Chem 345 – Organic Reactions
Chapter 18
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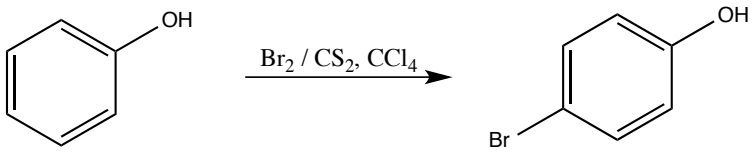
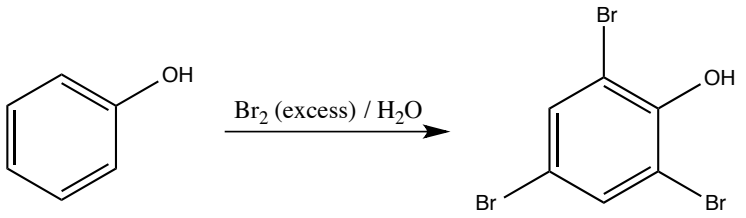
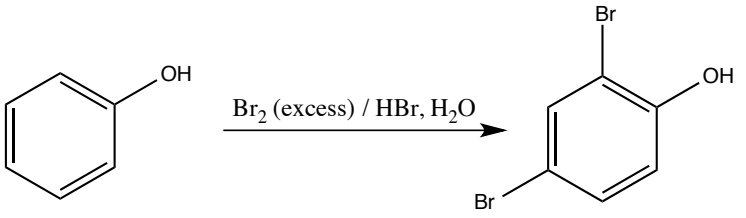
http: www.chem.wisc.edu/areas /clc (Resource page)

Phenol Reactivity Toward Electrophilic Aromatic Substitution (EAS)

Reactions:

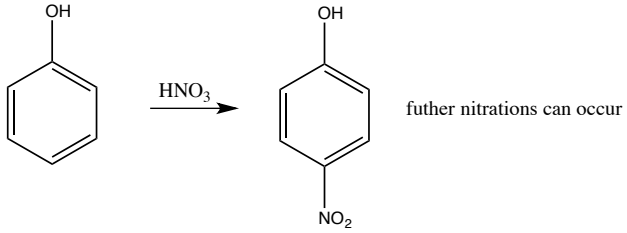




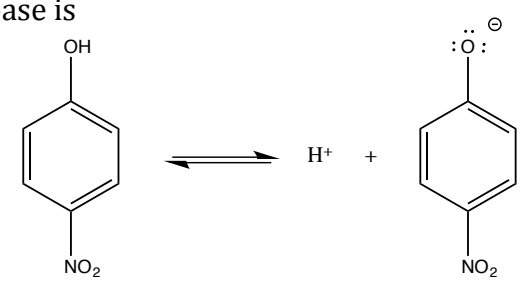


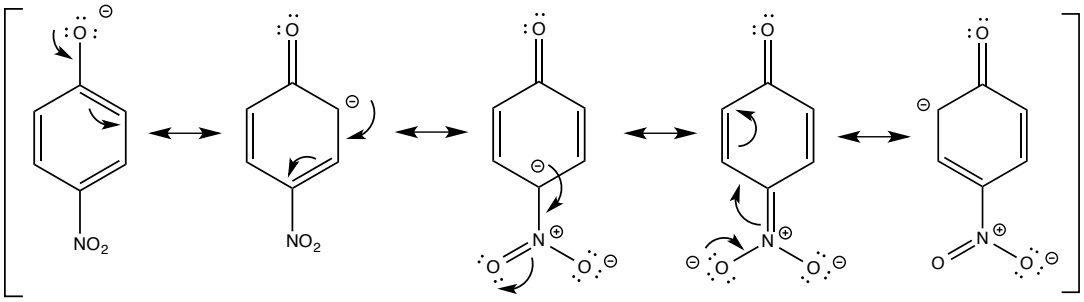
Phenols are very active in electrophilic aromatic substitution reactions. Conditions can be monitored to achieve selective substitution. The more acidic the environment where the reaction takes place the less reactive the phenol becomes. In the first example the aprotic solvents are not good at absorbing protons therefore the solution becomes acidic very fast as the reaction proceeds.

In the case of bromine and water the mono-brominated product will make the phenol more acidic – recall the inductive effect of the bromine - and easier to ionize in water. The conjugate base of a phenol is even more electrophilic so further substitutions are possible.

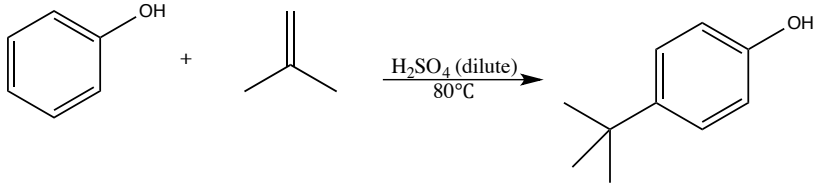


Electron withdrawing groups make phenols more acidic (see below). Notice that the conjugate base is resonance stabilized.



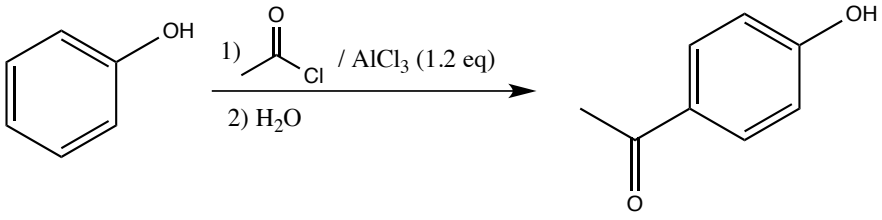


Phenols can undergo Friedel-Crafts alkylation. It's best to use reagents that can generate the electrophile without the use of Lewis acids.

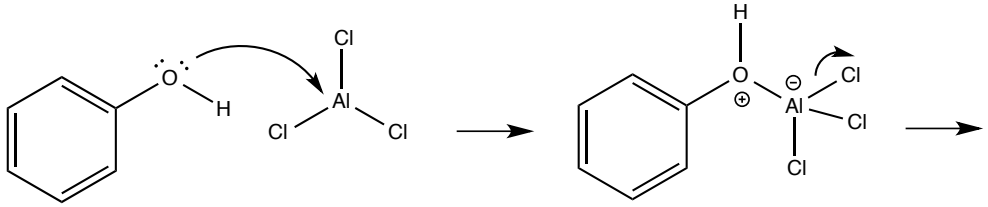


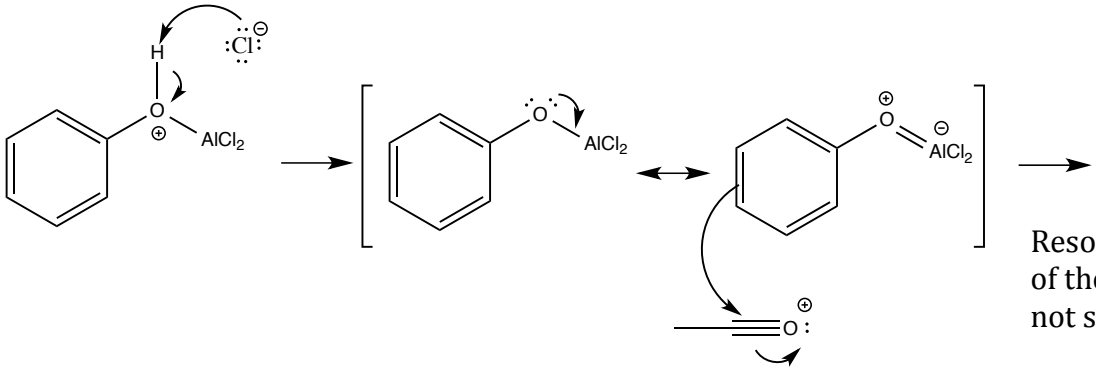
≈ 85% yield

Friedel-Crafts acylation on phenols require harsher conditions, e.g., high temperature. The phenol becomes a complex with $AlCl_3$ and consequently its activity is decreased. The major products are *mono*-acylations.



Mechanism





Resonance structures of the intermediate not shown.