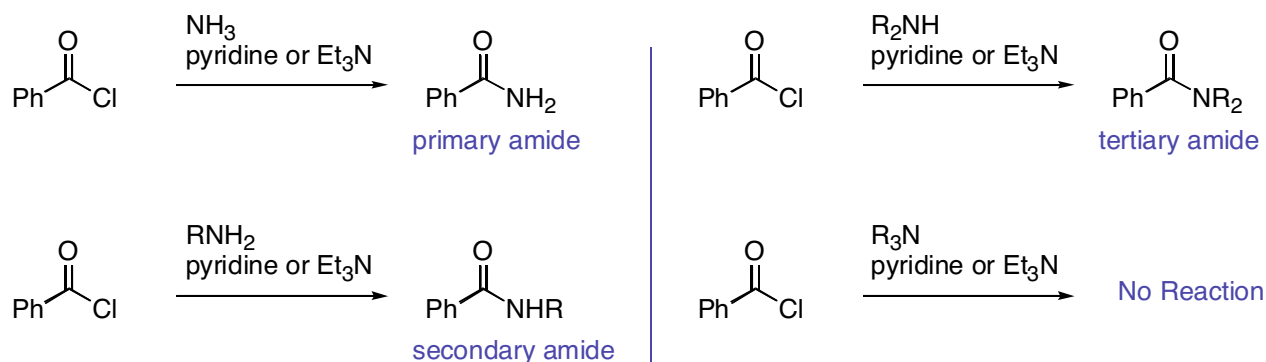


These notes can be obtained at: <http://www.ndsu.nodak.edu/instruct/grcook/chem342/notes.shtml>

## Chapter 21: Carboxylic Acid Derivatives and Nucleophilic Acyl Substitution Reactions

### Preparation of amides

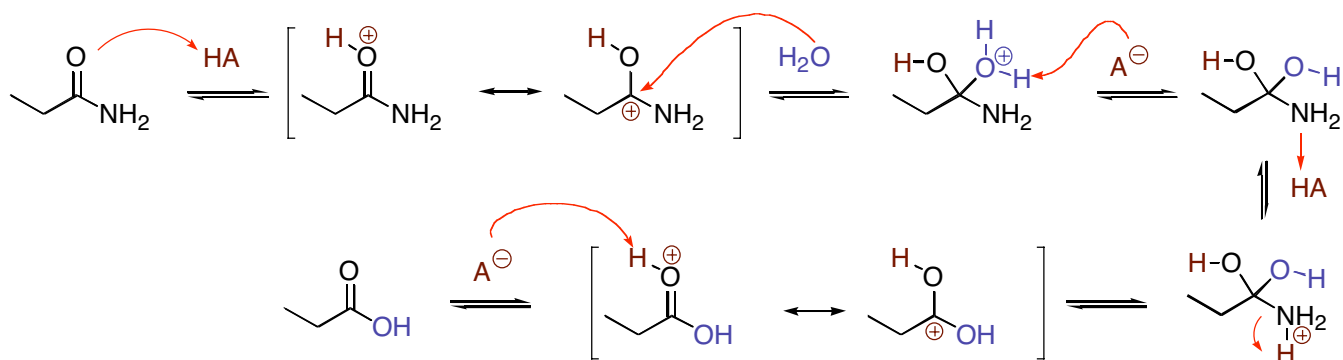
Amides are best prepared from acid chlorides. Note that tertiary amines do not react as there is no proton to come off. Tertiary amines are often added as a base in acylation reactions.



### Hydrolysis of amides

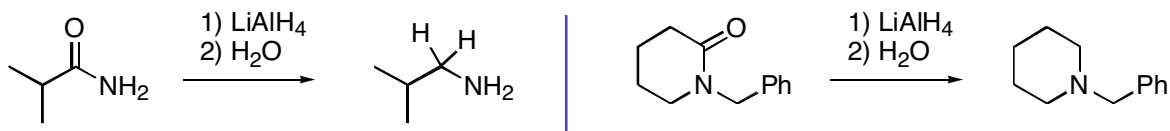
Amides can be hydrolyzed under acidic conditions. Base catalyzed hydrolysis is extremely difficult as NH<sub>2</sub><sup>-</sup> is a terrible leaving group.

#### Acid Catalyzed Hydrolysis of Amides



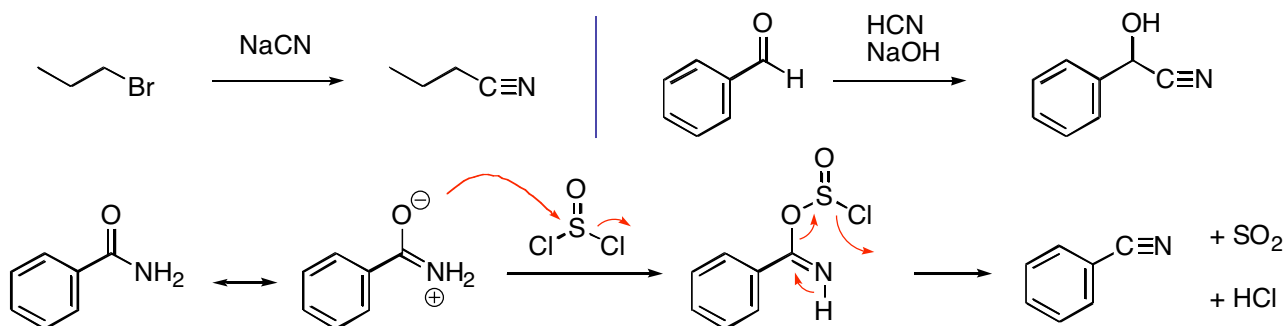
## Reduction of amides

As amines are poor leaving groups, the reduction of amides is slightly different than the reduction of esters. The carbonyl carbon is reduced to a  $\text{CH}_2$  and the amino group remains.



## Preparation of Nitriles

Nitriles can be made with the addition of a carbon using cyanide as a nucleophile in substitution or addition chemistry. Alternatively, they can be prepared from primary amides by dehydrating with  $\text{SOCl}_2$ .



## Reactions of Nitriles

Nitriles can be hydrolyzed under acidic conditions to the amide or all the way to the carboxylic acid.  $\text{LiAlH}_4$  reduces all the way to the amine. DIBAL stops at the aldehyde stage and Grignard reagents add only one to afford ketones.

