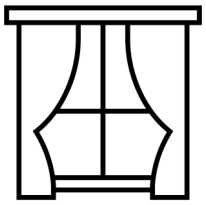
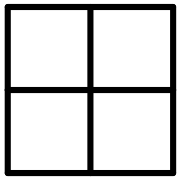




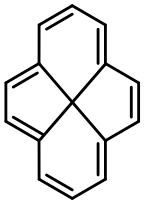
Window

Criteria

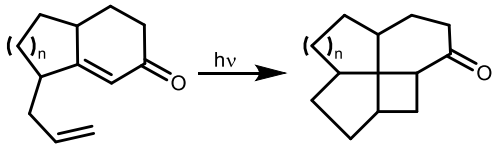
- Cycloalkanes all connected to a common quaternary carbon center
- Each cycloalkane must share three carbons with each neighbor

Origins

- Imagined as a theoretical compound with a planar tetracoordinate carbon (R. Hoffmann, *JACS*, **1970**, *92*, 4992)



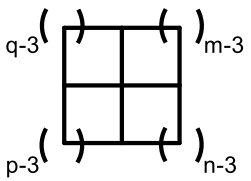
- Georgian and Saltzman synthesized first fenestranes* and coined the phrase (*Tet. Lett.*, **1972**, *42*, 4315)



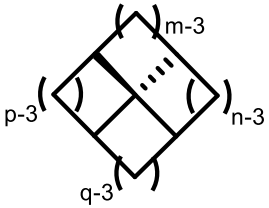
n = 1,2

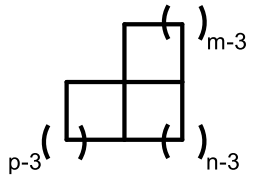
*Technically, only the all cyclobutane case is a true fenestrane, otherwise it's a rosettane

Nomenclature



[m.n.p.q] fenestrane





[m.n.p] fenestrane

Disclaimer

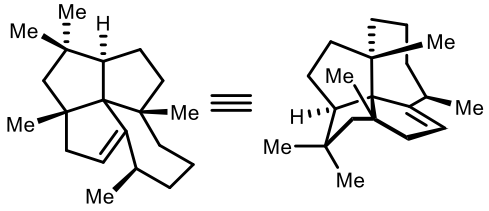
Only [m.n.p.q] fenestrane-bearing *natural products* will be discussed.

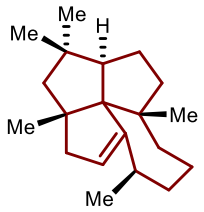
Helpful Reviews

Chem. Rev., **1987**, *87*, 399
Chem. Rev., **2006**, *106*, 4787
Angew. Chem. Int. Ed., **2013**, *52*, 12786
Tet. Lett., **2016**, *57*, 3665

(–)-laurenene

-Isolated in 1979 from the Rimu tree (*D. cupressinum)* (*J. Chem. Soc., Perkins Trans. 1,* **1979**, 1774)





[5.5.5.7] fenestrane

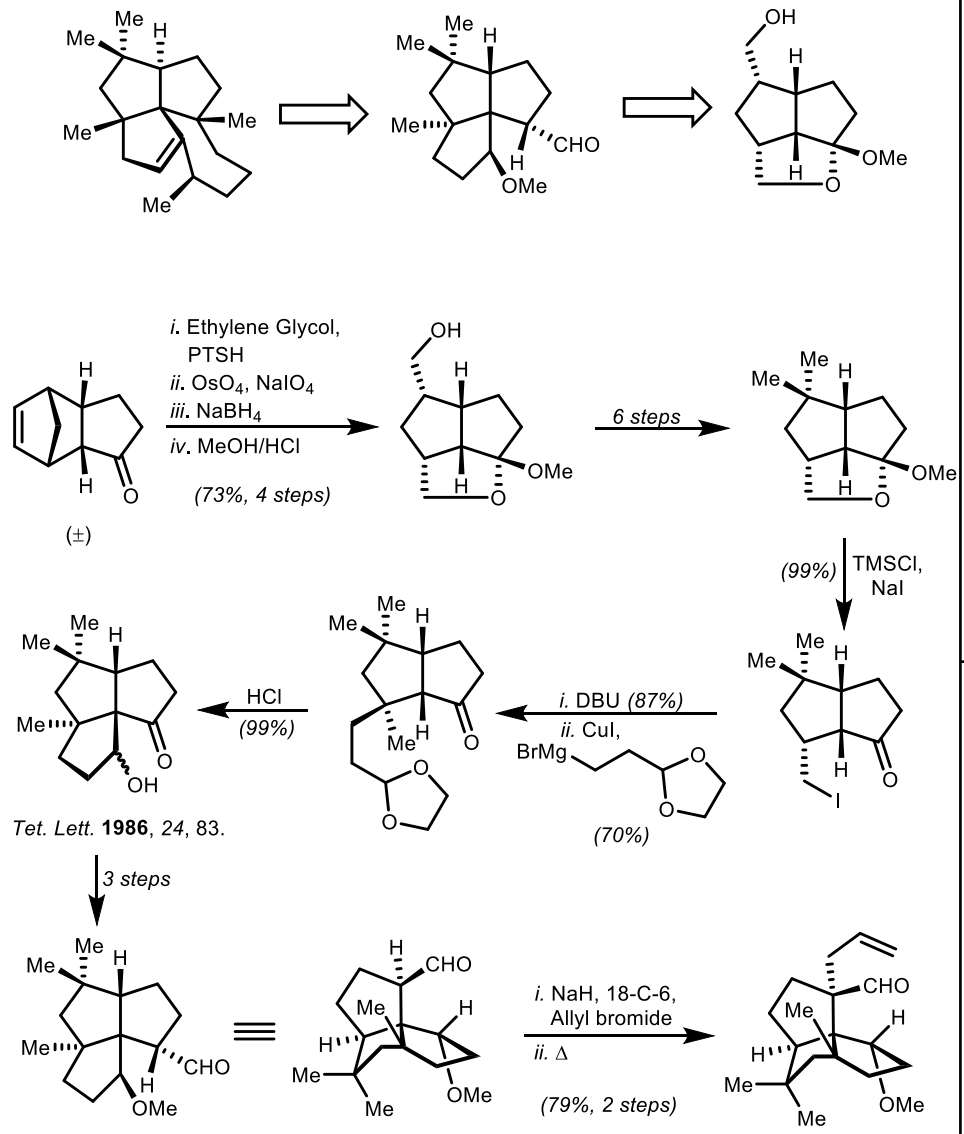
-No known biol. activity
-Only known natural product with an all carbon fenestrane scaffold

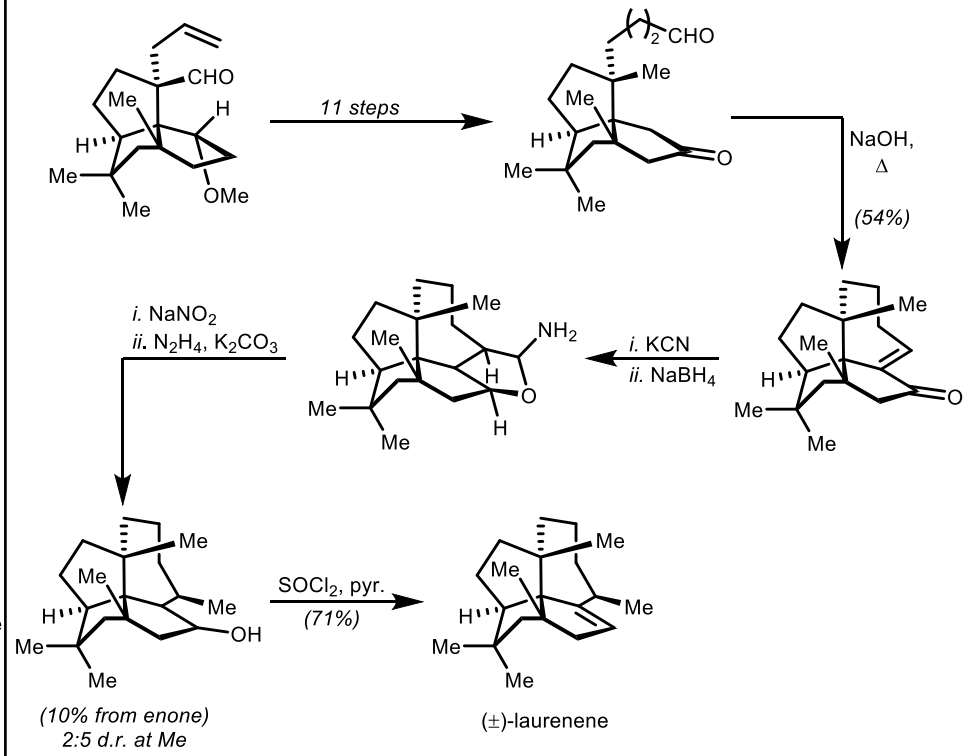
Fenestrane Natural Products

Isaac Falk

Ito et al., 1987

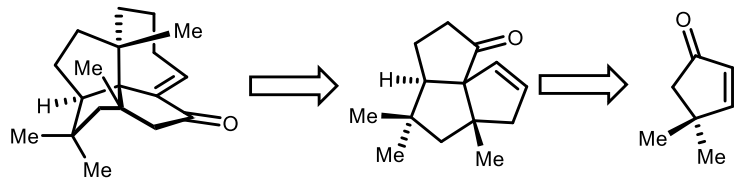
Tet. Lett., **1987**, *28*, 2537.





Paquette et al., 1988

J. Org. Chem., **1998**, *53*, 477.

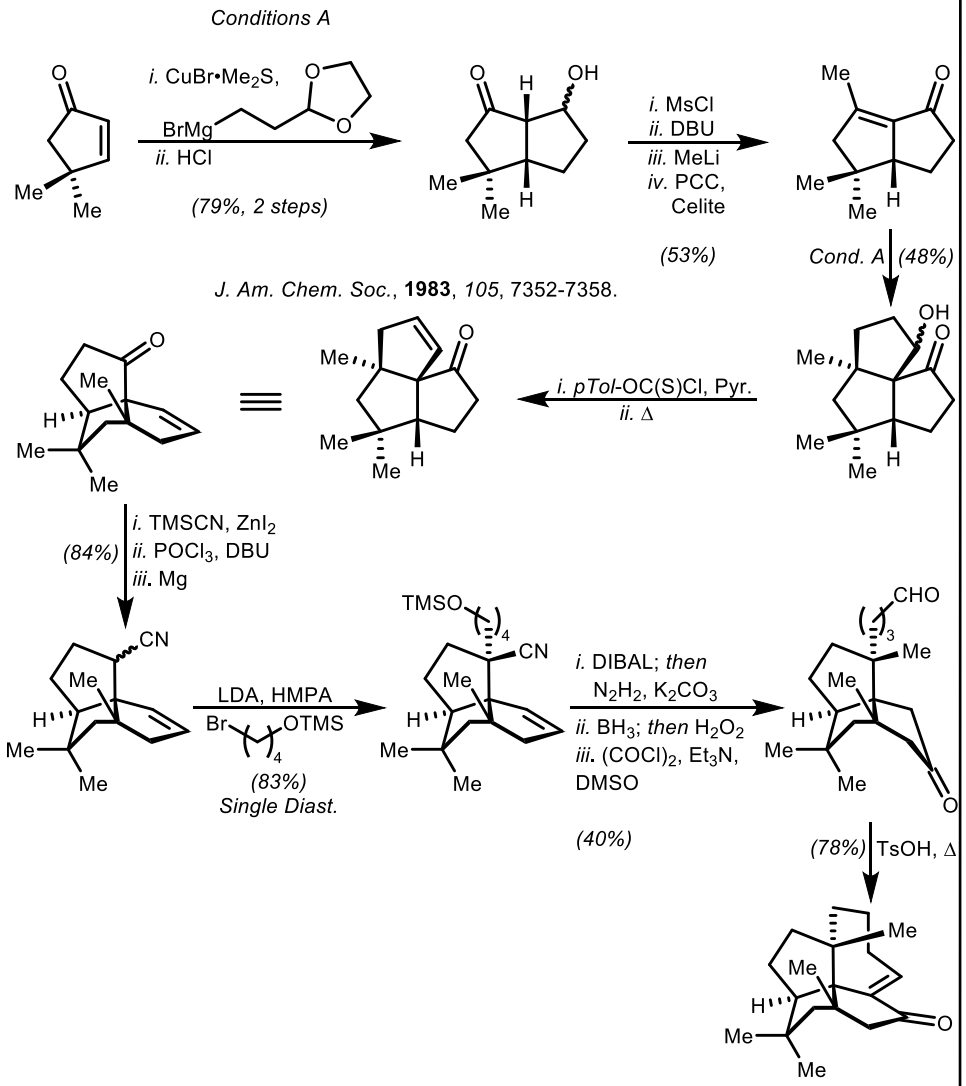


Fenestrane Natural Products

Isaac Falk

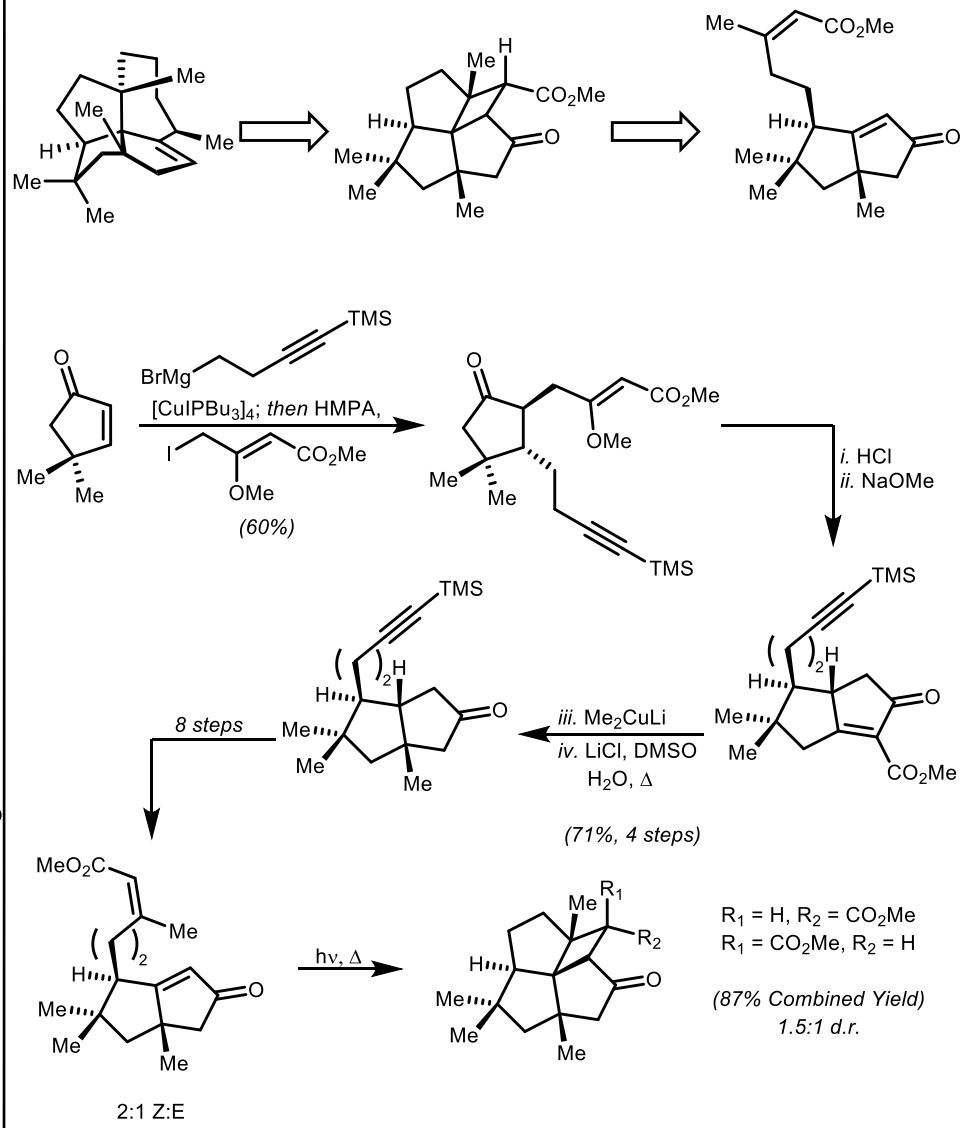
Paquette et al., 1988

J. Org. Chem., **1988,** *53*, 477-481.



Crimmins et al., 1987

J. Am. Chem. Soc., **1987**, *109*, 6199-6200.

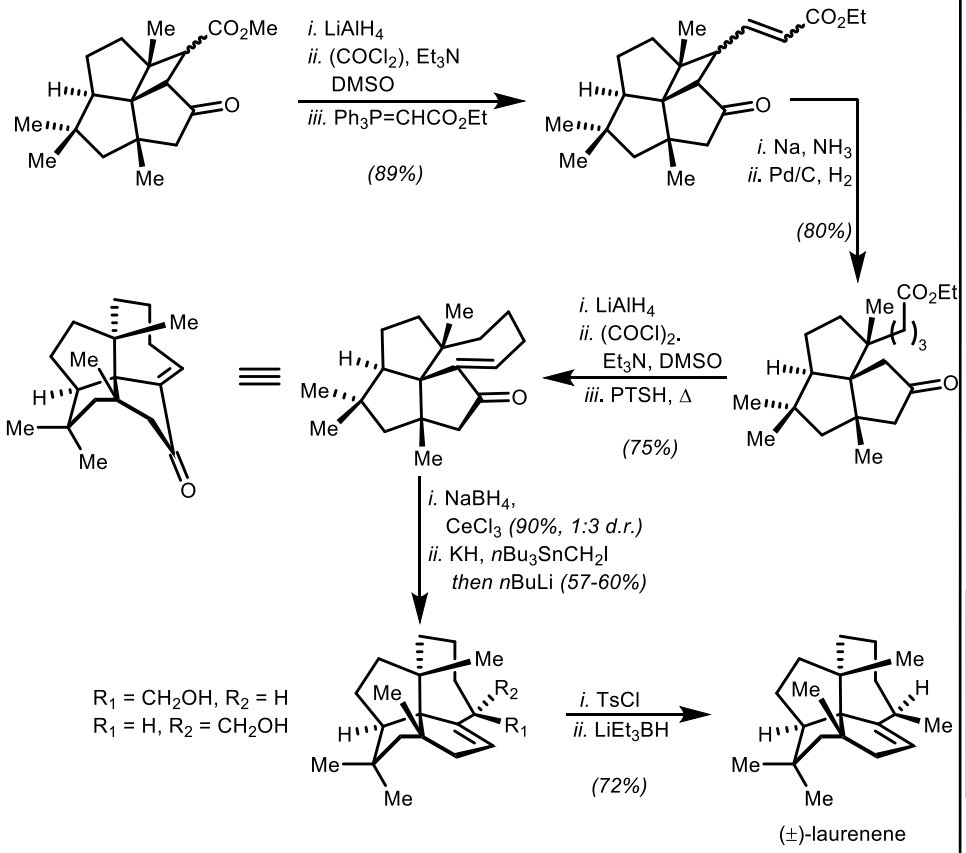


Fenestrane Natural Products

Isaac Falk

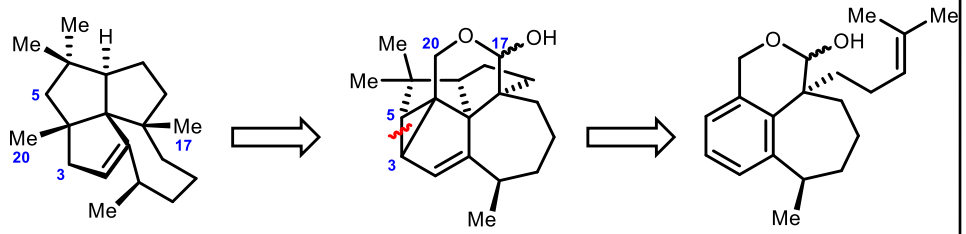
Crimmins et al., 1987

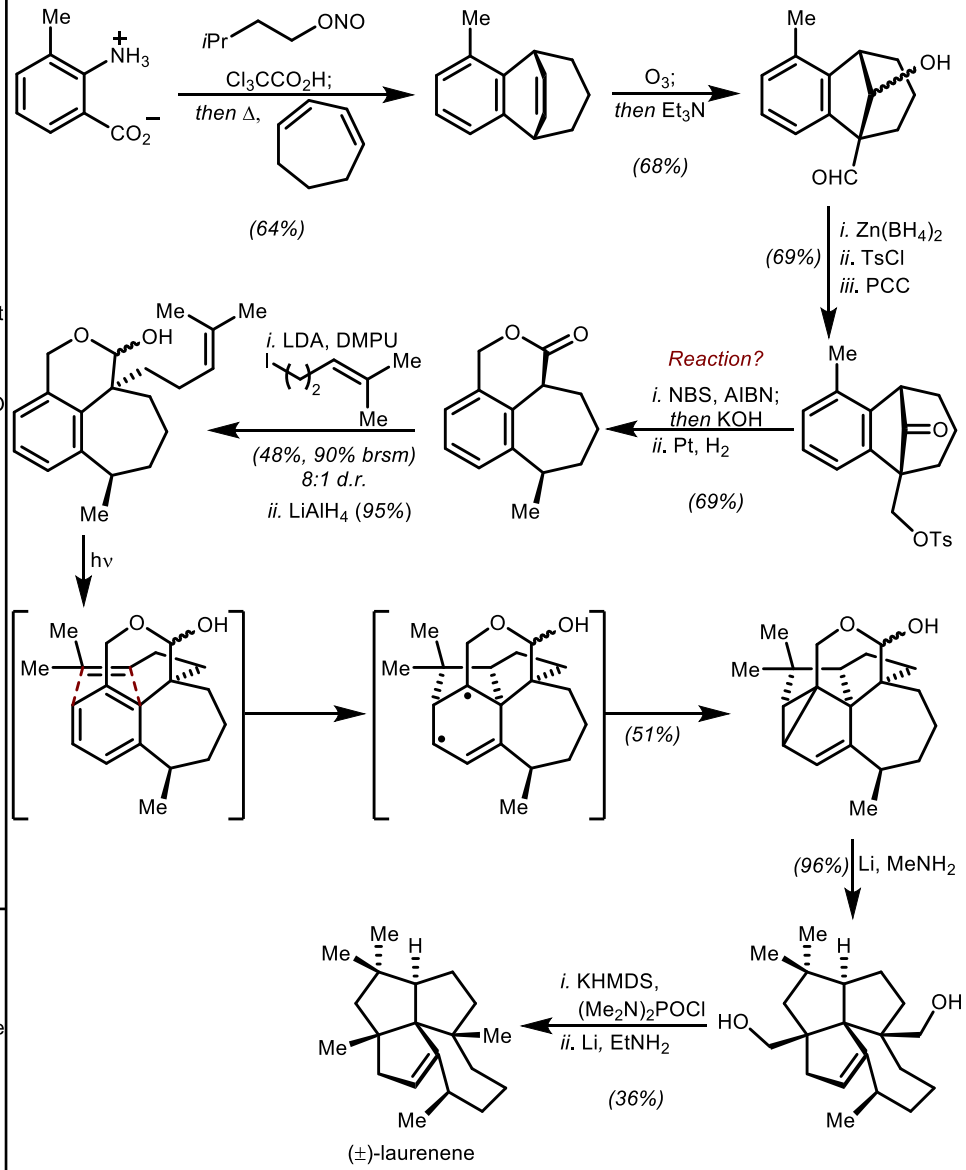
J. Am. Chem. Soc., **1987**, *109*, 6199-6200.



Wender et al., 1988

J. Am. Chem. Soc., **1988**, *110*, 4858-4860.

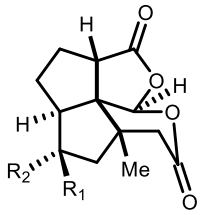




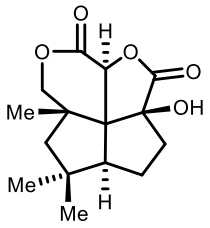
Fenestrane Natural Products

Isaac Falk

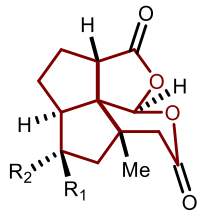
Dioxafenestranes



(–)-penifulvin A (R_1,R_2 = Me)
(–)-penifulvin B (R_1 = CH_2OH, R_2 = Me)
(–)-penifulvin C (R_1 = Me, R_2 = CH_2OH)



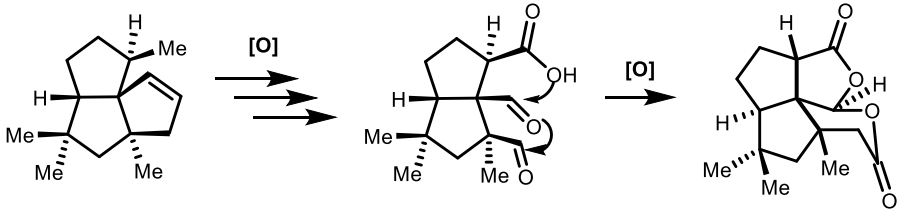
(–)-asperaculin A



[5.5.5.6] fenestrane

- (–)-penifulvin A isolated in 2006 (*Org. Lett.,* **2006**, *8*, 1225-1228.) from *P. griseofulvem* fungus, (–)-asperaculin A in 2012 from *A. aculeatus* fungus (*J. Nat. Prod.*, **2012**, *74,* 1650-1652.)
- (–)-penifulvin A has antiinsectan activity toward a major crop pest, the fall armyworm

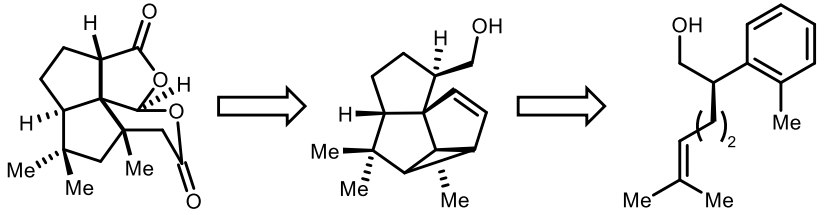
Proposed Biosynthesis*

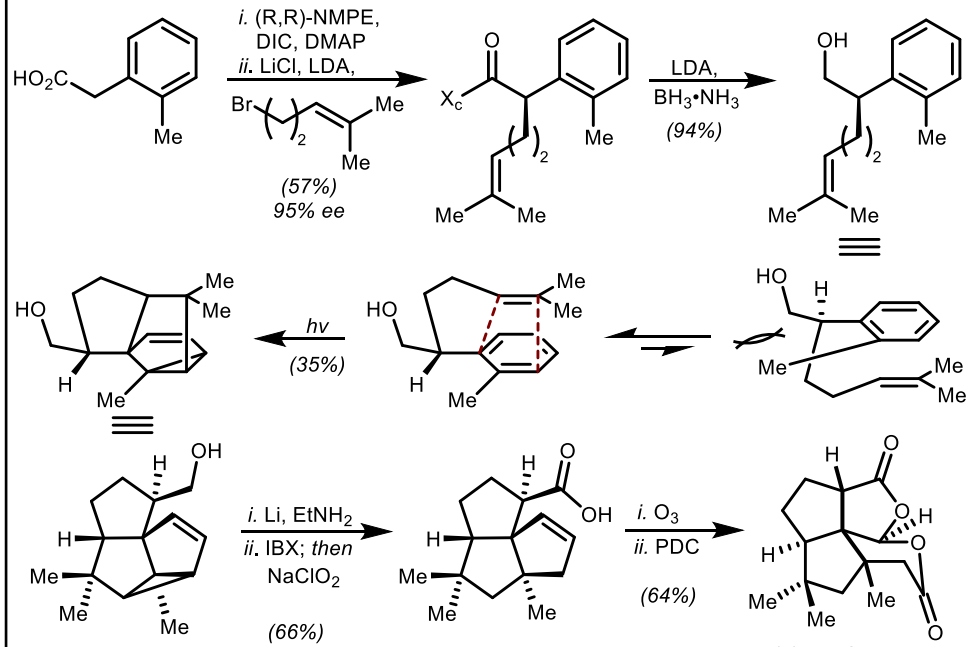


*Revised biosynthesis *Angew. Chem. Int. Ed.*, **2019**, *58*, 6569-6573.

Mulzer (Gaich Ph.D.) **2009/2010**

J. Am. Chem. Soc., **2009**, *131*, 452-453.





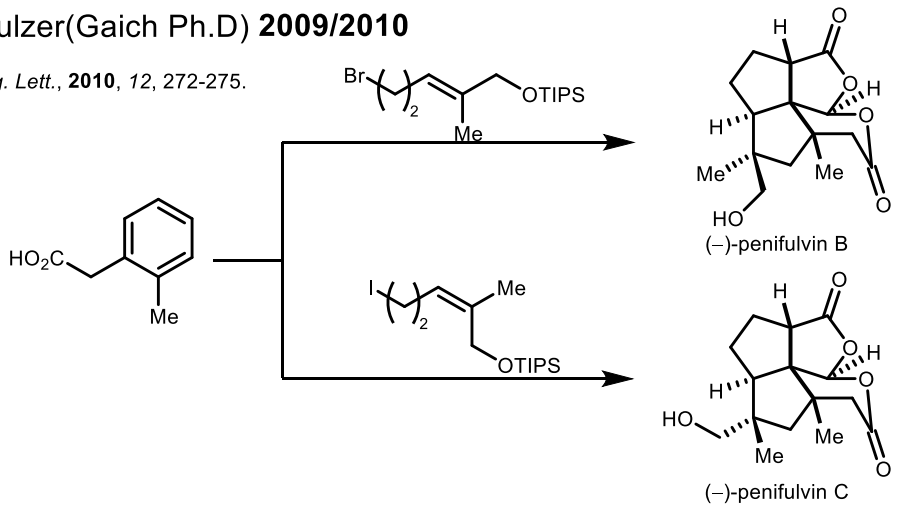
(–)-penifulvin A

Fenestrane Natural Products

Isaac Falk

Mulzer(Gaich Ph.D) **2009/2010**

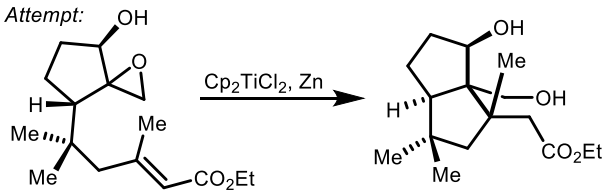
Org. Lett., **2010**, *12*, 272-275.



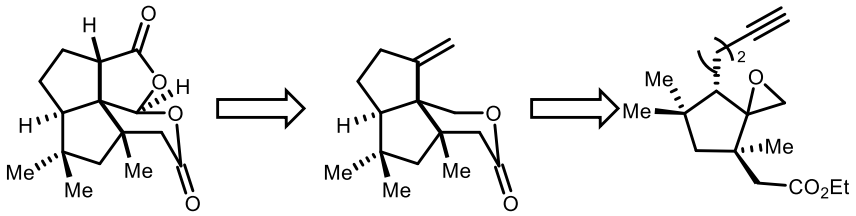
Chakraborty *et al.*, 2010/2014

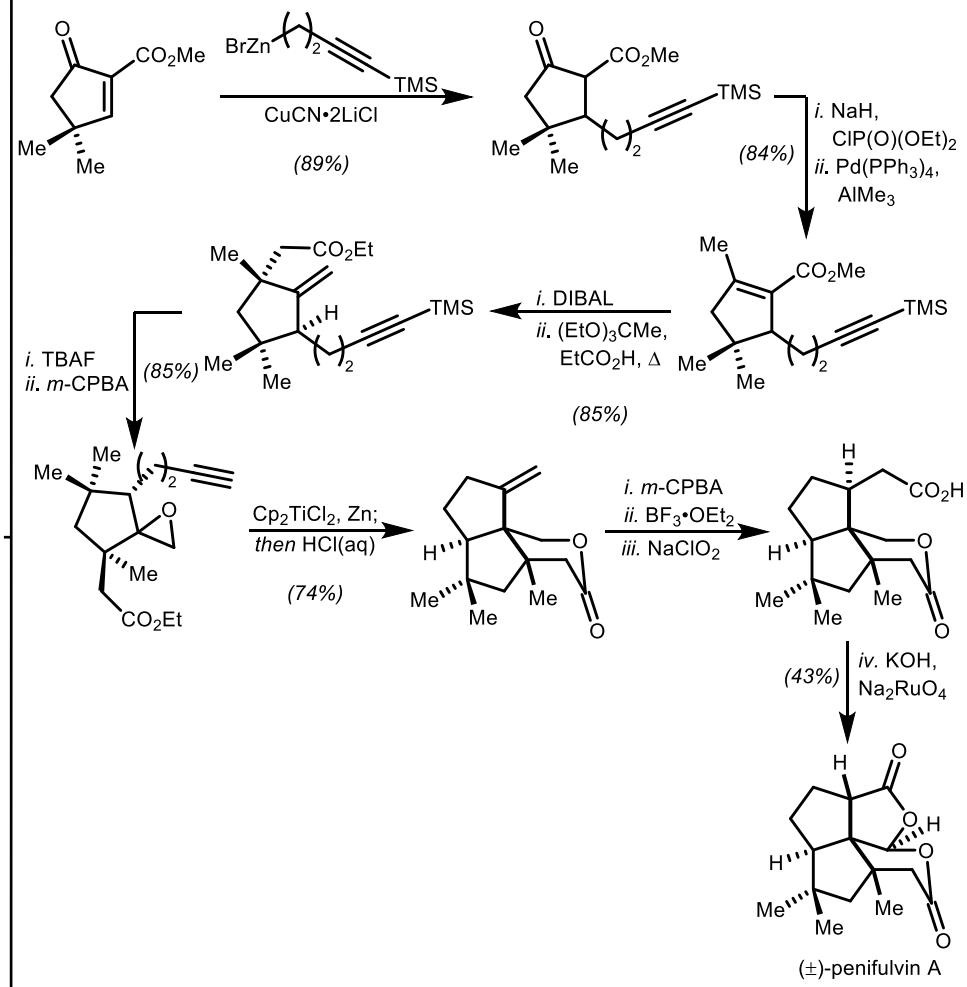
Tet. Lett. **2010**, *51*, 4425-4428.

First Generation Attempt:



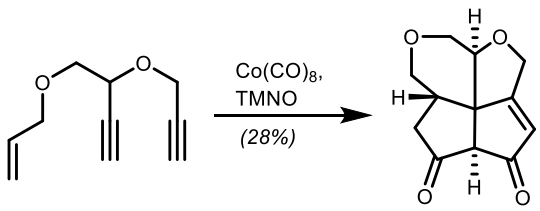
Second Generation Attempt:
Org. Lett., **2014**, *16*, 2618-2621.



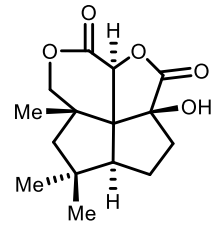


Mehta *et al.*, **2012**

Tet. Lett., **2012**, *53*, 4558.



(All carbon var. Keese et *al.,* H*elv. Chim. Acta.,* 1**996,** ,*79,* 461.)



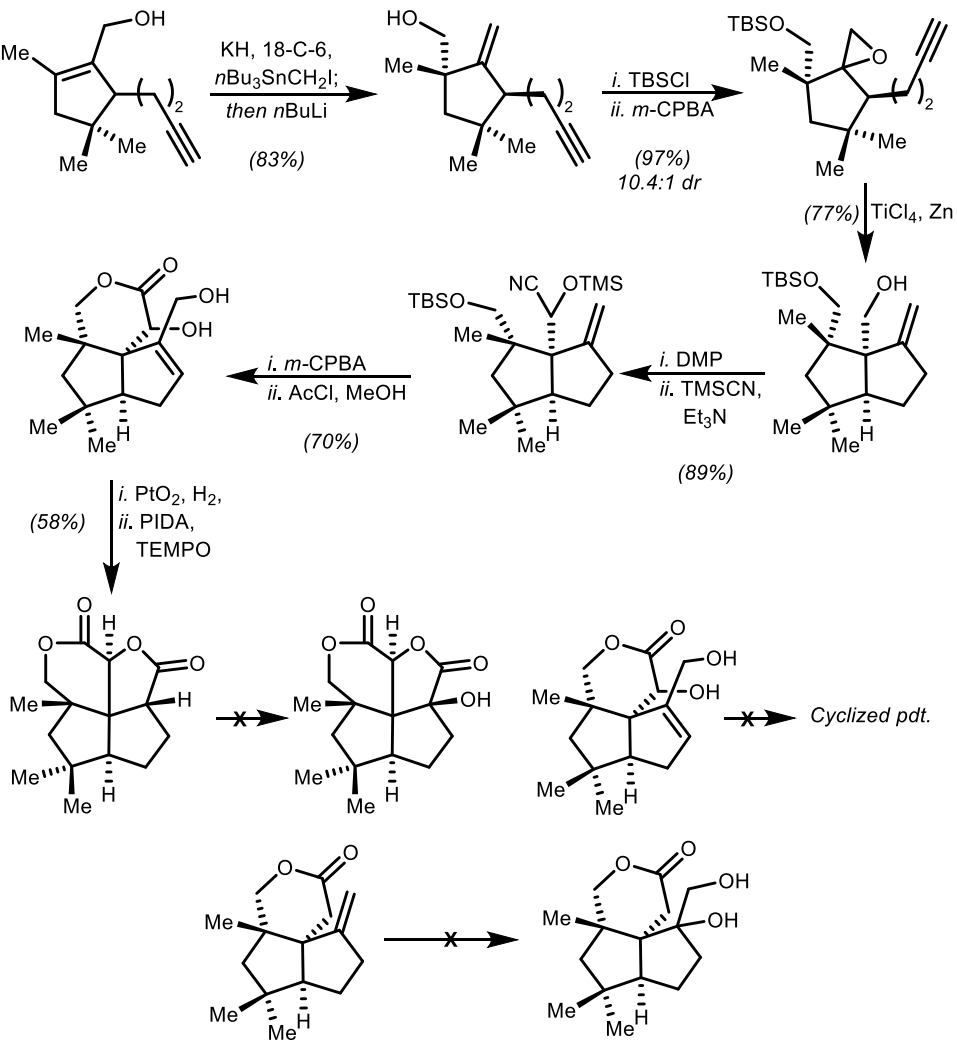
(–)-asperaculin A

Fenestrane Natural Products

Isaac Falk

Chakraborty *et al.*, **2017**

Org. Lett., **2017**, *19*, 682

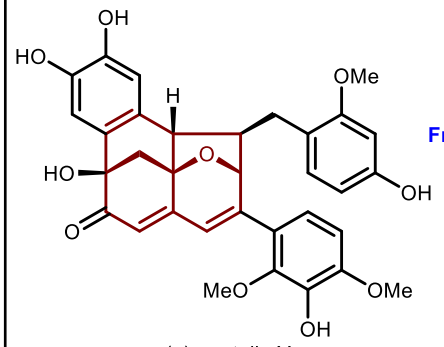


- To date no synthesis of (–)-asperaculin A

Oxafenestranes

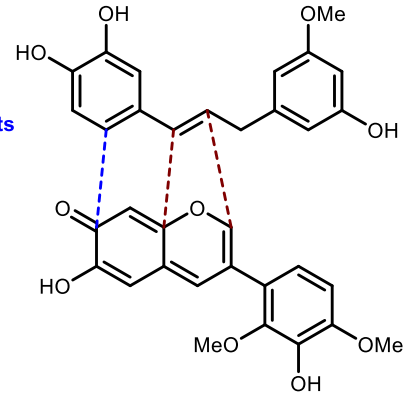
Trauner et al., **2015**

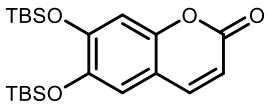
Angew. Chem. Int. Ed., **2015**, *54*, 5079.



(±)-santalin Y
[6.6.6.5] fenestrane

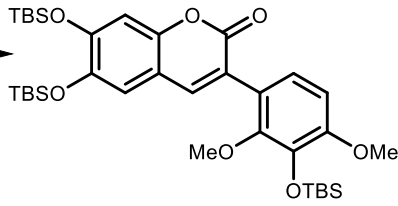
[3+2],
Friedel-Crafts



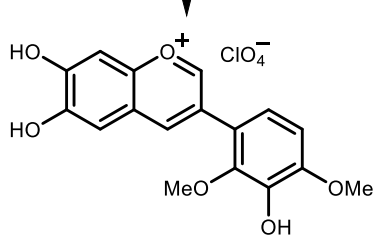


3 steps from commercial

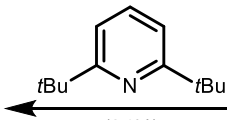
TMPMgCl, $ZnCl_2$; *then*
$Pd(OAc)_2$, S-Phos, Ar-Br
(84%)

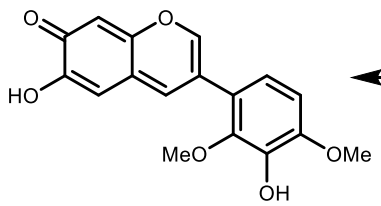


i. DIBAL
(41%) ii. $HClO_4$, AcOH
iii. TBAF



Angew. Chem. Int. Ed., **2013**, *52*, 9509.



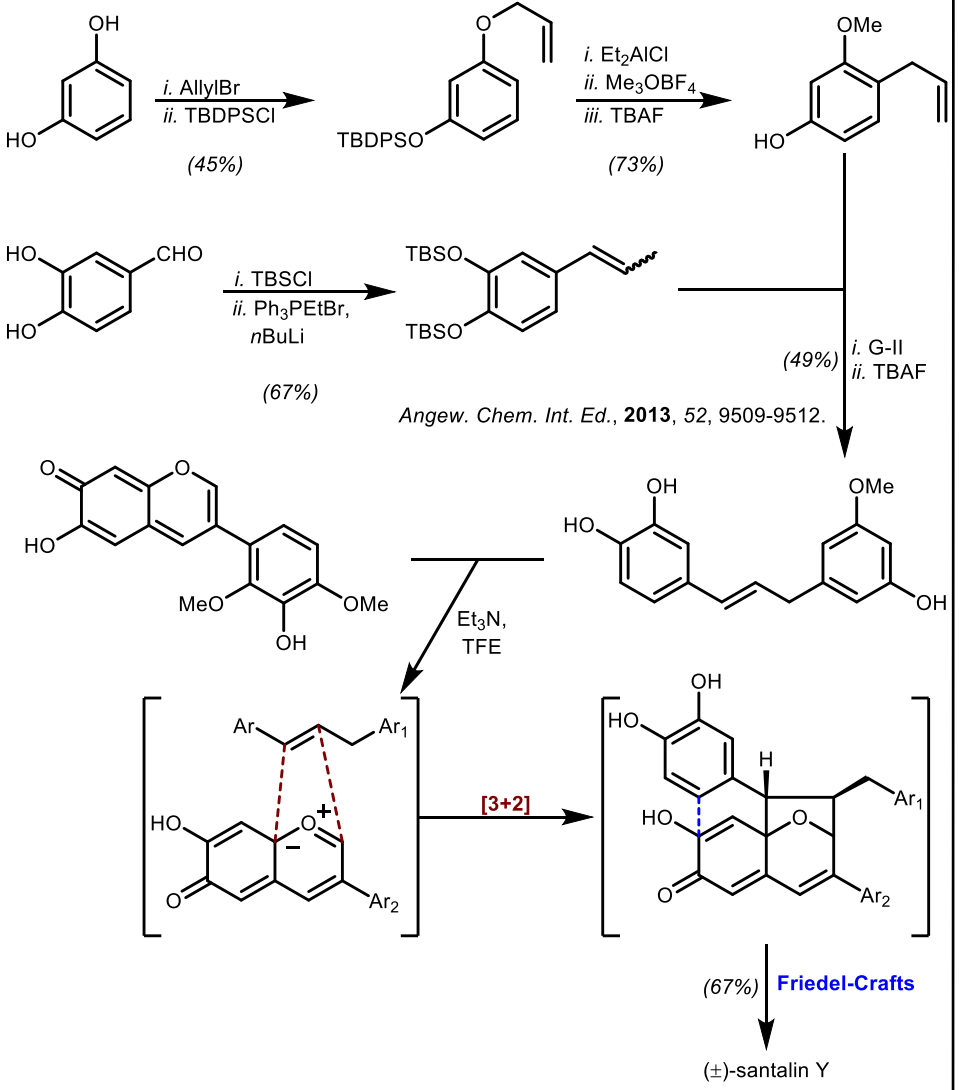


Fenestrane Natural Products

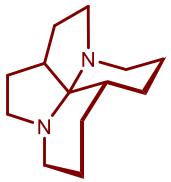
Isaac Falk

Trauner et al., **2015**

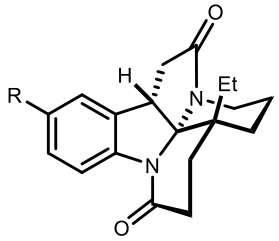
Angew. Chem. Int. Ed., **2015**, *54*, 5079.



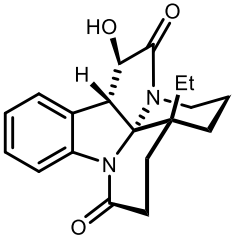
Diazafenestranes



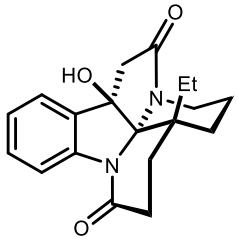
[5.5.6.6] fenestrane



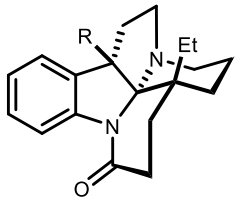
(–)-leuconoxine (R = H)
(*Phytochemistry*, **1994**, *35*, 169)
(–)-leuconodine C (R = OH)
(*J. Nat. Prod.*, **2013**, *76*, 957)



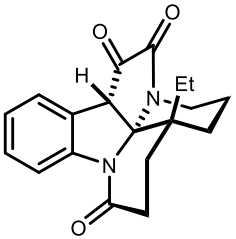
(–)-leuconondine A
(*J. Nat. Prod.*, **2013**, *76*, 957)



(–)-leuconodine B/
(–)-scholarisine G
(*Planta Med.*, **2009**, *75*, 1537)

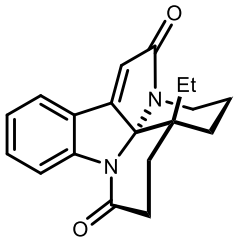


(–)-leuconodine D (R = H)
(–)-leuconodine E (R = OH)
(*J. Nat. Prod.*, **2013**, *76*, 957)



(–)-leuconodine F
(*J. Nat. Prod.*, **2007**, *70*, 1380)

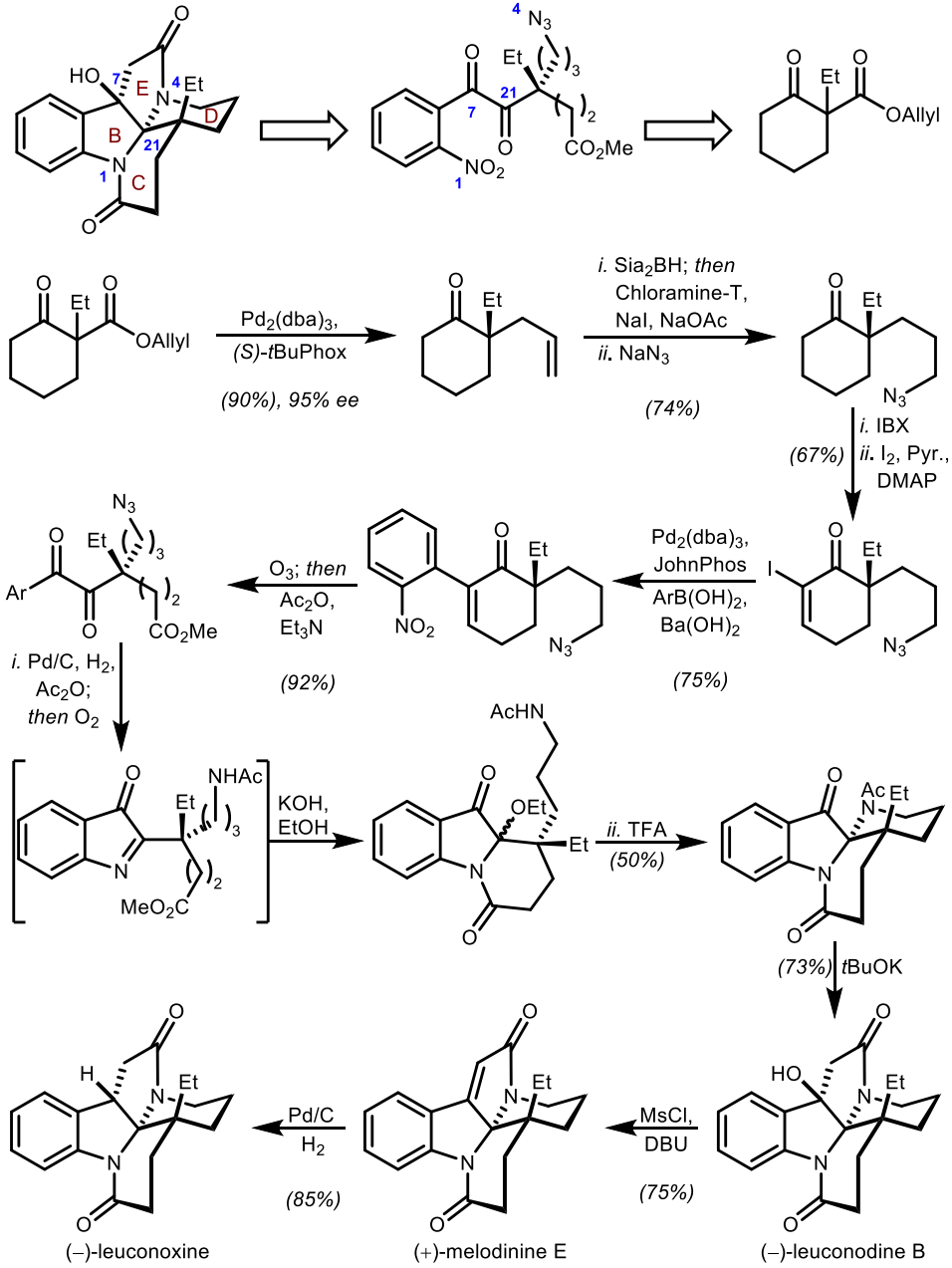
- Isolated from members of the Apocynacae family
- Some members have weak-moderate anticancer activity
- 11 total synthesis of diazafenestranes
  - Seven published between 2014 and 2015



(+)-melodinine E
(*J. Nat. Prod.*, **2010**, *73*, 22)

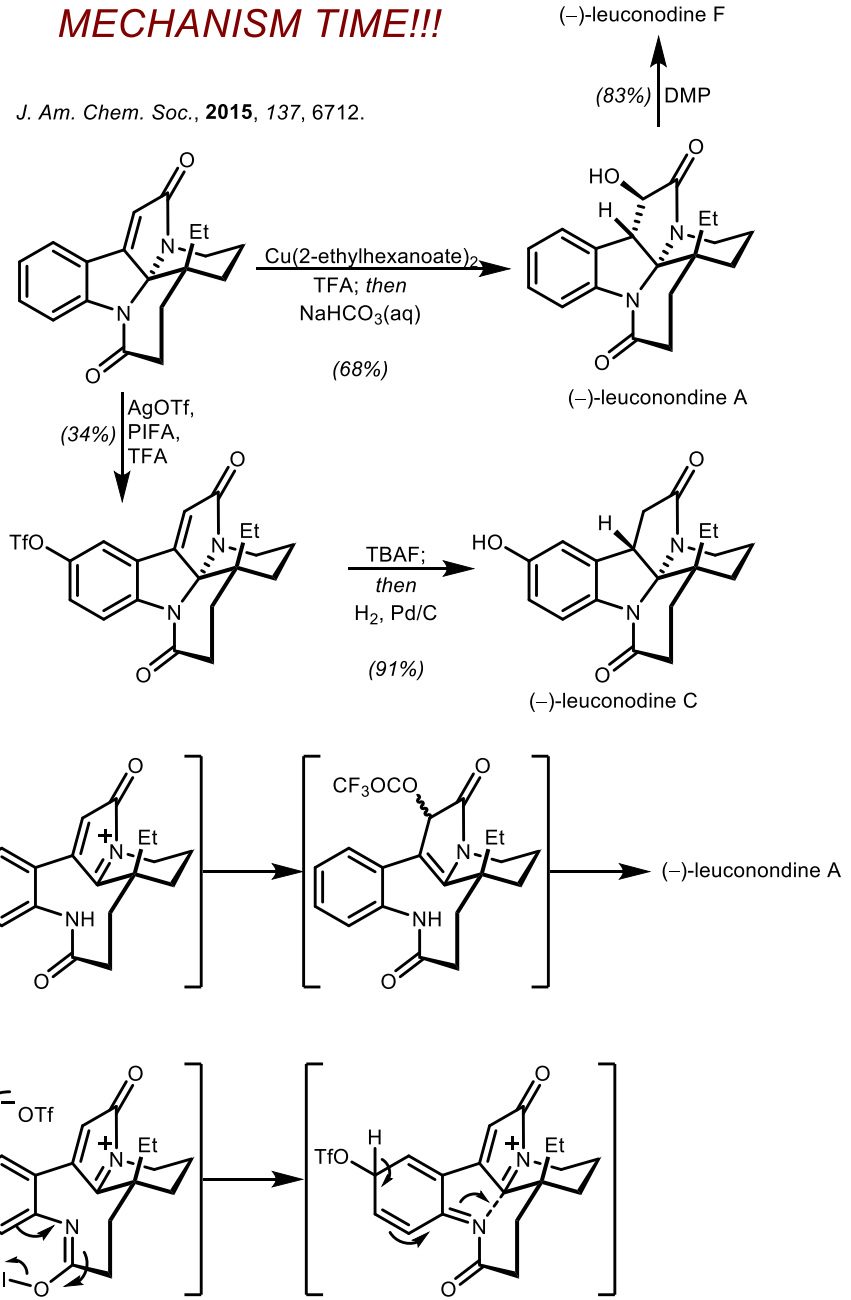
Zhu et al. **2013/2015**

J. Am. Chem. Soc., **2013**, *135*, 19127.



MECHANISM TIME!!!

J. Am. Chem. Soc., **2015**, *137*, 6712.

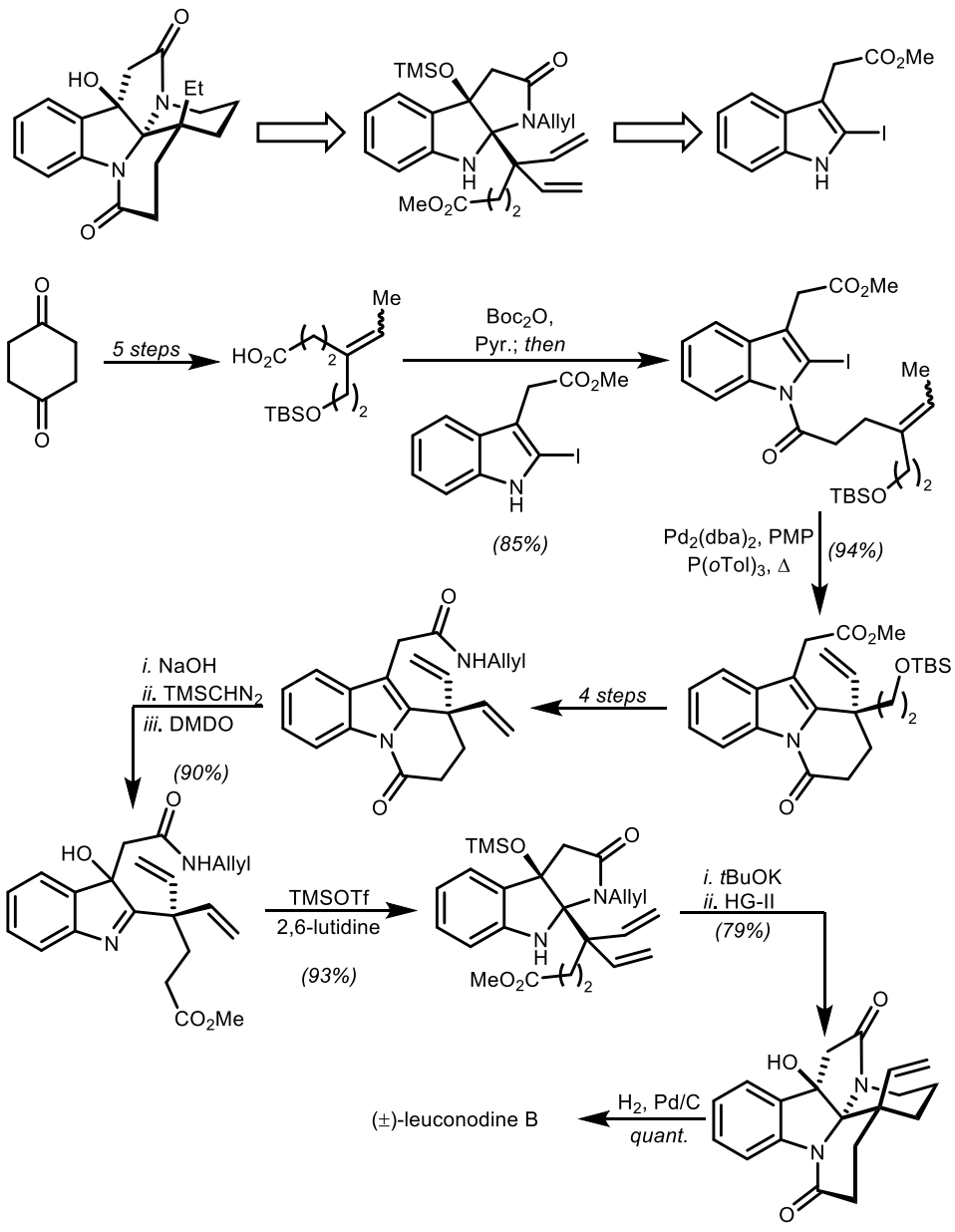


Fenestrane Natural Products

Isaac Falk

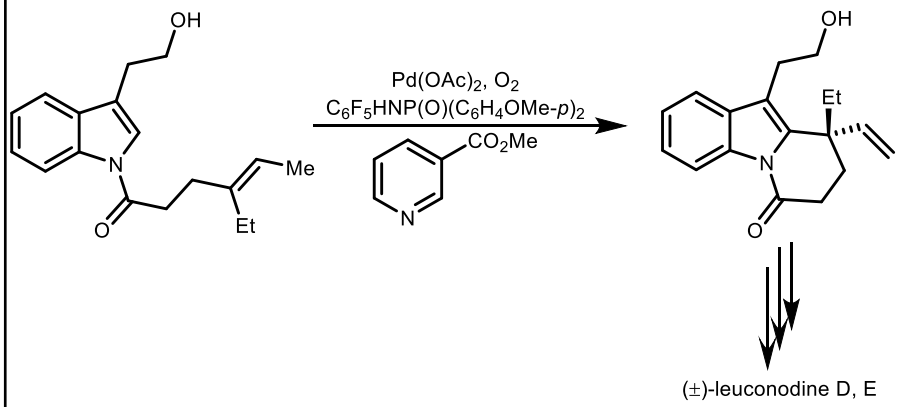
Tokuyama *et al.*, **2014**

Org. Lett., **2014**, *16*, 2526-2529.



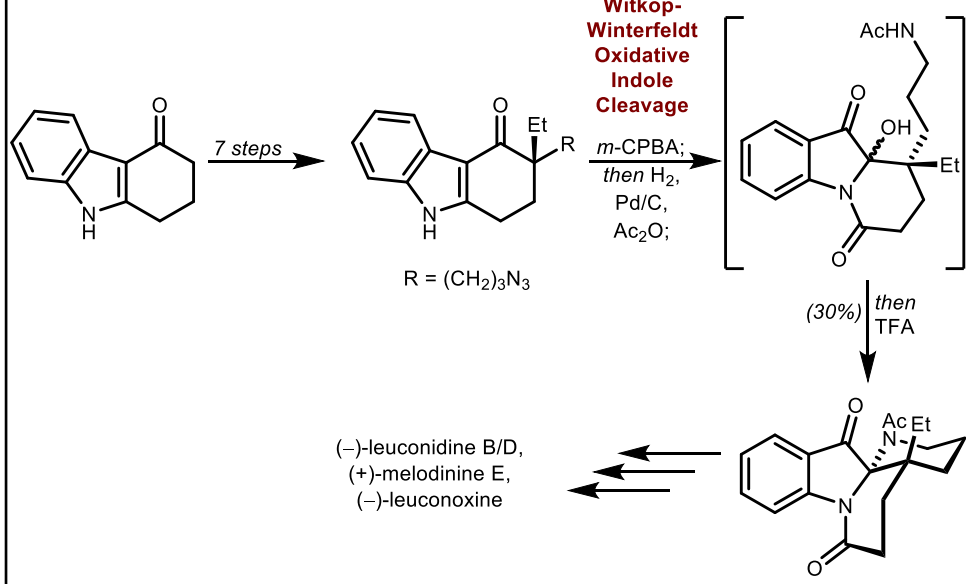
Han *et al.*, **2019**

J. Org. Chem., **2019**, *84*, 13890.



Dai *et al.*, **2014**

Org. Lett., **2014**, *16*, 6216.



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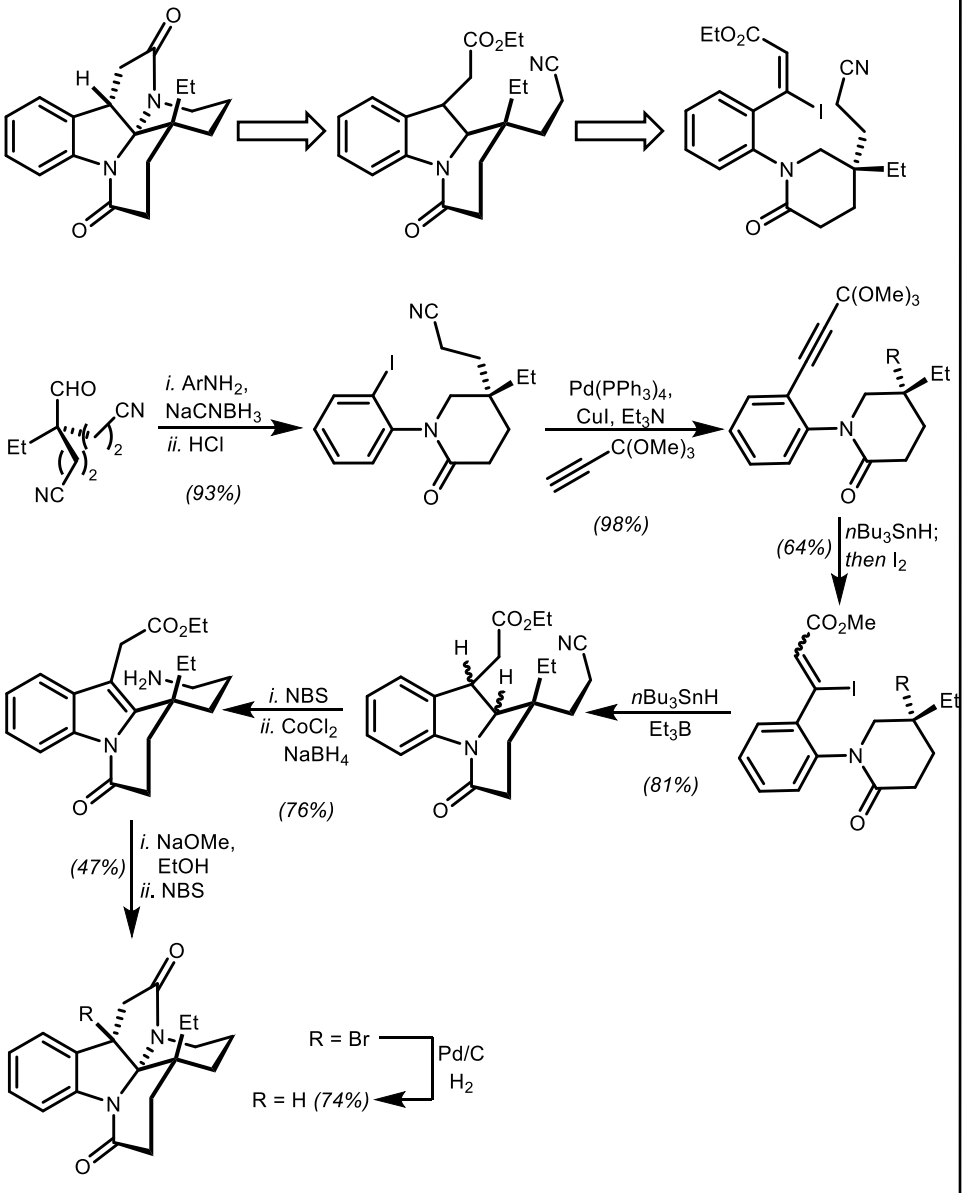

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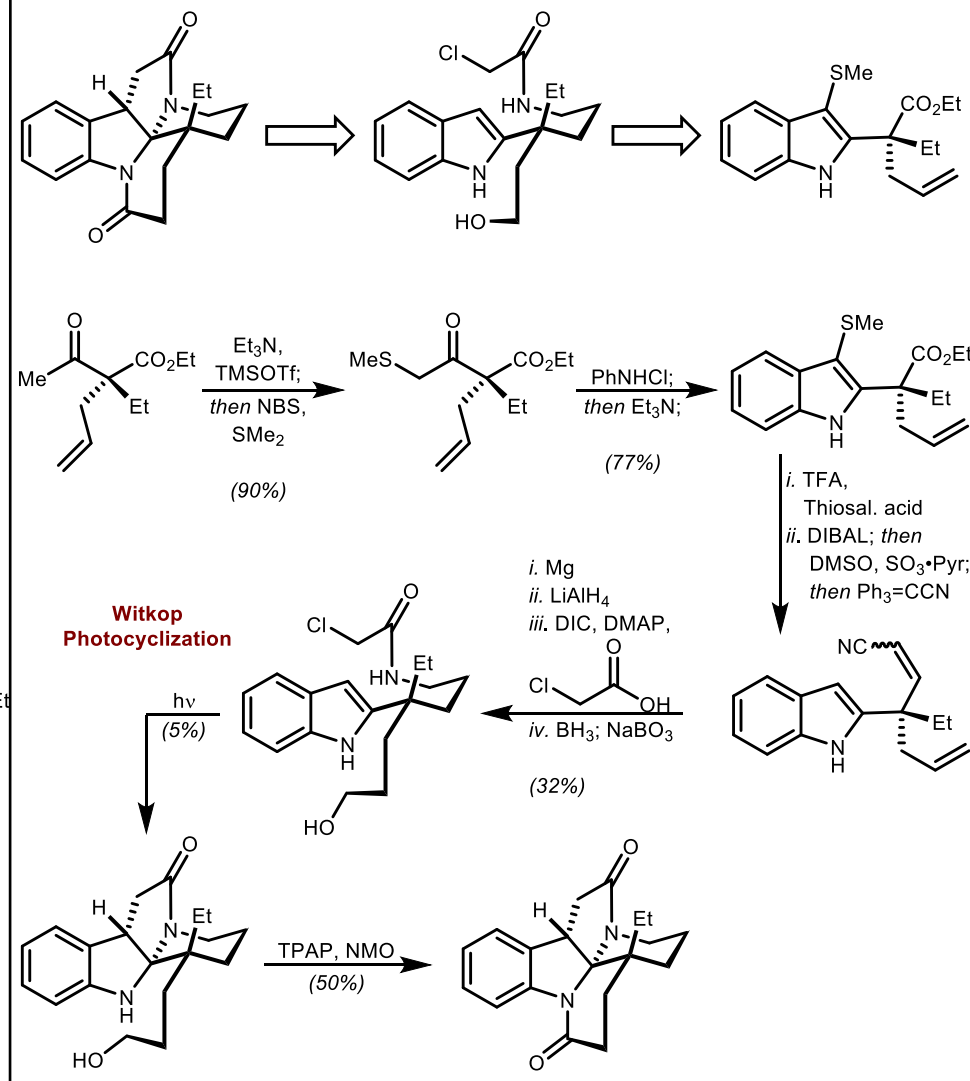

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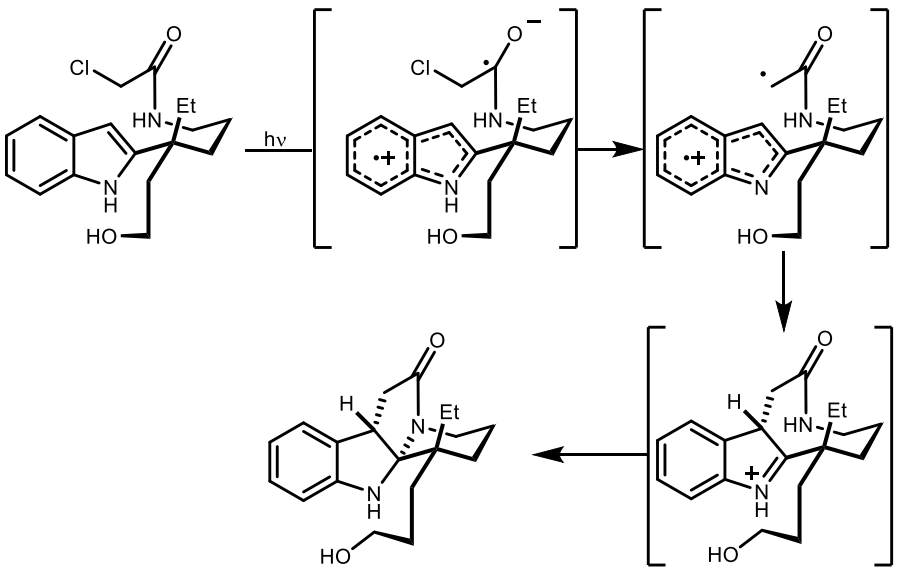

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