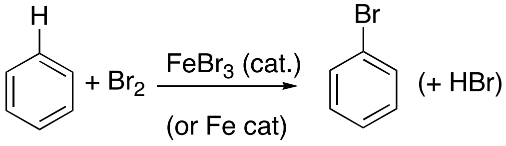
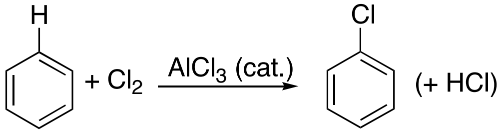
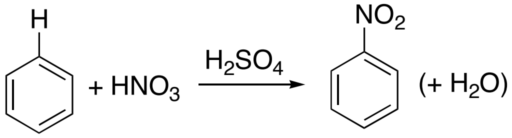
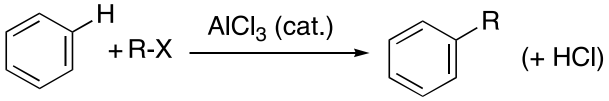
5 Major Electrophilic Aromatic Substitution Reactions

		Activating/ Deactivating	**Ortho/Para Or Meta Directing**	**Book**
1		Deactivating	Ortho/Para	17.2
		Deactivating	Ortho/Para	17.2

The halides are unique in being deactivating but ortho/para directing. All other o/p-directors are activating, and all other deactivating groups are m-directors. **Mech**

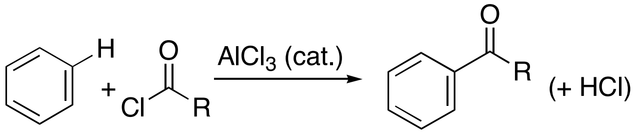
2		Deactivating	Meta	17.3

The product can be reduced to Ar-NH_2 by Fe/HCl or Sn/HCl. Nitration/Reduction provides an effective way to introduce an NH_2 group. Reduction converts m-directing NO_2 group into an o/p-directing NH_2 group. **Mech required.**

3		**Activating**	Ortho/para	17.10

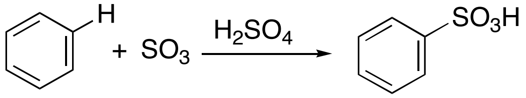
a. Restricted to 3°, 2°, or ethyl halides. 1° halides suffer carbocation rearrangements.
b. Since product is more active than starting material, polyalkylation is often a serious problem.
c. Fails with strongly deactivated benzenes.

Mech required.

4		Deactivating	Meta	17.11

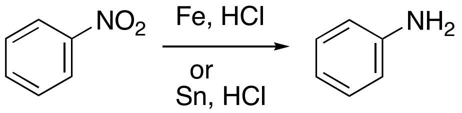
a. The product can be reduced to -CH_2R by Zn(Hg)/HCl.
b. The acylation-reduction sequence provides an effective way to introduce a 1° alkyl group.
c. Reduction converts meta-directing acyl group into an ortho/para-directing alkyl group.

Mech required.

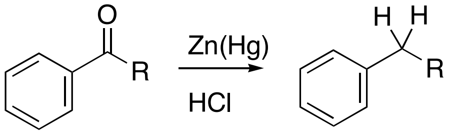
5		Deactivating	Meta	17.4

The sulfonyl group is a useful para-blocking group, since it can later be removed upon treatment with H_2O/H^+. **No mech required.**

5 Major Aromatic Support Reactions

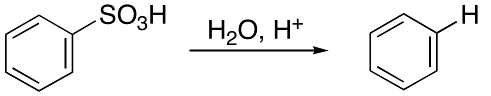
		Activating/ Deactivating	**Ortho/Para Or Meta Directing**	**Book**
6		Activating	Ortho/Para	19.21

- Reduction converts meta-director into an ortho-para director.
- Fe, Sn, or several other reducing metals can work. No mech required.

7		Activating	Ortho/Para	17.12

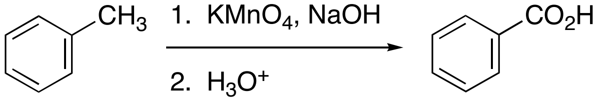
- Clemmensen reduction converts meta-director into an ortho-para director.
- Acylation (#4) followed by Clemmensen Reduction (#7) is the standard method for introducing a 1° alkyl group. (Direct alkylation with a 1° alkyl halide, reaction #3, fails due to cation rearrangement problems…)

No mech required.

8		------	------	17.4

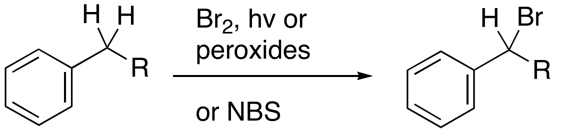
- The sulfonyl group is a useful and reversible para-blocking group, since it can be temporarily put on (reaction 5) but then can be removed later upon treatment with H_2O/H^+ (reaction 8).
- The sulfonation/other reaction/desulfonation sequence is crucial for clean ortho-substitution of an o/p director.

No mech required.

9		Deactivating	Meta	17.14

- Oxidation converts ortho/para-director into a meta-director.
- Side alkyl chains longer than methyl can also be oxidized to benzoic acid in the same way, although more time and heat is required.
- For test purposes, just writing $KMnO_4$ will be OK. But the real reaction requires a basic solution for the $KMnO_4$ to work, so an acidic workup step is actually required to isolate the neutral carboxylic acid.

No mech required.

10		------	------	17.14

- Bromination occurs via free-radical mechanism.
- It is selective for substitution at the benzylic position because the benzylic radical intermediate is resonance-stabilized.
- Note: keep distinct $Br_2/FeBr_3$ from Br_2/peroxides!
- Product is subject to S_N2 substitutions (benzylic bromides are especially good, better than normal 2° bromides) and E2 eliminations with bulky bases.
- "NBS" is N-bromosuccinimide, which functions just like Br_2/peroxides, but is much more convenient and cleaner because it avoids competing reactions caused by lots of Br_2 and HBr.

Mech required.