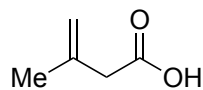


# Total Synthesis of (+)-Hapeforin G

Wei Zhang, Zhenyu Zhang, Jun-Chen Tang, Jin-Teng Che, Hao-Yu Zhang, Jia-Hua Chen and Zhen Yang

JACS 2020, 142, 19487-19492



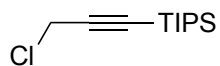
1-9



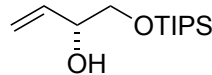
10-16



- 1) n-BuLi, **1**, -78 °C then HMPA, **2**
- 2) DCC, DMAP, **3**
- 3) Grubbs II (7% mol)
- 4) CeCl<sub>3</sub> (10 eq.), CH<sub>3</sub>MgBr (10 eq.)
- 5) TBAF
- 6) TBSCl (1.05 eq.), imidazole
- 7) KHMDS, TMSCl
- 8) TPAP, NMO
- 9) PPH<sub>3</sub>=CH<sub>2</sub>



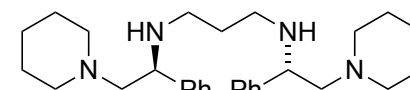
**2**



**3**

- 10) Co<sub>2</sub>(CO)<sub>8</sub> (0.2 eq.), CO, 120 °C
- 11) TBAF
- 12) NaOH, H<sub>2</sub>O<sub>2</sub>
- 13) TPAP, NMO
- 14) KHMDS, 18-crown-6, CH<sub>3</sub>I, -78 °C
- 15) KHMDS, PhSeBr, -78 to -40 °C
- 16) NaHCO<sub>3</sub>, H<sub>2</sub>O<sub>2</sub>

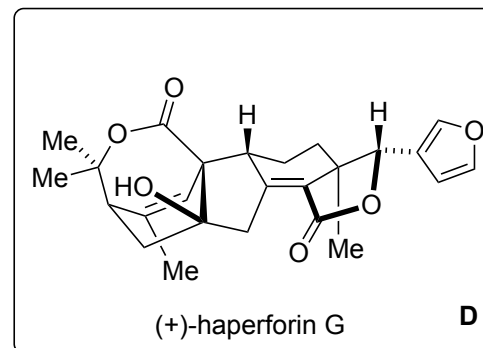
- 1) Rationalize the stereoselectivity of this reaction.  
*Hint: the new stereocenter has R absolute configuration.*

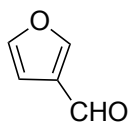


**1**

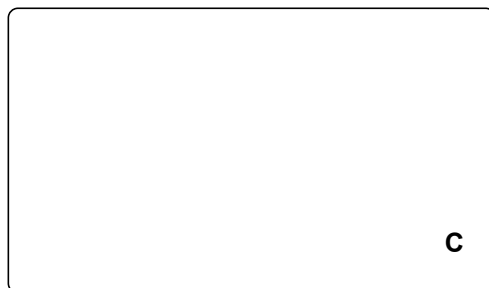
- 3) Grubbs II structure?  
7) *Hint: Only one functional group is protected.*

- 10) Name of reaction?
- 11) *Hint: Global deprotection*
- 12) Name of reaction?

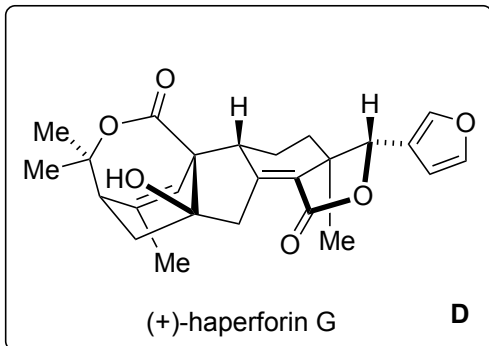




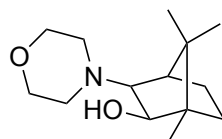
17-20



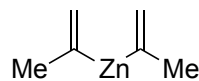
21-23



- 17) **4** (10% mol), Et<sub>2</sub>Zn (3 eq.), **5** (1 eq.), -30 °C  
 18) NIS, *tert*-butyl vinyl ether, -30 °C  
 19) Pd(OAc)<sub>2</sub> (10% mol), DPPF (30% mol), 130 °C  
 20) H<sub>2</sub>CrO<sub>4</sub>



**4**



**5**

- 21) [Ir(ppy)<sub>2</sub>(dtbbpy)]PF<sub>6</sub> (2.5% mol), DIPEA, Hantzsch ester, Blue LED  
 22) *t*BuOK, -78 °C  
 23) SOCl<sub>2</sub>, pyridine  
 24) DBU, 50 °C

17) How would you make ligand **4**?

*Hint: the new stereocenter has R absolute configuration.*

18) *Hint: the product is an inconsequential mixture of diastereomers*

19) Propose mechanism for this reaction.

*Hint: The iodine is transferred in this reaction.*

20) Name of reagent?

21) Propose a mechanism for this step.