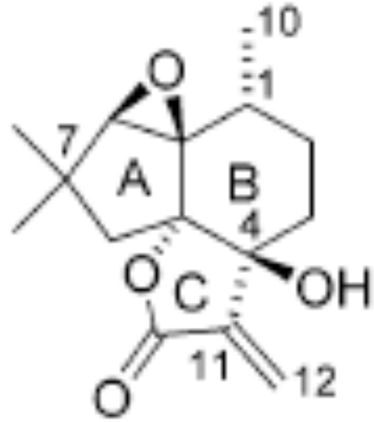
Anodic Oxidation reactions
First asymmetric synthesis of (-)-Alliaciol A

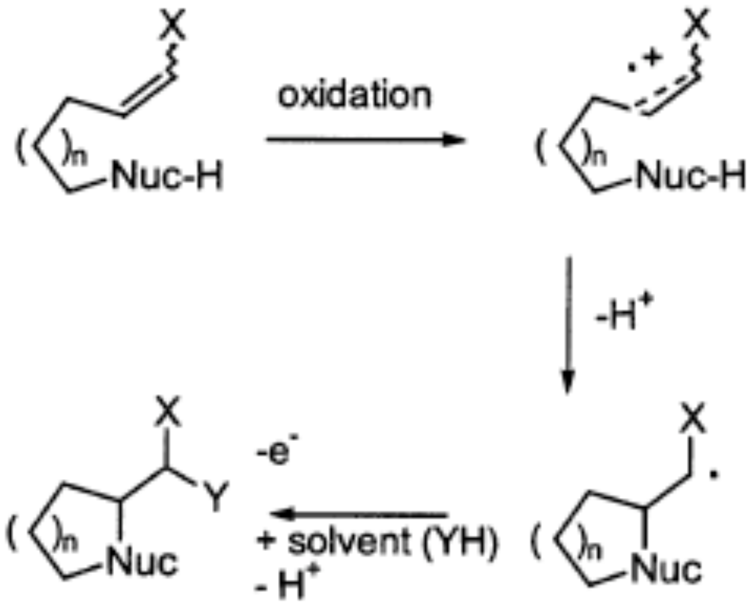


1. **(+)-Alliacol A**

John Mihelcic and Kevin D. Moeller*

J. AM. CHEM. SOC. 2004, *126*, 9106−9111

General mechanism for anodic oxidations of enol ethers



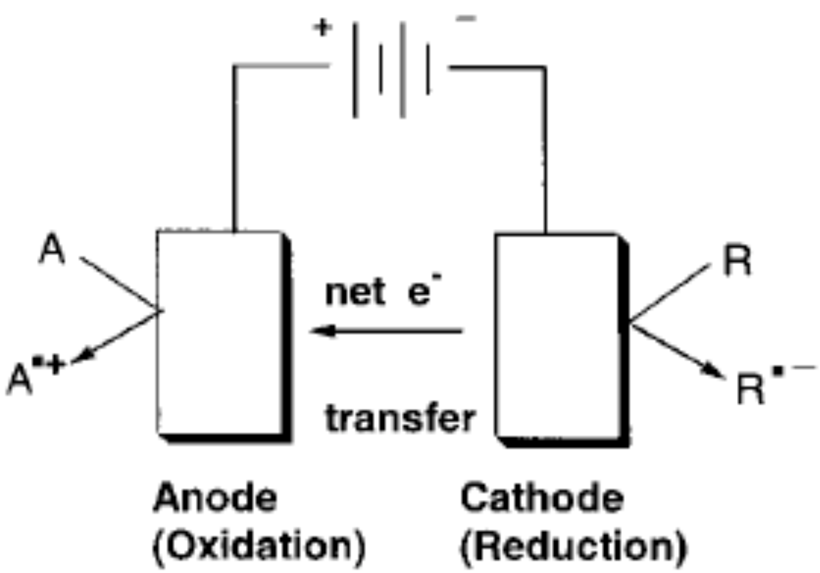
Kevin D. Moeller

Reversal of polarity of functional groups

⇩

Useful umpolong reactions (coupling of nucleophiles)

Anodic oxidation setup

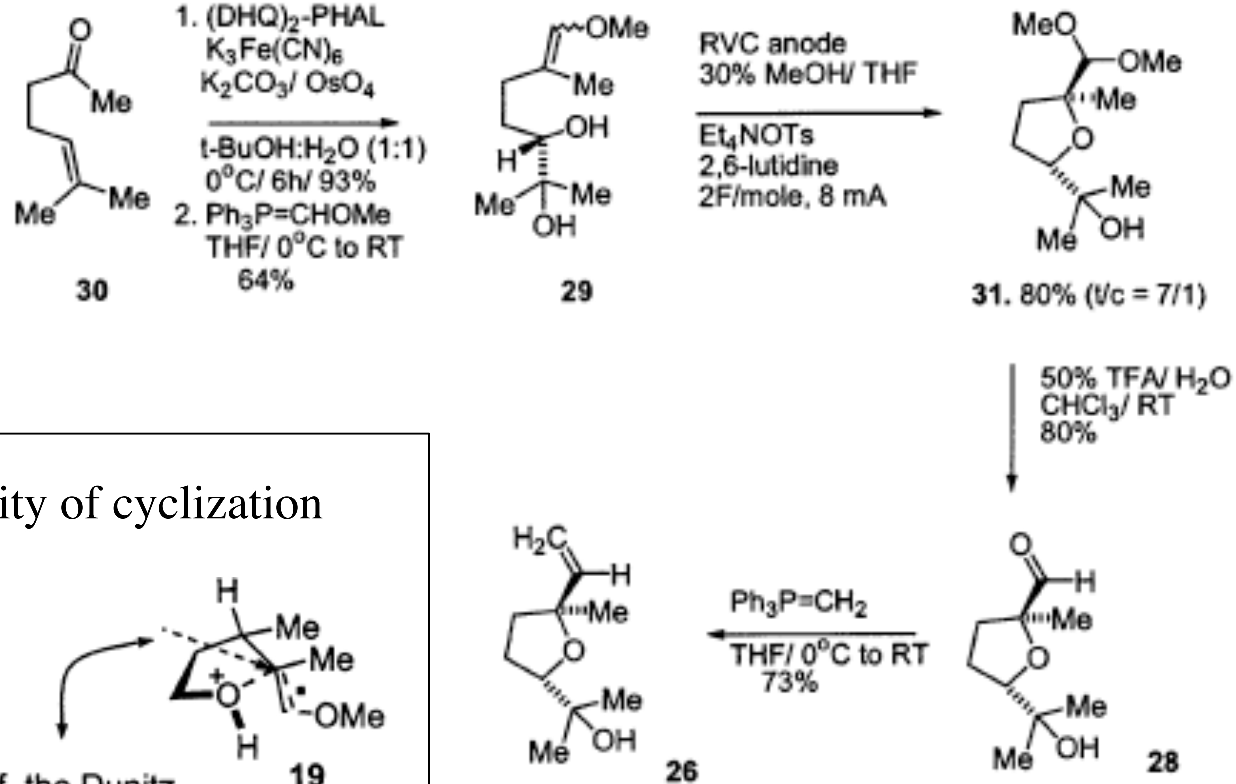


Constant Current -- potential varies
Controlled Potential -- current varies

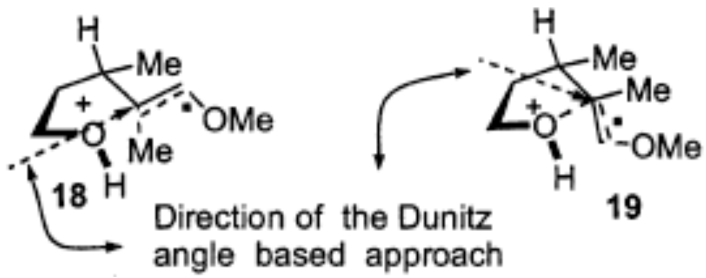
Anode materials: **Carbon or Platinum**
Solvents: **MeOH, AcOH, CH_3CN, CH_2Cl_2**
THF, H_2O
Electrolytes: **Et_4NOTs, $LiClO_4$, Bu_4NBF_4,**
Bu_4NPF_6

Kevin D. Moeller* Tetrahedron 56 (2000) 9527–9554

Coupling of enol ethers and O-nucleophiles:
Total synthesis of (+)-Linalool Oxide



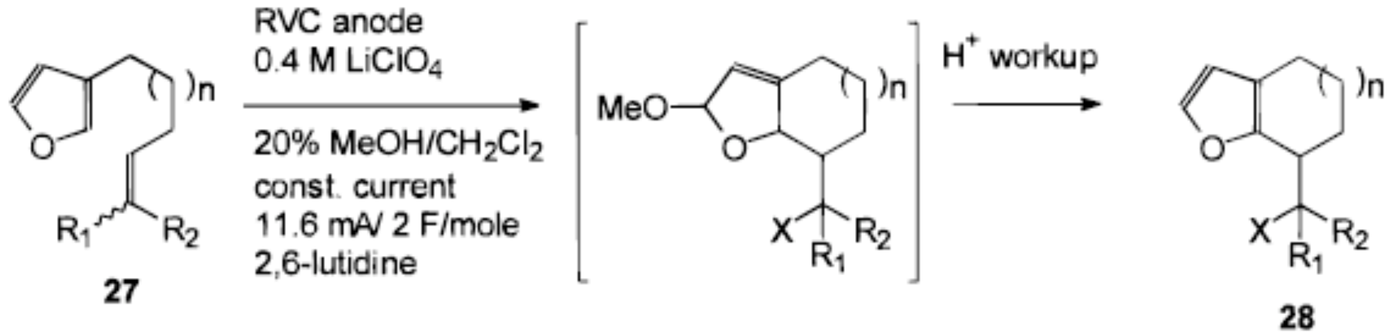
Stereoselectivity of cyclization



Bin Liu, Shengquan Duan, Angela C. Sutterer, and Kevin D. Moeller*

J. AM. CHEM. SOC. 2002, *124*, 10101−10111

Anodic coupling of silyl enol ethers with furans

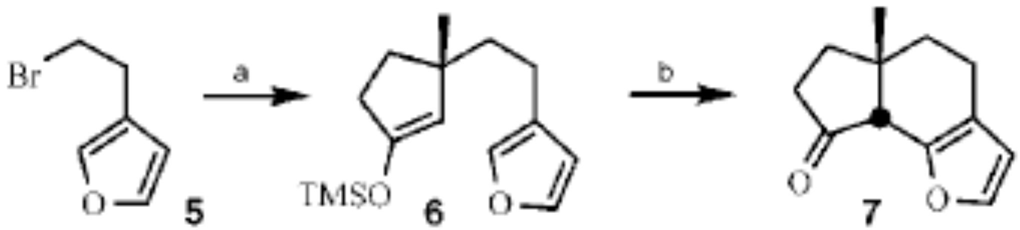


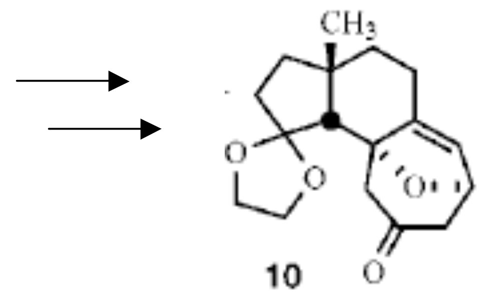
1	**27a**: R_1 = SMe, R_2 = H, n = 1		**28a**: 54% (R_1 = SMe, X = OMe) **28b**: 17% (R_1 = OMe, X = OMe)
2	**27a**: R_1 = SMe, R_2 = H, n = 1	MeOH solvent	**28a**: 67% (R_1 = SMe, X = OMe) **28b**: 10% (R_1 = OMe, X = OMe)
3	**27b**: R_1 = OMe, R_2 = H, n = 1		**28b**: 75% (X = OMe)
4	**27c**: R_1 = Ph, R_2 = H, n = 1		**28c**: 71% (X = OMe)
5	**27d**: R_1 = CH_2TMS, R_2 = H, n = 1		**28d**: 49% (no X, R_1 = CH_2)[a]
6	**27e**: R_1 = CH_2TMS, R_2 = CH_3, n = 1		**28e**: 51% (no X, R_1 = CH_2)
7	**27f**: R_1 = CH_3, R_2 = CH_3, n = 1		**28f**: 24% (X = OMe) **28e**: 51% (no X, R_1 = CH_2)
8	**27g**: R_1 = OMe, R_2 = H, n = 2		**28g**: 62% (X = OMe)
9	**27g**: R_1 = OMe, R_2 = H, n = 2	MeOH solvent	**28g**: 58% (X = OMe)
10	**27h**: R_1 = Ph, R_2 = H, n = 2		**28h**: 41% (X = OMe)[b]
11	**27h**: R_1 = Ph, R_2 = H, n = 2	MeOH solvent	**28h**: 48% (X = OMe)[b]
12	**27i**: R_1 = CH_3, R_2 = CH_3, n = 2		**28i**:[c] 26% (no X, R_1 = CH_2)[b] **28ii**: 6% (X = OMe)[b]
13	**27j**: R_1 = OMe, R_2 = H, n = 3		**28j**:[d] 32% (X = OMe)[b,e]

[a] The product formed cleanly but was volatile. [b] Unoptimized yield. [c] This reaction also led to an uncyclized product resulting from oxidation of the furan ring (see text). [d] This reaction also led to an uncyclized product resulting from oxidation of the enol ether (see text). [e] This reaction used n-Bu_4NBF_4 as the electrolyte. The yield using $LiClO_4$ was 24%.

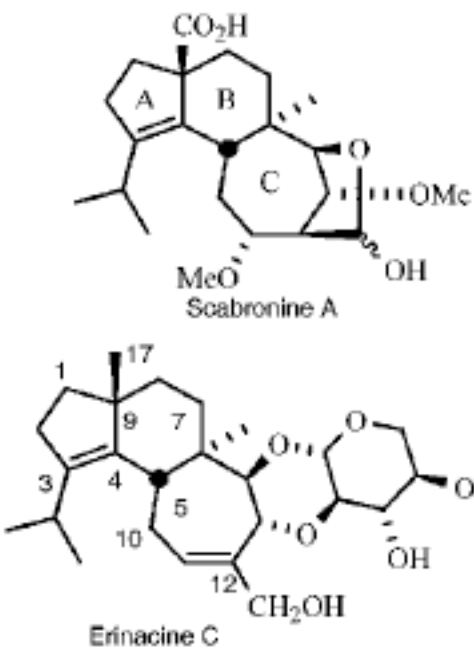
Dallas G. New, Zerom Tesfai, and Kevin D. Moeller* *J. Org. Chem.* **1996**, *61*, 1578−1598

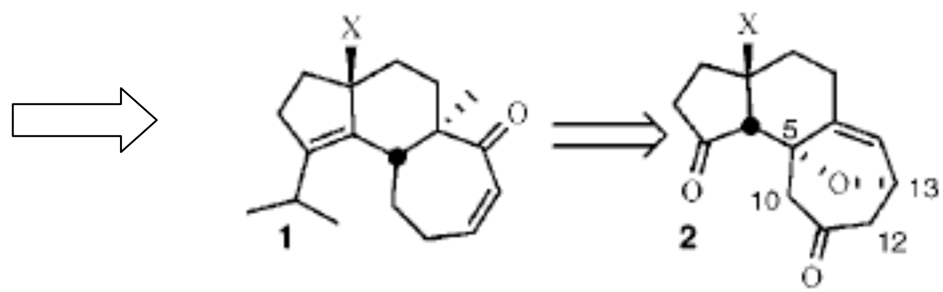
Anodic coupling for the synthesis of cis-fused furans: Synthesis of the cyanthin core





Key: a) Mg, CuI, TMSCl then **4a** b) carbon anode, iPrOH, CH_3CN, $LiClO_4$, lut., 65% overall from **4a**





Dennis L. Wright,* Christopher R. Whitehead, E. Hampton Sessions,[†]
Ion Ghiviriga,[§] and Dean A. Frey

Org. Lett. **2001**, *3*, 2685

Introduction on alliacene family of antiboitics

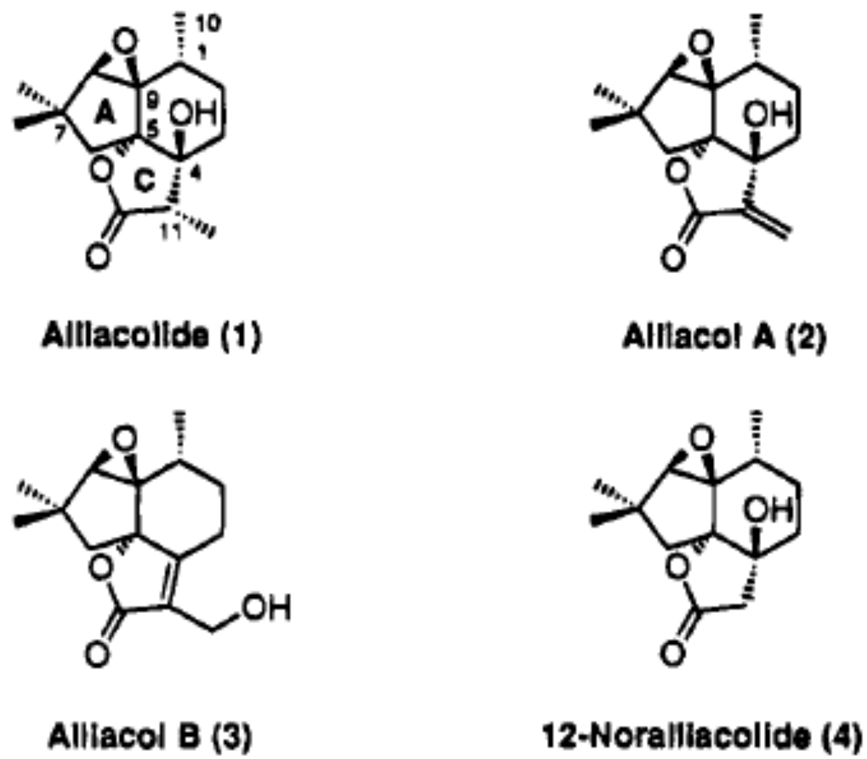


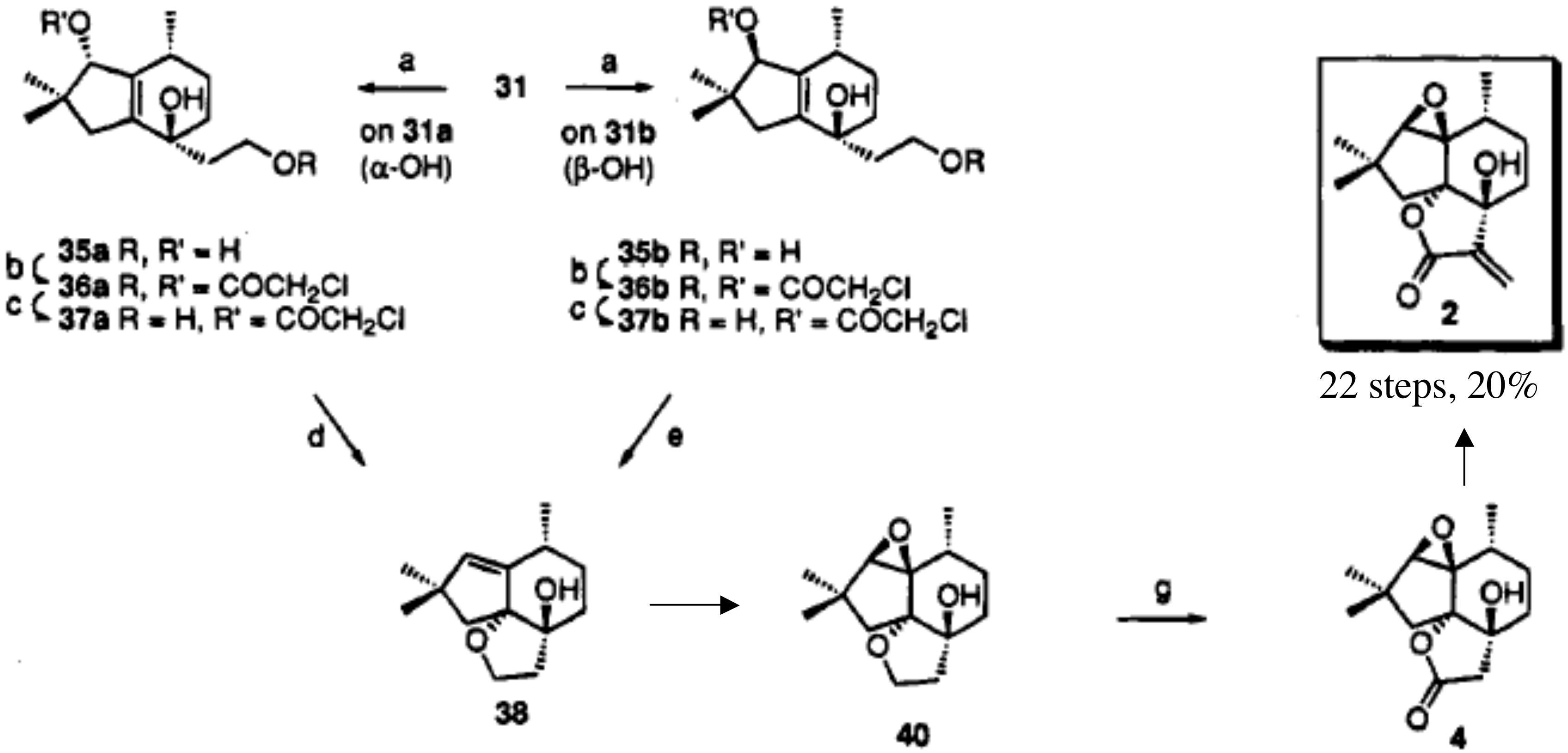
Figure 1. Several sesquiterpene metabolites isolated from cultures of *Marasmius Alliaceus*.

Alliacol A

Isolation : 1977
from fungus
Marasmius Alliaceous

Anti-microbial activity
against Ehrlich carcinoma

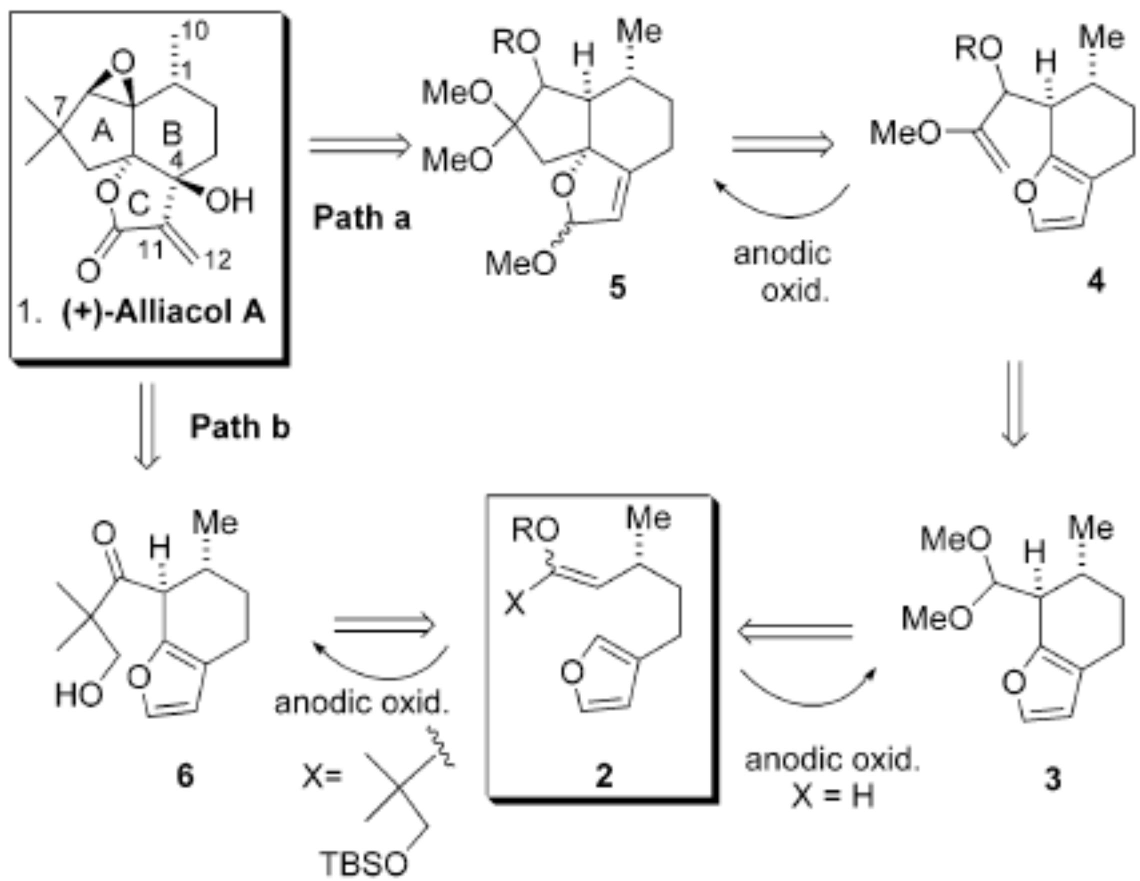
First stereoselective synthesis of Alliacol A (racemic)



James J. La Clair,*,†,§ Peter T. Lansbury,*,† Ben-xin Zhi,†,|| and Karst Hoogsteen‡

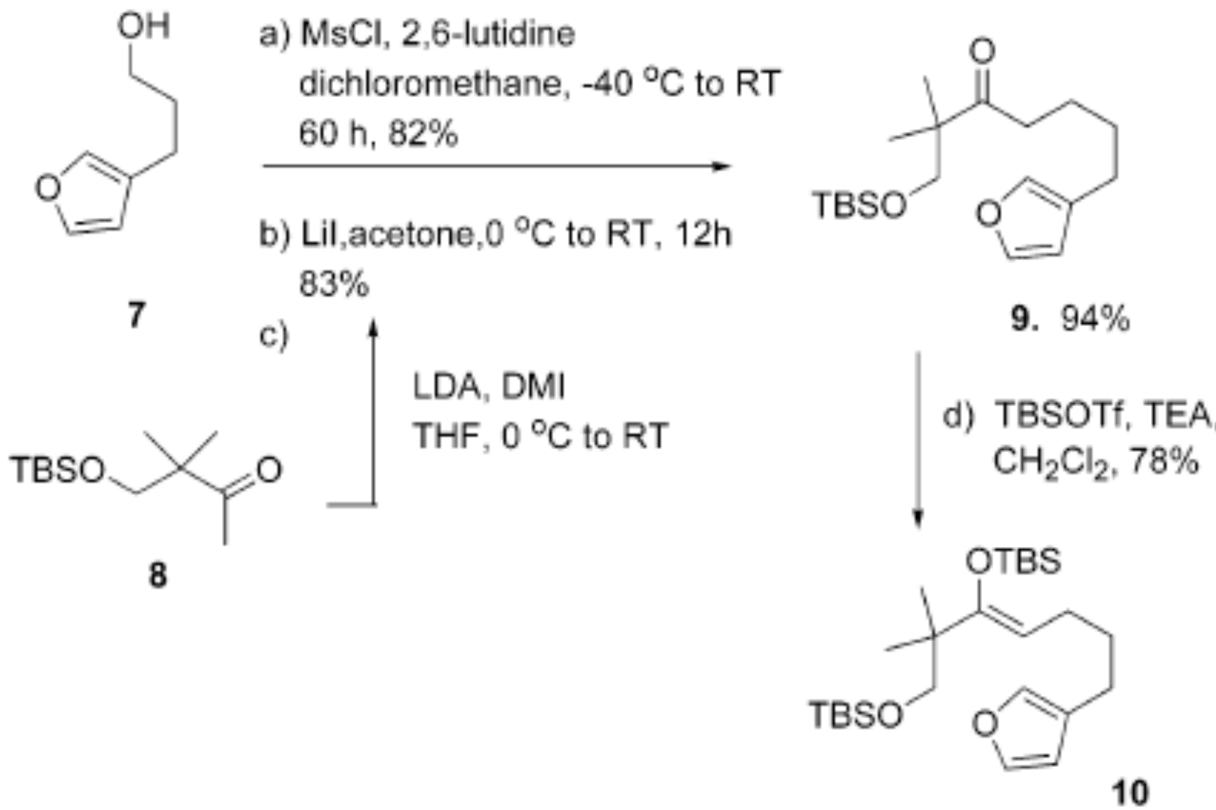
J. Org. Chem. **1995,** *60,* 4822–4833

Moeller's retrosynthesis

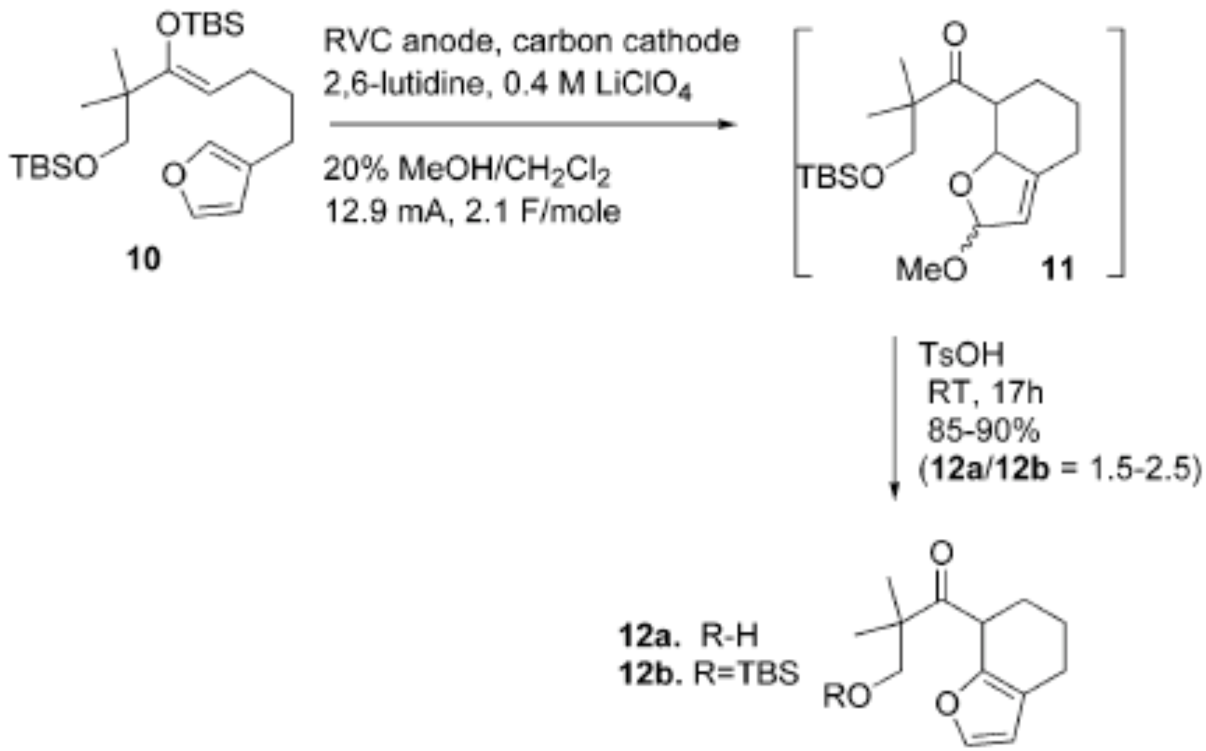


J. AM. CHEM. SOC. **2004**, *126*, 9106−9111

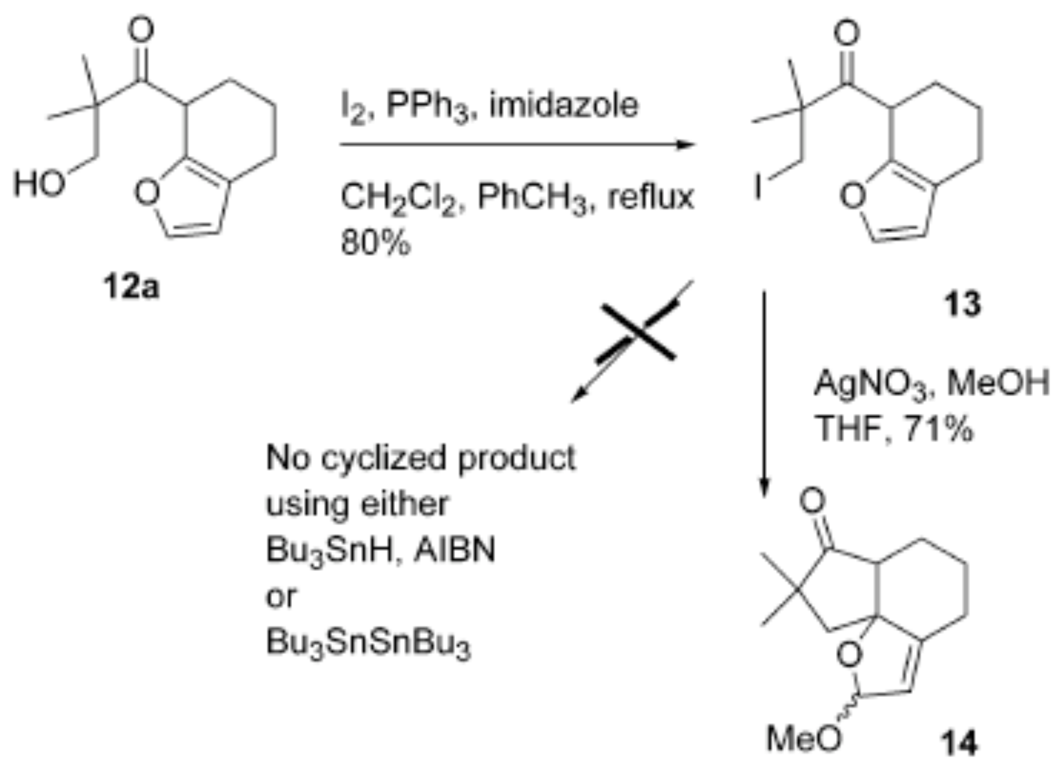
Construction of model compound 10



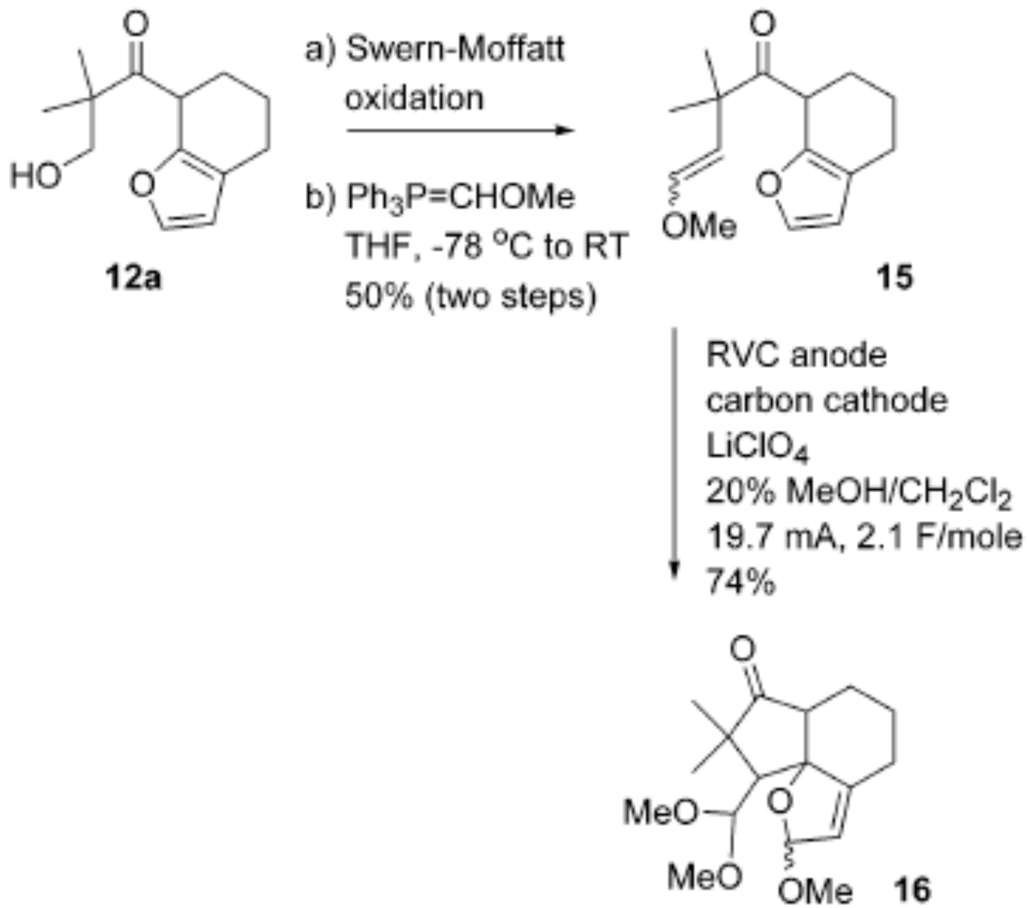
Anodic oxidation of model compound



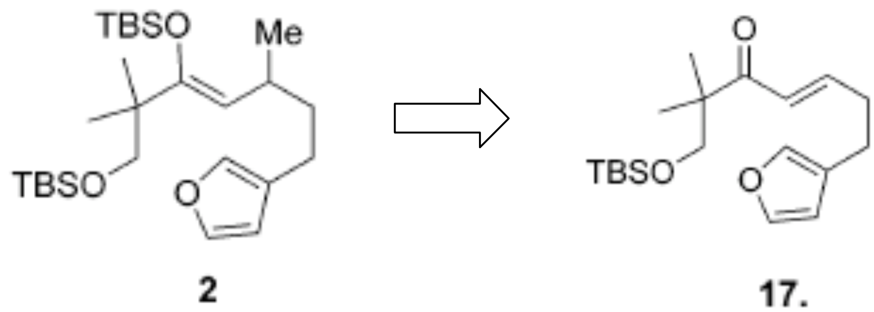
Finishing the tricyclic core: Friedel crafts option

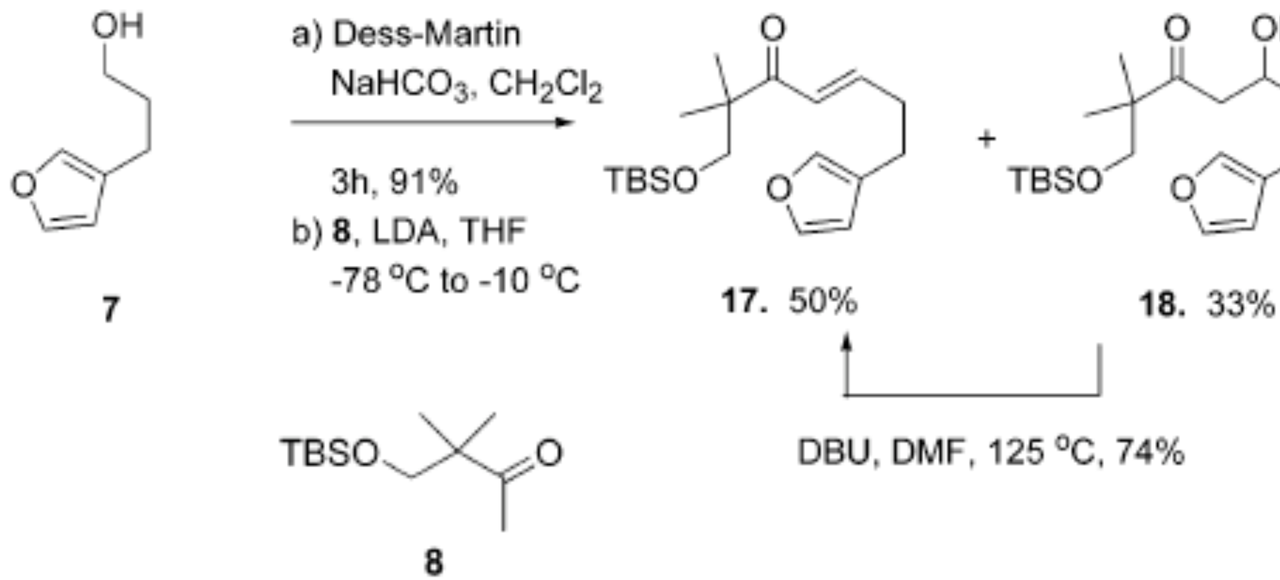


Finishing the tricyclic core: Anodic oxidation option

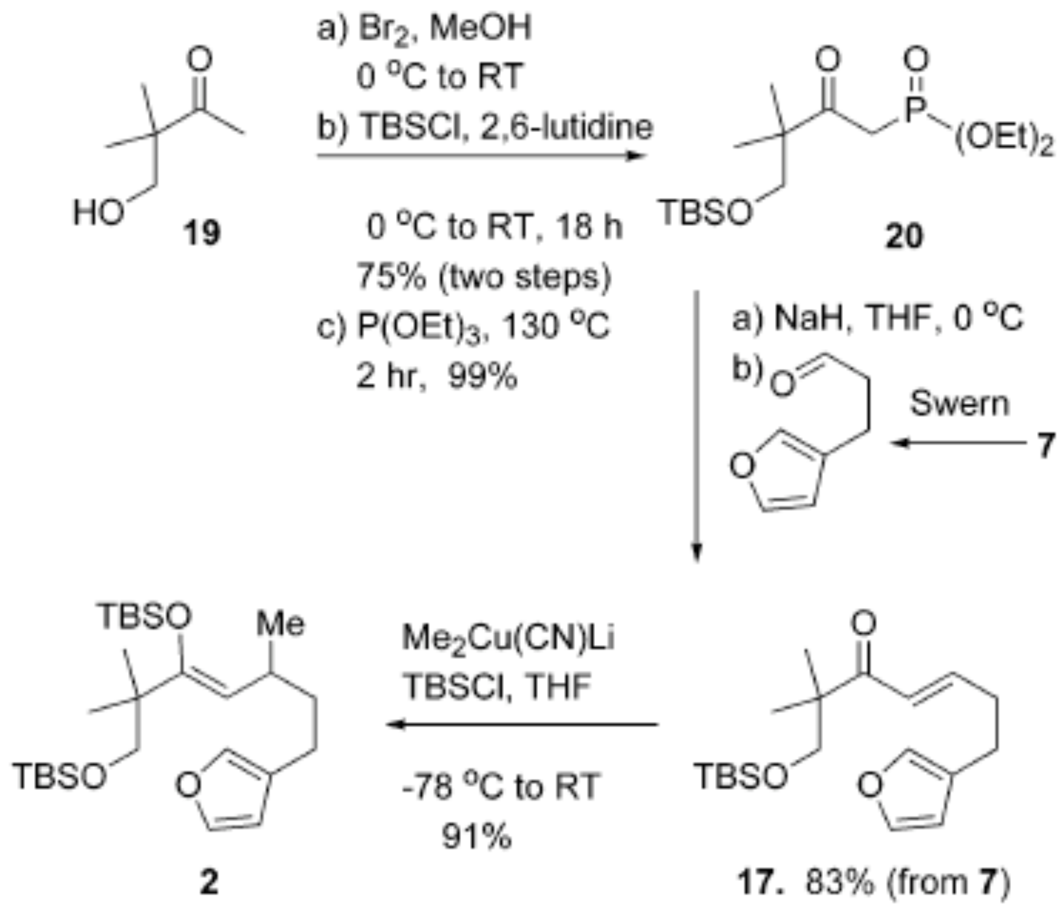


Back to the real molecule: Effords towars enone 17

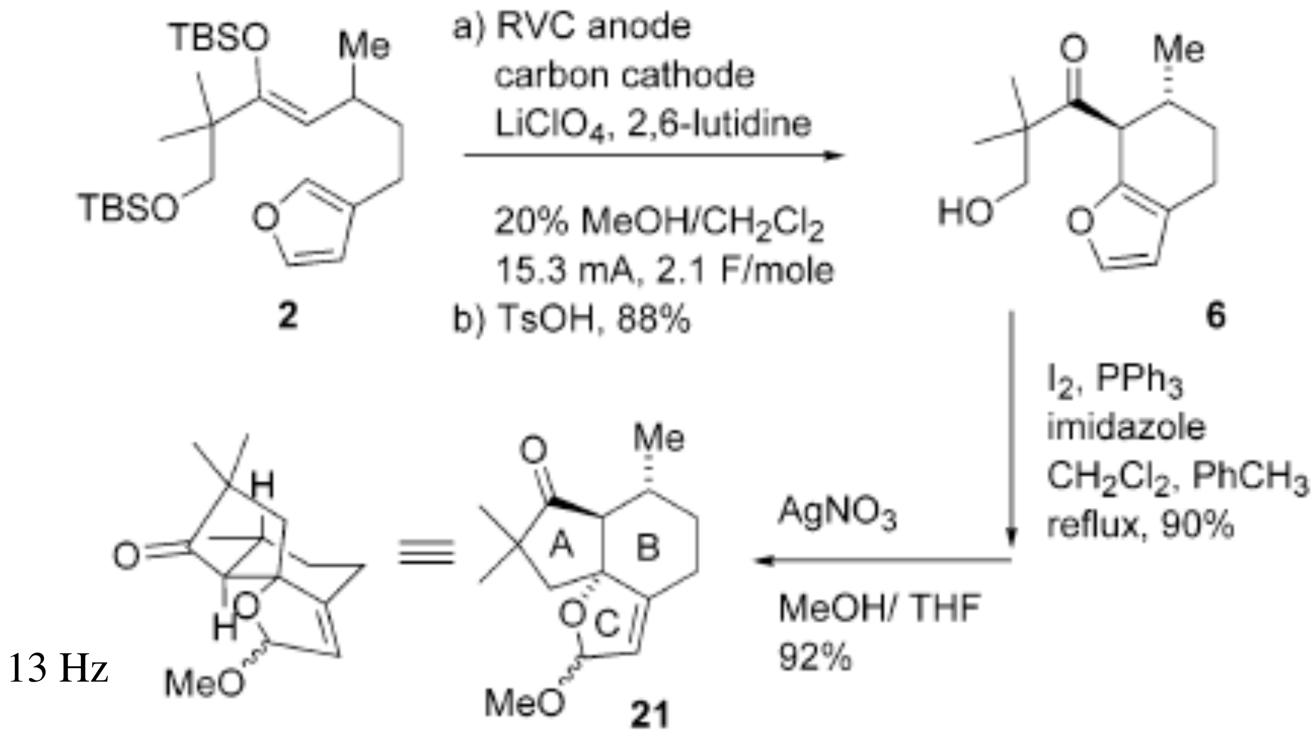




Alternative strategy and completion of electrolysis substrate 2

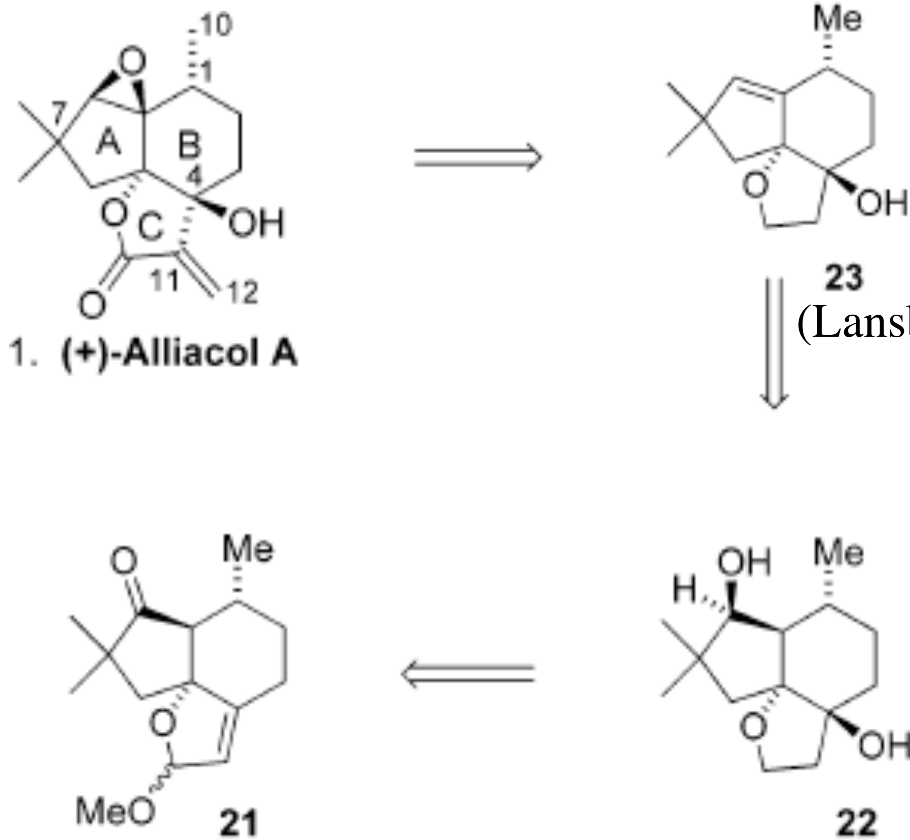


Key steps and completion of tricyclic core



COSY, HMQC

Strategy for the end-game

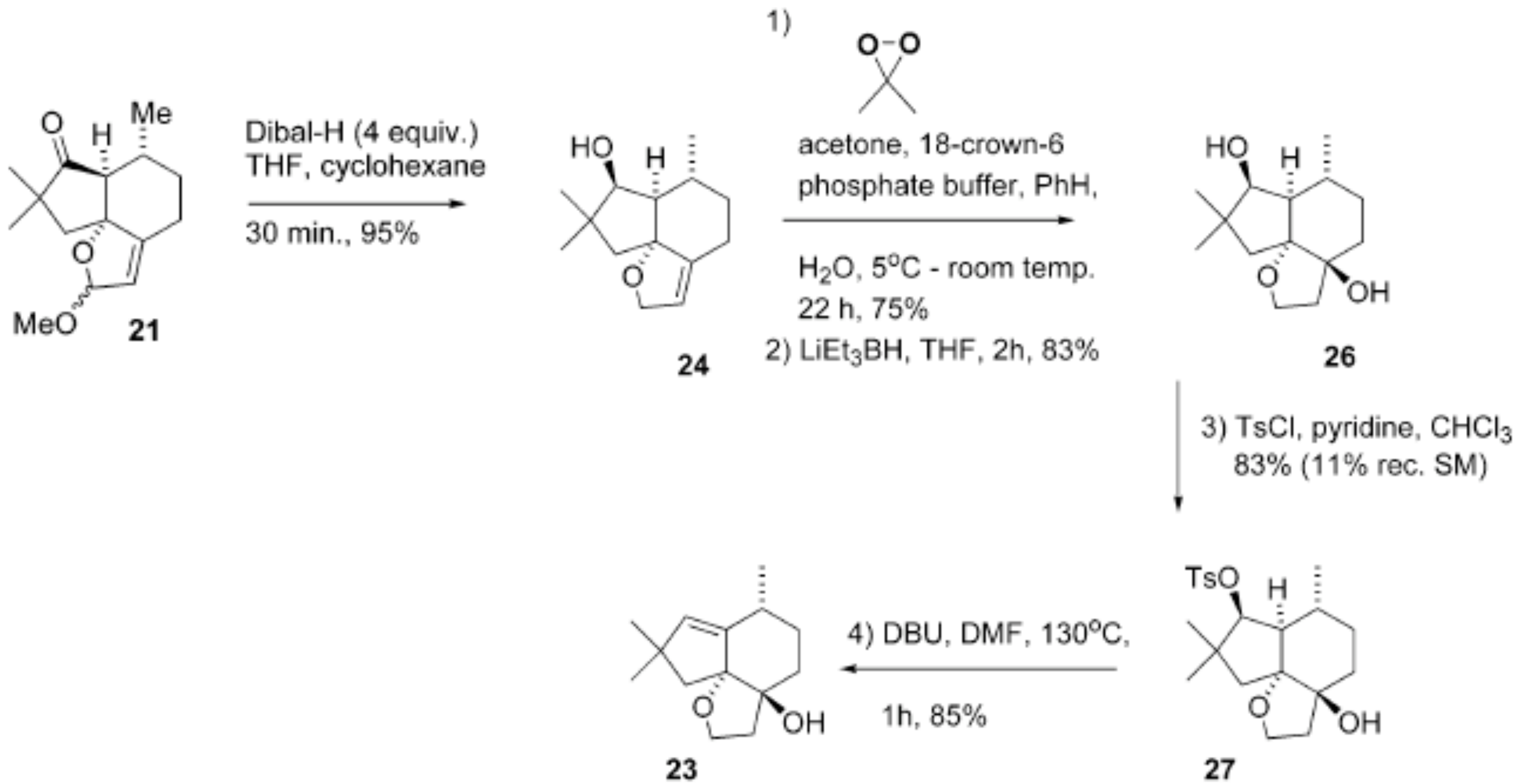


1. **(+)-Alliacol A**

23
(Lansbury's intermediate)

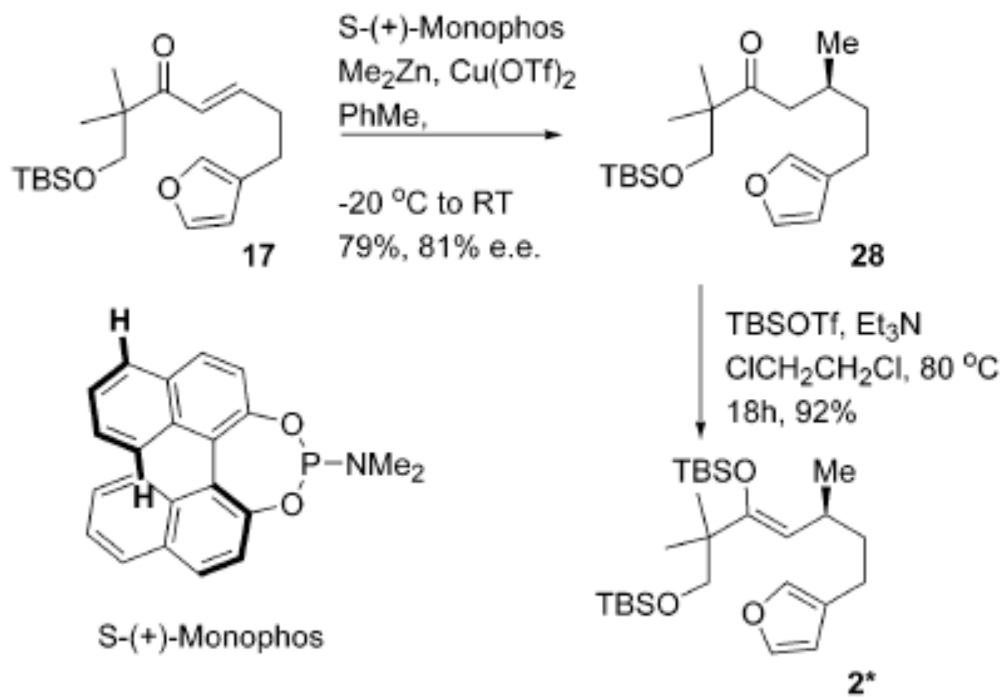
22

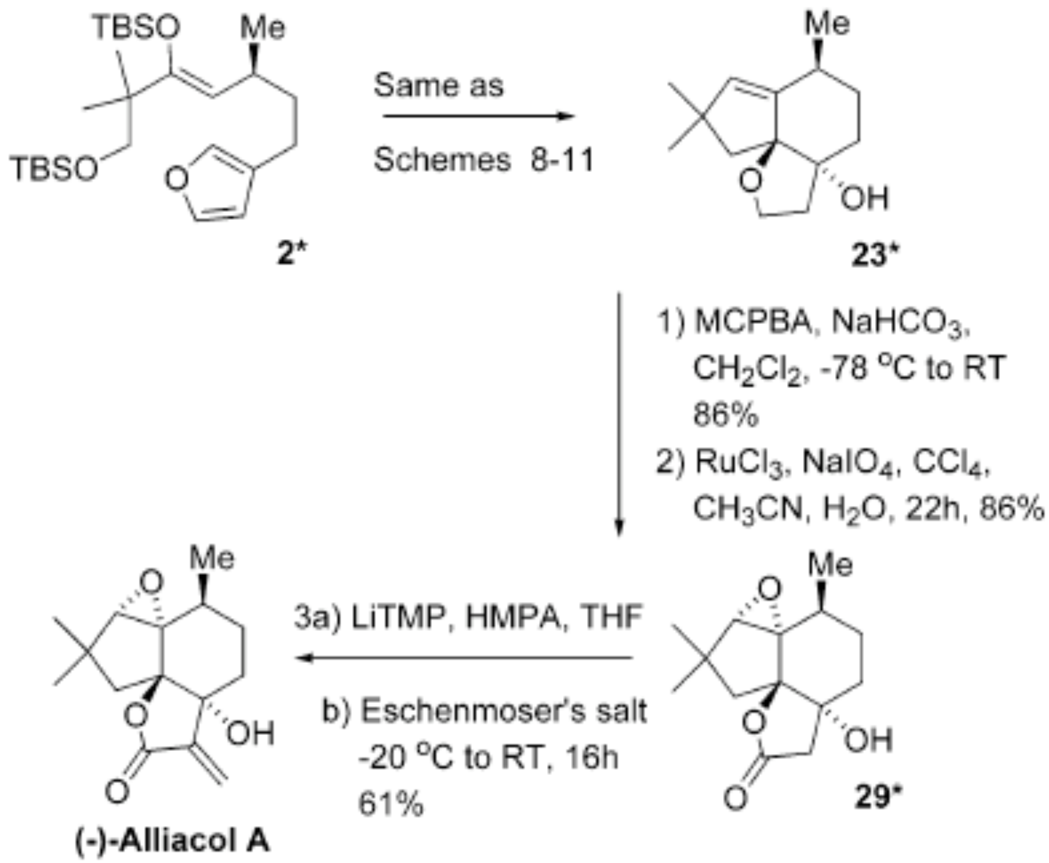
21



(18% over 13 steps)

Completing the asymmetric synthesis

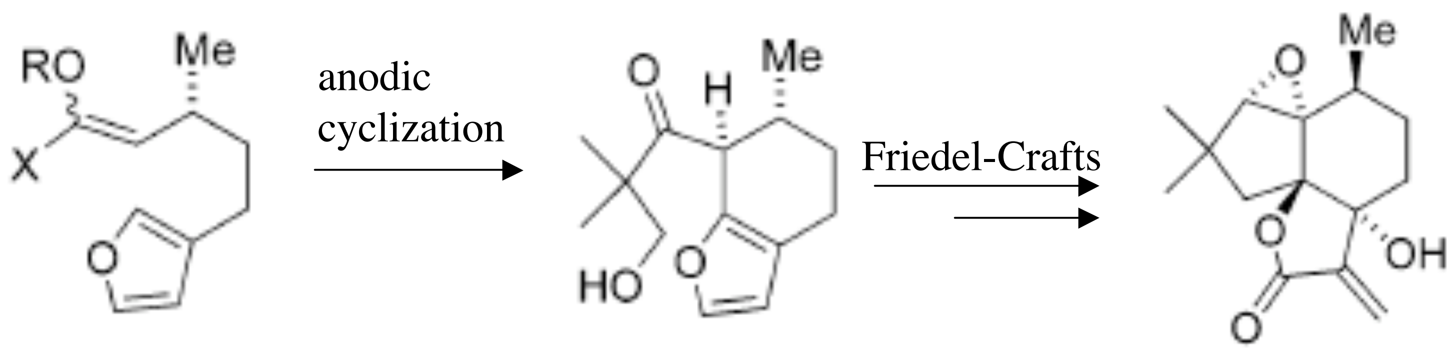



TBSO
Me
TBSO
O
2*
Same as
Schemes 8-11
Me
O
OH
23*
1) MCPBA, NaHCO3,
CH2Cl2, -78 °C to RT
86%
2) RuCl3, NaIO4, CCl4,
CH3CN, H2O, 22h, 86%
O
Me
O
OH
O
(-)-Alliacol A
3a) LiTMP, HMPA, THF
b) Eschenmoser's salt
-20 °C to RT, 16h
61%
O
Me
O
OH
O
29*

Conclusion

The anodic oxidation of enol ethers is a useful umpolong reaction for making tetrahydrofurans or fused furans

The first asymmetric synthesis of (-)-Alliacol A was accomplished using stereoselective anodic oxidation and Friedel Crafts reactions as key steps.



(-)-Alliacol A