


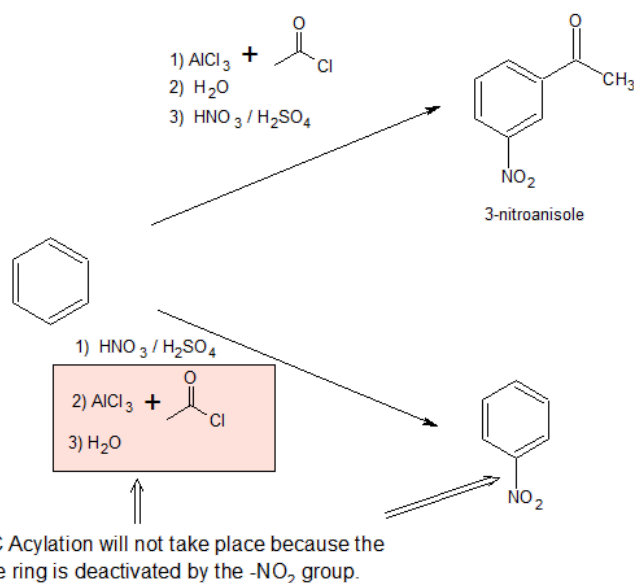
## 18.8: SYNTHETIC STRATEGIES FOR DI-SUBSTITUTED BENZENES

### 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.

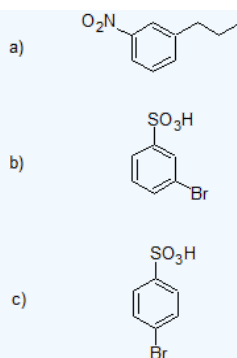
ortho, para-directing			meta-directing	
Resonance Donors	Inductive Donors	Halogens	Carbonyls	Other Withdrawing Groups
$\text{—NH}_2$ $\text{—OH}$ $\text{—OR}$ $\text{—NHCOCH}_3$	$\text{—R}$ 	$\text{—F}$ $\text{—Cl}$ $\text{—Br}$ $\text{—I}$	$\text{—C(=O)—H or R}$ $\text{—C(=O)—OH}$ $\text{—C(=O)—OR}$	$\text{—SO}_3\text{H}$ $\text{—CN}$ $\text{—NO}_2$ $\text{—NH}_3^+$
← 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.



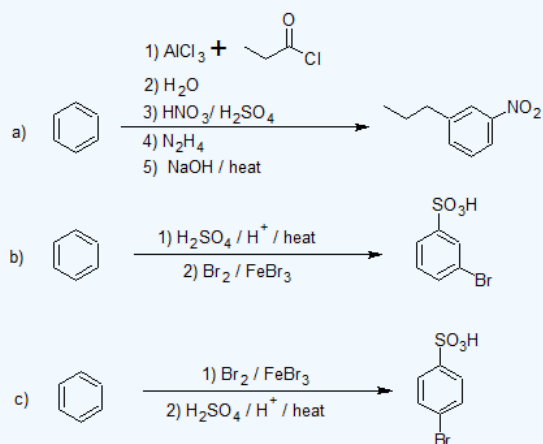
### Exercise

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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