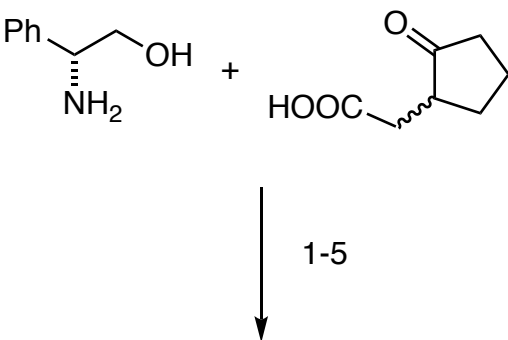


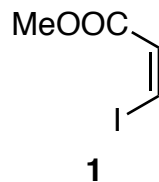
**Total Synthesis of (+)-Halichlorine: An Inhibitor of VCAM-1 Expression**

D. Trauner, J. B. Schwarz, and S. J. Danishefsky  
*Angew. Chem. Int. Ed.* **1999**, *38*, 3542-3545.



1-5

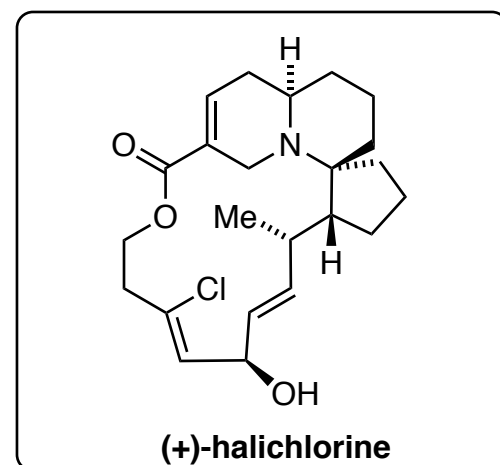
- 1) PhMe, reflux
- 2) allyltrimethylsilane, TiCl<sub>4</sub>
- 3) Na, NH<sub>3</sub>
- 4) Boc<sub>2</sub>O, DMAP
- 5) LHMDS then MeI



**1**

- 6) LiOH, H<sub>2</sub>O/THF
- 7) ClCOOEt, NEt<sub>3</sub> then NaBH<sub>4</sub>, MeOH
- 8) TBDPSCI, NEt<sub>3</sub>, DMAP
- 9) 9-BBN, THF then **1**, [Pd(dppf)Cl<sub>2</sub>], AsPh<sub>3</sub>, Cs<sub>2</sub>CO<sub>3</sub>, DMF/H<sub>2</sub>O
- 10) TFA, DCM then K<sub>2</sub>CO<sub>3</sub>, H<sub>2</sub>O

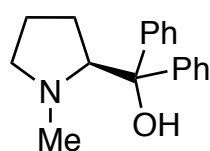
6-9



**(+)-halichlorine**

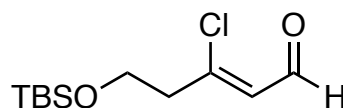
12-20

- 11) *t*-BuOAc, LHMDS
- 12) H<sub>2</sub>CO, EtOH
- 13) LHMDS, then [Cp<sub>2</sub>Zr(H)Cl]
- 14) HF/py
- 15) TPAP, NMO
- 16) N<sub>2</sub>CHP(O)(OMe)<sub>2</sub>, KO<sup>*t*</sup>-Bu



**2**

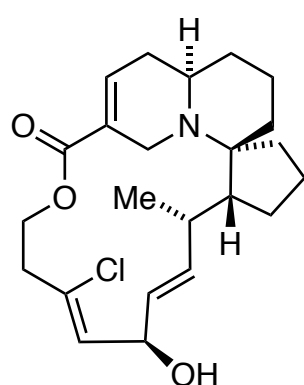
*Soai's chiral amino alcohol*



**3**

- 17) [Cp<sub>2</sub>Zr(H)Cl] then ZnMe<sub>2</sub>, then **2** then **3**
- 18) TBSOTf, 2,6-lutidine
- 19) NH<sub>4</sub>F, MeOH/H<sub>2</sub>O
- 20) EDCI, DMAP, DMAP · HCl
- 21) HF/py

12-20



**(+)-halichlorine**

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?

**Bonus Question: what is VCAM-1?**