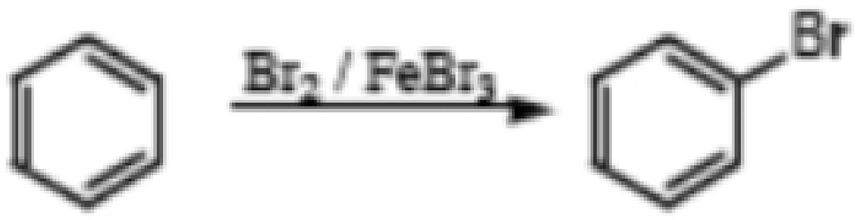
Substitution Reactions of Aromatic Compounds

Simple alkenes tend to undergo addition reactions:

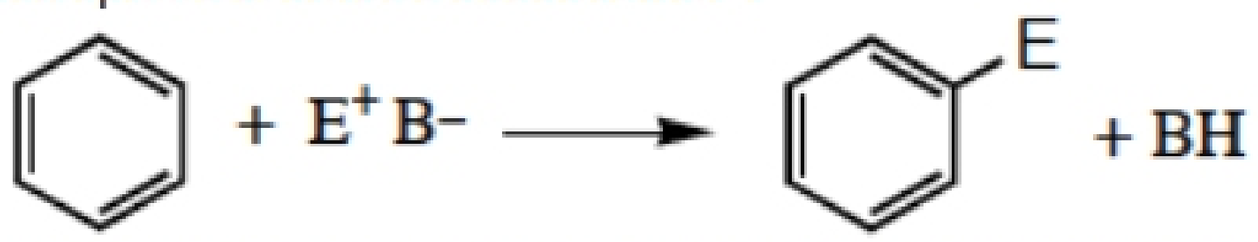
The elements of the reagent (HBr or Br_2) are simply added to the starting material. This is called, unsurprisingly, an *addition* reaction.

Aromatic compounds do not react in this manner; and it usually takes a catalyst to initiate reaction with halogens:

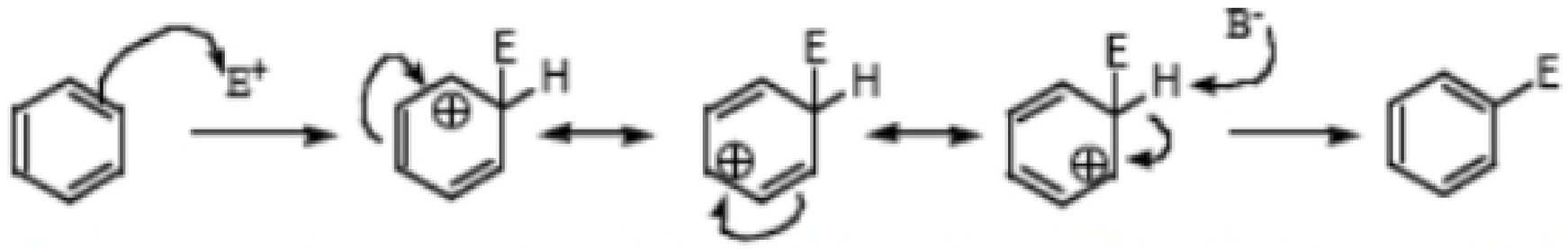


What we have done in this case is *substitute* a bromine atom for a hydrogen atom. Hence the reaction is termed an "aromatic substitution."

Because the benzene ring is quite electron-rich, it almost always behaves as the nucleophile in a reaction - which means that the substitution on benzene occurs by the addition of an electrophile to benzene; thus, the reactions are termed "electrophilic aromatic substitution":



There is basically one simple mechanism for all electrophilic aromatic substitutions:



The benzene acts as a nucleophile, attacking the electrophile with a pair of its π-electrons. This initial step destroys the aromaticity of the molecule! The resulting positive charge is delocalized over the *ortho* and *para* positions. The conjugate base of the initial electrophile then assists in removing the now extraneous proton, and restores aromaticity.

Note that addition of the conjugate base to the cyclohexadienyl cation (an addition reaction) does not occur because the addition reaction is much less exothermic than the rearomatization reaction and cannot compete with it.

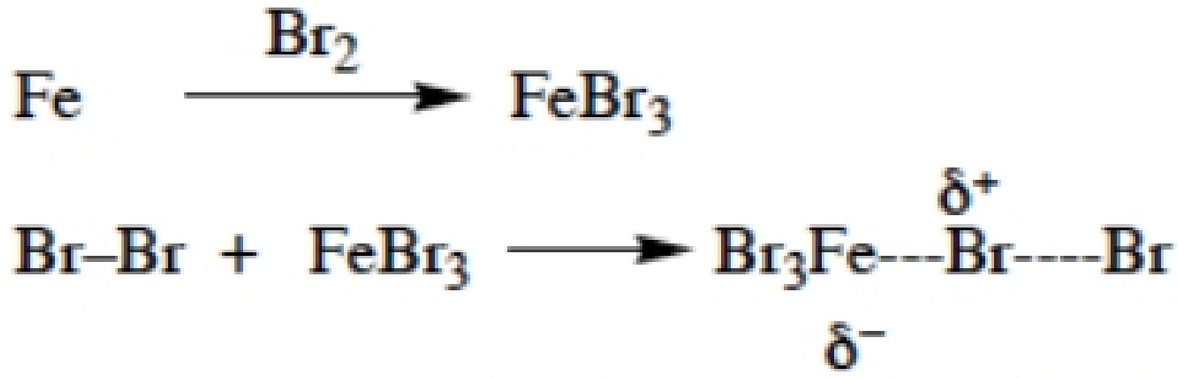
Because all electrophilic aromatic substitutions proceed in this way, the only thing that matters is the preparation of a "reactive' electrophile.

Why a "reactive" electrophile? As you can see, the first step of the reaction involves destroying aromaticity. In order to do this, there must be a

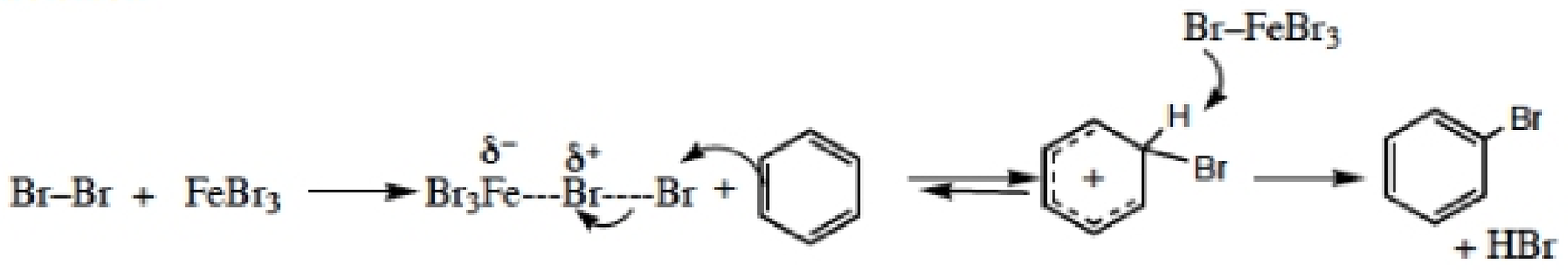
significant energetic driving force. This driving force comes in the form of a very reactive (unhappy) electrophile. How are such electrophiles generated?

Halogenation

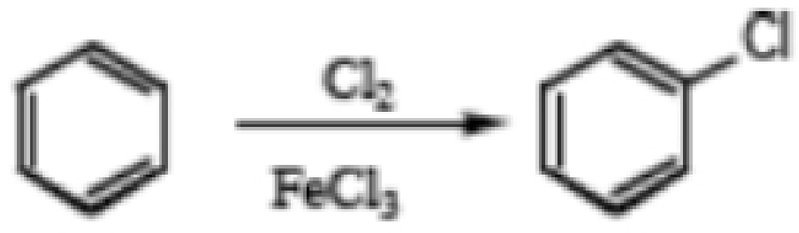
As you can imagine, halogens bearing a positive charge are particularly reactive. We will focus on preparing halogen electrophiles from Br, Cl and I.
Bromine: Allowing bromine to react with iron metal first generates $FeBr_3$, which then interacts with the remaining Br_2 to form a highly Lewis acidic system that is capable of reacting with weakly nucleophilic aromatic compounds:



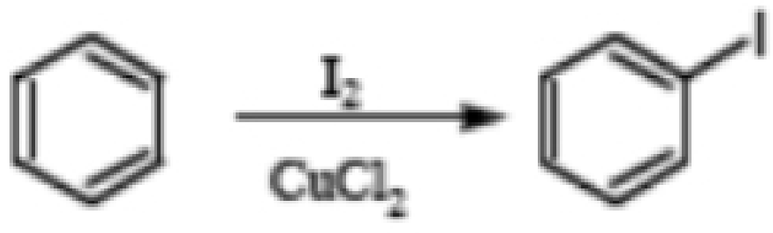
The reaction proceeds by the mechanism shown below to give brominated benzene:



Chlorine: The same chemistry shown for bromine also works with chlorine togenerate "Cl+." A mixture of benzene, chlorine and iron(III)chloride yields the chlorobenzene:

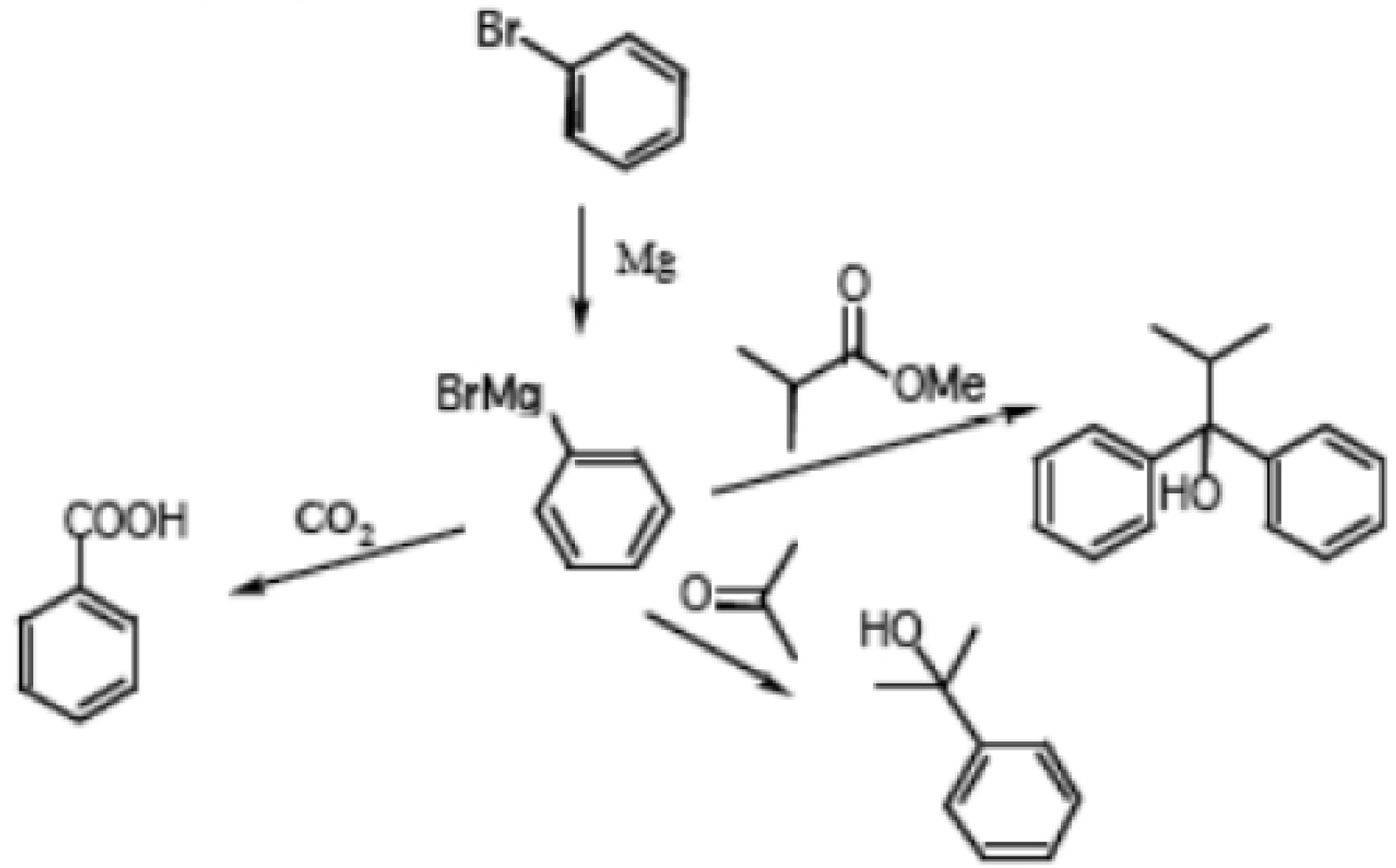


Iodine: It is a little more difficult to make iodine sufficiently electrophilic. For relatively activated compounds, where a mild source of "I+" is required, copper salts are often used as a catalyst:



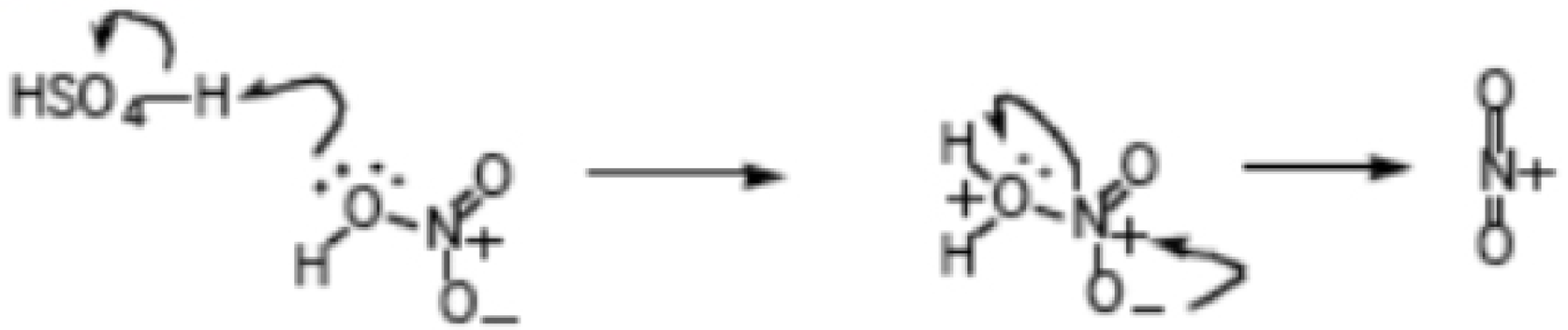
Reaction then proceeds by the standard mechanism, with I+ as the electrophile, to give iodinated benzenes.
What good are aromatic halides? The halogens are excellent synthetic "handles" – they can be easily converted into other functional groups. For

example, bromobenzenes can be turned into Grignard reagents, and then reacted with aldehydes, ketones, etc....

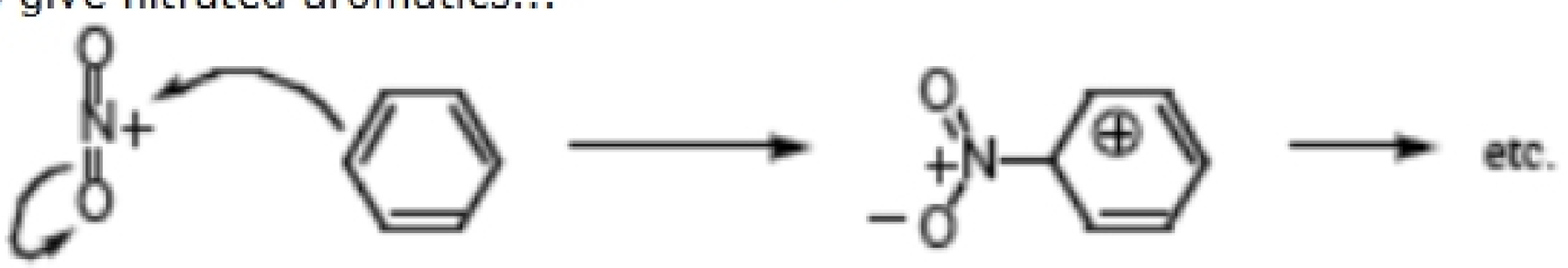


Nitration

We can also make a highly electrophilic form of NO_2 (from HNO_3/H_2SO_4), the nitronium ion:



Which can then react with aromatic compounds via the standard mechanism to give nitrated aromatics...



Why nitrate aromatics? There are a couple of good reasons to nitrate things. The first is in the manufacture of explosives – highly nitrated organic molecules are frequently used as explosives (trinitrotoluene (TNT), nitroglycerine, etc.). The second reason is that nitro-groups are generally easy to reduce to amines. And since it is nearly impossible to make an amine electrophilic (in order to add it to an aromatic ring under electrophilic aromatic substitution conditions), aromatic nitro compounds are about the only precursors to aromatic amines: