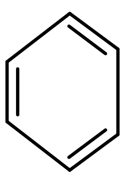
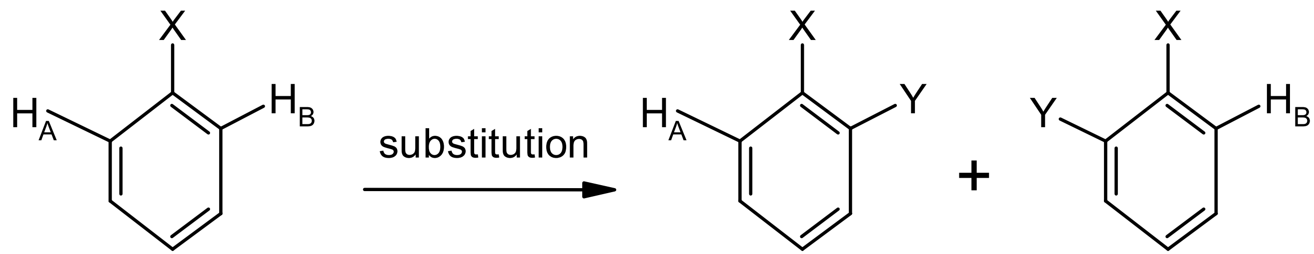
# Organic Chemistry – chemistry of aromatics

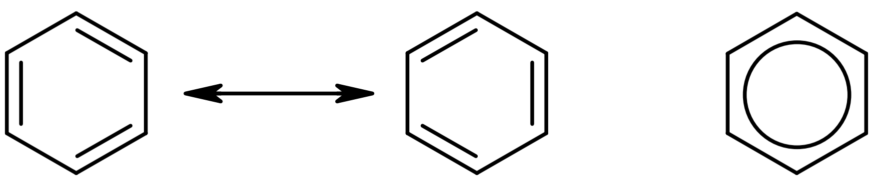
## History

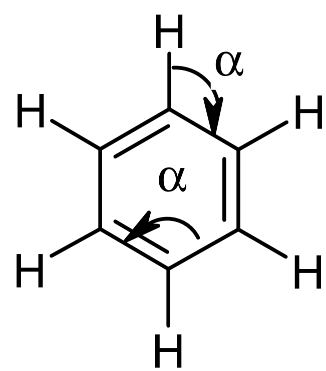
- discovery of benzene (M.Faraday – 1825)
- structure of benzene (F.A.Kekulé – 1864)
- conjugation, resonance structures

$C_6H_6$





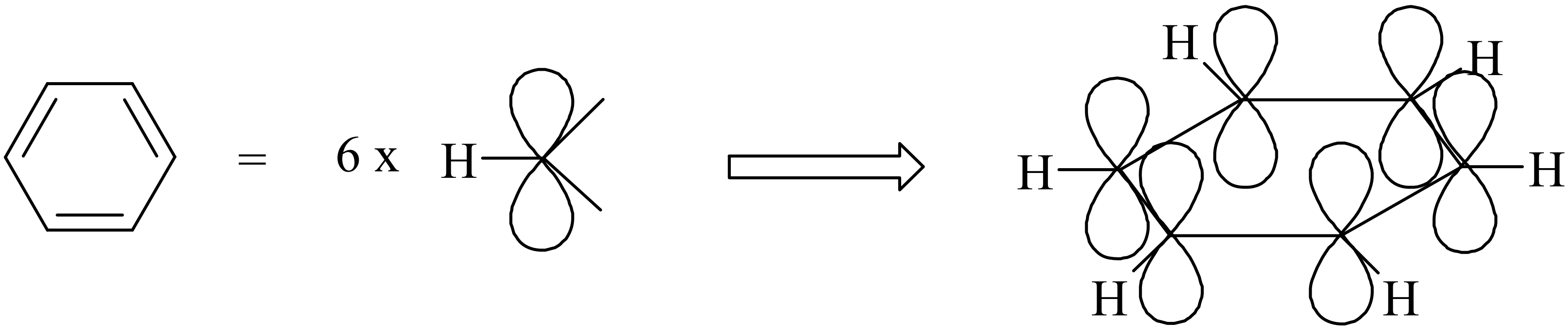






$\alpha$ = 120 °
C-H = 108,4 pm
C-C = 139,7 pm

# Organic Chemistry – chemistry of aromatics

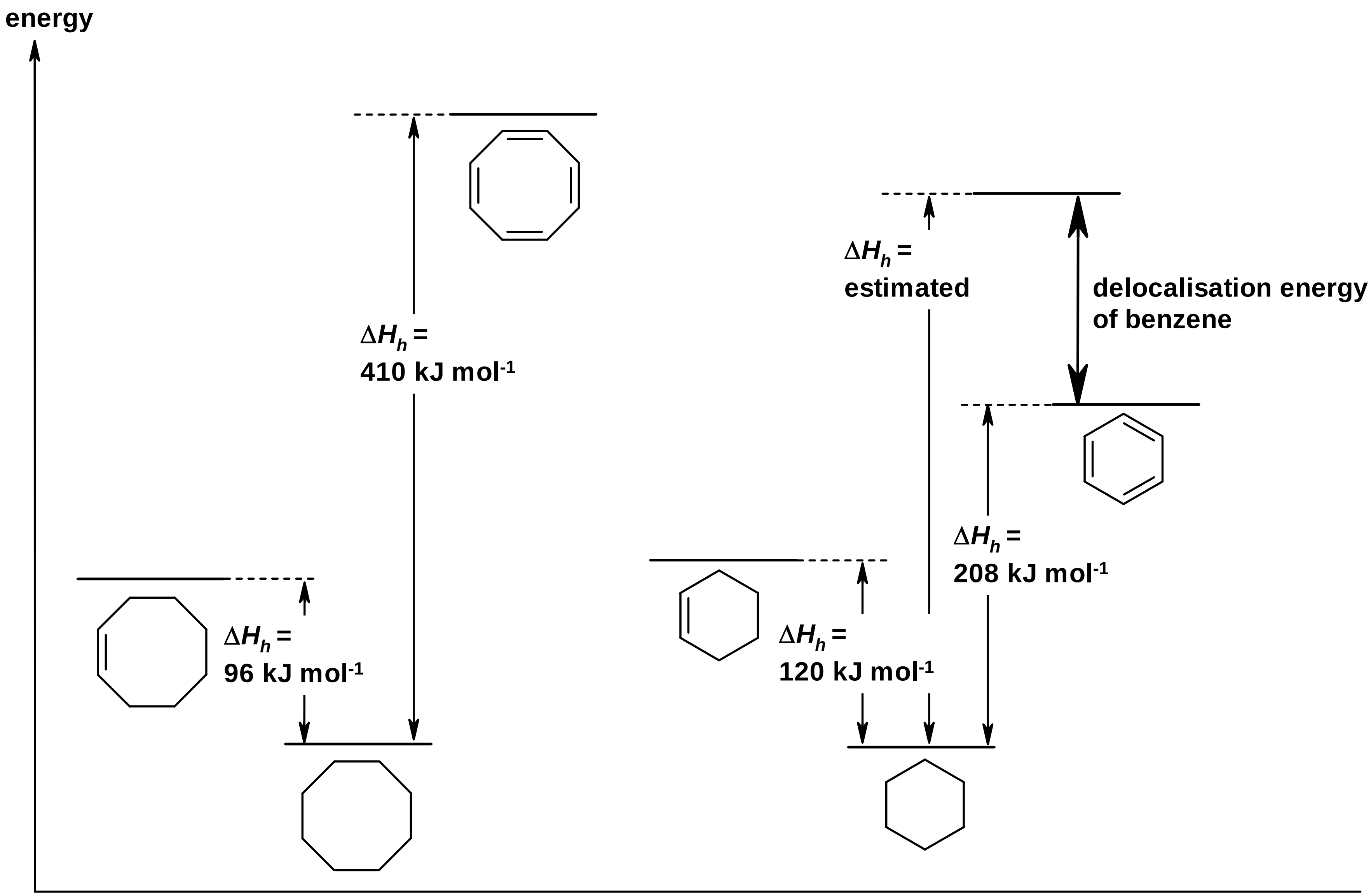
## Aromaticity




**Delocalisation of π – electrons**

**- is it favourfable process ???**

# Organic Chemistry – chemistry of aromatics



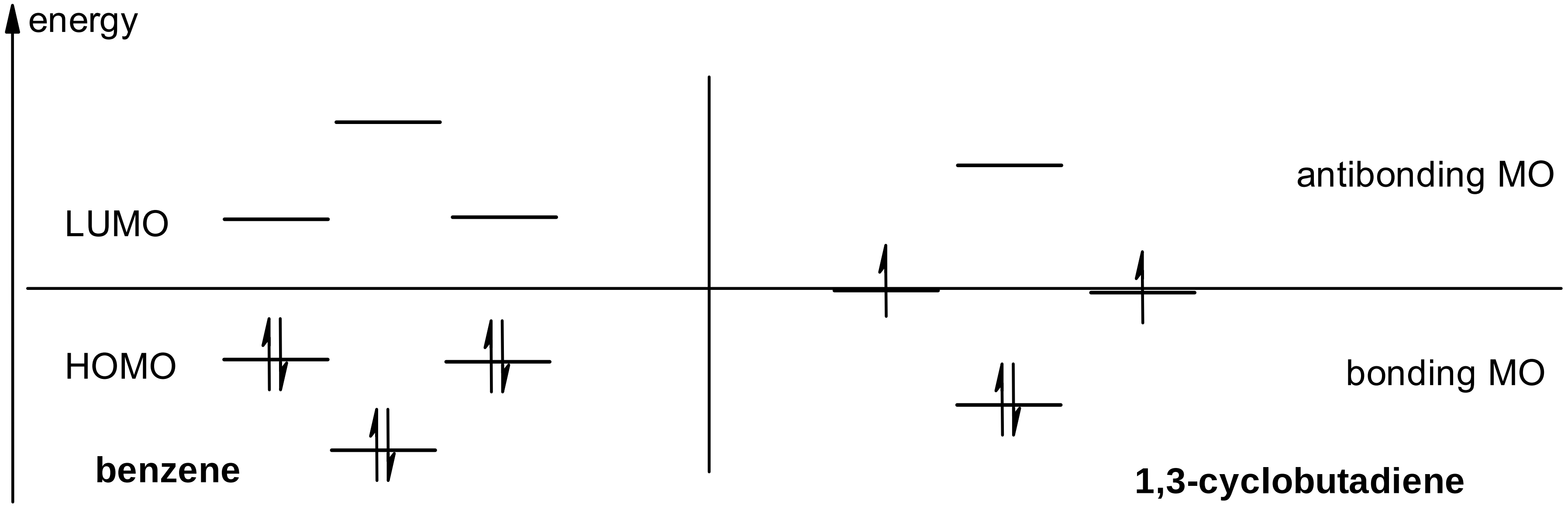
## Aromaticity

„Hückel rule“

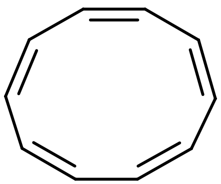
**Aromatic compounds have to have**

- cyclic structure
- conjugated systém of double bonds
- 4n + 2 (n = 1,2,3,4….. Π – electrons
- planar structure (shape) of aromatic part

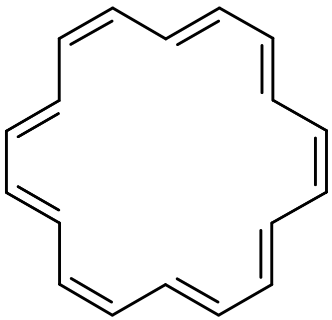
## Aromaticity – π - orbital picture



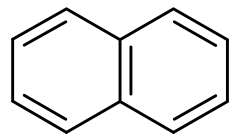
# Aromatic compounds



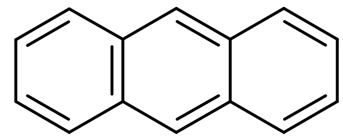
[10]-annulene



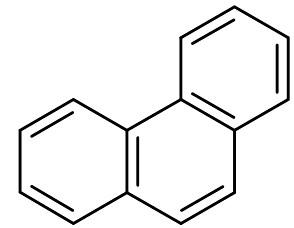
[18]-annulene



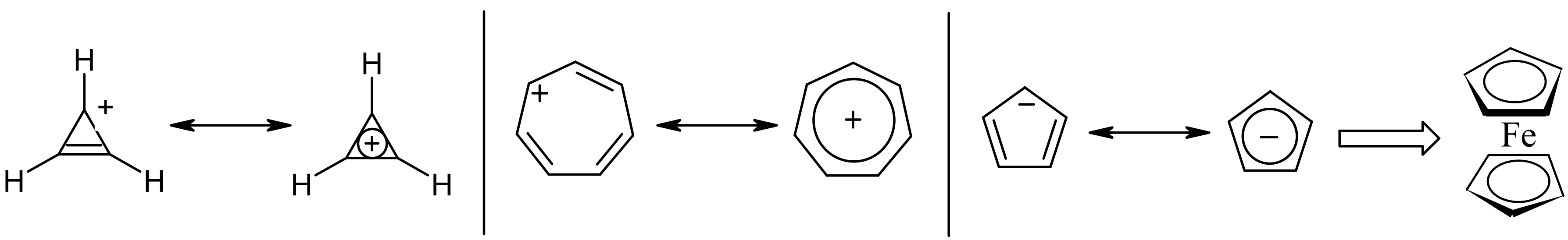
naphthalene



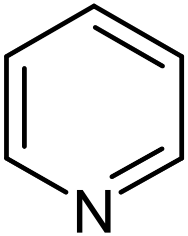
anthracene



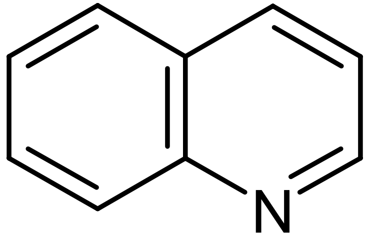
fenanthrene



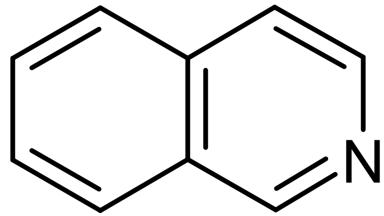
## Heteroaromatic compounds



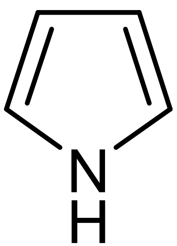

pyridine



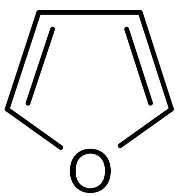

quinoline



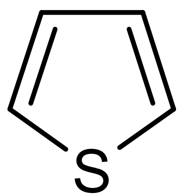

isoquinoline



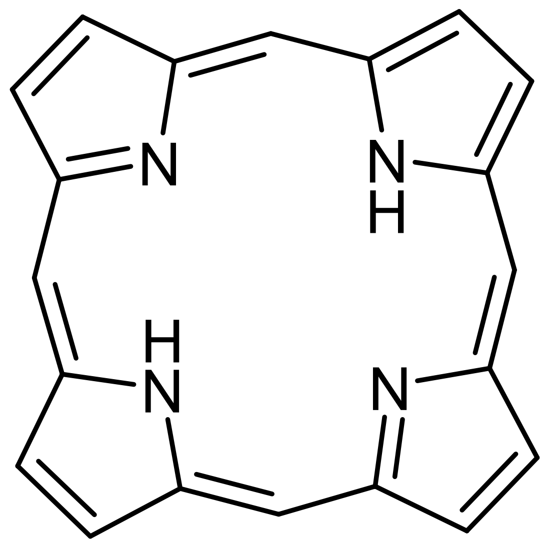

pyrrole




furane

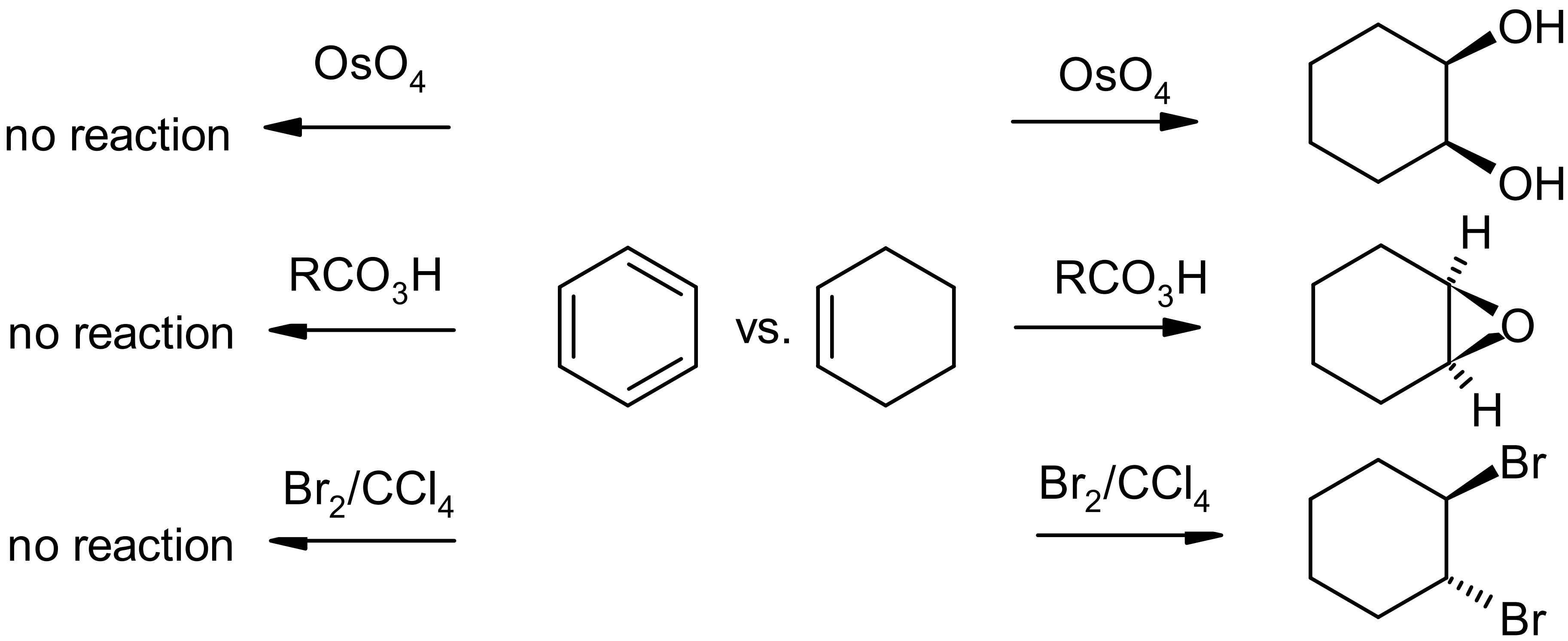



thiophene

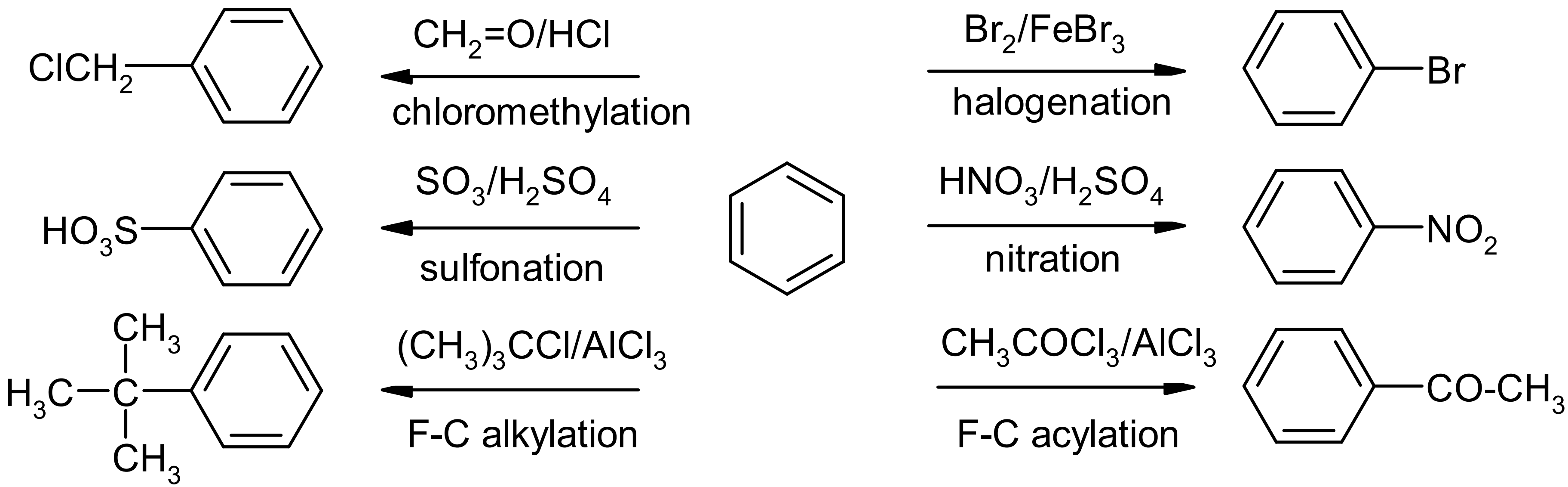



porfyrine

# Aromatic compounds - reactivity

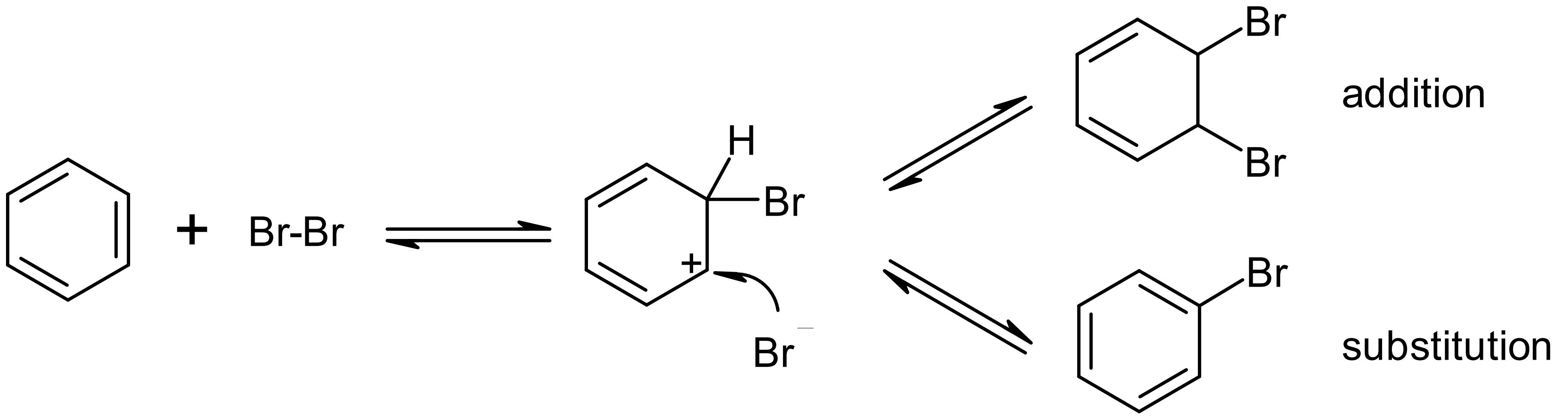


# Aromatic compounds – reactivity – $S_E$ aromatic

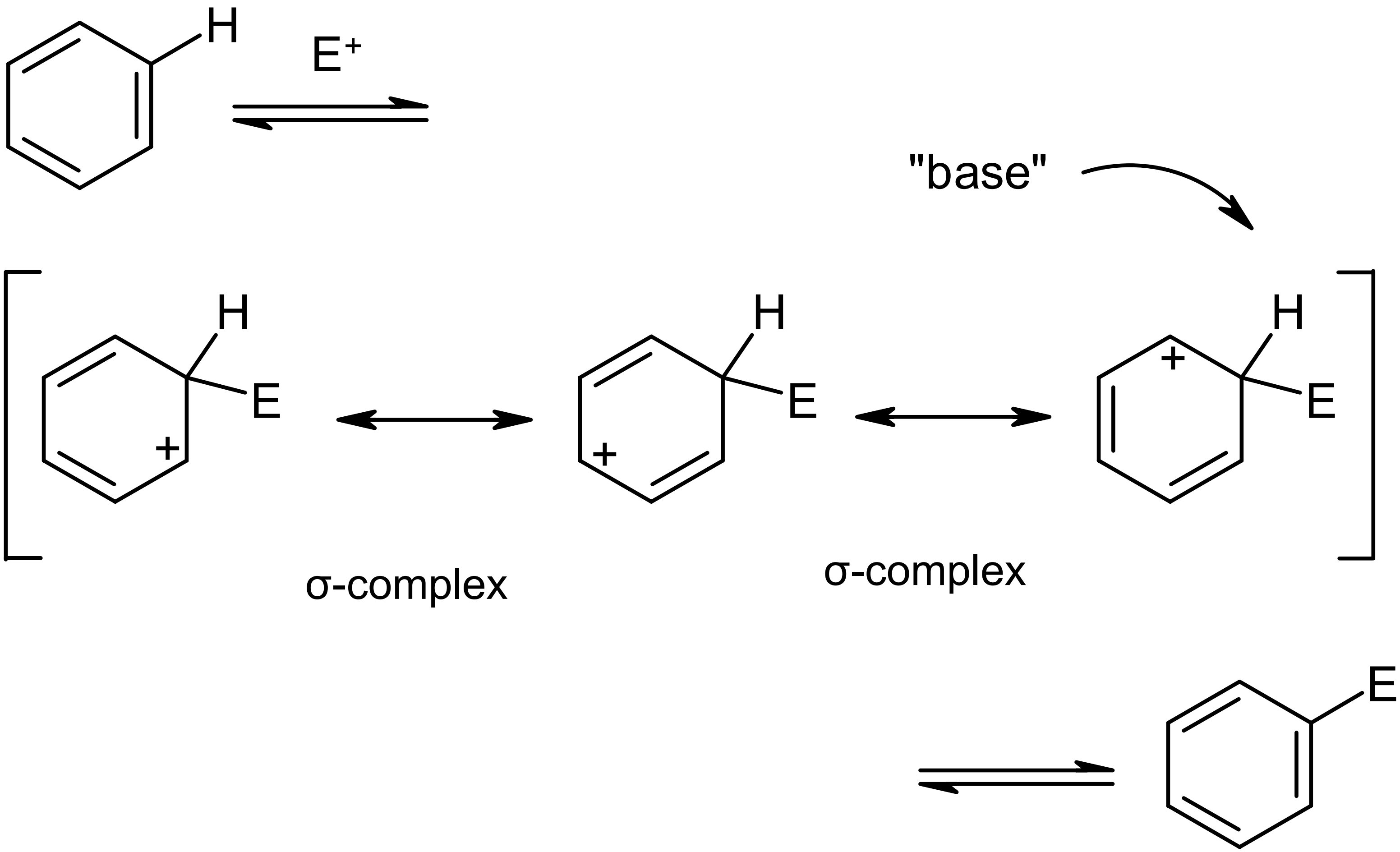


# Organic Chemistry – chemistry of aromatics

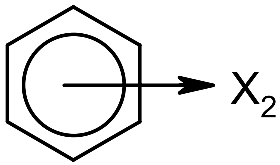
## Aromatic compounds – retention of aromatic character

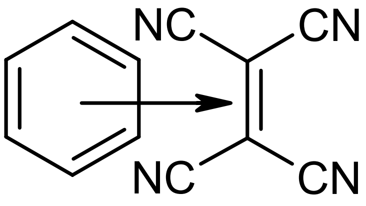


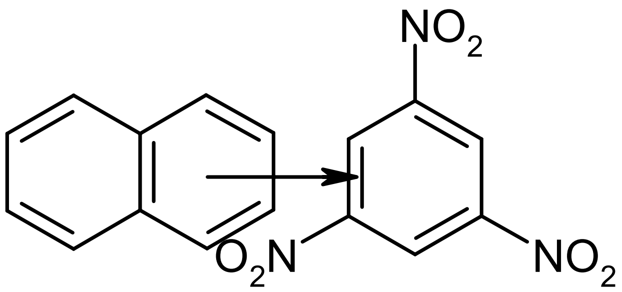
## Aromatic compounds – reactivity – $S_E$ aromatic



## Aromatic compounds – reactivity – $S_E$ aromatic



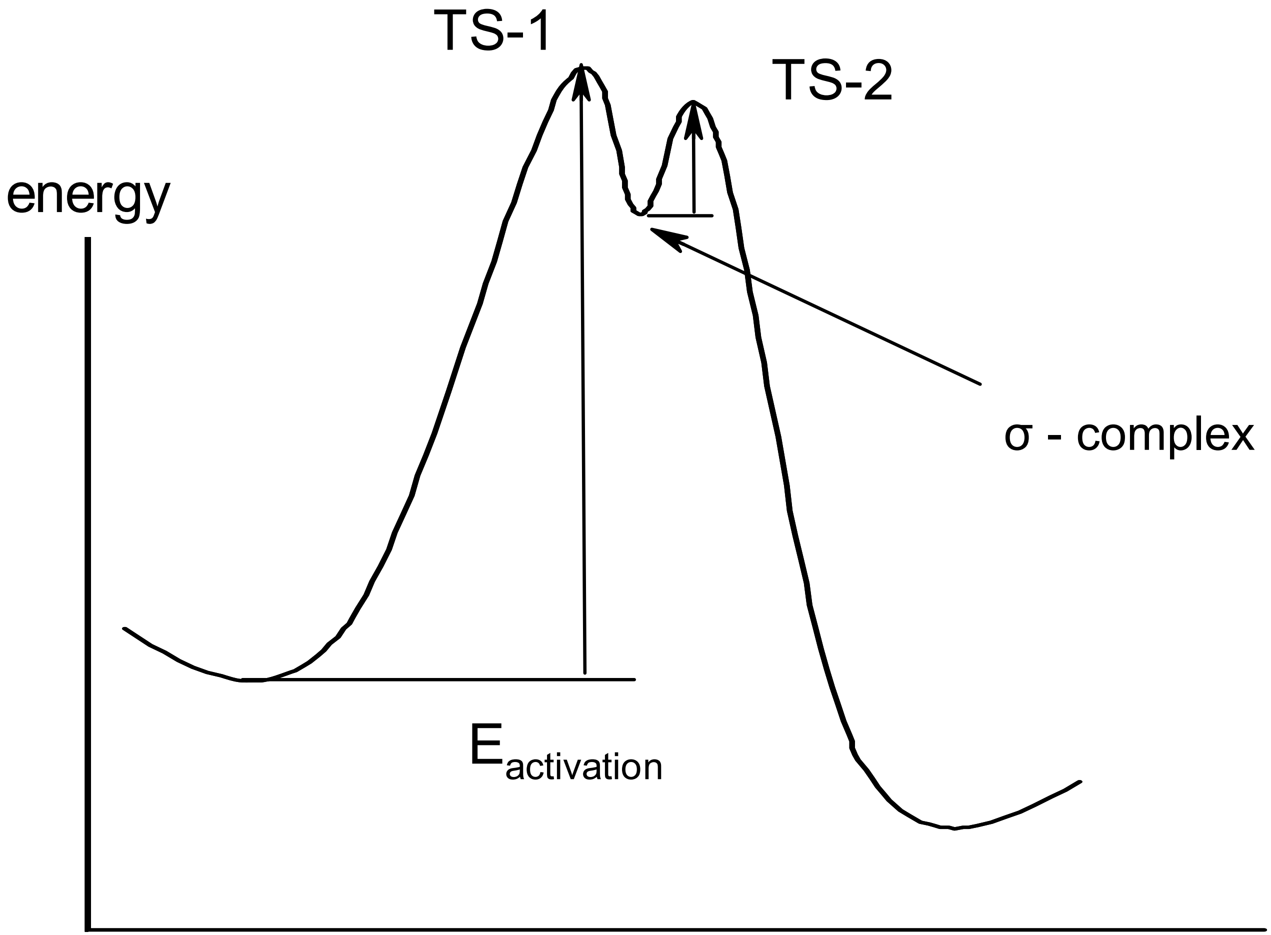




π – complexes

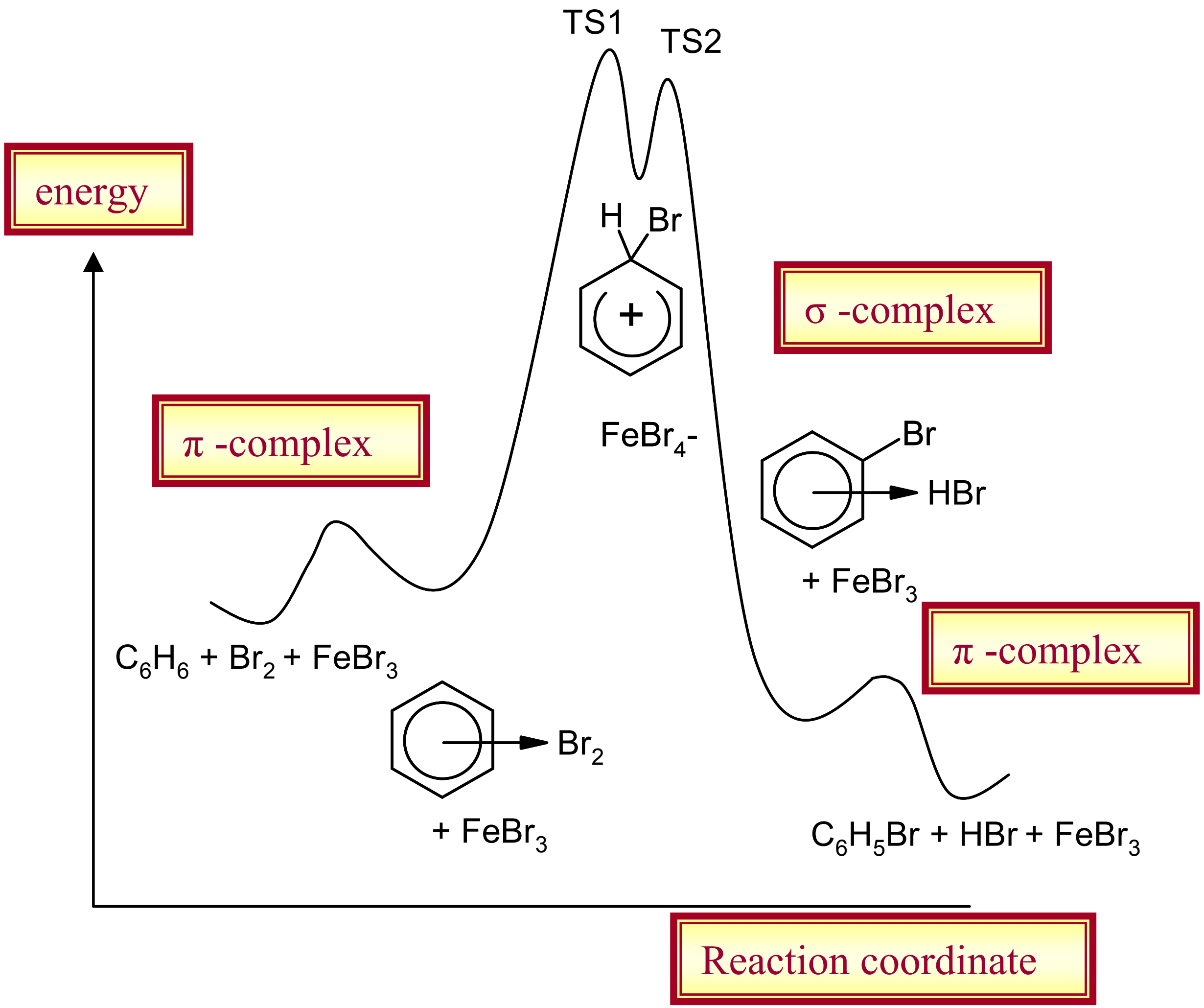
C-T (charge-transfer) complexes

## Aromatic compounds – reactivity – $S_E$ aromatic

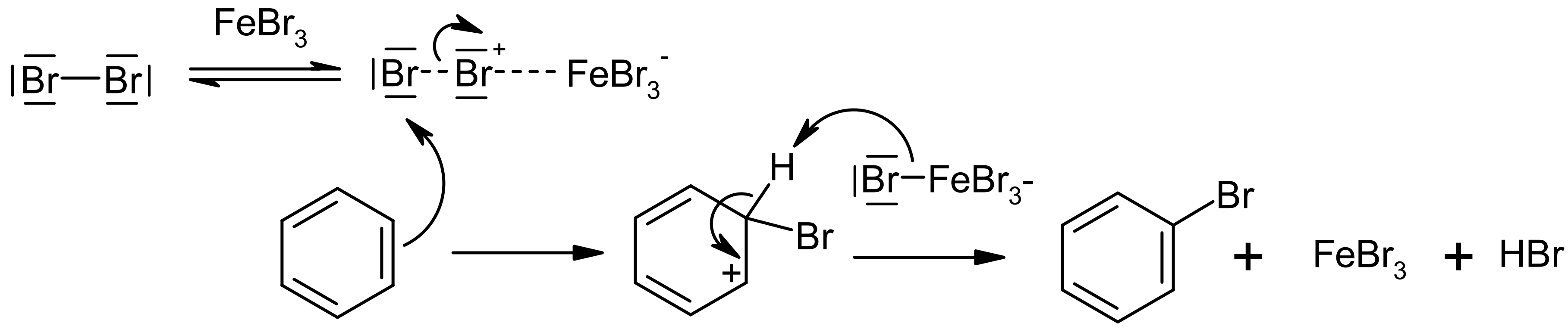


# Organic Chemistry – chemistry of aromatics

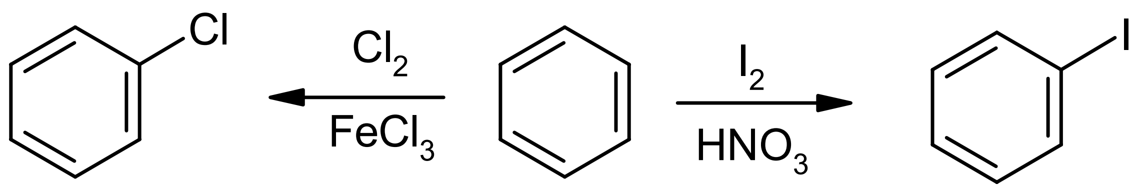
## Aromatic compounds – reactivity – $S_E$ aromatic



# Aromatic compounds – $S_E$ aromatic - halogenation




bromobenzene




chlorobenzene
(83%)

iodobenzene
(86%)

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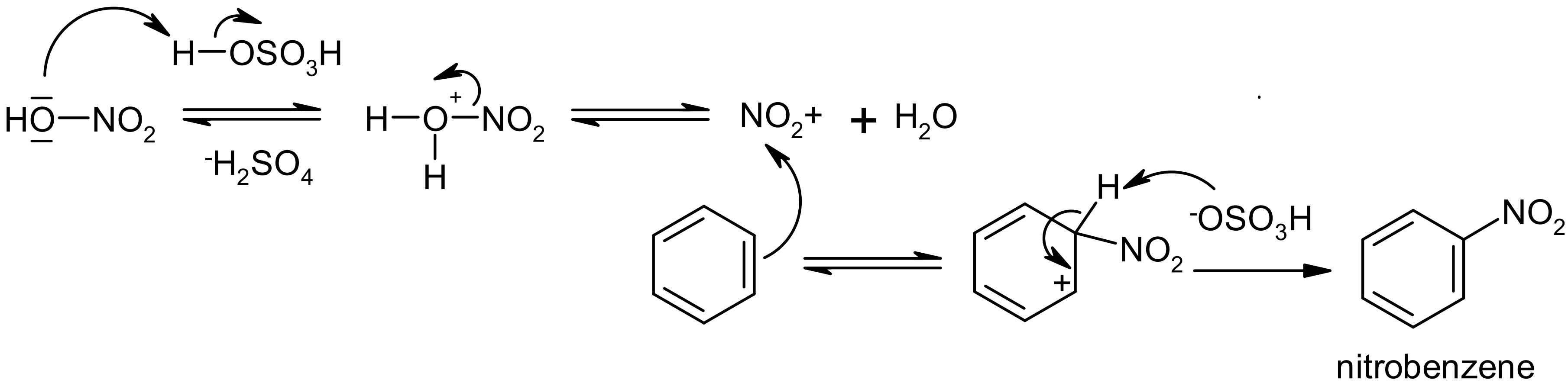
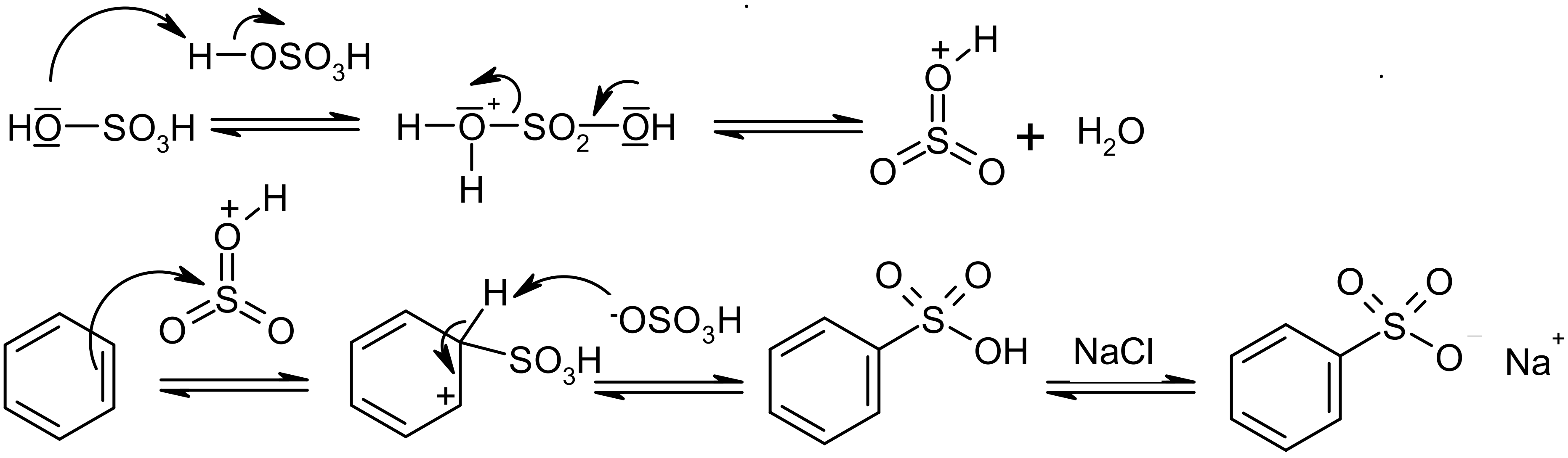
## Aromatic compounds – $S_E$ aromatic - nitration




**stable salts $NO_2^+X^-$ (X = $BF_4$, $ClO_4$, $PF_6$)**

# Organic Chemistry – chemistry of aromatics

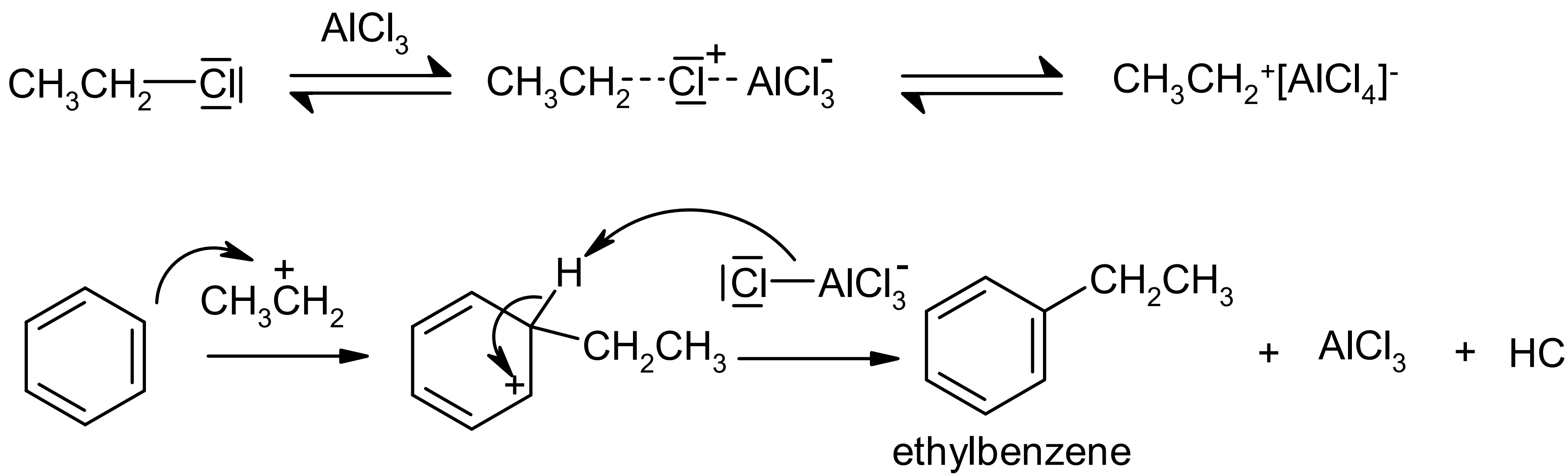
## Aromatic compounds – $S_E$ aromatic - sulfonation




benzenesulfonic acid

natrium-benzenesulfonate

# Aromatic compounds – $S_E$ aromatic – F-C alkylation



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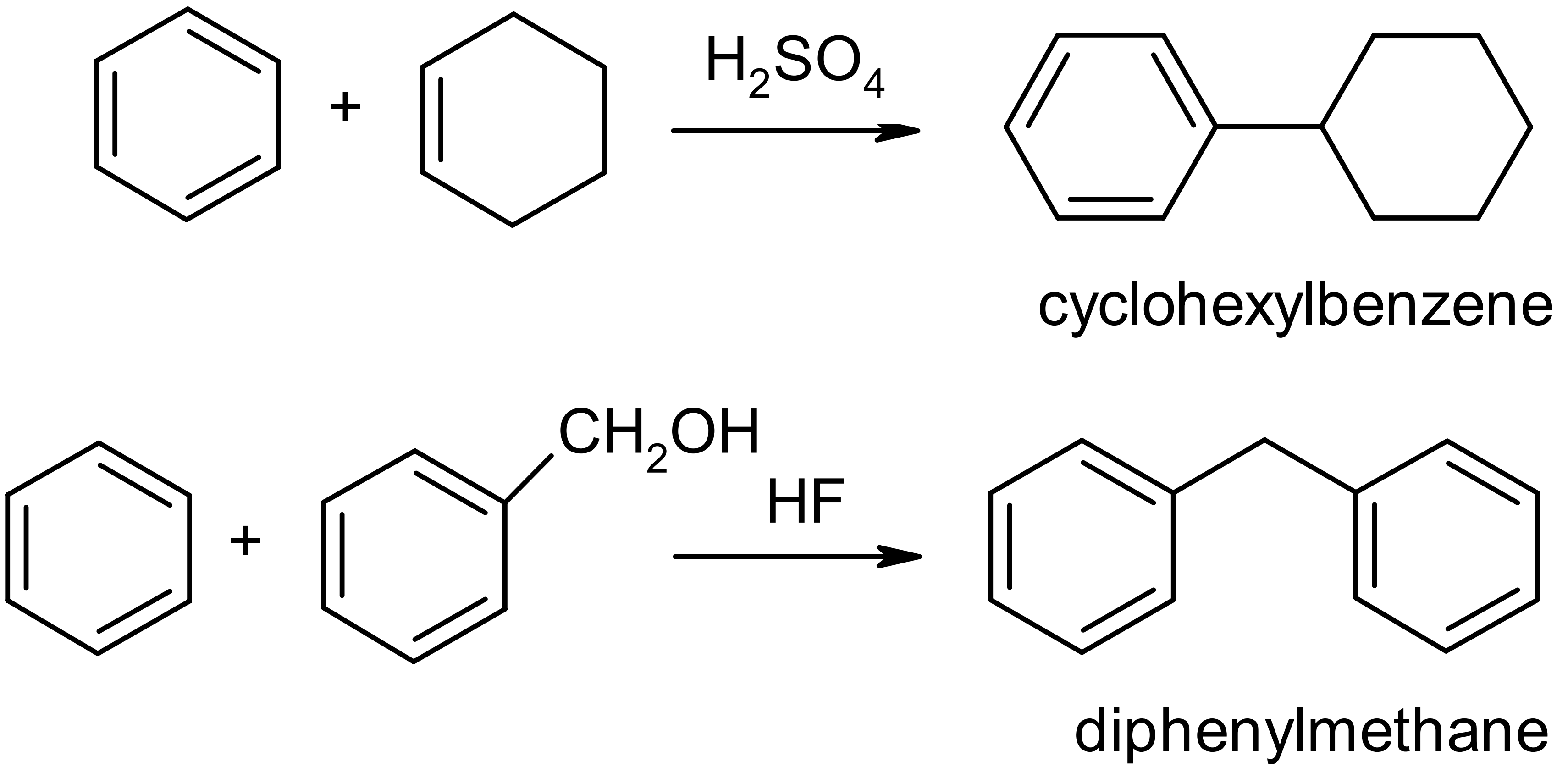
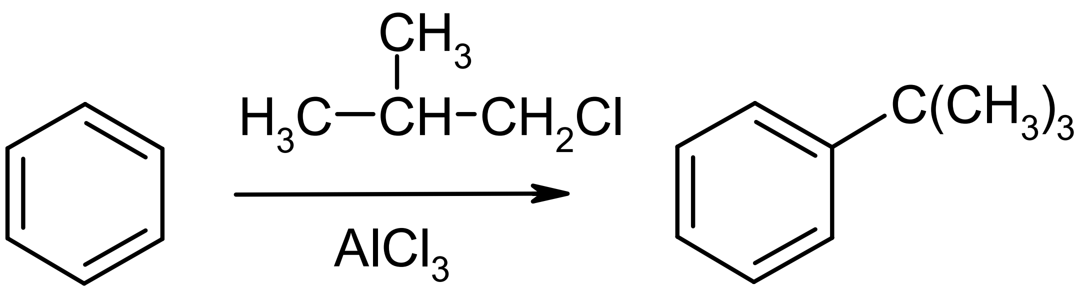
## Aromatic compounds – $S_E$ aromatic – F-C alkylation

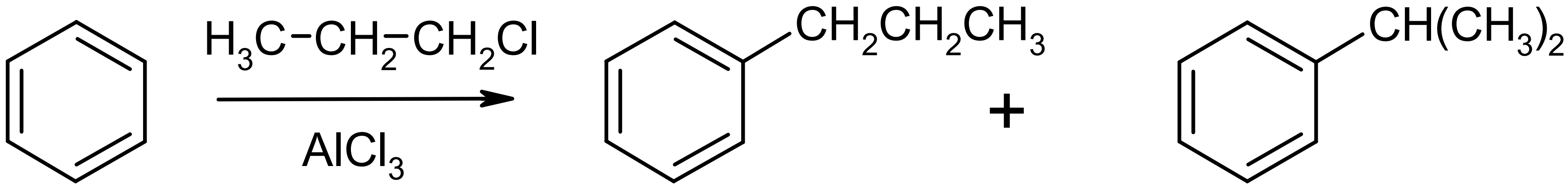


# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – F-C alkylation



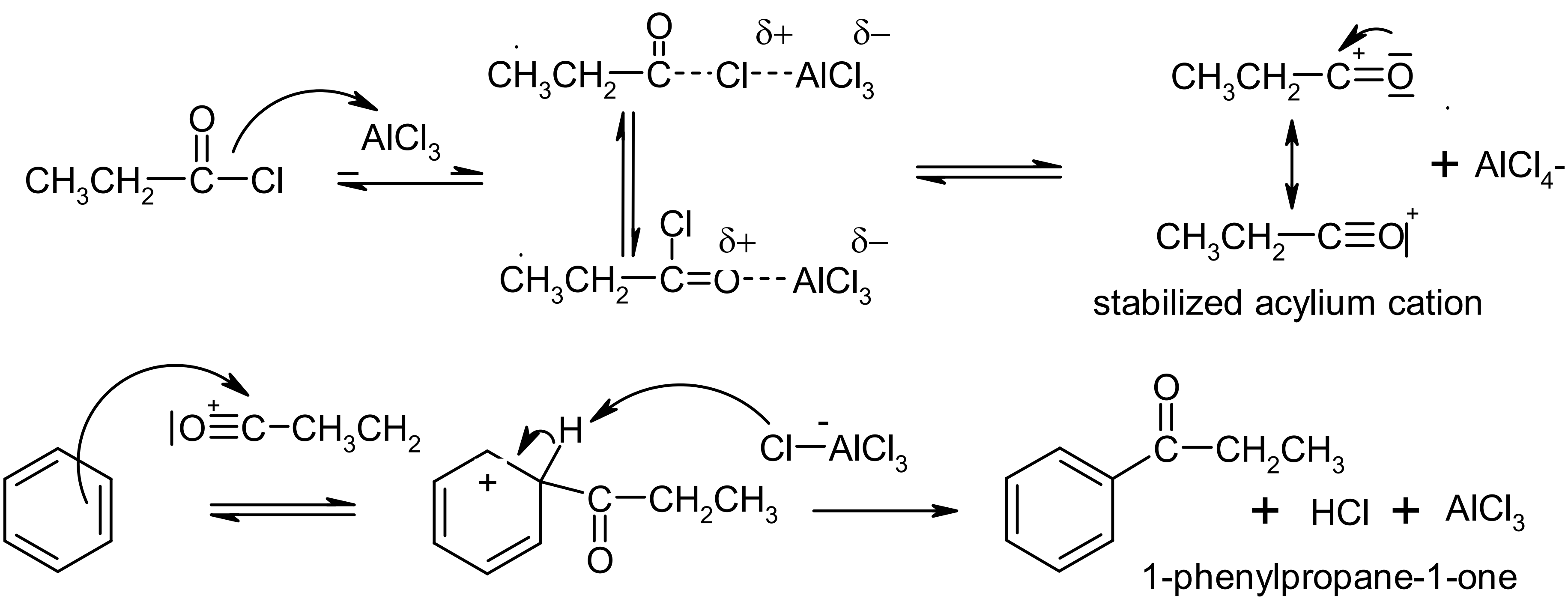

tert-butylbenzene



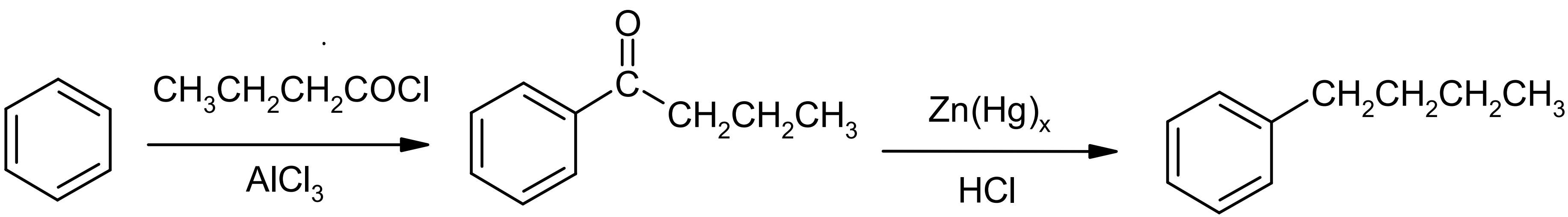

propylbenzene

isopropylbenzene

## Aromatic compounds – $S_E$ aromatic – F-C acylation

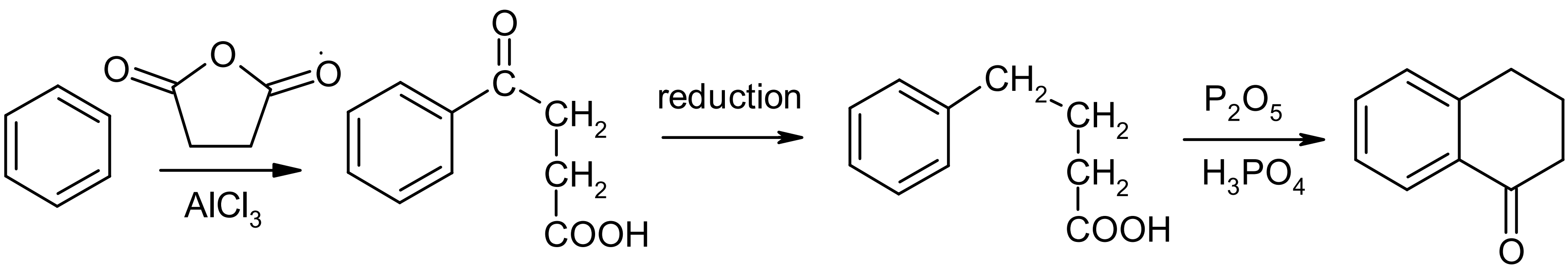


# Aromatic compounds – $S_E$ aromatic – F-C acylation



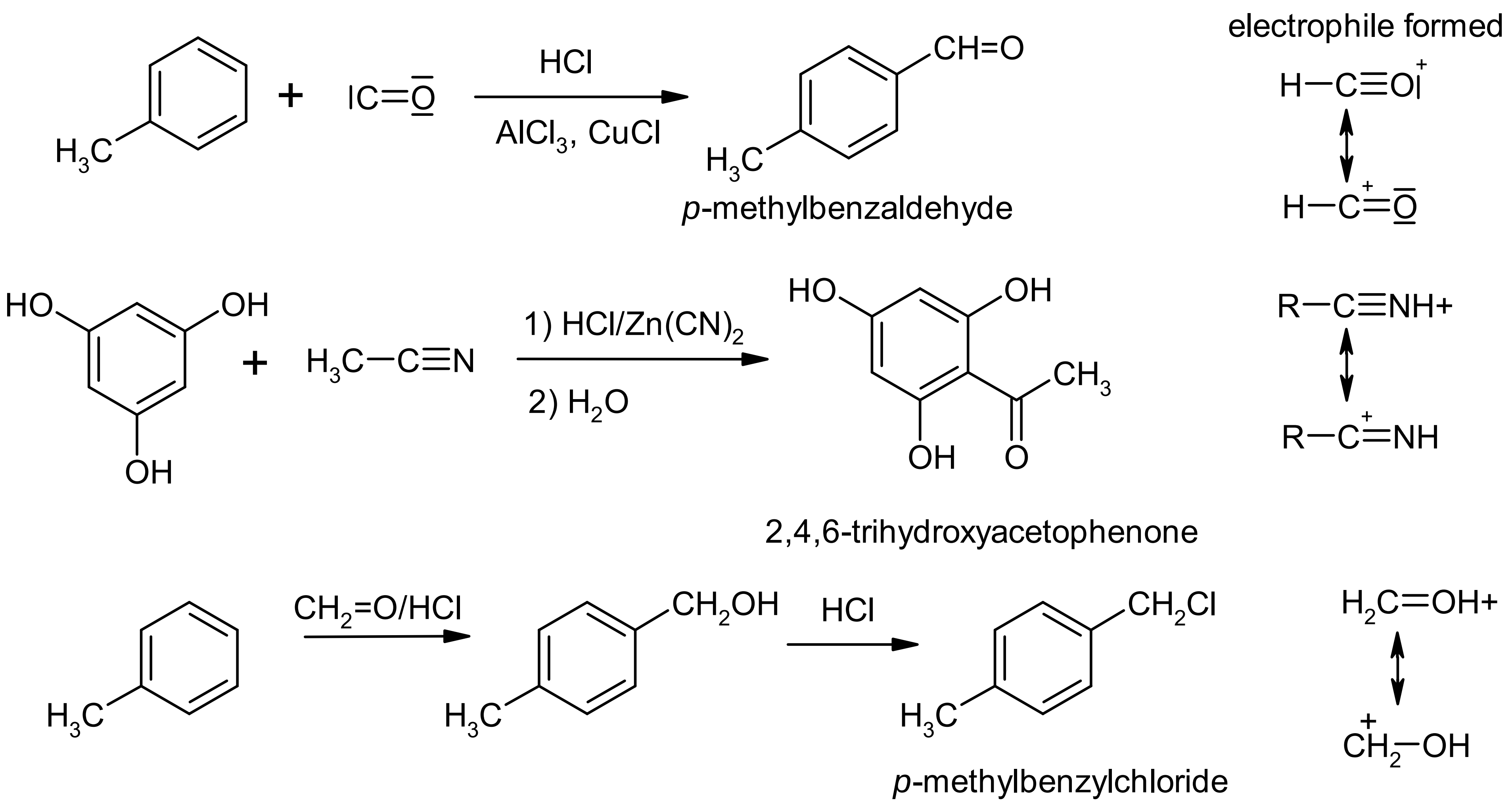

1-phenylbutane-1-one

butylbenzene



# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – varia

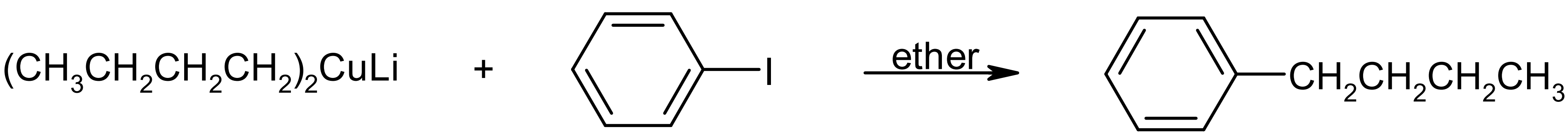


# Aromatic compounds – varia

$$R_2CuLi \quad + \quad R'X \longrightarrow R\text{-}R \quad + \quad RCu \quad + \quad LiX$$

$$\underset{\text{lithiumdimethylcuprate}}{(CH_3)_2CuLi} \quad + \quad \underset{\text{1-iododekane}}{CH_3(CH_2)_8CH_2I} \xrightarrow[-30\ ^\circ C]{\text{ether}} \underset{\text{undekane (90\%)}}{CH_3(CH_2)_8CH_2CH_3}$$

$$\underset{\text{lithiumdiphnylcuprate}}{(C_6H_5)_2CuLi} \quad + \quad \underset{\text{1-iodooktane}}{CH_3(CH_2)_6CH_2I} \xrightarrow{\text{ether}} \underset{\text{1-phenyloktane (99\%)}}{CH_3(CH_2)_6CH_2C_6H_5}$$

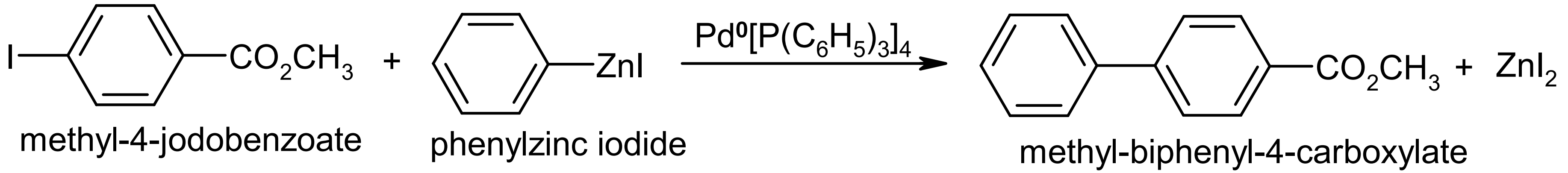



lithiumdibutylcuprate

butylbenzene (75%)

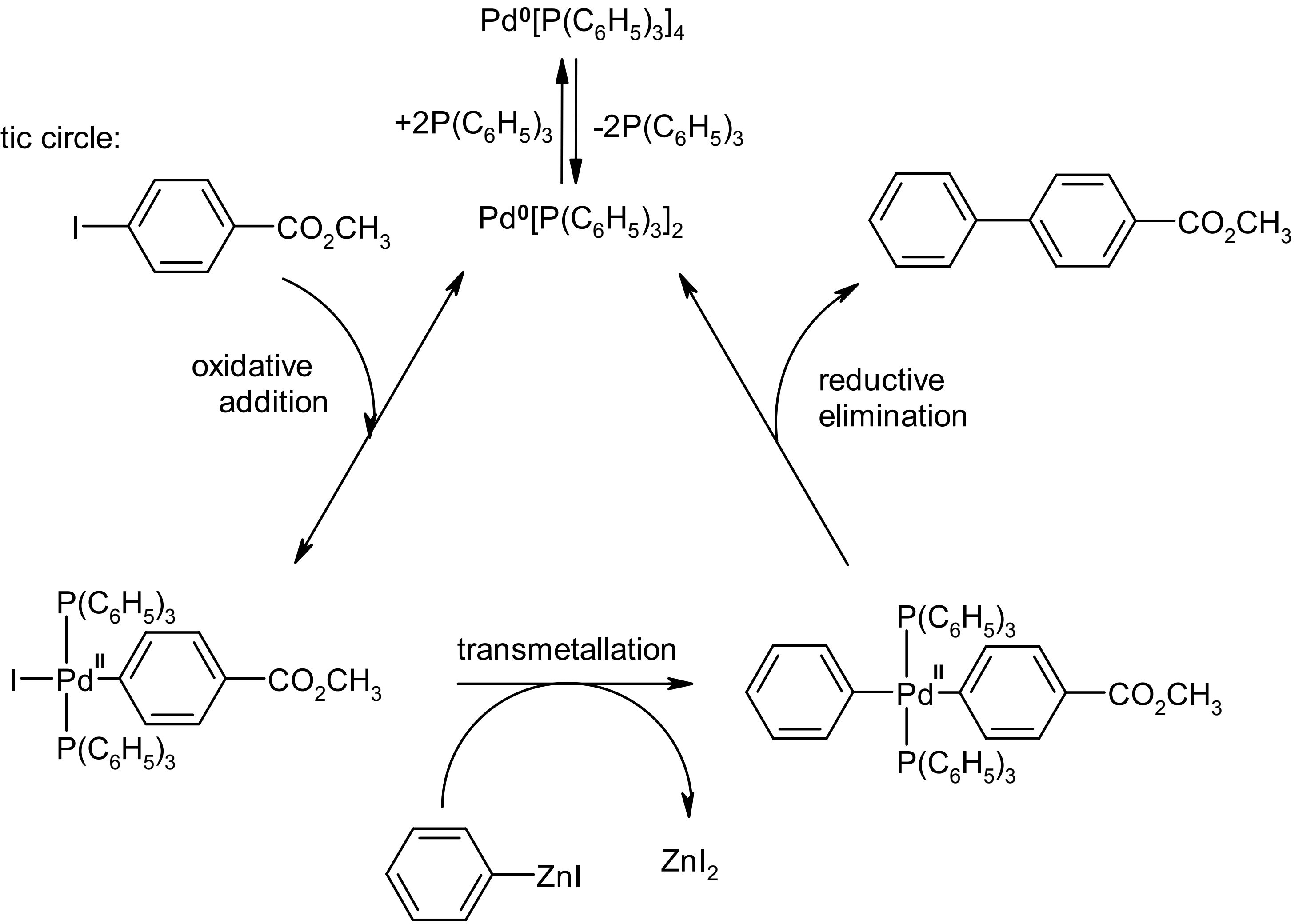
# Aromatic compounds – varia

Negishi reaction:

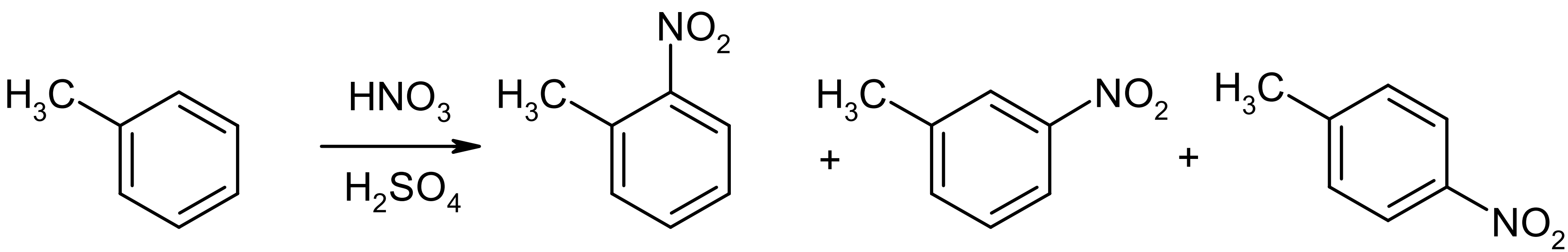


# Aromatic compounds – varia

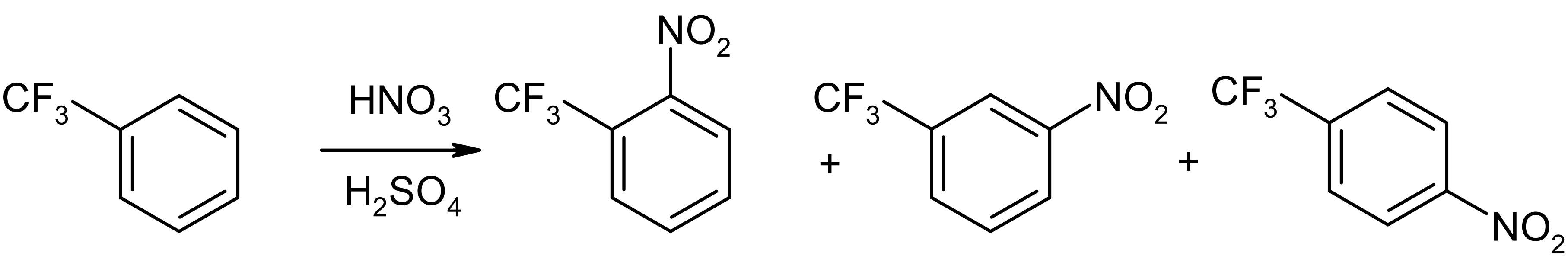
Catalytic circle:



# Aromatic compounds – $S_E$ aromatic – directive effect



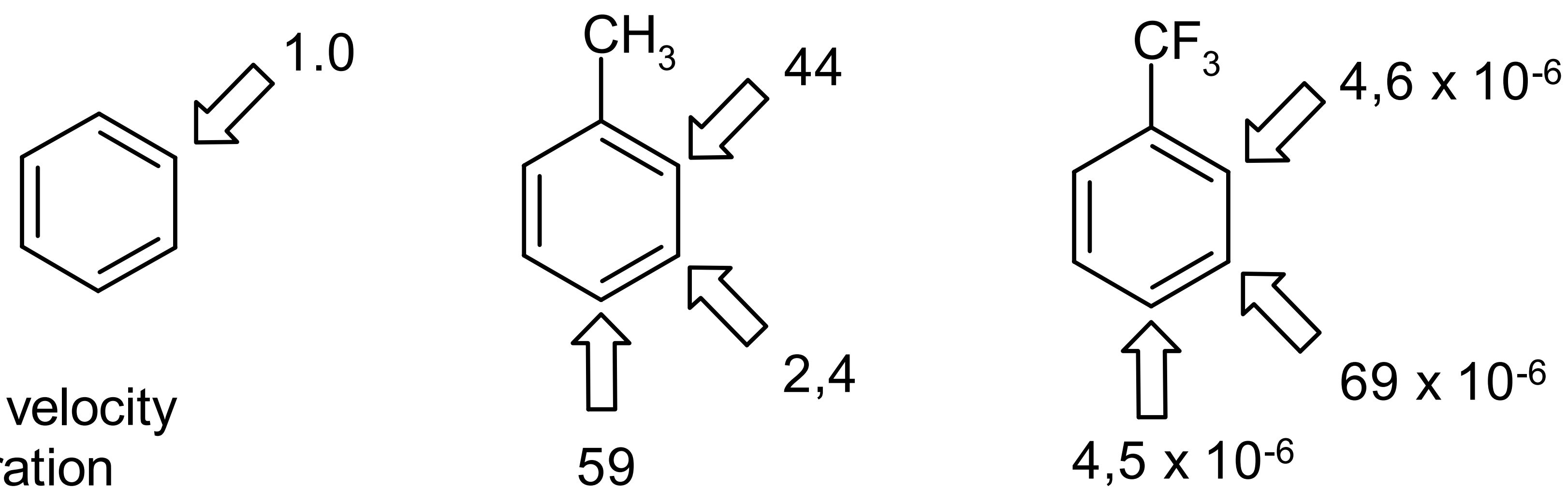

**2-nitrotoluene (63%)** | 3-nitrotoluene (3%) | **4-nitrotoluene (34%)**




2-nitro(trifluoromethyl)benzene (6%) | **3-nitro(trifluoromethyl)benzene (91%)** | 4-nitro(trifluoromethyl)benzene (3%)

# Organic Chemistry – chemistry of aromatics

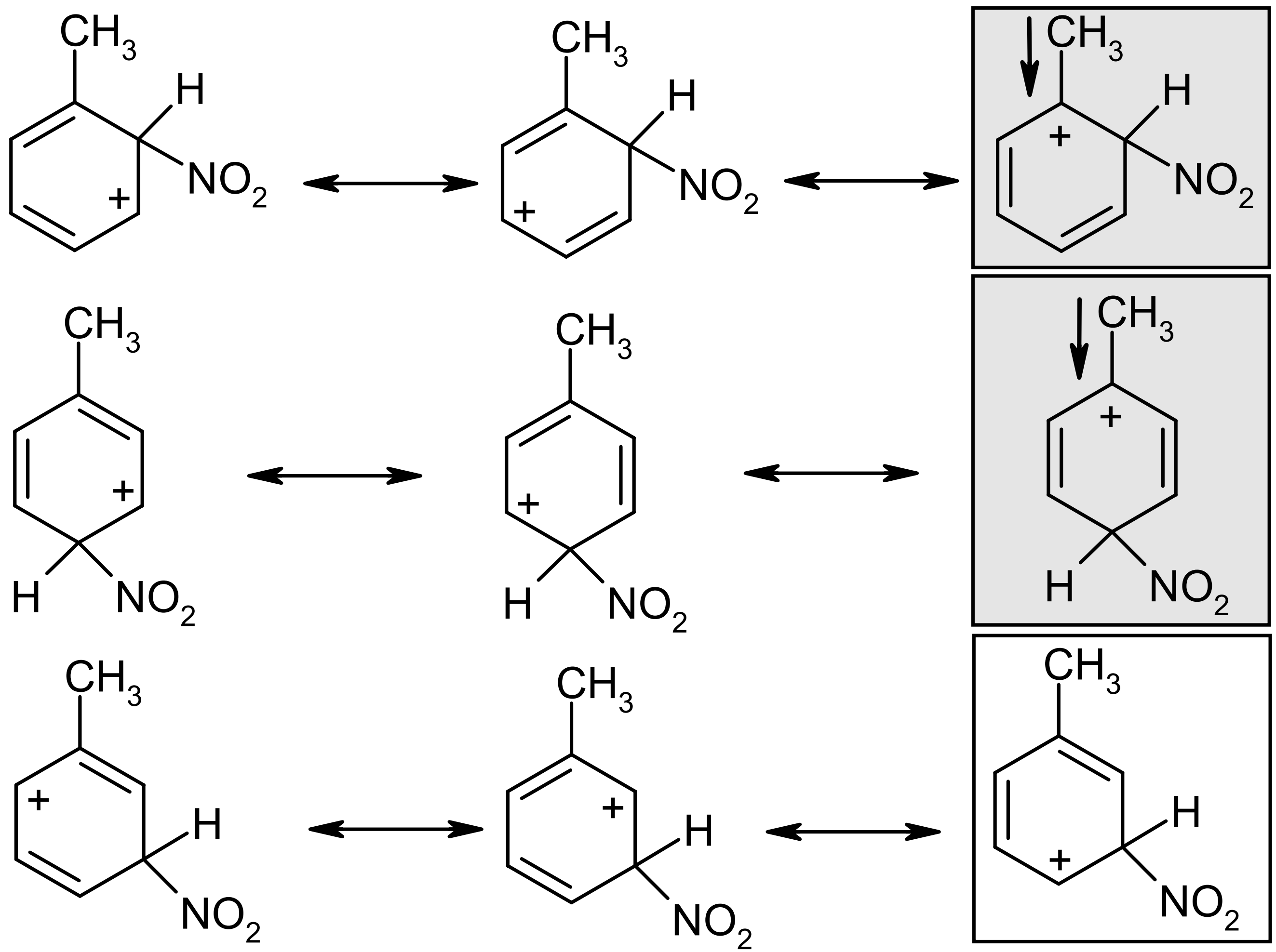
## Aromatic compounds – $S_E$ aromatic – directive effect




relative velocity of nitration

# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – directive effect




*ortho* substitution

+I

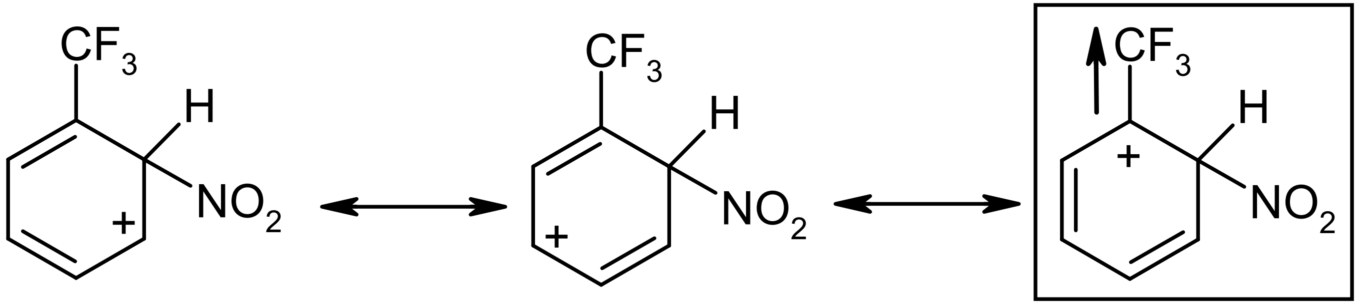
$H_3C$—Ar

*para* substitution

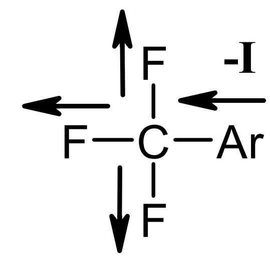
*meta* substitution

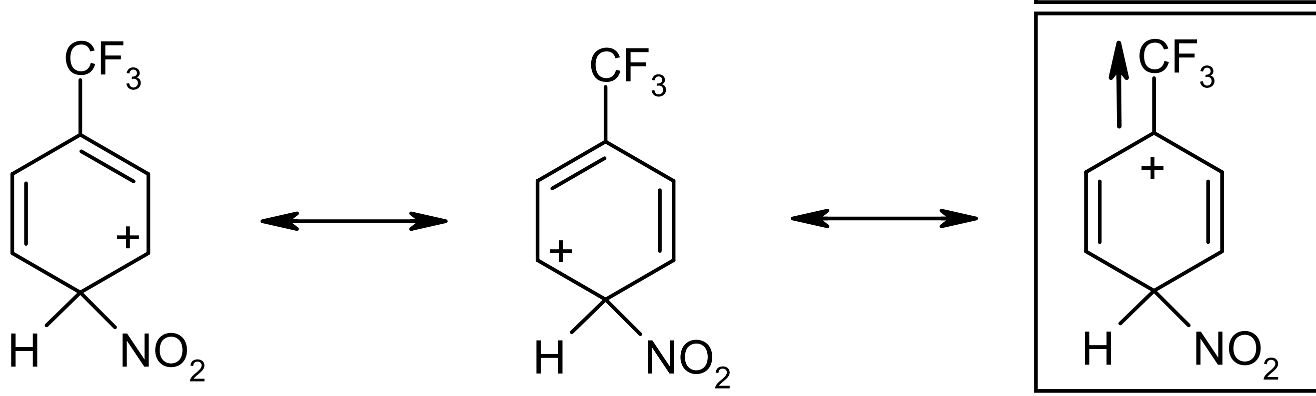
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – directive effect

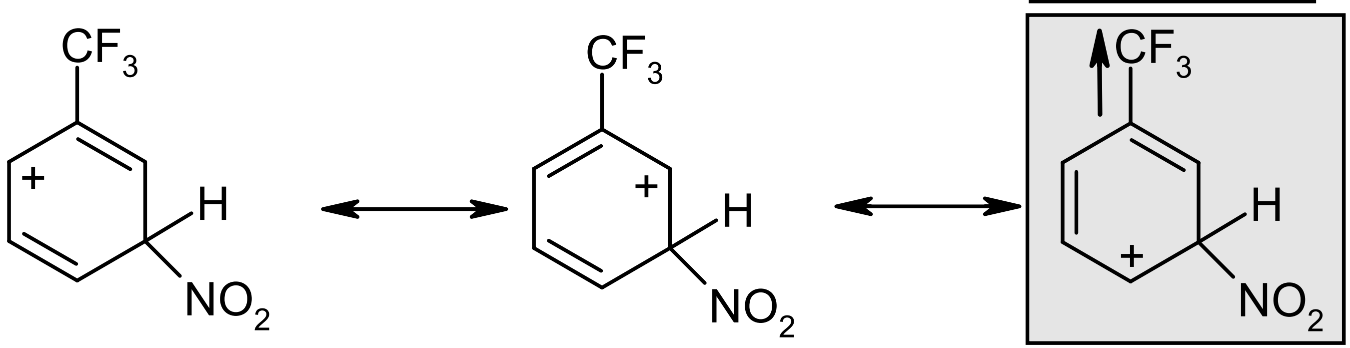



*ortho* substitution



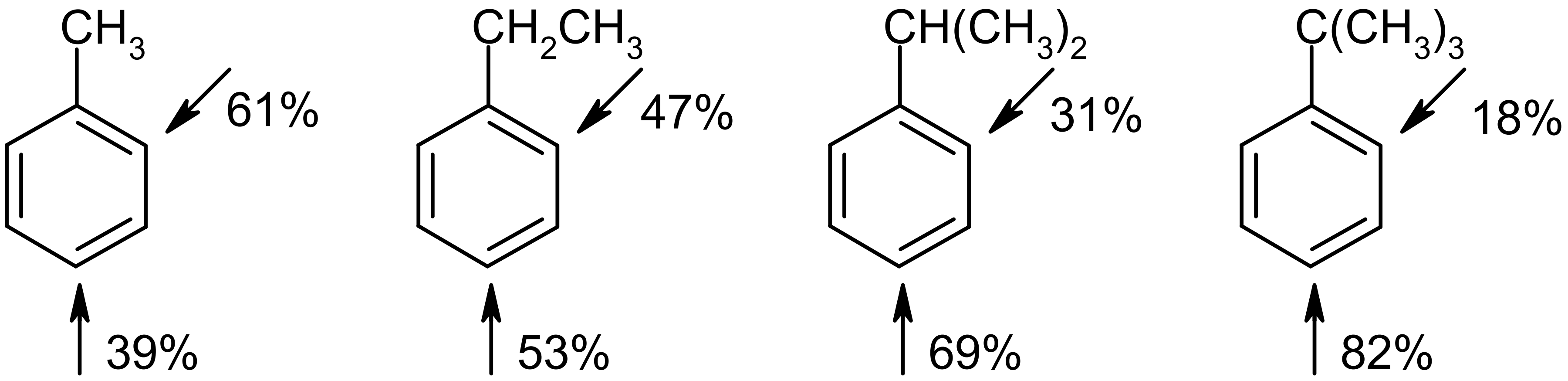

*para* substitution




*meta* substitution

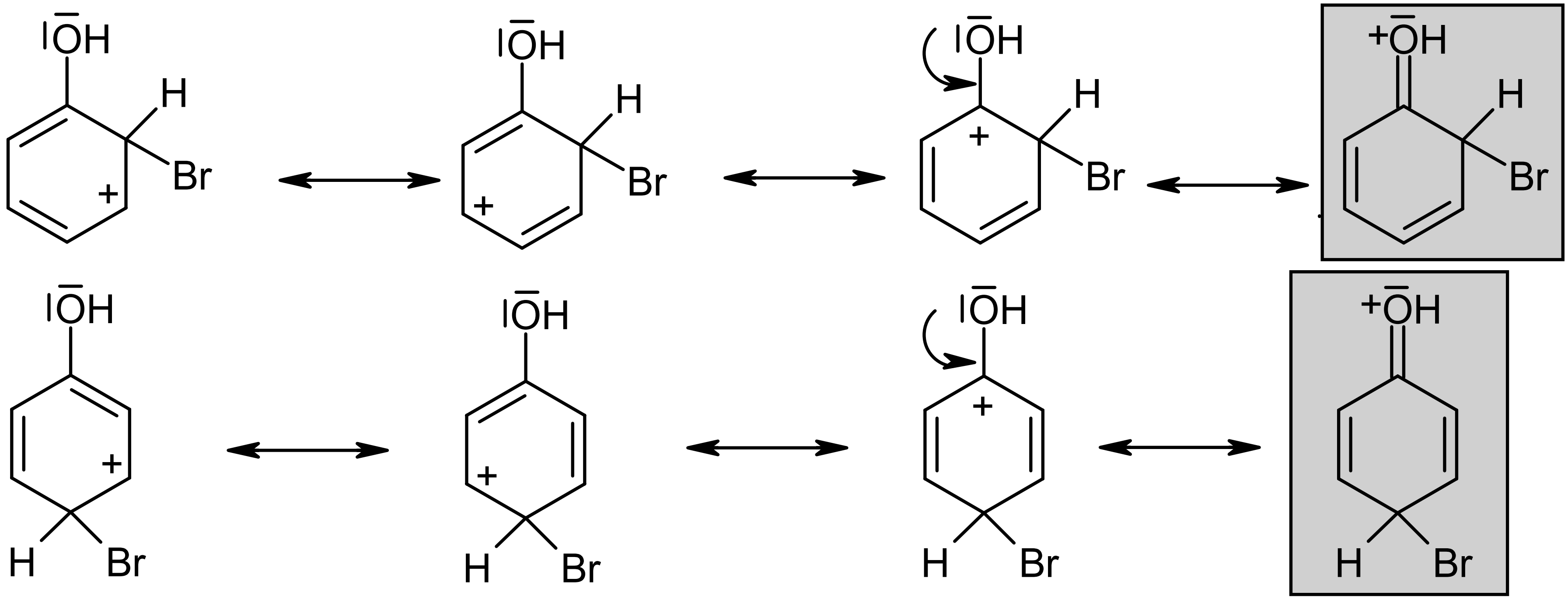
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – directive effect




## Steric effect

## Aromatic compounds – $S_E$ aromatic – directive effect



## - I +M substituents

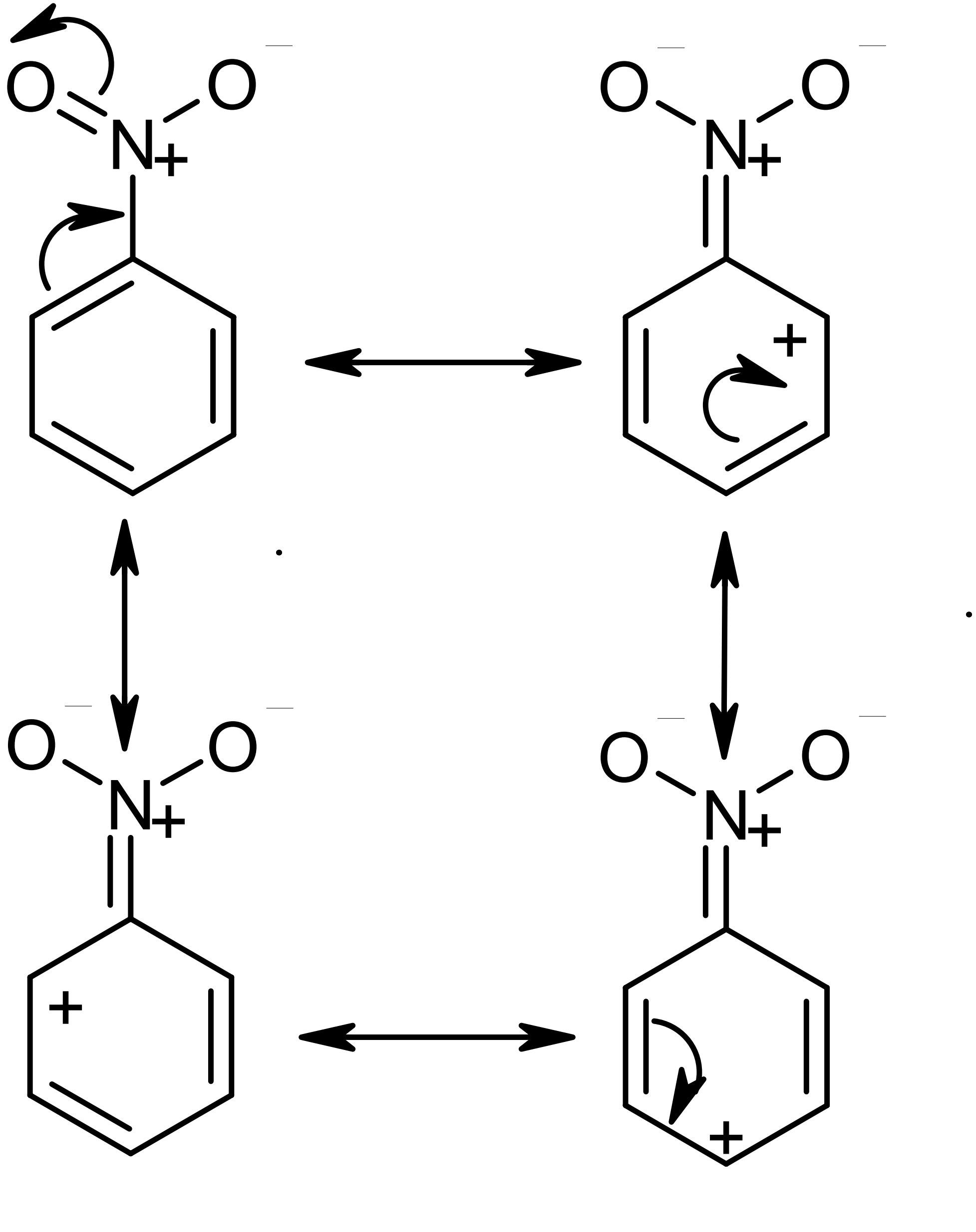
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – directive effect

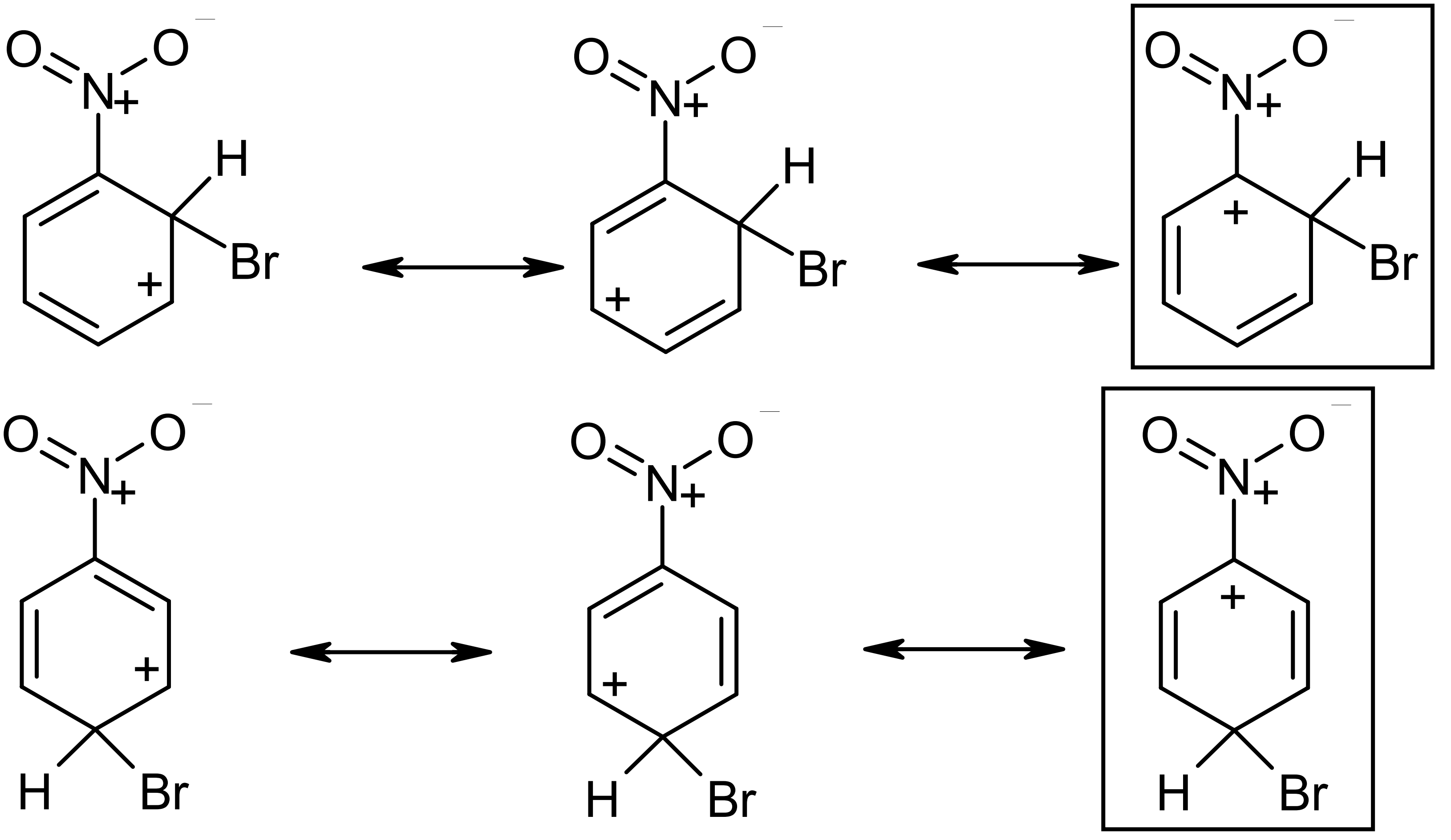
| Velocity of $S_EAr$ | Substituent | Name | Oriention |
|---|---|---|---|
| super activating | $-\overline{N}H_2$ | amino | *ortho*/*para* |
| | $-\overline{N}R_1R_2$ | alkylamino ($R_1$=H)<br>dialkylamino ($R_1$,$R_2\neq$H) | *ortho*/*para* |
| Strongly activating | $-\underline{\overline{O}}H$ | hydroxy | *ortho*/*para* |
| | $-H\overline{N}-C(=O)-R$ | acylamino | *ortho*/*para* |
| | $-\underline{\overline{O}}-R$ | alkoxy | *ortho*/*para* |
| | $-\underline{\overline{O}}-C(=O)-R$ | acyloxy | *ortho*/*para* |
| activating | -R, -Ar | alkyl, aryl | *ortho*/*para* |
| | $-CH=CR_2$ | alkenyl | *ortho*/*para* |
| reference | H | | |

# Organic Chemistry – chemistry of aromatics

| Velocity $S_EAr$ | Substituent | Name | Oriention |
|---|---|---|---|
| reference | H | | |
| weakly deactivating | $-\overline{\underline{X}}\vert$ (X=F, Cl, Br, I) | halogen | *ortho*/*para* |
| | $-CH_2-\overline{\underline{X}}\vert$ | halogenmethyl | *ortho*/*para* |
| strongly deactivating | $-C(=O)-Y$ | acyl (Y=R)<br>acylchloride (Y=Cl)<br>carboxylic acid (Y=OH)<br>ester (Y=OR) | *meta* |
| | $-C\equiv N\vert$ | cyano | *meta* |
| | $-SO_3H$ | sulfonic acid | *meta* |
| Very strongly deactivating | $-CF_3$ | trifluormethyl | *meta* |
| | $-\overset{+}{N}(=O)-O^-$ | nitro | *meta* |



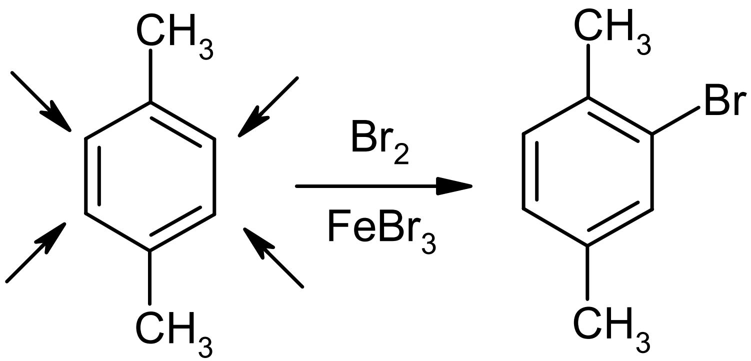
## Aromatic compounds – $S_E$ aromatic – directive effect



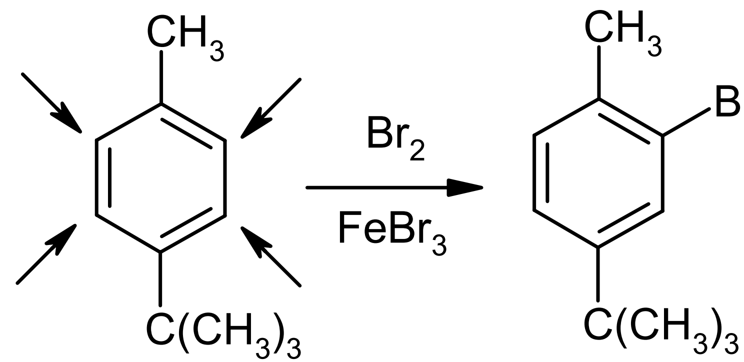
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – multiple effect

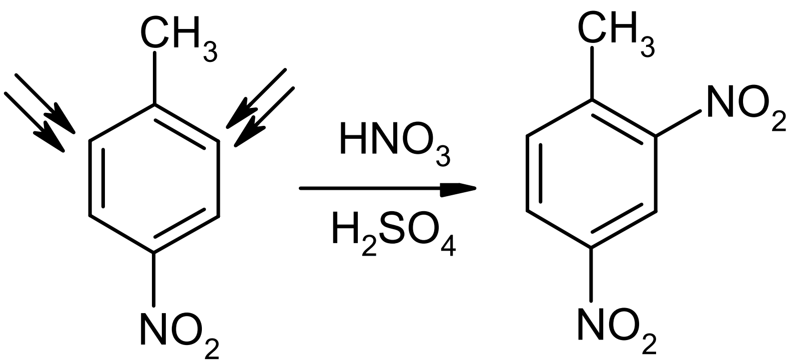
a)



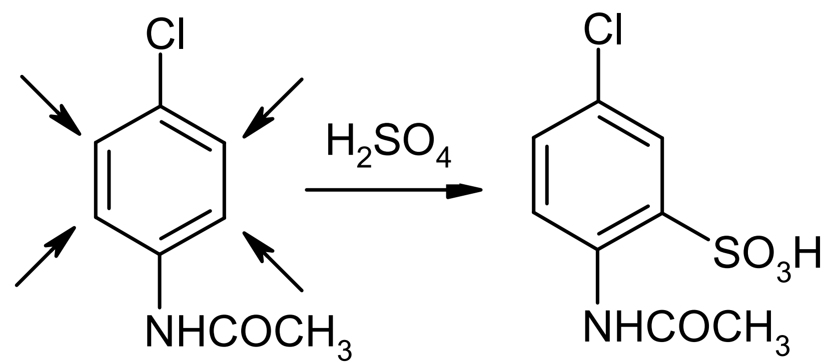

b)



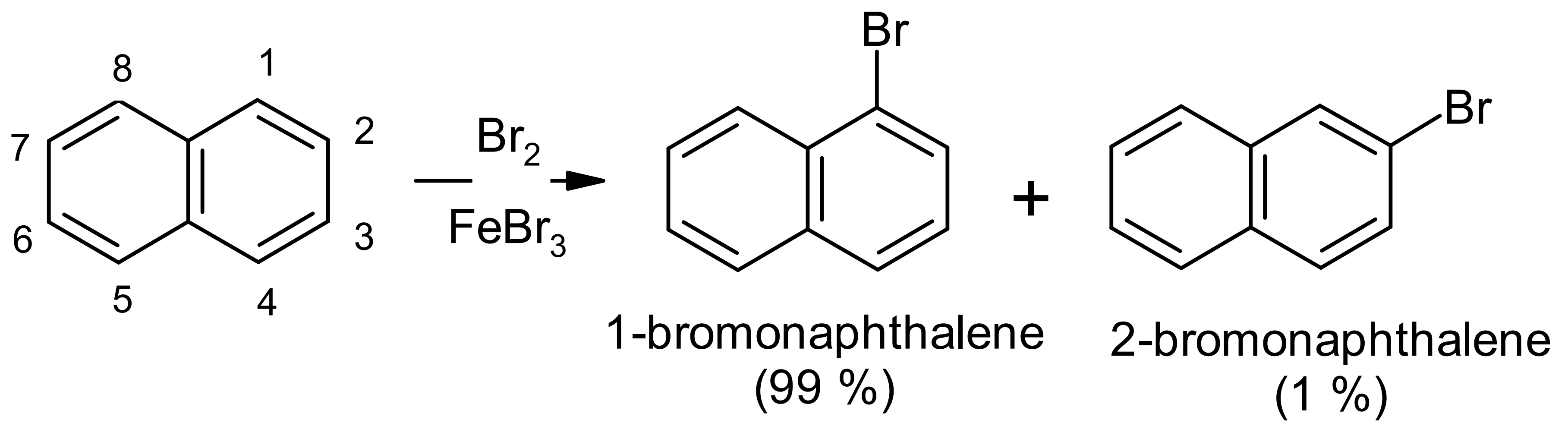

c)

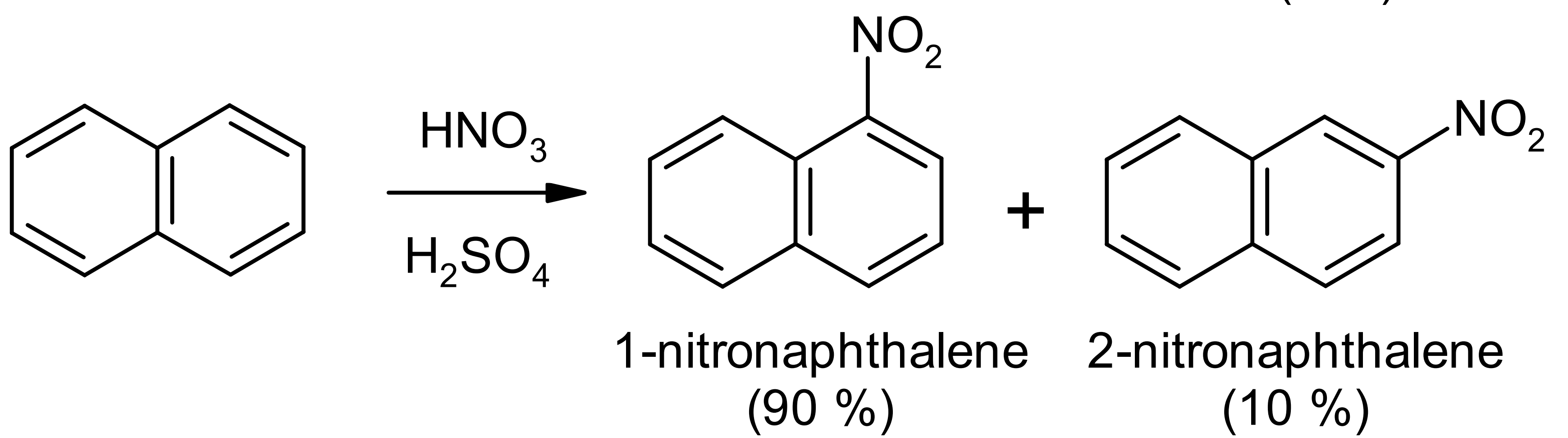



d)

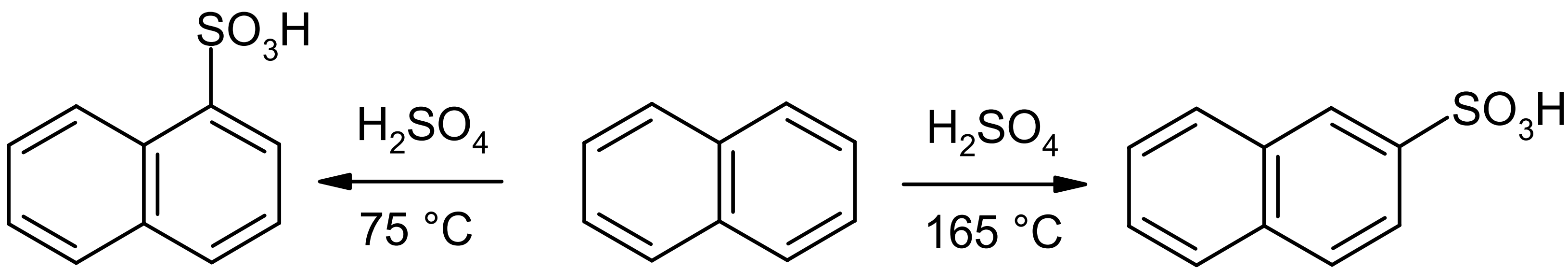


# Aromatic compounds – $S_E$ aromatic – naphthalene



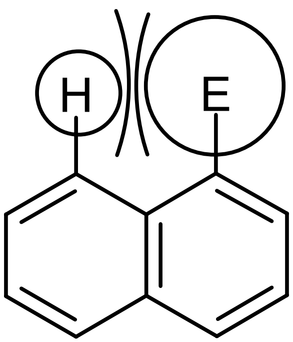



# Aromatic compounds – $S_E$ aromatic – naphthalene



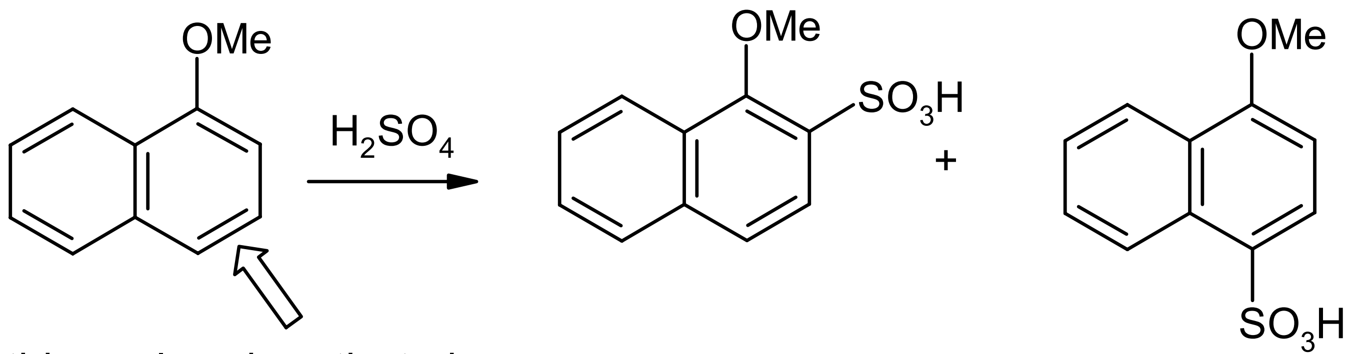

naphthalene-1-sulfonic acid acid (98 %)

naphthalene-2-sulfonic acid (88 %)



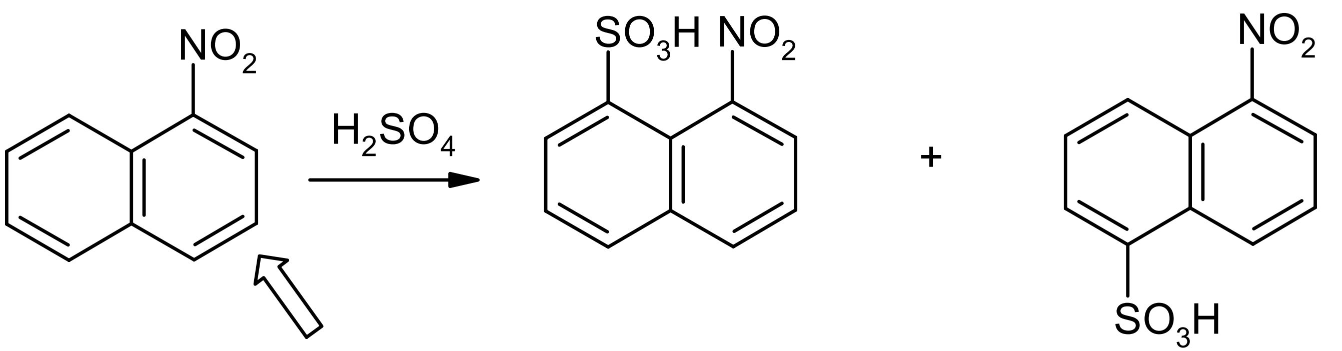
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – naphthalene




this nucleus is activated

Me = $CH_3$

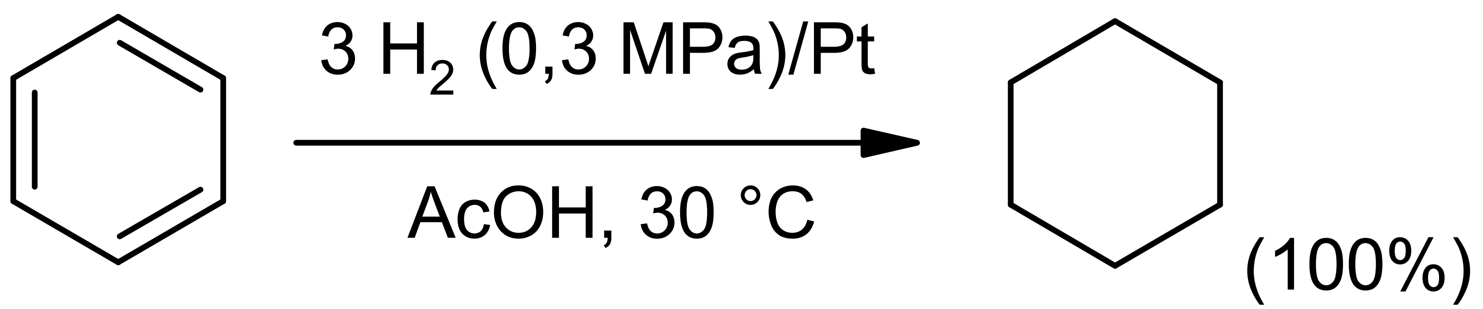


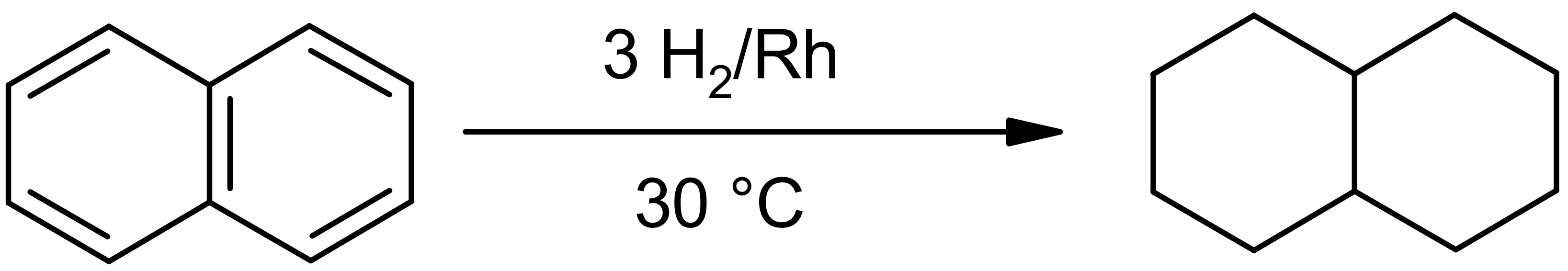

this nucleus is deactivated

8-nitronaphthalene-1-sulfonic acid

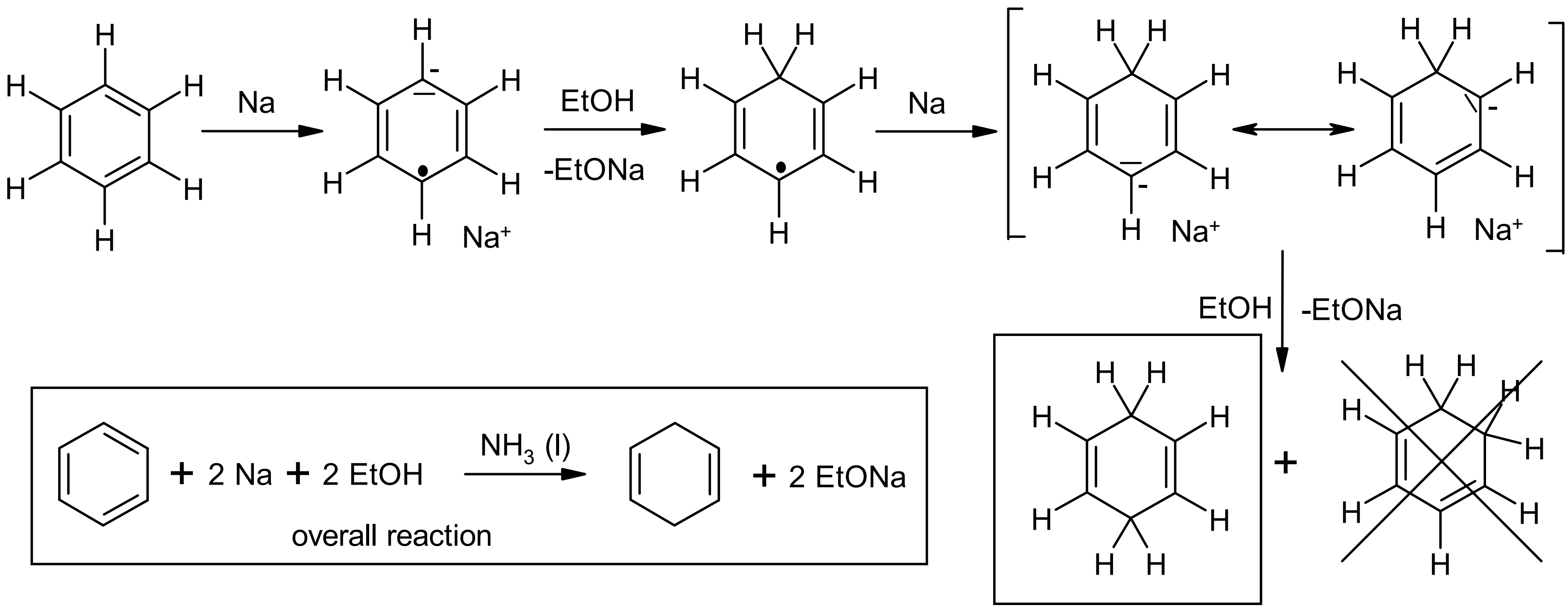
5-nitronaphthalene-1-sulfonic acid

## Aromatic compounds – $S_E$ aromatic – reduction



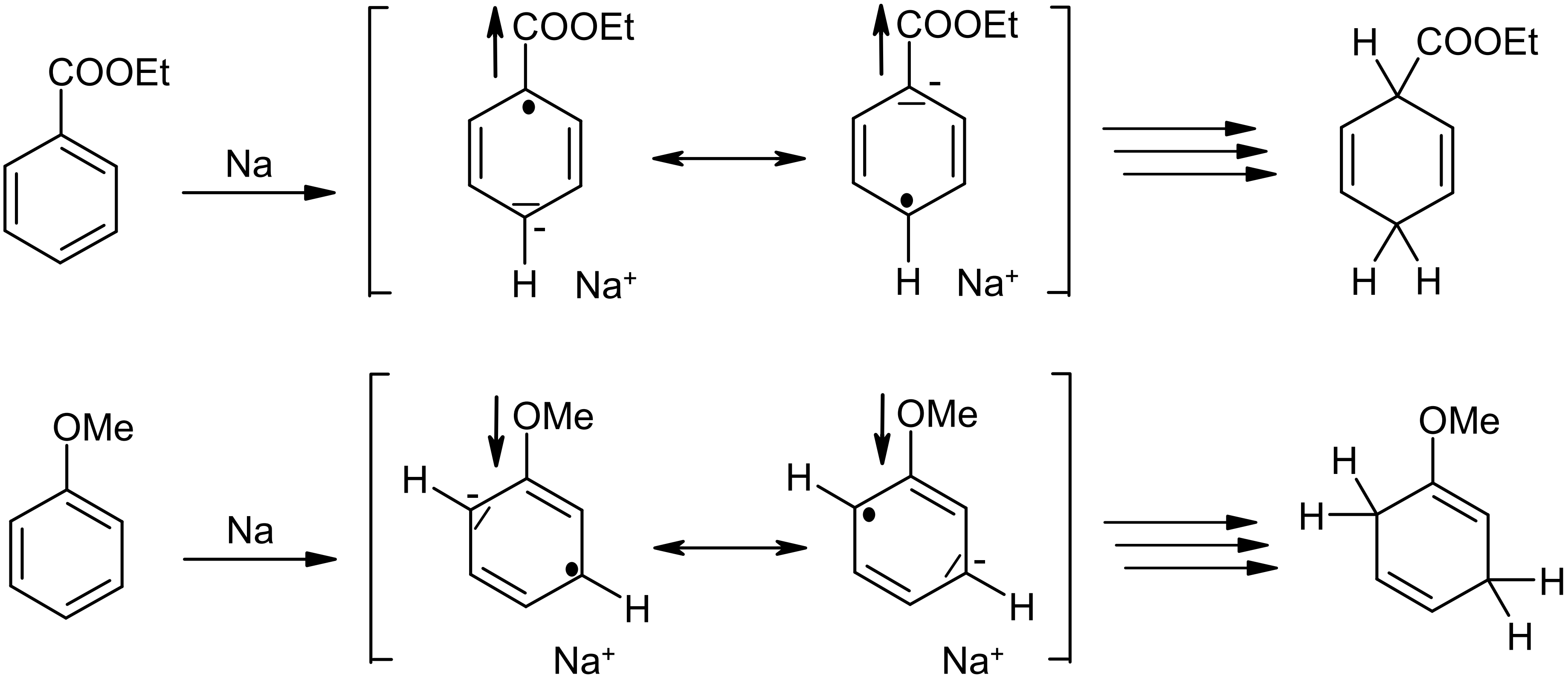
# Aromatic compounds – $S_E$ aromatic – reduction




Et = $C_2H_5$

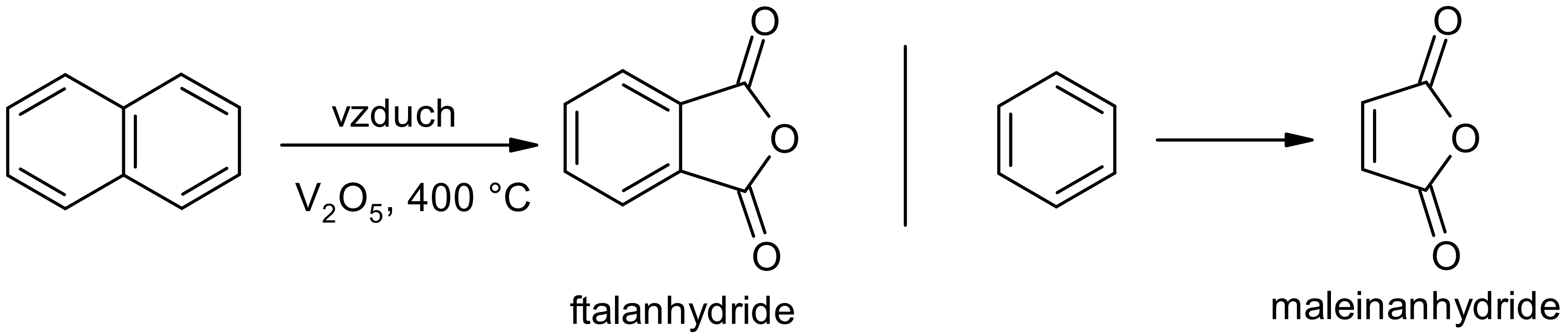
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – reduction



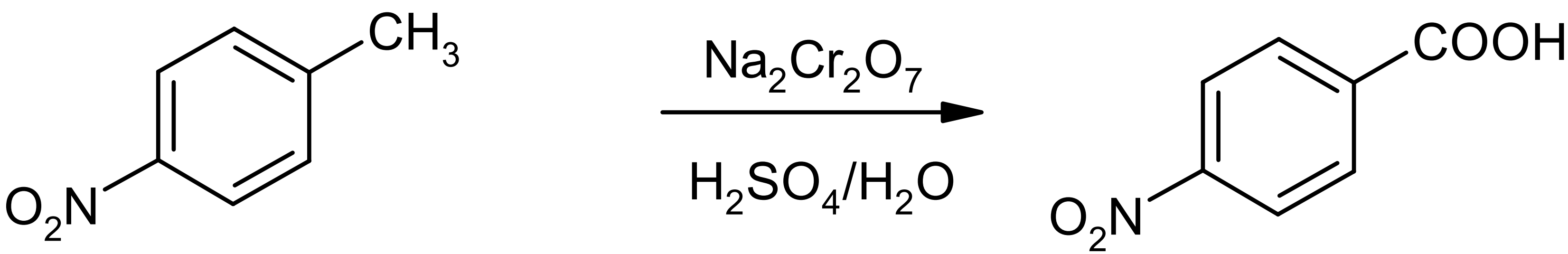

Me = $CH_3$, Et = $C_2H_5$

## Aromatic compounds – $S_E$ aromatic – oxidation

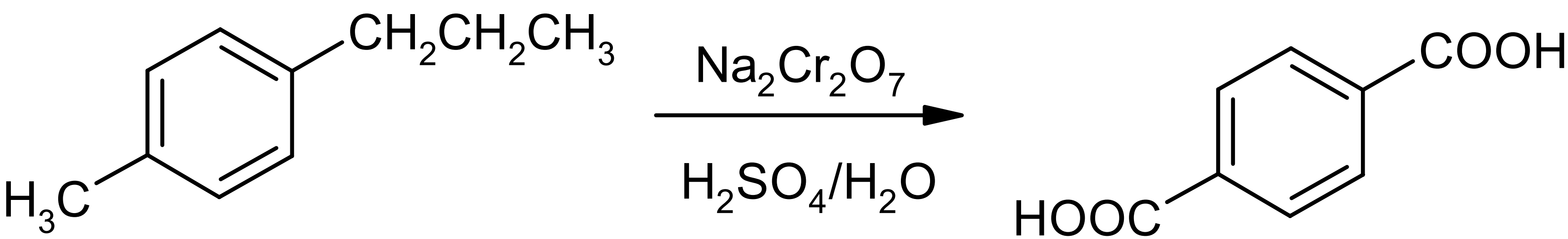


# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – $S_E$ aromatic – oxidation



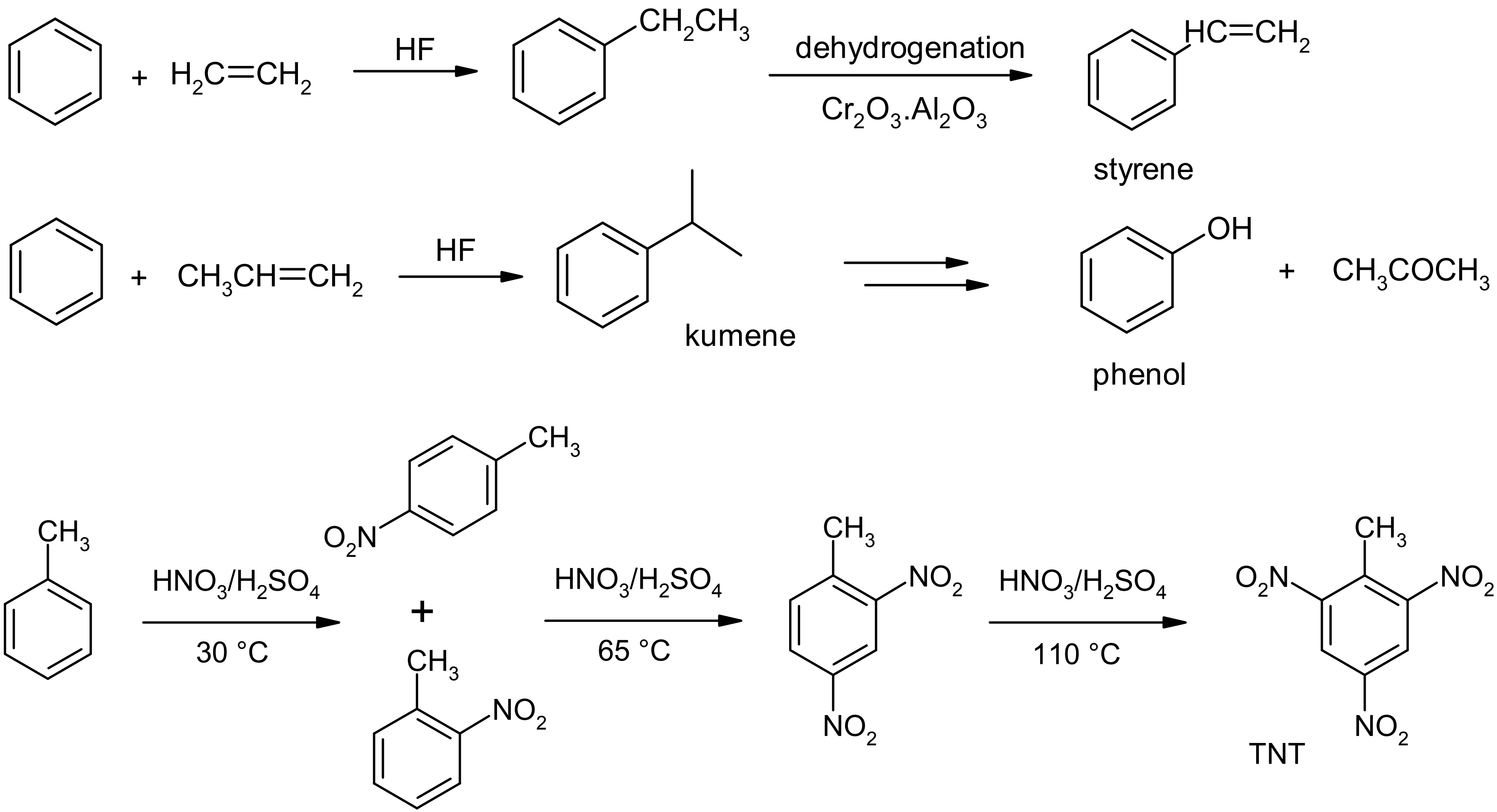

*p*-nitrobenzoic acid



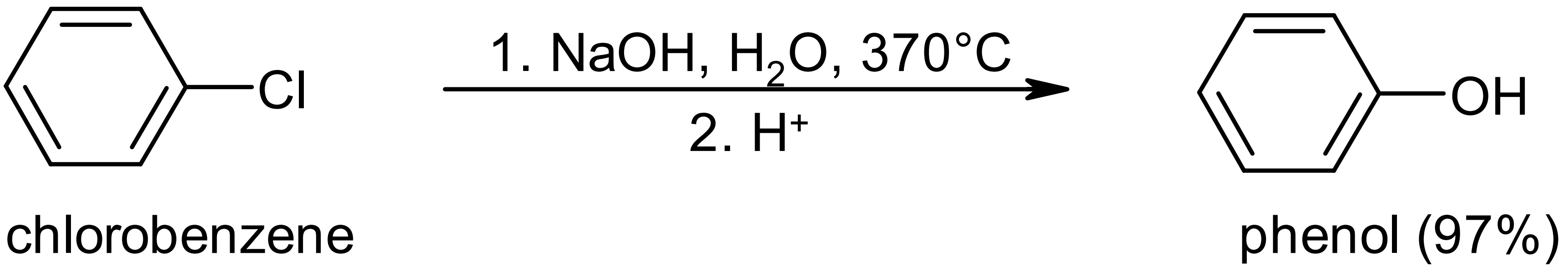

benzene-1,4-dicarboxylic acid
(tereftaphthalic acid)

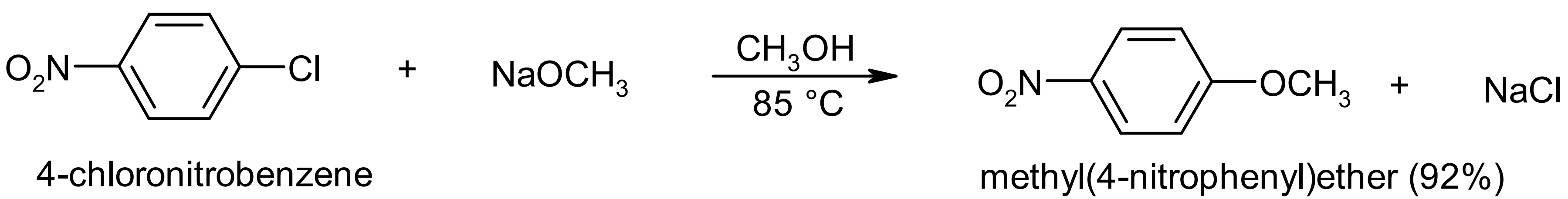
# Organic Chemistry – chemistry of aromatics

## Aromatic compounds – technically important



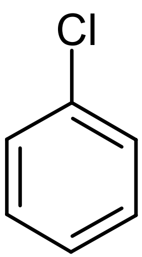
# Phenols - $S_N$ on aromatic halogen



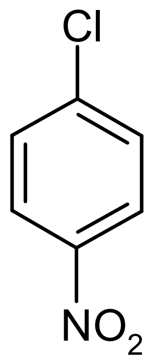
# Phenols - $S_N$ on aromatic skeleton

Relative velocity reaction with $NaOCH_3$:



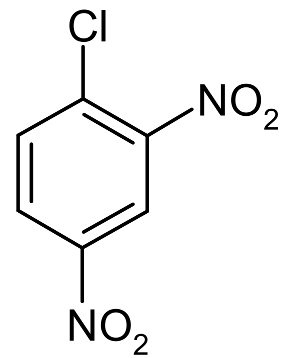
chlorobenzene

1,0



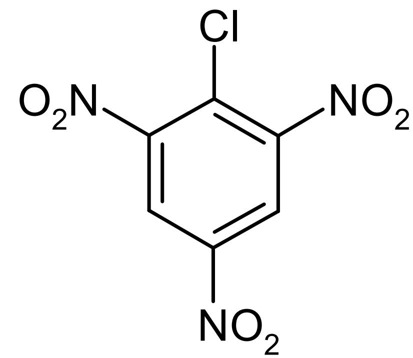
1-chloro-
4-nitrobenzene

$7 \times 10^{10}$



1-chloro-
2,4-dinitrobenzene

$2,4 \times 10^{15}$



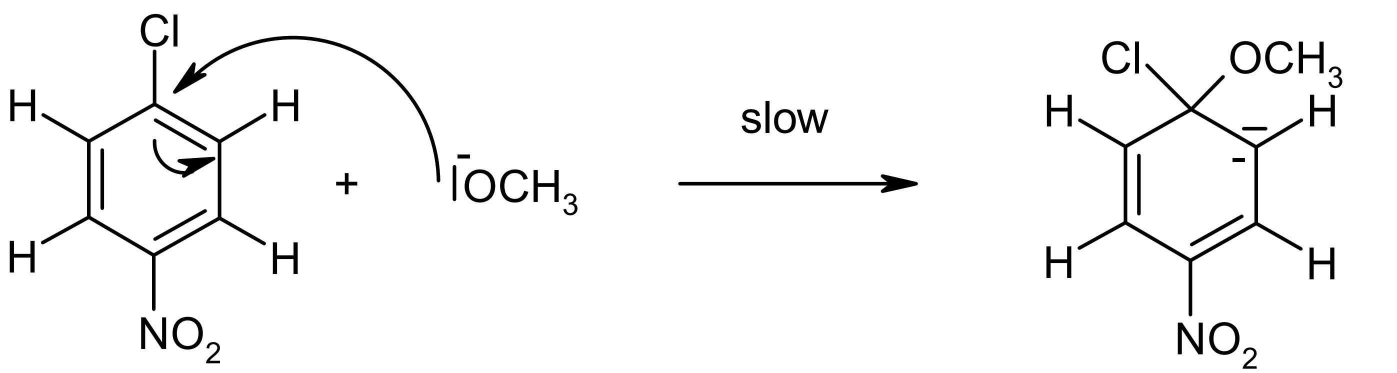
2,4,6-trinitro-
chlorobenzene

too high to be determined

# Organic Chemistry – chemistry of aromatics

## Phenols - $S_N$ on aromatic skeleton - mechanism

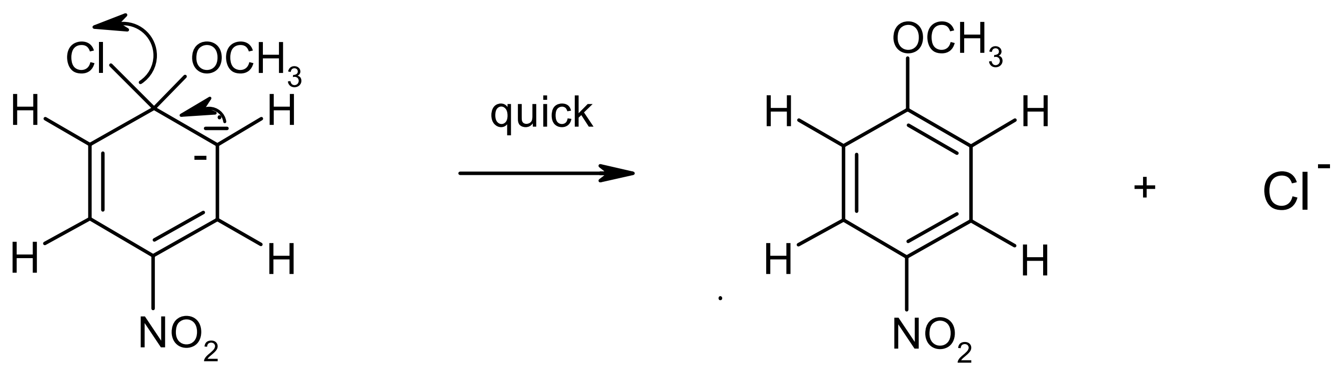
1. step:




4-chloronitrobenzene

cyclohexadienyl anion

2. step:

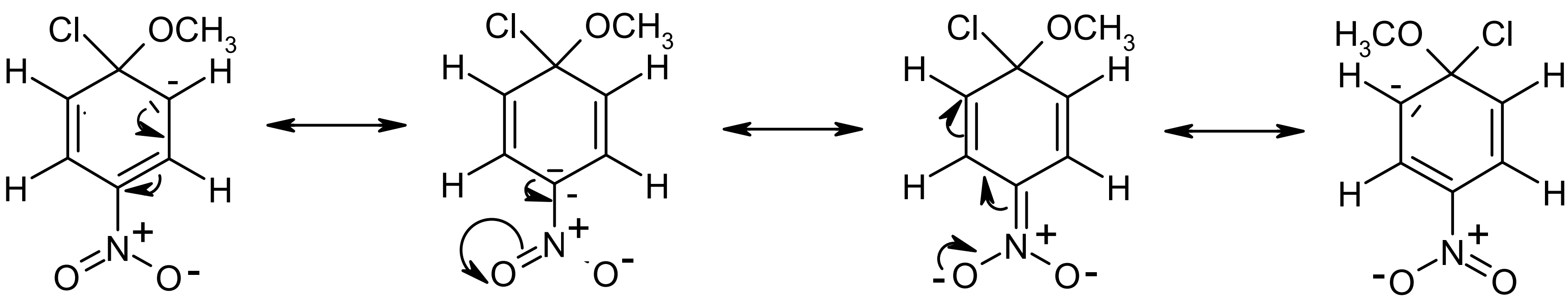



cyclohexadienyl anion

methyl(4-nitrophenyl)ether

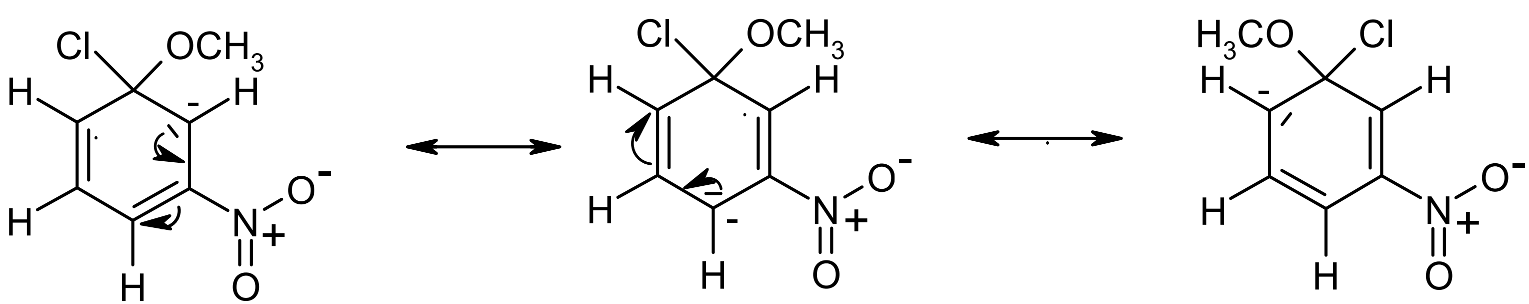
# Phenols - $S_N$ on aromatic skeleton - mechanism

4-nitrochlorobenzene:



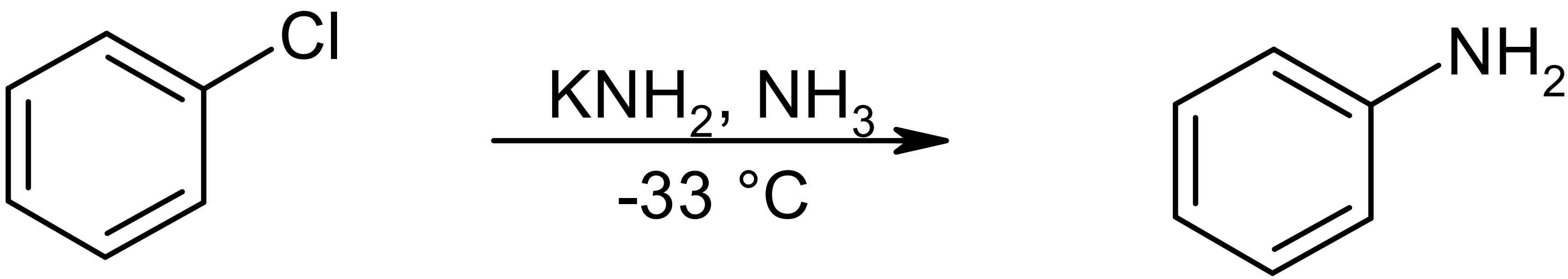

The most stable mesomeric structure
(negative charge on oxygen)

3-nitrochlorobenzene:




Negative charge can be located on carbon atoms only

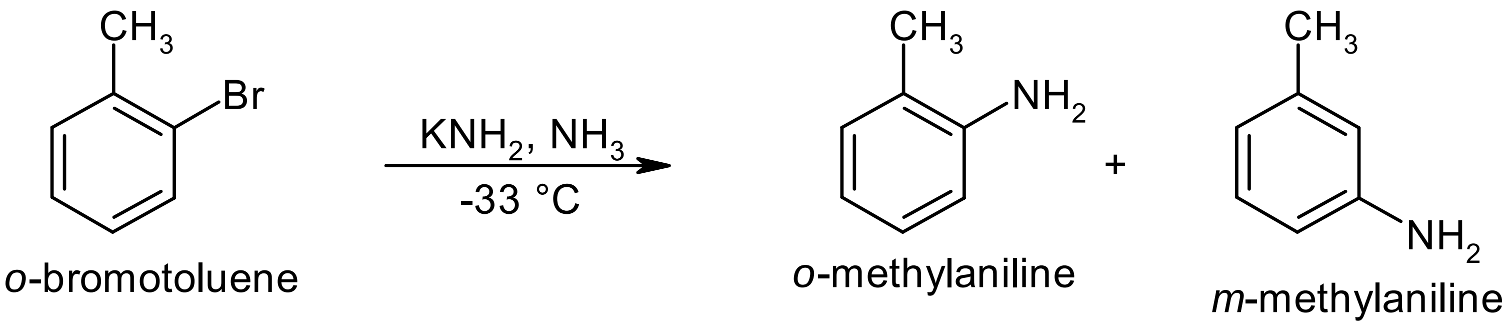
## $S_N$ on aromatic skeleton – addition-elimination mechanism

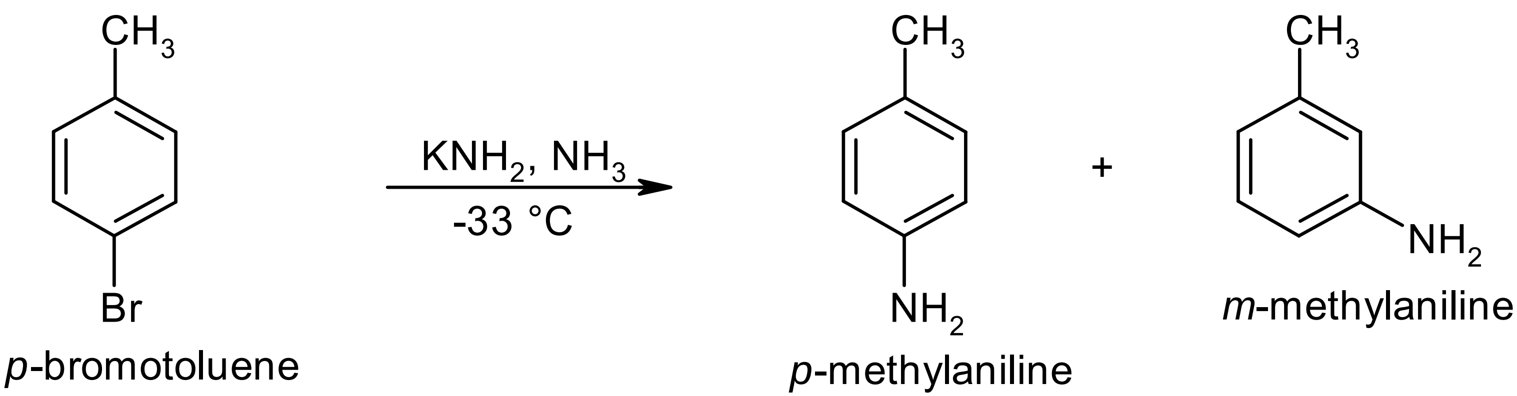


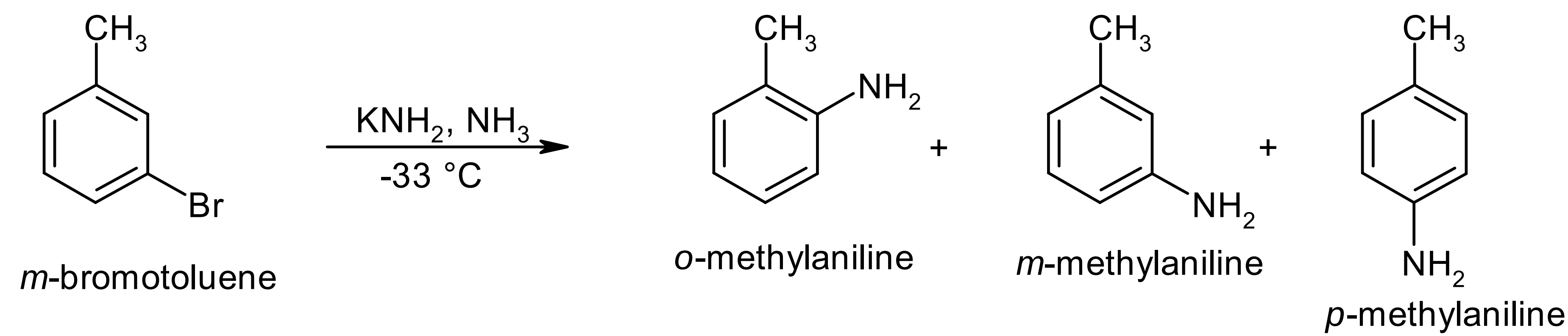

chlorobenzene

aniline (52%)

# Organic Chemistry – chemistry of aromatics



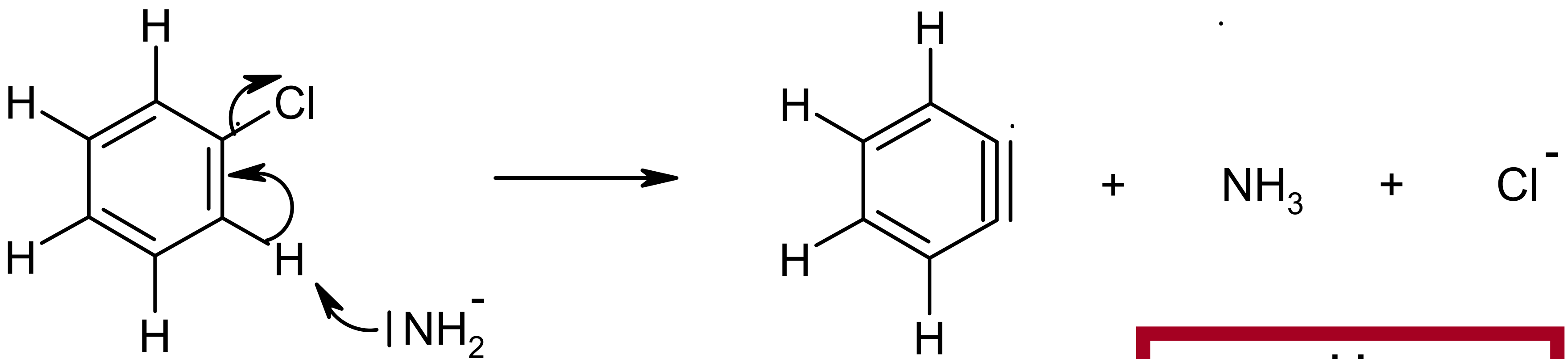



# Organic Chemistry – chemistry of aromatics

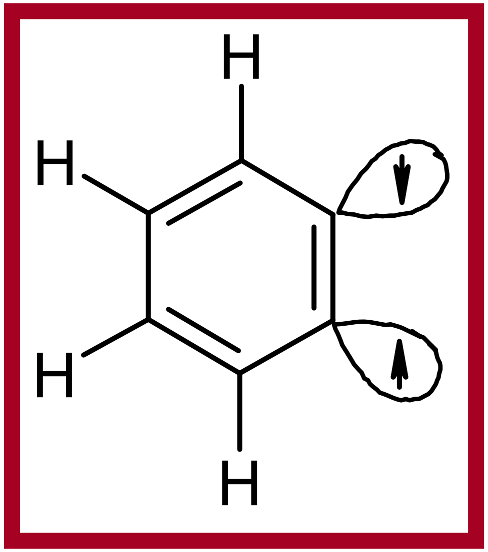
## $S_N$ on aromatic skeleton – addition-elimination mechanism

1. step - elimination:

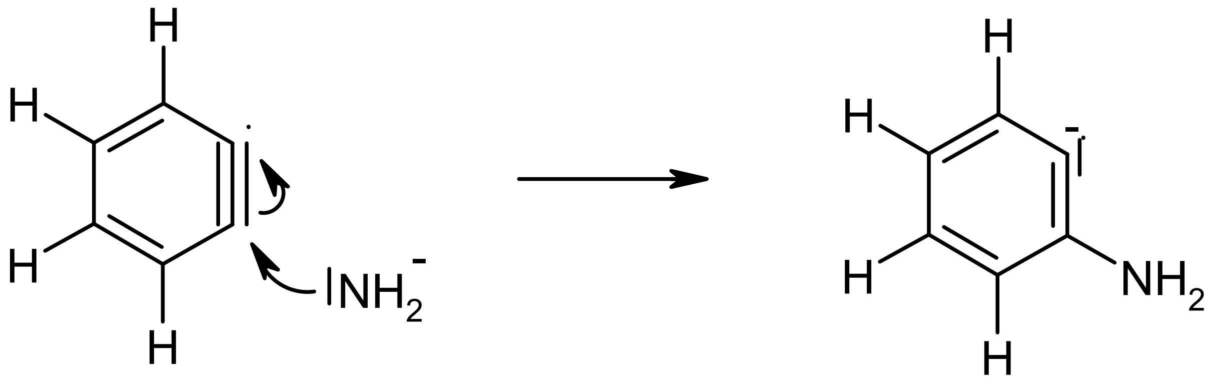



chlorobenzene

benzyne



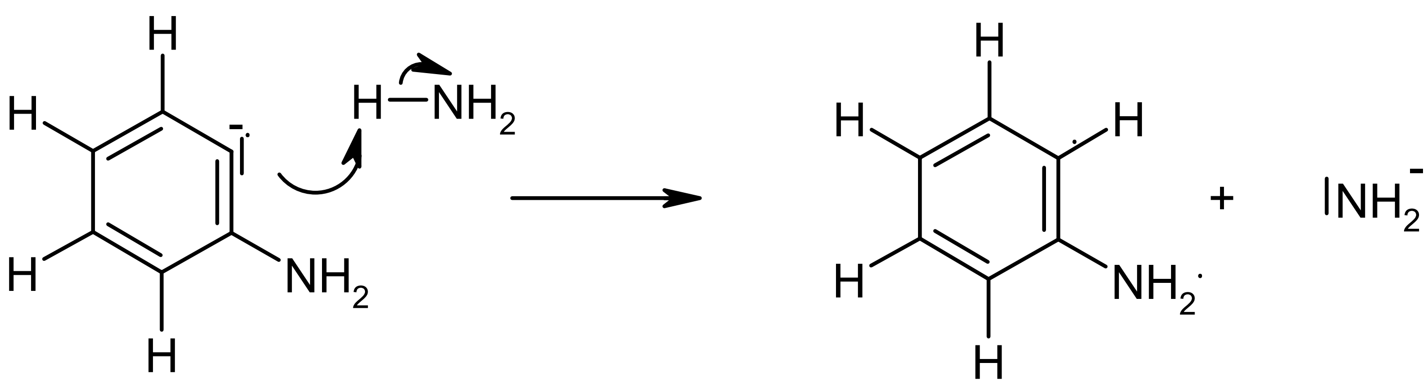
2. step - addition amide anion:



benzyne

aryl anion

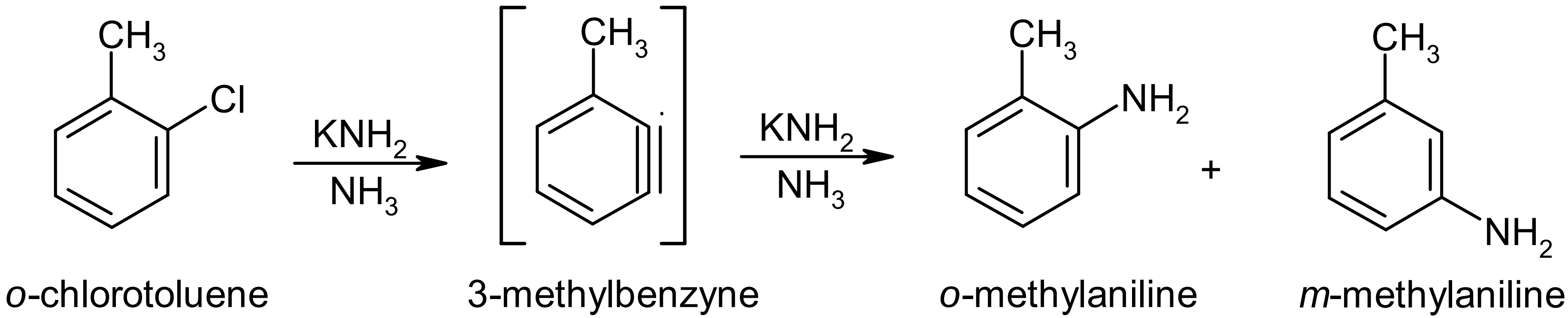
3. step - protonation:



aryl anion

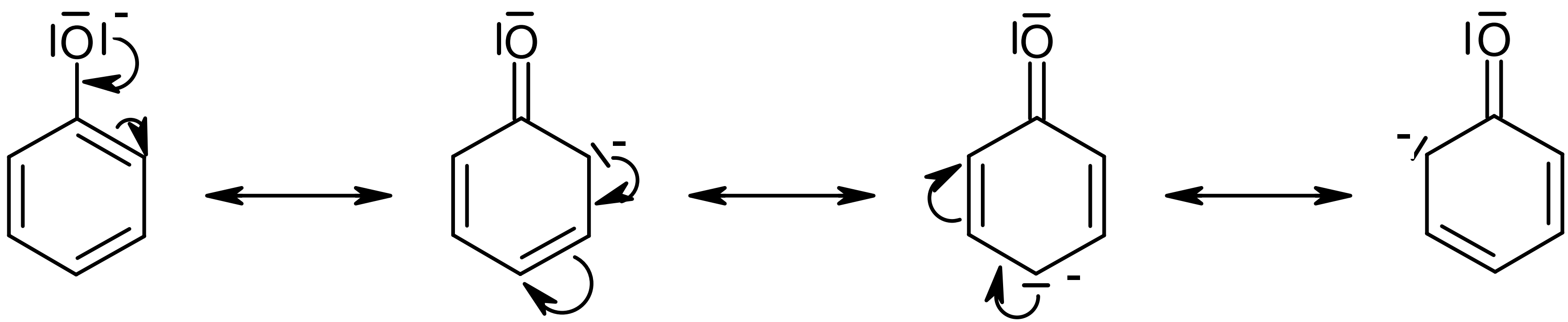
aniline

# $S_N$ on aromatic skeleton – addition-elimination mechanism



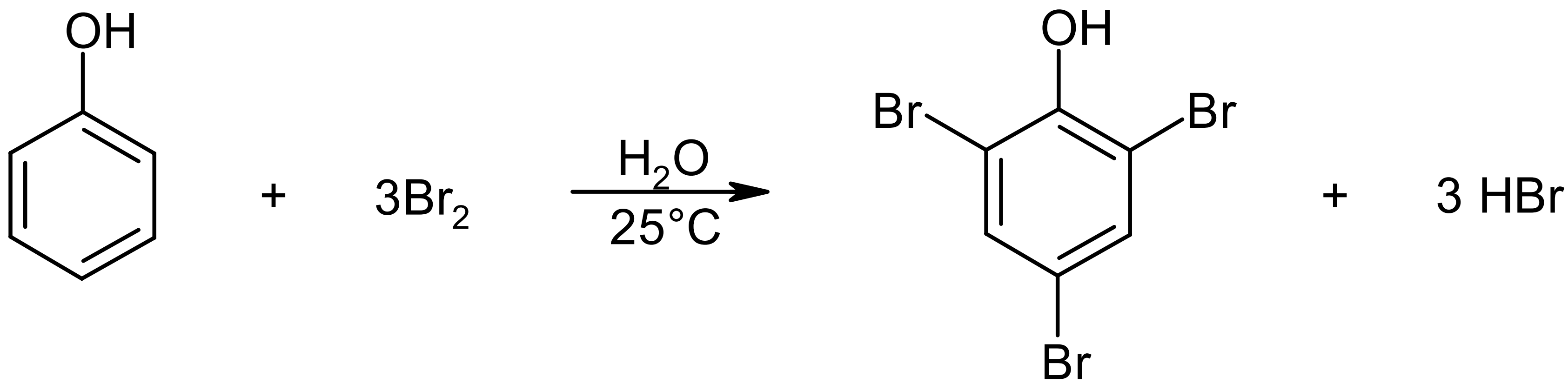
# Organic Chemistry – chemistry of aromatics

## Phenols – acidity – stabilisation od anion by resonance



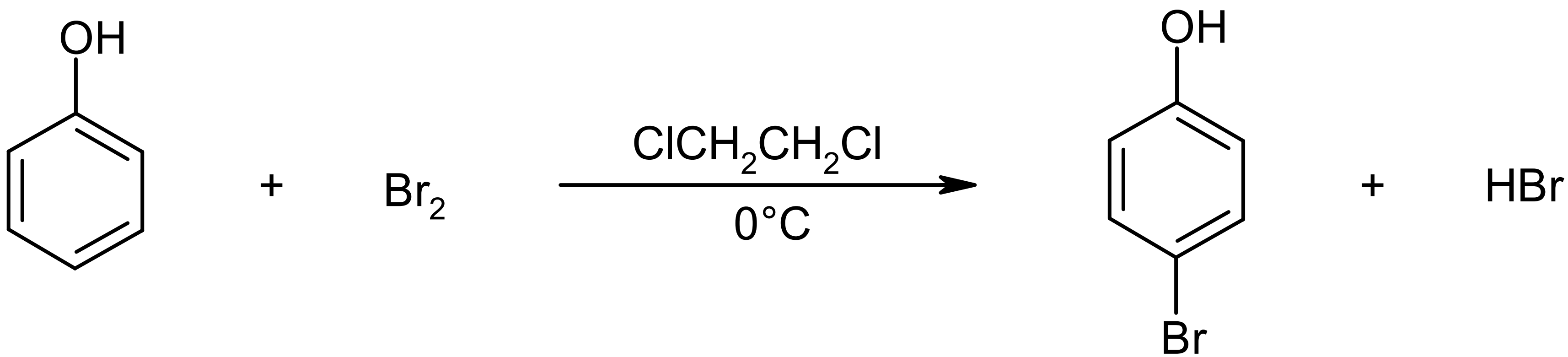
| Compounds | $pK_a$ | Compounds | $pK_a$ |
|---|---|---|---|
| Phenol | 10,0 | 3-nitrophenol | 8,4 |
| 2-methylphenol | 10,3 | 4-nitrophenol | 7,2 |
| 3-methylphenol | 10,1 | 2.4-dinitrophenol | 4,0 |
| 4-methylphenol | 10,3 | 3,5-dinitrophenol | 6,7 |
| 2-nitrophenol | 7,2 | 2,4,6-trinitrophenol | 0,4 |

## Phenols – are extremely reactive aromatics




phenol

2,4,6-tribromophenol

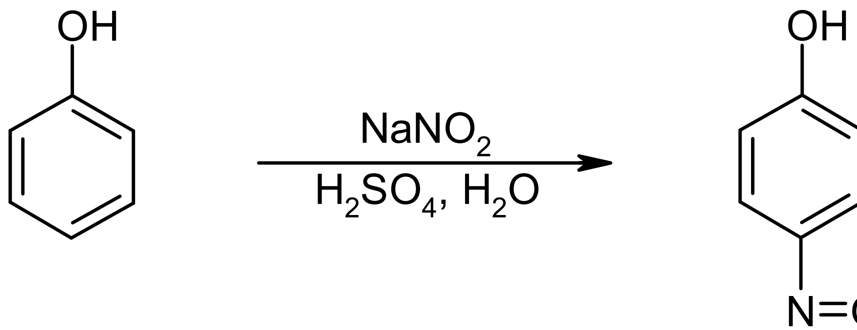



phenol

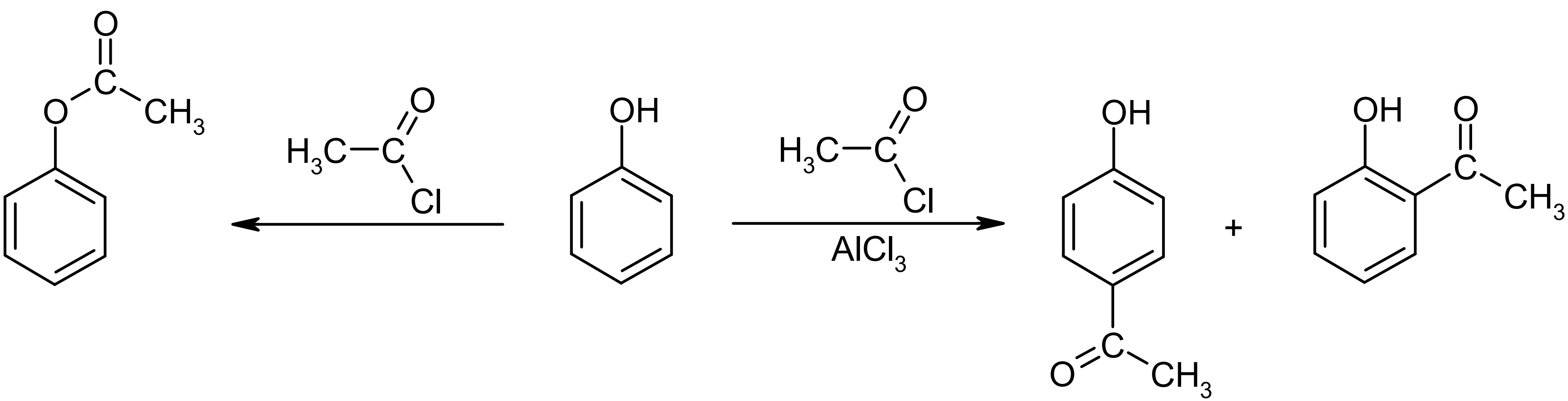
4-bromophenol (93%)

# Organic Chemistry – chemistry of aromatics

## Phenols – are extremely reactive aromatics

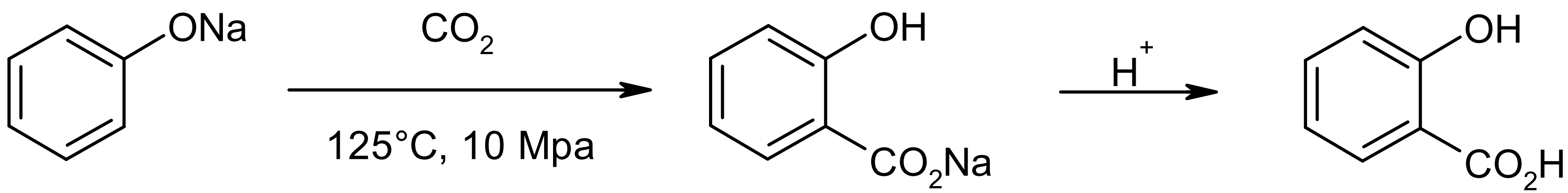



phenol 4-nitrosophenol




phenyl-acetate phenol 4-hydroxyacetophenone (74%) 2-hydroxyacetophenone (16%)

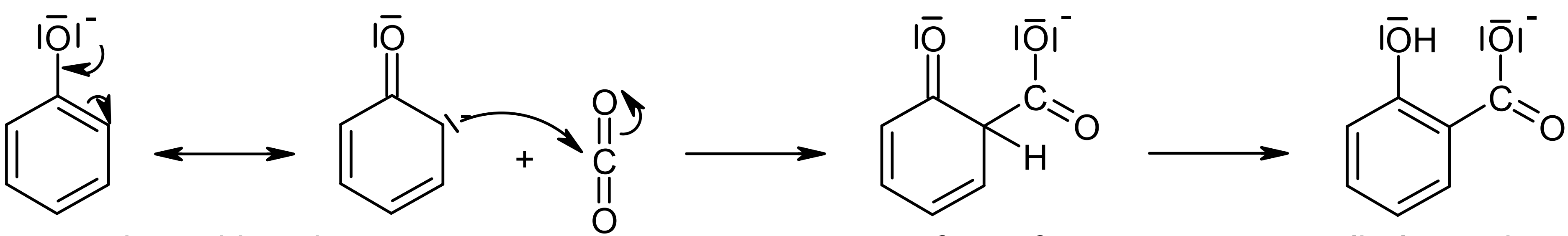
# Phenols – are extremely reactive aromatics




sodium phenoxide

sodium salicylate

salicylic acid (79%)

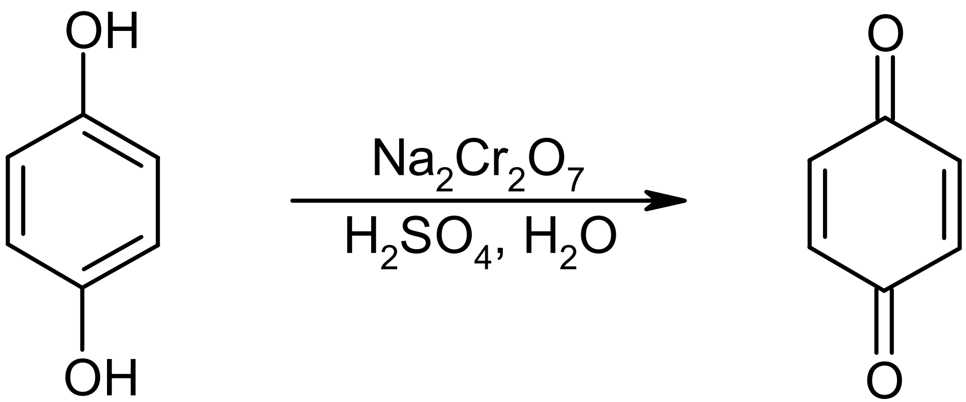



phenoxide anion

oxoform of salicylate anion

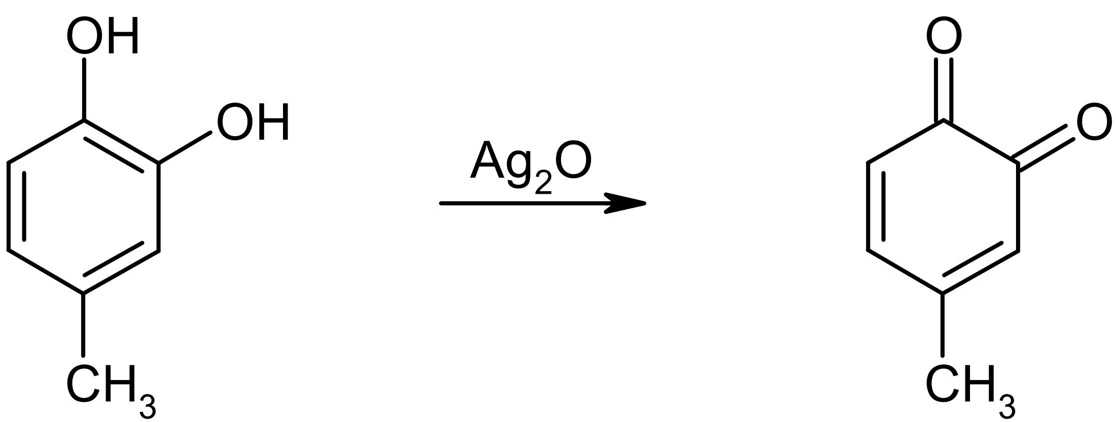
salicylate anion

# Phenols – oxidation to quinones




hydroquinone

*p*-benzoquinone (81%)

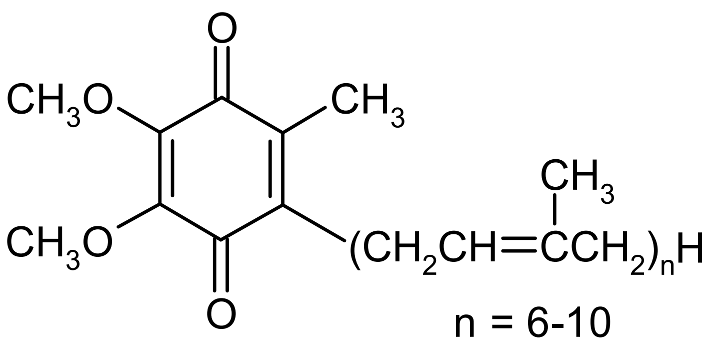



4-methylbenzene-1,2-diol

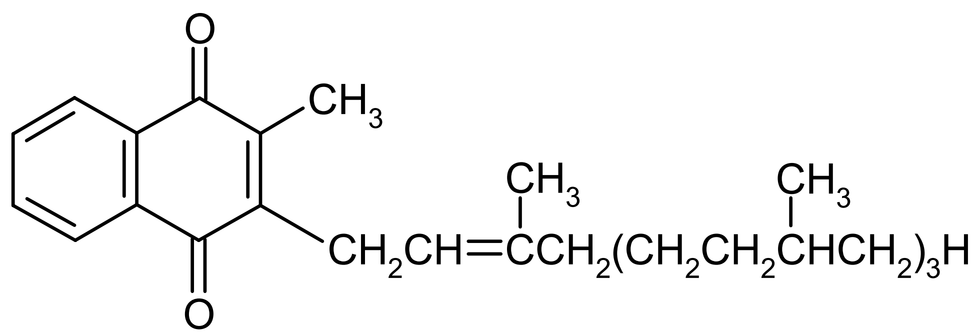
4-methylbenzo-1,2-quinone (68%)

# Organic Chemistry – chemistry of aromatics

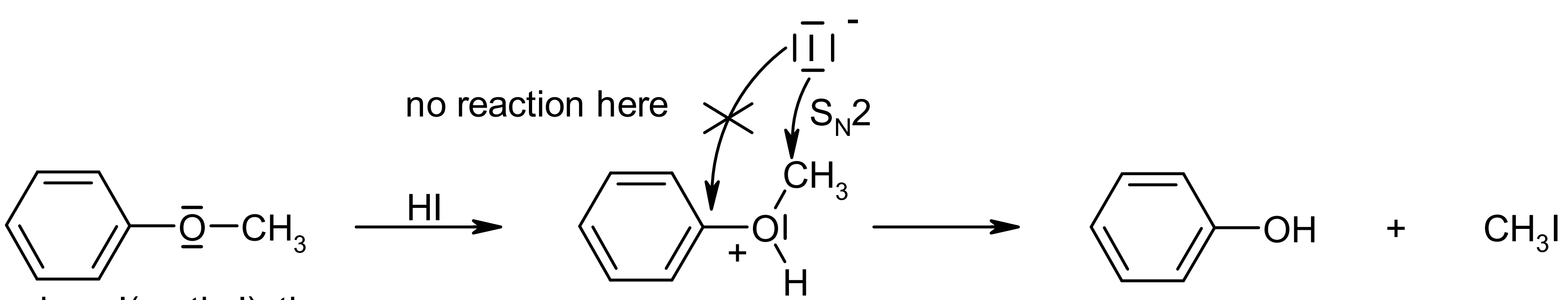
## Phenols – oxidation to quinones and cleavage of ethers




ubiquinone (koenzyme Q)




vitamine K

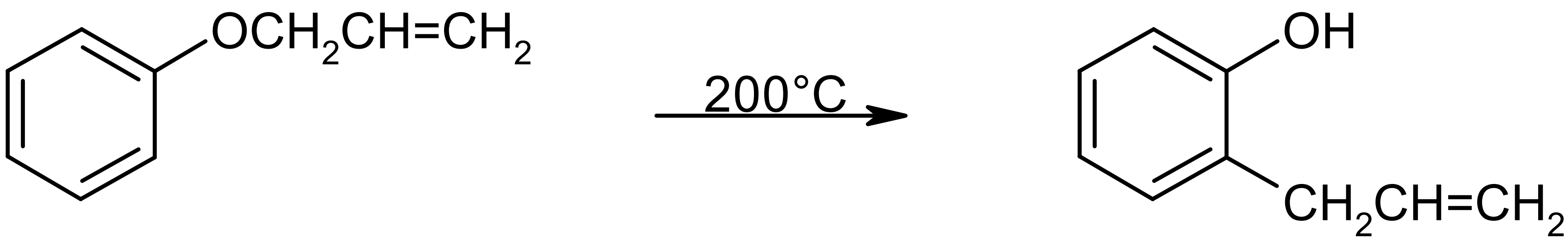



phenyl(methyl)ether (anisole)

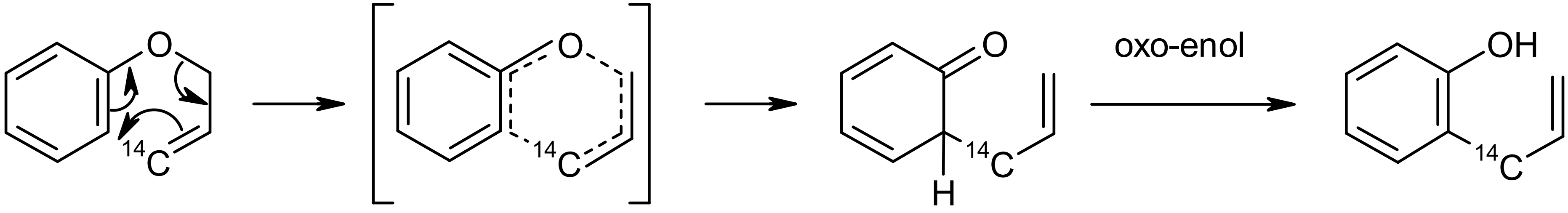
phenol

iodomethane

# Phenols – Claisen rearrangement of allylarylethers

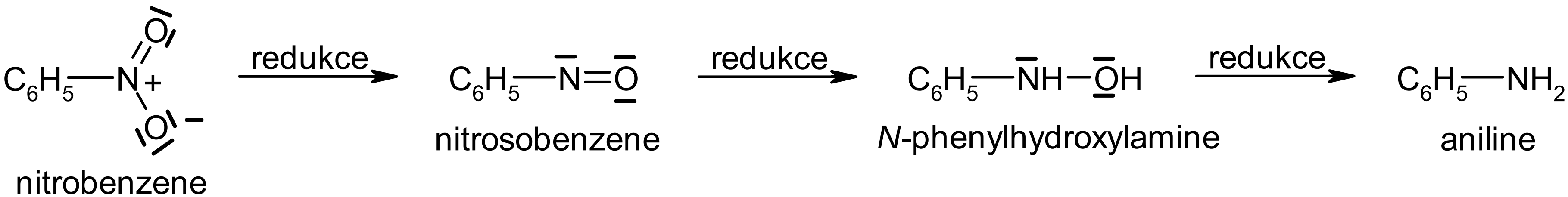


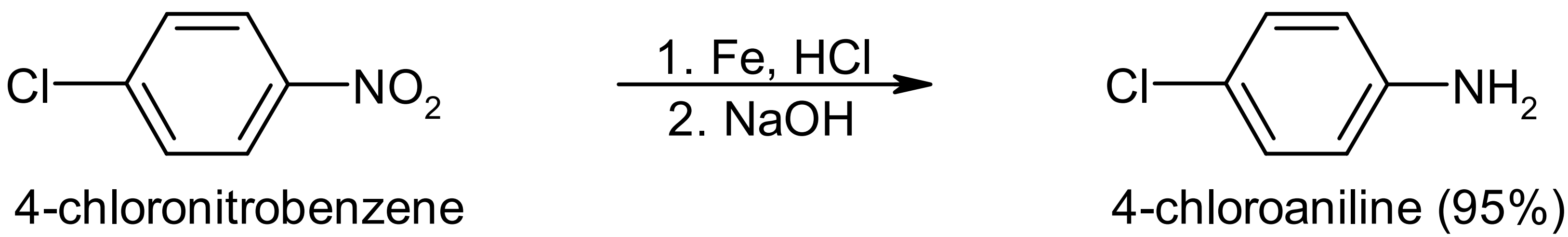

allyl(phenyl)ether — 2-allylphenol (75%)

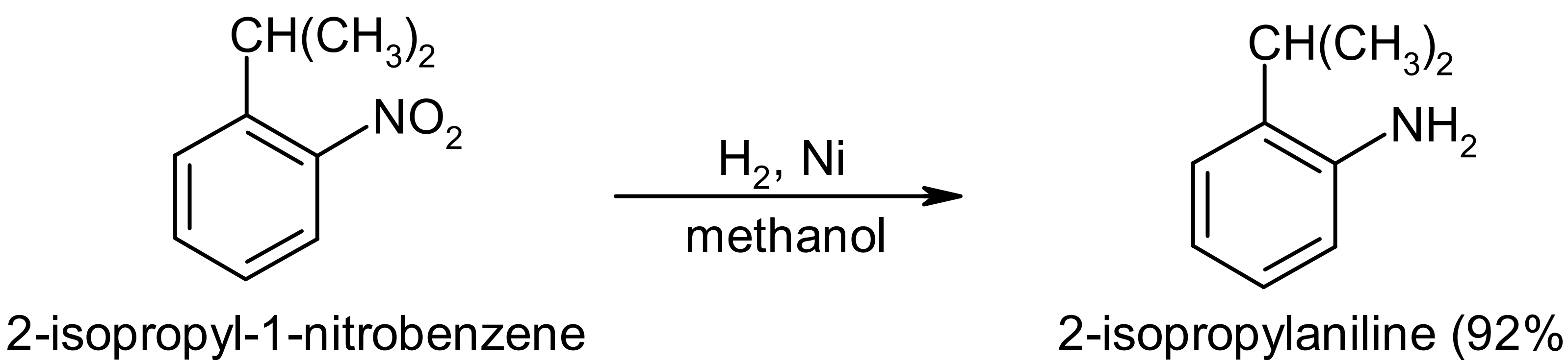



allyl(phenyl)ether — transition state — 6-allylcyclohexa-2,4-diene-1-one (enolform of product) — 2-allylphenol

# Aromatic amines – preparation –reduction of nitrocompounds

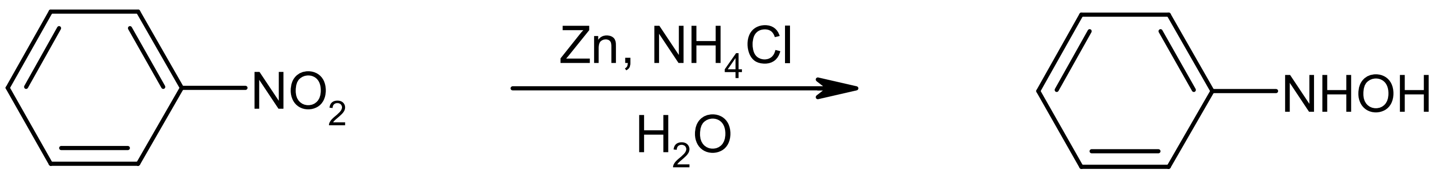


# Organic Chemistry – chemistry of aromatics

## Aromatic amines – preparation –reduction of nitrocompounds




*N*-phenylhydroxylamine

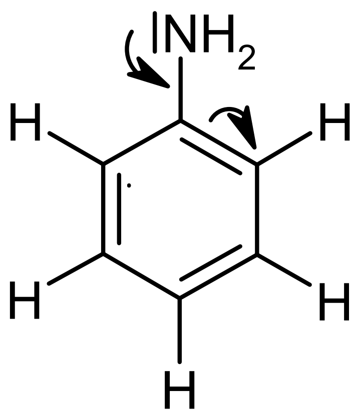
$$C_6H_5{-}NHOH \rightleftharpoons C_6H_5{-}\overset{+}{N}(\text{—}\bar{O}^-)H_2 + O{=}N{-}C_6H_5 \xrightarrow{-H_2O} C_6H_5{-}\overset{+}{N}(\text{—}\bar{O}^-){=}N{-}C_6H_5$$

*N*-phenylhydroxylamine; nitrosobenzene; azoxybenzene

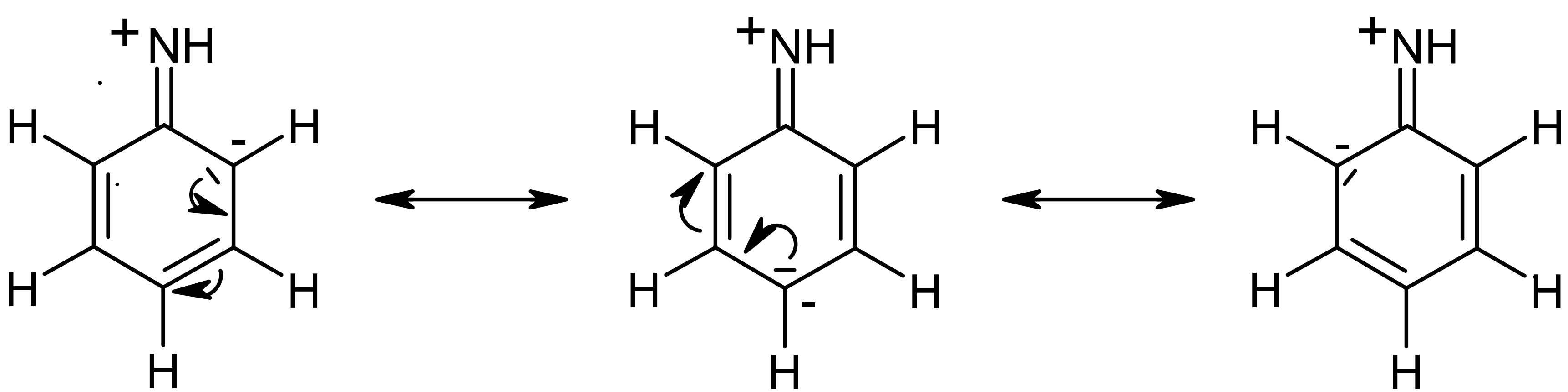
$$C_6H_5{-}\overset{+}{N}(\text{—}\bar{O}^-){=}N{-}C_6H_5 \xrightarrow{Zn,\ OH^-} C_6H_5{-}N{=}N{-}C_6H_5 \xrightarrow{Zn,\ OH^-} C_6H_5{-}NH{-}NH{-}C_6H_5$$

azoxybenzene; azobenzene; 1,2-diphenylhydrazine

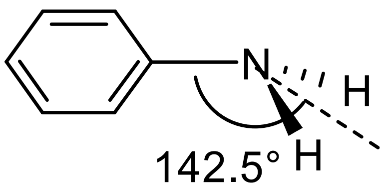
## Aromatic amines - structure



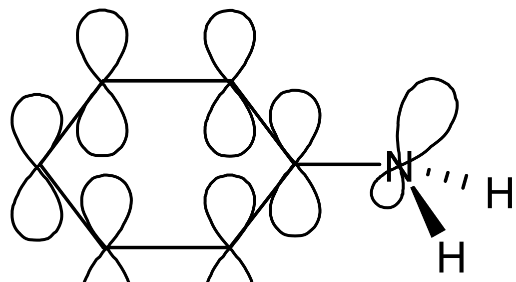

aniline
benzenamine
aminobenzene
phenylamine



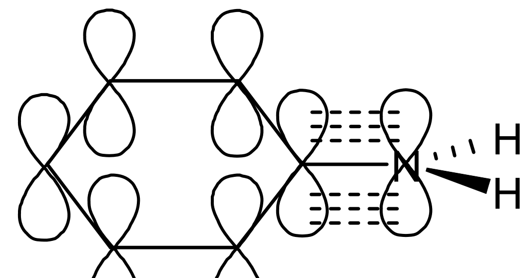
# Aromatic amines - structure




aniline

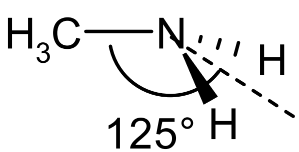



*sp*³

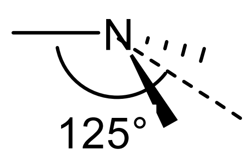



*sp*²

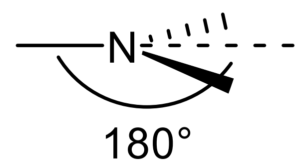
aniline - conjugation of nonbonded electrons




methylamine



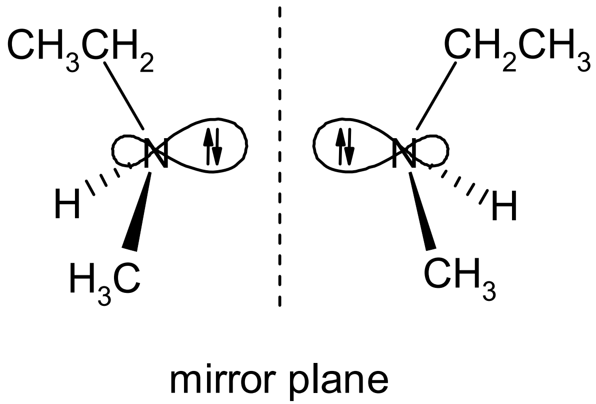

*sp*³ hybridisationace on N

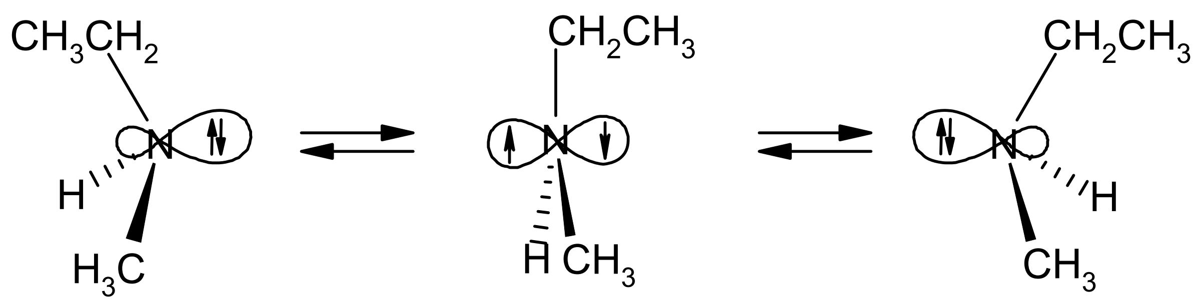


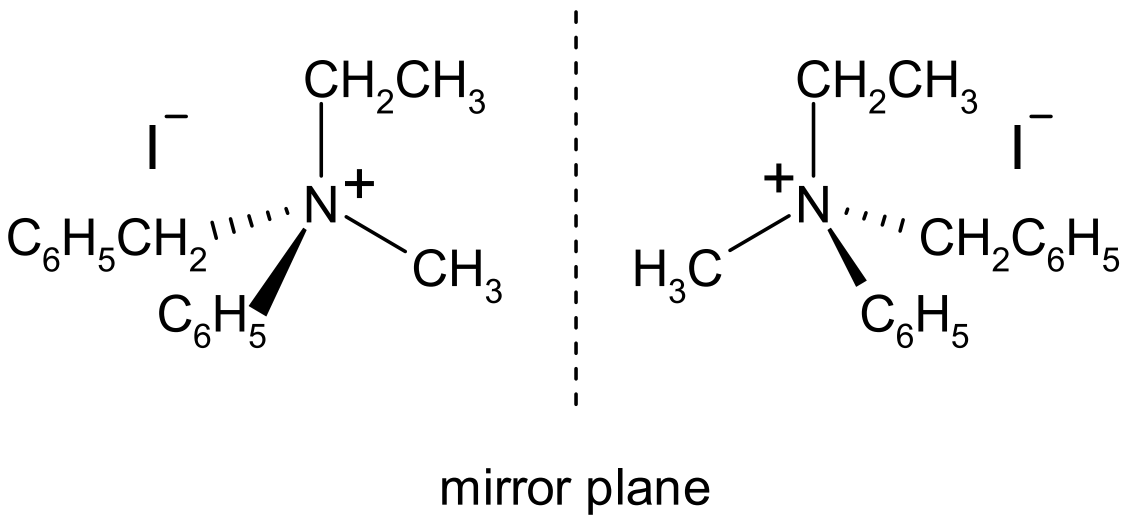

*sp*² hybridisation on N

# Organic Chemistry – chemistry of aromatics

## Aromatic amines – structure, chirality

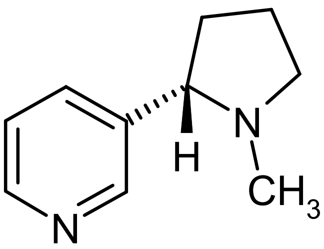


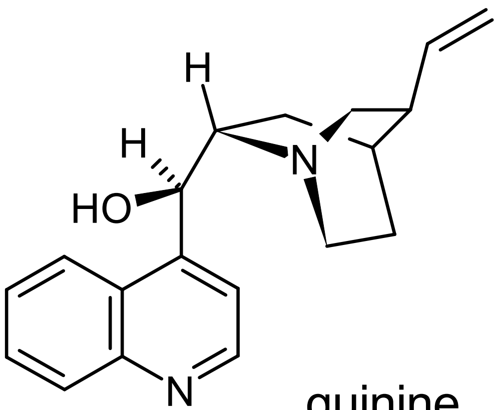



# Organic Chemistry – chemistry of aromatics

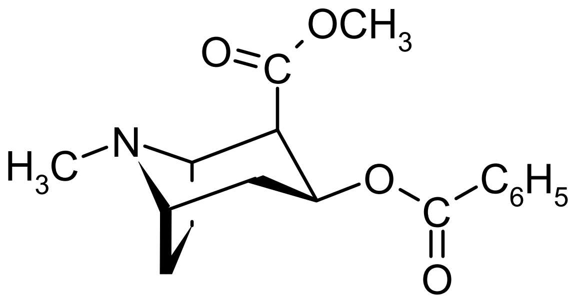
## Amines – natural compounds



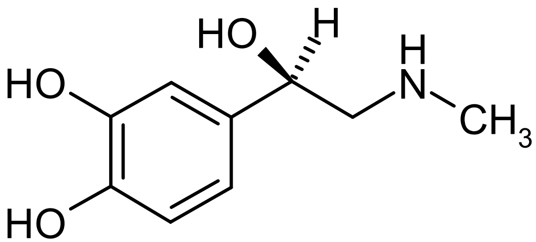

nicotine



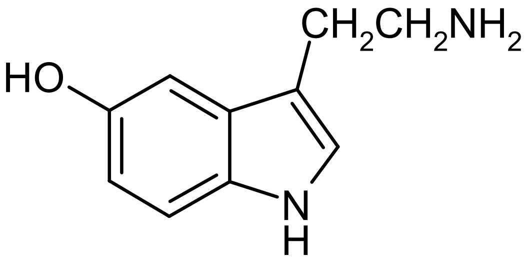

quinine



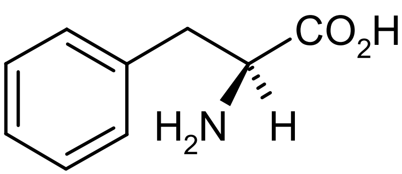

cocaine




adrenaline




serotonine




L-phenylalanine

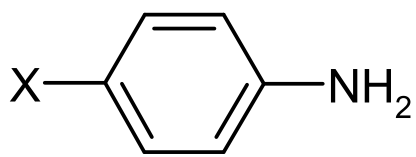
# Amines – basicity

$$R_3N| \;+\; H-\overline{\underline{O}}-H \;\rightleftharpoons\; R_3\overset{+}{N}-H \;+\; {}^{-}|\overline{\underline{O}}-H$$

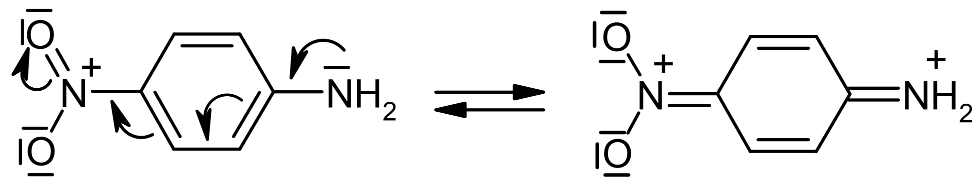
$$K_b = \frac{[R_3NH^+][OH^-]}{[R_3N]} \qquad pK_b = -\log K_b$$

| Amine | p$K_b$ | Amine | p$K_b$ |
|---|---|---|---|
| amoniak | **4,7** | **secondary amines** | |
| **primary amines** | | $(CH_3)_2NH$ | **3,3** |
| $CH_3NH_2$ | **3,4** | $(CH_3CH_2)NH$ | **2,9** |
| $CH_3CH_2NH_2$ | **3,2** | $C_6H_5NHCH_3$ | **9,2** |
| $(CH_3)_2CHNH_2$ | **3,4** | **Tertiary amines** | |
| $(CH_3)_3CNH_2$ | **3,6** | $(CH_3)_3N$ | **4,3** |
| $C_6H_5NH_2$ | **9,4** | $(CH_3CH_2)_3N$ | **3,2** |
| | | $C_6H_5N(CH_3)_2$ | **8,9** |

# Aromatic amines – basicity – role of substituent




| X | $pK_b$ |
|---|---|
| H | 9,4 |
| $CH_3$ | 8,7 |
| $CF_3$ | 11,5 |
| $O_2N$ | 13,0 |



# Amines – as acids – deprotonation of them

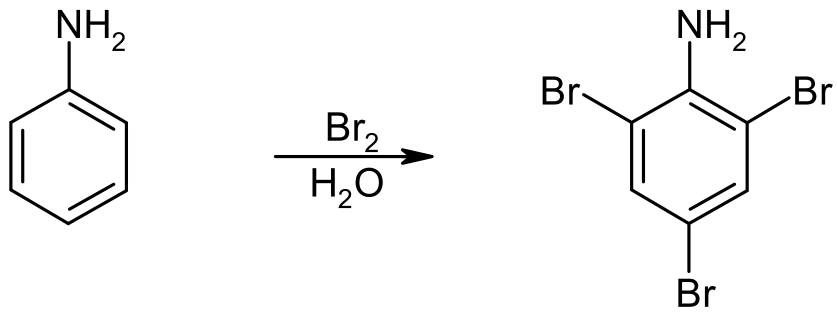
$$R{-}NH_2 \quad + \quad H{-}O{-}H \quad \underset{}{\overset{K_a}{\rightleftharpoons}} \quad R{-}NH^- \quad + \quad H_3O^+$$

$$K_a = \frac{[RNH^-][H_3O^+]}{[RNH_2]} = \sim 10^{-35} \qquad pK_a = -\log K_a = \sim 35$$

$$(CH_3)_2CH{-}NH{-}CH(CH_3)_2 \xrightarrow[-\ CH_3CH_2CH_2CH_3]{CH_3CH_2CH_2CH_2Li} (CH_3)_2CH{-}N^-{-}CH(CH_3)_2 \ Li^+$$

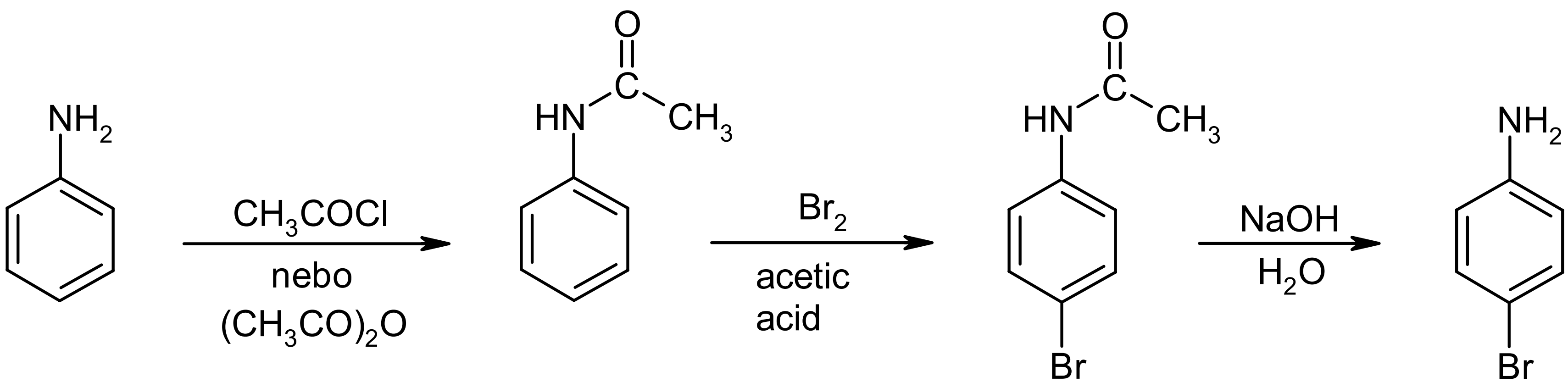
diisopropylamine → lithium-diisopropylamide, LDA

# Aromatic amines – reactivity $S_EAr$




aniline

2,4,6-tribromoaniline (quantitative)



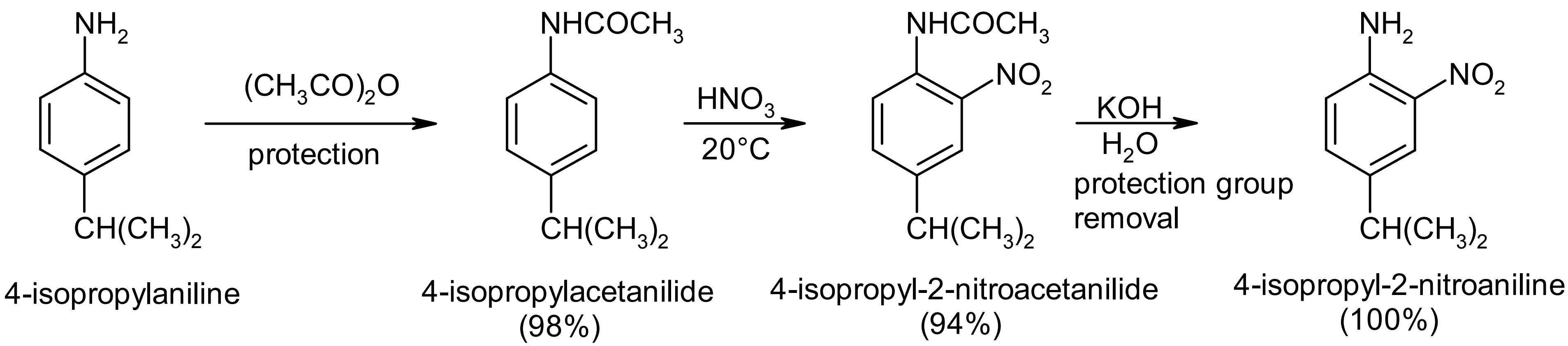

acetanilide

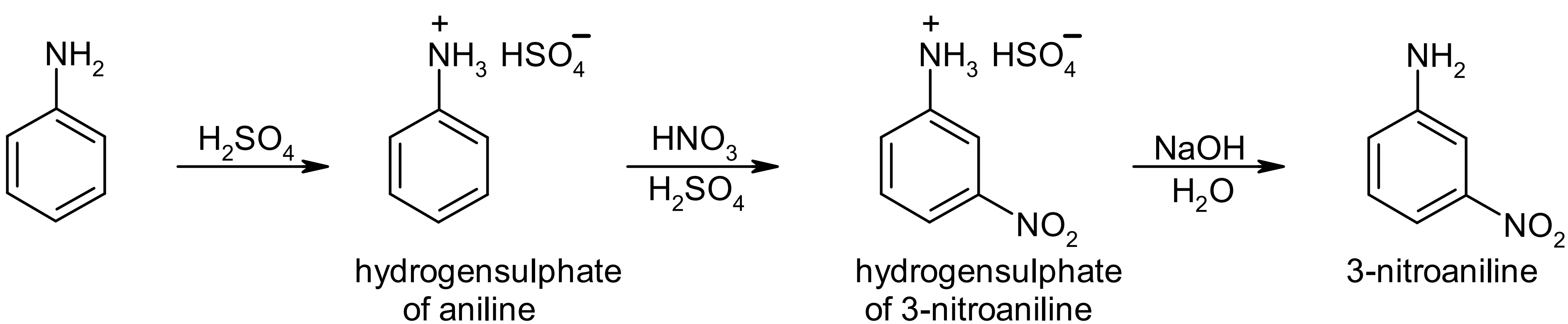
4-bromoacetanilide (main product)

4-bromoaniline

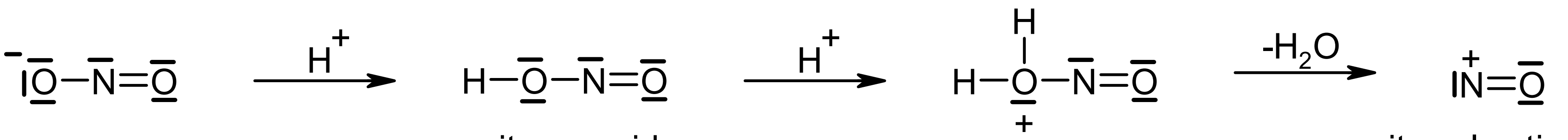
# Organic Chemistry – chemistry of aromatics

## Aromatic amines – reactivity $S_EAr$

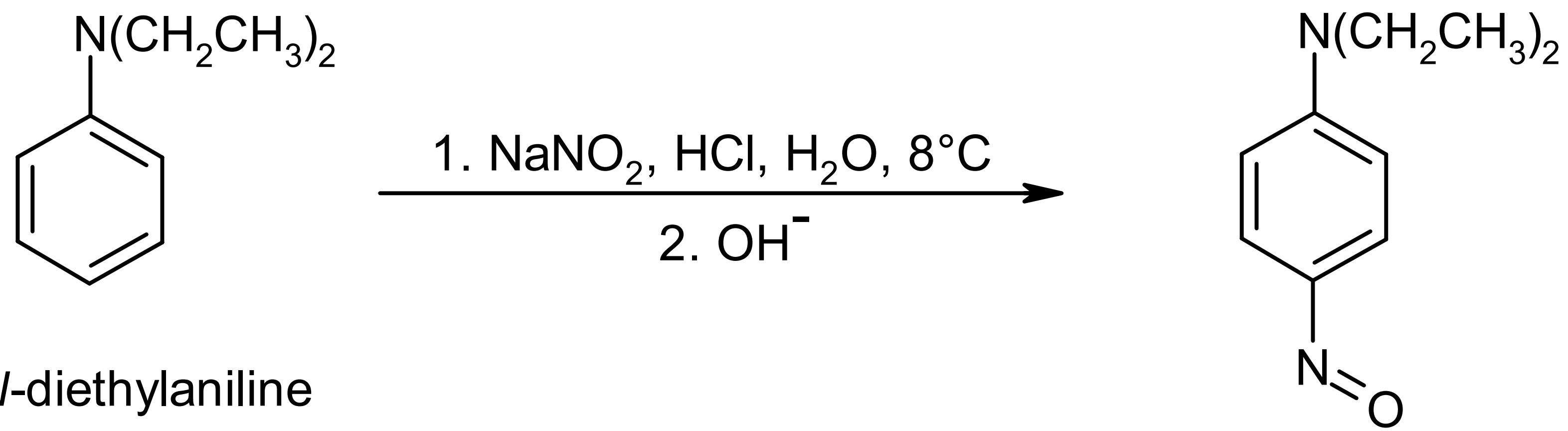


# Aromatic amines – reactivity $S_EAr$



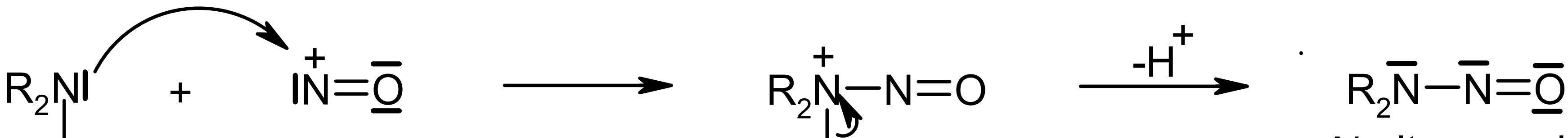

nitrous anion → nitrous acid → nitrosyl cation



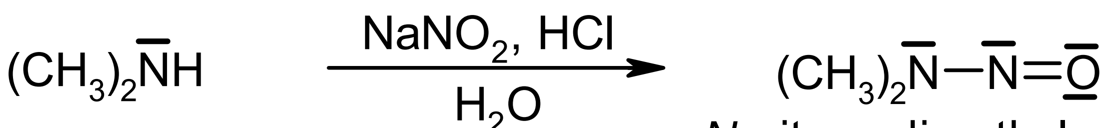

*N,N*-diethylaniline

*N,N*-diethyl-4-nitrosoaniline (95%)

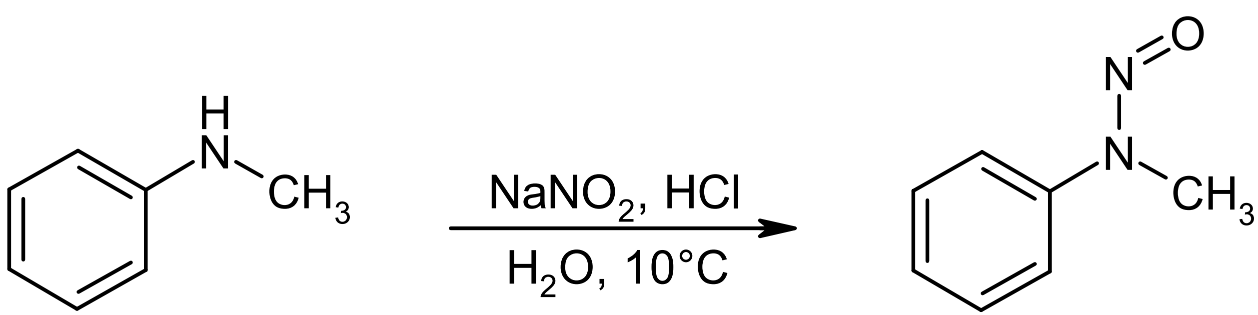
# Aromatic amines – reactivity $S_EAr$




*N*-nitrosoamine




*N*-nitrosodimethylamine
(90%)

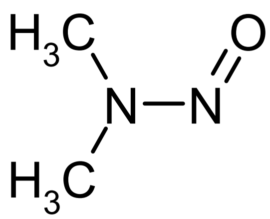



*N*-methylaniline

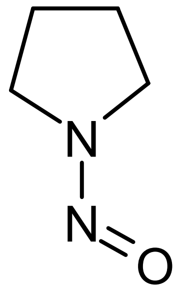
*N*-methyl-*N*-nitrosoaniline (90%)

# Organic Chemistry – chemistry of aromatics

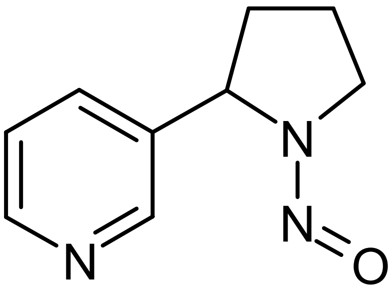
## Aromatic amines – reactivity $S_EAr$




*N*-nitrosodimethylamine
(found e.g. in beer)

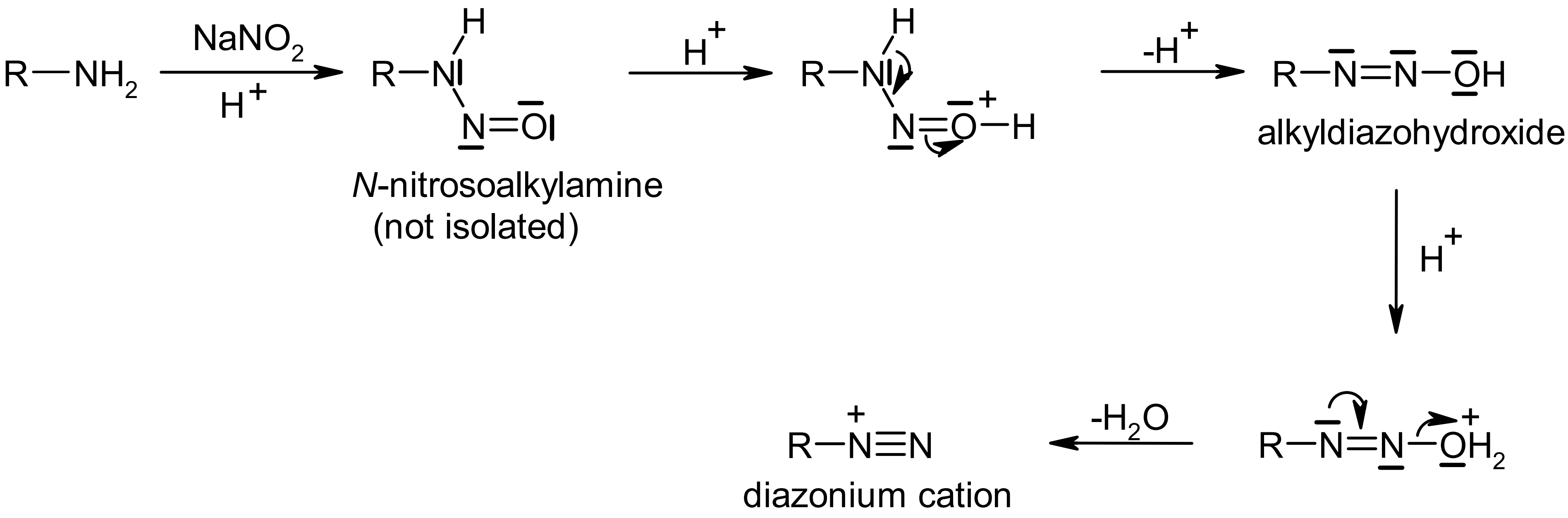



*N*-nitrosopyrrolidine
(in roasted beans)

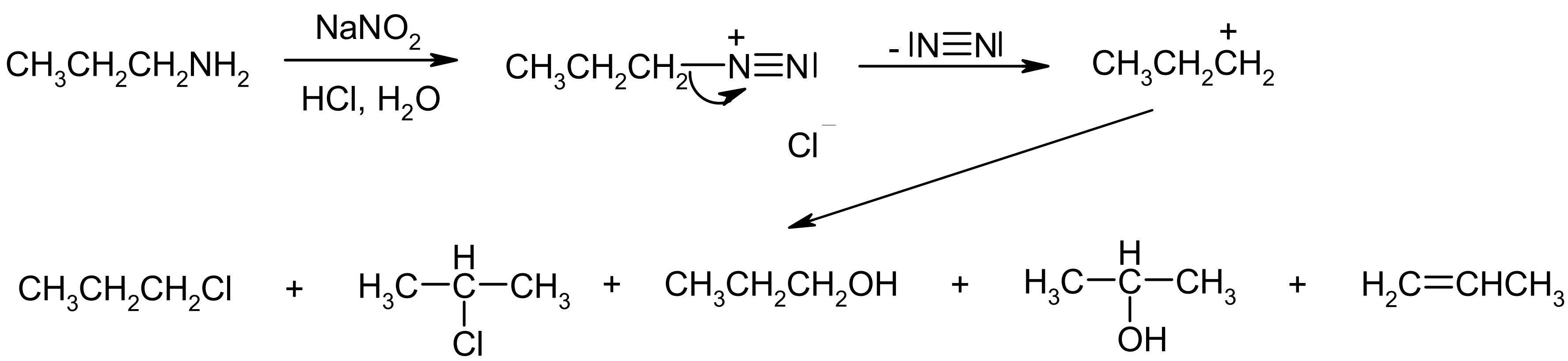


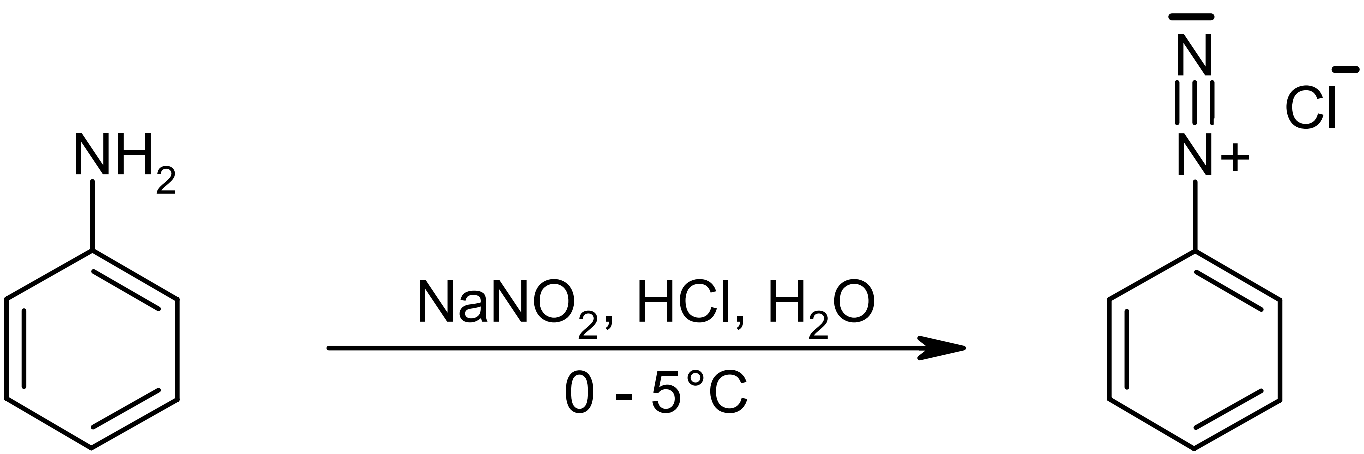

*N*-nitrosonornicotin
(i tobacco smoke)

# Amines – reactivity – diazonium salt formation



# Amines – reactivity – diazonium salt formation

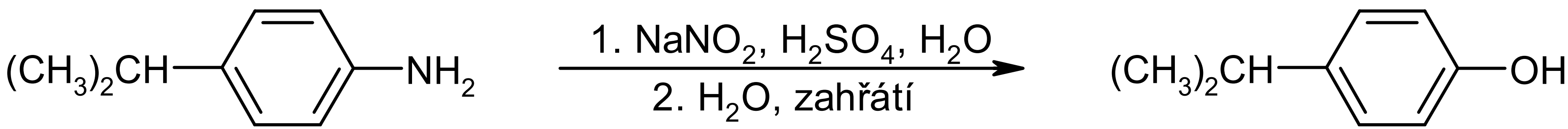



benzendiazoniumchloride

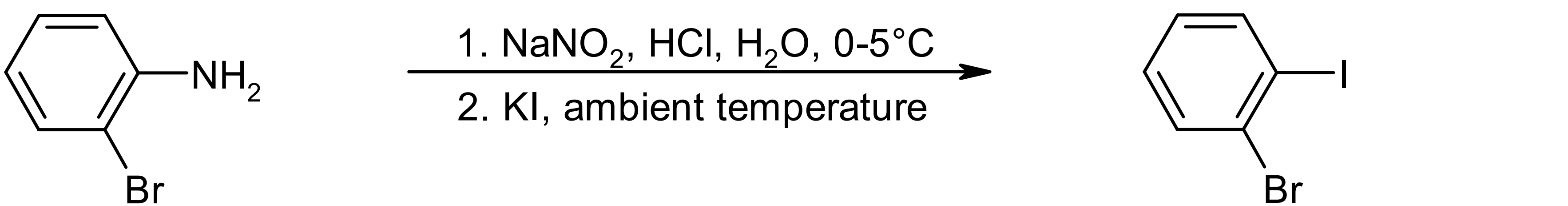
# Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$

$$Ar-\overset{+}{N}\equiv N| \xrightarrow{-N_2} Ar^+ \xrightarrow{H_2O} Ar-OH + H^+$$




4-isopropylaniline

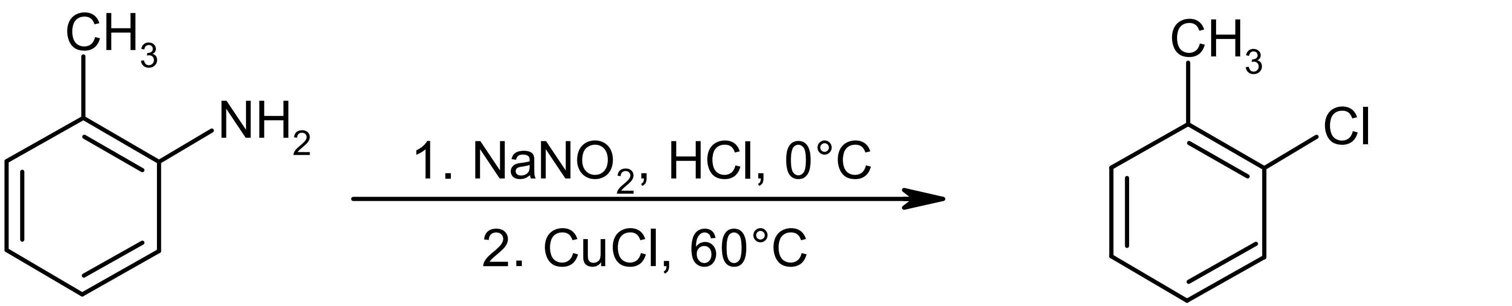
4-isopropylphenol (73%)



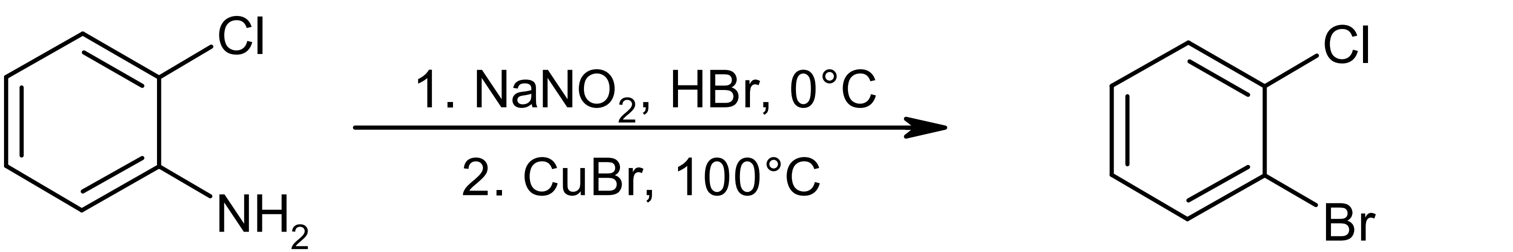

2-bromoaniline

1-bromo-2-iodobenzene (72-83%)

## Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$



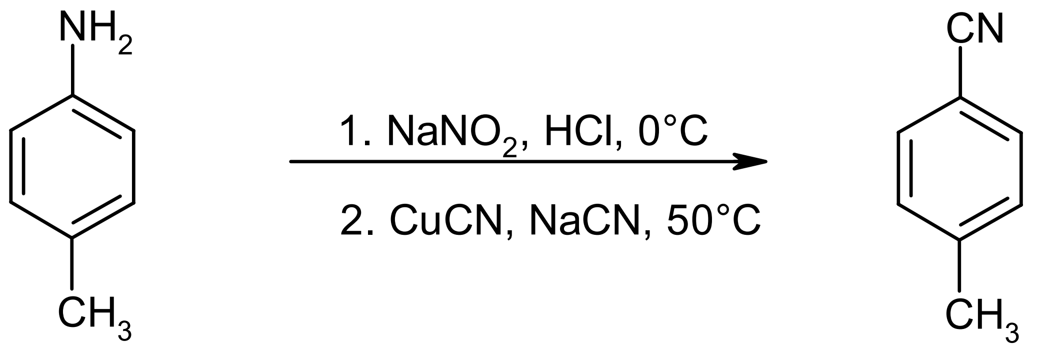

2-methylaniline → 2-chlorotoluene (79%)




2-chloroaniline → 1-bromo-2-chlorobenzene (73%)

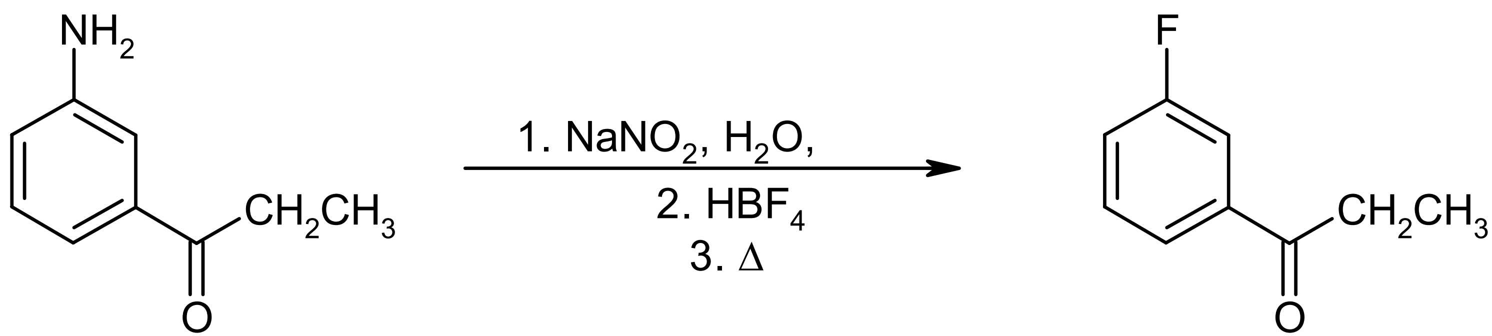
# Organic Chemistry – chemistry of aromatics

## Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$




4-methylaniline → 4-methylbenzonitrile (70%)

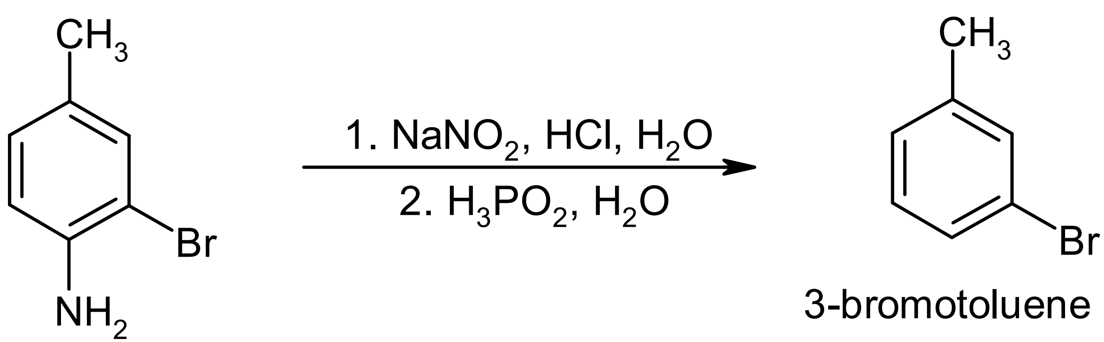
$$Ar-\overset{+}{N}\equiv N| \ BF_4^- \xrightarrow{\Delta} Ar-F + BF_3 + N_2$$




1-(3-aminophenyl)propane-1-one → 1-(3-fluorophenyl)propane-1-one (68%)

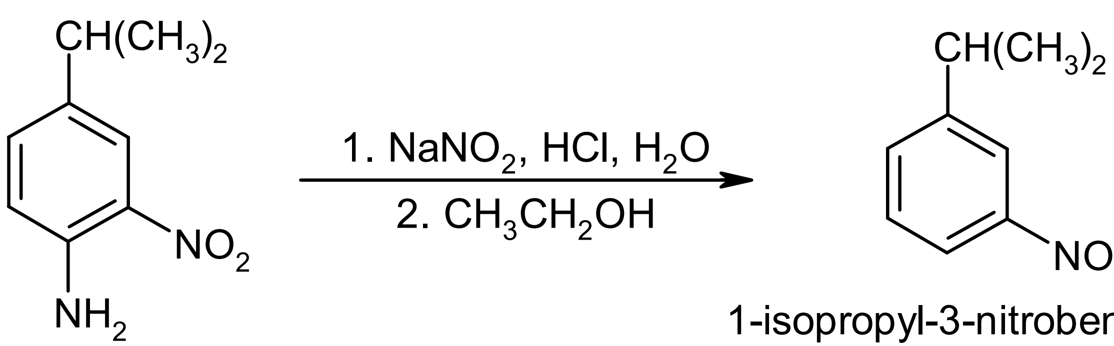
# Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$

$$Ar-\overset{+}{N}\equiv N| \xrightarrow{H_3PO_2} Ar-H + N_2$$




2-bromo-4-methylaniline

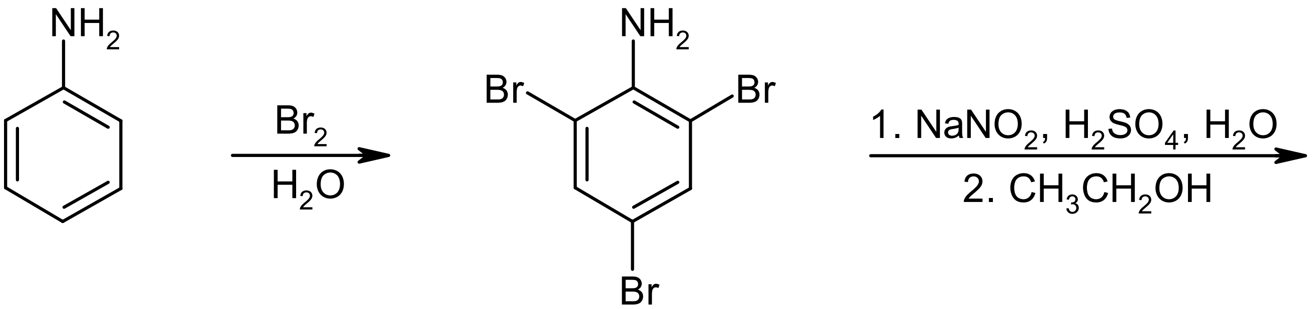
3-bromotoluene (85%)




4-isopropyl-2-nitroaniline

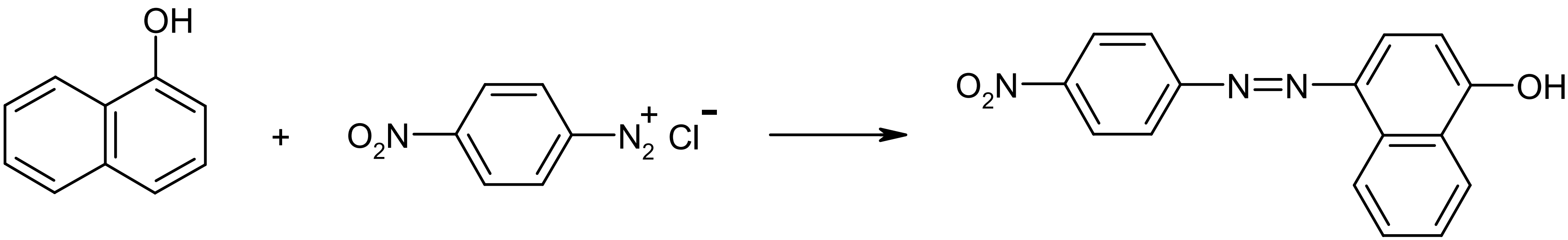
1-isopropyl-3-nitrobenzene (59%)

# Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$




2,4,6-tribromoaniline (100%)

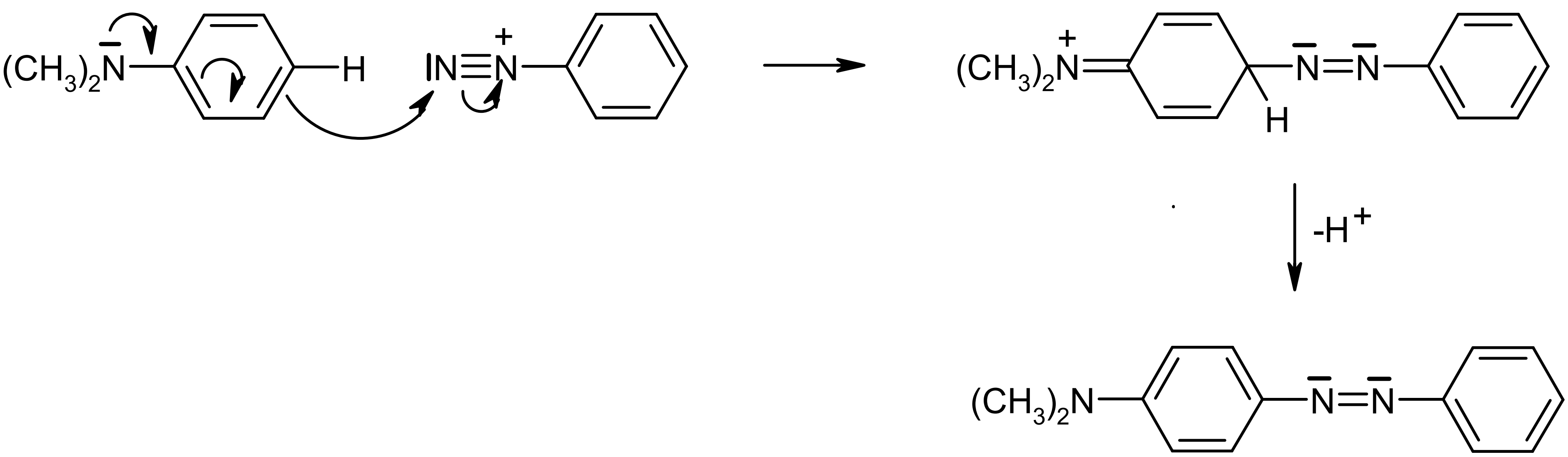
1,3,5-tribromobenzene (75%)




4-(4-nitrophenyldiazenyl)-1-naphtol

# Organic Chemistry – chemistry of aromatics

## Amines – reactivity - diazonium salt synthetic utilisation – $S_{N(R)}$




4-(dimethylamino)azobenzene