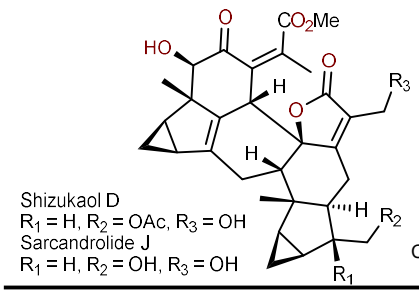
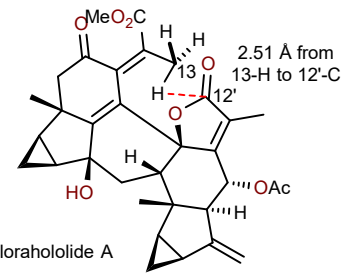
Shizukaol D (Liu, 2017)

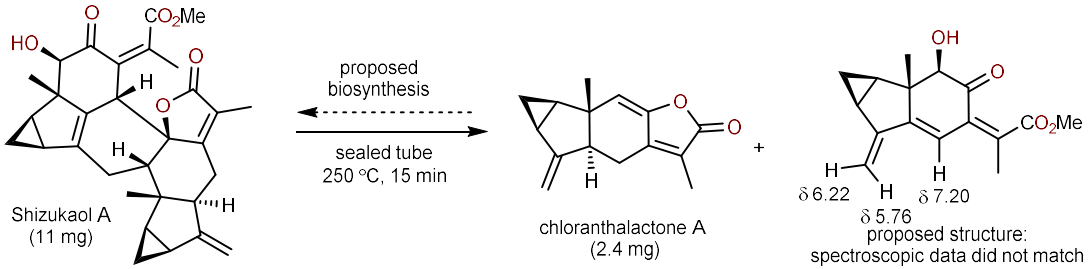




- The first member of lindenane sesquiterpenoid [4+2] dimer family, shizukaol A isolated in 1990
- Shizukaol D can activate AMP-activated protein kinase, increase ACC phosphorylation in HepG2 cells, and repress the growth of human liver cancer cells.
- Sarcandrolide J shares the same molecular architecture as shizukaol D, although they were isolated from *Sarcandra glabra* and *Chloranthus serratus*, respectively.
- The first total synthesis of lindenane sesquiterpenoid [4+2] dimers

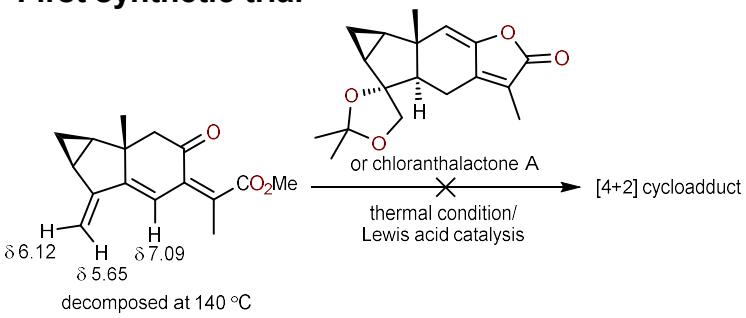
Liu, B. *Angew. Chem. Int. Ed.* **2017**, *56*, 637. https://doi.org/10.1002/anie.201610484

Pyrolysis of shizukaol A

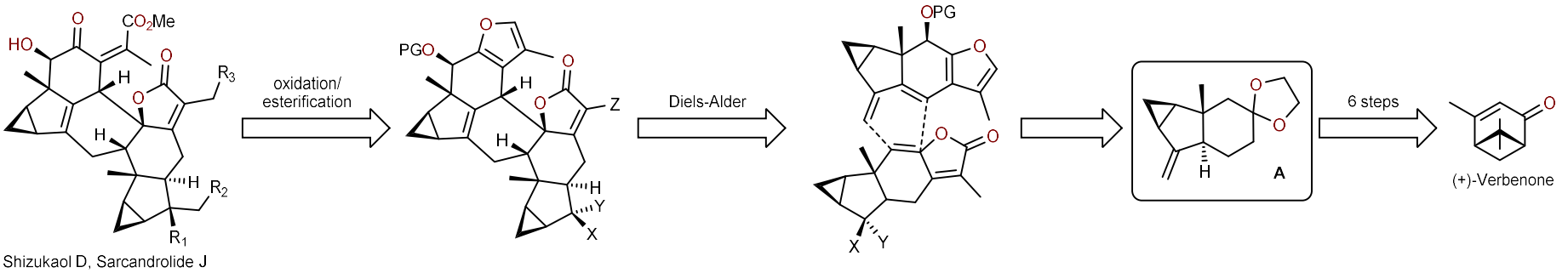


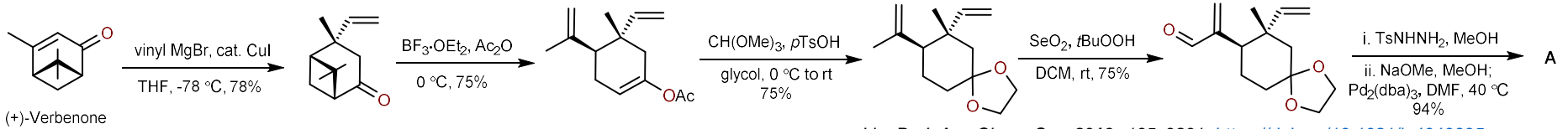
Kawabata, J. *Agric. Biol. Chem.* **1979**, *43*, 885. https://doi.org/10.1271/bbb1961.43.885

First synthetic trial



Retrosynthetic analysis

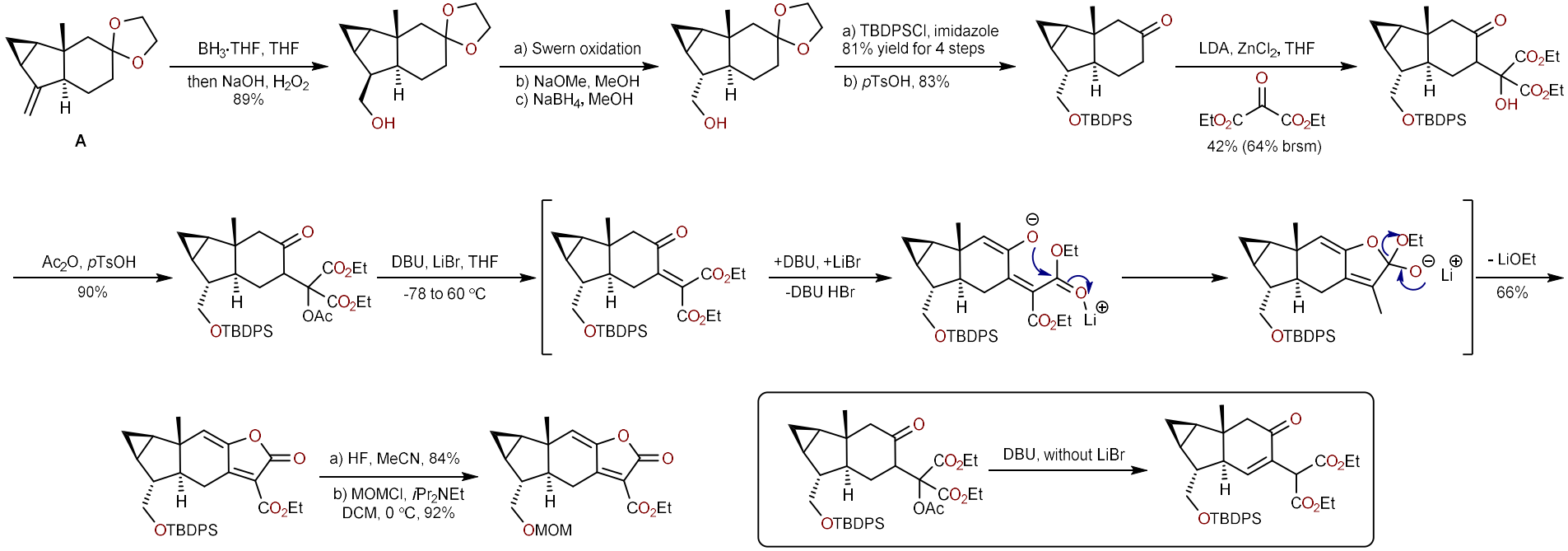




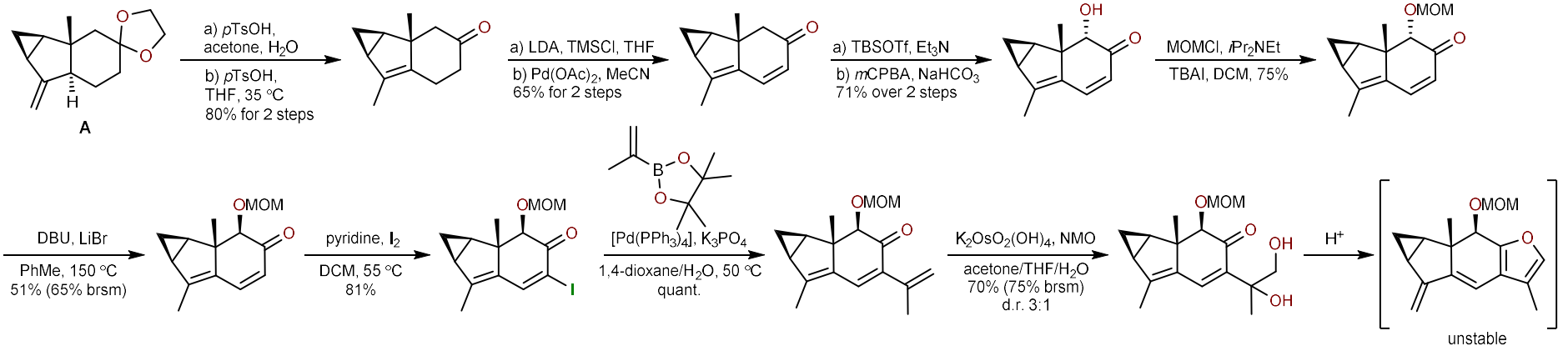
Liu, B. *J. Am. Chem. Soc.* **2013**, *135*, 9291. https://doi.org/10.1021/ja4040335

Shizukaol D (Liu, 2017)

Synthesis of the dienophile

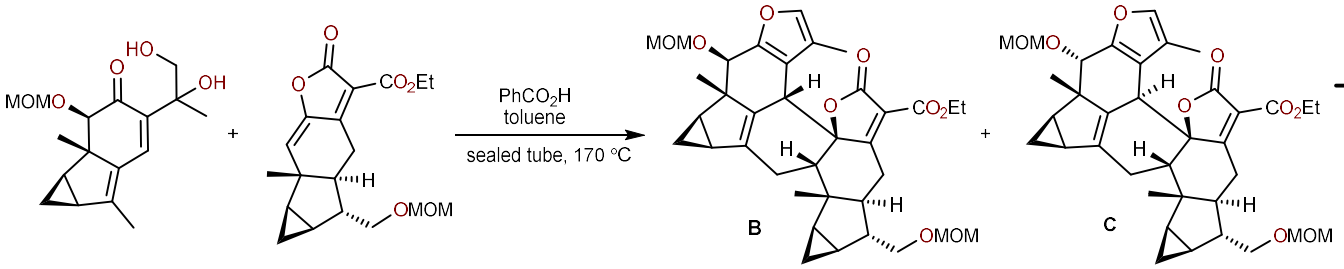


Synthesis of the diene surrogate



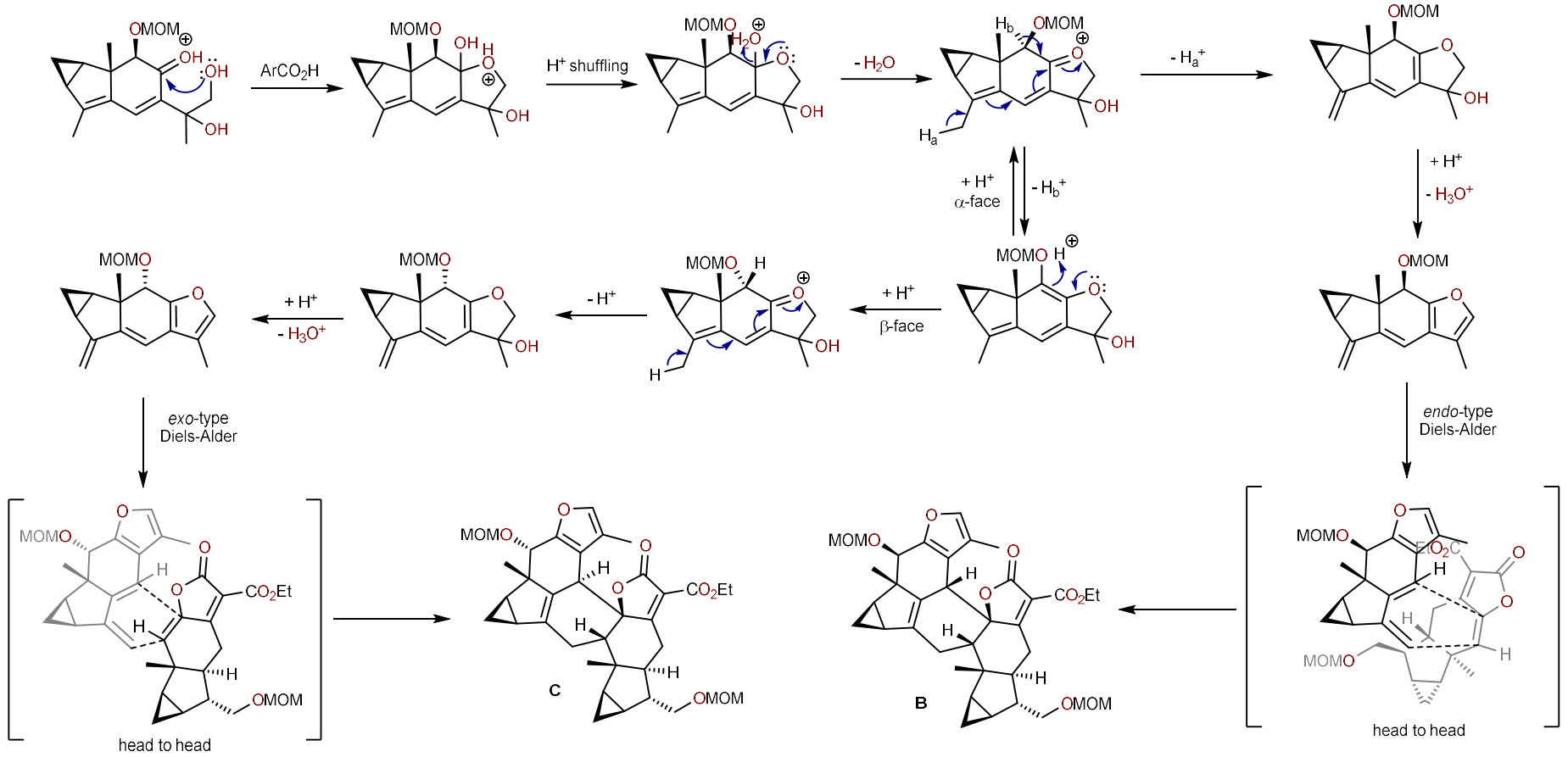
Shizukaol D (Liu, 2017)

Diels-Alder reaction



Diene surrogate	Dienophile	$PhCO_2H$	t [h]	Yield [%] B	C
1 equiv	2.5 equiv	5 equiv	6	trace	-
3.8 equiv	1 equiv	10 equiv	3	51	9
5 equiv	1 equiv	10 equiv	3	83	14

Mechanistic rationale



Shizukaol D (Liu, 2017)

End-game