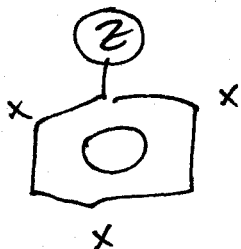
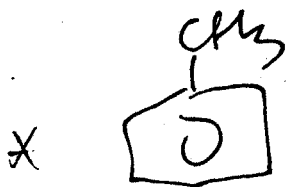


# ortho vs. Para Substitution

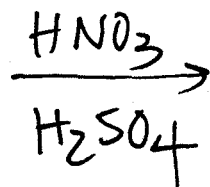


Expect twice as much ortho as para substitution -

2 ortho positions  
1 para position.



61% ortho    39% para



50% ortho    50% para



18% ortho    82% para

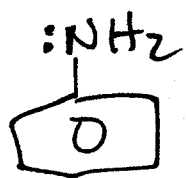
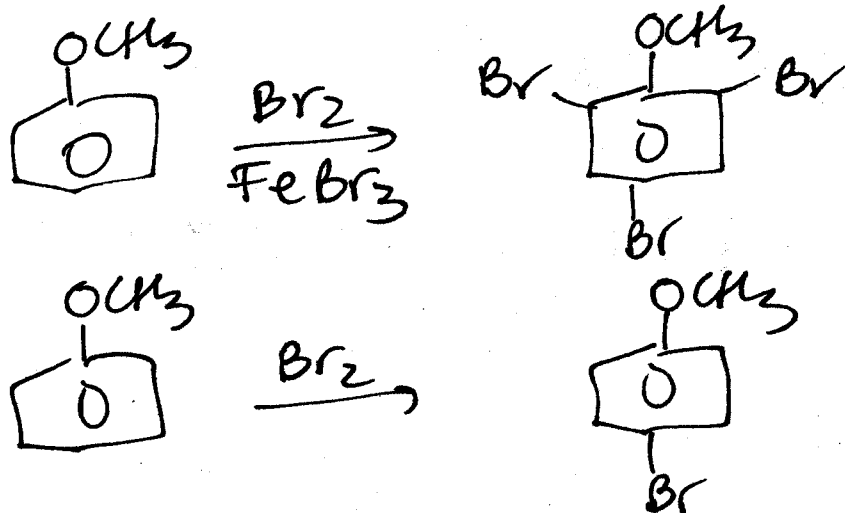
Why?

STERICS

In general - para is the major product

other considerations:

- when halogenating compounds w/ strong activators (OH, OR) - don't use the Lewis acid!



- a) can't be nitrated because 1° amines easily oxidized

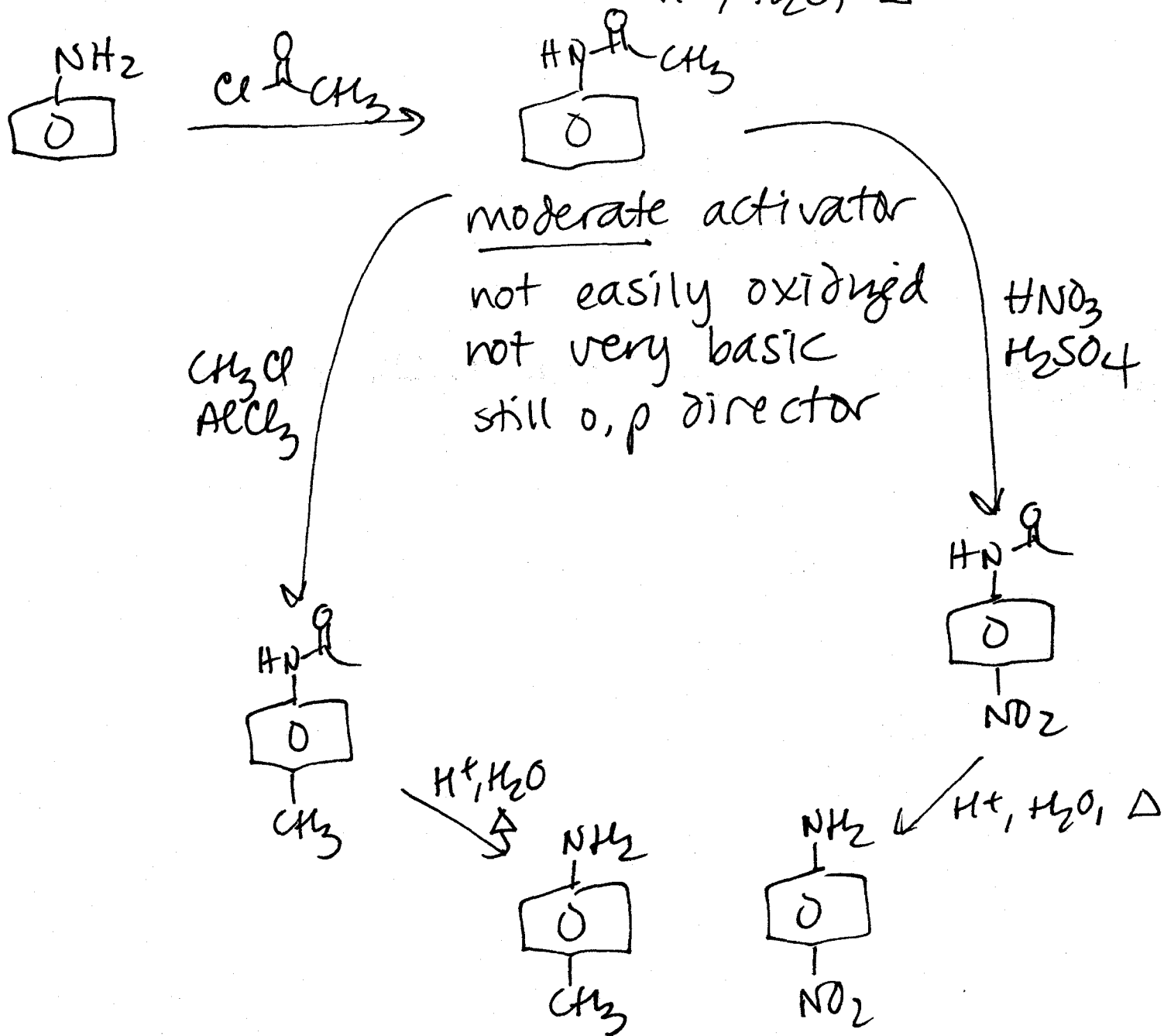
( $\text{HNO}_3$  is an oxidizer)

- b) can't do Friedel-Crafts - because N is a good base. Reacts w/  $\text{AlCl}_3$

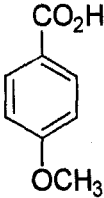
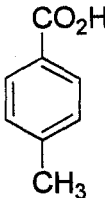
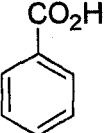
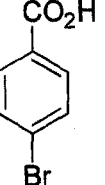
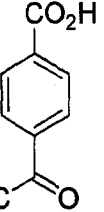
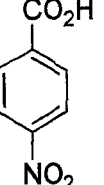
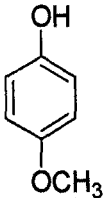
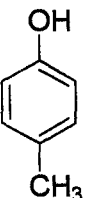
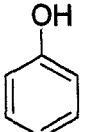
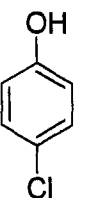
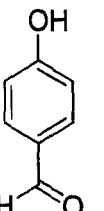
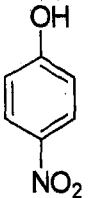
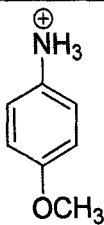
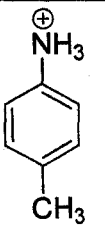
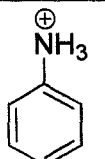
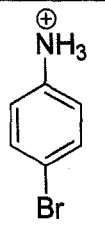
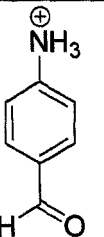
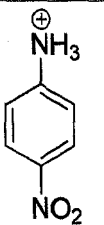


pos. charged N is strong deactivator

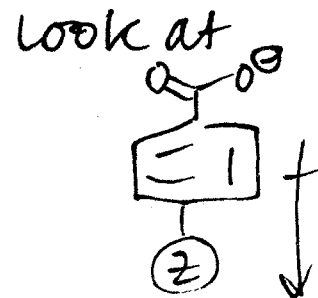
workaround: amine + acid chloride  $\rightarrow$  amide



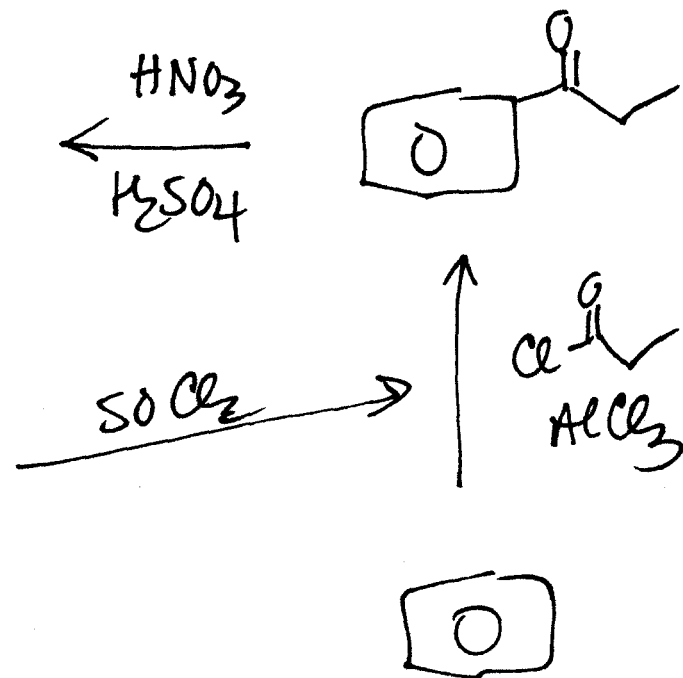
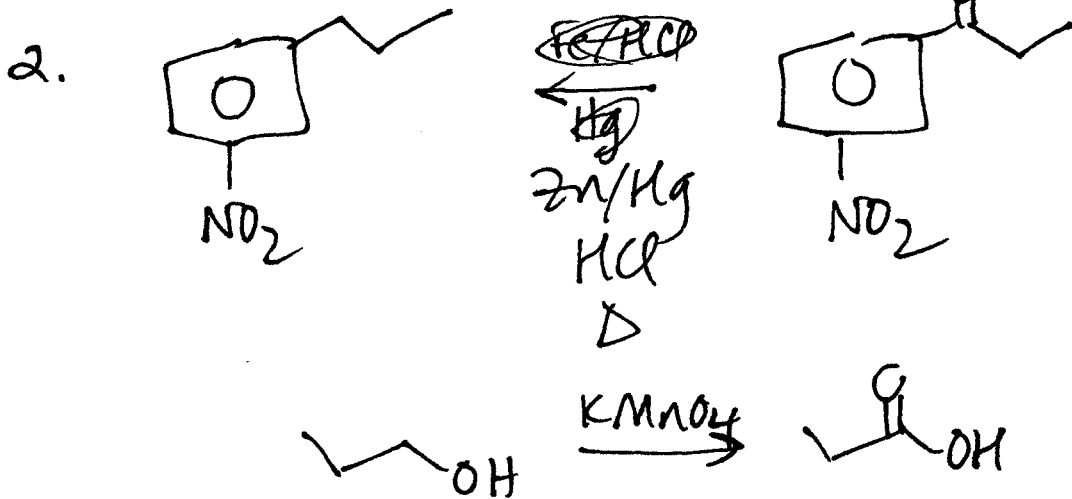
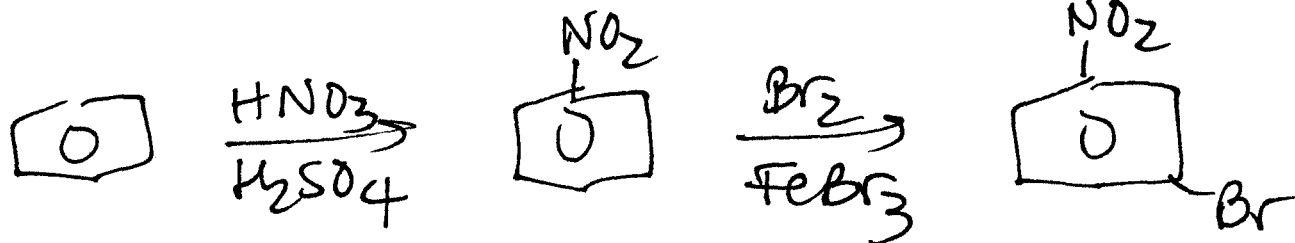
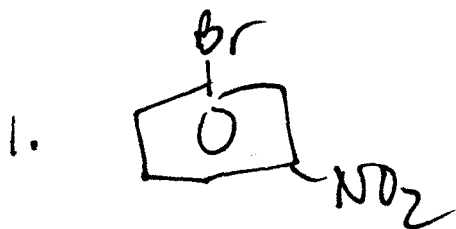
# Effect of substituents on $pK_a$

					
4.47	4.34	4.20	4.00	3.70	3.44
					
10.20	10.19	9.95	9.38	7.66	7.14
					
5.29	5.07	4.58	3.91	1.76	0.98

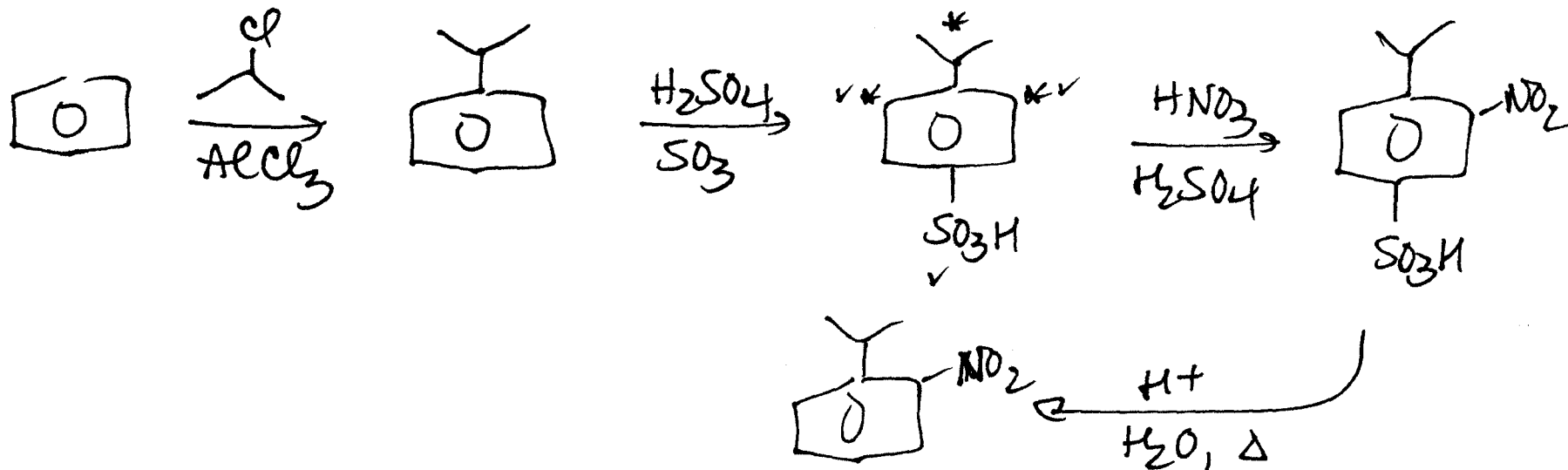
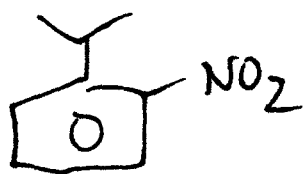
$e^-$  donors decrease acidity  
 $e^-$  withdrawers increase acidity



# Syntheses



3.

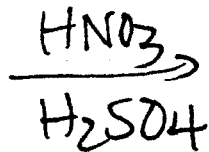
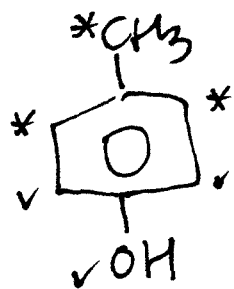


Directing Effects w/ Lots of Substituents

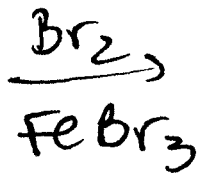
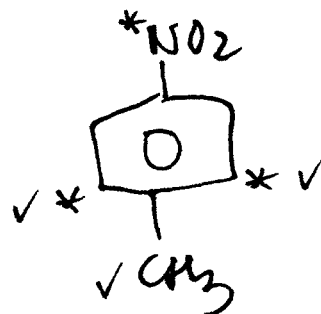
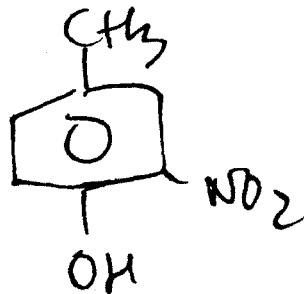
- consider directing effects of each individual substituent

- reinforcing - GOOD

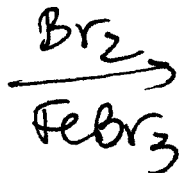
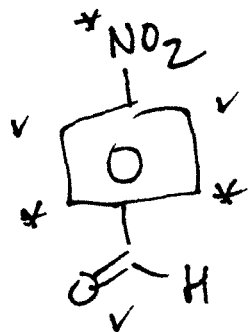
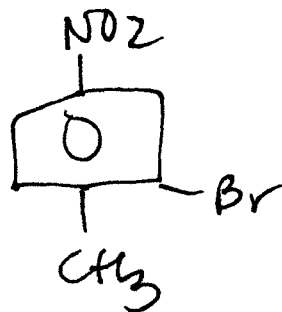
- conflicting - NOT SO GOOD - whichever subst. is higher up on the table (best activator) wins.



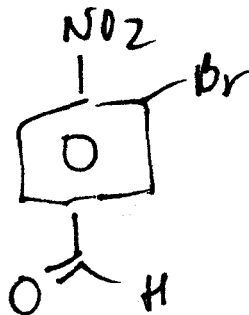
?



?



?



strong  
act.



strong  
deact.