

# Fluorine and Physorg

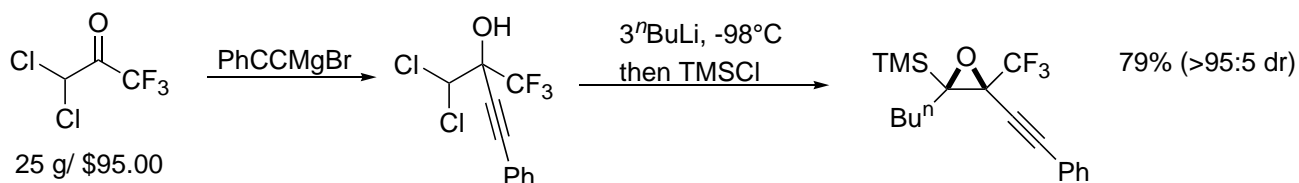
Nathan Shapiro, 4/25/07

## 1. Fluorine and anions

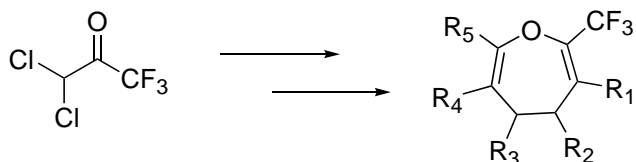
a. Rationalize the trend

HCX <sub>3</sub>	$\left\{ \begin{array}{l} X = \text{F} \\ X = \text{Cl} \\ X = \text{Br} \\ X = \text{CH}_3 \end{array} \right.$	<u>pKa</u>	<u>X electronegativity</u>
		30	3.98
		16	3.16
		14	2.96
>45	2.55		

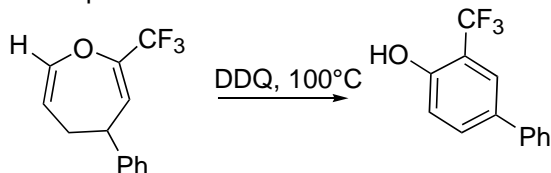
b. Shimizu and Hiyama (kyoto university) have developed a way to synthesize CF<sub>3</sub>-substituted tri and tetra substituted epoxides using this 2 pot procedure. Rationalize the diastereoselectivity.



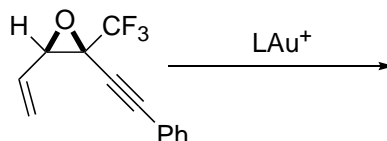
c. Show how this methodology can be applied towards the synthesis of 2-trifluoromethyl-4,5-dihydrooxepins



d. The oxepins can also be converted to the corresponding phenols. Devise another synthesis of the given phenol.

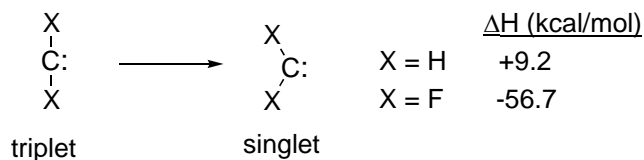


e. Just for fun predict the product of this reaction:

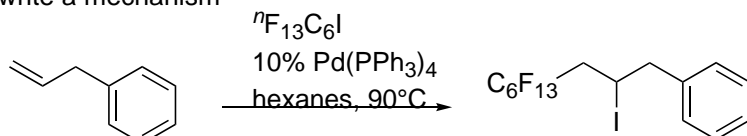


## 2. Rad Fluorine

a. rationalize

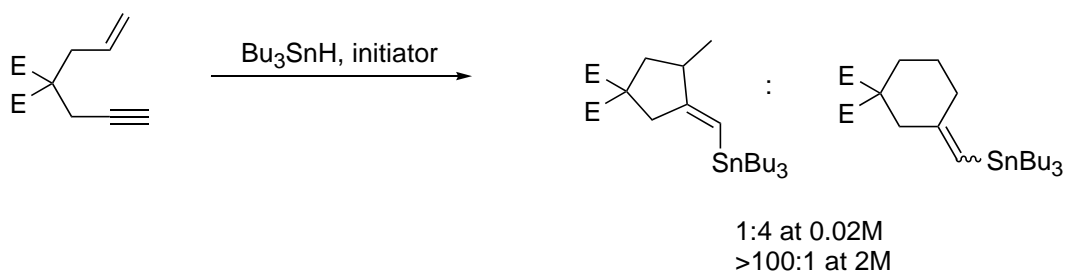
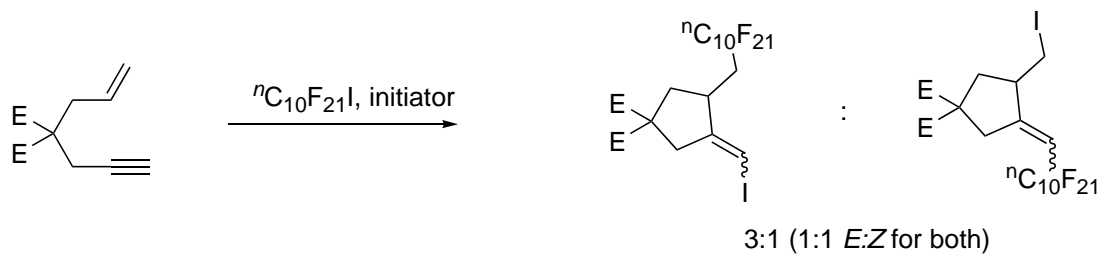


b. write a mechanism



c. propose an enantioselective version

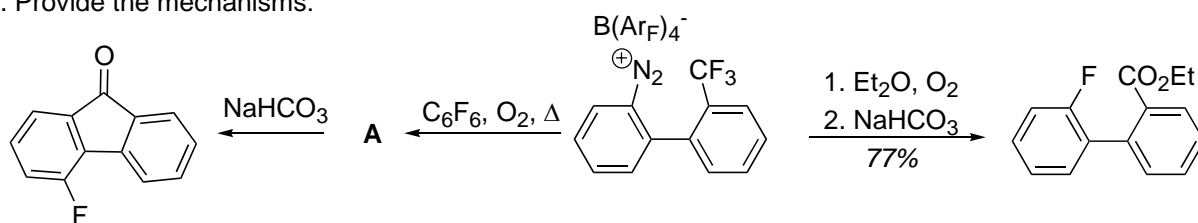
d. compare and rationalize the selectivity of the following reactions:



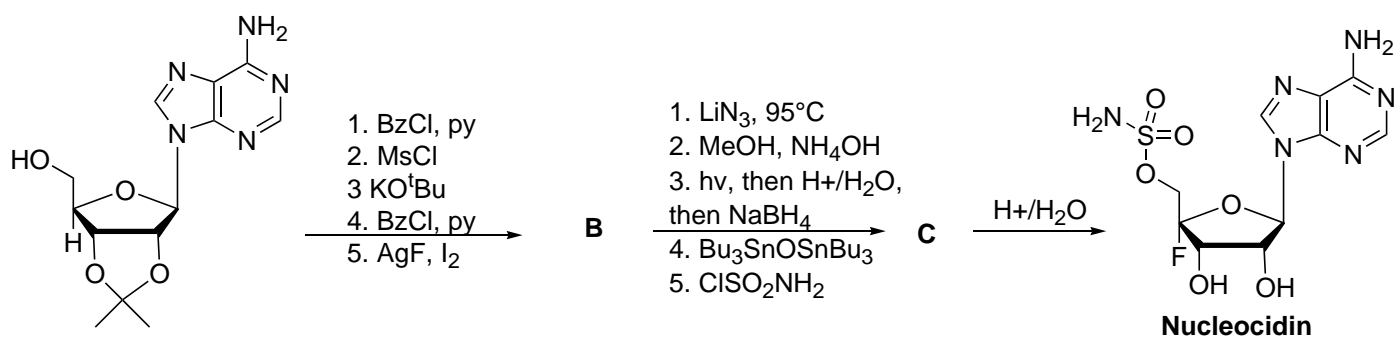
### 3. Fluorine and cations

sorry no physorg warmup

a. Provide the mechanisms:



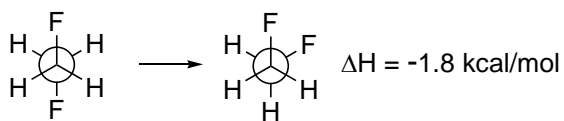
b. Follow along in Moffatt's not so elegant total synthesis of Nucleocidin, a now extinct natural product:



c. In fact, displacement of the the alkyl iodide in **B** proved extremely difficult (hence the convoluted sequence). Provide a rationale.

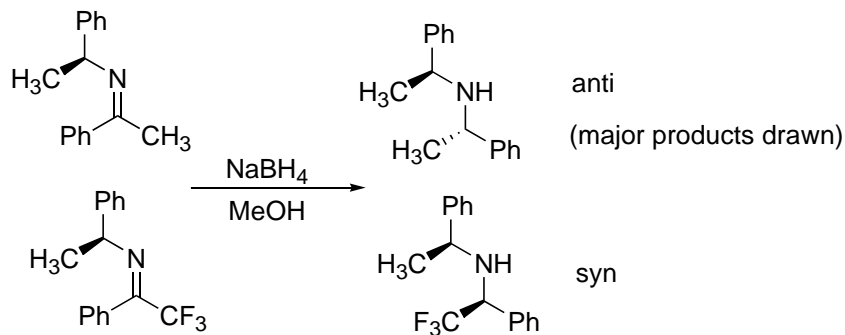
#### 4. Fluorine on selectivity

a. Rationalize the following observation and trend:

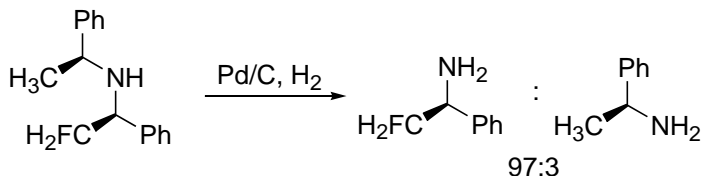


	C-X BDE (kcal/mol)	
	X=F	X=Cl
CXH <sub>3</sub>	110	85
CX <sub>2</sub> H <sub>2</sub>	120	80
CX <sub>3</sub> H	128	78
CX <sub>4</sub>	131	73

b. Rationalize the diastereoselectivity

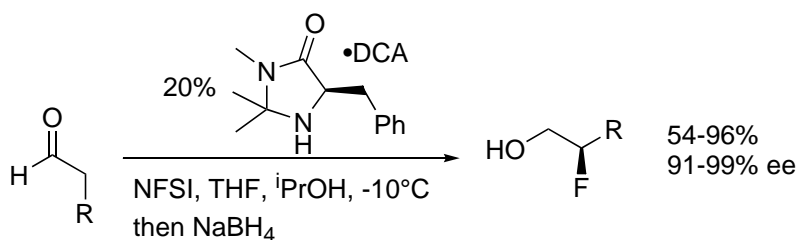


c. Rationalize the chemoselectivity



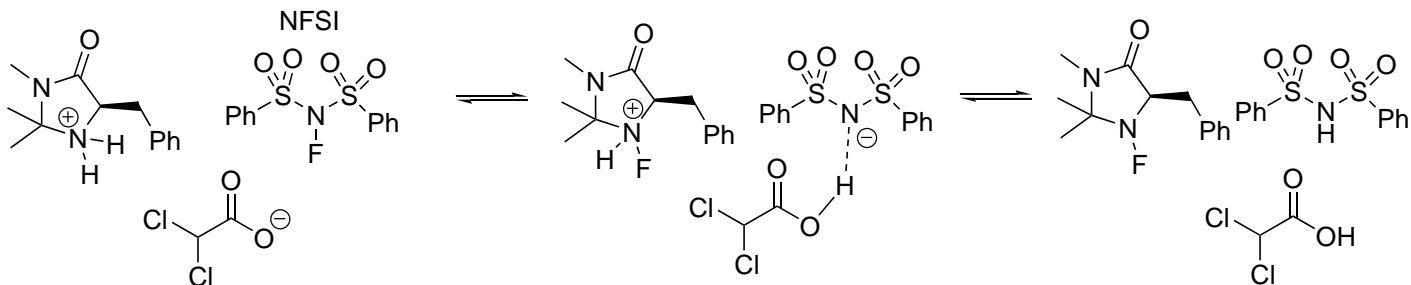
#### 5. A FluorUsual Suspect

The devious MacMillian (or perhaps MacFluorian), developed this organocatalytic enantioselective fluorination:



a. In the paper they propose this proceeds via enamine catalysis, draw the enantiodetermining transition state:

b. One could envision other possible mechanisms, predict the equilibrium:



c. In the introduction they tote these alpha-fluoroaldehydes as valuable synthons; however, in order to determine the enantiomeric excess the aldehydes were first reduced with NaBH<sub>4</sub>. Why? Would you have done the same?