Lecture 5

Effect of Substituents on Orientation in S_EAr

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Reference textbook

- “Organic Chemistry” by Paula Yurkanis Bruice, 8th Edn.
- This lecture – Chapter 18, in particular 18.13, 18.14, 18.15

Learning Objectives – Lecture 5

Section 2– Substituted benzenes and electrophilic aromatic substitution

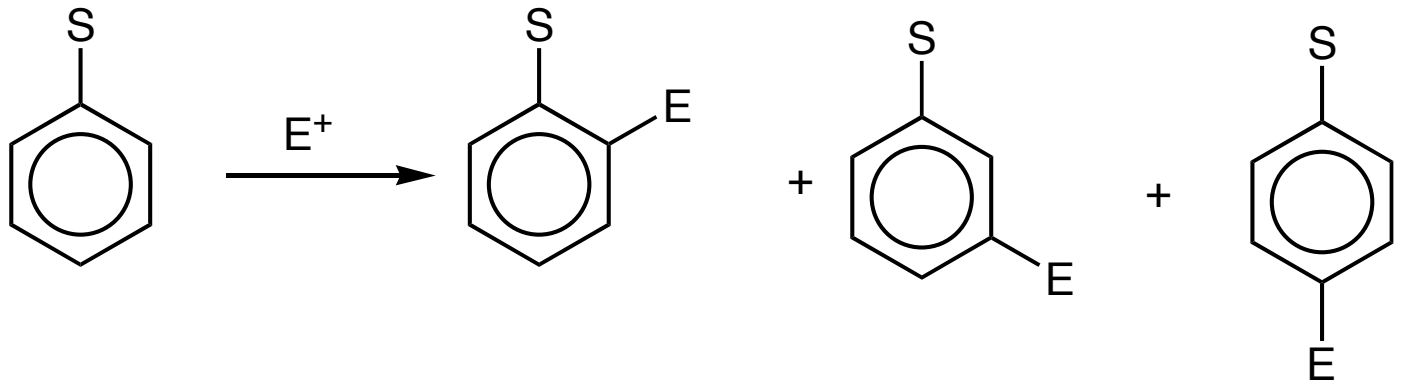
Describe and account for the differences in how an electron-donating (+I or +M) or weakly deactivating substituent affects the reactivity of different positions relative to it (ortho-, meta- and para-) in the aromatic ring towards electrophilic aromatic substitution.
Describe and account for the differences in how an electron-withdrawing (-I or -M) substituent affects the reactivity of different positions relative to it (ortho-, meta- and para-) in the aromatic ring towards electrophilic aromatic substitution
Appreciate that the overall directing and reactivity effects of some substituents (e.g. halogens) may be based on some combination of opposing inductive and mesomeric effects
Understand that steric effects also play a part in determining the relative reactivity of the different sites in an aromatic ring
Predict and account for the effects of common substituents on the chemical shifts of aromatic protons in 1H NMR spectra of substituted benzene derivatives

Lecture Outline: L5

1. **Introduction**
2. **Electron Donating Substituents**
3. **Electron Withdrawing Substituents**
4. **Steric considerations**
5. **Mixed examples**

1. Introduction

When substituted benzenes react with electrophiles where does the new substituent attach?



ortho (1,2-) meta (1,3-) para (1,4-)

- All activating and weakly deactivating (the halogens) substituents direct E^+ to the **ortho and para positions**.
- All other deactivating groups direct E^+ to the **meta position**.

1. Introduction – Table from Lecture 4

(refer to Table 18.1 page 923)

Strongly Activating towards S_EAr

—NH_2	Ortho/Para	+M >> –I
—NHR	Ortho/Para	+M >> –I
—NR_2	Ortho/Para	+M >> –I
—OH	Ortho/Para	+M >> –I
—OR	Ortho/Para	+M >> –I

Activating towards S_EAr

—NHCOR (amide)	Ortho/Para	+M > –I
—OCOR (ester)	Ortho/Para	+M > –I
—Alkyl	Ortho/Para	+I

1. Introduction – Table from Lecture 4

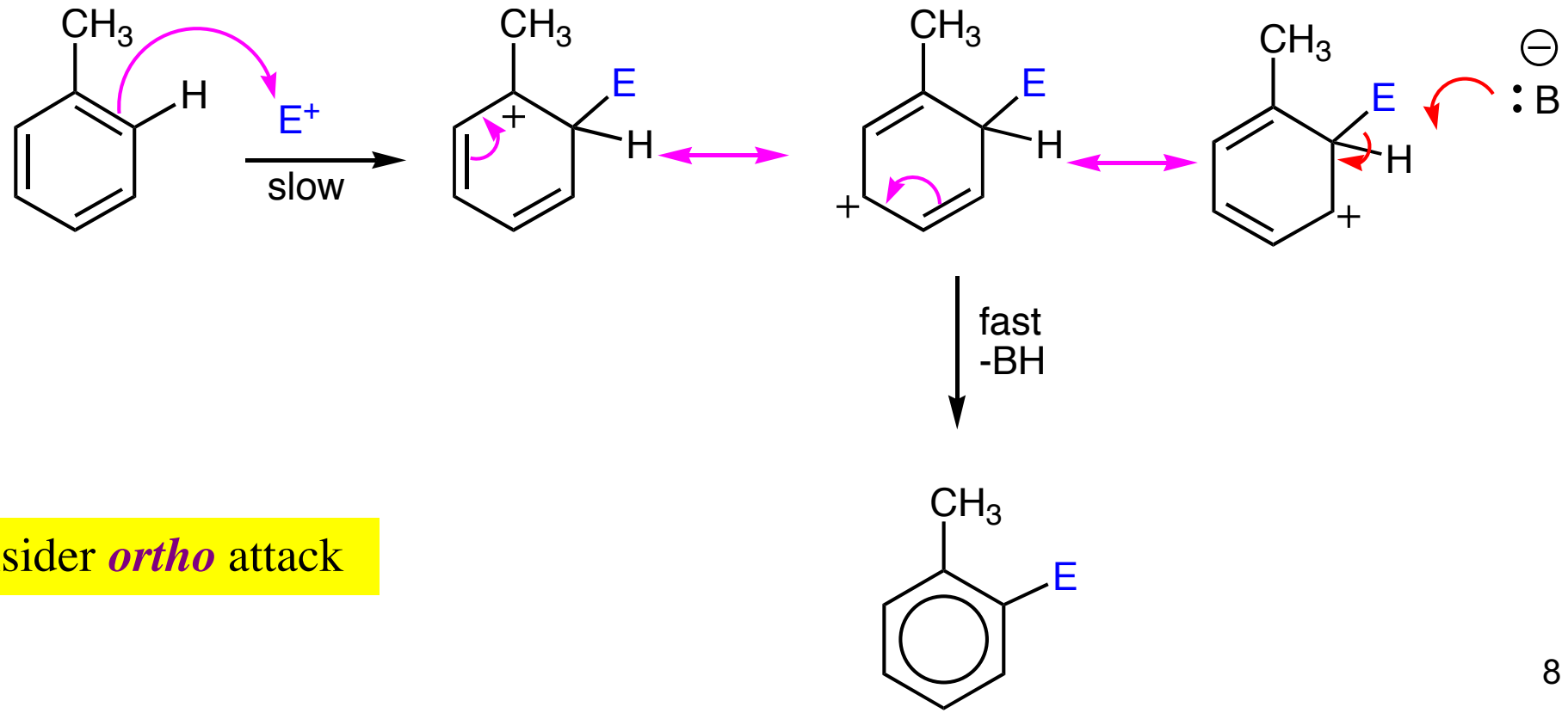
(refer to Table 18.1 page 923)

Weakly Deactivating towards S_EAr		
—F, —Cl, —Br, —I	Ortho/Para	–I > +M
Deactivating towards S_EAr		
—COH (aldehyde)	Meta	–I, –M
—COR (ketone)	Meta	–I, –M
—COOR (ester)	Meta	–I, –M
—COOH (acid)	Meta	–I, –M
—COCl (acid chloride)	Meta	–I, –M
Strongly Deactivating towards S_EAr		
—NO_2	Meta	–I, –M
—CN	Meta	–I, –M
—SO_3H	Meta	–I, –M
—NH_3^+	Meta	strong –I
—NR_3^+	Meta	strong –I

2. Electron donating substituents

- Recall from Lecture 4, +I and +M substituents activate the Ar ring to S_EAr and speed up the S_EAr reaction (relative to 'S' being H)
- But what relative ring position(s) is more activated than others?

Methylbenzene (toluene), the CH_3 group is inductively donating (+I)

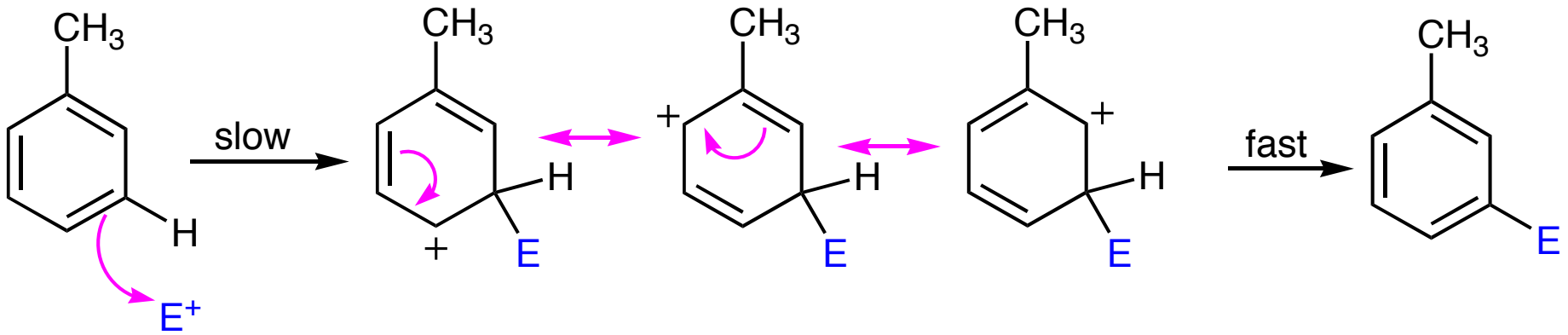


Consider *ortho* attack

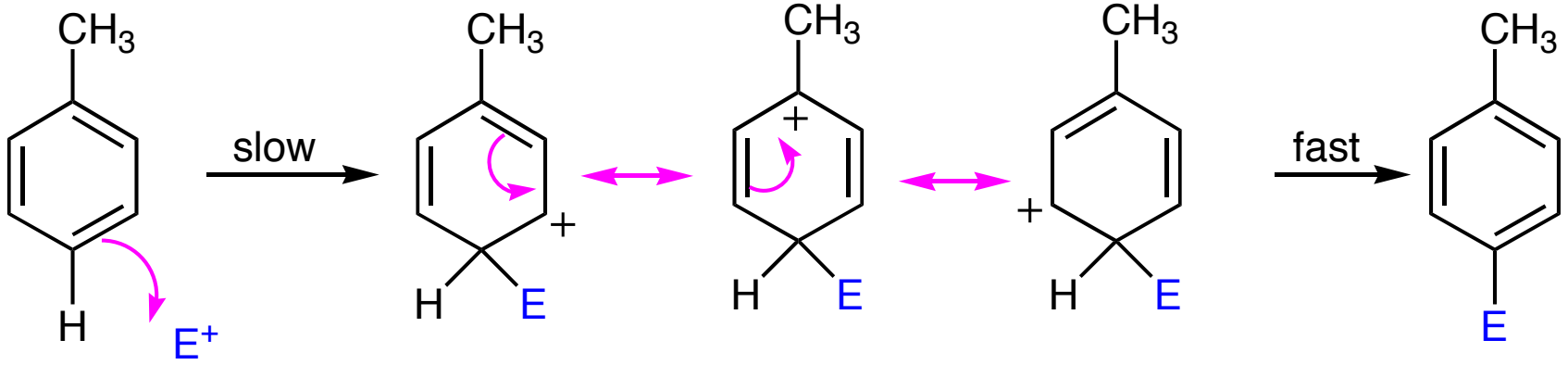
2. Electron donating substituents

Methylbenzene (toluene), the CH_3 group is inductively donating (+I)

Consider *meta* attack



Consider *para* attack

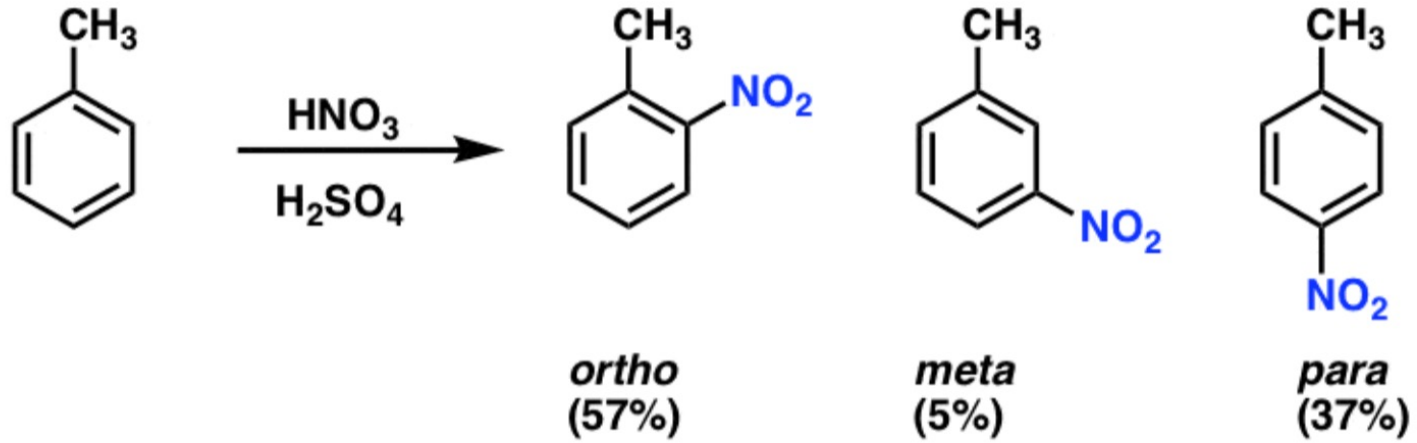


2. Electron donating substituents

Methylbenzene (toluene), the CH_3 group is inductively donating (+I)

- Conclusion – S_EAr with a +I substituent present **directs to *ortho* and *para*** E+ reaction as these have **more stable intermediates** than that of *meta*.
- The transition states leading to their formation are **lower in energy**.
- Thus **ΔE_a is smaller**
- Hence the *ortho* and *para* products are formed faster.

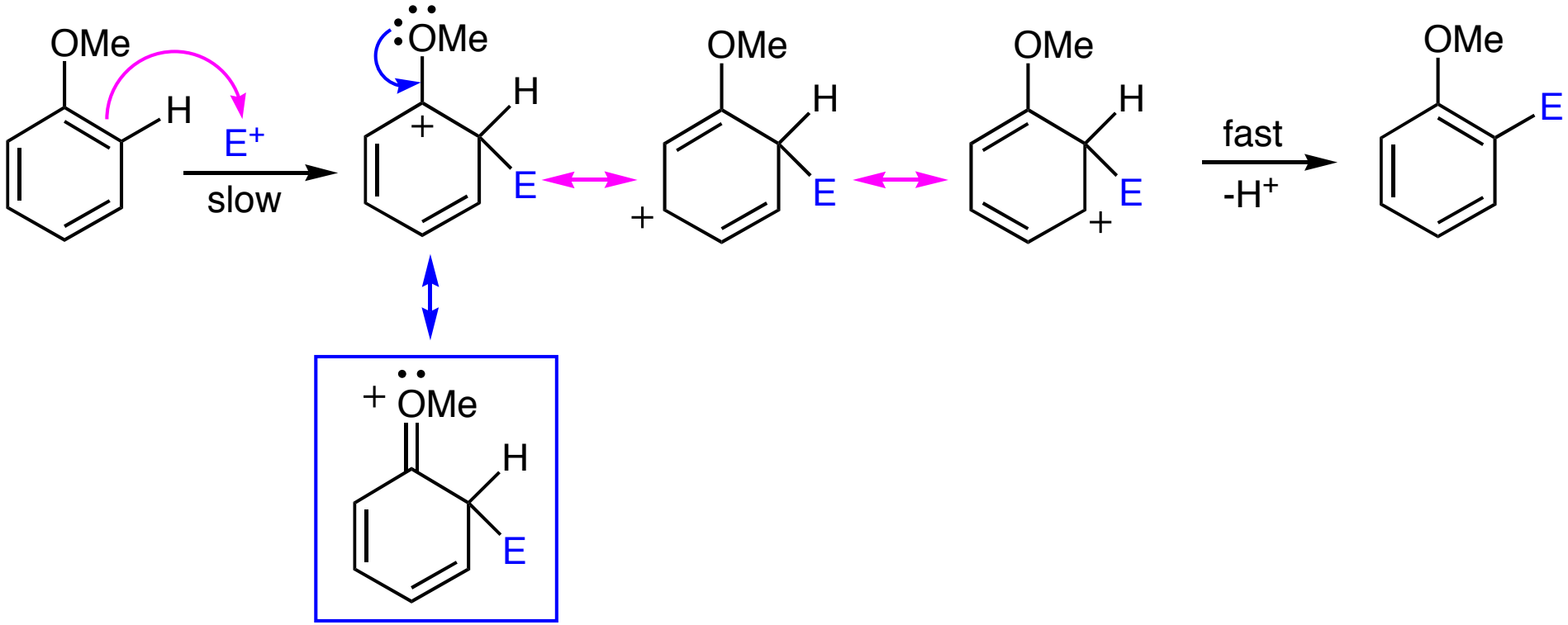
Now you can fully explain your lab 1 results !



2. Electron donating substituents

Methoxybenzene is mesomerically electron donating (+M) (+M > –I)

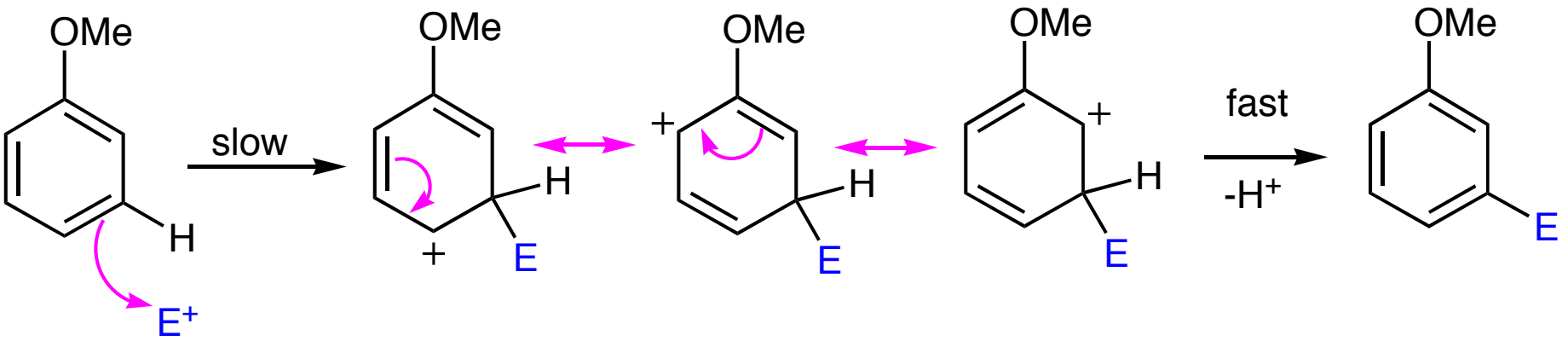
Consider *ortho* attack



2. Electron donating substituents

Methoxybenzene is mesomerically electron donating (+M) (+M > –I)

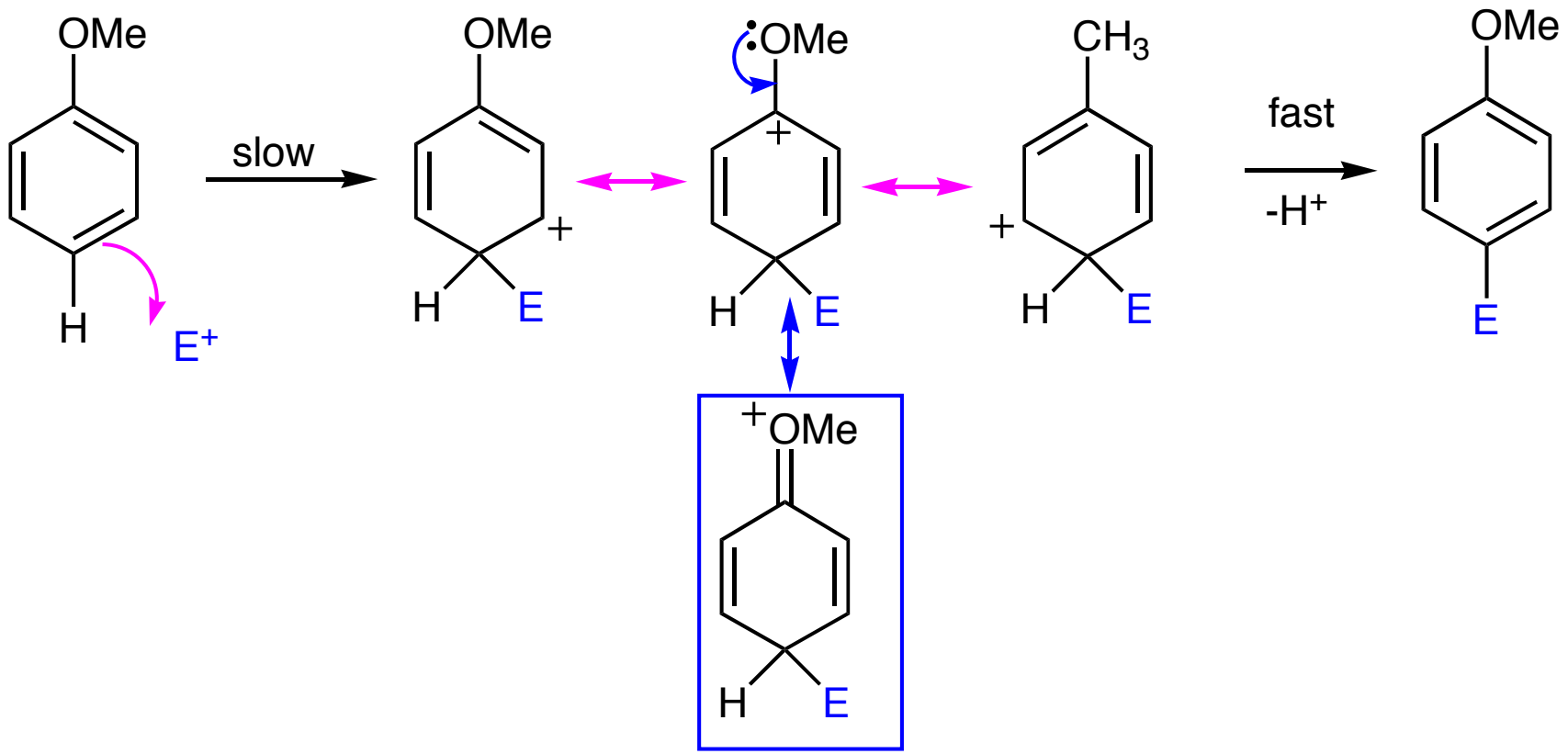
Consider *meta* attack



2. Electron donating substituents

Methoxybenzene is mesomerically electron donating (+M) (+M > –I)

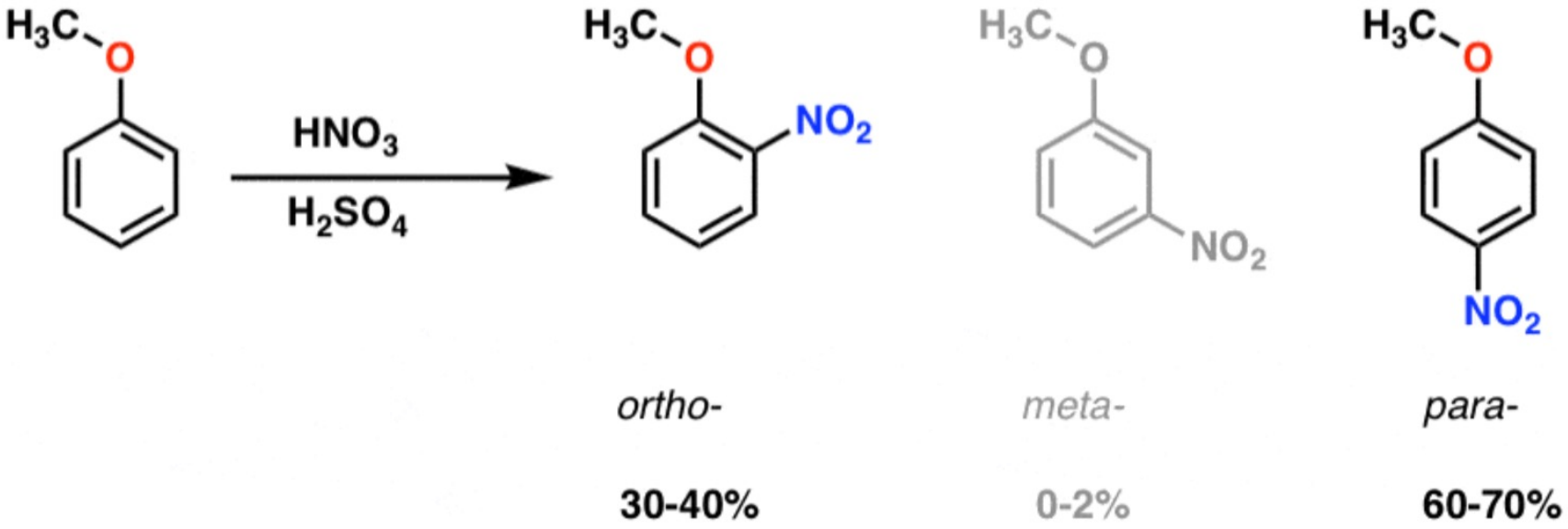
Consider *para* attack



2. Electron donating substituents

Methoxybenzene is mesomerically electron donating (+M) (+M > –I)

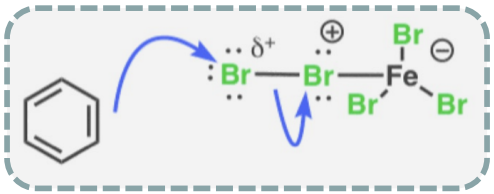
- Both ***ortho* and *para*** substitution have an 'extra' **very stable intermediate** while *meta* does not.
- Therefore +M substituents are ortho, para directing

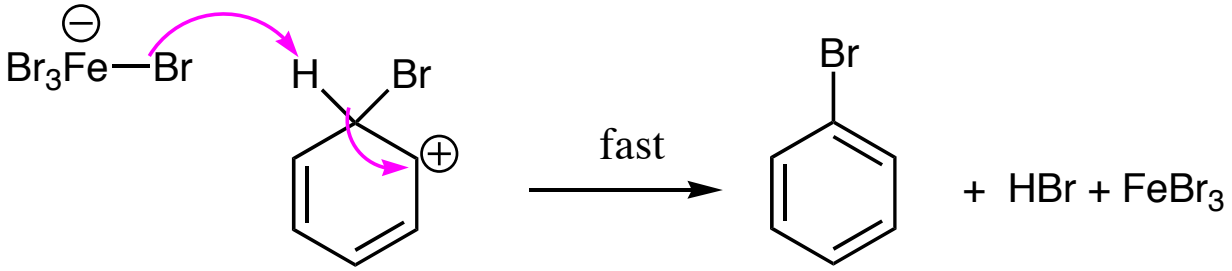


2. Electron donating substituents

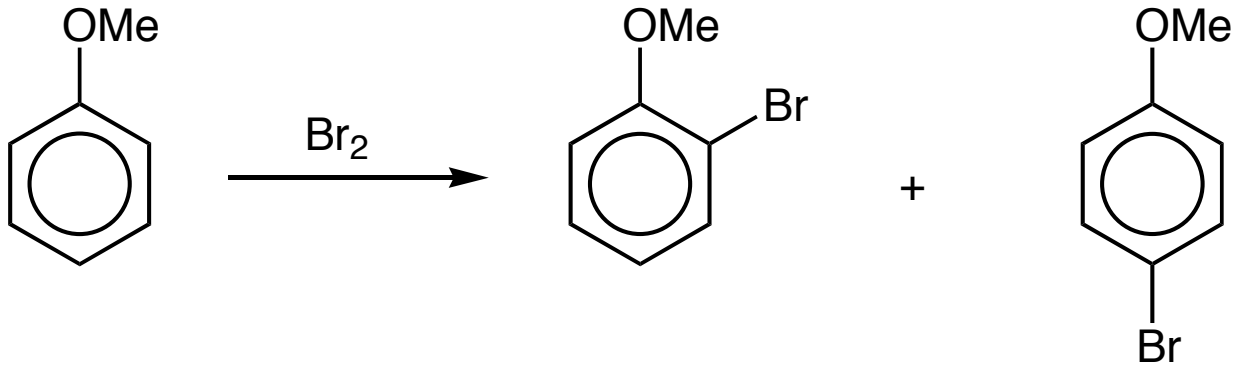
Methoxybenzene is mesomerically electron donating (+M) (+M > –I)

- Now with an **activating substituent** a **less reactive E+** can sometimes be used…
- Recall - to brominate benzene, bromine had to be turned into a better E+





- But bromination of methoxybenzene is fast and occurs without a catalyst ….

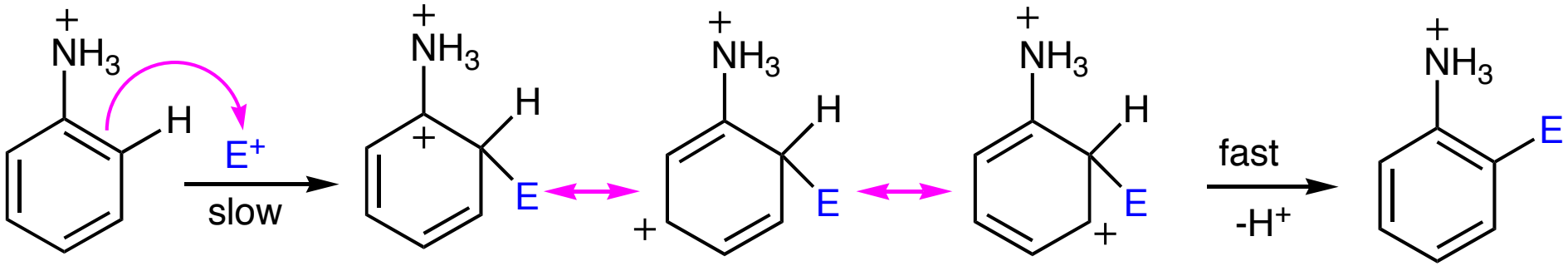


3. Electron withdrawing substituents

- Recall from Lecture 4, -I and -M substituents **deactivate** the Ar ring to S_EAr and slow down the S_EAr reaction (relative to 'S' being H)
- But what relative ring position(s) is more activated than others?

An anilinium ion (protonated analine) is strongly inductively withdrawing (-I)

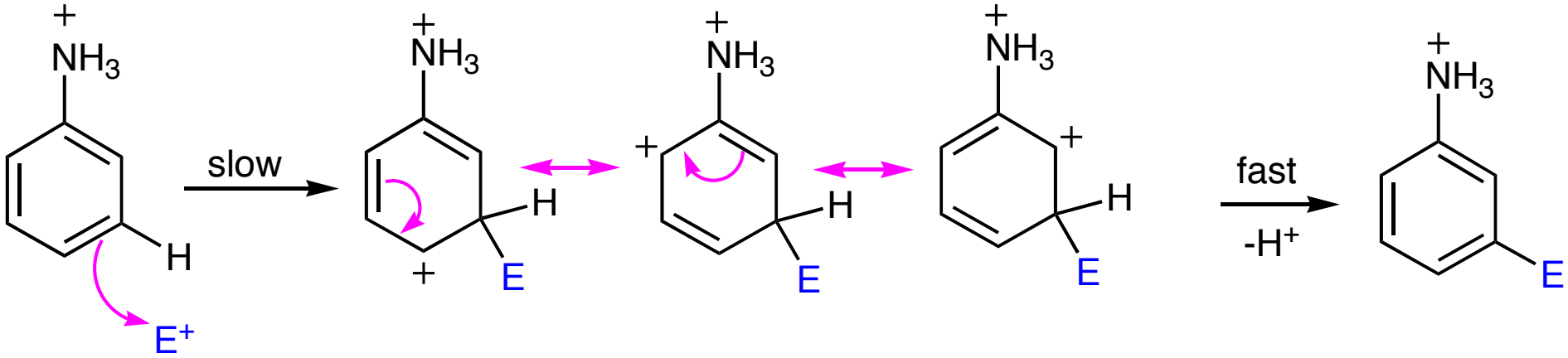
Consider ***ortho*** attack



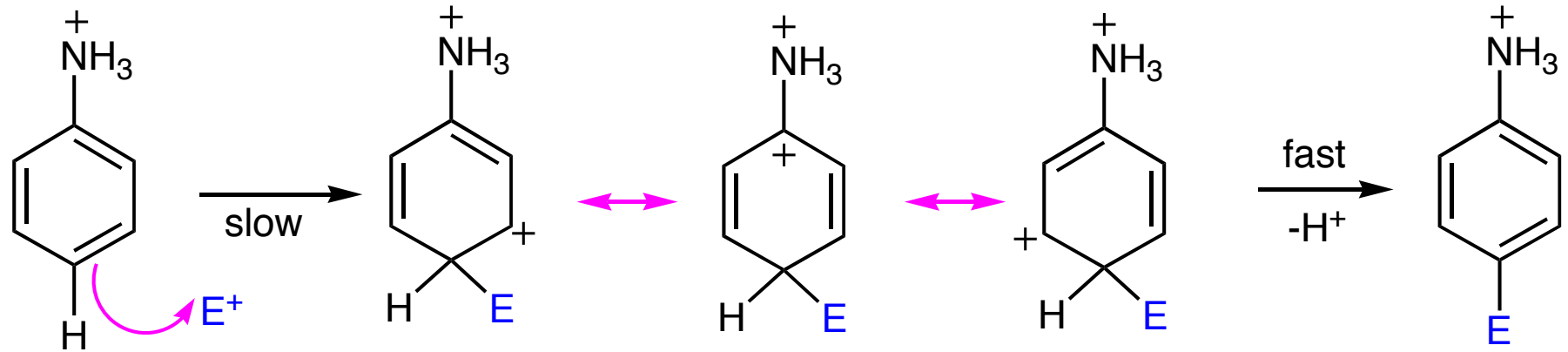
3. Electron withdrawing substituents

An anilinium ion (protonated analine) is strongly inductively withdrawing (-I)

Consider *meta* attack



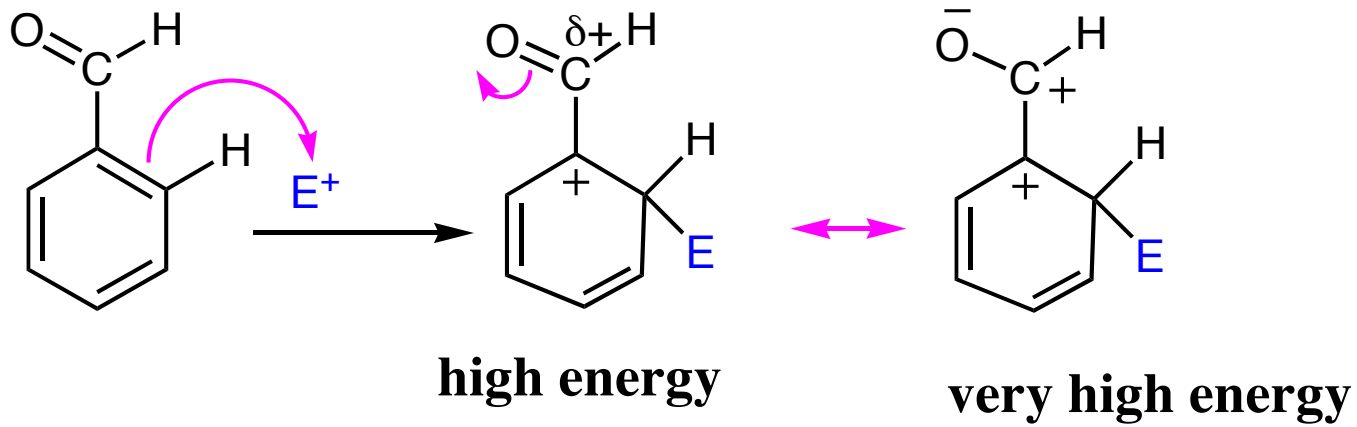
Consider *para* attack



3. Electron withdrawing substituents

All –M substituents are also all -I

Consider *ortho* attack

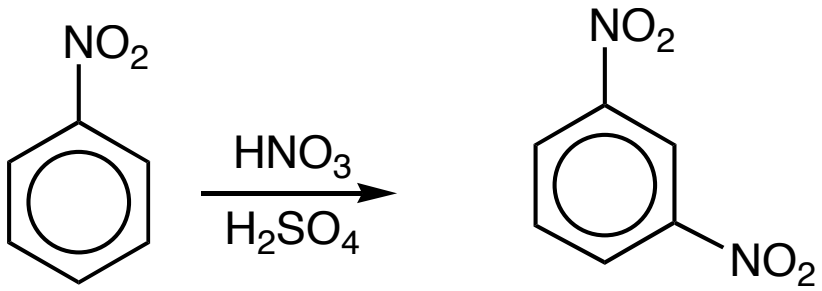


- S_EAr para substitution results in **similar high energy contributors**.
- However, the meta pathway does not.
- **Thus -M substituents are meta directing.**

3. Electron withdrawing substituents

All –M substituents are also all -I

e.g. Nitration of nitrobenzene, NO_2 group is deactivating and meta directing



The rate is 10^{-4} **slower** than that of benzene. Forcing conditions are required.

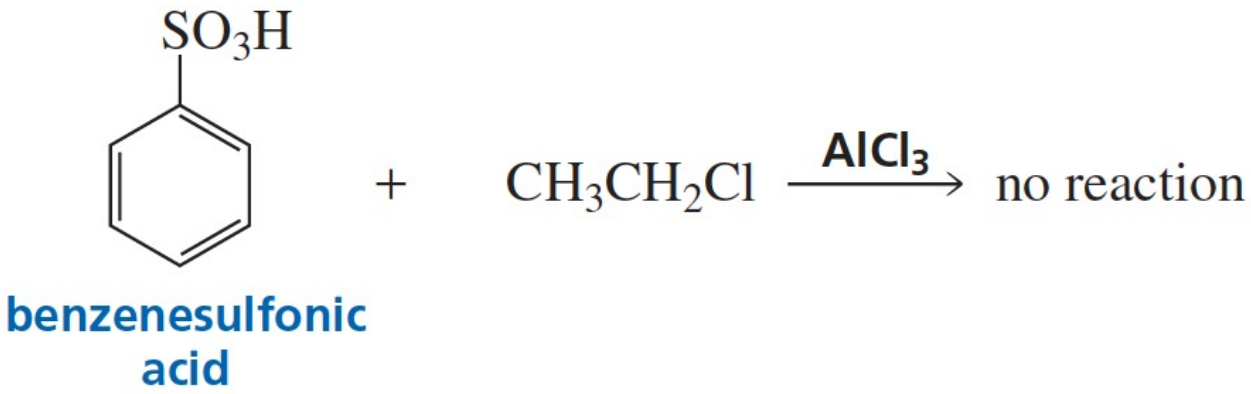
Much more forcing nitration conditions will result in possibly tri-nitro products. But since each nitro group is deactivating the rates of these further substitution reactions is even slower.

*Does this also explain why **di-NO_2 products were not formed** in lab 1…..?*

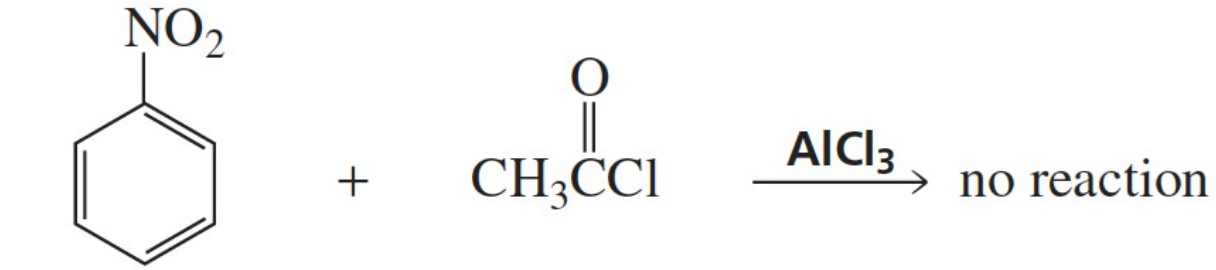
3. Electron withdrawing substituents

All –M substituents are also all -I

- Friedel Crafts acylation and alkylation are the slowest of the S_EAr's
- If a benzene ring has a moderate or strongly deactivating group a Friedel Crafts reaction will not even occur



benzenesulfonic acid



nitrobenzene

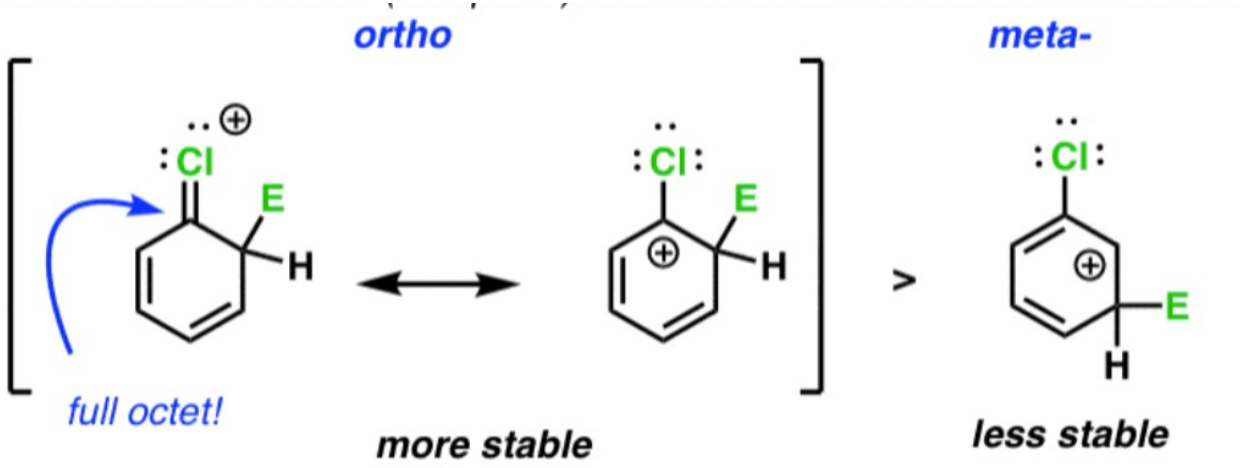
3. Electron withdrawing substituents - halogens

- Halogens are an interesting case, although electron withdrawing (-I) and classified as **weakly deactivating** for S_EAr are o/p directing

  … why?

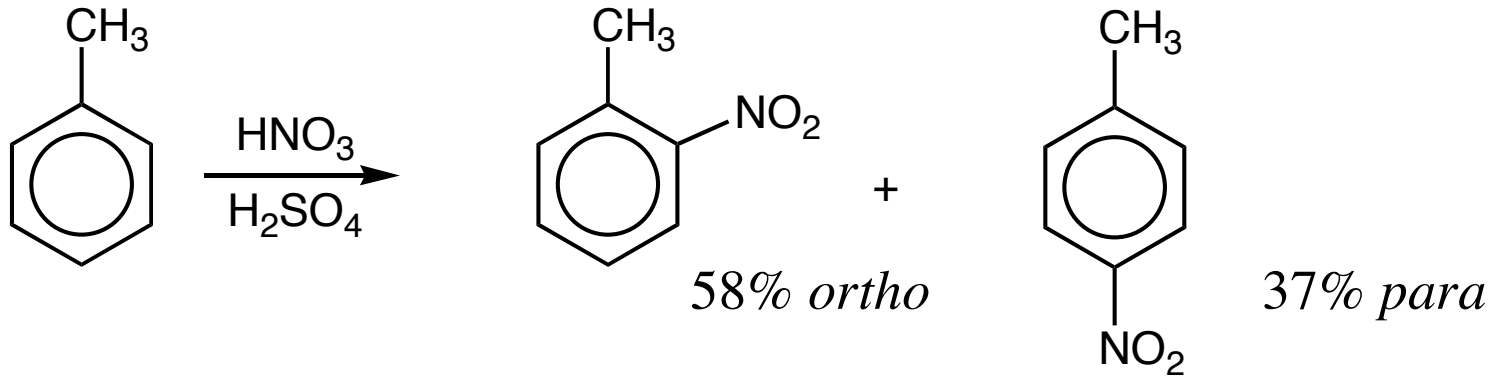
- **Weakly deactivating** just means S_EAr is comparatively slower to if an 'H' was the substituent instead.

- Halogens are the only 'deactivating' group that is NOT meta directing, instead o/p

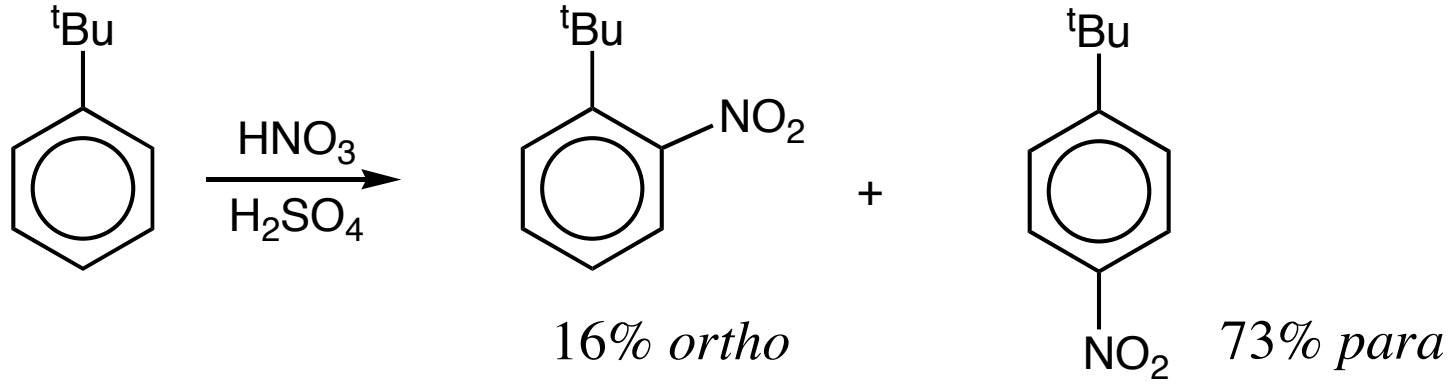


4. Steric considerations

- Often with small sized substituents the products are the expected statistical ratio based on activation/deactivation of o, m, p positions

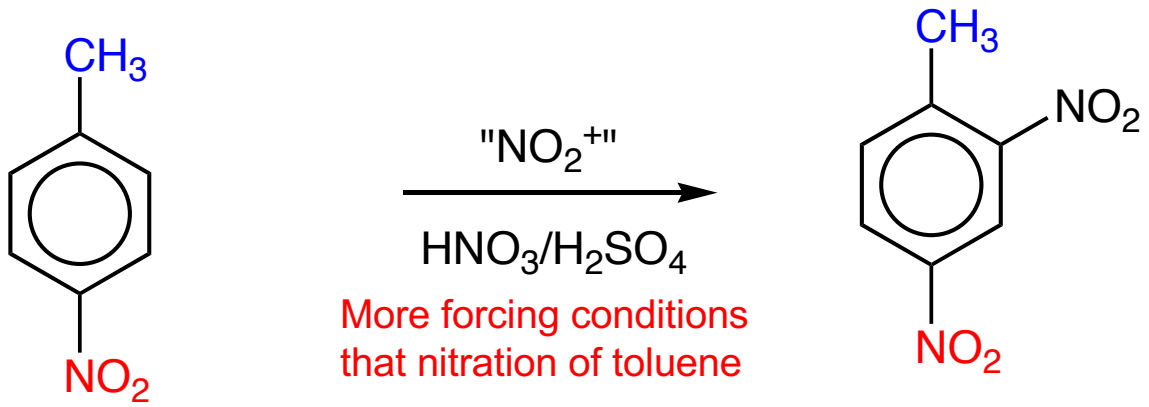


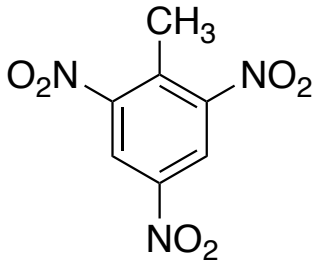
- But if the substituent is LARGE the para position is favoured, **steric factors**



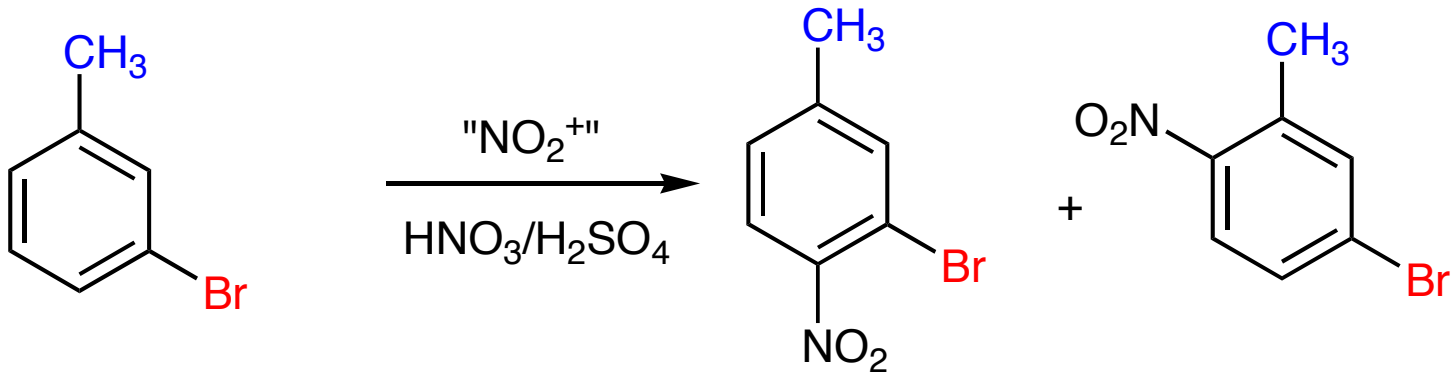
5. Mixed examples

- What about a phenyl with 2 substituents?
- This may be additive or opposing in ‘directing’ and ‘activating’ aspects.





It’s actually quite hard to make this…

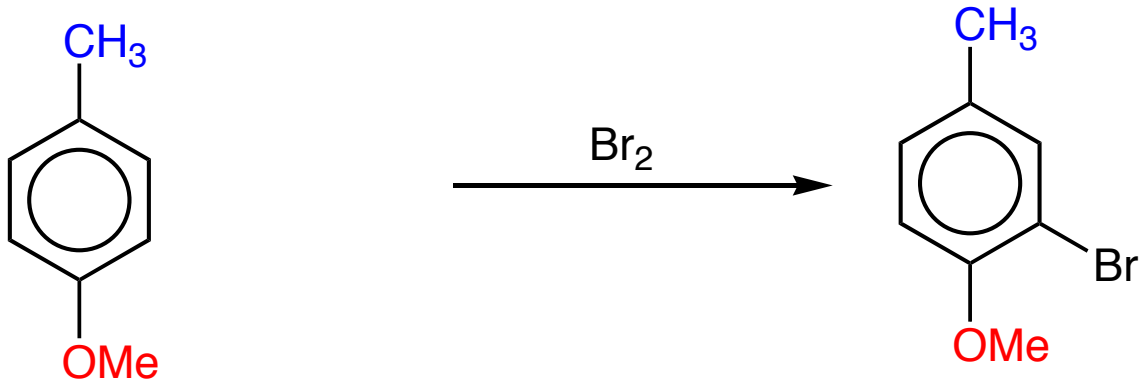


3-bromo-4-nitrotoluene 5-bromo-2-nitrotoluene

Methyl and bromo groups direct to their *o* and *p* positions
e.g. “ortho to bromo” “ortho to methyl”, specify o, m, or p in relation to something…

5. Mixed examples

- If two groups direct to different positions the group with the stronger activating properties wins.



The **methoxy +M effect (strongly activating)** is much greater than the alkyl +I effect (activating)