Chemistry, University of Texas

ISIS Web of Knowledge statistics as of August 11, 2007 ★

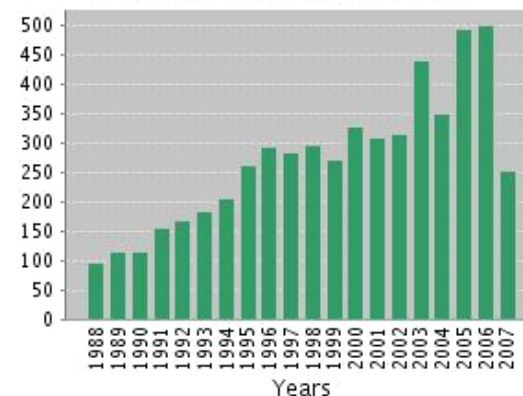
Total Publications: 240

Total Citations: 6118

Published Items in Each Year



Citations in Each Year

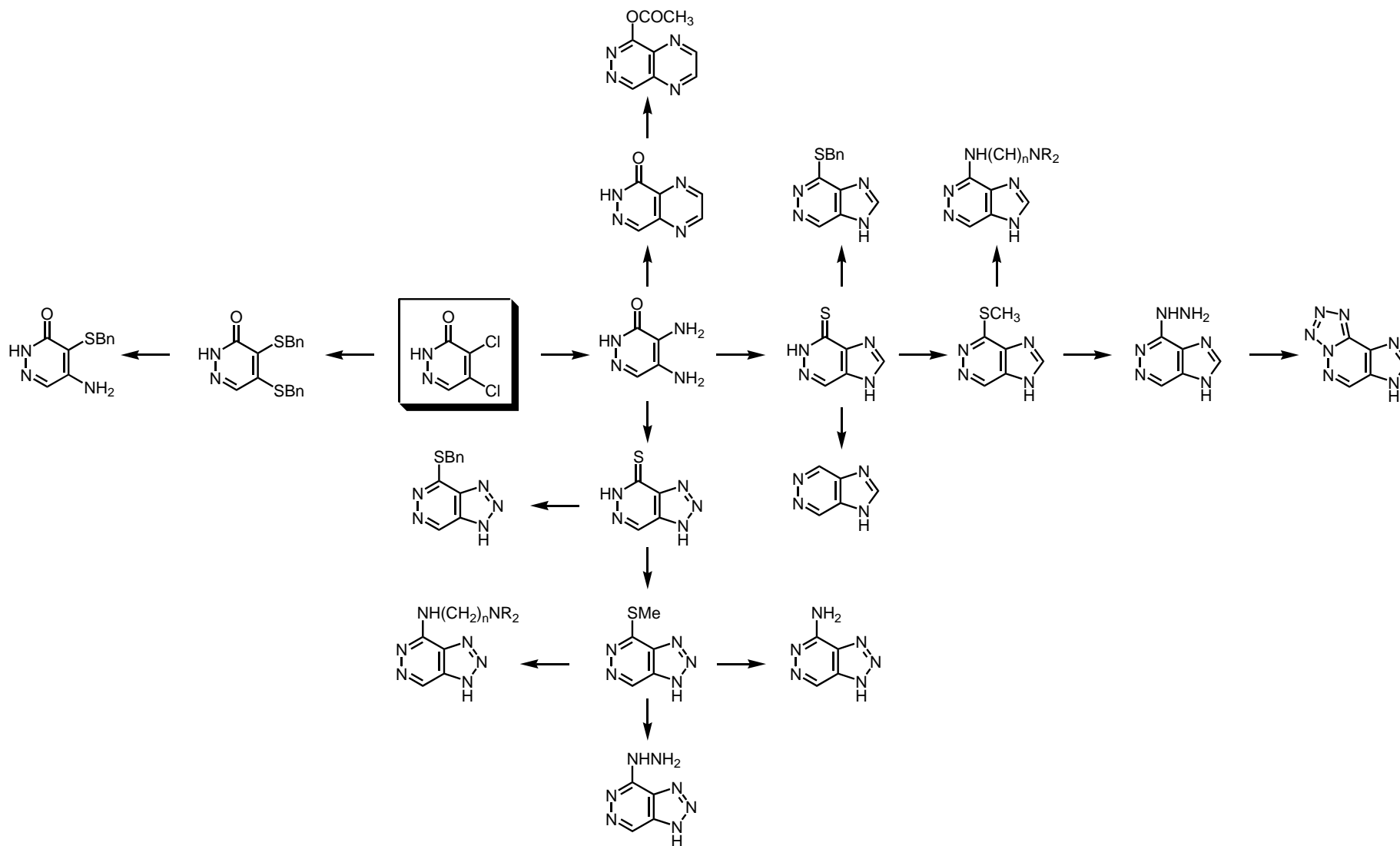


Five Most Cited Papers

1. **Martin, SF**
Methodology for the construction of quaternary carbon centers
Tetrahedron 36 (4): 419-460 1980
Times Cited: 385
2. **Martin SF, Dodge JA**
Efficacious modification of the Mitsunobu reaction for inversions of sterically hindered secondary alcohols
Tetrahedron Letters 32 (26): 3017-3020 JUN 24 1991
Times Cited: 265
3. Deiters A, **Martin SF**
Synthesis of oxygen- and nitrogen-containing heterocycles by ring-closing metathesis
Chemical Reviews 104 (5): 2199-2238 MAY 2004
Times Cited: 252
4. Doyle MP, Austin RE, Bailey AS, et al.
Enantioselective Intramolecular Cyclopropanations of Allylic and Homoallylic Diazoacetates and Diazoacetamides Using Chiral Dirhodium(II) Carboxamide Catalysts
Journal of the American Chemical Society 117 (21): 5763-5775 MAY 31 1995
Times Cited: 155
5. **Martin SF**
Synthesis of Aldehydes, Ketones, and Carboxylic Acids from Lower Carbonyl Compounds by C-C Coupling Reactions
Synthesis(9): 633-665 1979
Times Cited: 153

Undergraduate Career

Synthesis of Imidazo [4,5-d]-pyridazines



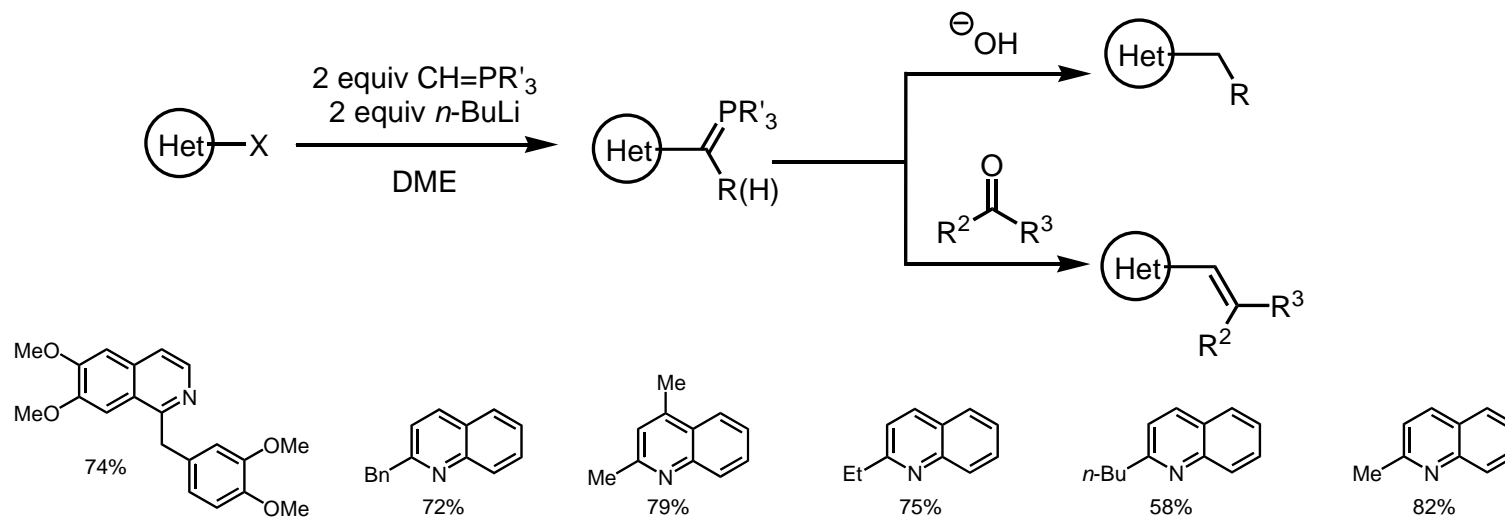
(a) Martin, S.F. and Castle, R. N.; *J. Het. Chem.* **1969**, 6, 93.

CU Synthesis Lit Group – CIR:SF Martin – Tran 4

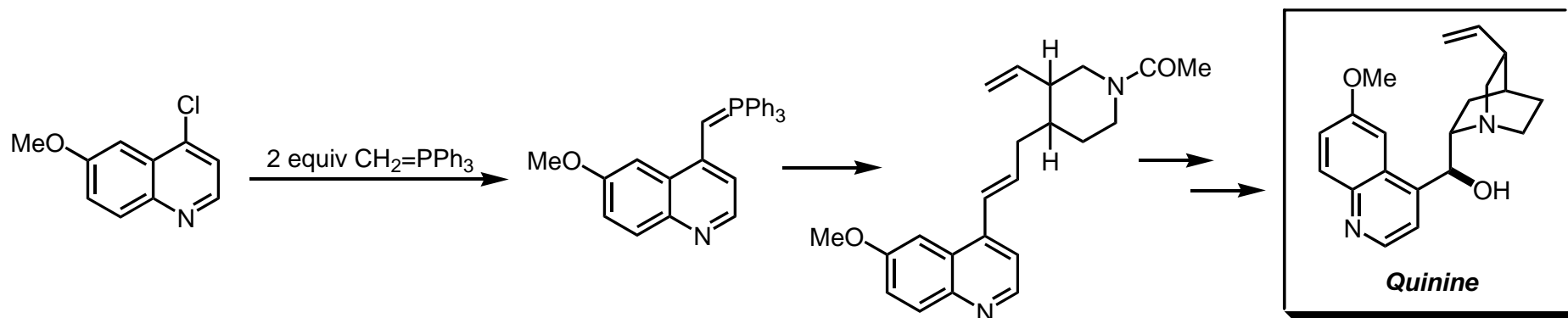
Graduate Career

7 Publications and 1 Patent

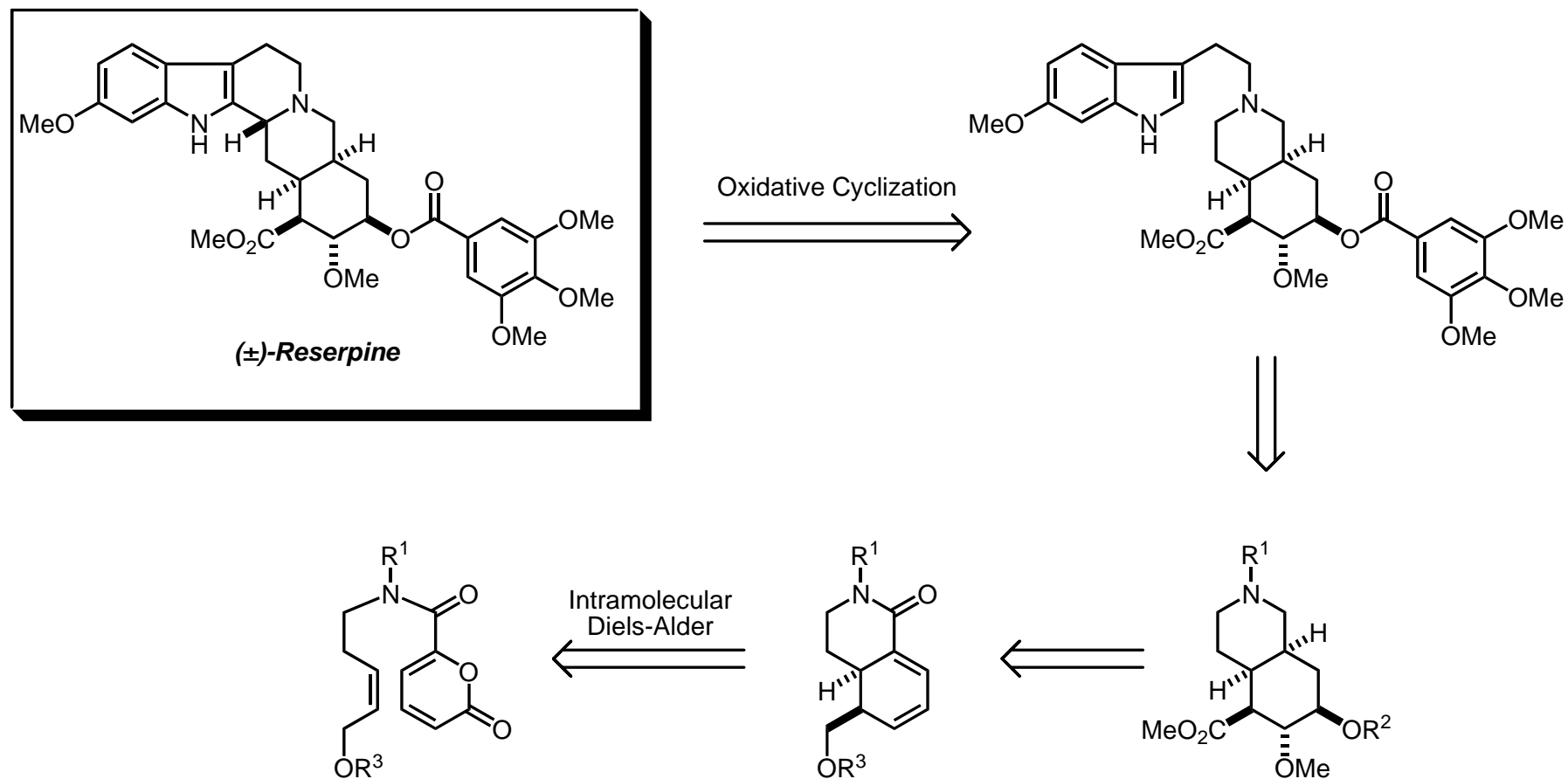
A facile method for alkylation and alkenylation of heterocycles *JACS* 1972, 94, 2874.



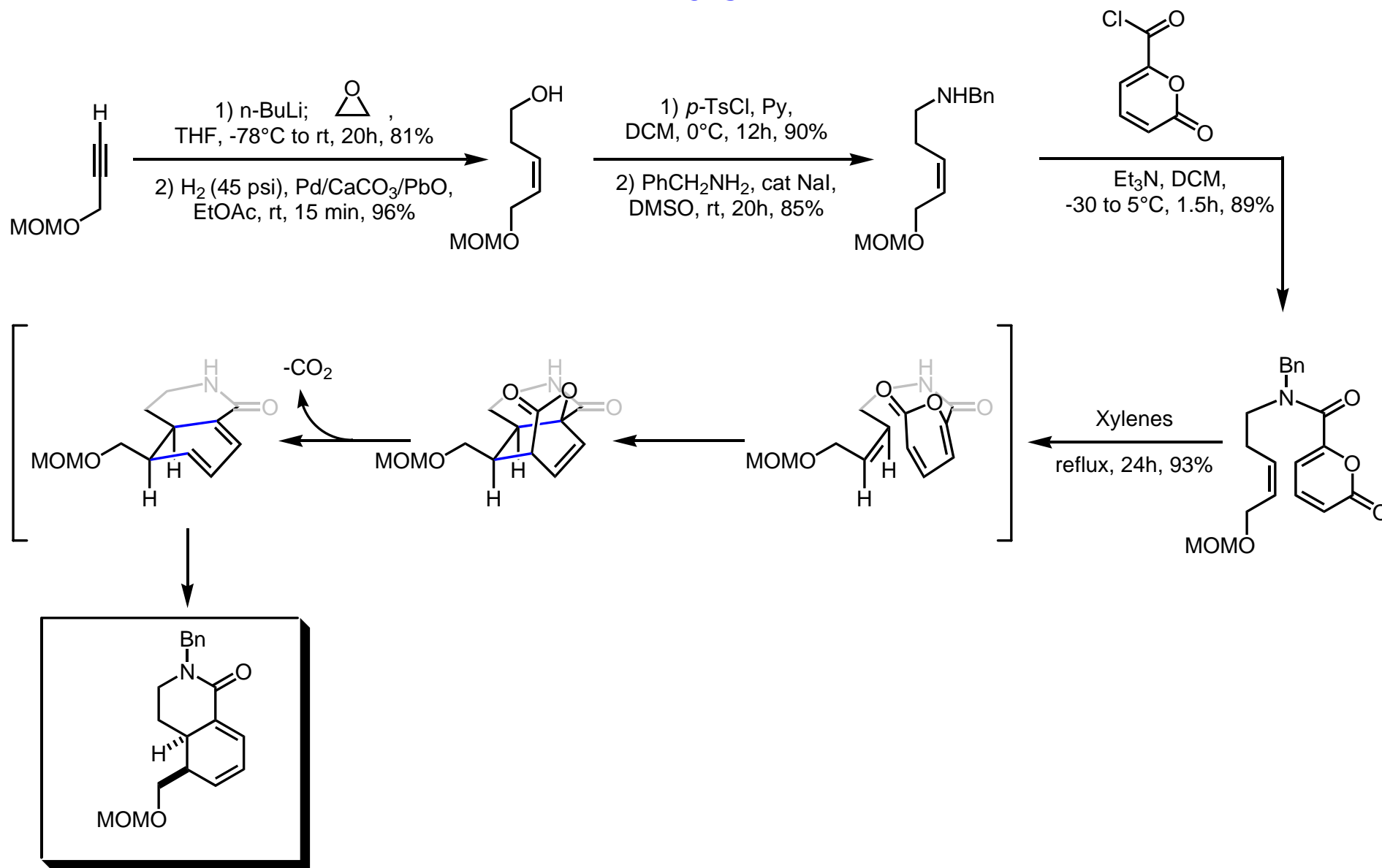
A facile synthesis of Quinine and related Cinchona alkaloids *JACS* 1972, 94, 6128.



Synthesis of (\pm)-Reserpine: Retrosynthesis



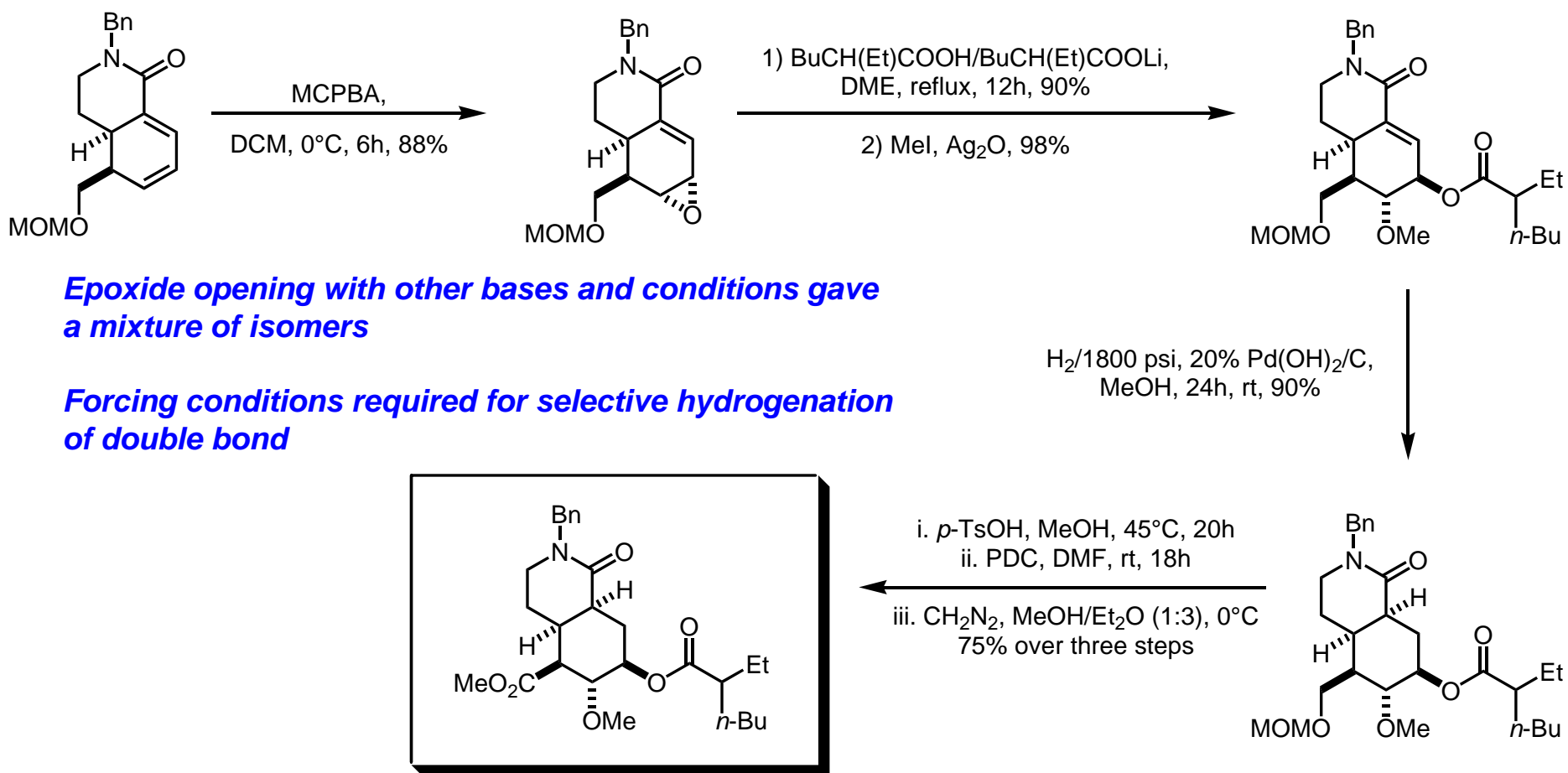
Synthesis of (\pm)-Reserpine: Intramolecular Diels-Alder



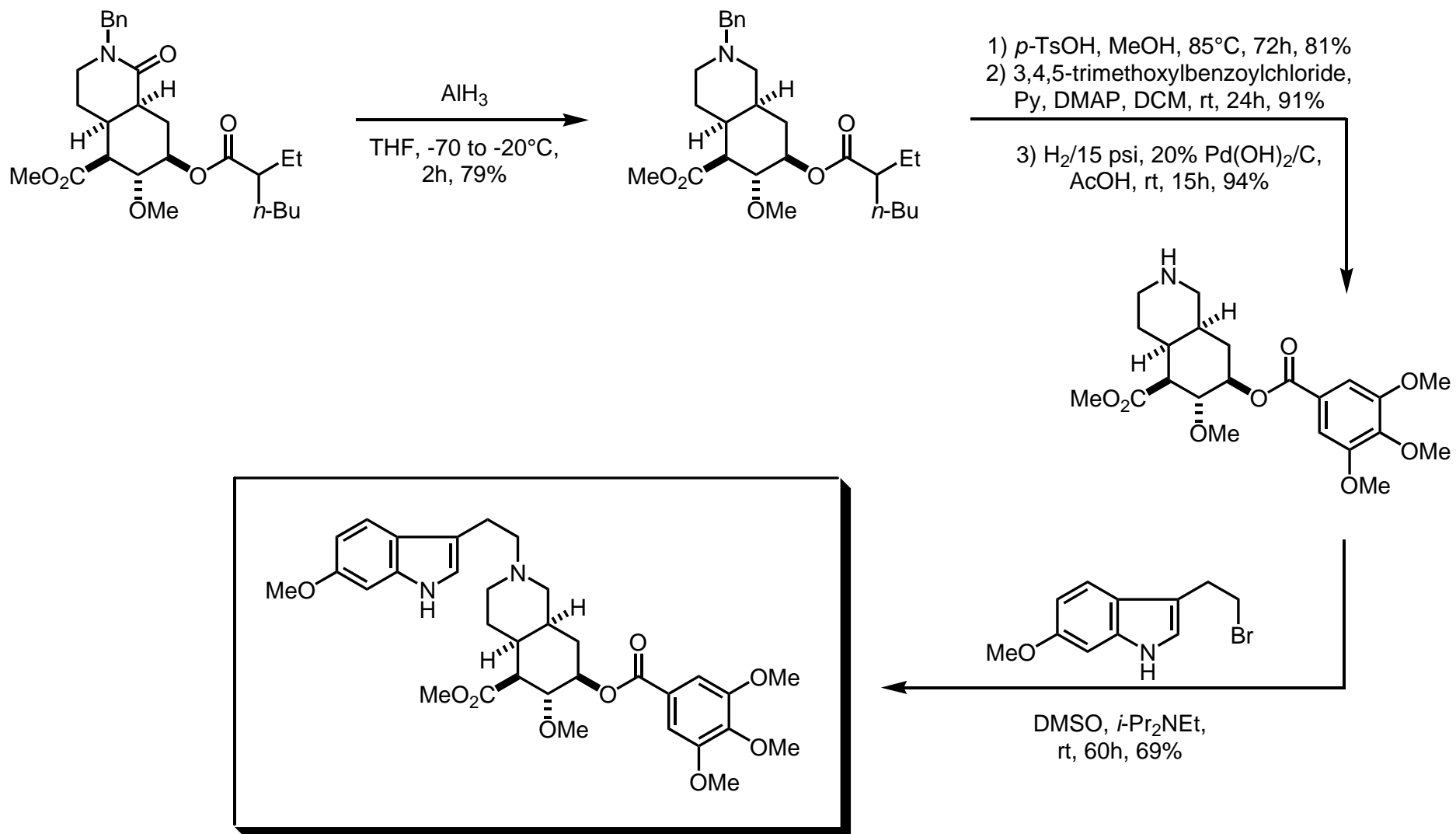
(a) *JACS* **1985**, *107*, 4074 (b) *JACS* **1987**, *109*, 6124

CU Synthesis Lit Group – CIR:SF Martin – Tran 7

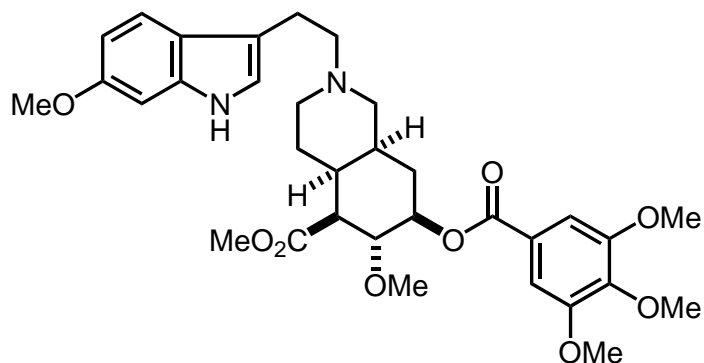
Synthesis of (\pm)-Reserpine: Refunctionalization of E ring



Total Synthesis of (\pm)-Reserpine

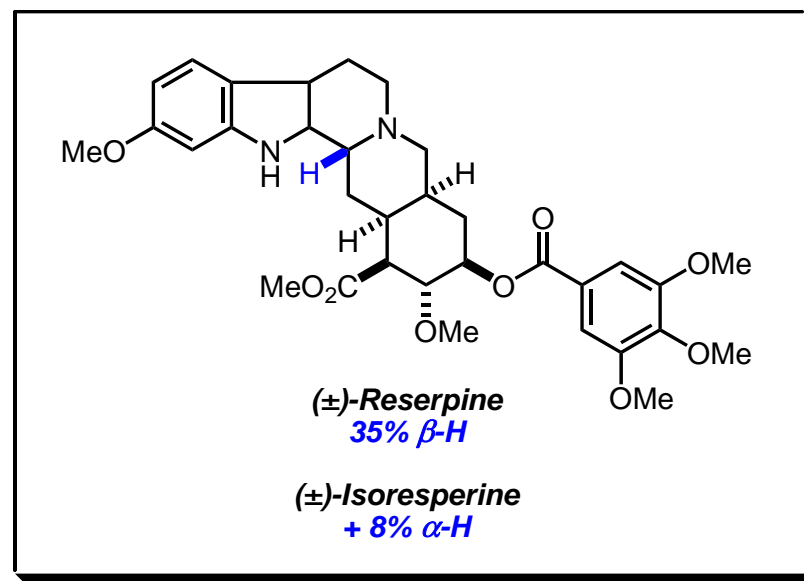
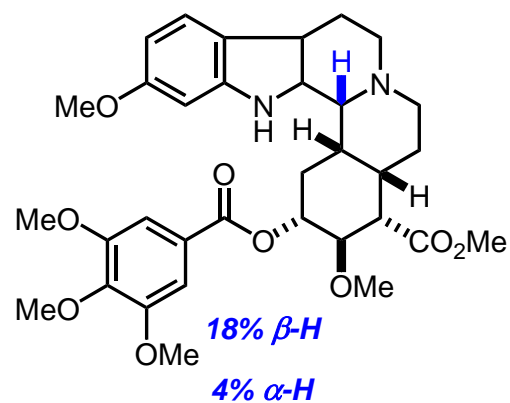


Total Synthesis of (\pm)-Reserpine



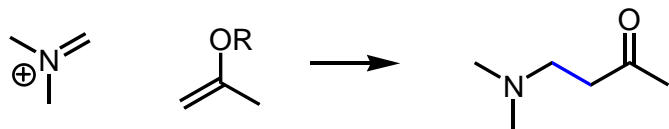
i. Hg(OAc)₂ (10 equiv), 5% HOAc (aq), 85°C, 1.5h
ii. H₂S

iii. Zn, 7% HClO₄ (aq)/Acetone/THF (1:1:1)
reflux, 20 min

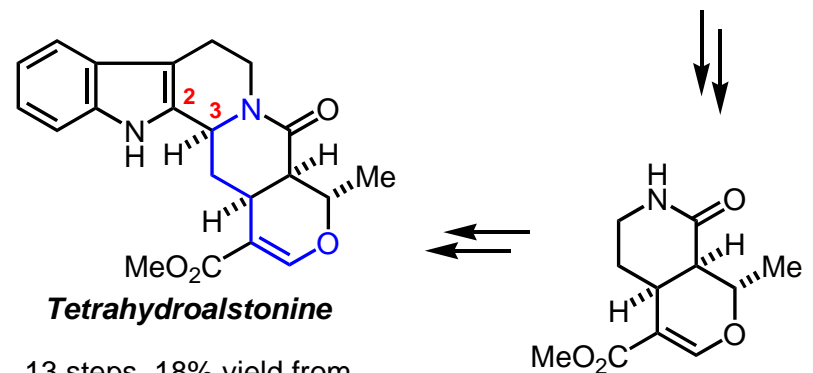
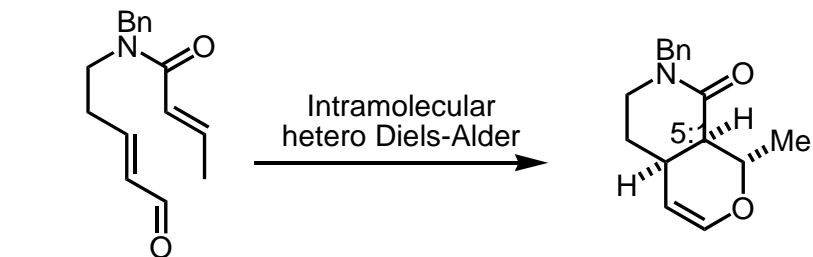
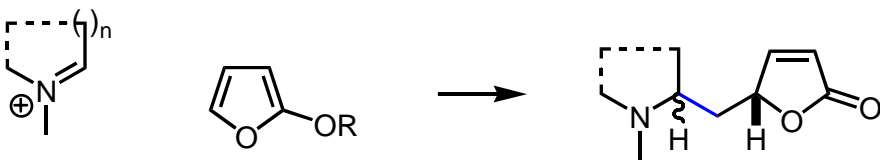
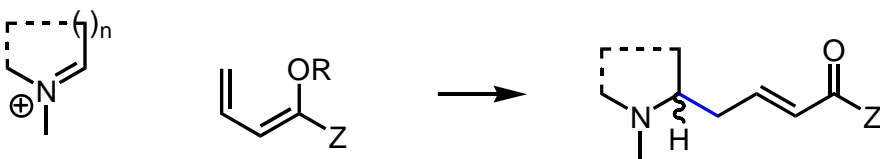
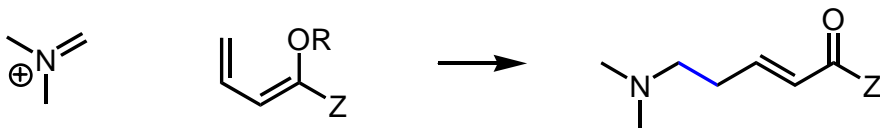


The vinylogous Mannich reaction in alkaloid synthesis

Mannich Reaction



Vinylogous Mannich Reaction

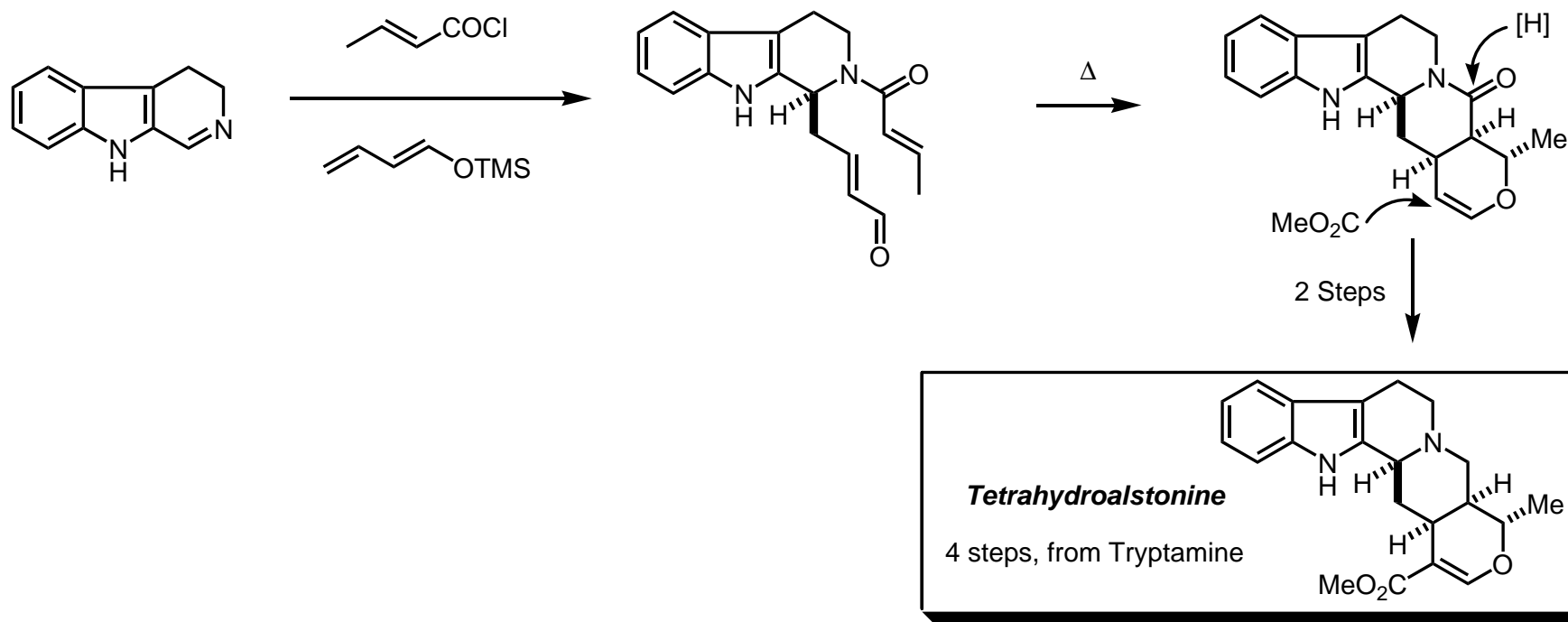


Tetrahydroalstonine
13 steps, 18% yield from commercially available starting materials

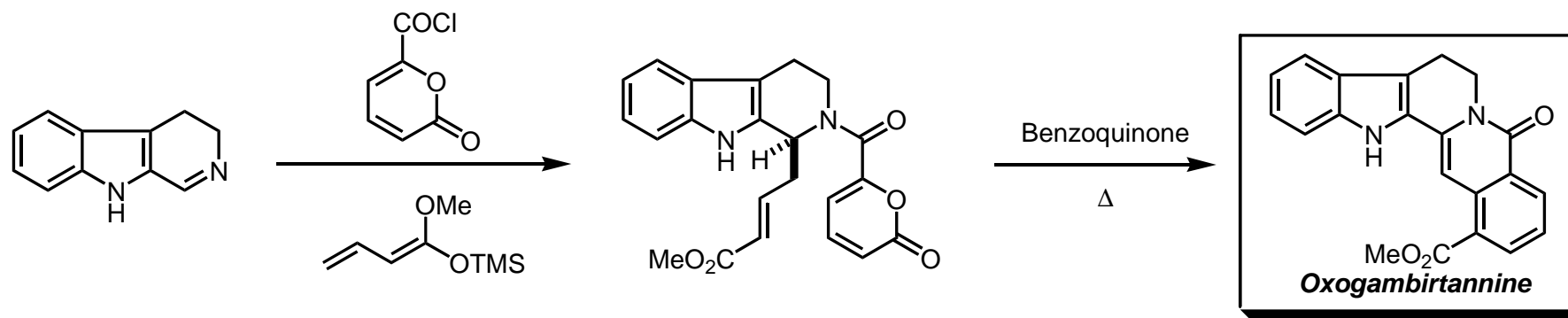
Stereoselectivity in C2-C3 bond formation is uncertain. A more concise and efficient route to yohimboid alkaloids may be found using vinylogous mannich reactions (VMR).

The vinylogous Mannich reaction in alkaloid synthesis

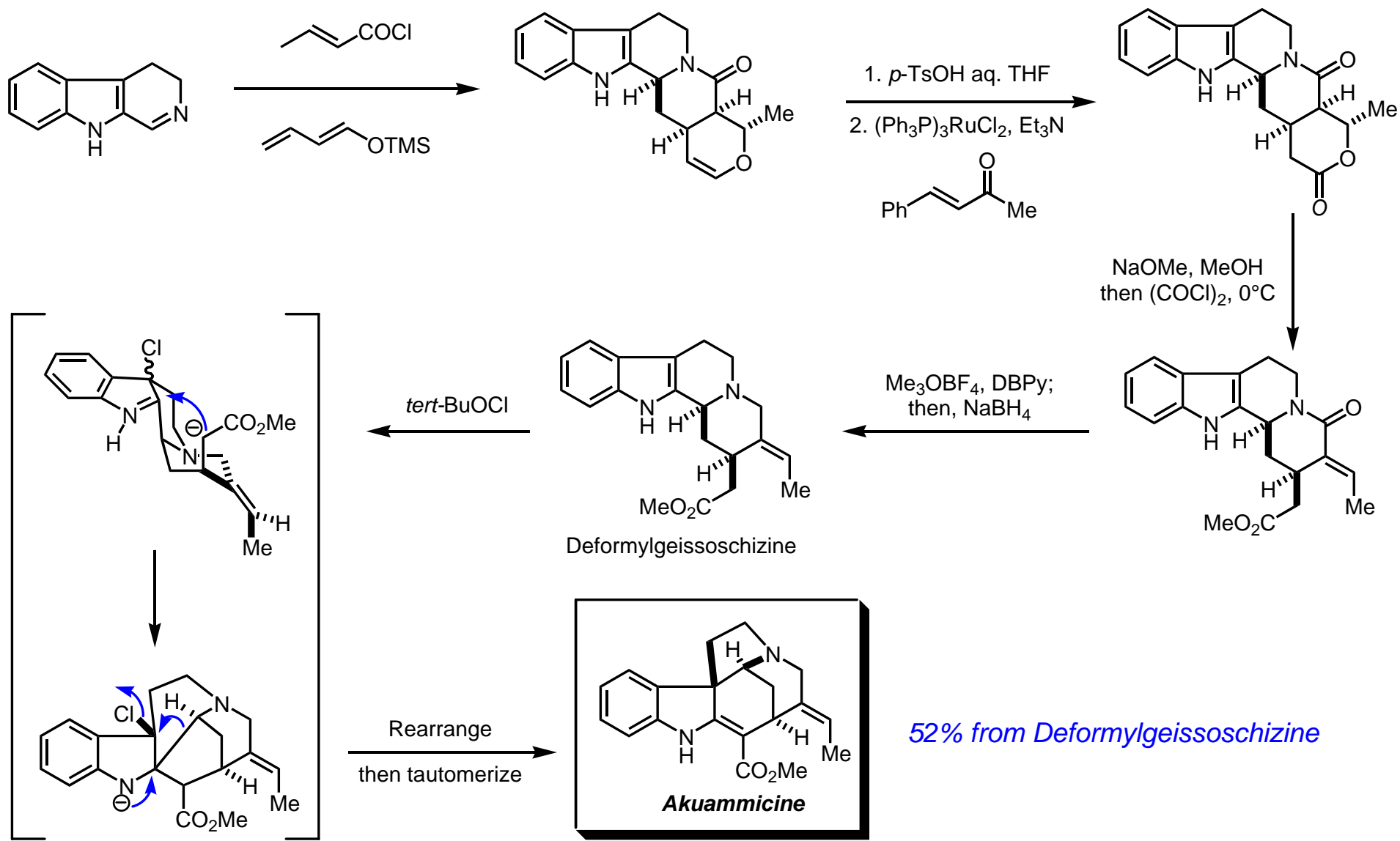
A more concise and efficient route using vinylogous Mannich reaction



Other variants of the vinylogous Mannich/intramolecular hetero Diels-Alder reaction

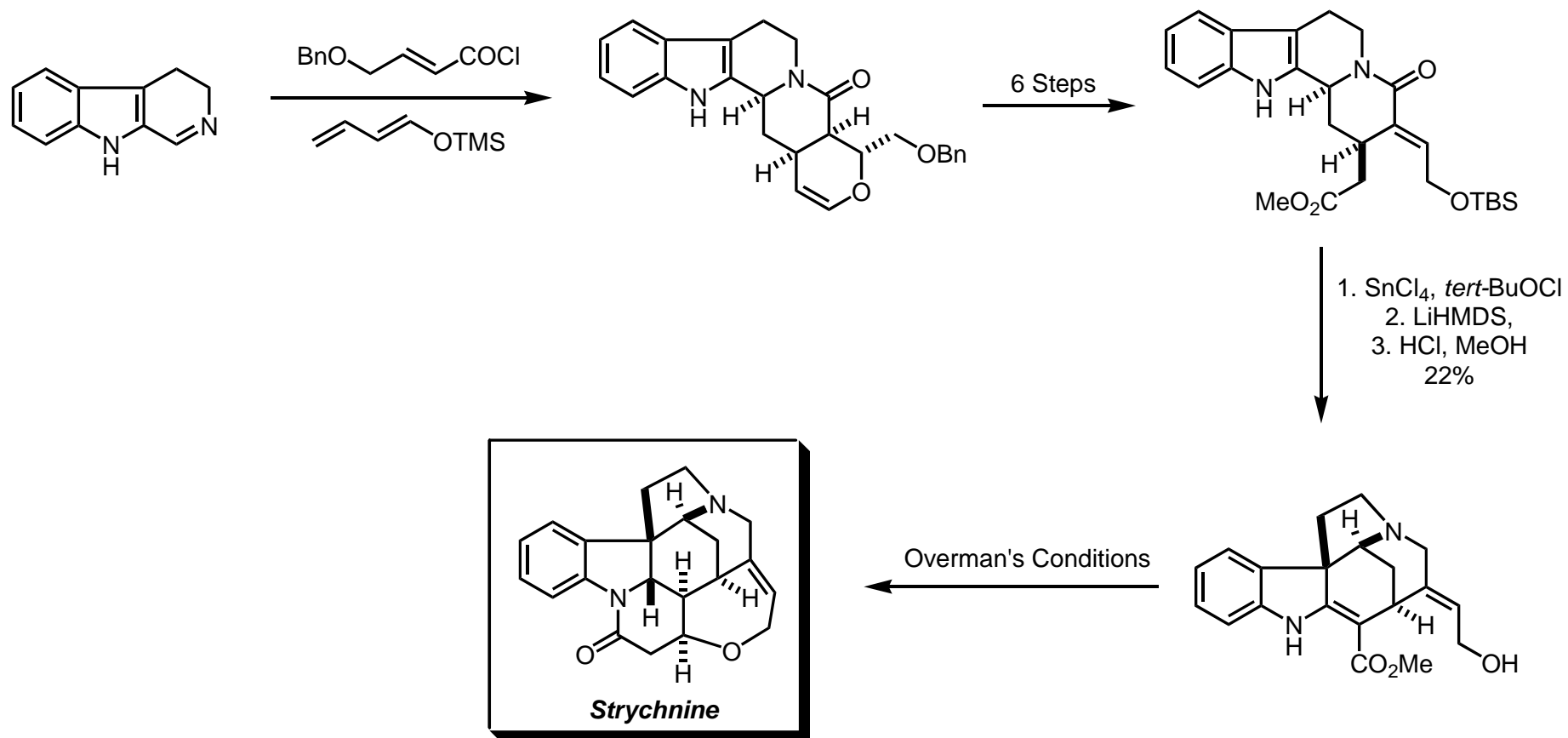


The vinylogous Mannich reaction in alkaloid synthesis: (\pm)-Akuammicine



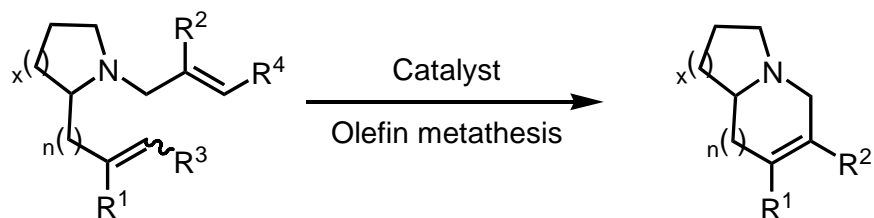
(a) *Acc. Chem. Res.* **2002**, 35, 895. (b) *JACS* **1996**, 118, 9804.

The vinylogous Mannich reaction in alkaloid synthesis: (\pm)-Strychnine

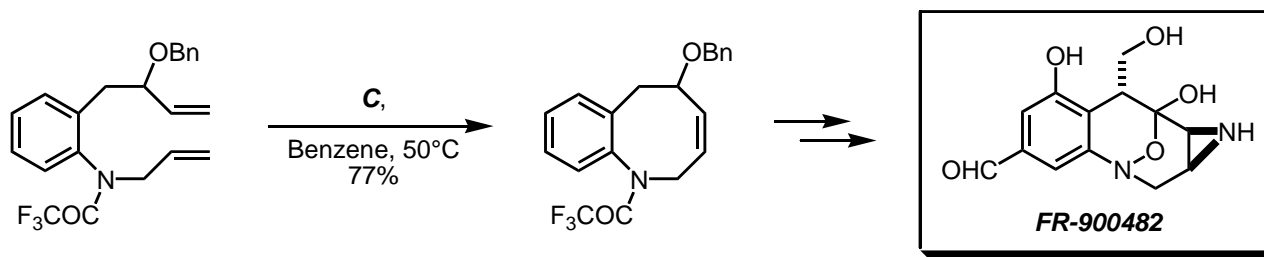
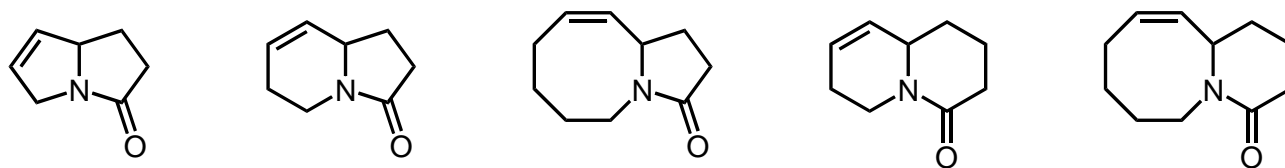
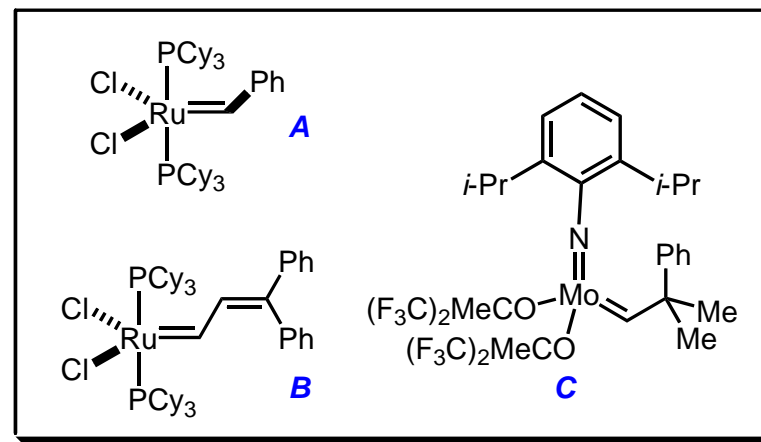


(a) *Acc. Chem. Res.* **2002**, 35, 895. (b) *JACS* **2001**, 123, 8003. (c) Overman, LE *JACS* **1993**, 115, 9293.

Nitrogen heterocycles by olefin metathesis

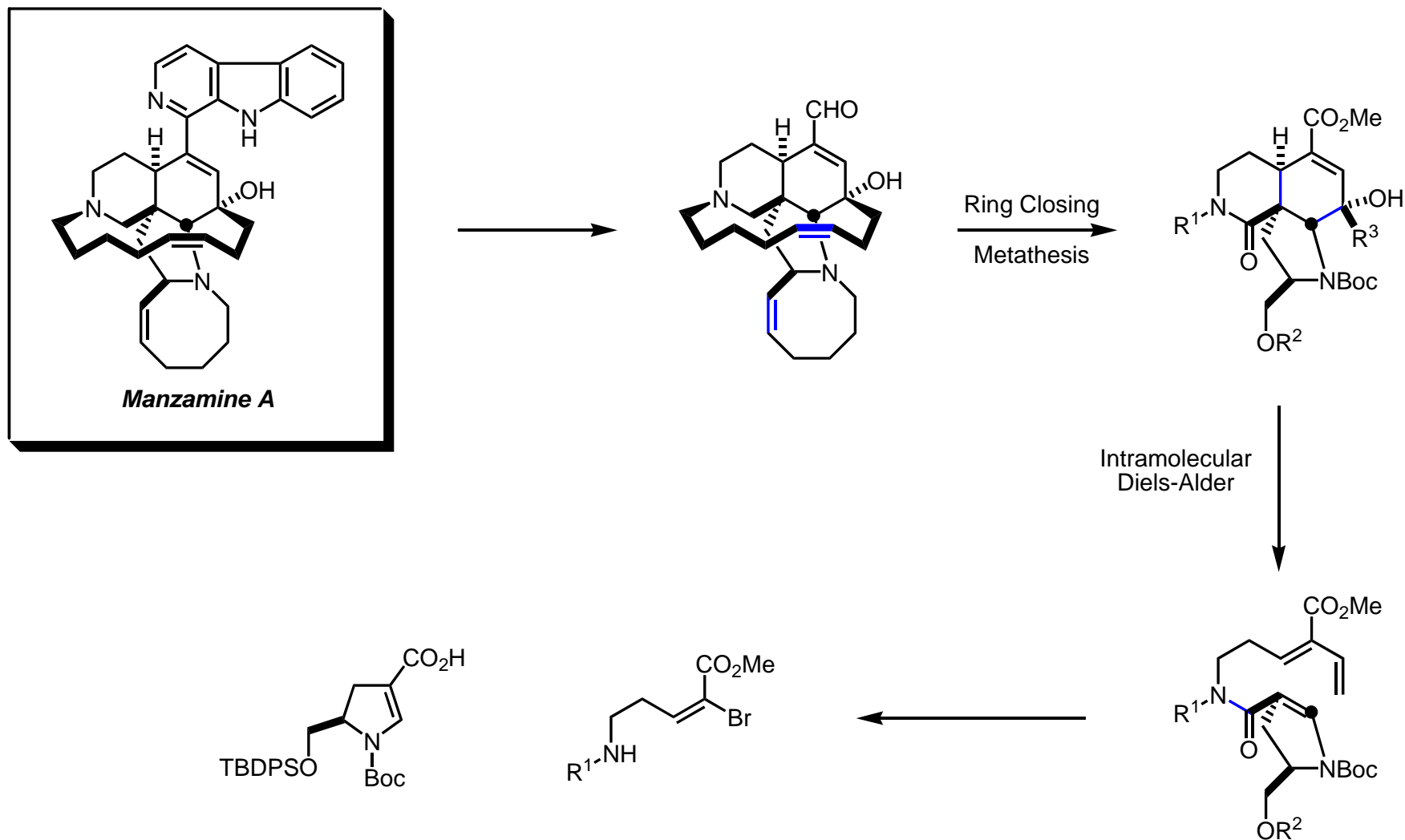


Olefin metathesis allows for the facile synthesis of fused nitrogen heterocycles, including medium sized rings!



(a) *TL* **1994**, 35, 6005 (b) *Chem. Rev.* **2004**, 104, 2199. (c) *JACS* **2000**, 122, 10781.

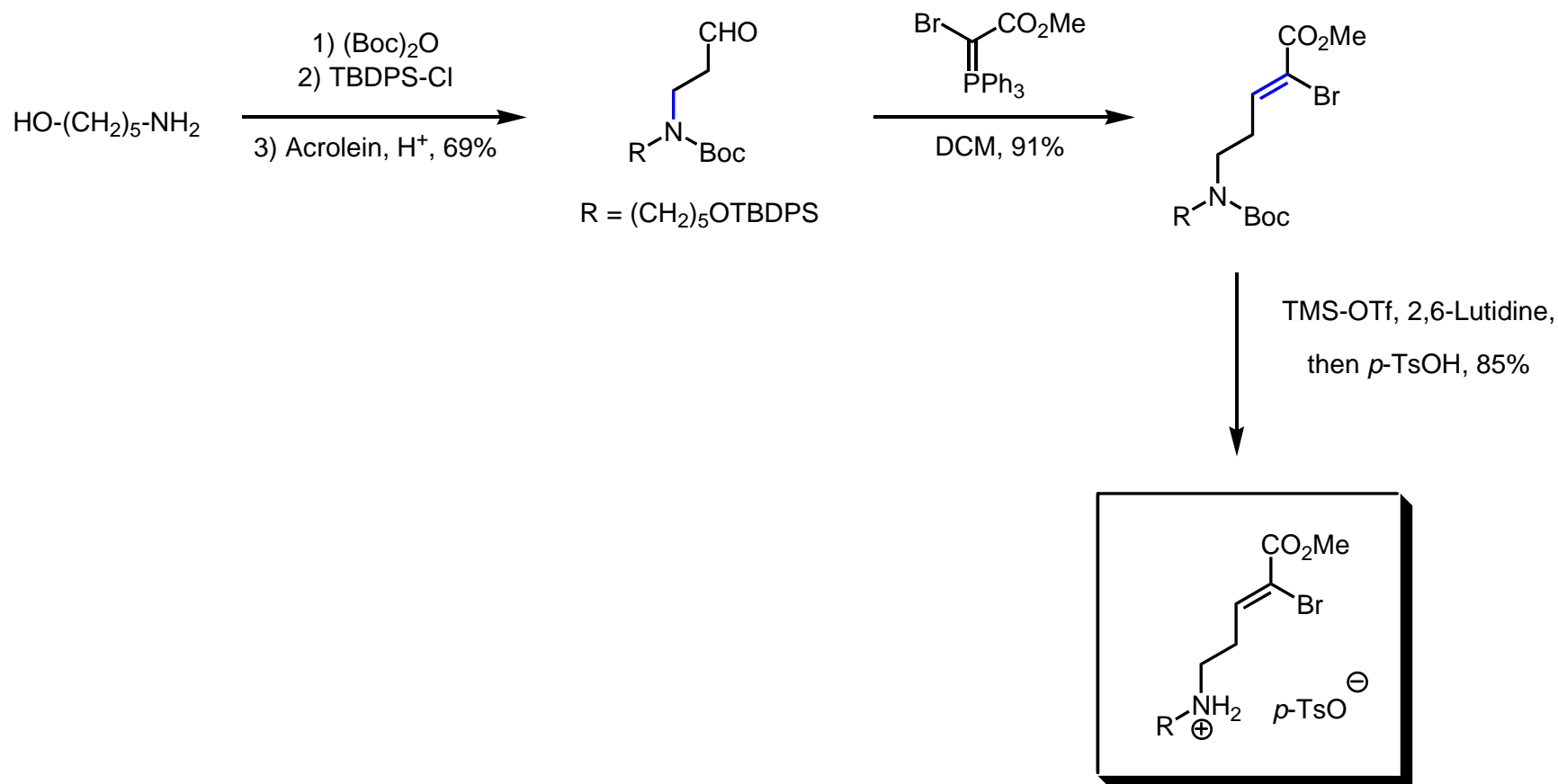
Total Synthesis of (\pm)-Manzamine



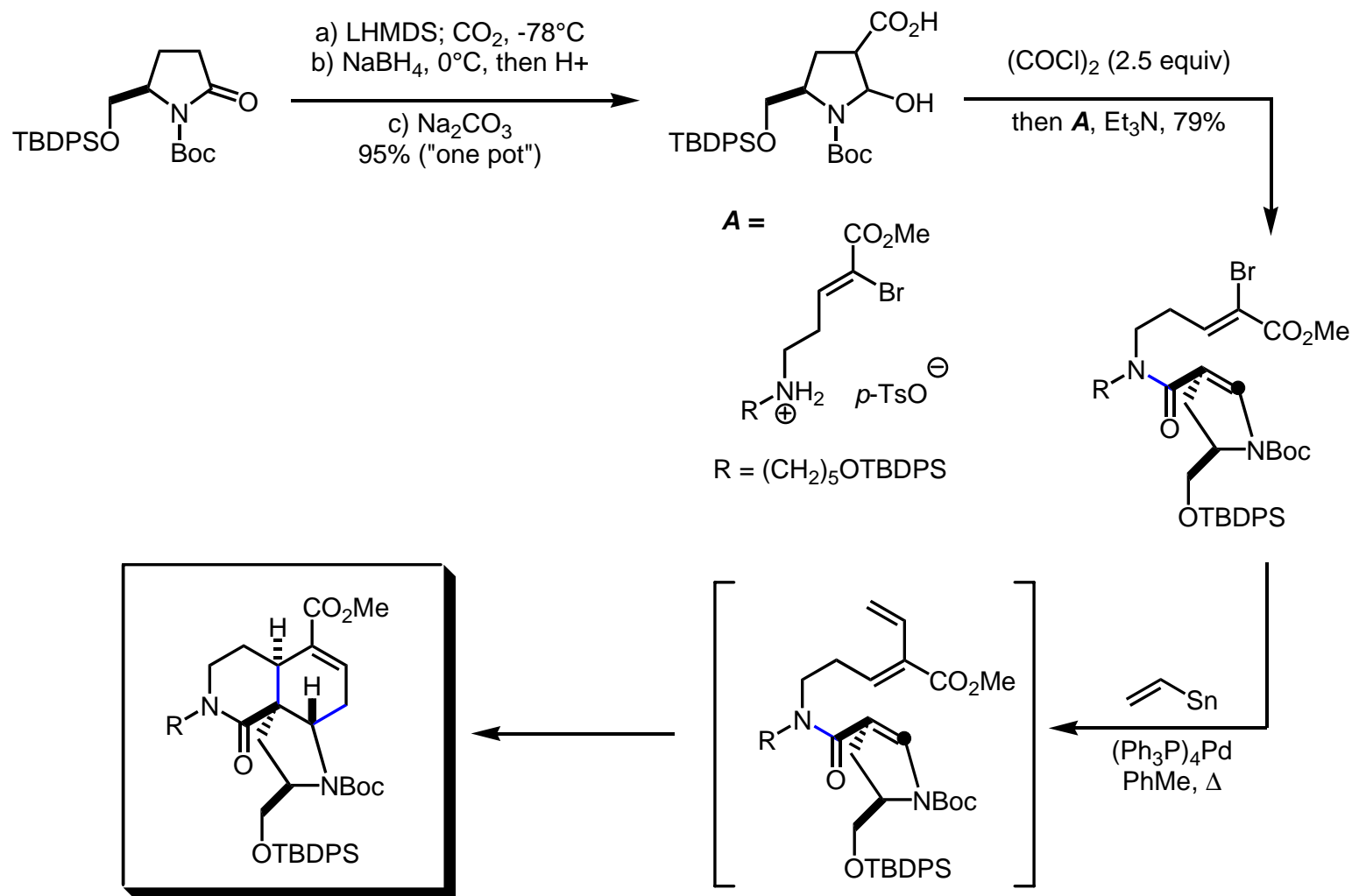
(a) *JACS* **1999**, 121, 866 (b) *JACS* **2002**, 124, 8584

CU Synthesis Lit Group – CIR:SF Martin – Tran 16

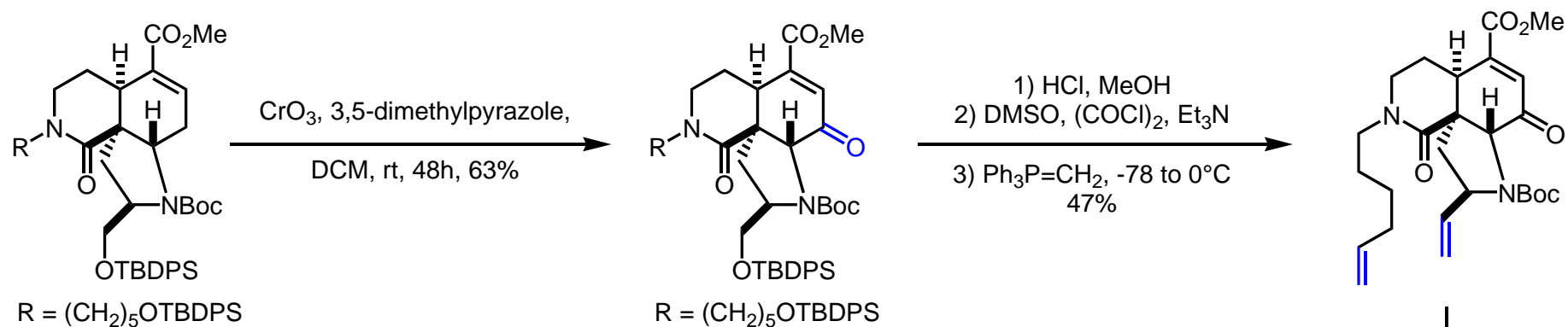
Total Synthesis of (\pm)-Manzamine



Total Synthesis of (±)-Manzamine

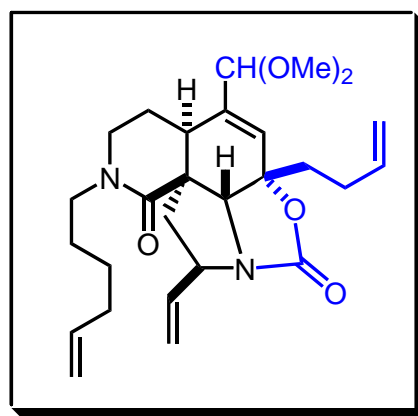


(±)-Manzamine: Synthesis of RCM Precursor



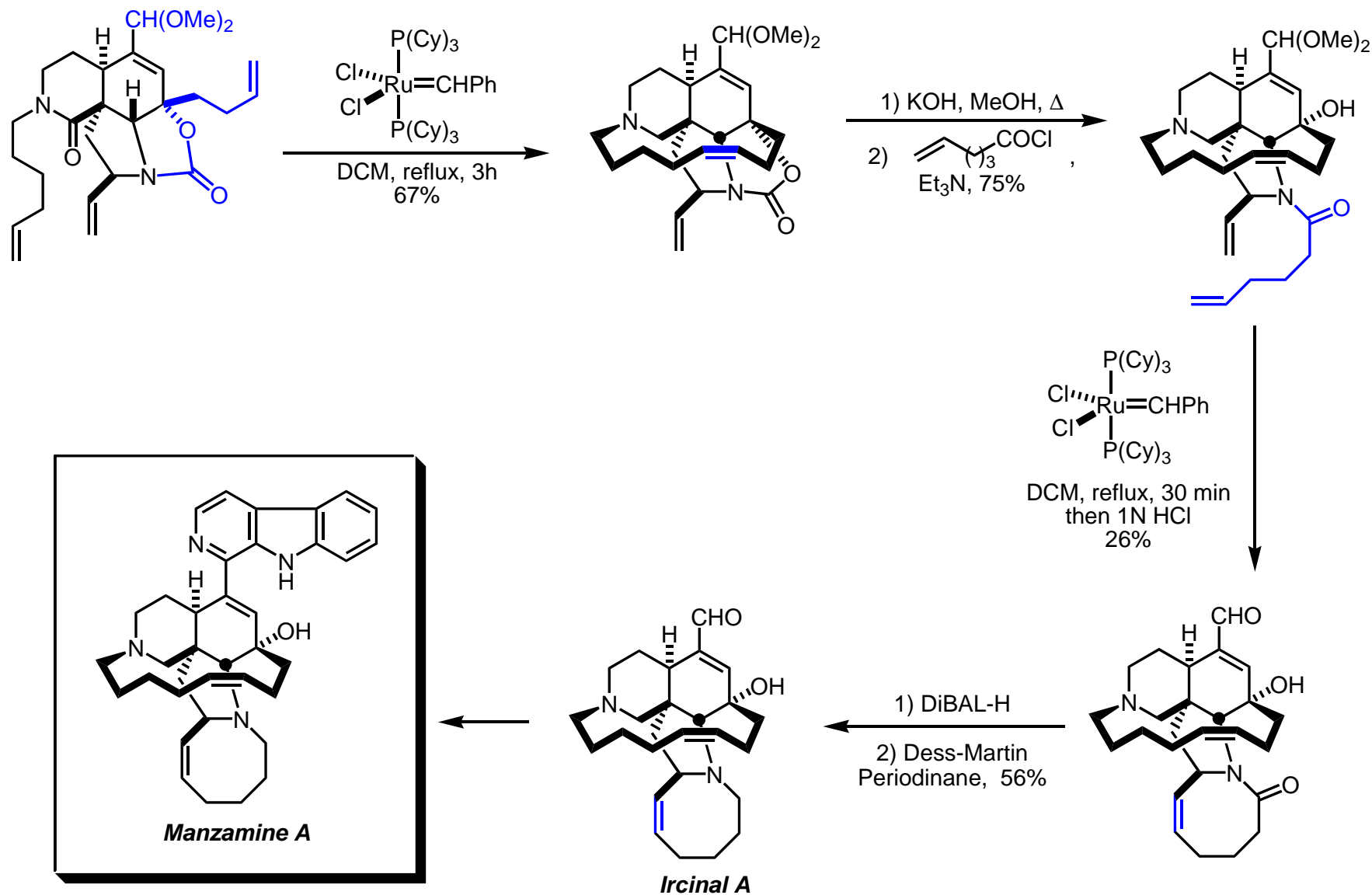
Allylic oxidation was troublesome and best achieved with Salmond's protocol

1) xs DIBAL-H
2) Dess-Martin
Periodinane, 53%



1) MeOH, HC(OMe)₃, H⁺
2) CH₂=CHCH₂CH₂Li
-78 to -20°C, 55%

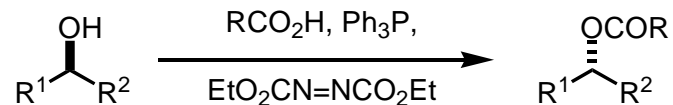
Total Synthesis of (±)-Manzamine



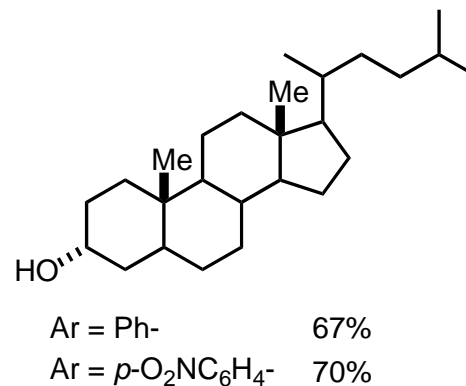
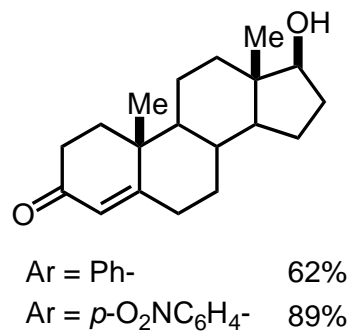
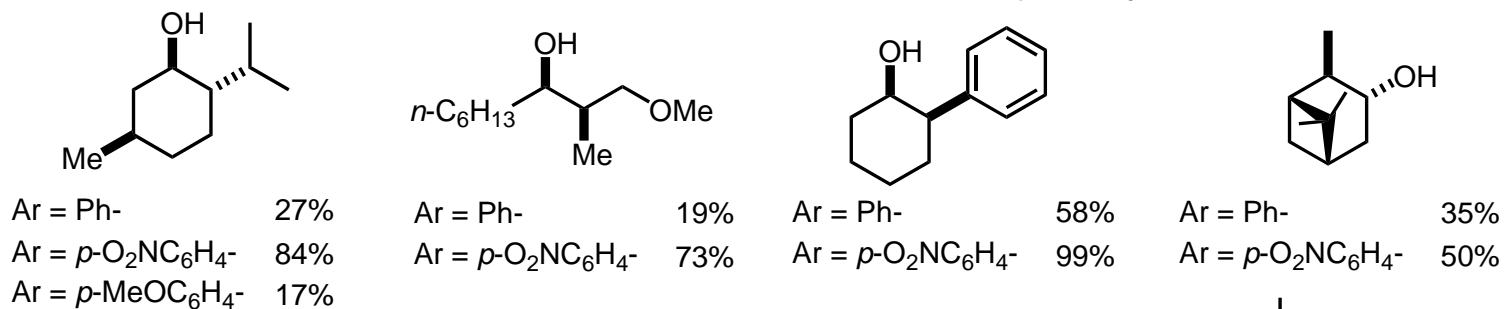
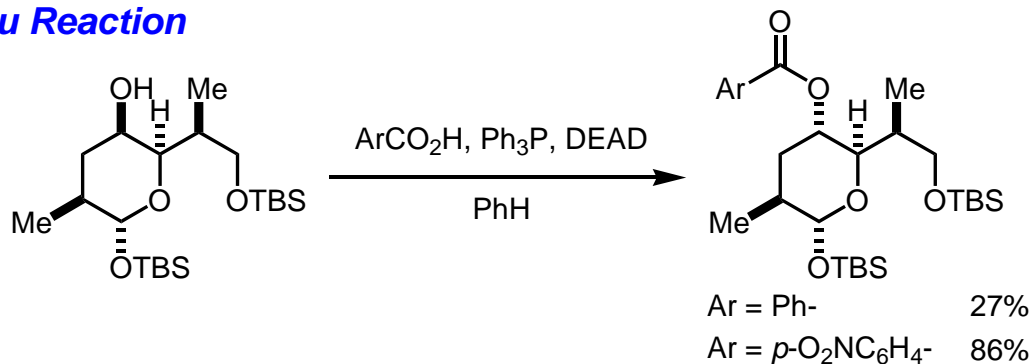
(a) *JACS* **1999**, 121, 866 (b) *JACS* **2002**, 124, 8584 (c) *JOC*, 1992, 57, 2480

A modified Mitsunobu

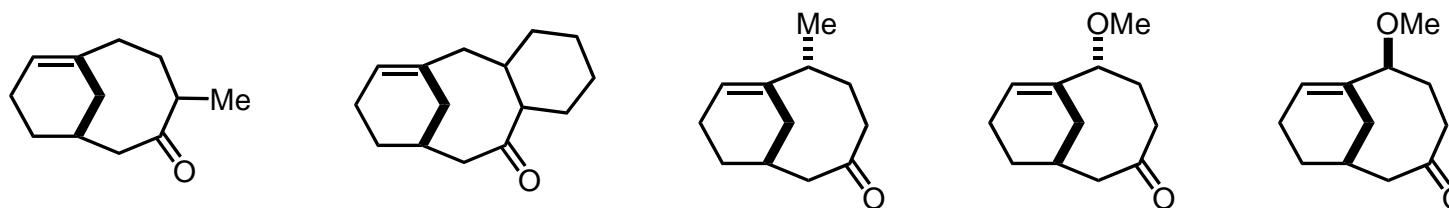
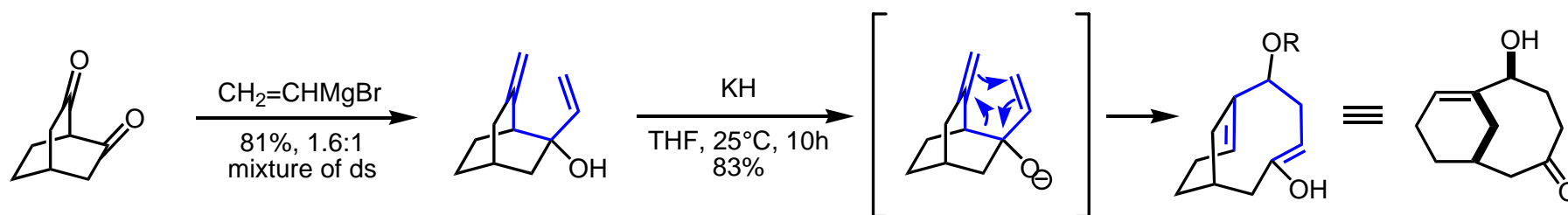
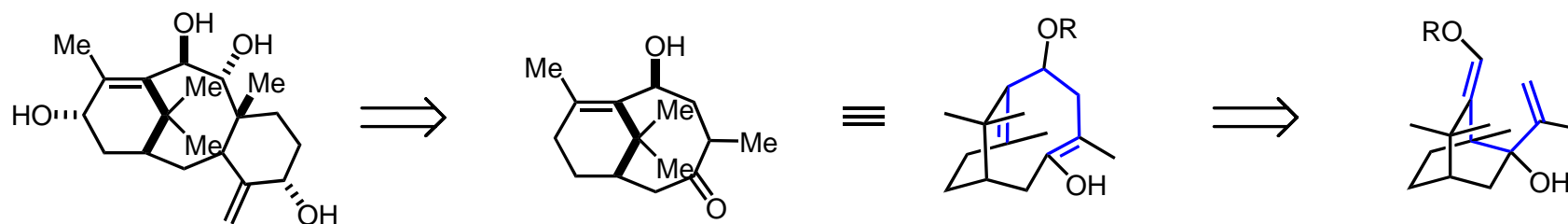
Mitsunobu Reaction



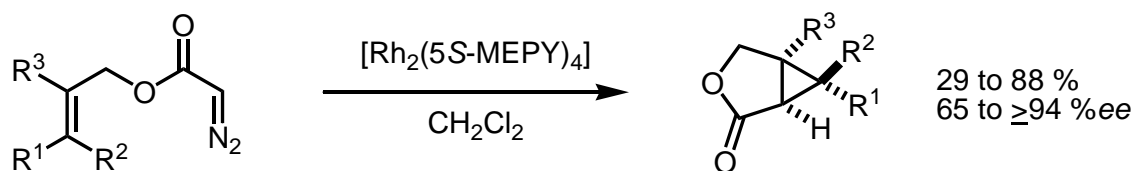
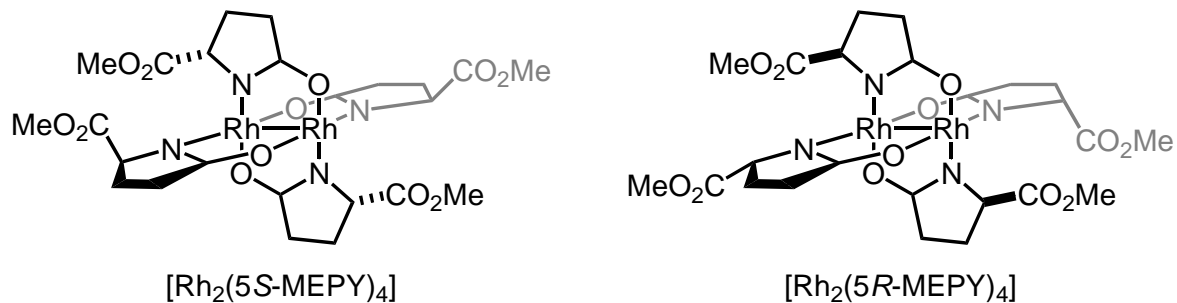
Modified Mitsunobu Reaction



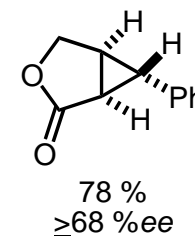
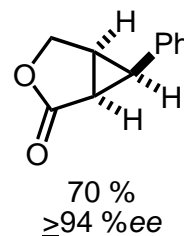
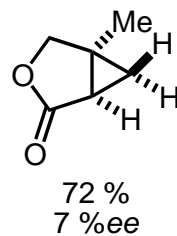
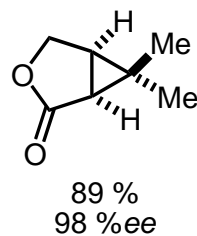
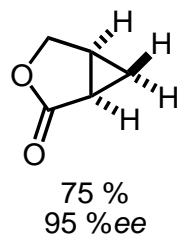
Alkoxide-accelerated sigmatropic rearrangements: Taxane diterpenes



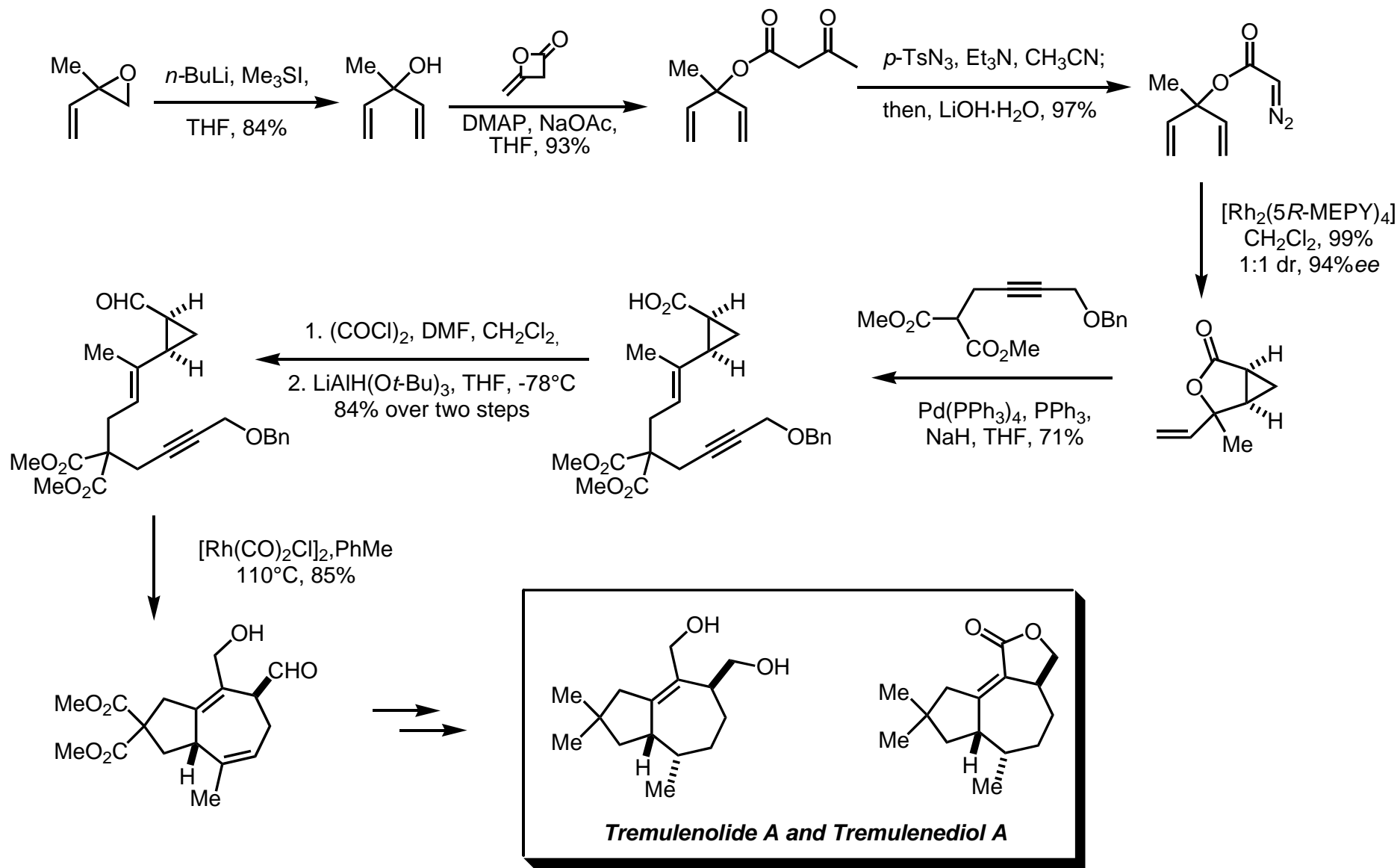
Enantioselective intramolecular cyclopropanations



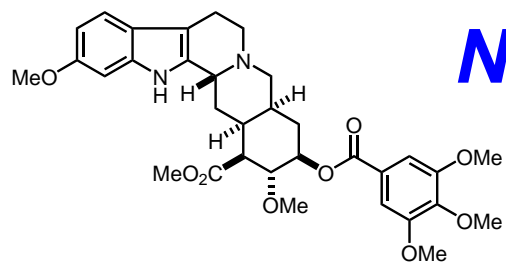
- *2,2 disubstituted olefins gives poor enantioselectivity*
- *Z olefins give greater levels of enantioselectivity than E isomers*



Enantioselective intramolecular cyclopropanations

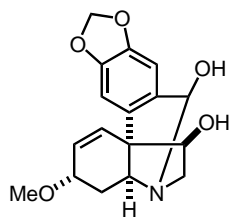


Natural Product Synthesis



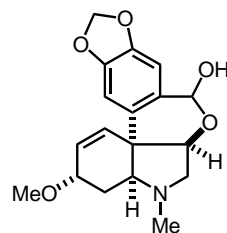
(±)-Reserpine

JACS 1985, 107, 407
JACS 1987, 109, 6124



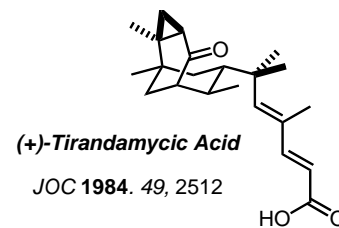
(±)-Haemanthidine

JOC 1987, 52, 1962
JACS 1984, 106, 6431



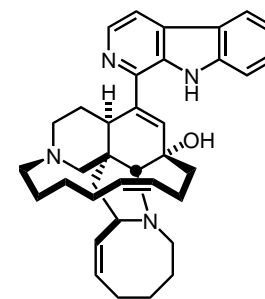
(±)-Pretazettine

JOC 1987, 52, 1962
JACS 1984, 106, 6431



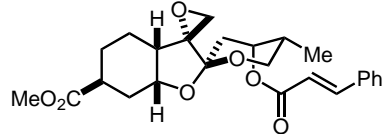
(+)-Tirandamycic Acid

JOC 1984, 49, 2512



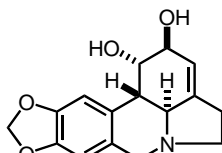
Manzamine A

JACS 2002, 124, 8584
JACS 1999, 121, 866
TL 1994, 35, 691



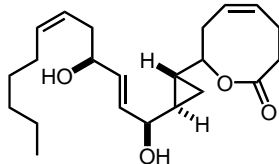
(+)-Phyllanthocin

JOC 1987, 52, 3706



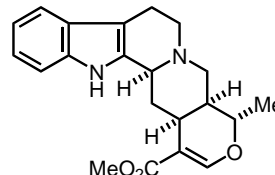
Lycorine

JOC 1982, 47, 3634



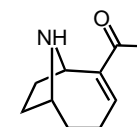
Solandelactone E

JACS 2007, 129, 510



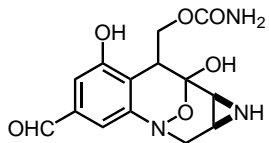
(±)-Tetrahydroalstonine

TL 1997, 38, 7641
JACS 1988, 110, 5925



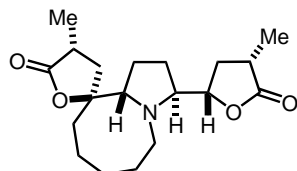
(+)-Anatoxin-a

OL 2004, 6, 1329



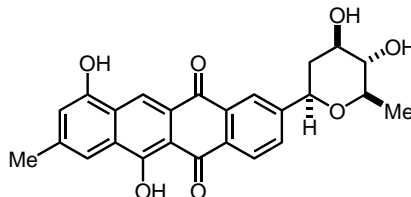
FR-900482

TL 1995, 36, 1169



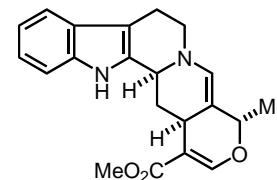
(+)-Croomine

JACS 1996, 118, 3299



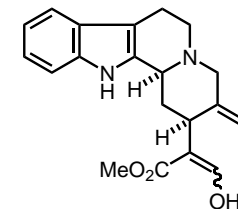
Galtamycinone

TL 2003, 44, 1075



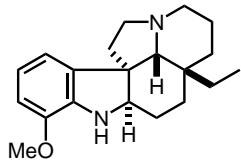
(±)-Cathenamine

JACS 1988, 110, 5925



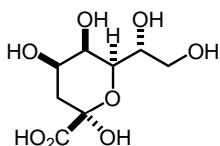
Geissoschizine

(±) JACS 1988, 110, 5925
(+) OL 1999, 1, 79
(+) JACS 2003, 125, 4541



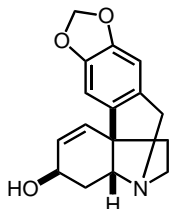
Aspidospermine

JACS 1980, 102, 3294



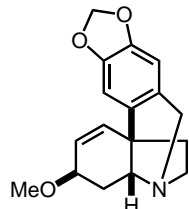
(+)-KDO

JOC 1991, 56, 6600



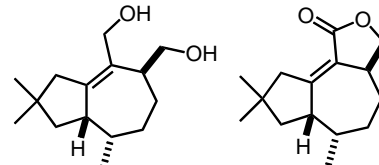
(±)-Crinine

TL 1987, 28, 503



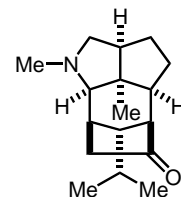
(±)-Bulphanisine

TL 1987, 28, 503



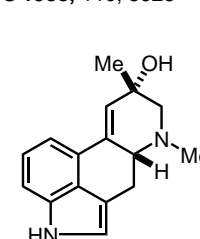
Tremulenolide A and Tremulenediol A

OL 2005, 7, 4535



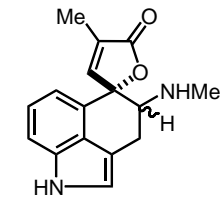
(±)-Dendrobine

JOC 1991, 56, 642



Setoclavine

JACS 2001, 123, 5918



Rugulovasines A = β -H
Rugulovasines B = α -H

JACS 2001, 123, 5918