ASAP report

Reporter: Wenquan Peng

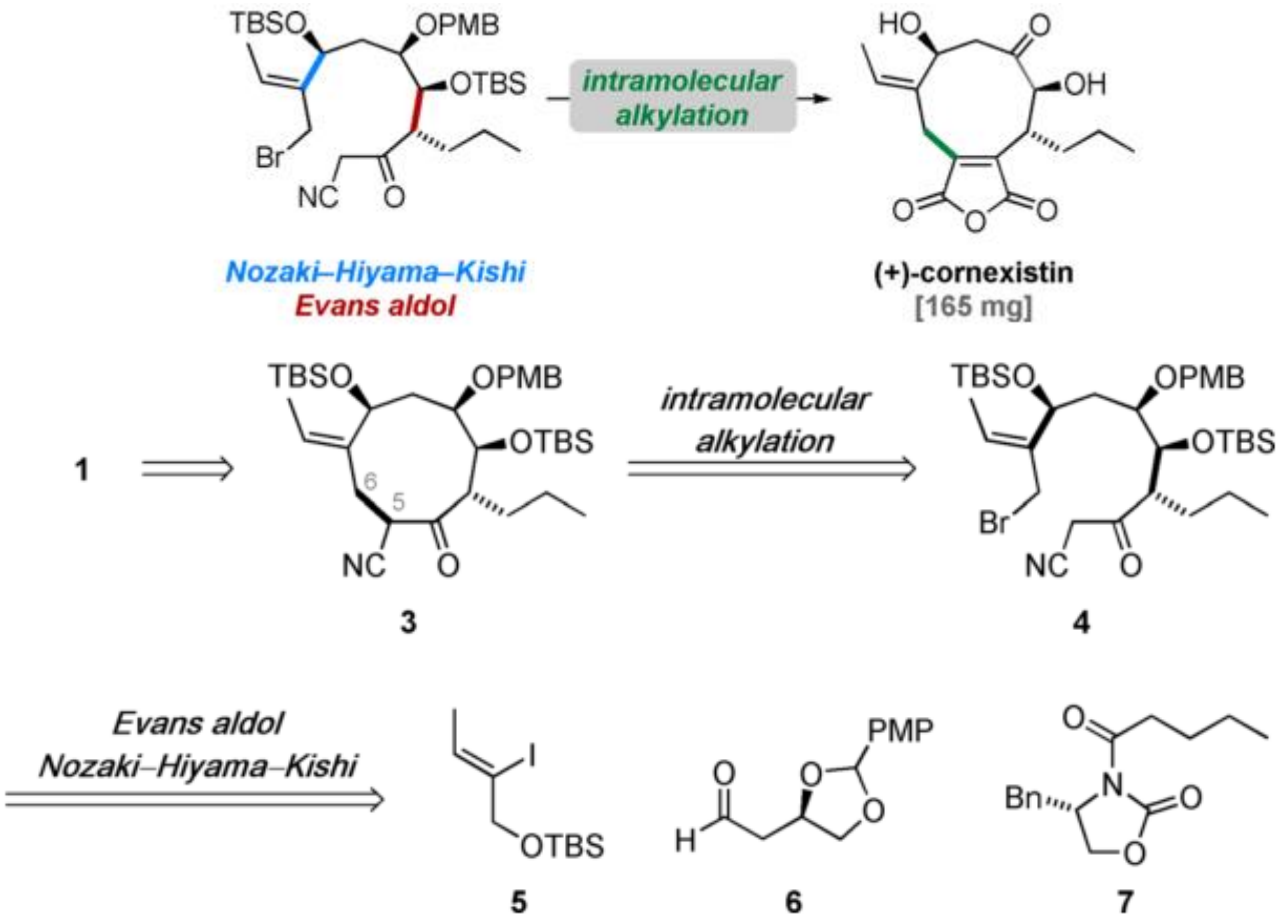
Supervisors: Prof. Tao Ye

Dr. Yian Guo

Oct. 19th, 2020

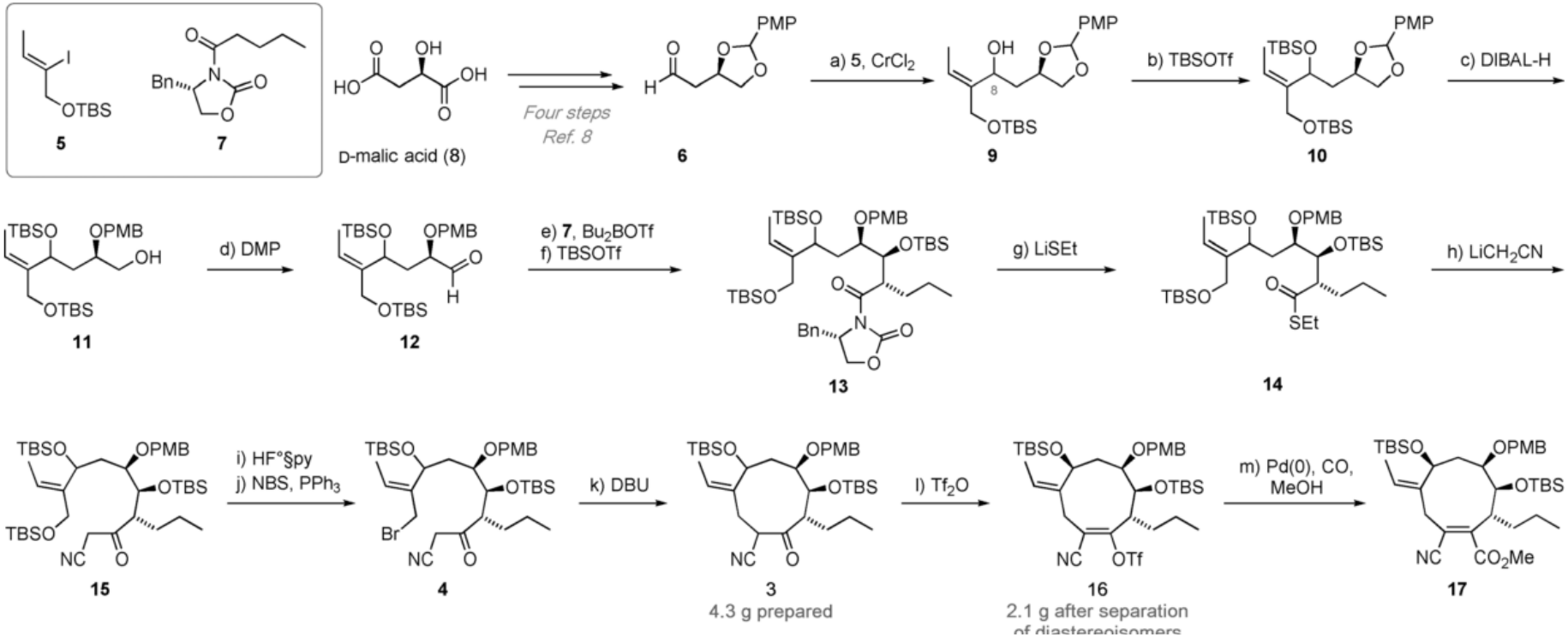
A brief introduction to a total synthesis

Part I :Total Synthesis of (+)-Cornexistin

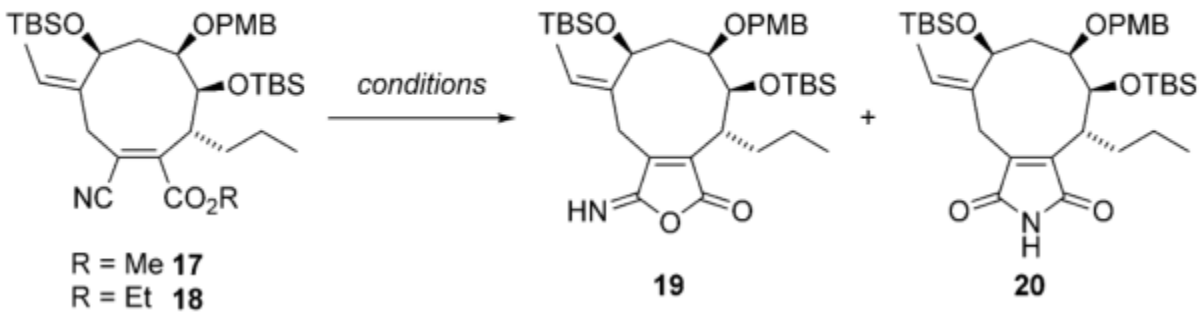


Christian Steinborn *et al.*, *Angew. Chem. Int. Ed.* 2020, **59**, 1–5

A brief introduction to a total synthesis

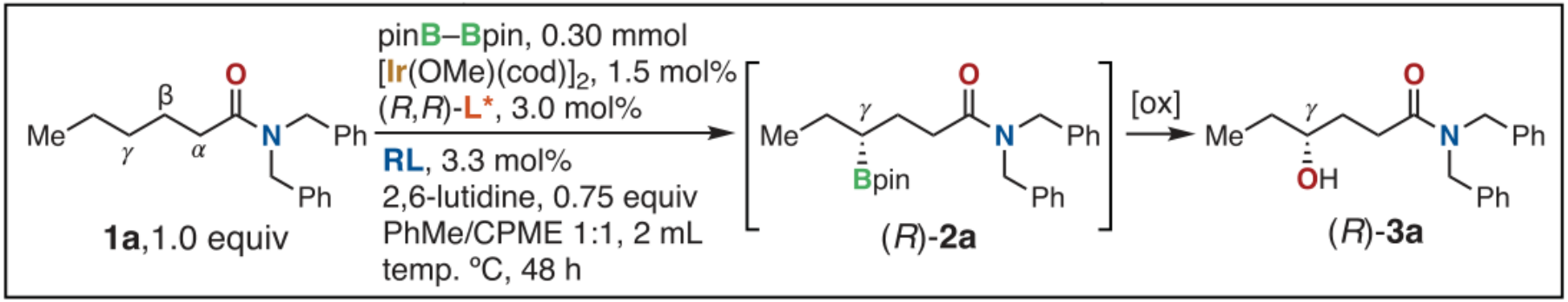


Hydrolysis of nitrile **17**.



A brief introduction to a methodology

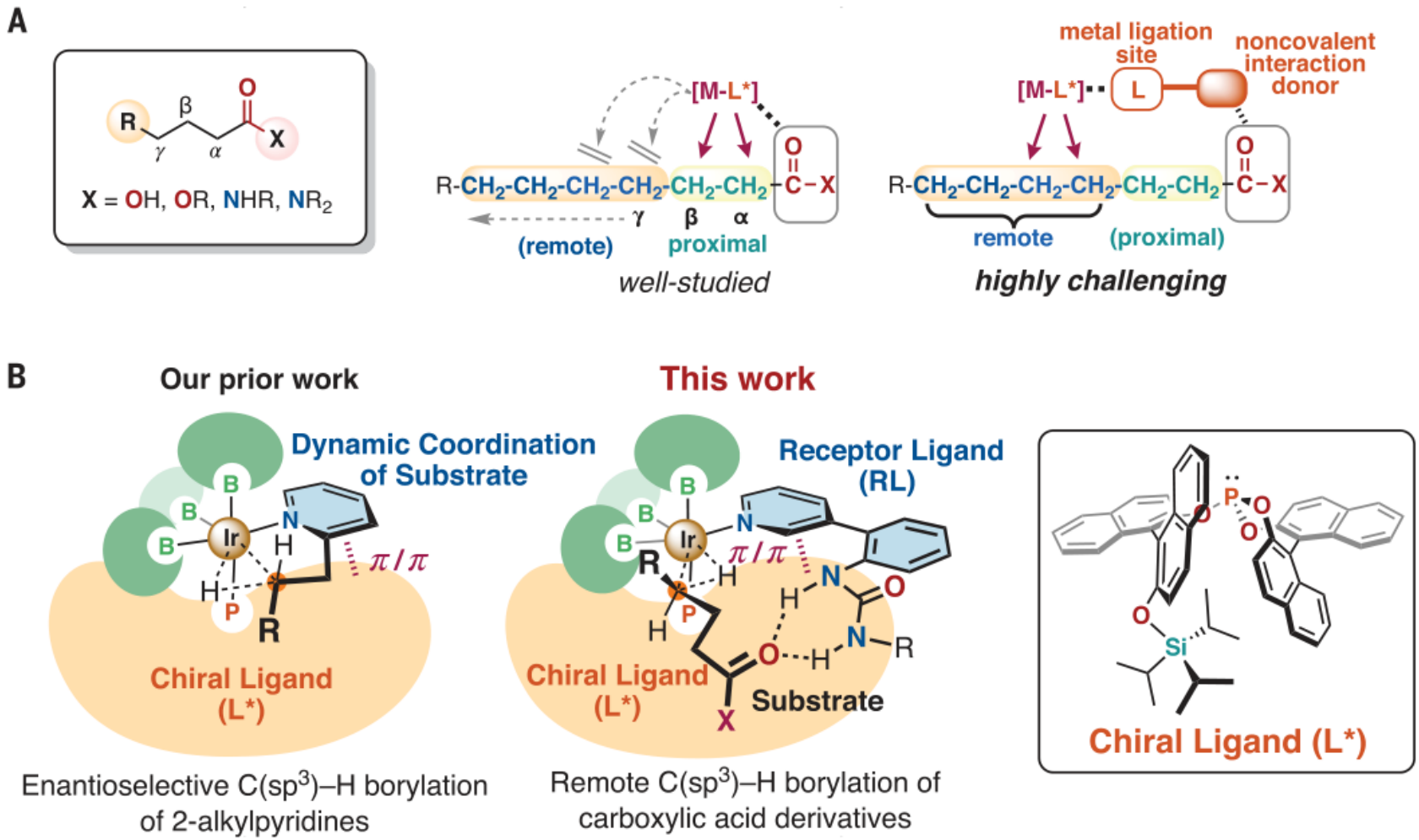
Part II: Asymmetric remote C–H borylation of aliphatic amides and esters with a modular iridium catalyst



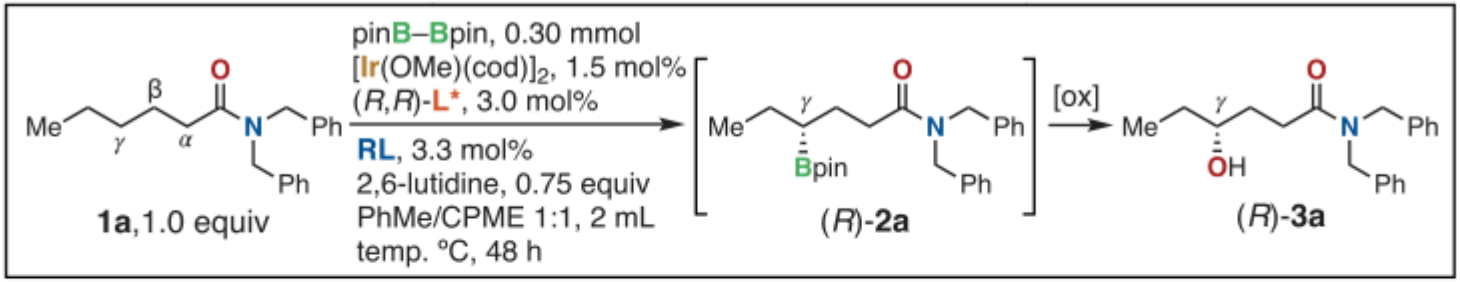
Reyes *et al.*, *Science*. **369**, 970–974 (2020)

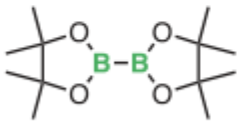
A brief introduction to a methodology

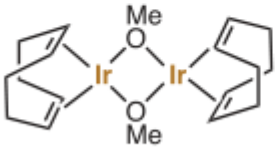
Part II: Asymmetric remote C–H borylation of aliphatic amides and esters with a modular iridium catalyst



R. L. Reyes *et al.*, *J. Am. Chem. Soc*. **141**, 6817–6821 (2019)




pinB–Bpin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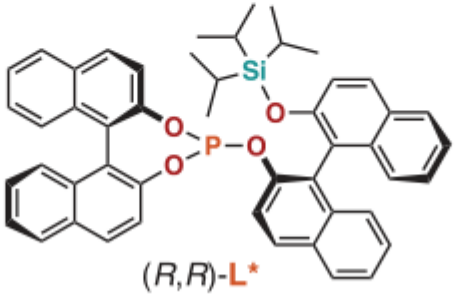
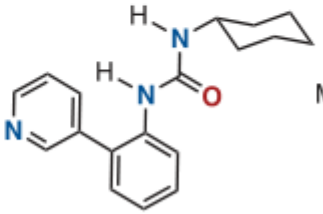
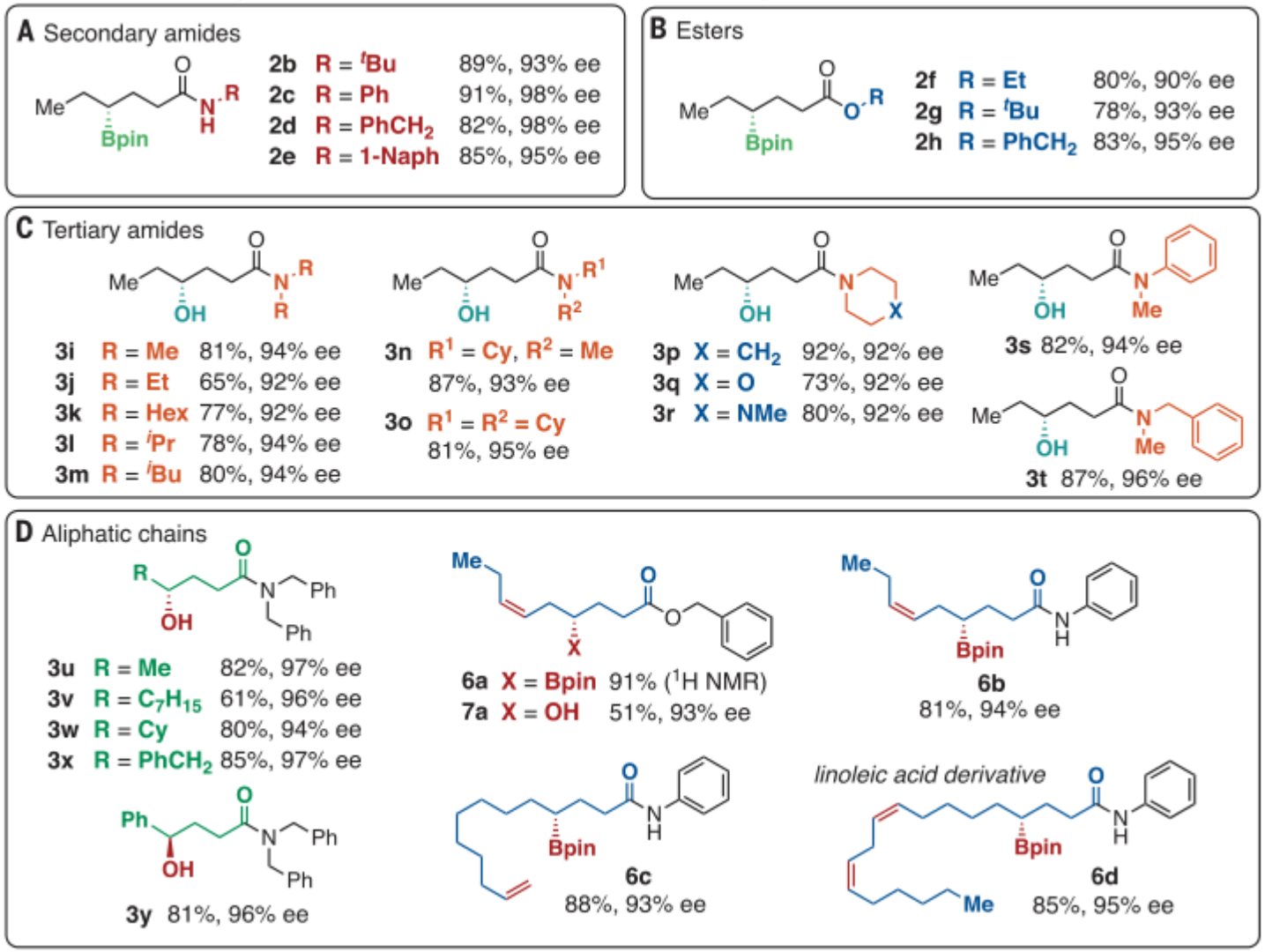

(R,R)-L*

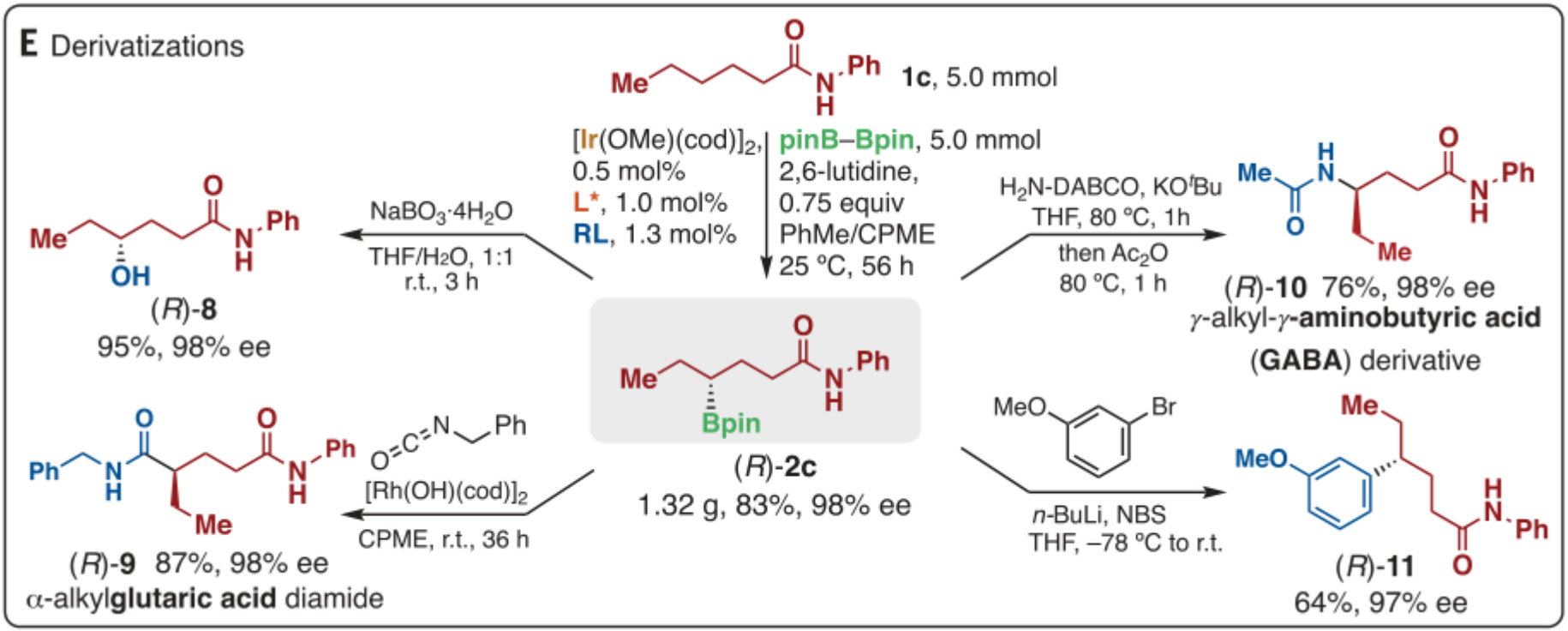

receptor ligand (RL)

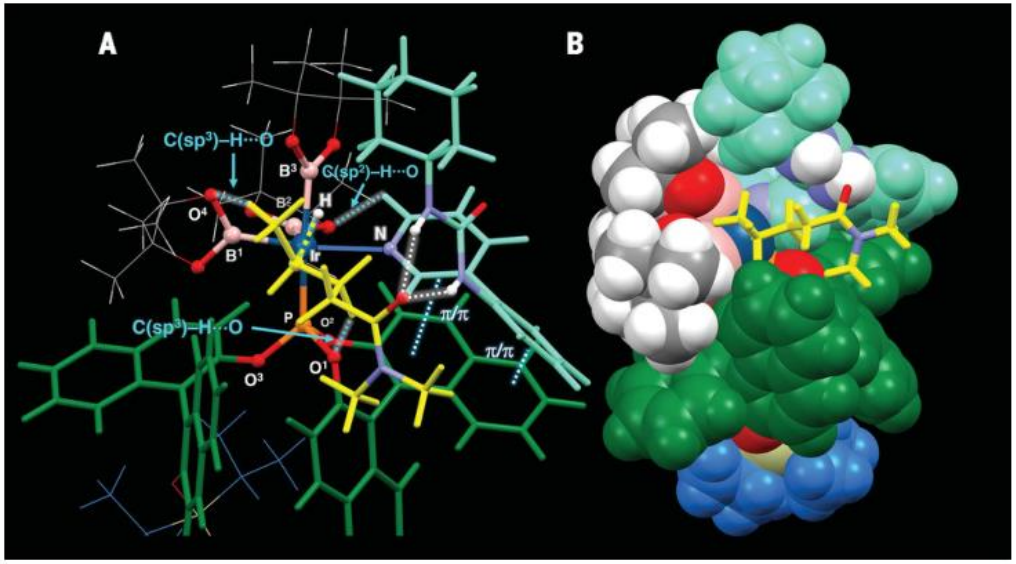
2,6-lutidine

entry	RL	2,6-lutidine	temp. °C	yield of **2a**, %*	ee %
1	+	+	25	99	>99.9
2	+	+	40	75	90
3	+	+	60	51	89
4	+	+	80	38	87
5	–	+	25	0	–
6	+	–	25	87	89
7†	+	+	25	39	85
8‡	+	+	25	0	–

A brief introduction to a methodology

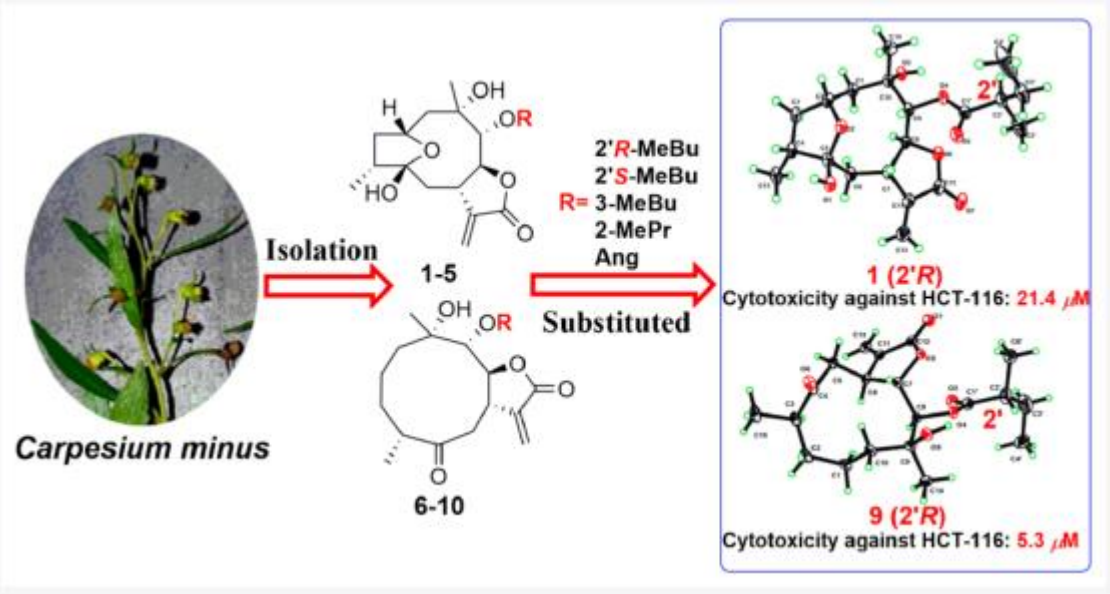


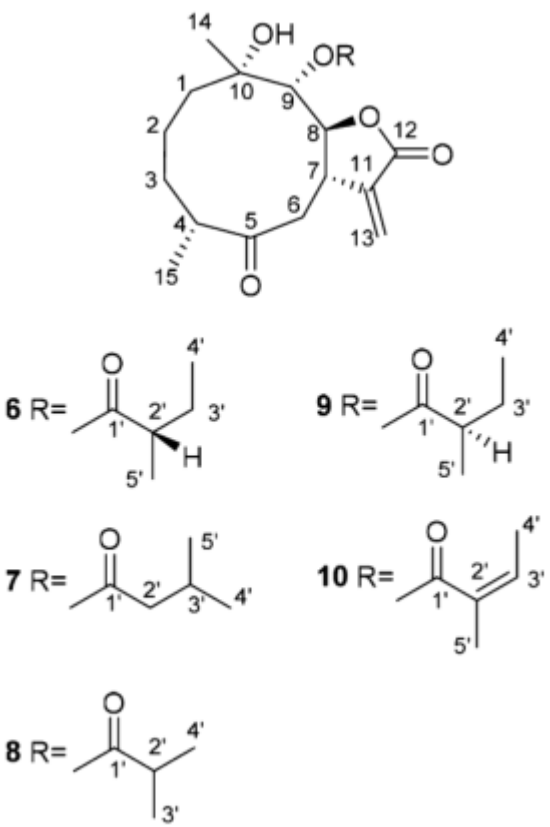




X. Liu *et al.*, *Angew. Chem. Int. Ed*. **59**, 2745–2749 (2020).
R. L. Reyes *et al.*, *J. Am. Chem. Soc*. **141**, 6817–6821(2019).

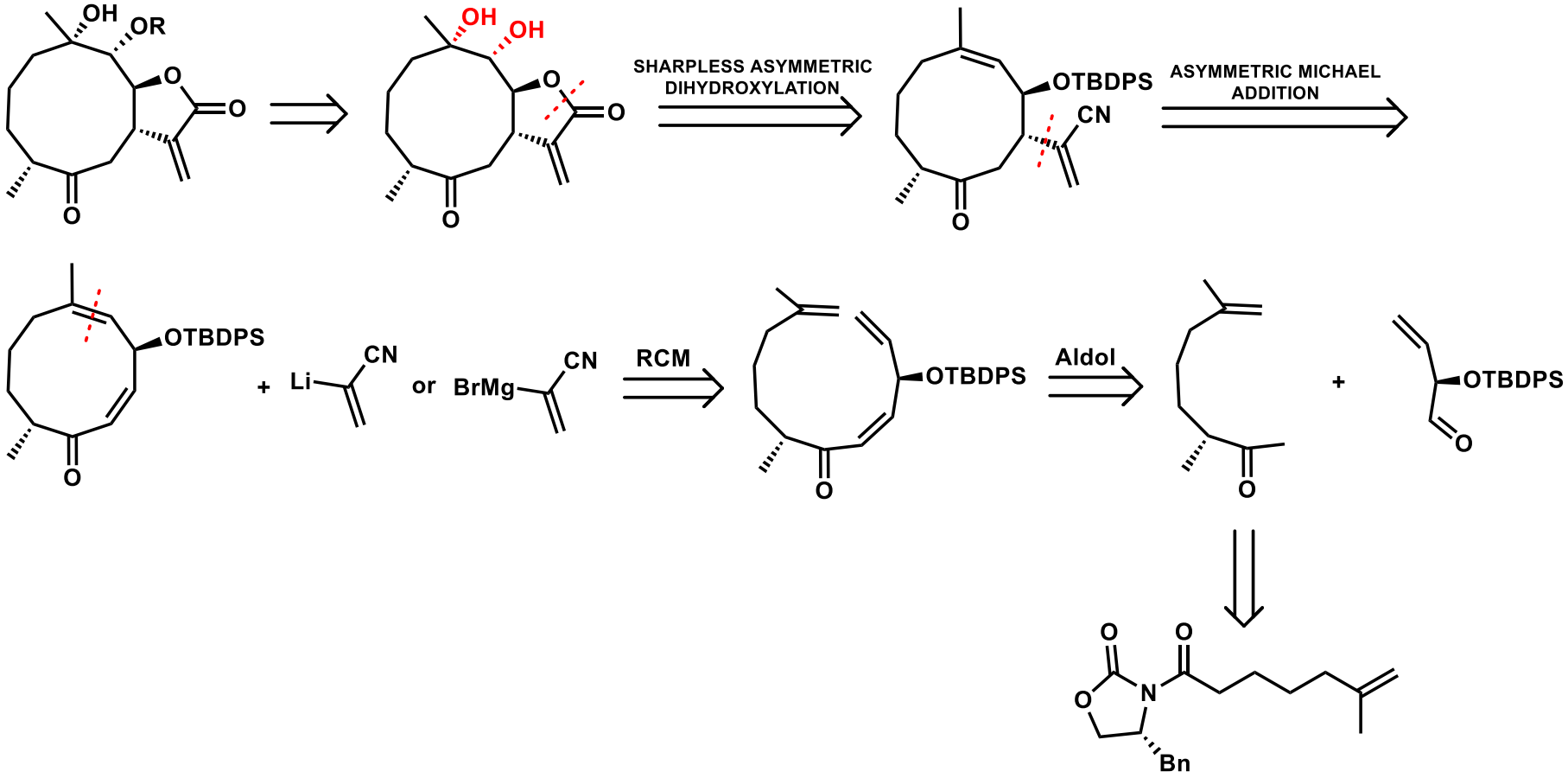
A brief introduction to a separation of natural products





Li zhu *et al.*, *J. Nat. Prod*. **ASAP** (2020).

A brief introduction to a separation of natural products



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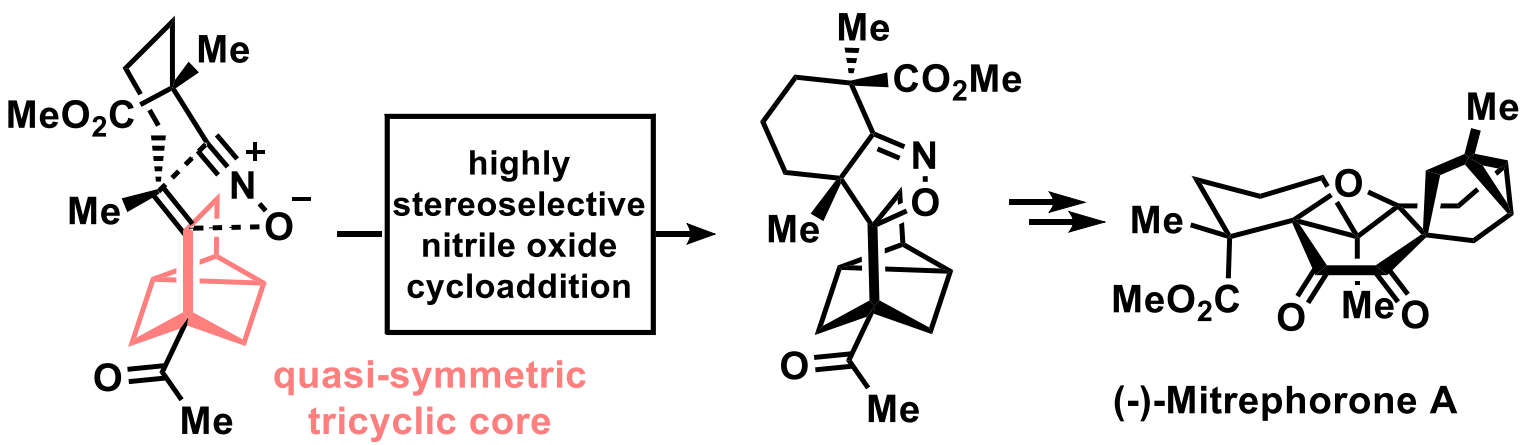
Article

Total Synthesis of (−)-Mitrephorone A Enabled by Stereoselective Nitrile Oxide Cycloaddition and Tetrasubstituted Olefin Synthesis

Michael Schneider, Matthieu J. R. Richter, and Erick M. Carreira*



The introduction of author

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•V-Card (vcf, 1kb)

***Prof*. Erick M. Carreira**

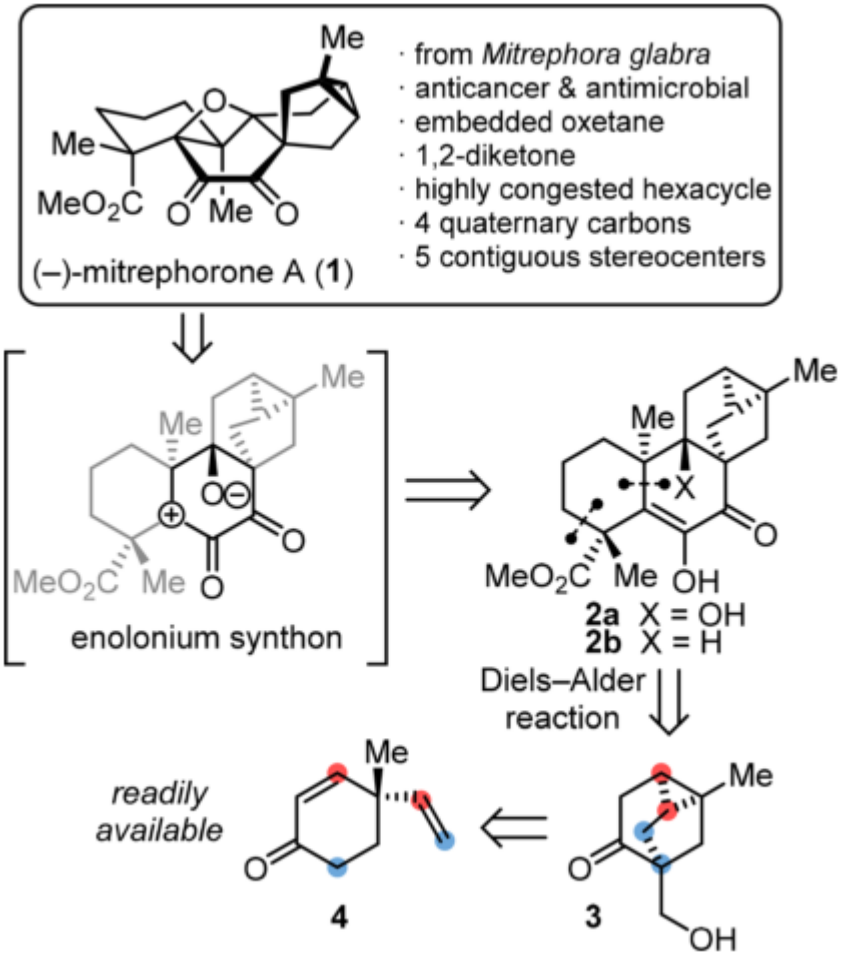
Experiences

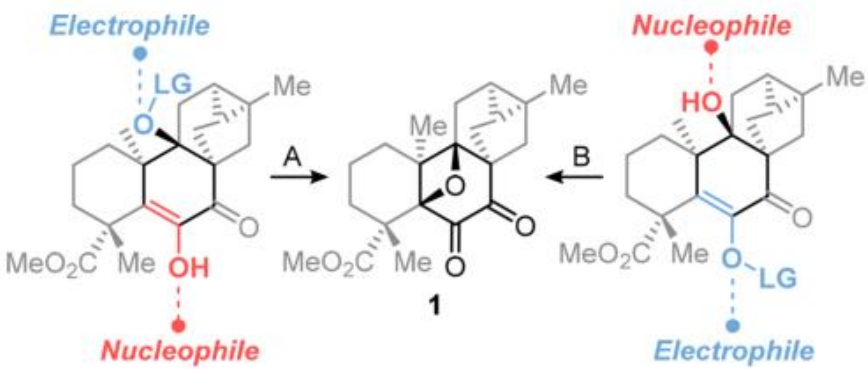
1984 University of Illinois at Urbana-Champaign, **B.S**. Scott E. Denmark;
1990 Harvard University, **Ph.D**. David A. Evans;
1992 California Institute of Technology, **Postdoctoral**, Peter Dervan;
1996 California Institute of Technology, Associate Professor;
1997 California Institute of Technology, Professor;
1998-now Swiss Federal Institute of Technology Zurich, Professor.

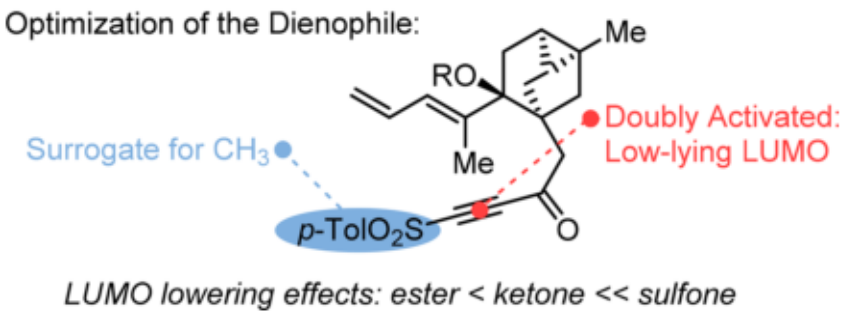
Research interests

1. Total synthesis of bioactive molecules
2. Development of synthetic strategy
3. Pharmacochemistry

Introduction to previous work





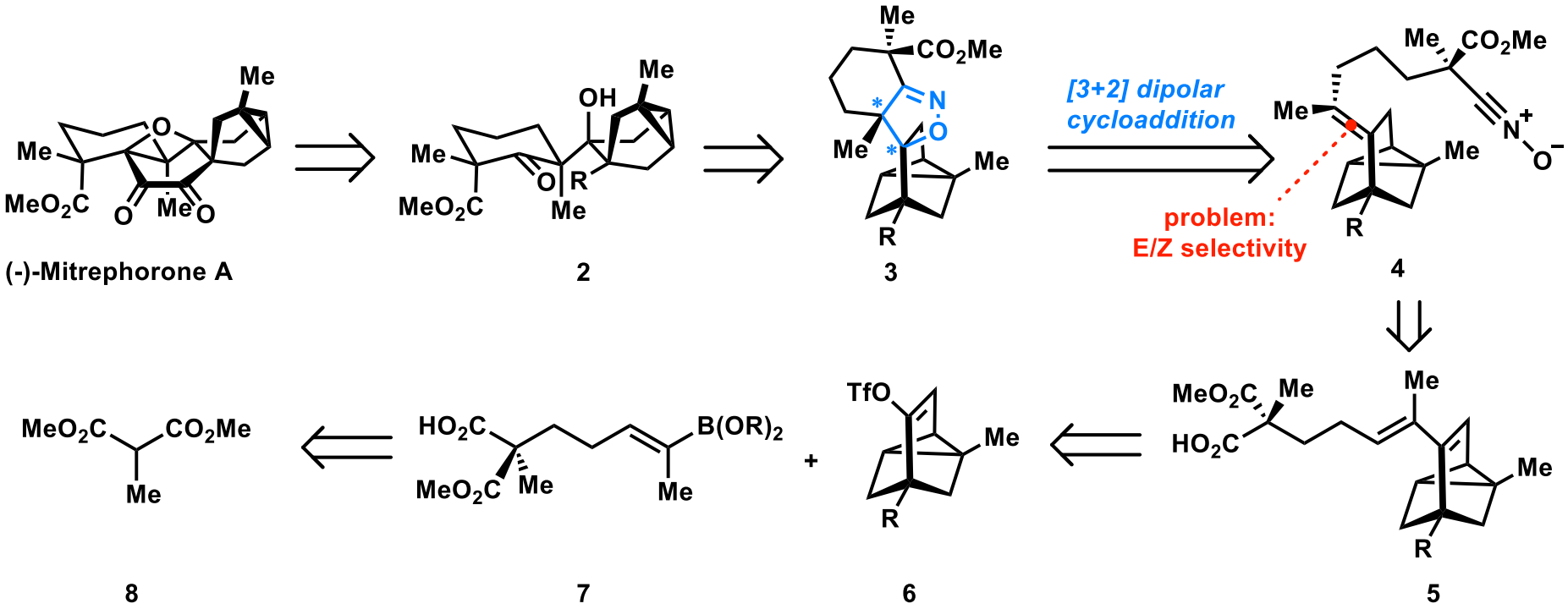


carbonyl-olefin photocycloadditions, Prins-type cyclizations, and oxidative ring closures

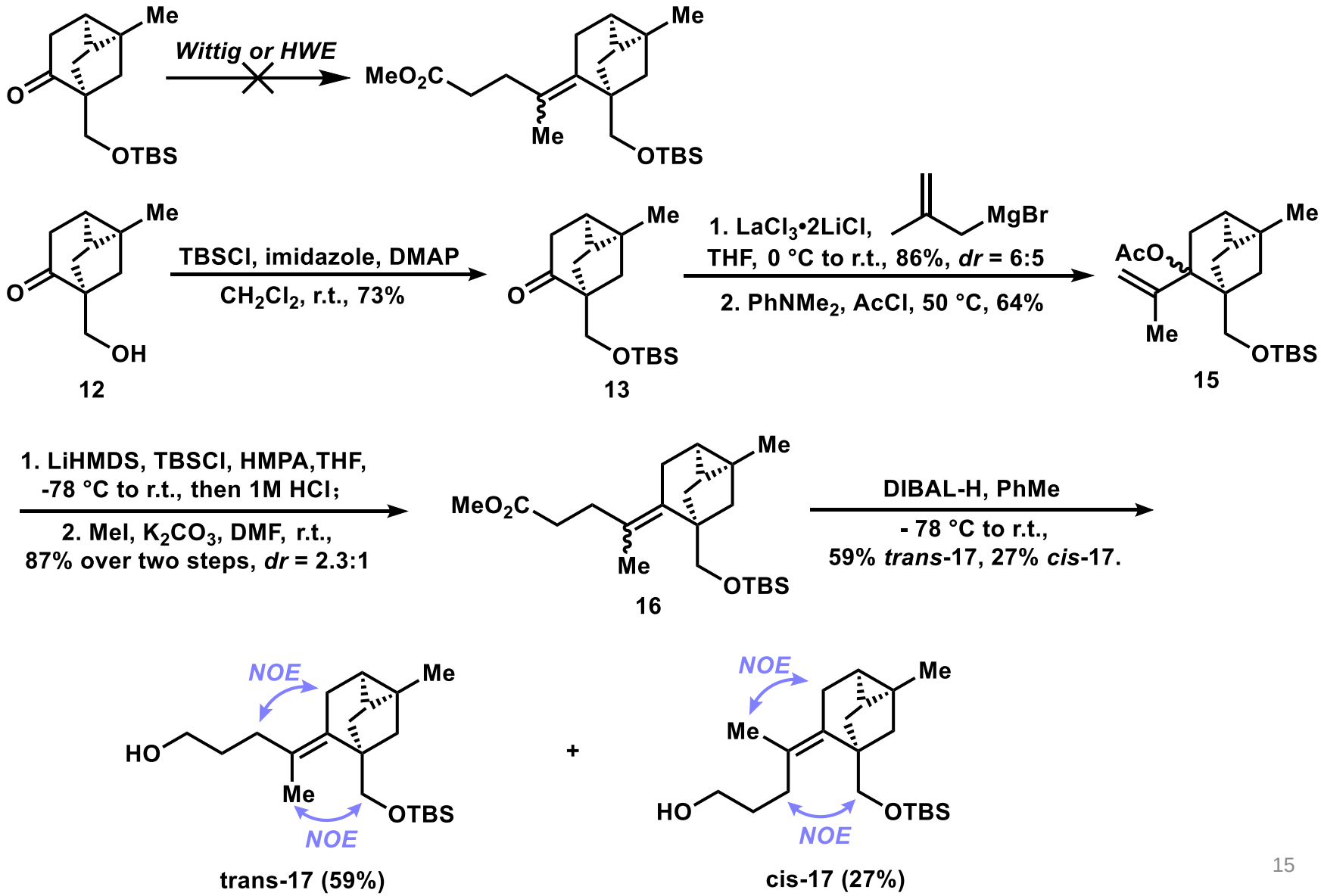
Matthieu J. R. Richter *et al.*, *J. Am. Chem. Soc*. 2018, **140**, 16704−16710

Retrosynthetic analysis

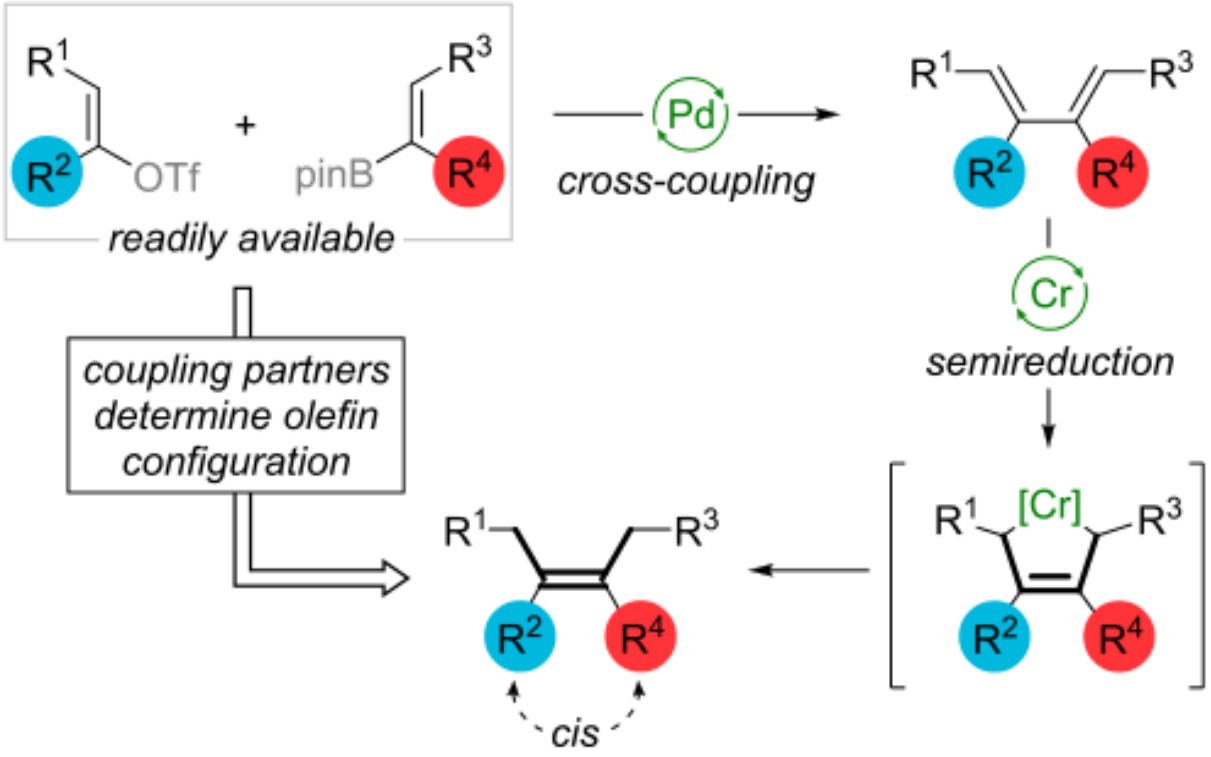
This Work:



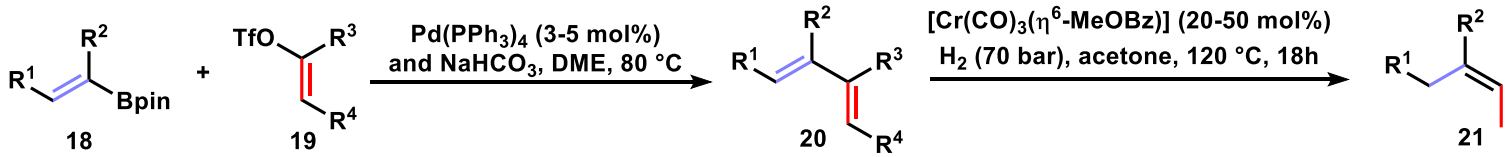
Synthesis of Tetrasubstituted Olefin via Ireland−Claisen Rearrangement

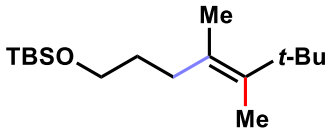


Conceptual Approach to Tetrasubstituted Olefin Synthesis via Cross-Coupling and 1,4-Semihydrogenation

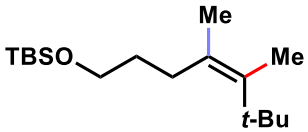


Synthesis of Tetrasubstituted Olefins via Cross-Coupling and Semihydrogenation

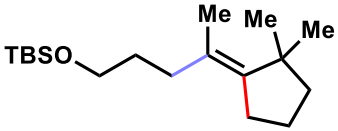




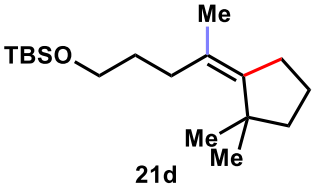
21a
Step1: 98%
Step2: 95%



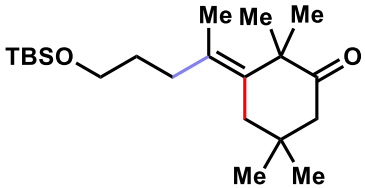
21b
Step1: 67%
Step2: 87%



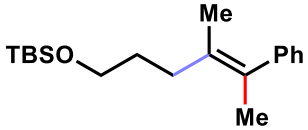
21c
Step1: 99%
Step2: 90%



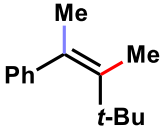
21d
Step1: 75%
Step2: 87%



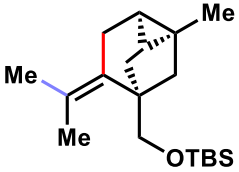
21e
Step1: 97%
Step2: 95%



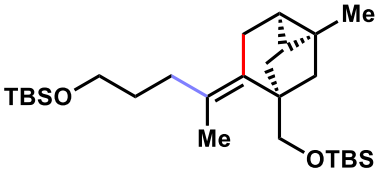
21f
Step1: 79%
Step2: 93%



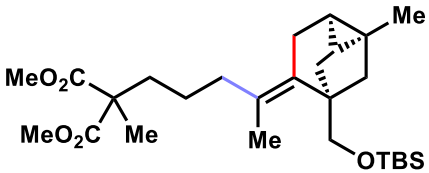
21g
Step1: 79%
Step2: 84%



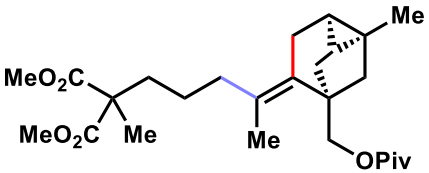
21h
Step1: 65%
Step2: 92%



21i
Step1: 68%
Step2: 90%

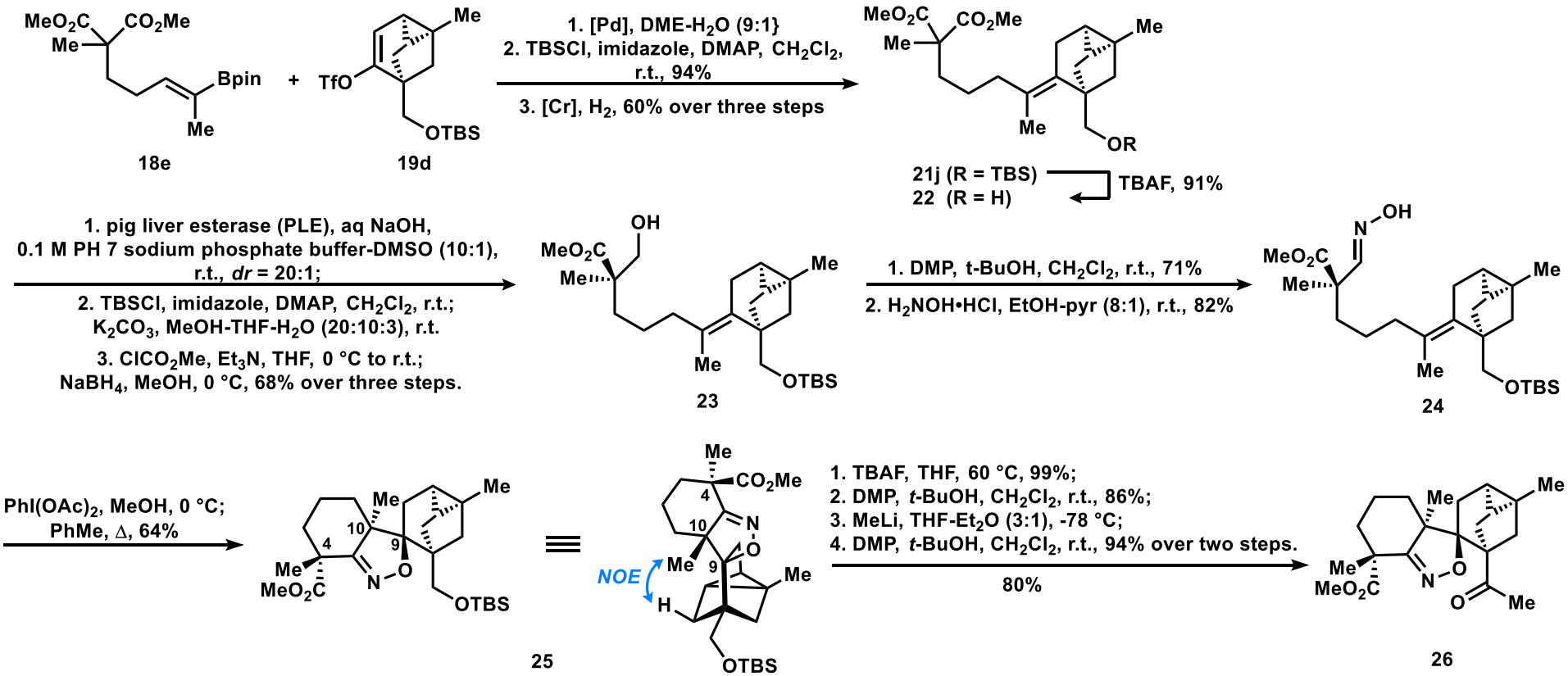


21j
Step1: 62%
Step2: 97%



21k
Step1: 98%
Step2: 98%

Synthesis of Isoxazoline 26 via Nitrile Oxide Cycloaddition



PLE (pig liver esterase/猪肝酯酶)

Putative transition states for nitrile oxide cycloaddition

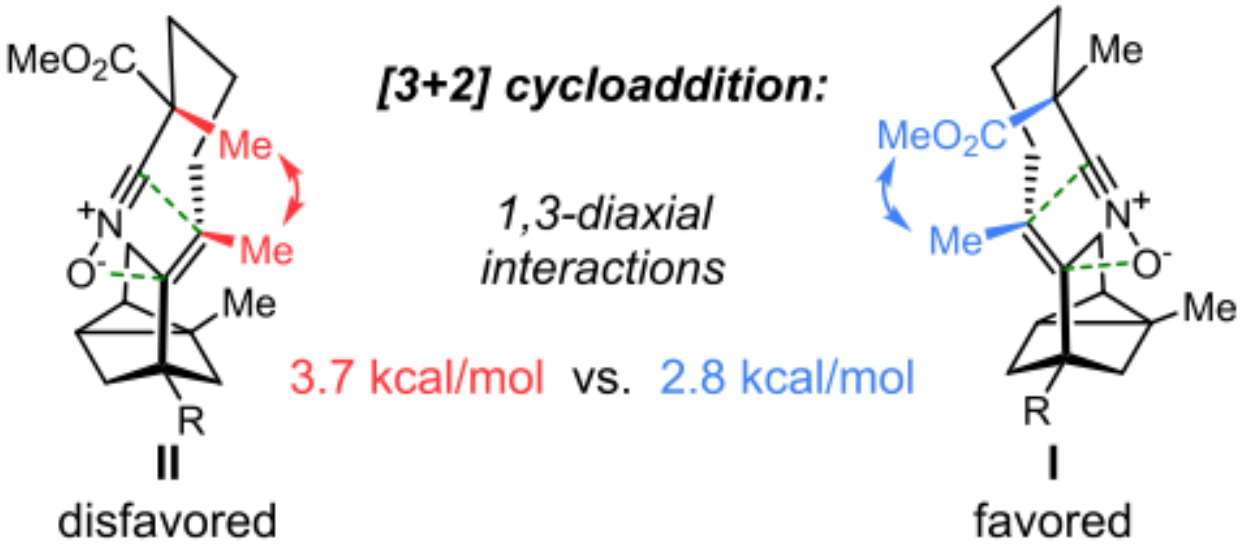
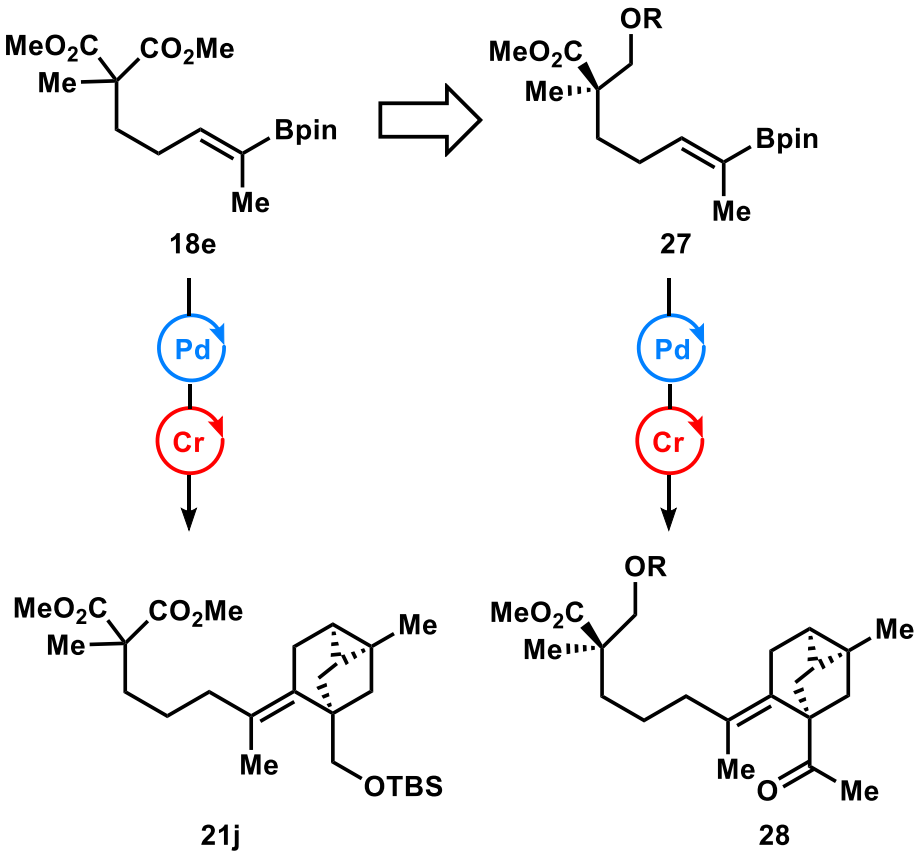
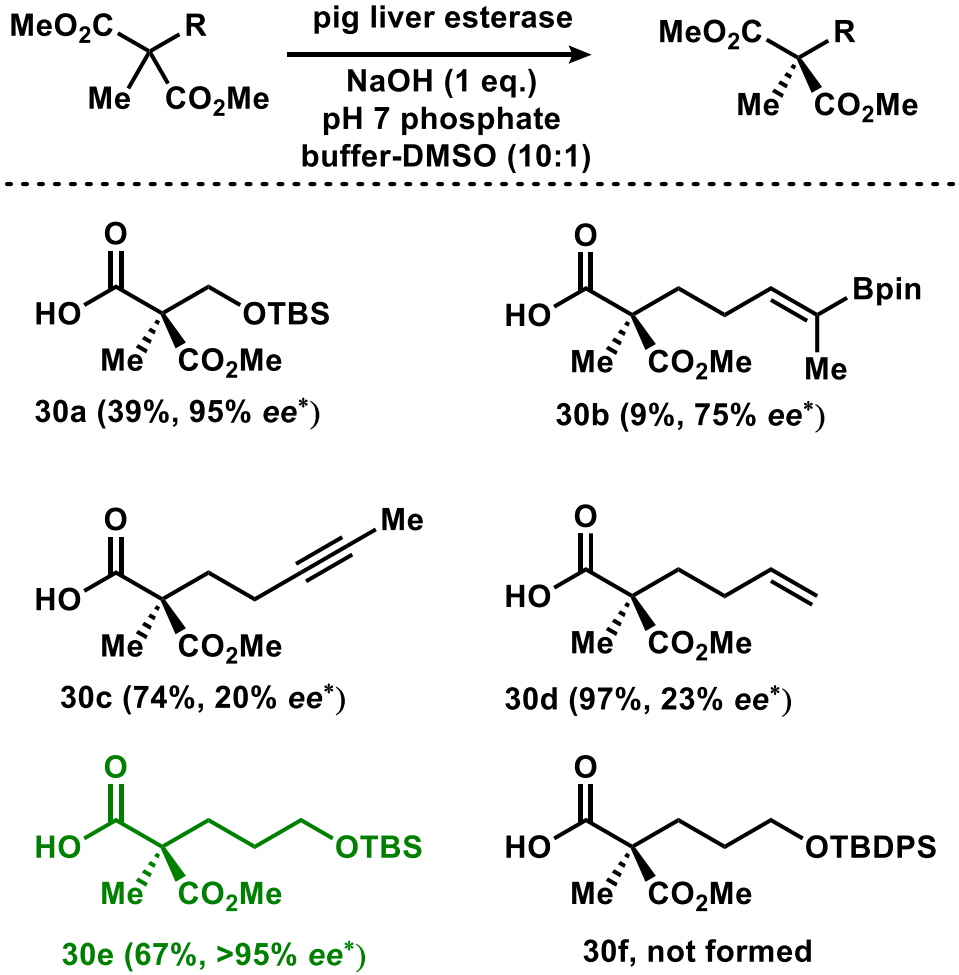


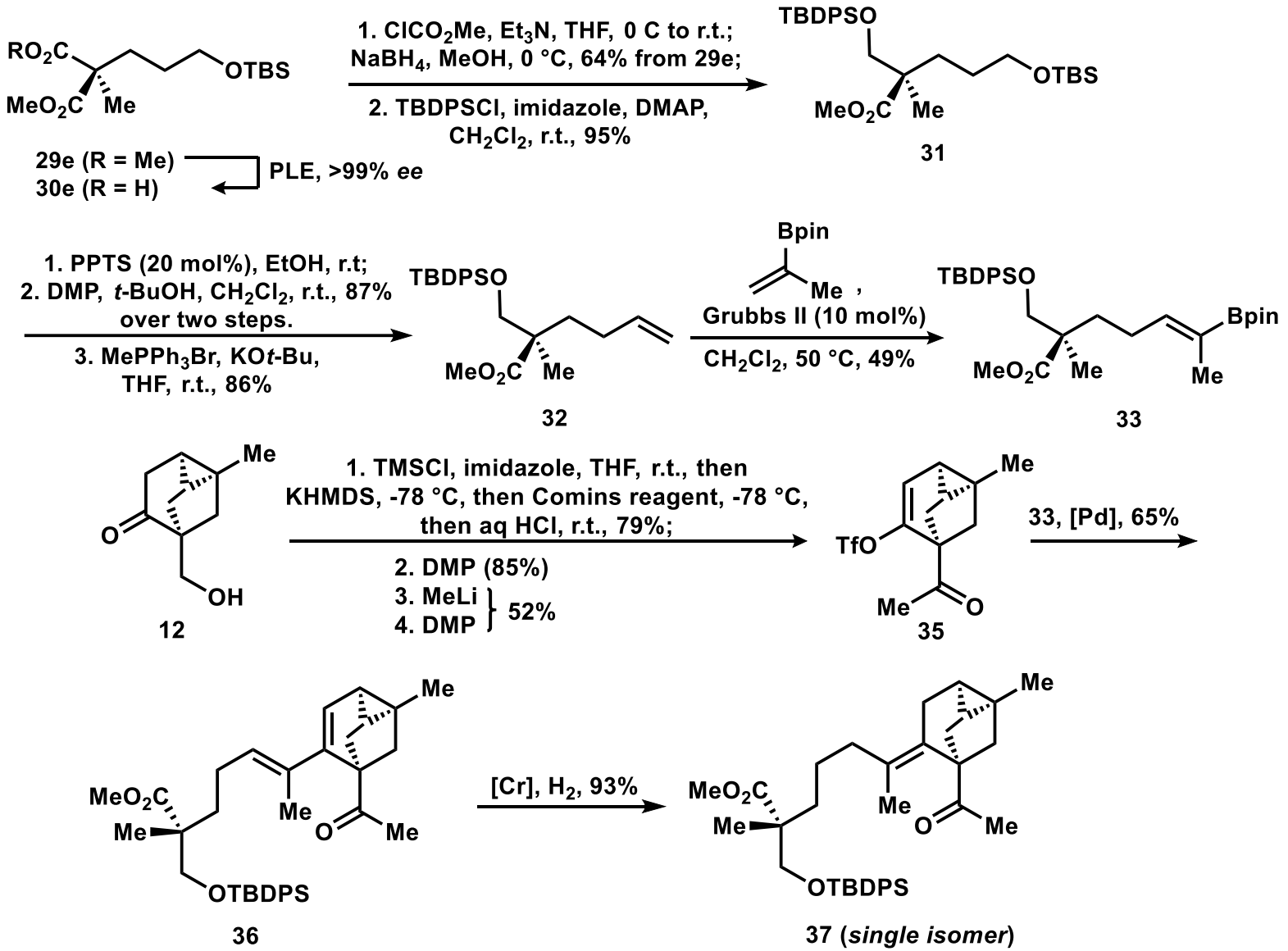
Figure 1. Putative transition states for nitrile oxide cycloaddition.

Optimize the route toward isoxazoline 26

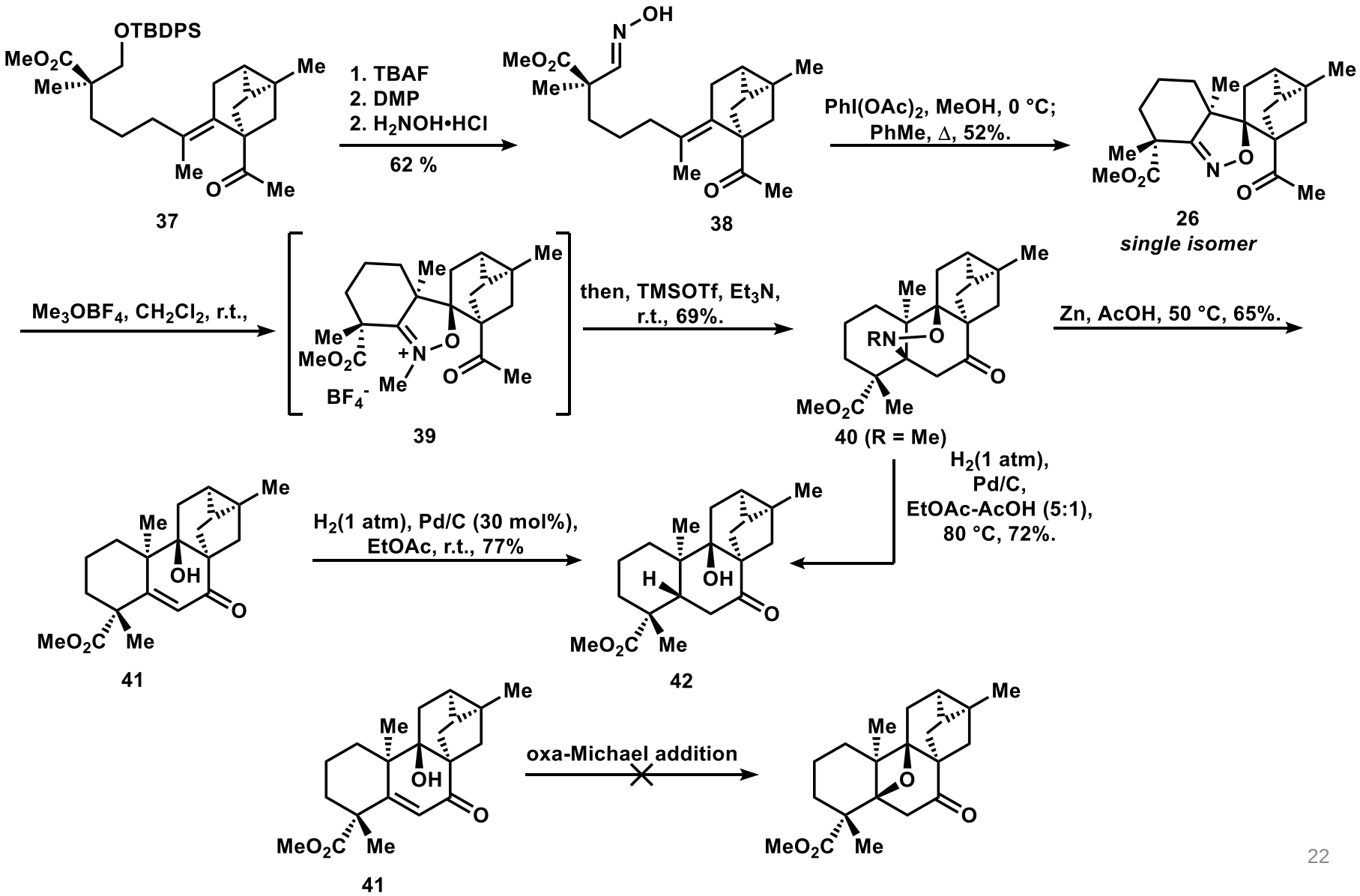




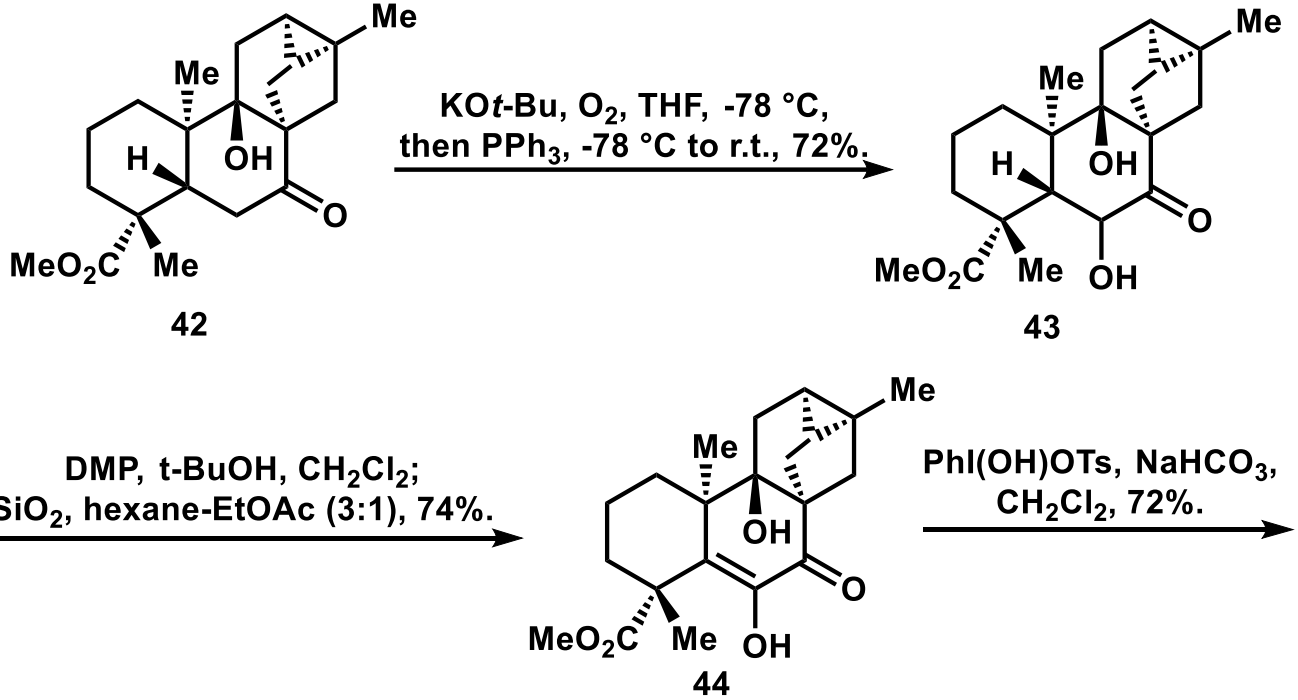
Synthesis of Vinyl Boronate 33 and Tetrasubstituted Olefin 37

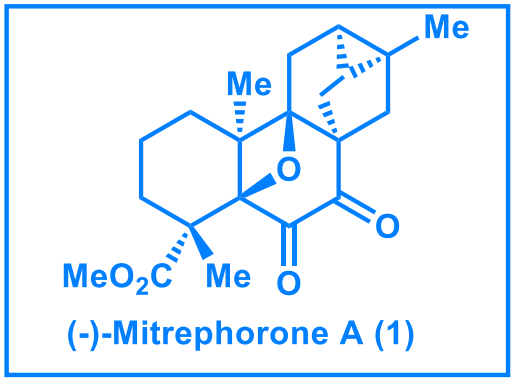


Synthesis of 42 via Nitrile Oxide Cycloaddition

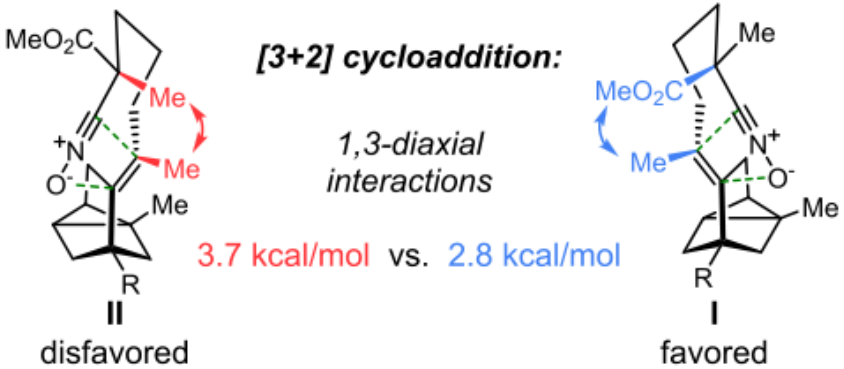


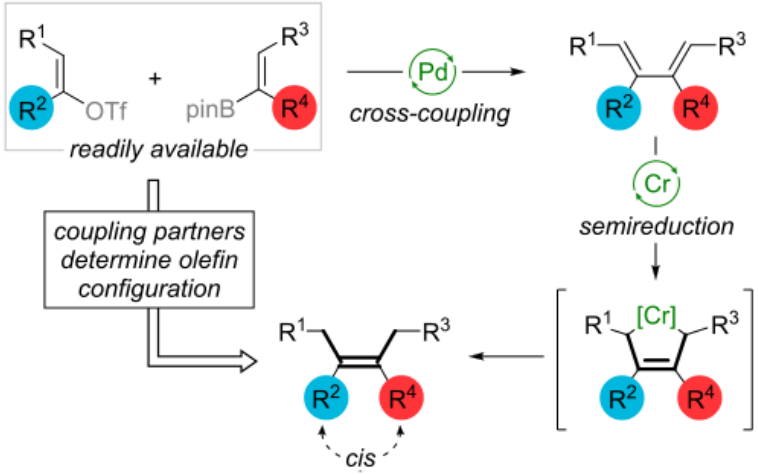
Completion of the Synthesis

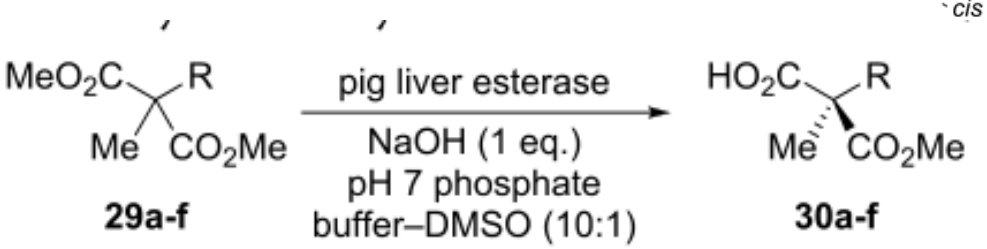


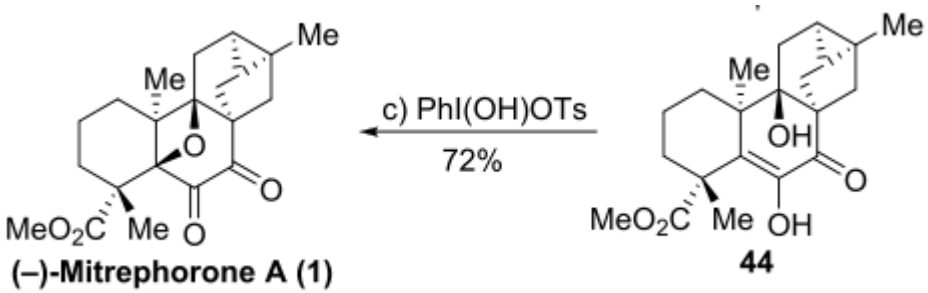


Summary


[3+2] cycloaddition:
1,3-diaxial interactions
3.7 kcal/mol vs. 2.8 kcal/mol
II
disfavored
I
favored

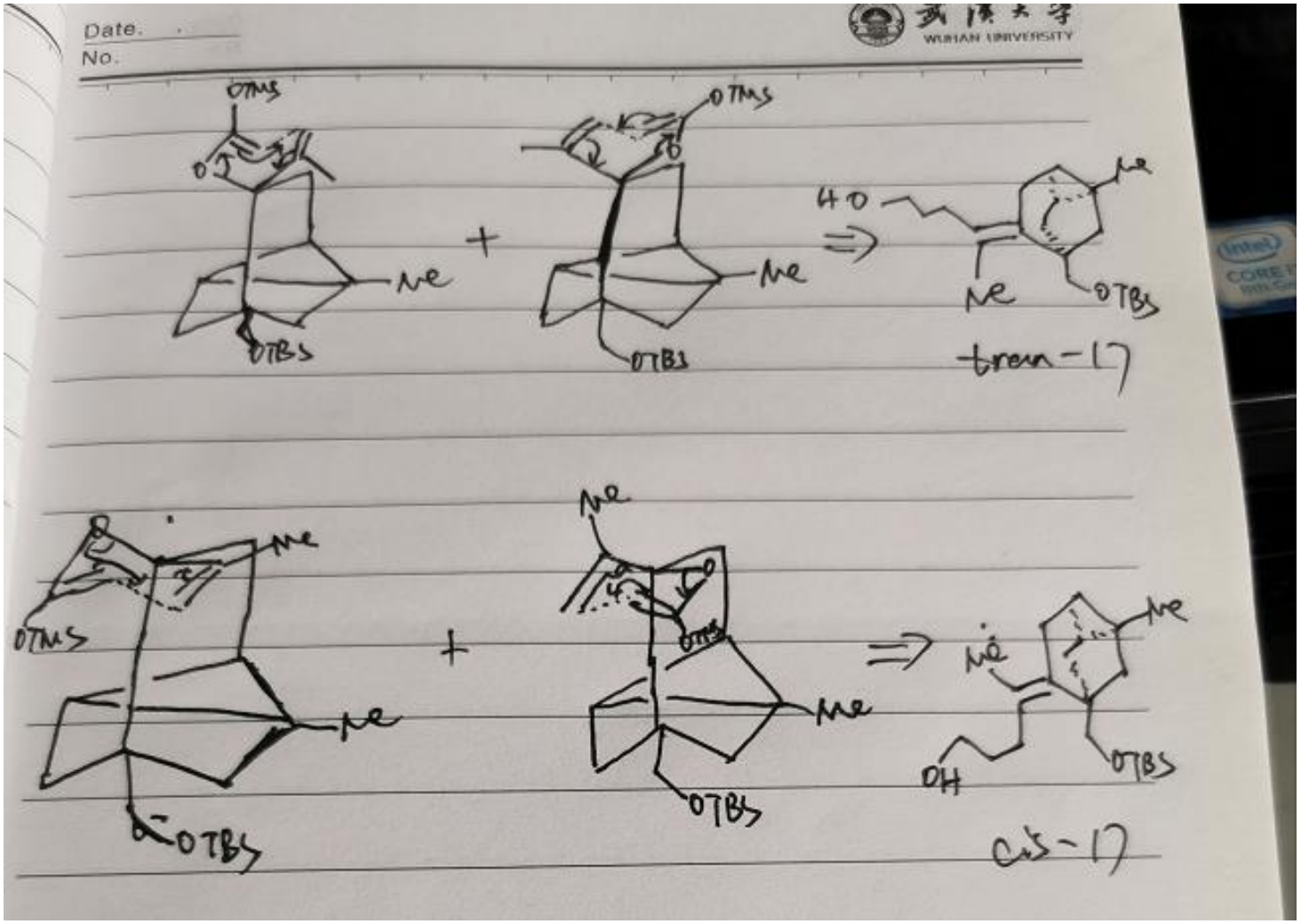

readily available
cross-coupling
semireduction
coupling partners determine olefin configuration
cis


pig liver esterase
NaOH (1 eq.)
pH 7 phosphate buffer–DMSO (10:1)
29a-f
30a-f


c) PhI(OH)OTs
72%
(–)-Mitrephorone A (1)
44

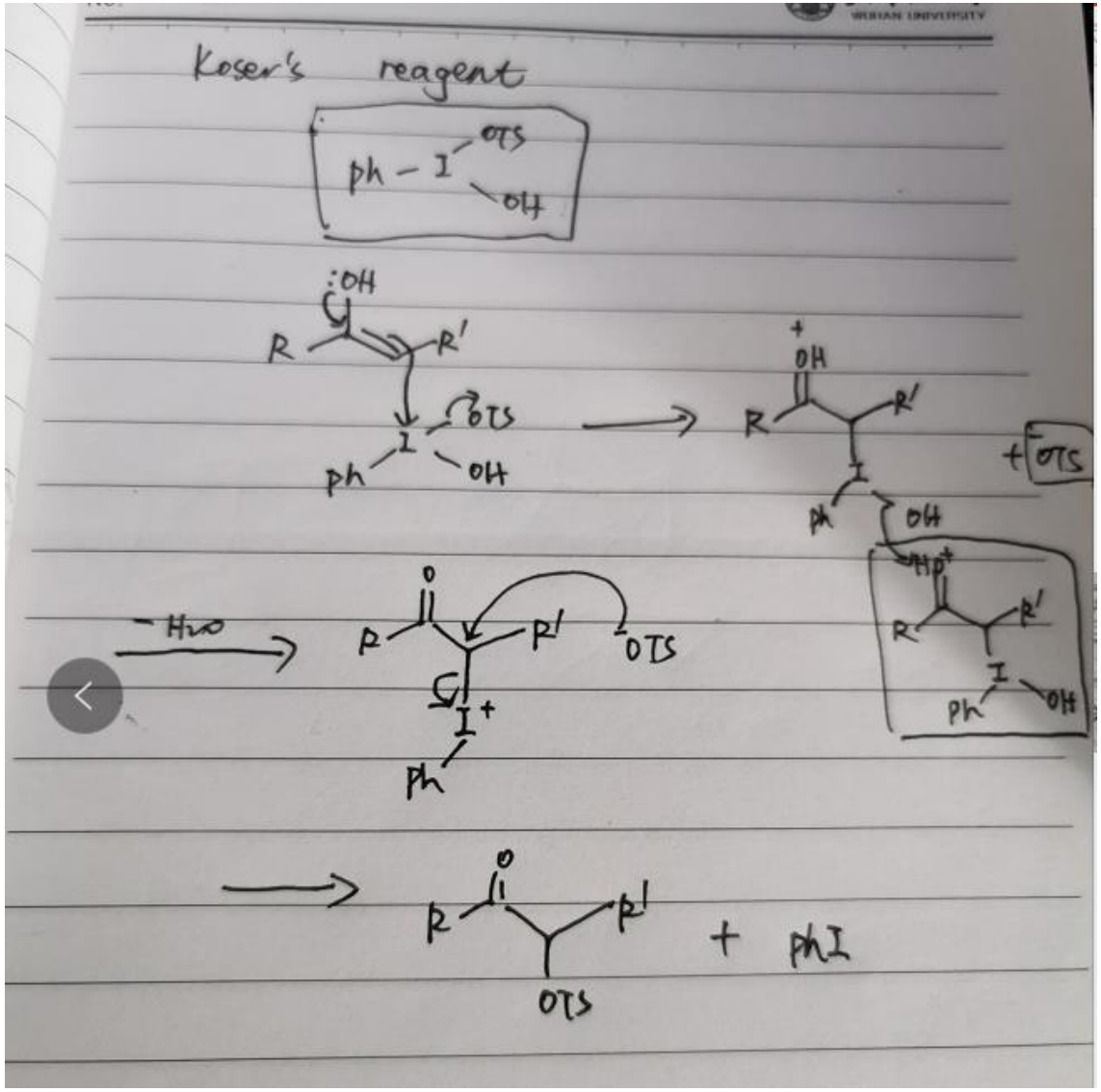
Support materials

Ireland−Claisen Rearrangement



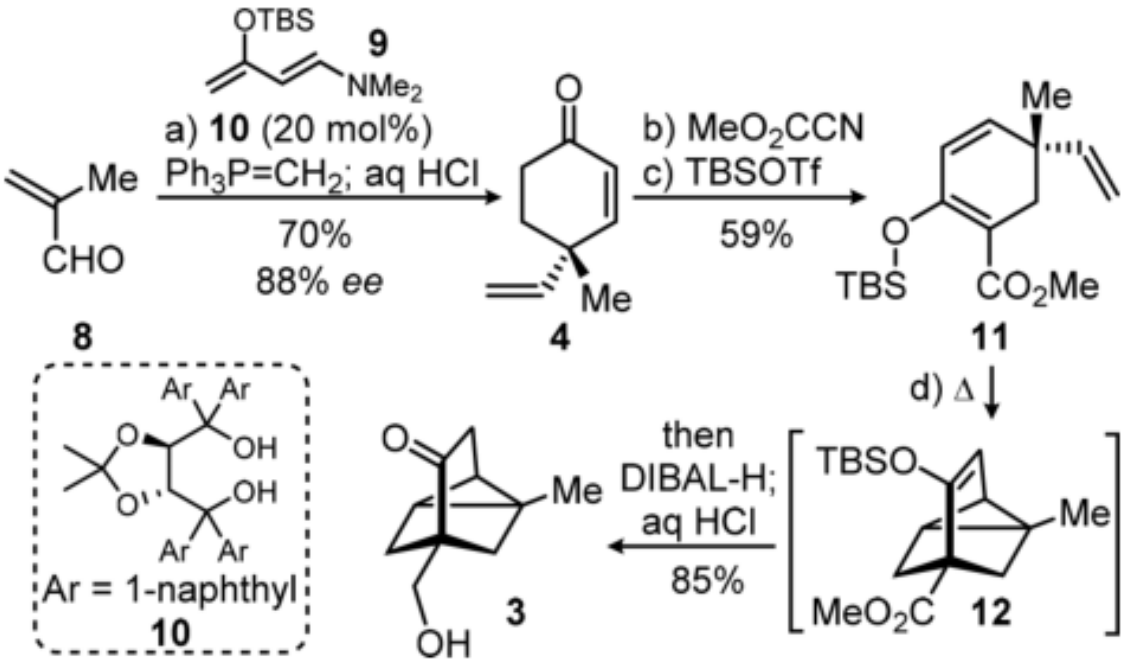
Support materials

Koser's reagent



Support materials

Scheme 4. Construction of the Tricyclooctane Core[a]



[a]Reagents and conditions: (a) Rawal's diene (**9**), (*S*,*S*)-1-Np-TADDOL (**10**) (20 mol %), PhMe, −80 °C, then $Ph_3P{=}CH_2$, −78 °C to RT, then 1 M aq HCl, RT, 70%, 88% *ee*; (b) LDA, THF, −78 °C, then HMPA, MeO_2CCN; (c) LiHMDS, *t*-$BuMe_2SiOTf$, THF, −78 °C, 59% (2 steps); and (d) propylene oxide, PhMe, 190 °C, then DIBAL-H, −78 °C, then 1 M aq HCl, −78 °C to RT, 85%.