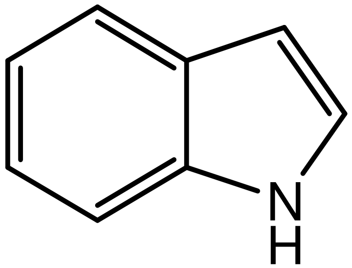
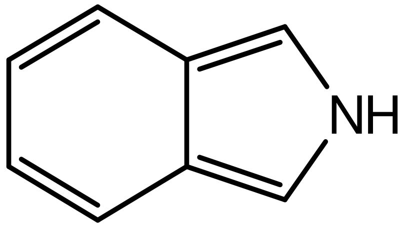
Indole and Isoindole



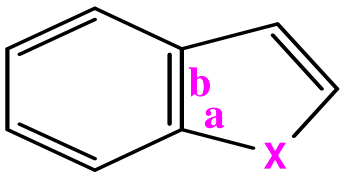


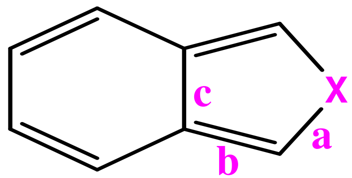
SAYANWITA PANJA
DEPT. OF CHEMISTRY
SHAHID MATANGINI HAZRA GOVT. GENERAL DEGREE COLLEGE FOR WOMEN

Introduction

- As a result of the fusion between benzene ring and 5-memebered heterocyclic ring there are two possible aromatic structures differ in position of fusion:

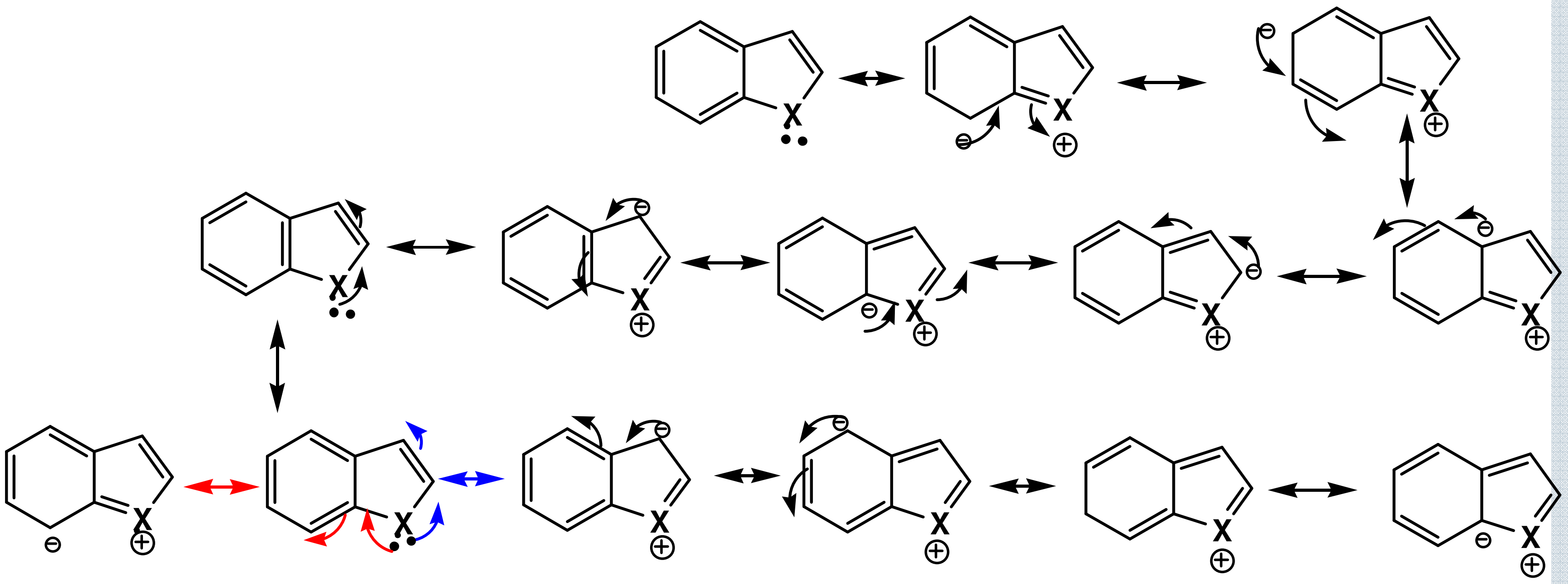
(a) Indole and its analogs **(b) Isoindole and its analogs**





(a)	X =	(b)
Indole	N	Isoindole
Benzo[b]thiophene	S	Benzo[c]thiophene
Benzo[b]furan	O	Benzo[c]furan

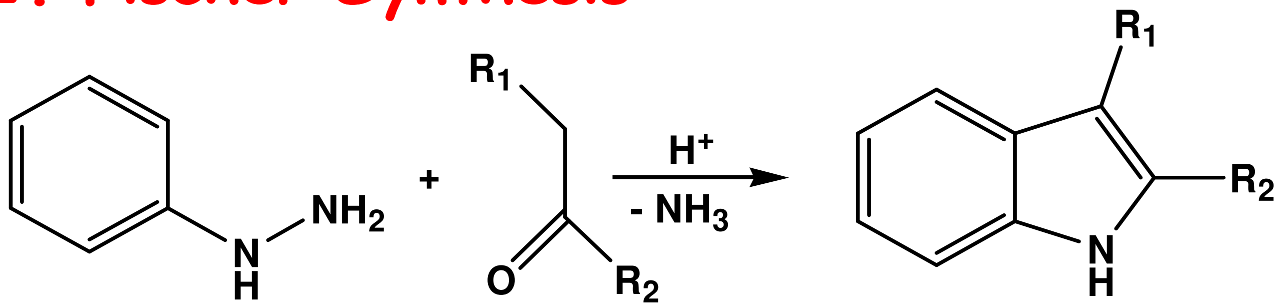
Resonance structures of indole and its analogs



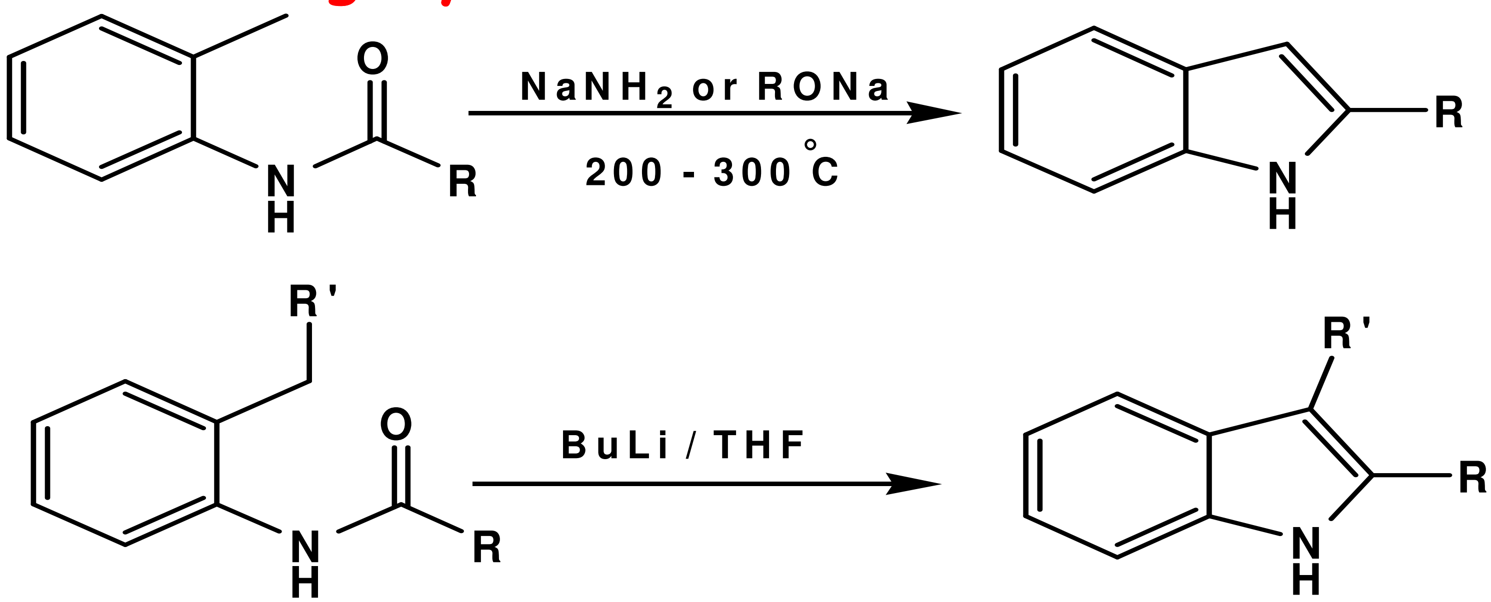
❖It appears from these resonance structures that all C atoms bear – ve. charge while the hetero atom bears + ve. charge

Synthesis of Indole

1. Fischer Synthesis



2. Madelung Synthesis



Comparison with pyrrole

- Pyrroles, indoles and isoindoles have a partially positive nitrogen, and partially negative carbons therefore these carbons react easily with electrophilic reagents, and resist substitution by nucleophilic reagents.
- Indoles, like pyrroles are non basic due to if protonation on nitrogen occurs, the aromaticity would be lost. Similar to pyrrole protonation occurs at ring carbons

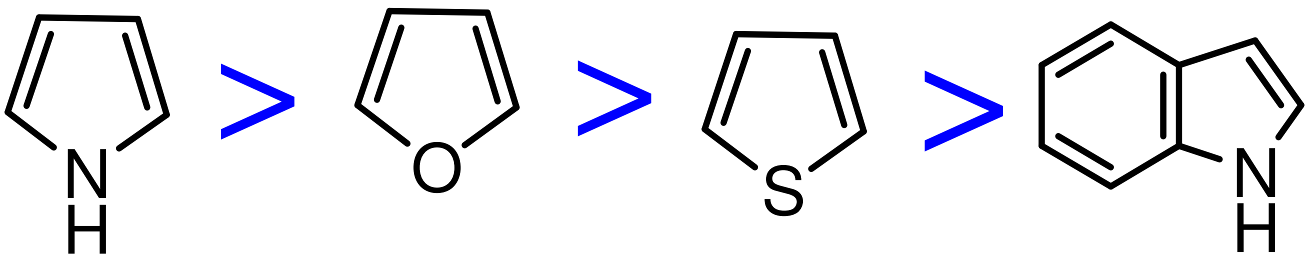
The main differences between indole and pyrrole include:

1. The reactivity order in the electrophilic substitution
2. the regioselectivity in electrophilic substitution

1. The reactivity order in the electrophilic substitution

- Generally indole and its analogs are less reactive compared to the corresponding single heterocyclic rings therefore the electrophilic aromatic substitution is slower with these compounds
- This can be attributed to the fact that the share of each carbon atom of the –ve charge in these compound is lesser due to delocalization of the charge on the benzene (as appeared from the resonance structure of indole.

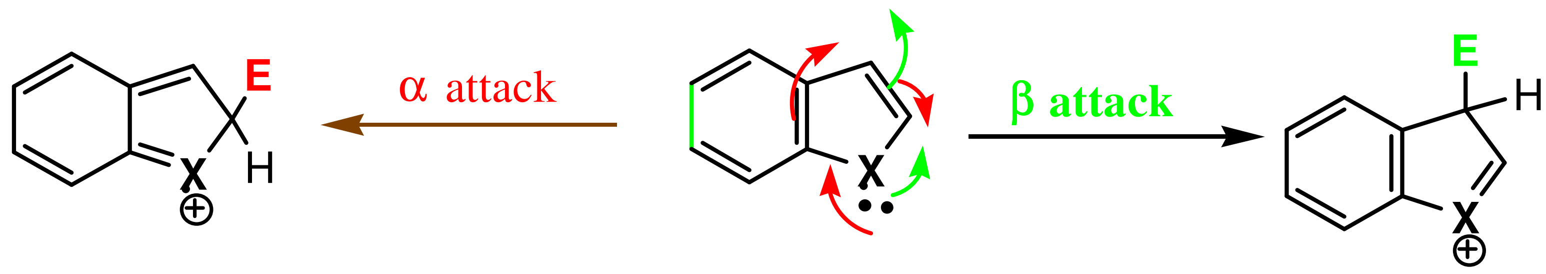
Reactivity order in electrophilic aromatic substitution:



2. The regioselectivity in E. substitution

- Fusion of the benzene ring with heterocyclic rings alter the regioselectivity from the α- position in the single heterocylic compounds (e.g. pyrrole) to β- position in indole
- This β preference in case of indole can be attributed to the extra stability experienced by the cations resulted from β attack (cation I) over that resulted from α attack (cation II). Where the attack at the β position does not disturb the aromaticity of the benzene ring thus the +ve. charge in the intermediate is delocalized round the benzene ring and gets more stabilization.

2. The regioselectivity in E. substitution



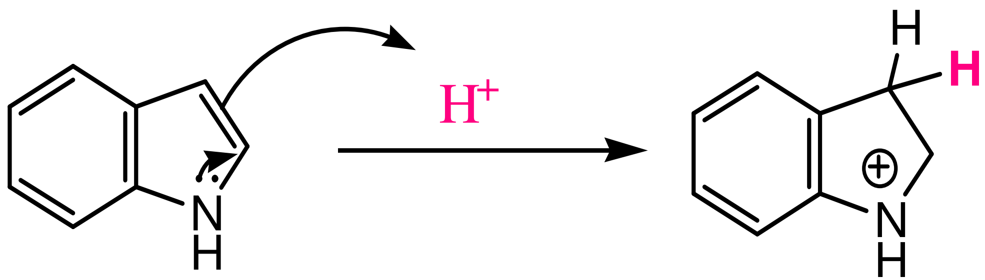
Cation II

Cation I

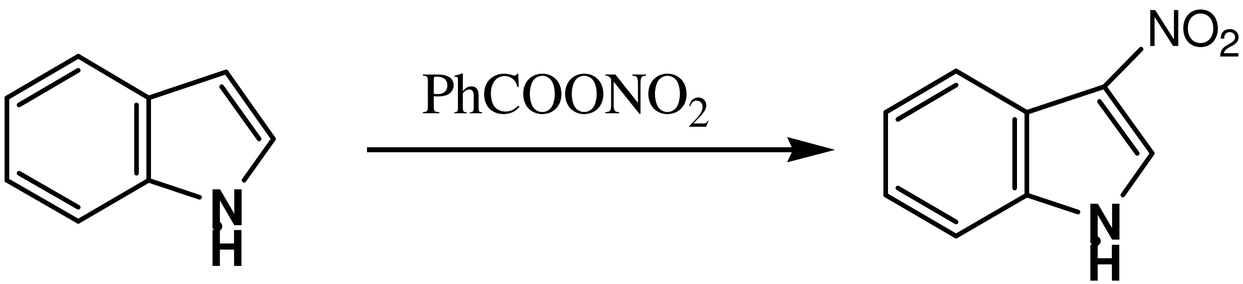
More preferred
the 6-membered ring is aroamtic

Electrophilic substitution reactions

1- Protonation

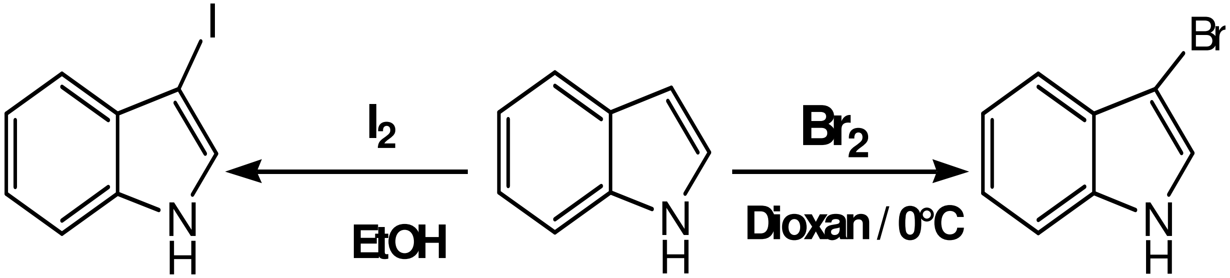


2- Nitration

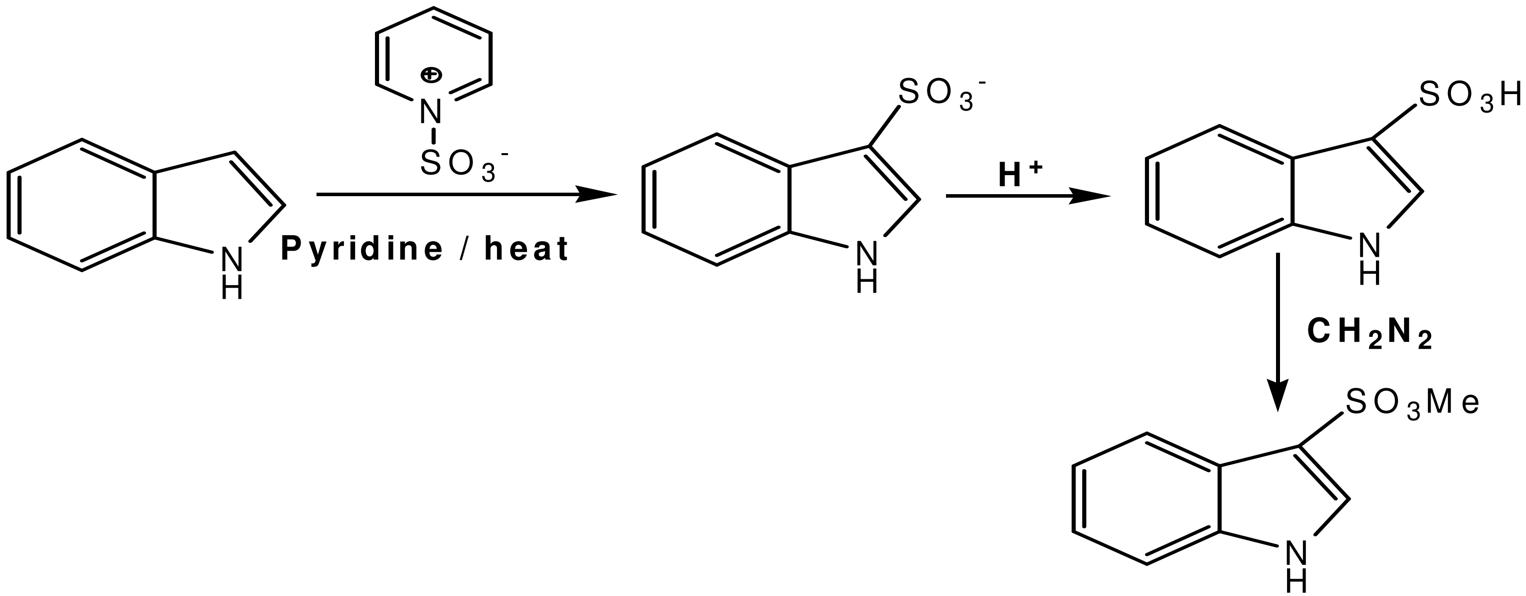


Electrophilic substitution reactions

3- Halogenations

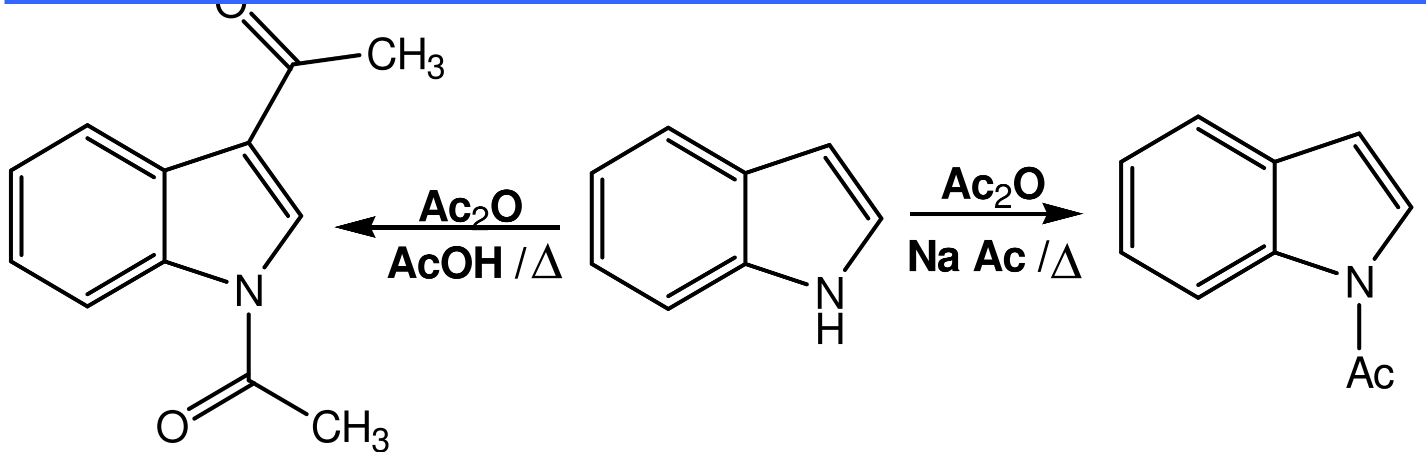


4- Sulphonation

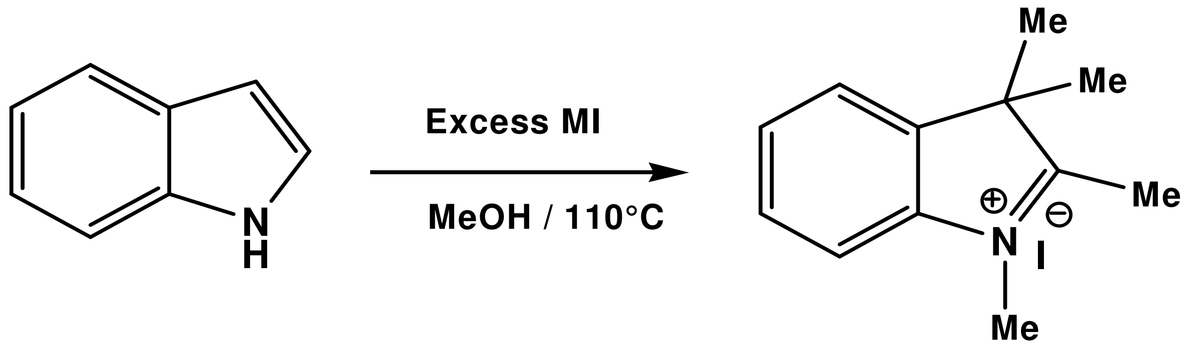


I-Electrophilic substitution reactions

5- Acylation

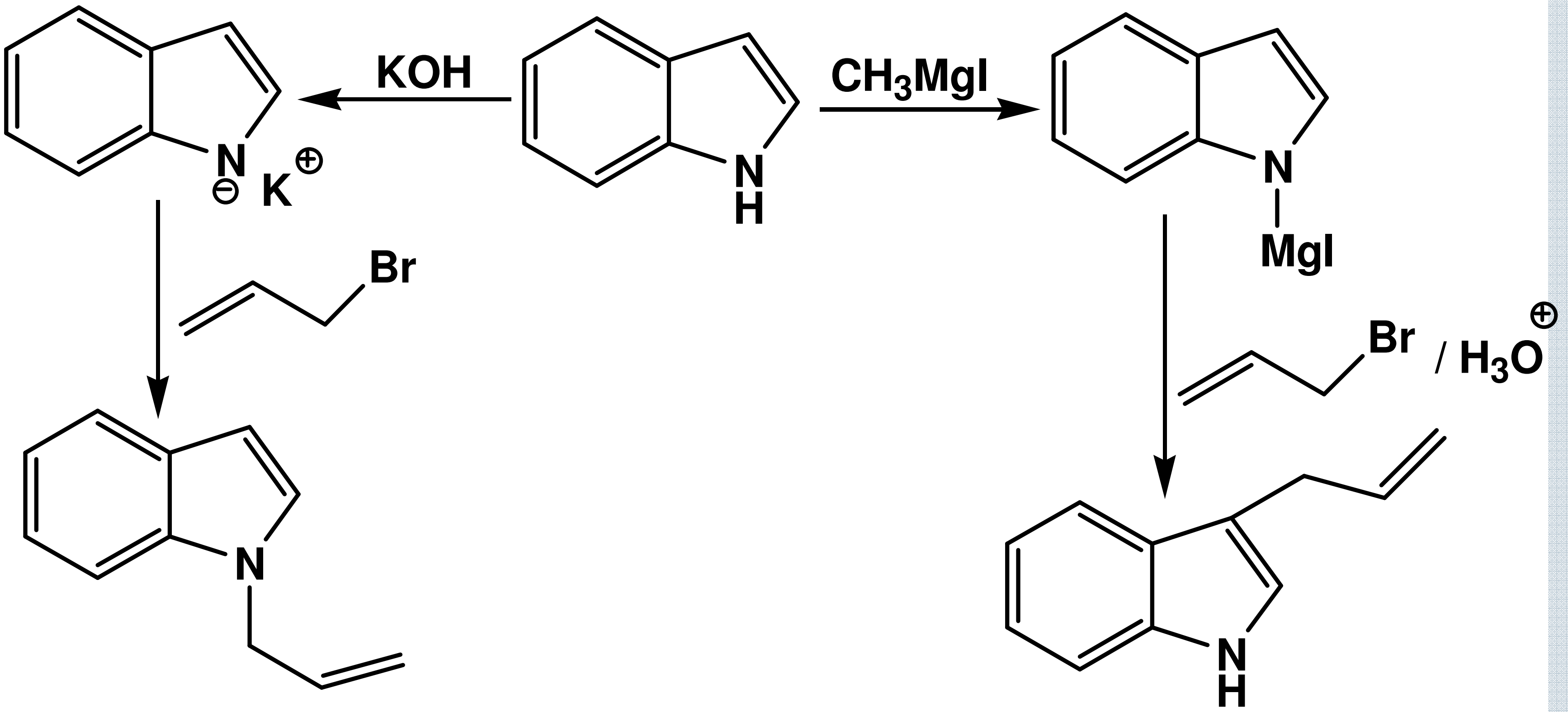


6- Alkylation

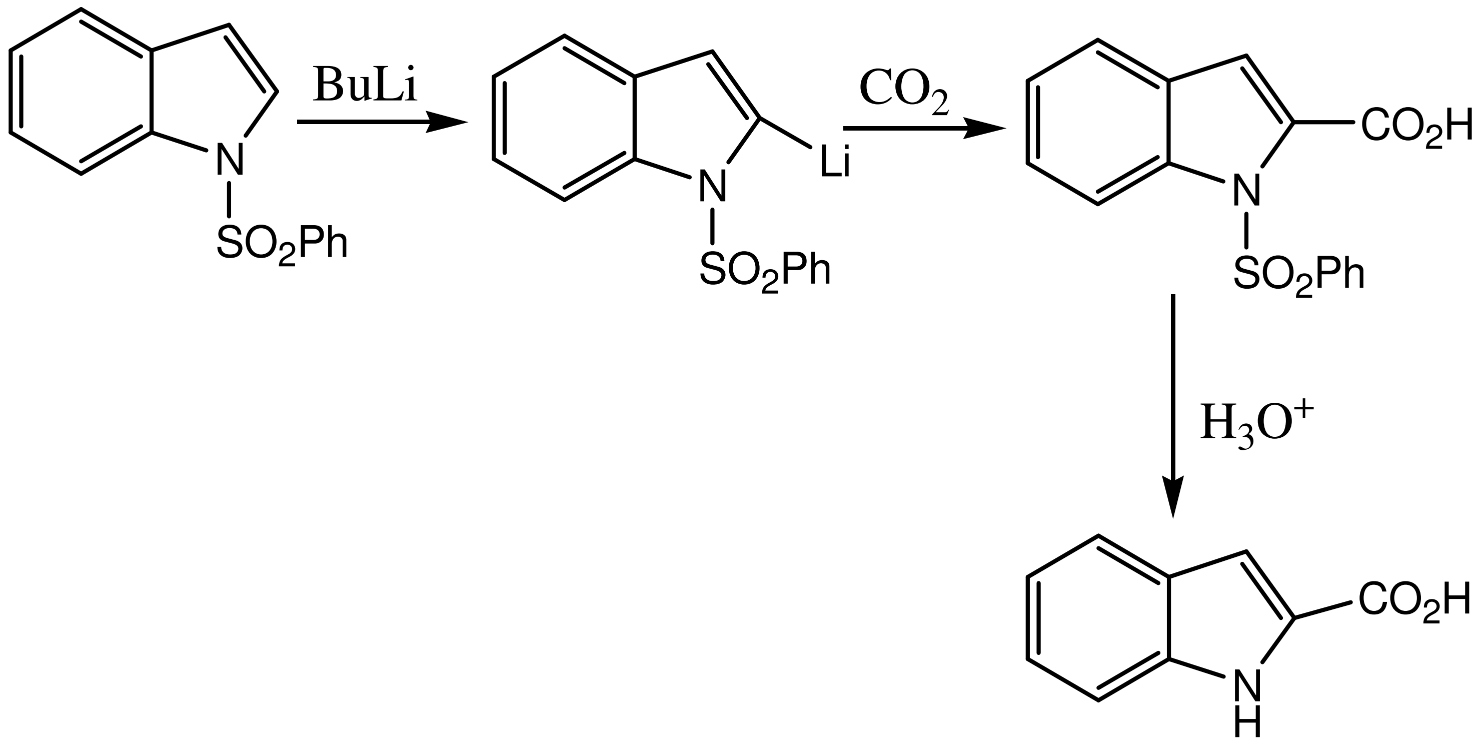


1,2,3,3-Tetramethyl-3*H*-indolium iodide

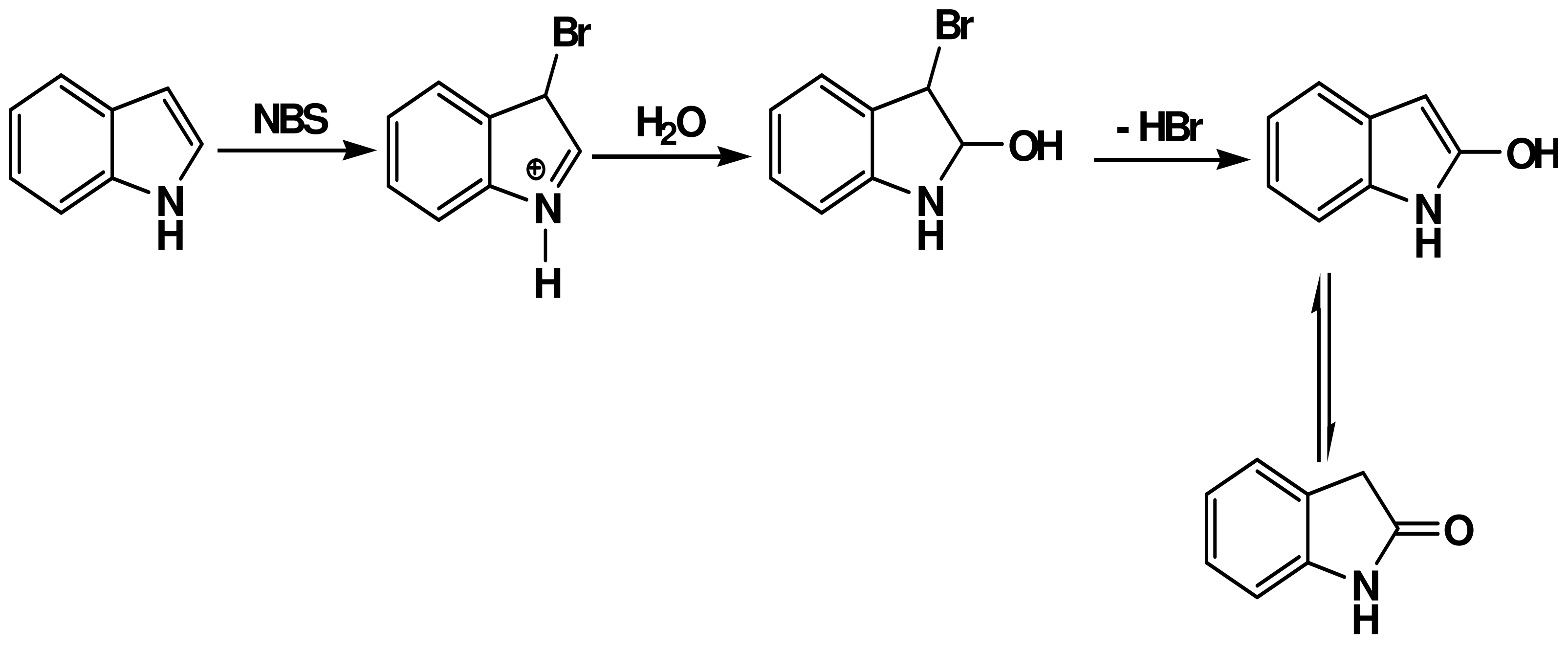
II-Nucleophilic substitution



Nucleophilic substitution

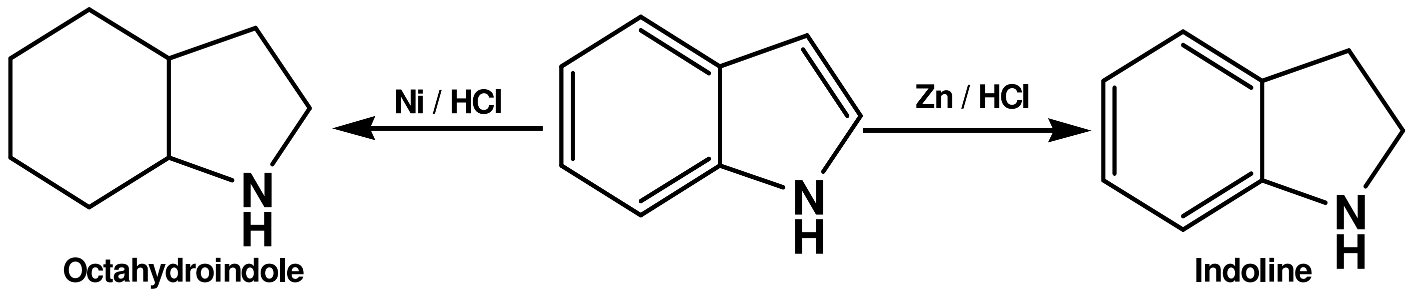


Oxidation of Indole



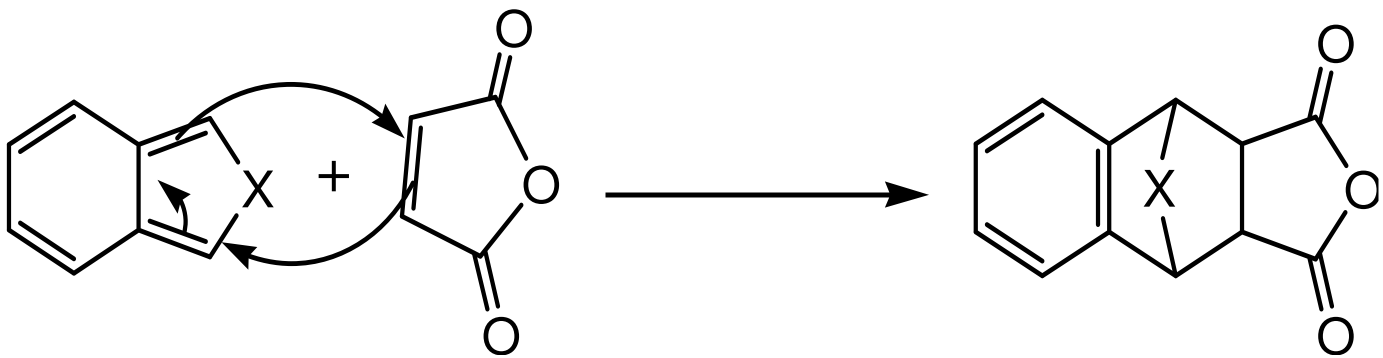
Oxindole

Reduction of Indole



Diels Alder Reaction

- Indole and its analogs do not undergo D.A.R. while isoindole and its analogs do thus this reaction is used to differentiate between these compounds.



Thank You