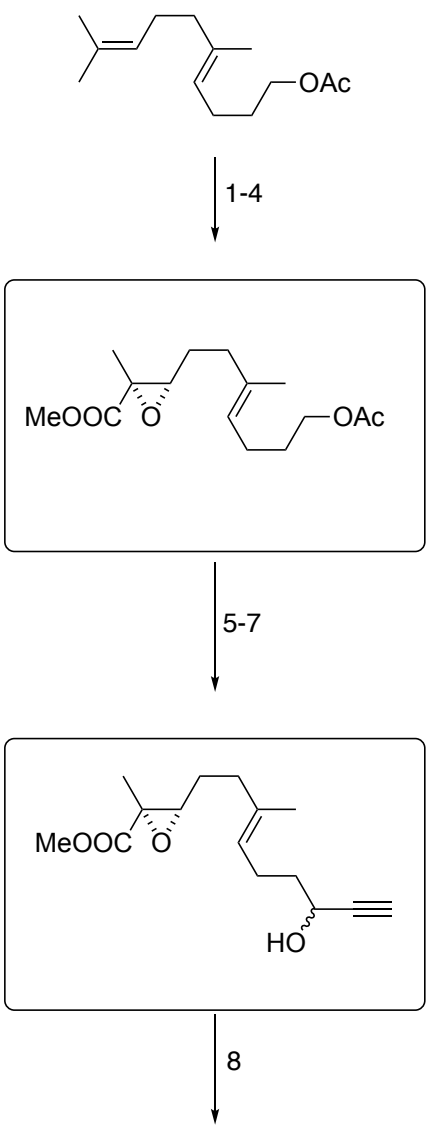
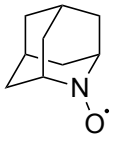
Bioinspired Total Synthesis of Sespenine

Yu Sun, Pengxi Chen, Deliang Zhang, Martin Baunach, Christian Hertweck, Ang Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 9012-9016.



1) *t*-BuOOH, SeO_2
2) $Ti(O\textit{i}\text{-}Pr)_4$, (+)-DET, *t*-BuOOH, -40°C
3) AZADO, $PhI(OAc)_2$, H_2O
4) MeI, K_2CO_3

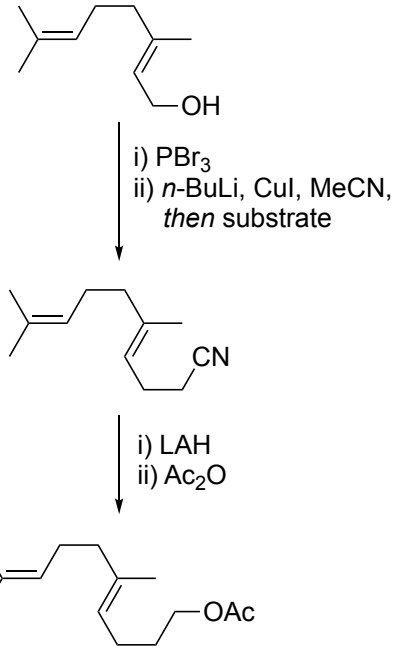
AZADO = 

5) K_2CO_3, MeOH
6) DMP
7) $CeCl_3$,

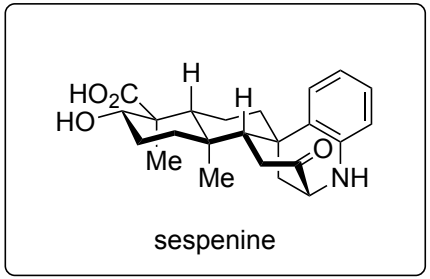
8) $[Cp_2TiCl_2]$, Mn, *i*-Pr_2NEt_2, TMS-Cl
then aq. HCl workup

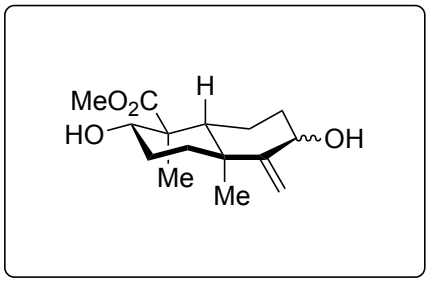
How would you synthesize the starting material?

T. Hirukawa, M. Oguchi, N. Yoshikawa, T. Kato, *Chem. Lett.* **1992**, *21*, 2343.

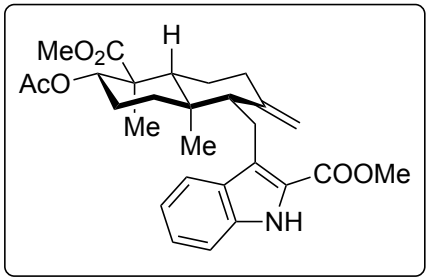


Please provide a mechanism for step 8.

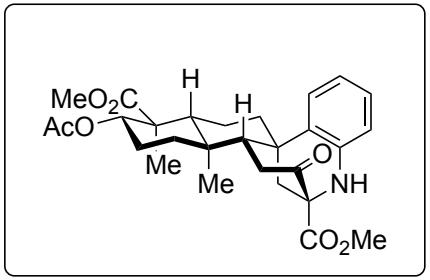




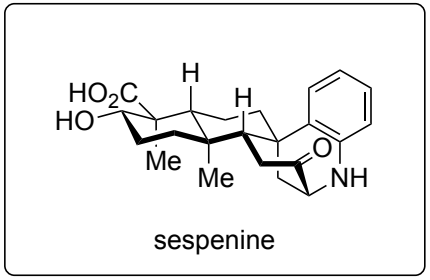
9-12



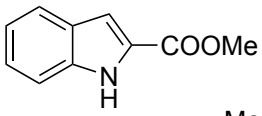
13,14

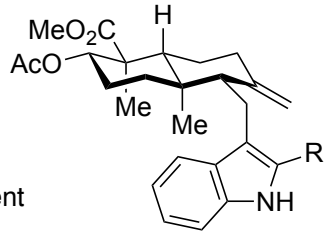


15,16



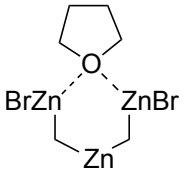
sespenine

X = 



9) IBX
10) Ac_2O, NEt_3
11) $Bi(OTf)_3$, **X**
12) $TiCl_4$, Nysted reagent

Structure of Nysted's reagent?

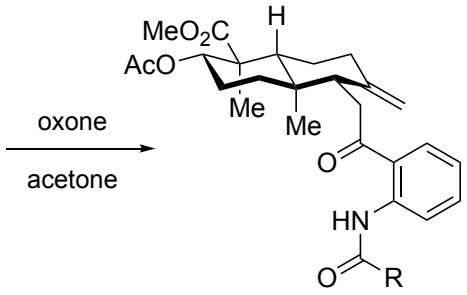


13) oxone, acetone
14) AcOH

15) NaCl, Δ
16) LiOH

What could be the reason for using the C2-substituted indol, while in the end that position is not functionalized?

Electronics reduce the overoxidized side product:



R = H
major product

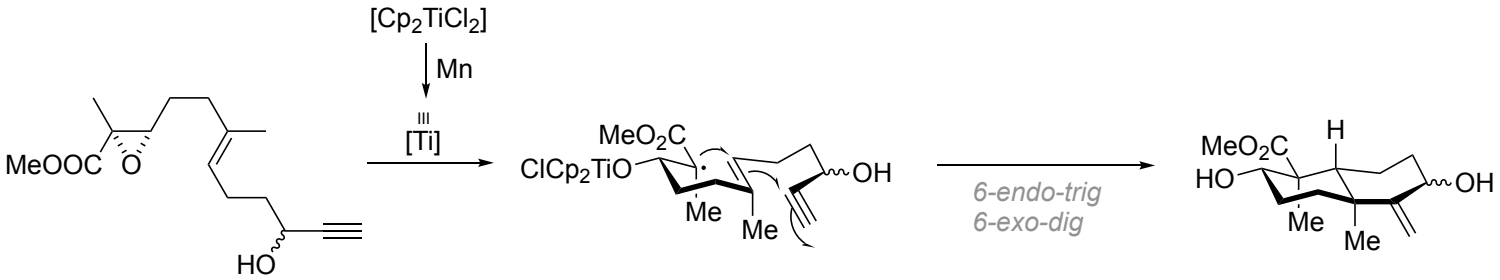
R = COOMe
minor side product

Please explain the transformation of step 14 with a mechanism.

What is the name associated with the reaction in step 15?

Krapcho demethoxycarbonylation

Mechanism of step 8



Mechanism of step 14