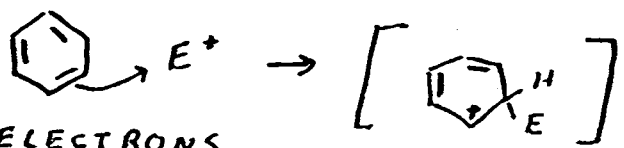


ELECTROPHILIC AROMATIC SUBSTITUTION

RING ELECTRONS  
ATTACK ELECTROPHILE



THE SIGMA  
COMPLEX  
RESONANCE  
STABILIZED

AROMATICITY IS LOST  
HIGHLY ENDOOTHERMIC  
RATE DETERMINING

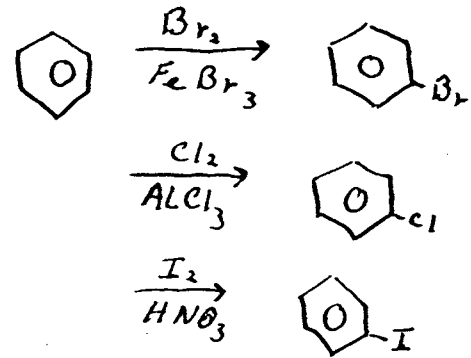
ABSTRACTION OF H<sup>+</sup>



SUBSTITUTION  
PRODUCT  
AROMATIC  
EXOTHERMIC

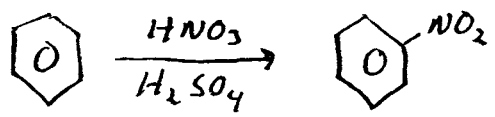
ANY DIFFERENT ELECTROPHILES CAN BE USED  
SUMMARY PG 720-722

HALOGENATION



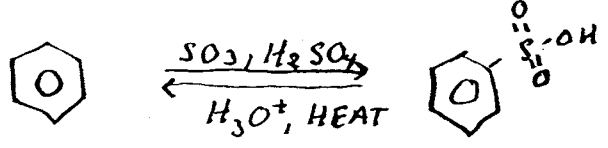
PG 672  
FOR MECHANISM  
FIGURE 17-2 FOR RCD

NITRATION



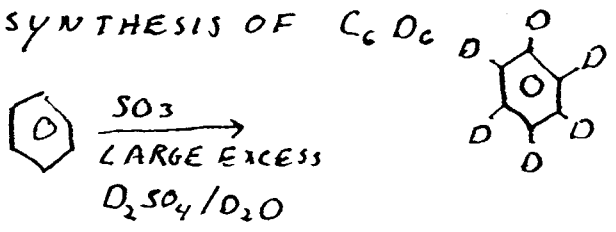
HNO<sub>3</sub> + H<sub>2</sub>SO<sub>4</sub> PRODUCE THE NITRONIUM ION  
+ NO<sub>2</sub>  $\ddot{O}=\overset{+}{N}=\ddot{O}$   
WHICH IS THE ELECTROPHILE

SULFONATION



SO<sub>3</sub> IS THE ELECTROPHILE  
SULFONATION IS REVERSIBLE

SINCE DESULFONATION SUBSTITUTES A H ON THE RING, IT PROVIDES  
A SYNTHESIS OF C<sub>6</sub>D<sub>6</sub>



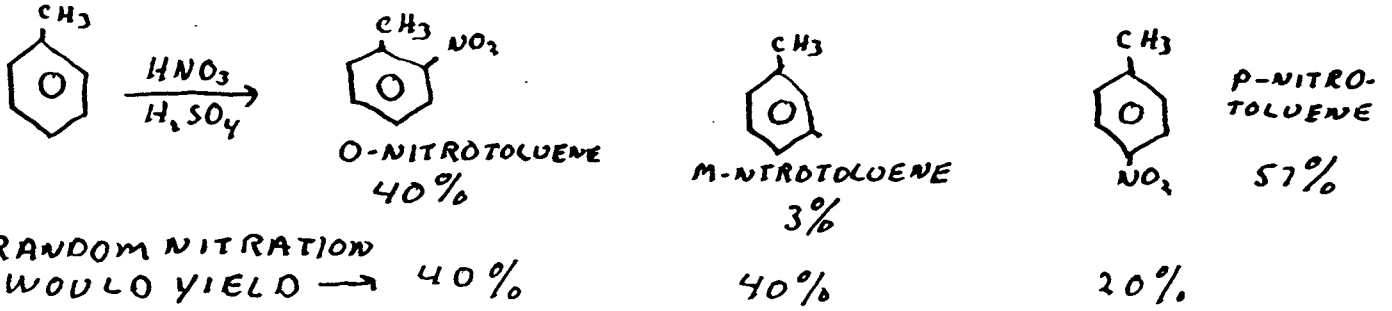
ACTIONS OF SUBSTITUTED BENZENES  
ACTIVATION, DEACTIVATION, DIRECTING GROUPS

# NITRATION OF TOLUENE

TOLUENE REACTS 25X FASTER THAN BENZENE

TOLUENE IS "ACTIVATED" AND THE METHYL IS THE ACTIVATOR

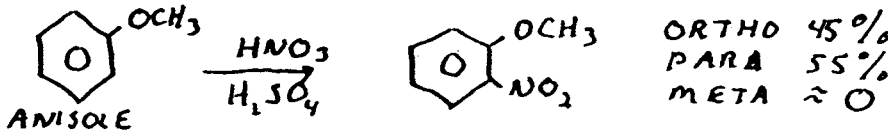
ACTIVATED RINGS ARE SUBSTITUTED MOSTLY AT O, P POSITIONS



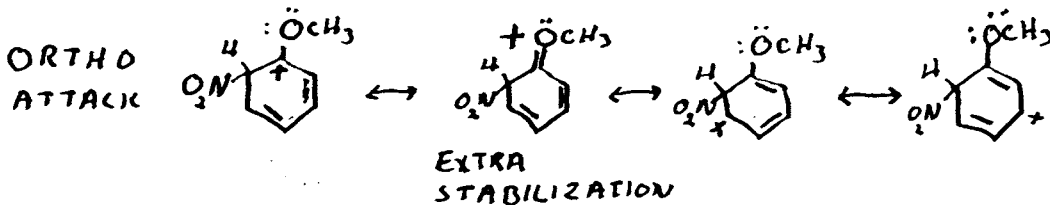
THE STRUCTURE OF THE SIGMA COMPLEX REVEALS O, P SUBSTITUTION IS STABILIZED BY A 3° CATION, WHILE META IS NOT PG 675

THE STABILIZING EFFECT OF ANY ELECTRON DONATING GROUP HAS THIS SAME POSITIONAL PREFERENCE AND REACTION RATE ENHANCEMENT  
 TREMELY STRONG ACTIVATION COMES FROM SUBSTITUENTS WITH BONDING ELECTRONS

ANISOLE REACTS 10,000 TIMES FASTER THAN BENZENE

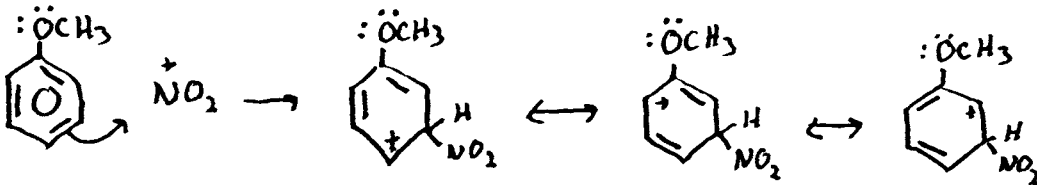


RESONANCE STRUCTURES OF THE SIGMA COMPLEX

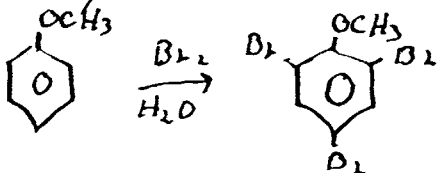


YOU SHOULD BE ABLE TO DRAW RESONANCE STRUCTURES FOR PARA ATTACK

BUT THERE IS NO EXTRA STABILIZATION FOR META ATTACK



THE METHOXY GROUP IS SO STRONGLY ACTIVATING THAT NO  $F_2$   $B_2$  IS NEEDED



MINO ( $-NH_2$ ) GROUPS LIKEWISE ACTIVATE SEE SUMMARY OF ACTIVATING, O, P DIRECTORS PG 745 680

# DEACTIVATING SUBSTITUENTS (META DIRECTORS)

NITROBENZENE REACTS  $10^5$  X SLOWER THAN BENZENE  
 O, P POSITIONS ARE MOST STRONGLY DEACTIVATED, LEAVING  
 META POSITIONS MOST REACTIVE (LEAST DEACTIVATED)

IN NITROBENZENE, THE NITROGEN CARRIES A FORMAL + CHARGE

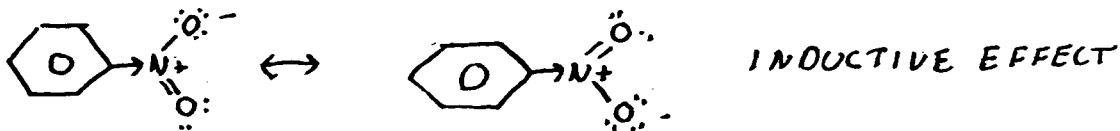
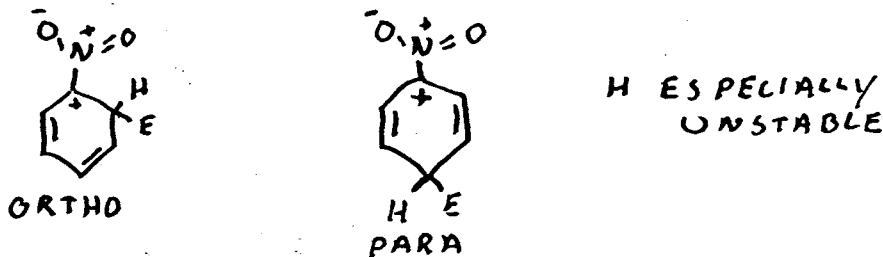


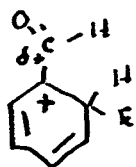
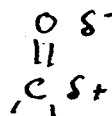
FIGURE 17-4 SHOWS THE RCD FOR NITROBENZENE REACTIONS  
 O AND P SIGMA COMPLEXES ARE HIGHLY DESTABILIZED IN RESONANCE  
 FORMS WHERE THE + CHARGE IS ON THE CARBON BEARING THE NITROGEN



MOST DEACTIVATING GROUPS  
 ARE O, P META DIRECTORS

ANY SUBSTITUENT WITH A FORMAL + CHARGE OR PARTIAL + CHARGE  
 DEACTIVATES AND META DIRECTS

FOR EXAMPLE, THE CARBONYL GROUP



ORTHO ATTACK (AND PARA) IS DESTABILIZED

DEACTIVATING META DIRECTORS ARE SUMMARIZED ON PG 747 680

NALLY, HALOGENS

THE HALOGENS ARE BOTH INDUCTIVELY WITHDRAWING AND RESONANCE DONATING  
 THIS COMBINATION MAKES HALOGENS DEACTIVATING, BUT O, P DIRECTING

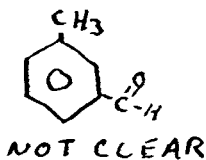
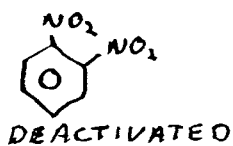
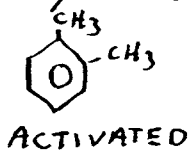
SEE FIGURE 17-5

ALL DIRECTING EFFECTS ARE SUMMARIZED ON PG 749 680

EFFECTS OF MULTIPLE SUBSTITUENTS

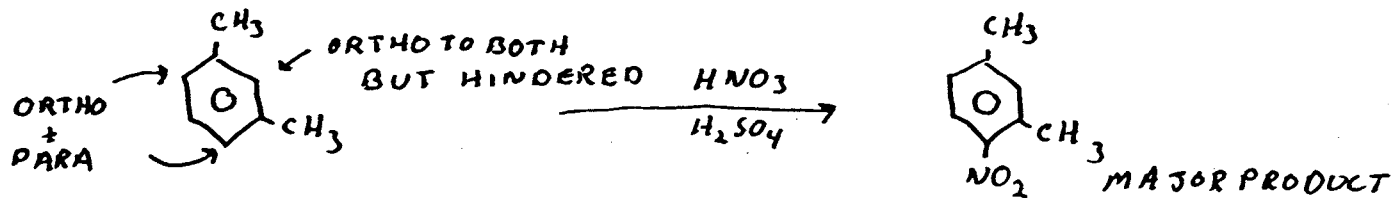
IMPLY SUM UP THE DIRECTING EFFECTS. OFTEN THE RESULT IS CLEAR

BUT NOT ALWAYS

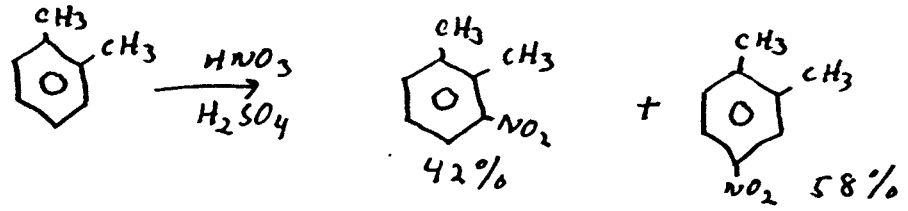


# ACTIVATORS WIN

THE ORIENTATION OF SUBSTITUTION IS ALSO OFTEN CLEAR



HOWEVER, MIXTURES ARE POSSIBLE



ACTIVATING GROUPS ARE USUALLY STRONGER THAN DEACTIVATING GROUPS

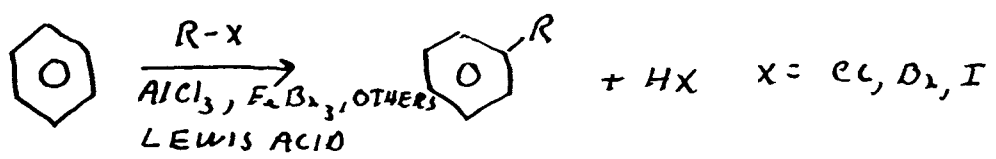
STRONG ACTIVATORS THAT STABILIZE VIA RESONANCE RANK HIGHEST

OH, -OR, -NR<sub>2</sub>

MODERATE O, P DIRECTORS -R, -X ARE NEXT

META DIRECTORS LAST SEE SOLVED PROBLEM 1

FEEDL-CRAFTS ALKYLATION



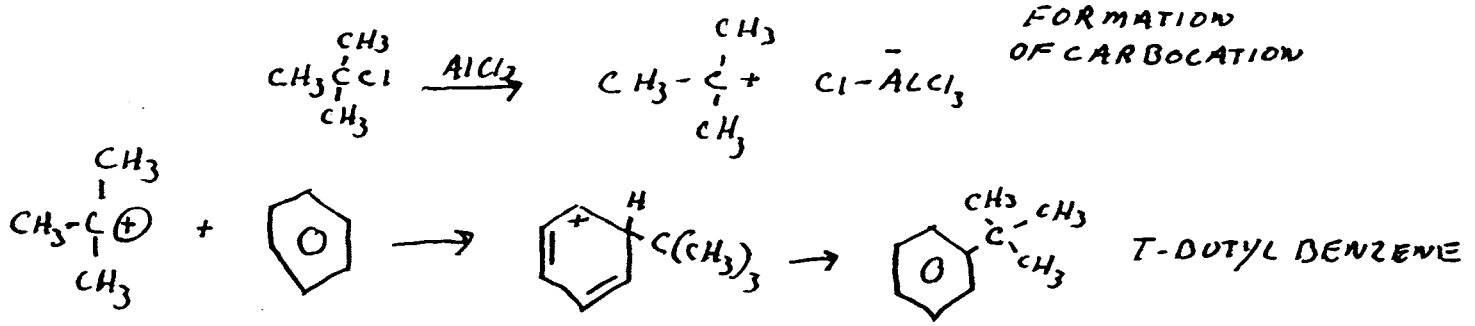
ALKYL HALIDES

ALKYLATE THE RING IN THE PRESENCE OF LEWIS ACIDS

THIS IS A TYPICAL ELECTROPHILIC AROMATIC SUBSTITUTION

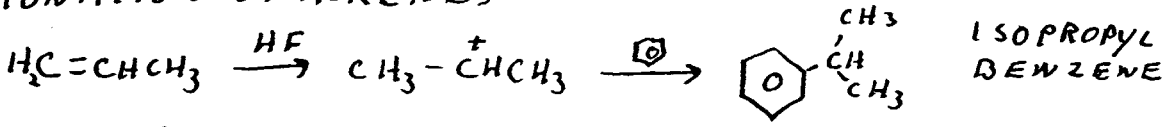
CARBOCATION IS THE ELECTROPHILE

FORMATION OF CARBOCATION



ALTERNATIVE CARBOCATION SOURCES MAY ALSO BE USED, SUCH AS

PROTONATION OF ALKENES



THE F<sup>-</sup> ANION IS A POOR

NUCLEOPHILE, NOT TOO REACTIVE TOWARDS THE CATION

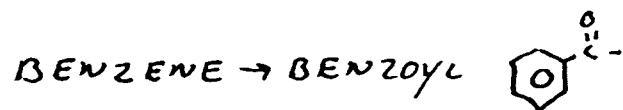
## LIMITATIONS OF FRIEDEL-CRAFTS ALKYLATION

- 1) WORKS ONLY WITH ACTIVATED RINGS
- 2) CARBOCATION REARRANGEMENTS
- 3) AFTER ALKYLATION, RING IS MORE ACTIVATED, GIVING POLY ALKYLATION PRODUCTS

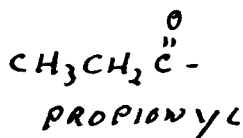
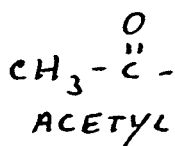
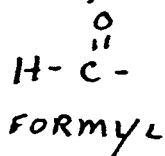
OF THESE 3 LIMITATIONS ARE OVERCOME BY

## FRIEDEL CRAFTS ACYLATION

ITS VERY SIMILAR, BUT THE ELECTROPHILE IS THE ACYLIUM ION  
 IN ACYL GROUP IS  $R-\overset{\overset{O}{\parallel}}{C}-$  NAMED BY DROPPING THE E FROM THE  
 ALKANE NAME AND ADD -OYL

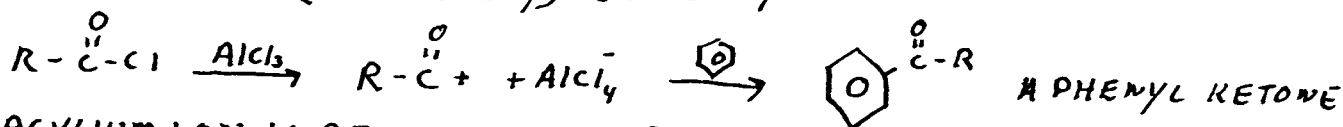


SMALL ACYL GROUPS GET COMMON NAMES



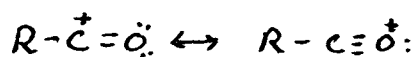
WHEN AN ACYL GROUP IS BONDED TO A CHLORINE, ITS CALLED  
 AN ACID CHLORIDE

FRIEDEL-CRAFTS ACYLATION IS THE STANDARD ELECTROPHILIC SUBSTITUTION  
 THE ELECTROPHILE (SIMPLISTICALLY) IS THE ACYLIUM ION



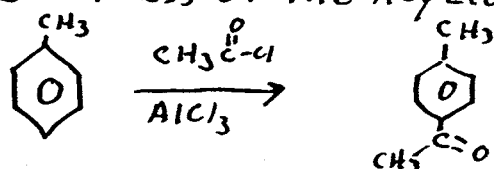
THE ACYLIUM ION IS RESONANCE-STABILIZED

SO NO REARRANGEMENTS



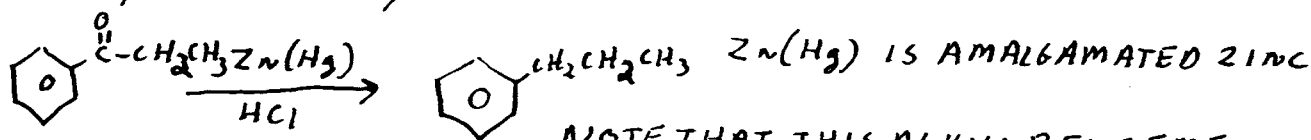
BUT THE ACYLATED PRODUCT IS DEACTIVATED TOWARD FURTHER SUBSTITUTION

THE BULKINESS OF THE ACYLIUM COMPLEX OFTEN FAVORS PARA SUBSTITUTION



ACYLATION AND ALKYLATION ARE SUMMARIZED ON PG 759

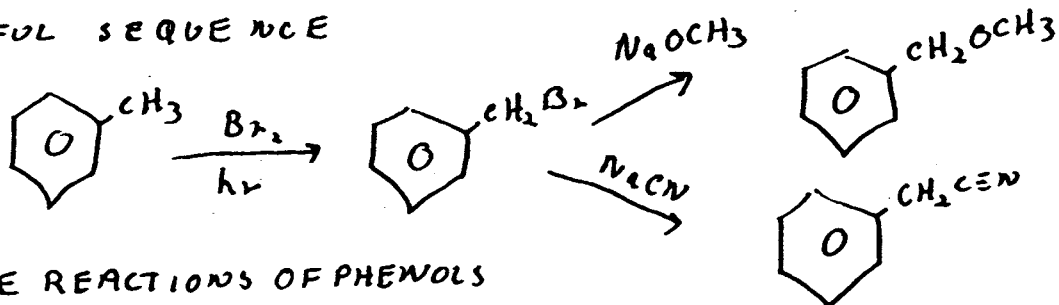
FREQUENTLY THE PHENYL KETONE IS REDUCED TO THE ALKANE



THIS IS CALLED THE  
 CLEMMENSEN REDUCTION

NOTE THAT THIS ALKYL BENZENE  
 COULD NOT BE MADE BY ALKYLATION  
 DUE TO REARRANGEMENT PROBLEMS

## USEFUL SEQUENCE

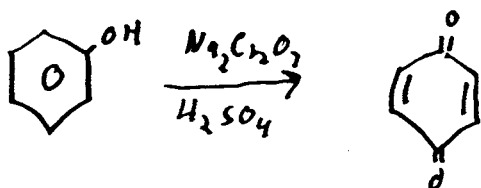


## UNIQUE REACTIONS OF PHENOLS

PHENOLS UNDERGO MOST OF THE USUAL ALCOHOL REACTIONS SUCH AS ESTERIFICATION AND ALKOXIDE FORMATION

ALSO:

### OXIDATION TO QUINONES



PHENOLS ALSO MAKE STRONG SUBSTRATES FOR ELECTROPHILIC AROMATIC SUBSTITUTION. PHENOXIDES ARE EVEN MORE REACTIVE.

## SKILLS

KNOW THE MOST COMMON ELECTROPHILIC AROMATIC SUBSTITUTIONS; HALOGENATION, NITRATION, SULFONATION, FRIEDEL-CRAFTS

KNOW THE MECHANISM OF ELECTROPHILIC AROMATIC SUBSTITUTION

KNOW RESONANCE STRUCTURES FOR O,P AND M DIRECTION

PREDICT THE POSITIONS OF SUBSTITUTION IN MULTI-SUBSTITUTED RINGS

DESIGN SIMPLE SYNTHESIS INVOLVING POSITION OF SUBSTITUTION AND SIDE-CHAIN REACTIONS

## THESE

PROBLEMS ARE FROM WADE, 4<sup>TH</sup> ED

16, 17a  
21c, 42, 43

10R2, 19A

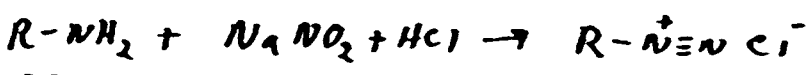
3, 8

5B, 51, 14

52, 35, 36, 37B,C  
47

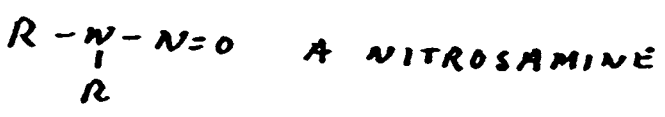
# DIAZONIUM SALTS

ALCYLAMINES REACT WITH NITROUS ACID TO FORM DIAZONIUM SALT



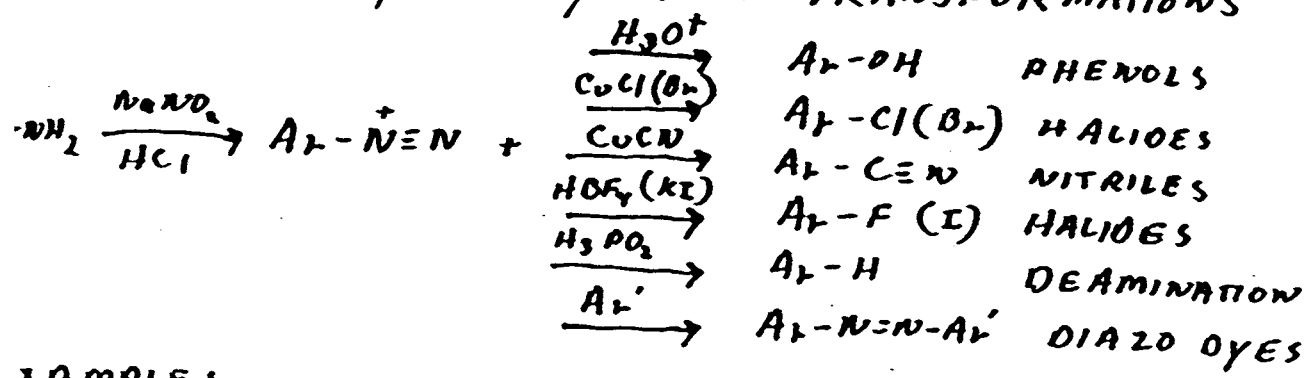
PRIMARY DIAZONIUM SALTS DECOMPOSE TO FORM CARBOCATIONS  $R^+$ , WHICH THEN EITHER REARRANGE, ELIMINATE H TO FORM AN ALKENE OR UNDERGO NUCLEOPHILIC SUBSTITUTION

SECONDARY DIAZONIUM SALTS FORM NITROSAMINES, ONE OF THE MOST POTENT CLASSES OF CARCINOGEN KNOWN



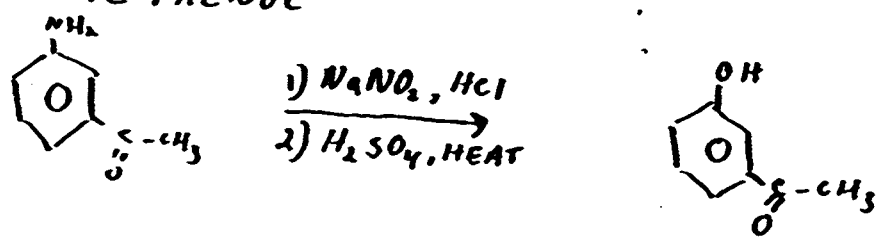
THE MAIN USEFULNESS OF DIAZONIUM SALTS IS WITH AROMATIC AMINES, WHICH MAY BE CONVERTED INTO A WIDE VARIETY OF FUNCTIONALITIES AFTER DIAZOTIZATION

A SUMMARY OF ARYL AMINE TRANSFORMATIONS

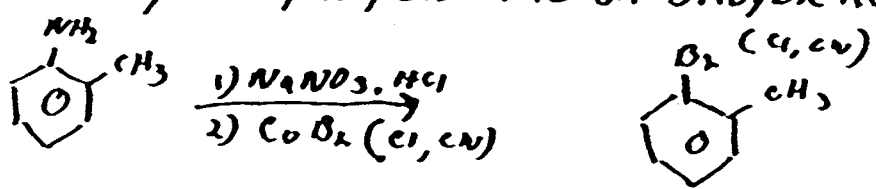


## EXAMPLES

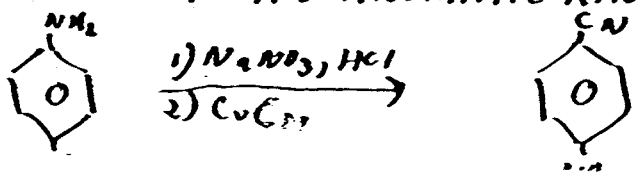
HYDROLIS TO THE PHENOL



REPLACEMENT BY CL, Br, CN THE SANDMEYER REACTION



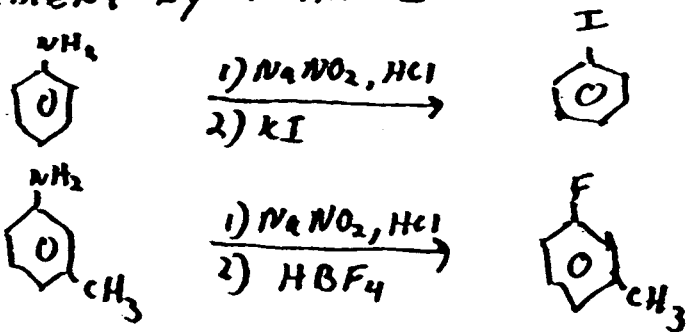
THIS IS A USEFUL WAY TO ATTACH A NEW CARBON TO AN AROMATIC RING



ONCE YOU HAVE THE NEW CARBON ON THE RING, YOU CAN GO ON TO MODIFY IT

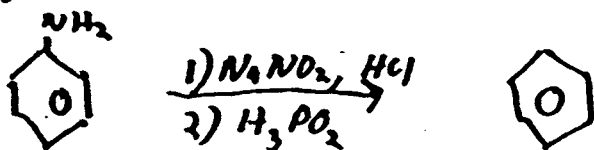
# 10 MORE DIAZONIUM REACTIONS

## REPLACEMENT BY F AND I

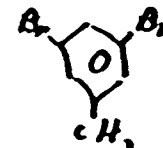


THIS IS THE BEST WAY TO GET F OR I ONTO AN AROMATIC RING

## DEAMINATION

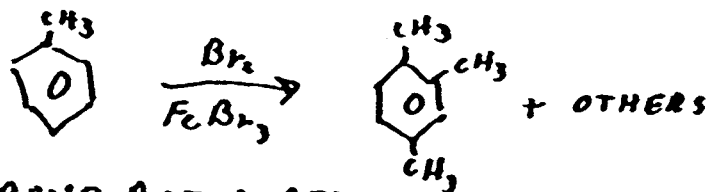


AN AMINO GROUP MAY BE ADDED TO A RING TO ACTIVATE IT AND DIRECT SUBSTITUTION

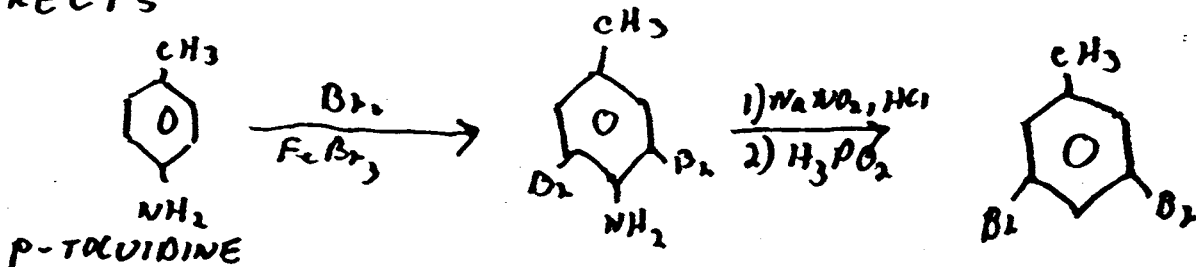
A GOOD EXAMPLE IS THE SYNTHESIS OF  FROM TOLUENE

## DIRECT BROMINATION OF TOLUENE

GIVES A MIXTURE OF ORTHO AND PARA SUBSTITUTION



AN AMINO GROUP ACTIVATES AND DIRECTS



DIAZOCOUPLING PRODUCES AZO DYES



THESE HIGHLY CONJUGATED SYSTEMS ARE STRONGLY COLORED  
USED IN TEXTILES



# CHAPTER 16 + 17

TOPIC	QUESTIONS
RULES FOR AROMATICITY	15-31
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O, M, P DIRECTORS	31-40, 42, 52
REAGENTS AND REACTIONS	38, 43, 41
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