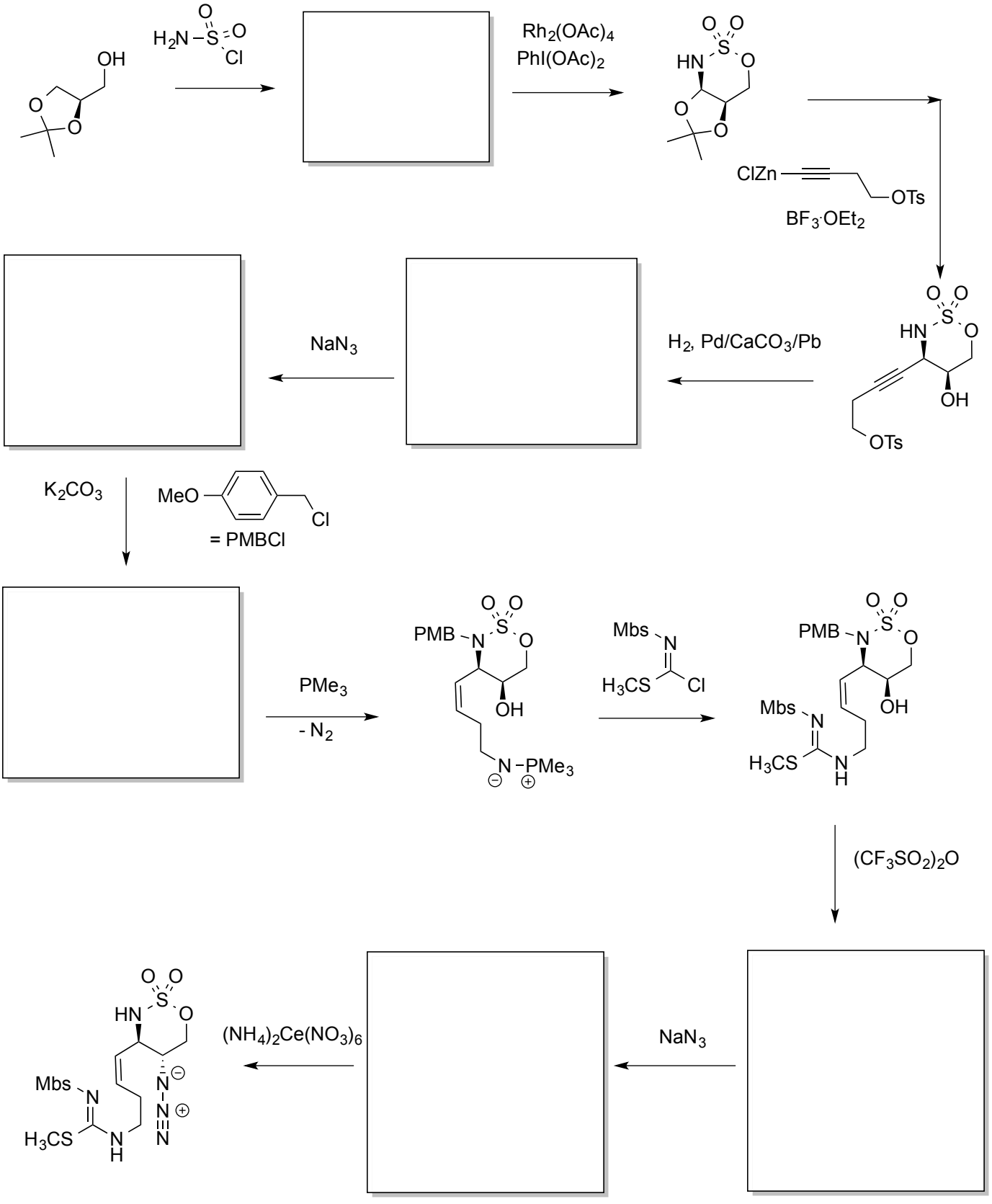
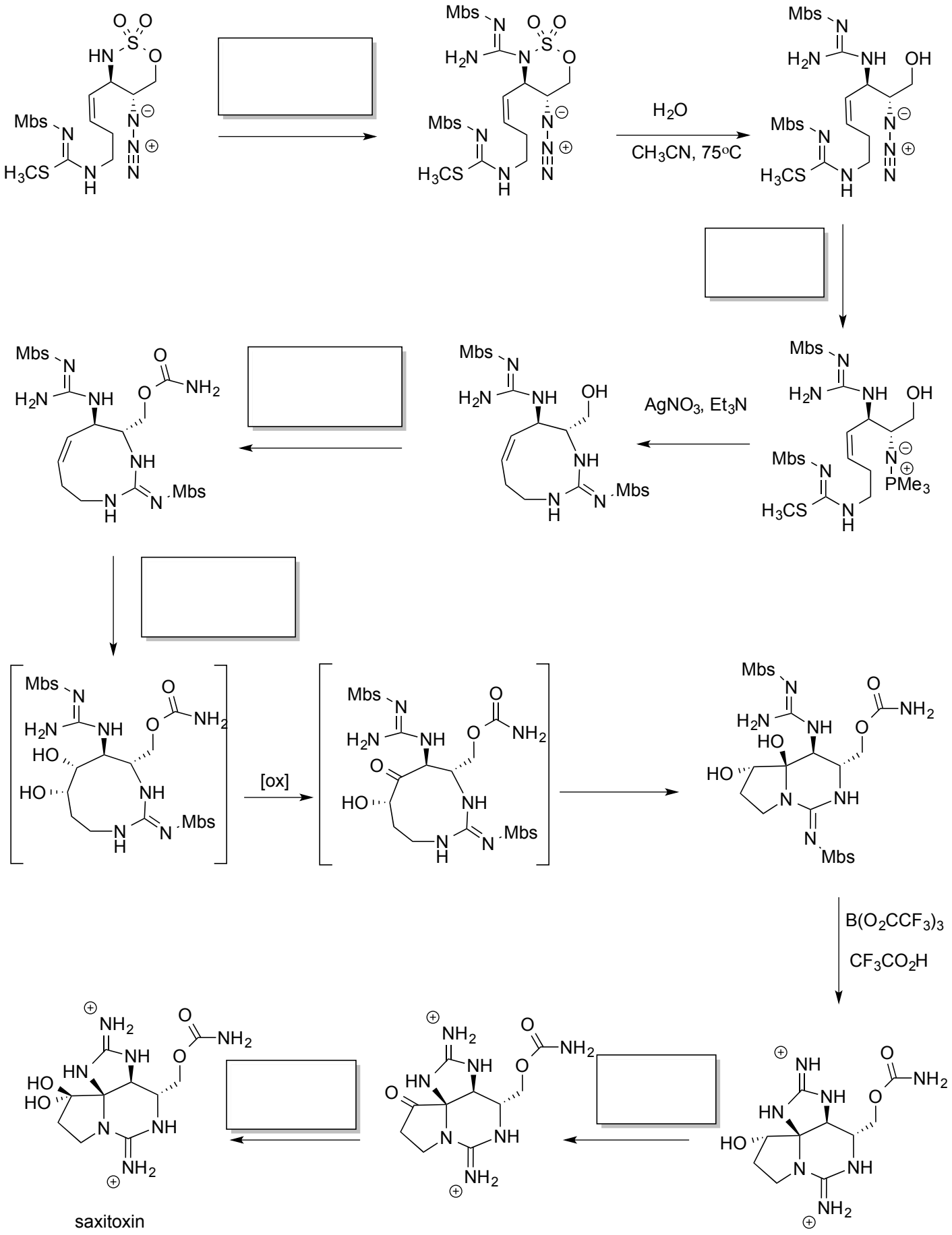
Synthesis of saxitoxin, DuBois, Stanford, 2006.

Saxitoxin, produced by red tide algae, is a potent blocker of voltage-gated Na^+ channels, causing paralysis. DuBois set out to synthesize saxitoxin and then systematically alter the structure, testing the effects of these derivatives in order to gain insight into the structure and function of sodium ion channels.



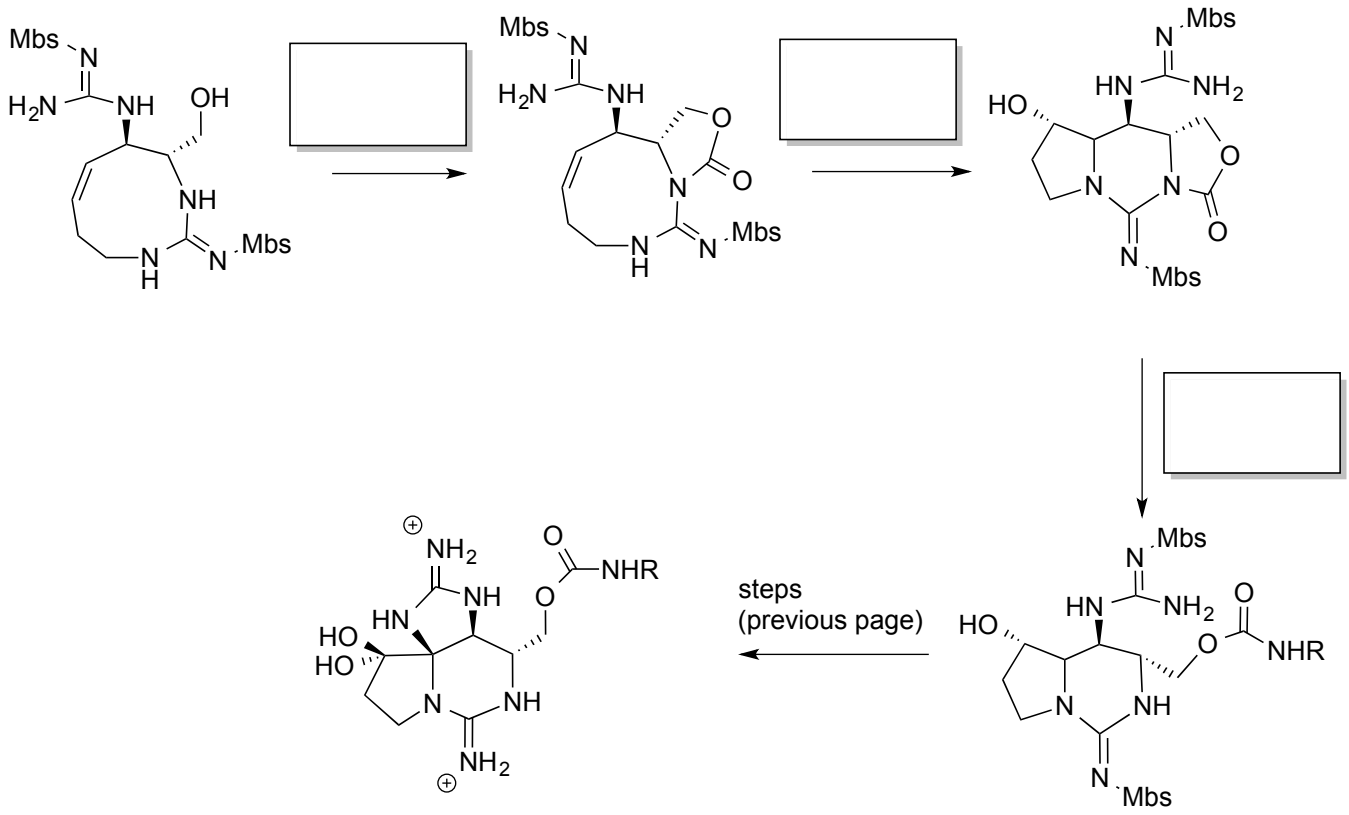
Ce(IV): oxidative cleavage of benzyl group

Saxitoxin, part 2



saxitoxin

Saxitoxin, part 3: As a first step in studying saxitoxin, DuBois modified the amide side chain and tested the activity of the new compounds against voltage-gated sodium channels.



Derivatives **9** - **13**

DuBois studied how well these derivatives block sodium ion channels. IC_{50} is the concentration needed to cut the activity of the channels in half.

Derivative	R = (in NHR)	IC_{50} (nM)
Saxitoxin	H	2.9 +/- 0.1
9	heptyl	26 +/- 3
10	isopropyl	83 +/- 13
11	$C_6H_{12}NH_3^+$	19 +/- 0.8
12	$C_6H_{12}CO_2^-$	135 +/- 7

What does this data tell you about the portion of the channel where the carbamate group sits (that's the O-(C=O)NHR part)? Be specific in discussing both steric and charge effects.