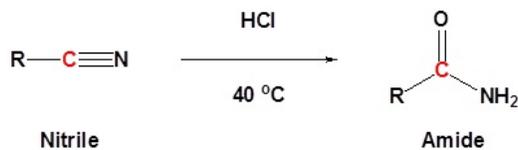


22.7: AMIDE CHEMISTRY

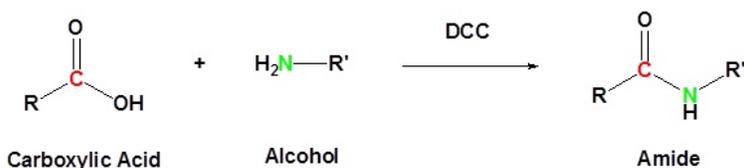
SYNTHESIS OF AMIDES

There are five synthetic routes to produce amides: nitrile conversion and the acyl nucleophilic substitution reactions of acid halides, acid anhydrides, and carboxylic acids.

Nitriles can be converted to amides. This reaction can be acid or base catalyzed



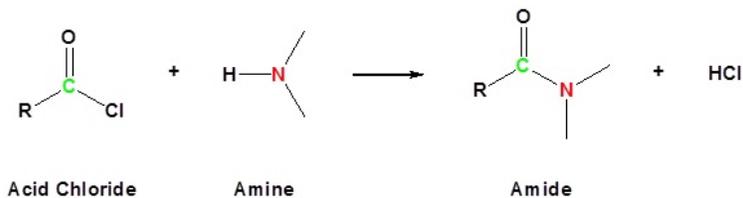
Carboxylic acid can be converted to amides by using DCC as an activating agent



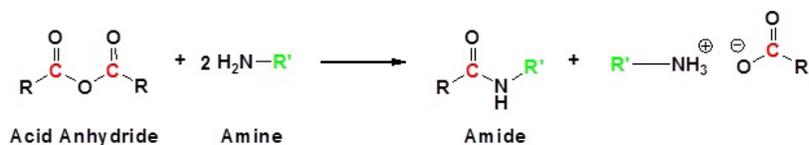
Direct conversion of a carboxylic acid to an amide by reaction with an amine.



Acid chlorides react with ammonia, 1° amines and 2° amines to form amides



Acid Anhydrides react with ammonia, 1° amines and 2° amines to form amides



HYDROLYSIS OF AMIDES

HYDROLYSIS UNDER ACIDIC CONDITIONS

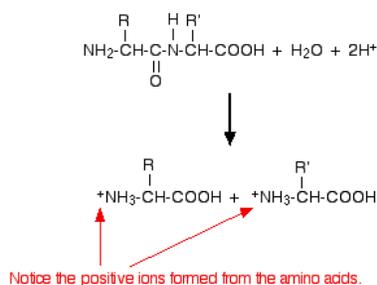
Taking acetamide (ethanamide) as a typical amide. If acetamide is heated with a dilute acid (such as dilute hydrochloric acid), acetic acid is formed together with ammonium ions. So, if you were using hydrochloric acid, the final solution would contain ammonium chloride and acetic acid.

HYDROLYSIS UNDER ALKALINE CONDITIONS

Also, if acetamide is heated with sodium hydroxide solution, ammonia gas is given off and you are left with a solution containing sodium acetate.

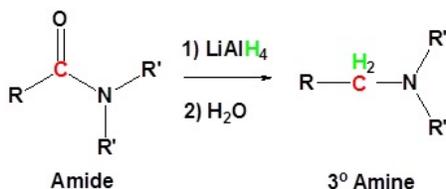
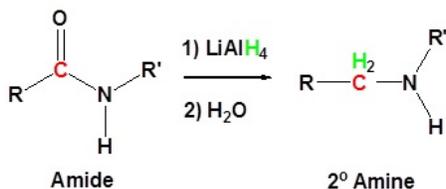
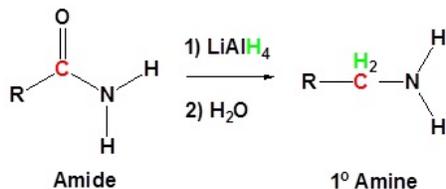
PEPTIDE HYDROLYSIS

Peptide hydrolysis of proteins is amide hydrolysis. What biologists and biochemists call a peptide link (in proteins, for example) is what chemists call an amide link. Apply either hydrolysis reaction above to the dipeptide below to produce two amino acids. The amines in the products are shown in their protonated form because this hydrolysis reaction was performed under acidic conditions.



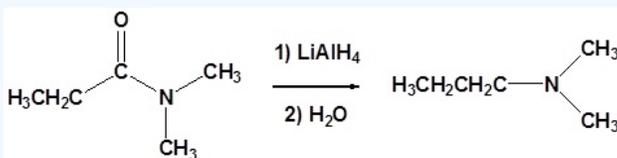
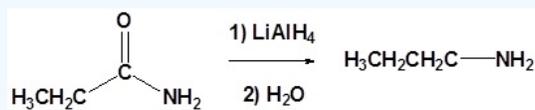
REDUCTION OF AMIDES INTO AMINES

Amides can be converted to 1°, 2° or 3° amines using LiAlH_4 followed by an aqueous work-up. Alkyl groups attached to the amide nitrogen do not affect the reaction. The amine classification correlates with the amide as shown in the reaction summary below.



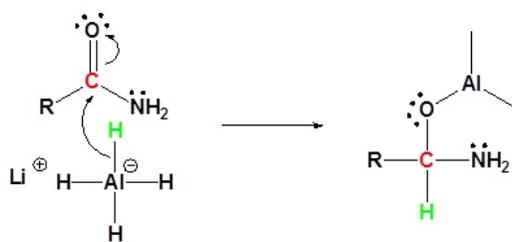
The reductions of propanamide and N,N-dimethylpropanamide are shown as examples.

Example: Amide Reductions

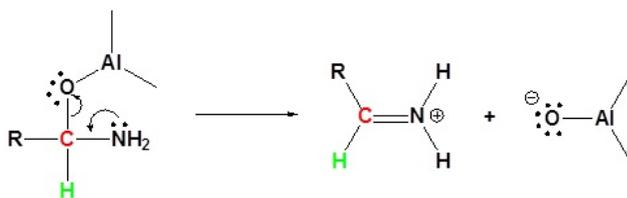


The mechanism begins with nucleophilic hydride reacting with the carbonyl carbon to produce the tetrahedral intermediate. An imine forms in concert with the loss on the leaving group. A second hydride nucleophile reacts with the imine carbon to produce the final product.

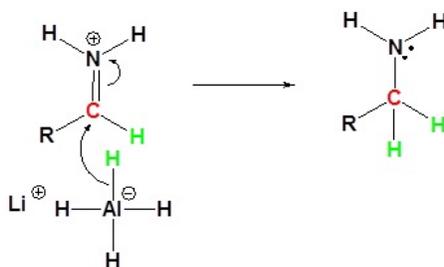
1) Nucleophilic reaction by the hydride



2) Imine formation with loss of leaving group

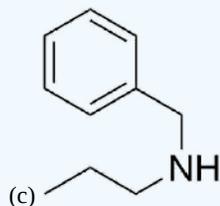
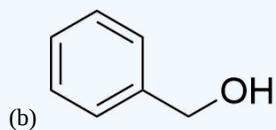
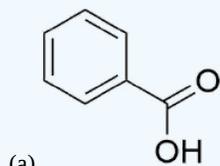


3) Nucleophilic reaction by the hydride



Exercise

11. How would you prepare the following compounds from N-Propyl benzamide?



12.

Propose a synthesis for the following.

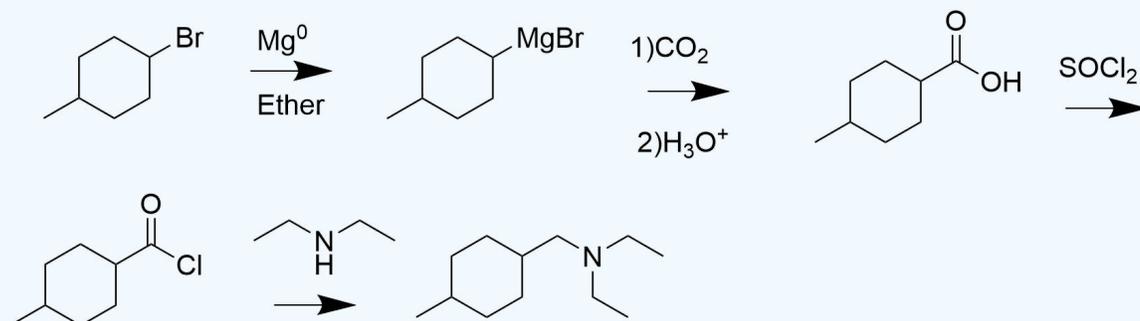


Answer

11.

- a) NaOH, H₂O
- b) NaOH, H₂O, then LiAlH₄
- c) LiAlH₄

12.



CONTRIBUTORS AND ATTRIBUTIONS

- Dr. Dietmar Kennepohl FCIC (Professor of Chemistry, [Athabasca University](#))
- Prof. Steven Farmer ([Sonoma State University](#))
- Jim Clark ([Chemguide.co.uk](#))

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