Syntheses of furanocembranoids and related natural products

Outline:

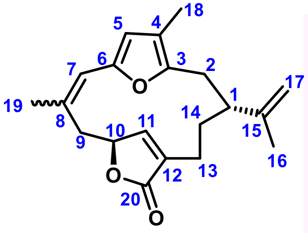
i. Overview
ii. Structural features and representative examples
iii. Biosynthesis
iv. a) Total syntheses
  Paquette — gorgiacerone (1992)
  Marshall — *ent*-rubifolide (1997)
  Trauner — bipinnatin J, rubifolide, isoepilophidione B, intricarene (2006), coralloidolides A, B, C, and E (2010)
  Pattenden — (*Z*)-deoxypukalide, (*E*)-deoxypukalide, deoxypseudopterolide (2010)
  Mulzer — 11-gorgiracerol, 11-epigorgiacerol (2012)
  Clark — 7-*epi*-Pukalide and 7-acetylsinumaximol B (2017)
 b) Synthetic studies
  Theodorakis — verrillin (2013)
  Sulikowski — bielschowskysin (2013)
  Mulzer — bielschowskysin (2013)
  Roche — bielschowskysin (2018)
  Stoltz — ineleganolide (2017, 2018)
 c) Not covered
  Paquette — acerosolide (1993)
  Marshall — kallolide B (1996)
  Marshall — kallolide A (1998)
  Marshall — deoxypukalide (2001)
  Pattenden — bis-deoxylophotoxin (2001)
  Rawal — bipinnatin J (2006)
  Pattenden — bippinatin J, intricarene (2006)
  Donohoe — (Z)-deoxypukalide (2008)
  Theodorakis — norcembrenolide B, scabrolide D (2011)
  Mulzer — 17-deoxyprovidencin (2014)
  Trauner — intricarene (2014)
  Furstner — sinulariadiolide (2019)
  Other synthetic studies (Nicolaou — bielschowskysin, Lear — bielschowskysin, Barriault — havellockate, Trost — rameswaralide, Vanderwal — ineleganolide, Ito — Yonarolide, Mehta — plumarellides and mandapamates...)

Reviews:
Trauner, *Nat. Prod. Rep.* **2008**, *25,* 298-317
Pattenden, *Nat. Prod. Rep.* **2011**, *28,* 1269-1310
Stoltz, *Chem. Rev.* **2017**, *117*, 7878–7909


gorgonian corals, northwestern Atlantic Ocean and the Carribean sea

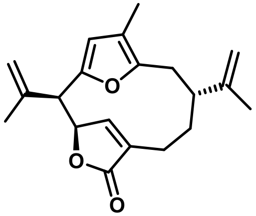

soft corals, Indo Pacific reefs

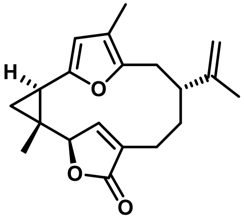
ii. Structural features and representative examples



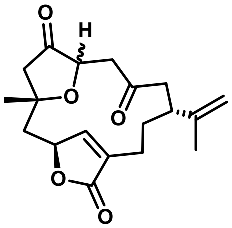
furanocembranoids

- most furanocembranoids have ***Z*** olefins, but most of the corresponding **C7-C8** epoxides are derived from the ***E*** diastereomer
- only **C1** and **C9** are spared of oxidation *in vivo*
- **C18** can be in all oxidation states
- the furan moiety is often oxidatively cleaved *in vivo* to give enediones that are converted to a variety of different products


pseudopteranes



gersolanes



norcembranoids

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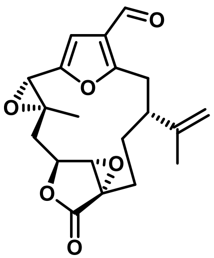
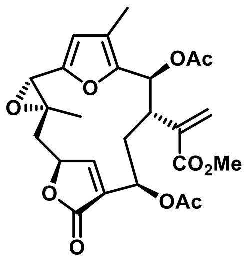
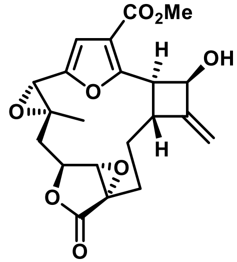
Furanocembranoids



lophotoxin
neurotoxin

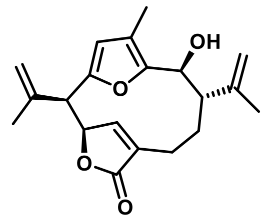


bipinnatin I
potent cytotoxin

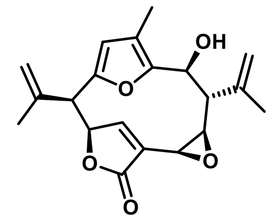


providencin
cytotoxin

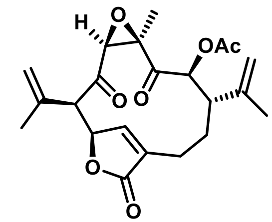
Pseudopteranes



kallolide A
strong anti-inflamatory activity

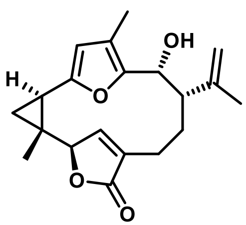


pseudopterolide
cytotoxin

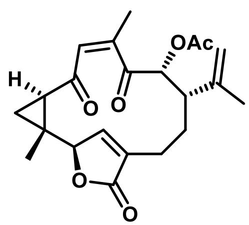


kallolide I

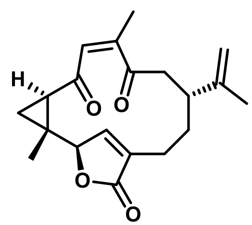
Gersolanes



pinnatin A
potent cytotoxin

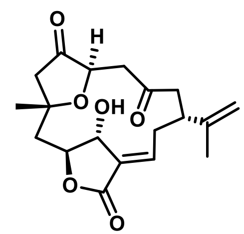


pinnatin B
cytotoxin

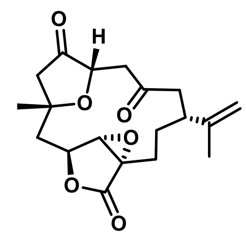


gersolide

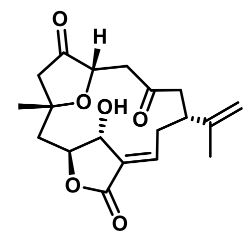
Norcembranoids



sinuleptolide
strong anti-inflamatory activity
cytotoxin

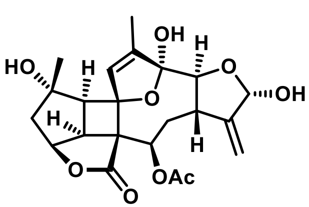


scabrolide D

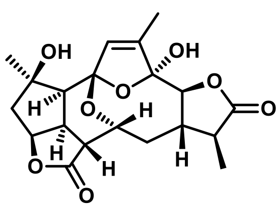


5-epi-sinuleptolide
cytotoxin

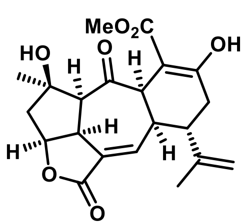
Complex polycyclic furanocembranoid derivatives



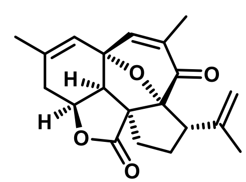
bielschowskysin
very potent cytotoxin
antimalaric



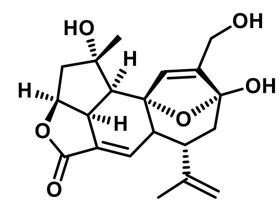
verrillin
uknown bioactivity



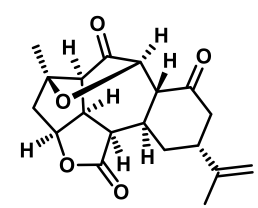
rameswaralide
cytotoxin



intricarene
cytotoxin



plumarelide
moderate hemolytic activity



ineleganolide
antileukemic

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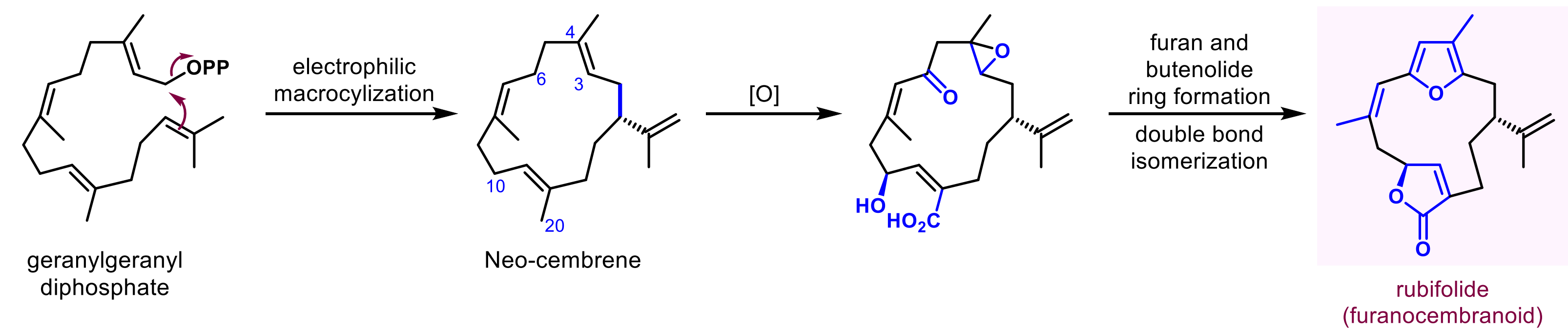
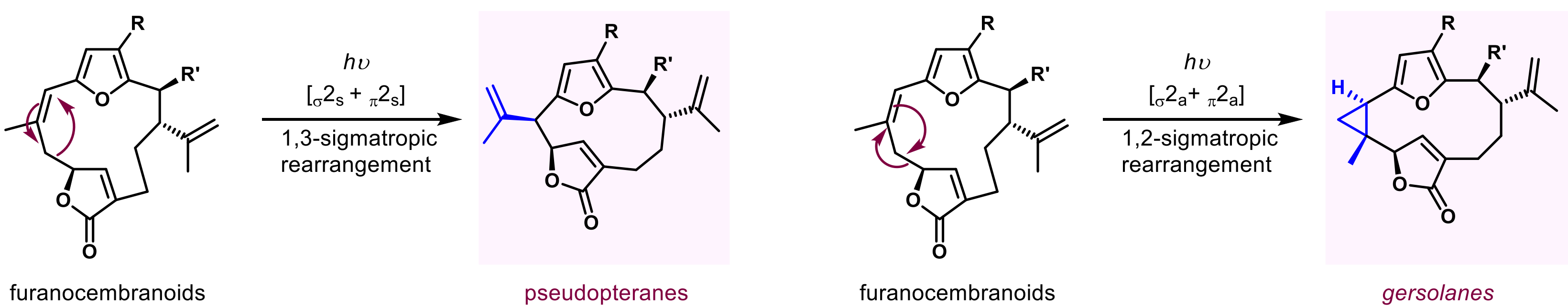
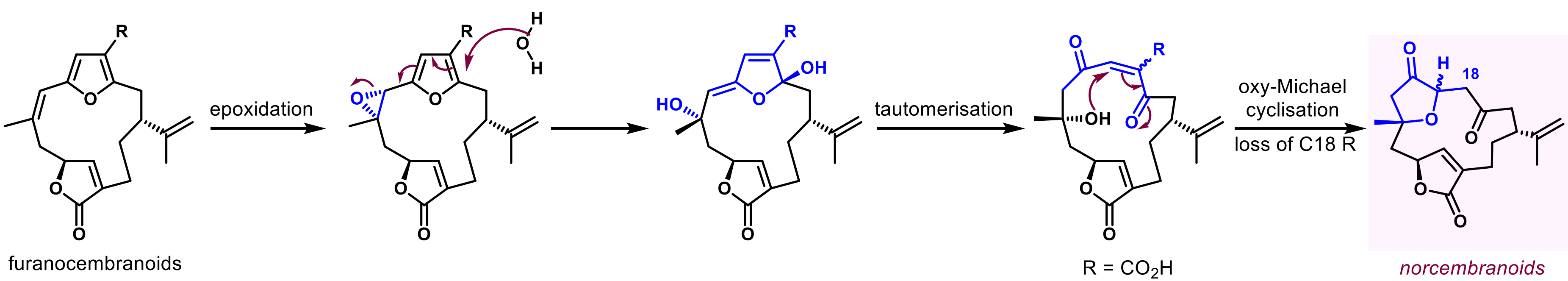
iii. Biosynthesis





R' = H or OH when R = Me
R' = H when R = CO_2Me



R = CH_3, CHO, CO_2H, CO_2Me

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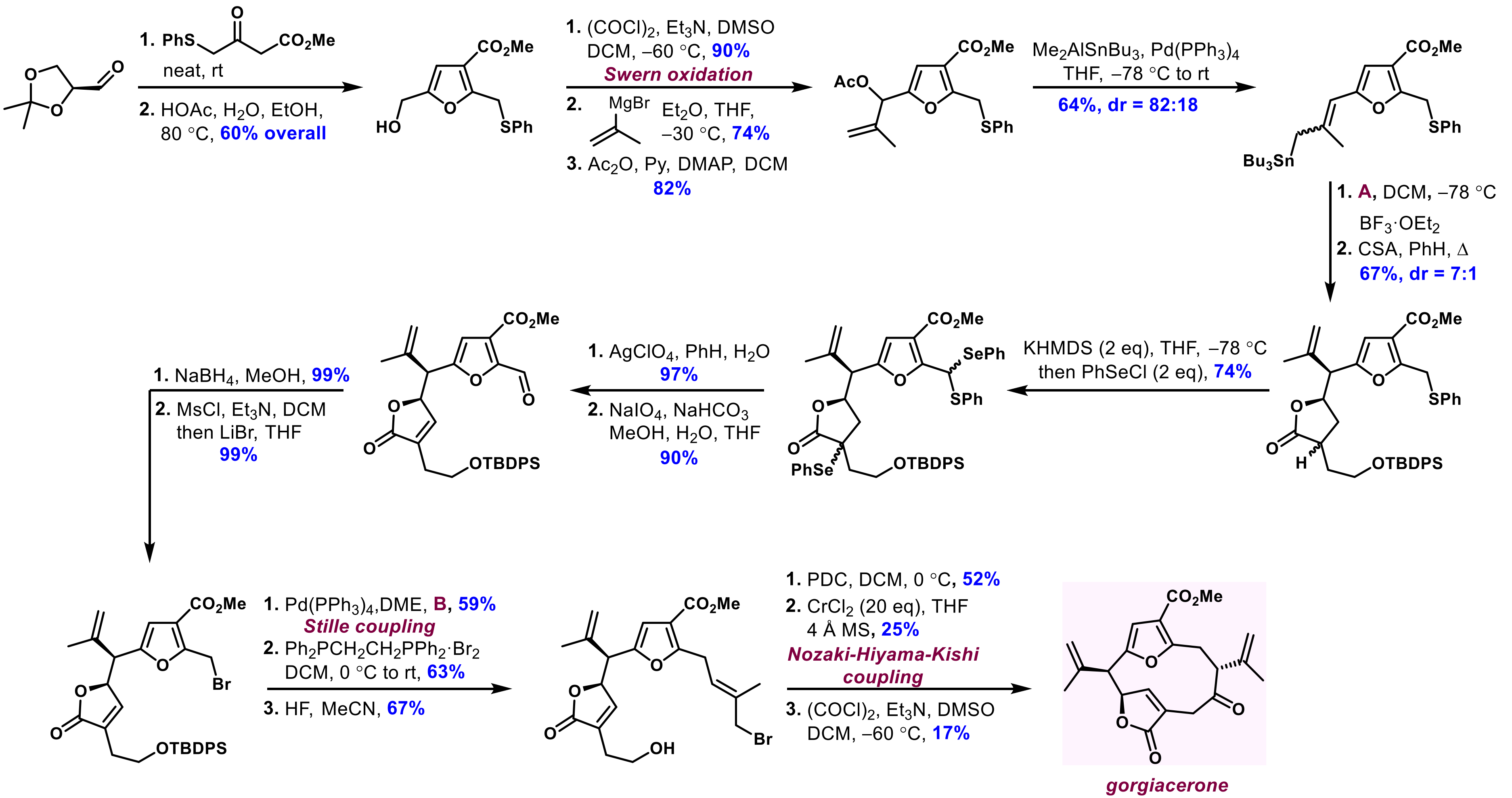
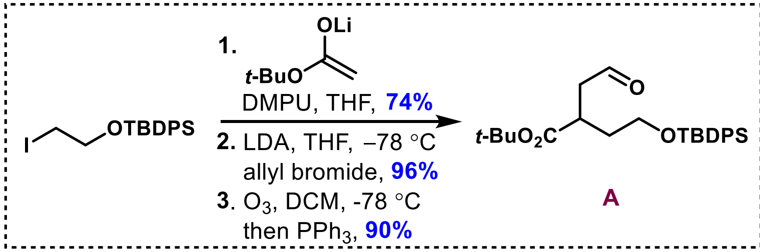
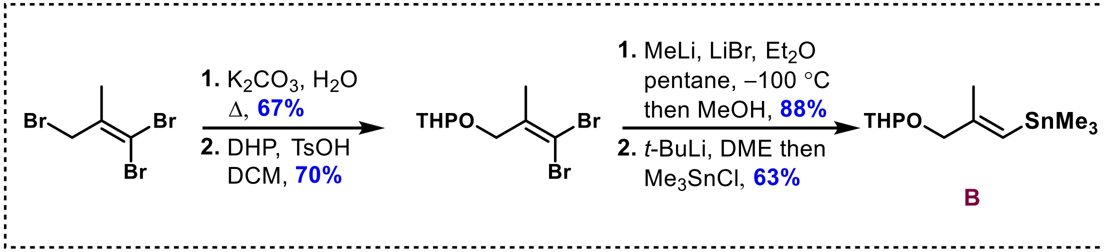
iv. a) Total syntheses: Paquette, *J. Am. Chem. Soc.* **1992**, *114*, 3910–3926; *J. Am. Chem. Soc.* **1992**, *114*, 3926-3936







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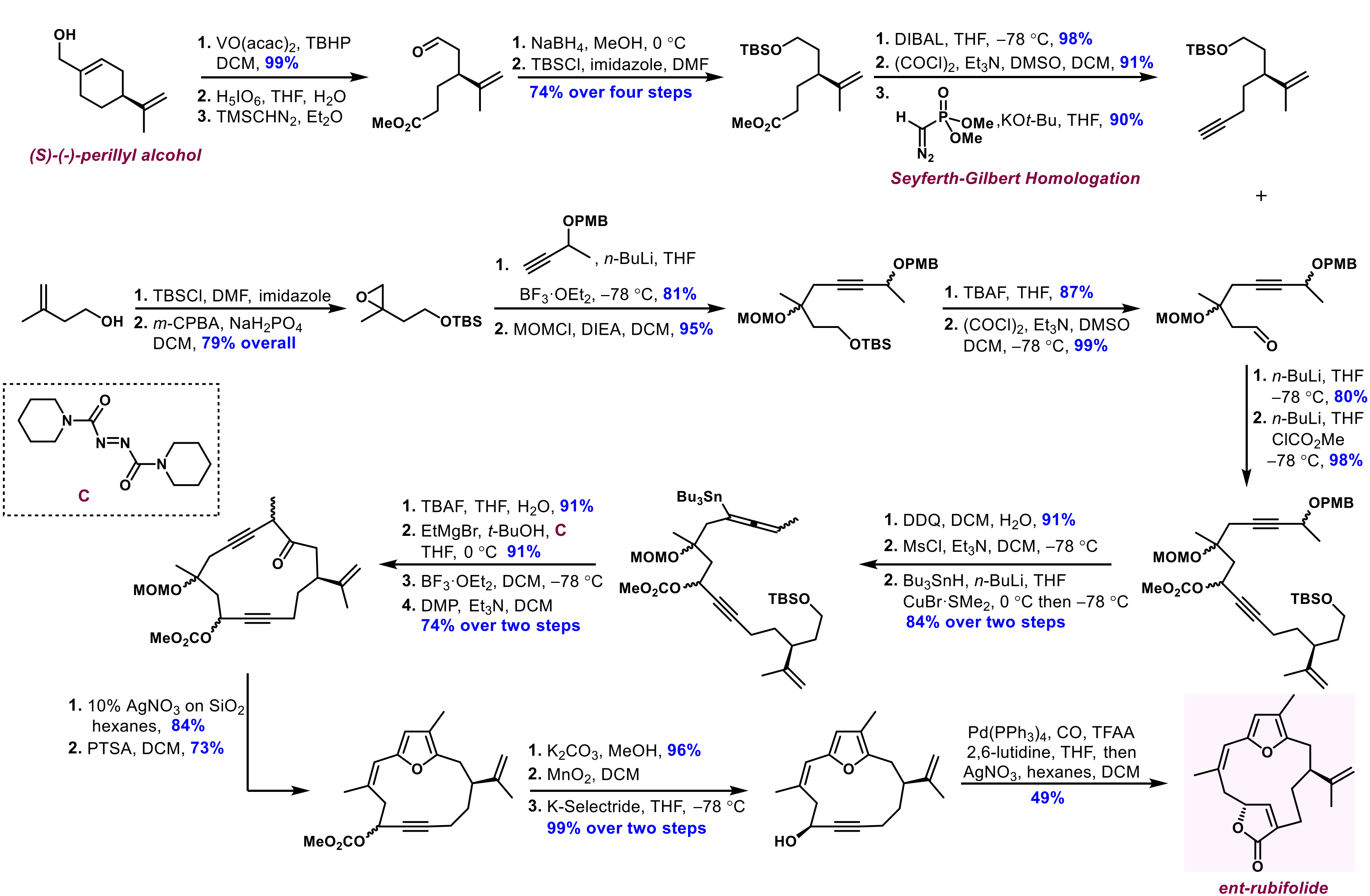
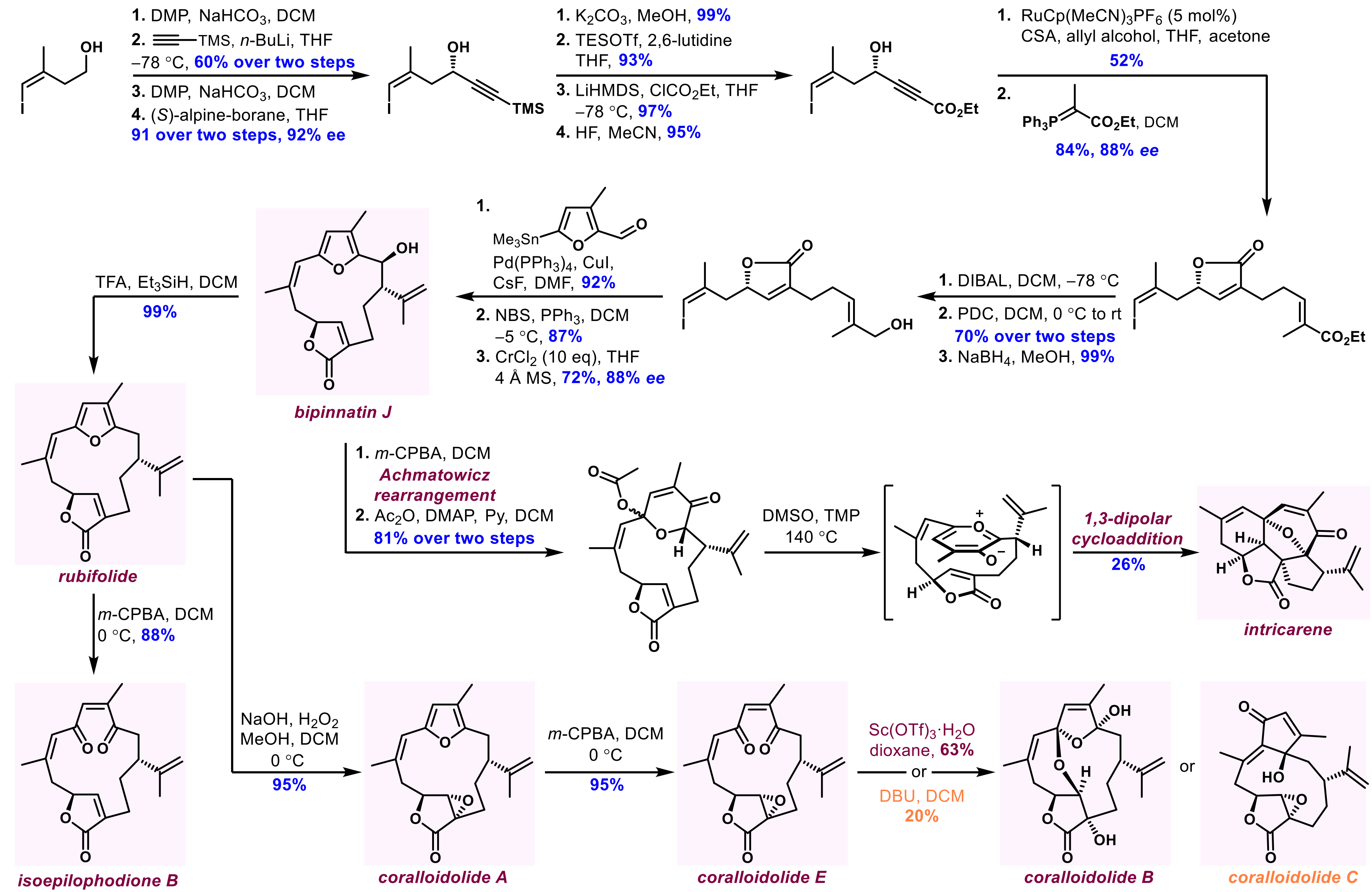
Marshall, *J. Org. Chem.* **1997**, *62*, 4313-4320



Syntheses of furanocembranoids and related natural products

Trauner, *Org. Lett.* **2006**, *8*, 5901–5904; *Angew. Chem. Int. Ed.* **2010**, *49*, 2619 –2621;



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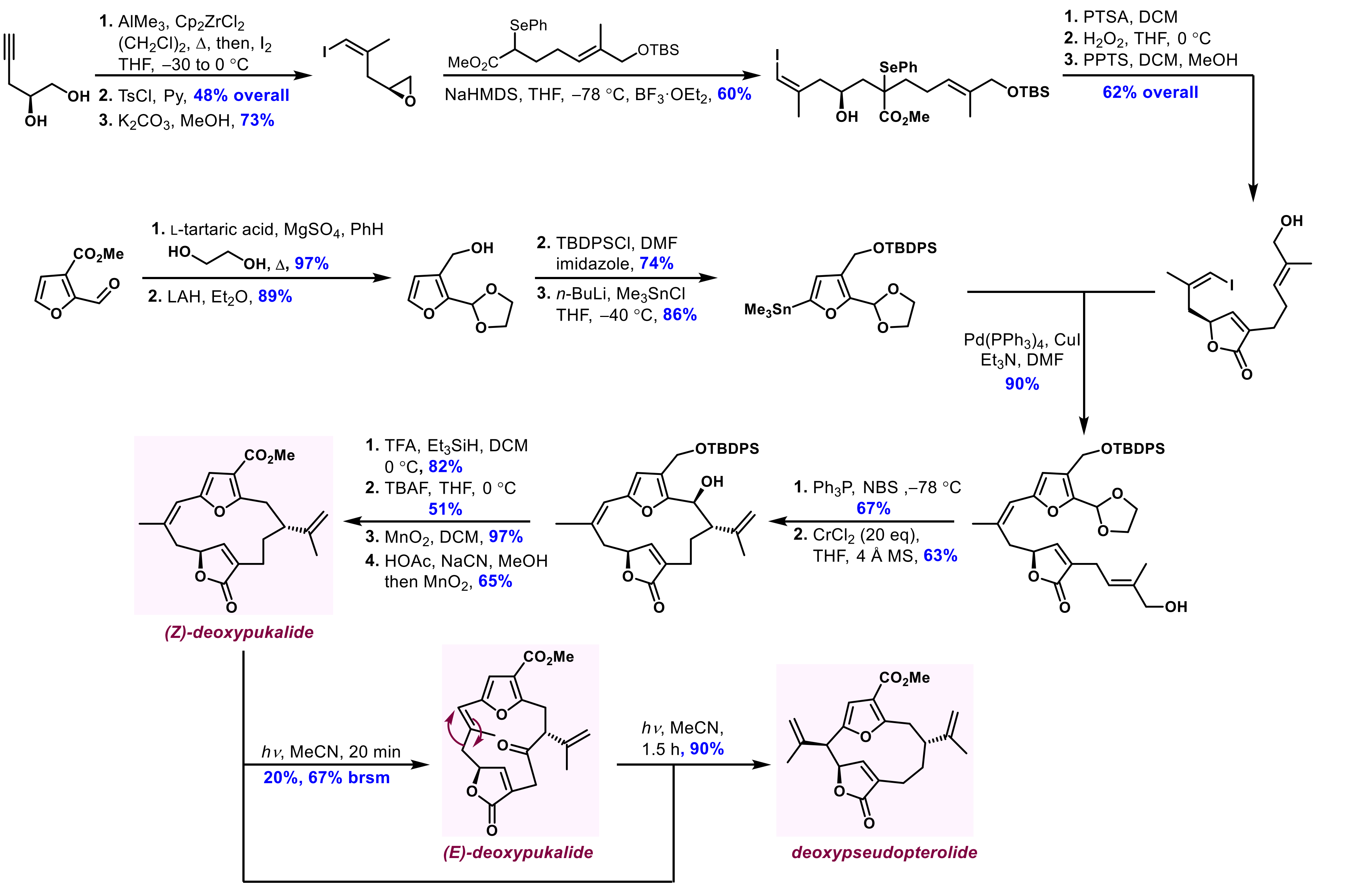
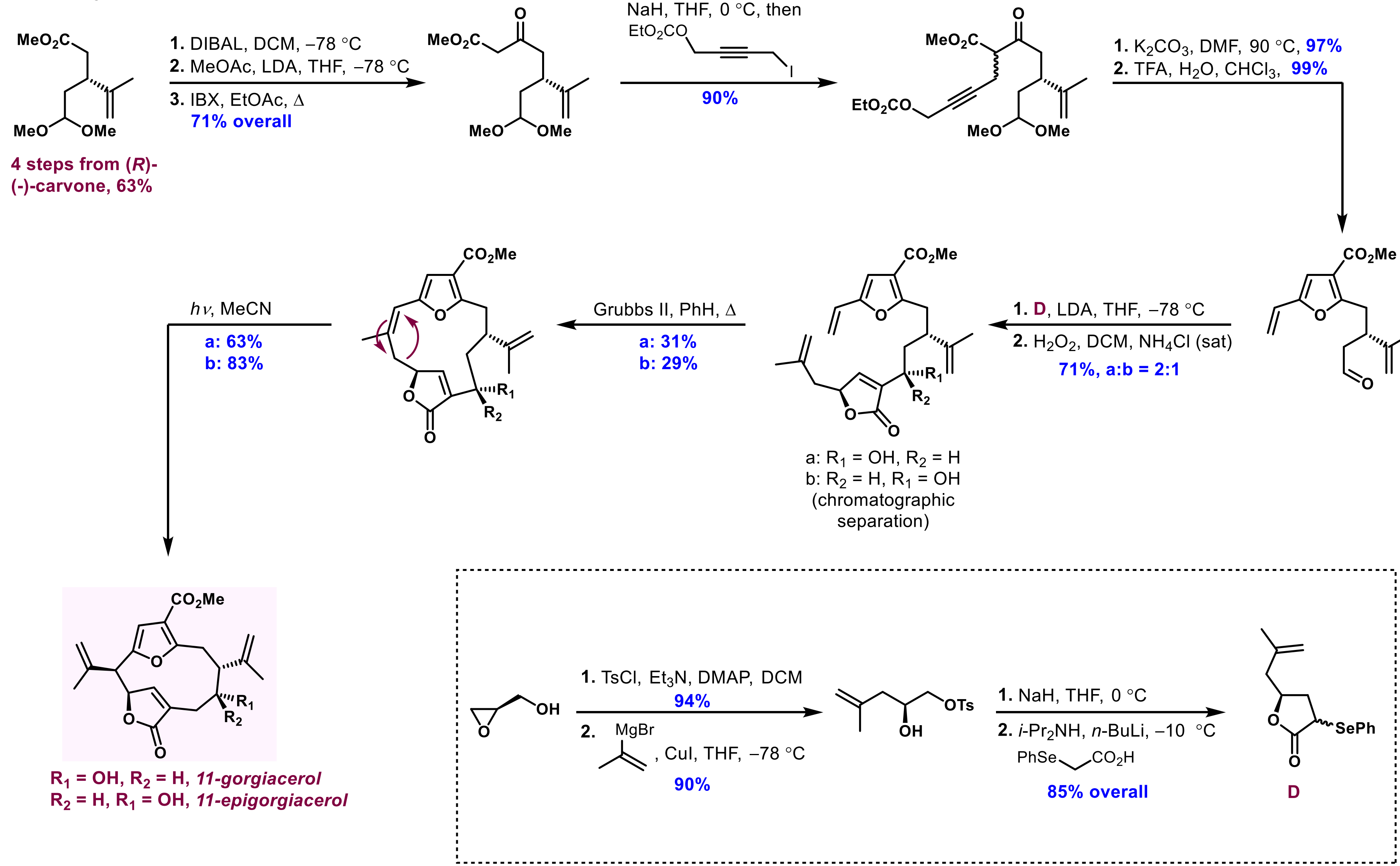
Pattenden, *Tetrahedron* **2010**, *66*, 2492–2500, *Tetrahedron* **2010**, *66*, 6546-6549



Syntheses of furanocembranoids and related natural products

Mulzer, *Org. Lett.* **2012**, *14*, 2834-2837



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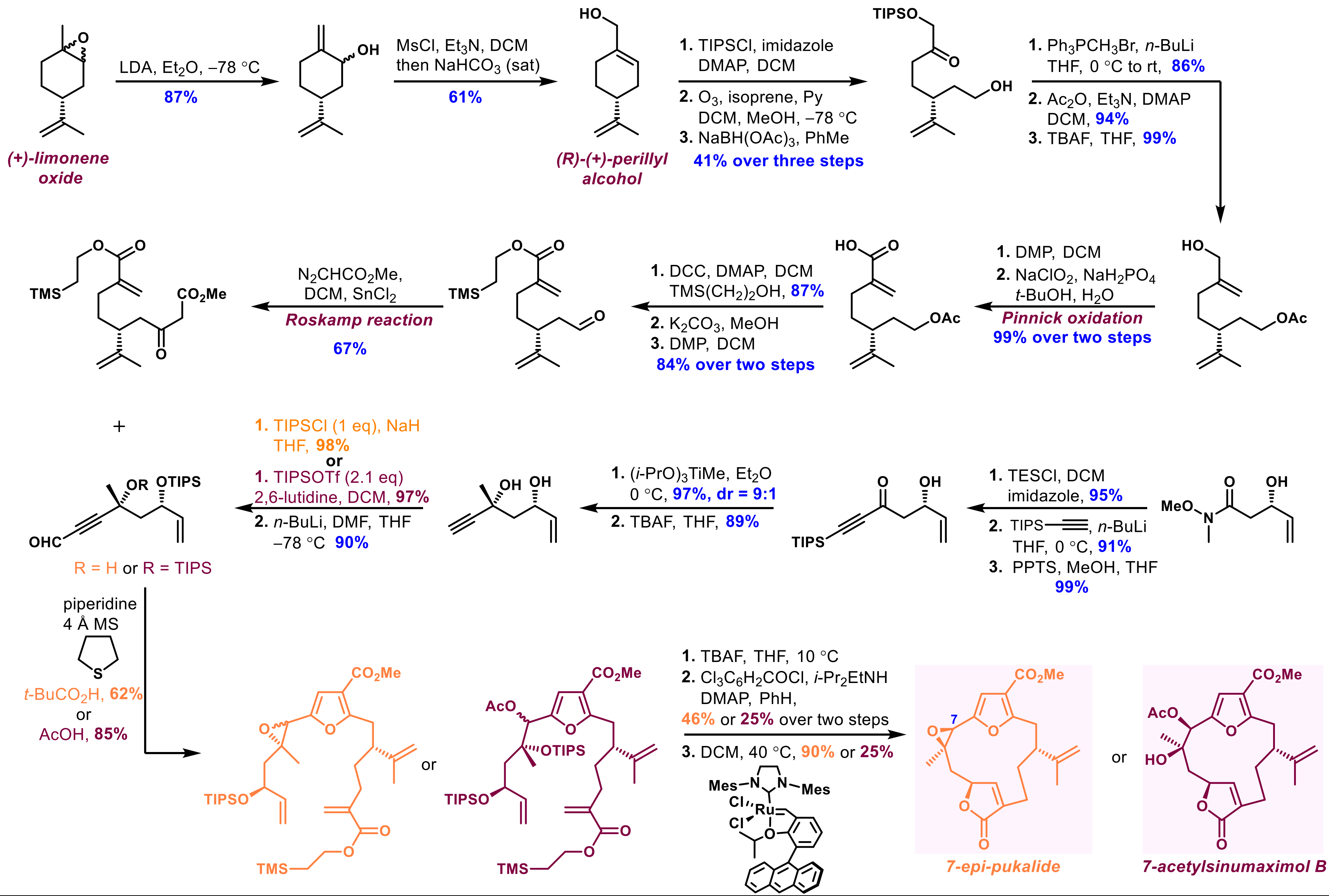
Clark, *Chem. Eur. J.* **2017**, *23*, 9761–9765



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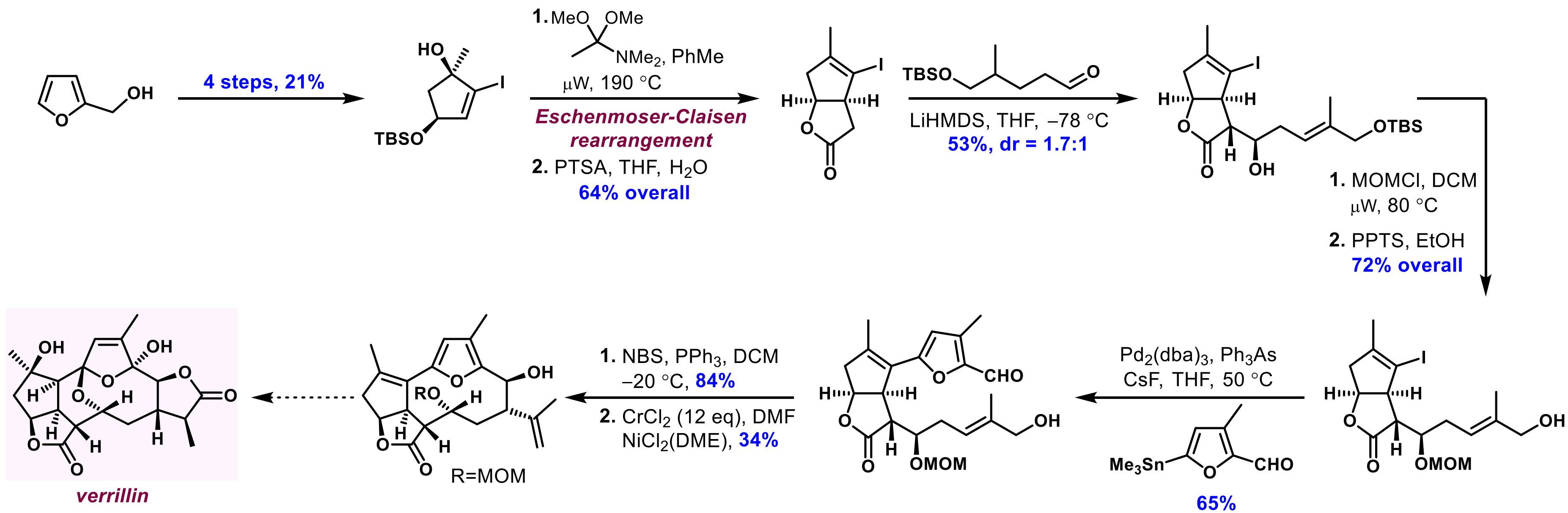
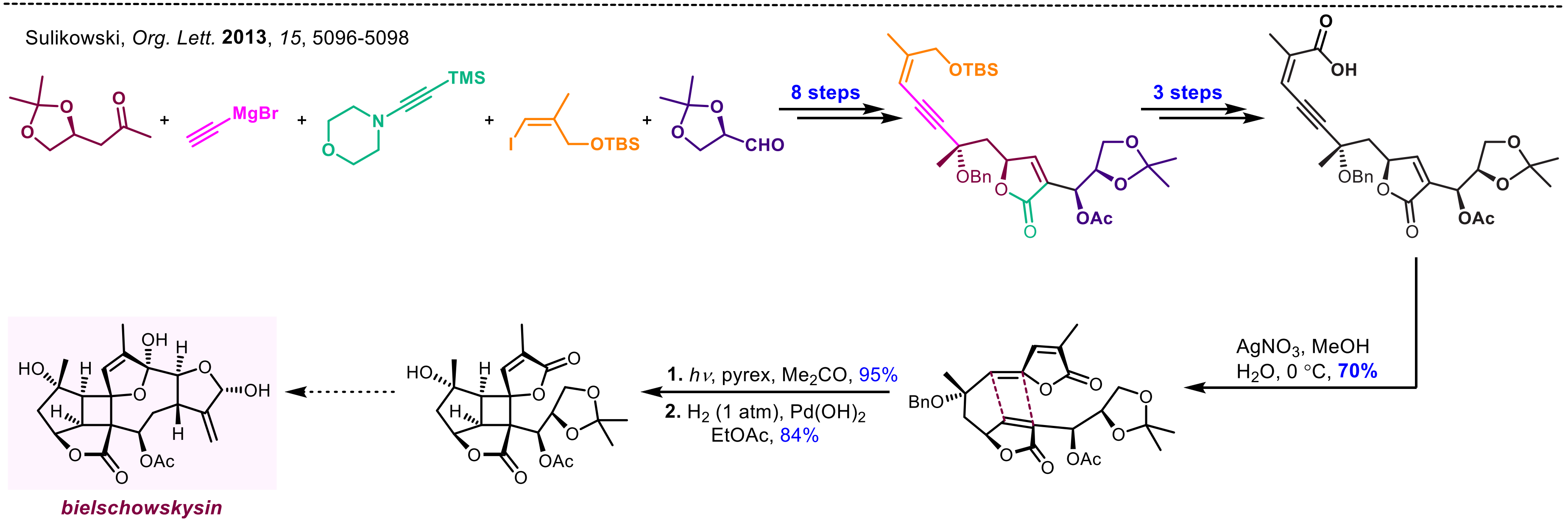
iv. b) Synthetic studies: Theodorakis, *Org. Lett.* **2013**, *15*, 2410-2413



Sulikowski, *Org. Lett.* **2013**, *15*, 5096-5098



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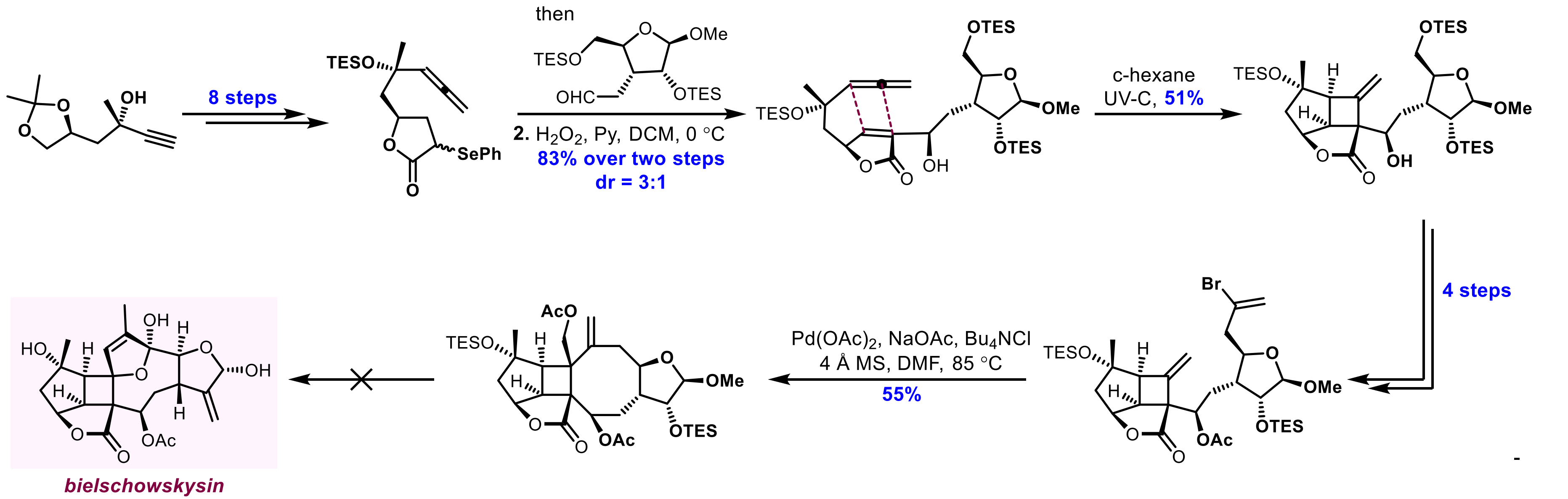
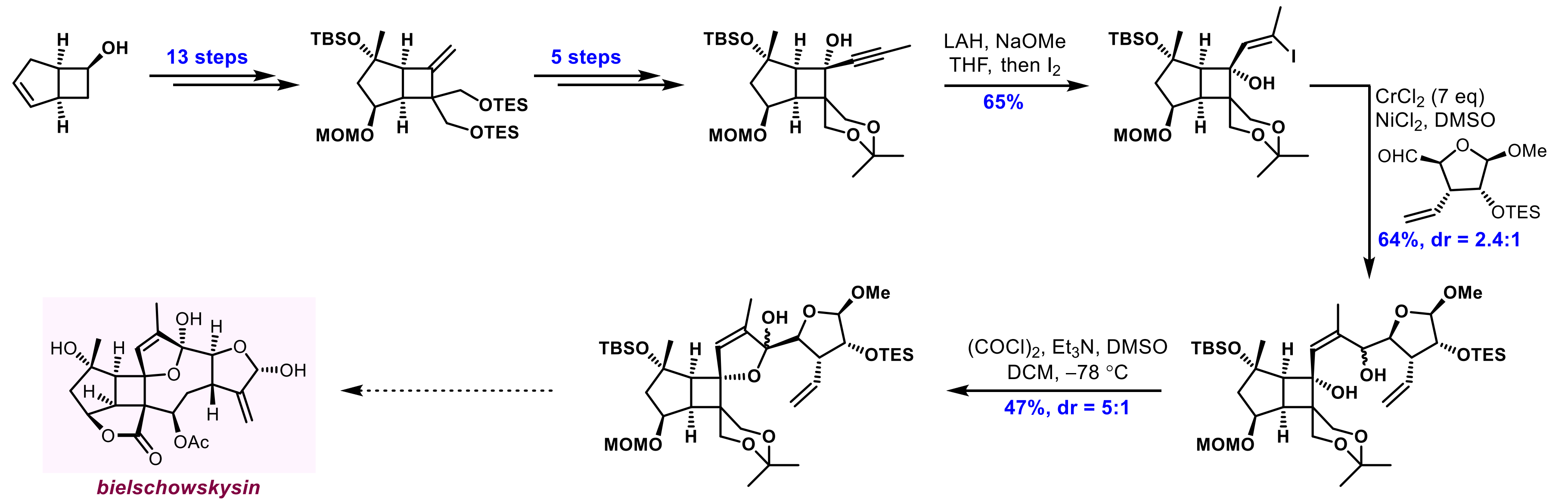
Mulzer, *Eur. J. Org. Chem.* **2013**, 8214-8244



Mulzer, *Eur. J. Org. Chem.* **2013**, 8245-8252



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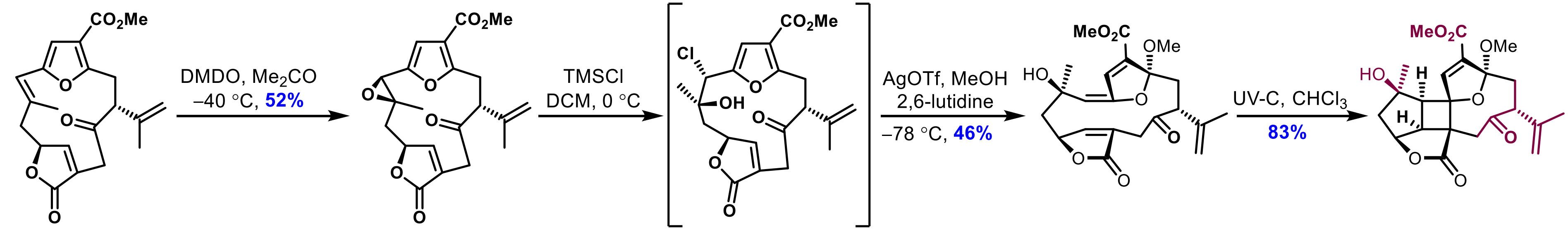
Roche, *Angew. Chem. Int. Ed.* **2018**, *57*,1316-1321



acerosolide

Stoltz, *Chem. Sci.* **2017**, *8*, 507-514; *J. Org. Chem.* **2018**, *83*, 3467-3485