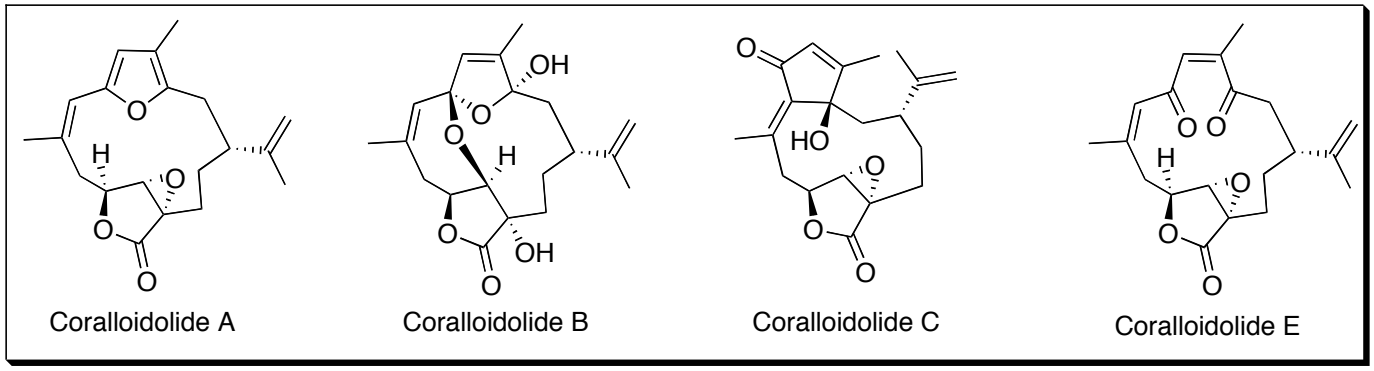
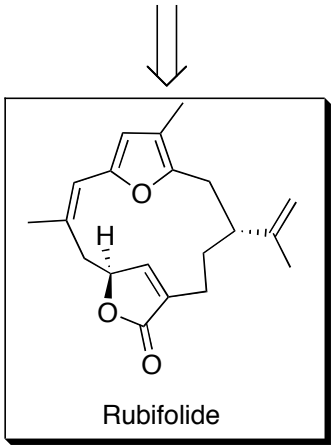
Total Synthesis of Coralloidolides A, B, C, and E

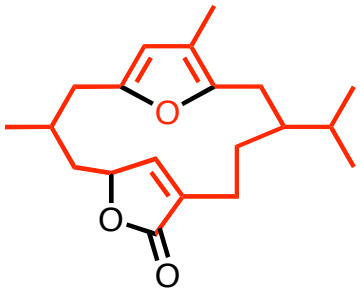




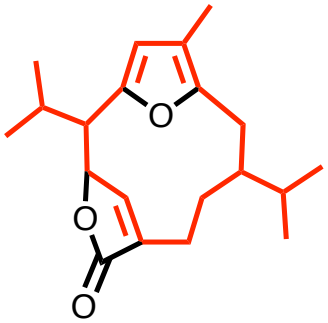
Melissa Sprachman
Current Literature
April 24, 2010

Kimbrough, T. J.; Roethle, P. A.; Mayer, P.; Trauner, D.
Angew. Chem. Int. Ed. **2010,** *49,* 2619-2621

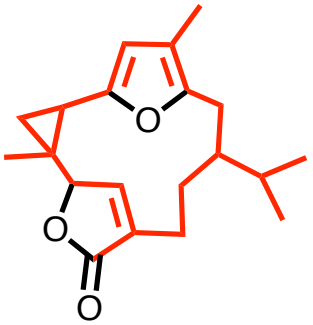
Furanocembranoids and Related Compounds



(furano)cembrane skeleton



pseudopterane skeleton



gersolane skeleton

Members of these classes are isolated from gorgonian corals; most are isolated from the Caribbean, but the coralloidolides were isolated from *Alcyonium coralloides* (by Pietra et al.), a Mediterranean Organism.

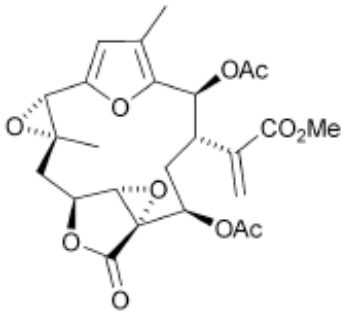
The coralloidolides are furanocembranes with the common structural feature of the 14-membered carbocyclic core.

Other common structural motifs of the furanocembranes are the furan and butenolide moeities; the coralloidolides feature these moeities intact (coralloidolide A) or further oxidized or hydrated.

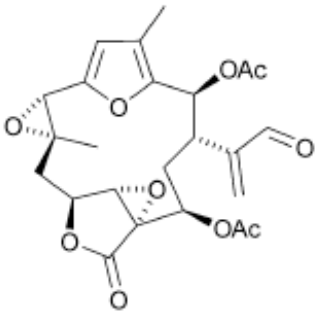

http://en.wikipedia.org/wiki/Gorgonian

Roethle, P. A.; Trauner, D. *Nat. Prod. Rep.* **2008,** *25,* 298-317.
D'Abrosio, M.; Fabbri, D.; Guerriero, A.; Pietra, F. *Helv. Chim. Acta* **1989,** *70,* 63-70.

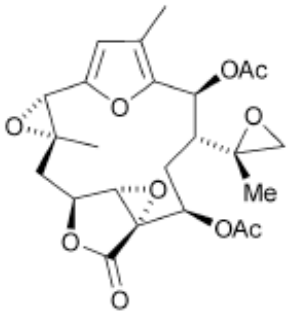
“Regular” Furanocembranoids



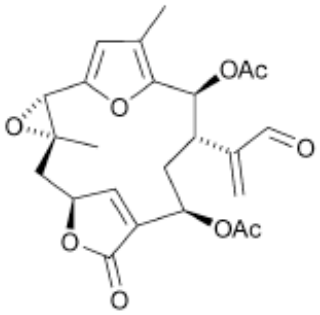
bipinnnatin A (**16**)



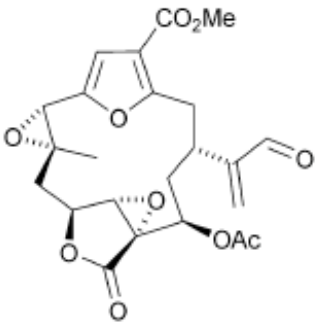
bipinnatin B (**17**)



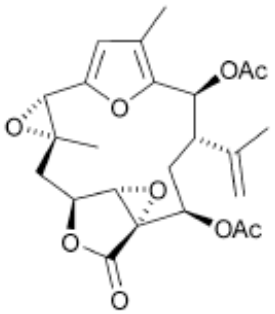
bipinnatin C (**18**)



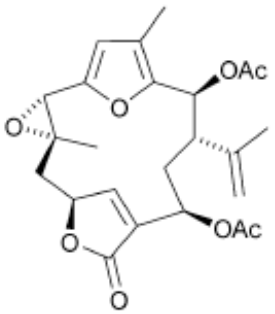
bipinnatin D (**19**)



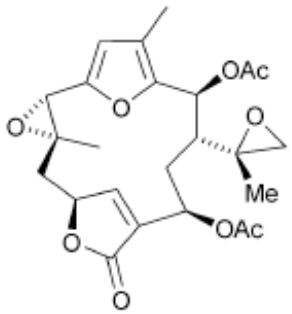
bipinnatin E (**20**)



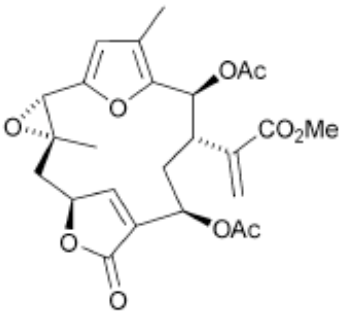
bipinnatin F (**21**)



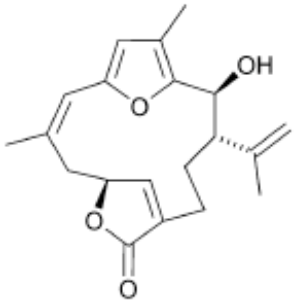
bipinnatin G (**22**)



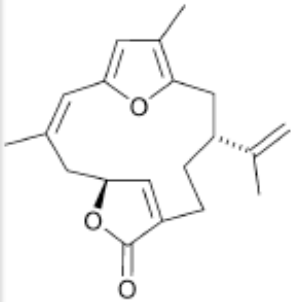
bipinnatin H (**23**)



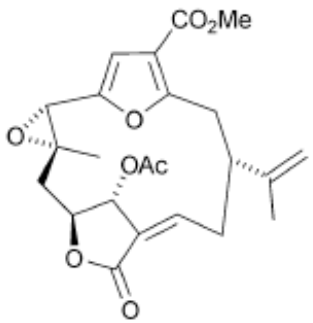
bipinnatin I (**24**)



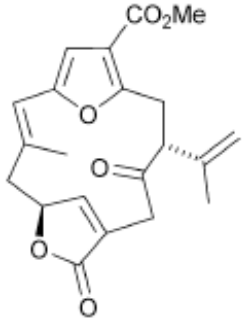
bipinnatin J (**25**)



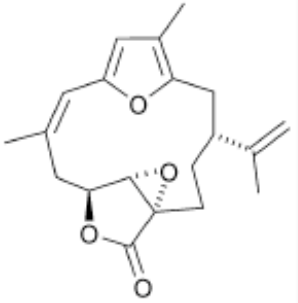
rubifolide (**26**)



unnamed (**27**)



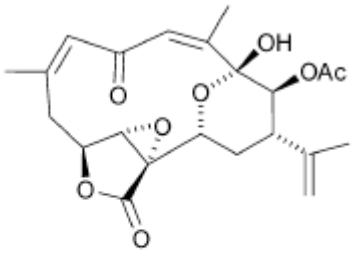
acerosolide (**28**)



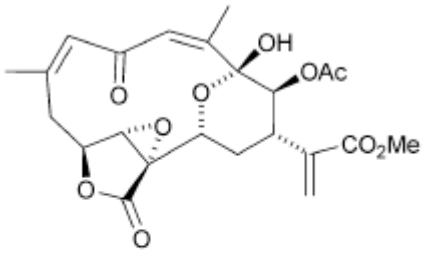
coralloidolide A (**29**)

Copied from Roethle, P. A.; Trauner, D. *Nat. Prod. Rep.* **2008,** *25,* 298-317.

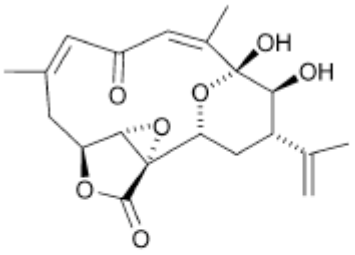
“Oxidized” Furanocembranoids



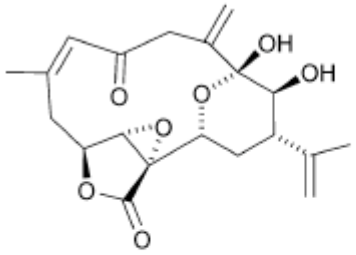
bipinnatolide B (**34**)



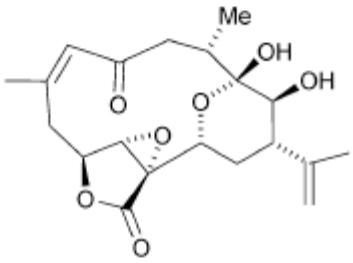
bipinnatolide E (**35**)



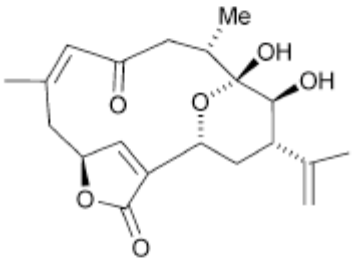
bipinnatolide F (**36**)



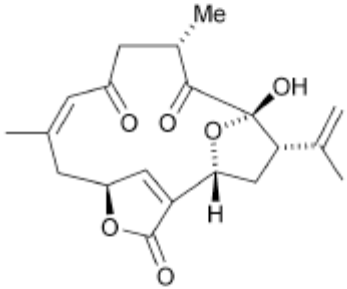
bipinnatolide G (**37**)



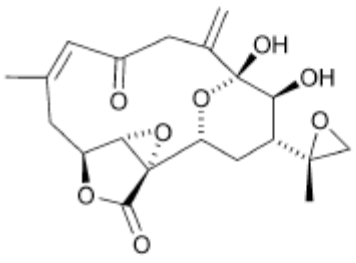
bipinnatolide H (**38**)



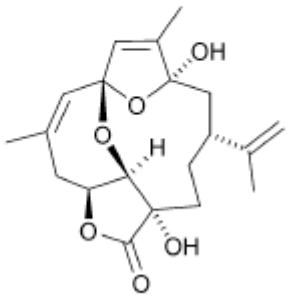
bipinnatolide I (**39**)



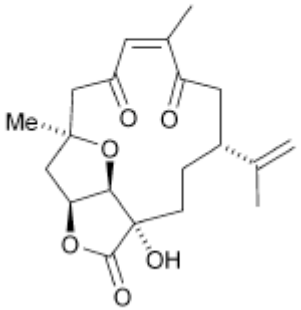
bipinnatolide J (**40**)



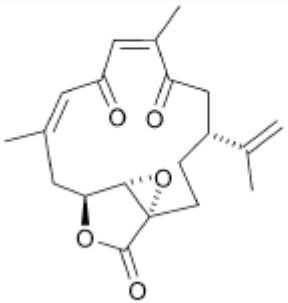
bipinnatolide K (**41**)



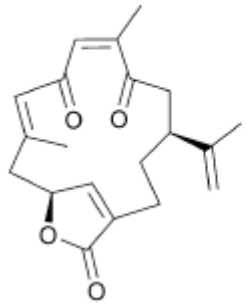
coralloidolide B (**42**)



coralloidolide D (**43**)



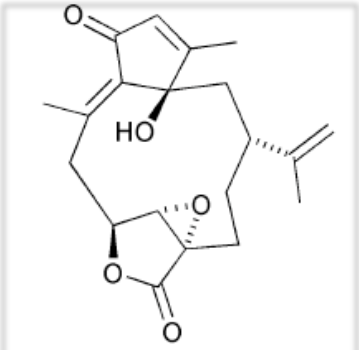
coralloidolide E (**44**)

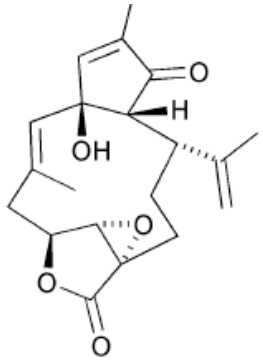


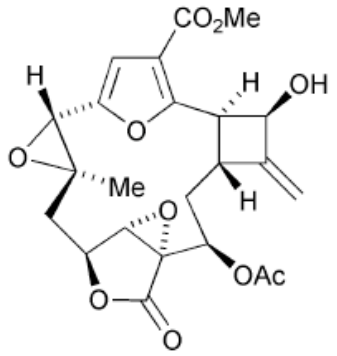
lophodione (**45**)

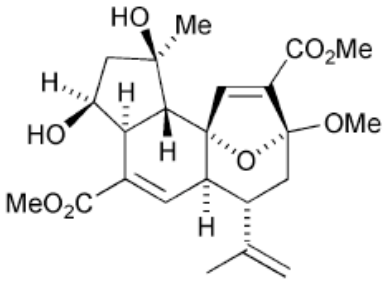
Copied from Roethle, P. A.; Trauner, D. *Nat. Prod. Rep.* **2008,** *25,* 298-317.

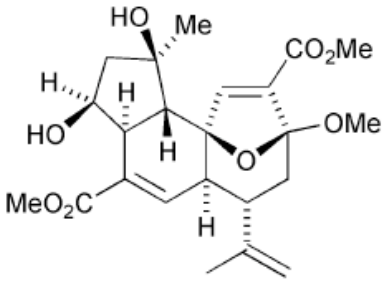
"Furanocembranoid derivatives with complex polycyclic carbon skeletons"

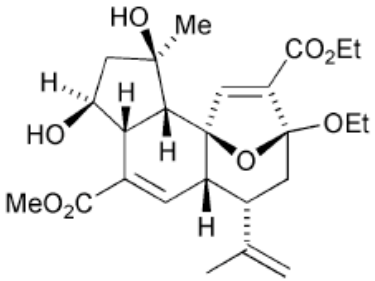

coralloidolide C (**93**)

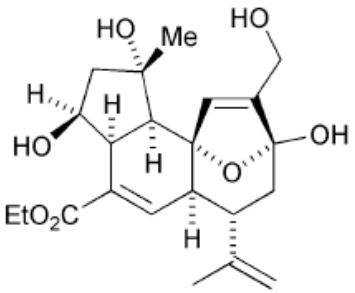

coralloidolide F (**94**)

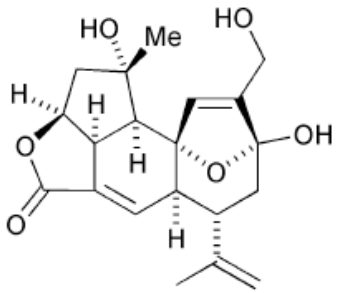

providencin (**95**)

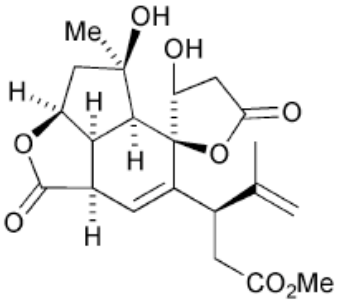

mandapamate (**96**)

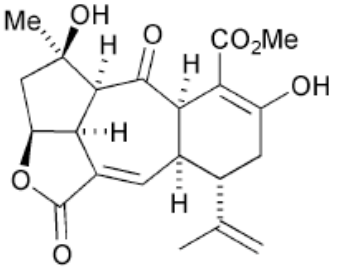

isomandapamate (**97**)


bishomoisomandapamate (**98**)


plumarellic acid ethyl ester (**99**)

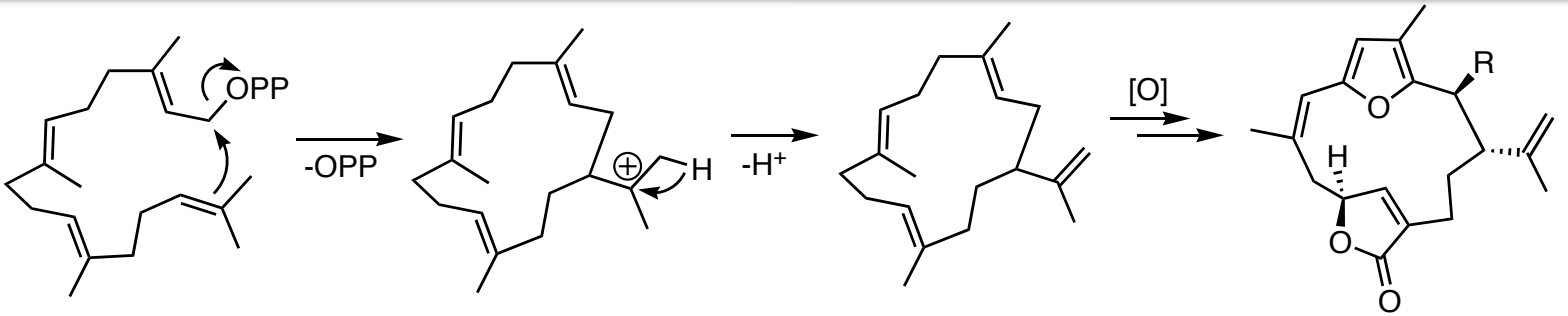

plumarellide (**100**)


havellockate (**101**)


rameswaralide (**102**)

Copied from Roethle, P. A.; Trauner, D. *Nat. Prod. Rep.* **2008,** *25,* 298-317.

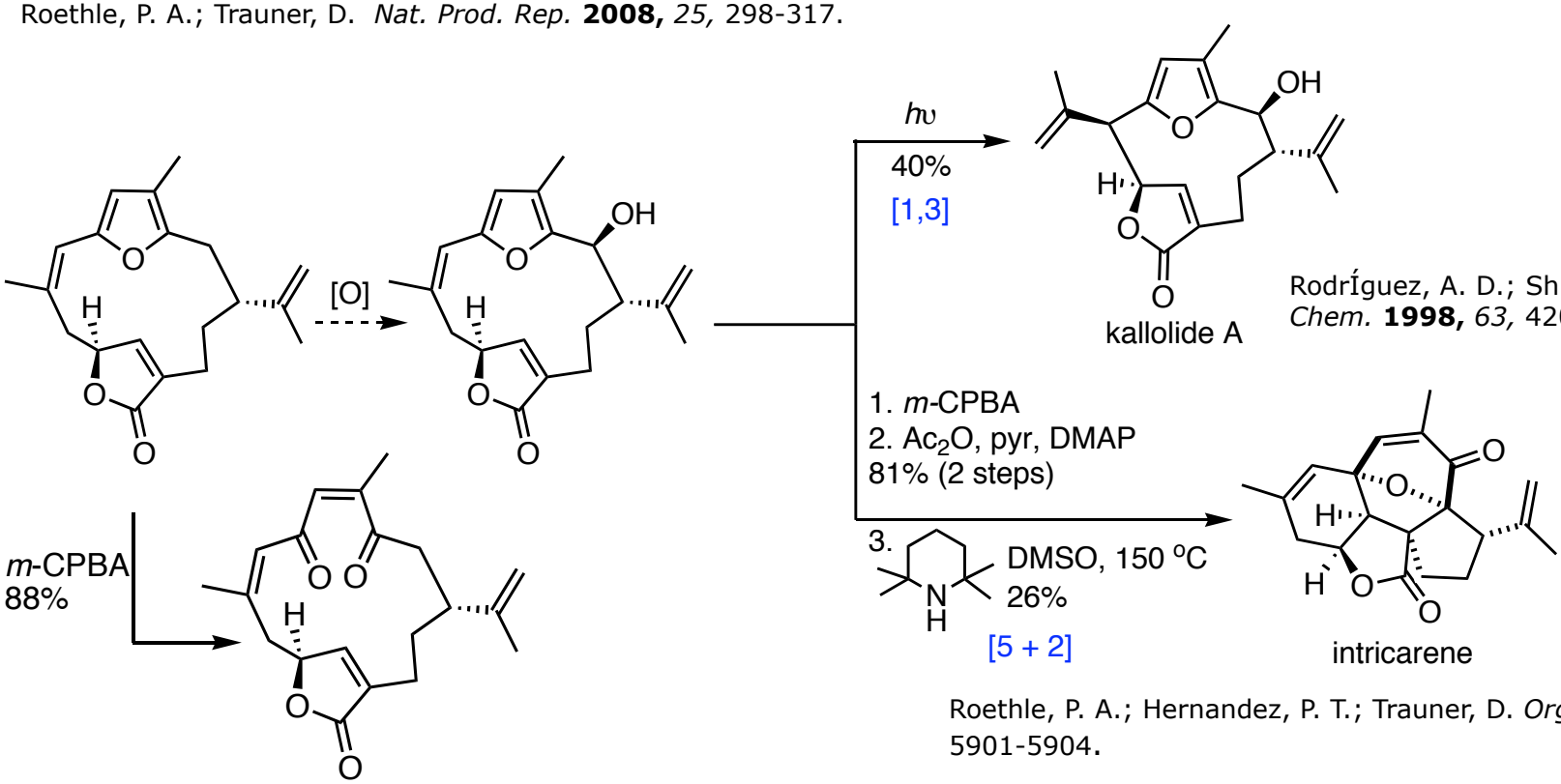
Cembrane Biosynthesis and Proposals



geranylgeranyl diphosphate

R = H: Rubifolide
R = OH: Bipinnatin J

Roethle, P. A.; Trauner, D. *Nat. Prod. Rep.* **2008,** *25,* 298-317.

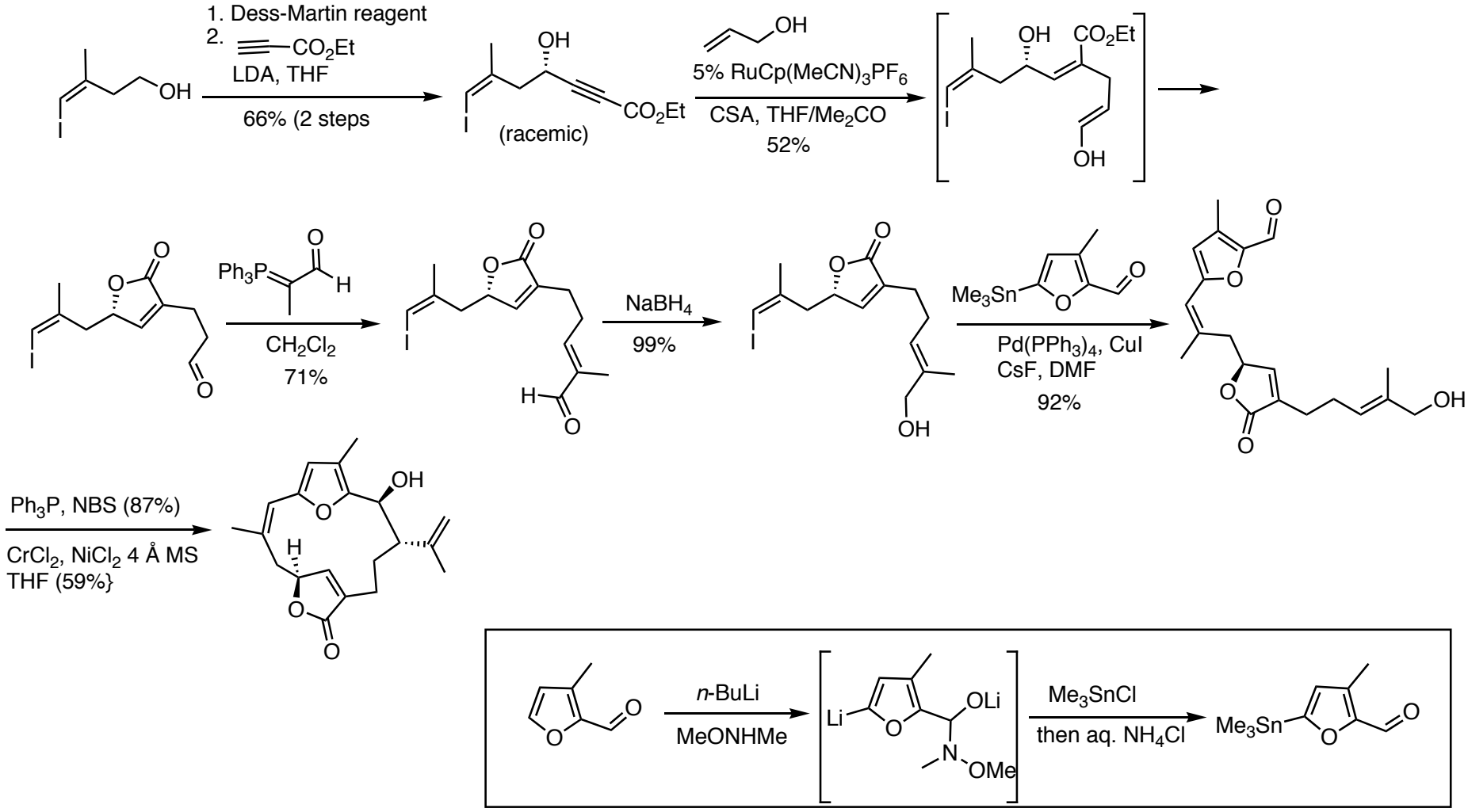


Rodríguez, A. D.; Shi, J.-G. *J. Org. Chem.* **1998,** *63,* 420-421.

Roethle, P. A.; Hernandez, P. T.; Trauner, D. *Org. Lett.* **2006,** *8,* 5901-5904.

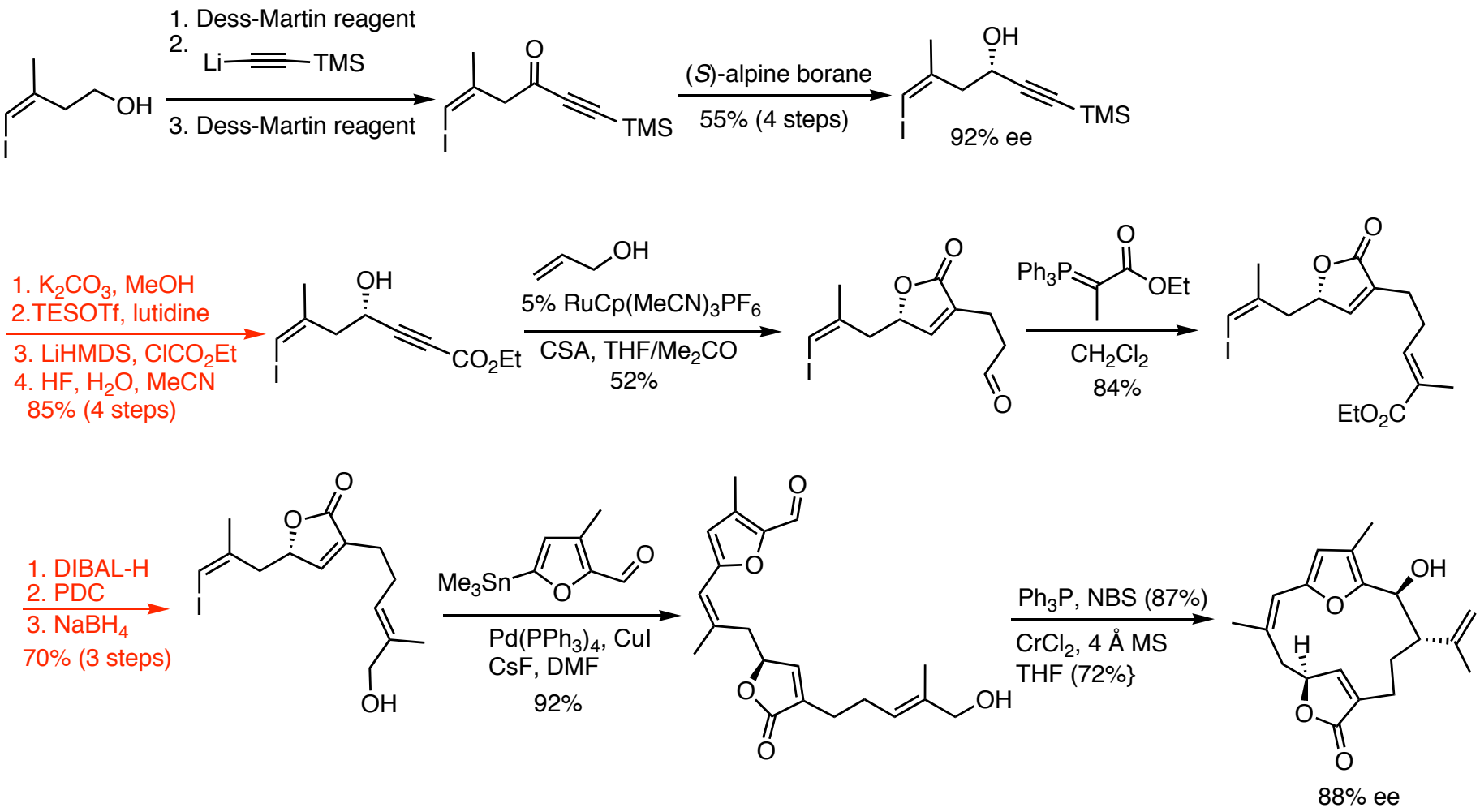
Also: Tang, B.; Bray, C. D.; Pattenden, G. *Tetrahedron Lett.* **2006,** *47,* 6401-6404.

Synthesis of Bipinnatin J



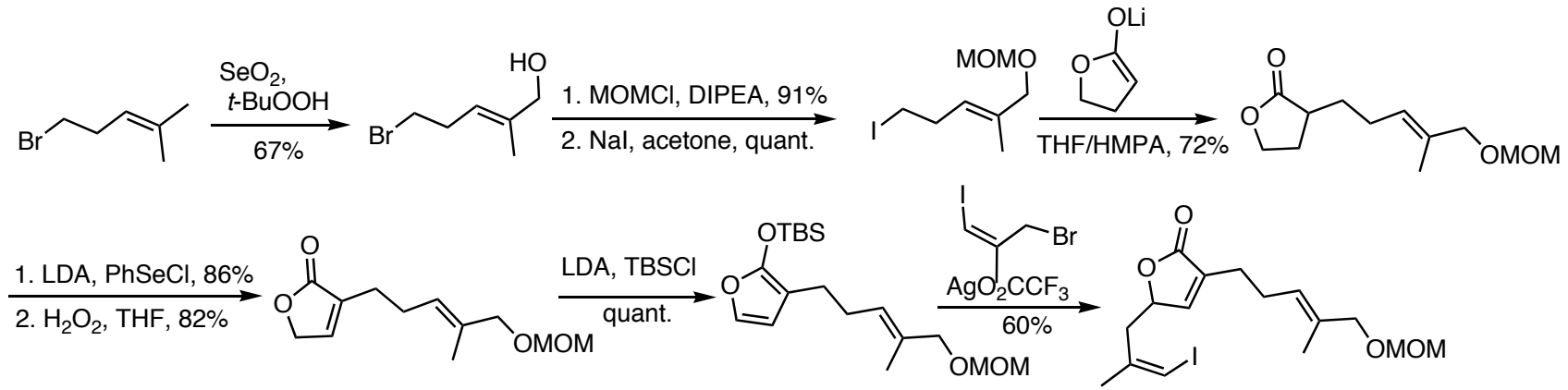
Roethle, P. A.; Trauner, D. *Org. Lett.* **2006,** *8,* 345-347.

Enantioselective Synthesis of Bipinnatin J



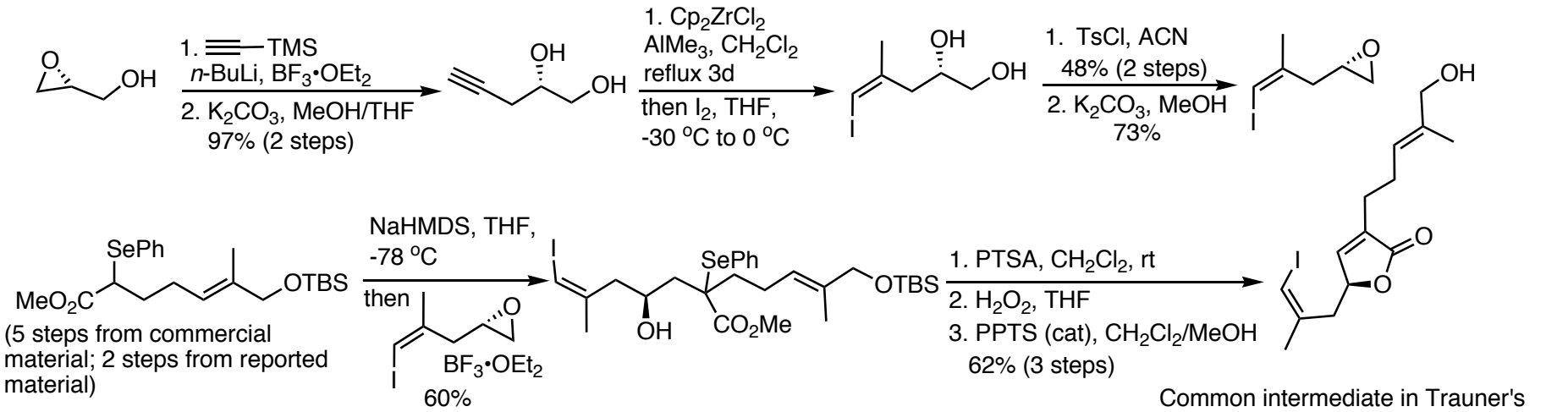
Roethle, P. A.; Hernandez, P. T.; Trauner, D. *Org. Lett.* **2006,** *8,* 5901-5904.

Other Approaches to Bipinnatin J



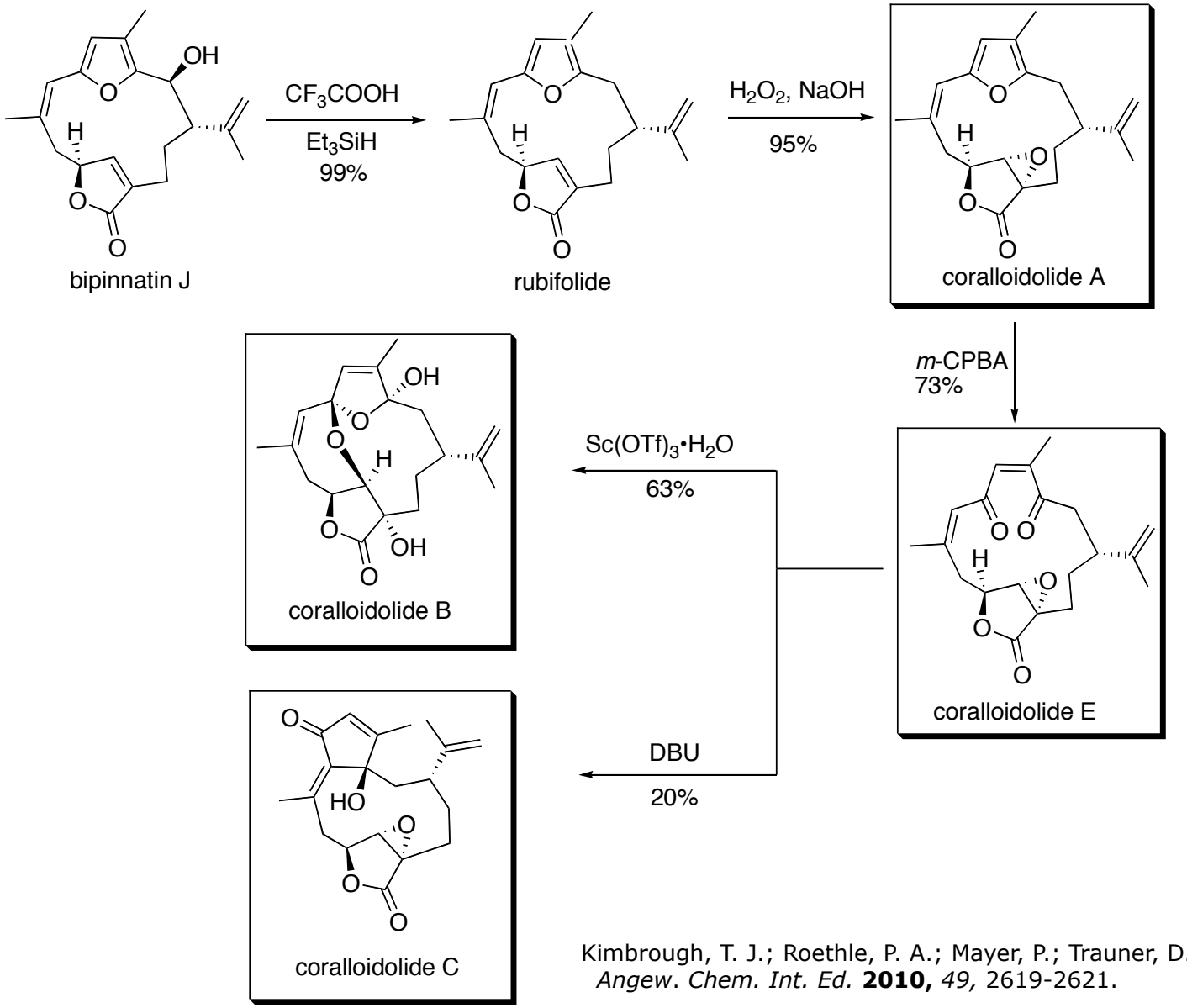
Huang, Q.; Rawal, V. H. **2006,** *8,* 543-545.

Enantioselective route:



Tang, B.; Bray, C. D.; Pattenden, G. *Tetrahedron Lett.* **2006,** *47,* 6401-6404.

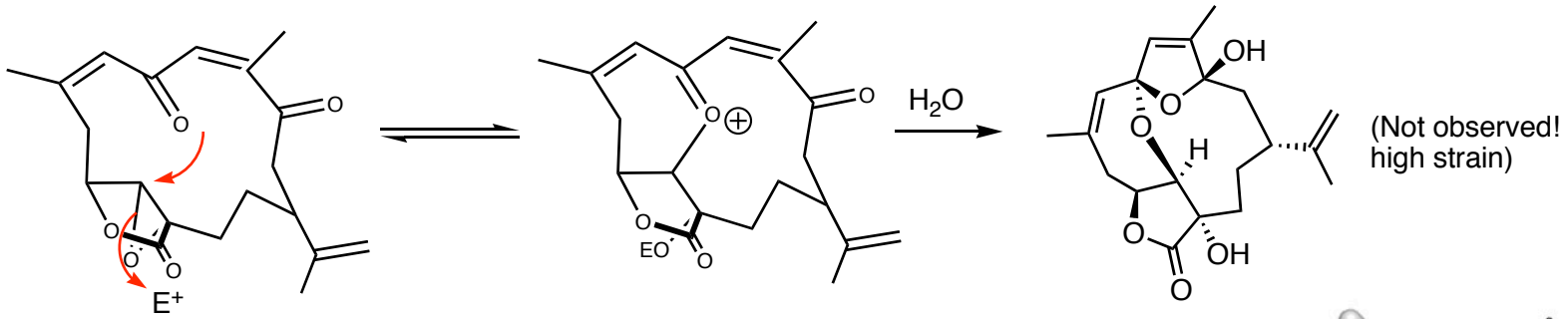
Synthesis of the Coralloidolides



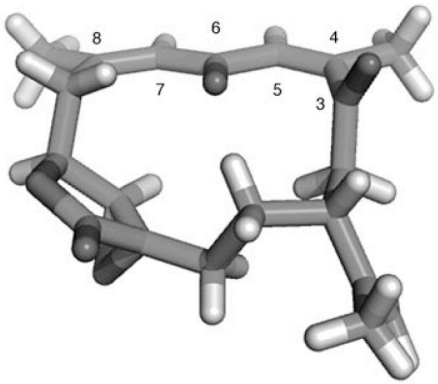
Kimbrough, T. J.; Roethle, P. A.; Mayer, P.; Trauner, D. *Angew. Chem. Int. Ed.* **2010,** *49,* 2619-2621.

Formation of Coralloidolide B

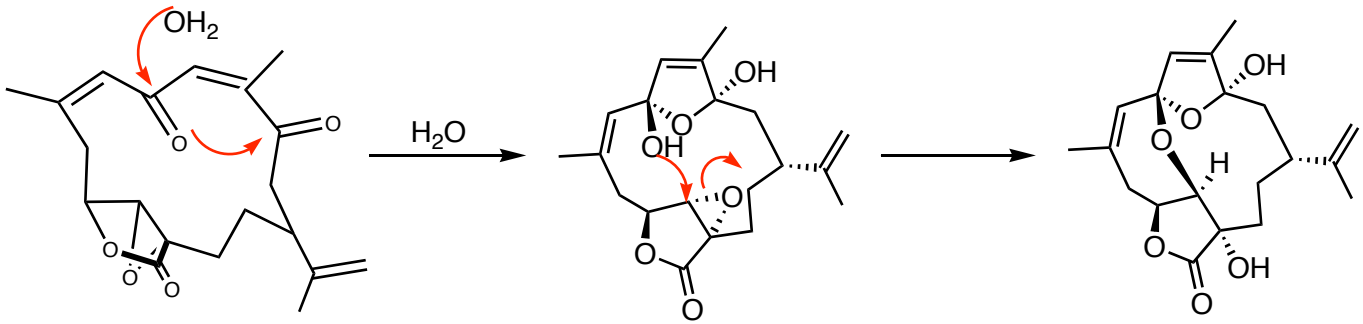
Via an oxocarbenium intermediate:



X-ray structure
Of coralloidolide E:



Stepwise hydrate formation followed by epoxide opening:

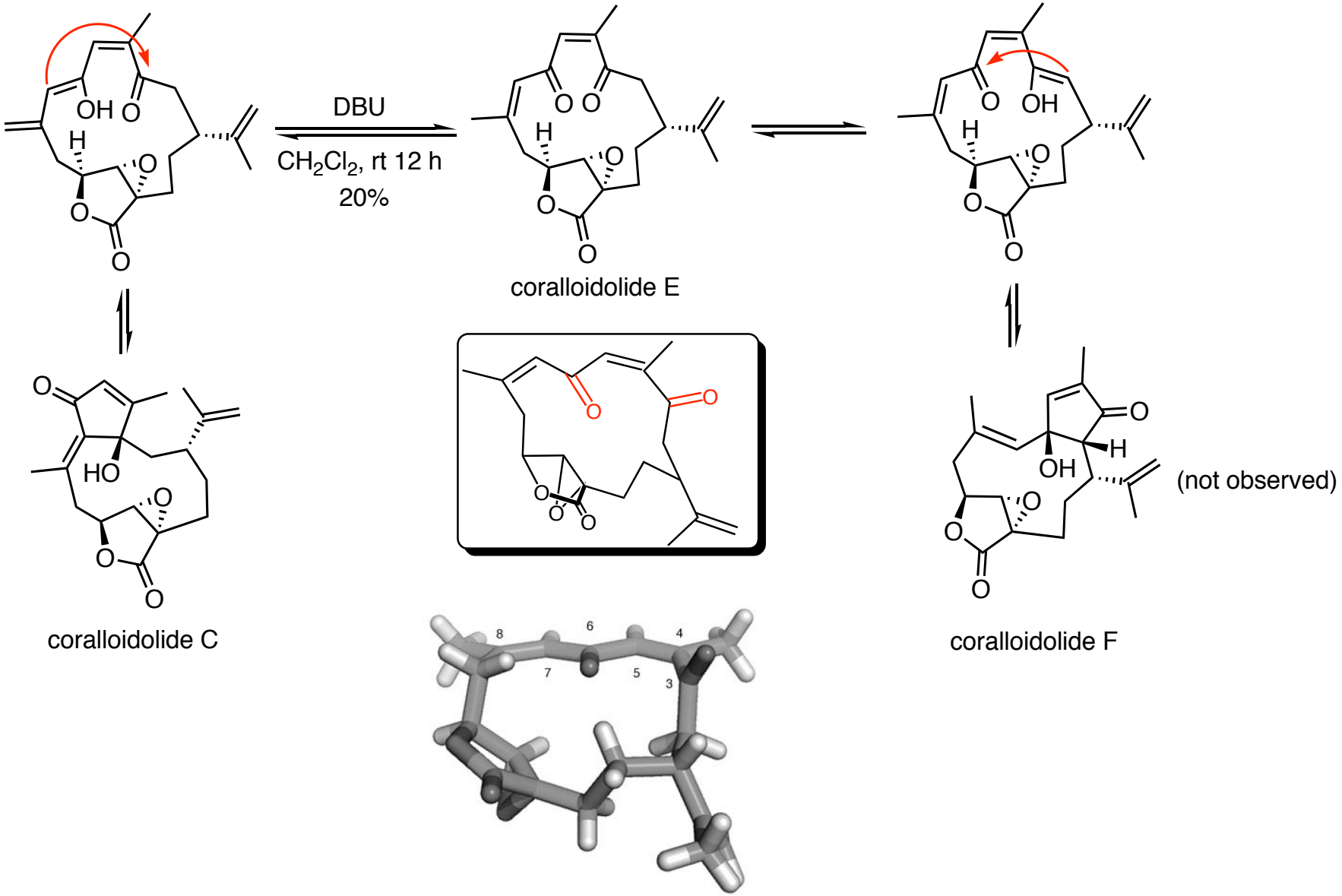


coralloidolide B

conditions: $Sc(OTf_3) \cdot xH_2O$, dioxane, rt, 3 h: 63% isolated

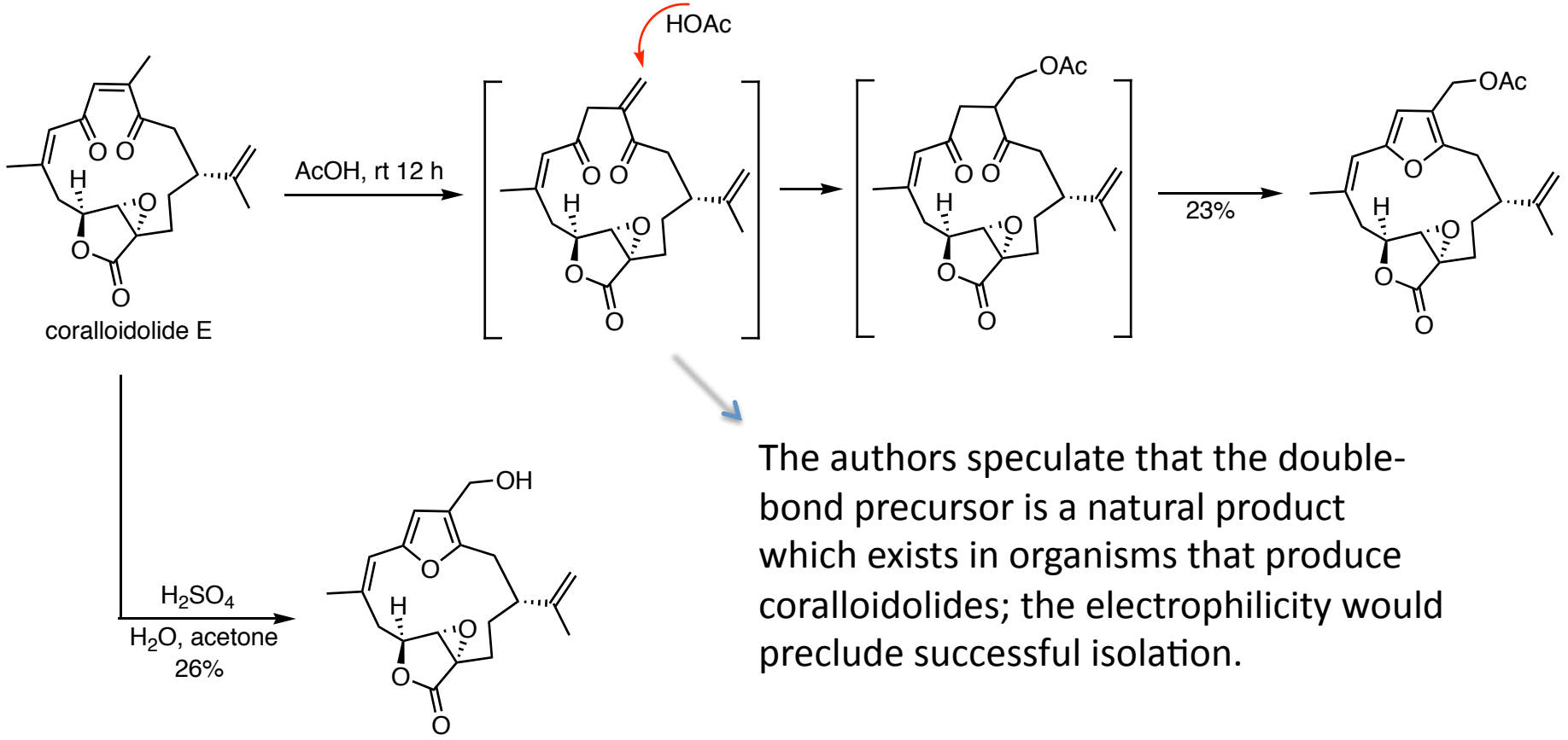
Kimbrough, T. J.; Roethle, P. A.; Mayer, P.; Trauner, D. *Angew. Chem. Int. Ed.* **2010,** *49,* 2619-2621.

Transannular Aldol Additions



Kimbrough, T. J.; Roethle, P. A.; Mayer, P.; Trauner, D. *Angew. Chem. Int. Ed.* **2010,** *49,* 2619-2621.

Products from Other Aldol Attempts



The authors speculate that the double-bond precursor is a natural product which exists in organisms that produce coralloidolides; the electrophilicity would preclude successful isolation.

Kimbrough, T. J.; Roethle, P. A.; Mayer, P.; Trauner, D. *Angew. Chem. Int. Ed.* **2010,** *49,* 2619-2621.

Summary and Outlook

- Trauner and coworkers have demonstrated the feasibility of preparing several coralloidolides from the common precursor rubifolide.

- The nature of the transformation (oxidative and acidic conditions) support the hypothesis that rubifolide may serve as a biosynthetic precursor to the coralloidolides.

- The asymmetric variant of the Trauner's synthesis of bipinnatin J (rubifolide precursor) suffers from the need to add several additional FGI's to install the correct stereocenters.

- Is the synthesis of coralloidolide D from rubifolide also feasible?