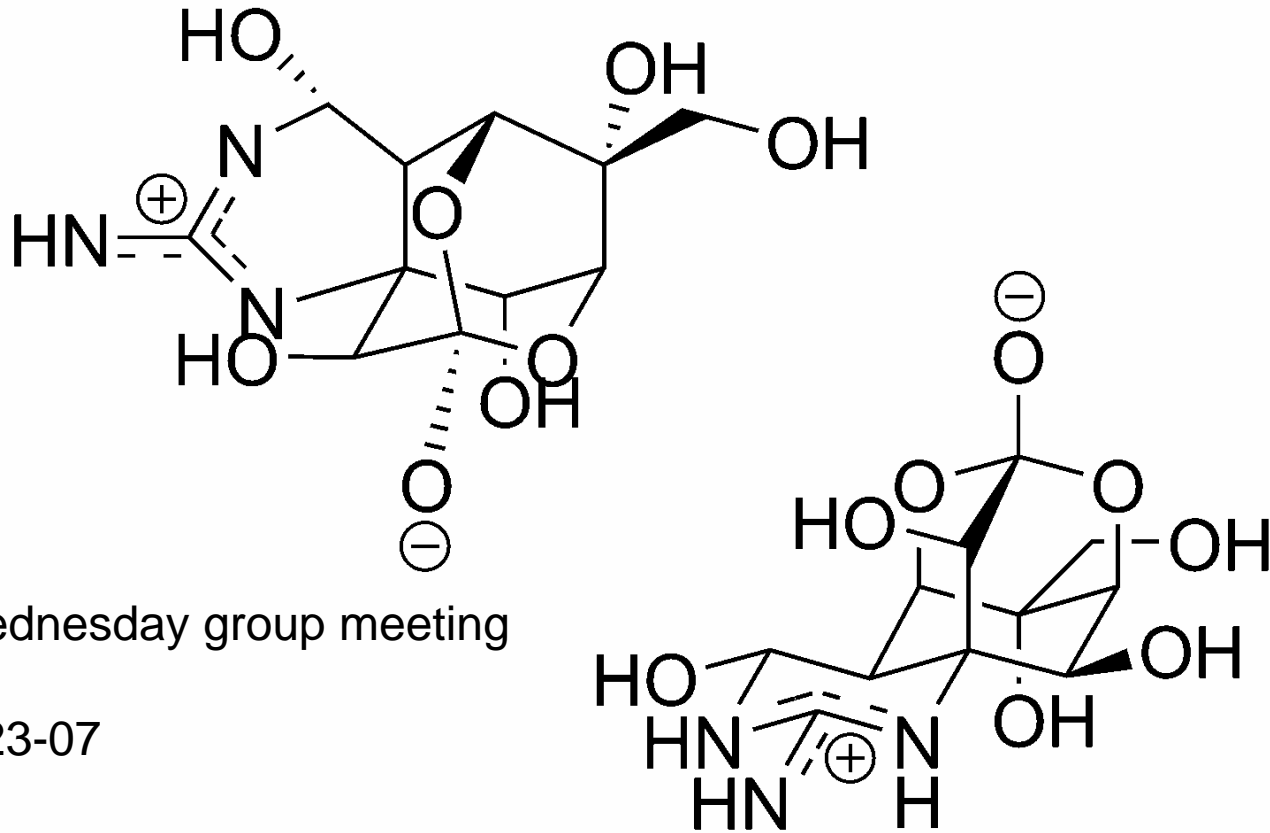


# Tetrodotoxin

by Kishi



Wednesday group meeting

5-23-07

Colin Hughes

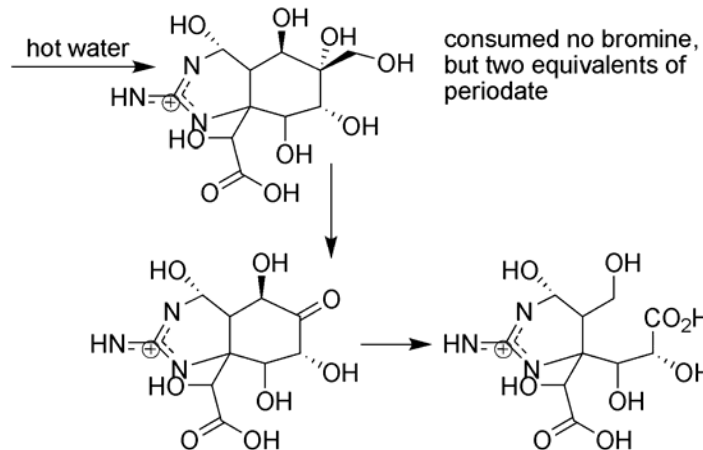
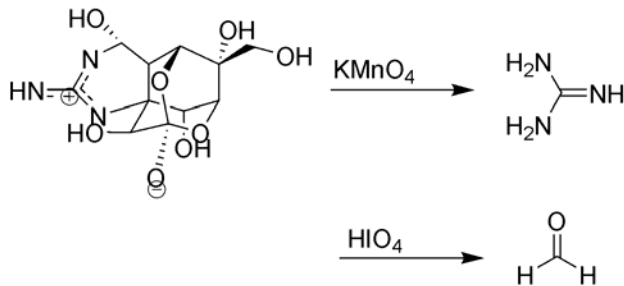
# Big in Japan

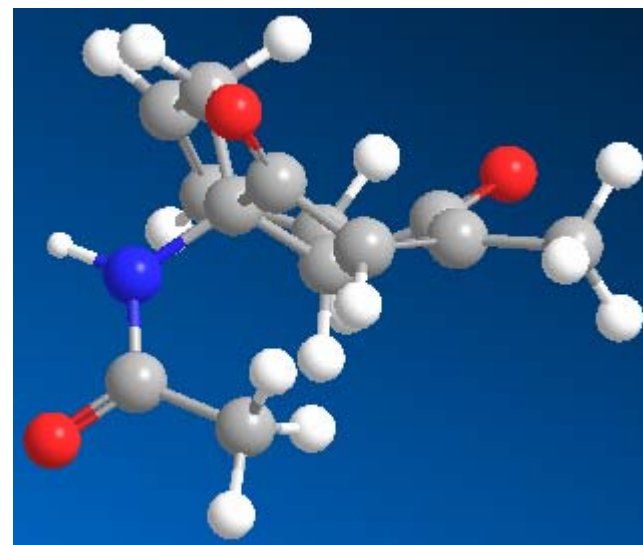
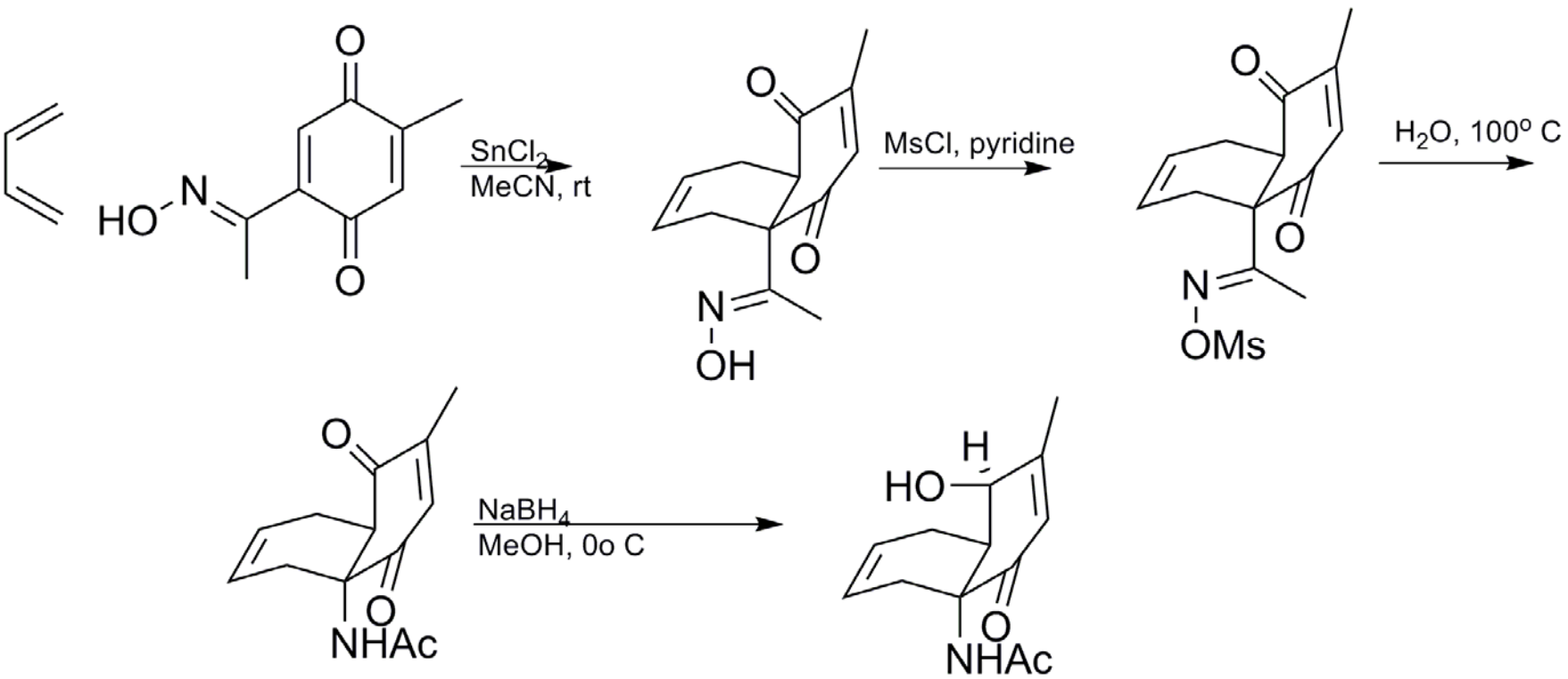
- Nearly killed Homer Simpson in a season two episode “one fish, two fish, blowfish, blue fish” when Homer ate “fugu”
- In addition to pufferfish, is found in newts, sea stars, and worms
- Very toxic! Works by blocking sodium channels
- No known antidote



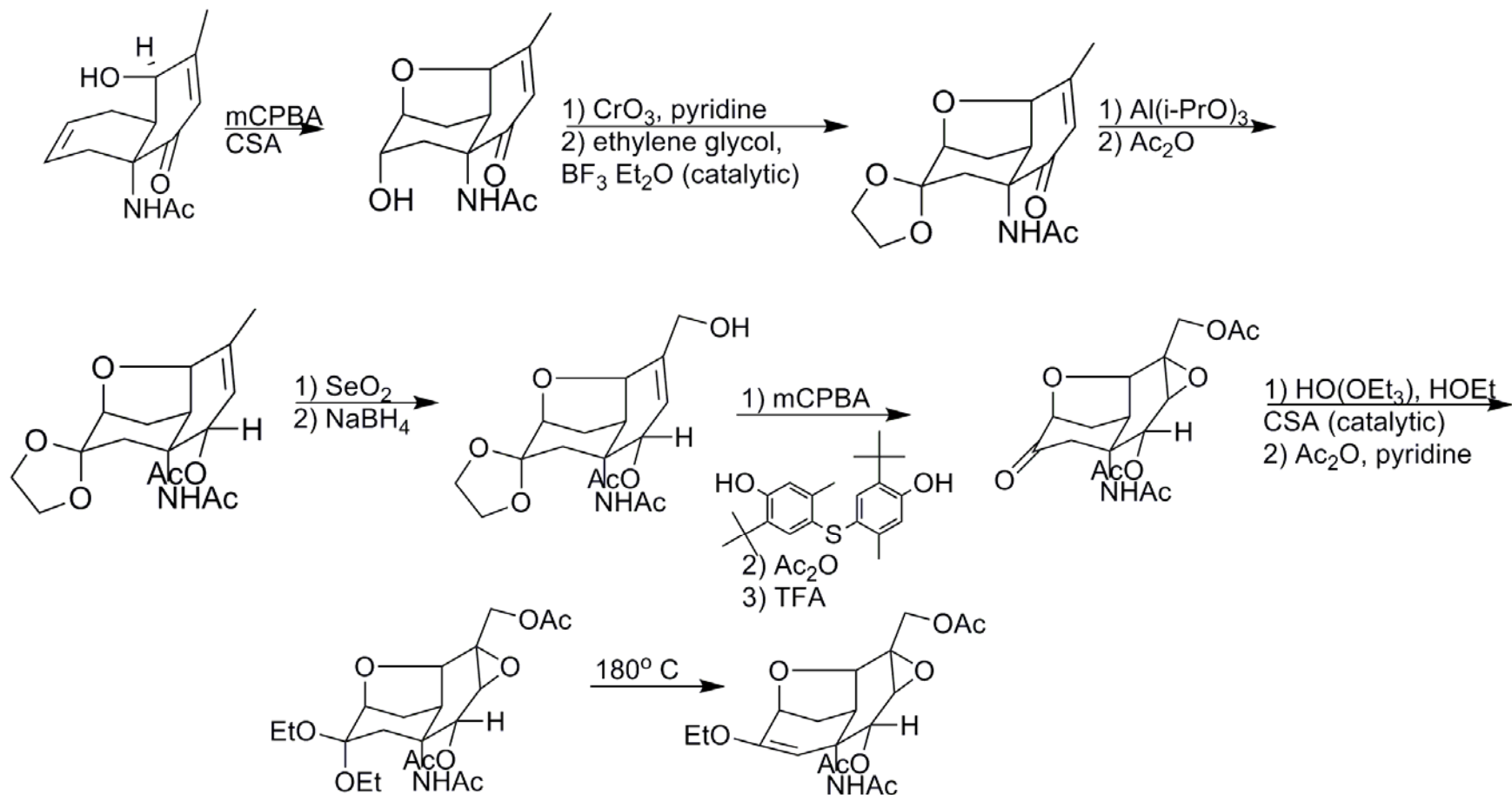
# How they determined the structure

- Originally assigned  $C_{12}H_{17}O_{10}N_3$
- Revised to  $C_{12}H_{19}O_9N_3$  then to  $C_{12}H_{17}O_8N_3$

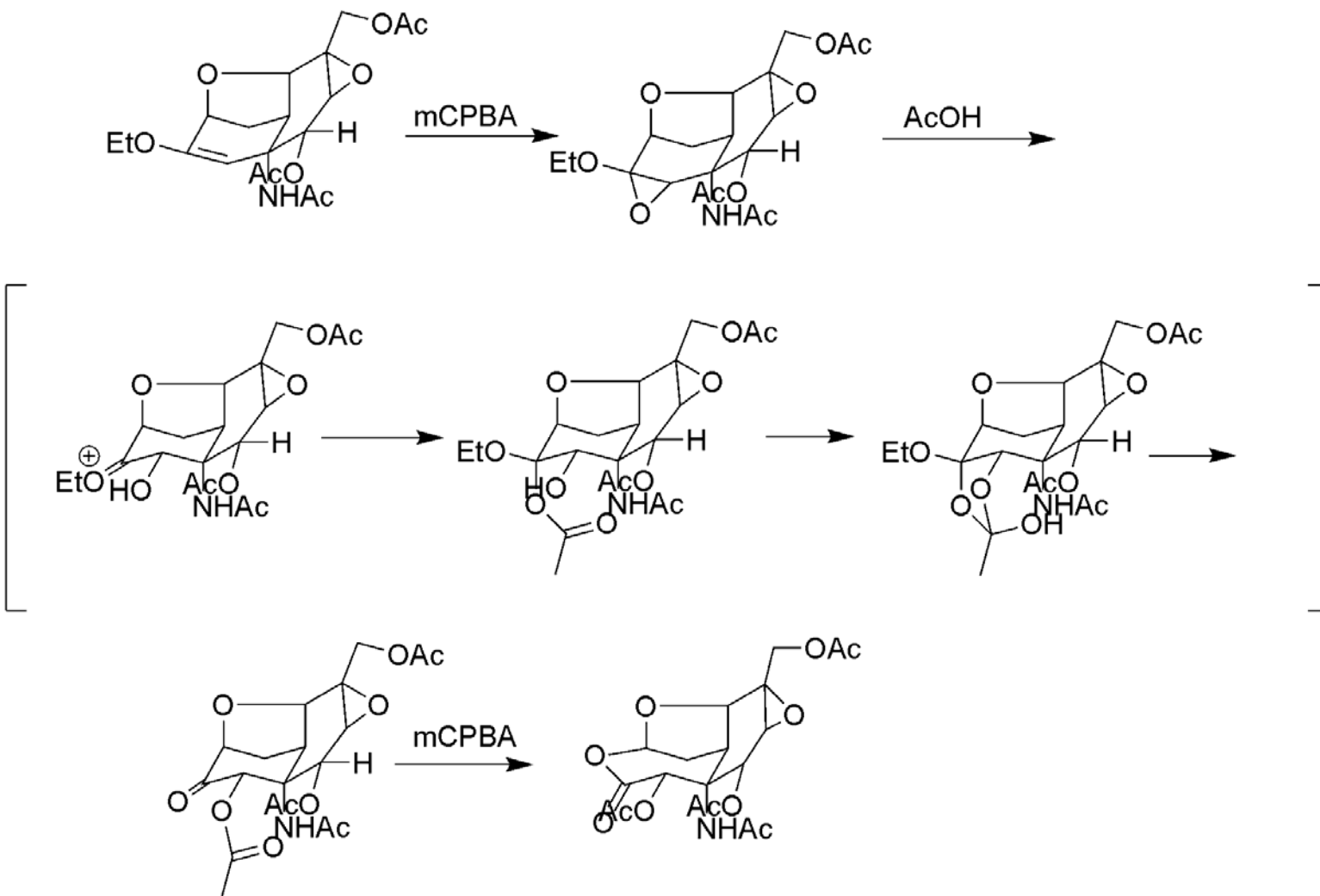




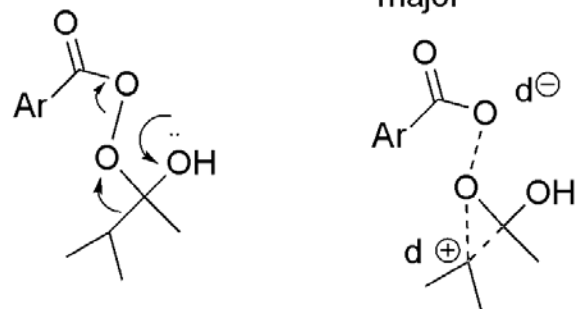
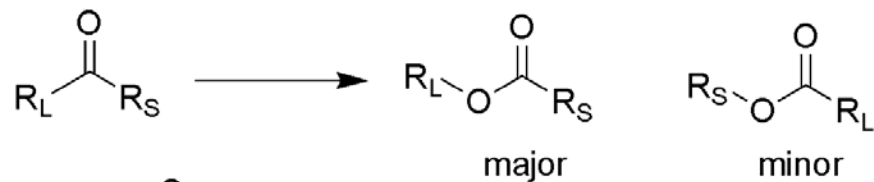
# Functionalization of the two olefins



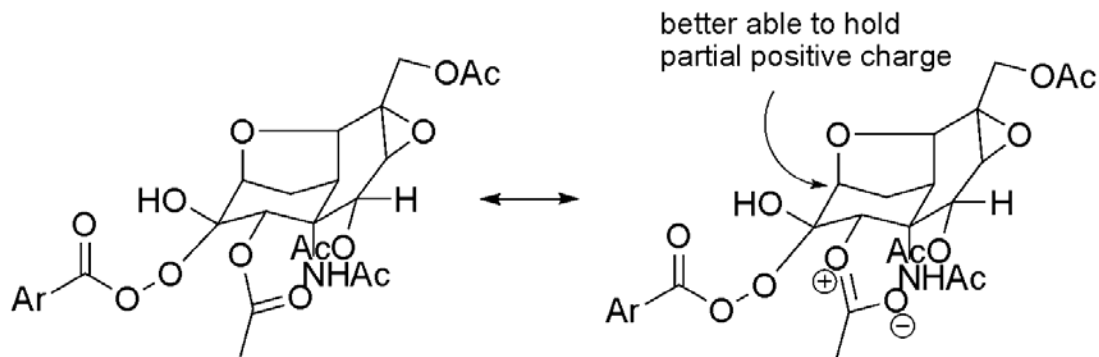
# A Selective Baeyer-Villiger



# Kishi's 1972 explanation



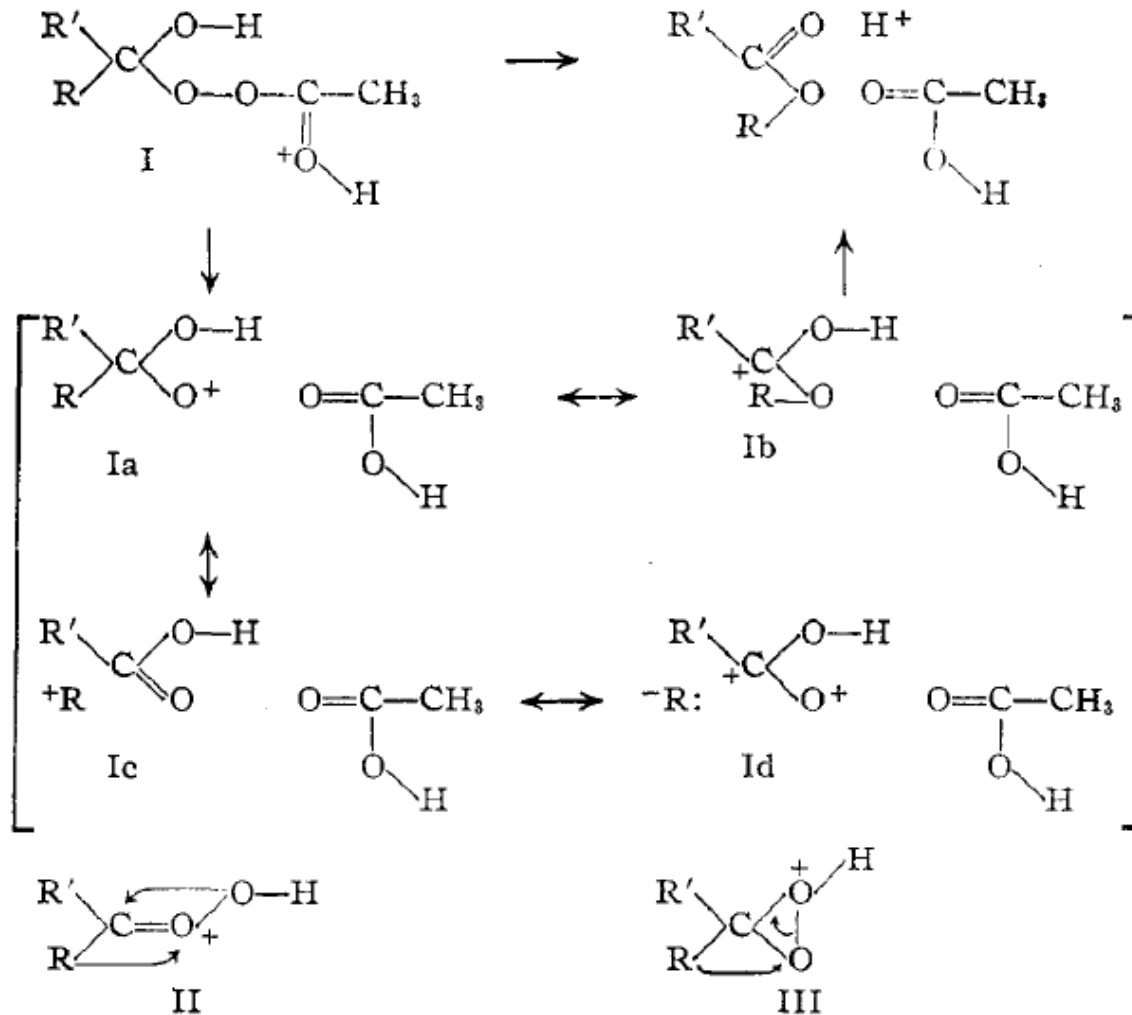
the larger the group, the better it can stabilize partial positive charge



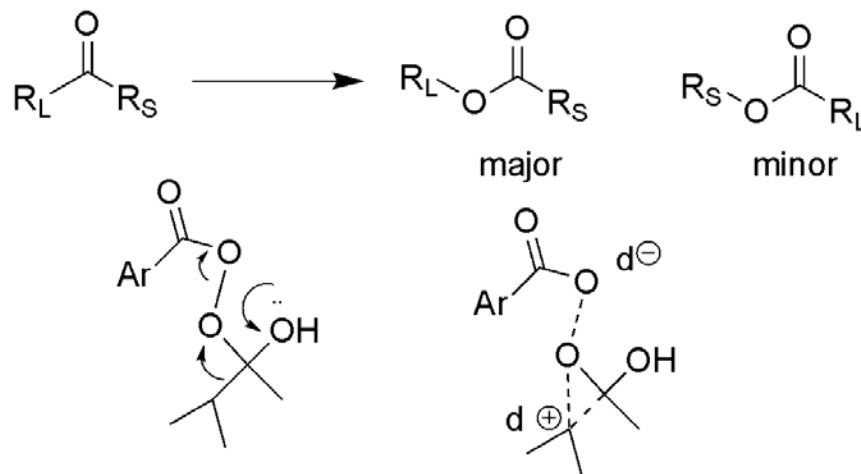
# Baeyer-Villiger oxidation, the true story

- Sterics? Electronics? Stereoelectronics?
- Not completely understood, but all three seem to play a part

# Pre-modern day

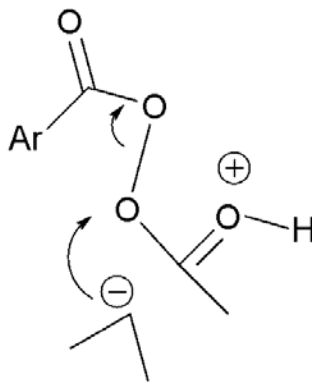


# Traditional Explanation: rule of thumb, or scientific explanation?

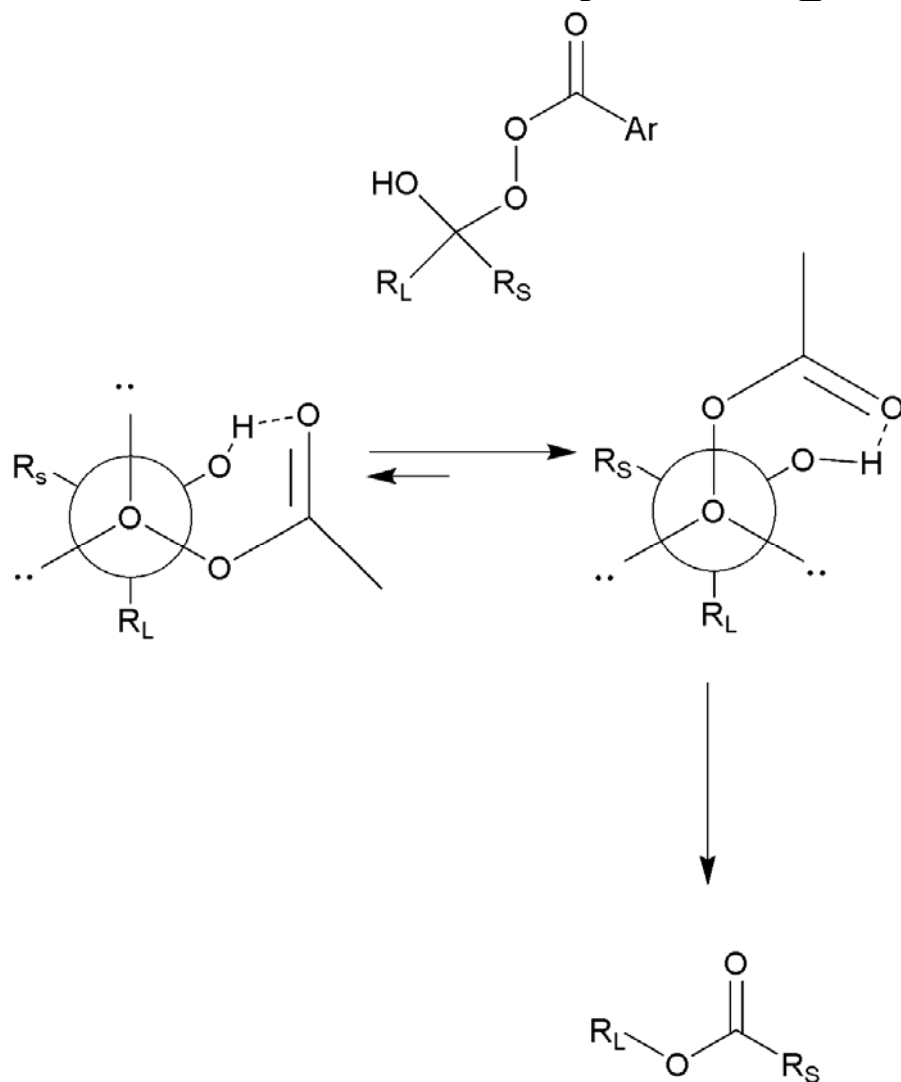


the larger the group, the better it can stabilize partial positive charge

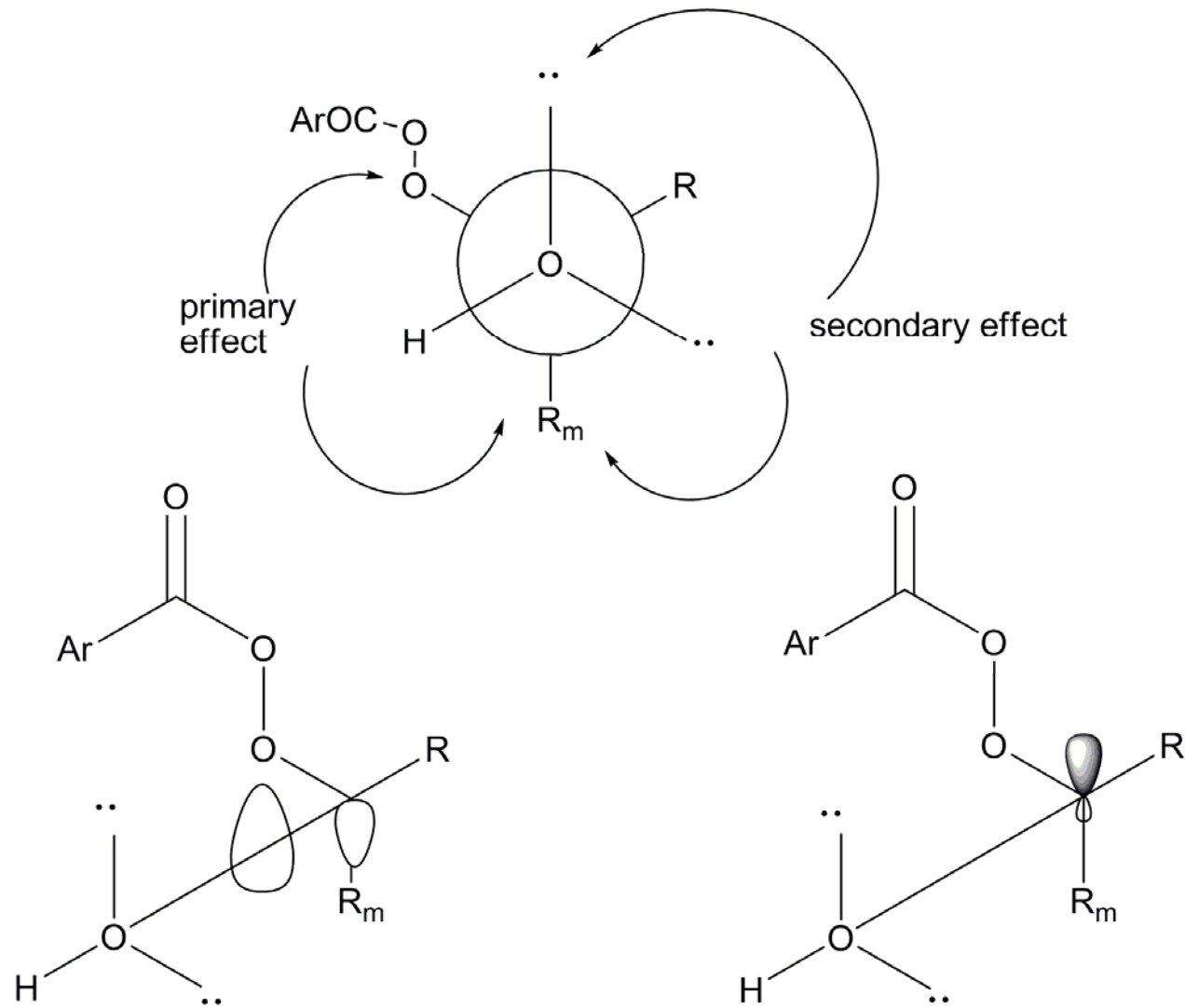
but why not an  $S_N2$  like?



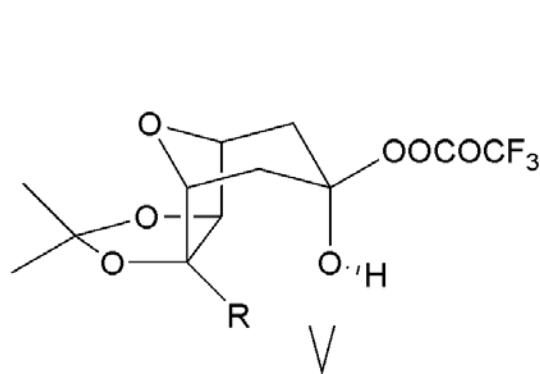
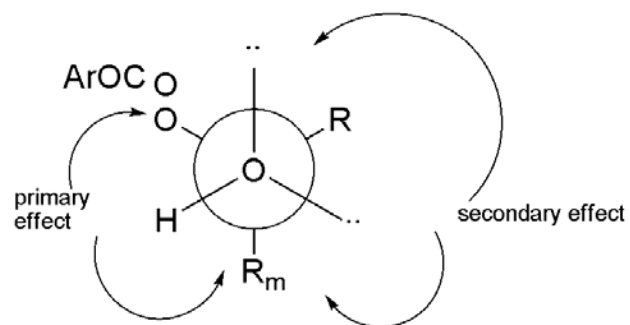
# Understanding through Newman projections and hydrogen bonding



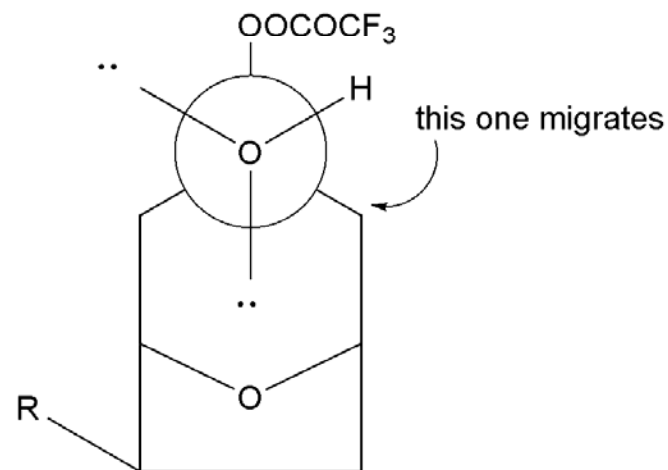
# stereoelectronics



# Secondary stereoelectronic effect



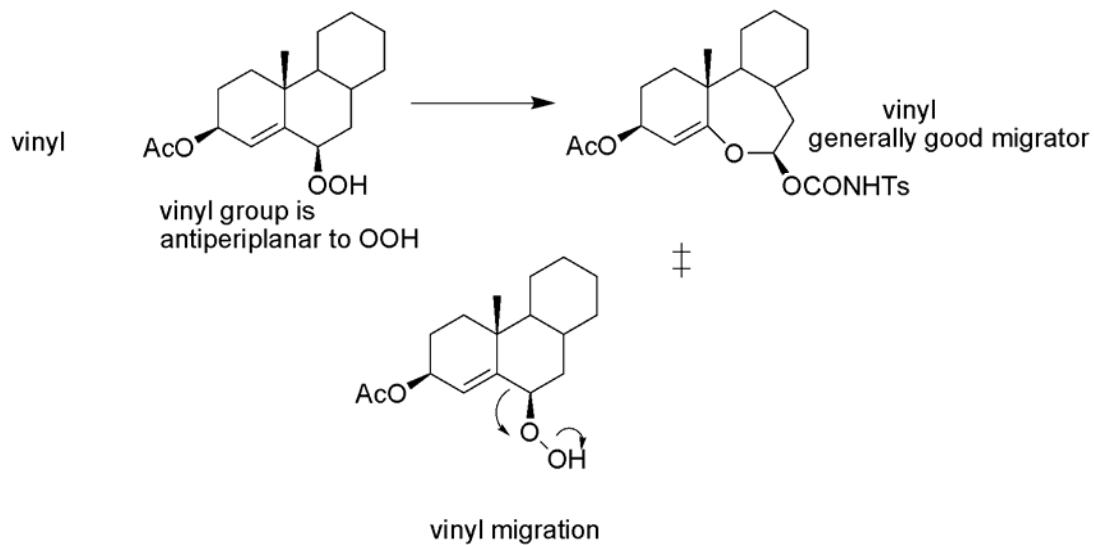
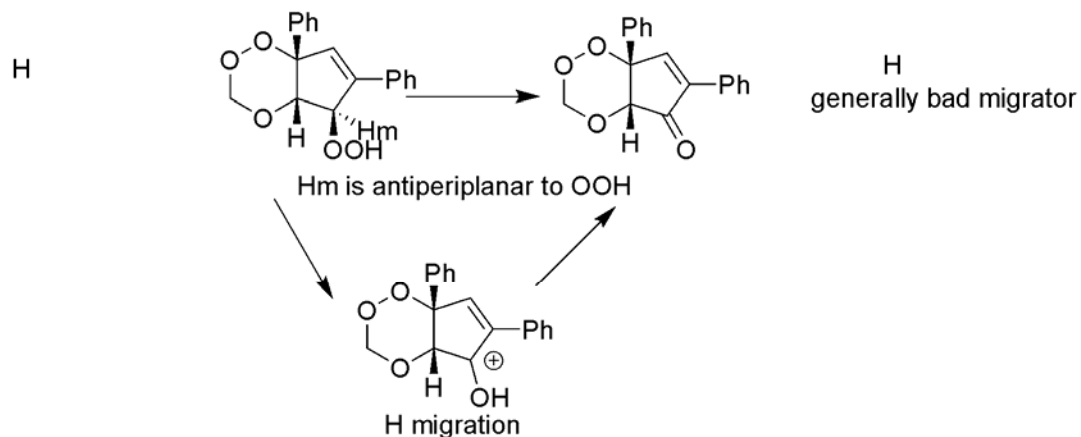
"Criegee intermediate"



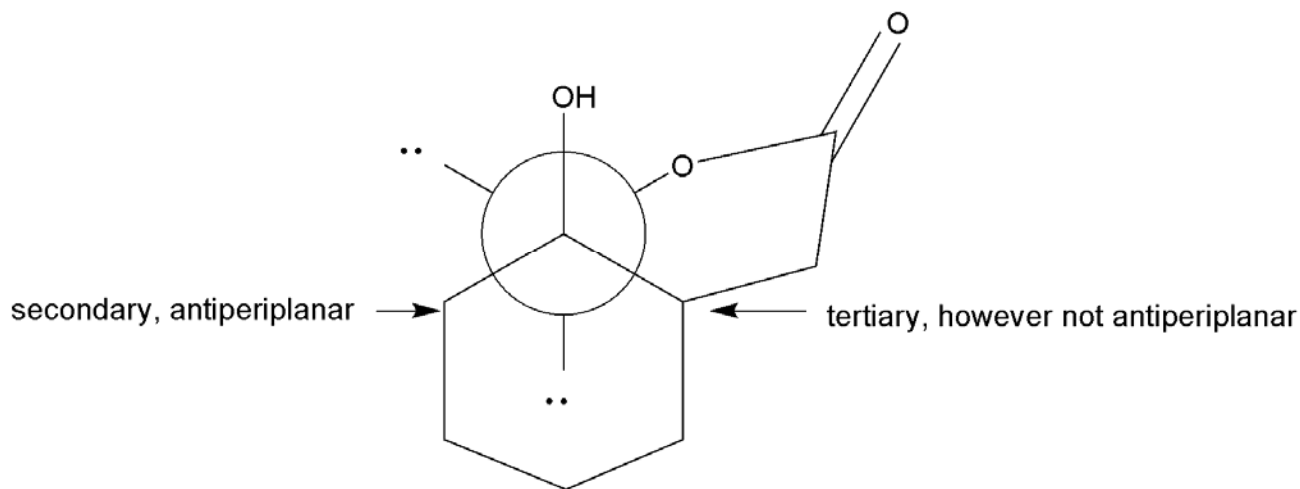
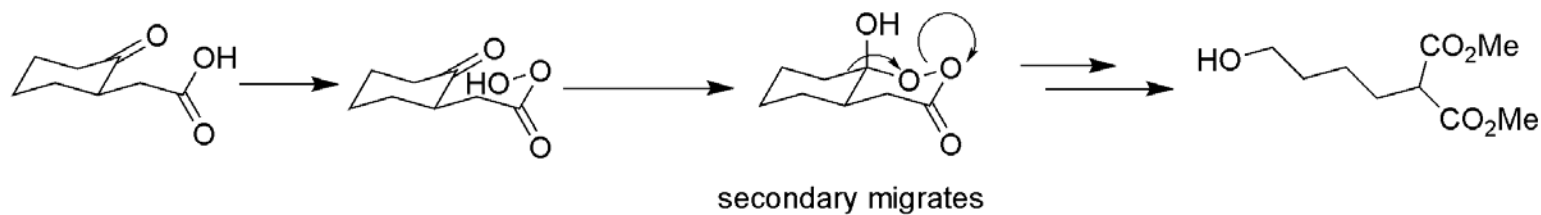
# Primary effect, Kishi 1998

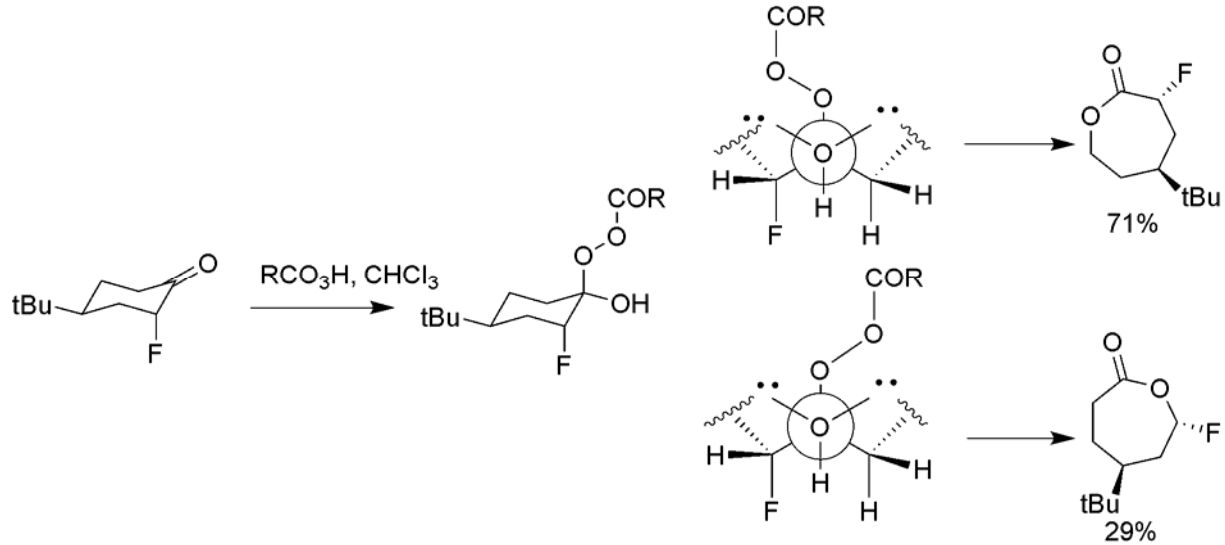
anti periplanar:

migrated

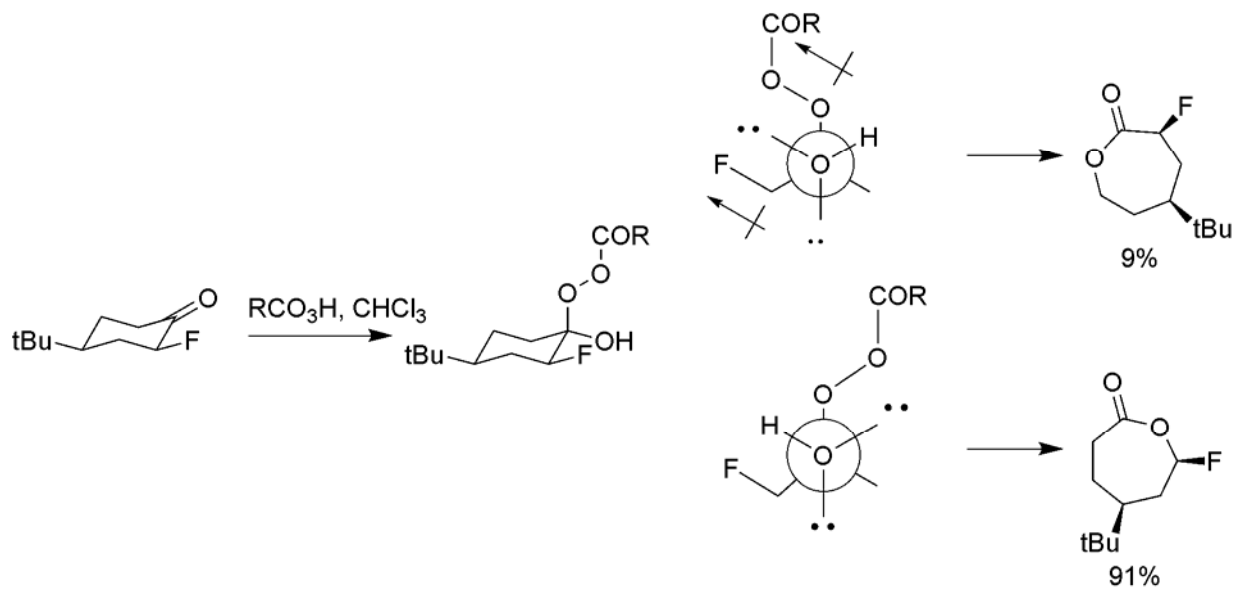


# Primary effect II



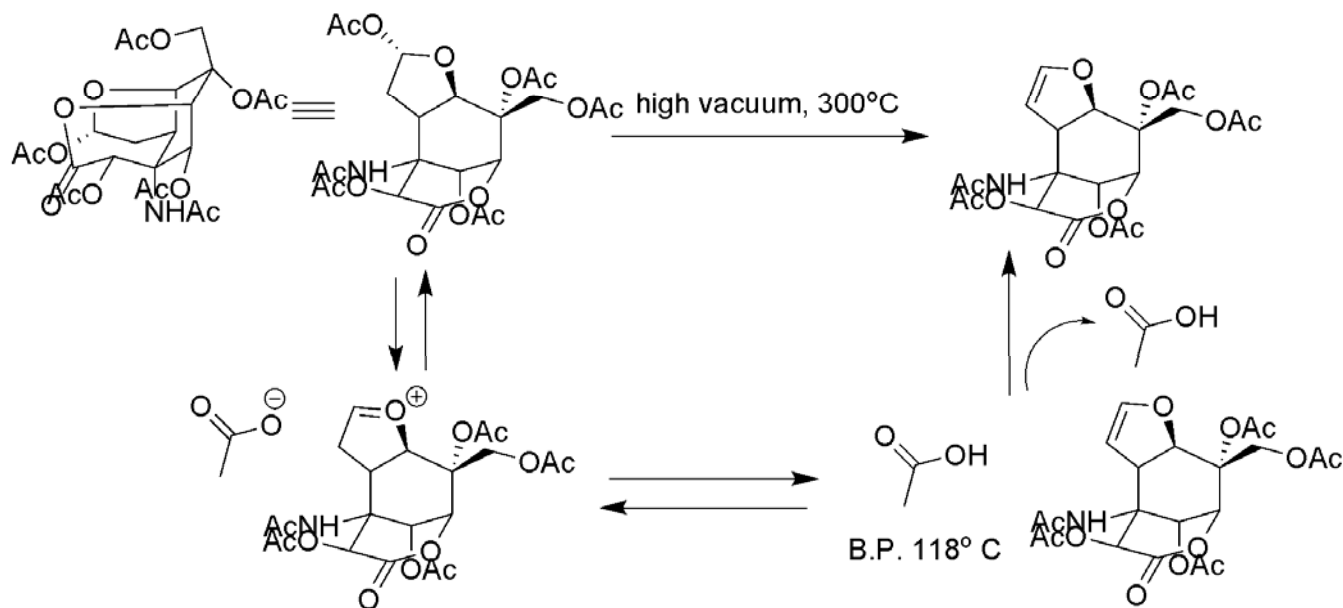
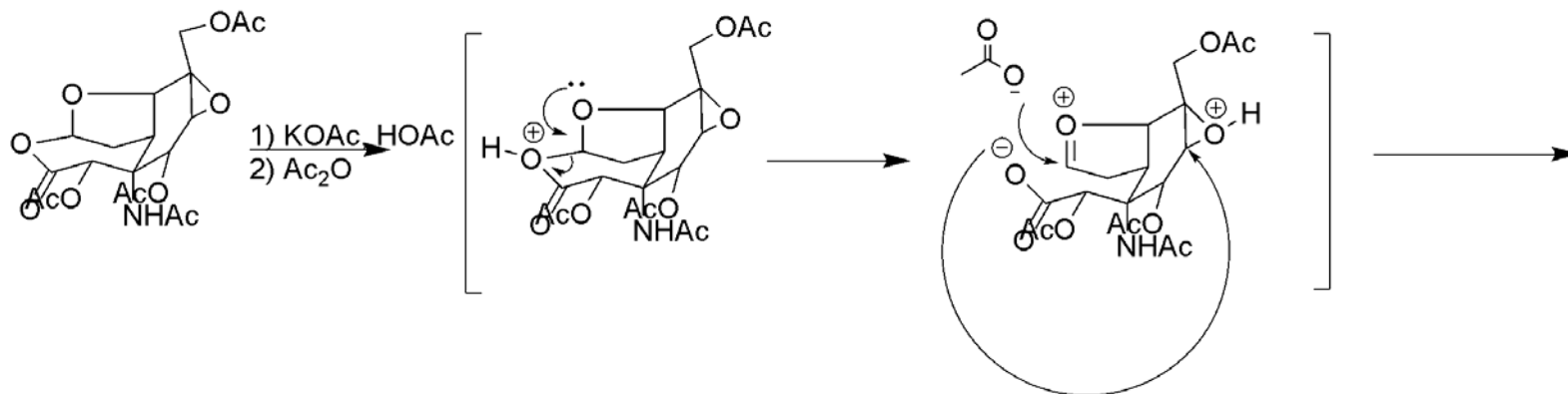


when experiments run in polar solvents, there is not a decrease in selectivity observed

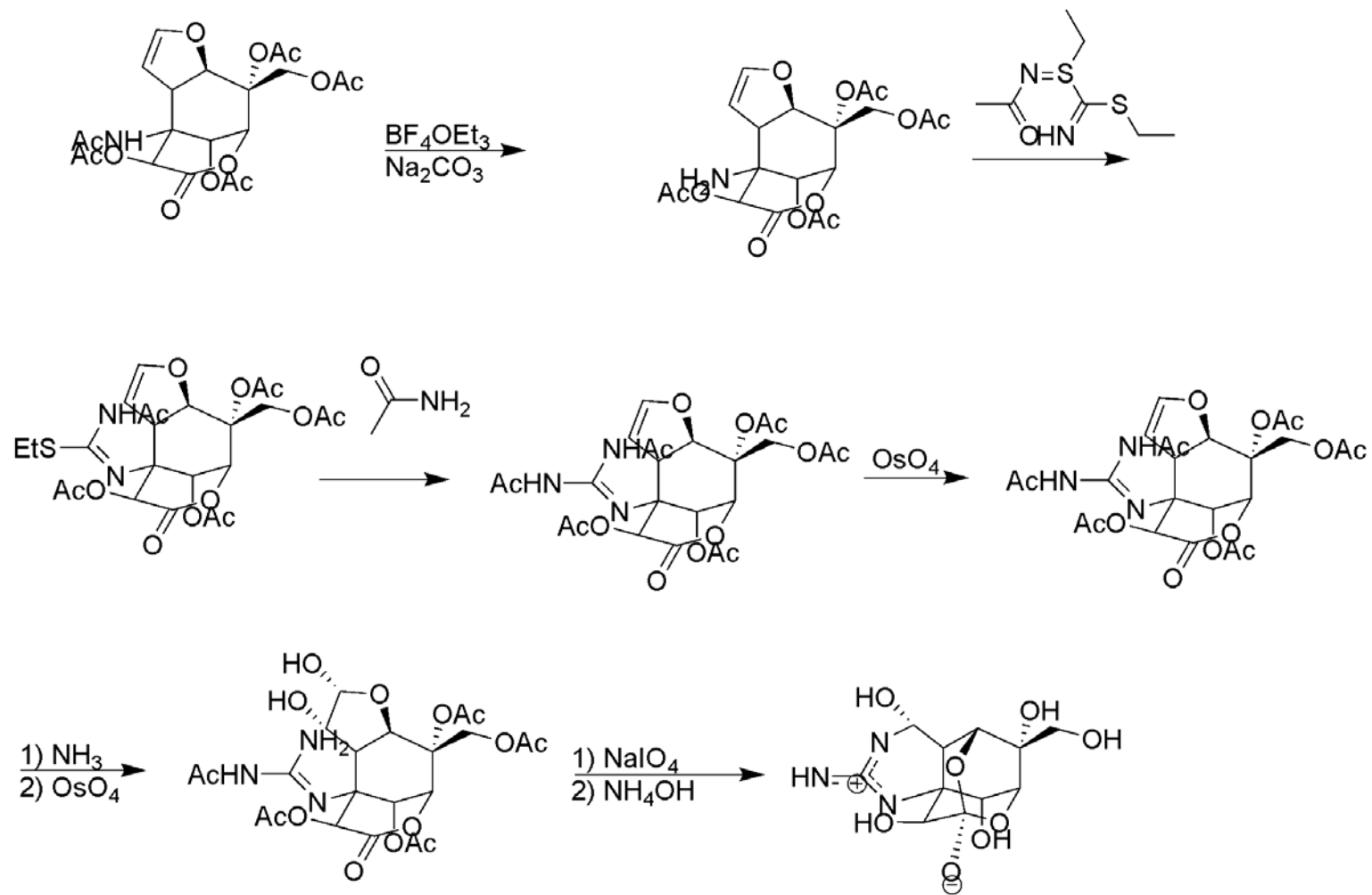


when experiments run in polar solvents, there is a decrease in selectivity observed

# Back to 1972



# Endgame



# Conclusions

- Tetrodotoxin's cage-like structure allows for good selectivity
- Baeyer-Villiger reactions are very interesting, and not completely understood
- Respect the old school chemists

# References

- *J. Am. Chem. Soc.* **1972**, 94, 9217, 9219
- *Tett. Lett.* **1970**, 59, 5127, 5129
- *Angew. Chem., Int. Ed.* **2000**, 39, 2852
- *J. Am. Chem. Soc.* **1998**, 120, 9217, 9392