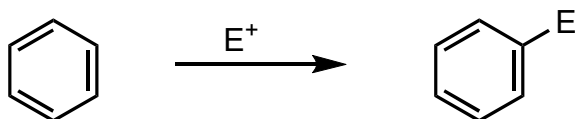


Chapter 5 - Aromatic Target Molecules

5.1 Electrophilic Aromatic Substitution (EAS)



<u>EAS Reaction</u>	<u>Conditions</u>	<u>Electrophile (E^+)</u>	<u>Mech. to make E^+ (1st steps in EAS)</u>
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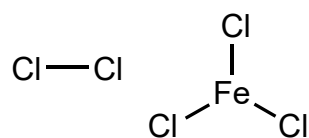
halogenation
-X

$Br_2/FeBr_3$

Br^{\oplus}

$Cl_2/FeCl_3$

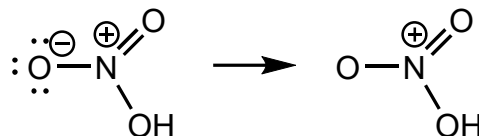
Cl^{\oplus}



nitration
- NO_2

$HNO_3,$
 H_2SO_4

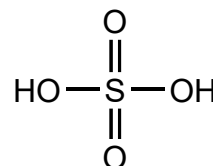
$O=N^{\oplus}=O$



sulfonation*
- SO_3H

$SO_3,$
 H_2SO_4

O
 \parallel
 $O=S^{\oplus}-O^{\ominus}$



*reaction is reversible (heat removes $-SO_3H$ group)

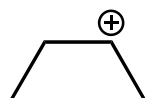
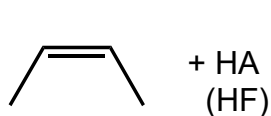
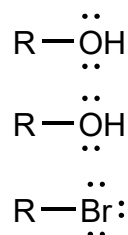
Friedel-Crafts
alkylation

ROH/HA

ROH/BF_3

$RX/AlCl_3$

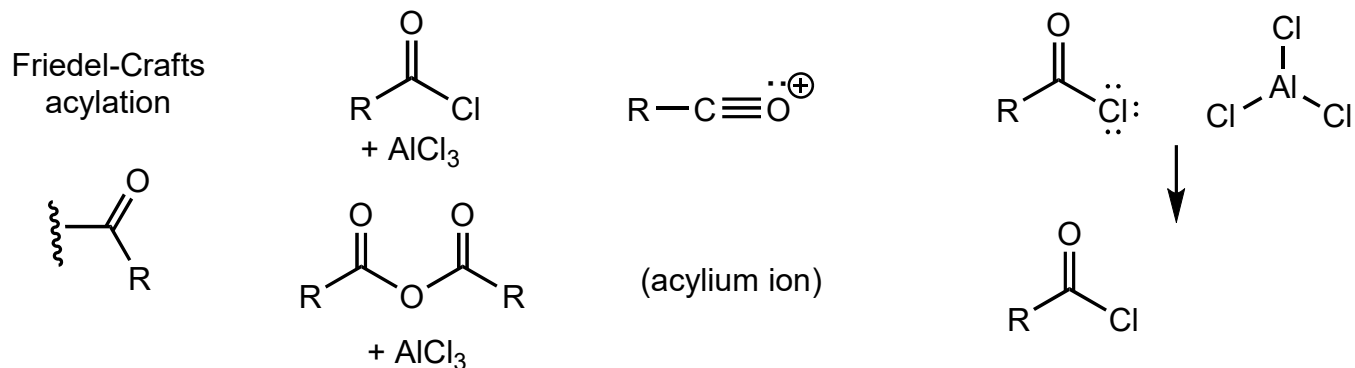
R^{\oplus}



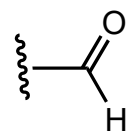
(carbocation)



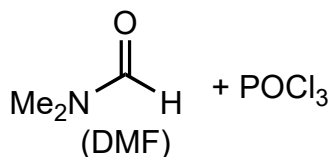
EAS Reaction **Conditions** **Electrophile (E⁺)** **Mech. to make E⁺ (1st steps in EAS)**



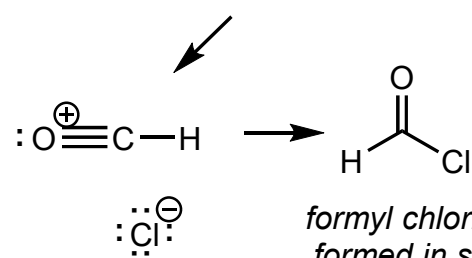
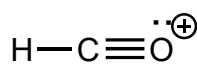
formylation



CO, HCl, AlCl₃
(Gattermann-Koch)



(Vilsmeier-Haack
for activated rings)

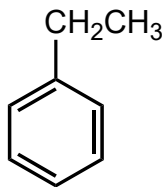
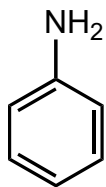
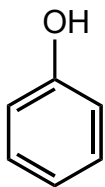


Electrophilic Aromatic Substitution on Substituted Rings

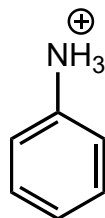
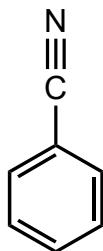
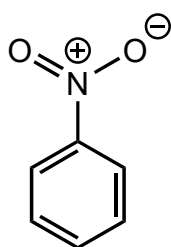
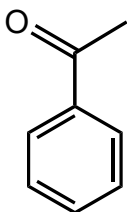
	EDG	EWG	X
type of group	 electron-donating group	 electron-withdrawing group	 halogen
reactivity (vs. PhH)			
regio-selectivity			
examples	$-\text{OH}$ $-\text{NH}_2$ $-\text{OR}$ $-\text{R}$ 	$-\text{NO}_2$ $-\text{CN}$ $-\text{NR}_3^{\oplus}$ $-\text{SO}_3\text{H}$ $-\text{CF}_3$ 	$-\text{Cl}$ $-\text{Br}$ $-\text{F}$ $-\text{I}$

Identifying electron-donating groups (EDG)

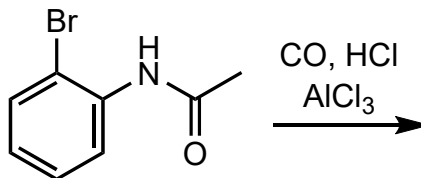
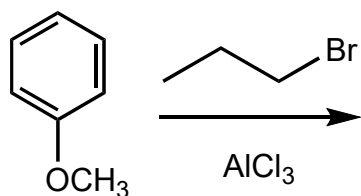
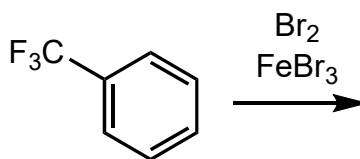
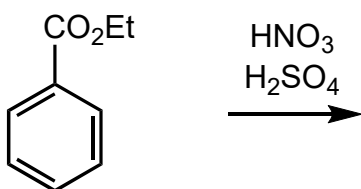
5-3



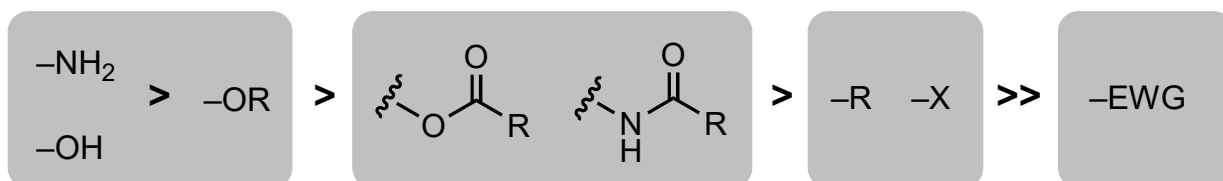
Identifying electron-withdrawing groups (EWG)



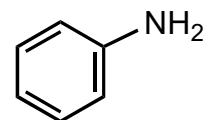
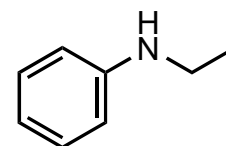
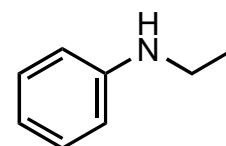
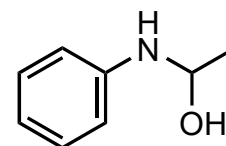
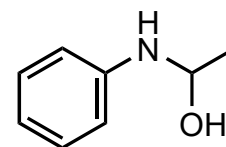
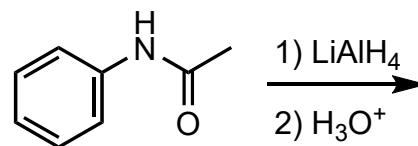
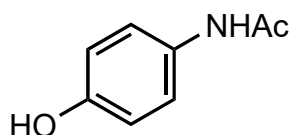
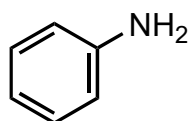
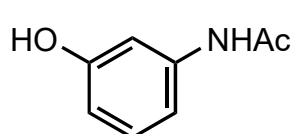
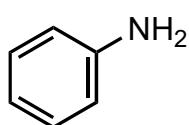
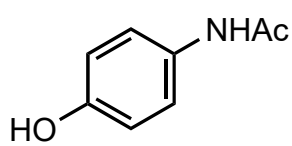
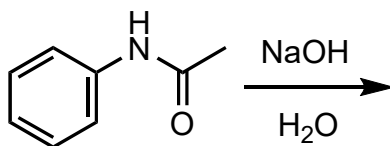
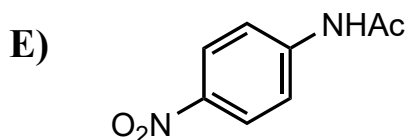
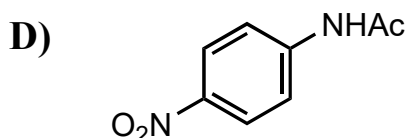
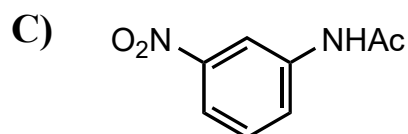
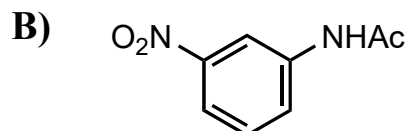
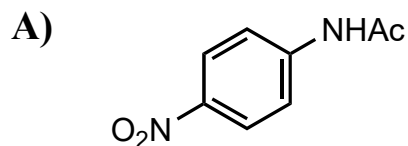
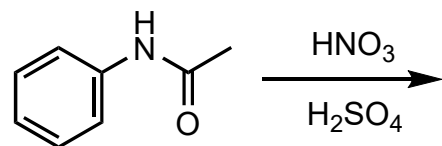
Predict the major product. First, determine whether substituent is an EDG or EWG.



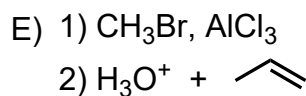
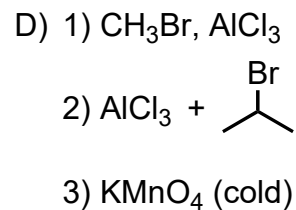
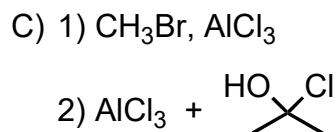
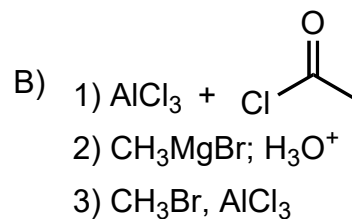
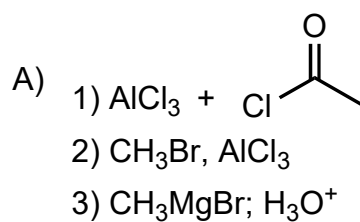
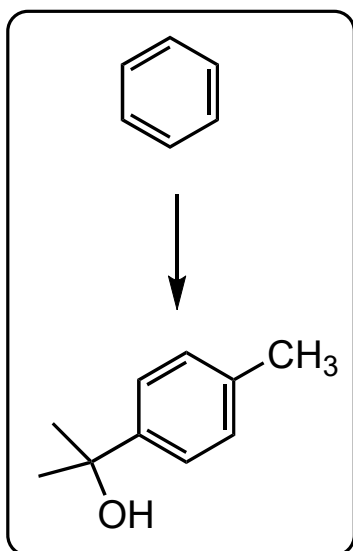
Directing power of substituents

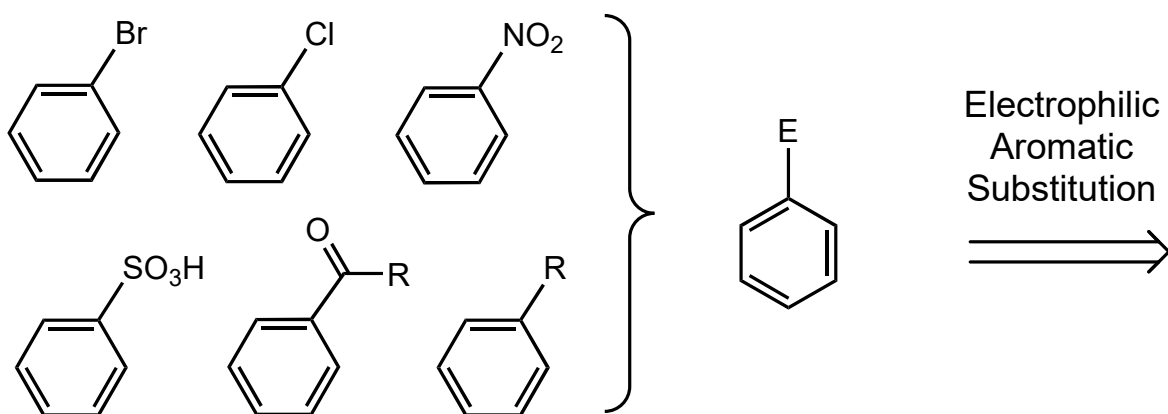


Predict the major products for the following reactions.



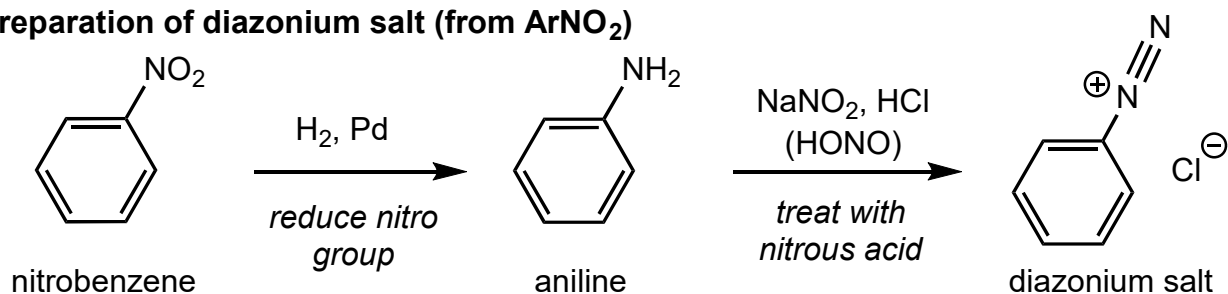
Provide the reagents necessary to transform the given starting material into the desired product.



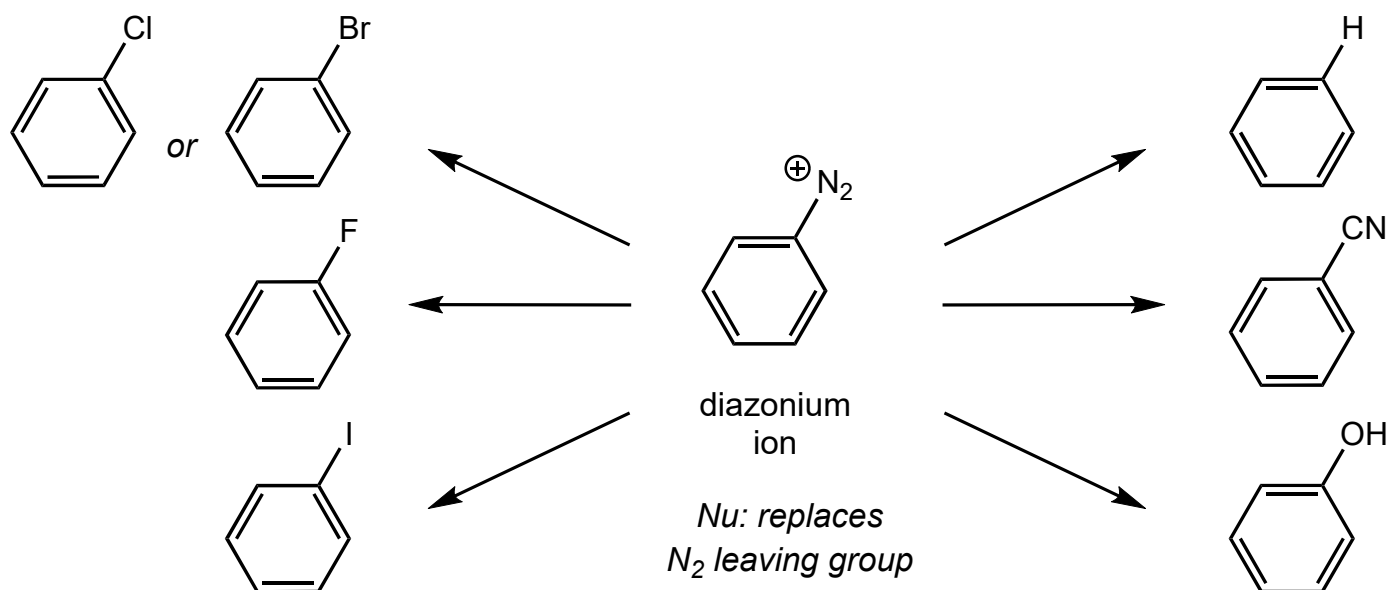


5.2 Aromatic Substitution via Diazonium Salts (ArN_2^+)

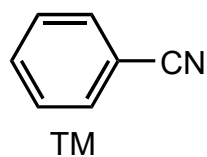
Preparation of diazonium salt (from ArNO_2)



Use of diazonium salts (copper reagents = Sandmeyer reaction)

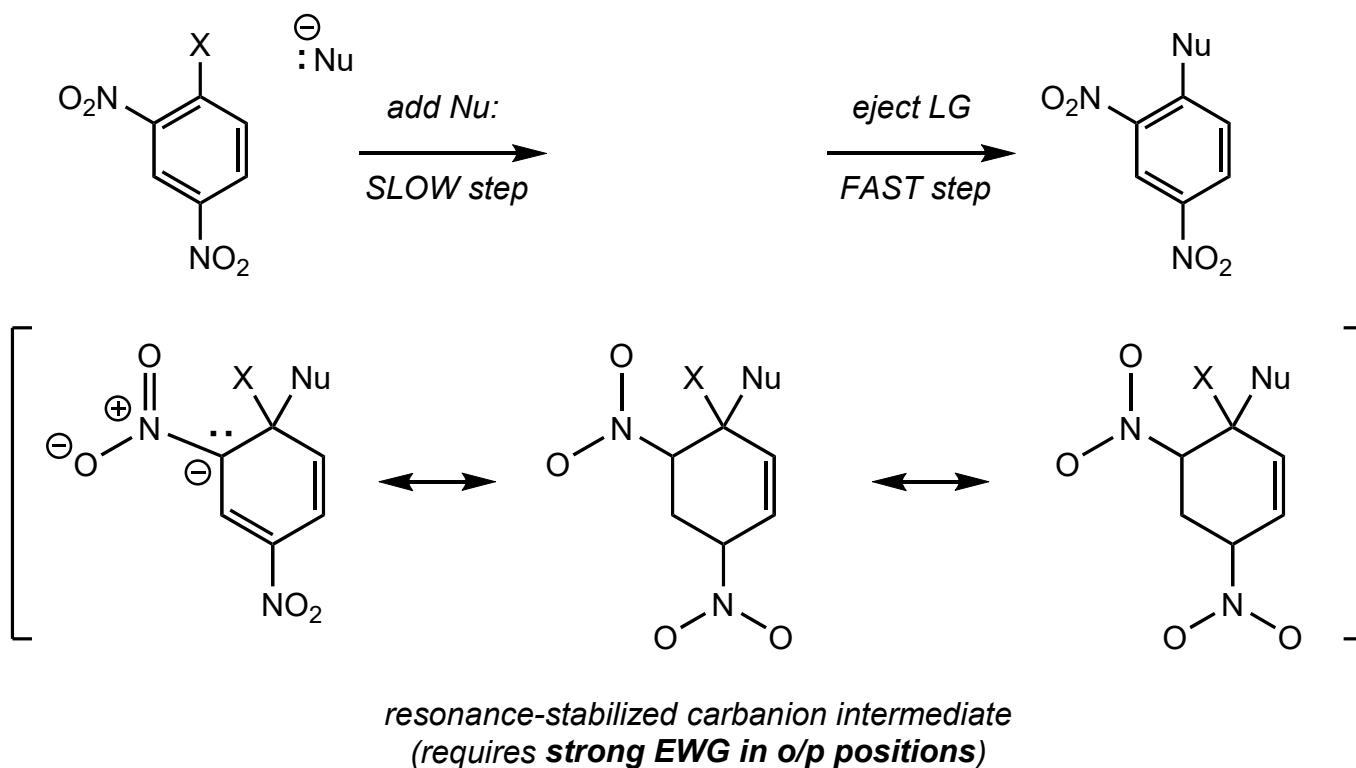


Show how you could prepare the following target molecule from benzene.

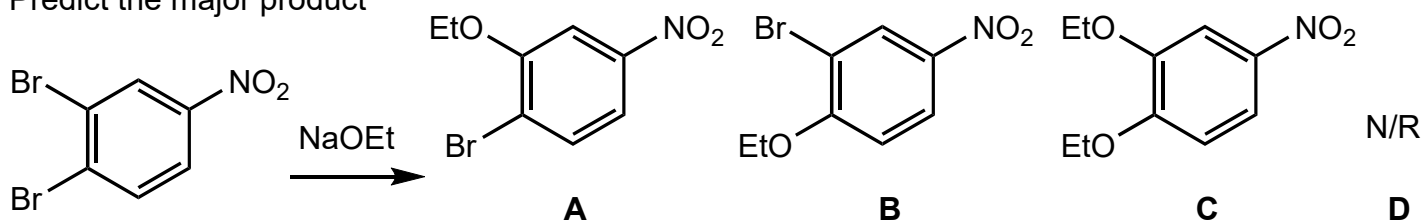


5.3 Nucleophilic Aromatic Substitution (S_NAr)

5-5

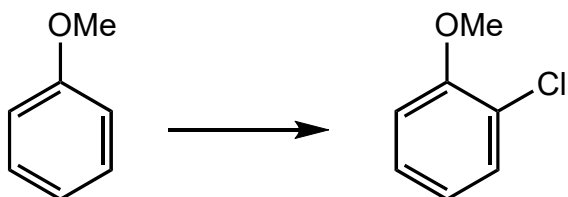


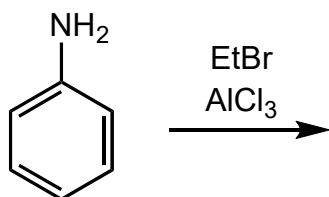
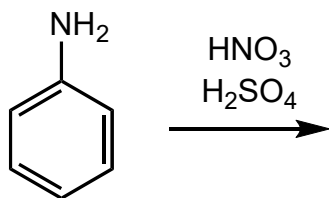
Predict the major product



Additional Synthetic Strategies: Protecting Groups and Blocking Groups

Transform the given starting material into the desired product.





Provide the structures **A** – **H**.

