

**Biography**

- Born 1936 in San Antonio, TX
for complete bio
(<http://heathcock.org/CHHJr/>)

Education

- Abilene Christian College; B.S., 1958
- University of Colorado; Ph.D., 1963
(A. Hassner)
- Columbia University; Postdoc, 1963-64
(G. Stork)

Professional Experience:

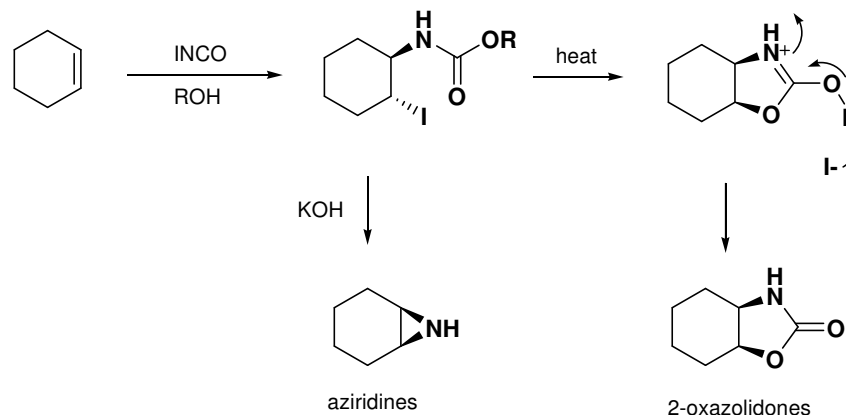
- Champion Paper & Fibre Company, Pasadena, TX; Supervisor, Chemical Tests, 1958-60
- University of California; Berkeley, CA
Assistant Professor, 1964-70; Associate Professor, 1970-75; Professor, 1975-present
Vice-Chairman, 1972-77; Chairman, 1986-89; Dean, College of Chemistry, 1999-2005;
Gilbert Newton Lewis Professor, 2003-05; Chief Scientist, QB3 Berkeley, California Institute
for Quantitative Biosciences, 2005-present
- Merck, Sharp & Dohme, Rahway, NJ; Consultant, 1968-78
- Abbott Laboratories, Abbott Park, IL; Scientific Advisory Committee, 1986-present
- Medicinal Chemistry A Study Section (NIH); Member, 1979-81; Chairman, 1981-83
- Organic Chemistry Division of the American Chemical Society
Executive Committee, 1976-79, 1984-86; Chairman, 1985; Ex officio 1986-present
- Organic Syntheses Editorial Board, 1980-88; Editor-in-Chief, 1986;
Board of Directors, 1992-present
- Chairman, 1986 Gordon Conference on Stereochemistry
- Editor-in-Chief, Journal of Organic Chemistry, 1989-1999
- Advisory Board, Bulletin of the Chemical Society of Japan
- Chair, Chemistry Division, American Association for the Advancement of Science, 2000

Honors and Awards:

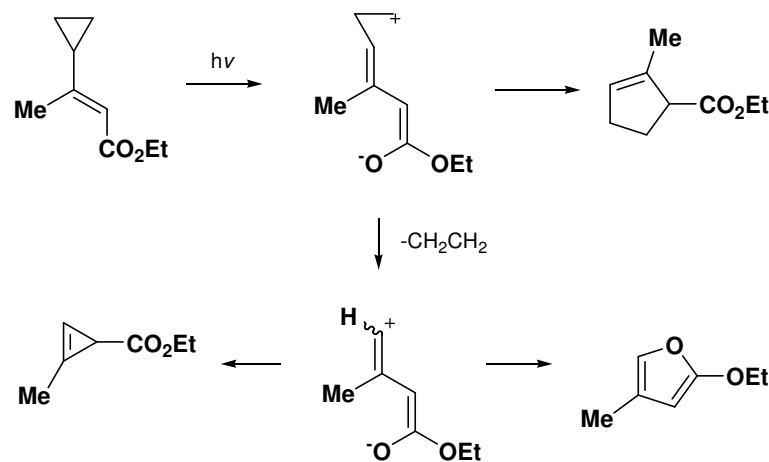
- National Science Foundation Predoctoral and Postdoctoral Fellow, 1961-64
- Alfred P. Sloan Foundation Fellow, 1967-69
- Humboldt United States Senior Scientist Award, 1978
- Miller Research Professor, UC Berkeley, 1982-83, 1991-92
- Ernest Guenther Award, American Chemical Society, 1986
- Allan R. Day Award, Philadelphia Organic Chemists Club, 1989
- Award for Creative Work in Synthetic Organic Chemistry, American Chemical Society, 1990
- A. C. Cope Scholar Award, American Chemical Society, 1990
- Prelog Medal, ETH, 1991
- American Academy of Arts and Sciences, 1991
- Pfizer Award in Synthetic Organic Chemistry, 1993
- National Academy of Sciences, 1995
- Centenary Medal, Royal Society of Chemistry, 1996
- H. C. Brown Award, American Chemical Society, 2002
- Paul Gassman Award for Distinguished Service, American Chemical Society, 2004

Graduate Work:

Iodine isocyanate as a reagent: *JOC*, 1967, 32, 540

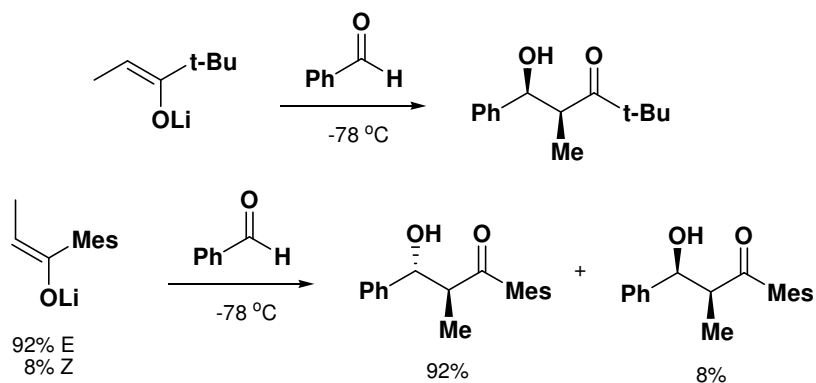
**Independent Research:**

First paper as PI: *JACS*, 1965, 87,5264

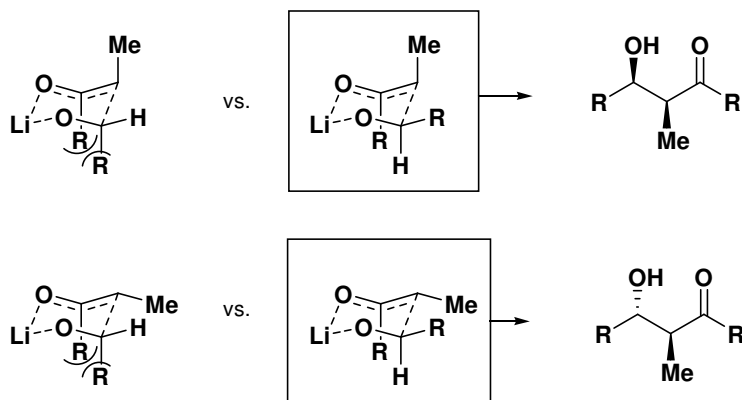


Aldol ReactionFirst paper on aldol: *JACS*, 1977, 99, 247.

- Conformation of Dubois results: Kinetic stereoselection
Z-enolates -> erythro (syn)
E-enolates -> threo (anti)
- Main contributions focuses on Li enolates utilizing bulky substituents

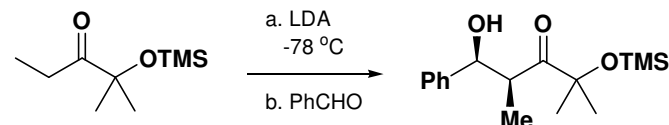


-Stereochem can be explained through Zimmerman-Traxler

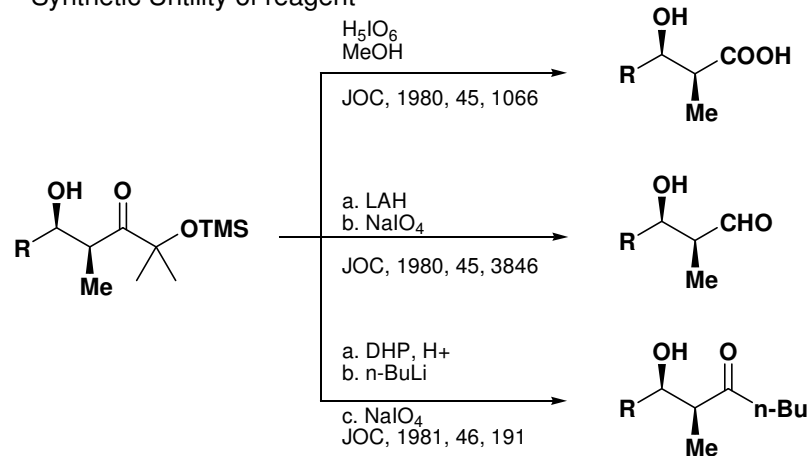


- As a result, several reagents were developed

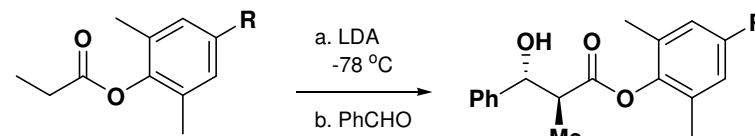
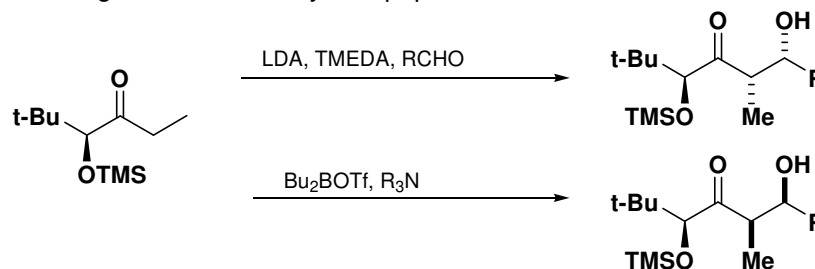
Used for erythro selectivity: Z-enolate



- Synthetic Utility of reagent

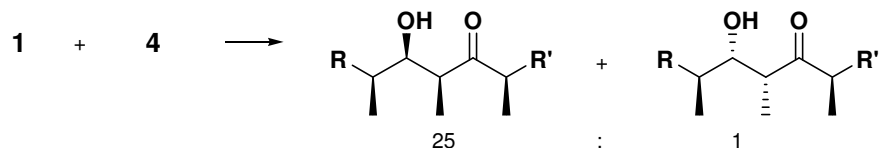
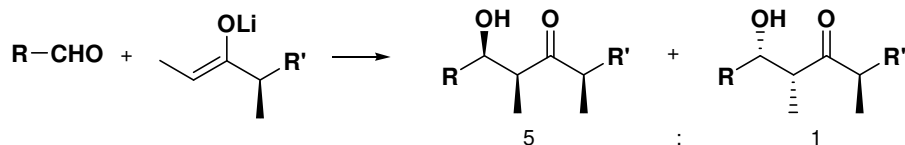
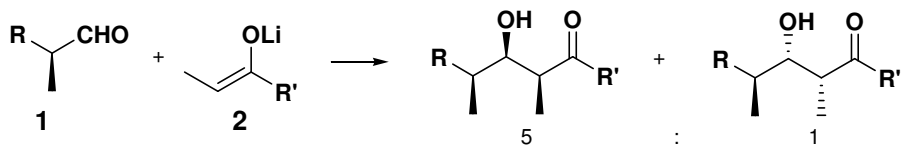


Used for threo selectivity: E-enolate

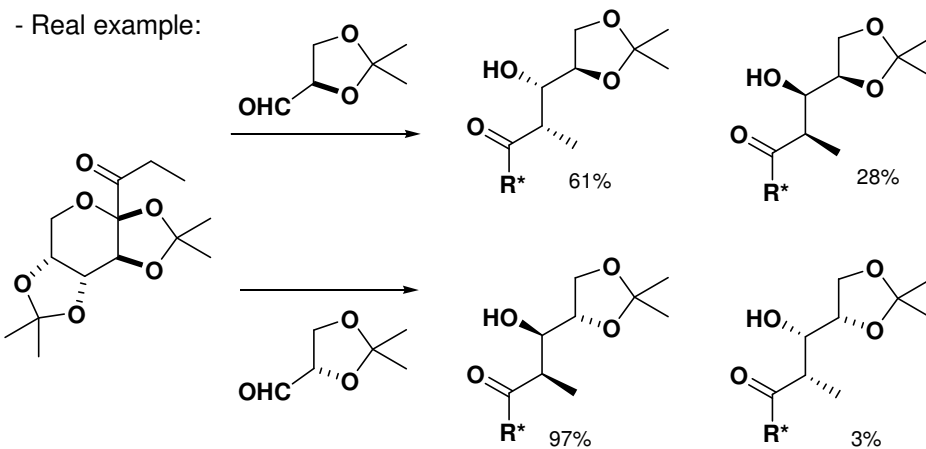
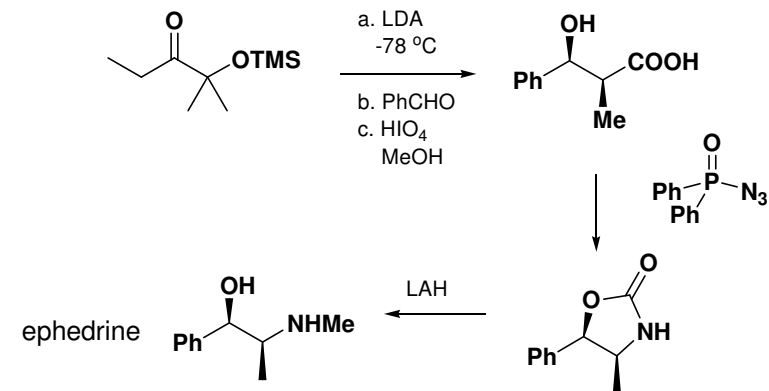
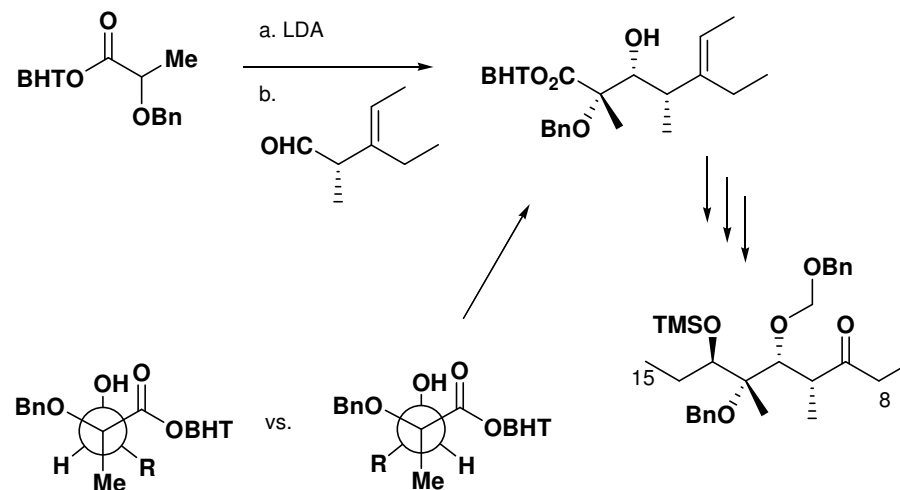
Chiral Reagent: Unfortunately less popular than Evans: *JOC*, 1991, 56, 2499

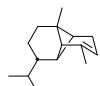
Aldol Reaction cont'dDouble Diastereoselectivity: *JACS*, 1979, 101, 7076

- Matched and mismatched aldols
- Best way to have excellent dr is through double diastereoselection (BOTH components chiral)

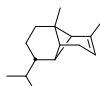


- Real example:

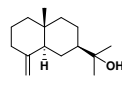
-Application of aldol and erythro reagent: *JOC*, 1980, 45, 1066- Application of aldol reaction C8 to C15 of Erythromycin A:
JOC, 1988, 53, 4730



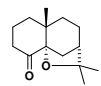
copaene (1966)



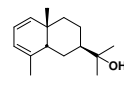
ylangene (1967)



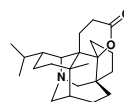
B-eudesmol (1968)



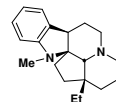
nor-ketoagarofuran (1968)



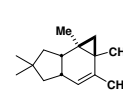
(+)-occidentolol (1972)



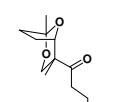
daphnilactone (1989)



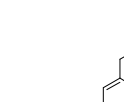
vallesamidine (1989)



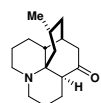
isovelleral (1990)



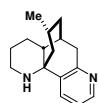
(-)-secodaphniphylline (1990)



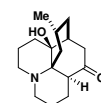
proto-daphniphylline (1990)



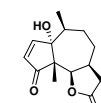
lycopodine (1978)



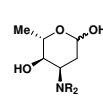
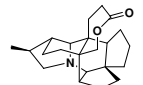
lycodine (1979)



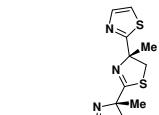
lycododine (1981)



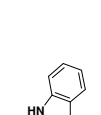
parthenin (1982)

ritosamine R = H
megalosamine R = Me (1983)

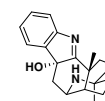
bukittinggine (1992)



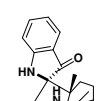
(-)-mirabazole C (1992)



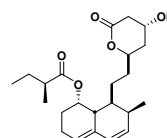
(-)-alloaristolone (1992)



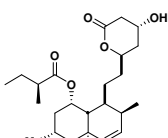
(-)-serratoine (1992)



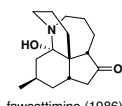
(+)-aristolone (1992)



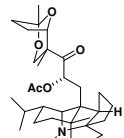
(+)-compactin (1985)



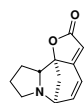
(+)-dihydronevinolin (1986)



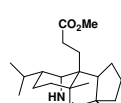
fawcettimine (1986)



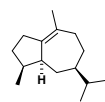
(+)-methyl homodaphniphyllate (1986)



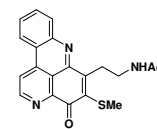
norsecurinine (1987)



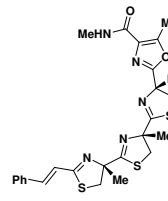
methyl homosecodaphniphyllate (1988)



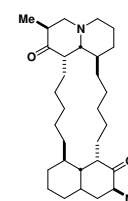
a-bulnesene (1971)



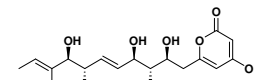
diplamine (1994)



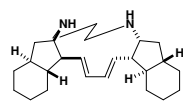
(-)-thiazazole (1994)



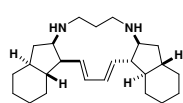
petrosin (1994)



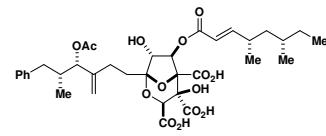
ACRL toxin IIIb (1994)



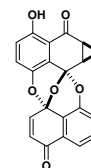
(-)-papuamine (1996)



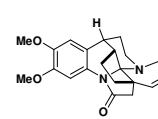
(-)-haliconadamine (1996)



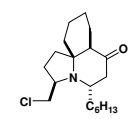
zaragozic acid A (1996)



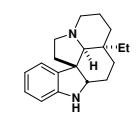
preussomerin G (1999)



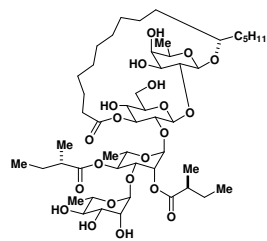
isoschizogamine (1999)



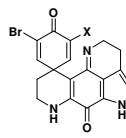
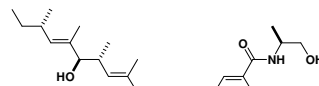
cylindricine A (1999)



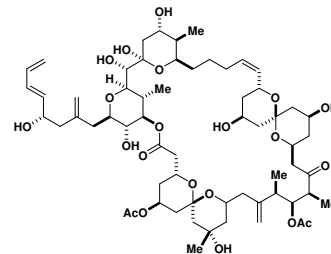
aspidozpermidine (2000)



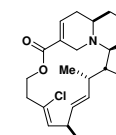
Tricolorin A (1997)

discorhabdin C X = Br
discorhabdin E X = H (1999)

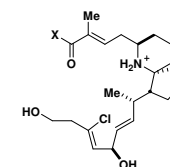
myxalamide A (1999)



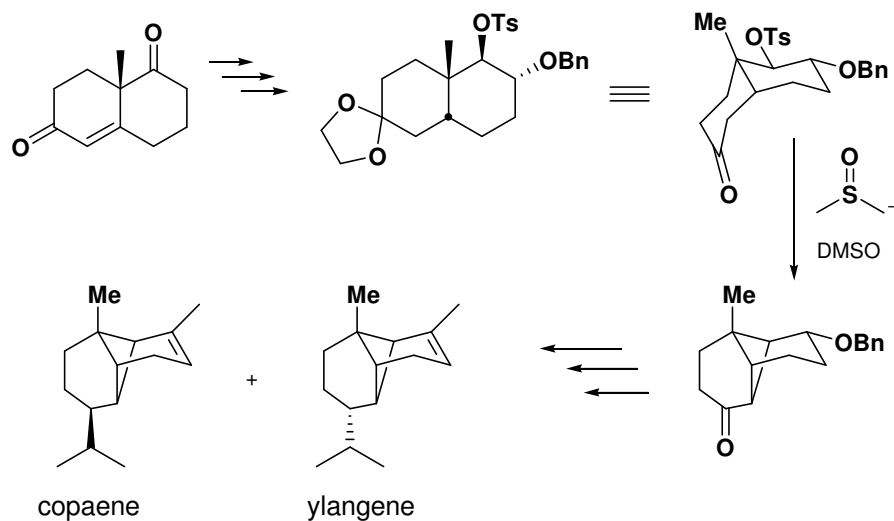
spongistatin 2 (2003)



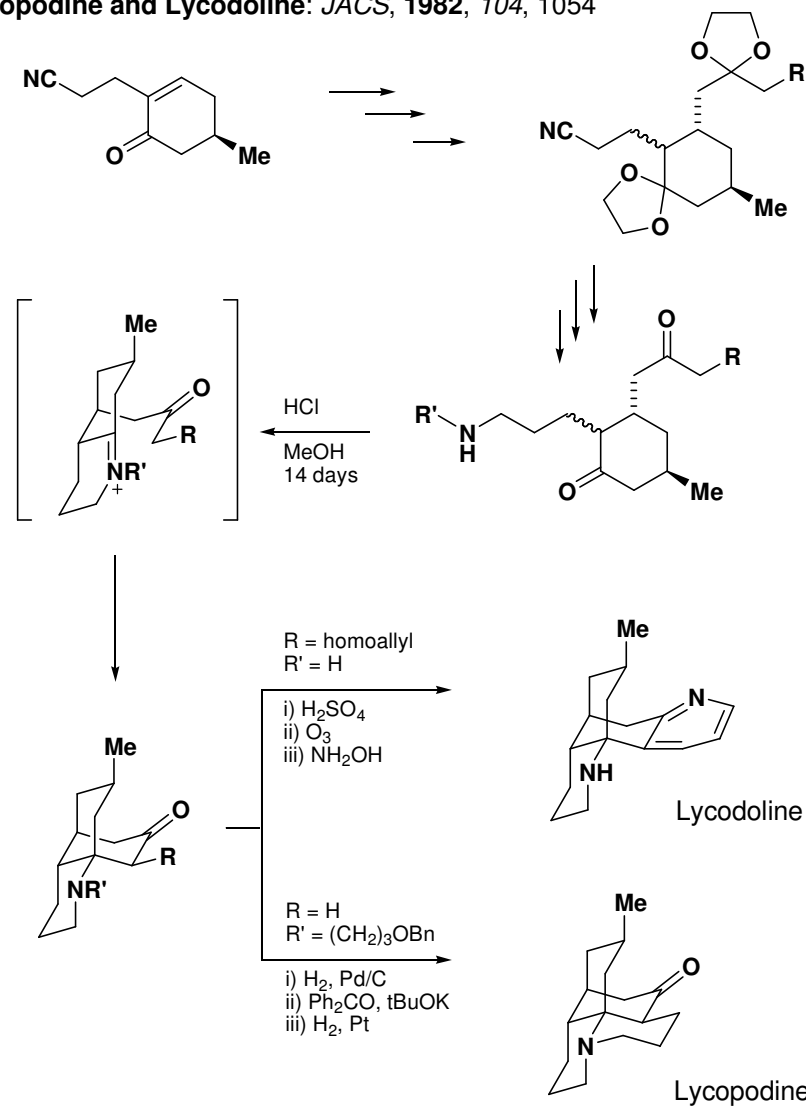
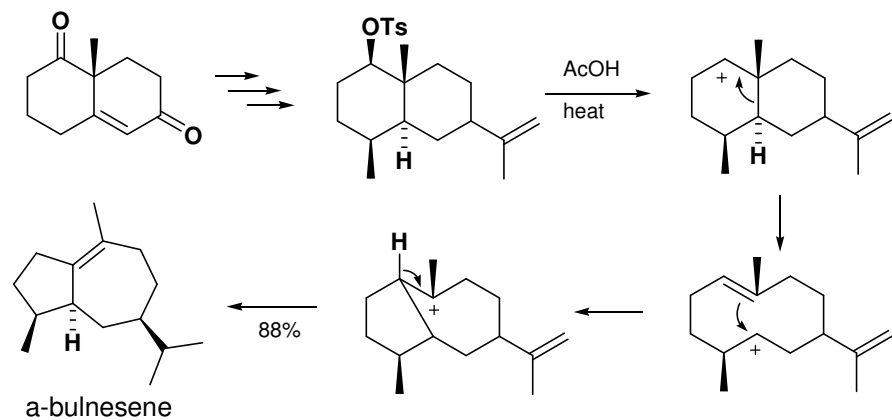
halichlorine (2004)

pinnaic acid X = O (2004)
taupinnaic acid X = NH(CH₂)₂SO₃⁻

Sesquiterpenes

Copaene and Ylangene: *JACS*, 1967, 89, 4133

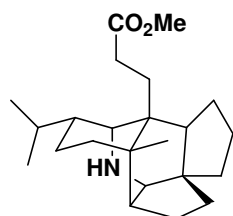
Lycopodium Alkaloids

Lycopodine and Lycodoline: *JACS*, 1982, 104, 1054Bulnesene: *JACS*, 1971, 93, 1746

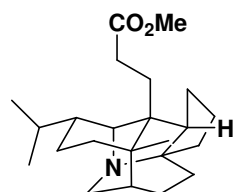
Daphniphyllum Alkaloids

- Isolated from Yuzuriha tree
- Vermicide and asthma cure early 1900's
- 38 members

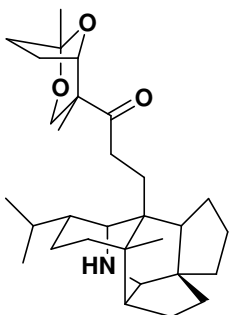
JOC, 1992, 57, 2531



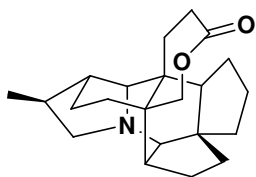
methyl homosecodaphniphyllate (1988)



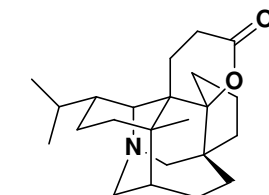
methyl homodaphniphyllate (1986)



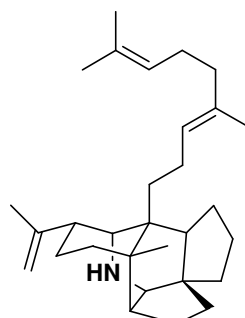
(-)-secodaphniphylline (1990)



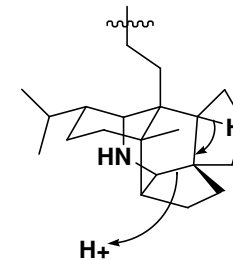
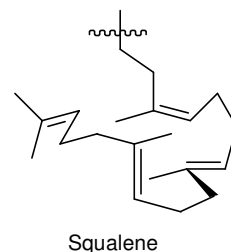
bukittingine (1992)



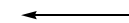
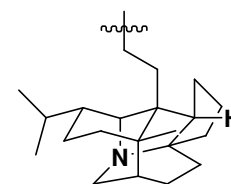
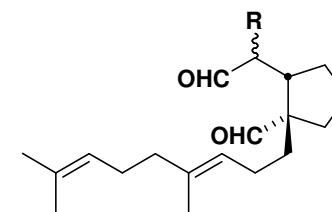
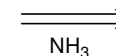
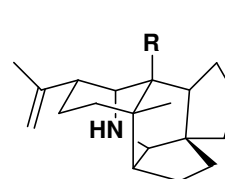
daphnilactone (1989)



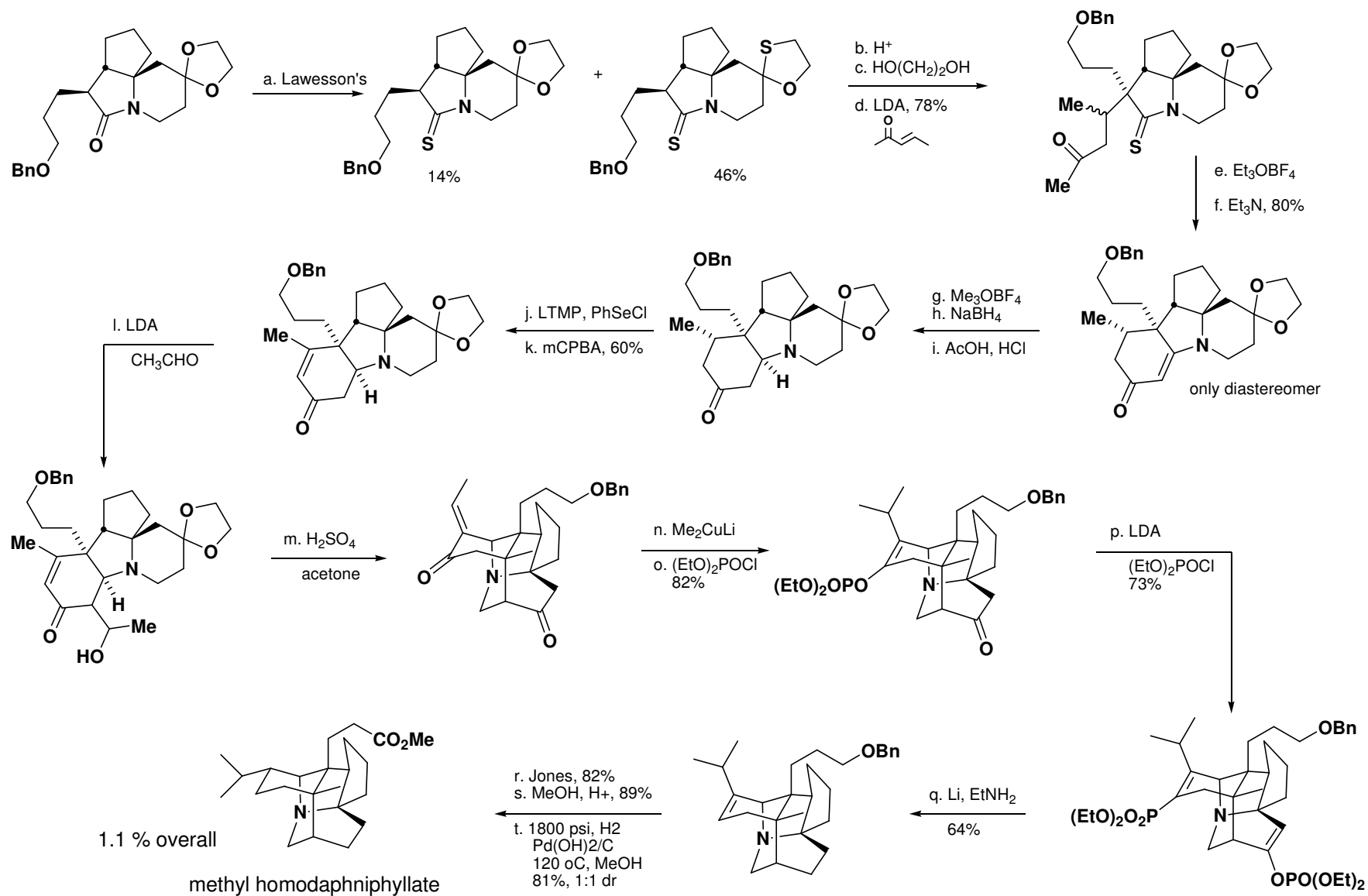
proto-daphniphylline (1990)

Proposed Biosynthesis (abbreviated)

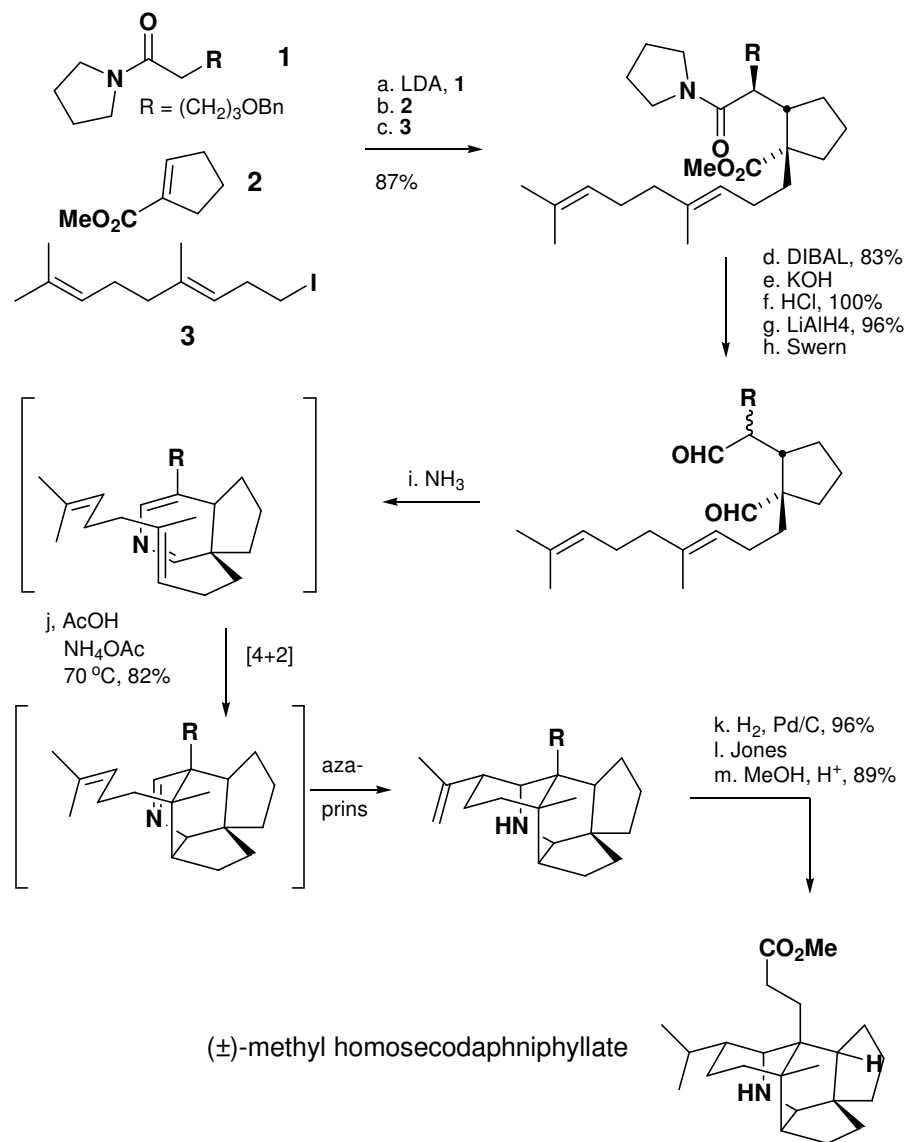
H⁺

**Key retrosynthetic step**

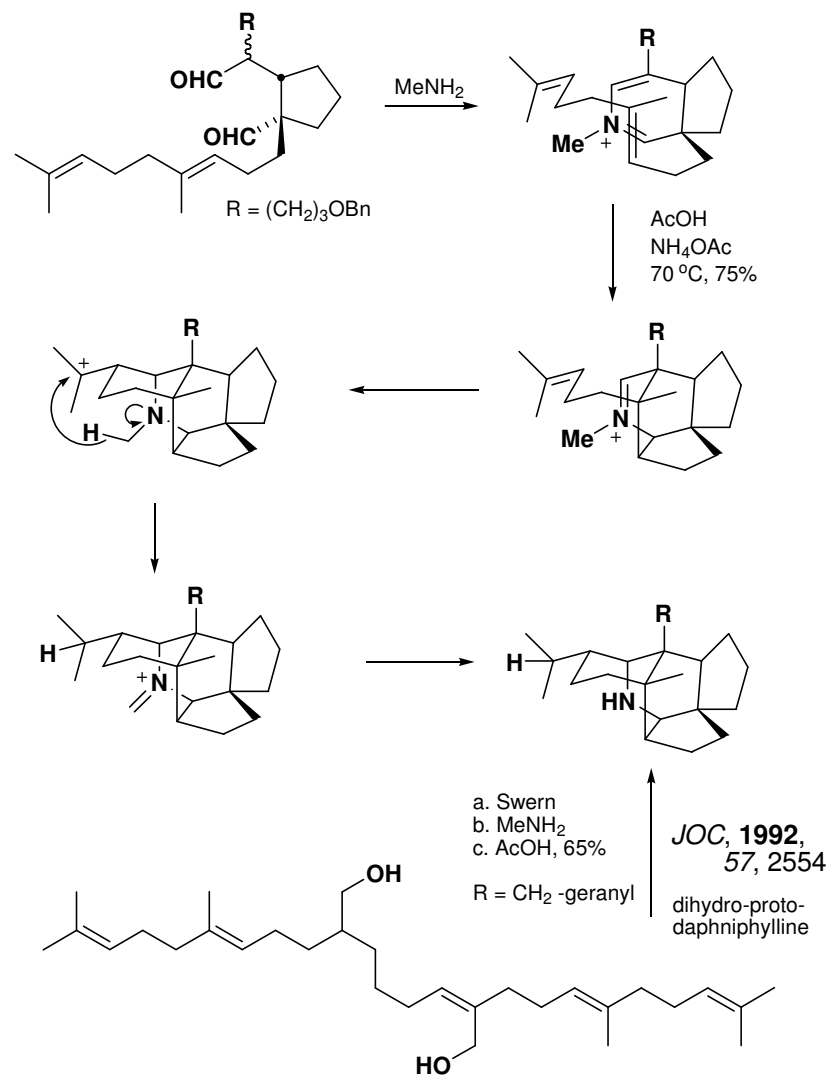
"Classic" Synthesis of methyl homodaphniphyllate: *JACS*, 1986, 108, 5650; *JOC*, 57, 2531

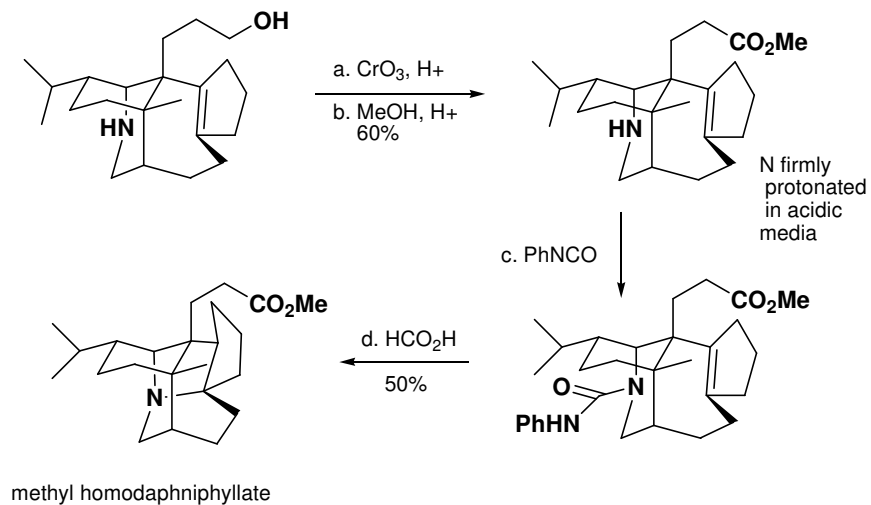
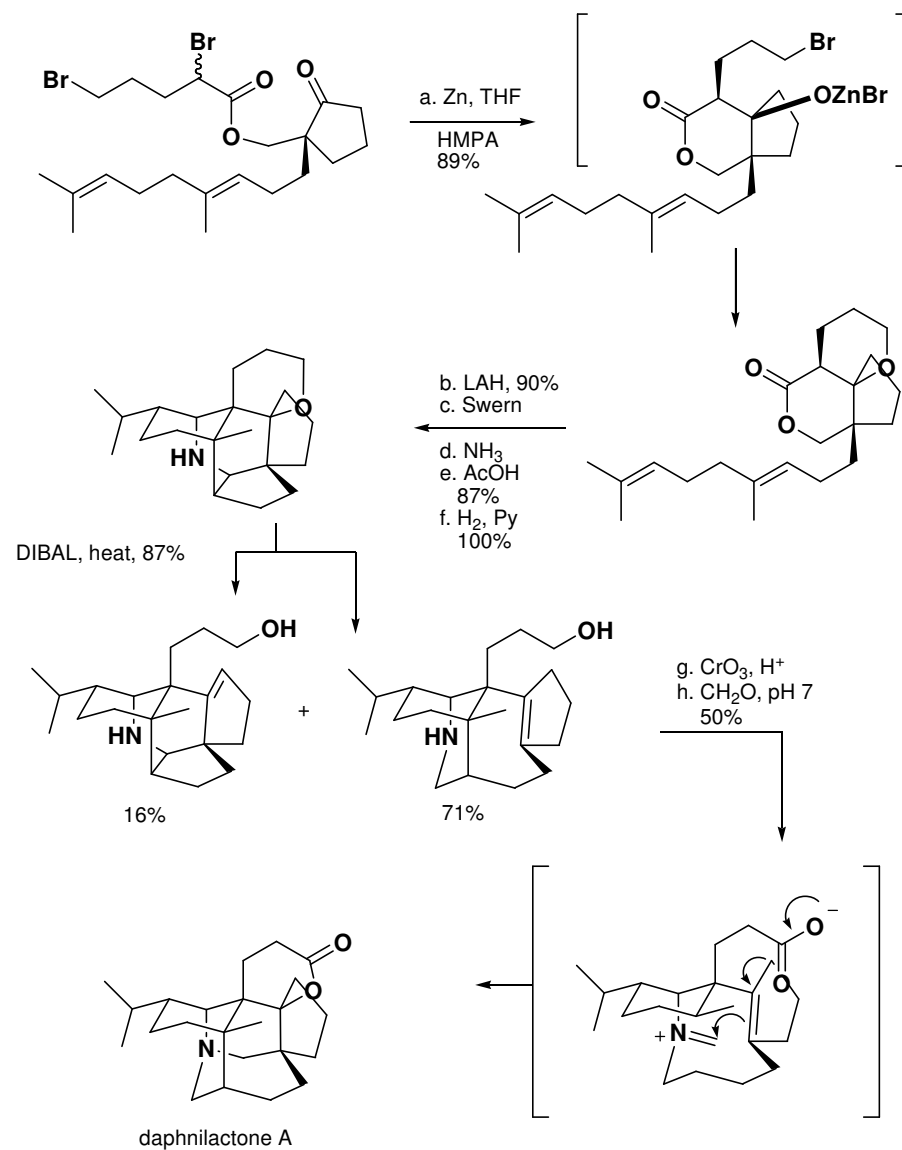
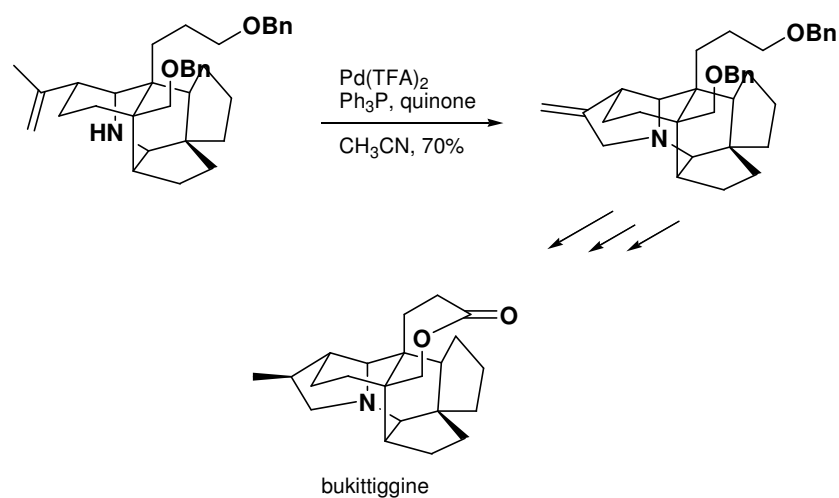


First Generation Biomimetic Synthesis

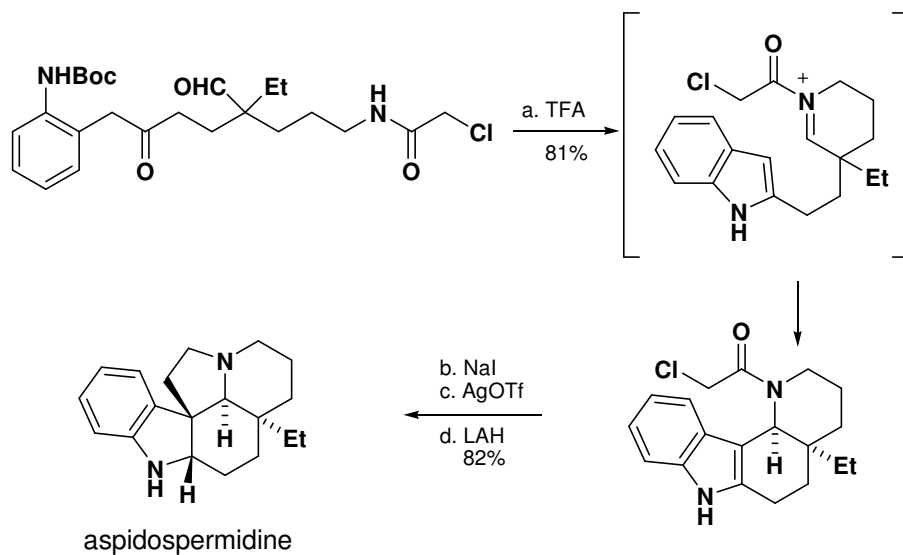
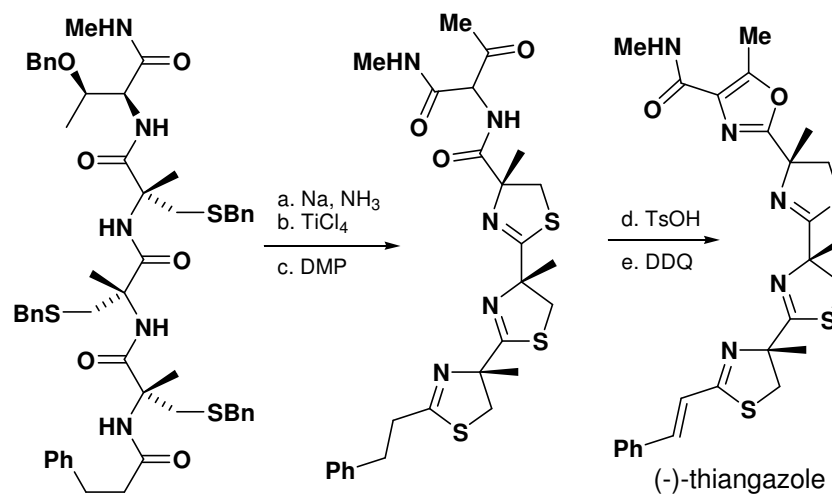
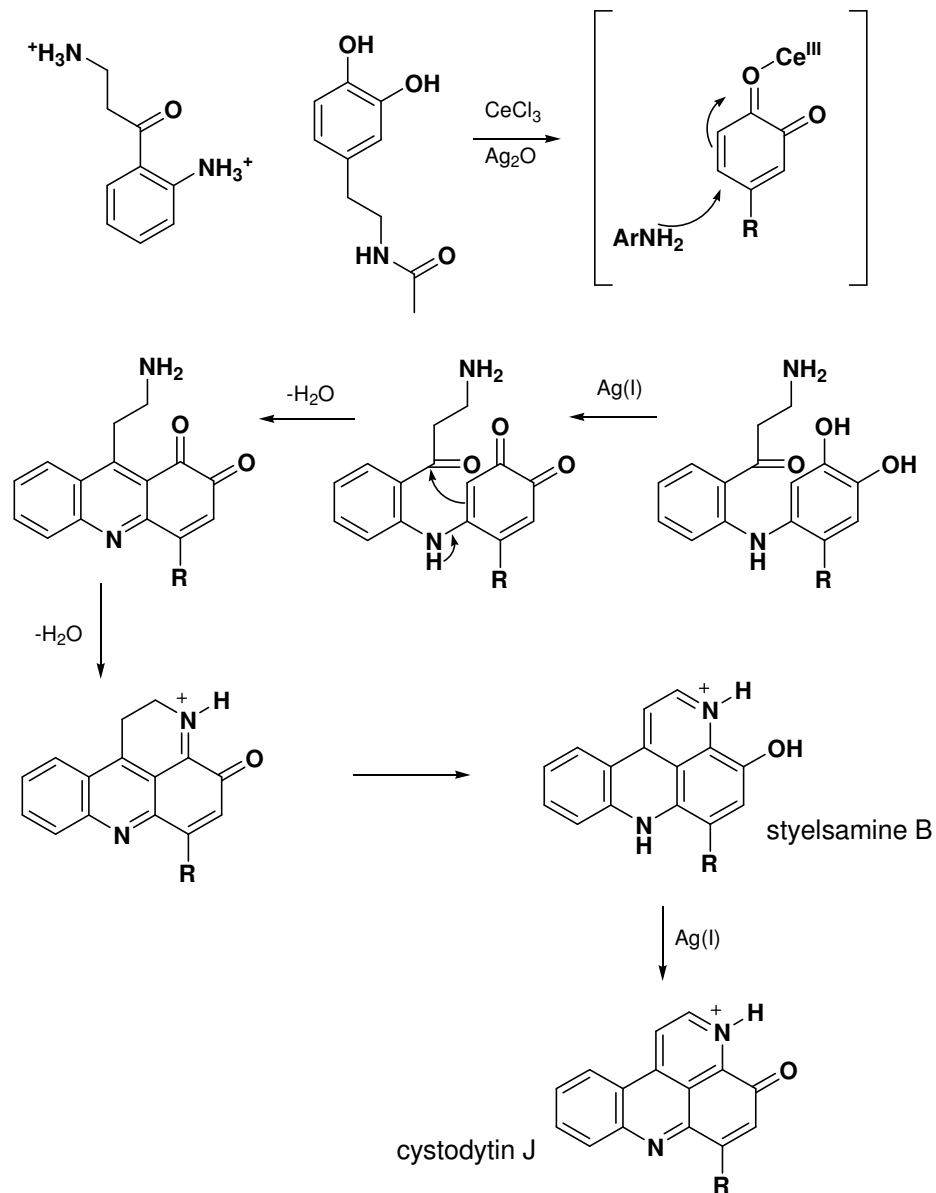
Second Generation Biomimetic Synthesis *JOC*, 1992, 57, 2544

footnote (23): "This serendipitous discovery resulted from use of a lecture bottle of methylamine that was mislabeled as ammonia by the vendor."

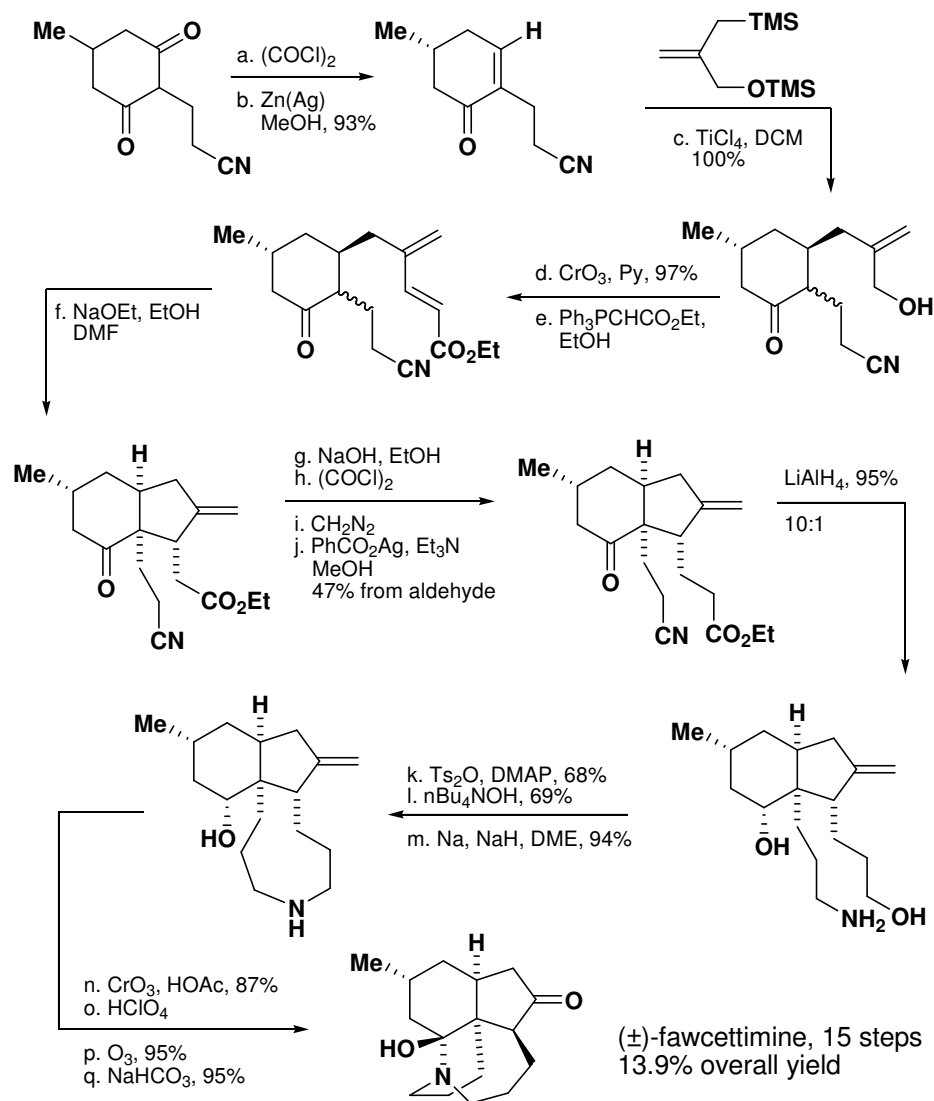


Daphnilactone A and methyl homodaphniphyllate: *JOC*, 1992, 57, 2585Bukittigine: *JOC*, 1992, 57, 2575

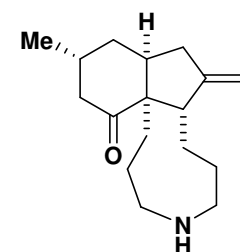
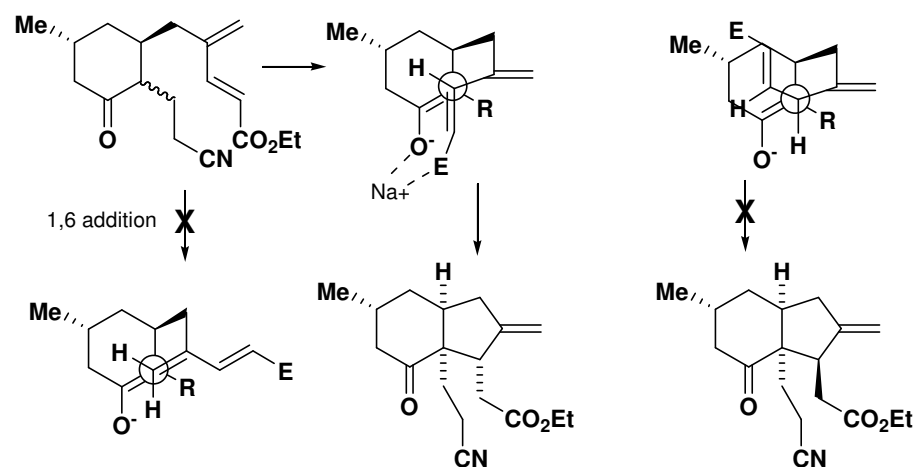
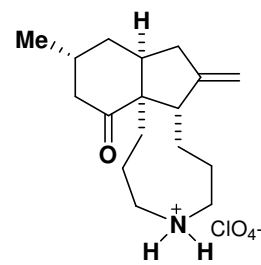
Heterocycles

Aspidospermidine: *JOC*, 2000, 65, 2642*(-)-Thiangazole*: *JOC*, 1994, 59, 4733Styelsamine B and Cystodytin J: *Org. Lett.*, 2001, 3, 4323

Protecting Group Free Synthesis

(±)-Fawcettimine: *JACS*, 1986, 108, 5022, full account: *JOC*, 1989, 54, 1548

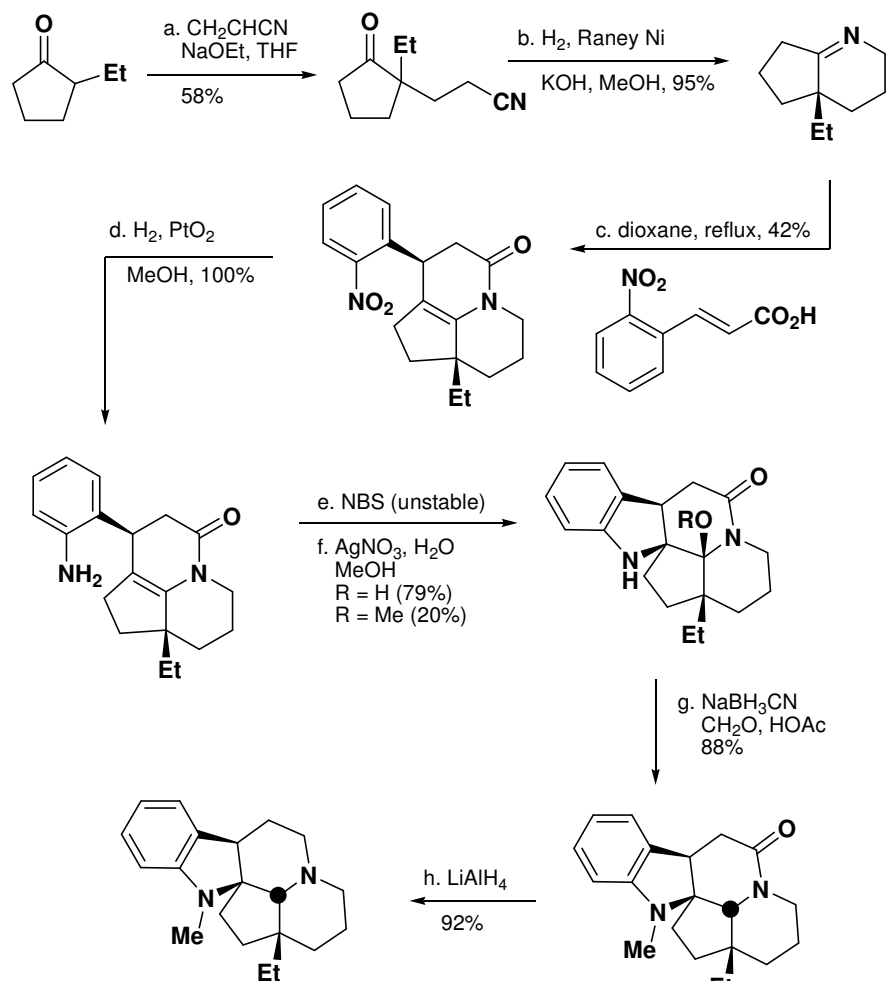
Keys to Synthesis

Michael Addition: 2 potential conformers, one diastereomer formed
1,4- vs. 1,6 addition-exists in amino ketone exclusively;
closes only when C-4 is up (4S)

-protonated amine serves as "protection" to ozonolysis

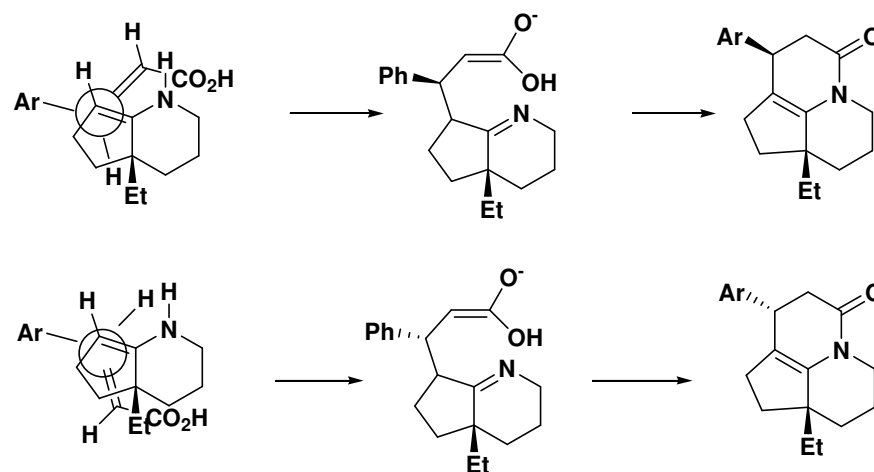
-base serves to deprotonate and epimerize C-4
to give exclusively fawcettimine

Protecting Group Free Synthesis cont'd

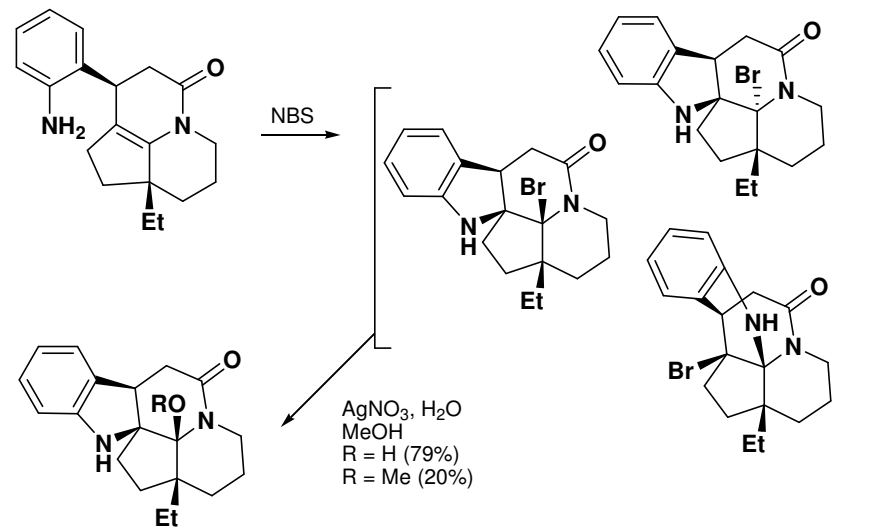
(±)-Vallesamidine: *JACS*, 1989, 111, 1528, full account: *JOC*, 1990, 55, 798(±)-vallesamidine, 8 steps
18.5% overall yield

Keys to Synthesis

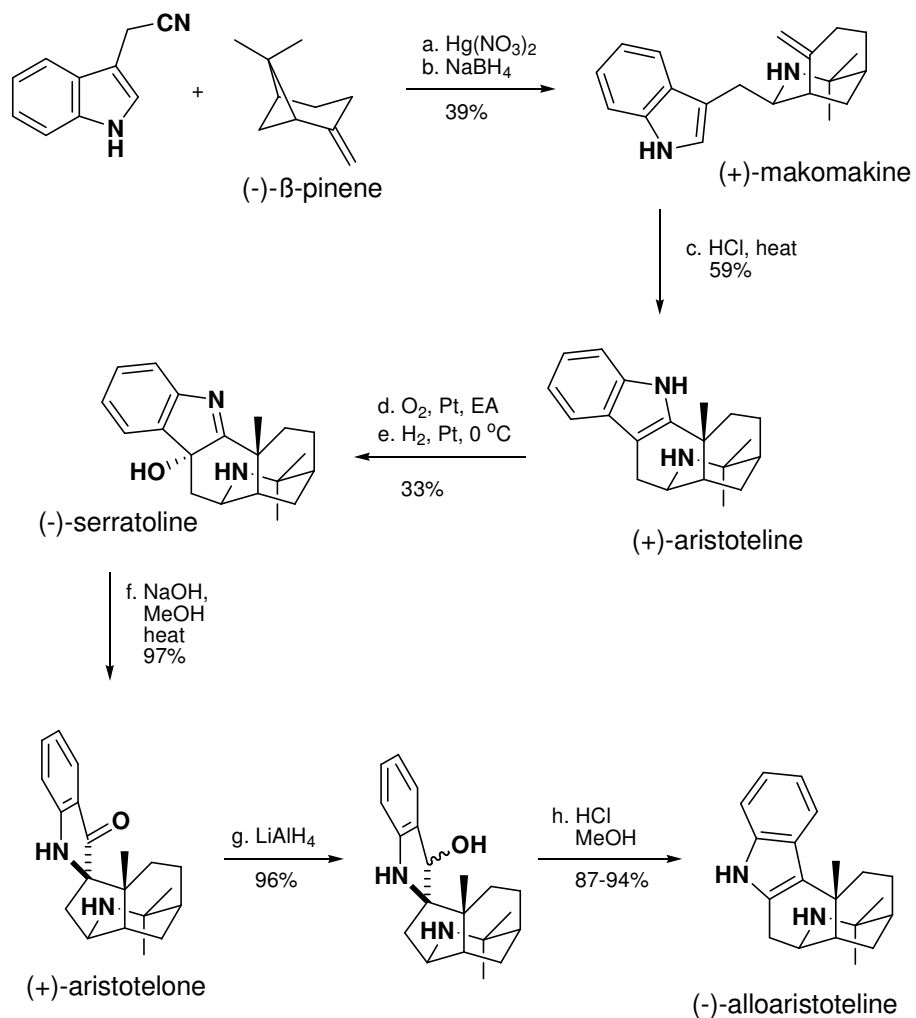
Michael annulation



Indoline Formation



Protecting Group Free Synthesis

Aristolonia alkaloids: *JOC*, 1993, 58, 564

Protecting Group Free Synthesis

Isovelleral: *JOC*, 1990, 55, 3004