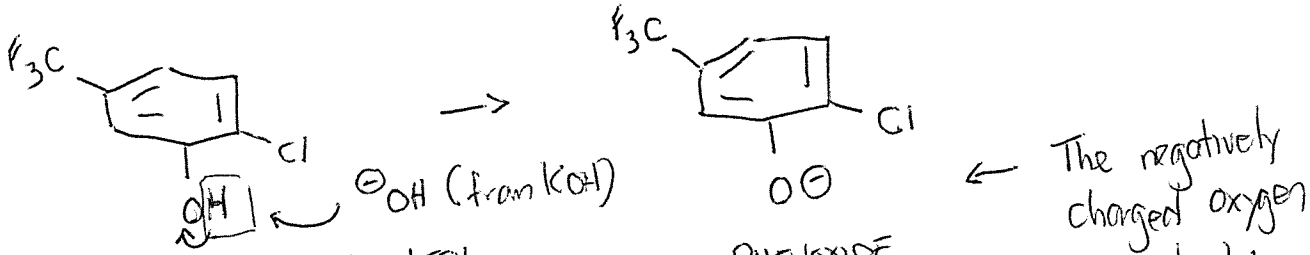
16.16 This is an example of an NAS reaction.

The nucleophile is the phenoxide anion derived from reaction of KOH (a strong base) with the 2-chloro-5-trifluoromethyl phenol reagent

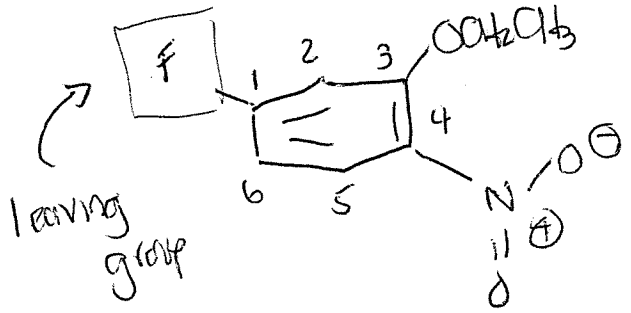


2-CHLORO-5-TRIFLUOROMETHYL PHENOL
(The H of the phenol is acidic)

PHENOXIDE ANION

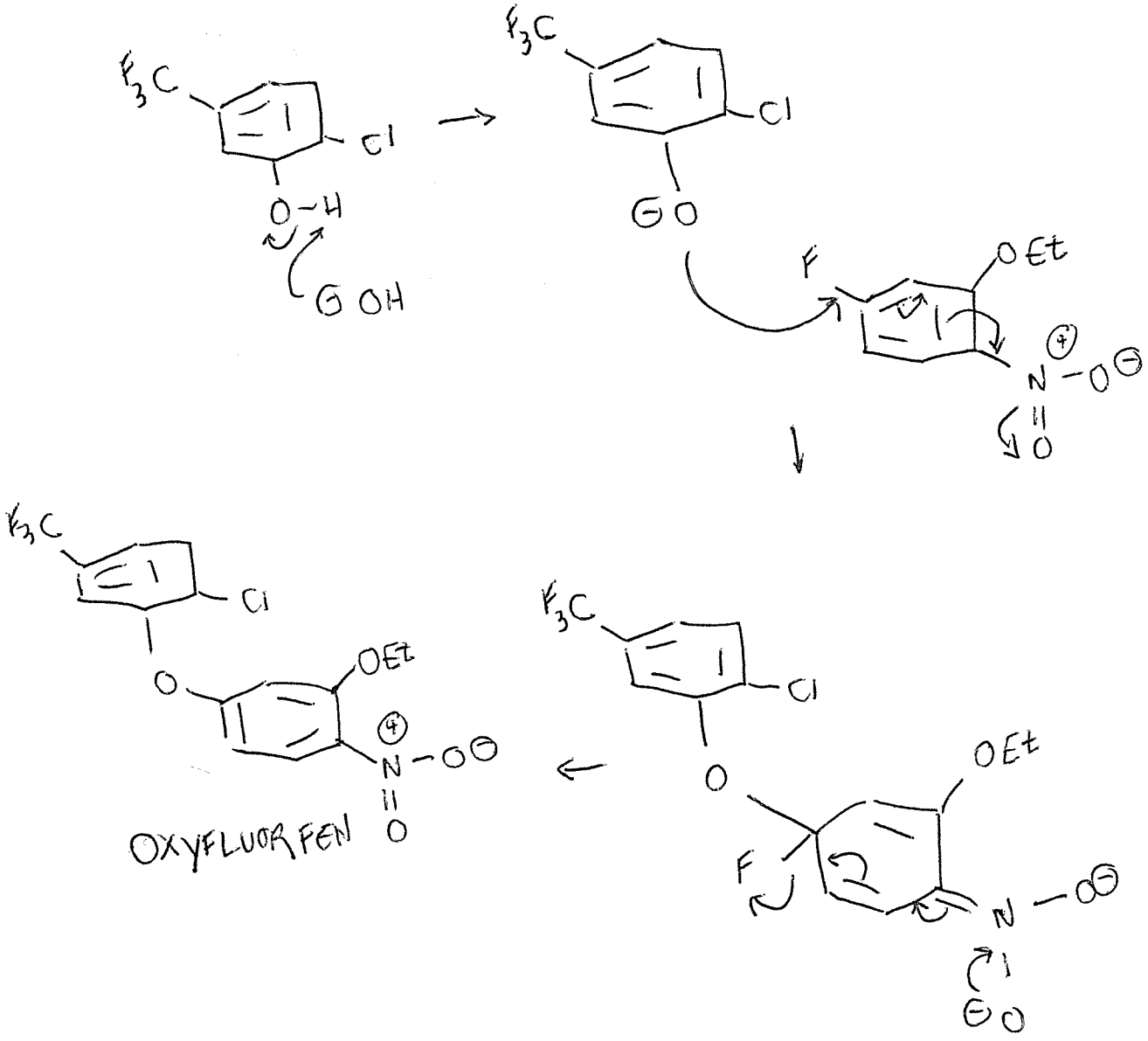
← The negatively charged oxygen is nucleophilic

The leaving group (F) of 2-ethoxy-1-fluoro-4-nitrobenzene is para to the nitro group, which is an EWG by resonance. The C_1 atom (bonded to the fluorine leaving group) reacts with the Nucleophile (Oxygen of phenoxide anion) in an NAS reaction.



leaving group

16.16 (cont'd)

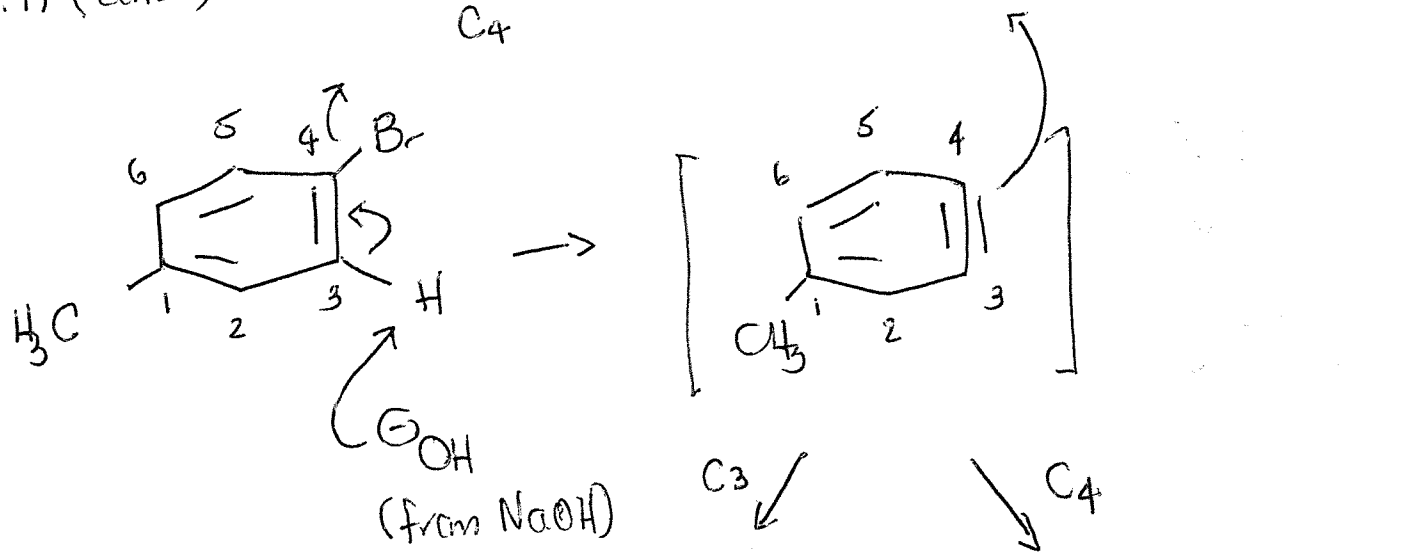


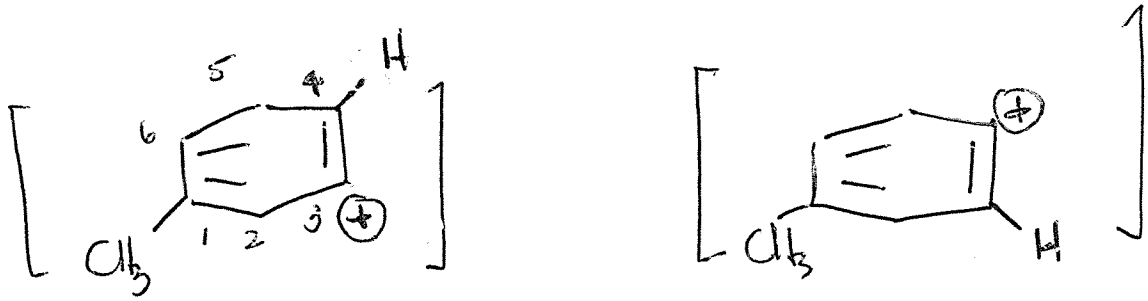
16.17. This is an example of a BENZYNE reaction. The leaving group is bromide ion. NaOH serves as base <u>and</u> as reagent to substituted in the benzyne reaction.

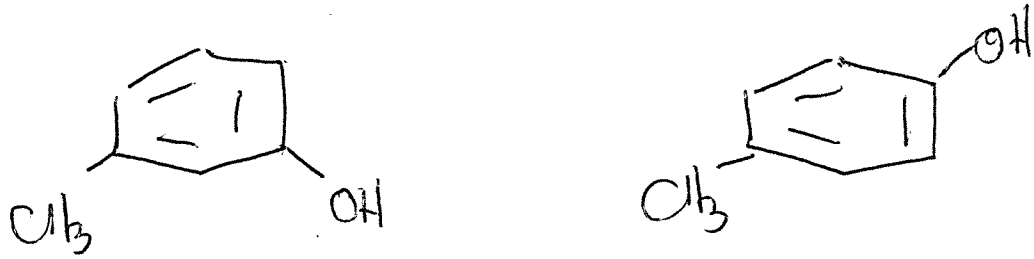
16.17 (cont'd)

H from H_2O reacts @ C_3 or C_4

HO-H





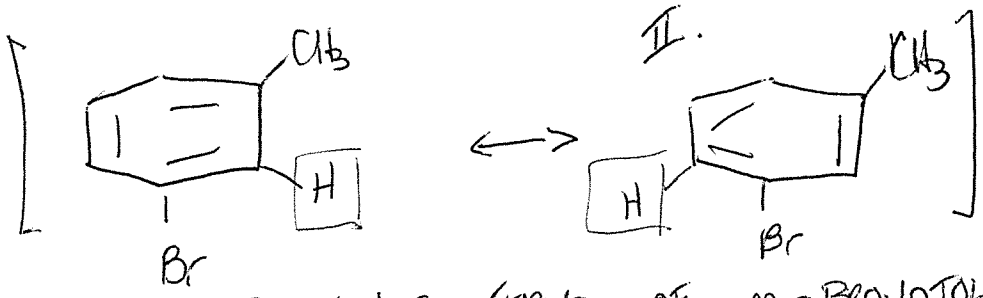


META

PARA

* If H @ C_5 reacted initially w/ NaOH, same two products would be generated.

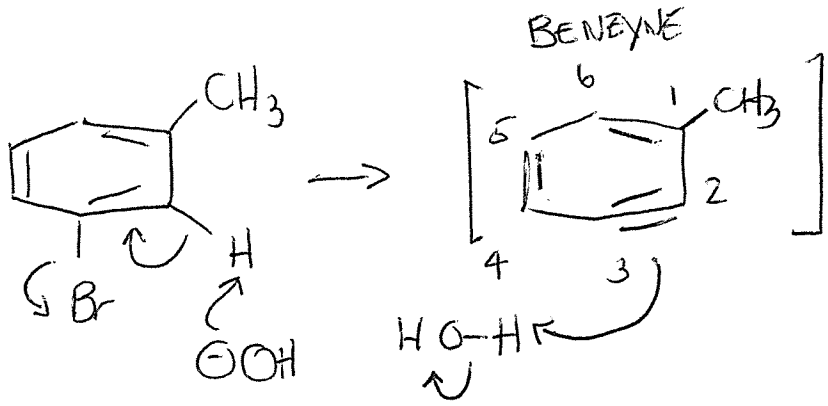
I. II.

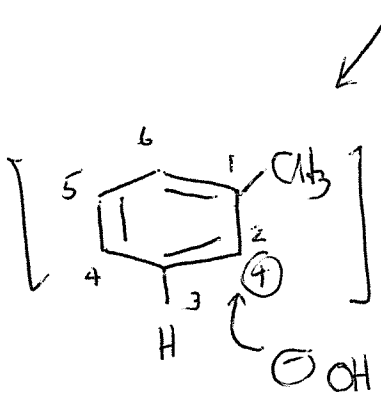


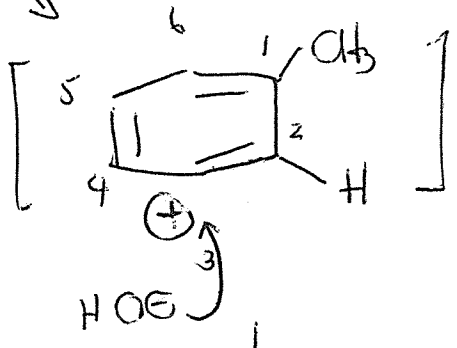
RESONANCE FORMS OF m-BROMOTOLUENE

Consider the benzyne reaction, and the resulting products from each resonance form independently.

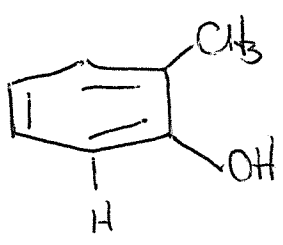
I.



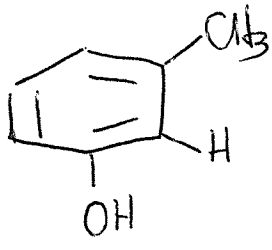




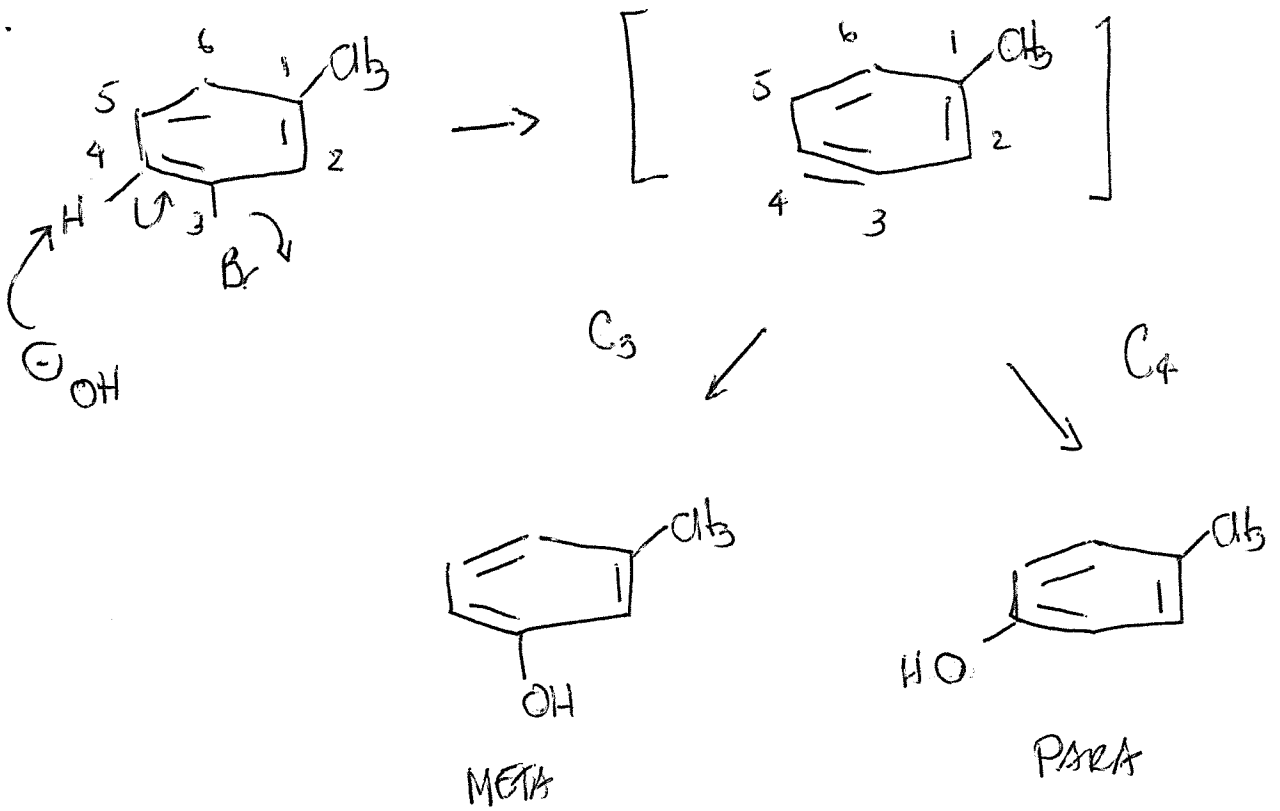
ORTHO-



META-



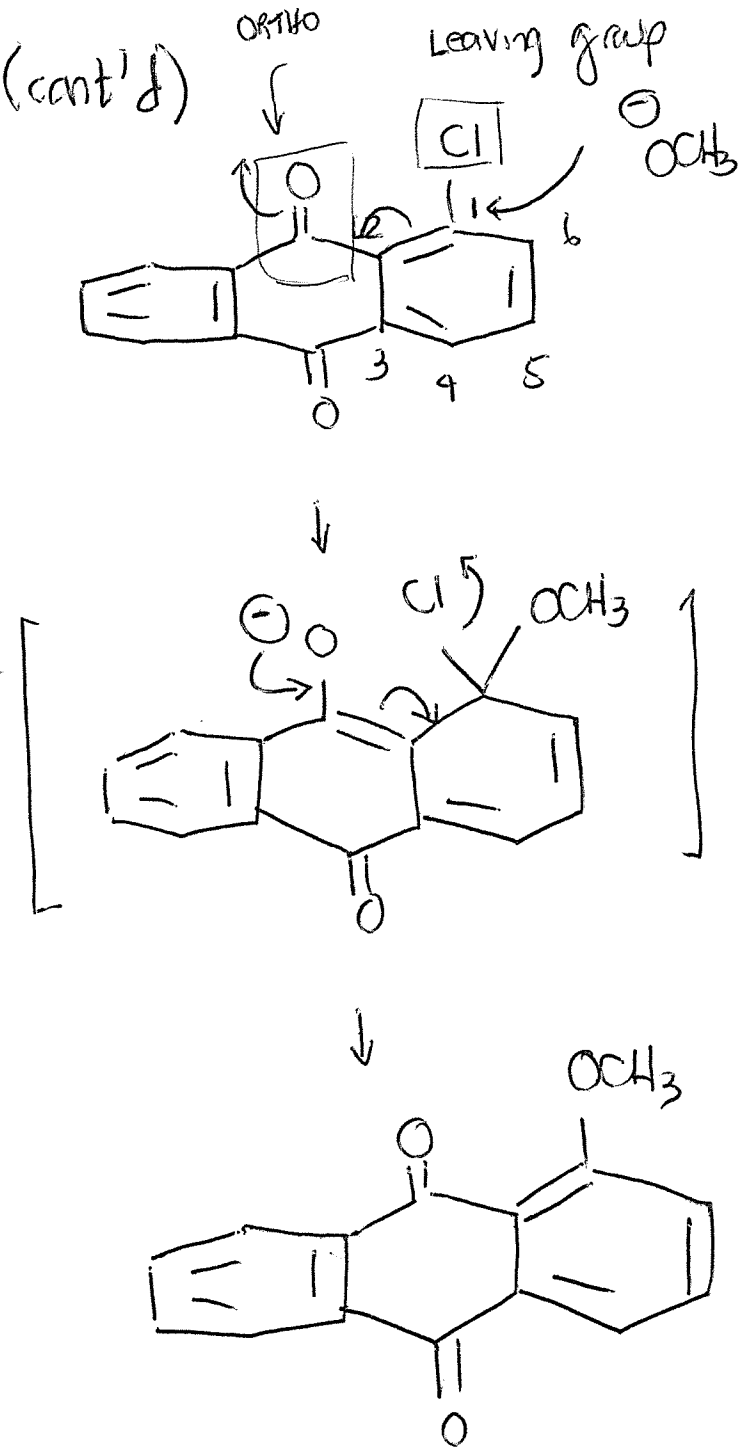
II.



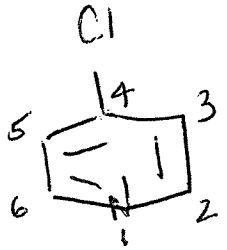
So from meta-bromotoluene, 3 products are generated (m- and o- from resonance form I and m- and p- from resonance form II) Meta is the MAJOR product.

16.61 This is an example of an NAS reaction. CH_3O^- is the nucleophile. The chlorine of 1-chloroanthraquinone is the leaving group. One carbonyl group is ORTHO to the Cl so the NAS mechanism is allowed.

16.61 (cont'd)



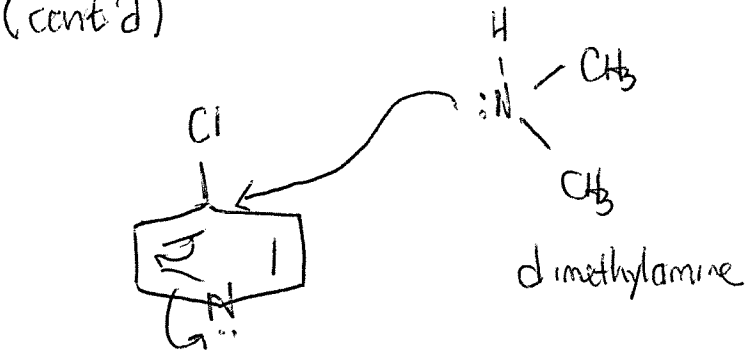
16.62.



4-chloropyridine

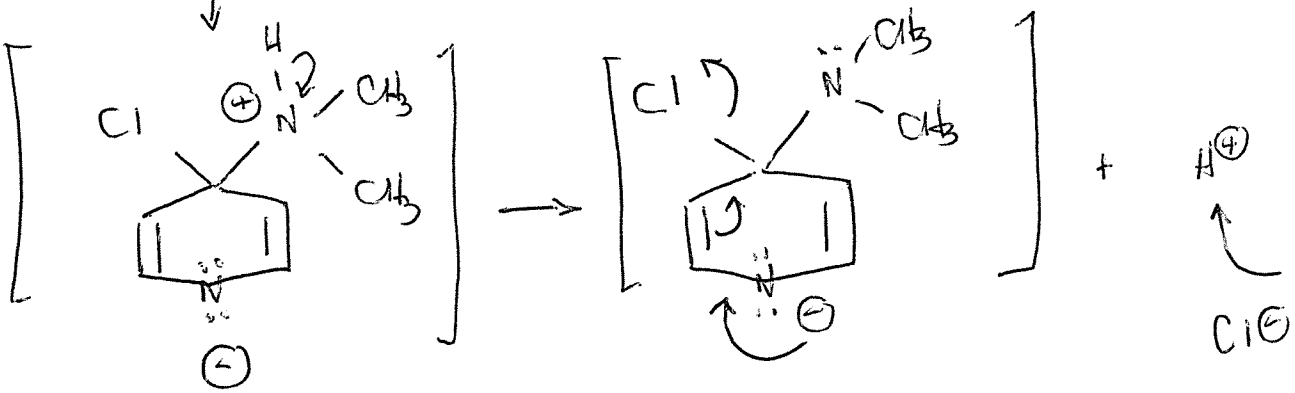
4-chloropyridine can react with a nucleophile in a NAS. The N atom of the ring, serves as an "internal" EWG.

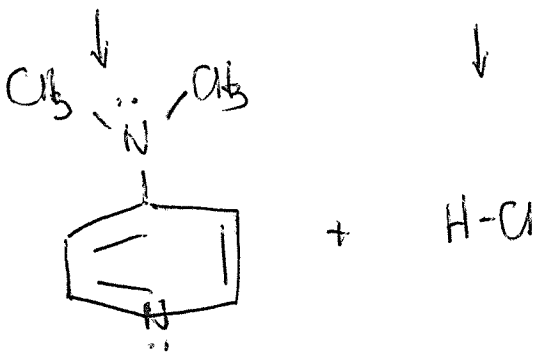
16.62 (cont'd)



dimethylamine

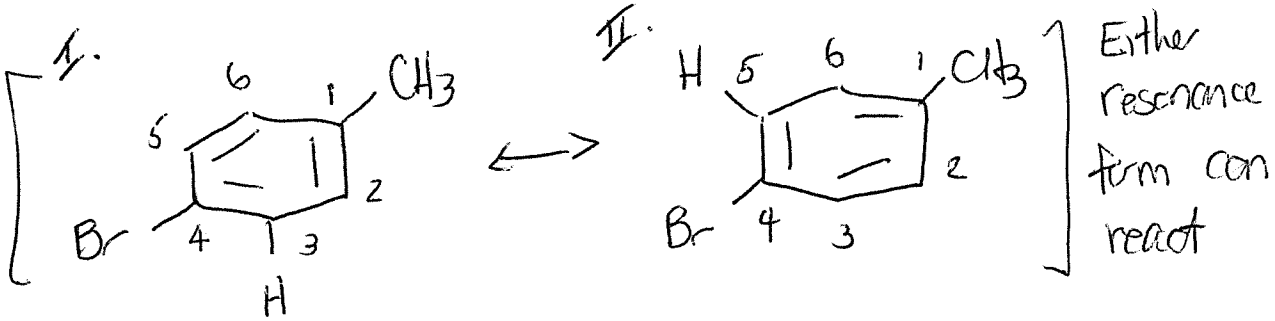
The lone pair e⊖ on dimethyl amine N serves as the nucleophile.





16.63 This problem is very similar to 16.17

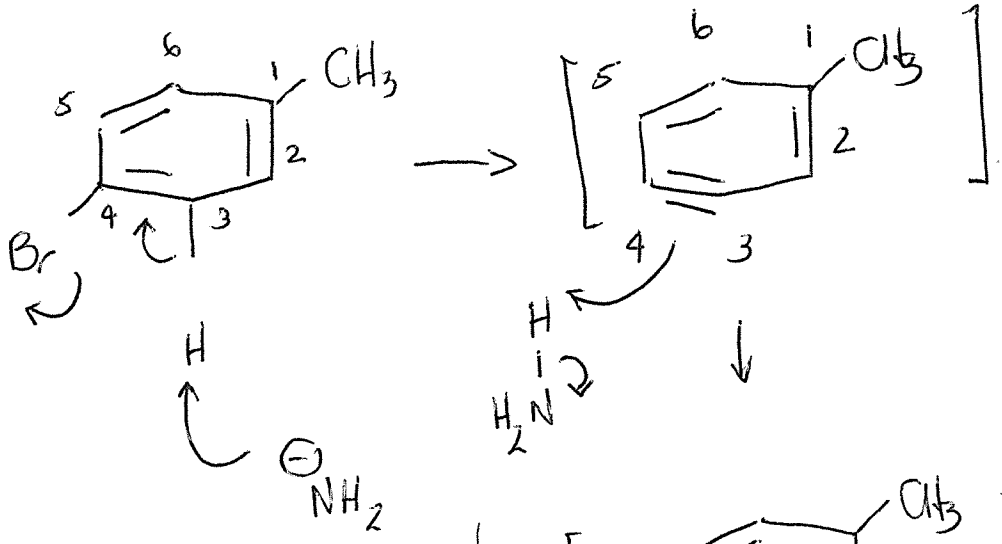
p-Bromotoluene reacts with potassium amide (KNH_2, strong base) in a benzyne reaction.

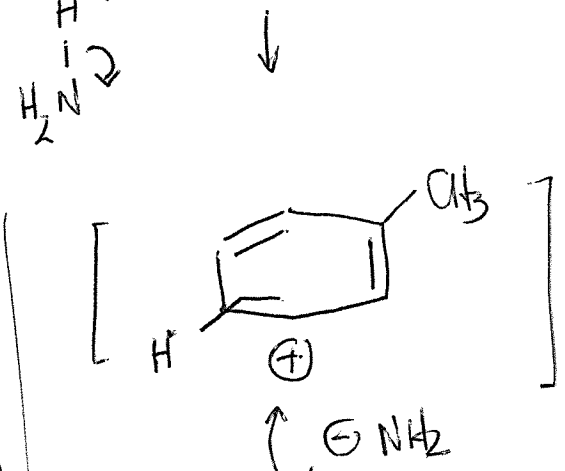


Either resonance form can react

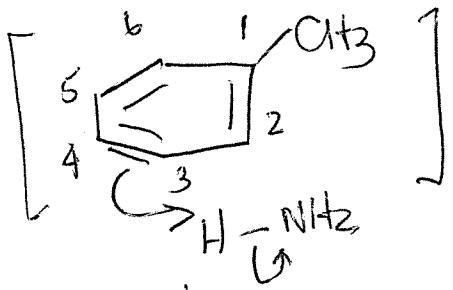
16.63 (cont'd)

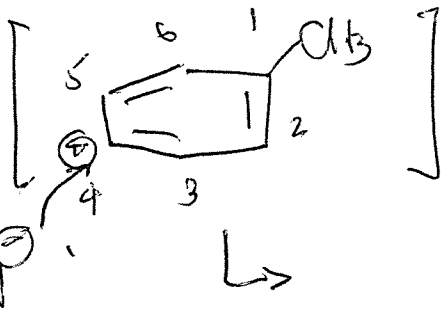
I.



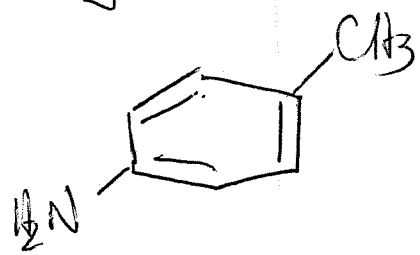


The same benzyne intermediate can react to give the para product





META-methyl aniline



PARA-methyl aniline