Total Synthesis of Unsymmetrically Oxidized Nuphar Thioalkaloids via Copper-Catalyzed Thiolane Assembly

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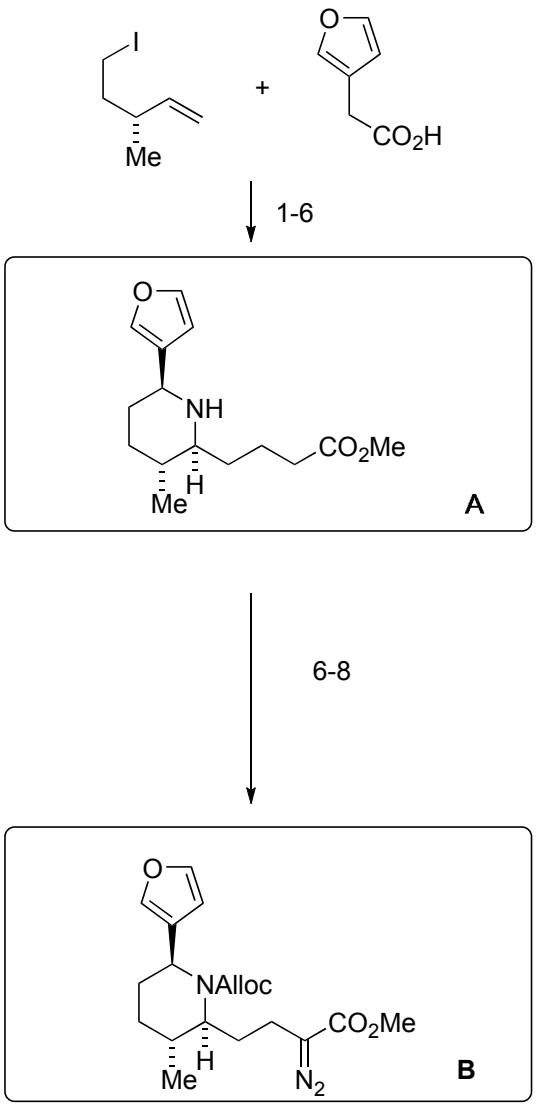
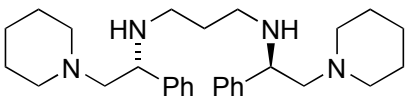
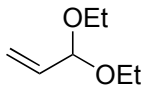


1) **1**, *n*-BuLi, THF, –78°C
2) *i*-Pr_2NEt, $(PhO)_2P(O)N_3$
2,2,2-trichloroethanol, 80°C
3) **2**, HGII (5mol%)
4) $Ph_3P{=}CHCO_2Me$
5) Cd- Pb Couple, THF,
1M NH_4OAc
6) $RhCl(PPh_3)_3$ (5 mol%)
H_2 (300 psi)

6) AllocCl, *i*-Pr_2NEt, THF
7) $KN(SiMe_3)_2$, $PhCO_2Me$
8) $(4\text{-}NO_2C_6H_4)SO_2N_3$, DBU



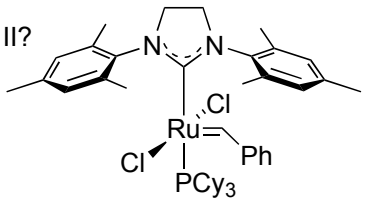
1

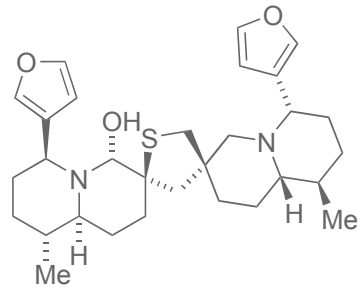


2

Explain the mechanism in Step 2

Structure of Grubbs II?

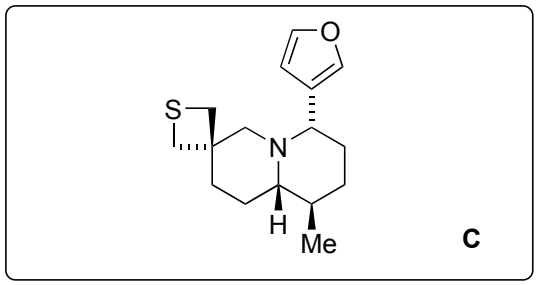




(–)-6-hydroxythionuphlutine

A

9-14

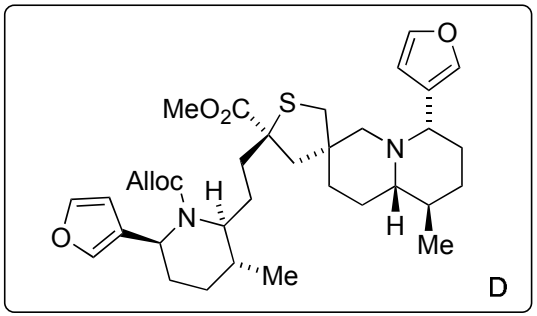


C

9) AcOH, 110°C
10) LDA, 4-$MeOC_6H_4OCOCl$ 10 equiv., –78°C
11) $NaBH_4$ 7 equiv.
12) MsCl 3 equiv., *i*-Pr_2NEt
13) $Na_2S•9H_2O$, *n*-Bu_4NI
14) *i*-Bu_2AlH

B + **C**

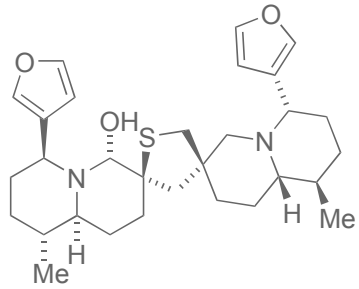
15



D

15) $Cu(hfacac)_2$ (5 mol %), 100°C (μW)

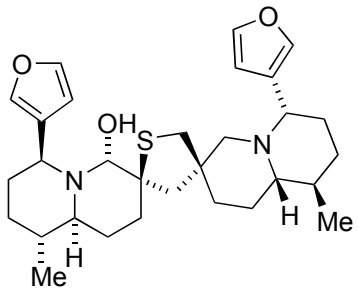
Mechanism of 15?



(–)-6-hydroxythionuphlutine

D

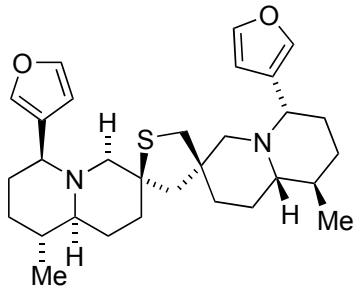
16-17



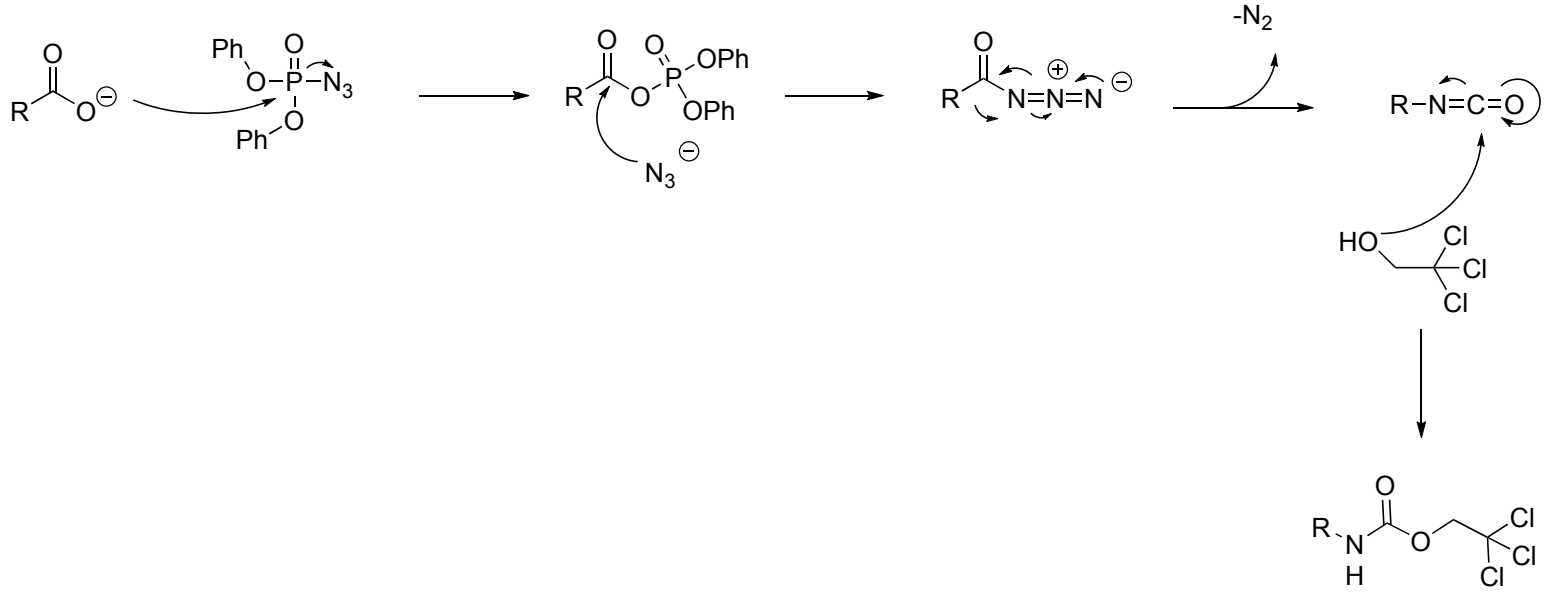
(–)-6-hydroxythionuphlutine

16) $Pd(PPh_3)_4$, $PhSiH_3$
17) *i*-Bu_2AlH

In the last step a side product was isolated in 10% yield. What is the side product?



Step 2:



Step 15: