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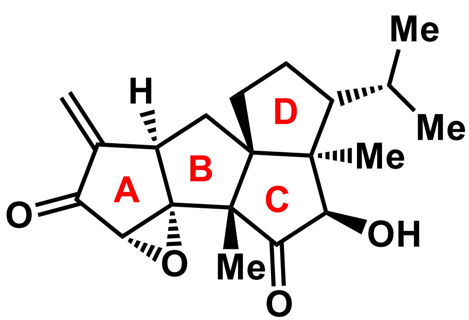
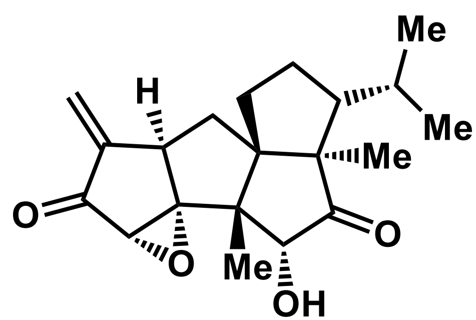
Communication

Concise Total Syntheses of (−)-Crinipellins A and B Enabled by a Controlled Cargill Rearrangement



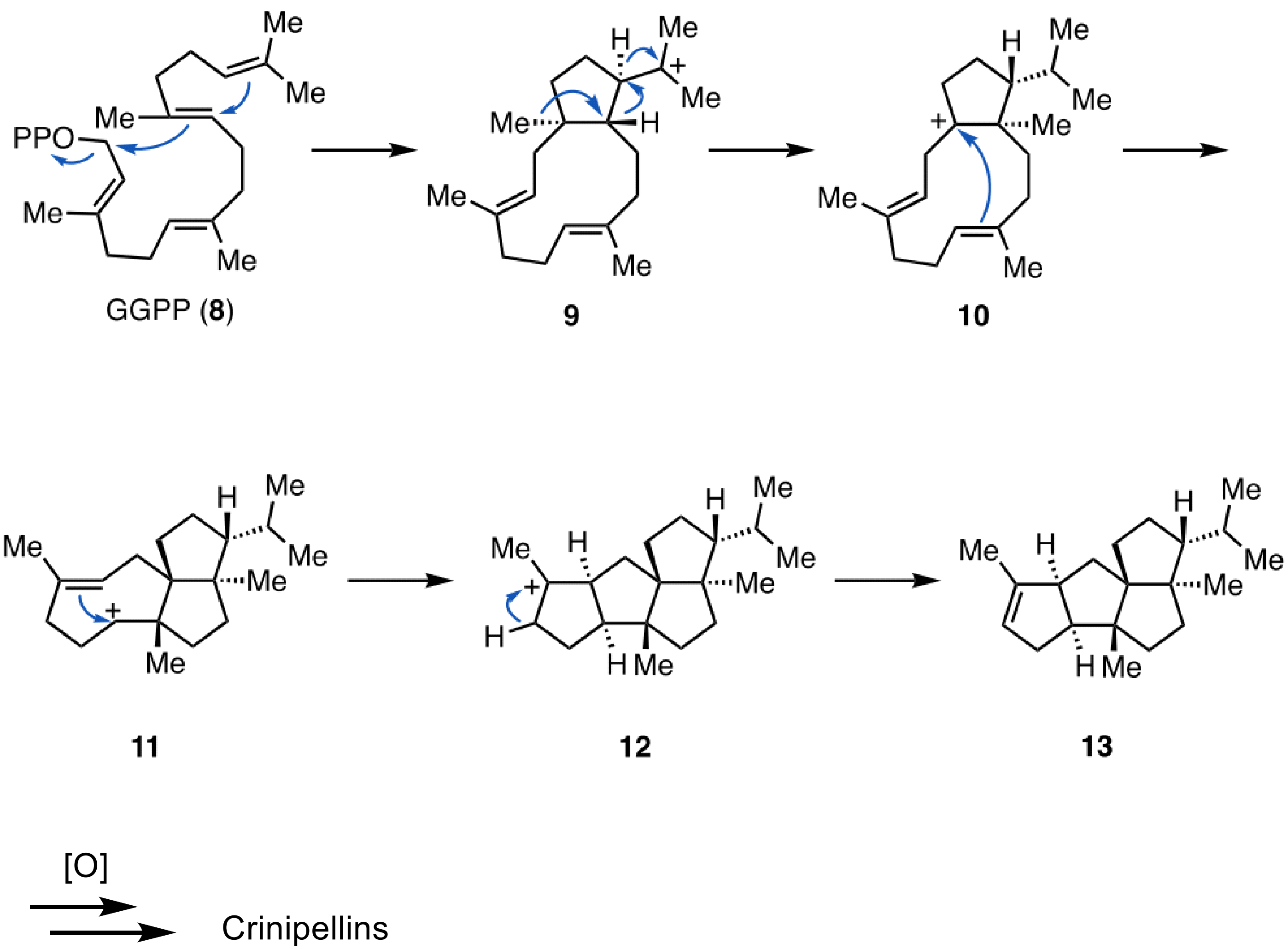
(-)-Crinipellin A (**1**)



(-)-Crinipellin B (**2**)

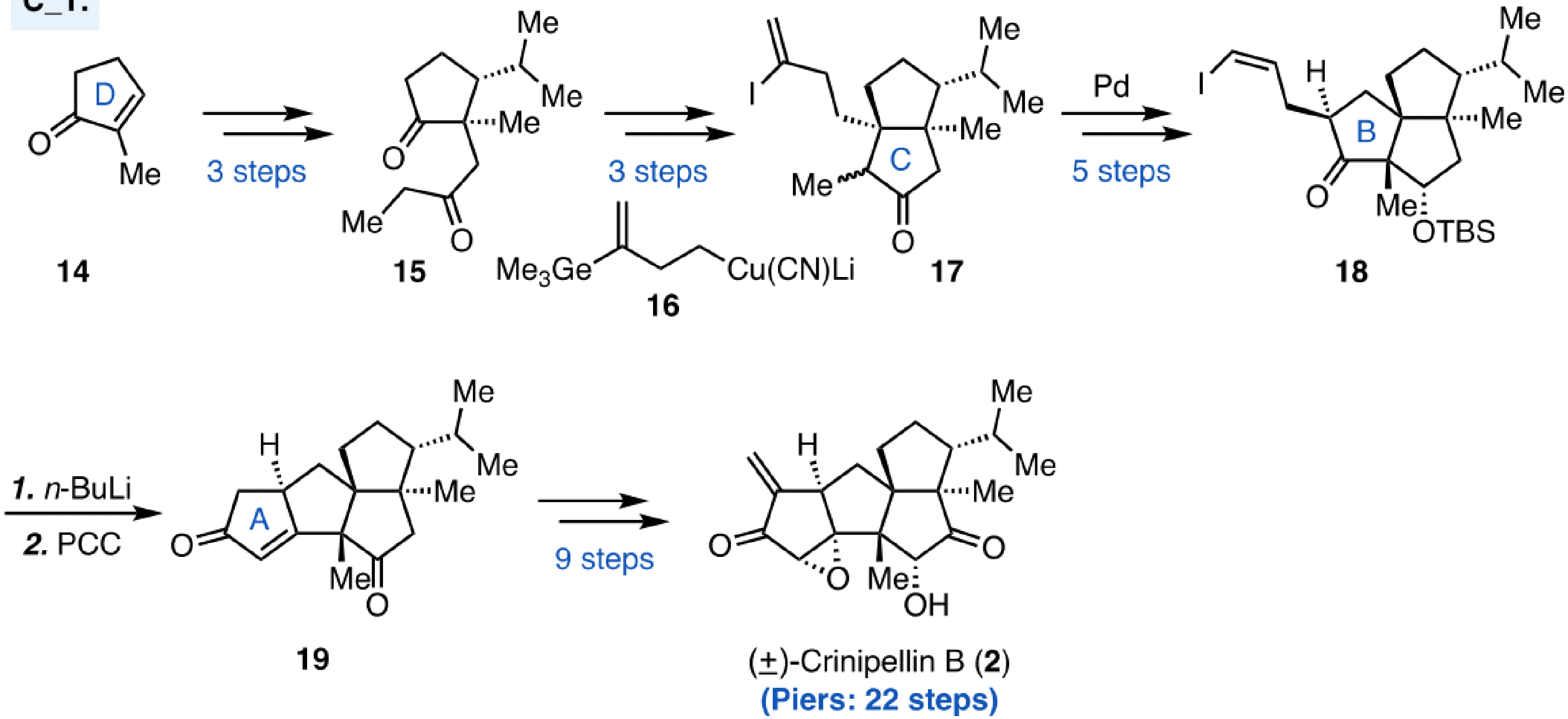
J. Am. Chem. Soc. **2024**, *146*, 21250.

Plausible Biosynthesis of Crinipellins



Highlight of the previous total syntheses from the groups of Piers, Lee, Yang, and Ding

C_1:



J. Org. Chem. **1993**, *58*, 11.

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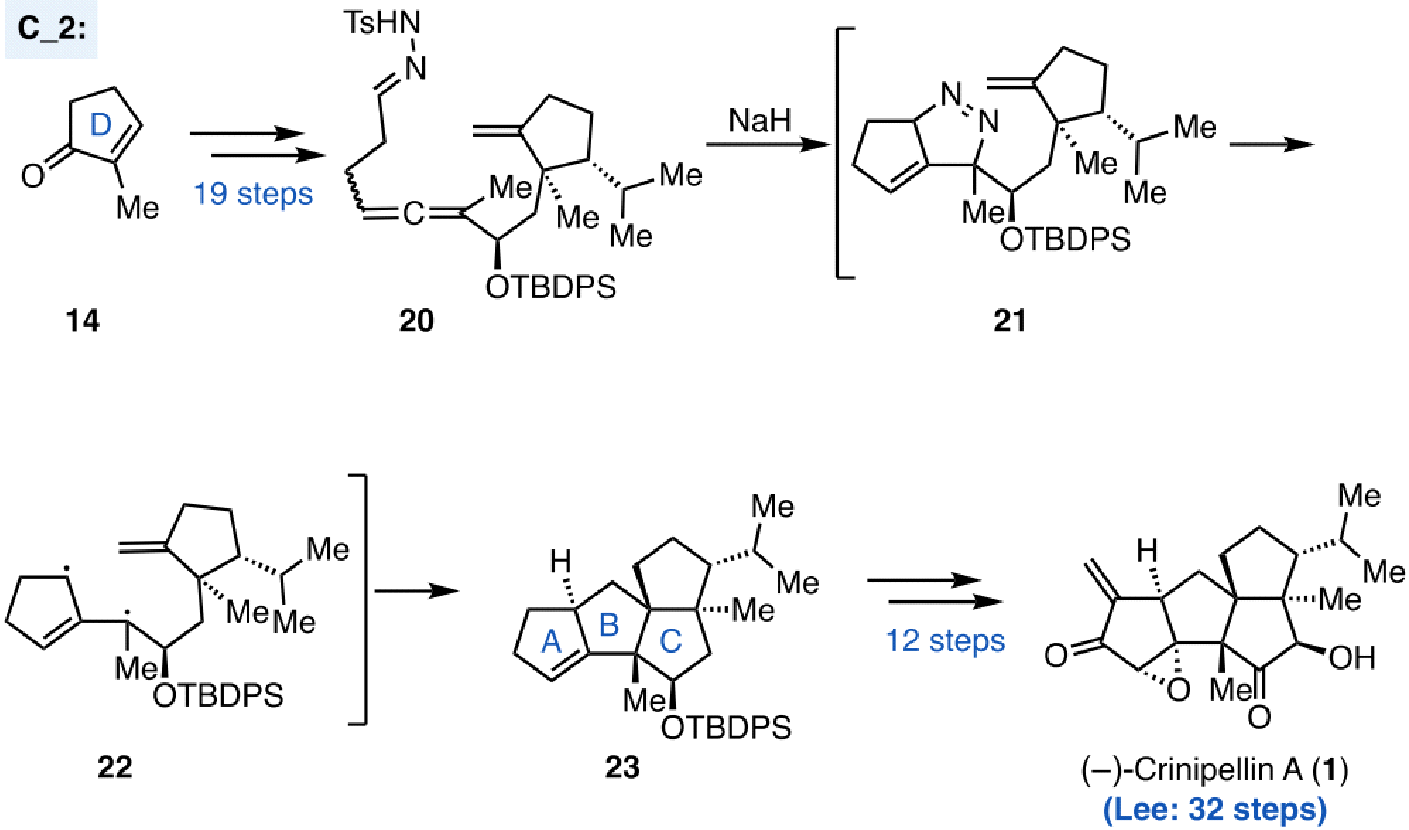
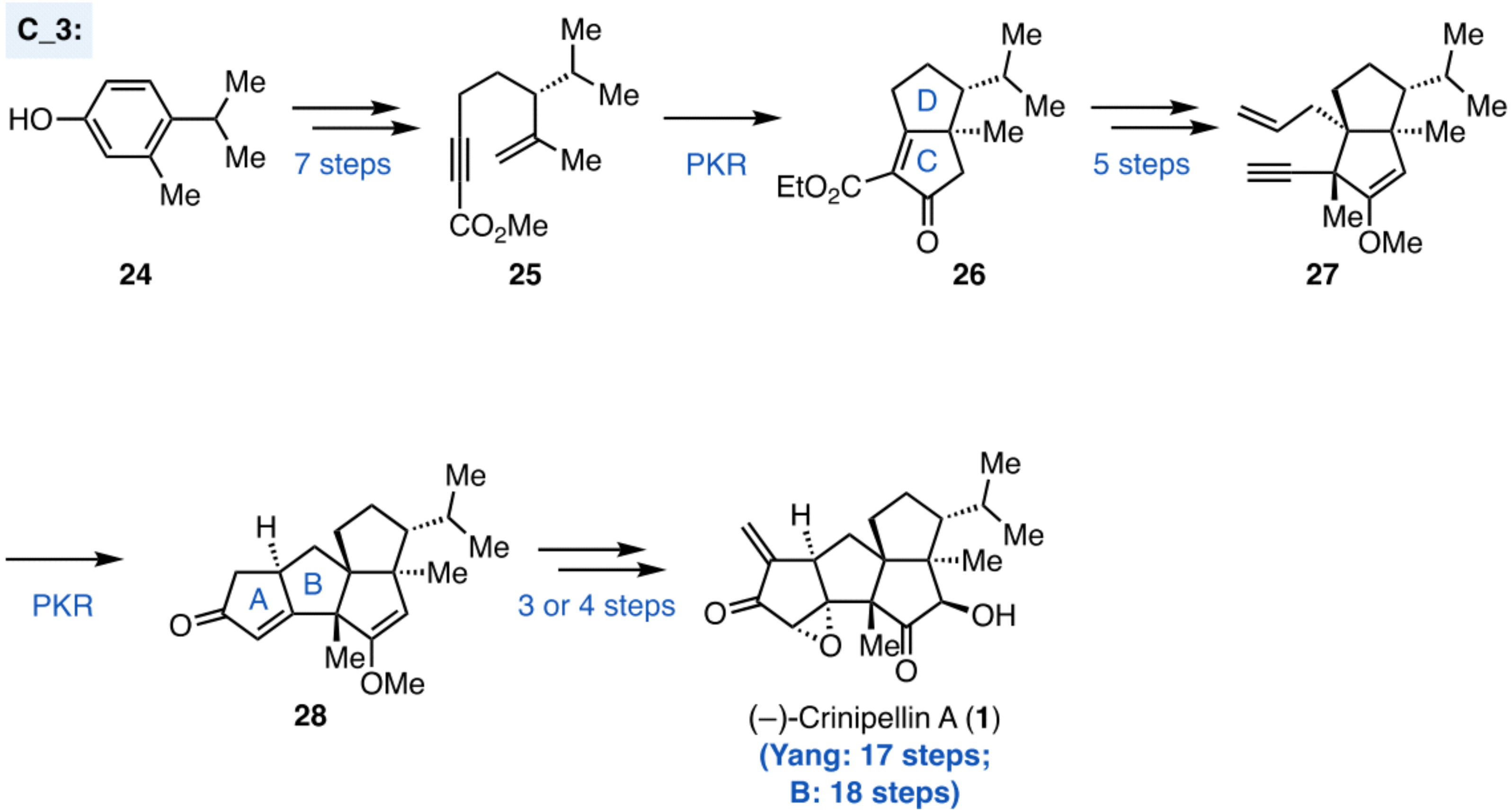
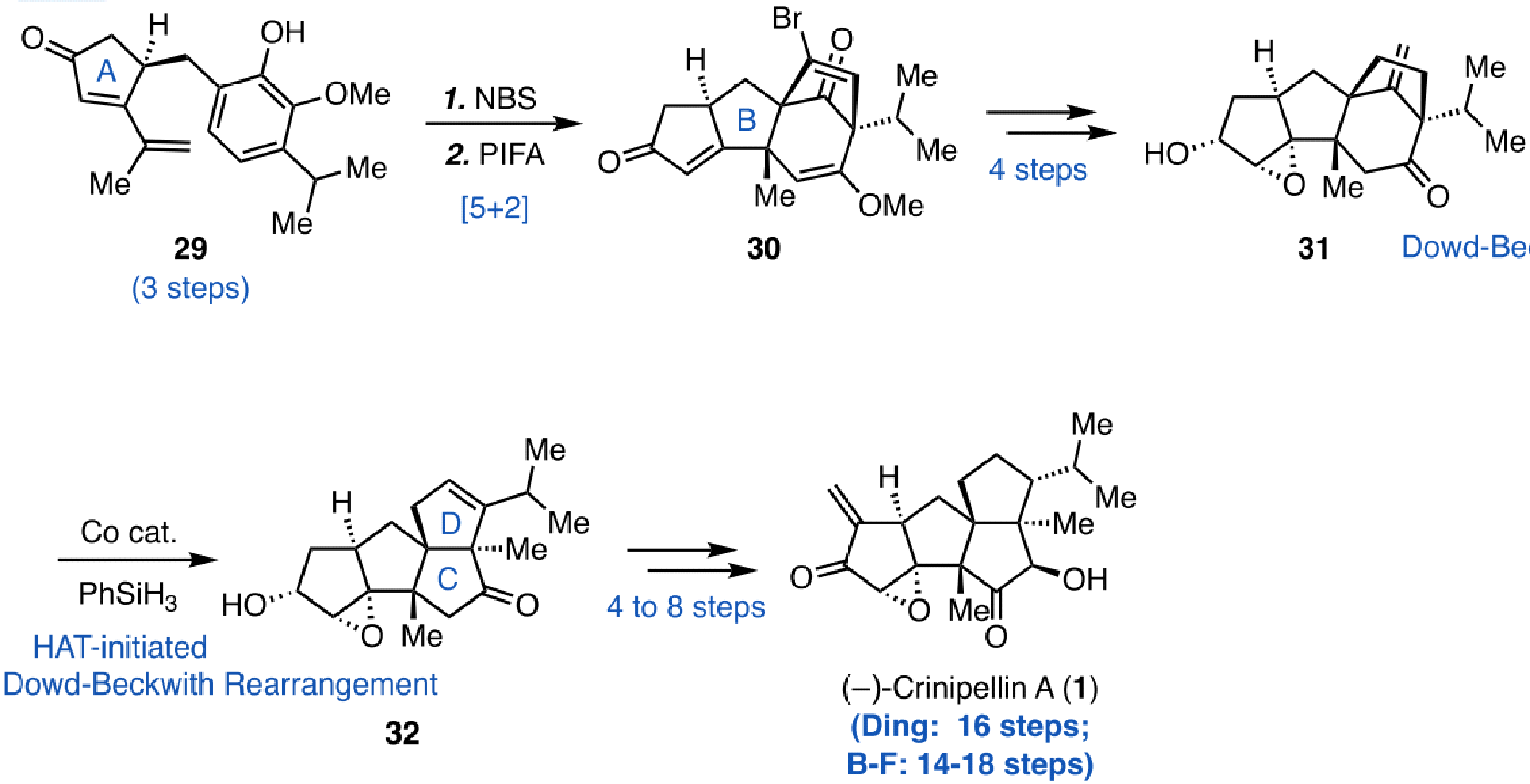


J. Am. Chem. Soc. **2014**, *136*, 10274.



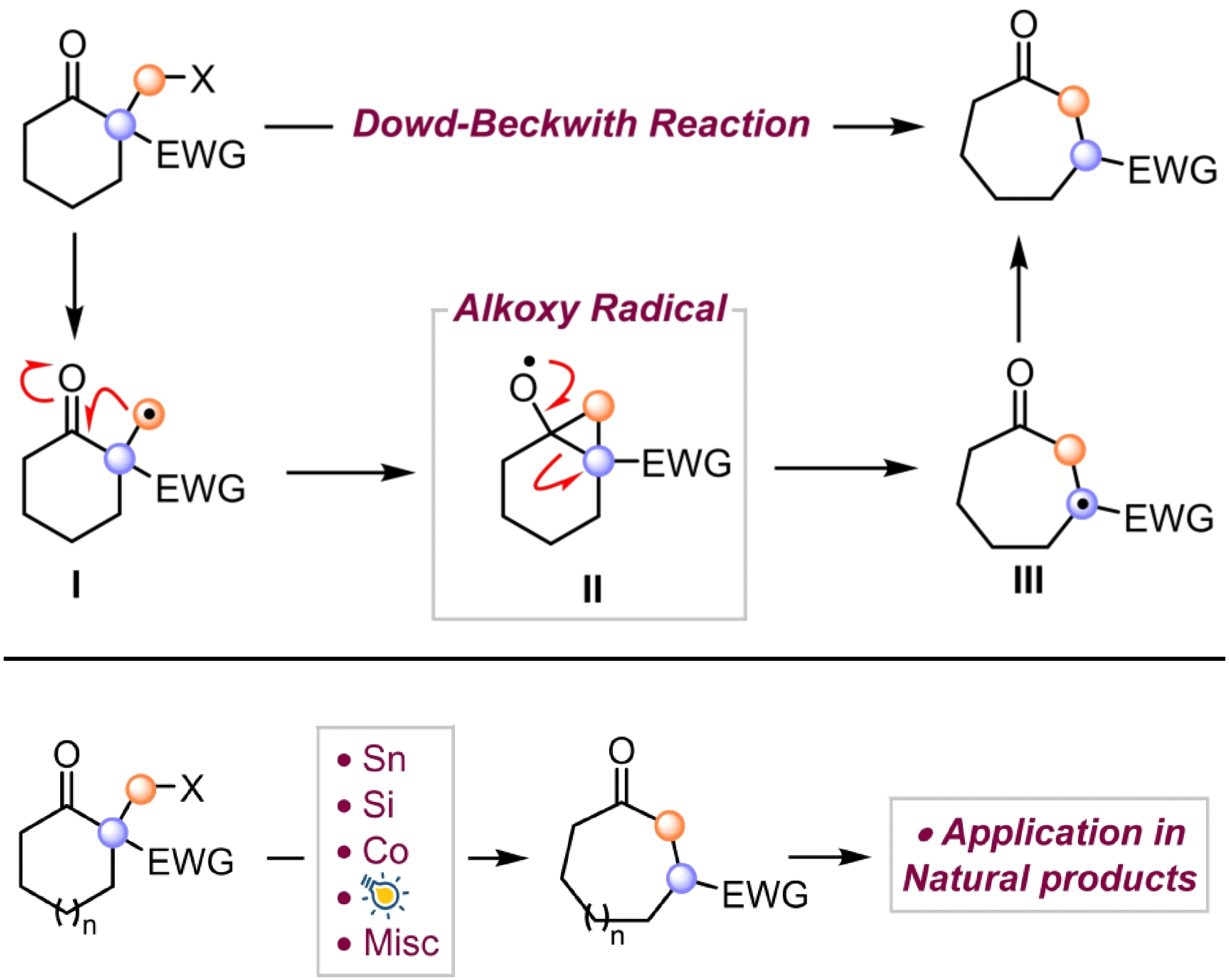
Angew. Chem., Int. Ed. **2018**, *57*, 8744.

C_4:



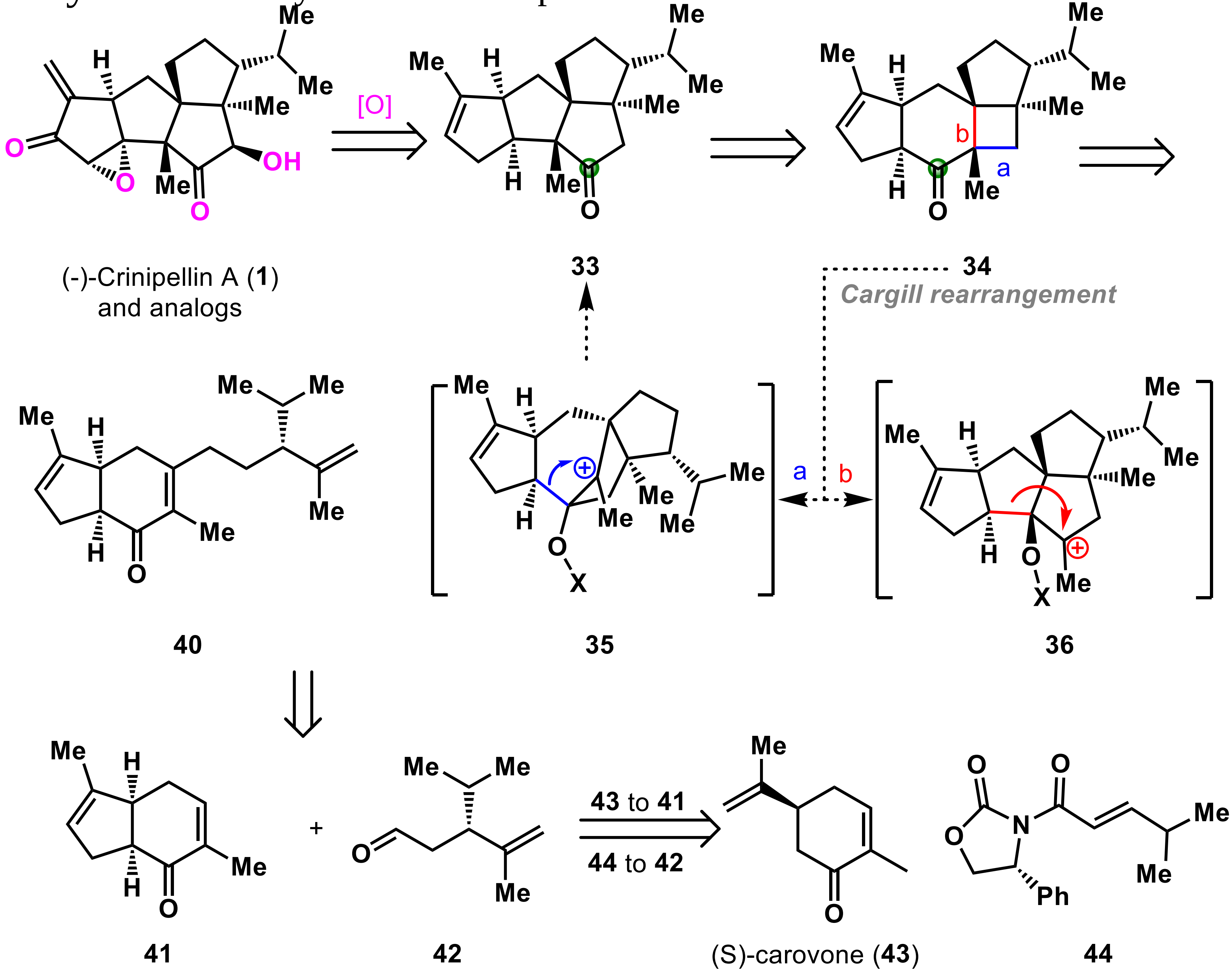
J. Am. Chem. Soc. **2022**, *144*, 2495.

The Dowd–Beckwith Reaction



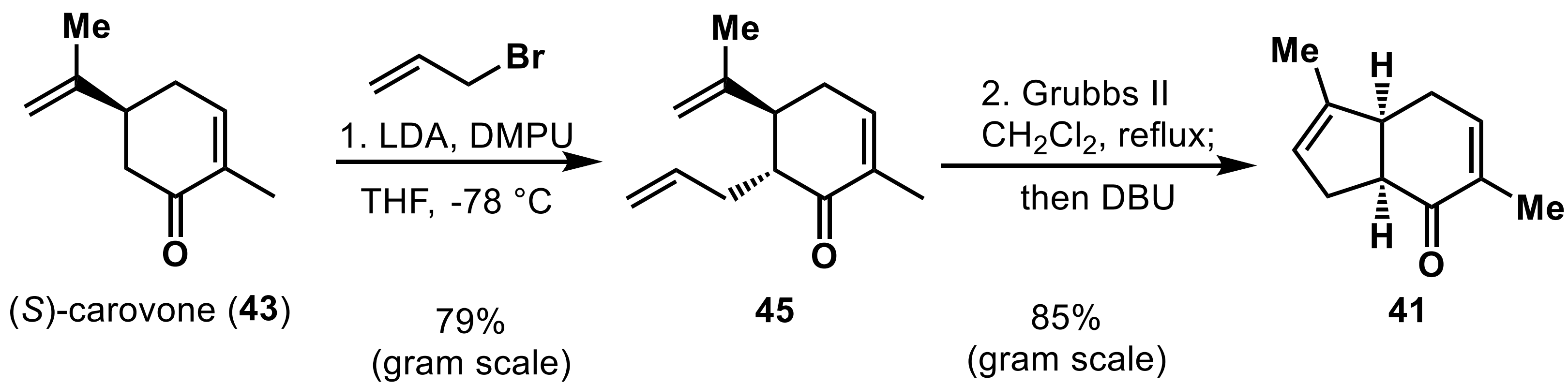
Chem. Eur. J. **2022**, *28*, e202202025

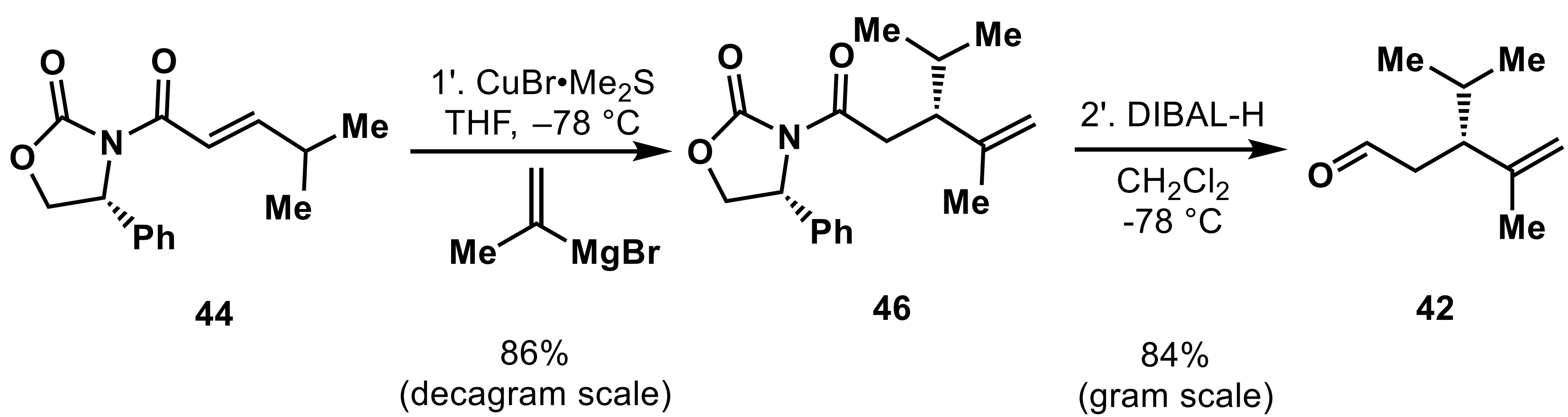
Retrosynthetic Analysis of the Crinipellins



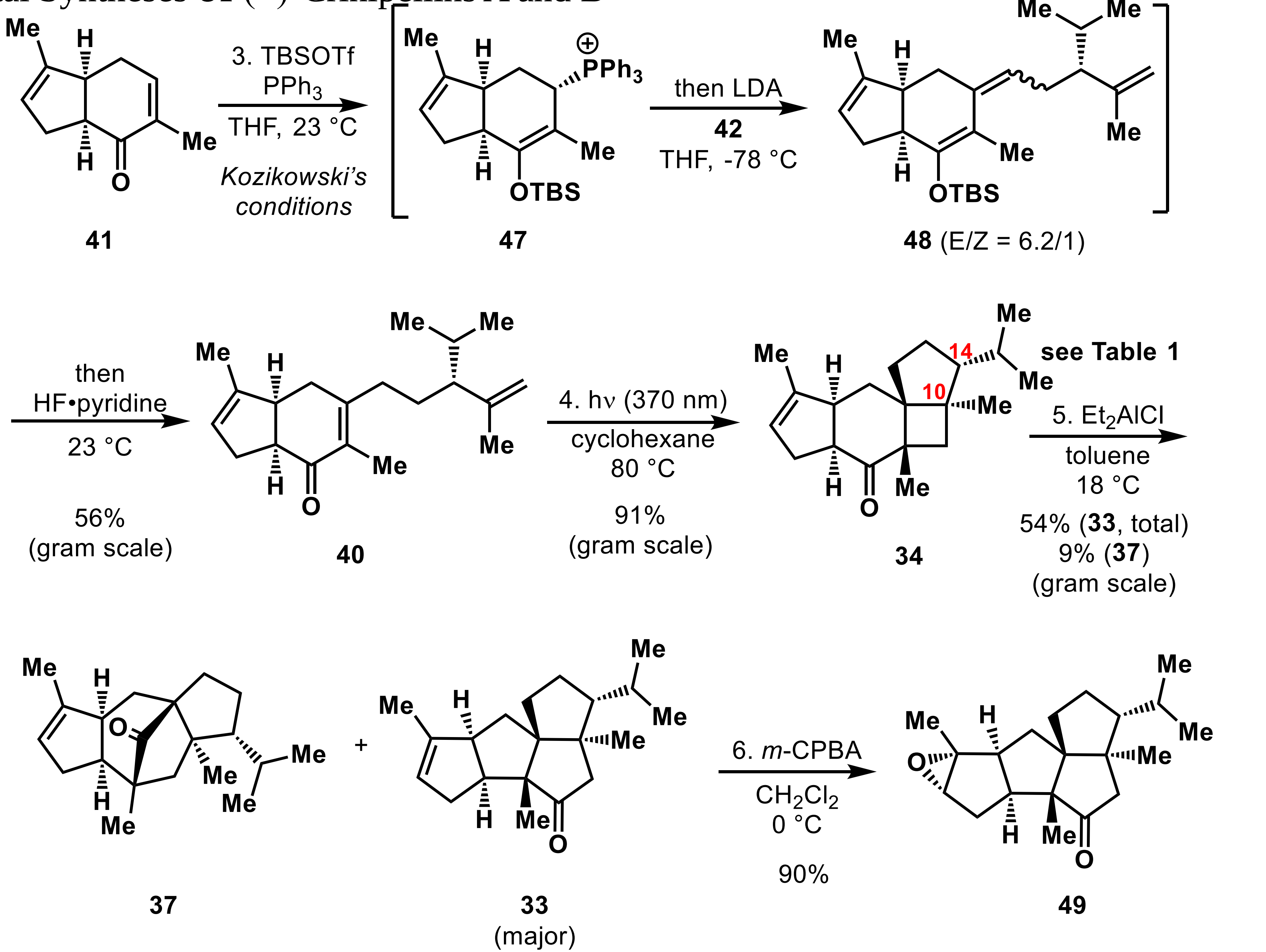
(-)-Crinipellin A (**1**) and analogs; **33**; **34**; **35**; **36**; **40**; **41**; **42**; (S)-carovone (**43**); **44**

The Syntheses of **41**and **42**





Total Syntheses of (−)-Crinipellins A and B



Cargill Rearrangement

Cargill重排是在酸(Bronsted酸或Lewis酸)催化下，二环[n.2.0]型桥环化合物发生重排反应，转化为二环[n-1.2.1]桥环化合物的反应。该反应已广泛应用于具有二环[3.2.1]辛烯骨架的天然产物的构建。

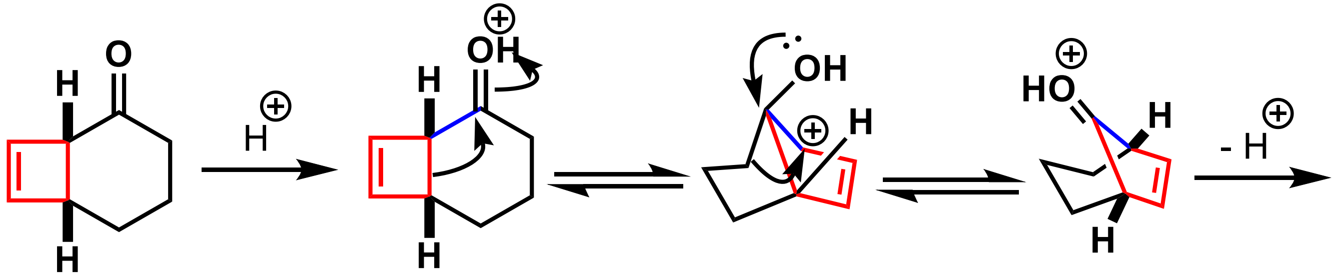
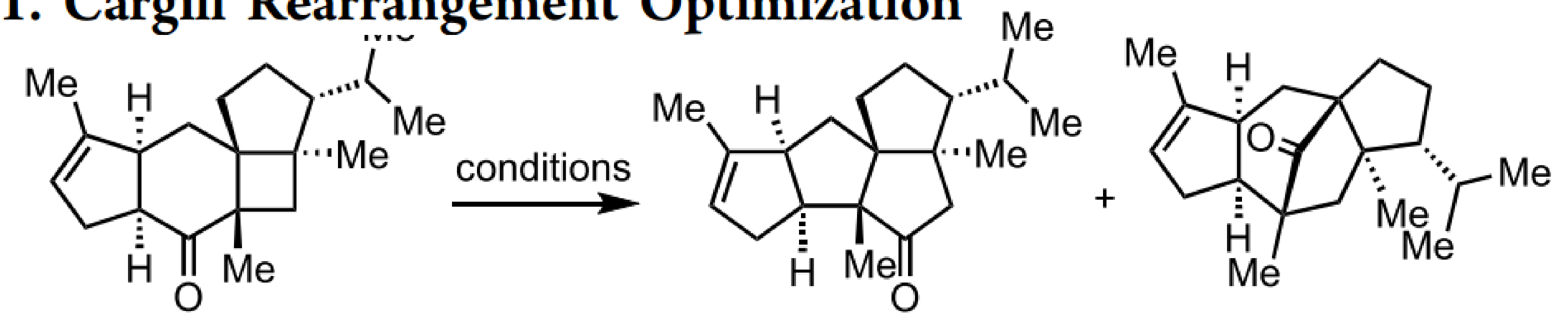
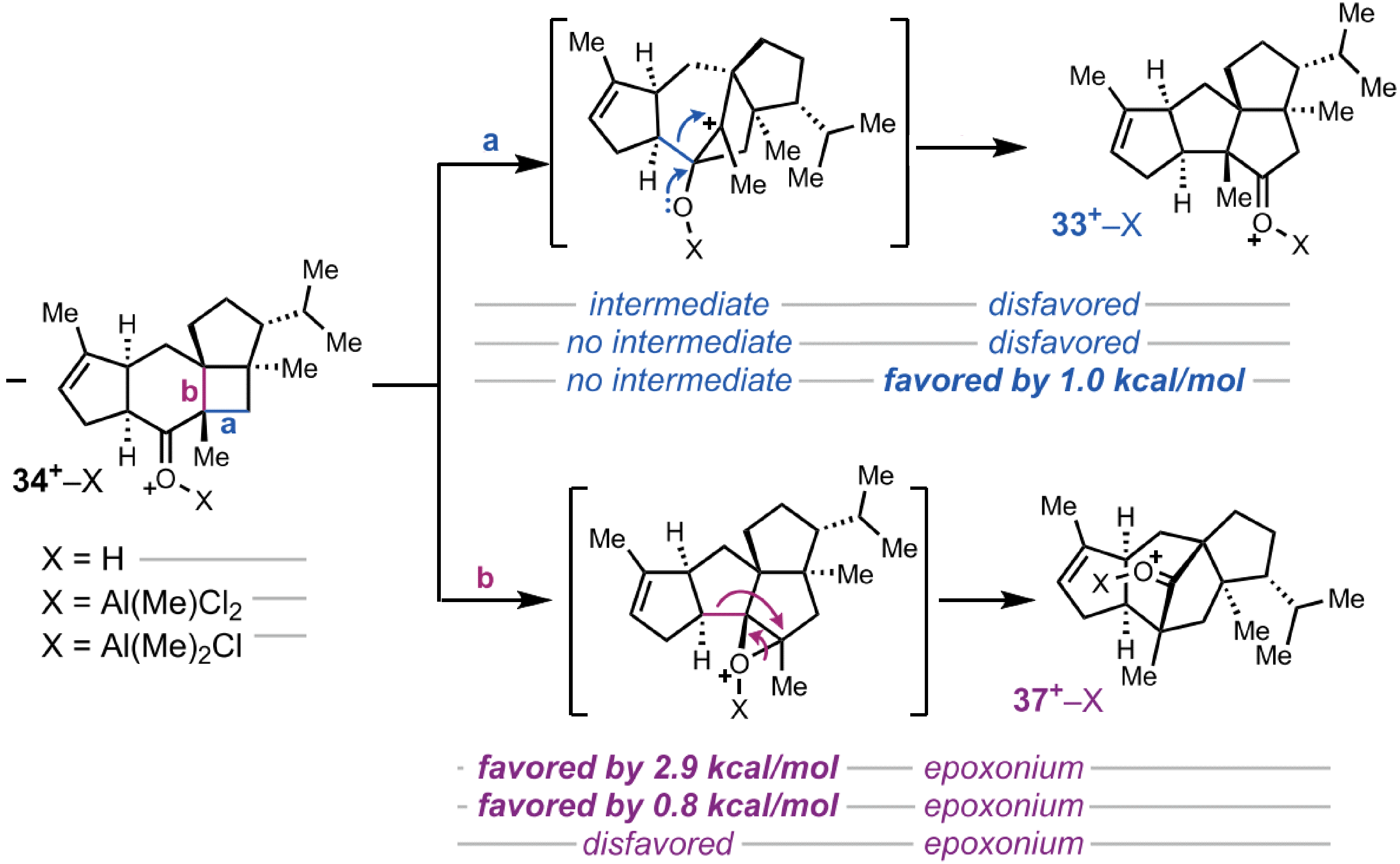


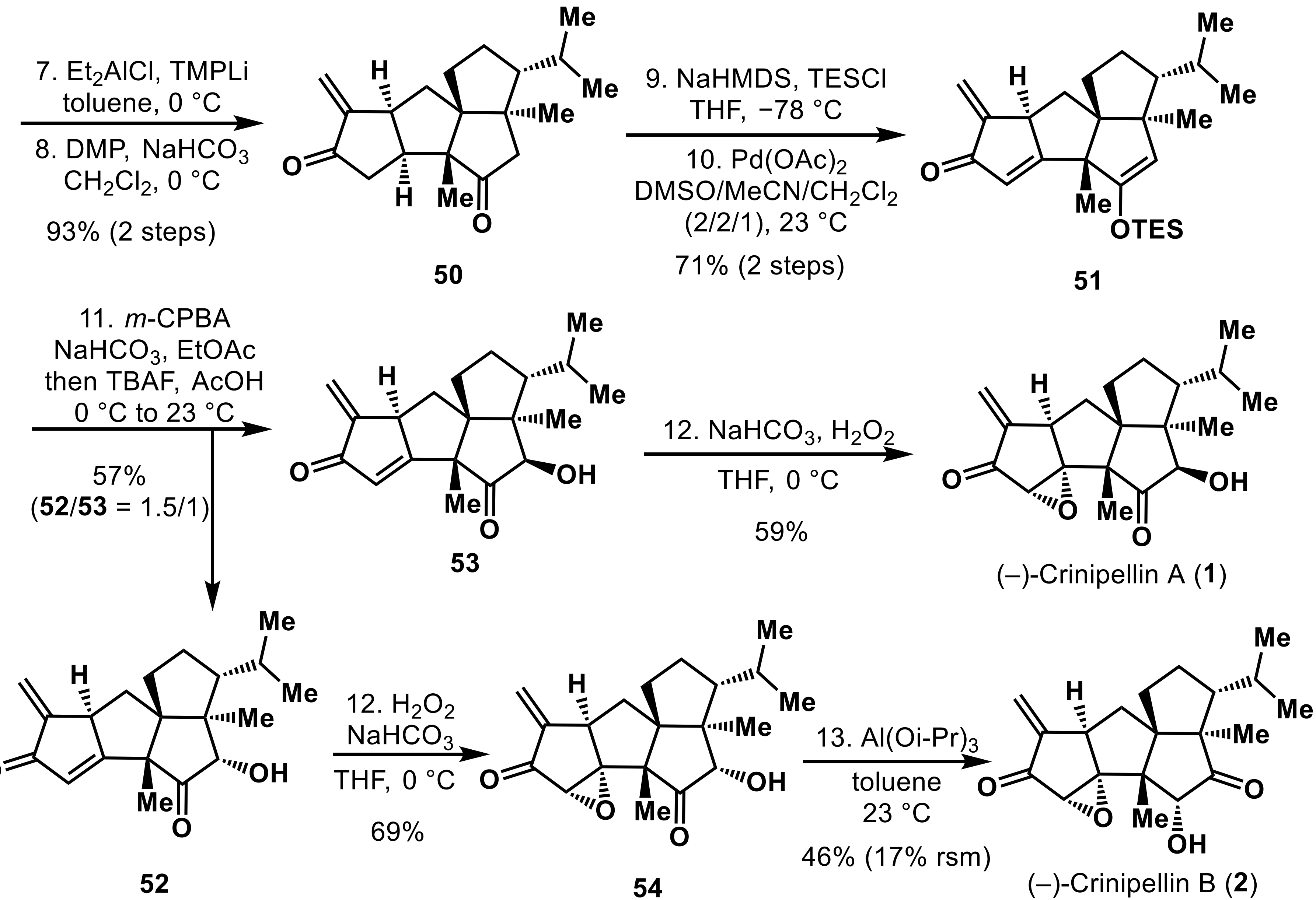
Table 1. Cargill Rearrangement Optimization



entry	reaction conditions (equiv)	results (**33**/**37**/**34**)
1	*p*-TsOH (1.0), PhH, 80 °C	18%/45%/0%[a]
2	*p*-TsOH (1.0), LiCl, toluene, 23 °C	0%/0%/85%[a]
3	Tf_2NH (1.0), CH_2Cl_2, 23 °C	9%/51%/0%[a]
4	$Mg(ClO_4)_2$ (1.0), CH_2Cl_2, 23 °C	0%/0%/91%[a]
5	$ZnCl_2$ (1.0), CH_2Cl_2, 23 °C	0%/79%/0%[a]
6	$ZnBr_2$ (1.0), CH_2Cl_2, 23 °C	0%/21%/69%[a]
7	$InCl_3$ (1.0), toluene, 23 °C	8%/82%/0%[a]
8	BF_3•Et_2O (1.0), CH_2Cl_2, 23 °C	7%/59%/0%[a]
9	$AlCl_3$ (1.0), CH_2Cl_2, 23 °C	5%/42%/0%[a]
10	Me_2AlCl (1.0), CH_2Cl_2, 23 °C	32%/45%/0%[a]
11	Me_2AlCl (1.0), LiCl, CH_2Cl_2, 23 °C	33%/40%/0%[a]
12	$EtAlCl_2$ (1.0), CH_2Cl_2, 23 °C	28%/46%/0%[a]
13	$EtAlCl_2$ (1.0), LiCl, CH_2Cl_2, 23 °C	32%/48%/0%[a]
14	Et_2AlCl (1.0), CH_2Cl_2, 23 °C	35%/23%/0%[a]
15	Et_2AlCl (1.0), LiCl, CH_2Cl_2, 23 °C	52%/25%/0%[a]
16	Et_2AlCl (1.0), toluene, 23 °C	65%/16%/0%[a]
17	Et_2AlCl (1.0), LiCl, toluene, 23 °C	59%/10%/0%[a]
18	Et_2AlCl (1.0), toluene, 18 °C (gram scale)	54%[b]/9%/0%[c]

Computational results on mechanisms of the Cargill rearrangements.




7. Et2AlCl, TMPLi
toluene, 0 °C
8. DMP, NaHCO3
CH2Cl2, 0 °C
93% (2 steps)
50
9. NaHMDS, TESCl
THF, −78 °C
10. Pd(OAc)2
DMSO/MeCN/CH2Cl2
(2/2/1), 23 °C
71% (2 steps)
51
OTES
11. m-CPBA
NaHCO3, EtOAc
then TBAF, AcOH
0 °C to 23 °C
57%
(52/53 = 1.5/1)
53
12. NaHCO3, H2O2
THF, 0 °C
59%
(–)-Crinipellin A (1)
52
12. H2O2
NaHCO3
THF, 0 °C
69%
54
13. Al(Oi-Pr)3
toluene
23 °C
46% (17% rsm)
(–)-Crinipellin B (2)