Aromatics IV

Rxns of Substituted Benzenes

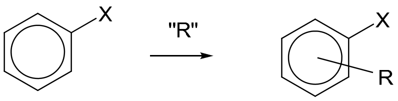
Misc.

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 ↓

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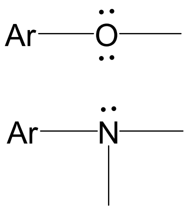
inductive withdrawal ....

very important for

– Cl, – Br, (– I)

less important for

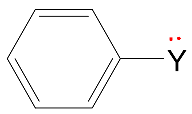


(Ar stands for aromatic ring system)

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 ↑

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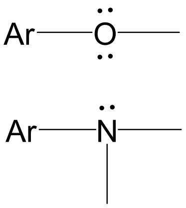
donating effect ...

- 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

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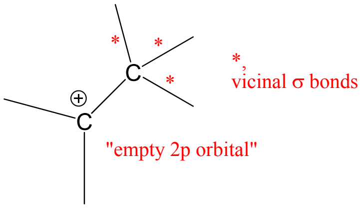
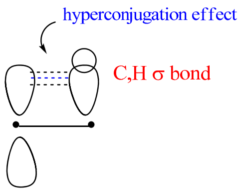
e^- Donation by Hyperconjugation

(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

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hyperconjugation ...

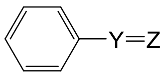
apply to aromatic systems:

- very approximate resonance hybrid:

- e^-'s fed into ring

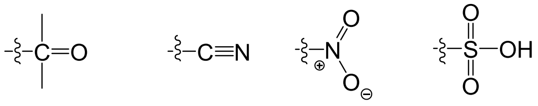
e^- Withdrawal by Conjugation

applies to systems like



where Z is e/n; esp. "Z" = $\ddot{\underset{\cdot\cdot}{\text{O}}}$

e.g.



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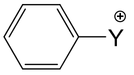
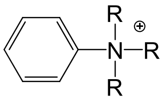
also:



e.g.



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

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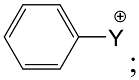
e^- withdrawal ...

- effect explained by resonance:

(similar resonance for  ; do as HMWK!)

∴ less e^- density in ring

∴ less attractive for "E^+"

Direction of Substitution

- depends on "nature" of "X"
- determined by stability of intermediate arenium ion

A.)

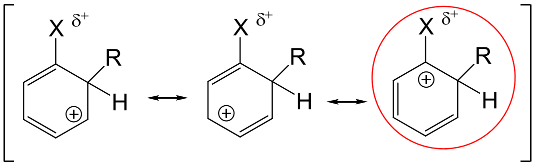
meta substitution has better resonance stabilization (no unfavorable structures)

(see schematic next page)

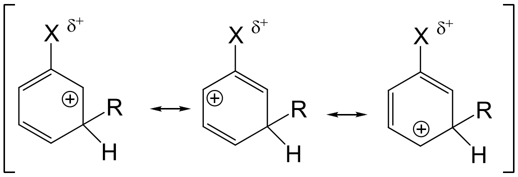
∴ **meta product favored**

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

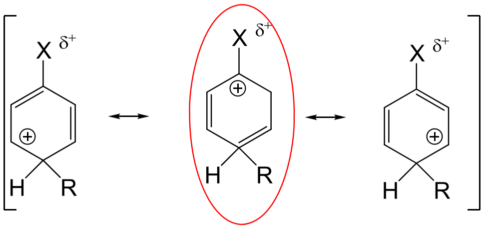
ortho:



meta:



para:



○ unfavorable resonance structure, due to proximity of pos. charges

B.)

- 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

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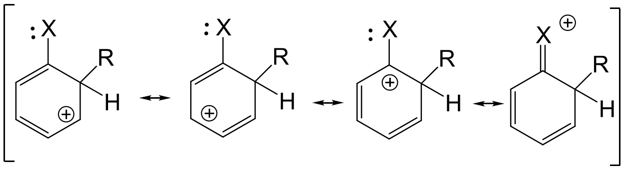
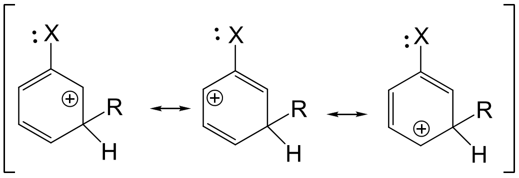
Resonance structures of “EDG”arenium ions, differing in substitution pattern

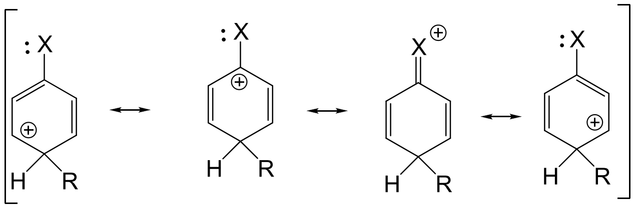
ortho:



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

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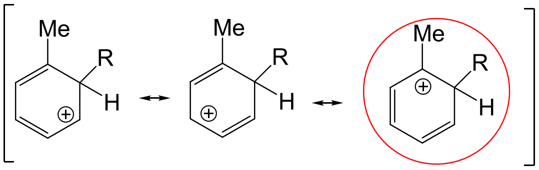
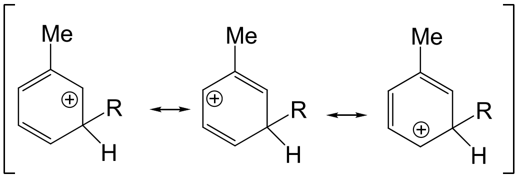
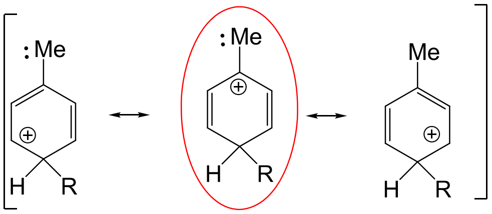
ortho:



meta:



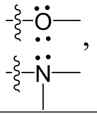
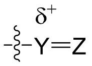
para:



◯ 3^{o} cation

Summary of Reactivity Ranking

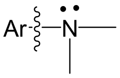
Aromatic Substitution Patterns Overall Summary

Substituent	Reactivity	Orientation/ Direction	Explanation
alkyl			
EDG's 			
halo			
EWG's 			

Notes:

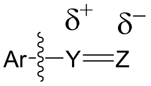
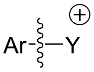
Fridel – Crafts Alkylation/ Acylation

not possible if

1.) 

b/c irreversible side reaction;

i.e., protonation

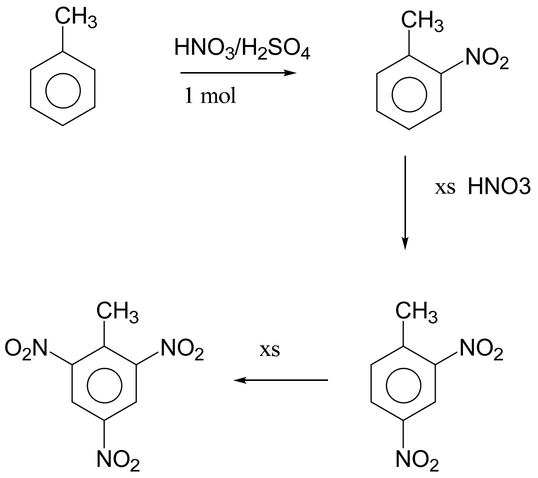
2.)  or 

b/c too strongly deactivating

Multi – Substitution

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

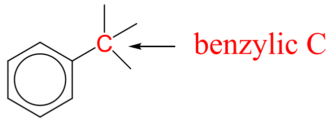
e.g.



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

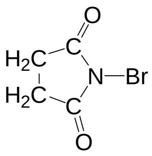
"alkyl" must not be 4° (quaternary)
can be sp^2, sp

(procedure can be useful as
traditional, analytical tool)

Practice

2.) NBS Bromination

N-bromosuccinimide, NBS,



produces Br_2 at low conc^n.

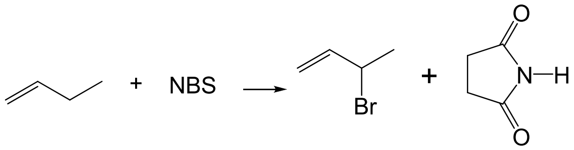
rxn conditions: NBS/CCl_4, hν

rxn introduces Br at benzylic/allylic position

Overall Rxn

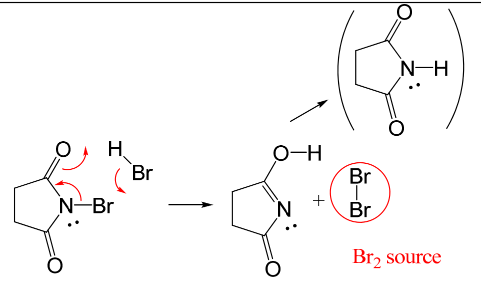
Note:

similarly: allylic bromination



Mech. of Benzylic Bromination

Aside:
Mech. of Benzylic/Allylic Bromination w/ NBS



then typical radical rxn:

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

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

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

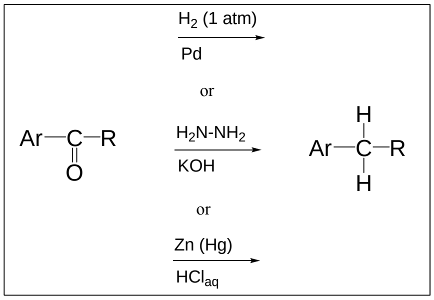
$$Br\cdot + R{-}H \longrightarrow R\cdot + HBr$$

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: (*mild*)	H_2 (1 atm) /Pd
2.) Wolff- Kishner Reduction:	$H_2N\text{-}NH_2$ / KOH (*hydrazine*)
3. Clemmensen Reduction:	Zn (Hg)/ $HCl_{(aq)}$



$$Ar{-}\overset{}{\underset{\displaystyle O}{\underset{\|}{C}}}{-}R \xrightarrow[Pd]{H_2\ (1\ atm)} \text{ or } \xrightarrow[KOH]{H_2N\text{-}NH_2} \text{ or } \xrightarrow[HCl_{aq}]{Zn\ (Hg)} Ar{-}CH_2{-}R$$

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

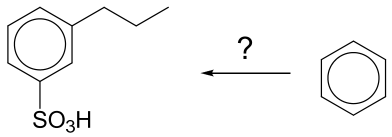
$$Ar\text{-}NO_2 \rightarrow Ar\text{-}NH_2$$

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