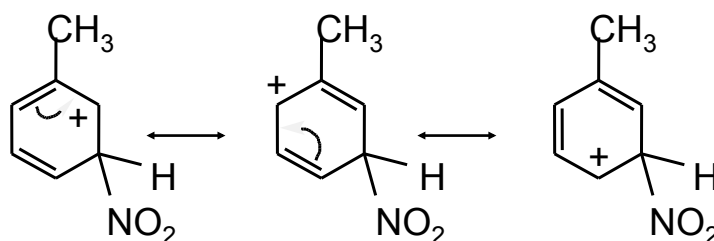


## Lecture 11

## EAS



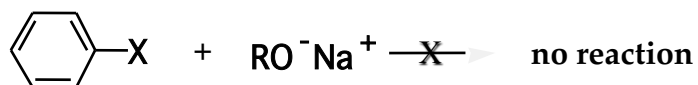
February 23, 2016

Chemistry 328N



## Synthesis: Alkyl-Aryl Ethers

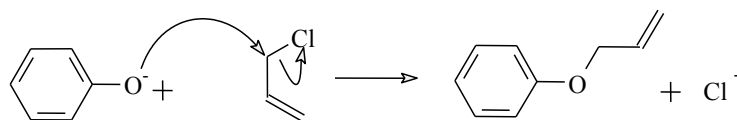
- Alkyl-aryl ethers can be prepared by the Williamson ether synthesis
  - but only using phenoxide salts and alkyl halides
  - **aryl halides are unreactive to  $S_N2$  reactions**



Chemistry 328N



## Alkyl-Aryl Ethers



$\text{S}_{\text{n}}2$  reactions are accelerated by:

- polar aprotic solvents

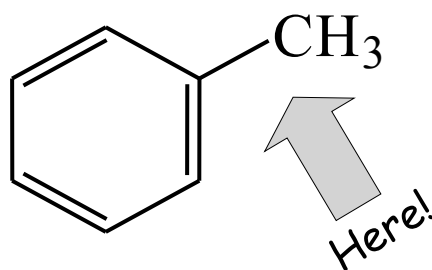
Remember: methyl  $>$   $1^\circ >$   $2^\circ$  and  $3^\circ$  is a no go!

{Review chapter 9??}

Chemistry 328N



## Reactions at Benzyl Carbons

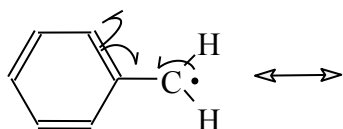


Chemistry 328N



## Benzylic Reactions

- Benzylic radicals (and cations) are easily formed because of the resonance stabilization of these intermediates
  - the benzyl radical is a hybrid of four contributing structures

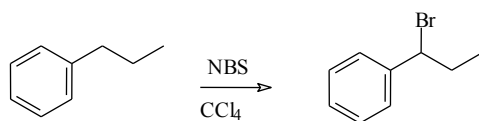


Chemistry 328N

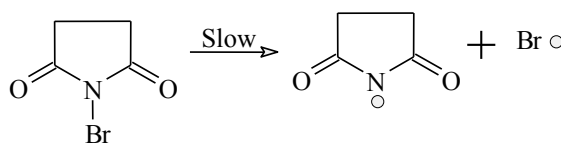


## Benzylic Bromination

- Bromination occurs by a radical mechanism



A Regioselective reaction !!



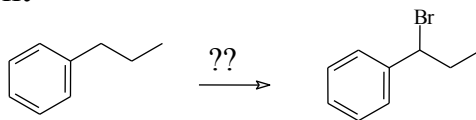
NBS = N-bromosuccinimide

Chemistry 328N

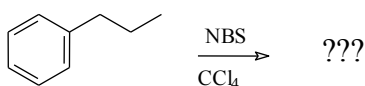


## Flash Card Tricks!!!

- front



- Back

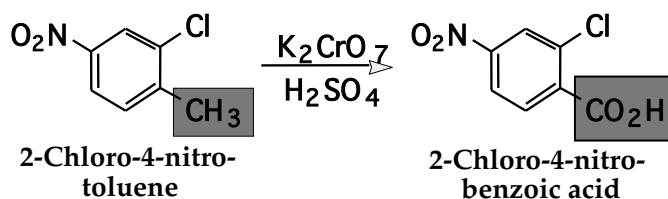


Chemistry 328N



## Benzylic Oxidation

- Benzene is unaffected by strong oxidizing agents such as  $\text{H}_2\text{CrO}_4$  and  $\text{KMnO}_4$ 
  - halogen and nitro substituents are also unaffected by these reagents
  - alkyl groups with at least one hydrogen on the benzylic carbon are oxidized to a carboxyl group

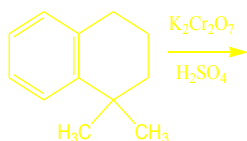
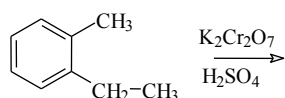


Chemistry 328N



## Benzylic Oxidation

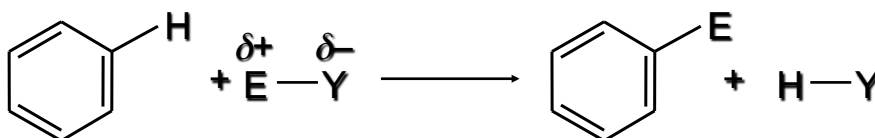
If there is more than one alkyl group on the benzene ring, each is oxidized to a  $-\text{CO}_2\text{H}$  group



Chemistry 328N



## Electrophilic Aromatic Substitution

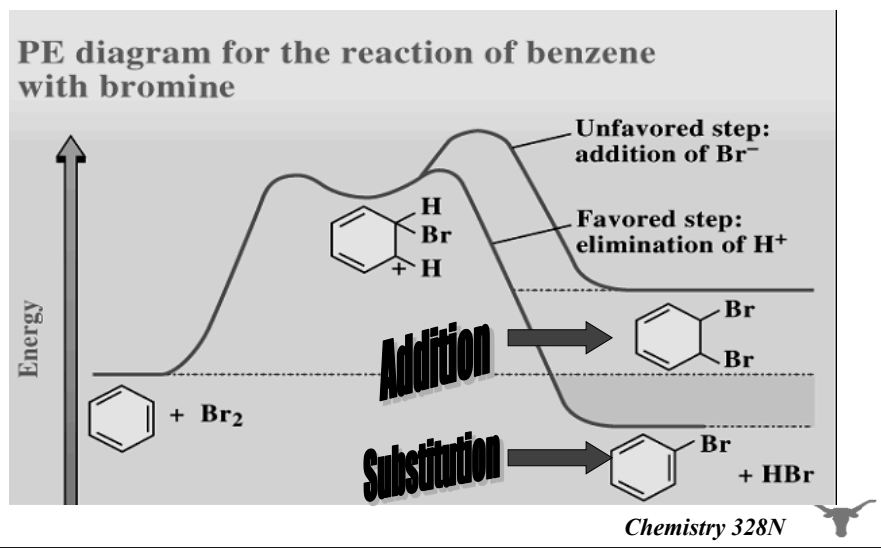


- Electrophilic aromatic substitution: a reaction in which a hydrogen atom of an aromatic ring is replaced by an electrophile
- We study
  - several common types of electrophiles,
  - how they are generated, and
  - the mechanism by which they replace hydrogen is the same for all

Chemistry 328N

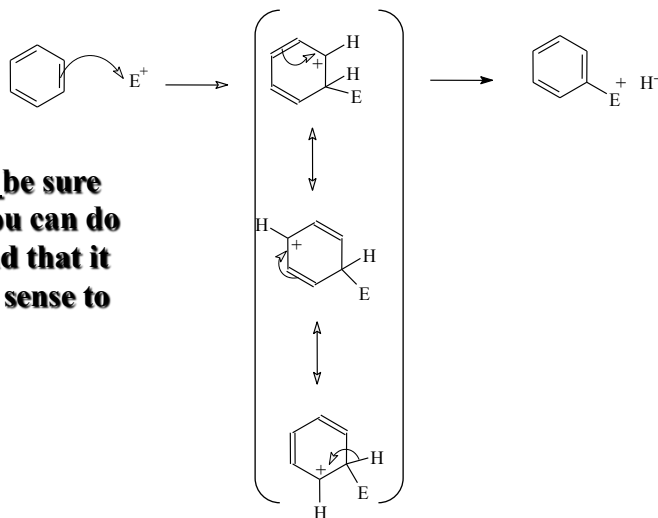


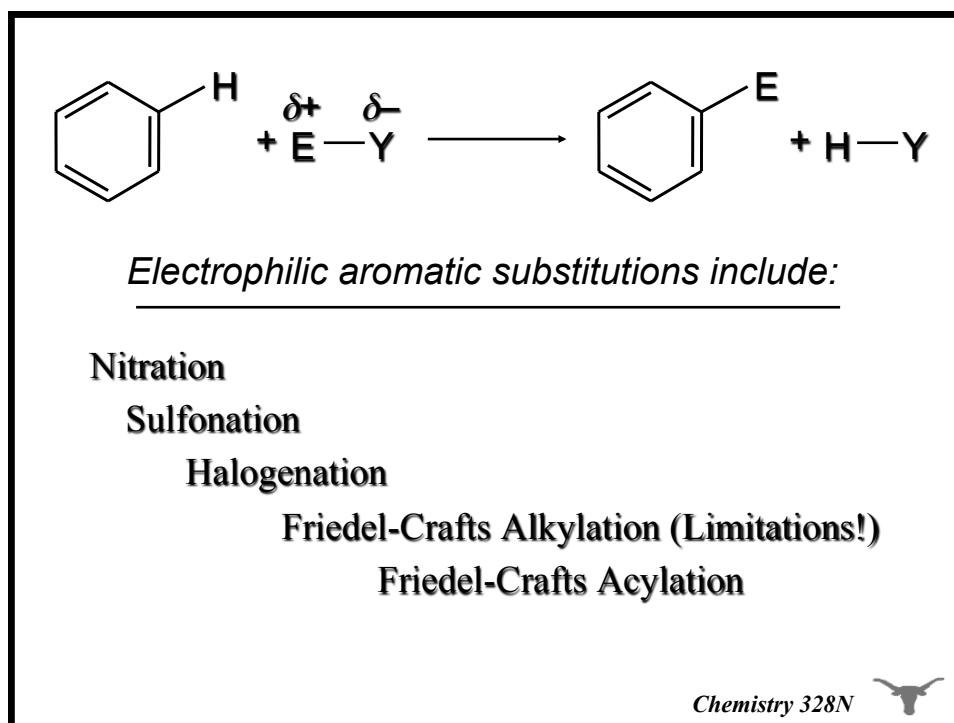
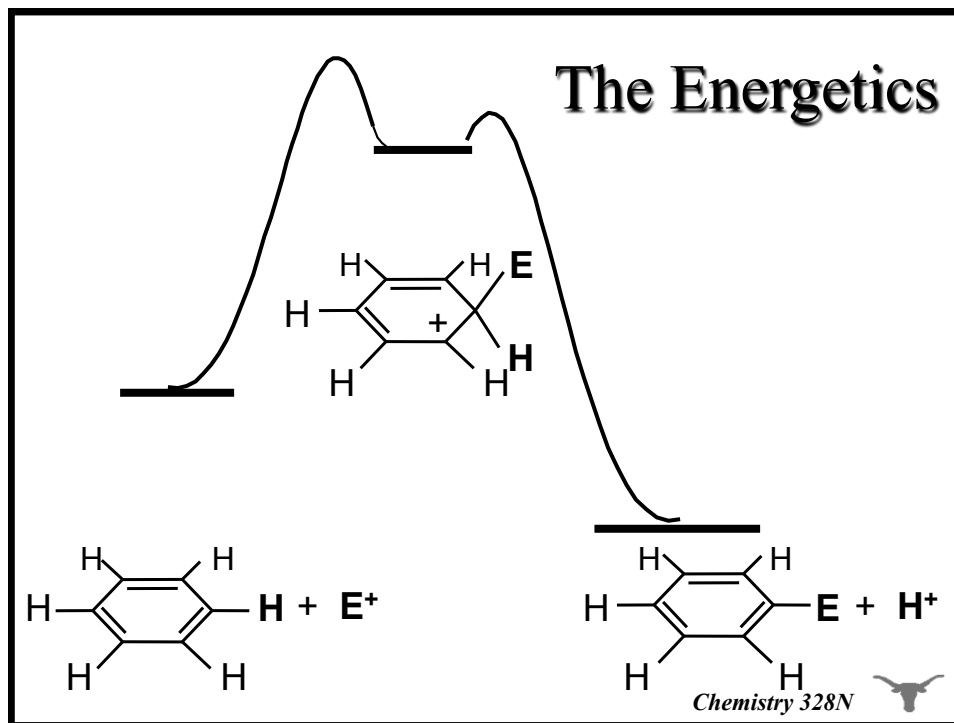
## Electrophilic Aromatic Substitution



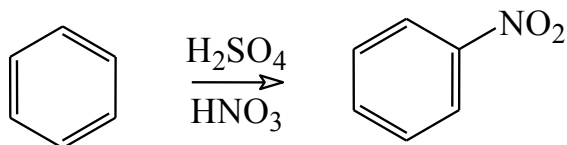
## Electrophilic Aromatic Substitution

**Please be sure that you can do this and that it makes sense to you!!**





## Nitration



Chemistry 328N



## Chlorination

- Chlorination requires requires a Lewis acid catalyst, such as  $\text{AlCl}_3$  or  $\text{FeCl}_3$

Step 1: formation of a chloronium ion

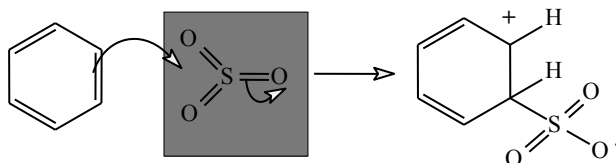
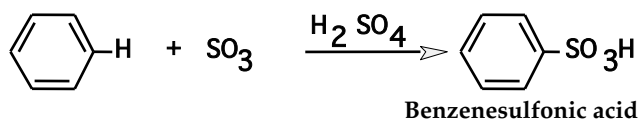
Step 2: EAS

Chemistry 328N





## Sulfonation

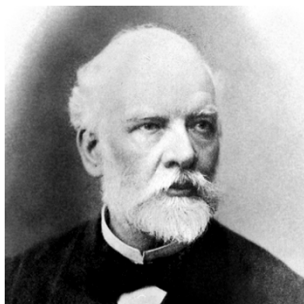


Sulfonation can be reversed by Heating in  $\text{H}_2\text{O}$

Chemistry 328N

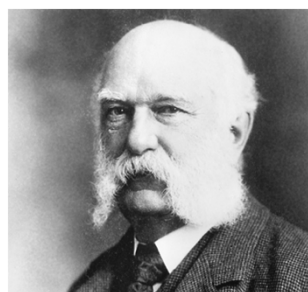


## *The Friedel-Crafts Reaction.. Circa 1877*



Courtesy Edgar Fahs Smith Collection,  
Van Pelt Library, University of Pennsylvania

Charles Friedel



Courtesy Edgar Fahs Smith Collection,  
Van Pelt Library, University of Pennsylvania

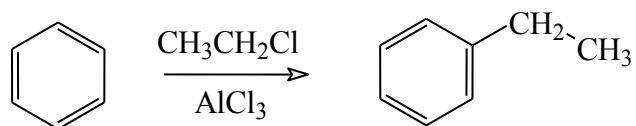
James Craft


Making C-C bonds is.... **a BIG deal**

Chemistry 328N

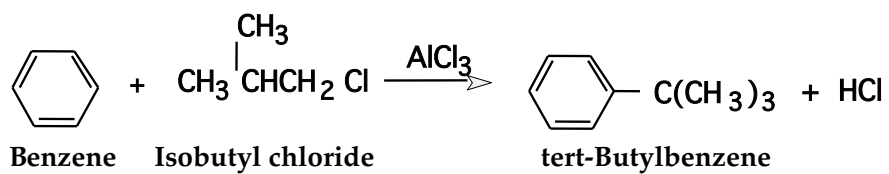



## Friedel-Crafts Alkylation



Chemistry 328N 

## Problem #1

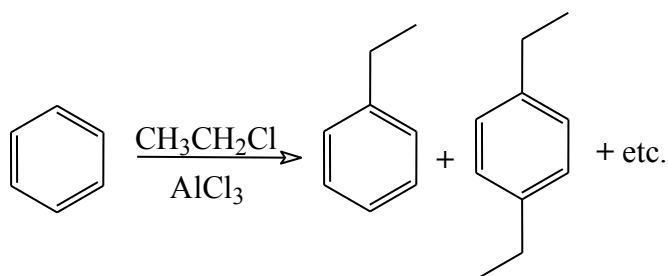


Chemistry 328N 

## Problem #2

They are tough to stop!

Product is more reactive than the starting material

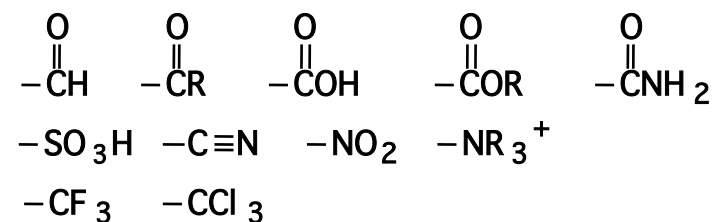


Chemistry 328N



## Problem #3

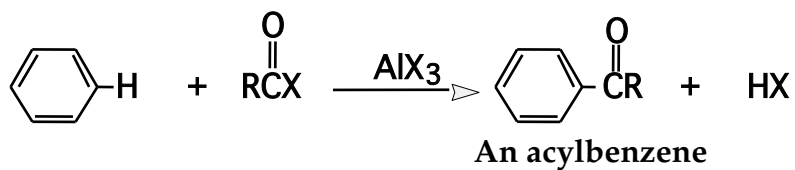
alkylation **fails** on benzene rings bearing one or more strongly electron-withdrawing groups



Chemistry 328N



## Friedel-Crafts Acylation

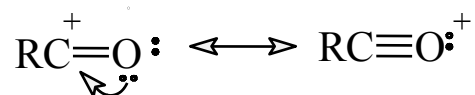


Chemistry 328N



## Friedel-Crafts Acylation

- An acylium ion is a resonance hybrid of two major contributing structures



- F-C acylations are free of ONE major limitation of F-C alkylations; acylium ions do not rearrange
- They still do not work on deactivated Rings
- They stop after one substitution

Chemistry 328N



# Hydrogenolysis

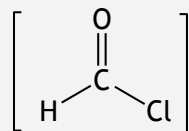


There are two nice tricks hidden here  
Please be sure to remember this reaction!!!

Chemistry 328N



# Another word of caution




Does not exist!!

Please do not propose Friedel Crafts acylation with  
Formyl Chloride as a route to aryl aldehydes.

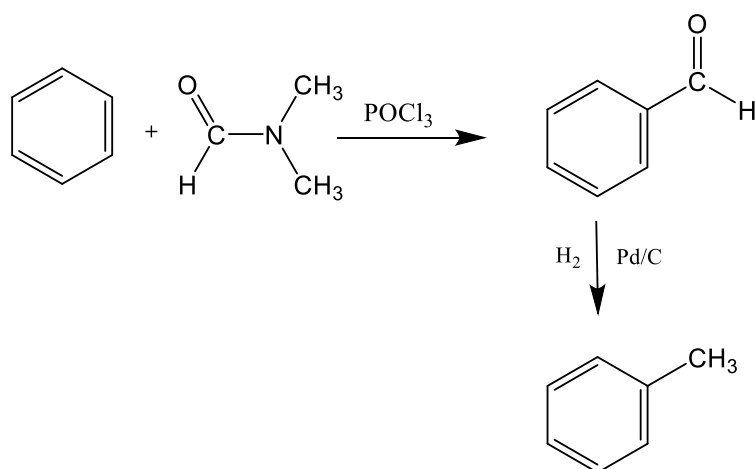
Chemistry 328N



## Gatterman-Koch Reaction

Chemistry 328N 

## Vilsmeier Reaction



Chemistry 328N 