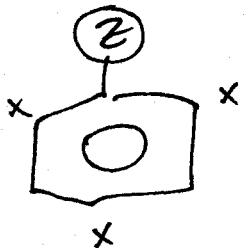


Ortho vs. Para Substitution

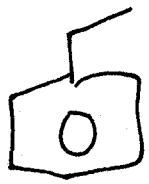


Expect twice as much ortho as para substitution -

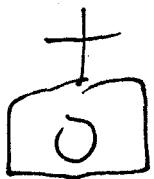
2 ortho positions
1 para position.



61% ortho 39% para



$\xrightarrow[\text{H}_2\text{SO}_4]{\text{HNO}_3}$
50% ortho 50% para



18% ortho 82% para

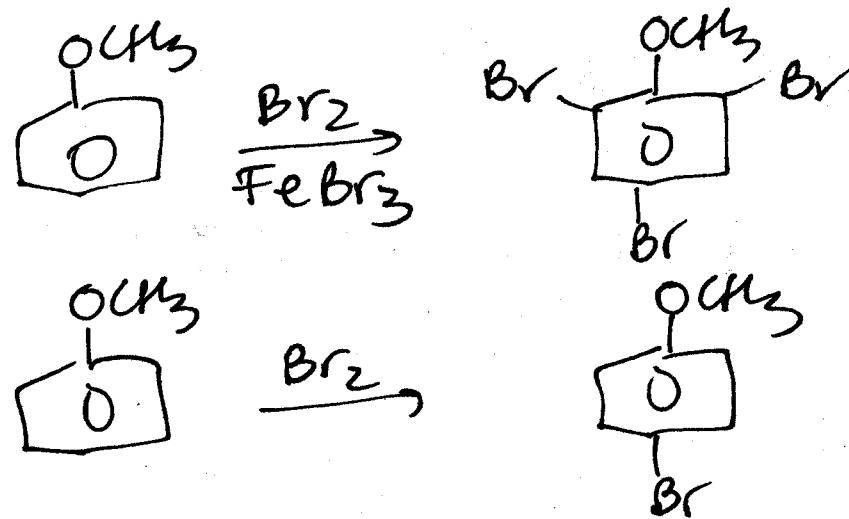
Why?

sterics

In general - para is the major product

other considerations:

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

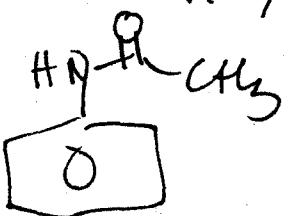
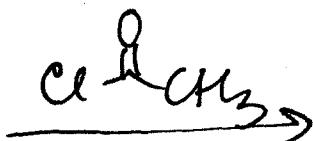
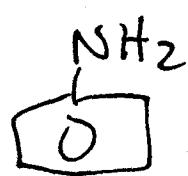


- a) can't be nitrated because 1° amines easily oxidized

(HNO₃ is an oxidizer)

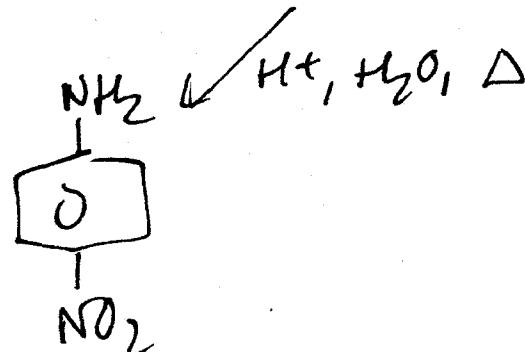
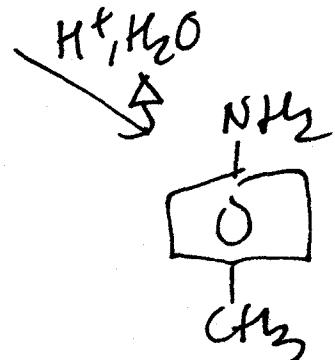
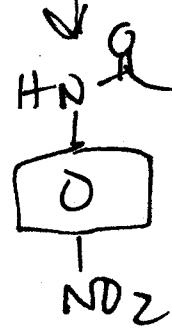
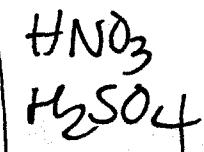
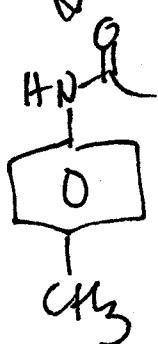
- b) can't do Friedel-Crafts - because N is a good base. Reacts w/ AlCl₃
- $\text{N}^{\oplus}\text{AlCl}_3$ pos. charged N is strong deactivator

workaround: amine + acid chloride \rightarrow amide



moderate activator

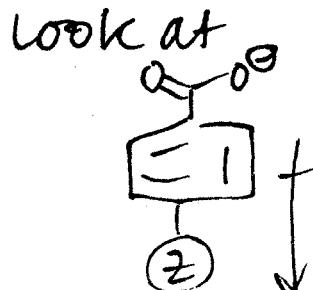
not easily oxidized
not very basic
still o, p director



Effect of substituents on pK_a

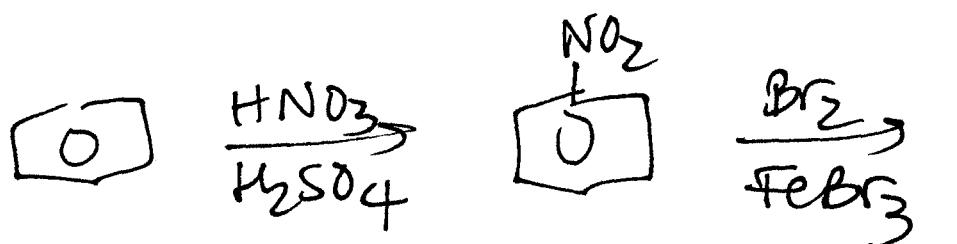
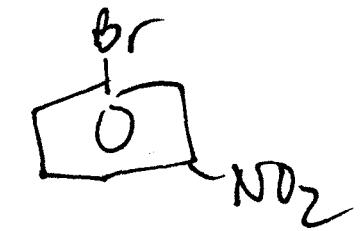
<chem>Oc1ccccc1C(=O)O</chem>	<chem>Cc1ccccc1C(=O)O</chem>	<chem>c1ccccc1C(=O)O</chem>	<chem>Brc1ccccc1C(=O)O</chem>	<chem>CC(=O)c1ccccc1C(=O)O</chem>	<chem>[N+](=O)[O-]c1ccccc1C(=O)O</chem>
4.47	4.34	4.20	4.00	3.70	3.44
<chem>Oc1ccccc1O</chem>	<chem>Cc1ccccc1O</chem>	<chem>c1ccccc1O</chem>	<chem>Clc1ccccc1O</chem>	<chem>CC(=O)c1ccccc1O</chem>	<chem>[N+](=O)[O-]c1ccccc1O</chem>
10.20	10.19	9.95	9.38	7.66	7.14
<chem>[NH3+]c1ccccc1O</chem>	<chem>[NH3+]Cc1ccccc1O</chem>	<chem>[NH3+]c1ccccc1</chem>	<chem>[NH3+]Br</chem>	<chem>[NH3+]CC(=O)c1ccccc1O</chem>	<chem>[NH3+]c1ccccc1[N+](=O)[O-]</chem>
5.29	5.07	4.58	3.91	1.76	0.98

σ^+ donors decrease acidity
 σ^- withdrawers increase acidity

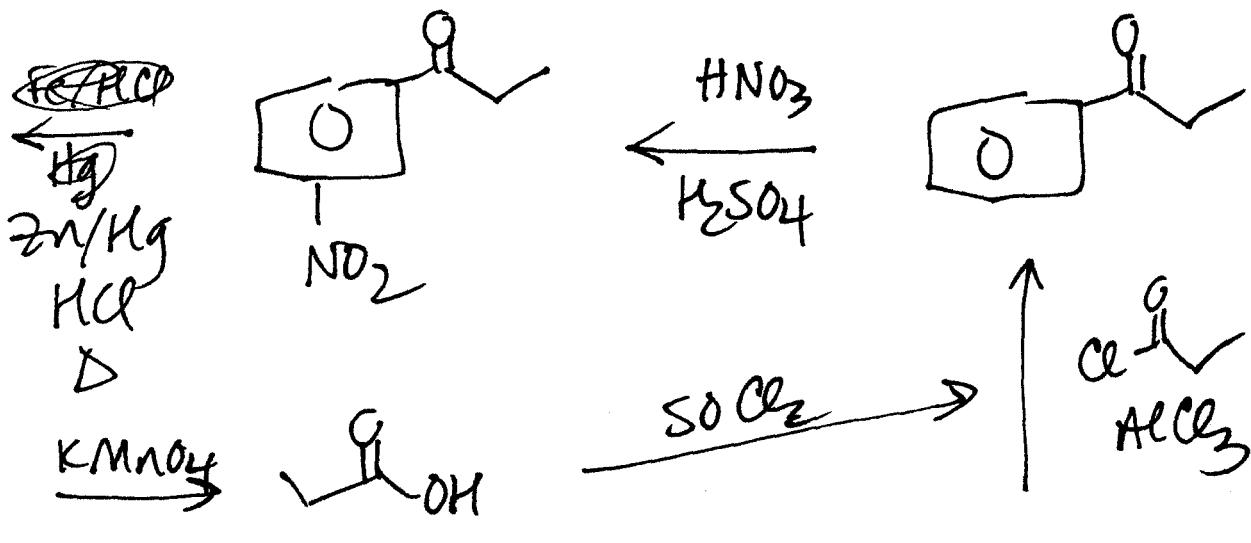
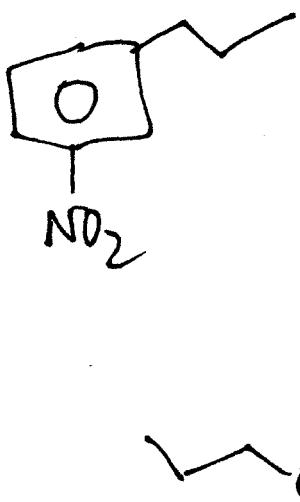


Synthesis

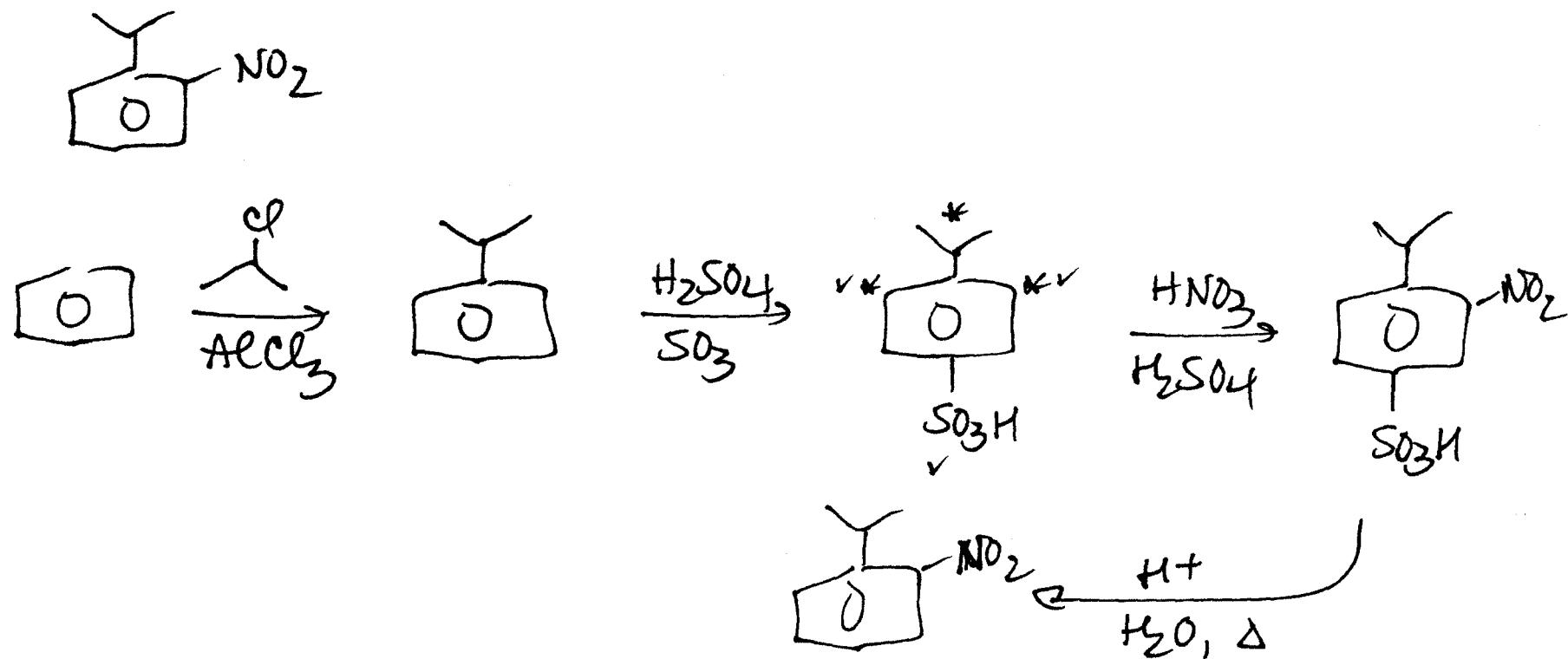
1.



2.

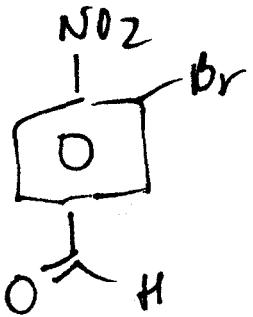
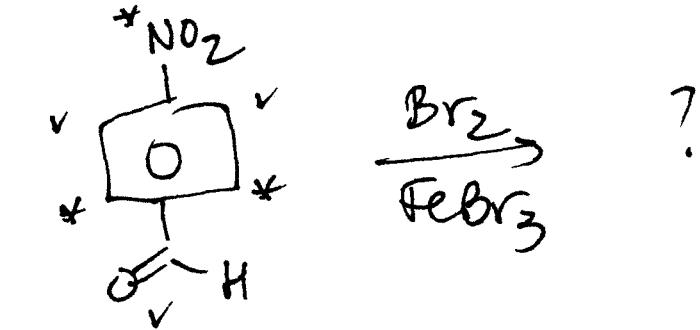
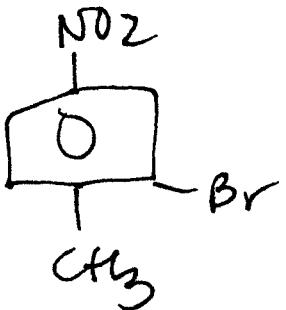
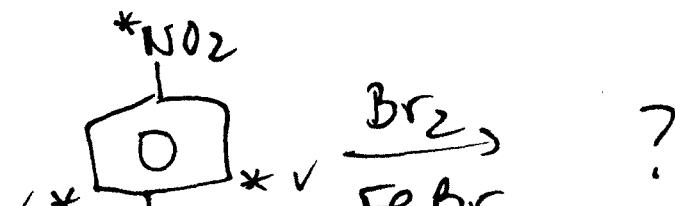
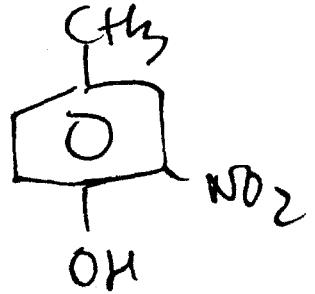
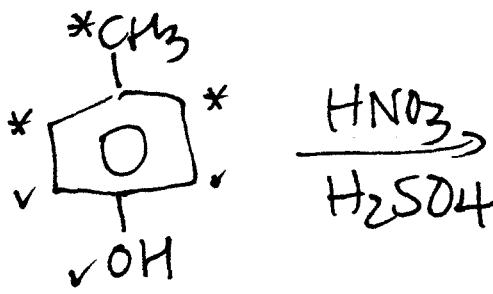


3.



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
react.