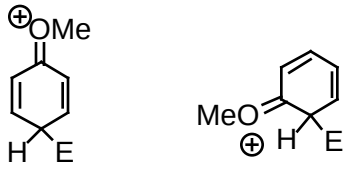
Chemistry 304B, Spring 1999 Lecture Notes 12

Review sessions:
Saturday: 3 pm Rm 124
Sunday: 8 pm Rm 324

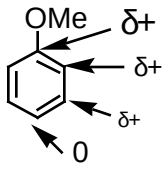
Exam: 7:30 pm-9:30 pm "Open book"
Anything that is not alive.

From last time:

Resonance effects:



Inductive effects:



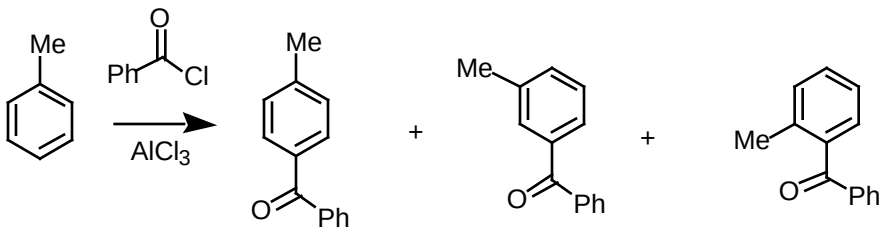
Ortho and para position **activated** by resonance donation from -OMe

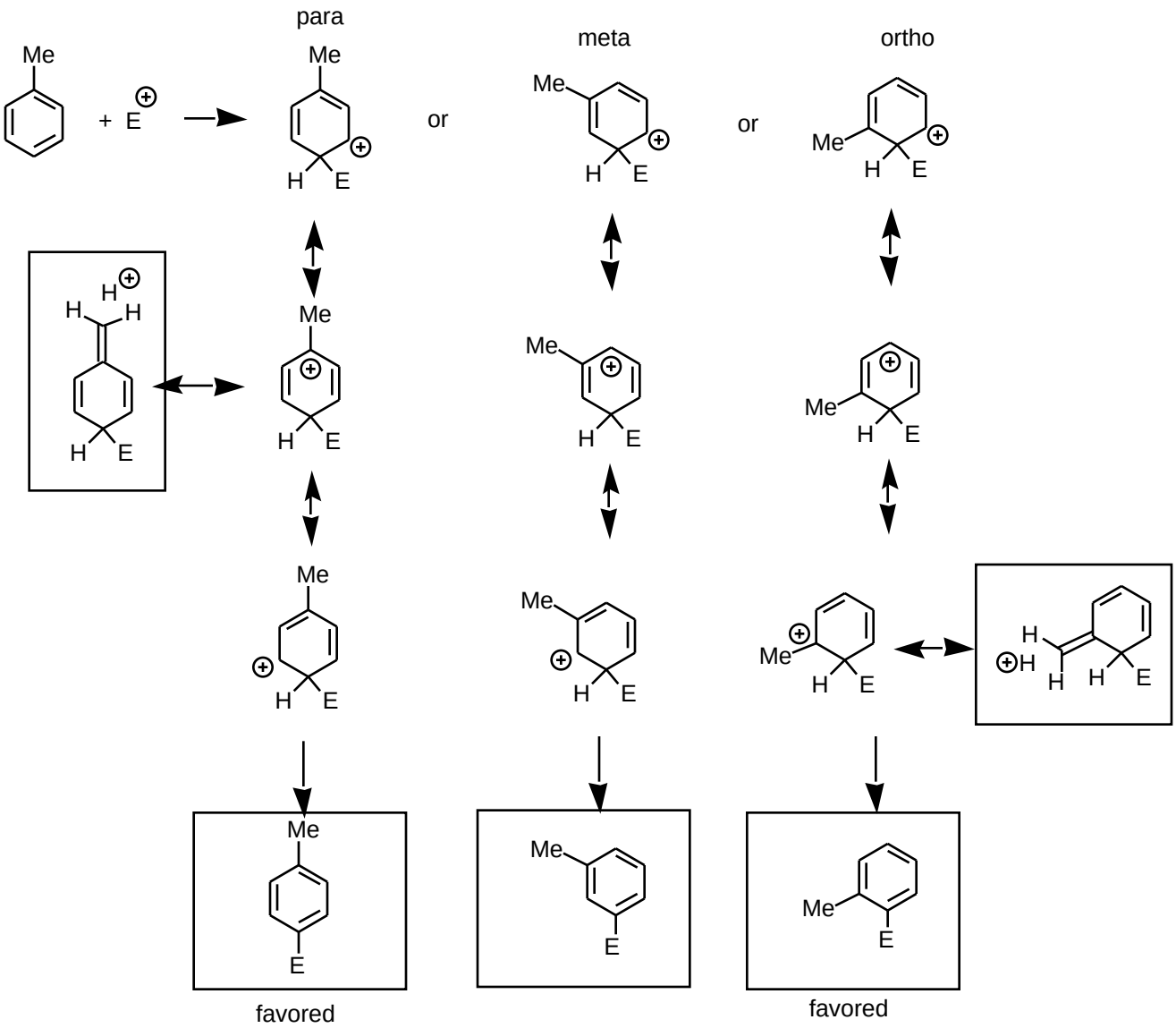
Ortho position **deactivated** by (1) inductive withdrawal and
(2) steric hindrance in the approach of the electrophile

What about rate effects? -OMe gives strong acceleration.
TS energy for *para/ortho* is lowered by resonance interaction of cation with -OMe

Inductive and resonance effects oppose each other in the case of a -OMe substituent--
how to know which dominates?
Do the experiment and memorize the result → resonance dominates for -OMe
Strong rate acceleration, strong o/p director

Methyl (toluene):



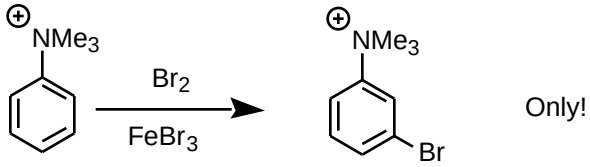


Note: Me has no inductive effect. Ortho is still <u>disfavored</u> relative to para. Must be a <u>steric effect.</u>

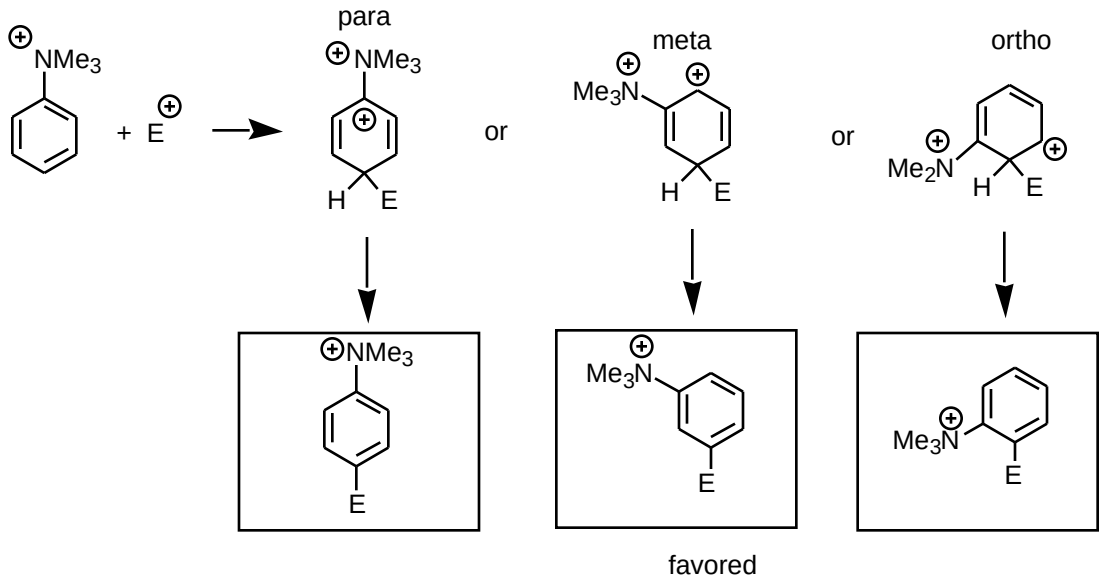
"Extra" resonance structures for *para* and *ortho* substitution (hyperconjugation).

Accelerate the reaction moderately

Trimethylammonium Ion



Only!



$^{+}NMe_3$ is a strong meta director. More precisely, it is a strong inhibitor of substitution o/p
Overall reduction in rate of substitution.

Also:see Table 14.1

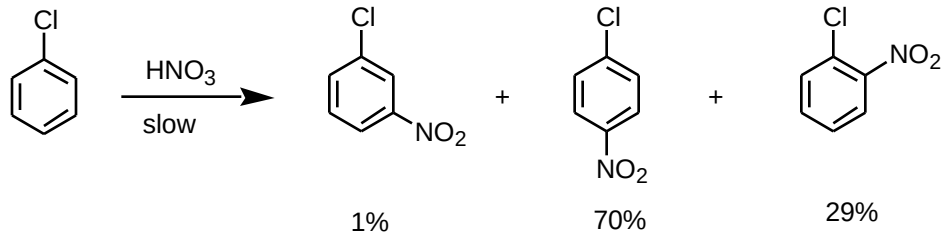
$^{+}NMe_3$, $-NO_2$, -CN, SO_2OH, acyl, $-CF_3$ → reduce the rate and prefer META addition
Inductive withdrawing (all)
Resonance withdrawing (some of them)

$-NH_2$, $-NMe_2$, -OH, -alkyl → increase the rate and prefer ORTHO/PARA addition.

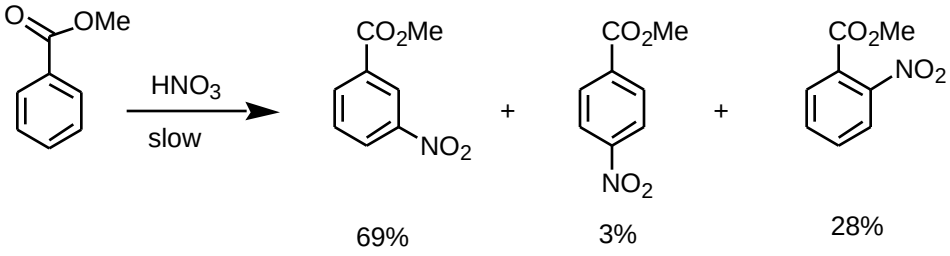
Halides: Dominant inductive effect → reduce the rate of addition

BUT: the halide atoms (F > Cl > Br > I) show (weak) resonance donation. Addition at all positions is slowed by the general inductive effect, but addition at ortho/para is selectively increased (partially compensated) by resonance donation.

Reverse of the effect with -OMe.
The halides slow the rate of addition of electrophiles BUT show ortho/para selectivity.



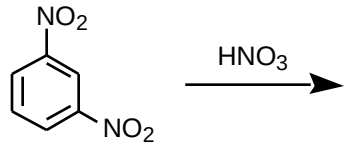
Acyl groups:

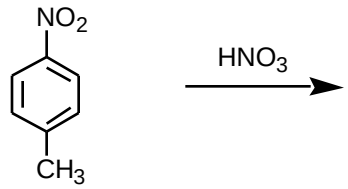


Why both META and ORTHO?

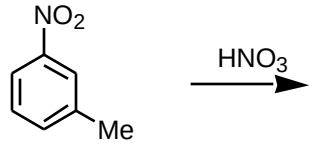
Multiple Substituents: Balancing effects.

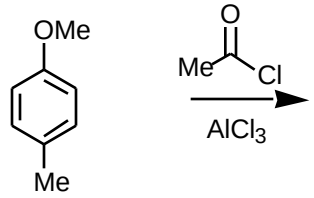
Easy ones:





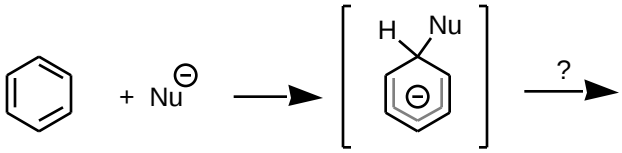
Conflicting:

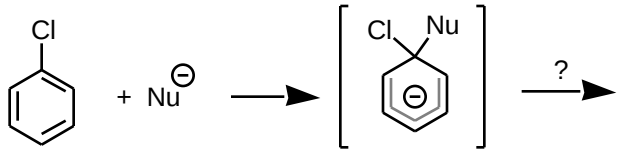




Read pp 665-670 for more examples and control strategies.

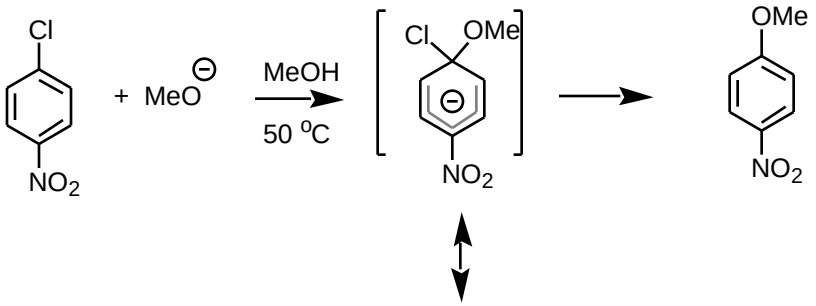
What about the reverse reactivity? Nucleophilic Aromatic Substitution

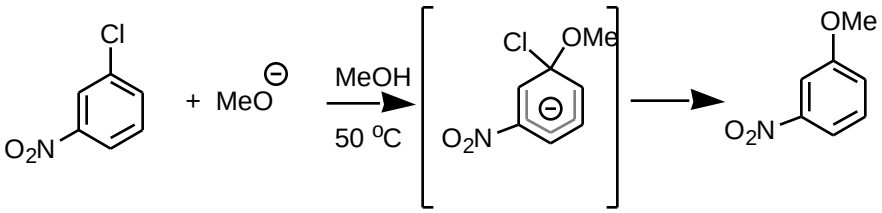


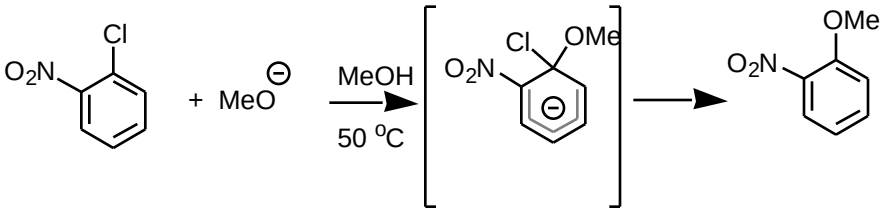


Need to stabilize the anionic intermediate (and TS leading to it)

Nitro group is strongly activating:







Other electron withdrawing groups can also activate aryl halides toward nuclophilic addition, but often the group itself reacts with the nucleophile. Nitro is the most common successful one.

Summary: S_NAr is possible if one (or more) strongly electron withdrawing groups is present and oriented ortho or para to a good leaving group (halide).
"Site specific substitution--direct replacement of a leaving group.

Odd case: