Journal Years in Review: Organic Letters 1999

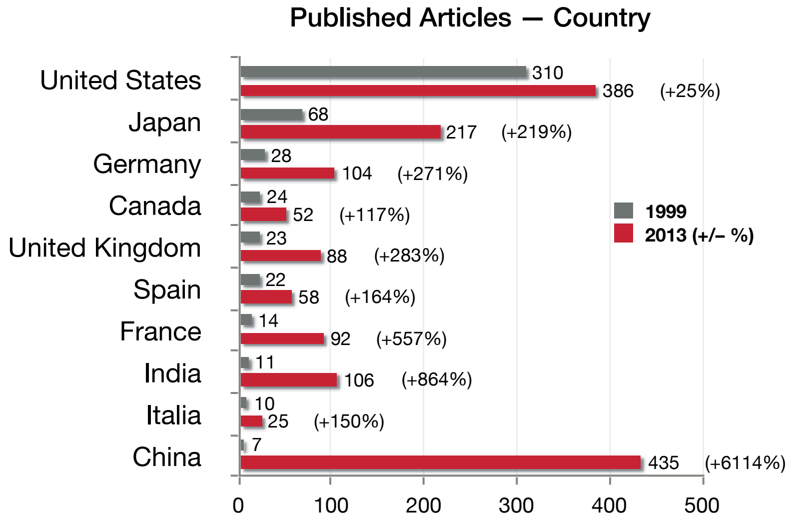
Gaich-Group Seminar

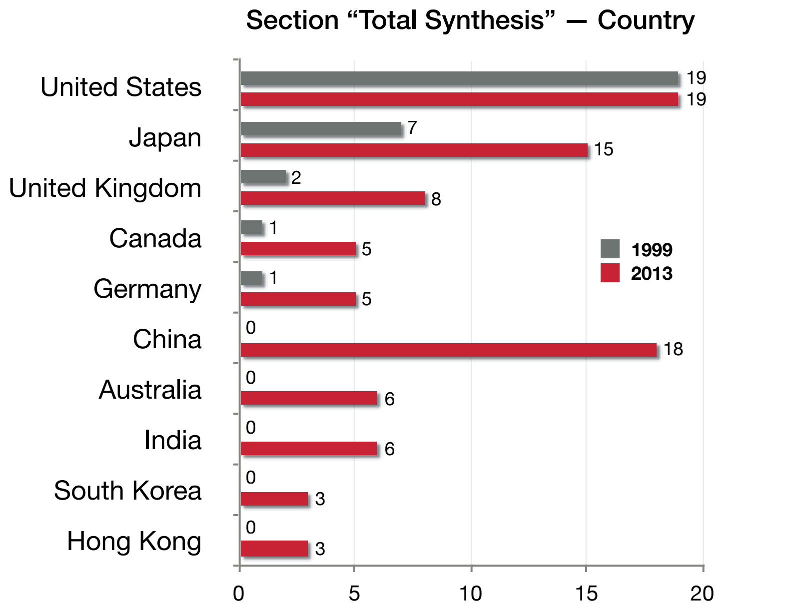
Erik Stempel
31.07.2014

Introduction / Analysis

- OL facts 1999 (2013 in parentheses):
  - Impact Factor: 3.367 (6.142, +82%)
  - 2 184 pages (6 308, +189%)
  - 561 published articles (1 738, +210%)
  - 29 "Total Syntheses" as topic (93, +221%)

- Most prolific authors of 1999:
  - E. J. Corey (8)
    A. B. Smith (8)
  - D. L. Comins, (4)
    Y. Fujiwara, (4)
    K. N. Houk, (4)
    M. E. Jung, (4)
    T. Kitamura, (4)
    A. Jain, (4)
    T. Nakata, (4)
    J. D. Rainier, (4)
    W. R. Roush, (4)
    J. F. Stoddart, (4)
    P.A. Wender (4)





- Scopus / SciFinder

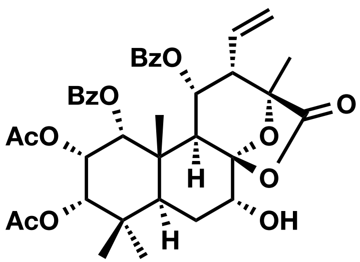
Introduction / Analysis (II)

- Most cited papers (general):
  - *Synthesis and activity of a new generation of ruthenium-based olefin metathesis catalysts coordinated with 1,3-dimesityl-4,5-dihydroimidazol-2-ylidene ligands* (R. H. Grubbs, p. 953)
    - Number of citations: 2497
  - *The Heck Reaction in Ionic Liquids: A Multiphasic Catalyst System* (J. D. Holbrey, p. 997)
    - Number of citations: 423
  - *Enantioselective Synthesis of α-Amino Nitriles from N-Benzhydryl Imines and HCN with a Chiral Bicyclic Guanidine as Catalyst* (E. J. Corey, p. 157)
    - Number of citations: 370

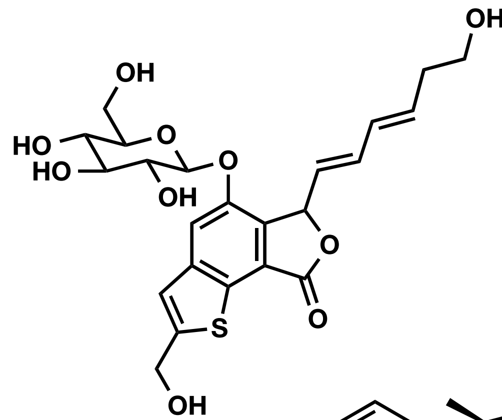
- Most cited papers (section „Total Synthesis“):
  - *Total Synthesis of (+)-Laurencin* (M. T. Crimmins, p. 2029)
    - Number of citations: 93
  - *Asymmetric Total Synthesis of (+)-Dictamnol* (P. A. Wender, p. 137)
    - Number of citations: 87
  - *An Enantioselective Total Synthesis of (+)-Geissoschizine* (S. F. Martin, p. 79)
    - Number of citations: 64

- Scopus / SciFinder

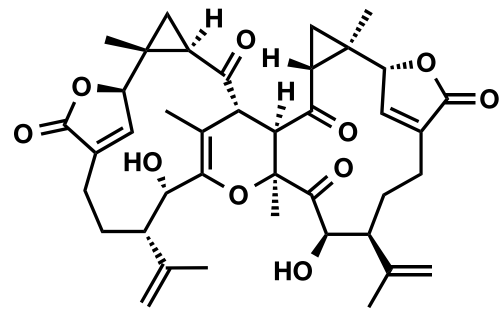
Isolated Natural Products



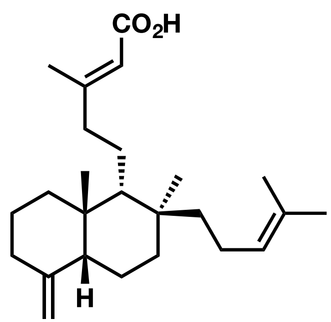
staminolactone A (**1**)



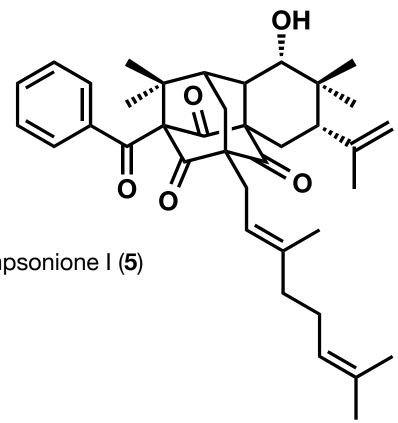
echinothiophene (**4**)



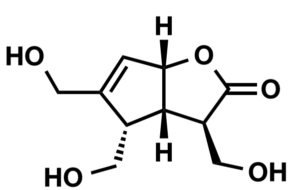
bisgersolanolide (**6**)



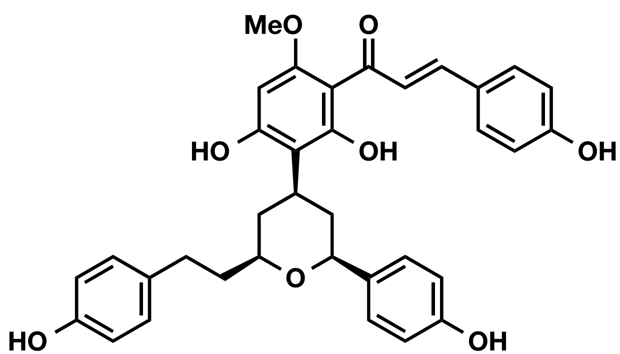
bilosespen A (**2**)
(synthesis: *Org. Lett.* **2003**, *5*, 4741–4743)



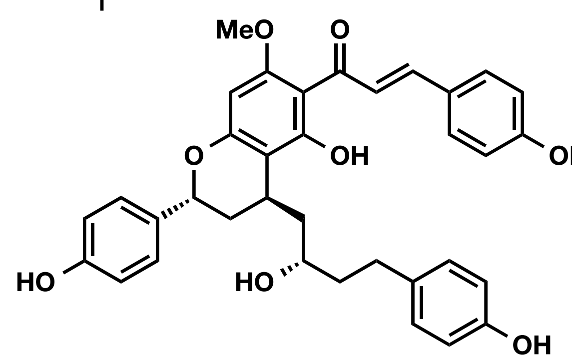
sampsonione I (**5**)



borreriagenin (**3**)



epicalyxin F (**7**)



epicalyxin F (**8**)
(revised structure and synthesis: *Org. Lett.* **2007**, *9*, 4955–4958.)

- (i) S. Kadota *Org. Lett.* **1999,** *1*, 1367–1370. (ii) A. D. Rodríguez *Org. Lett.* **1999,** *1*, 337–340. (iii) Y. Kashman *Org. Lett.* **1999,** *1*, 471–472. (iv) K. Y. Sim *Org. Lett.* **1999,** *1*, 879–882. (v) J. Schripsema *Org. Lett.* **1999,** *1*, 1169–1171. (vi) T. Nikaoido *Org. Lett.* **1999,** *1*, 197–198. (vii) S. Kadota *Org. Lett.* **1999,** *1*, 1733–1736.

Selected Detailed Syntheses

(+)-Dictamnol — Wender

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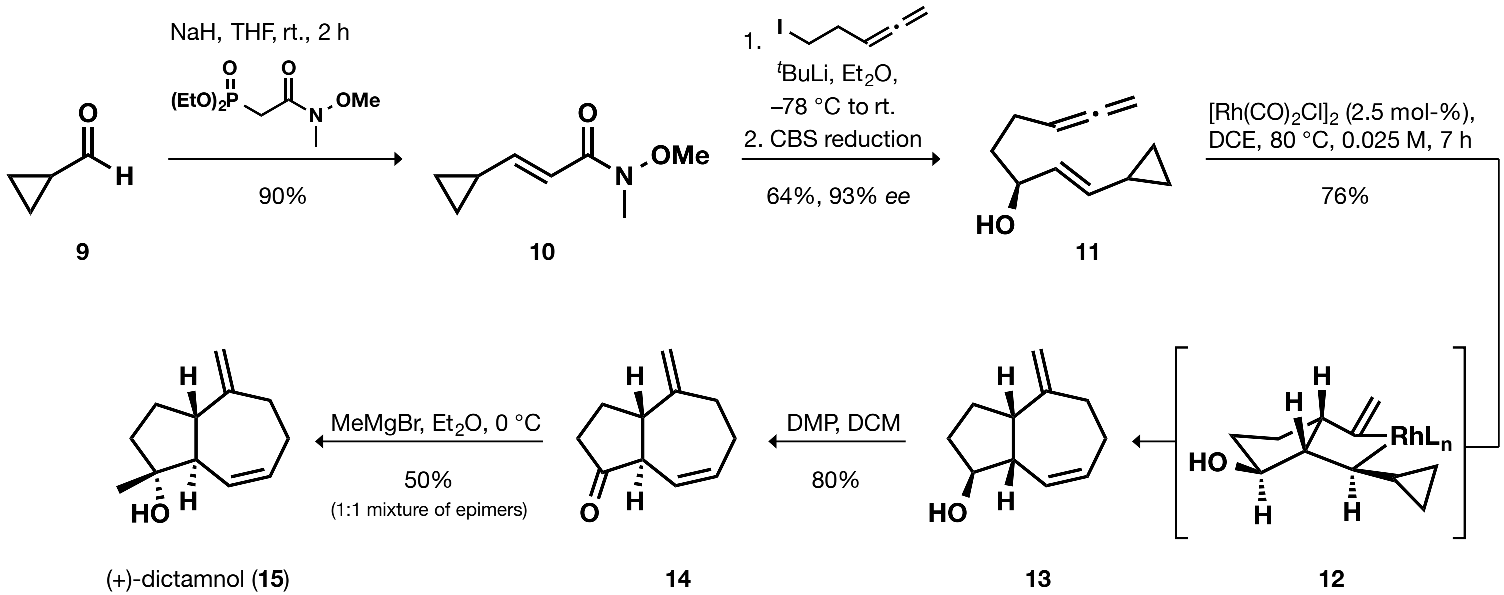
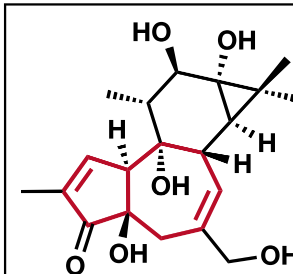


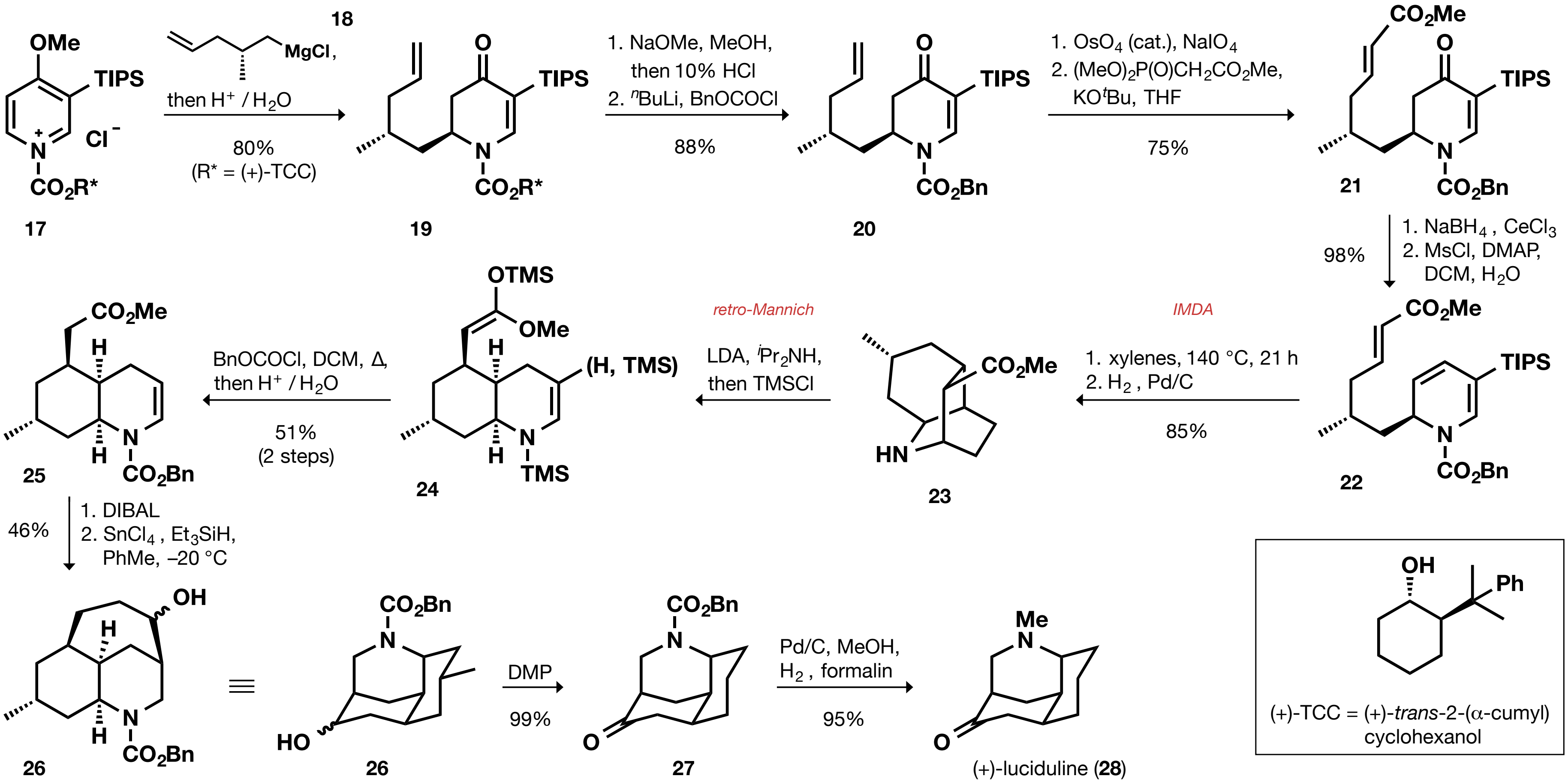
- Key features:
  - concise synthesis, 6 steps, 18% overall yield (9% pure epimer)
  - fast access to cycloaddition precursor
  - [5+2] cycloaddition
  - asymmetric center is used to control relative stereochemistry during CA process



phorbol (**16**)

- P. A. Wender *Org. Lett.* **1999,** *1*, 137–139.

(+)-Luciduline — Comins



- Key features:
  - concise synthesis, 14 steps, 10% overall yield
  - IMDA–retro-Mannich sequence for the synthesis of *cis*-decahydroquinoline skeleton

- D. L. Comins *Org. Lett.* **1999,** *1*, 229–231.

(±)-Culmorin — Takasu

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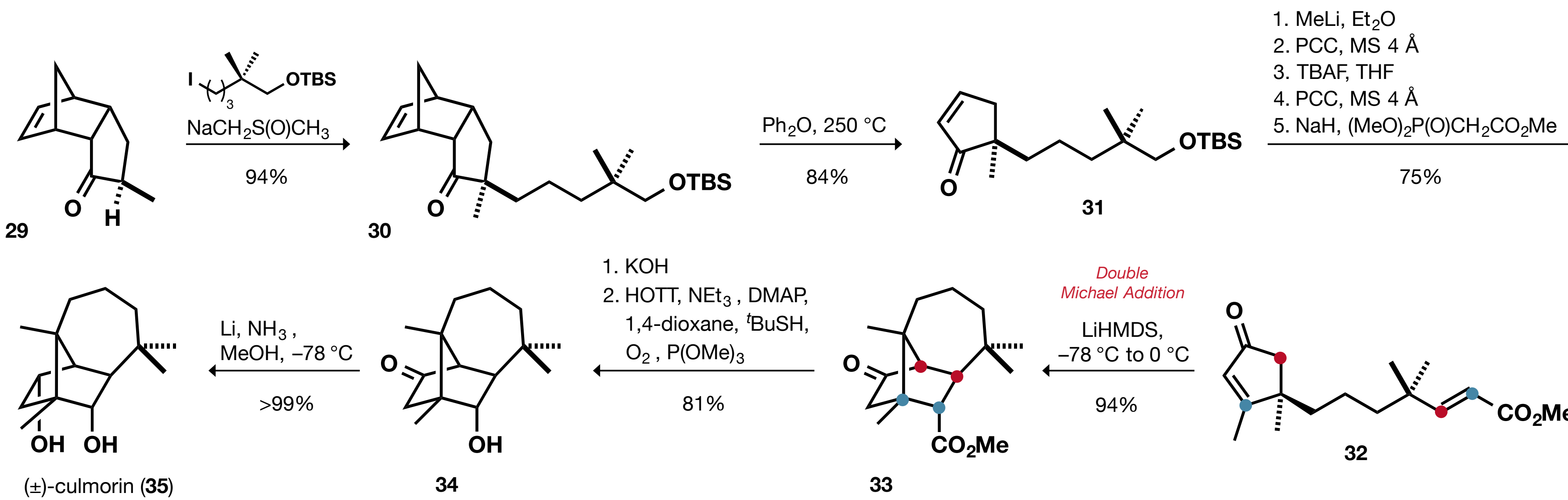
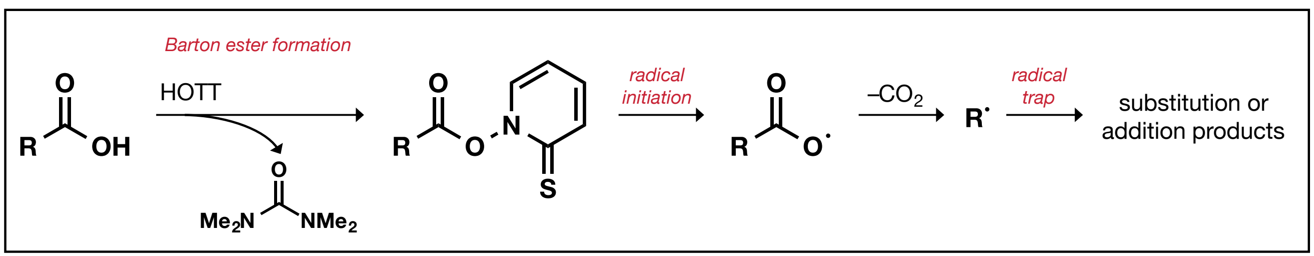
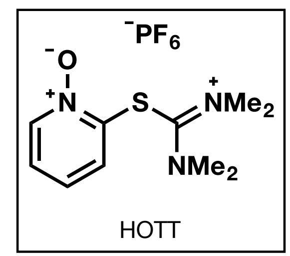


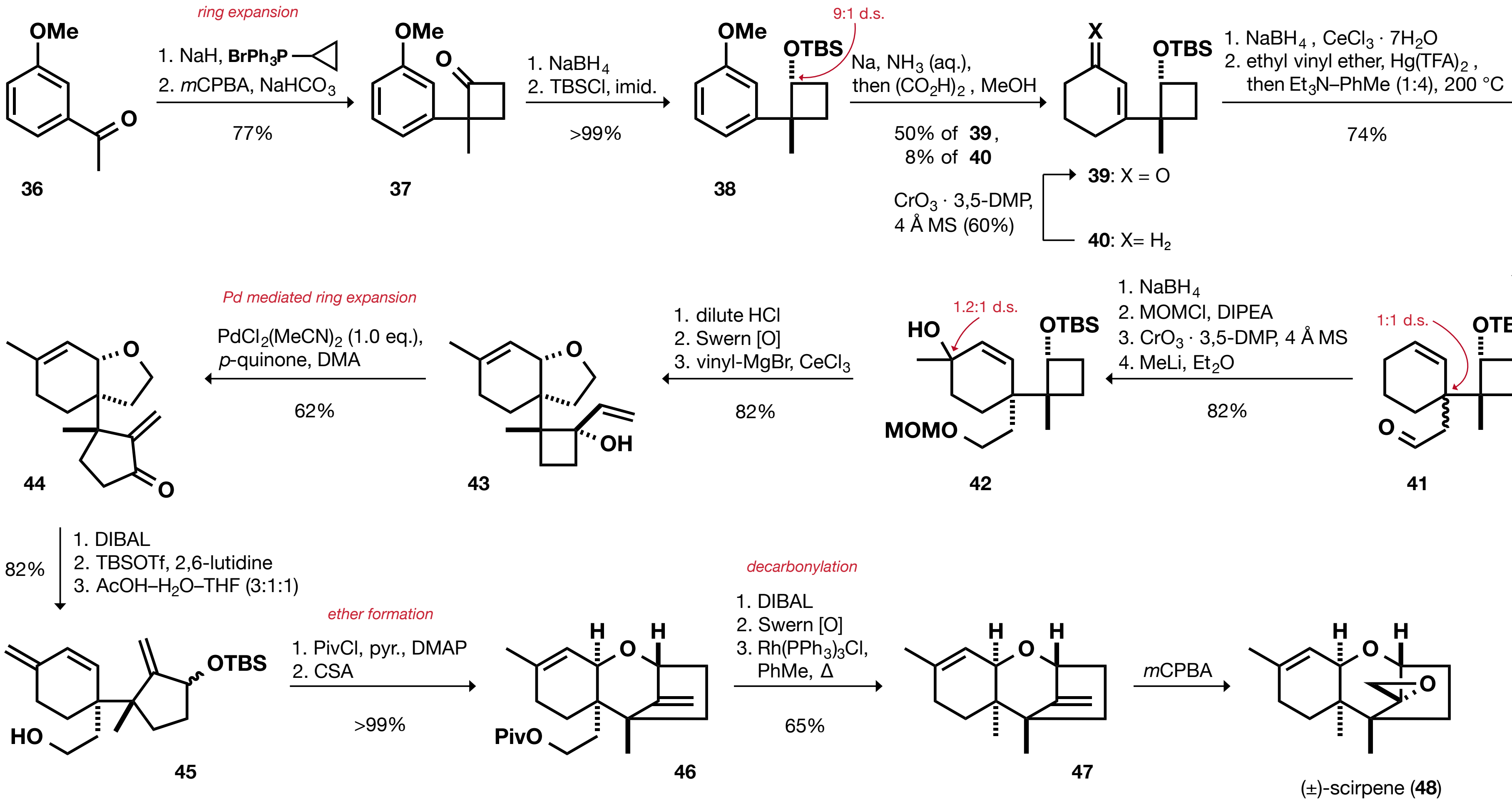




- Key features:
  - 11 steps, 45% overall yield
  - construction of the culmorin framework *via* double Michael addition

- K. Takasu *Org. Lett.* **1999,** *1*, 391–393.

(±)-Scirpene — Nemoto

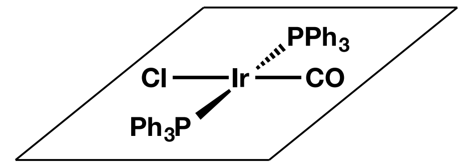


- Features:
    - quite long (maybe overcomplicated?) synthesis, 25 steps, 4% overall yield
    - take-home message: ring-expansions, decarbonylation using Wilkinson's catalyst

- H. Nemoto *Org. Lett.* **1999,** *1*, 517–519.

Excursus: Decarbonylation with $Rh(PPh_3)_3Cl$

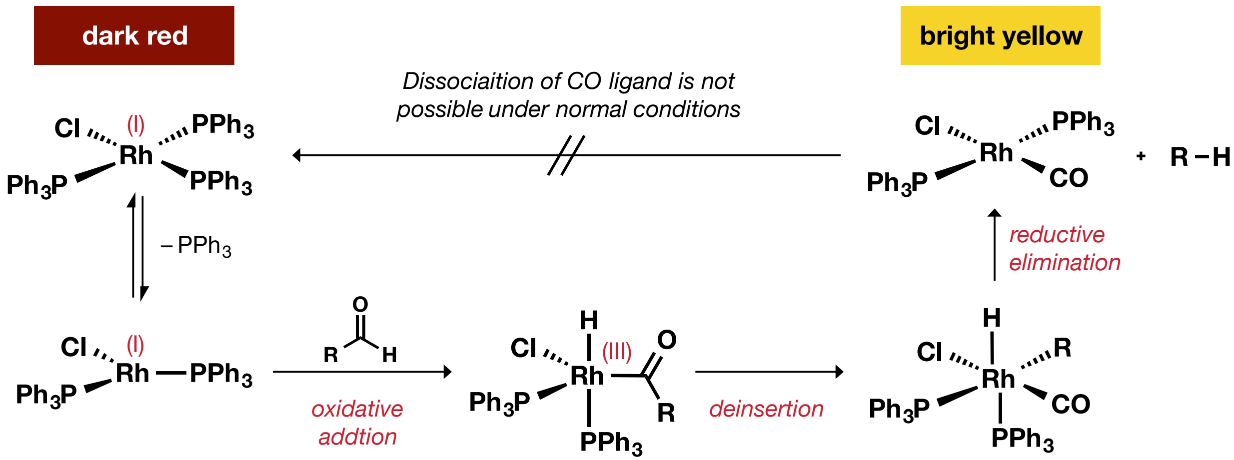
- $Rh(PPh_3)_3Cl$ reacts with CO to give *trans*-$RhCl(CO)(PPh_3)_2$. This complex is structurally analogous to *Vaska's complex*, but much less reactive.



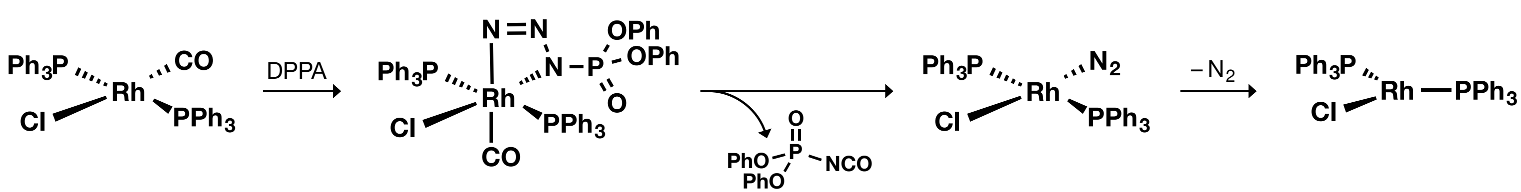
Vaska's complex

- The same complex arises from the decarbonylation of aldehydes.

- The process is non-catalytic → stoichiometric amounts of the complex is required



- Catalytic cycle possible by addition of stoichiometric amounts of DPPA.



(±)-Catharanthine — Fukuyama

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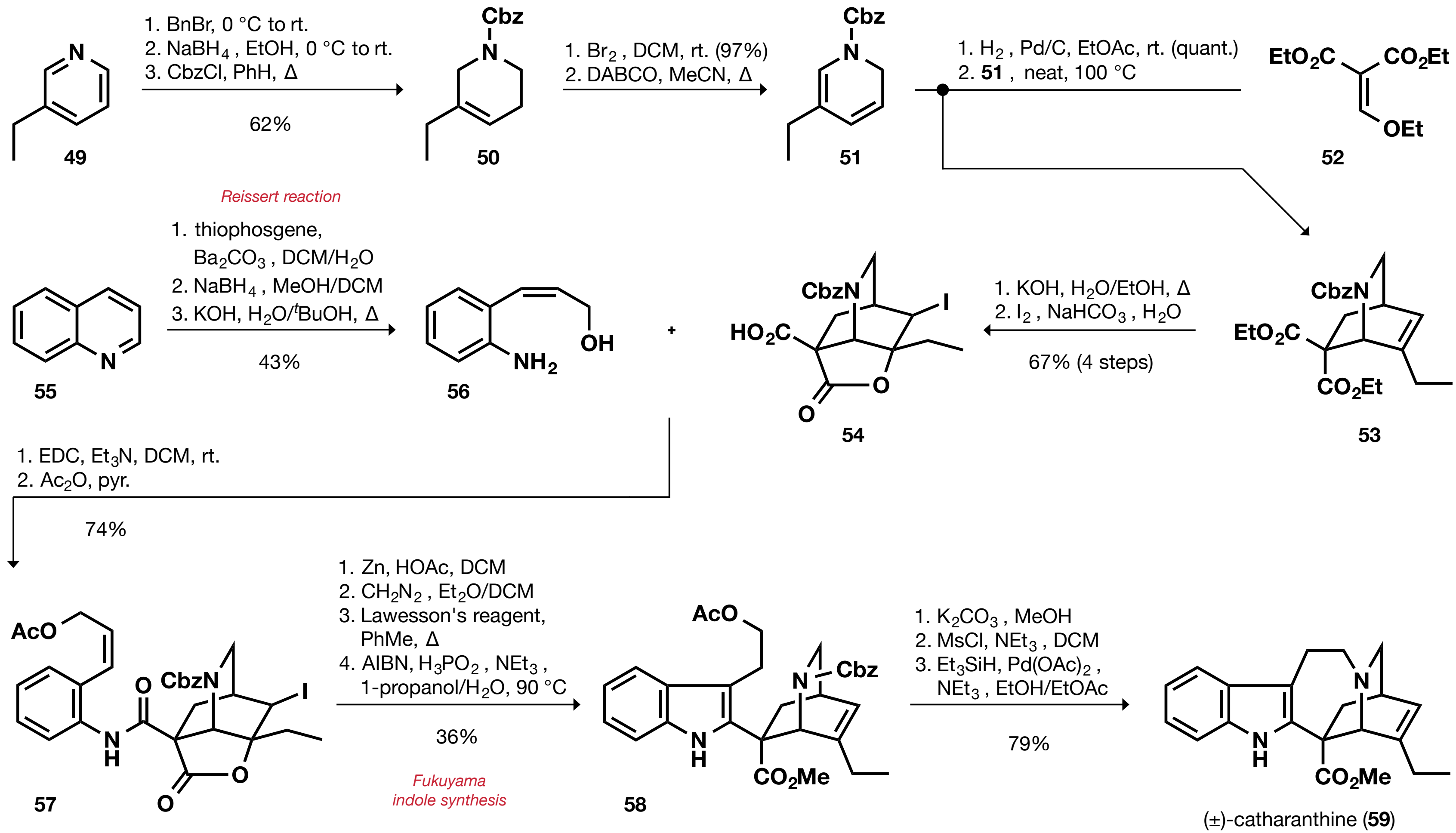
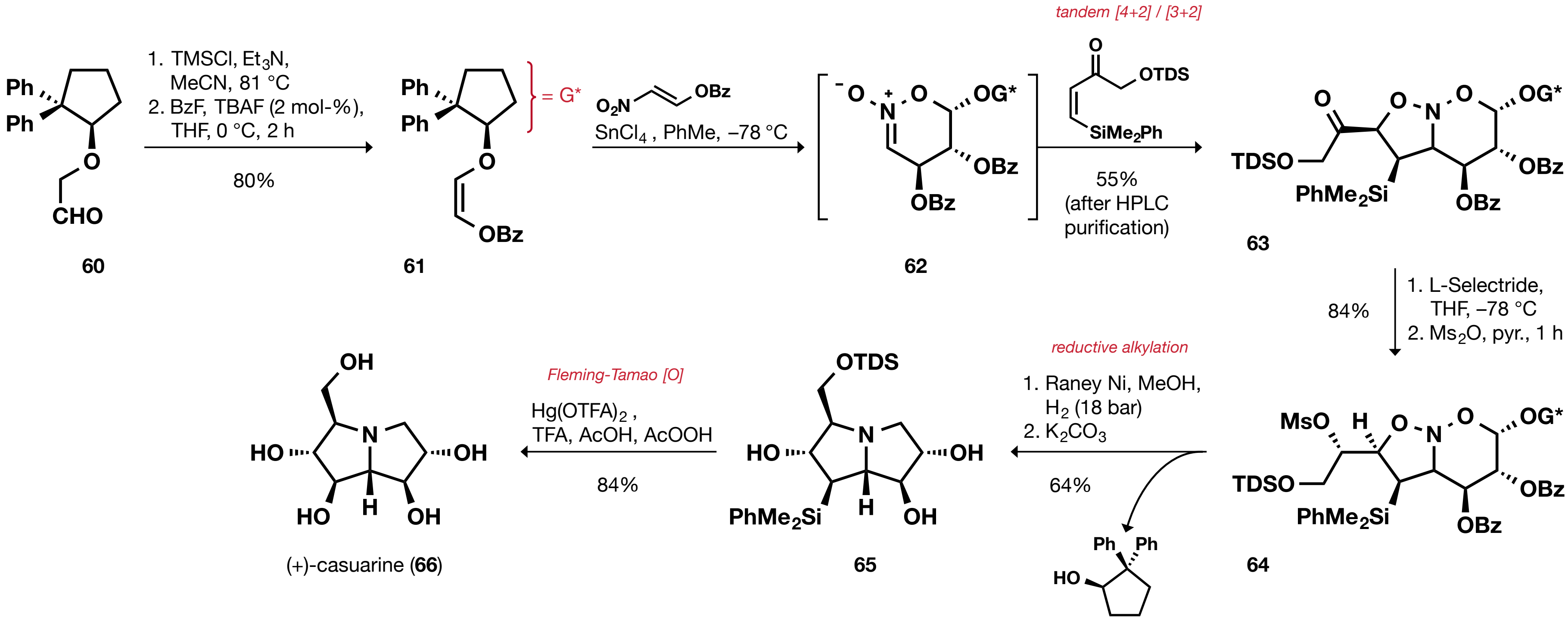


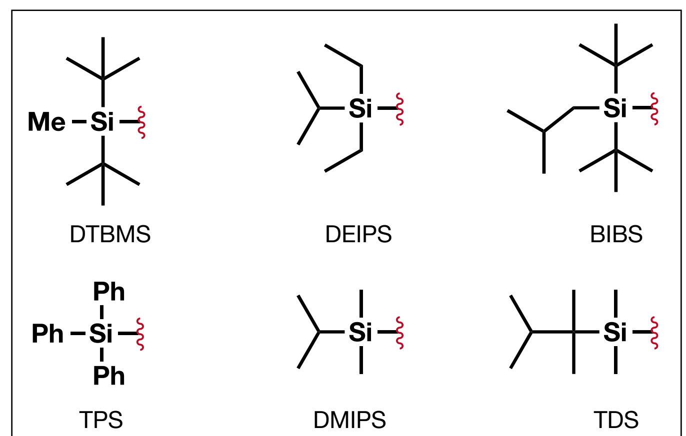
- Key features:
  - convergent synthesis, 17 steps (longest linear sequence), 8% overall yield
  - take-home message: formation of 1,2-dihydropyridine, Reissert reaction, indole synth.

- T. Fukuyama *Org. Lett.* **1999,** *1*, 973–976.

(+)-Casuarine — Denmark

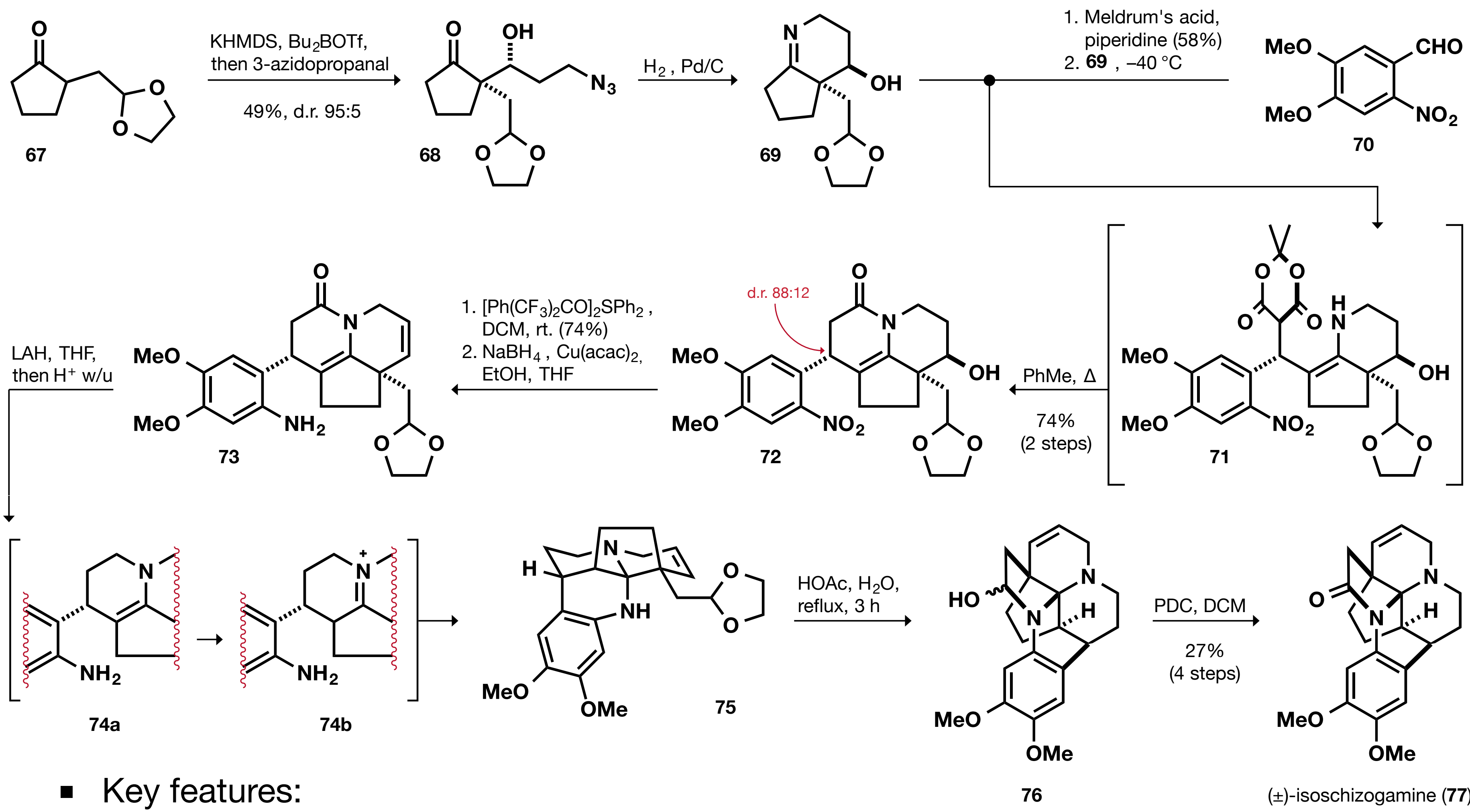


- Key features:
  - 8 steps, 20% overall yield
  - tandem [4+2] / [3+2] nitroalkene cycloaddition → creates 5 of 6 stereocenters present in the molecule
  - reductive alkylation with Raney Ni
  - Fleming–Tamao oxidation



- S. E. Denmark *Org. Lett.* **1999,** *1*, 1311–1314.

(±)-Isoschizogamine — Heathcock

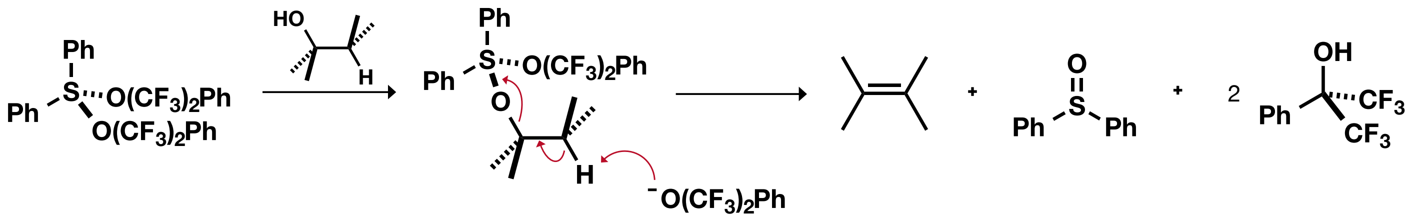


- Key features:
  - convergent synthesis, 8 steps (longest linear sequence), 7% overall yield
  - take-home message: cyclizations, dehydration, clever use of Meldrum's acid

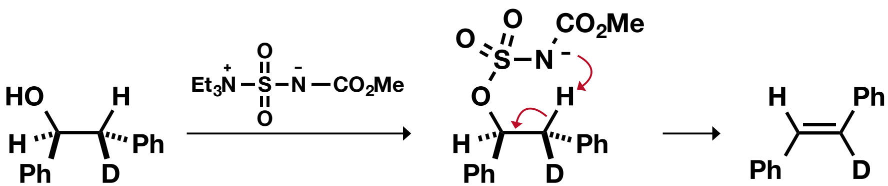
- H. Heathcock *Org. Lett.* **1999,** *1*, 1315–1317.

Excursus: Dehydrating Reagents

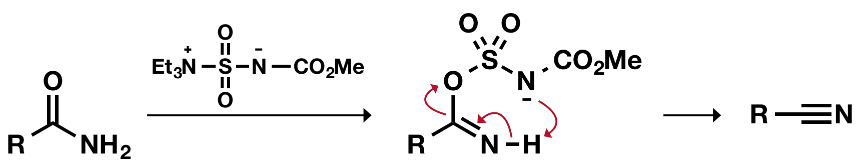
- **Martin's sulfurane**
  - dehydrates 2° and 3° alcohols to give olefins, *anti*-elimination



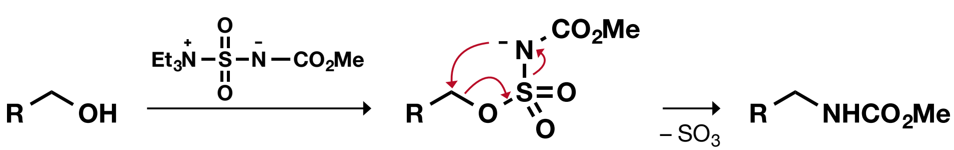
- **Burgess reagent**
  - dehydration of 2° and 3° alcohols, usually proceeds *via* a *syn*-elimination



  - dehydration of amides to nitriles

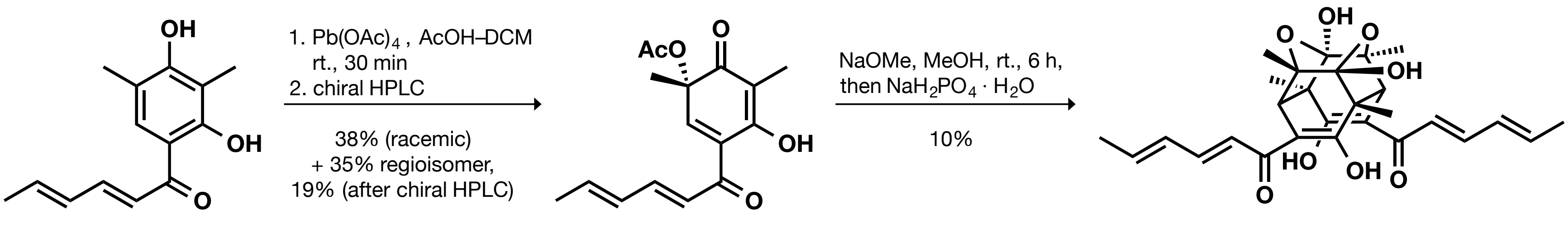


  - conversion of 1° alcohols to carbamates

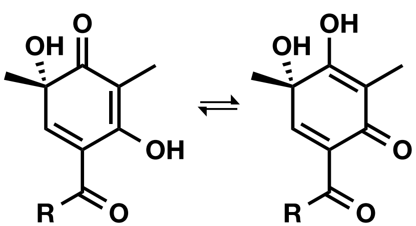


- J. J. Li *Name Reactions* **2009**, Springer Verlag Berlin, 339–340.
- K. C. Nicolaou *Chem. Eur. J.* **2004**, *19*, 5581–5606.

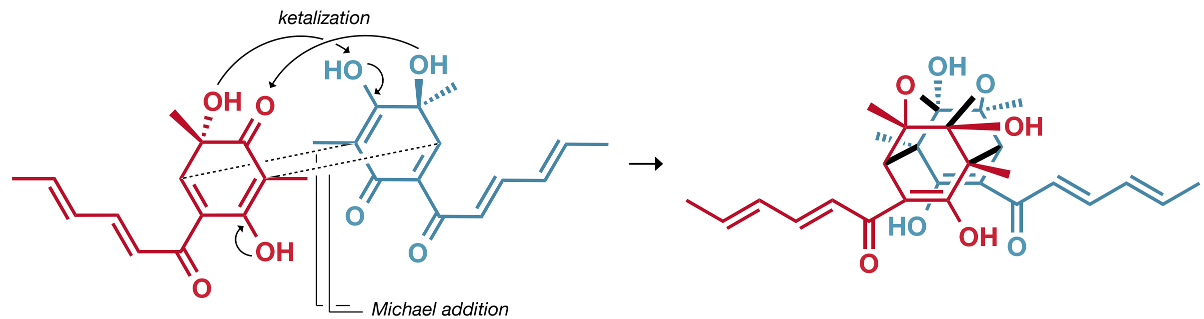
(–)-Trichodimerol — Corey



sorbicillin (**78**) **79** (–)-trichodimerol (**80**)

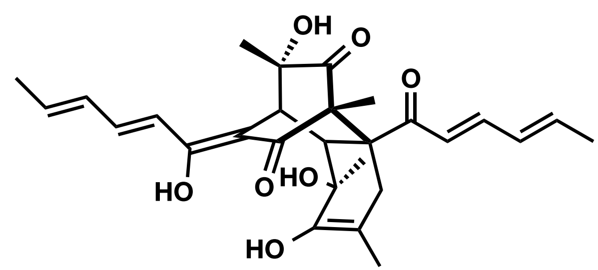


81 **82**



- Key features:
  - biomimetic 2-step-synthesis
  - cascades

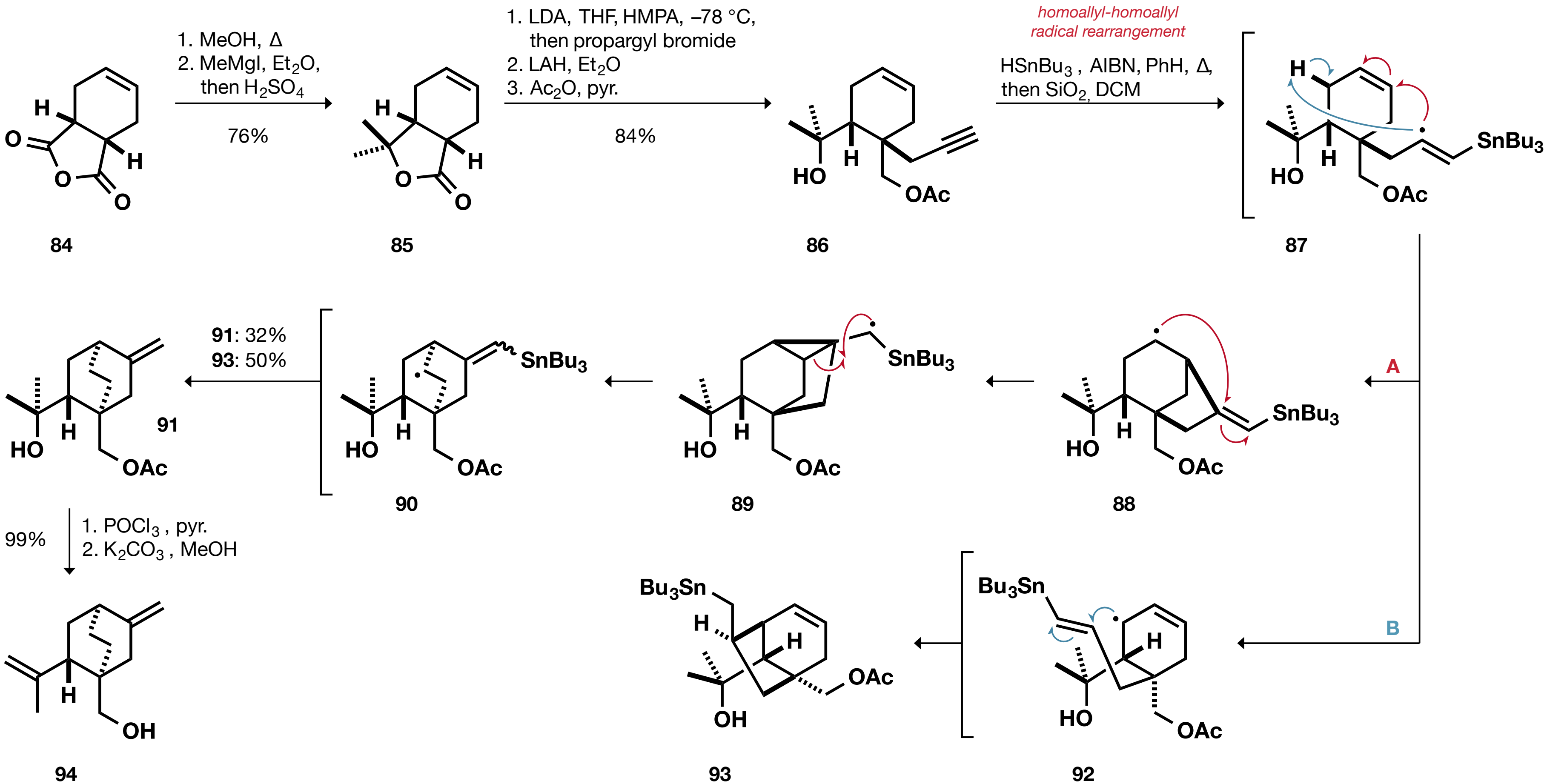
By-product *via* Diels-Alder reaction



(–)-bisorbicillinol (**83**)

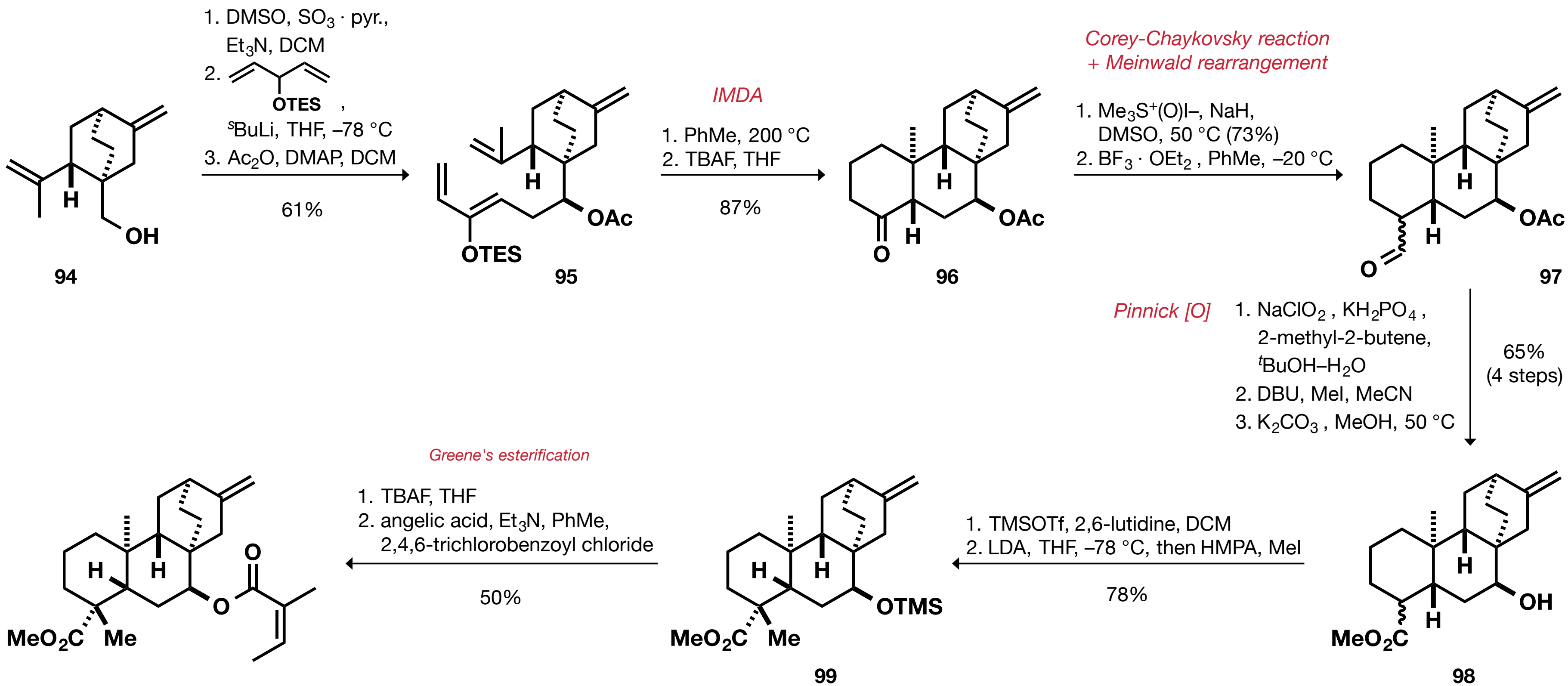
- E. J. Corey *Org. Lett.* **1999,** *1*, 1503–1504.
- K. C. Nicolaou *J. Am. Chem. Soc.* **2000**, *122* (13), 3071–3079.

(±)-Methyl Gummiferolate — Toyota (I)



▪ M. Toyota *Org. Lett.* **1999,** *1*, 1627–1629.

(±)-Methyl Gummiferolate — Toyota (II)

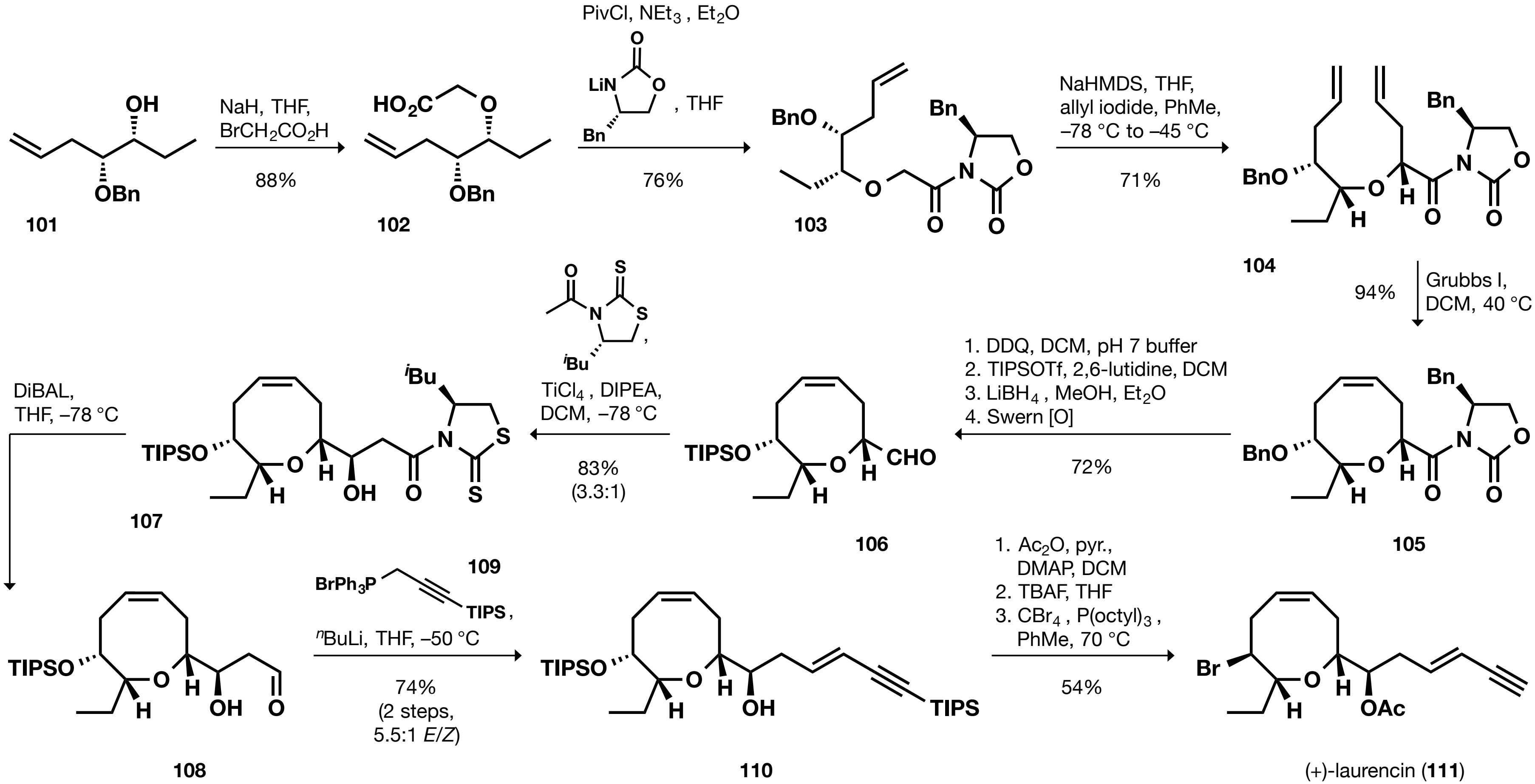


(±)-methyl gummiferolate (**100**)

- Key features:
  - 22 steps, 2% overall yield
  - take-home message: homoallyl-homoallyl radical rearrangement, diene synthesis, C1 elongation *via* Corey-Chaykovsky / Meinwald rearrangement sequence

- M. Toyota *Org. Lett.* **1999,** *1*, 1627–1629.

(+)-Laurencin — Crimmins

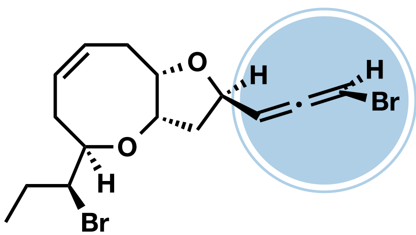


- Features:
  - straightforward synthesis, fast access to oxocene core
  - 14 steps, 8% overall yield

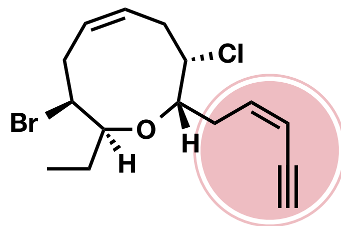
- M. T. Crimmins *Org. Lett.* **1999,** *1*, 2029–2032.

Excursus: Some N. P. From *Laurencia* Species

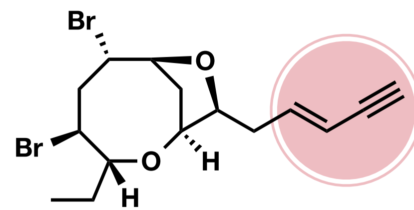
- red algae
- marine organisms that feed on *Laurencia* species have produced a diverse collection of natural products containing medium ring ethers



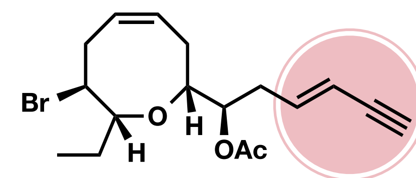
Laurallene (**112**)



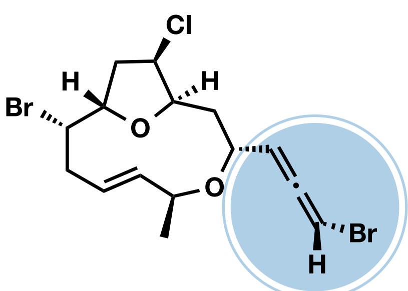
Obtusenyne (**113**)



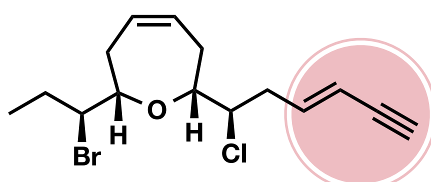
Bromifucin (**114**)



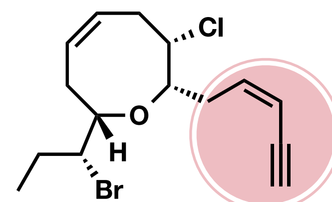
(+)-Laurencin (**115**)



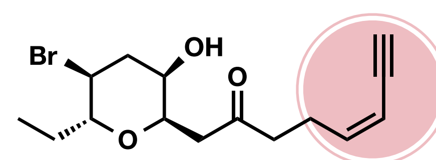
Obtusallene IV (**116**)



(+)-Isolaurepinnacin (**117**)



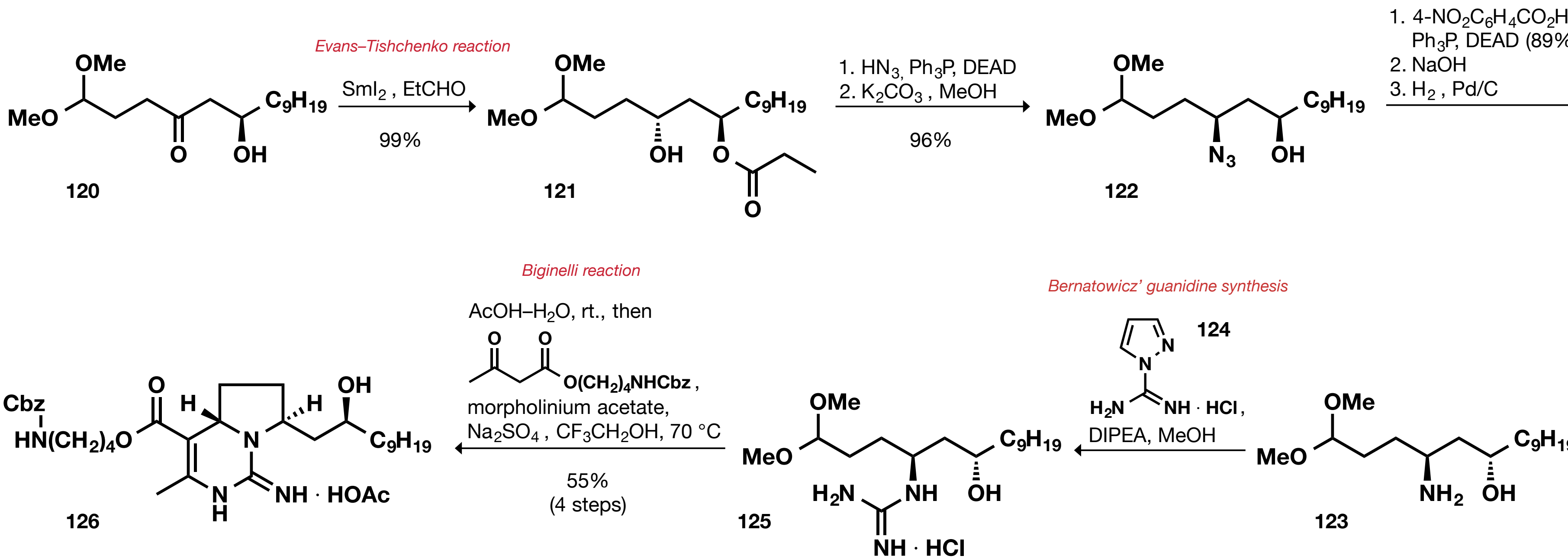
(3*Z*)-13-Epipinnatifidenyne (**118**)

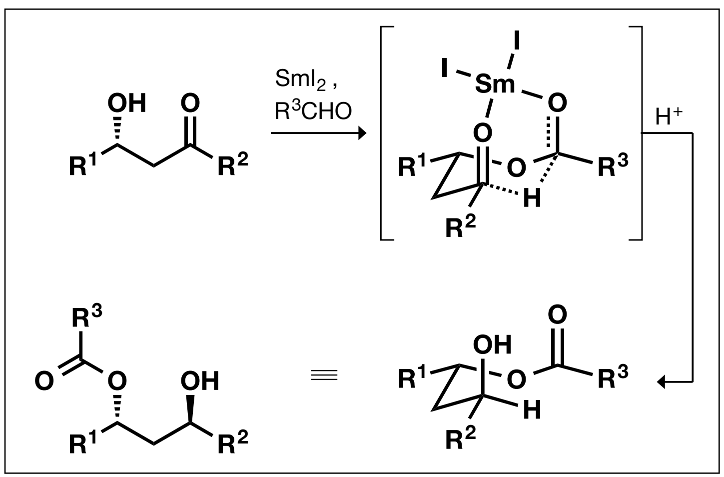


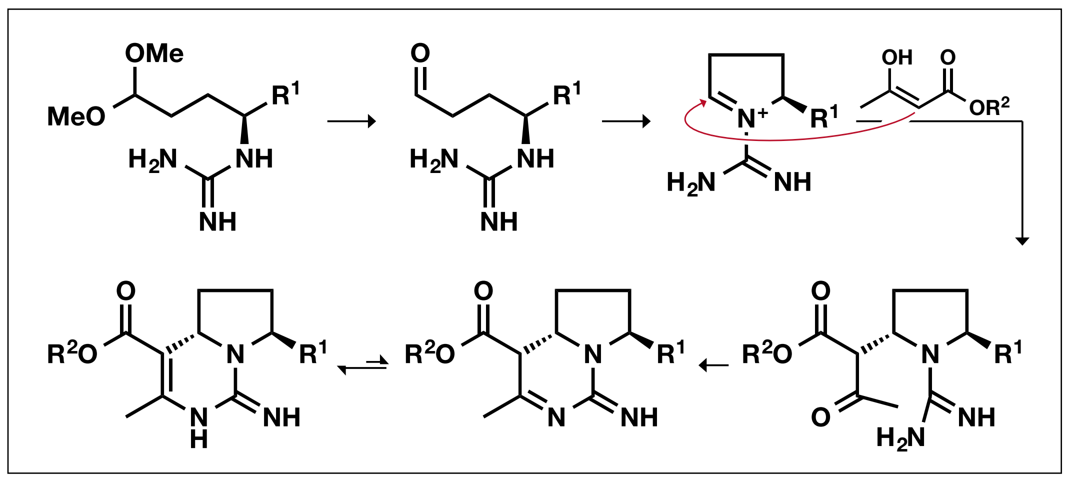
Scanlonenyne (**119**)

- D. J. Faulkner *Nat. Prod. Rep.* **1999**, *16*, 155–198.

(–)-Batzelladine D — Overman (I)

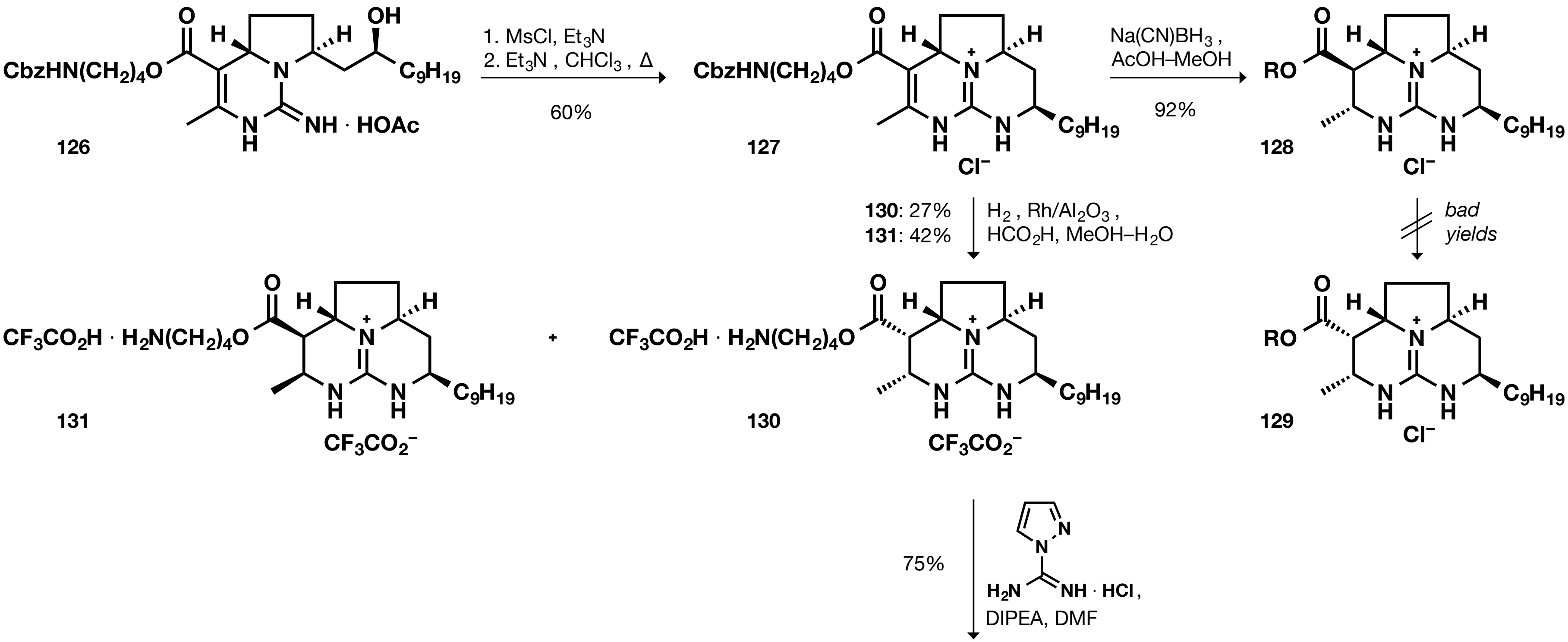




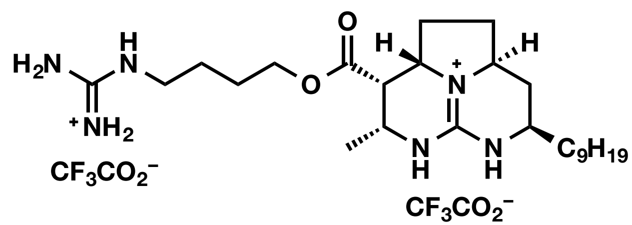


▪ L. E. Overman *Org. Lett.* **1999,** *1*, 2169–2172.

(–)-Batzelladine D — Overman (II)



- Key Features:
  - 13 steps, 6% overall yield
  - Evans-Tishchenko reaction
  - tethered Biginelli condensation
  - guanidine synthesis



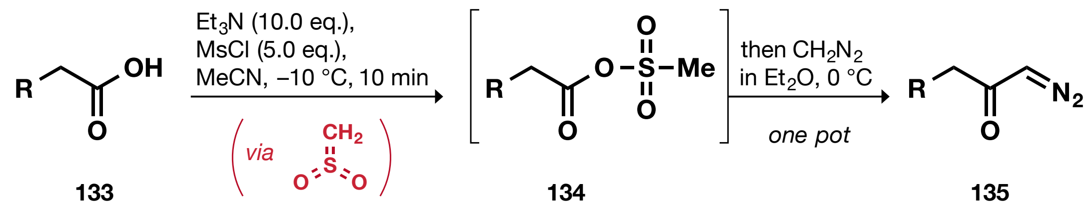
(–)-batzelladine D bistrifluoroacetate (**132**)

Selected Methodologies

Miscellaneous (I)

Synthesis of Hindered α-Diazoketones

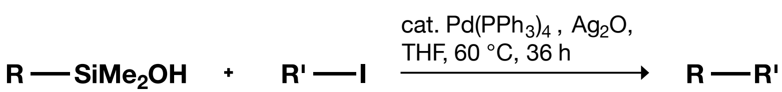
- mild one-pot protocol for the conversion of sterically demanding carboxylic acids into α-diazoketones *via* acyl mesylates



133 134 135

Palladium-Catalyzed Cross-Coupling of Silanols with Organic Halides

- Pd-catalyzed cross-coupling of silanols is achieved by the addition of Ag_2O as an activator

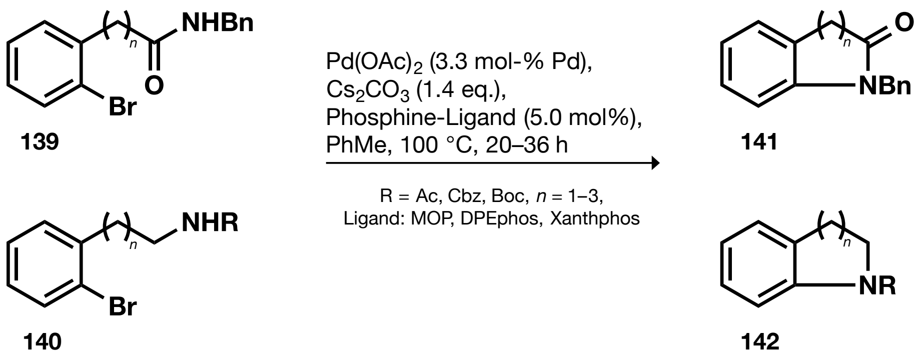


136 137 138

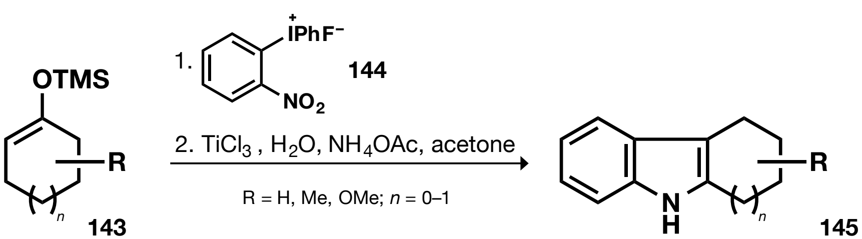
- scope: R and R’ are almost exclusively electron-rich aryl rests

- K. C. Nicolaou *Org. Lett.* **1999**, *1*, 883–886.
- A. Mori *Org. Lett.* **1999**, *1*, 299–301.

Miscellaneous (II)

- **Pd-Catalyzed Cyclization Reactions of Secondary Amides and Carbamates**
  - five-, six-, and seven-membered rings are formed efficiently from secondary amide or secondary carbamate precursors
  - ligands which are capable of chelation (e.g. bisphosphines) are essential
  - 

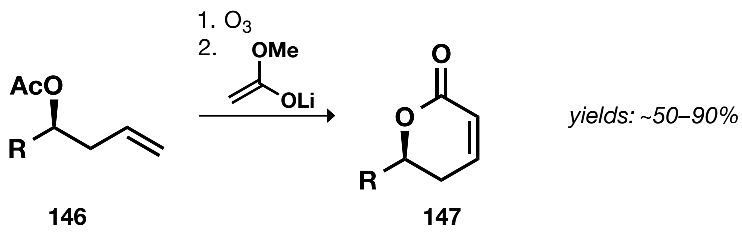
    yields: 79–95%

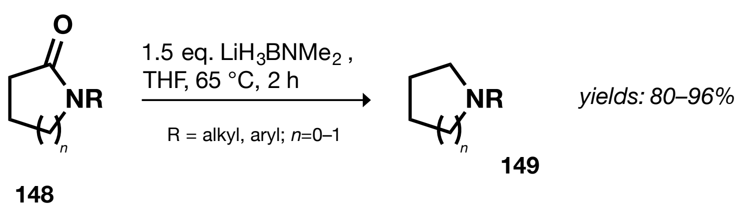
- **Regiocontrolled Synthesis of Carbocycle-Fused Indoles**
  - two-step procedure: 1) regiospecific arylation of silyl enol ether with *o*-$NO_2Ph(IPh)^+F^-$
    2) reduction of the aromatic nitro group with $TiCl_3$ followed by spontaneous aromatization/indolization
  - 

    yields: 60–89%

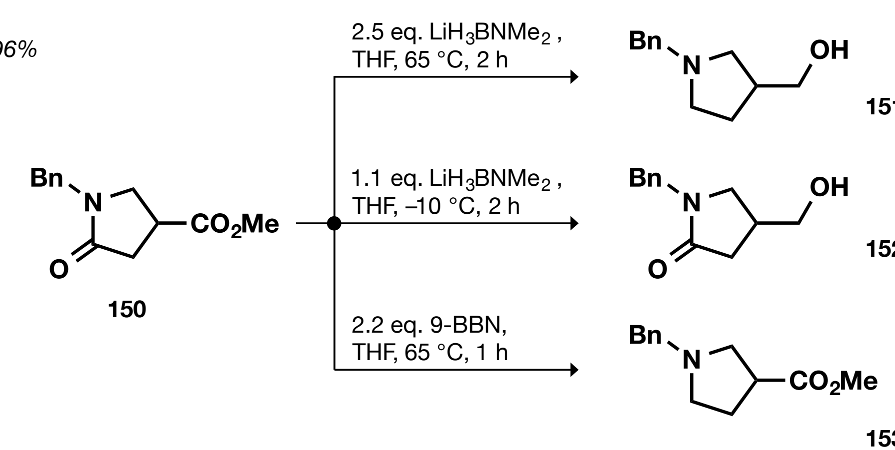
- L. Buchwald *Org. Lett.* **1999**, *1*, 35–37.
- V. H. Rawal *Org. Lett.* **1999**, *1*, 673–676.

Miscellaneous (III)

- **A Versatile Preparation of α,β-Unsaturated Lactones from Homoallylic Alcohols**
  - new method for the one-pot synthesis of α,β-unsaturated lactones from β-acetoxy aldehydes by reaction with the lithium enolate of methyl acetate
  - 

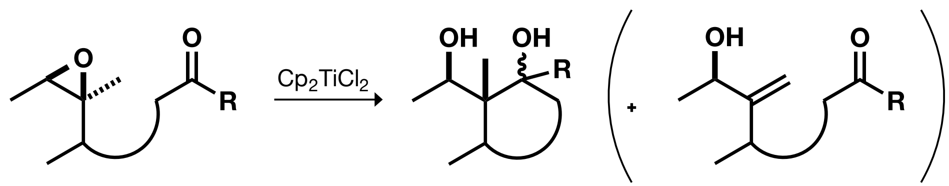
- ***N,N*-Dialkylaminoborohydrides — Facile Reduction of *N*-Alkyl Lactams**
  - five- and six-membered lactams are reduced to the corresponding cyclic amines using lithium dimethylaminoborohydride (LiH_3BNMe_2)
  - 

    - selective reductions:



- G. Keck *Org. Lett.* **1999**, *1*, 411–413.
- B. Singaram *Org. Lett.* **1999**, *1*, 799–801.

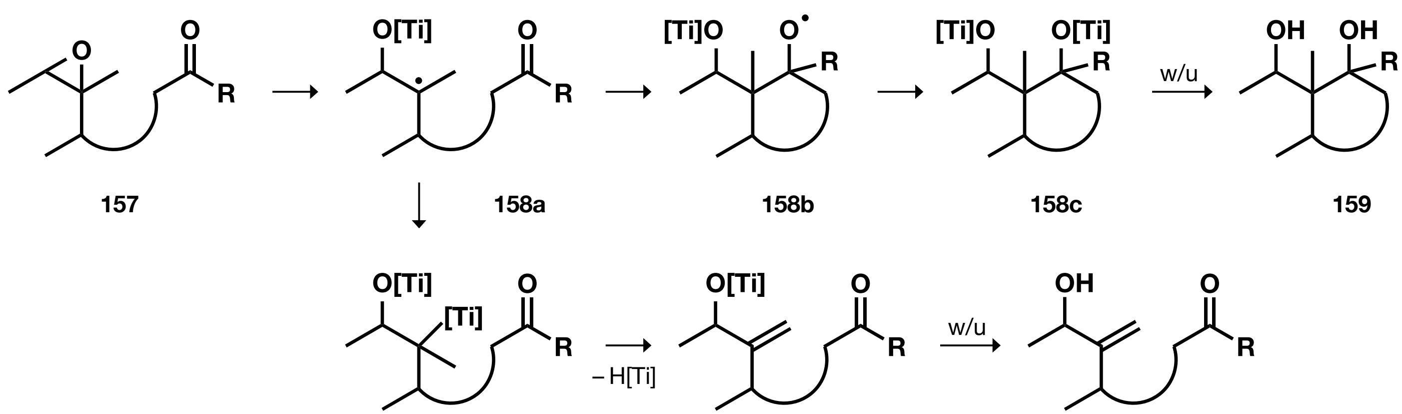
Miscellaneous (IV)

- **Radicals from Epoxides. Intramolecular Addition to Aldehyde and Ketone Carbonyls**
  - Titanocene dichloride reacts with epoxides by C—O homolysis
  - resultant radicals undergo intramolecular addition to aldehydes and ketones to afford cycloalkanols in good yield
  - 

    common minor by-product

    154 155 156

  - mechanism:



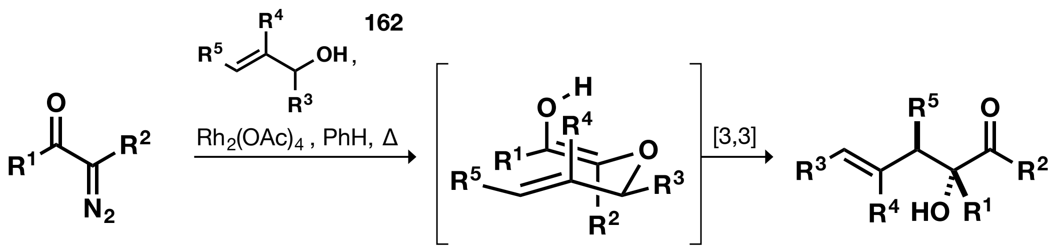
157 158a 158b 158c 159

158d 158e 160

  - comment: small scope, but looks promising with additional optimization work

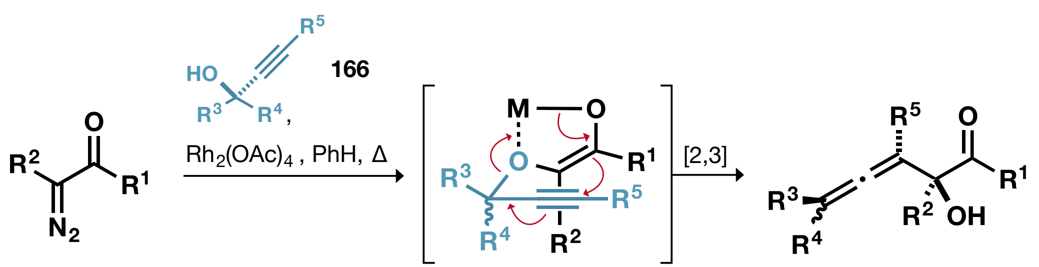
- A. Fernàndez-Mateos *Org. Lett.* **1999**, *1*, 607–609.

Miscellaneous (IV)

- **Rhodium Carbenoid-Initiated Claisen Rearrangement**
  - reaction of α-diazoketones with allylic alcohols in the presence of Rh(II) catalysts
  - intermediate undergoes Claisen rearrangement to furnish α-hydroxyketones
  - 

161 163 164

- **Facile Preparation of Allenic Hydroxyketones**
  - treatment of propargylic alcohols with α-diazoketones in the presence of Rh(II) catalysts yields allenic hydroxyketones
  - mechanistic proposal: intermediate undergoes [2,3]-sigmatropic rearrangement

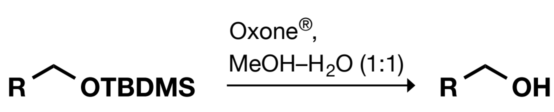


165 167 168

- J. Wood *Org. Lett.* **1999**, *1*, 371–374.
- M. E. Jung *Org. Lett.* **1999**, *1*, 367–369.

A Mild, Efficient, Inexpensive, and Selective Cleavage of Primary TBMDS Ethers by Oxone® in aq. Methanol

- Oxone® in a 50% aqueous methanolic solution cleaves primary alkyl and aryl TBDMS ethers
- high selectivity
  - deprotection of primary TBDMS ethers within few hours
  - secondary, tertiary and phenolic TBDMS ethers are unaffected
  - deprotection of TBDMS ethers possible in the presence of TPDPS ethers and certain acid-labile protecting groups (THP, *N*-Boc, …)
- mild conditions, inexpensive
- mechanism unknown

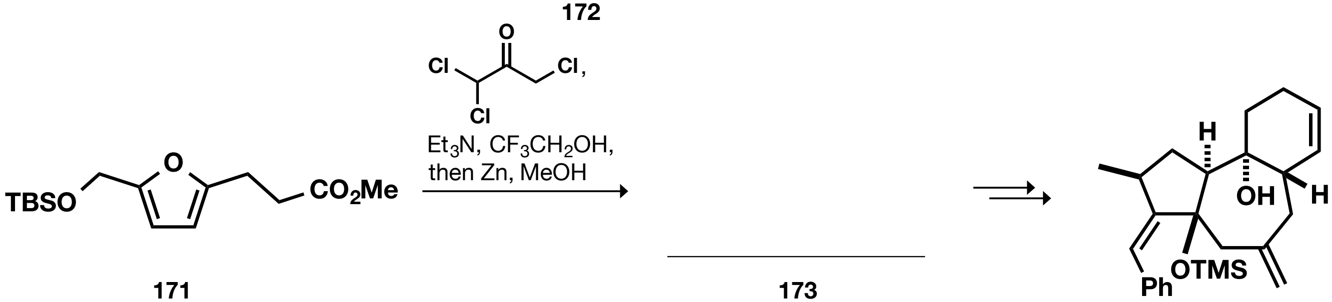


169 **170**

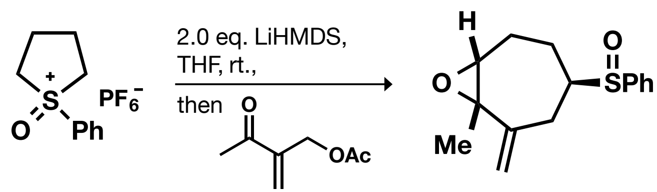
- own experience:
  - full conversion
  - easy handling, no precautions required
  - clean product, no purification necessary
  - *proceeds even faster with ultrasonic!*

- G. Sabitha *Org. Lett.* **1999**, *1*, 1701–1703.

Easy “Denksports”



171 173 174

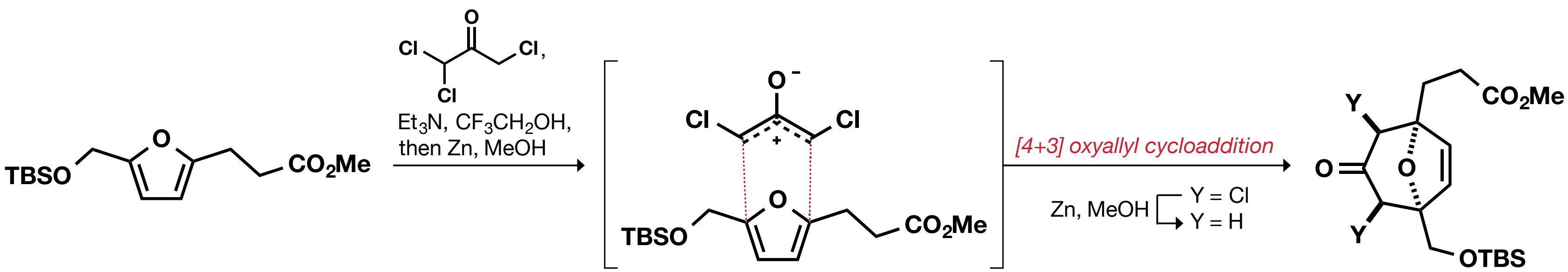


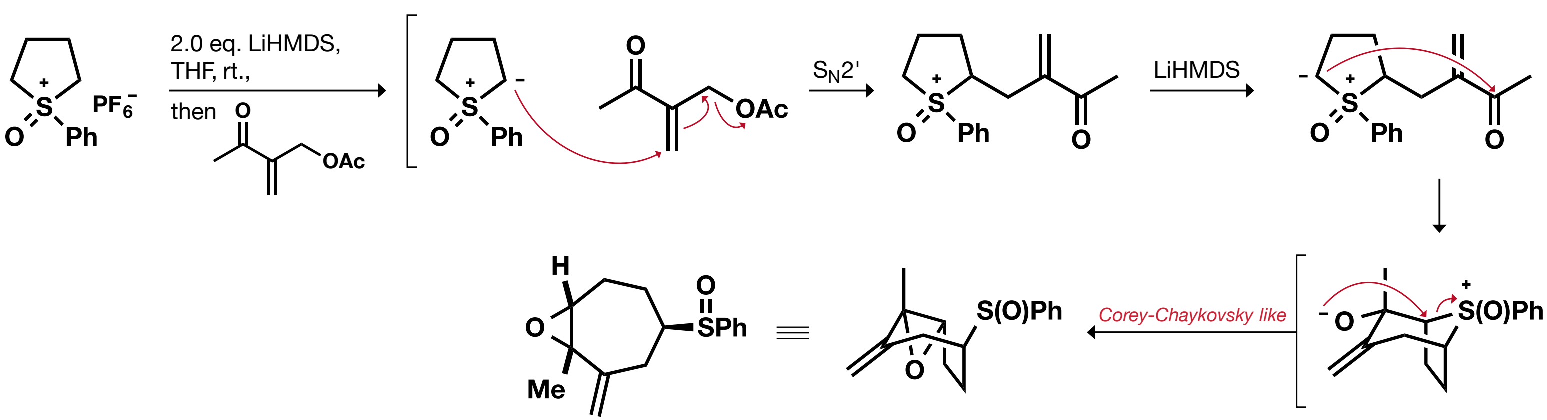
175 176 177

Thanks for your attention.

Questions?

Solutions





- K. Cha *Org. Lett.* **1999**, *1*, 523–525.
- T. Fujimoto *Org. Lett.* **1999**, *1*, 427–430.