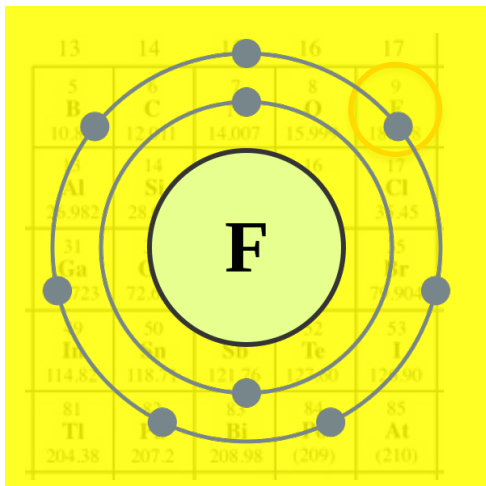


# Exotic Molecules Using F-Chemistry

Synthetic methodologies for organofluorine compounds has been important because introduction of the fluorinated functional groups has been quite useful for medicinal, agrochemical, and materials developments. The introduction of fluoro-functional groups into the lead or seed organic compounds has been one of the required approaches to improve/express the desired characteristics . In addition, one promising approach for stabilizing the strained molecular skeleton is to employ electron-withdrawing perfluoroalkyl substituents because the atomic p character of this group concentrates toward electronegative substituents (Bent 1961).



**Electronegativity (Pauling): 4.0**

**Ionization energy: 1680 kJ mol<sup>-1</sup>**

**Electron affinity: -328.1 kJ mol<sup>-1</sup> (Cl: -348.5)**

**Bond-dissociation energy (F<sub>2</sub>): 158.8 kJ mol<sup>-1</sup> (I<sub>2</sub>: 151.1)**

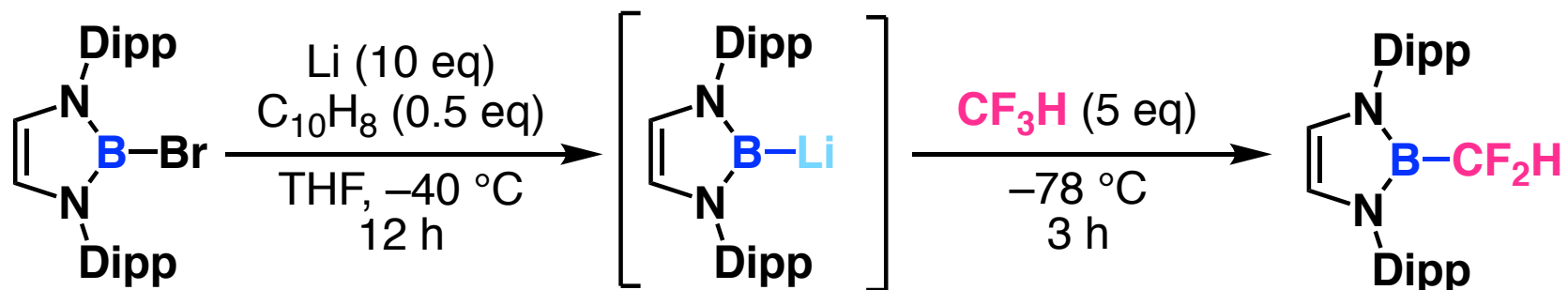
**van der Waals radius: 135 pm (H: 120 pm)**



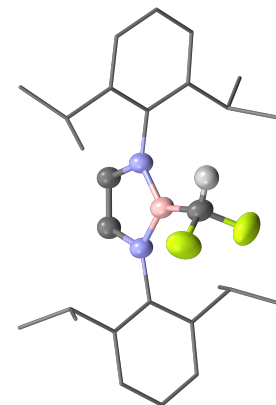
***Mimic effect = Bioisosteres***

# Difluoromethylboron Skeleton ( $\text{BCF}_2\text{H}$ )

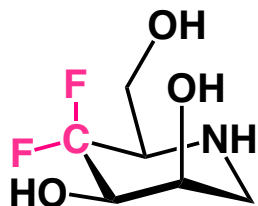
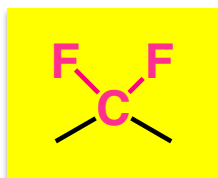
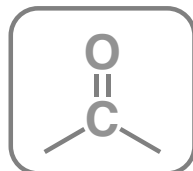
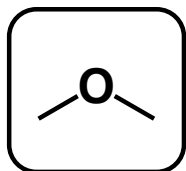
Chem. Commun. 2017, 53, 5546.



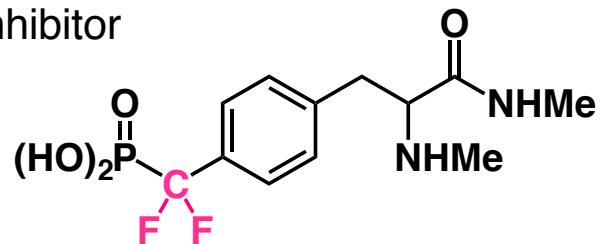
Dipp = 2,6-*i*Pr<sub>2</sub>C<sub>6</sub>H<sub>3</sub>



## Bioisosteres : Examples



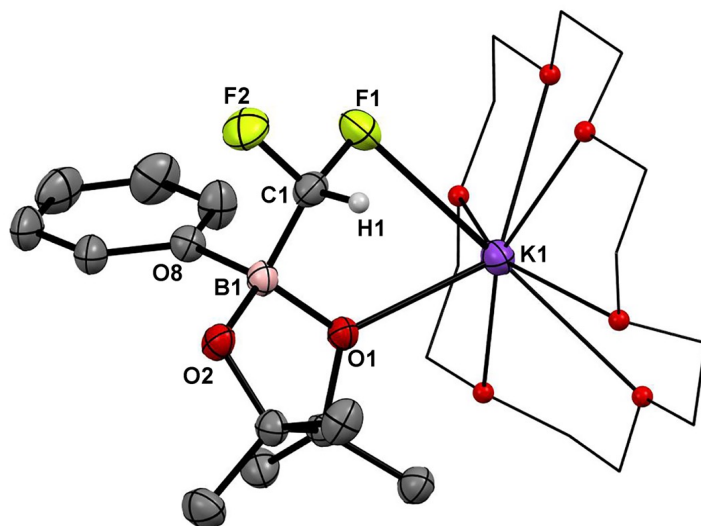
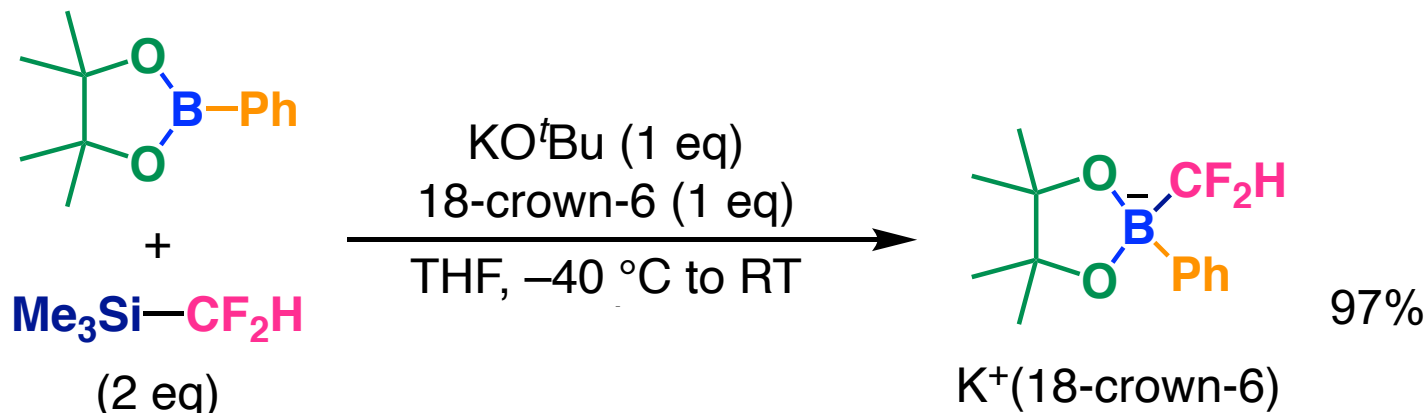
Glycosidase inhibitor



PTP inhibitor

# Reaction of pinBPh for a CF<sub>2</sub>H-Borate

## Use of Silicate Intermediate



## Bond distances (Å)

B1-C1 1.619(7)

B1-C8 1.624(6)

B1-O1 1.498(6)

B1-O2 1.475(6)

**O1-K1 2.637(3)**

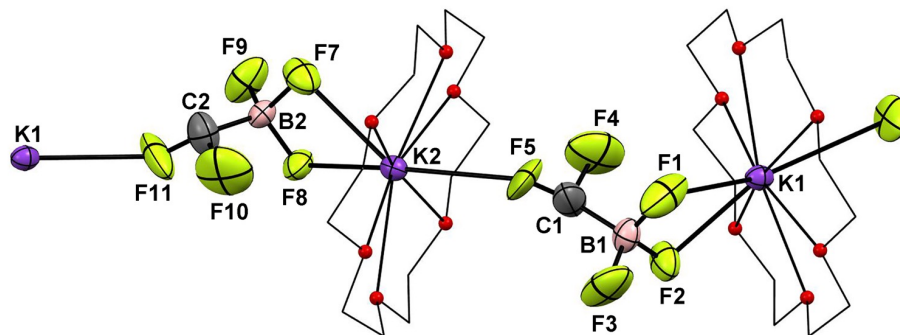
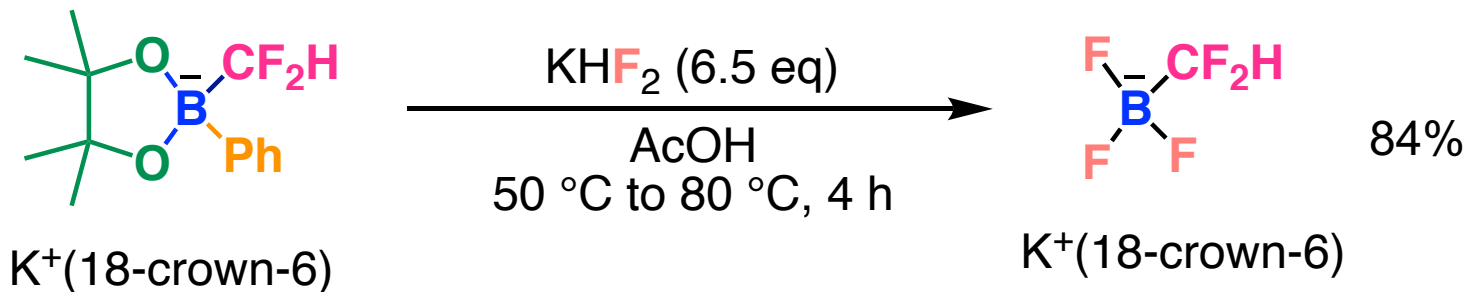
C1-F1 1.406(5)

C1-F2 1.399(5)

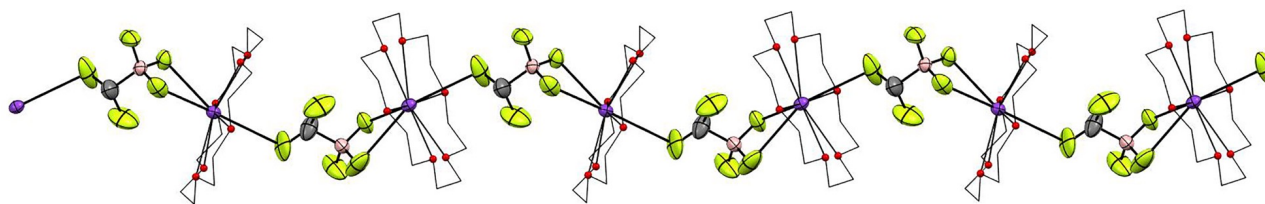
**F1-K1 3.020(3)**

(*T* = 166 K)

# $[F_3B-CF_2H]^- K^+(18-crown-6)$



Monoclinic,  $P2_1/c$  (#14)  
 $a = 15.6623(11)$   
 $b = 16.2527(11)$   
 $c = 17.1082(18)$  Å  
 $\beta = 117.174(2)^\circ$   
 $V = 3875.0(6)$  Å<sup>3</sup>  
 $Z = 8$   
 $R1 = 0.0666$  ( $I \geq 2\sigma(I)$ )  
 $wR = 0.1890$  (all data)

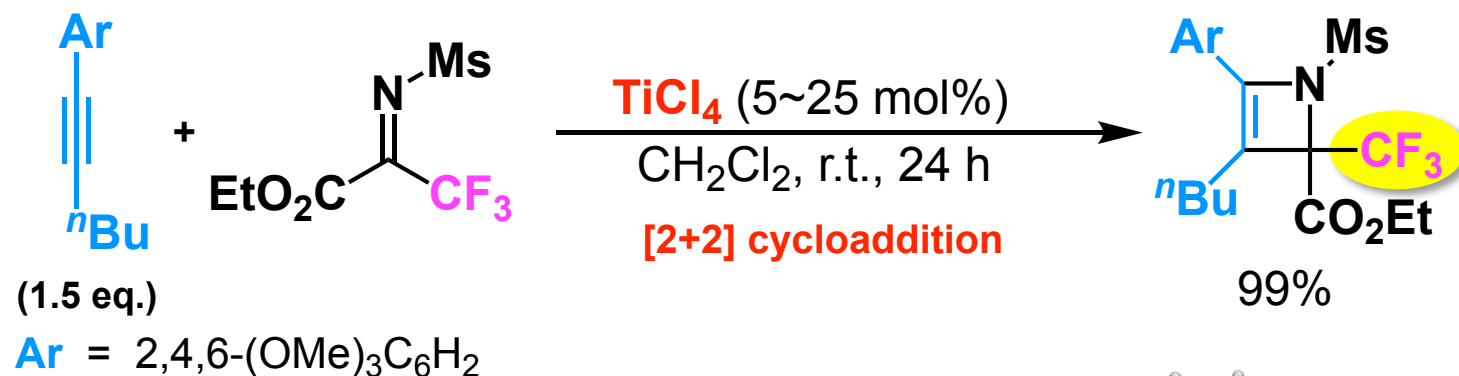


(along  $a$  axis)

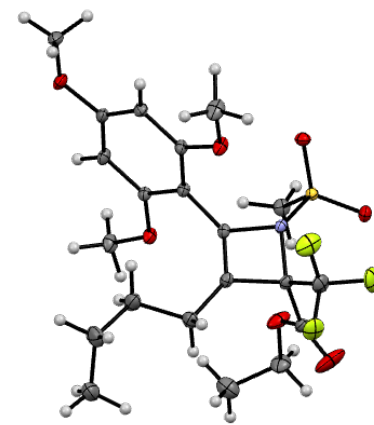
# Ti-Mediated [2+2] Cycloaddition



2-azetine



Electron-withdrawing  $\text{CF}_3$  group stabilizes the 2-azetine skeleton.



X-ray structure