

Lecture 3

Electrophilic aromatic substitution – introduction, mechanism, reactions

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Reference textbook

- “Organic Chemistry” by Paula Yurkanis Bruice, 8th Edn.
- This lecture – Chapter 18, all sections within and including 18.1 to 18.6

Learning Objectives – Lecture 3

Section 2– Substituted benzenes and electrophilic aromatic substitution

Recall abbreviations commonly used to represent fragments of organic molecules in chemical structures, to include aryl, phenyl, benzyl and benzoyl groups

Give general and specific mechanisms for electrophilic aromatic substitution reactions, to include resonance-stabilisation of reaction intermediates

Account for the preference of aromatic compounds to undergo electrophilic substitution rather than electrophilic addition reactions typical of alkenes

Sketch a general energy profile for electrophilic aromatic substitution reactions, and identify the rate-determining step of the reaction

Apply the general mechanism for electrophilic aromatic substitution to a range of electrophiles, to include nitration, halogenation, sulfonation, acylation and alkylation reactions of aromatic compounds

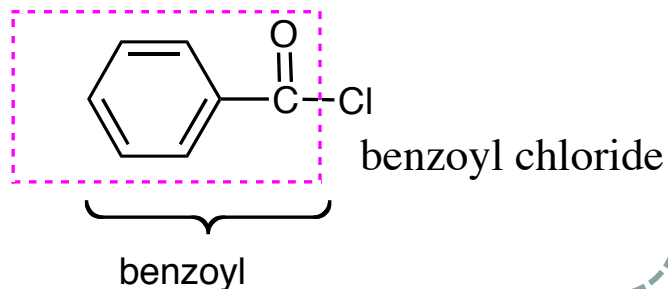
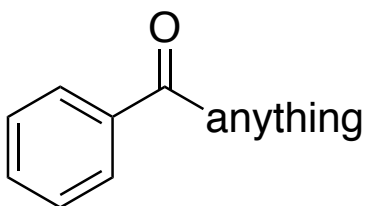
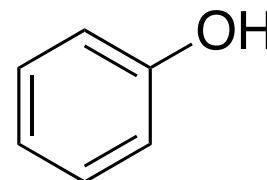
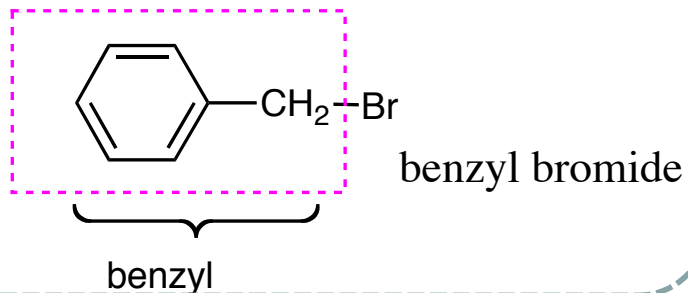
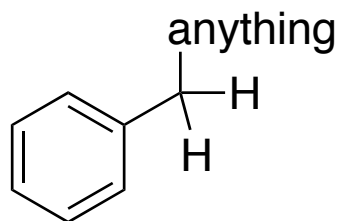
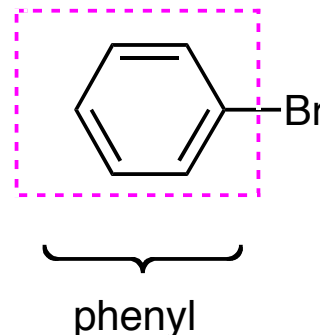
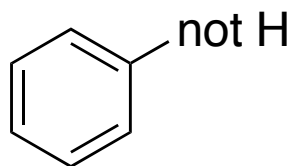
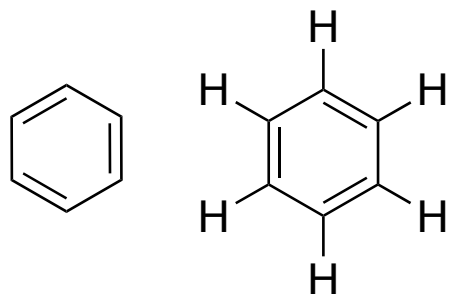
Recall the reagents required to generate the electrophiles encountered in this course, and give mechanisms for their formation

Lecture Outline: L3

- 1. Definitions and abbreviations**
- 2. Electrophilic Aromatic Substitution – General overview**
 - a. General reaction
 - b. Energy profile diagram
 - c. General mechanism, resonance
- 3. Electrophilic Aromatic Substitution – Specific reactions**
 - a. Nitration
 - b. Halogenation
 - c. Sulfonation
 - d. Acylation
 - e. Alkylation

1. Definition and abbreviations

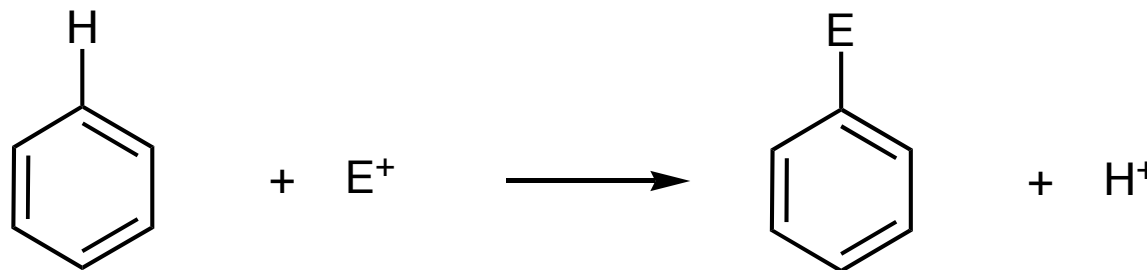
What's the difference between benzene, benzyl, benzoyl, aryl, phenyl, phenol?



What about aryl (Ar)?

2. Electrophilic Aromatic Substitution – General overview

a. General reaction



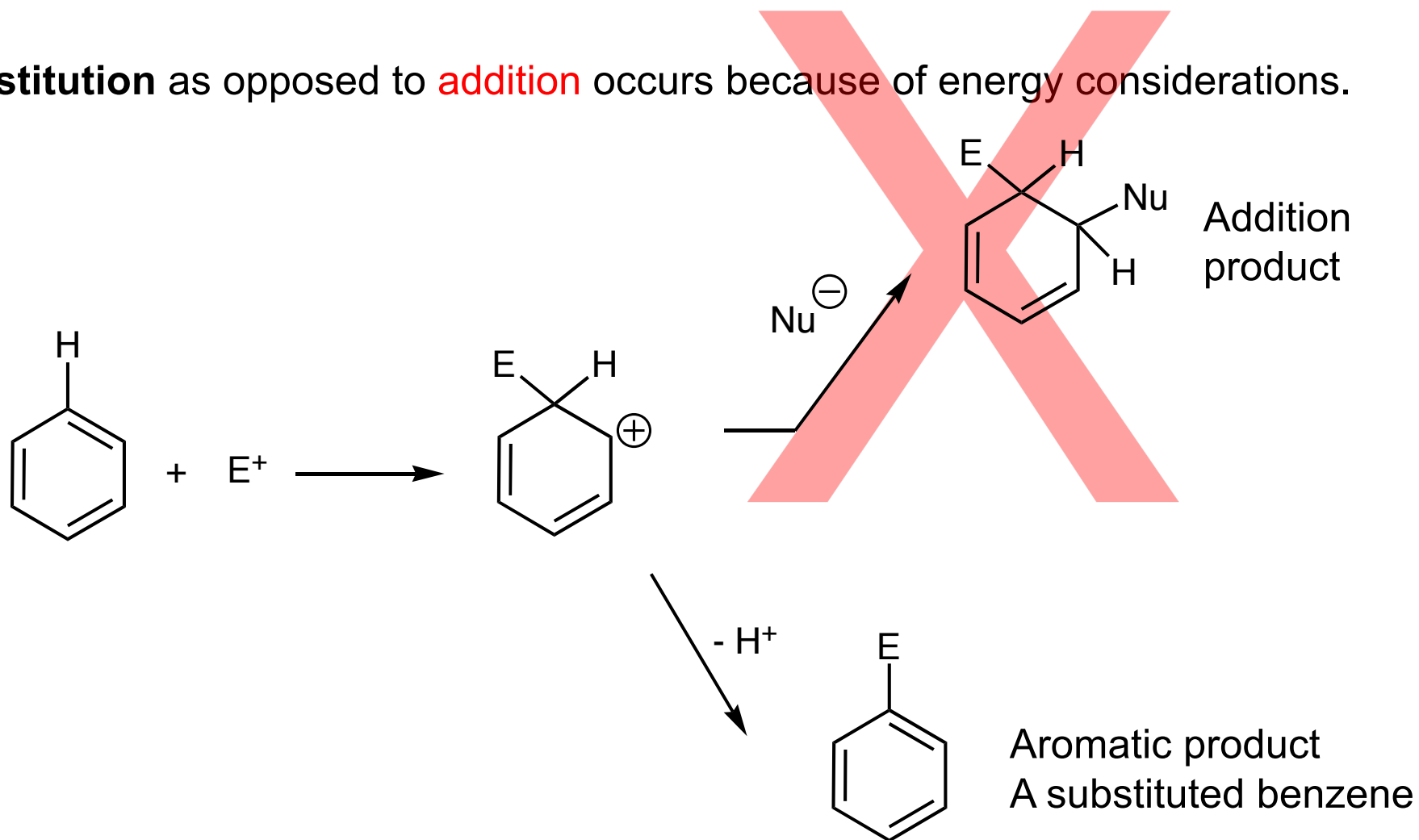
Two step mechanism

- Step 1 is same as that for electrophilic addition reaction to C=C.
- Step 2 — elimination of H⁺

2. S_EAr – General overview

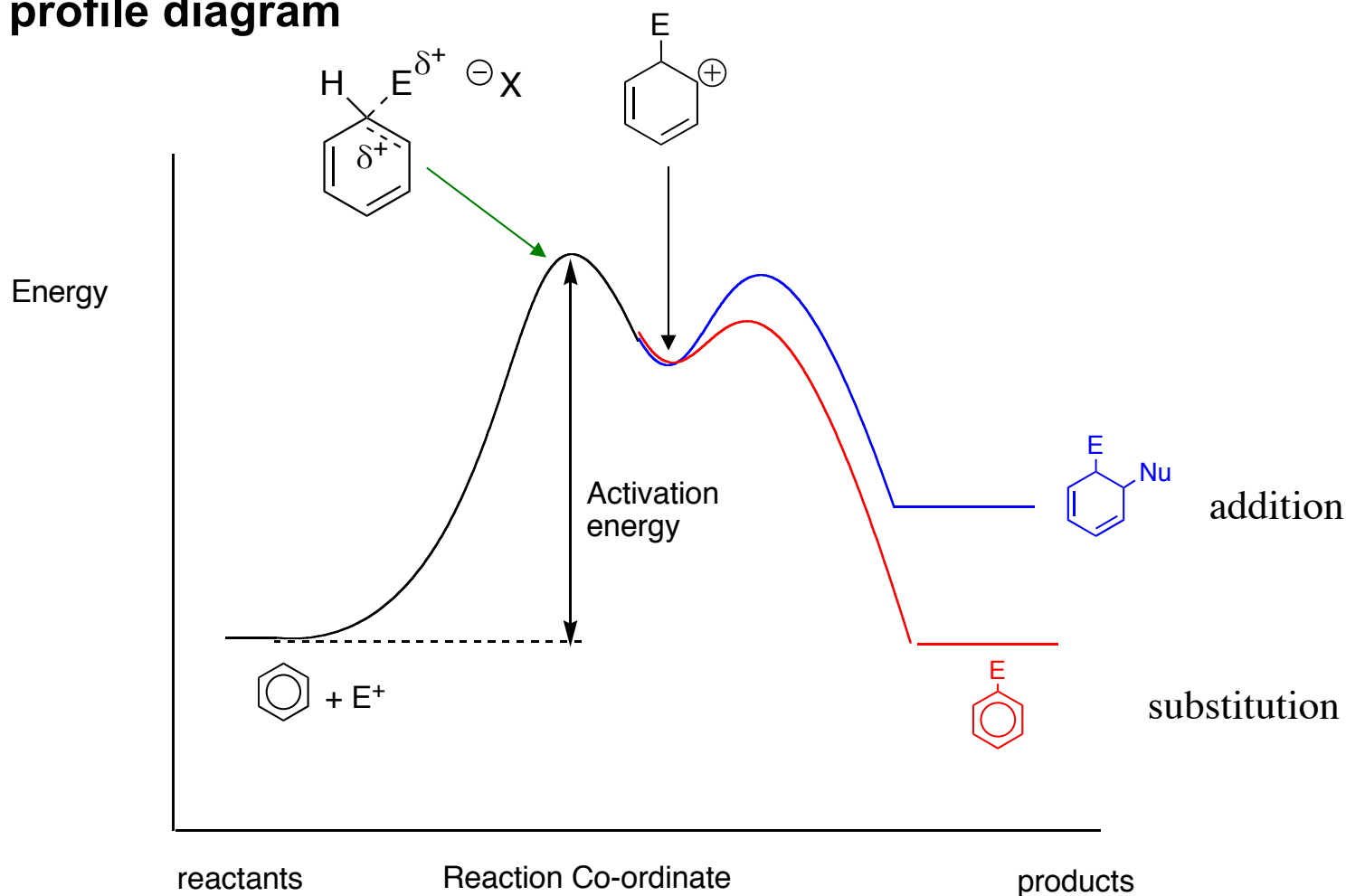
a. General reaction

Substitution as opposed to **addition** occurs because of energy considerations.



2. S_EAr – General overview

b. Energy profile diagram

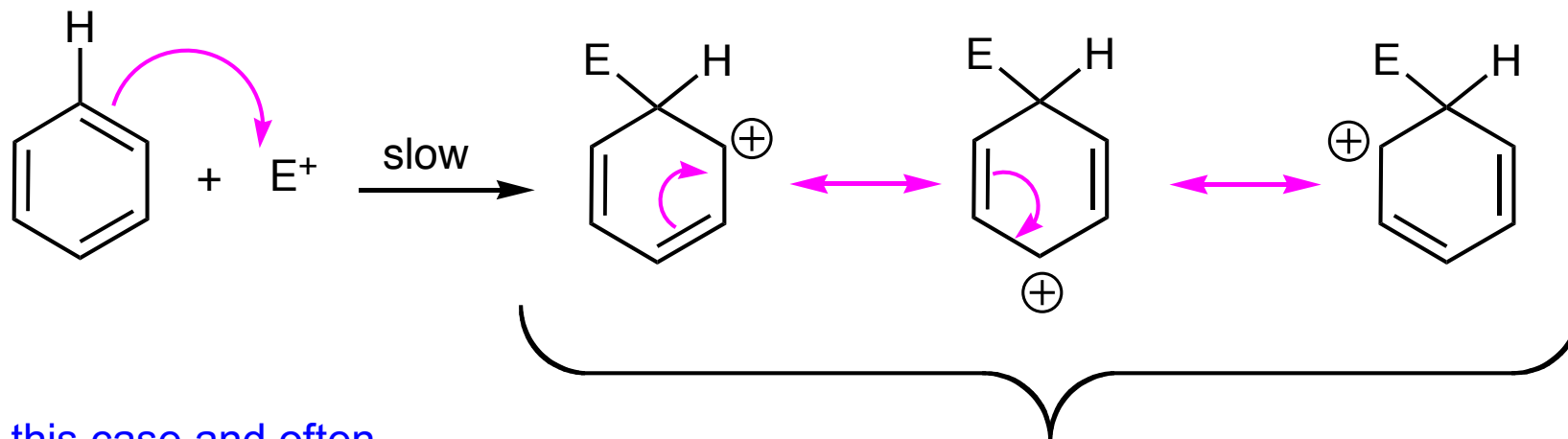


- The slower, **rate-limiting step** is the aromatic starting material attacking an electrophile, which produces a much less stable **non-aromatic carbocation intermediate**.
- The subsequent **deprotonation step** is fast and exergonic as a **lower energy 'stable' aromaticity** is 're'-generated.


2. S_EAr – General overview

c. General mechanism, resonance

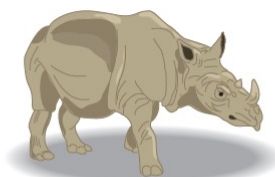
Step 1 – addition of an electrophile to the electron rich aromatic ring



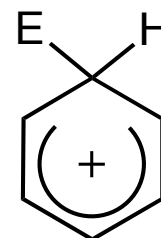
Arenium ion or Wheland Intermediate

In this case and often when showing mechanisms, use **valence bond structures** and not delocalised structures, ie benzene above not written as  because can't easily show indicative mechanism.

Real structure:



rhinoceros
resonance hybrid

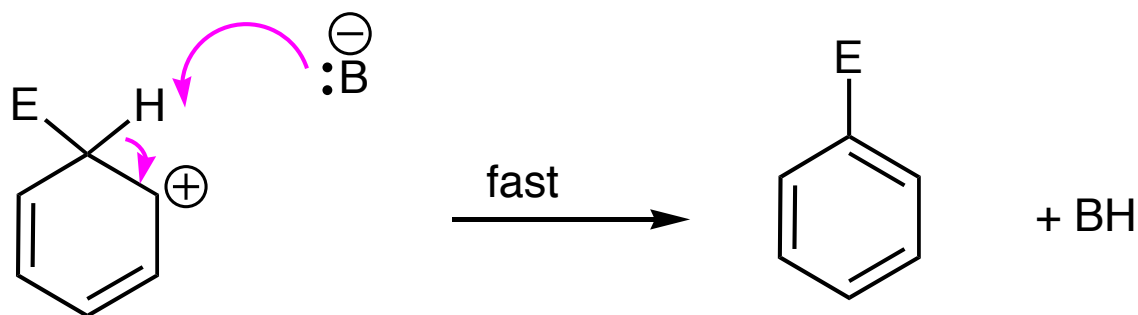


5 sp² hybridised carbons

2. S_EAr – General overview

c. General mechanism, resonance

Step 2 – Fast loss of H⁺ aided by a weak base



- General method example is using benzene.
- Further substitution may occur depending on E⁺, this can be reduced or avoided by using a large excess of benzene.
- We will see in lecture 4 onwards how substituents around an aromatic ring influence S_EAr.

3. S_EAr – Reactions

- a. Nitration
- b. Halogenation
- c. Sulfonation
- d. Acylation
- e. Alkylation

All follow the **SAME** two step reaction mechanism

Only differ in the 'E⁺', the electrophile

As per Learning Objectives, we will also learn the mechanisms of how these electrophiles are generated

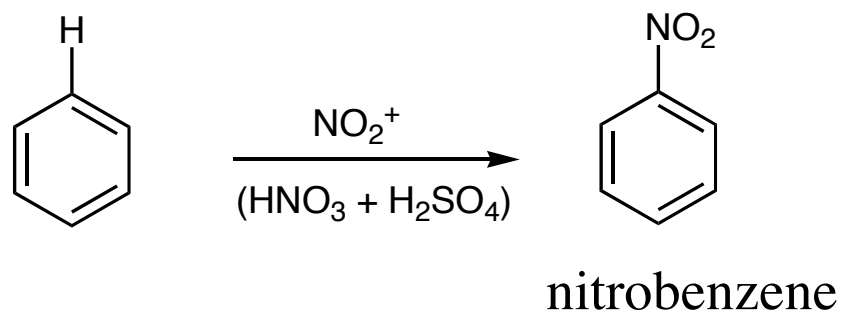
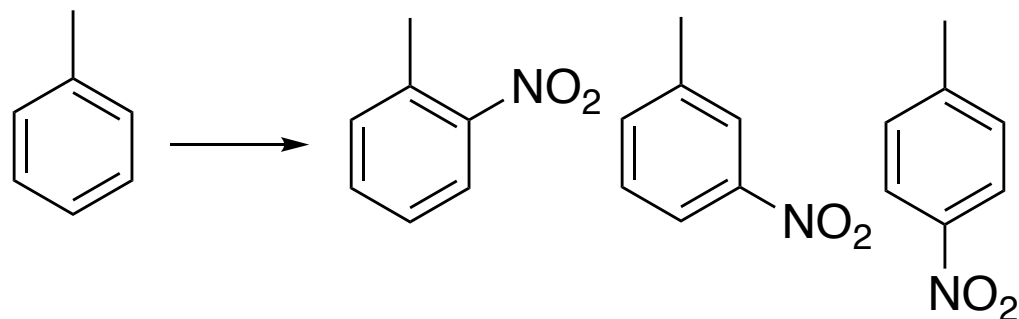
*it makes sense that as benzene is not very reactive, we will need a 'good' and quite 'reactive' electrophile for a reaction to occur, therefore it makes sense this is often something **not** 'straight out of a bottle' but needs to be generated itself in situ.*

3. S_EAr – Reactions

a. Nitration

Who remembers the first lab of 202?

Nitration of aromatic hydrocarbons: Measurement of reactivities by the competition technique



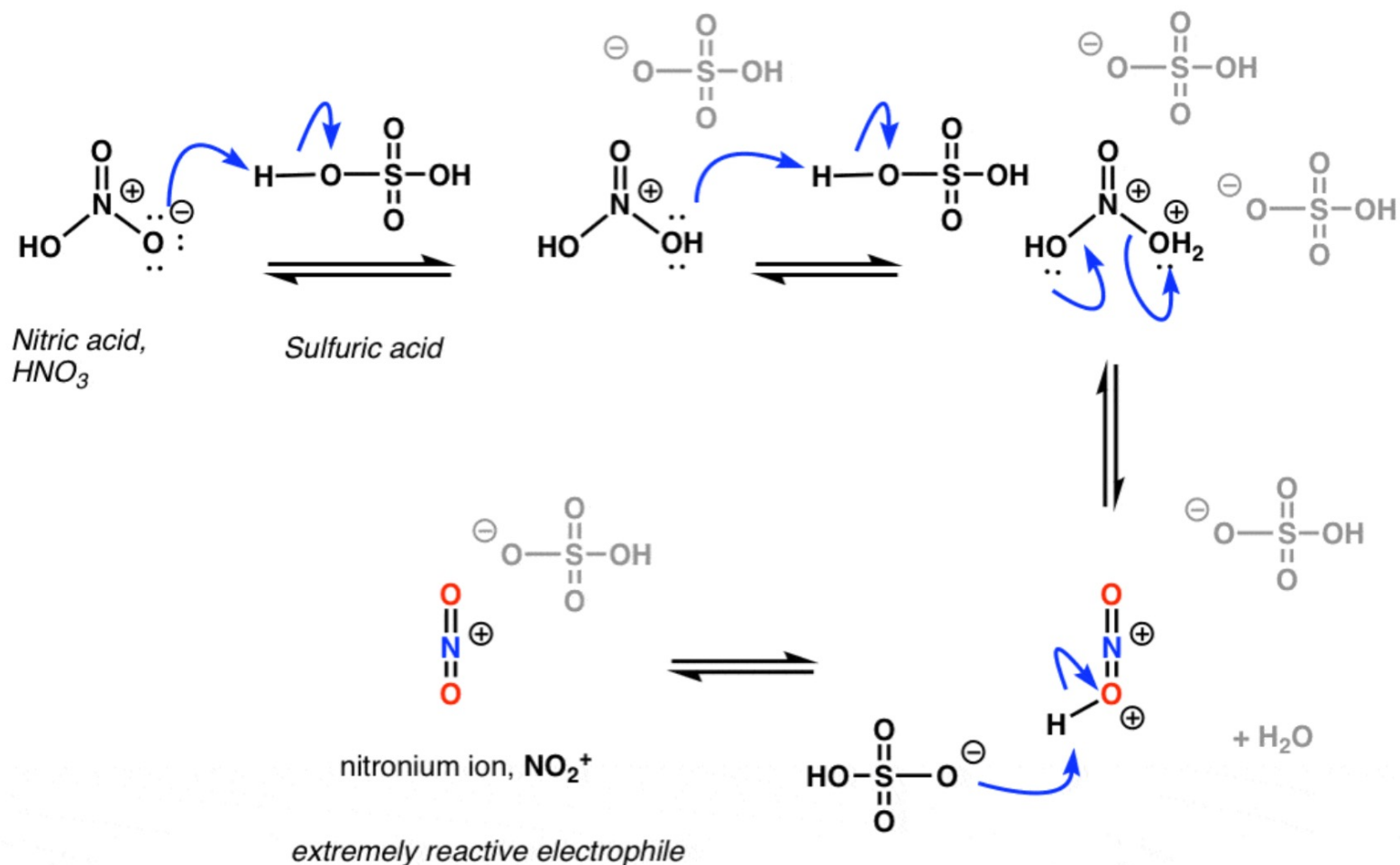
3. S_EAr – Reactions

<https://www.masterorganicchemistry.com/2018/04/30/electrophilic-aromatic-substitutions-2-nitration-and-sulfonation/#mech>

a. Nitration

Generate the electrophile, the nitronium ion **⁺NO₂**

Option A, use nitric acid and sulfuric acid -

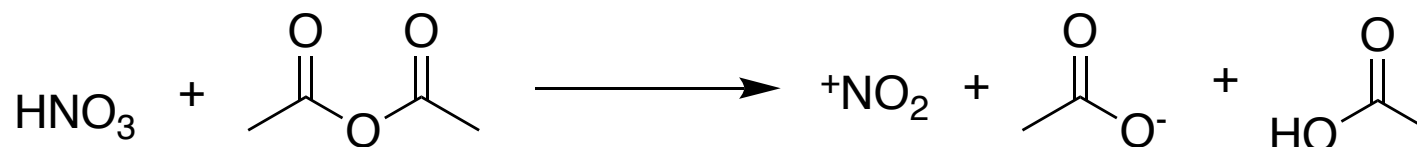


3. S_EAr – Reactions

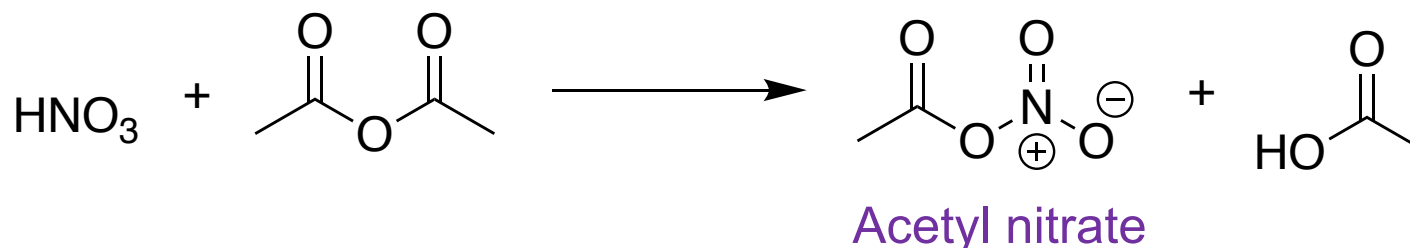
a. Nitration

Generate the electrophile

Option B, **and what you did in the lab**, use nitric acid and acetic anhydride –



There is actually some debate as to what the E⁺ species is here, it might not be the nitronium ion, it is likely ...

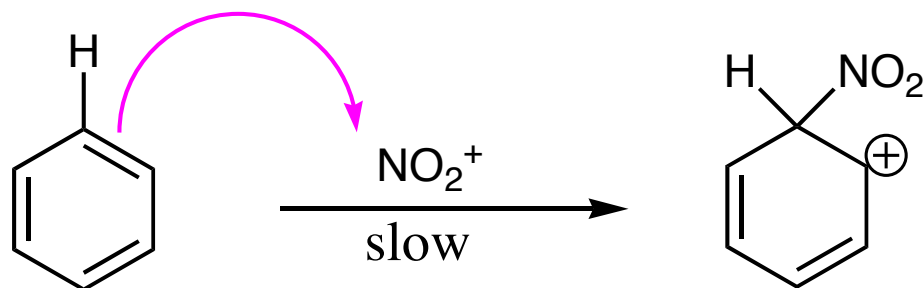


But for the purposes of learning Objective “Recall the reagents required to generate the electrophiles encountered in this course, and give mechanisms for their formation” **you can just learn and understand Option A (HNO₃, H₂SO₄) on the previous slide.**

3. S_EAr – Reactions

a. Nitration

Reaction step 1 – addition of the electrophile (**nitronium ion**) to the Ar ring

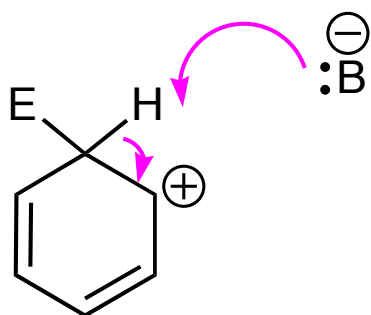
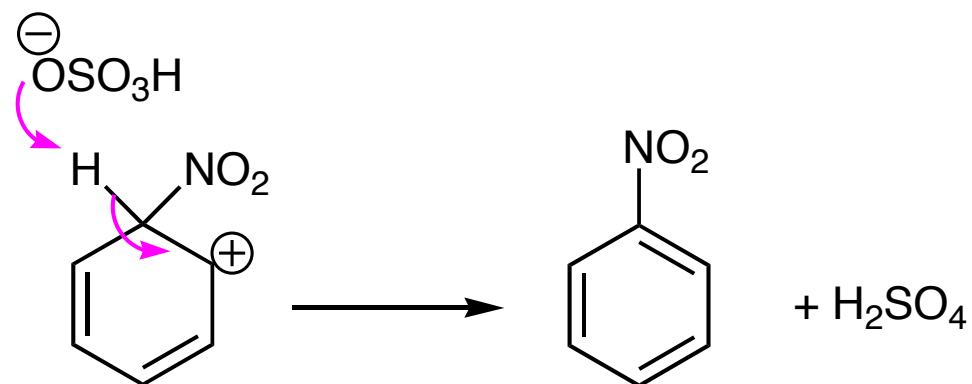


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3. S_EAr – Reactions

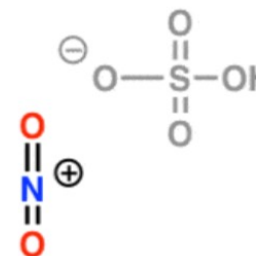
a. Nitration

Reaction step 2 – elimination of H⁺



What is 'B' ?

Nitric acid and sulfuric acid react to give



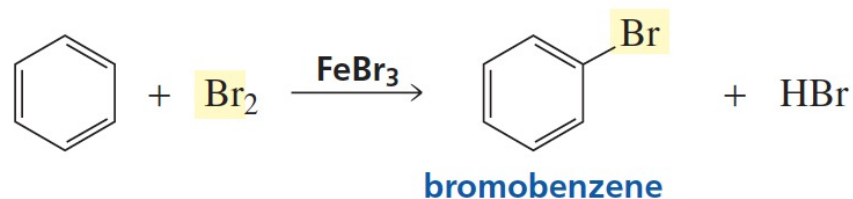
nitronium ion, NO_2^+

BREAK

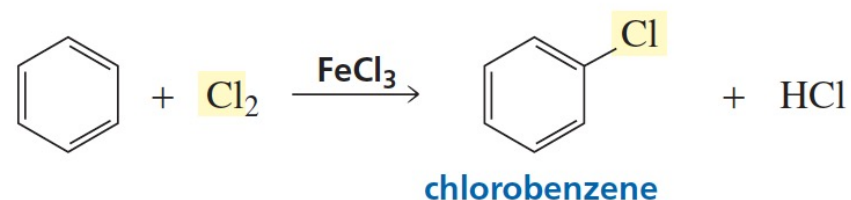
3. S_EAr – Reactions

b. Halogenation

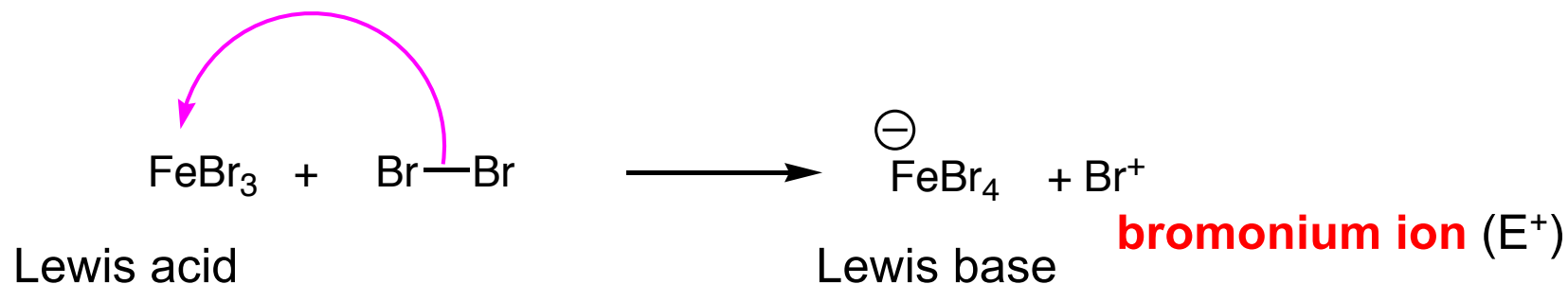
bromination



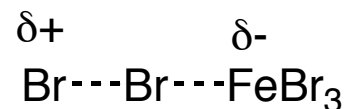
chlorination



Generate the electrophile, a **halonium ion**



The real reactive species would be:

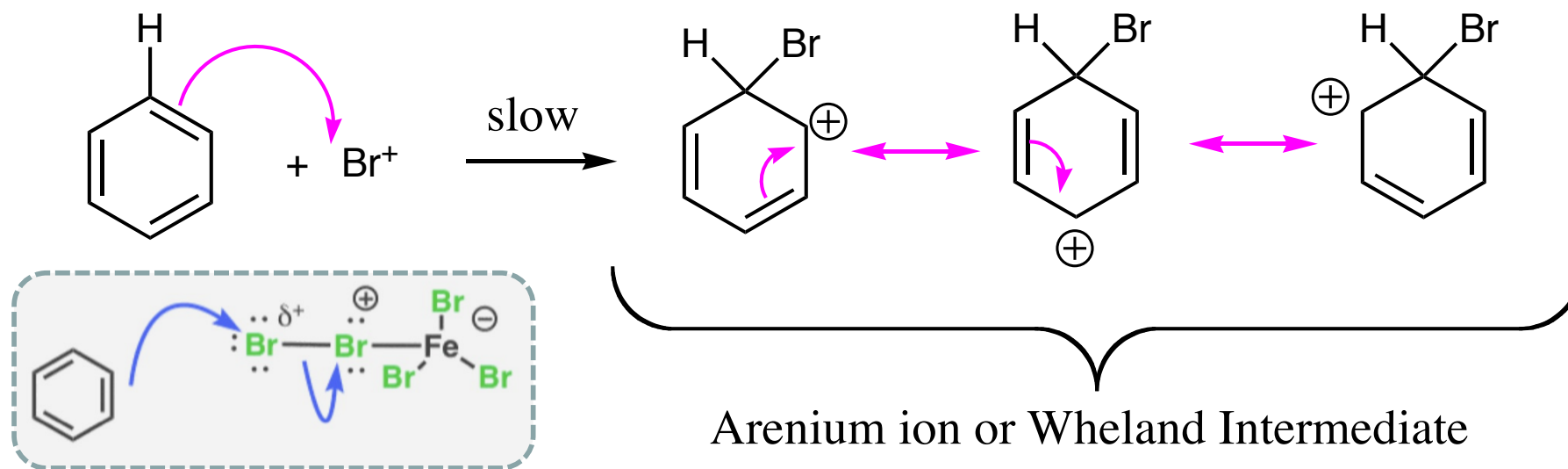


Why isn't 'just' Br₂ suitable as the electrophile in S_EAr with BENZENE?

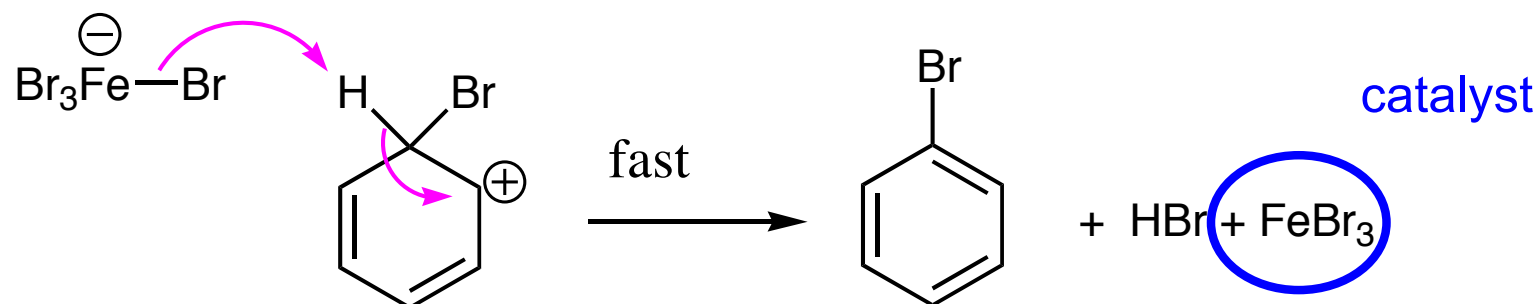
3. S_EAr – Reactions

b. Halogenation

Reaction step 1 – addition of the electrophile ('bromonium ion') to the Ar ring

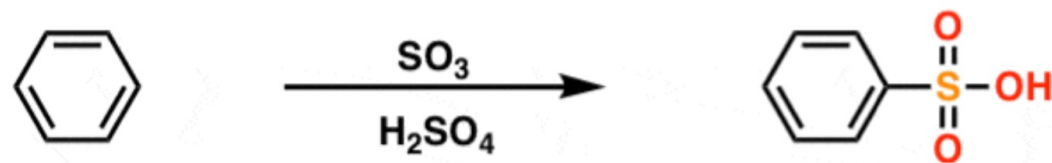


Reaction step 2 – elimination of H⁺



3. S_EAr – Reactions

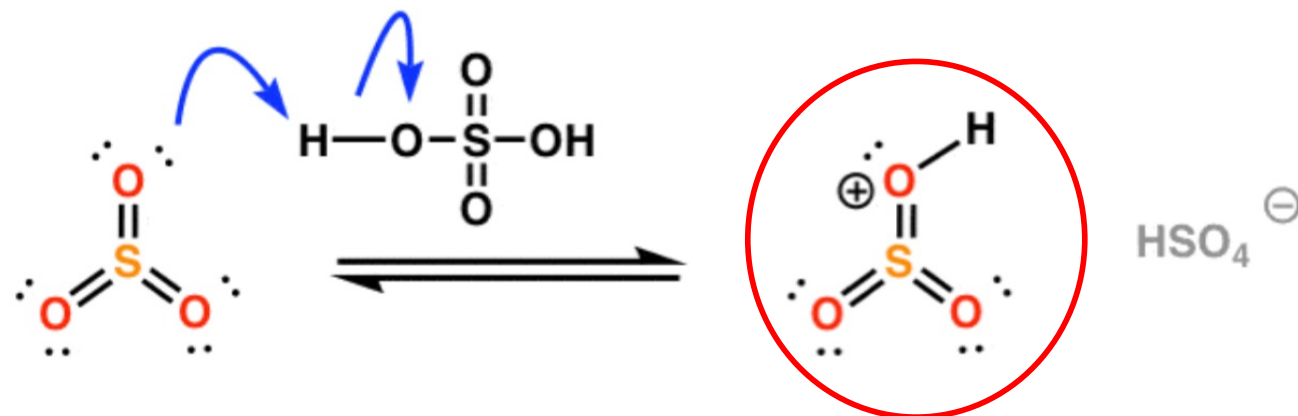
c. Sulfation



'fuming' sulfuric acid is a mixture of SO₃ and H₂SO₄

Generate the electrophile, a **sulfonium ion**

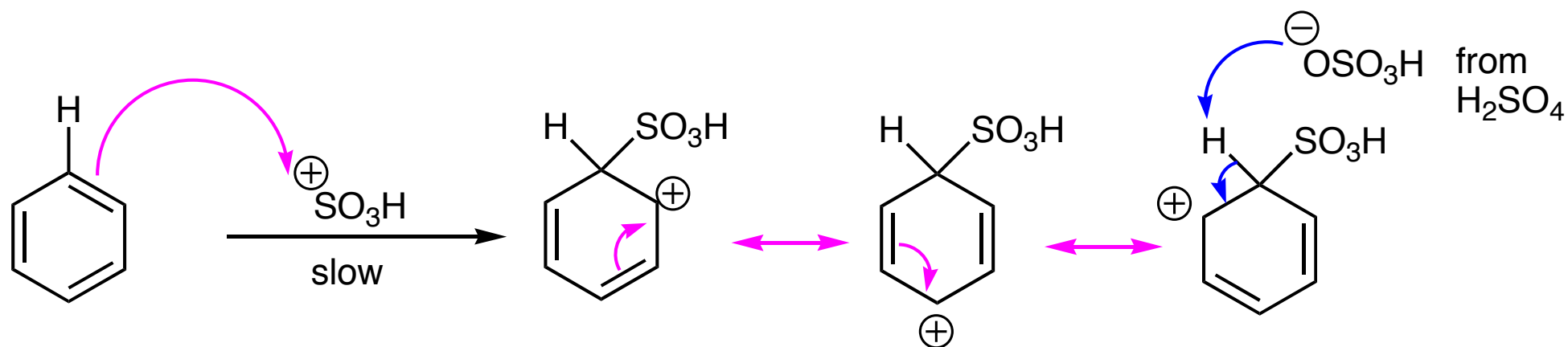
The electrophile is a protonated form of SO₃ from fuming sulfuric acid.



3. S_EAr – Reactions

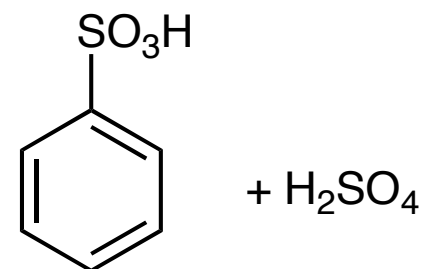
c. Sulfation

Reaction step 1 – addition of the electrophile (**sulfonium ion**) to the Ar ring



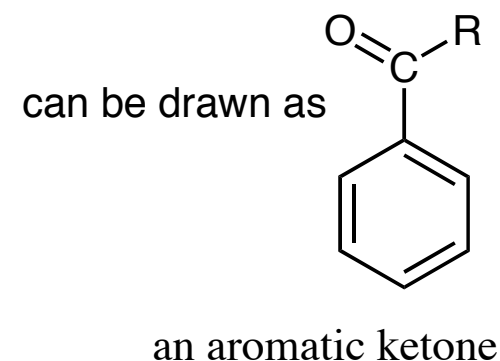
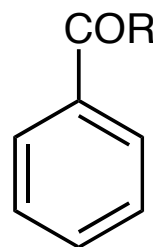
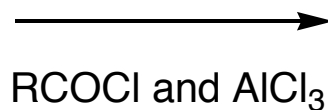
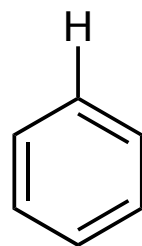
Reaction step 2 – elimination of H⁺

benzenesulfonic
acid



3. S_EAr – Reactions

d. Acylation

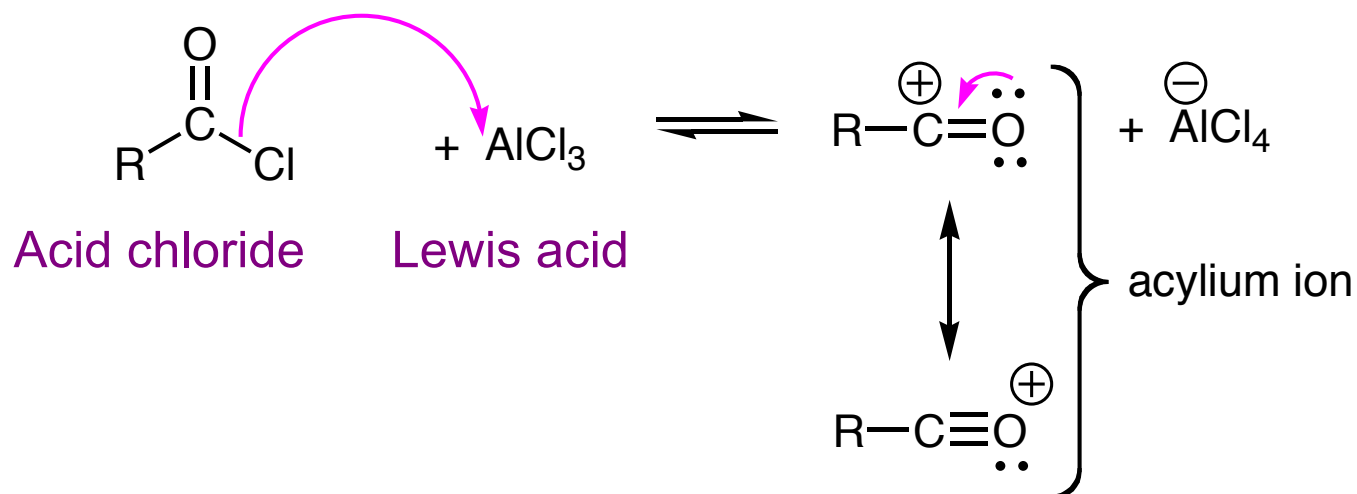


- In the previous S_EAr reaction examples, a new C-N, C-S, or C-halogen bond was made.
- **Here a new C-C bond is made**
- S_EAr acylation and alkylation are named after the chemists Friedel and Crafts
 - called **Friedel-Crafts Acylation** and *Friedel-Crafts Alkylation*
 - the general mechanism is the same as previously discussed for S_EAr.

3. S_EAr – Reactions

d. Acylation

Generate the electrophile, a **acylium ion**



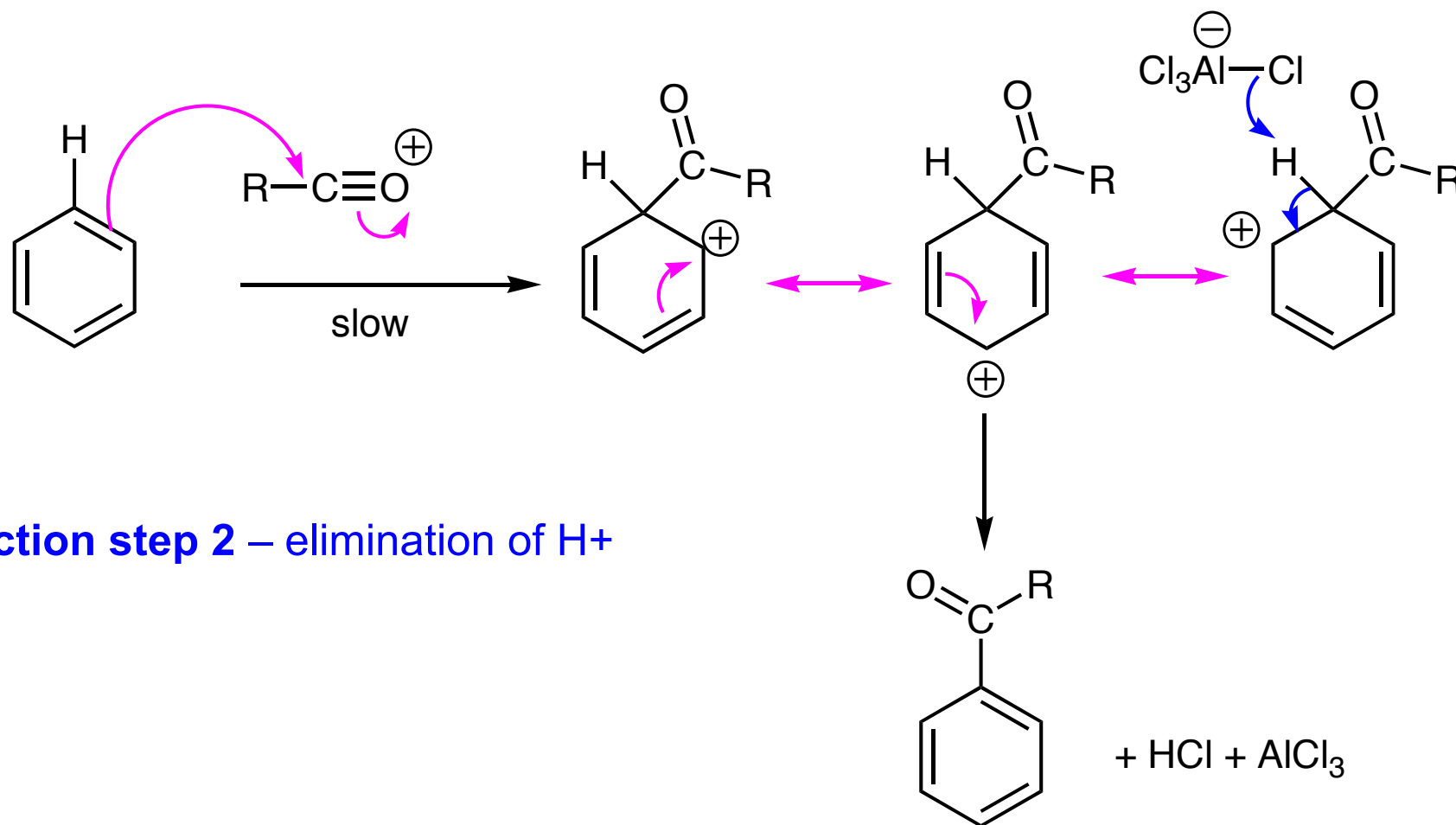
The acylium ion is stabilised by resonance.

Which is the most stable resonance contributor? i.e. which is the lowest in energy?

3. S_EAr – Reactions

d. Acylation

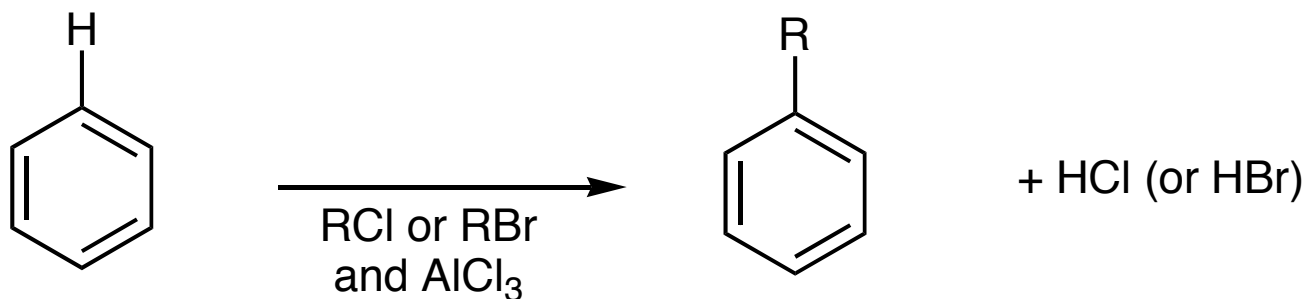
Reaction step 1 – addition of the electrophile (**acylium ion**) to the Ar ring



Reaction step 2 – elimination of H^+

3. S_EAr – Reactions

e. Alkylation



- Another S_EAr reaction that forms a new C-C bond
- S_EAr alkylation also named after the chemists Friedel and Crafts
 - **Friedel-Crafts Alkylation**
 - the general mechanism is the same as previously discussed for S_EAr.

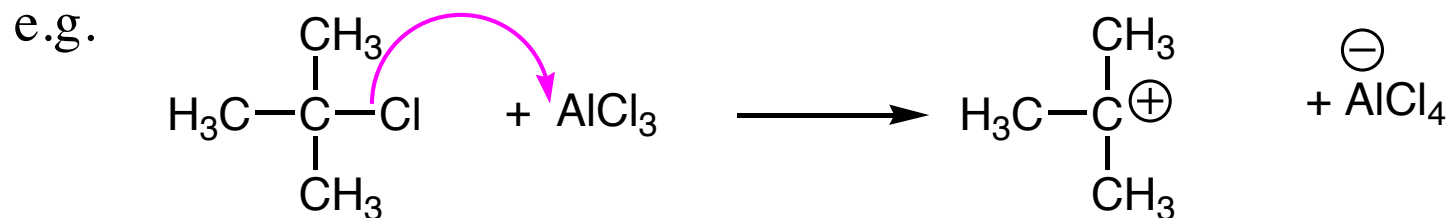
3. S_EAr – Reactions

e. Alkylation

Generate the electrophile, a '**carbocation**'



For secondary or tertiary alkyl halides, full dissociation to a 'formal' carbocation is likely



For primary alkyl halides, full dissociation to a "free" carbocation is **unlikely**

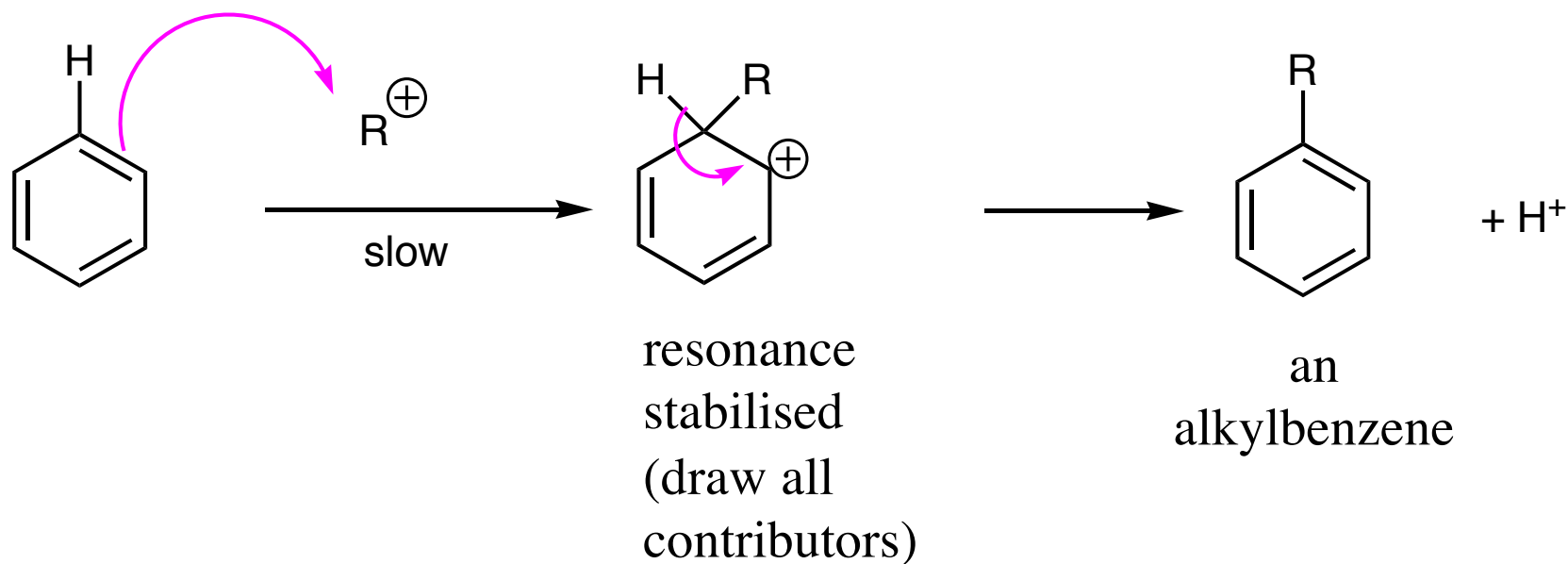


3. S_EAr – Reactions

e. Alkylation

Reaction step 1 - addition of the electrophile ('**carbocation**') to the Ar ring

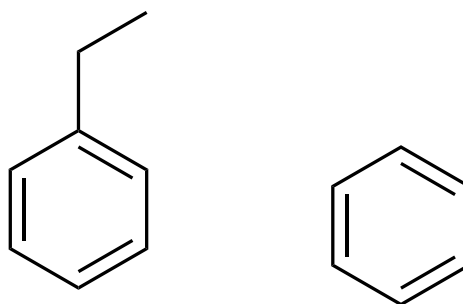
Reaction step 2- loss of H⁺



3. S_EAr – Reactions

e. Alkylation

Interesting fact - an phenyl alkyl compound is often a better nucleophile than benzene..

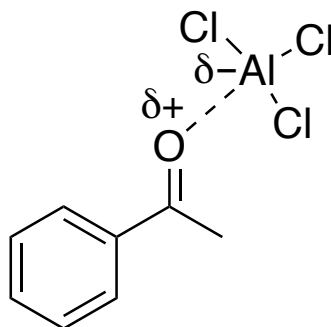
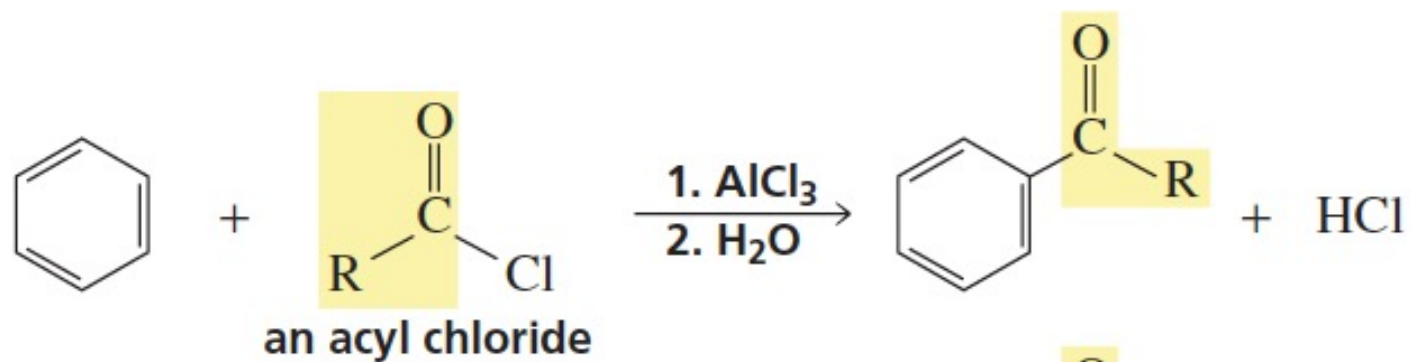
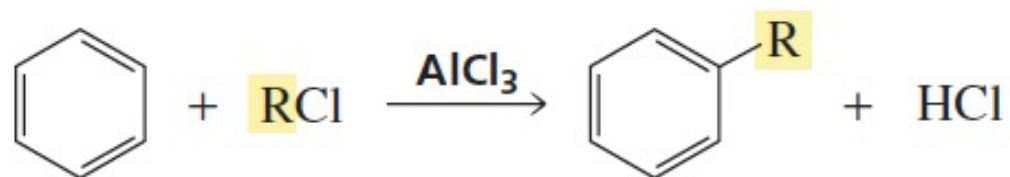


- We will learn why this is in coming lectures.....
- This can be managed experimentally by having a large excess of benzene starting material

3. S_EAr – Reactions

Comparing Friedel Crafts Acylation to Alkylation

Can the Lewis acid, e.g. AlCl₃, be used in a catalytic amount?



3. S_EAr – Reactions

A common 'problem' with FC Alkylation

The carbocation will **rearrange** to the most stable carbocation.....

More about this in the next lecture !