

Literature Report IX

Total Synthesis of Euphorbialoid A

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Date: 2025-1-6

Taguchi, J.; Fukaya, S.; Fujino, H.; [Inoue, M.](#) *J. Am. Chem. Soc.* **2024**, *146*, 34221-34230

CV of Prof. Masayuki Inoue (井上将行)



Background:

- **1989-1993** B.S., The University of Tokyo
- **1993-1998** Ph.D., The University of Tokyo
- **1998-2000** Postdoctoral Fellow, Sloan-Kettering Institute for Cancer Research
- **2000-2003** Assistant Prof., Tohoku University
- **2003-2007** Associate Prof., Prof., The University of Tokyo

Research:

Total Synthesis and Functional Analysis of Biologically Active Natural Products

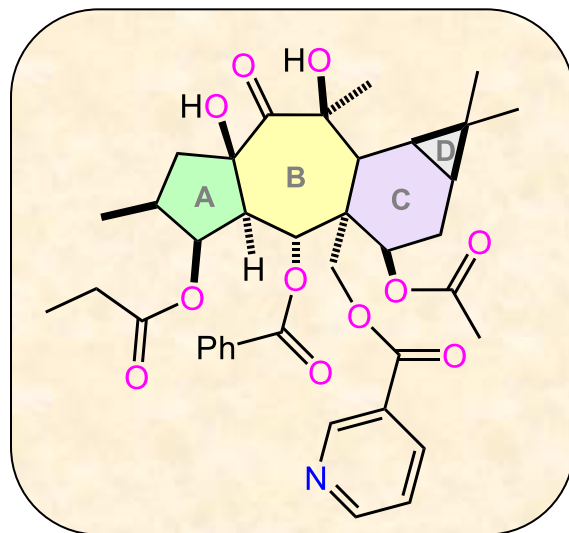
Contents

1 Introduction

2 Total Synthesis of Euphorbialoid A

3 Summary

Introduction



Euphorbialoid A (1)

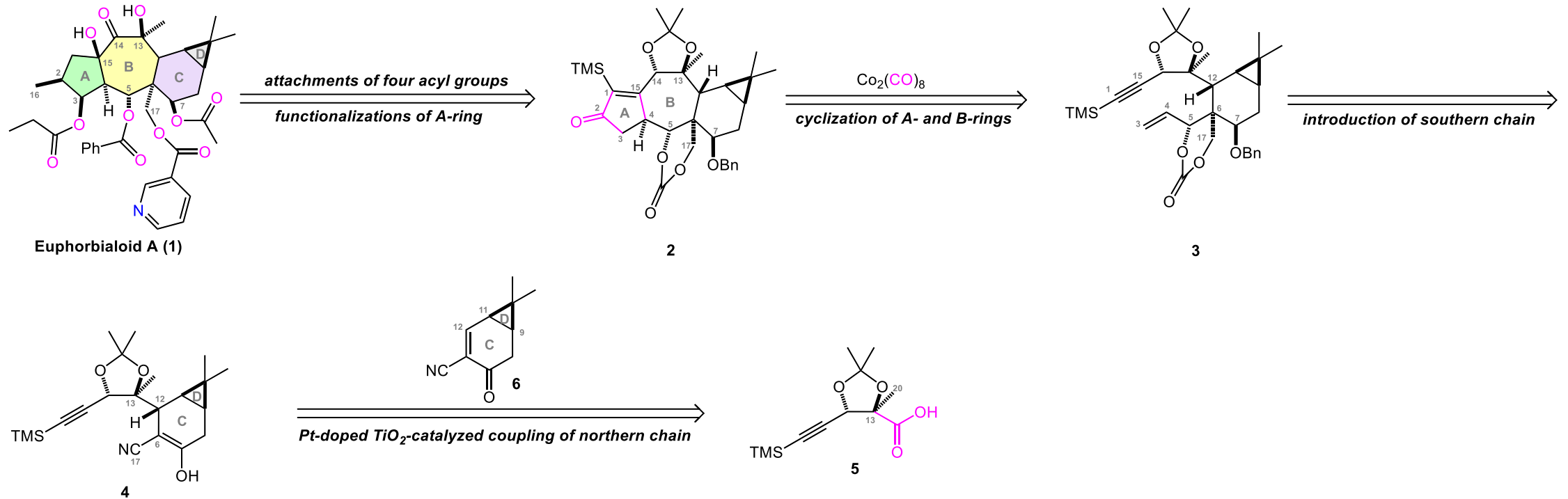


Euphorbia Prolifera 土瓜狼毒

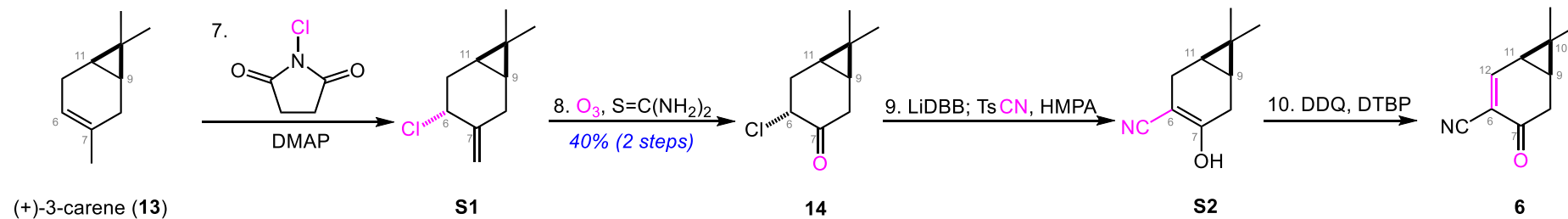
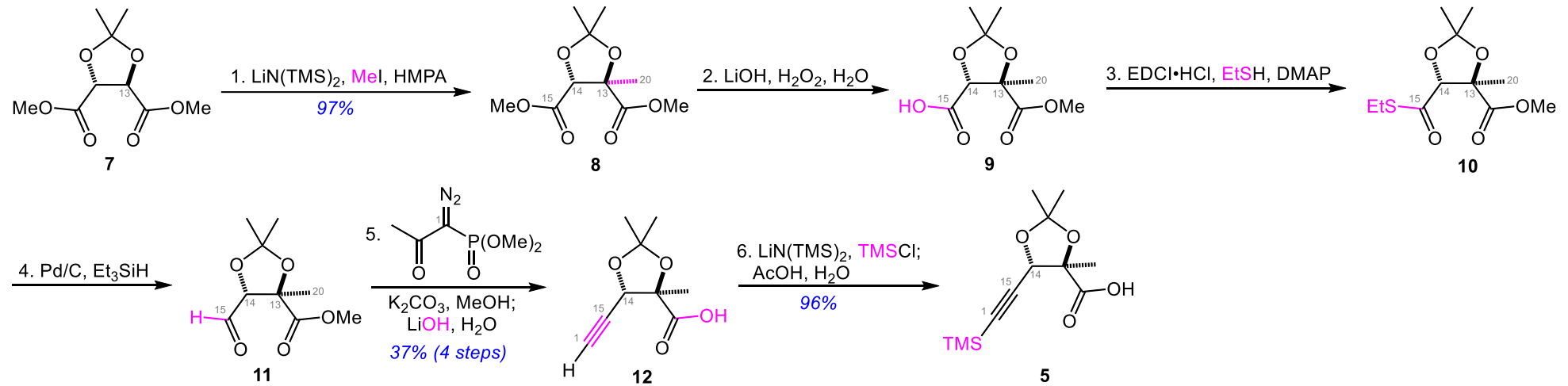
- ◆ The characteristic **5/7/6/3**-membered ABCD ring of premyrsinane diterpenoids
- ◆ The diterpenoids has **11 contiguous** stereogenic carbons
- ◆ The most notable structural feature of 1 lies in the **seven oxygen** functionalities that decorate the ABCD-ring skeleton

Xu, J.; Jin, D.-Q.; **Guo, Y.** *Bioorg. Med. Chem. Lett.* **2012**, 22, 3612–3618

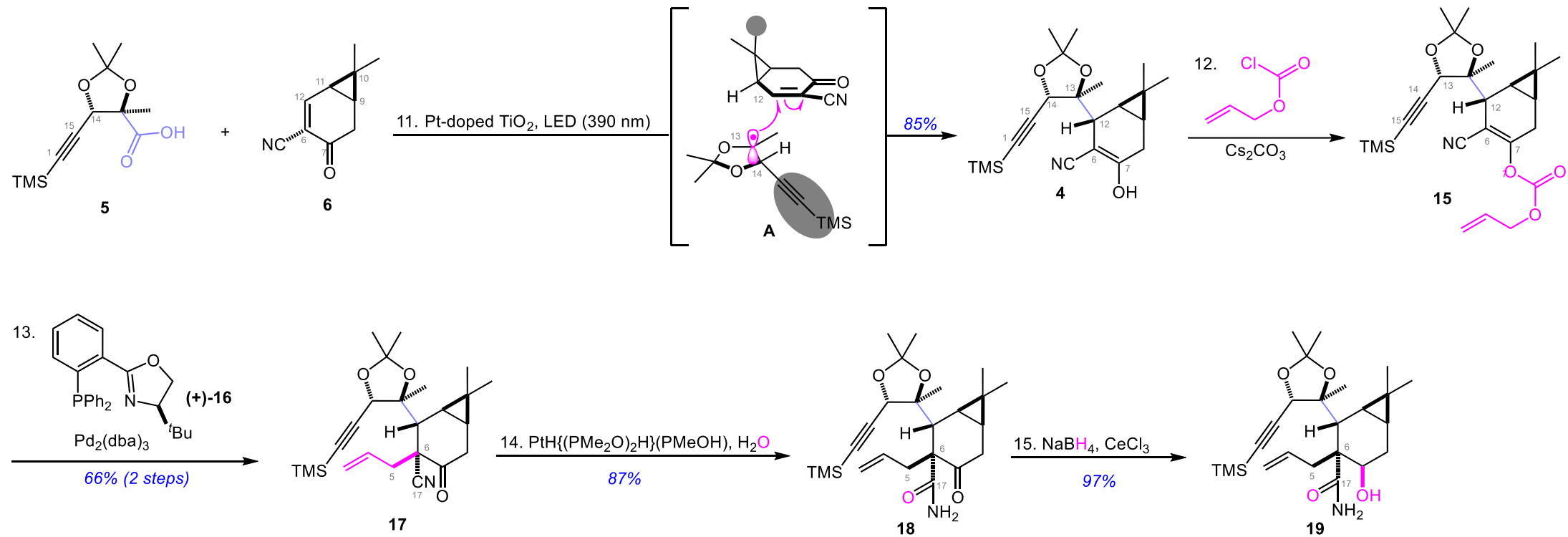
Retrosynthetic Analysis of Euphorbialoid A



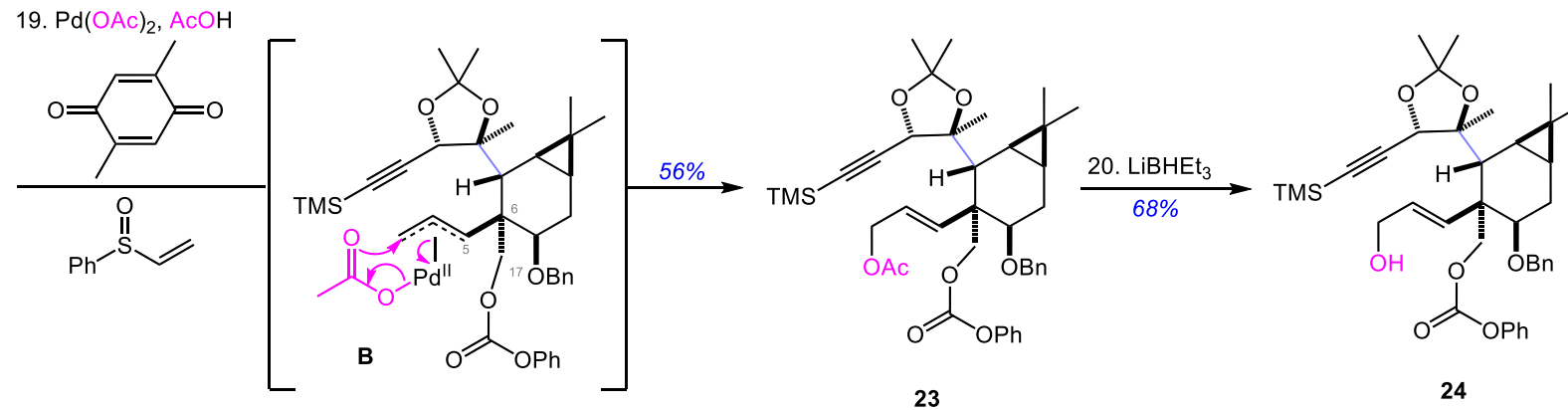
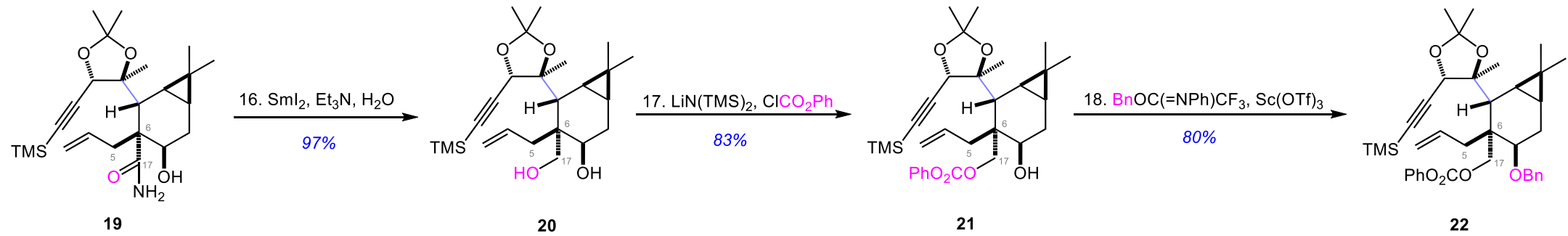
Preparation of Carboxylic Acid 5 and Enone 6



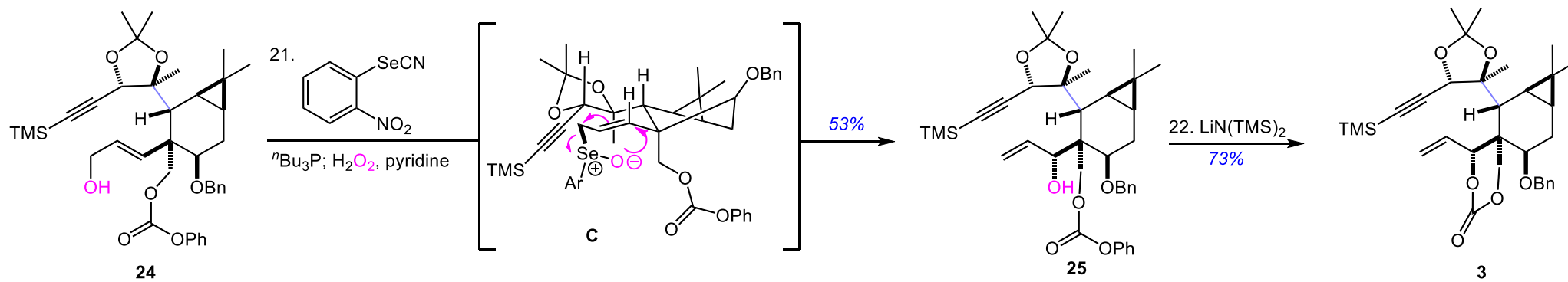
Construction of the ABCD-Ring Skeleton



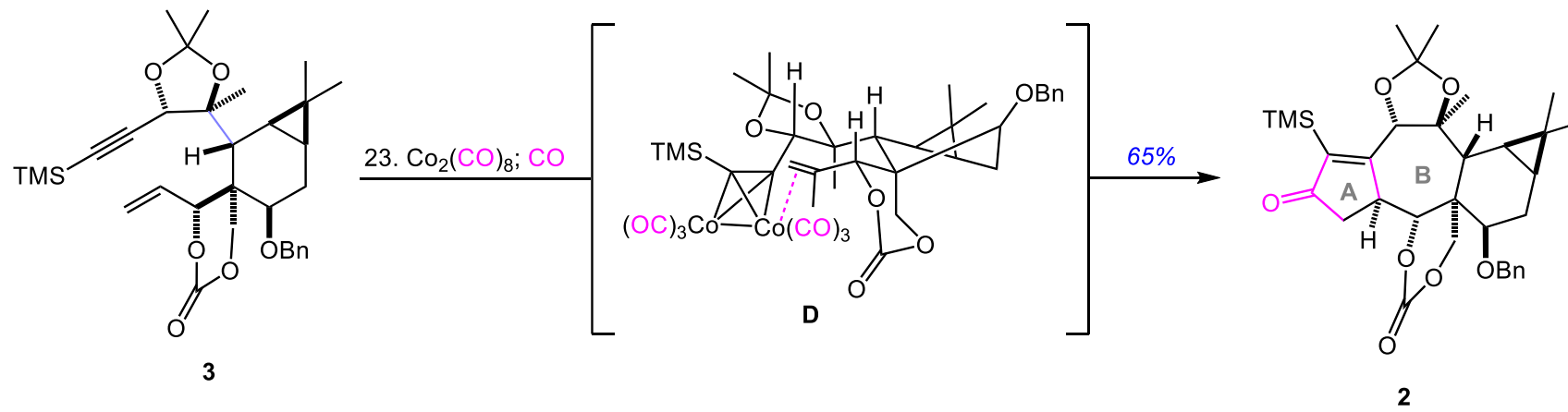
Construction of the ABCD-Ring Skeleton



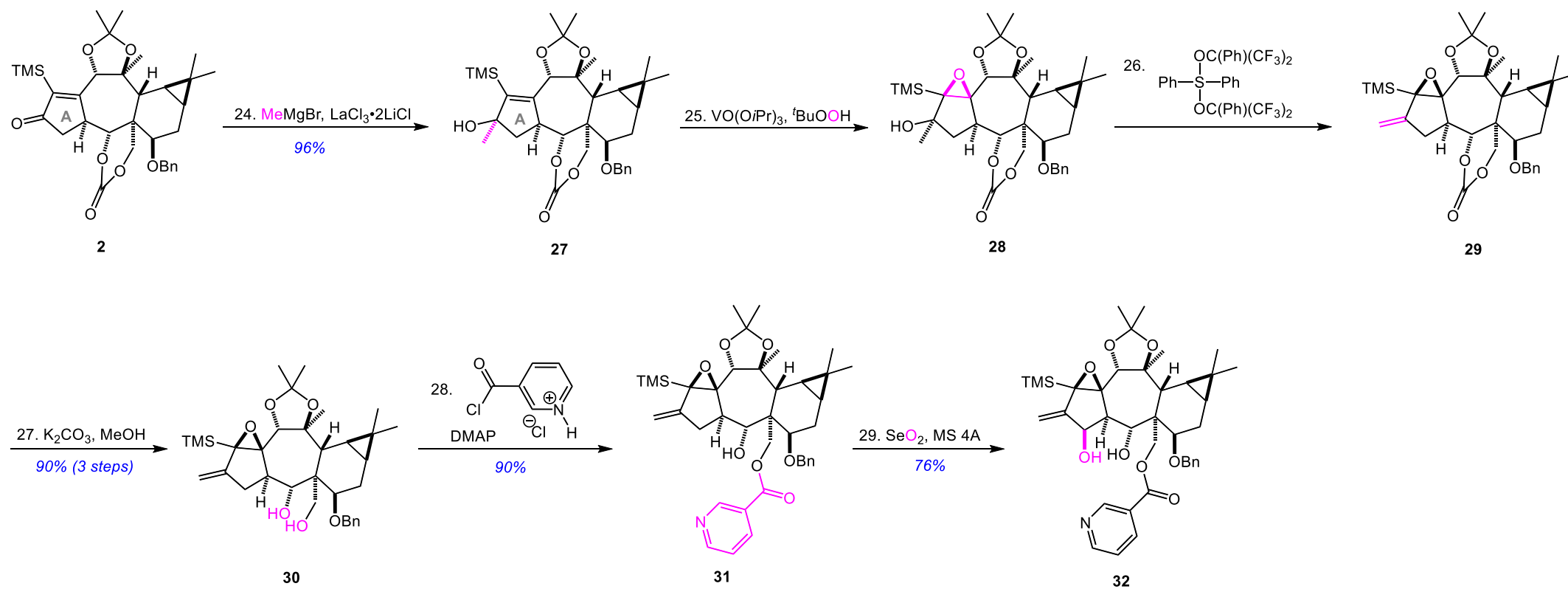
Construction of the ABCD-Ring Skeleton



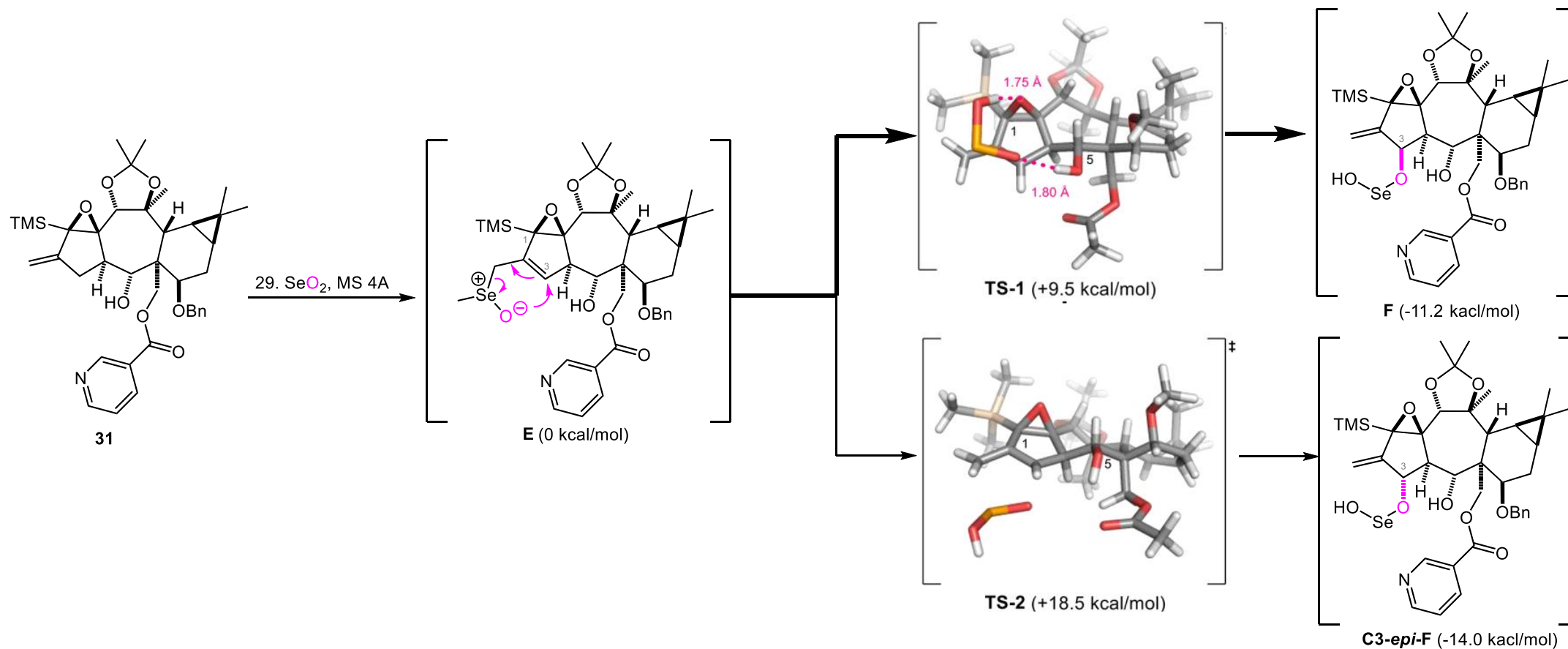
Construction of the ABCD-Ring Skeleton



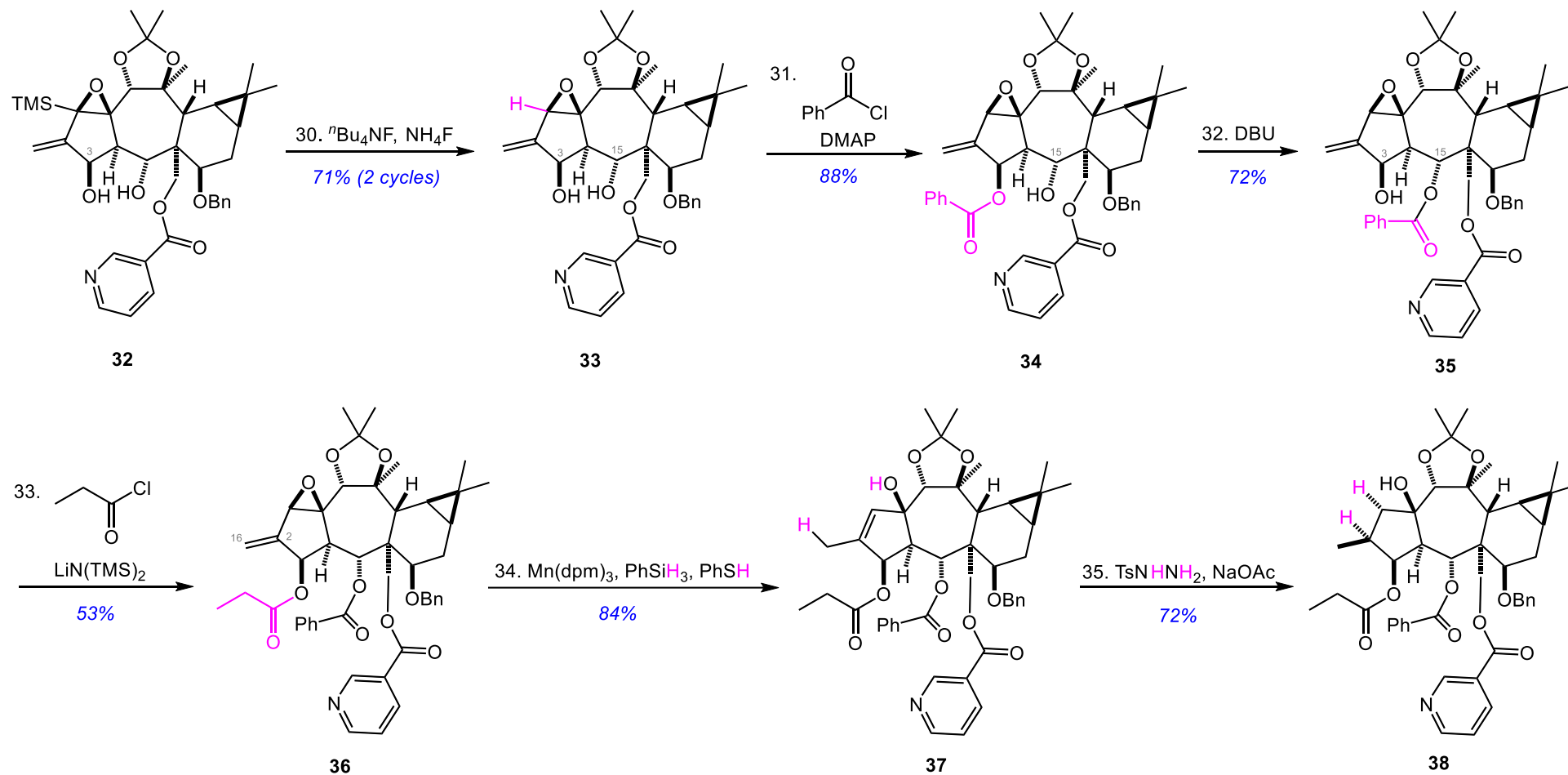
Total Synthesis of Euphorbialoid A



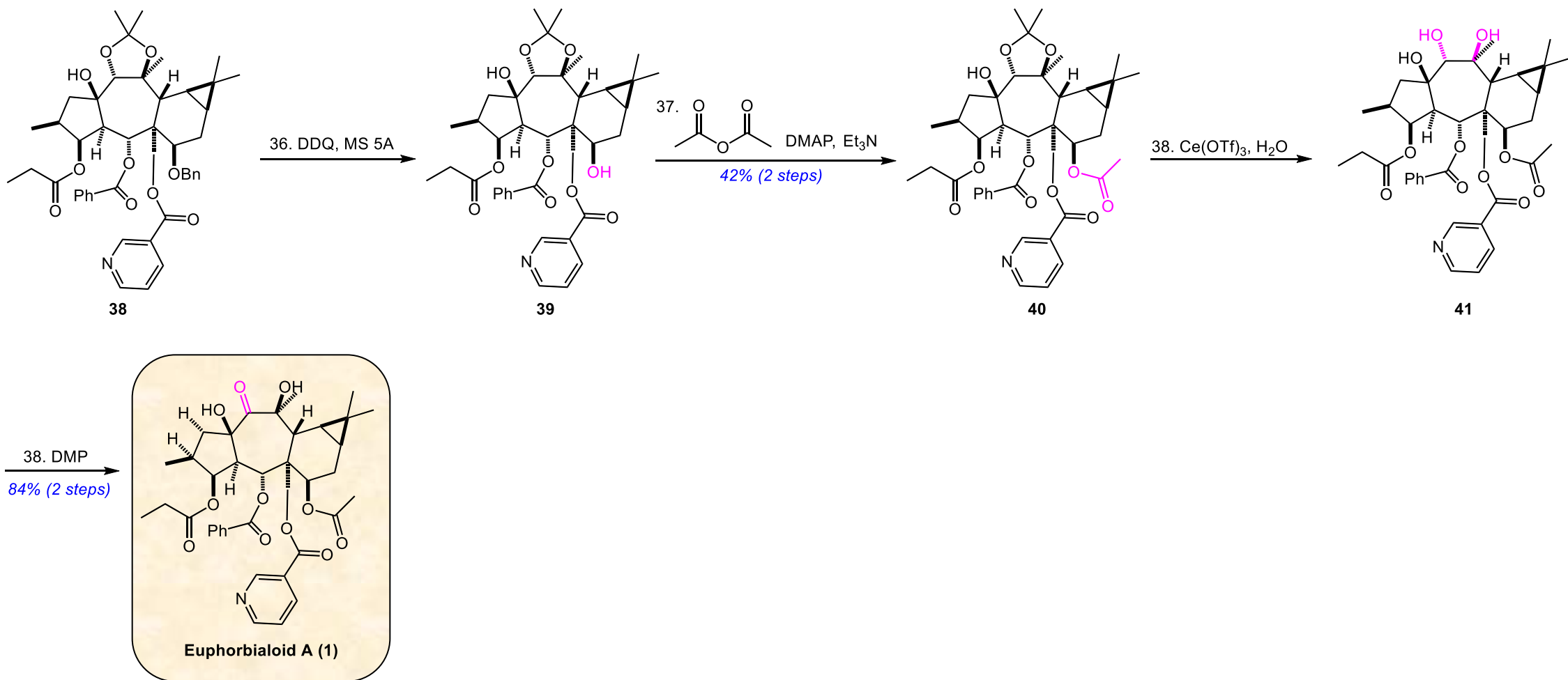
Rationale for the Stereochemical Outcome of C3- Allylic Oxidation



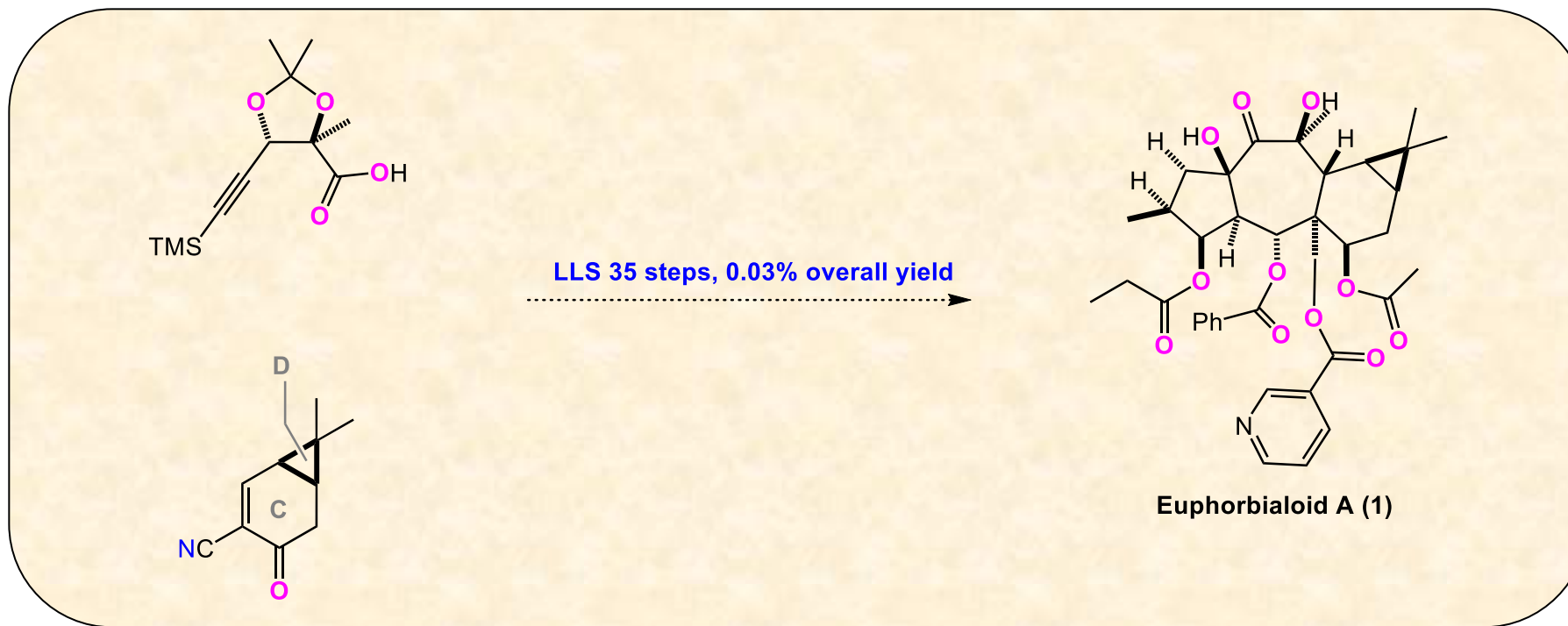
Total Synthesis of Euphorbialoid A



Total Synthesis of Euphorbialoid A



Summary



- Pt-doped TiO_2 -catalyzed radical coupling
- Co-mediated Pauson-Khand reaction
- Pd-catalyzed decarboxylative allylation
- Attachments of four acyl groups

Writing Strategy

□ The First Paragraph

Euphorbialoid A
的来源



Euphorbialoid A
的药物活性



介绍本文合成策略

- Euphorbialoid A (1, Scheme 1) was identified from the roots of *Euphorbia prolifera* by Guo in 2012, and revealed to possess a premyrsinane diterpenoid skeleton.
- Compound 1 inhibits lipopolysaccharide-induced nitric oxide production in murine microglial BV-2 cells with no significant cytotoxicity, thereby functioning as an *anti*-inflammatory agent.
- Herein, we report the development of a new strategy comprising two stages... The newly devised strategy and tactics described here enabled us to achieve the first total synthesis of euphorbialoid A.

Writing Strategy

□ The Last Paragraph

总结工作



本文亮点



展望

- In summary, we accomplished the first total synthesis of euphorbialoid A (1), a premyrsinane diterpenoid, in 35 steps as the longest linear sequence from *L*-tartrate derivative 7.
- The key reactions in the first stage are (1.1) stereo- and chemoselective Pt-doped TiO₂-catalyzed radical coupling to attach a northern chain with an alkynyl group to a 6/3-membered CD-ring...
- As we devised the first chemical construction of this class of diterpenoids and solved the unusual acylation problems, the valuable information gathered here would be highly useful for attaining the total syntheses of other premyrsinanes...

Representative examples

- ✓ To date, chemical construction of **1** or any other premyrsinane diterpenoids has not been achieved, **reflecting** the high degree of difficulty in assembling such intricate structures. (反映出...)
- ✓ The latter site-selective esterification reactions would be a **formidable** problem because of the need to accommodate the proximal acyl groups in a hindered matrix while impeding potential 1,3-acyl migration at the hydroxy groups. (强大的, 厉害的, 可怕的)
- ✓ **At the outset**, the C2-ketone and C15-olefin of **2** were transformed into the C2-methylene and C15 β -epoxide of **29**, respectively, in three steps. (一开始)

Acknowledgment

Thanks for your attention !