Total Synthesis of (+)-Halichlorine: An Inhibitor of VCAM-1 Expression

D. Trauner, J. B. Schwarz, and S. J. Danishefsky

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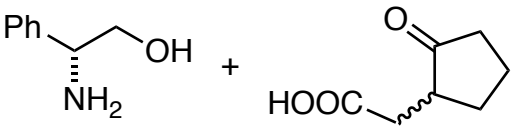

1-5

A

6-9

B

12-20

C

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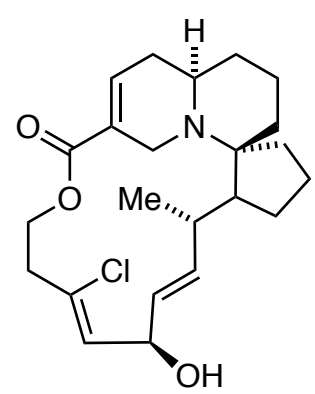
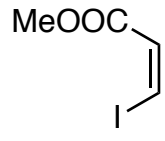


(+)-halichlorine

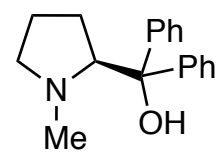
1) PhMe, reflux
2) allyltrimethylsilane, $TiCl_4$
3) Na, NH_3
4) Boc_2O, DMAP
5) LHMDS *then* MeI



1

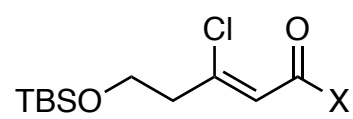
6) LiOH, H_2O/THF
7) ClCOOEt, NEt_3 *then* $NaBH_4$, MeOH
8) TBDPSCl, NEt_3, DMAP
9) 9-BBN, THF *then* **1**, $[Pd(dppf)Cl_2]$, $AsPh_3$, Cs_2CO_3, DMF/H_2O
10) TFA, DCM *then* K_2CO_3, H_2O

11) *t*-BuOAc, LHMDS
12) H_2CO, EtOH
13) LHMDS, then $[Cp_2Zr(H)Cl]$
14) HF/py
15) TPAP, NMO
16) $N_2CHP(O)(OMe)_2$, KO*t*-Bu



2

Soai's chiral amino alcohol



3

17) $[Cp_2Zr(H)Cl]$ then Zn_2Me, *then* **2** *then* **3**
18) DIBAL-H
19) TBSOTf, 2,6-lutidine
20) NH_4F, $MeOH/H_2O$
21) EDCI, DMAP, DMAP · HCl
22) HF/py

Bonus Question: what is VCAM-1?

1) What is the name of the structure formed in 1?

2) Please name the reaction and explain the Mechanism.

5) stereoselectivity?

11+12) please name the steps

15) which other methods can achieve this transformation?

16) Please name the transformation and give the Mechanism. What would be an alternative reaction for this transformation?

17) d.r.: 4:1

21) What is the role of DMAP · HCl?