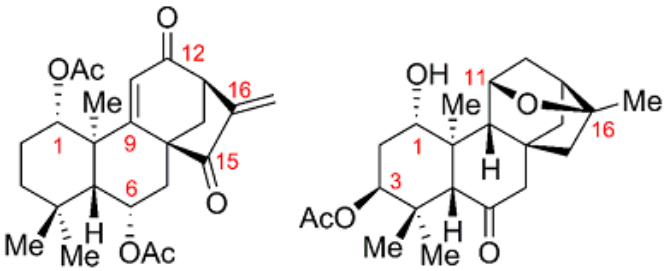
Convergent Route to ent-Kaurane Diterpenoids: Total Synthesis of Lungshengenin D and 1α,6α-Diacetoxy-ent-kaura-9(11),16-dien-12,15-dione

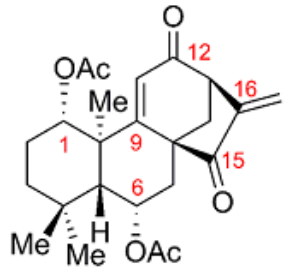


1α,6α-diacetoxy-*ent*-kaura-9(11),16-dien-12,15-dione (**2**)

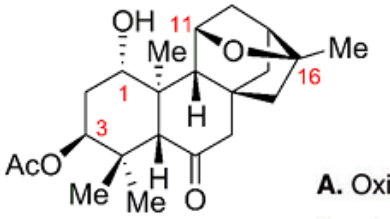
Lungshengenin D (**3**)

—Xiangbo Zhao,Wu Li,Junjie Wang,and Dawei Ma. *J.Am.Chem.Soc.***2017**

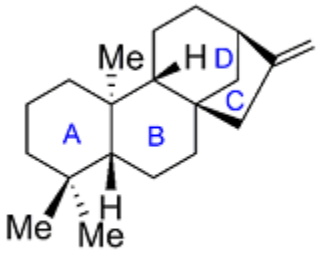
ent-Kaurane Diterpenoids



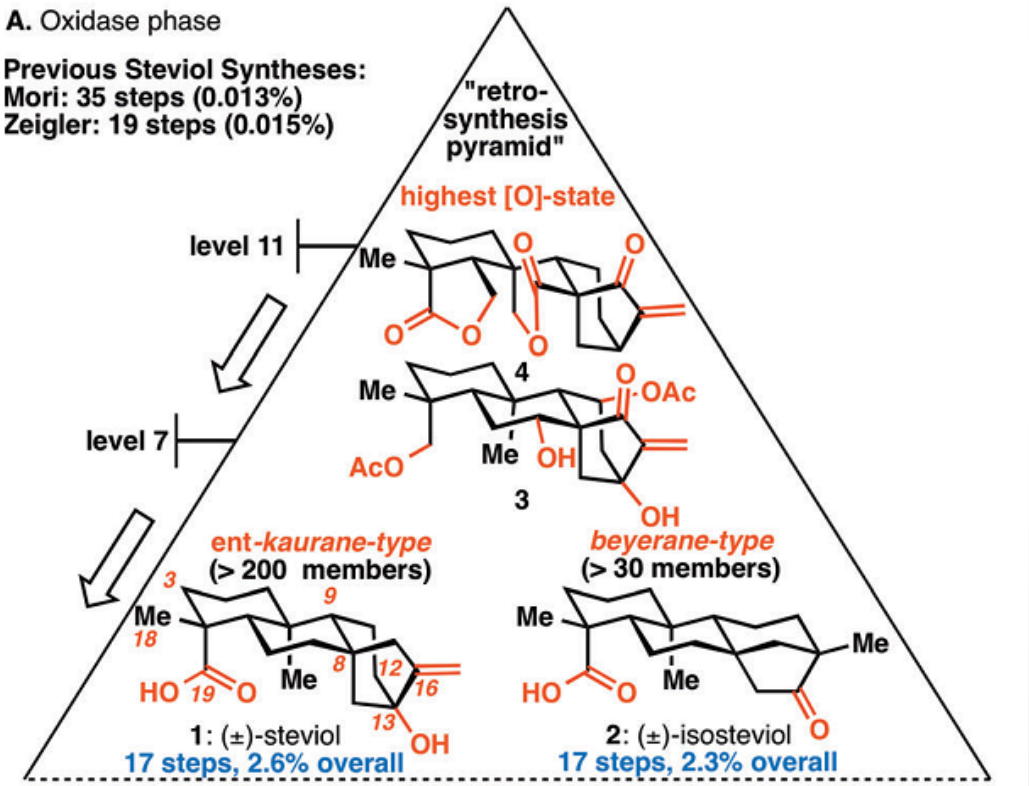
1α,6α-diacetoxy-*ent*-kaura-9(11),16-dien-12,15-dione (**2**)



Lungshengenin D

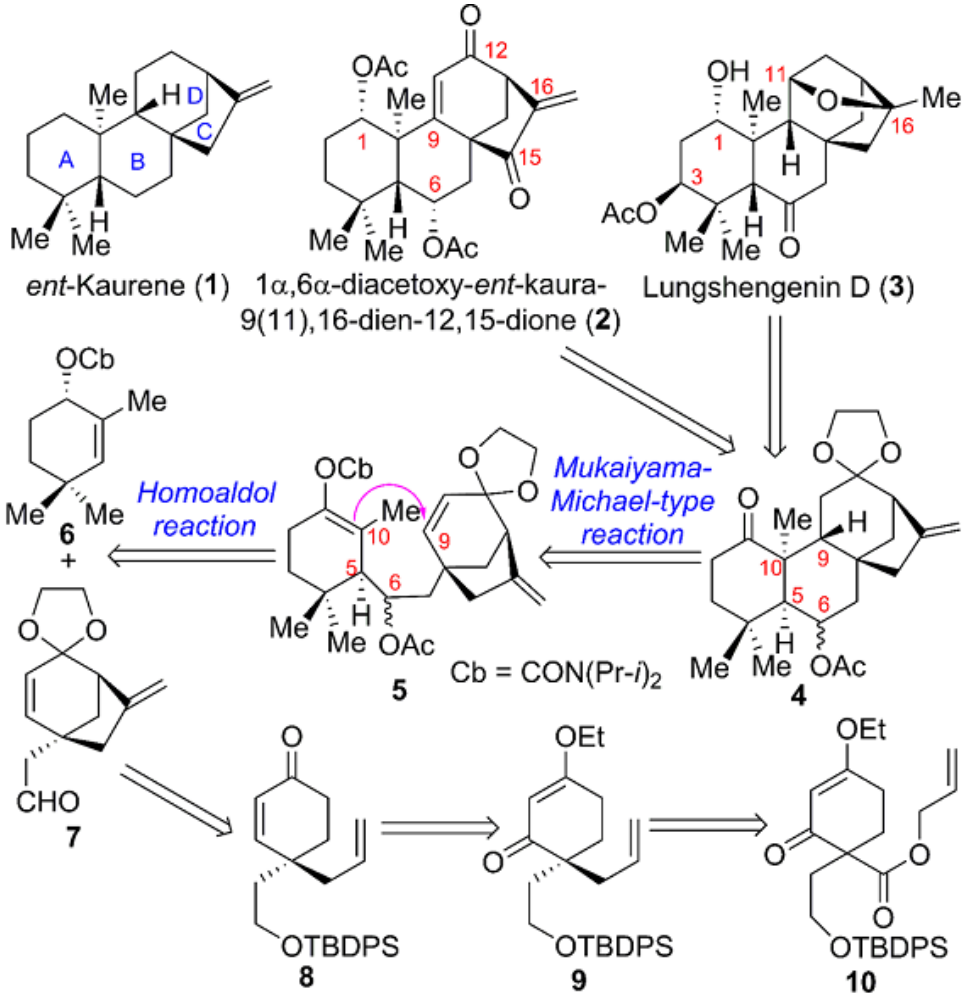


ent-Kaurene (**1**)



—Emily C. Cherney, Jason C. Green, and Phil S. Baran
Angew. Chem. Int. Ed. **2013**, 52, 9019 –9022

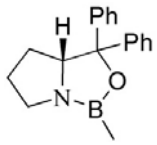
Retrosynthetic Analysis



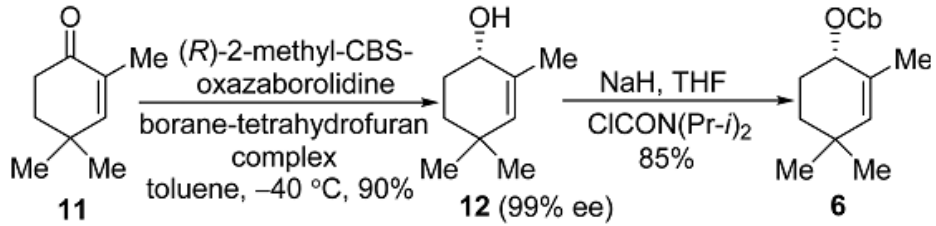
Feature

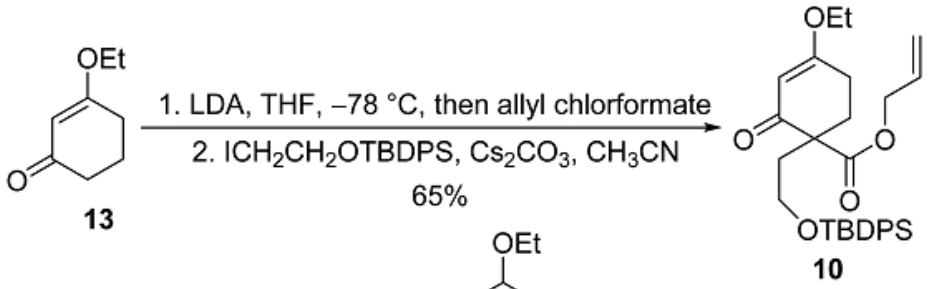
1. Mukaiyama–Michael-type reaction
2. Hoppe's homoaldol reaction
3. Toyota's Pd-catalyzed cycloalkenylation
4. Stoltz's Pd-catalyzed asymmetric allylic alkylation reaction

Synthesis of Building Blocks 6 and 7

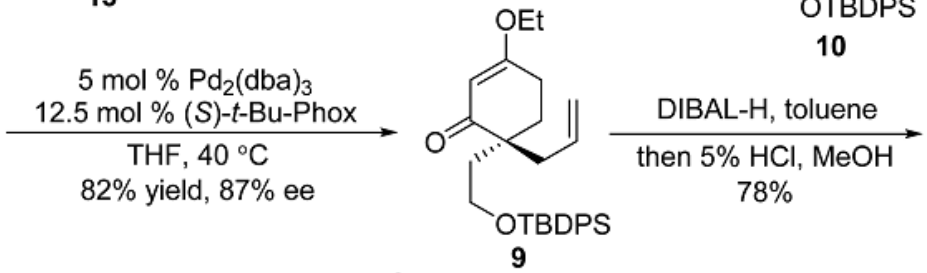


Typical Corey–Bakshi–Shibata's conditions

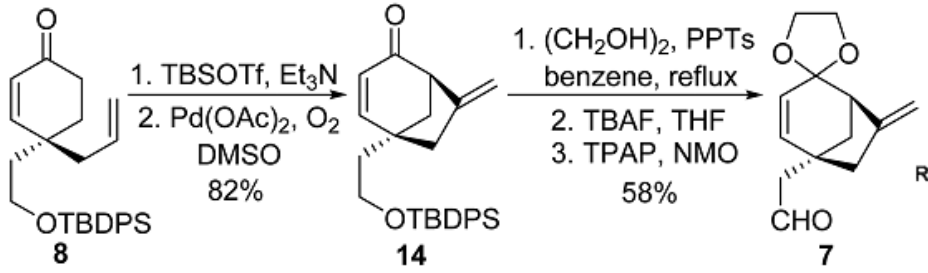




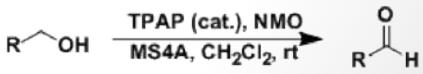
Stoltz's Pd-catalyzed asymmetric allylic alkylation reaction



Toyota's Pd-catalyzed cycloalkenylation

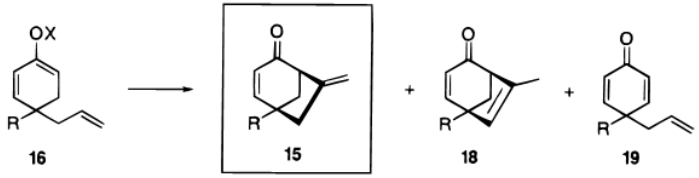


Ley-Griffith Oxidation



Toyota's Pd-catalyzed cycloalkenylation

Table 1. Pd-Catalyzed Cycloalkenylation Reaction of Cross-Conjugated Silyl Enol Ethers (**16**)[a]



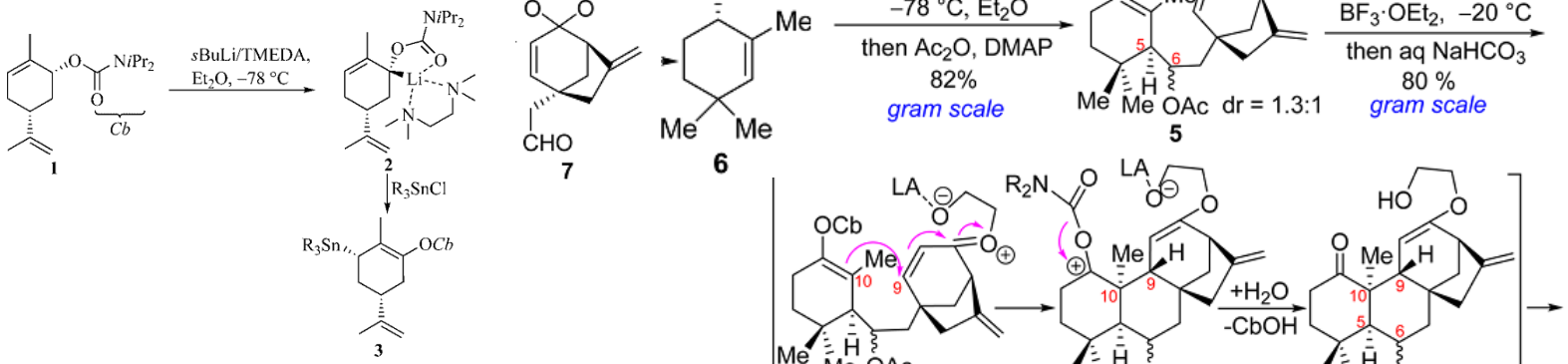
a: X = TMS, b: X = TES, c: X = TBDMS
R = $-CH_2CH_2OMOM$

					yield (%)			
run	X	$Pd(OAc)_2$ (mol %)	solvent (mol/L)	time (h)	**15**	**18**	**19**	**16**
1	TMS	10	DMSO (0.05)	17	62	trace	21	
2	TES	10	DMSO (0.05)	11	76	trace	14	
3	TBDMS	10	DMSO (0.05)	19	81	4	5	
4	TBDMS	5	DMSO (0.05)	4	82	3	3	
5	TBDMS	3	DMSO (0.05)	22	81	5	trace	
6	TBDMS	1	DMSO (0.05)	26	18	trace	trace	64
7	TBDMS	10	DMSO (0.1)	5	89	2	3	
8	TBDMS	10	DMSO (0.3)	15	78	3	5	
9	TBDMS	10	DMSO−H_2O[b] (0.05)	4.5	63	trace	trace	
10	TBDMS	10	MeCN (0.05)	13	37	trace	trace	57

[a] All reactions were carried out at 45 °C under O_2 (1 atm). [b] DMSO:H_2O (10:1 v/v).

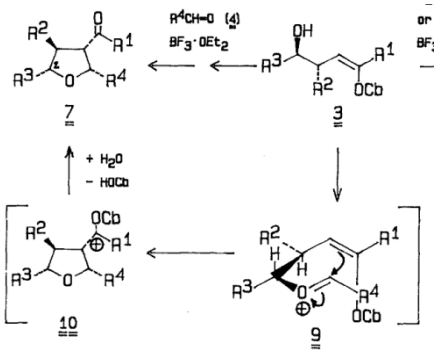
Homoaldol Reaction of 6 and 7 and Subsequent Cyclization

Hoppe's homoaldol reaction



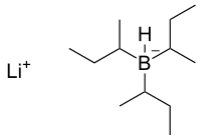
Becker, J.; Grimme, S.; Fröhlich, R.;
Hoppe, D. Angew. Chem., Int. Ed. ***2007***, 46, 1645

Mukaiyama–Michael-type reaction

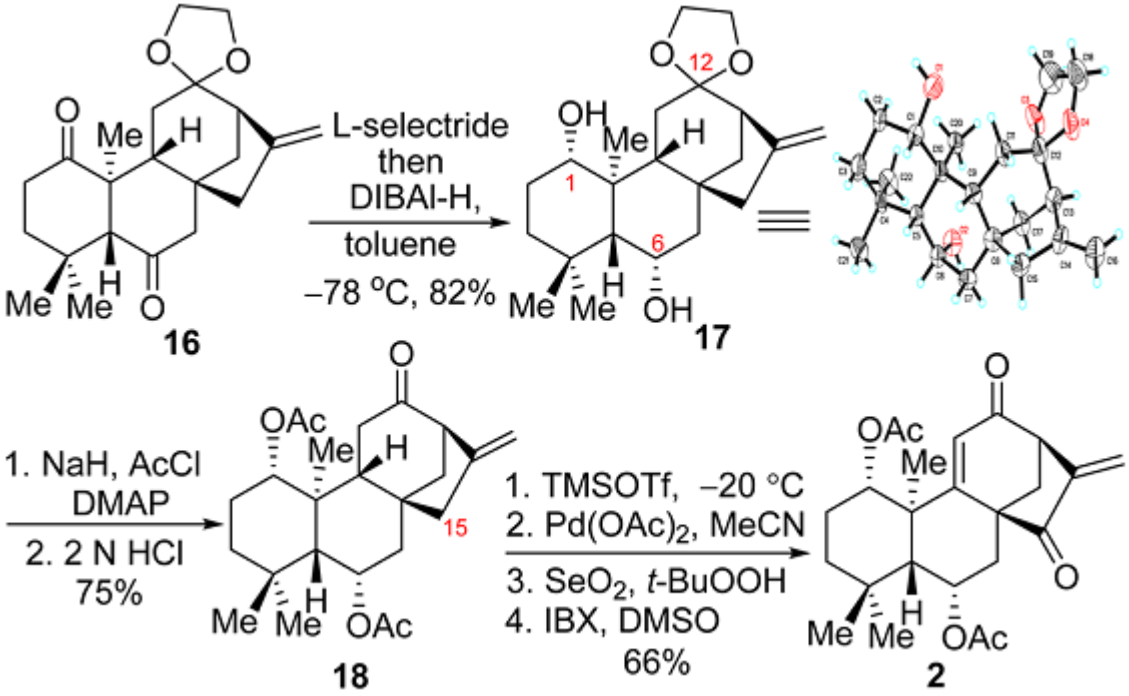


Hoppe, D.; Kramer, T.; Freire Erdbru¨gger, C.; Egert, E.
Tetrahedron Lett. ***1989***, 30, 1233.

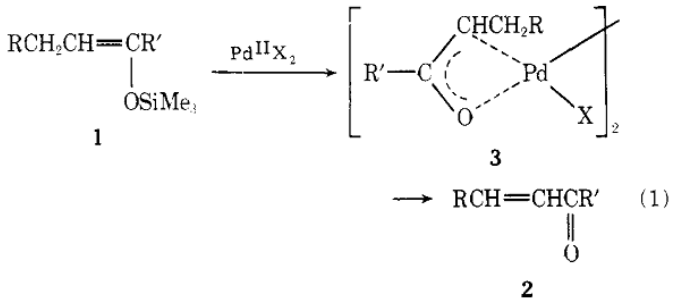
Total Synthesis of ent-Kaurane Diterpenoid 2



L-selectride



Saegusa's procedure



Total Synthesis of Lungshengenin D