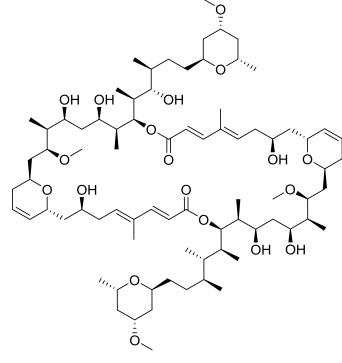
## Total Synthesis of Swinholide A: An Exposition in Hydrogen-Mediated C-C Bond Formation

Inji Shin, Suckchang Hong, and Michael J. Krische *J. Am. Chem. Soc.*, **2016**, *138*, 14246. DOI: 10.1021/jacs.6b10645

- Swinholide A, first isolated from the Okinawan marine sponge *Theonella swinhoei* in 1985, dimerizes actin (Kd ≈ 50 nM).
- Its ability to disrupt the actin cytoskeletal constructs confers cytotoxicity in the ng/mL range against diverse tumor cell lines, making it the most potent member of its class.
- Swinholide A contains a symmetric 44-membered macrodiolide ring.



Swinholide A





## **Previous Work**

## **Retro-synthetic Analysis**

$$[Ir(COD)CI]_2$$

$$CI$$

$$COOH$$

$$(s)-BINAP$$

$$OPMB$$

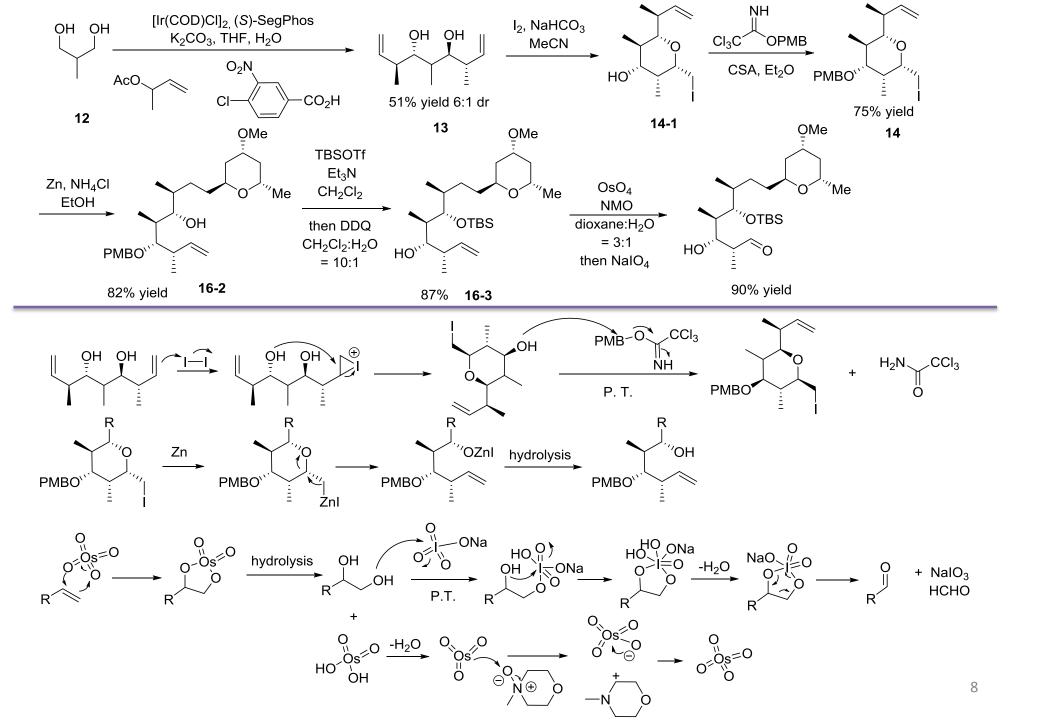
$$OP$$

OPMB TMS
OPMB 
$$I_2$$
OPMB  $K_2OsO_4H_2O$ 
 $K_3Fe(CN)_6$ 
 $K_2CO_3$ 
 $t_BuOH H_2O$ 
then NalO<sub>4</sub>  $60\%$  yield

TMS
OPMB  $K_2CO_3$ 
 $t_BuOH H_2O$ 
 $t_B$ 

Krische, M. J.Org. Lett. 2015, 17, 4686.

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Longest Linear Step: 15