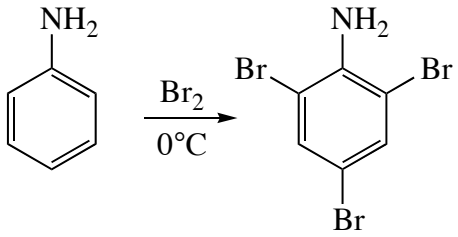
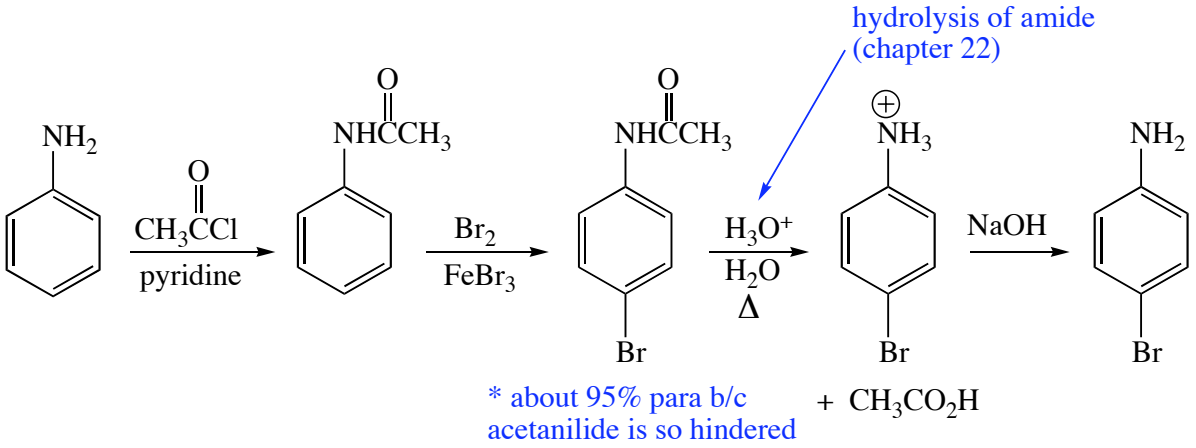
Problems with Aniline

A. Bromination Amine substituents are so strongly activating that halogenation is carried out without the Lewis acid catalyst ($FeBr_3$ or $FeCl_3$). Even at low temperature without a catalyst, multiple halogenation is observed.

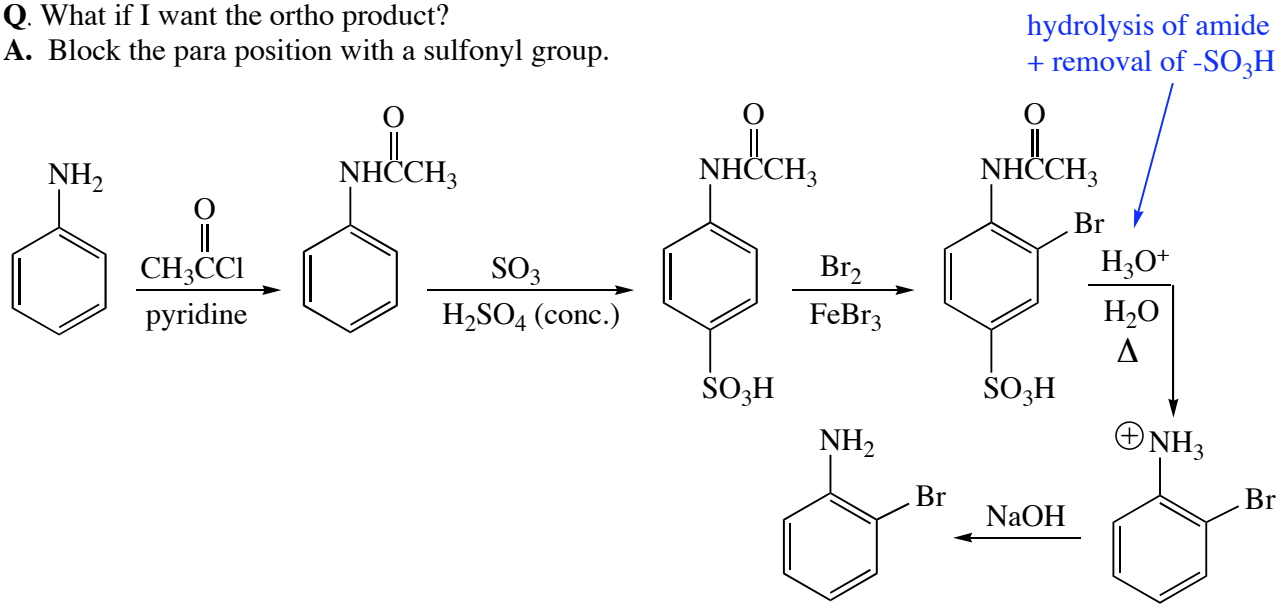


Solution: **Acylate the amine.** This turns the ring from strongly activated to *moderately* activated and allows monohalogenation:

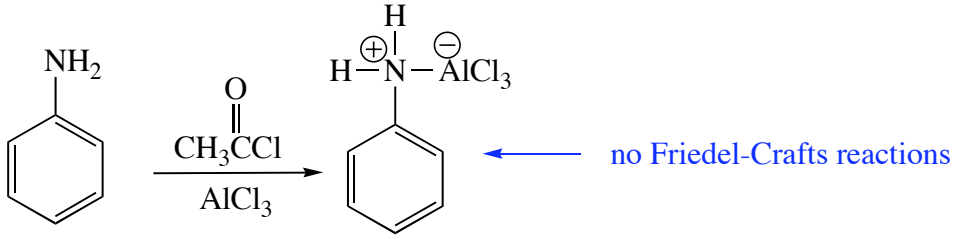


Q. What if I want the ortho product?

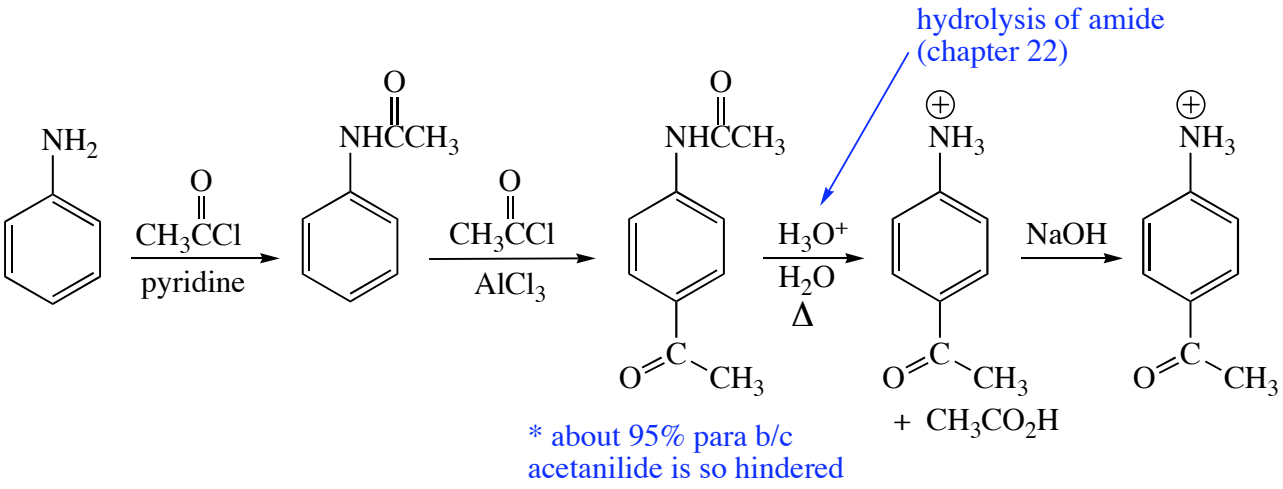
A. Block the para position with a sulfonyl group.



B. Friedel-Crafts Alkylation & Acylation. The amino groups -NH_2, -NHR, and NR_2 are changed into powerful deactivating groups by the Lewis acids used to catalyze Friedel-Crafts reactions. Deactivated, meta directing benzene derivatives *do not do* Friedel-Crafts reactions.

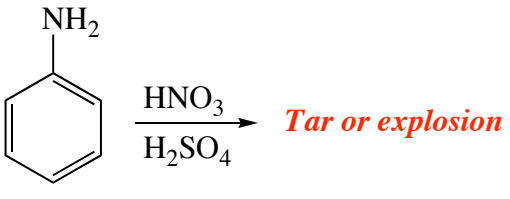


Solution: **Acylate the amine.** This turns the ring from strongly activated to moderately activated and allows Friedel-Crafts reactions to take place:

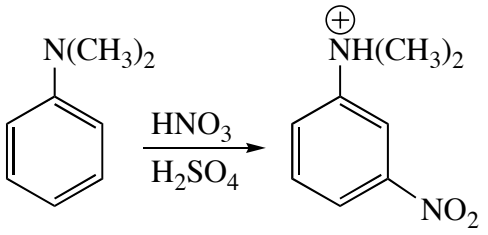


✳ *For ortho product, block para position with a sulfonyl group, like in a. Even though a sulfonyl group is deactivating, this effect is counteracted by the acetanilide group, so Friedel-Crafts acylation will work*

C. Nitration of Aniline Derivatives. Aniline derivatives cannot be nitrated because nitric acid is an oxidizing agent and primary amines are easily oxidized (nitric acid and aniline can be explosive). Only tertiary aromatic amines and acetamide derivatives can be nitrated.

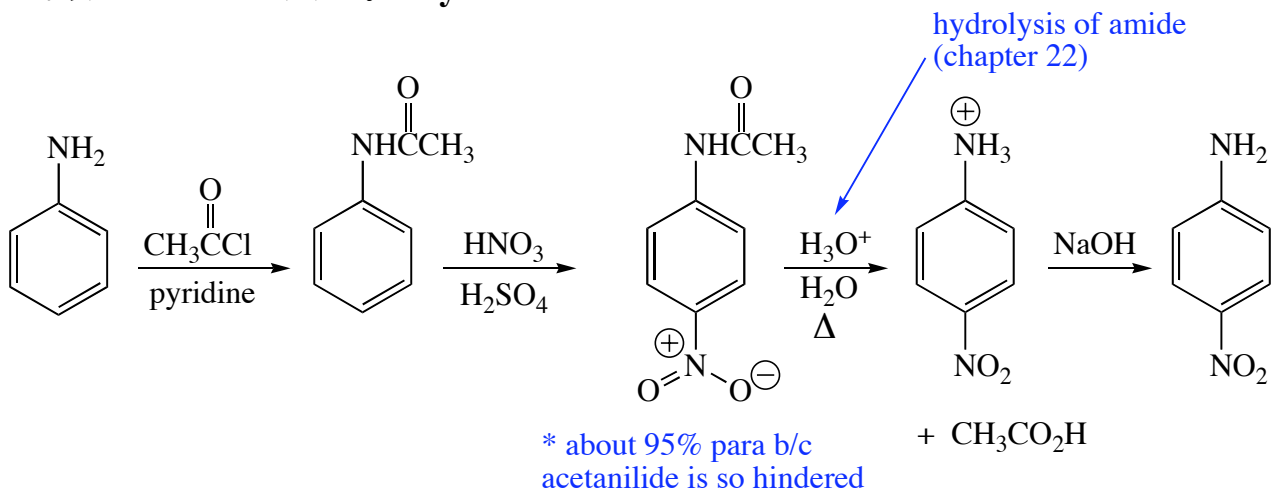


1° not safe or effective



2°, 3° okay, but nitrogen will be pronated in strong acid, becoming a meta director.

Solution for 1° Amines: **Acylate**



✳ *For ortho product, block para position with a sulfonyl group, like in a.*