Aromatics IV

Rxns of Substituted Benzenes

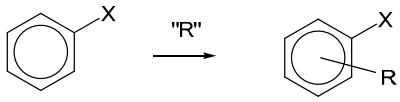
Misc.

Ref 15: 10 – 14 (both ed^{ns})

Prob 15: 9, 26, 27, 29 a-e, 34, 35 (both ed^{ns})

Adv Rdg 11: 1 – 15 (both ed^{ns})

General



2 Considerations:

A. Activation:

rxn faster or slower?

mostly determined by
e^- donating/ withdrawing power of X
(by induction or conjugation effect)

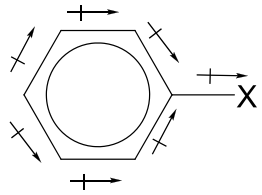
B. Direction:

where will new R go?
random?, o?, m?, p?

mostly determined by
stability of intermediate arenium cation

Deactivation by Inductive Withdrawal

- e/n atoms (X, O, N ...)
  polarize σ bonds
- withdraw e^- density from aromatic ring
- effect passed on by σ bonds



∴ less e^- density in ring

∴ less attractive for "E^+"

∴ rxn rate ↓

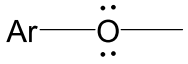
∴ "**deactivating"**

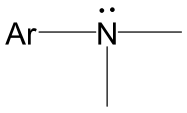
inductive withdrawal ....

very important for

– Cl, – Br, (– I)

less important for

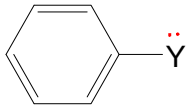




(Ar stands for aromatic ring system)

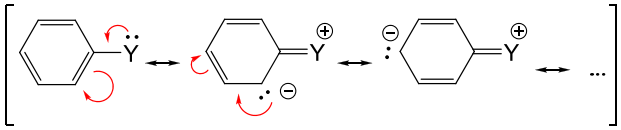
e^- Donation by Conjugation

"π bond effect"

• important for 

lone pair on Y

• explained by resonance:



∴ e^- density in ring ↑

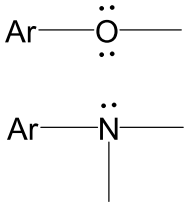
∴ more attractive for "E^+"

∴ rxn rate ↑

∴ "**activating"**

donating effect ...

• important for



• much less for $-Cl$, $-Br$, $(-I)$

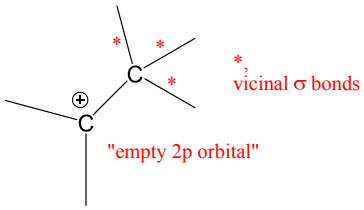
b/c valence (outer) p orbitals of Cl/ Br/ I
and p orbitals of C
are of different size

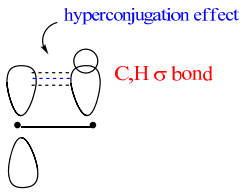
∴ less overlap; less effect

e^- Donation by Hyperconjugation

(σ bond e^-'s fed into p/π system)

recall from CHEM 261:





• empty p orbital and C,H σ bond line up

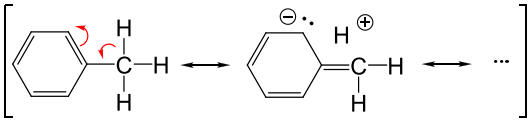
• σ bond feeds e^-'s into empty p AO

∴ pos. charge spread;
cation stabilized

hyperconjugation ...

apply to aromatic systems:

• very approximate resonance hybrid:

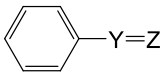


• e^-'s fed into ring

∴ "**activating"**

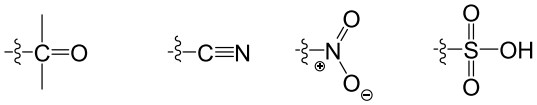
e^- Withdrawal by Conjugation

applies to systems like



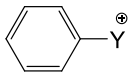
where Z is e/n; esp. "Z" = 

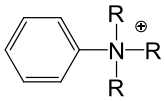
e.g.



---

also:

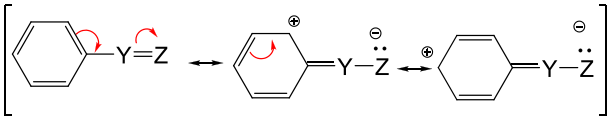


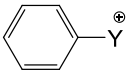
e.g. 

all the above are e^- withdrawing groups ("EWG")

e^- withdrawal ...

• effect explained by resonance:



(similar effect for  ; ~~do as HMWK!)~~

∴ less e^- density in ring

∴ less attractive for "E^+"

∴ "**deactivating"**

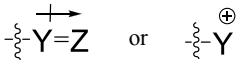
Direction of Substitution

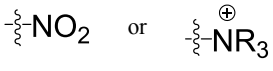
• depends on "nature" of "X"

• determined by stability of intermediate arenium ion

A.)

if "X" is an e^- withdrawing group (EWG)

such as: 

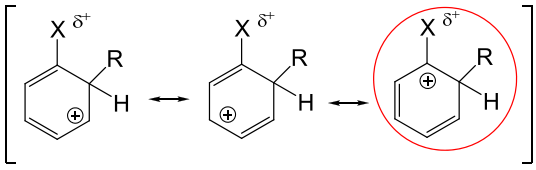
e.g., 

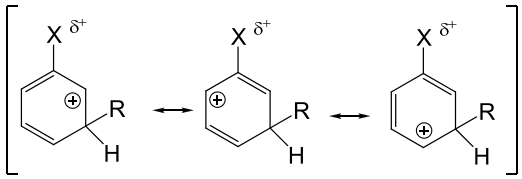
meta substitution has better resonance stabilization (no unfavorable structures)

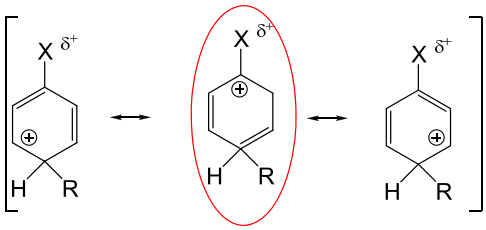
(see schematic next page)

∴ **meta product favored**

Resonance structures of "EWG"arenium ions, differing in substitution pattern

ortho: 

meta: 

para: 

unfavorable resonance structure, due to proximity of pos. charges

B.)

if "X" is an e^- donating group (EDG)

by conjugation: strongly: (—Ö: , —N— ...)

weakly: (—Cl: , —Br: ...)

or by hyperconjugation: (alkyl groups, $-CH_3$ ...)

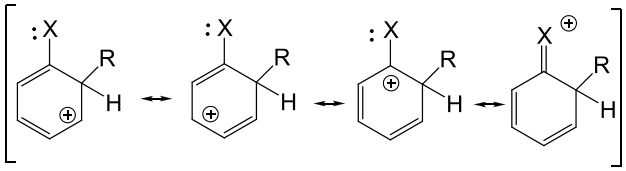
- o, p substitution allows "X:" lone pairs to participate more in resonance than m substitution
- b/c a 4th resonance structure is possible (see schematic next page)
- in o,p substitution pos. charge is more widely distributed = "delocalized"
- o,p arenium ion more stable

∴ **ortho, para product favored**

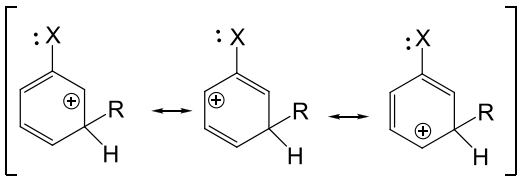
- p substitution often favored over o substitution due to steric reasons

Resonance structures of "EDG"arenium ions, differing in substitution pattern

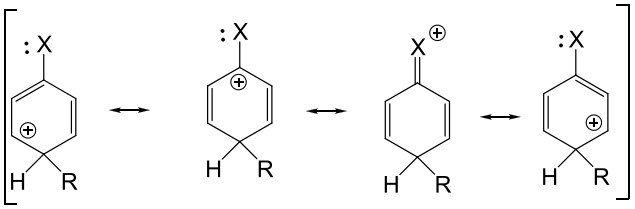
ortho:



meta:



para:



Alternative Explanation for Hyperconjugation in alkylbenzenes, e.g. methylbenzene

(see schematic next page)

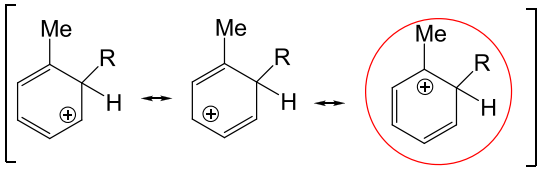
ortho & para give **two** 2° cations &
one 3° cation

meta gives **three** 2° cations

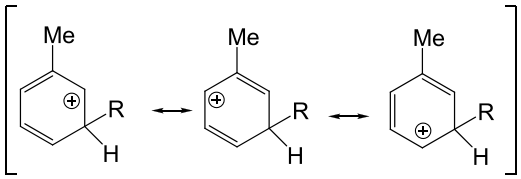
∴ ortho & para arenium ion are more stable

∴ ortho & para substitution is favored

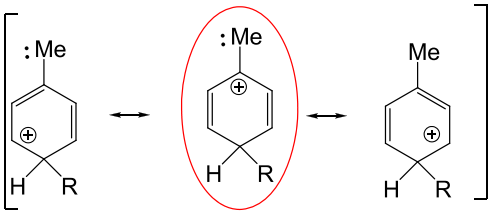
ortho:



meta:

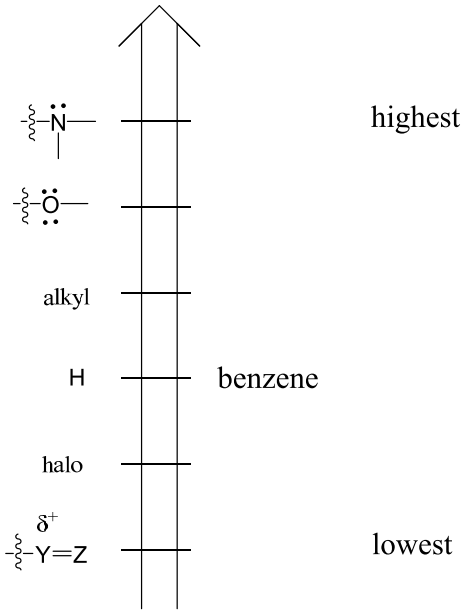


para:

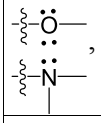
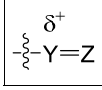


3° cation

Summary of Reactivity Ranking



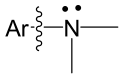
Aromatic Substitution Patterns Overall Summary

Substituent	Reactivity	Orientation/ Direction	Explanation
alkyl	↑	o,p	donation by hyperconjugation
EDG's 	↑↑	o,p	donation by conjugation
halo	↓	o,p	inductive withdrawal; donation by conjug^{n}
EWG's 	↓↓	m	withdrawal by conjugation

Notes:

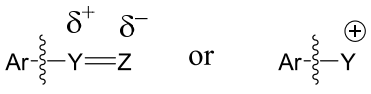
Fridel – Crafts Alkylation/ Acylation

not possible if

1.) 

b/c irreversible side reaction;

i.e., protonation

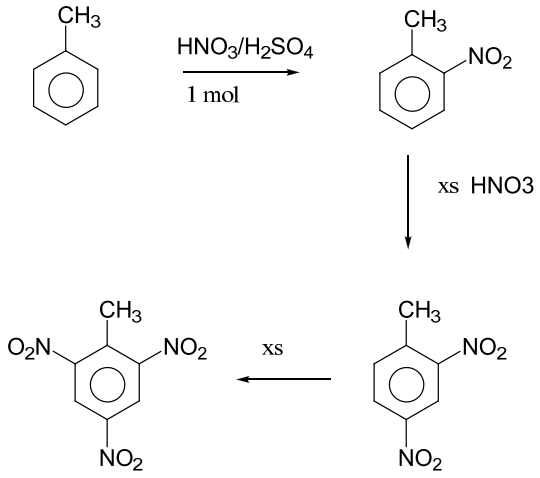
2.) 

b/c too strongly deactivating

Multi – Substitution

- extend ideas from di - substitution
- only simple cases are predictable

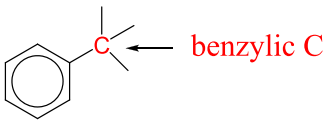
e.g.



TNT,

trinitrotoluene

Benzylic Rxns



specially reactive
b/c of hyper-conjugative effects (see before)

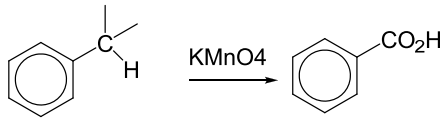
1.) $KMNO_4$ Oxidation (at ~ 70 °C)
of "alkyl" benzenes:

benzylic C is oxidised to carboxylic acid

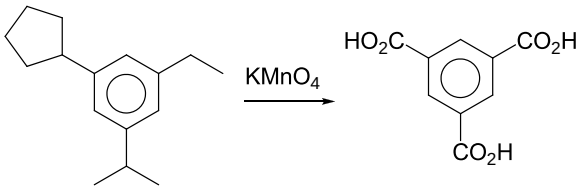
"alkyl" must not be 4° (quaternary)
can be sp^2, sp

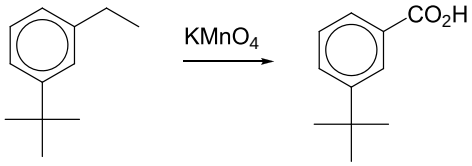
(procedure can be useful as
traditional, analytical tool)

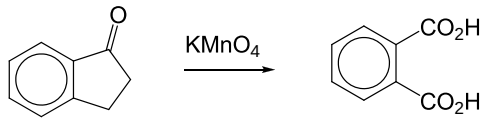
general:

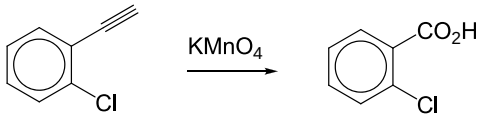


Practice



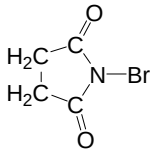






2.) NBS Bromination

N-bromosuccinimide, NBS,

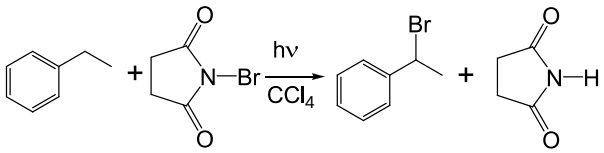


produces Br_2 at low conc^n.

rxn conditions: NBS/CCl_4, hν

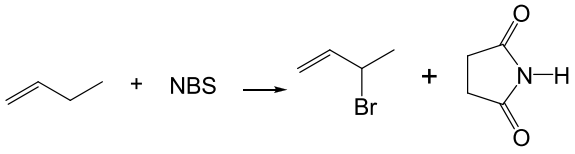
rxn introduces Br at benzylic/allylic position

Overall Rxn

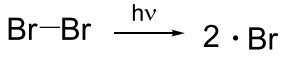


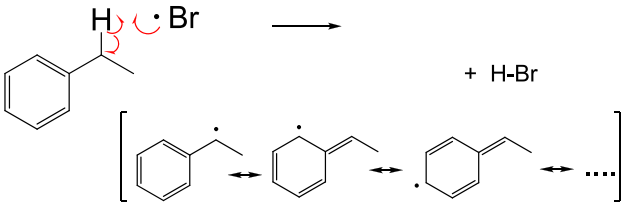
Note:

similarly: allylic bromination

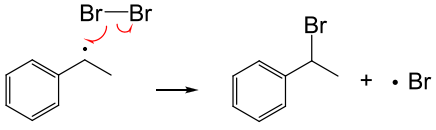


Mech. of Benzylic Bromination





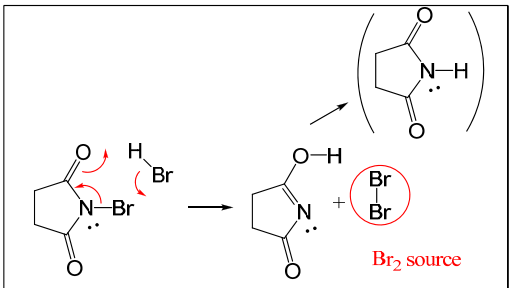
resonance stabilized radical



the 2 steps repeat = radical chain rxn follows

Aside:

Mech. of Benzylic/Allylic Bromination w/ NBS



then typical radical rxn:

$Br_2 \longrightarrow Br\cdot + \cdot Br$

$R{-}H + \cdot Br \longrightarrow R\cdot + HBr$

$R\cdot + Br{-}Br \longrightarrow R{-}Br + Br\cdot$

$Br\cdot + R{-}H \longrightarrow R\cdot + HBr$

The H-Br product is used up
in the generation of Br_2 from NBS

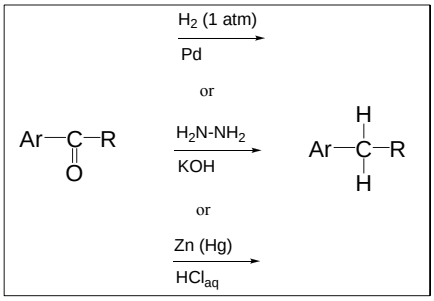
3.) Reduction of Aromatic Keto Group

available from F-C acylation
can be reduced by 3 different methods
to make "alkylated" aromatics

1.) catalytic hydrogenation: H_2 (1 atm) /Pd
(*mild*)

2.) Wolff- Kishner Reduction: $H_2N\text{-}NH_2$ / KOH
(*hydrazine*)

3. Clemmensen Reduction: Zn (Hg)/ $HCl_{(aq)}$



Note: Potential side rxn for 1.) and 2.):

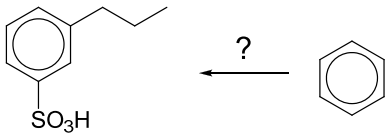
$Ar\text{-}NO_2 \rightarrow Ar\text{-}NH_2$

Synthesis Planning

(retro-synthetic analysis)

- apply knowledge from last few lectures
- restricted to 3 – 4 steps in CHEM 263)

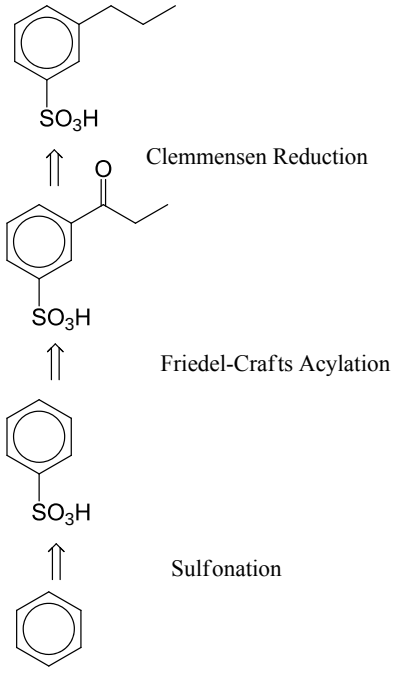
Ex.



Notes:

- start w/ the target molecule and work backwards;
- include several options to suit;
- sometimes, several schemes might succeed

Analysis Result



Reaction Details