

Wednesday,
May 19, 2004



Professor Satoshi Omura

Biography:

- Bachelors degree from Yamanashi University
- M.S. and Ph. D. from the Science University of Tokyo (1958)
- Ph. D. in Pharmacy from University of Tokyo
- Currently a professor and the president of the Kitasato Institute of Japan
- Research focuses on the isolation and discovery of microorganisms as well as biologically interesting substances which they produce

Biological diversity of Professor Omura's isolated chemicals

(Taken from *Microbiological Reviews*, 1986, 50, 259.)

Antibacterial:

A-73A, aurantins, factumycin, kinamycins, KM-8, LA-1, leucomycins, takaokamycin

Bacterial cell wall synthesis inhibitor:

AM-5289, asukamycin, azureomycin, nanaomycins, setomimycin, vineomycins

Antifolate:

AM-8402, diazaquinomycin

Antimycoplasmal:

2'-amino-2'-deoxyadenosine, cervinomycins, frenolicin B, OM-173

Antianaerobic:

clostomicin, luminamycin, lustromycin, thiotetromycin

Antiviral:

virantmycin, virustomycin

Antifungal:

AF-8 (albolleutin), cerulenin irumamycin, O-2867, prumycin

Antiparasitic:

avermectins, hitachimycin (stubomycin), setamycin

Anticancer:

OS-3256B, sporamycin

Herbicide:

herbimycins, karabemycin

Penicillinase inhibitor:

KA-107

Adenosine deaminase inhibitor:

adechlorin

Elastase inhibitor:

elasnin

Antiplaquet:

OM-3209

Alkaloid (chemical screening):

AM-2504 (prolimycin), 1,3-diphenethylurea, herquiline, NA-337 A, neoxaline, pyrimidin, quinoline-2-methanol, staurosporine, TM-64 (narcoactone)

Hybrid biosynthesis:

chimeramycins, mederrhodins

Chemical modification:

rokitamycin (3"-O-propionylleucomycin A, 5, 3,3",4"-tri-O-propionylspiramycin I, motilides

Neuritogenesis inducer:

lactacystin

HMG-CoA synthase inhibitor:

1233A

Acyl-CoA synthetase inhibitor:

triacsins

Acyl-CoA:cholesterol acyl-transferase (ACAT) inhibitor:

pyripropenes, terpendole, purpactines, glisoprenin

Glutamine synthetase inhibitor:

phosalacine, oxetin

Protein farnesyltransferase inhibitor:

pepticinnamin, gliotoxin

Cellulose biosynthesis inhibitor:

phthoramycin, phthoxazolin

Anticoccidial:

cytosaminomycin, fudecalone, hynapene

Gp-12-CD4 binding inhibitor:

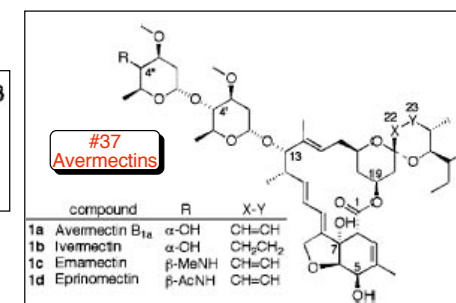
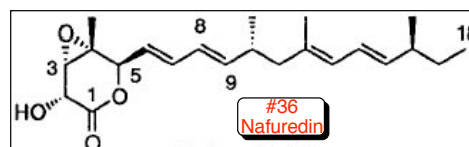
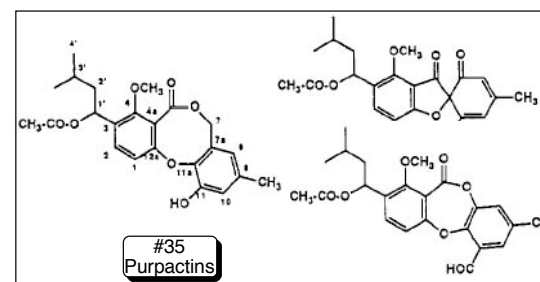
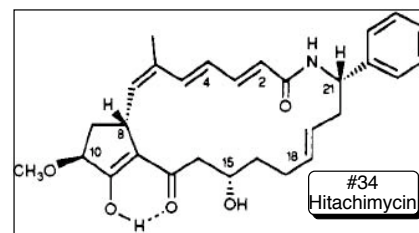
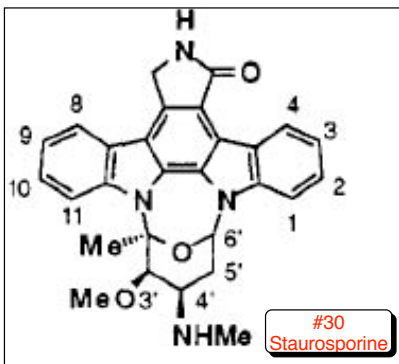
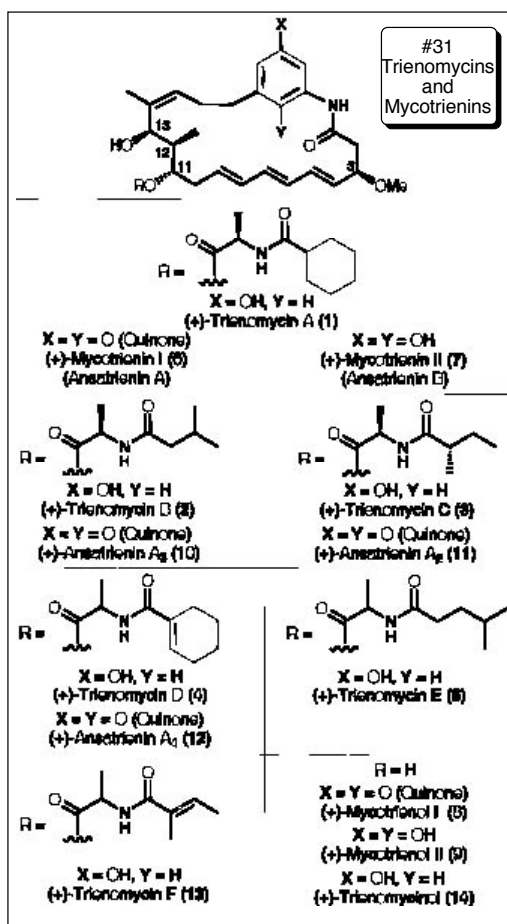
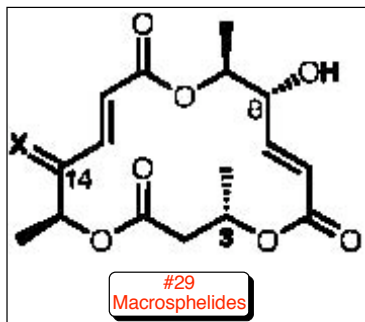
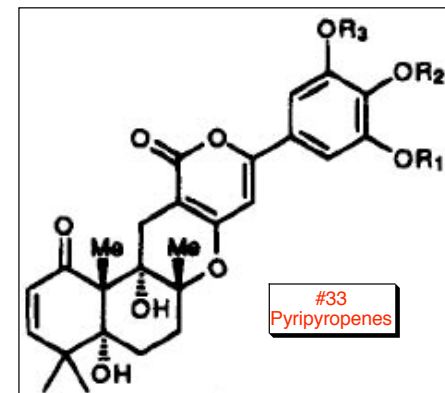
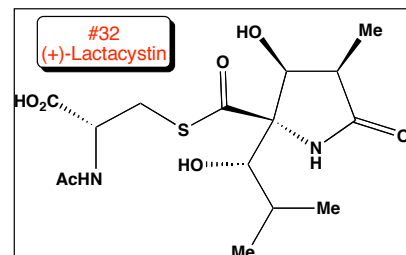
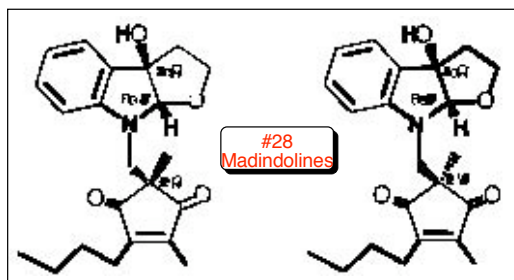
chloropectin, isochromophilones

Acetylcholine esterase inhibitor:

arisugacin

Others:

irumanolides, protylonolide

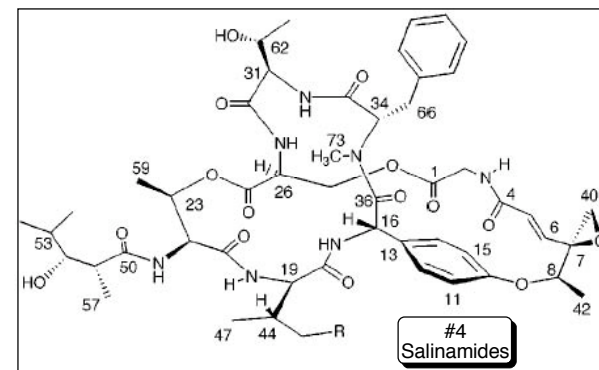
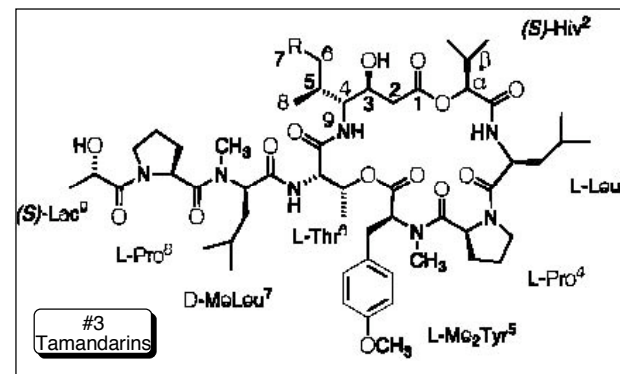
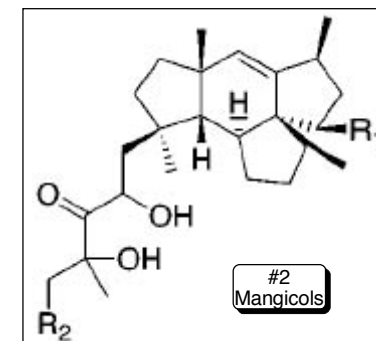
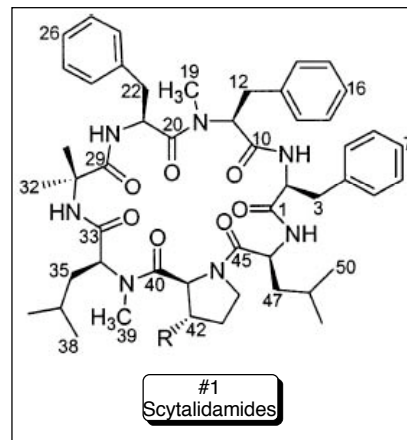


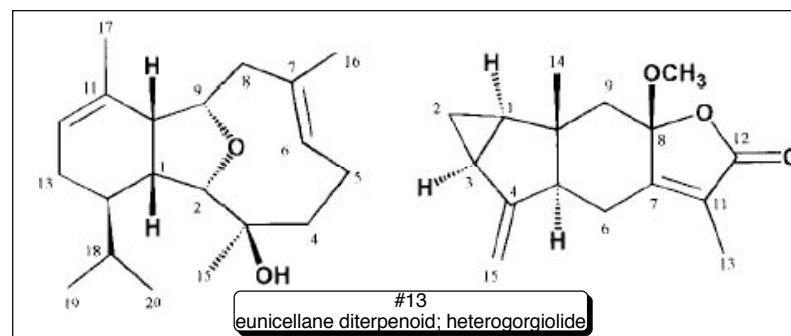
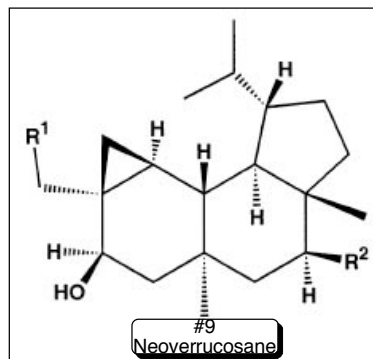
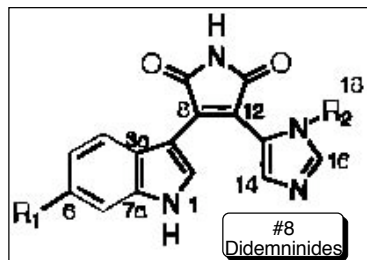
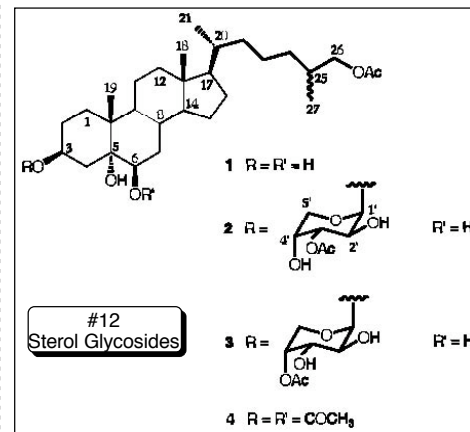
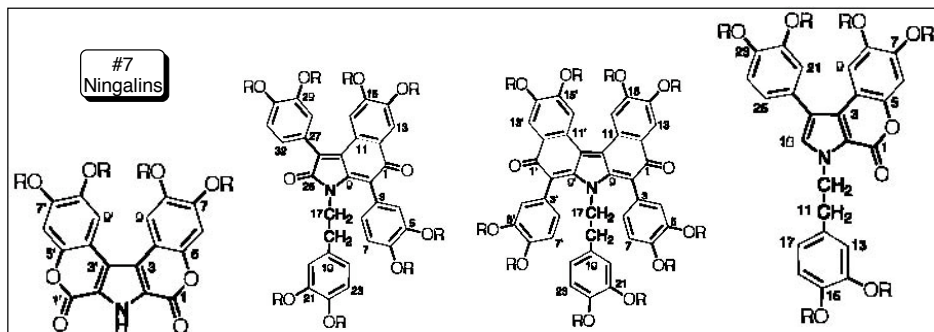
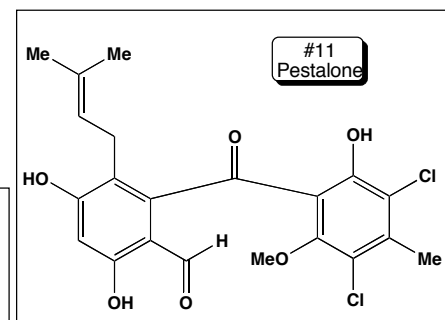
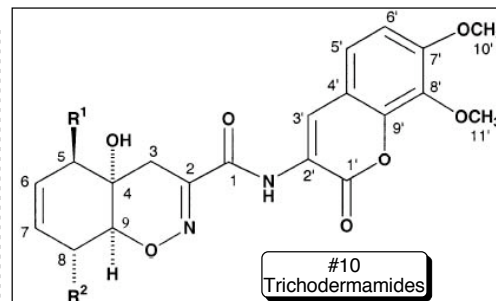
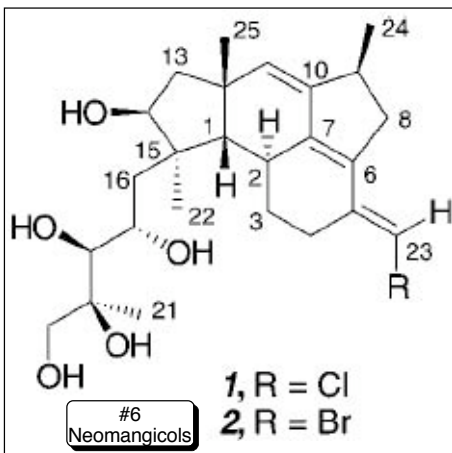
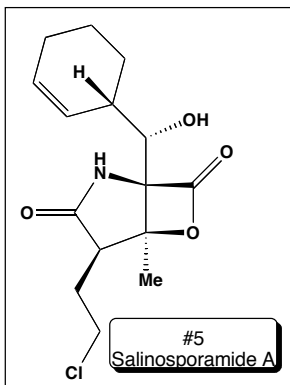


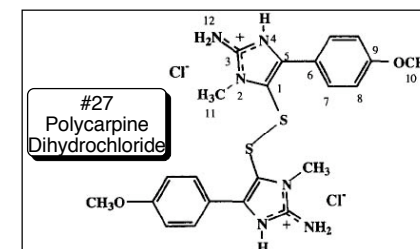
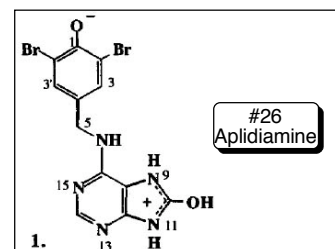
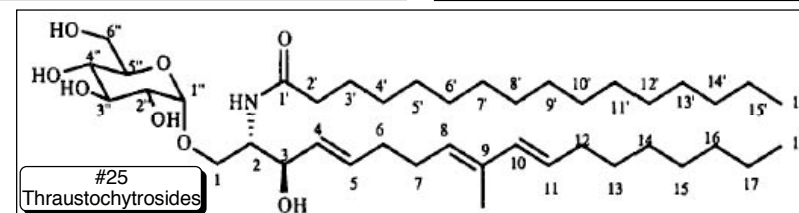
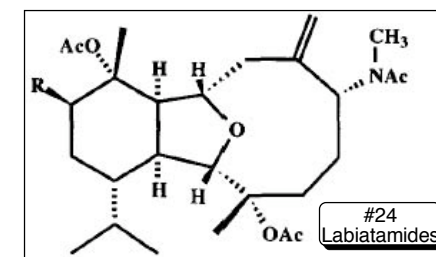
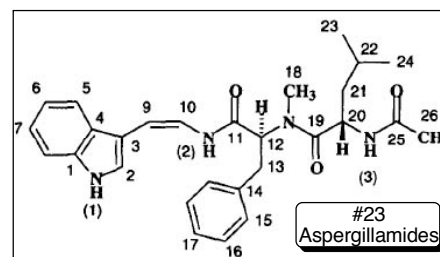
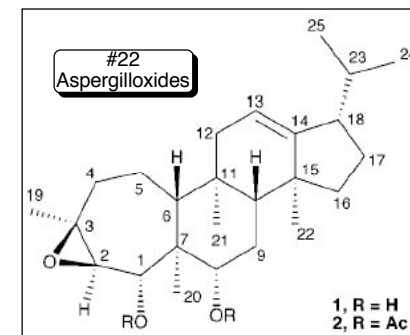
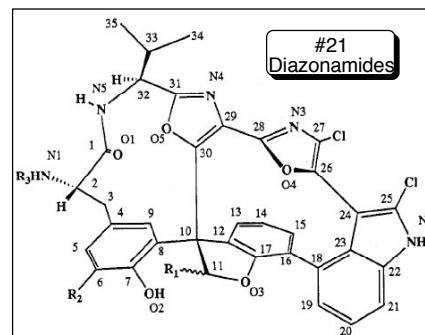
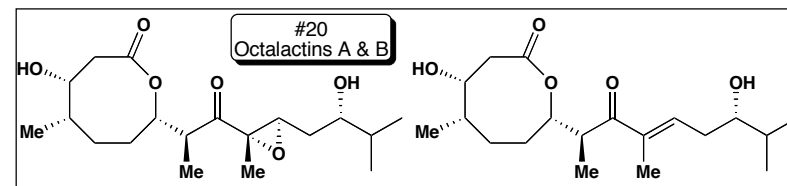
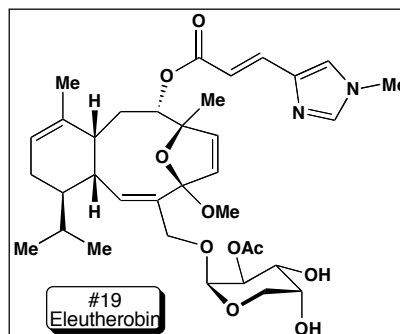
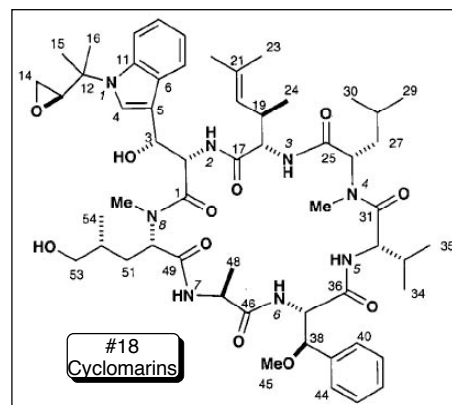
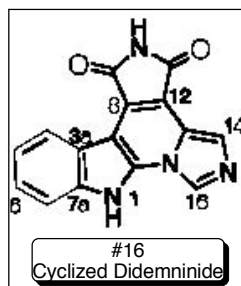
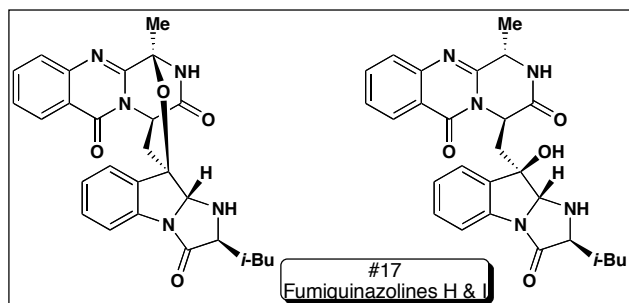
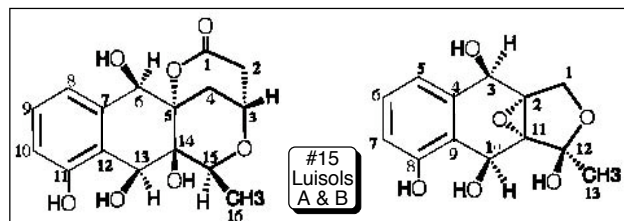
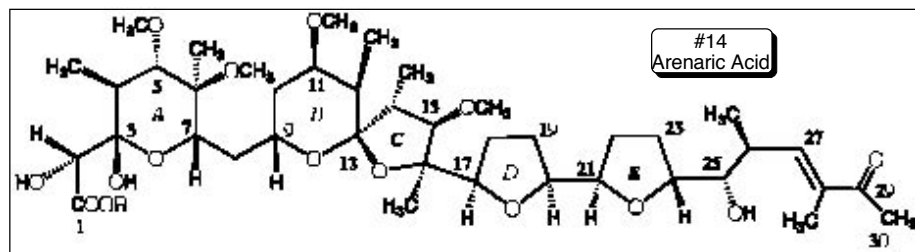
Professor William Fenical

Biography:

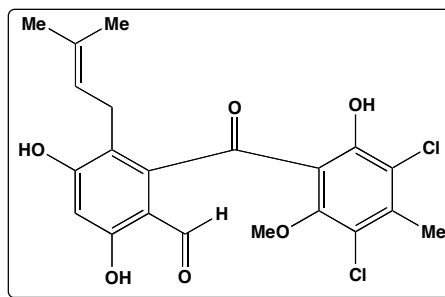
- Born in 1941, Chicago, Illinois
- B.S. in Biochemistry from California State Polytechnic University (1963)
- M.S. in organic chemistry from San Jose State University (1965)
- Ph. D. with professor D. R. Radlick at University of California, Riverside (1969)
- Began at Scripps Institute of Oceanography (SIO) as an assistant professor in 1973
- Became a professor of oceanography at SIO in 1983
- Became Director of Marine Research in 1989







Isolation of Pestalone
 "...potent antibacterial activity against drug-resistant bacteria."
 -Isolated as yellow crystals (Yes you could just do crystallography, but that's no fun!)



LREIMS: $m/z = 438/440/442$
 ->C₂₁ H₂₀ O₆ Cl₂

-11 Degrees of Unsaturation

IR

- Benzaldehyde
- Ketone
- Hydroxyl groups

UV: Aromatic Ring with
 extended chromophore

NMR

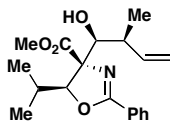
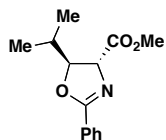
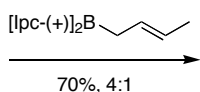
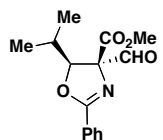
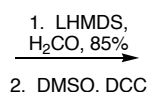
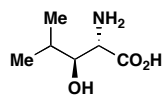
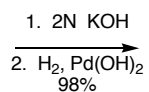
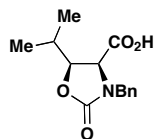
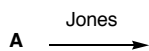
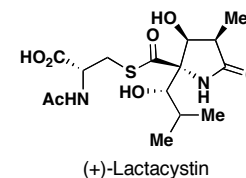
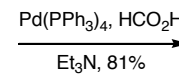
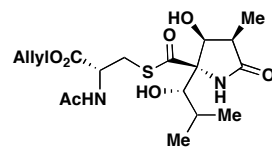
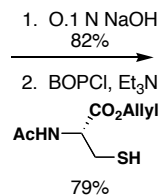
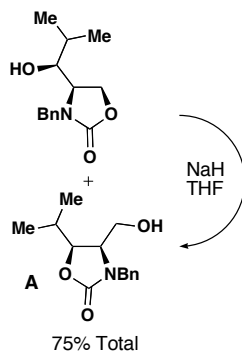
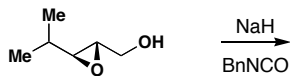
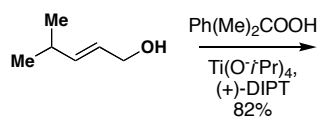
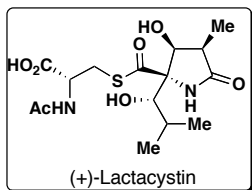
Proton: Two olefinic methyl groups
 One Aromatic resonance
 methoxy group
 three exchangeable phenols
 aldehyde

Carbon: Aldehyde and ketone confirmed
 Lots of aromatic/vinylic quat carbons
 One aromatic double

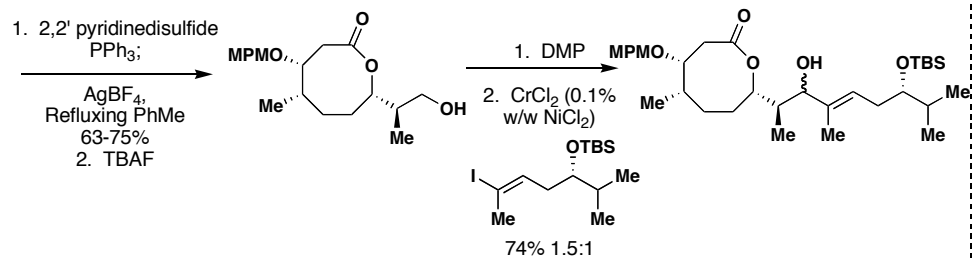
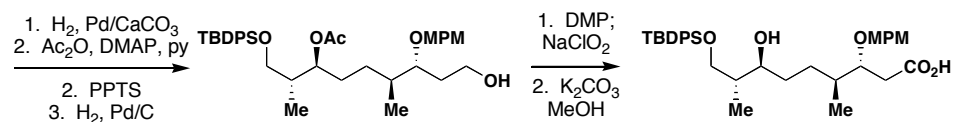
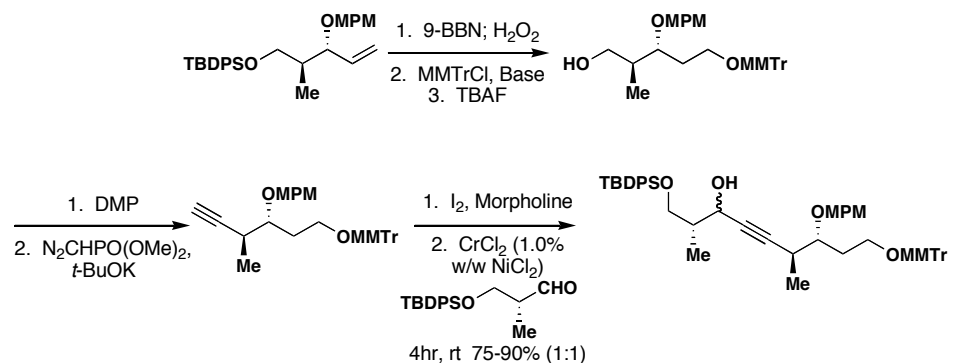
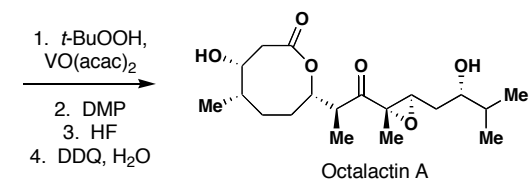
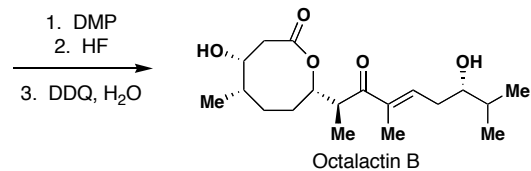
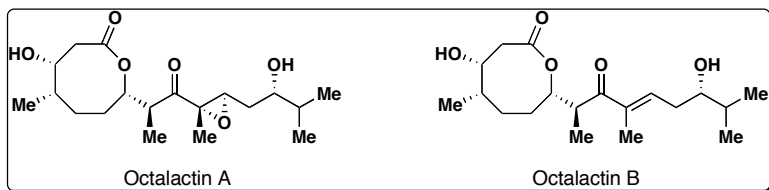
2D NMR: Isoprene Fragment
 -other modest assignments



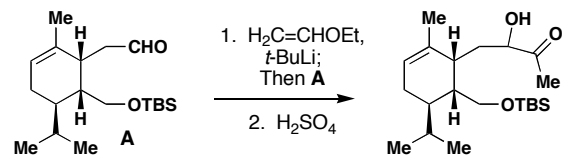
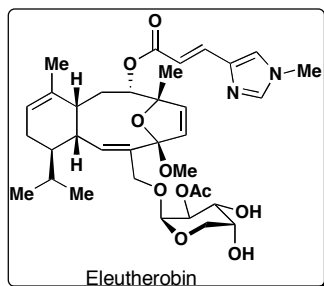
-Total Synthesis of (+)-Lactacystin
J. Am. Chem. Soc. **1996**, *118*, 3584.



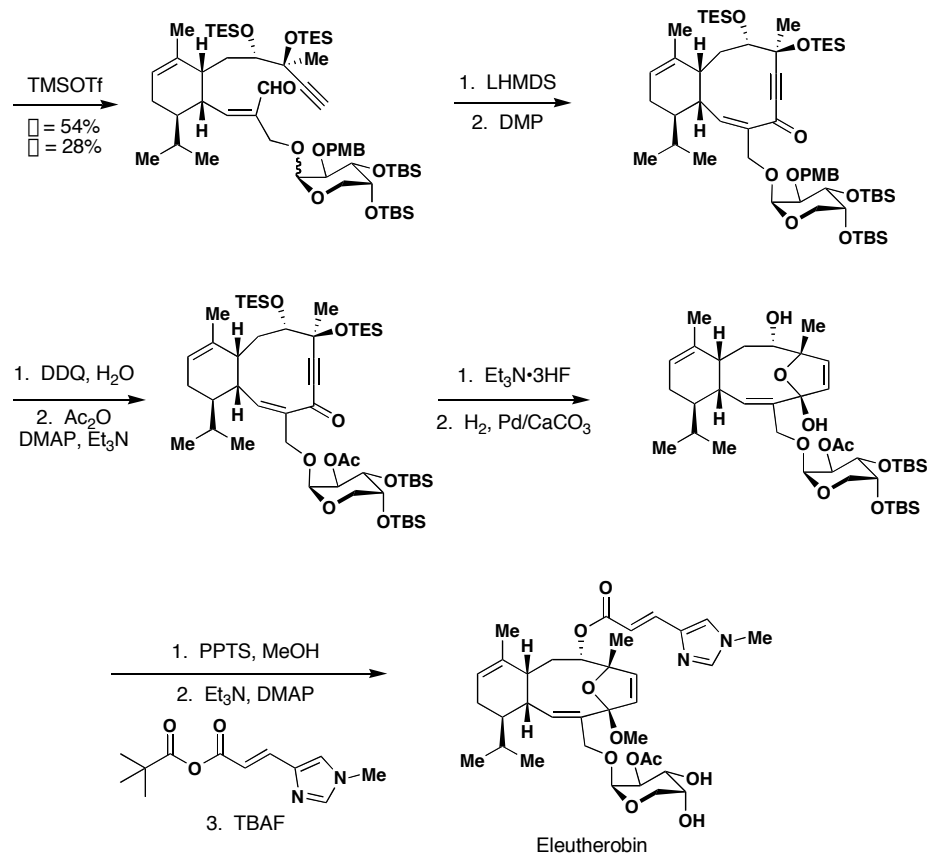
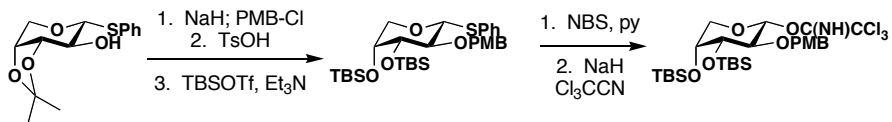
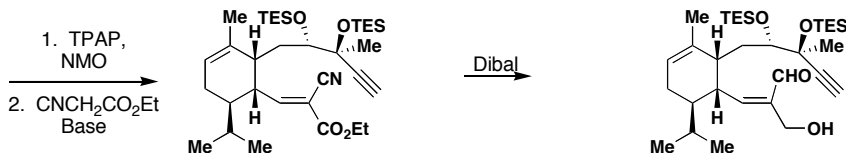
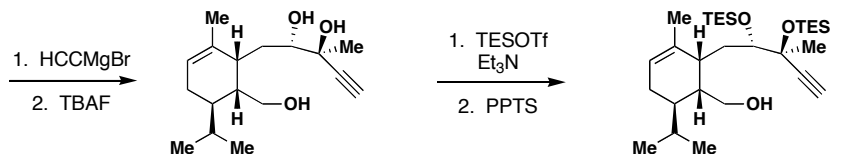
-Total Synthesis of Octalins A & B
Keith Buszek: *J. Am. Chem. Soc.* **1994**, *116*, 5511.



-Total Synthesis of Eleutherobin

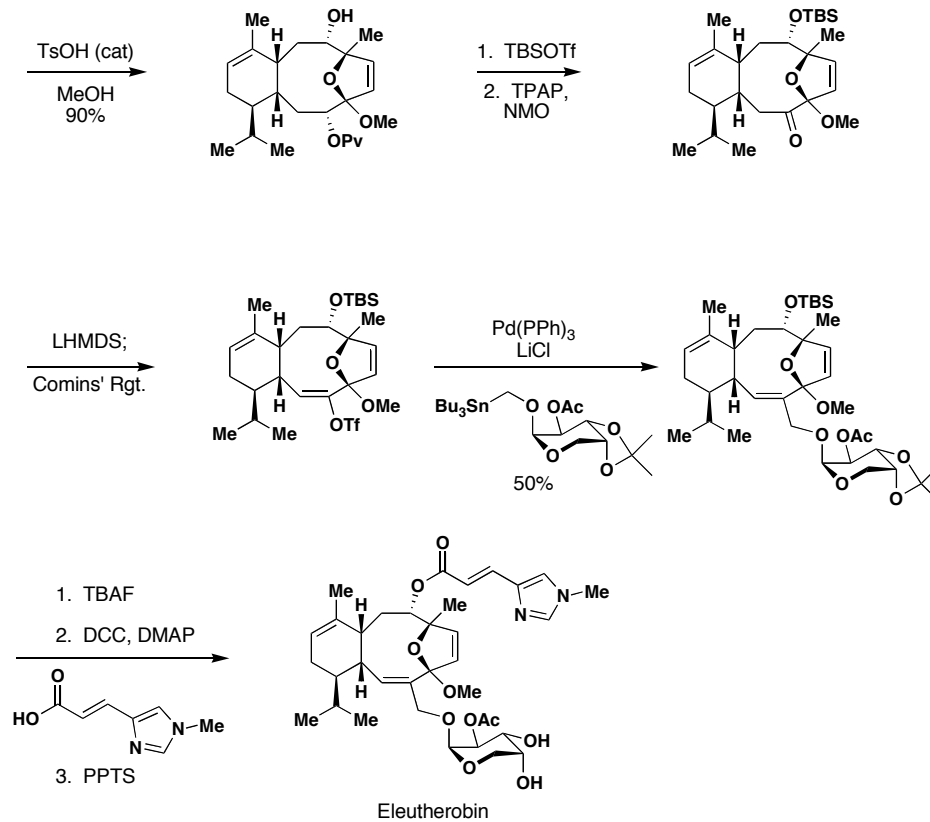
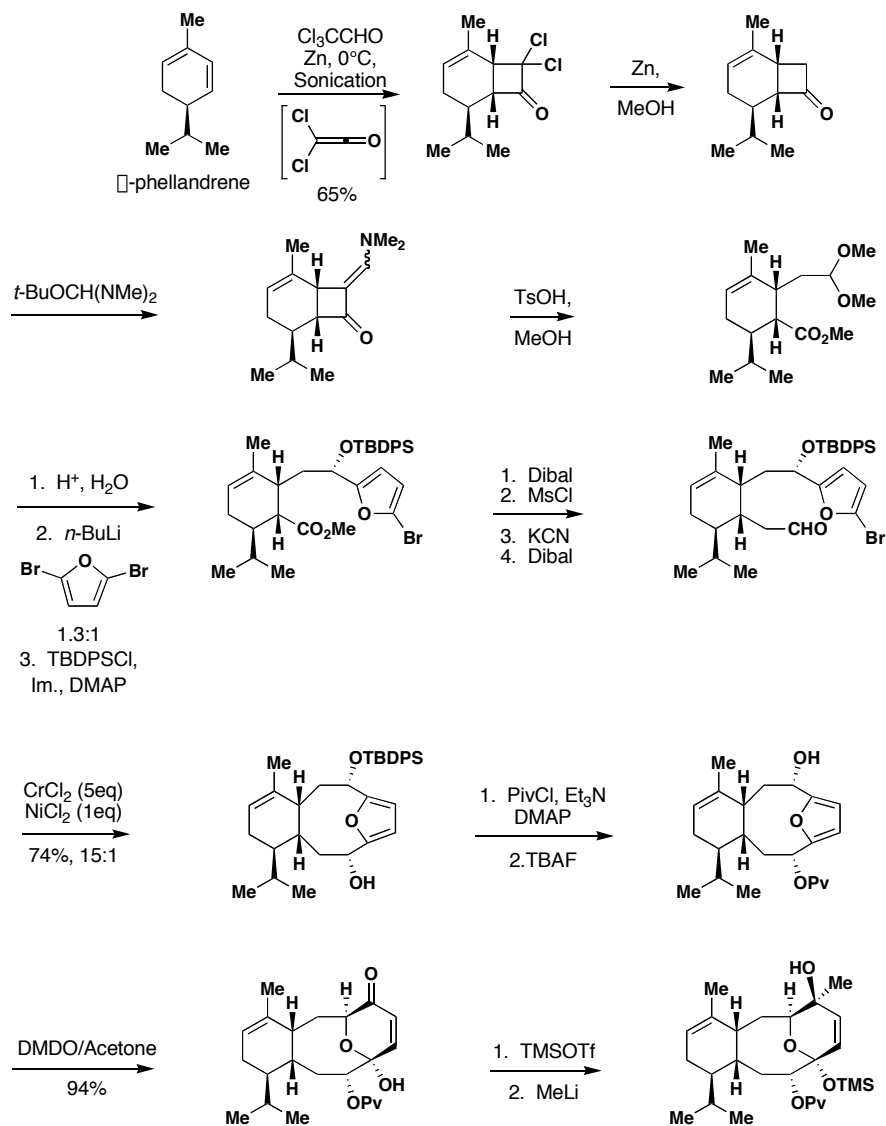
K.C. Nicolaou: *Angew. Chem. Int. Ed. Engl.* 1997, 36, 2520.

(+)-carvone derived



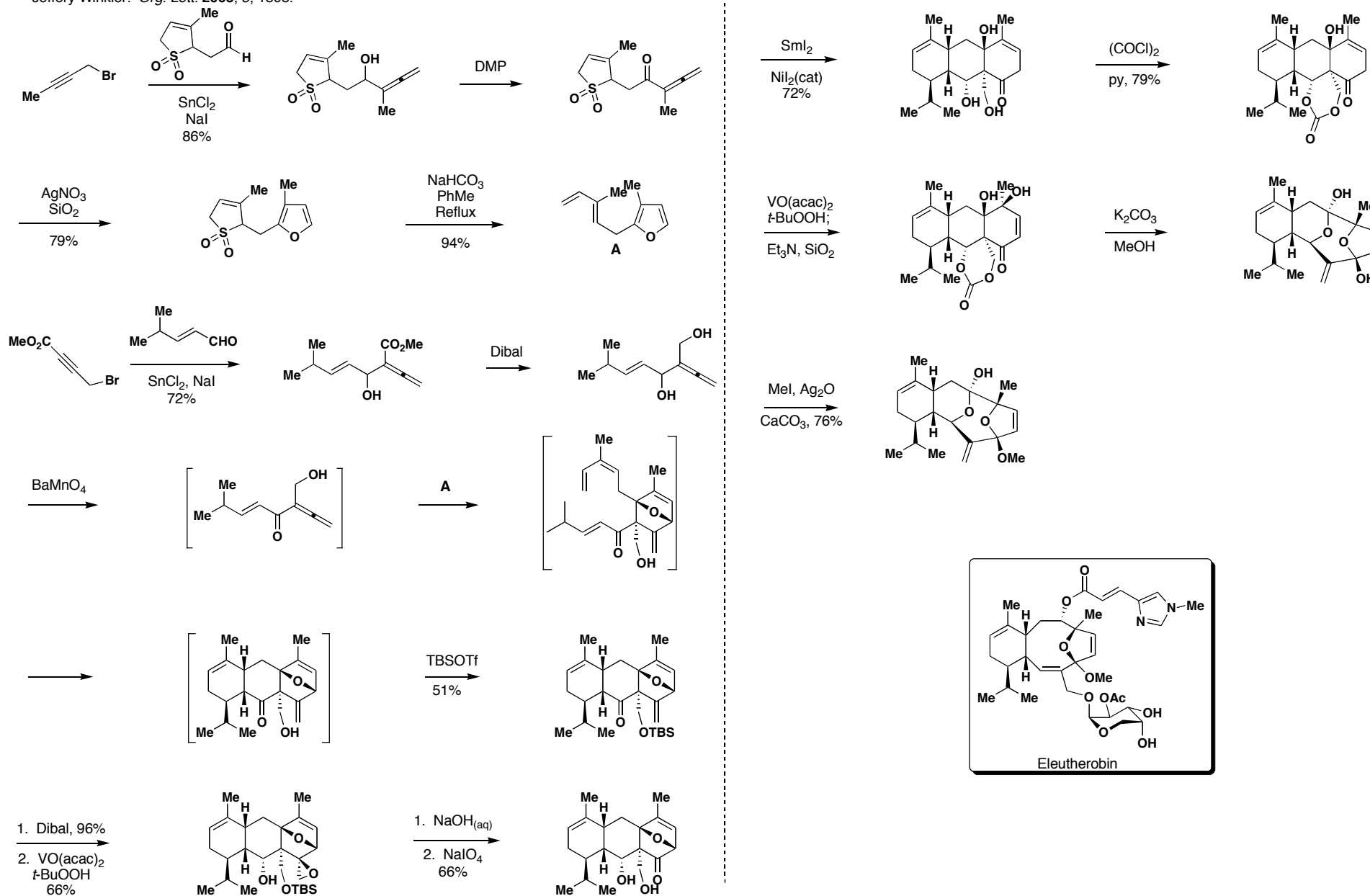
-Total Synthesis of Eleutherobin

Samuel Danishefsky: *J. Am. Chem. Soc.* **1999**, *121*, 6563.

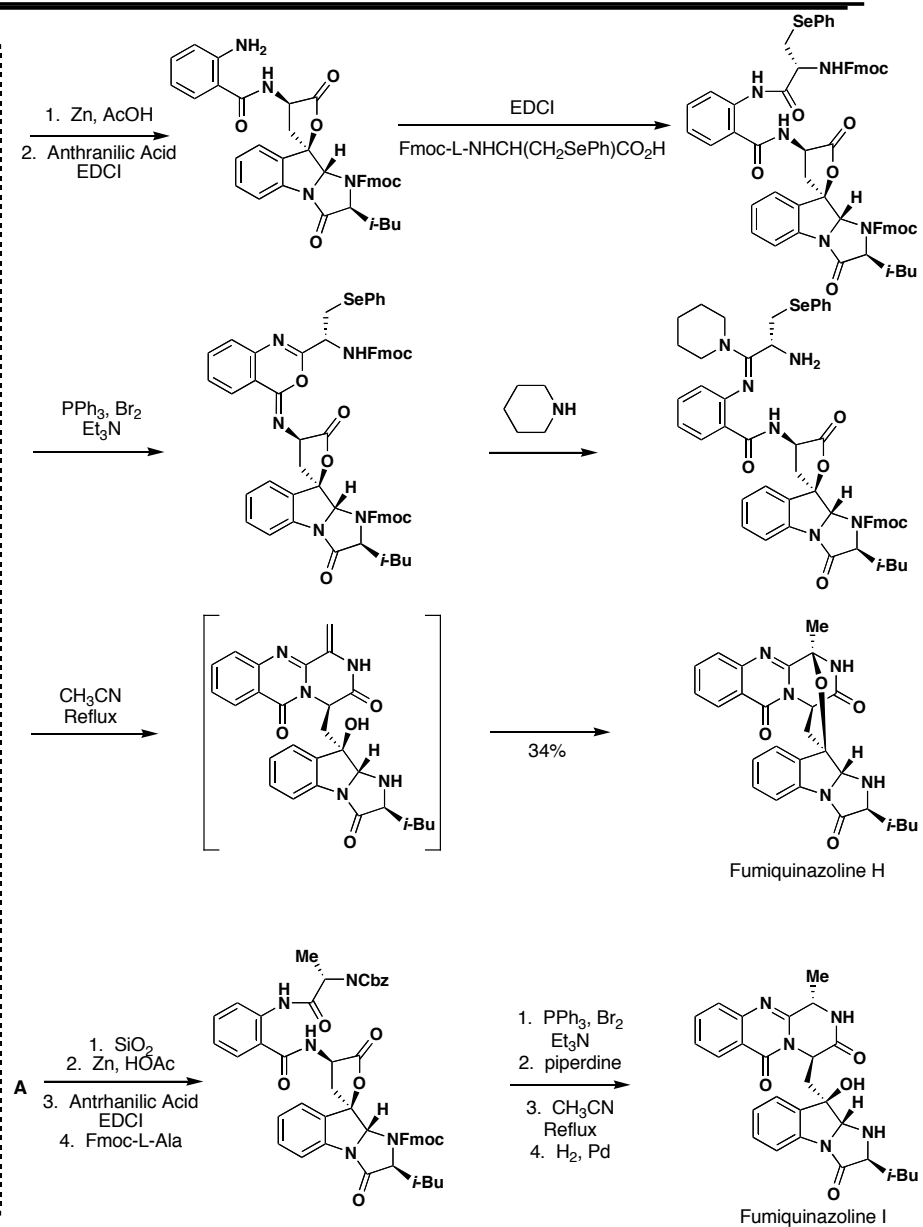
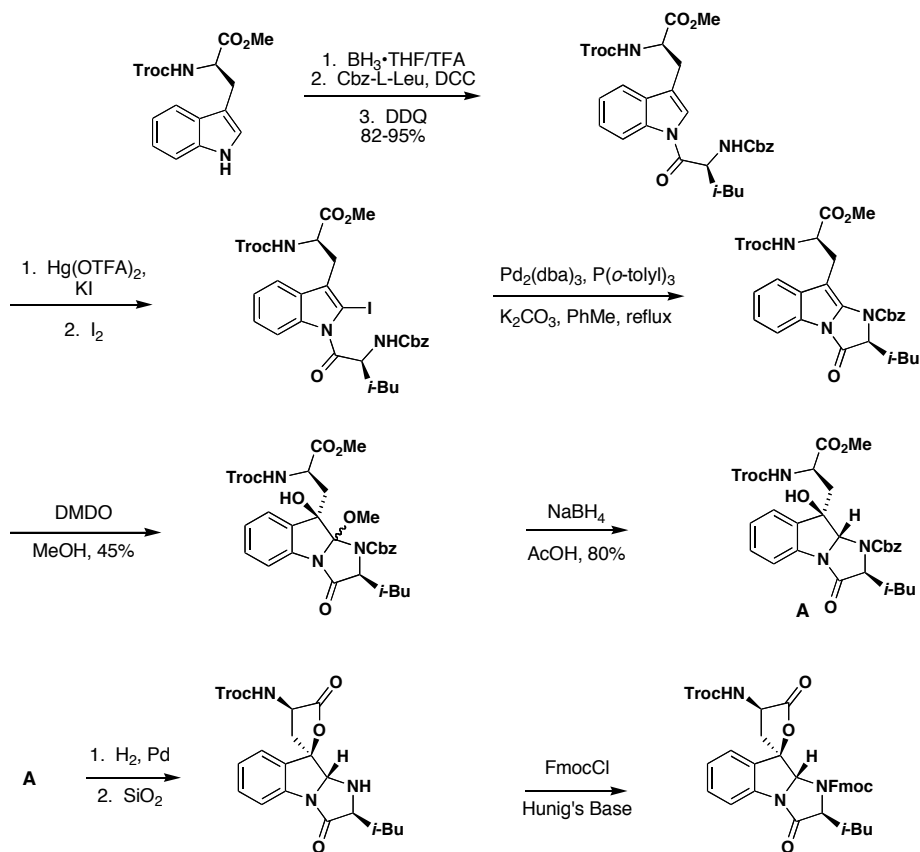
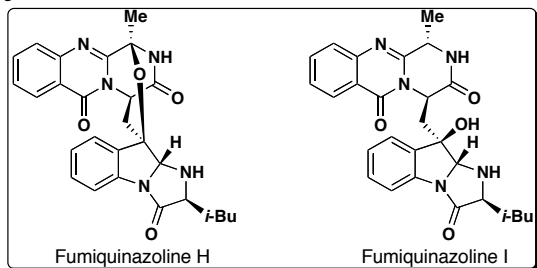


Eleutherobin

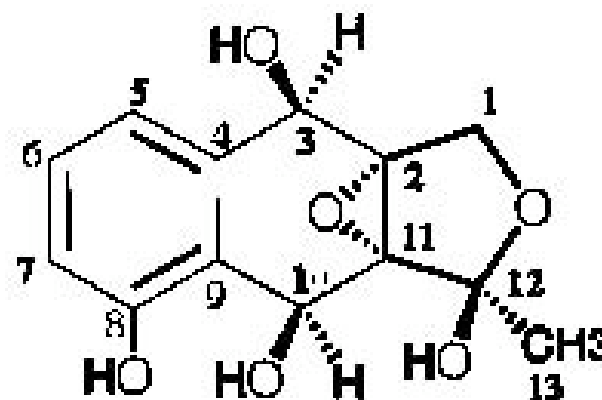
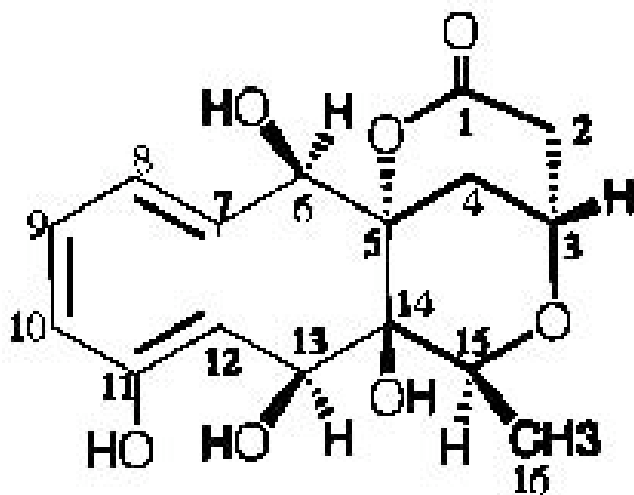
-Total Synthesis of Eleutherobin
Jeffery Winkler: *Org. Lett.* **2003**, 5, 1805.



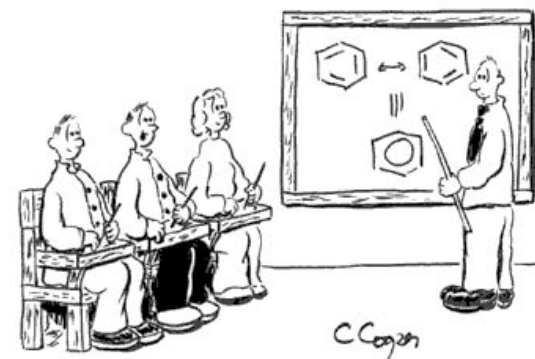
-Total Synthesis of Fumiquinazolines H & I
Barry Snider: *J. Org. Chem.* **2003**, *68*, 545.



The Baran Lab's Retrosynthetic Analysis of Luisols A and/or B:



“And I’ll thank you to wipe that smirk off your phase!”



“Define ‘resonance’? Sure, that’s where you live.”

References

Selected Natural Products:

1. *J. Org. Chem.* **2003**, *68*, 8767.
2. *J. Org. Chem.* **2000**, *65*, 4843.
3. *J. Org. Chem.* **2000**, *65*, 782.
4. *J. Org. Chem.* **1999**, *64*, 1145.
5. *Angew. Chem Int. Ed.* **2003**, *42*, 355.
6. *J. Org. Chem.* **1996**, *63*, 8346.
7. *J. Org. Chem.* **1997**, *62*, 3254.
8. *J. Org. Chem.* **1997**, *62*, 1486.
9. *J. Nat. Prod.* **2003**, *66*, 818.
10. *J. Nat. Prod.* **2003**, *66*, 423.
11. *J. Nat. Prod.* **2001**, *64*, 1444.
12. *J. Nat. Prod.* **2000**, *63*, 1427.
13. *J. Nat. Prod.* **1999**, *62*, 1322.
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