

**B.Sc. Semester-VI  
Organic Chemistry  
Paper-XIV**



**3. Heterocyclic Compounds**

**Coverage:**

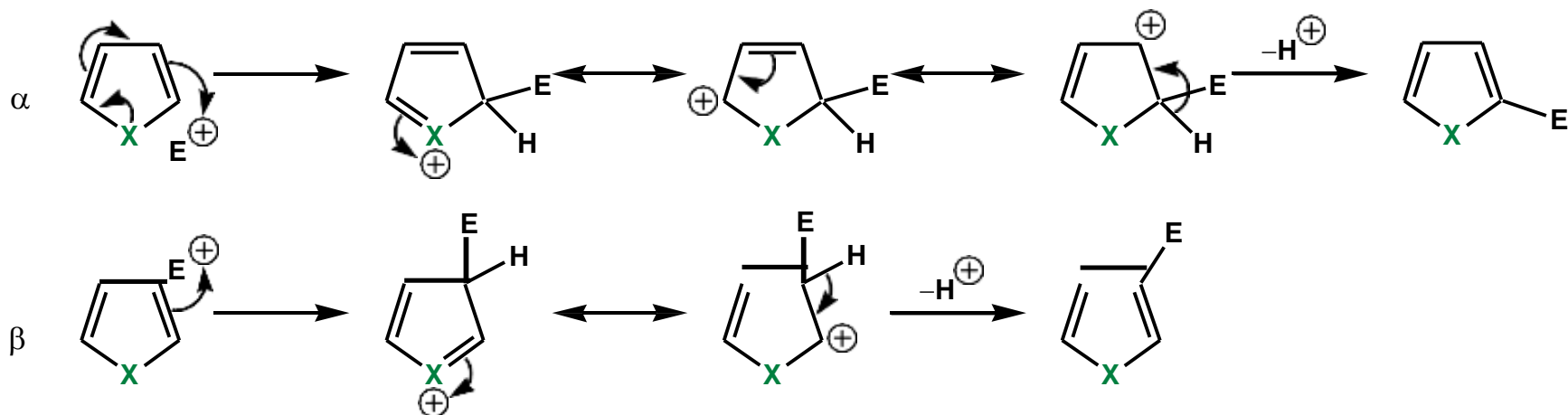
5. Furan, Pyrrole and Thiophene : (i) Electrophilic Substitution Reactions  
(ii) Deprotonation/Direct Metallation



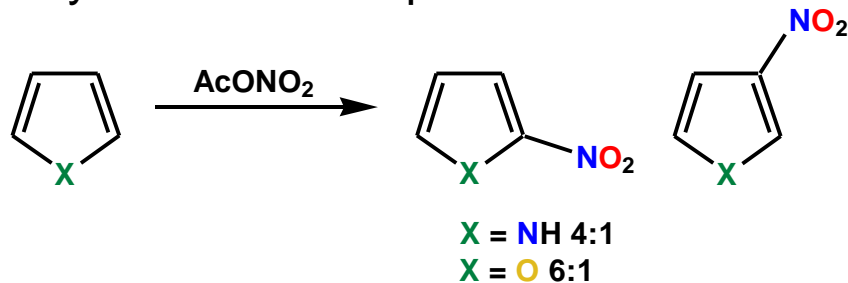
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# Furans, Pyrroles and Thiophenes – Electrophilic Substitution

## Electrophilic Substitution – Regioselectivity

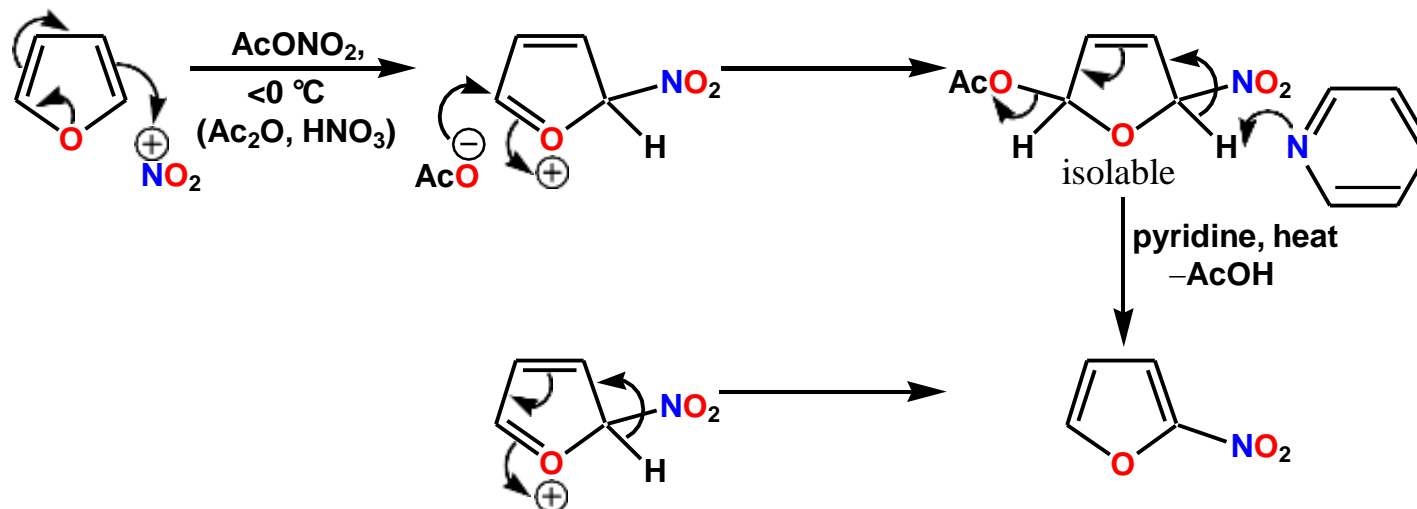


- Pyrrole > furan > thiophene > benzene
- Thiophene is the most aromatic in character and undergoes the slowest reaction
- Pyrrole and furan react under very mild conditions
- $\alpha$ -Substitution favoured over  $\beta$ -substitution more resonance forms for intermediate and so the charge is less localised (also applies to the transition state)
- Some  $\beta$ -substitution usually observed – depends on X and substituents



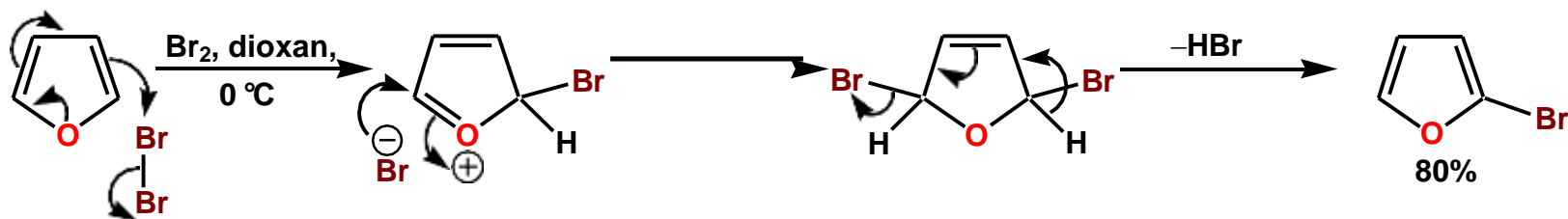
# Furans – Electrophilic Substitution

## Nitration of Furans



- Nitration can occur by an addition-elimination process
- When  $\text{NO}_2\text{BF}_4$  is used as a nitrating agent, the reaction follows usual mechanism

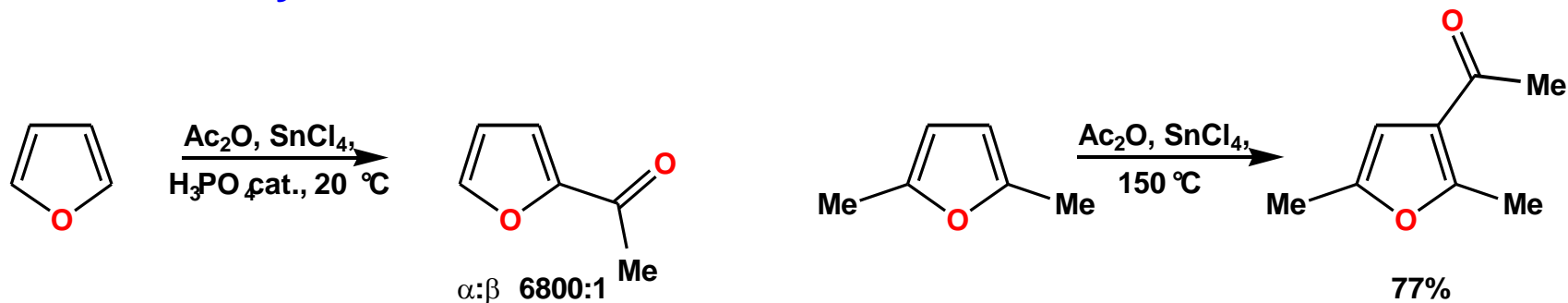
## Bromination of Furans



- Furan reacts vigorously with  $\text{Br}_2$  or  $\text{Cl}_2$  at room temp. to give polyhalogenated products
- It is possible to obtain 2-bromofuran by careful control of temperature

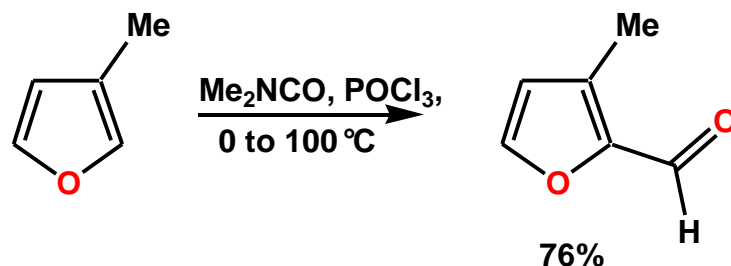
# Furans – Electrophilic Substitution

## Friedel-Crafts Acylation of Furan

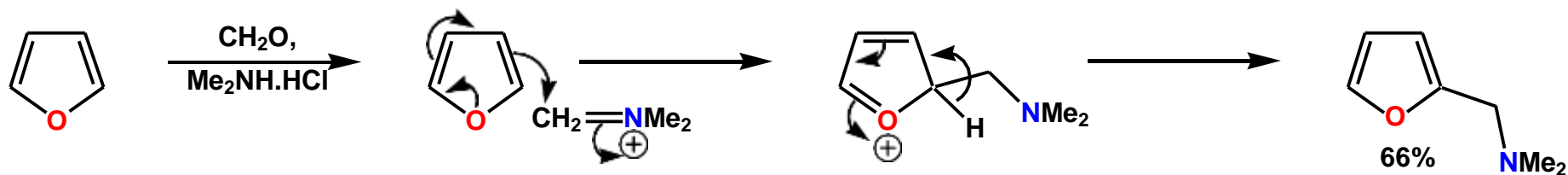


- Blocking groups at the  $\alpha$  positions and high temperatures required to give  $\beta$  acylation

## Vilsmeier Formylation of Furan

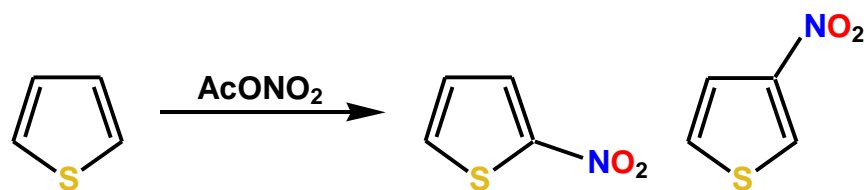


## Mannich Reaction of Furans



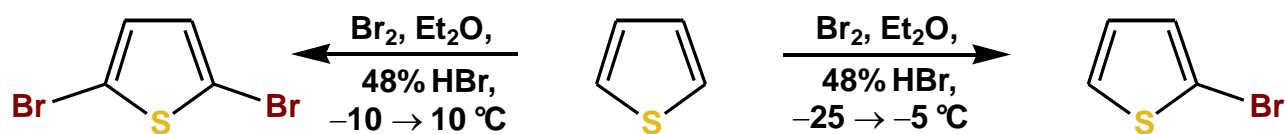
# Thiophenes – Electrophilic Substitution

## Nitration of Thiophenes



- Reagent AcONO<sub>2</sub> generated *in situ* from c-HNO<sub>3</sub> and Ac<sub>2</sub>O

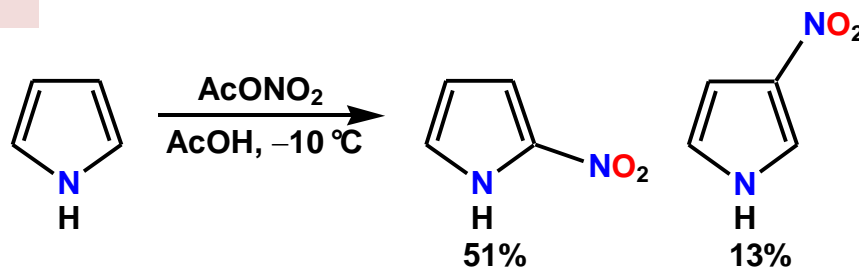
## Halogenation of Thiophenes



- Occurs readily at room temperature and even at -30 °C
- Careful control of reaction conditions is required to ensure mono-bromination

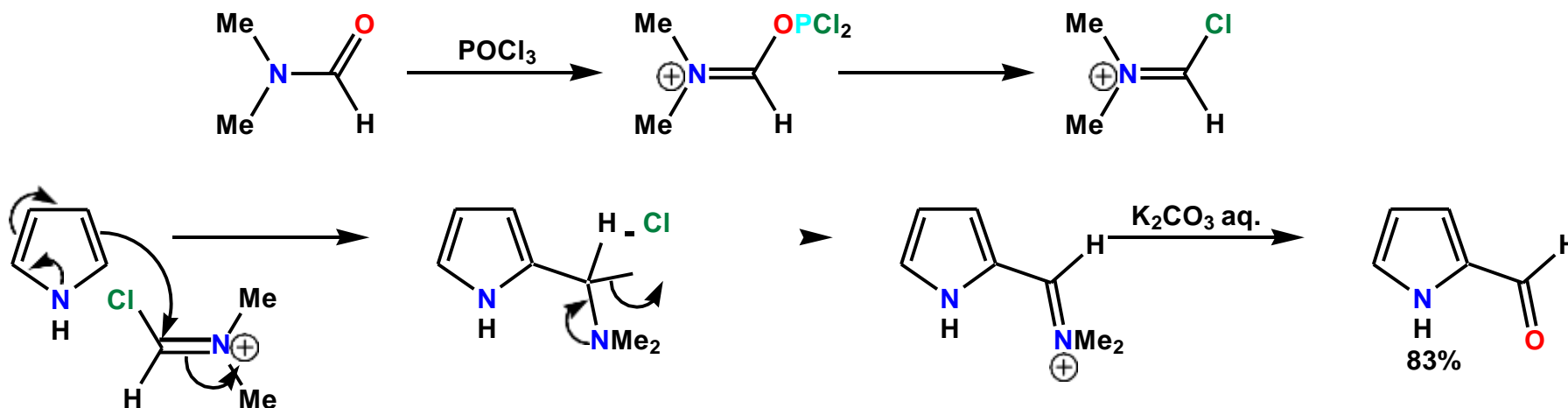
# Pyrroles – Electrophilic Substitution

## Nitration of Pyrroles

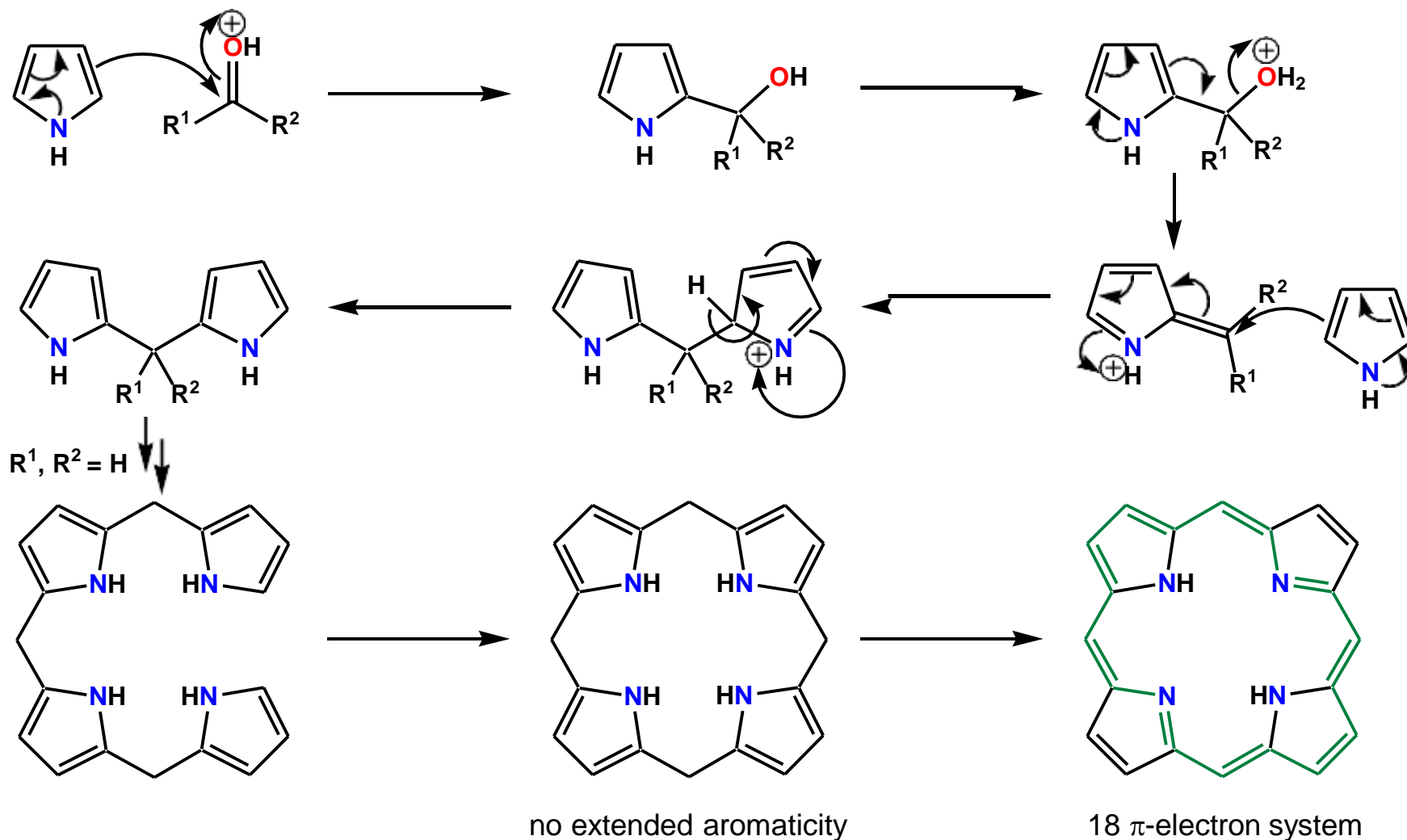


- Mild conditions are required ( $\text{c-HNO}_3$  and  $\text{c-H}_2\text{SO}_4$  gives decomposition)

## Vilsmeier Formylation of Pyrroles



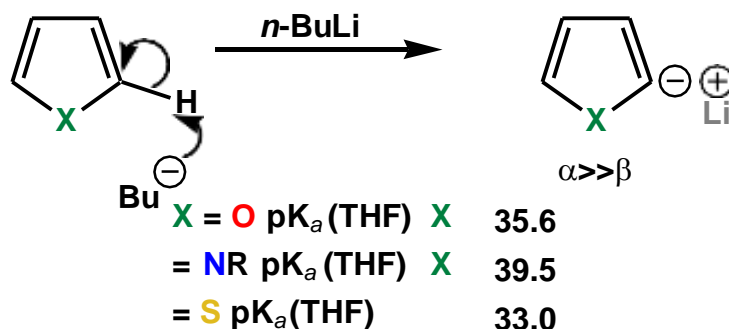
## Pyrroles – Porphyrin Formation



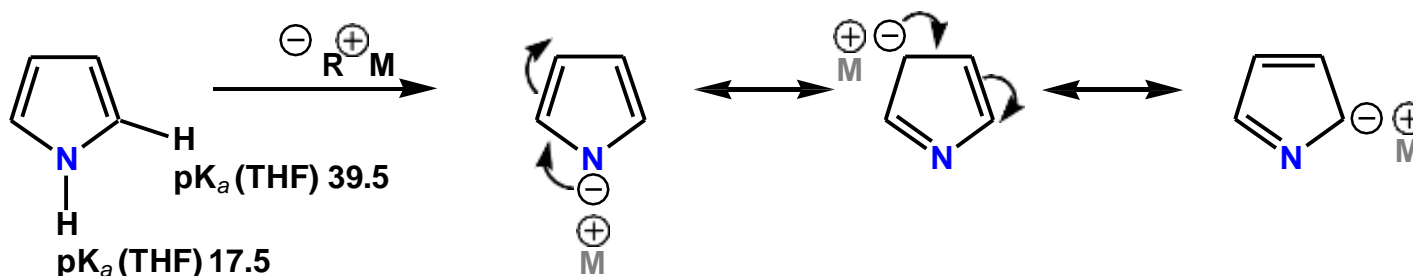
- The extended aromatic 18  $\pi$ -electron system is more stable than that having four isolated aromatic pyrroles

# Furans, Pyrroles Thiophenes – Deprotonation

## Metallation



## Deprotonation of Pyrroles

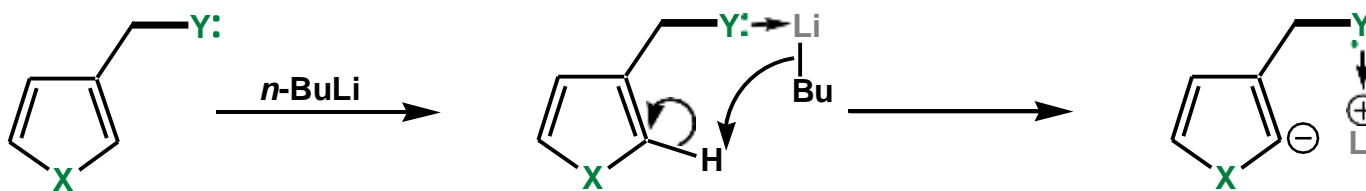


- Free pyrroles can undergo *N* or *C* deprotonation
- Large cations and polar solvents favour *N* substitution
- A temporary blocking group on *N* can be used to obtain the *C*-substituted compound



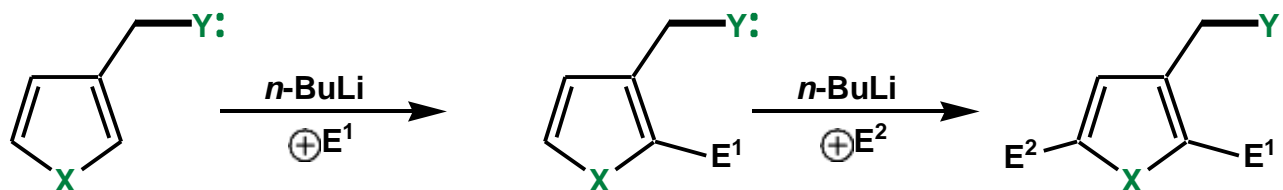
# Furans, Pyrroles Thiophenes – Directed Metallation

## Control of Regioselectivity in Deprotonation



Common directing groups: CO<sub>2</sub>H(Li), CH<sub>2</sub>OMe, CONR<sub>2</sub>, CH(OR)<sub>2</sub>

## Synthesis of $\alpha,\alpha'$ -Disubstituted Systems



## Use of a Trialkylsilyl Blocking Group

