Total Synthesis of *Pepluanol A*

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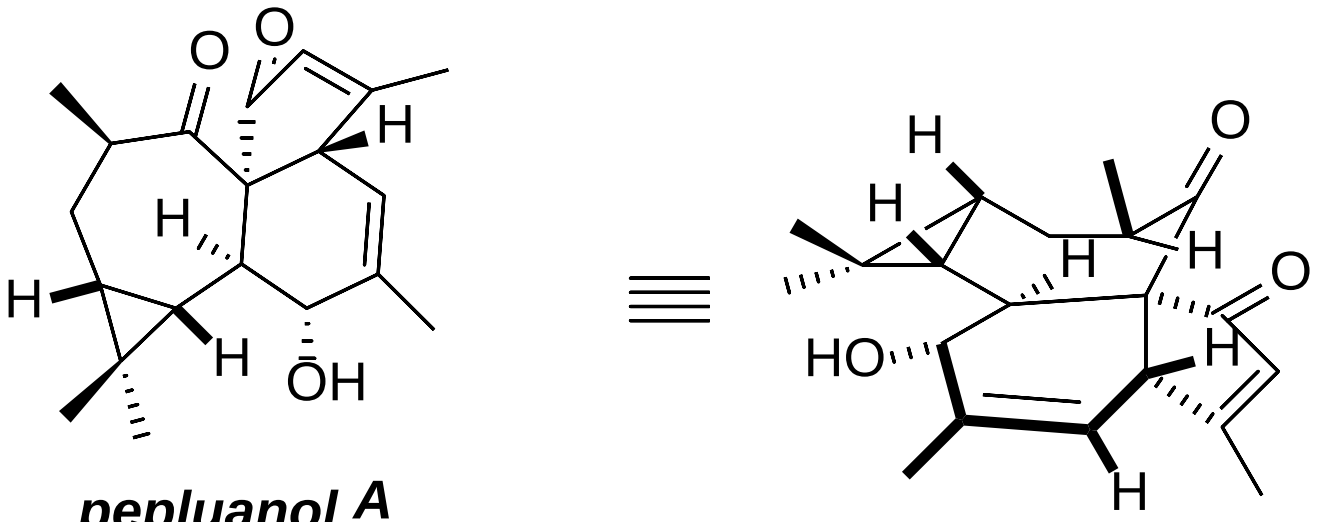
*JunXuan, Zhaobo Liu, An Zhu, Peirong Rao,Lei Yu,and Hanfeng Ding**

Isolation

E. peplus

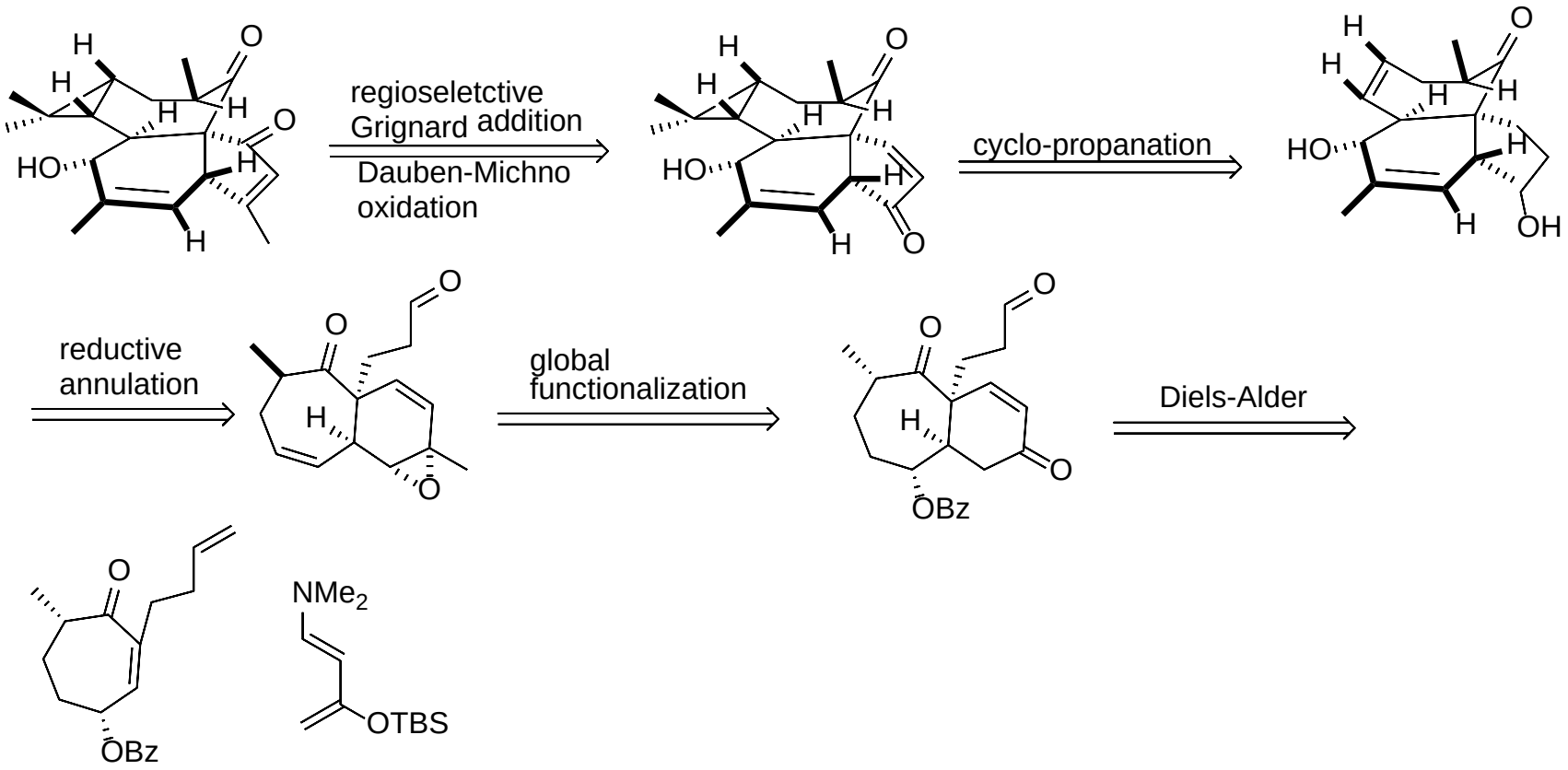
Structure



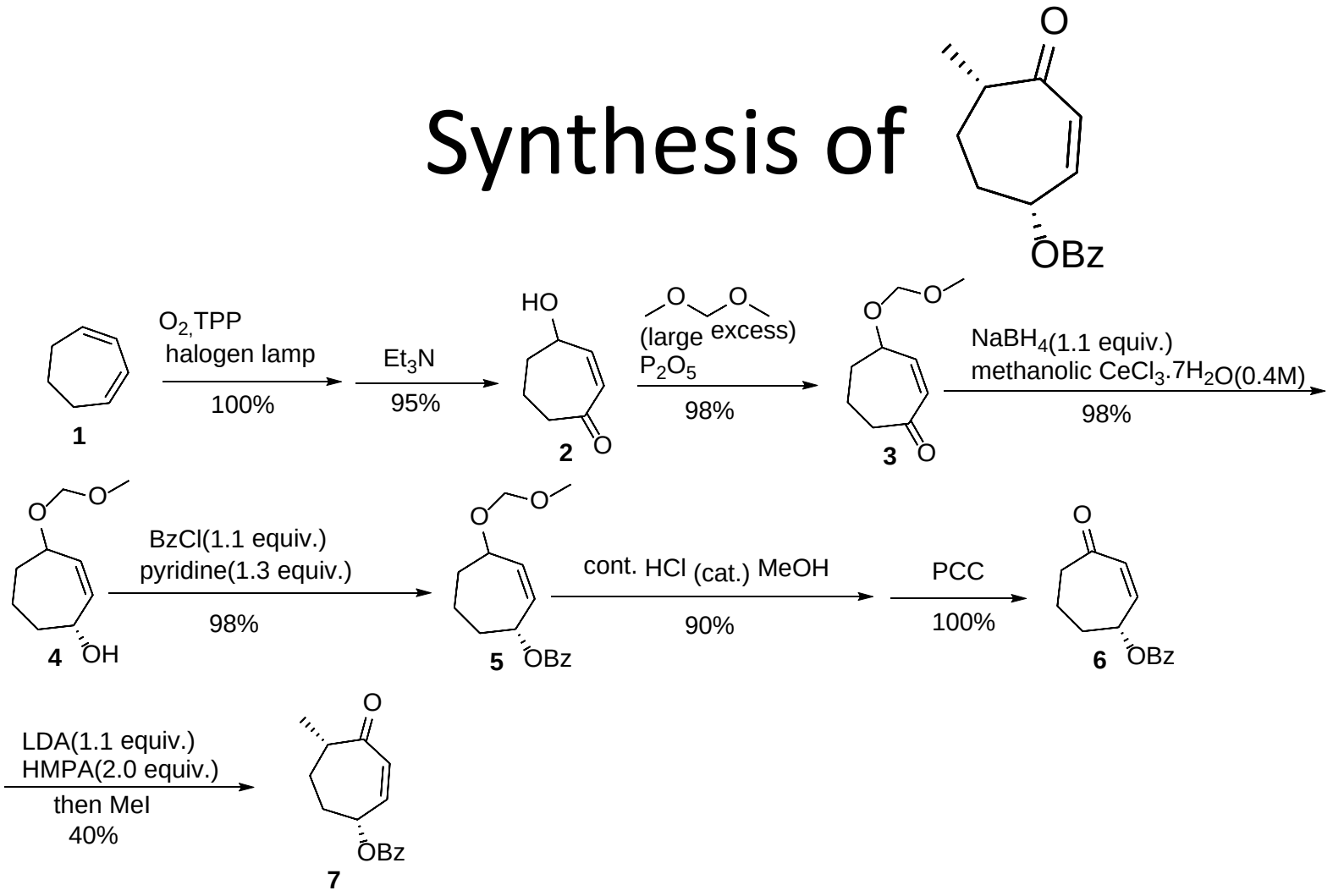
pepluanol A

- [3,4,6,7] tertracyclic ring

Retrosynthesis

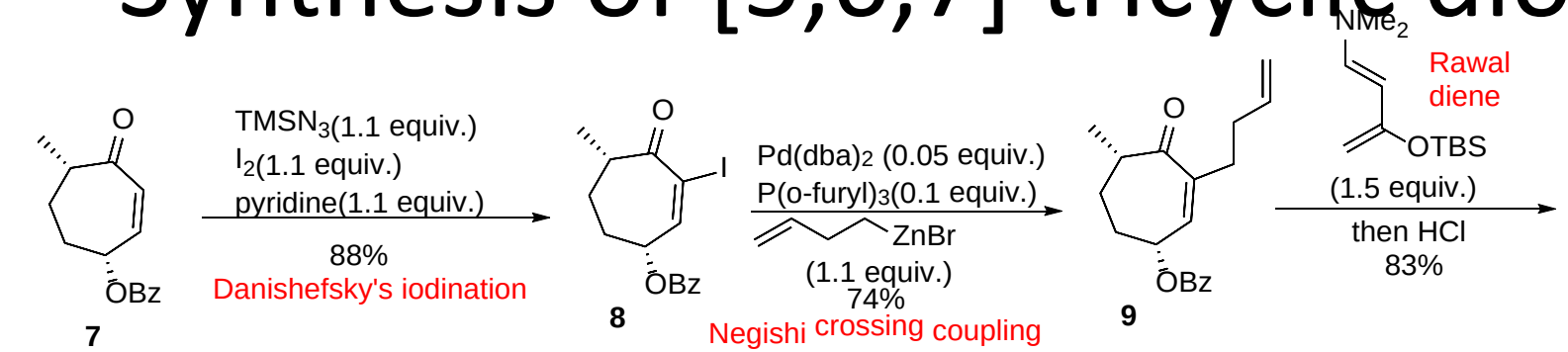


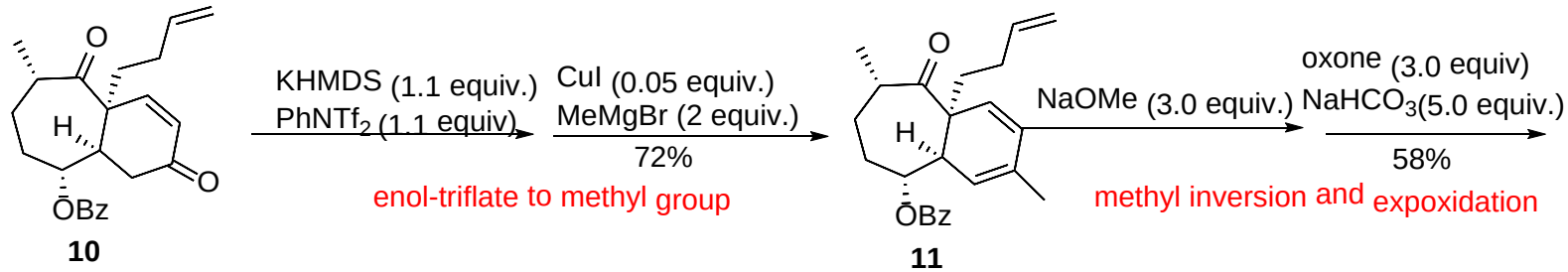
Synthesis of

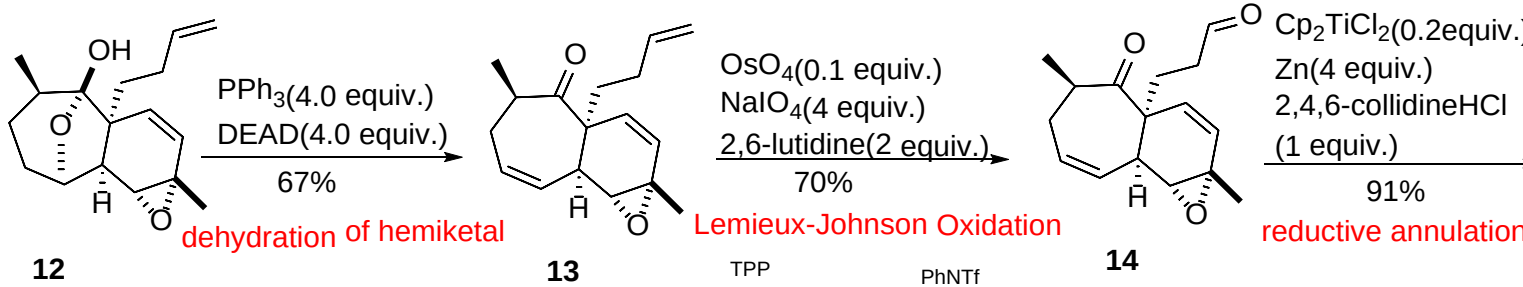


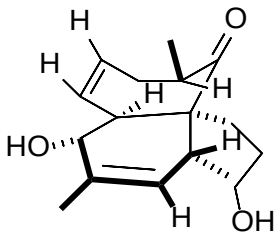
- A. J. Pearson; H. S. Bansal, *Tetrahedron Lett.* **1986**, *27*, 283.

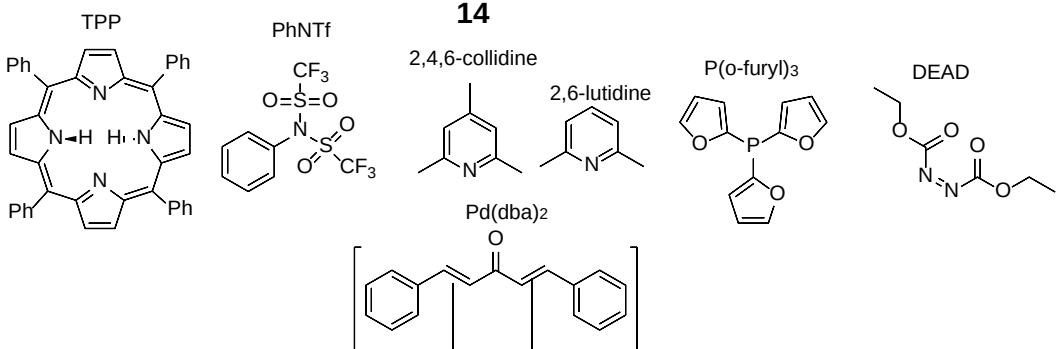
Synthesis of [5,6,7] tricyclic diol



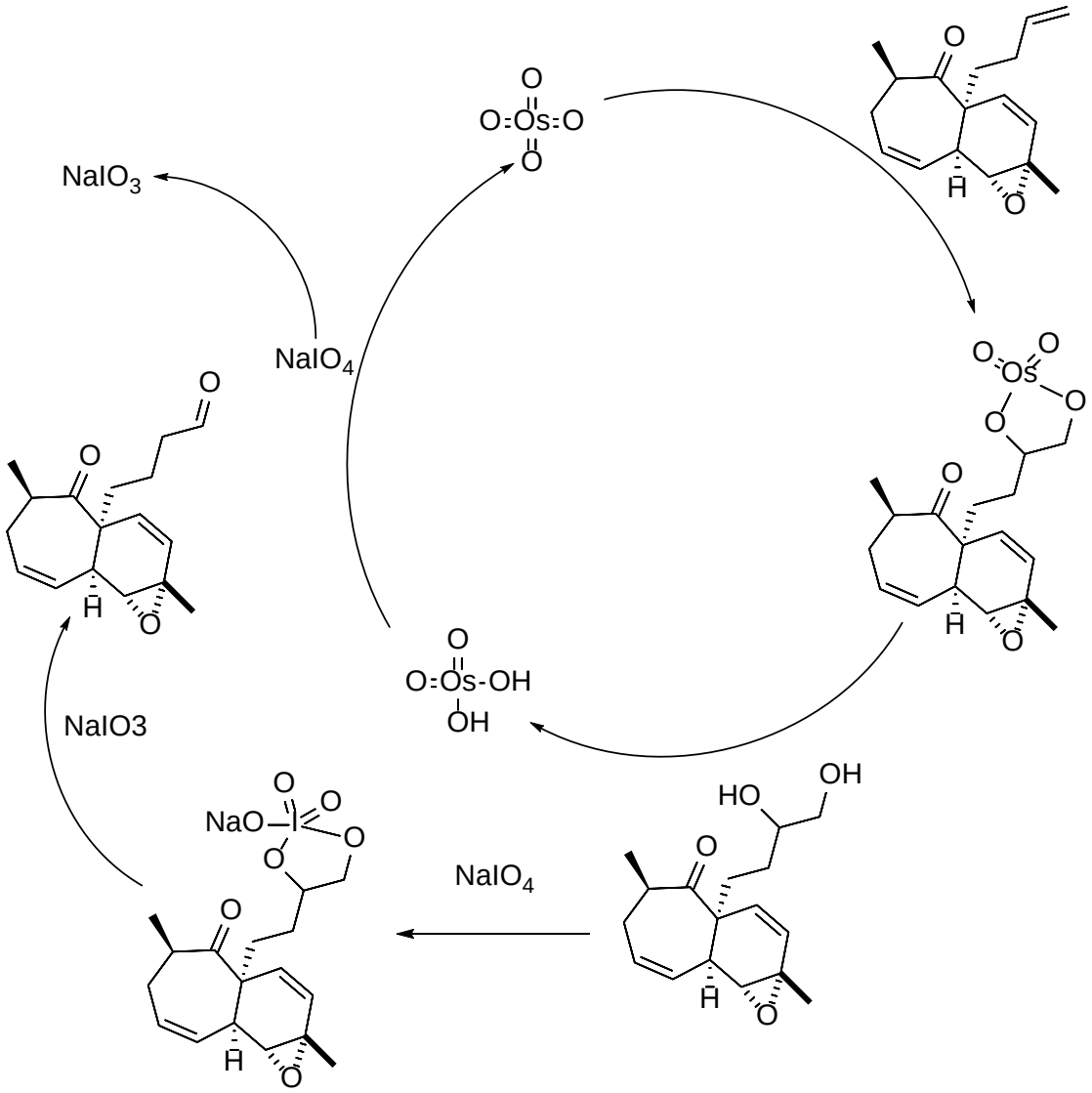








Lemieux-Johnson Oxidation



Optimization of reductive annulation

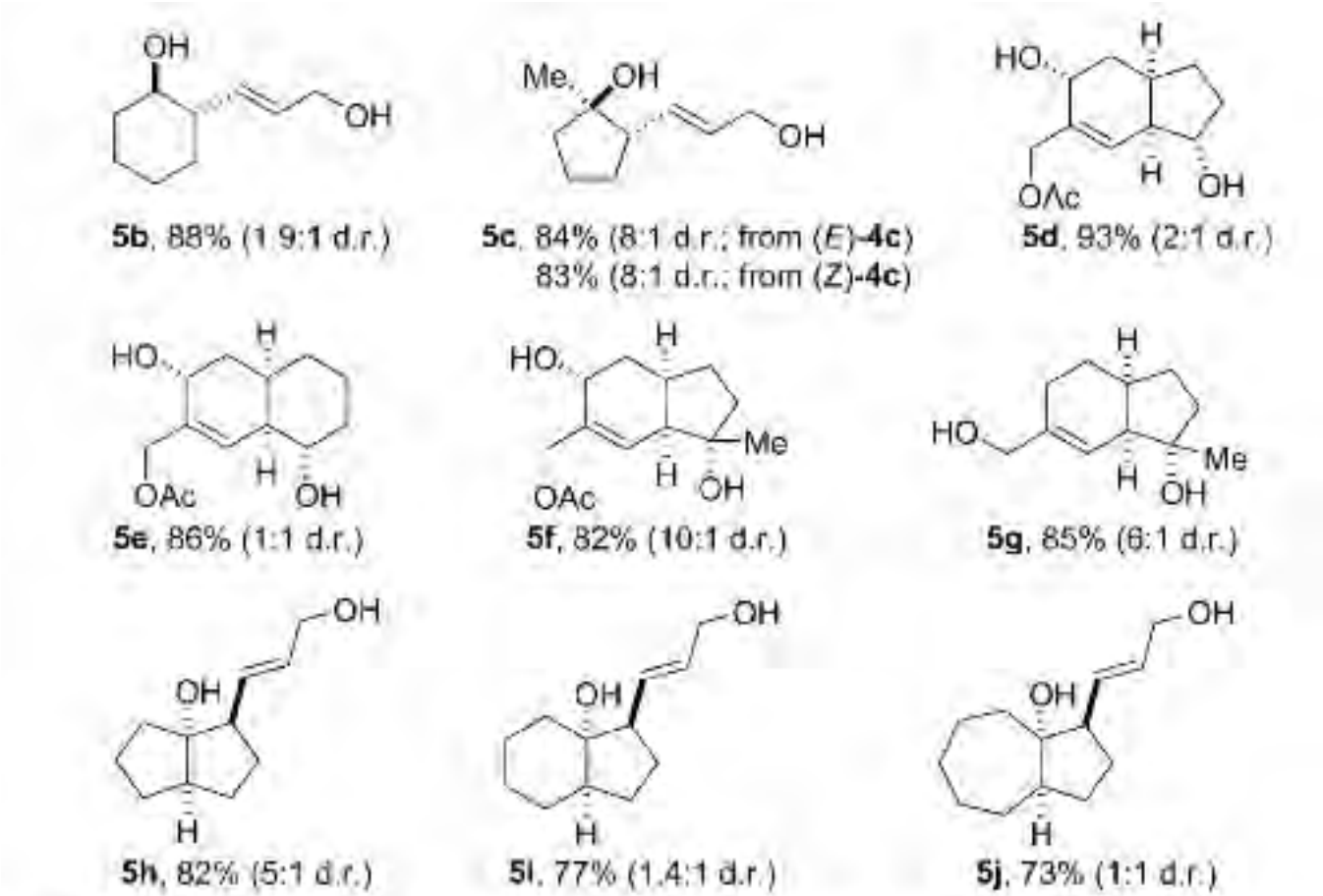
Table 1: Optimization on the reductive annulation of a vinyl epoxide-aldehyde.[a]

4a 5a

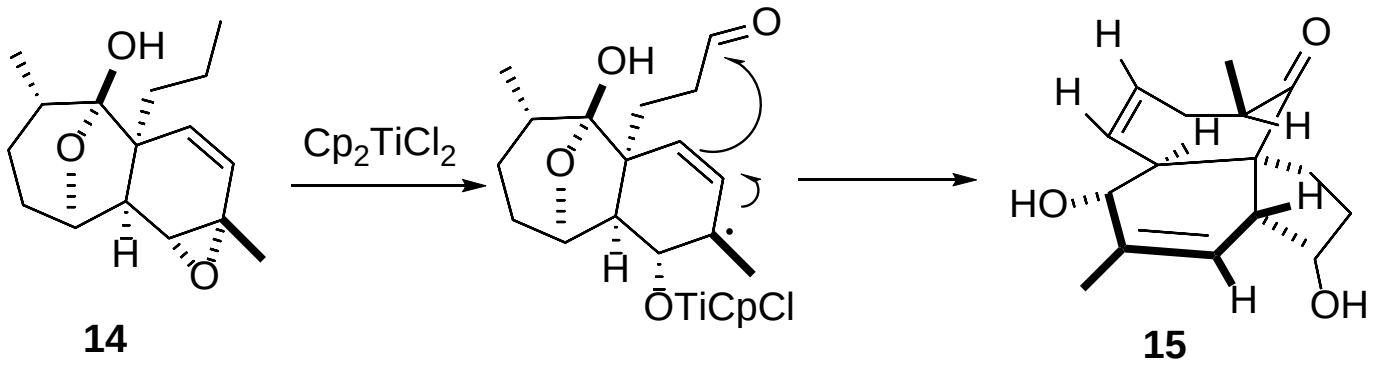
Entry	Reagent	Solvent	T [°C]	Yield [%][b] (d.r.)[c]
1	SmI_2/HMPA	THF	25	52 (> 20:1)
2	nBu_3SnH/AIBN	benzene	80	33 (1.3:1)
3	$nBu_3SnH/Et_3B/O_2$	toluene	25	< 5 (–)
4	$Pd(PPh_3)_4/SmI_2$	THF	−30	57 (1.2:1)
5	$CrCl_2$/LiI	THF	0	12 (1:2)
6	$SnCl_2$/TBAB	DMI	25	20 (1.5:1)
7	LiDBB	THF	0	78 (1.6:1)
8	Cp_2TiCl_2/Mn	THF	25	83 (1.5:1)
9	Cp_2TiCl_2/Zn	THF	25	88 (1.5:1)
10	Cp_2TiCl_2/Zn	THF	0	87 (1.5:1)
11	Cp_2TiCl_2/Zn/DIPA	THF	25	85 (1.5:1)
12	Cp_2TiCl_2/Zn/2,4,6-collidine·HCl	THF	25	95 (1.5:1)

Nice review of Cp_2TiCl_2 : *Org. Chem. Front.*, 2014, **1,** *15*

Optimization of reductive annulation

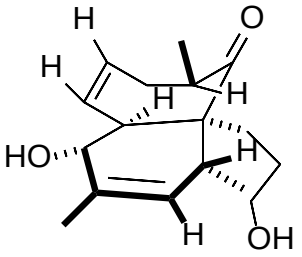


Scheme 1. Scope of the titanium(III)-catalyzed reductive annulation.



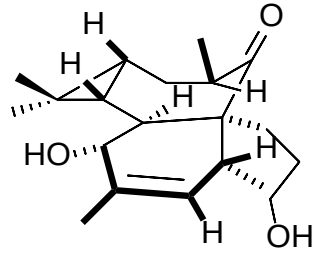
14 **15**

Final Modification

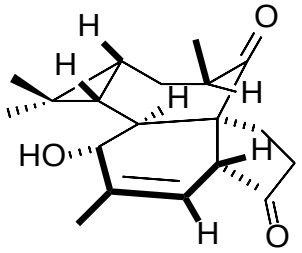


15

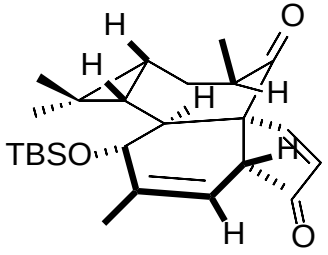
TEBAC (0.1 equiv.)
NaOH (aq., 50wt%)/$CHBr_3$
then
$Me_2Cu(SCN)Li_2$ (20 equiv)
HMPA (1.0 equiv.)
MeI (20 equiv.)
44%
cyclopropanation
bismethylation



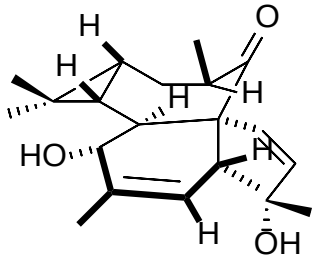
TEMPO (0.1 equiv.)
TBAC (1.0 equiv.)
NCS (2.0 equiv.)
$NaHCO_3$ (5.0 equiv.)
95%



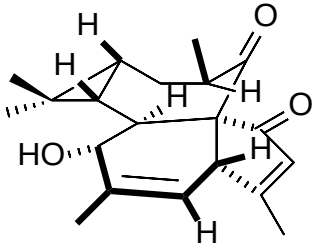
TMSOTf (4.0 equiv.)
Et_3N (10 equiv.)
then
$Pd(OAc)_2$ (2.0 euqiv.)
86%
Saegusa Oxidation



MeMgBr (2.0 equiv.)

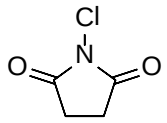


PCC (2.0 equiv)
NaOAc (2.0 equiv.)
SiO_2
then HCl (4.0 equiv.)
59%
Dauben-Michno Oxidation

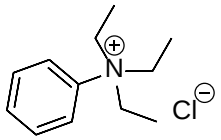


pepluanol A

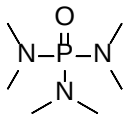
NCS



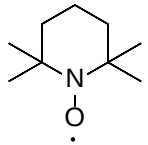
TEBAC



HMPA



TEMPO



Conclusion

- 22 steps
- Overall yield: 0.85%

- Thank you!