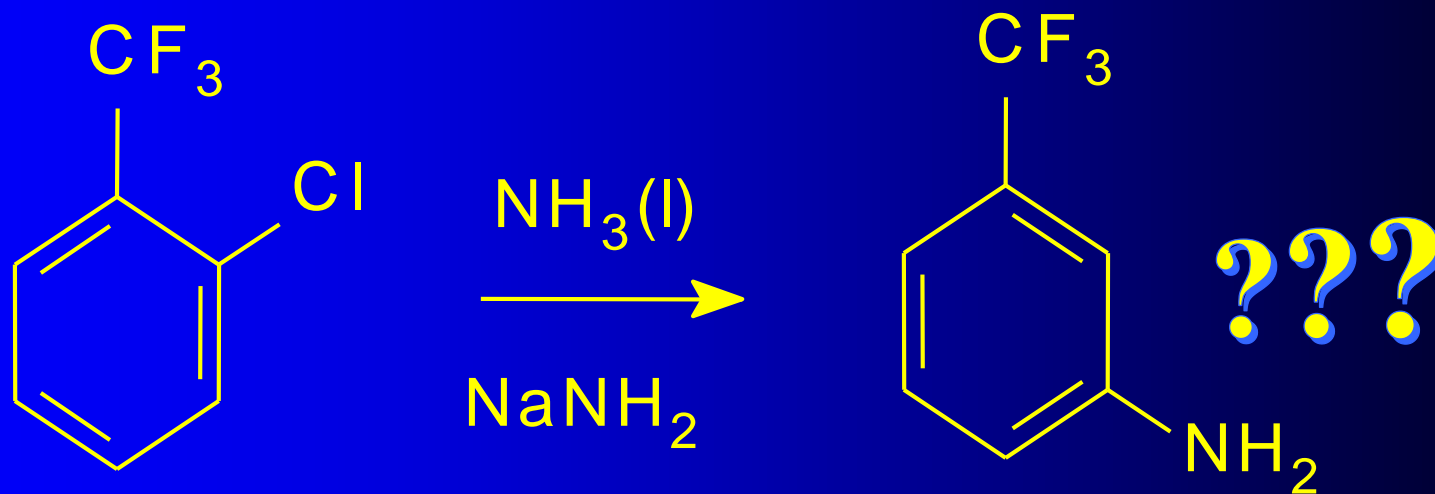
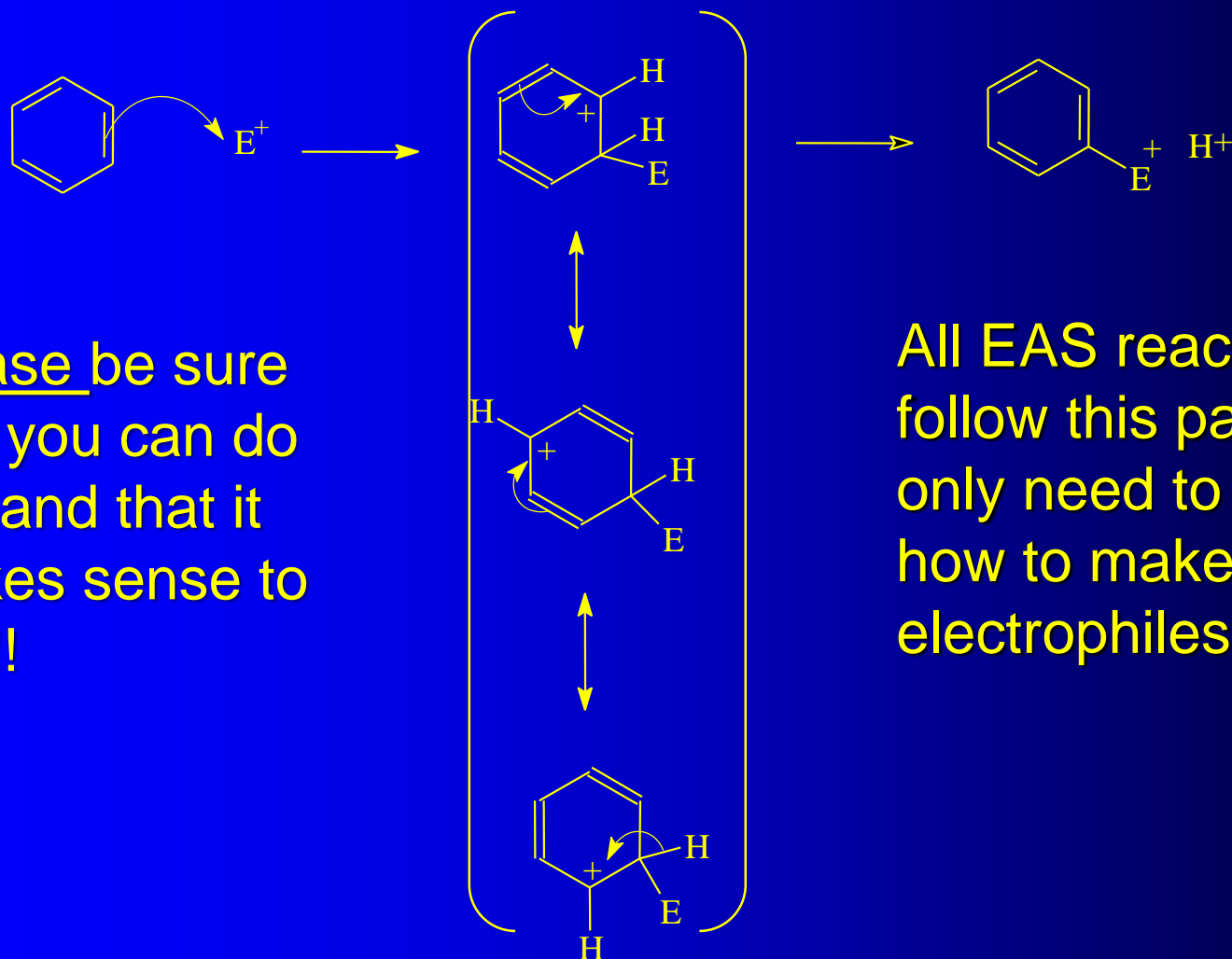


Lecture 13

Reactions of Benzene



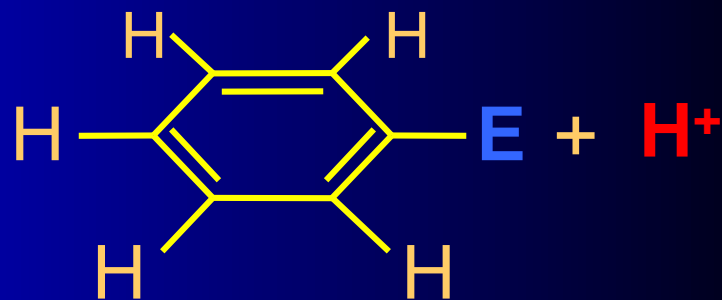
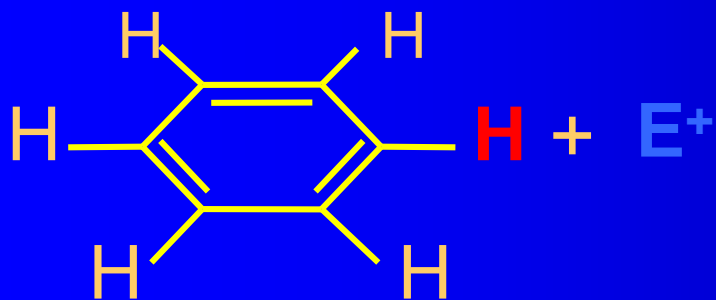
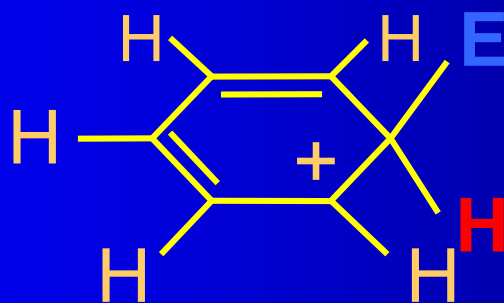
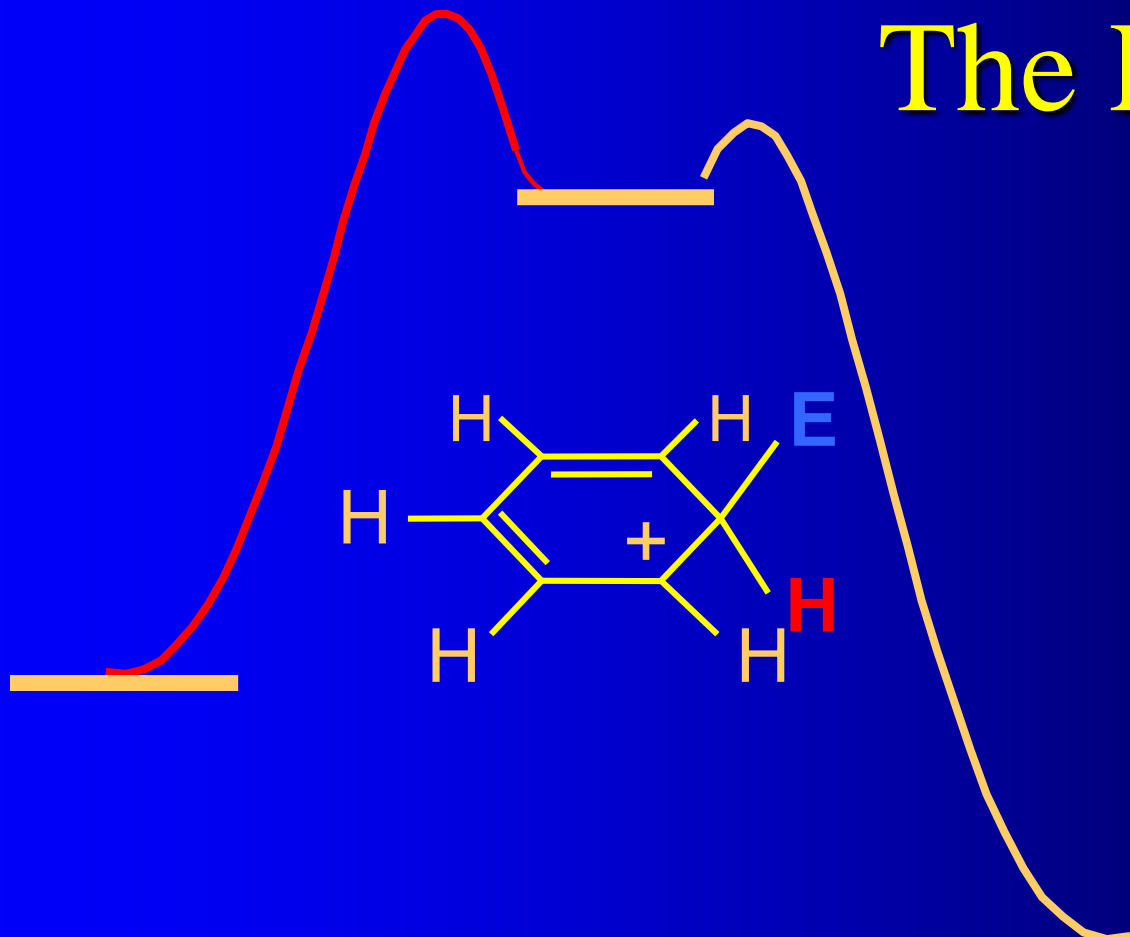
Electrophilic Aromatic Substitution

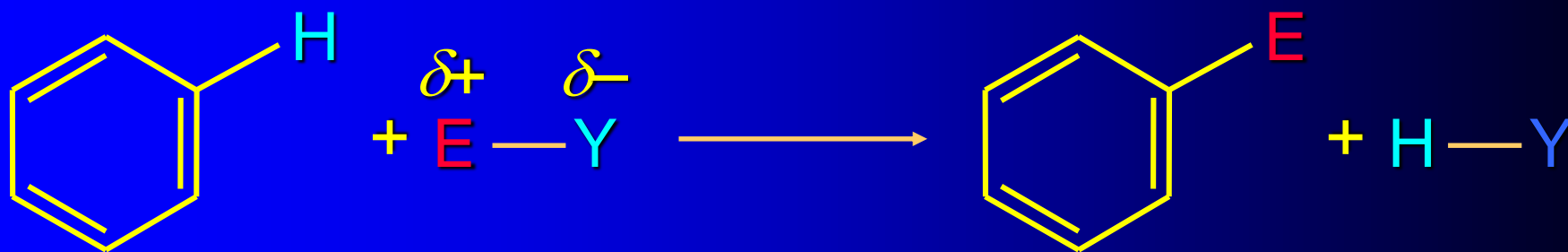


Please be sure that you can do this and that it makes sense to you!!

All EAS reactions follow this path so we only need to learn how to make different electrophiles, E^+

The Energetics





Electrophilic aromatic substitutions include:

Nitration

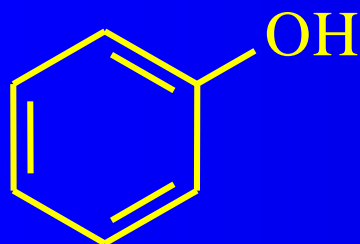
Sulfonation

Halogenation

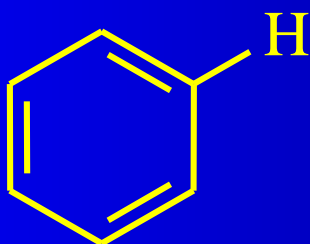
Friedel-Crafts Alkylation

Friedel-Crafts Acylation

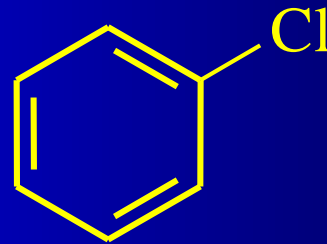
Relative rates of Nitration



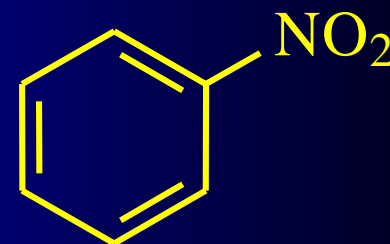
1000



1.0




0.033



6×10^{-8}



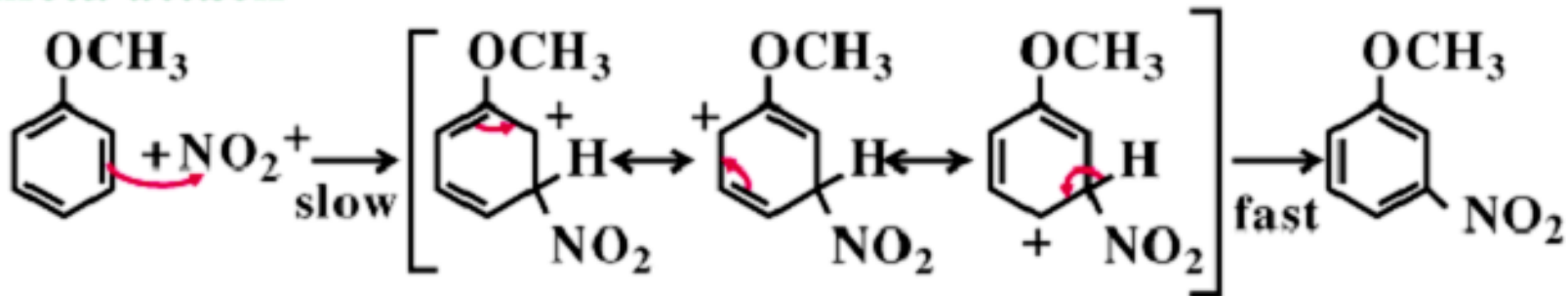
Effects of substitution on further electrophilic aromatic substitution

Ortho-Para Directing	Strongly activating	$-\ddot{\text{N}}\text{H}_2$	$-\ddot{\text{N}}\text{HR}$	$-\ddot{\text{N}}\text{R}_2$	$-\ddot{\text{O}}\text{H}$			Real Fast	
	Moderately activating	$-\ddot{\text{N}}\text{H}\overset{\text{O}}{\parallel}\text{CR}$	$-\ddot{\text{N}}\text{H}\overset{\text{O}}{\parallel}\text{CAr}$	$-\ddot{\text{O}}\text{R}$	$-\ddot{\text{O}}\overset{\text{O}}{\parallel}\text{CR}$	$-\ddot{\text{O}}\overset{\text{O}}{\parallel}\text{CAr}$		Pretty fast	
	Weakly activating	$-\text{R}$							Kinda slow
	Weakly deactivating	$-\ddot{\text{F}}:$	$-\ddot{\text{Cl}}:$	$-\ddot{\text{Br}}:$	$-\ddot{\text{I}}:$				Pretty slow
Meta Directing	Moderately deactivating	$\overset{\text{O}}{\parallel}-\text{CH}$	$\overset{\text{O}}{\parallel}-\text{CR}$	$\overset{\text{O}}{\parallel}-\text{COH}$	$\overset{\text{O}}{\parallel}-\text{COR}$	$\overset{\text{O}}{\parallel}-\text{CNH}_2$	$\overset{\text{O}}{\parallel}-\text{SOH}$	$-\text{C}\equiv\text{N}$	Slow
	Strongly deactivating	$-\text{NO}_2$	$-\text{NH}_3^+$	$-\text{CF}_3$	$-\text{CCl}_3$				Real Slow

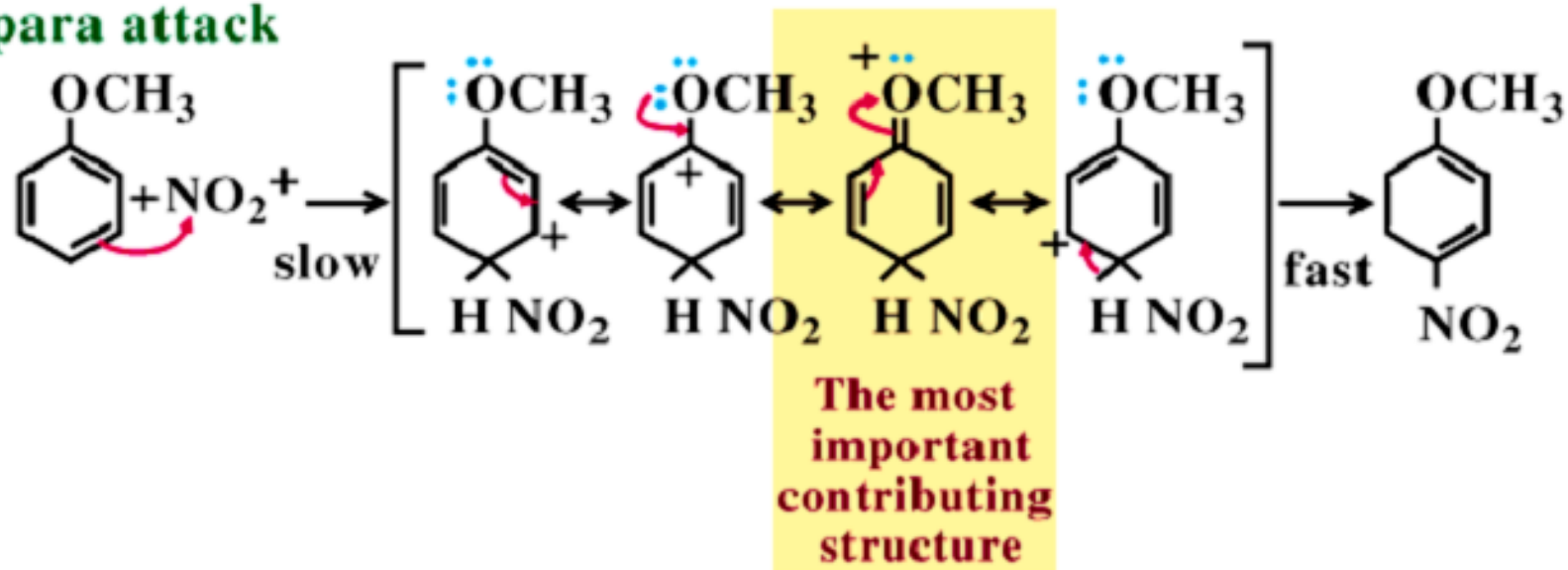


Adding a Second Substituent

meta attack



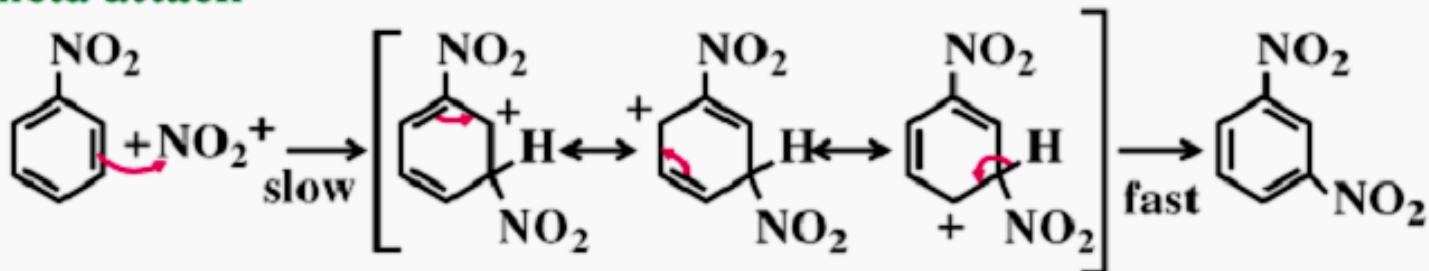
para attack



Methoxy is therefore an "o-p director"

Adding a Second Substituent

meta attack



para attack



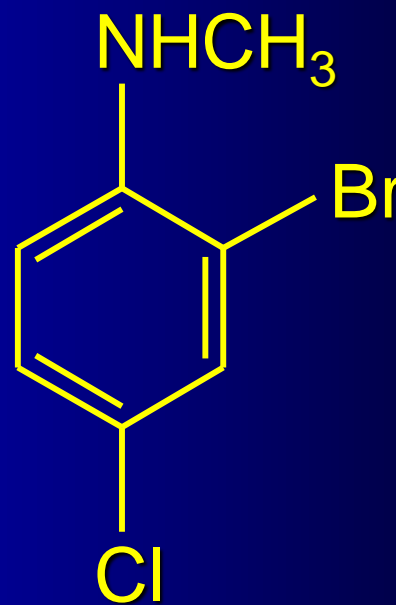
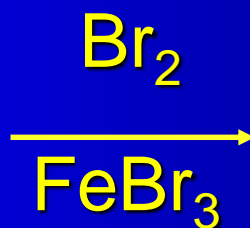
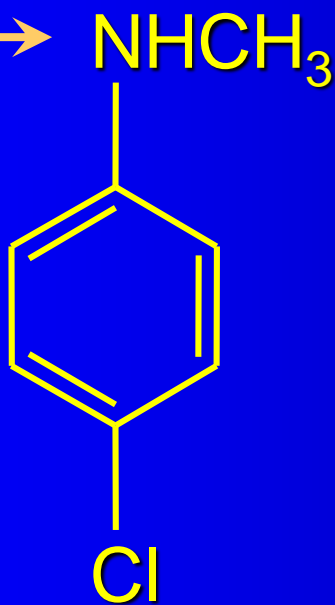
Nitro is therefore a "meta director"

Generalization

regioselectivity is controlled by the most activating substituent

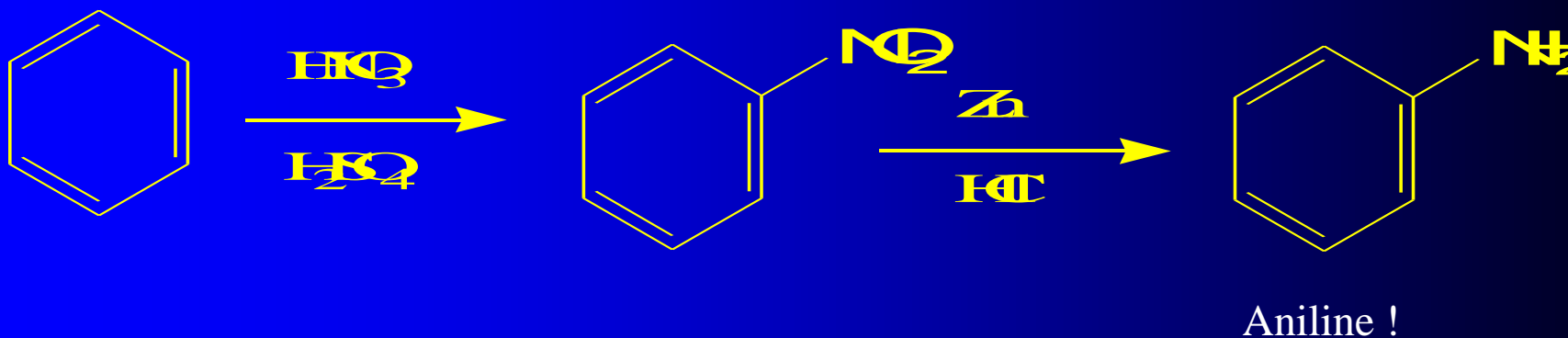
The "Best Man Wins"

strongly
activating →



87%

Reduction of the Nitro Group



The Nitro group is easily reduced. Many reducing agents can be employed for this transformation including Sn or Fe in HCl, H_2 with Pd/C, etc

Aniline dyes (Tyrian Purple)



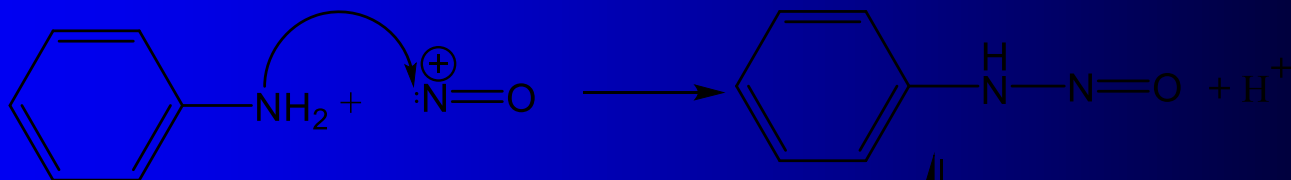
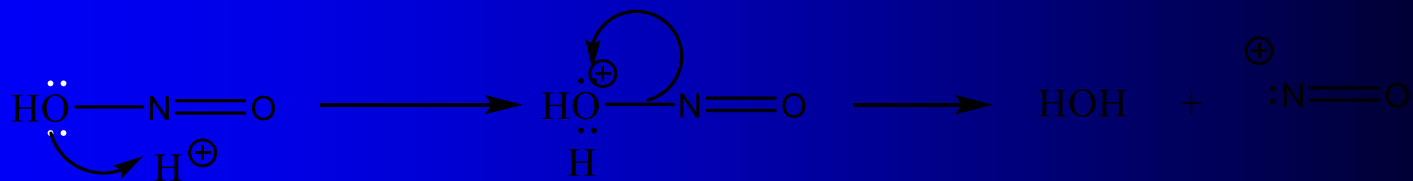
Aniline Dye



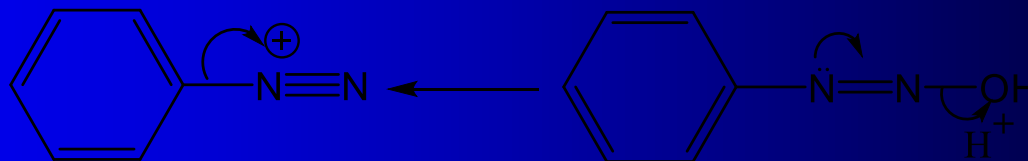
Royal Purple Previously
from shell fish secretions



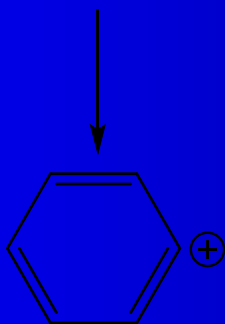
Diazonium Salts



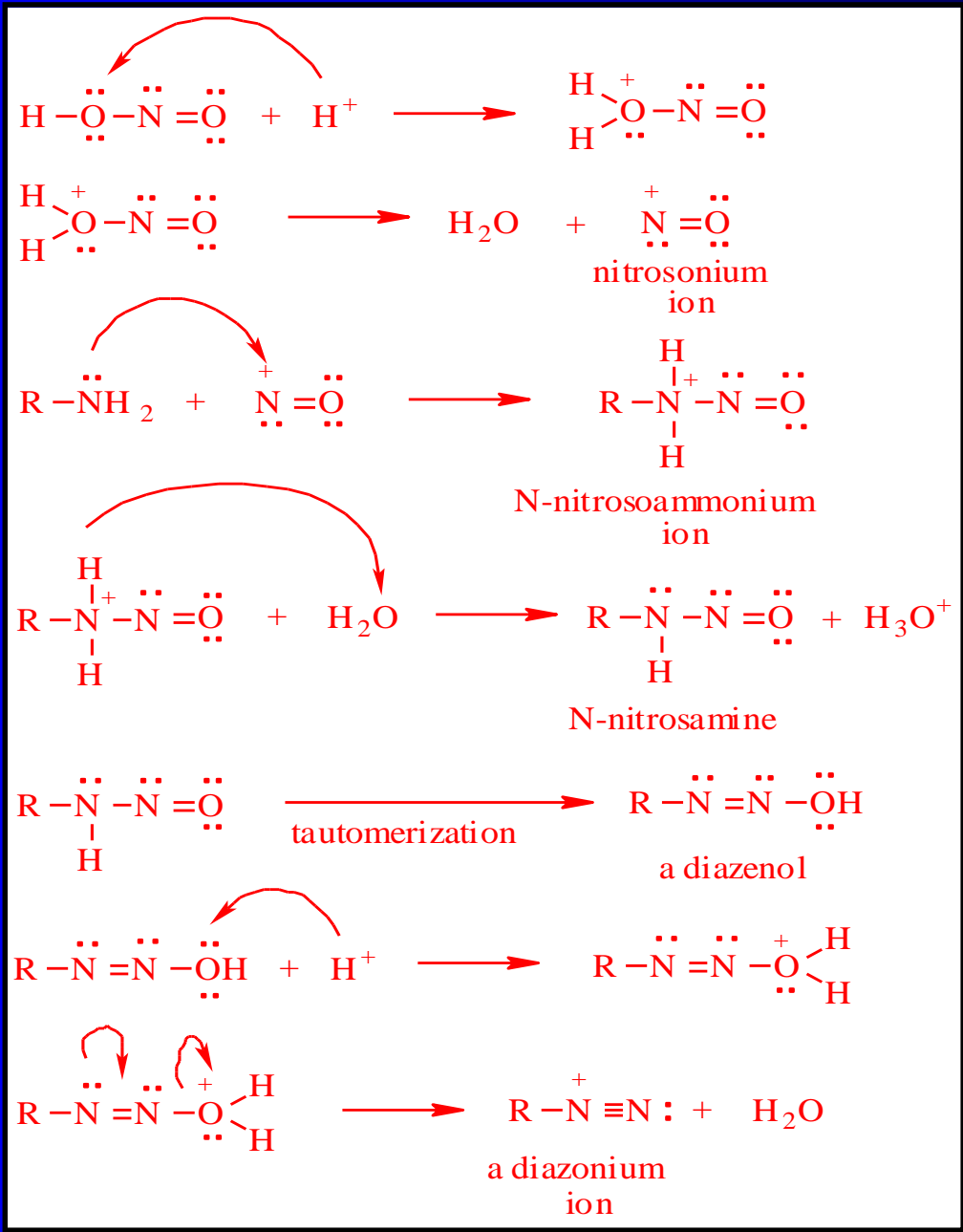
Diazonium Salt



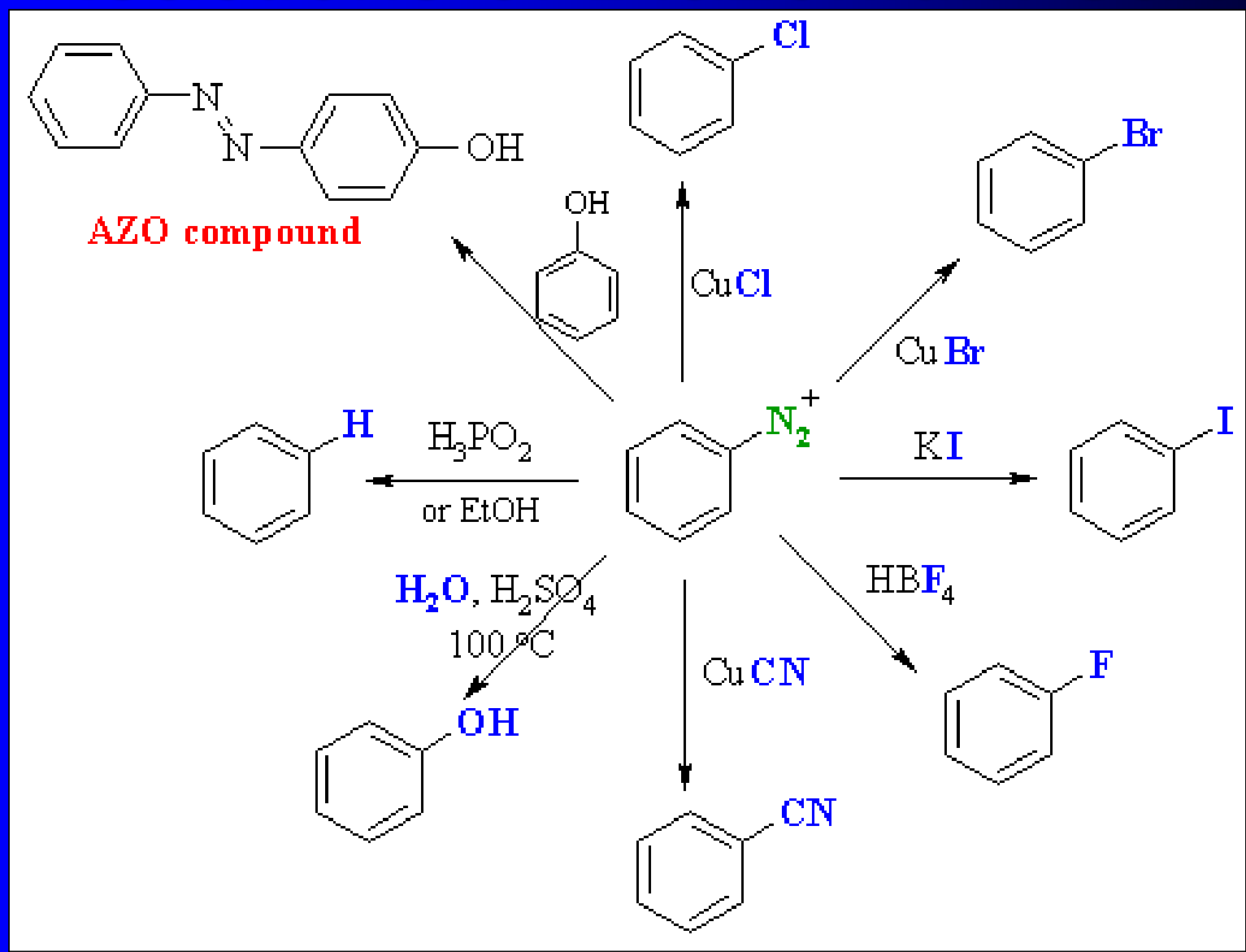
Acts like



Mechanism of Diazonium Salt formation

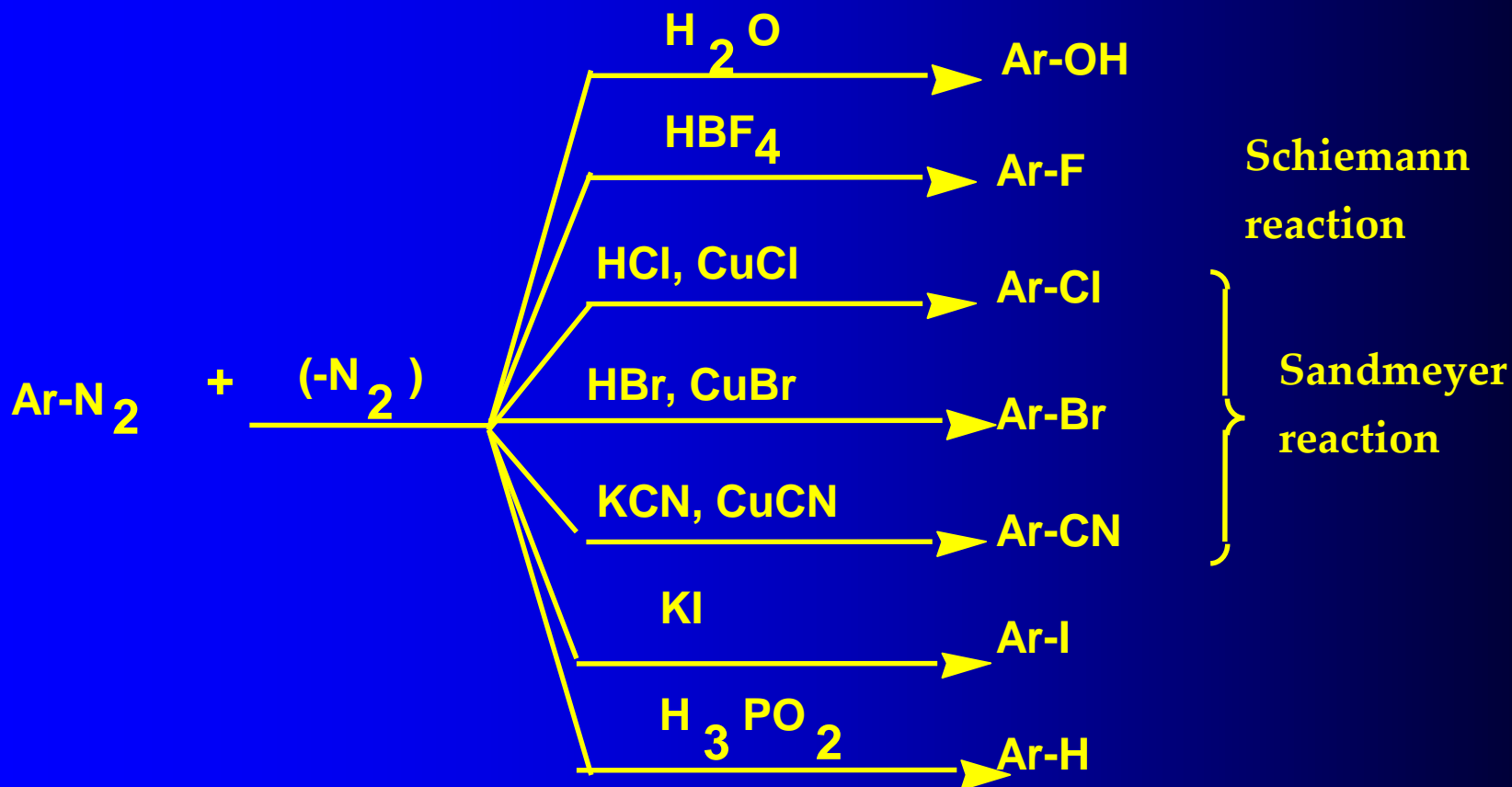


Reactions of Diazonium Salts

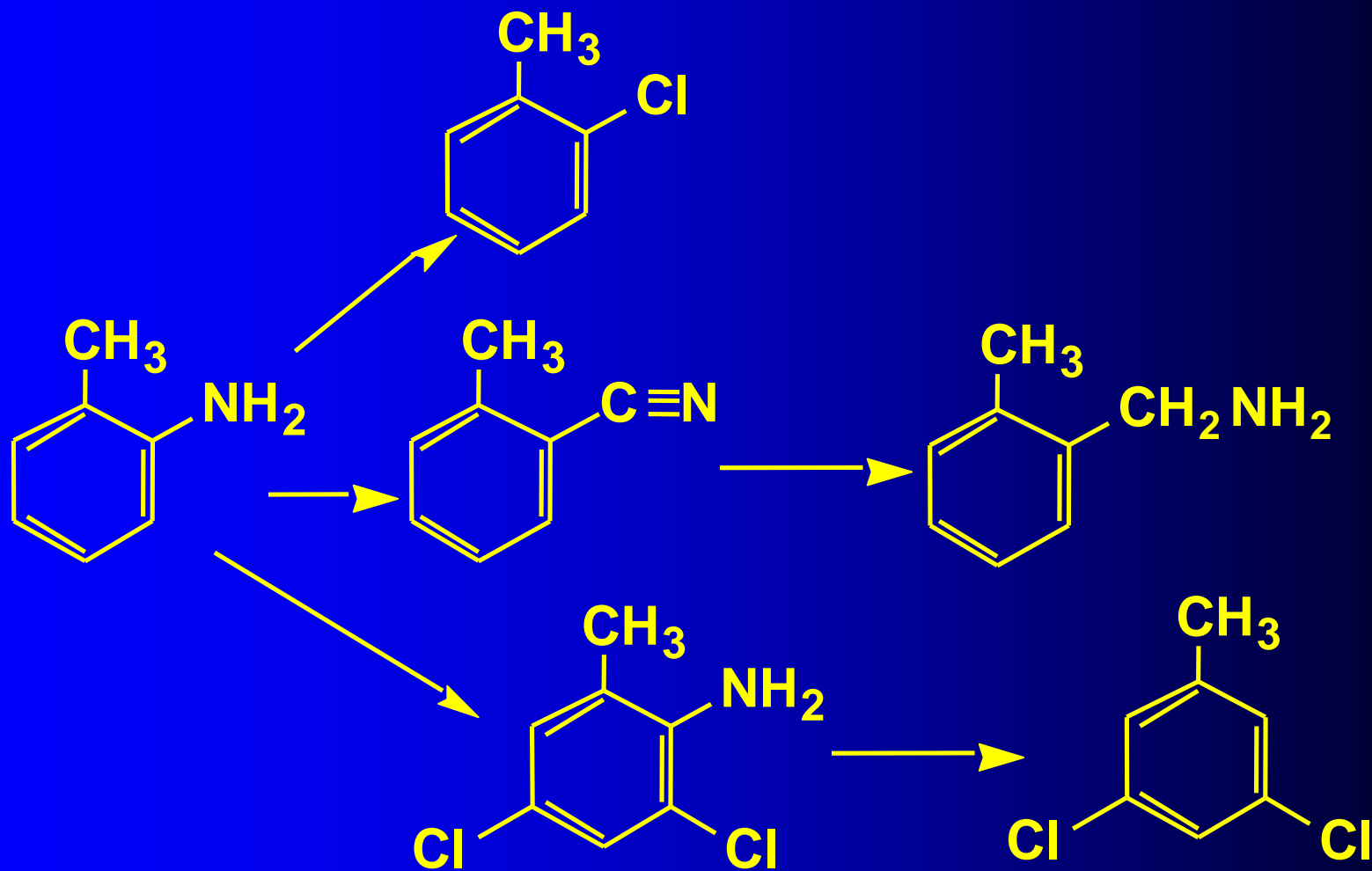


Diazonium Salts

- The $-\text{N}_2^+$ group of an arenediazonium salt can be replaced in a regioselective manner by these groups

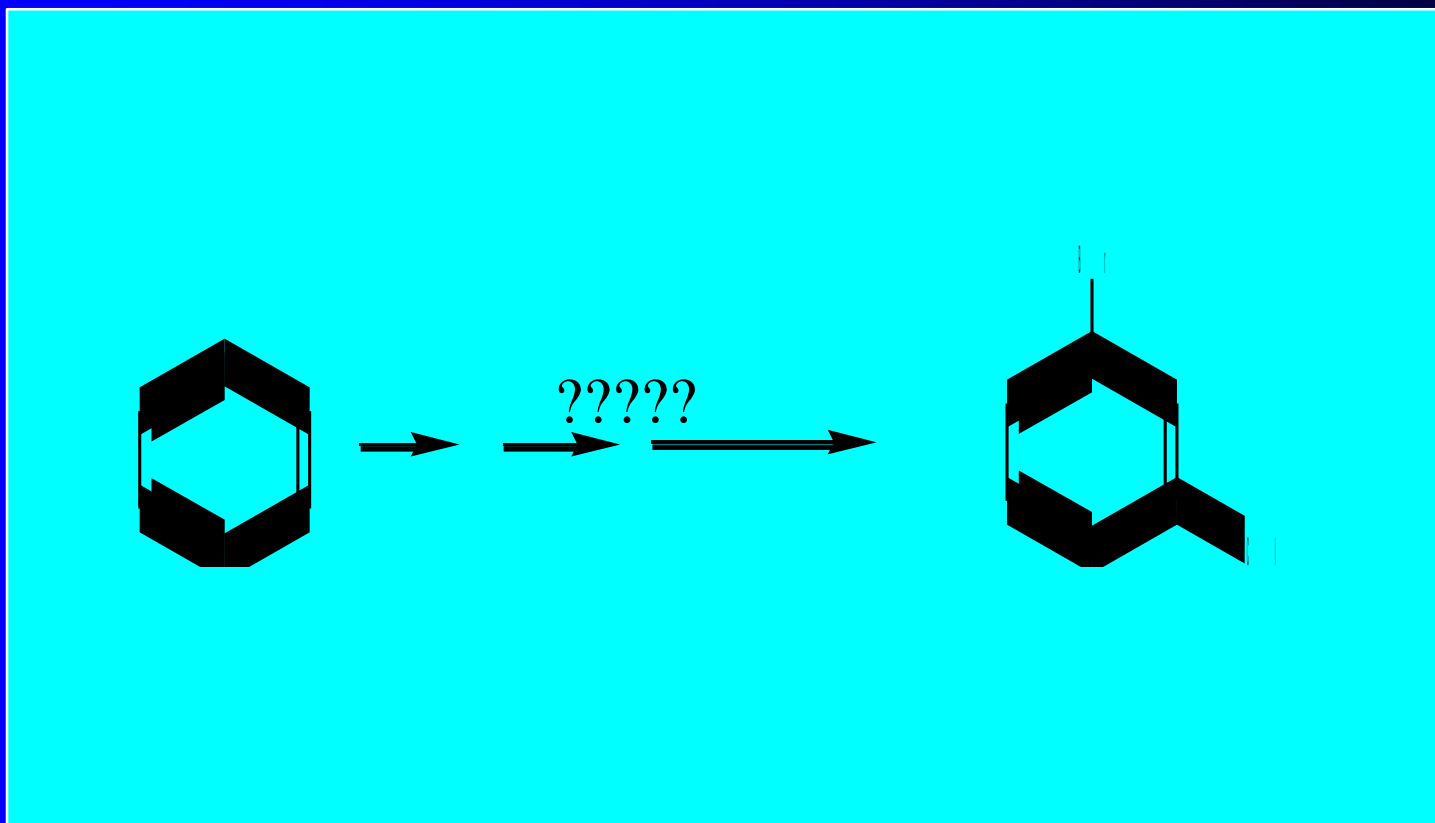


Practice

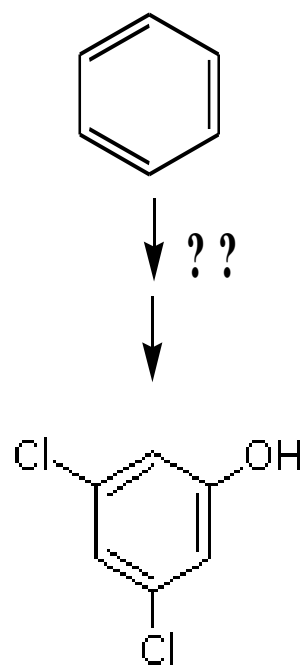


Practice...work backwards

Oh No....two o,p directors meta to one another???



Synthesis Strategy



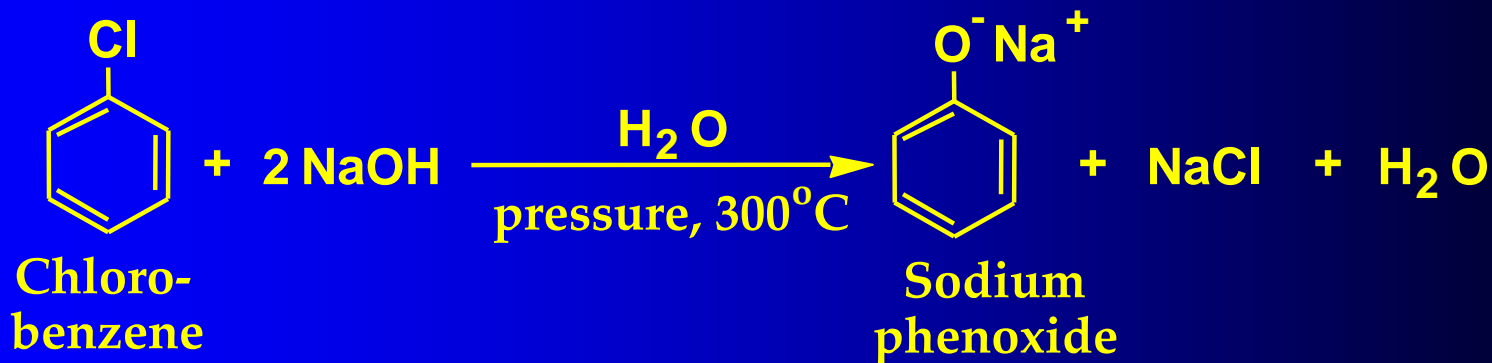
Substitution Reactions

- Aryl halides do not undergo nucleophilic substitution by either S_N1 or S_N2 pathways!

But.....

But....this is fact

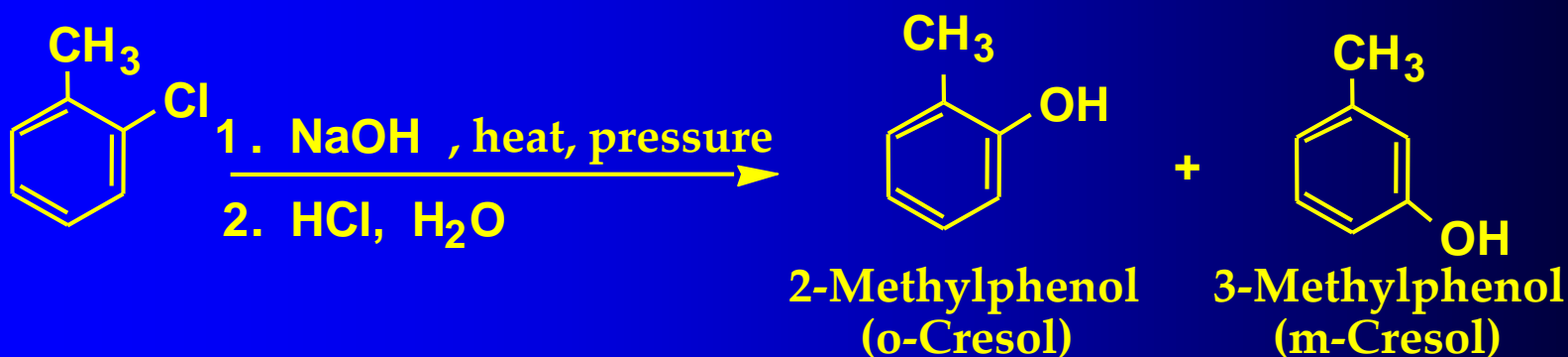
- When heated under pressure with aqueous NaOH, chlorobenzene is converted to sodium phenoxide



- neutralization with HCl gives phenol????? What is this??

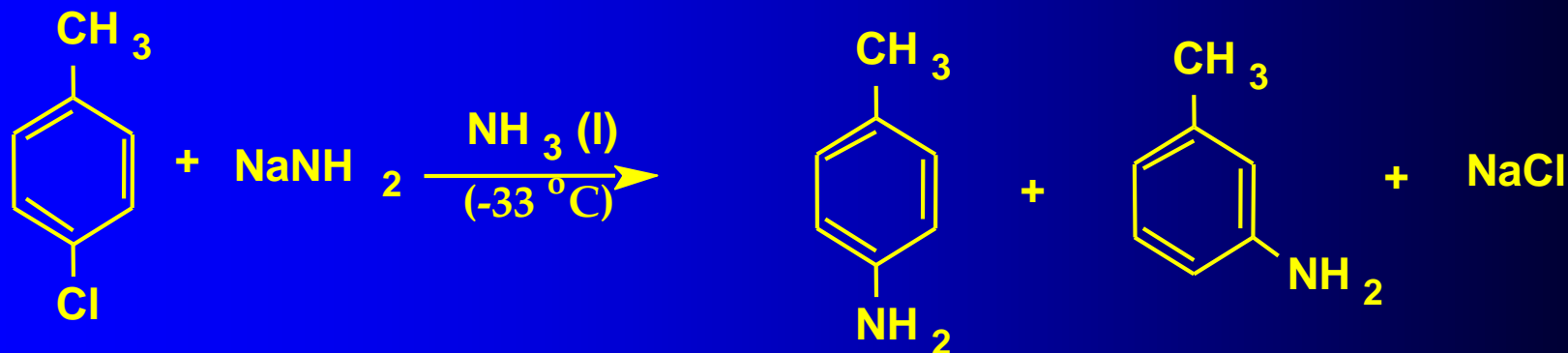
Also fact....

- The same reaction with 2-chlorotoluene gives a mixture of ortho- and meta-cresol???? Ortho and meta....huh????



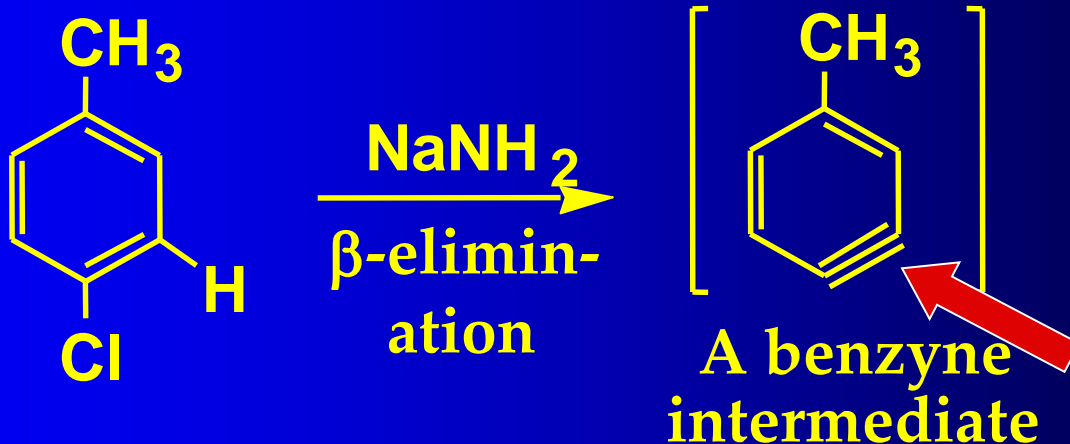
Also true

- The same type of reaction can be brought about by the use of sodium amide in liquid ammonia

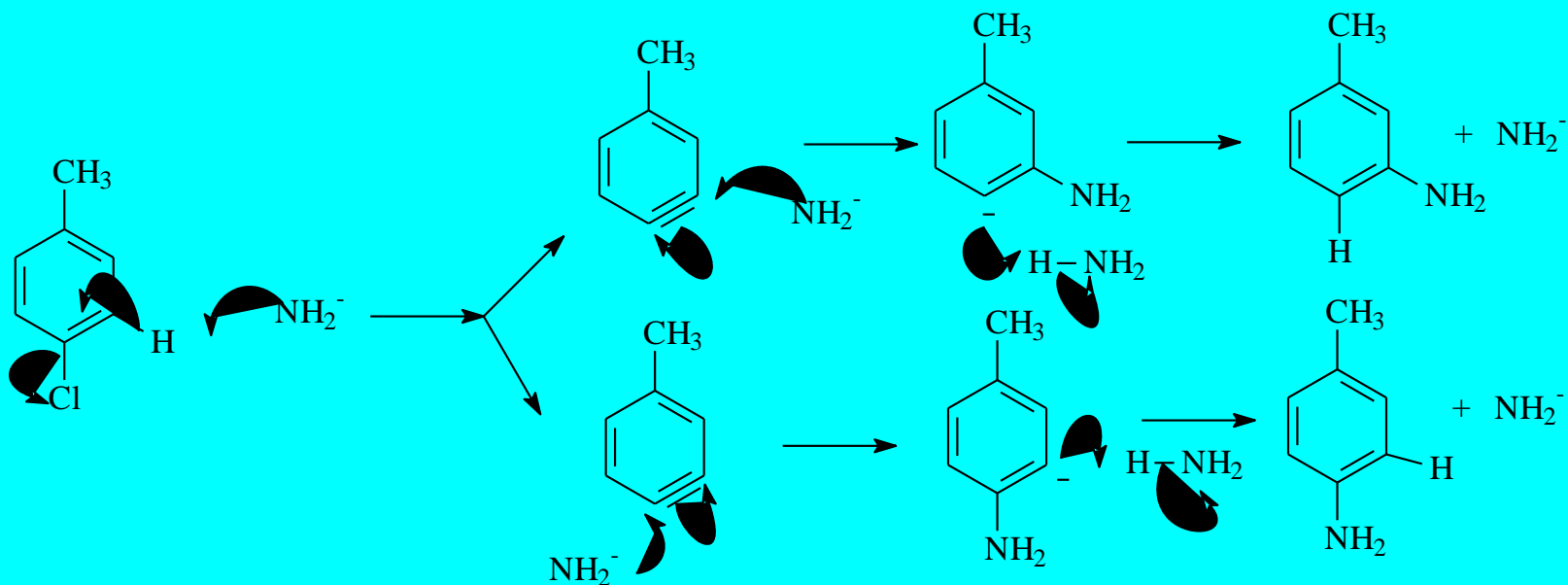


Proposed Benzyne Intermediate

- β -elimination of HX gives a “benzyne” intermediate, that then adds the nucleophile to give products

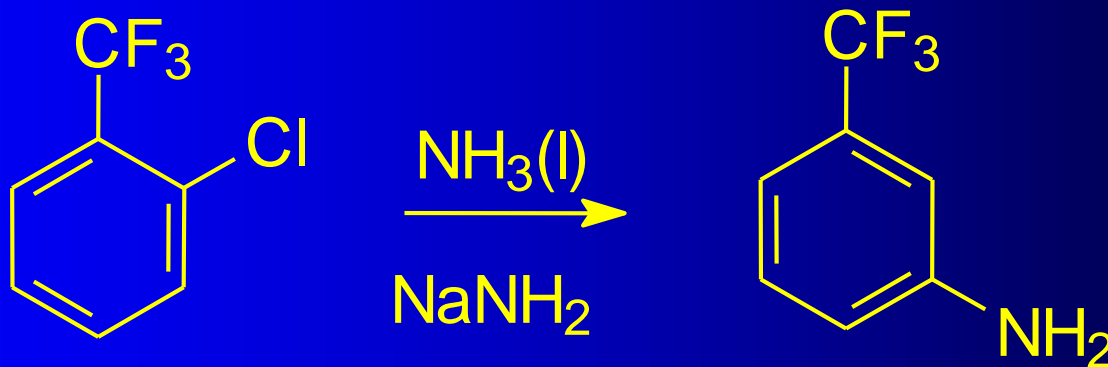


Proposed Benzyne Intermediate



Proposed Benzyne Intermediate

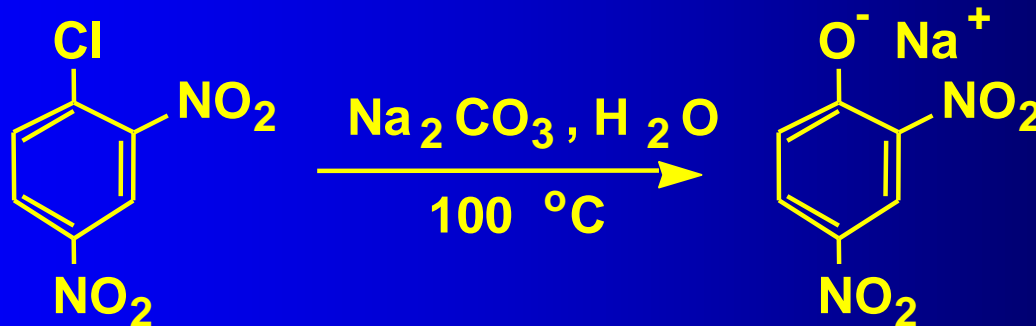
Another Mystery??



More than 95% of the product
is the meta isomer??

Nucleophilic Addition-Elimination

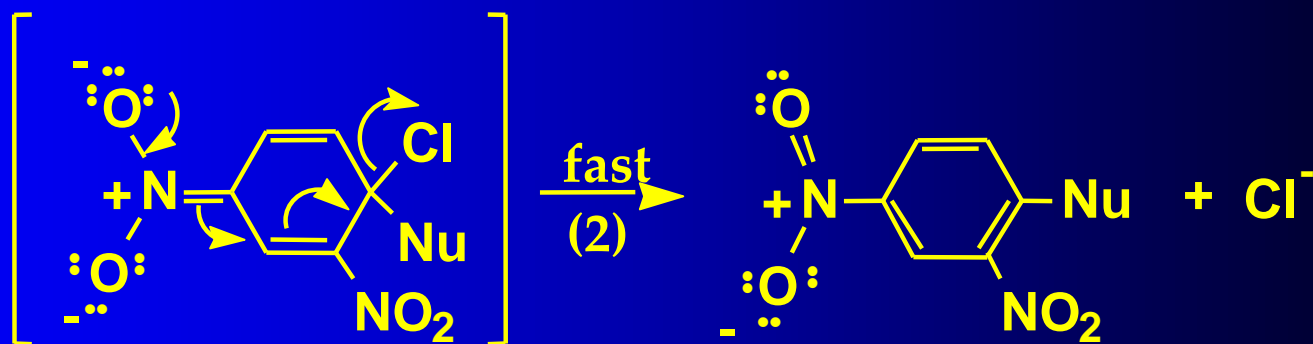
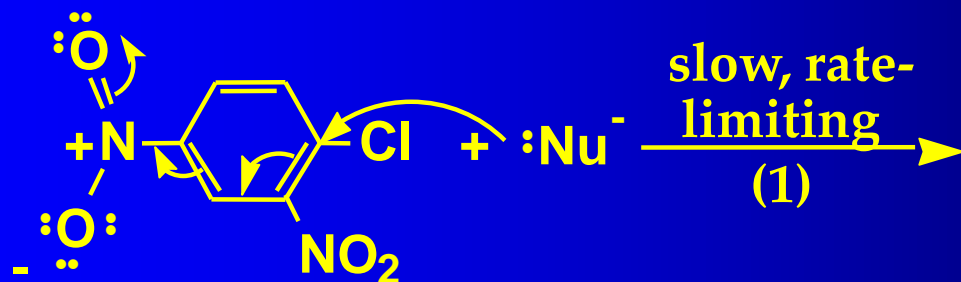
- When an aryl halide contains strongly electron-withdrawing $-\text{NO}_2$ groups ortho and/or para to X, nucleophilic aromatic sub. takes place readily



1-Chloro-2,4- dinitrobenzene

Sodium 2,4-dinitrophenoxide

Meisenheimer Complex



A Meisenheimer complex

Addition Elimination

