# Total Synthesis of (-)-Huperzine Q

(+)-Lycopladine B and C

$$MeO_2C$$
 $NBoc$ 
 $MeO_2C$ 
 $MeO_2C$ 

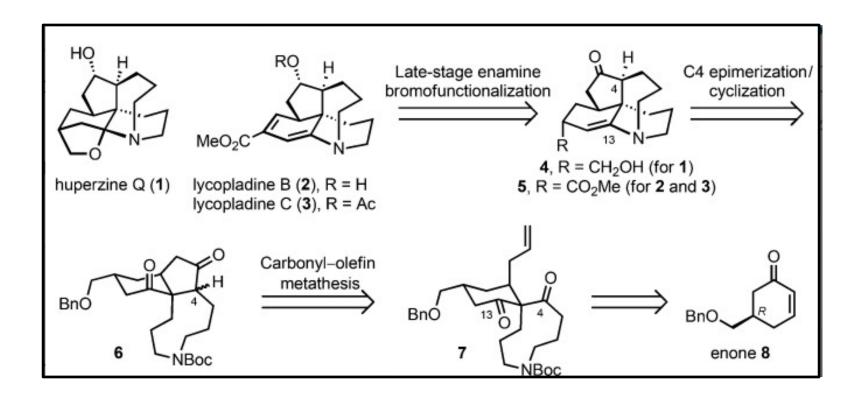
Niloofar Safaie CEM 852

Angew. Chem. Int. Ed. 2015, 54, 1011-1015.

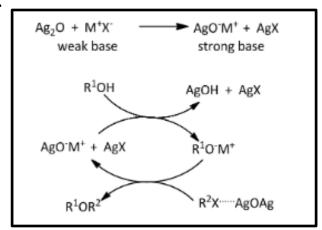
## Background

- Huperzine Q isolated by Zhu in 2002 and has unique aminal moiety and six steriogenic centers.
- It was synthesized by Takayoma in 19-steps.
- Lycopladine isolated by Kobayashi in 2006, however, no synthetic method has been reported.

# Retrosynthesis



Silver oxide increases basicity:



Tetrahedron: Asymmetry, 2009, 610-615.

#### Dess-Martin oxidation:

#### Ethylene has two important roles:

- 1) Converting bulky catalyst to more reactive species.
- 2) Avoiding side products reactions.

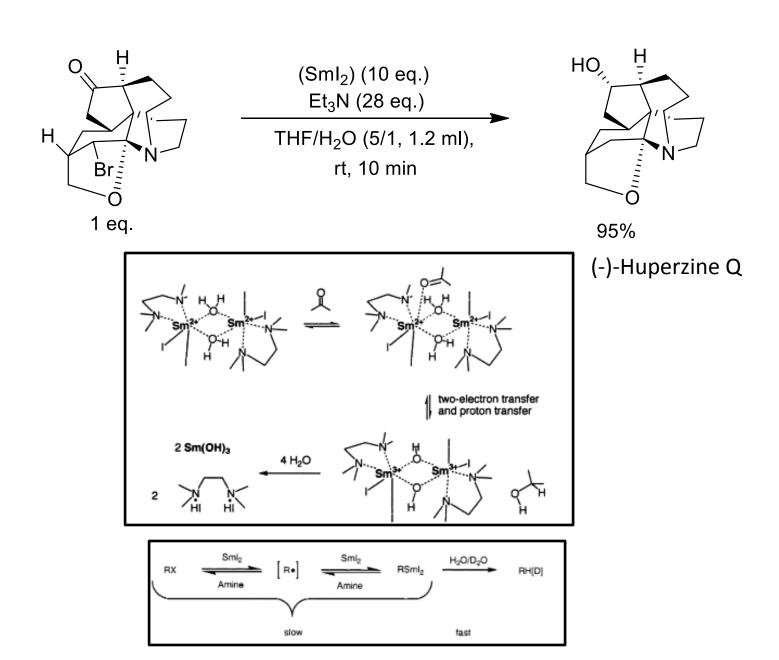
$$\begin{array}{c} \text{BH}_{3}\text{Me}_{2}\text{S (10 eq.)} \\ \text{Et}_{2}\text{O(5ml)} \\ \text{Then, NMO (10 eq.)} \\ \text{BnO} \\ \end{array}$$

NMO

$$\left[\begin{array}{c} O & O \\ O & O \\ O & O \end{array}\right] \oplus$$

TPAP (Lay-Griffith reagent)

#### Alkene halofunctionalization



Tetrahedron Lett. 2002, 43, 7197

J. Org. Chem. 2003, 68, 4870.

## Second molecule:

$$\frac{\text{CeCl}_3.7\text{H}_2\text{O (1 eq.), NaBH}_4 \text{ (leq.)}}{\text{MeO}_2\text{C}}$$

$$\frac{\text{MeO}_2\text{C}}{\text{1 eq.}}$$

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#### Luche reduction:

## (+)-Lycopladine B

$$\begin{array}{c} H \\ H \\ B \\ H \end{array} + n R - OH \\ \hline \begin{array}{c} Ioss \ of \\ n \ H - H \\ \hline \end{array} \\ \hline \begin{array}{c} Ioss \ of \\ n \ H - H \\ \hline \end{array} \\ \hline \begin{array}{c} Ioss \ of \\ n \ H - H \\ \hline \end{array} \\ \hline \begin{array}{c} Ioss \ of \\ n \ H - H \\ \hline \end{array} \\ \hline \begin{array}{c} Ioss \ of \\ Ios \$$

$$\begin{array}{c} \text{HO} \quad \overset{\text{H}}{\longrightarrow} \\ \text{MeO}_2\text{C} \\ \text{1 eq.} \end{array} \qquad \begin{array}{c} \text{Ac}_2\text{O (10 eq.) DMAP (0.5 eq)} \\ \text{pyridine (1 ml), rt, 7 h} \\ \text{MeO}_2\text{C} \\ \end{array} \qquad \begin{array}{c} \text{Ac}_2\text{O} \\ \text{N} \\ \text{DMAP} \end{array}$$

(+)-Lycopladine C