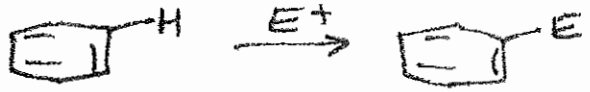
Ch.18 - Reactions of Aromatic Compounds

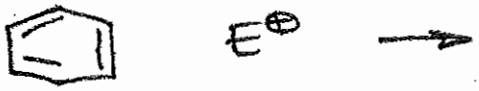
(18.1) Electrophilic Aromatic Substitution (EAS)



substitute $H^{\oplus}$ w/ $E^{\oplus}$

Mechanism (2 steps)

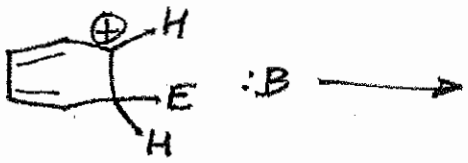
① Addition of $E^{\oplus}$ (needs special, reactive $E^{\oplus}$)



*difficult, slow step

*Note: ⊕ in intermediate is always ortho or para to E

② Loss of $H^{\oplus}$



*great, fast step
Why?

Electrophilic Aromatic Substitution on Substituted Benzenes

(18.7) 

(18.8) 

(18.9) 

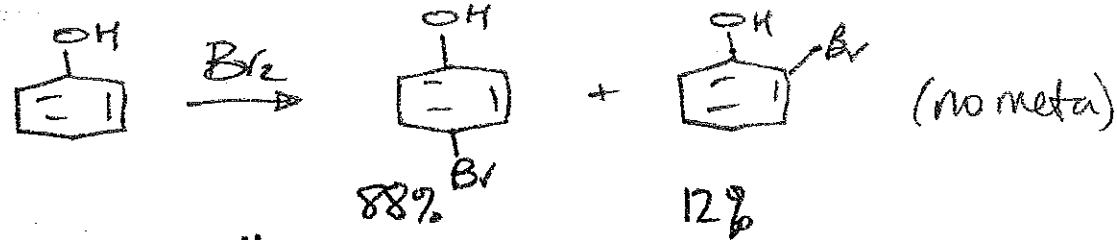
type of group:	e- donating group	e- withdrawing group	halogen

reactivity: (vs. PhH)

regioselectivity:

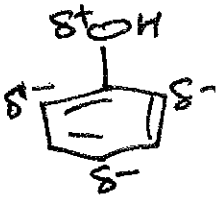
examples:

(18.7) Effects of Electron-Donating Groups (EDG)

ex. 

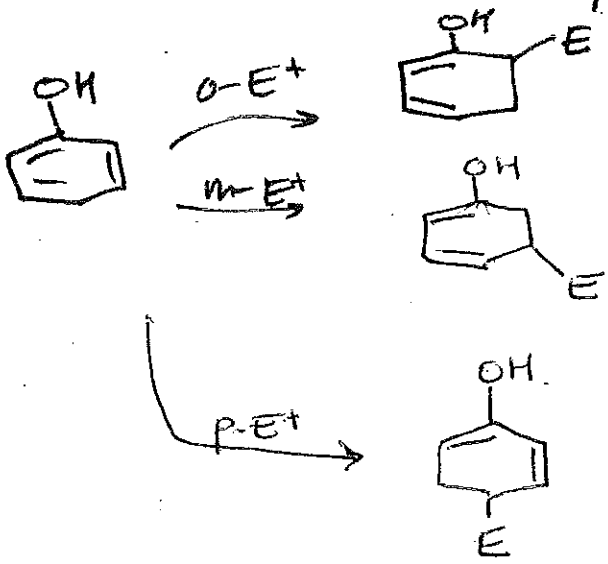
Why? What effect does EDG (OH) have?

*Reactivity → EDG makes ring more/less e⁻ rich
→ ring is a _____ nu: (vs. benzene)
→ _____ toward EAS

*Regioselectivity prediction: 

o/p sites more e⁻ rich

Prove it! Add E⁺ and look @ possible intermediates:



* is OH good or bad for ⊕?

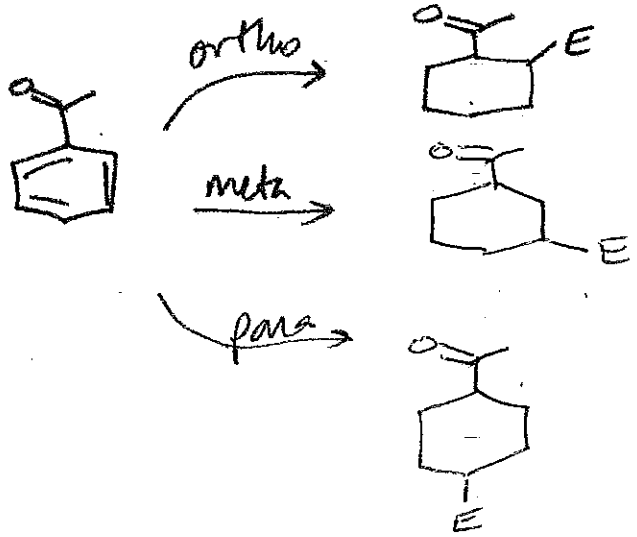
(18.8) Effects of electron-withdrawing groups (EWG)

What effect does EWG have on EAS?

* Reactivity → EWG adds/removes e⁻ density by resonance
→ ring is more e⁻ rich/deficient (vs. benzene)
→ ring is a _____ nu:
→ _____ toward EAS

* Regioselectivity  prediction:
→ $E^{\oplus}$ is repelled by o/p positions

Prove it! Add $E^{\oplus}$ + look @ competing intermediates



* is  good or bad for ⊕?

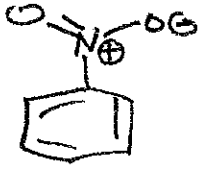
(18.9) Effects of Halogens on EAS

inductive withdrawal of e-density vs. resonance donation

Summary of Substituent Effects on EAS (18.10)

EDG  or  or 

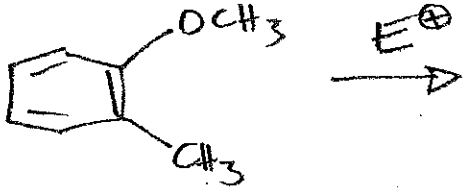
*all stabilize an adjacent ⊕ charge

EWG  or  or  or 

*all destabilize an adjacent ⊕ charge

(18.11) Directing Power of Substituents

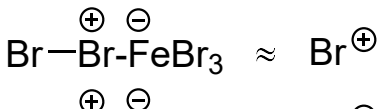
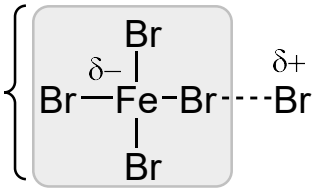
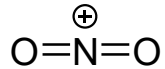
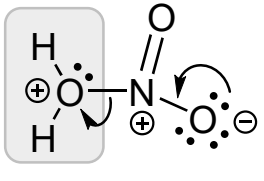
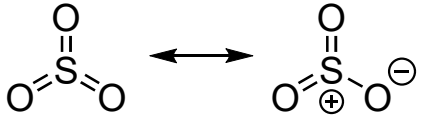
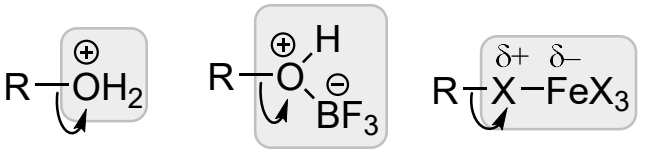
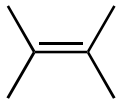
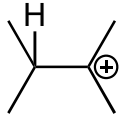
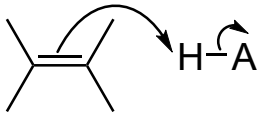
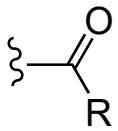
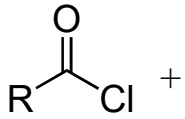
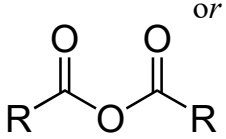
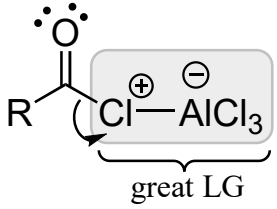
$-NH_2$, $-OH$ > $-OR$ > $-NHCOR$, $-OCOR$ > $-X$ > $-R$ >> EWG

EX: 

SkillBuilders 18.1, 18.2, 18.3

Electrophiles for Electrophilic Aromatic Substitution (EAS)

CHM 3150 Organic Chemistry II, Dr. Laurie S. Starkey, Cal Poly Pomona

Klein	EAS Reaction	Conditions	Electrophile (E^+)	Mech. to make E^+ (first steps in EAS)
18.2	**halogenation** –X	$Br_2/FeBr_3$ $Cl_2/FeCl_3$		great LG 
18.4	**nitration** –NO_2	HNO_3, H_2SO_4	 (nitronium ion)	great LG  *loss of water LG to make NO_2^+*
18.3	**sulfonation*** –SO_3H	SO_3, H_2SO_4		N/A (SO_3 is Electrophile)
18.5	**Friedel-Crafts alkylation** –R	ROH/HA *or* ROH/BF_3 *or* RX/FeX_3		 *loss of leaving group (LG) to make carbocation*
		or  + HA (HF)	 (carbocation - may rearrange, if unstable)	 *protonate pi bond to make carbocation*
18.6	**Friedel-Crafts acylation** 	 + $AlCl_3$ *or*  + $AlCl_3$	 (acylium ion)	 great LG

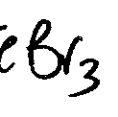
Electrophiles for EAS

(18.4) Nitration

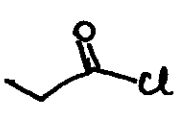
$\xrightarrow[H_2SO_4]{HNO_3}$

Mechanism (1st make $E^{\oplus}$)

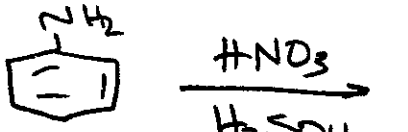
Making other Electrophiles:

$Br_2, FeBr_3$  $FeBr_3$

 , $AlCl_3$  $AlCl_3$

 , $AlCl_3$  $AlCl_3$

Electrophilic Aromatic Substitution (EAS)

* Ex. 

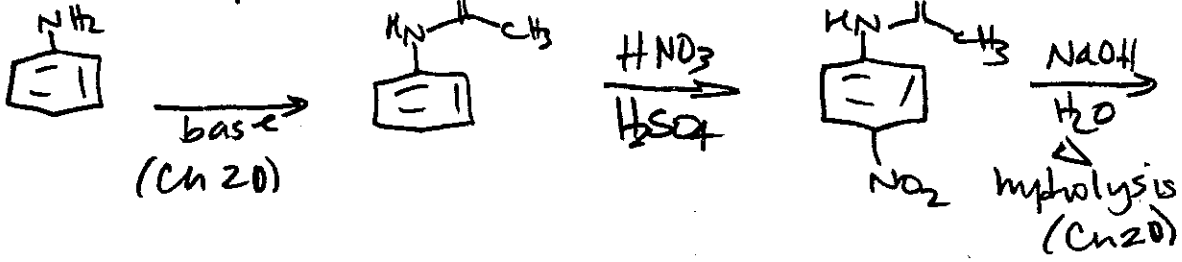
* what are we adding?
* where are we adding it?

Why?! 

amine = base

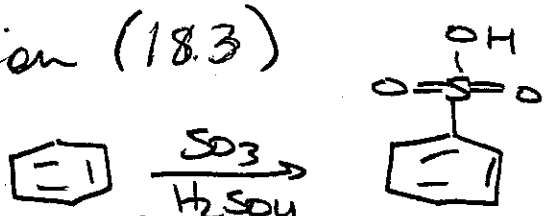
$H-ONO_3$ → acid

Workaround: protect amino group as an amide (22.8)



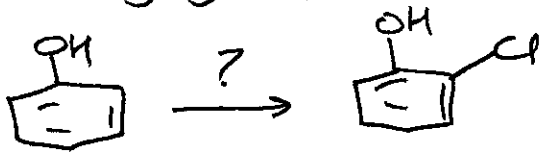
* EAS: Sulfonation (18.3)

* SkillBuilder 18.4 *



Δ(−SO_3H) reversible! −SO_3H can be removed

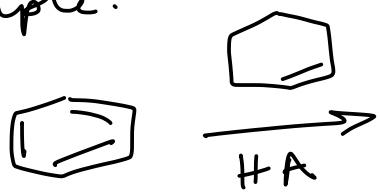
use as a blocking group

Transform: 

Friedel-Crafts Alkylation (18.5)

*Note: N/R for Friedel-Crafts if EWG is present.

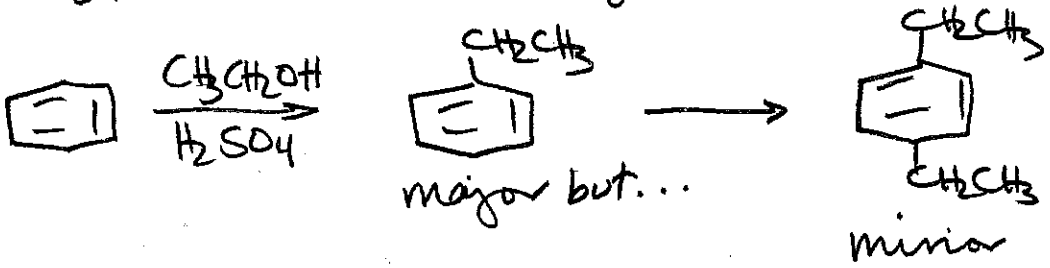
Example:



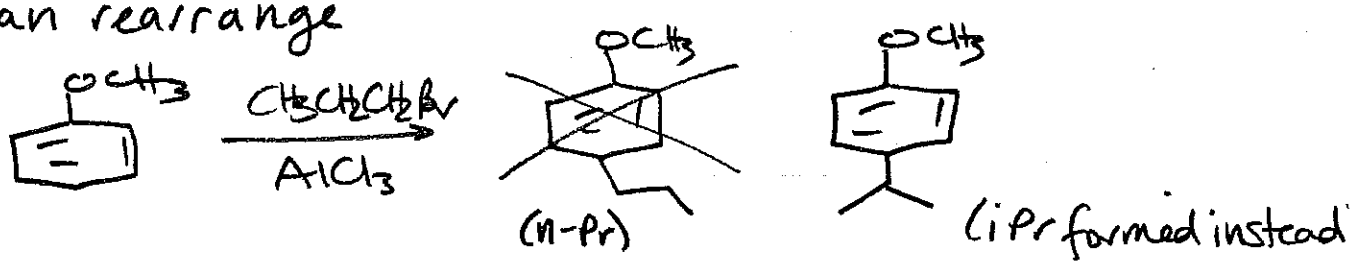
mechanism:

F.C. Alkylation Drawbacks

a) can over-react (dialkylation)



b) $C^{\oplus}$ can rearrange



mech: $CH_3CH_2CH_2\ddot{Br}:$ $AlCl_3$ ⟶

Lewis acid (vacancy)

Want n-propyl? Use Friedel-Crafts Acylation (18.6)

[red]

Reducing Agents: ? ⟶ H H

$Zn(Hg)/HCl$ (Clemmenson) — ok for any ketone/ald (18.21)

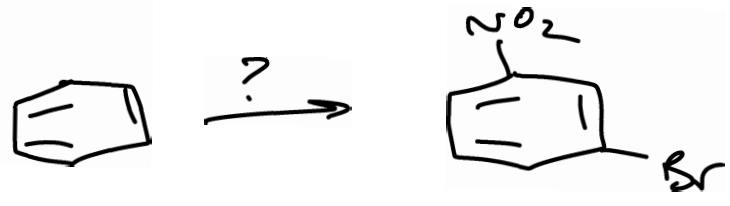
or $NH_2NH_2/KOH/\Delta$ (Wolff-Kishner)

or H_2/Pt (for benzylic C=O only!)

Synthesis with Electrophilic Ar. Substitution (EAS)

Transform:

Transform:



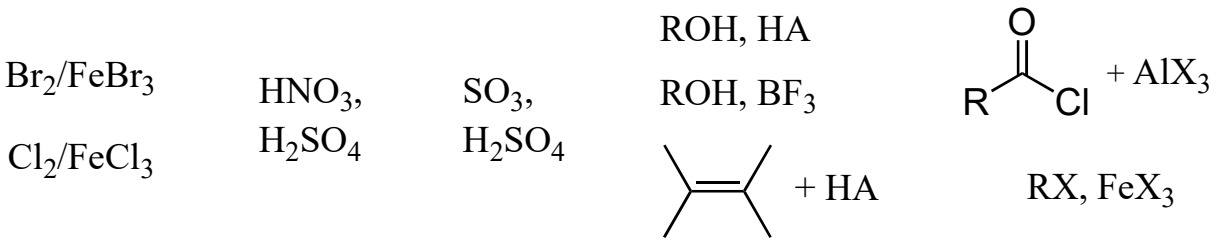
Hint: which do we add first?

* Skill Builders 18.4, 18.5, 18.6 *

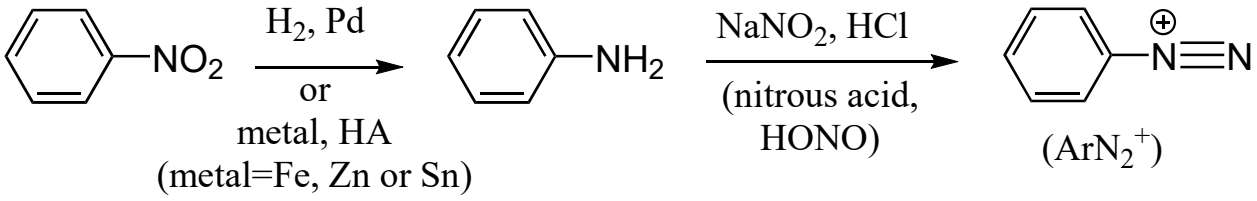
Try Problem 18.67

Reagents for Electrophilic Aromatic Substitution:

(Klein Sections 18.1-18.6, generate E^+)

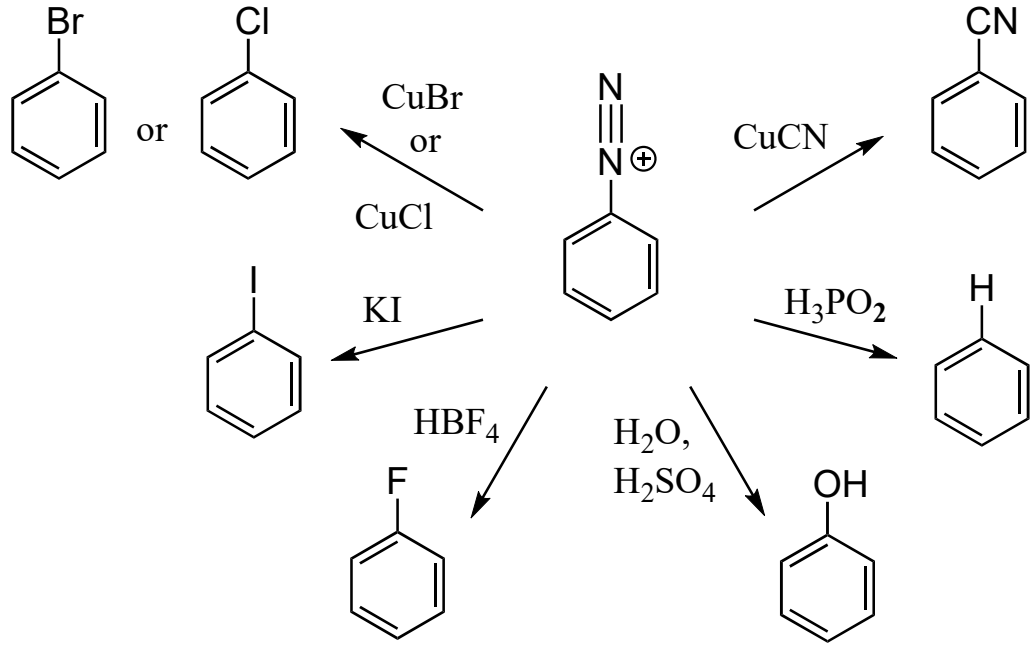


Preparation of Diazonium Salt (ArN_2^+):

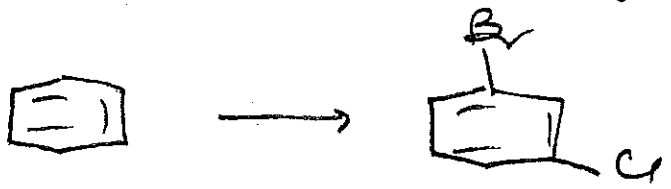


Reagents for Sandmeyer Reactions:

(Klein Section 22.11, react with ArN_2^+)

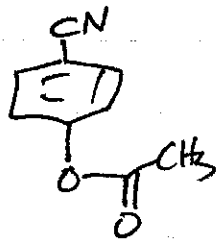


Apply $Ar N_2^+$ in synthesis (Try text problem 22.26)

Ex. 

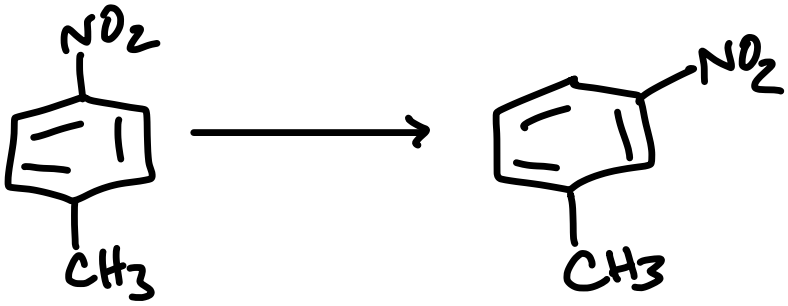
*can't be done with EAS alone!

Ex. Synthesize following TM from benzene or toluene.



Example: Transform

*Note: can't be made via Friedel-Crafts Alkylation (NO_2 is EWG, so N/R)



Reactions of Aromatic substituents (17.6)

↳ groups attached / side chains

a) Reduction Rxns (review)

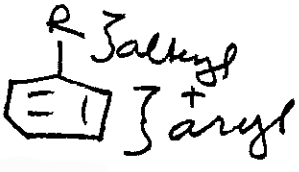
$ArNO_2 \xrightarrow{[red]} ArNH_2$

[red] = H_2/Pd or Sn/HCl

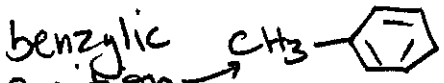
$ArCR \xrightarrow{[red]} ArCH_2R$

[red] = H_2/Pd or $Zn/Hg\ HCl$ or $NH_2NH_2/KOH/\Delta$

b) Oxidations of Arenes



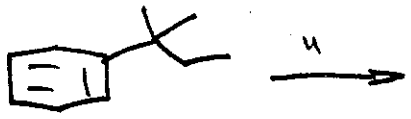
benzylic position → easily oxidized



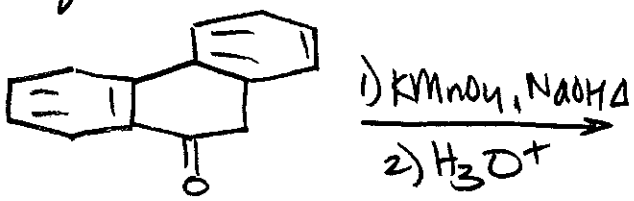
[ox] = $Na_2Cr_2O_7/H_2SO_4\ \Delta$ or 1) $KMnO_4, NaOH\ H_2O\ \Delta$ 2) H_3O^+

* benzylic [ox] even breaks c-c bonds!

* benzylic carbon can't be quaternary



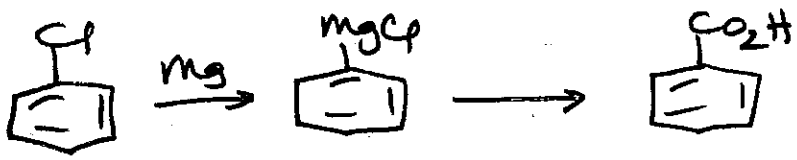
Ex.



Recall: Other benzoic acid preps (20.4)

via hydrolysis

via Grignard

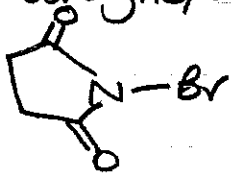


c) benzylic halogenation (10.5)

*easy to introduce a benzylic LG!

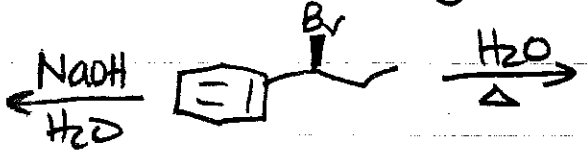
→ radical stabilities: benzylic/allylic/3° > 2° > 1° > methyl

→ NBS is also a source of Br.



d) benzylic substitutions

* S_N1 and S_N2 are both great with benzylic LG's



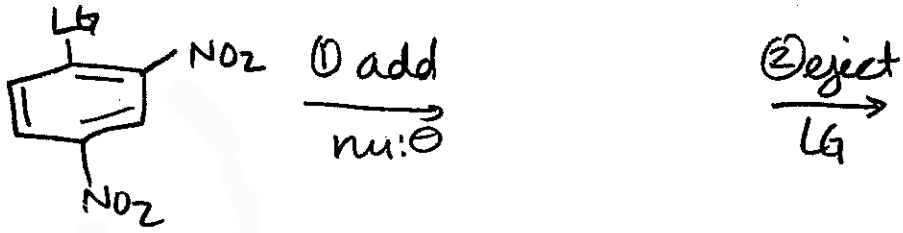
→ S_N2 favored over E2

→ benzylic TS. is stable

Ex. Transform

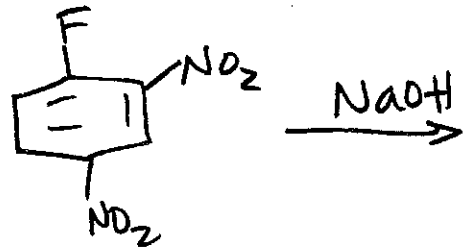
SkillBuilder 17.4

Nucleophilic Aromatic Substitution, S_NAr (18.13, 18.15) 18-16

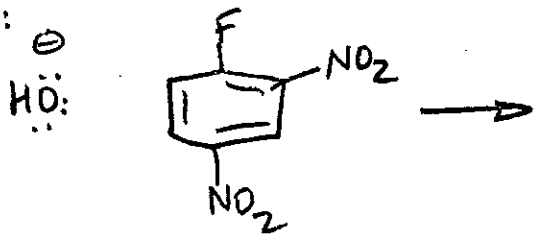


*o/p EWGs are needed to stabilize ⊖ intermediate
* ring is E⊕ so ring is _____ toward S_NAr by EWG
* LG ability: F > Cl > Br > I

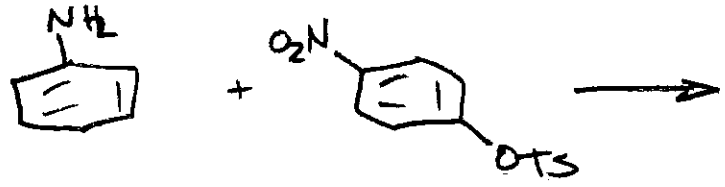
Ex.



mech:



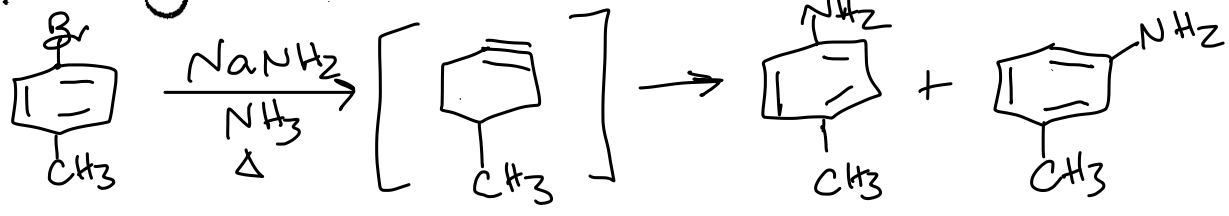
Ex



SkillBuilder 18.7

Note: skip benzyne (18.14) FYI see Educator 52:46–59:10

"Elimination-Addition" Mechanism



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Organic Chemistry II, CHM 3150, Dr. Laurie S. Starkey

Ch. 17-18 Summary (Klein): Aromaticity & Aromatic Substitution Reactions

I. Benzene (17.3)
- A) resonance stabilized (confirmed ΔH hydrogenation), 3-D sketch

II. Aromaticity
- A) definition and rules (17.1, 17.4) **SkillBuilder 17.2**
  - i) cyclic and planar; contiguous p orbitals
  - ii) (4n + 2) electrons in p orbitals (Hückel's rule, n = 0, 1, 2, etc.)
  - iii) Molecular Orbital (MO) theory to explain aromatic stability
- B) common aromatic compounds (furan, naphthalene, etc.) (17.5) **SkillBuilder 17.3**
- C) nomenclature: *ortho (o-), meta (m-), para (p-)* positions, common names (17.2) **SB 17.1**
- D) special topics: buckminsterfullerene (C_{60}, Bucky Ball) as a "new" form of carbon

III. Electrophilic Aromatic Substitution (EAS) (18.2 – 18.6)
- A) mechanism: formation of E^+ (one or more steps) addition of E^+ (slow step), loss of H^+

IV. EAS on substituted benzenes (18.7 – 18.11) **SkillBuilder 18.1, SkillBuilder 18.3**
- A) three categories of substituents (18.10)
  - i) electron-donating groups (EDG, 18.7)
  - ii) electron-withdrawing groups (EWG, 18.8)
  - iii) halogens (X = Cl, Br) (18.9)
- B) reactivity
  - i) EDG are activating (electron-rich ring, good Nu:)
  - ii) EWG/X are deactivating (electron-deficient ring, poor Nu:)
- C) regioselectivity (for *ortho*, *para* directors, *para* is usually major due to sterics)
  - i) regioselectivity can be explained by looking at resonance forms for:
    - a) starting material (Nu:) electron density (in certain cases only)
    - b) carbocation intermediate stability (can be used for all cases)
  - ii) EDG/X are *ortho*, *para* directors (because they stabilize adjacent carbocations)
  - iii) EWG are *meta* directors (because EWG's destabilize adjacent carbocations)
- D) directing power for disubstituted benzenes (18.11) **SkillBuilder 18.2**

V. Electrophiles for EAS
- A) –X ($Br_2/FeBr_3$ or $Cl_2/FeCl_3$) (18.2)
- B) $–NO_2$ (HNO_3/H_2SO_4) (18.4)
- C) $–SO_3H$ (SO_3/H_2SO_4), reaction is reversible (18.3) **SkillBuilder 18.4**
- D) –R (Friedel-Crafts Alkylation, via carbocation which can rearrange) (18.5)
  - i) RX + $AlCl_3$ *or* ROH + HA *or* ROH + BF_3 *or* alkene + HA
- E) –COR (Friedel-Crafts Acylation, $RCOX/AlCl_3$) (18.6)
  - i) can then reduce carbonyl to give desired 1˚ alkyl side chain

VI. Diazonium Salts (ArN_2^+, 22.10, 22.11)
- A) two-step preparation from $ArNO_2$
  - i) reduce nitro to amine: $–NO_2 \rightarrow –NH_2$ (H_2/Pd or Fe/Zn/Sn and HA)
  - ii) add nitrous acid $–NH_2 \rightarrow –N_2^+$ (HONO = $NaNO_2$/HCl)
- B) uses: replace its good LG (N_2) with the following groups
  - i) halogens: –Cl (CuCl), –Br (CuBr), –I (KI), –F (HBF_4)
  - ii) cyanide: –CN (CuCN)
  - iii) hydrogen: –H (H_3PO_2)
  - iv) hydroxyl –OH (H_2O/H_2SO_4)

VII. Aromatic Synthesis (18.12) **SkillBuilders 18.4, 18.5, 18.6**

VIII. Nucleophilic Aromatic Substitution (S_NAr, 18.13, 18.15) **SkillBuilder 18.7**
- A) two-step mechanism: add Nu:, eject LG (Addition-Elimination)
- B) EWG substituents ($–NO_2$) required

IX. Reactions of Benzylic Carbons (17.6) **SkillBuilder 17.4**
- A) oxidation (Na_2CrO_7 or $KMnO_4$) to oxidize benzylic carbons $\rightarrow$ benzoic acids
- B) substitution (S_N1, S_N2) and free-radical halogenation ($Br_2/h\nu$)

SKIP: Spectroscopy (17.8), Benzyne "Elimination-Addition" (18.4), [ox] of ArOH (12.12)