

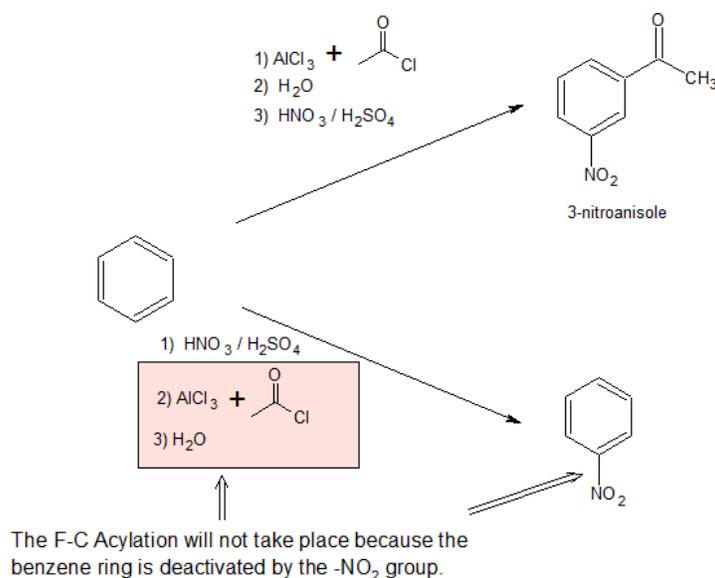
18.8: SYNTHETIC STRATEGIES FOR DI-SUBSTITUTED BENZENES

SYNTHETIC CONSIDERATIONS

To develop multiple step syntheses for di-substituted benzene derivatives, the regiochemistry of the substituents will determine the order of the reactions. The directing effects of the benzene substituents are summarized below.

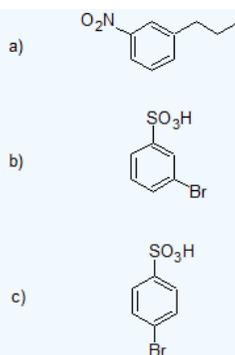
ortho, para-directing			meta-directing	
Resonance Donors	Inductive Donors	Halogens	Carbonyls	Other Withdrawing Groups
—NH ₂	—R	—F	—C(=O)—H or R	—SO ₃ H
—OH		—Cl	—C(=O)—OH	—CN
—OR		—Br	—C(=O)—OR	—NO ₂
—NHCOCH ₃		—I		—NH ₃ ⁺
← activating			deactivating →	

The limitations of the Friedel-Crafts reactions must also be considered. Friedel-Crafts alkylation and acylation reactions can only occur on benzene rings or benzene rings with ortho-, para-directors (activated rings or rings with halogens). Even though both acyl and nitro groups are meta-directors, benzene would need to be acylated before it is nitrated. To synthesize 3-nitroanisole [1-(3-nitrophenyl)ethan-1-one], the top reaction sequence is needed. The bottom reaction sequence will not produce the desired product as shown in the two synthetic pathways below.



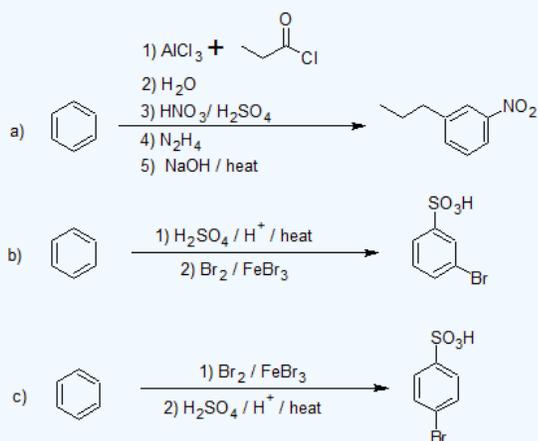
Exercise

22. Starting with benzene and using any synthetic reagents, propose a multiple step synthesis for each of the following compounds.



Answer

22.



CONTRIBUTORS AND ATTRIBUTIONS

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