

Module 3

NUCLEOPHILIC AROMATIC SUBSTITUTION

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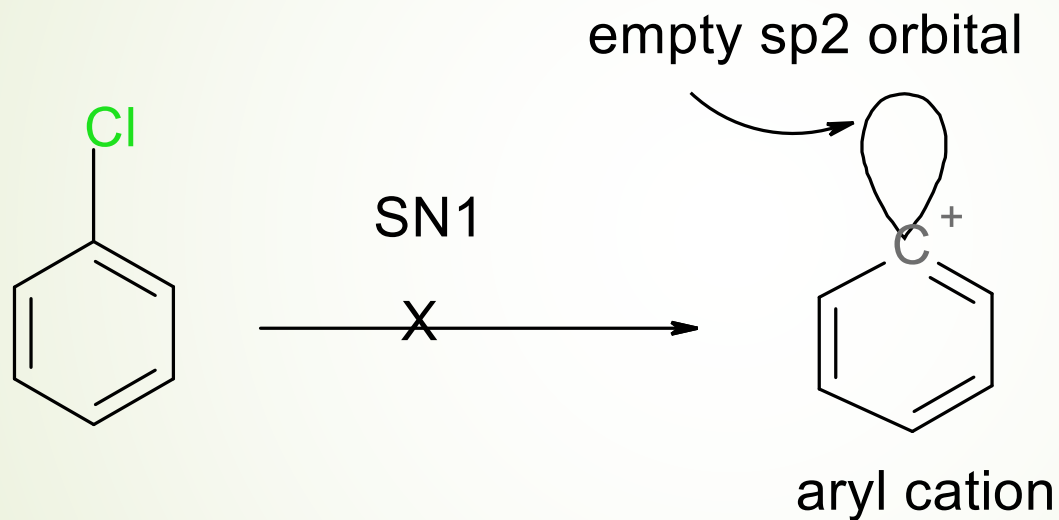
Objectives

After studying this module you will be able to ---

- Discuss the mechanism of nucleophilic substitutions in aromatic compounds.
- Predict the product of an addition elimination mechanism for the given reaction conditions.
- Analyse a given S_NAr mechanism and predict the products formed based on the mechanism.
- Discuss the structure of Benzyne`
- Choose the major and minor product in a given S_NAr reaction.
- Justify the formation of the ipso and cine products in a given S_NAr reaction.

Low reactivity of Aryl halides in S_N1

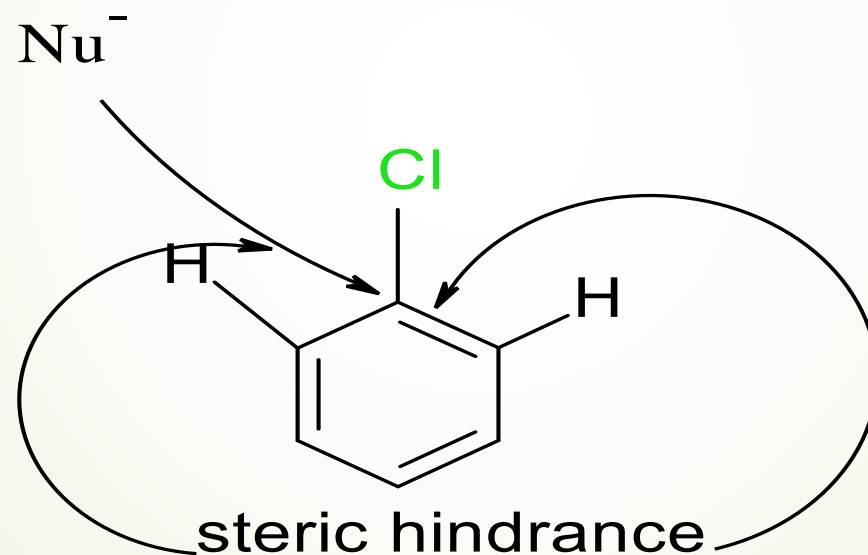
- Aryl halides do not undergo S_N1 reactions because formation of aryl carbocation is difficult for S_N1



- C-Cl bond is very strong so ionisation to form aryl cation not easy.
- Aryl cation is unstable.

Low reactivity of Aryl halides in S_N2

- S_N2 is not possible due to steric hindrance by the phenyl which prevents back side attack

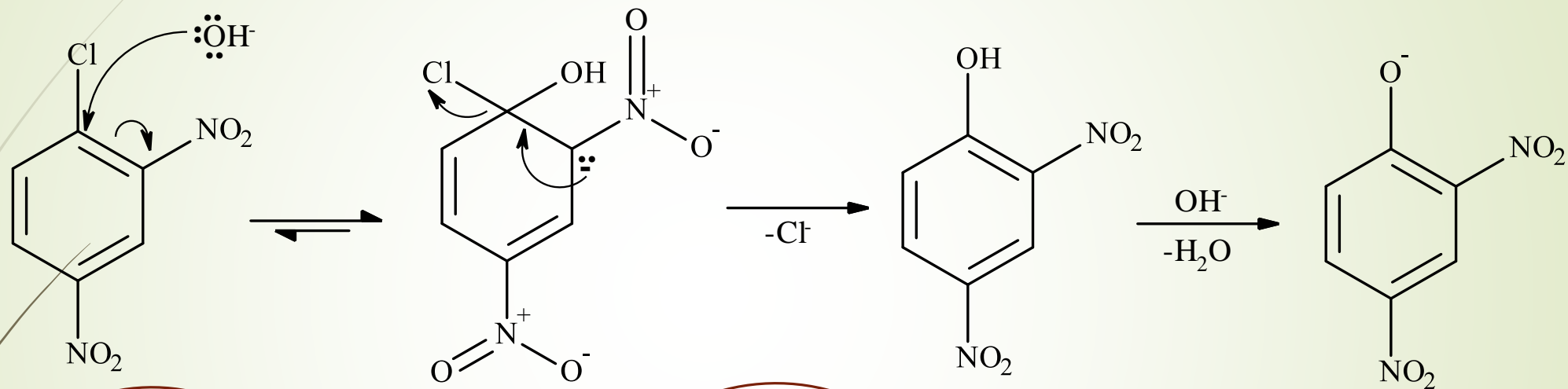


S_NAr mechanism

Two mechanisms for nucleophilic aromatic substitution – S_NAr

- Addition elimination reaction
- Elimination addition reaction

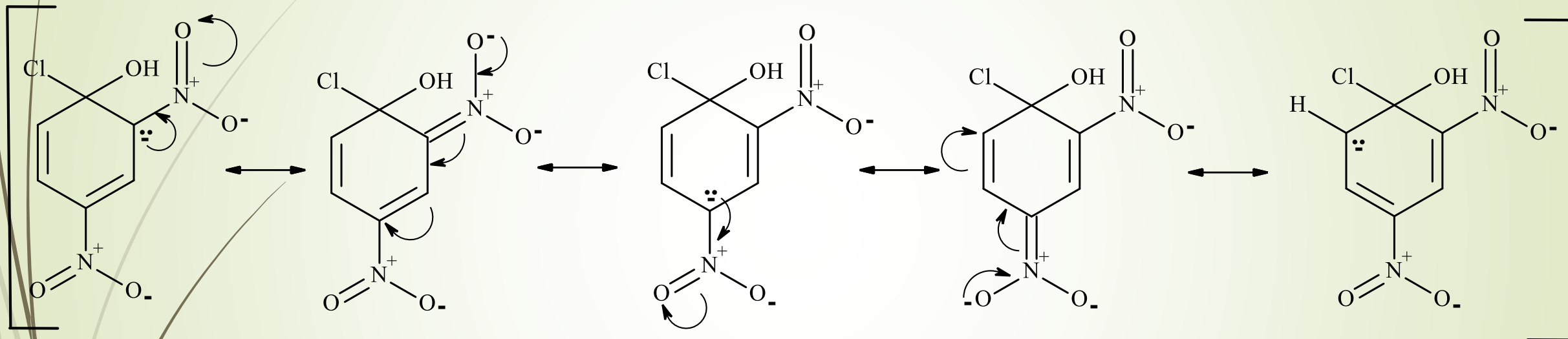
Addition Elimination Mechanism



Step I:
Attack of
nucleophile
to give
sigma
complex

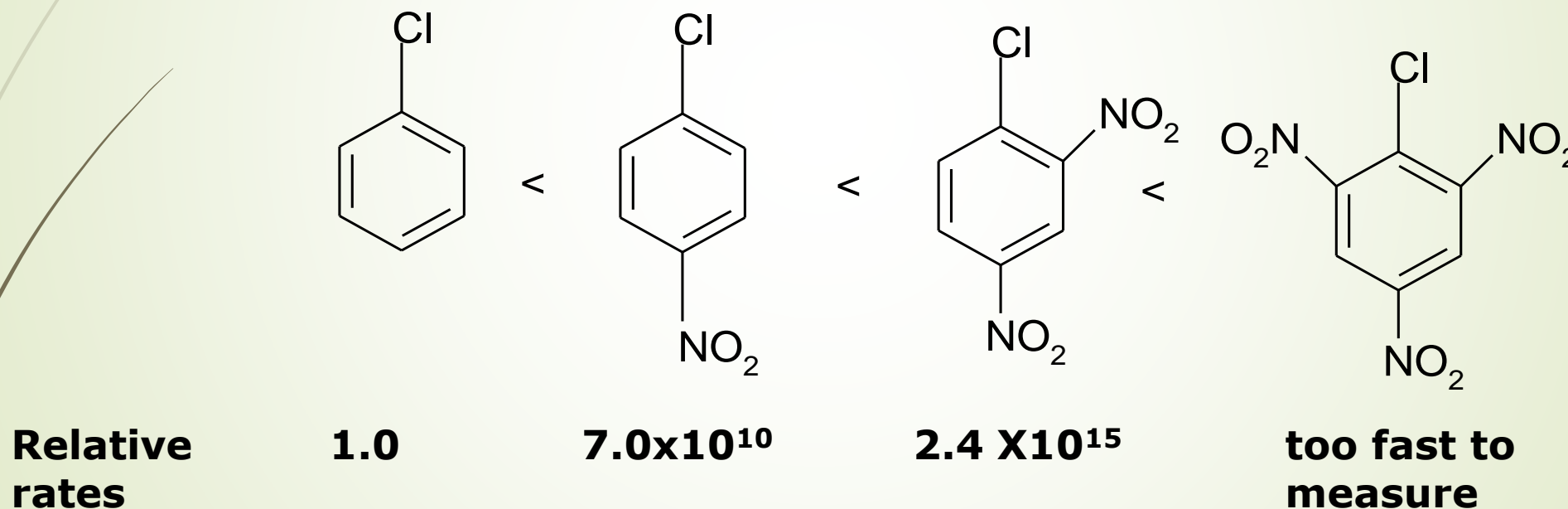
Step II: Loss
of leaving
group X $^-$

Stabilisation of sigma complex by resonance



Effect of electron withdrawing groups

- Presence of two or more nitro groups increases the rate of the reaction several folds, especially if the nitro groups are in the ortho and/or para positions w.r.t the leaving group



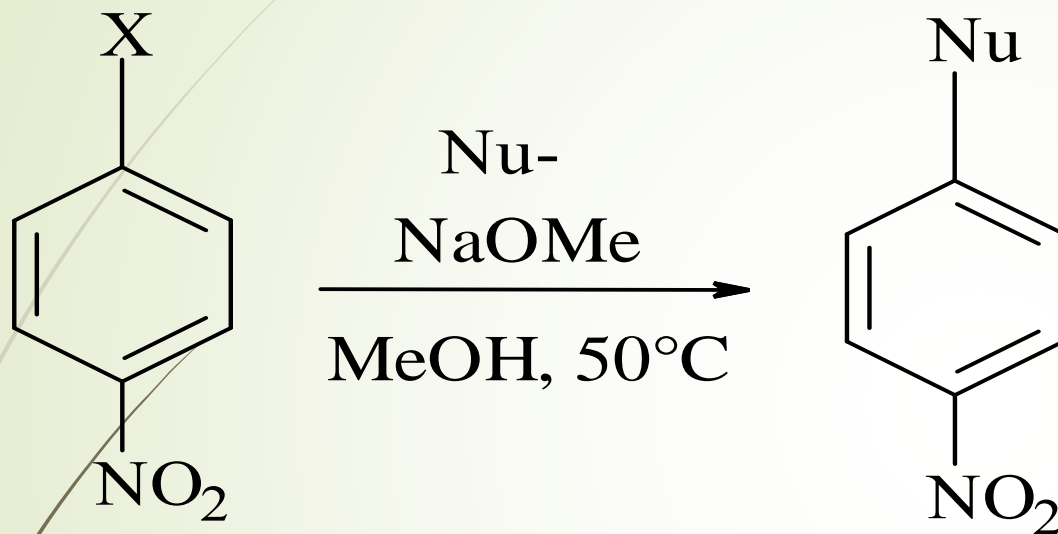
Kinetics of the reaction

Follows second order
rate law

$$\text{Rate} = k[\text{ArX}][\text{Nu}^-]$$

Implying that ArX
and nucleophile are
involved in the r.d.s

Effect of Leaving group in ArX



X	Relative rate
F	312.0
Cl	1.0
Br	0.8
I	0.4

Why p-nitrofluorobenzene is more reactive?

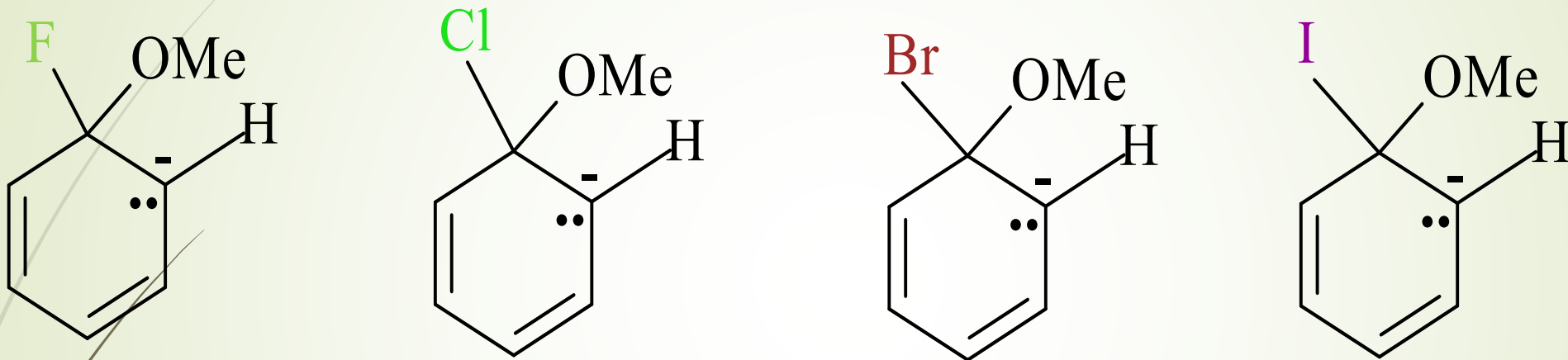
Step-1 r.d.s involves attack of nucleophile

- C-F bond more polarised due to greater electronegativity of F. Carbon more electrophilic. Attack of nucleophile faster.

Step-2 Electronegative F stabilises negatively charged intermediate

- C-F bond cleavage occurs after the r.d.s

Stability of Intermediate formed when X Changes

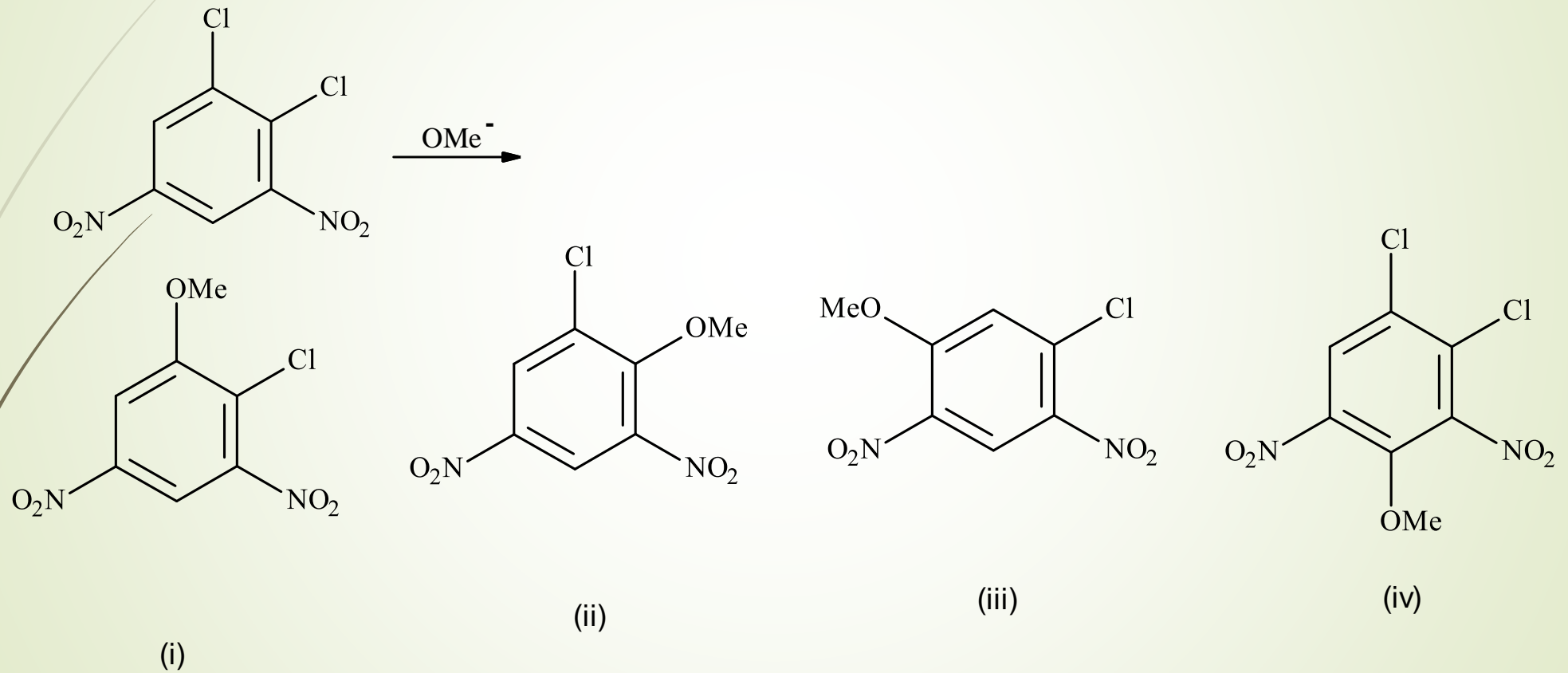


Most stabilised

Least stabilised

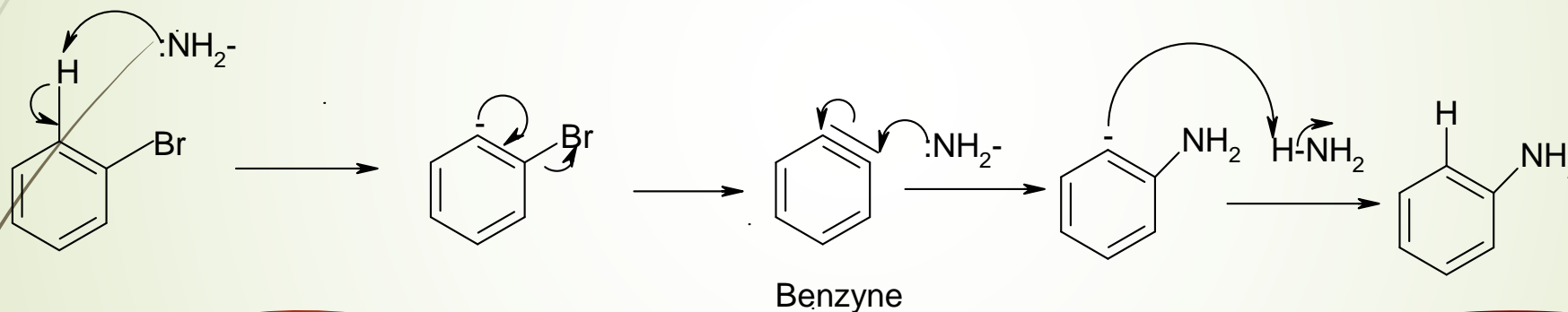
Problem 1

The major product formed in the following reaction is



Elimination Addition Mechanism

This mechanism operates when the nucleophile is a very strong base like NH_2^- and the substrate does not have strong electron withdrawing groups.

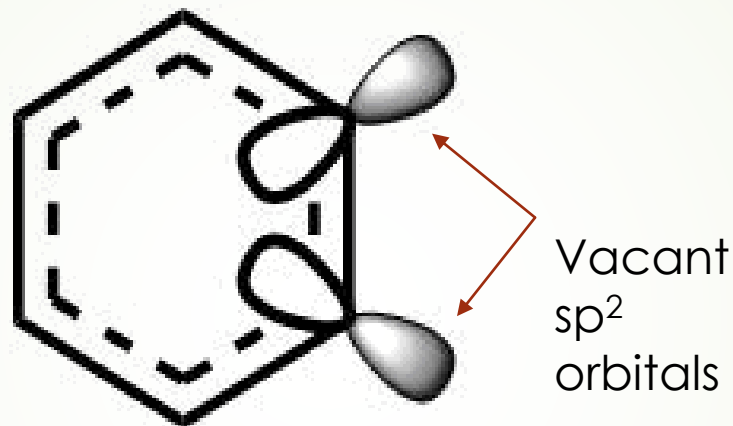


r.d.s is the
elimination of
 Br^- to form the
benzyne

Order of reactivity of
 ArX is
 $\text{ArI} > \text{ArBr} > \text{ArCl} > \text{ArF}$

Structure of Benzyne

Benzyne are highly reactive intermediates



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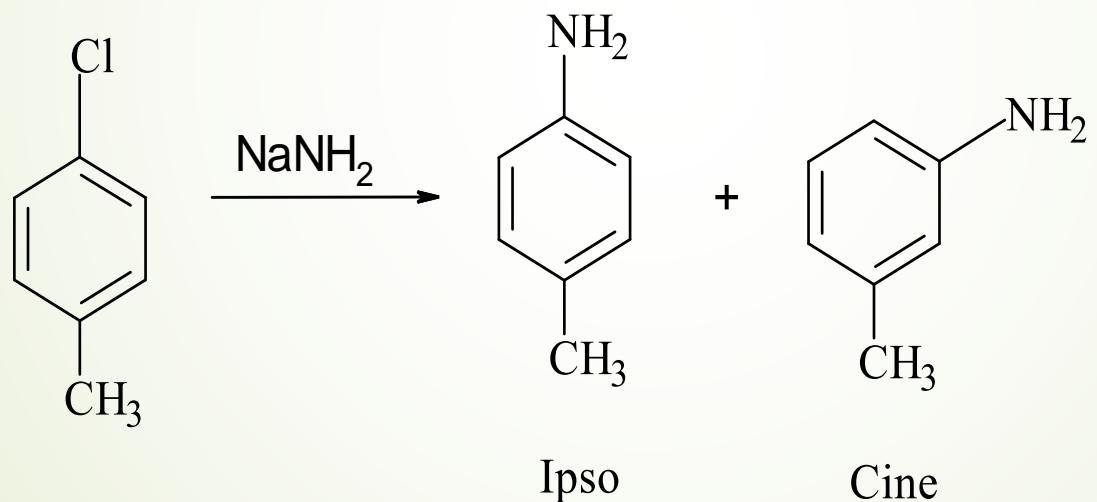
The triple bond is in a plane perpendicular to the plane of the π bonds

The π cloud is formed by overlap of planar p-orbitals.

The triple bond in benzyne is formed by overlap of sp^2 - sp^2 orbitals.

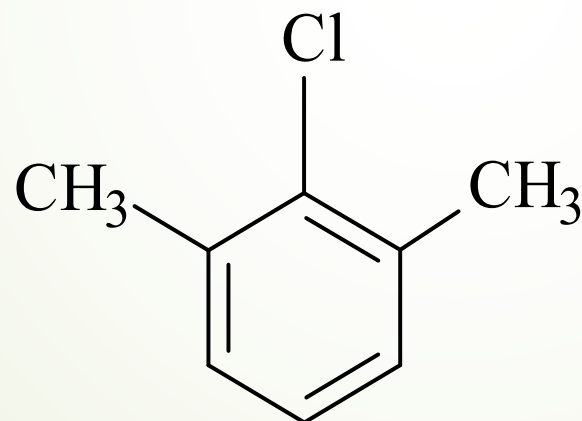
Ipsso and Cine Substitution products

The incoming nucleophile can add on the same carbon which carried the leaving group (ipso product) or on the adjacent carbon (cine product)

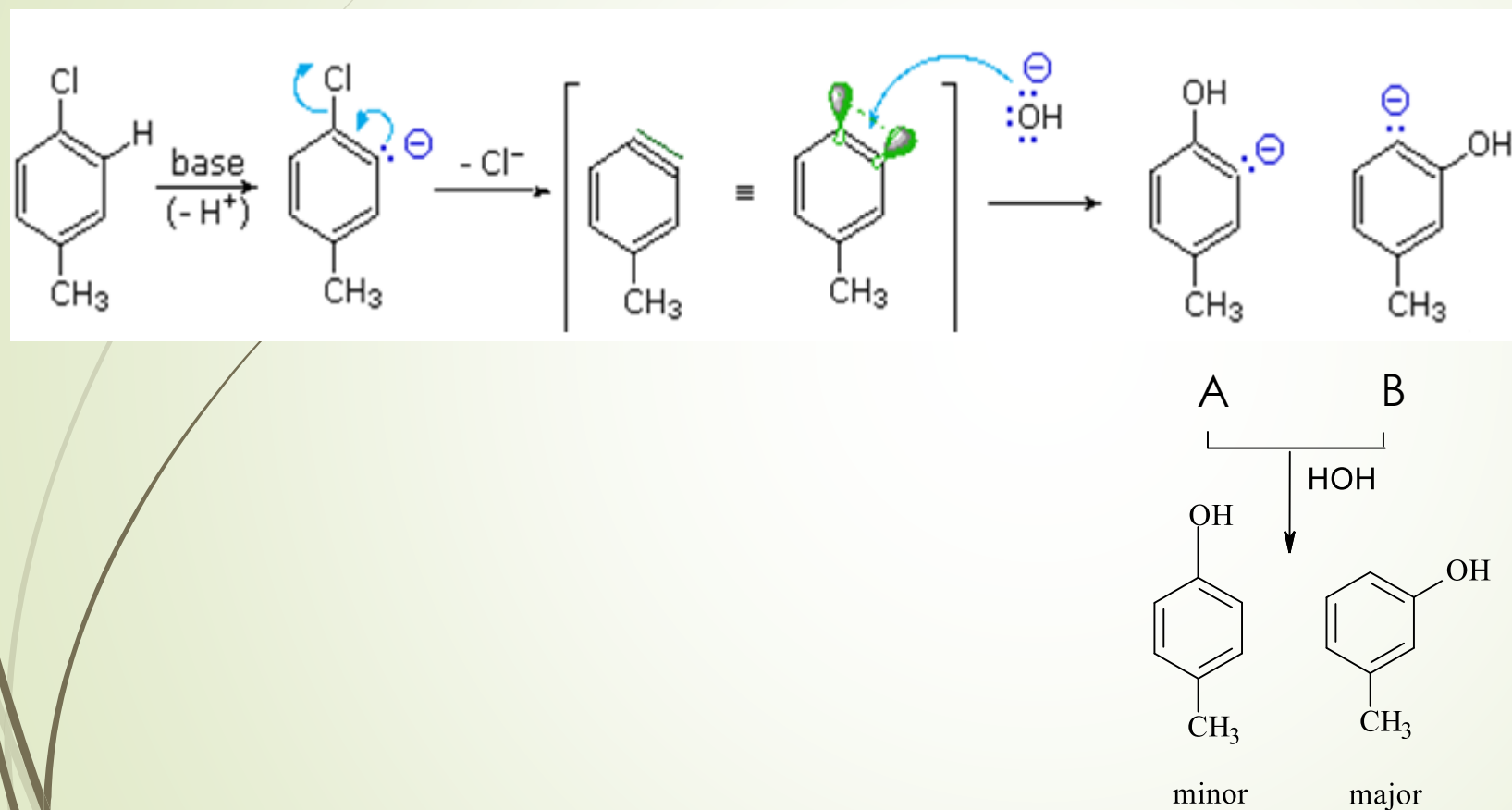


Proof for formation of benzyne intermediate

This aryl halide does not undergo substitution reaction with NaNH_2 in NH_3 as there is no β hydrogen which can be removed to form the benzyne intermediate



Which is the major product Ipso or Cine?

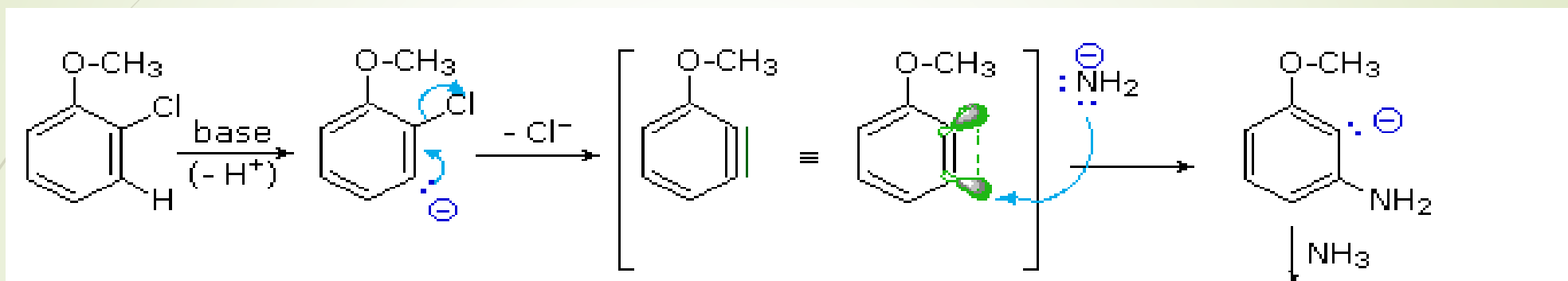


- Decided by the stability of intermediate carbanion

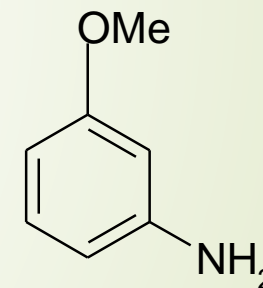
Here
Intermediate
B is more
stable than A

Presence of electron
releasing groups
like CH₃, in para
position favours cine
product

Which is the major product Ipso or Cine?

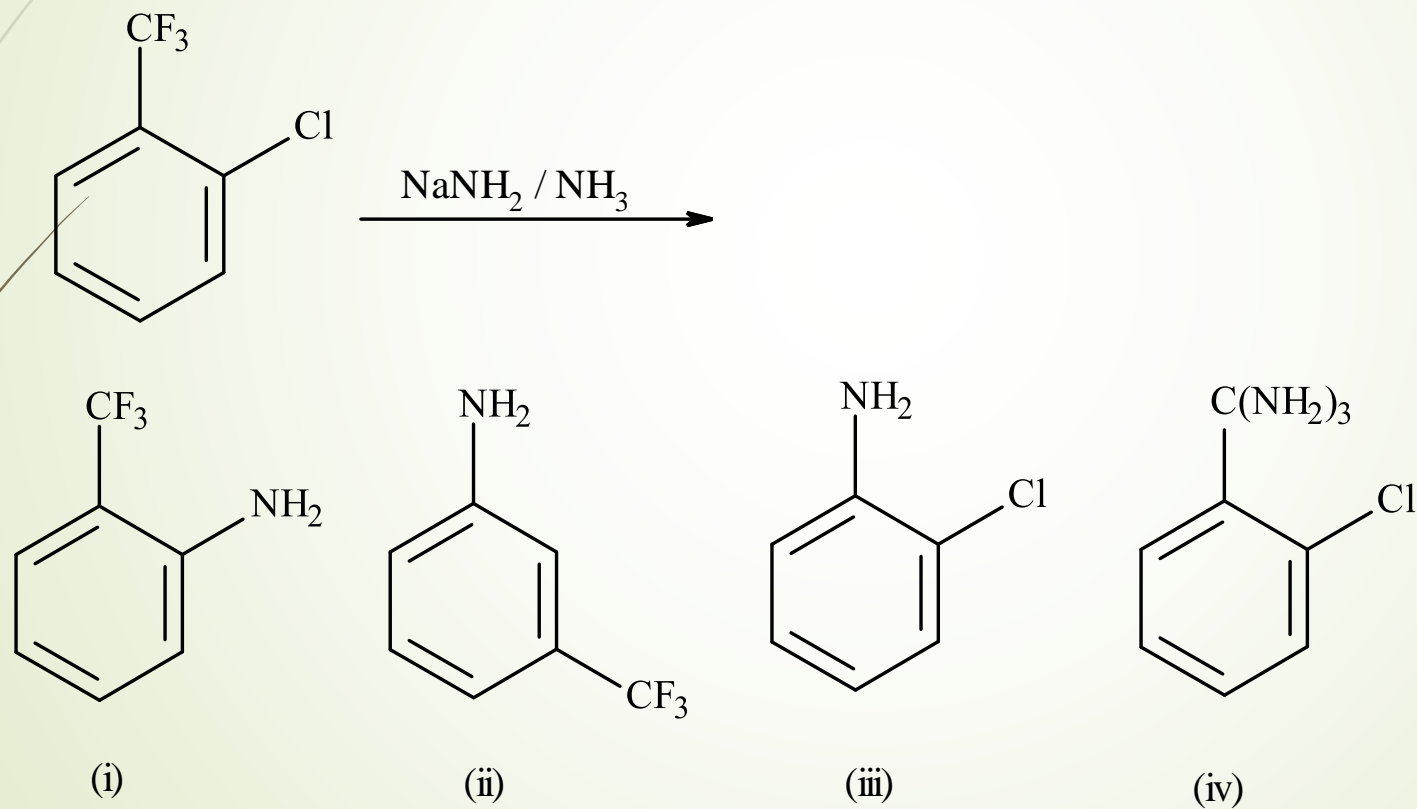


Presence of electron withdrawing groups like OH, OCH₃, in ortho position favours cine product



Problem 2

The major product formed in the following reaction is



Summary

Nucleophilic substitution on aryl halides can take place by

- i) *Addition elimination mechanism* ...favoured when strong electron withdrawing groups are present.

- ii) *Elimination addition mechanism via Benzyne intermediate*... favoured in the presence of strong nucleophile and base like NH_2^- and no strong electron withdrawing groups are present on the halide .

Thank You