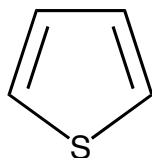
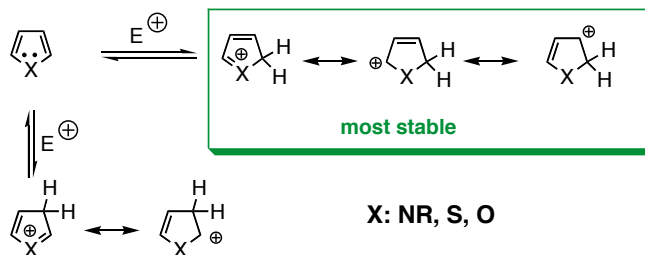


# THIOPHENES



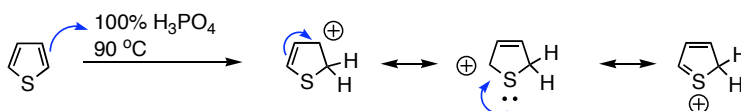
## Reactions with electrophiles at C

Preferably at C-2 / C-5 (cf pyrroles)



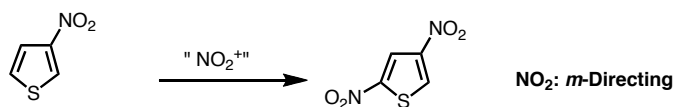
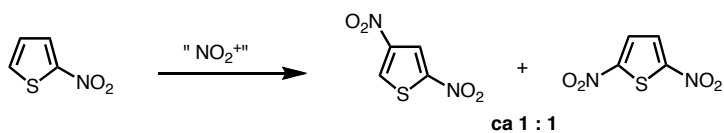
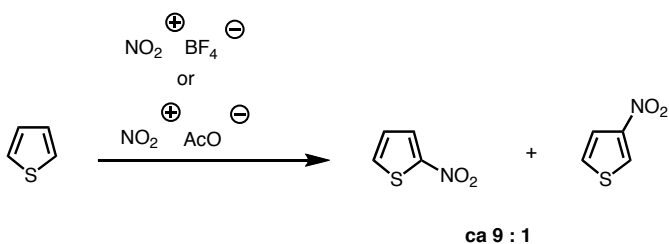
## -Protonation

- Much more stable under acidic conditions than pyrroles and furans
- Protonation at C-2 / C-5



## -Nitration

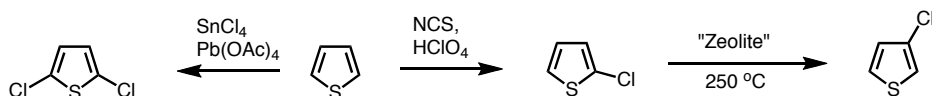
- Not complete selectivity
- Not HNO<sub>3</sub> (explosions)



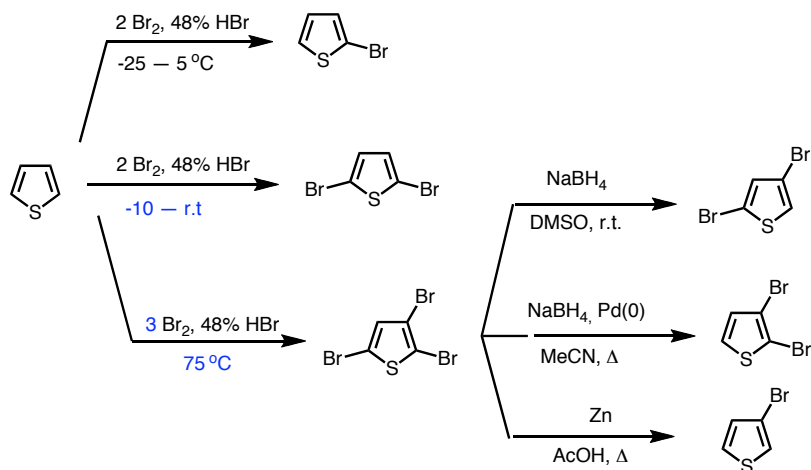
## -Halogenation

ca  $10^8$  times more reactive than PhH

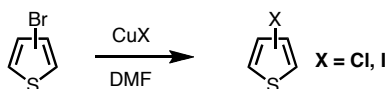
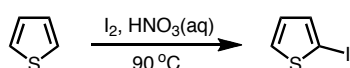
### Chlorination



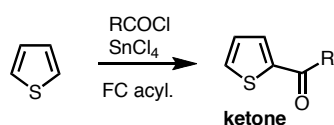
### Bromination



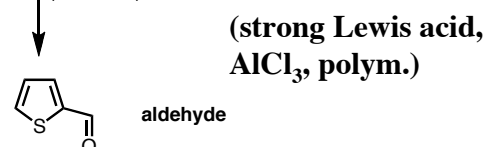
### Iodination



### -Acylation (FC alkylation not good react)

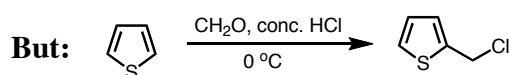
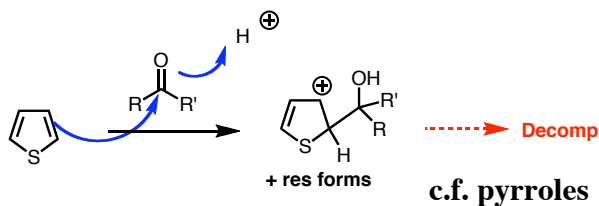


POCl<sub>3</sub>, DMF  
(Vilsmeier)



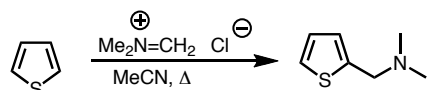
(strong Lewis acid,  
AlCl<sub>3</sub>, polym.)

### -Condensation with carbonyl comps



### -Condensation with imines / iminium ions - Mannich react.

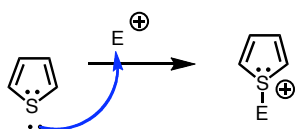
Thiophene (and furan): Preformed reagent generally required



(in case of pyrrol, Mannich reagent generated *in situ*)



## Reactions with electrophiles at Sulfur



- Possible for thiophene; S in 3rd row
- Not possible for furan / pyrrole; O and N in 2nd row
- Probably  $sp^3$  S. tetrahedral
- Works best for electron rich thiophenes

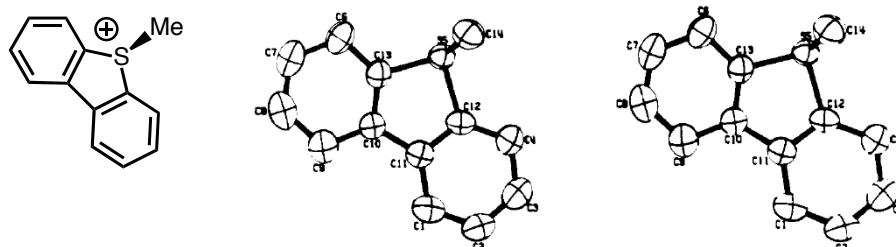
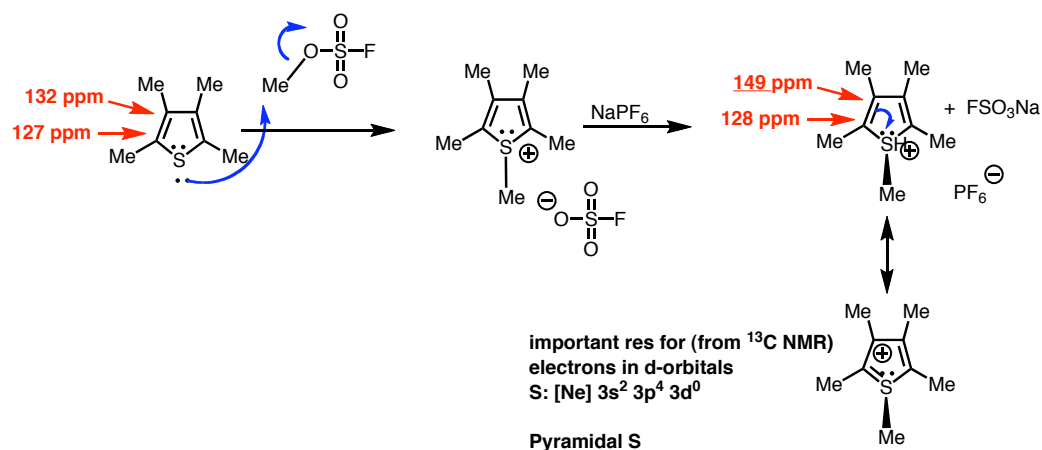
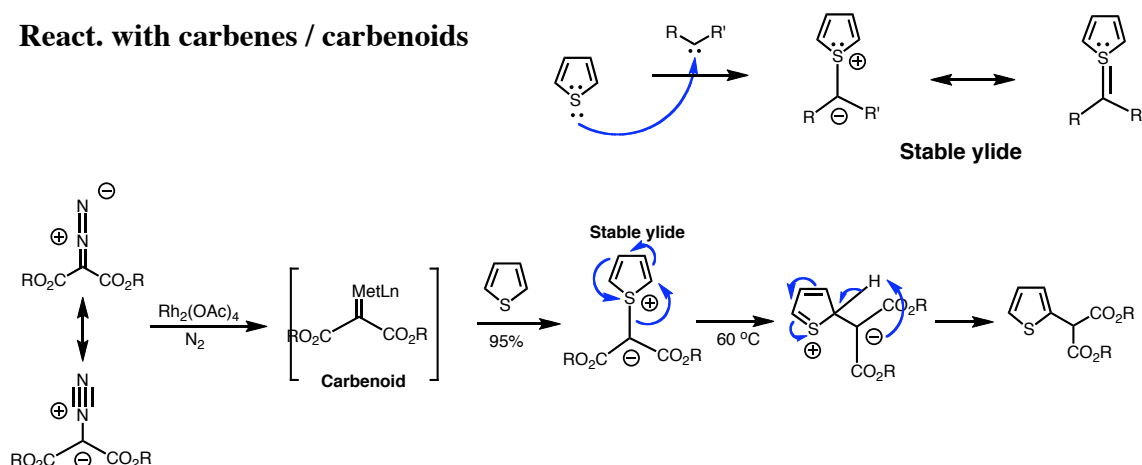
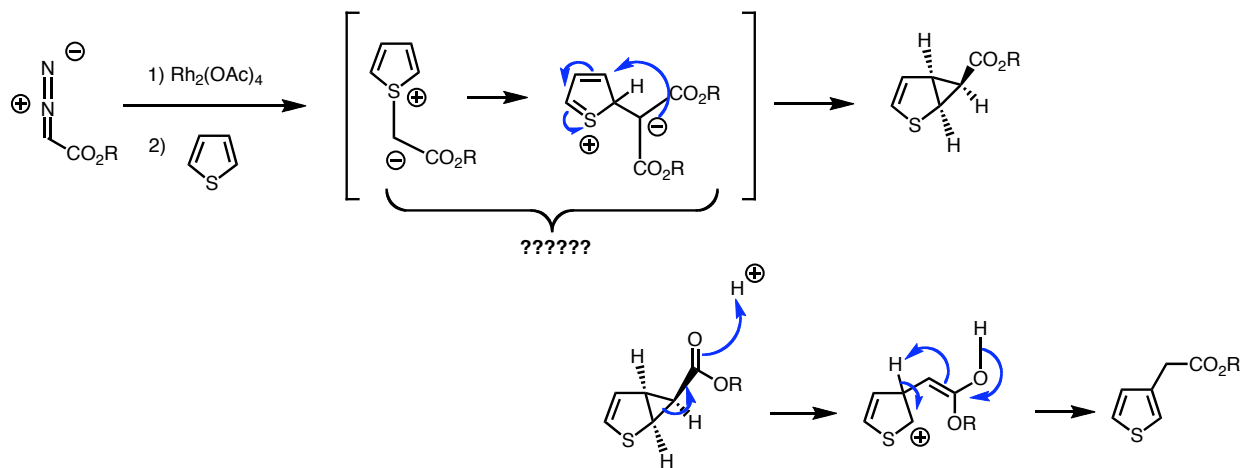


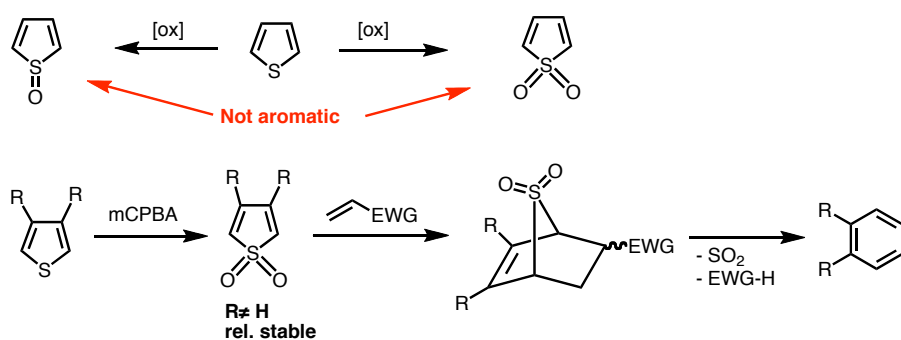
Figure 1. Stereoscopic representation of 5-methylbenzothiophenium tetrafluoroborate (1).

## React. with carbenes / carbenoids



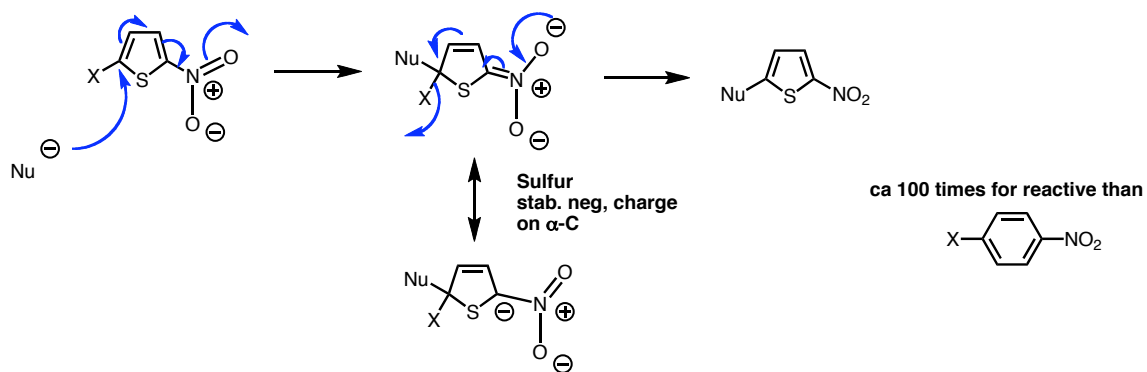


### Sulfoxides and sulfones

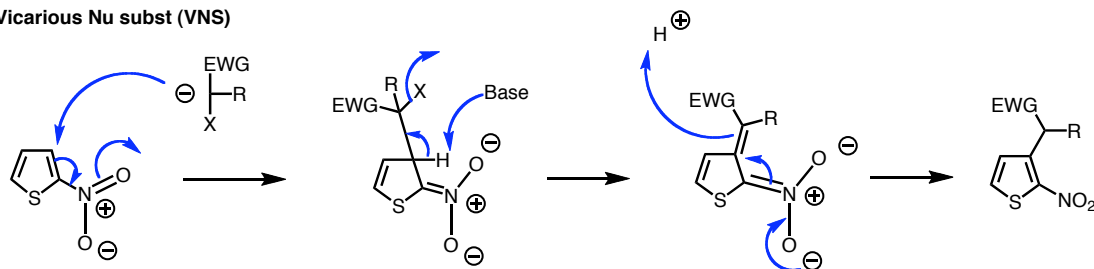


### Reactions with nucleophiles

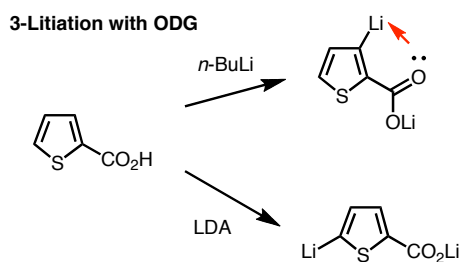
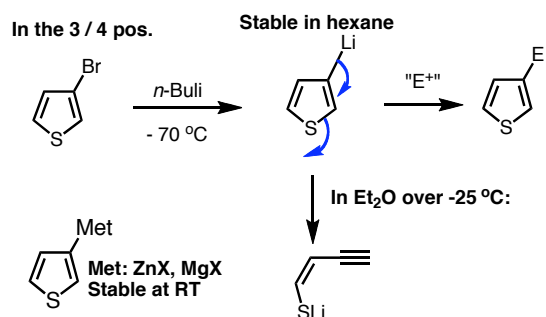
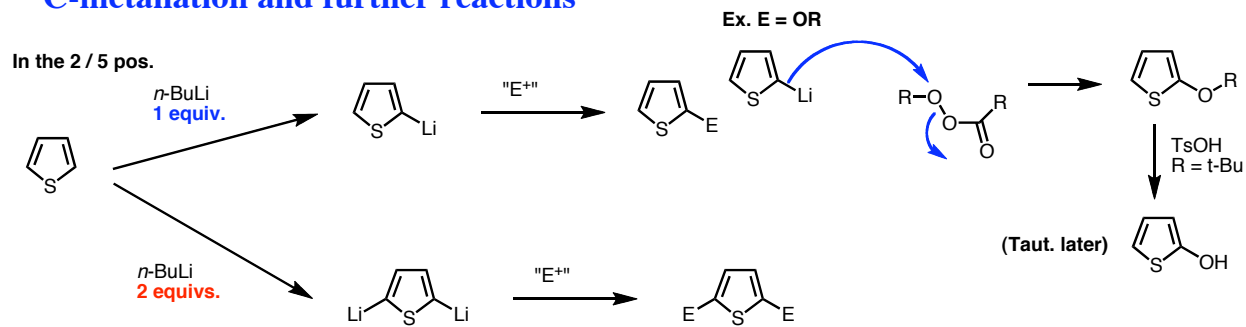
NB! Electron rich Aryl



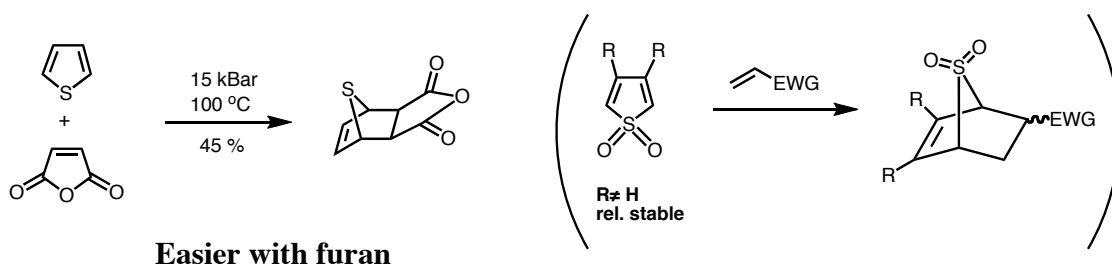
### Vicarious Nu subst (VNS)



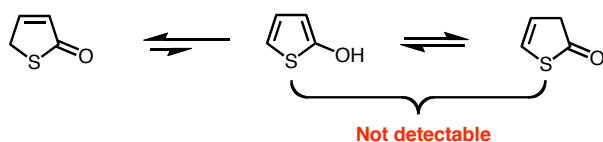
## C-m metallation and further reactions



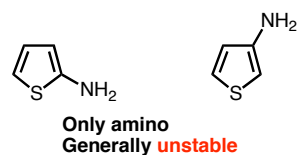
## Cycloadditions



## Oxythiophenes

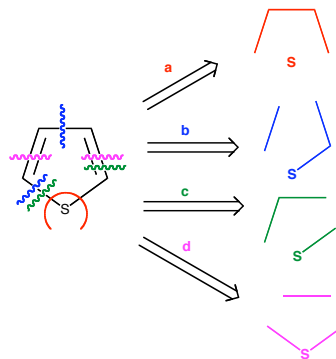


## Aminothiophenes

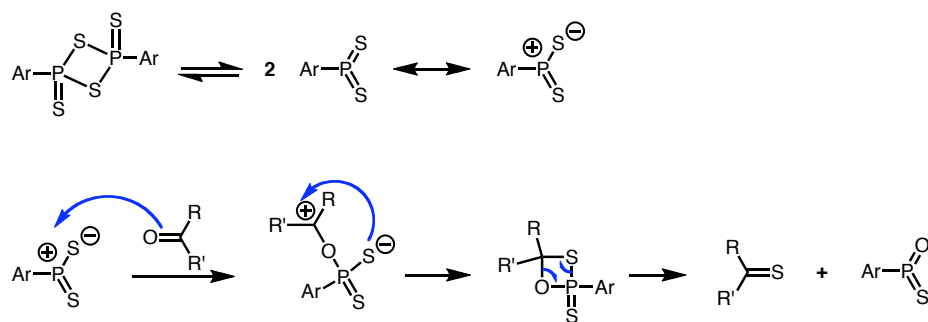
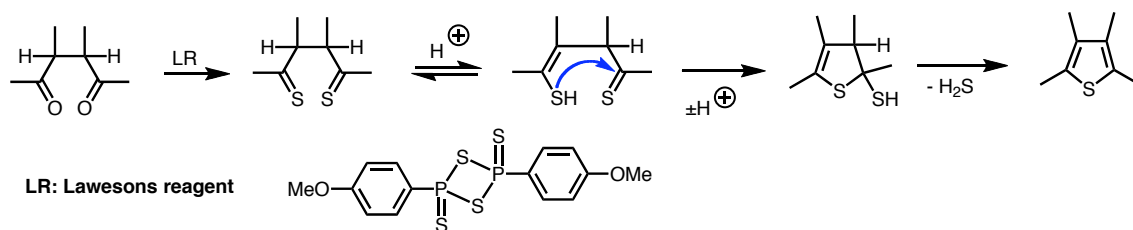


# Synthesis of Thiophenes

## Carbonyl condensations



### Strategy a



## Cycloadditions

