Total Synthesis of (+)-Haperforin G

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

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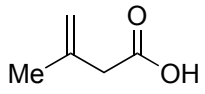


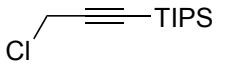
1-9

A

10-16

B

1) *n*-BuLi, **1**, −78 °C *then* HMPA, **2**
2) DCC, DMAP, **3**
3) Grubbs II (7% mol)
4) $CeCl_3$ (10 eq.), CH_3MgBr (10 eq.)
5) TBAF
6) TBSCl (1.05 eq.), imidazole
7) KHMDS, TMSCl
8) TPAP, NMO
9) $PPH_3{=}CH_2$



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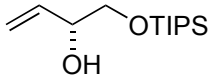
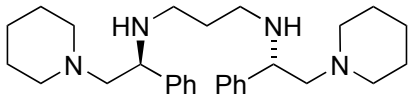


3

10) $Co_2(CO)_8$ (0.2 eq.), CO, 120 ℃
11) TBAF
12) NaOH, H_2O_2
13) TPAP, NMO
14) KHMDS, 18-crown-6, CH_3I, −78 °C
15) KHMDS, PhSeBr, −78 to −40 °C
16) $NaHCO_3$, H_2O_2

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



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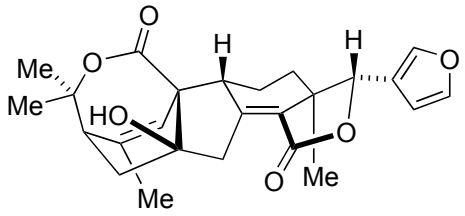
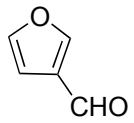
3) Grubbs II structure?
7) *Hint: Only one functional group is protected*.

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



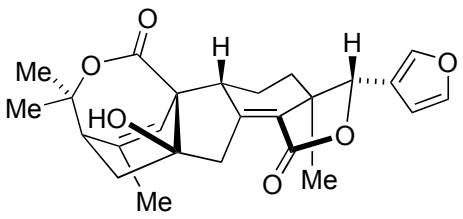
(+)-haperforin G **D**



17-20

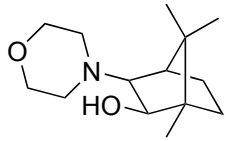
C

21-23



(+)-haperforin G **D**

17) **4** (10% mol), Et_2Zn (3 eq.), **5** (1 eq.), −30 °C
18) NIS, *tert*-butyl vinyl ether, −30 °C
19) $Pd(OAc)_2$ (10% mol), DPPF (30% mol), 130 °C
20) H_2CrO_4



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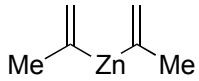

5

21) $[Ir(ppy)_2(dtbbpy)]PF_6$ (2.5% mol), DIPEA, Hantzsch ester, Blue LED
22) *t*-BuOK, −78 °C
23) $SOCl_2$, 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.