

ORGANIC CHEMISTRY 2 LECTURE GUIDE 2019

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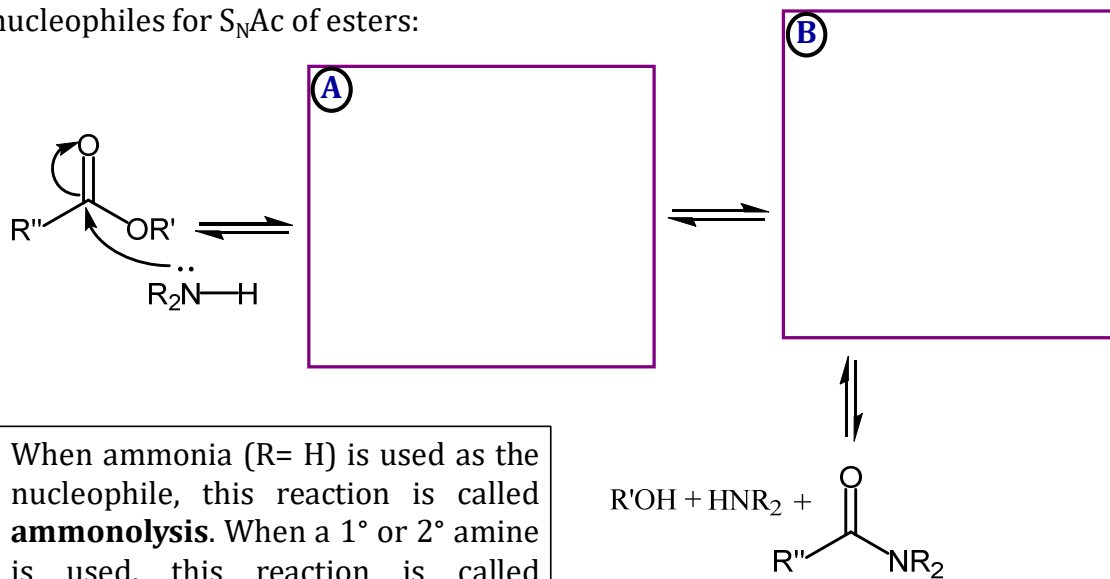
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Lesson VI.12. Amide Formation, Amide Hydrolysis and the Gabriel Synthesis

Ammonolysis and amidation

Ammonia, primary amines, or secondary amines can also be used as nucleophiles for S_NAc of esters:

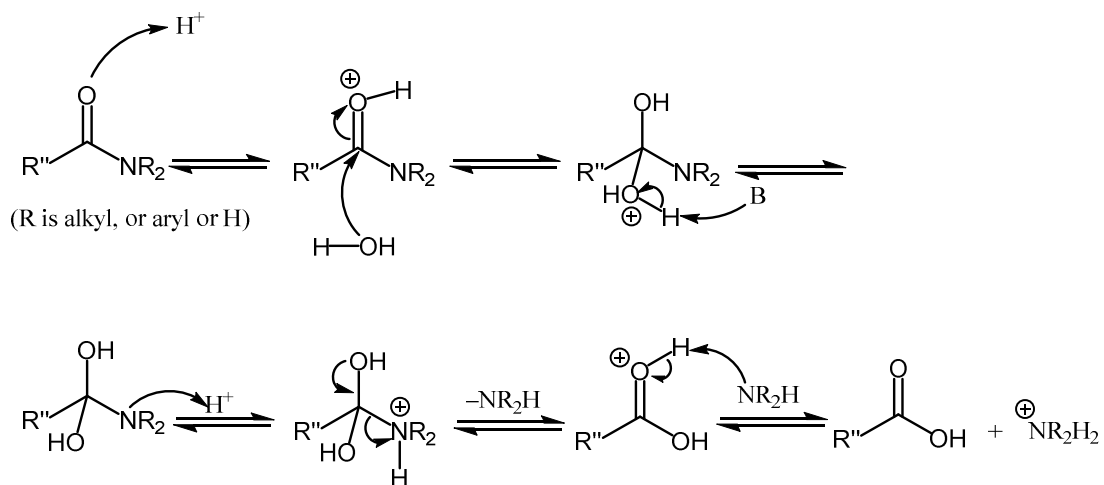


When ammonia (R= H) is used as the nucleophile, this reaction is called **ammonolysis**. When a 1° or 2° amine is used, this reaction is called **amidation**.

Notes

Lesson VI.12. Amide Formation, Amide Hydrolysis and the Gabriel Synthesis*Amide hydrolysis*

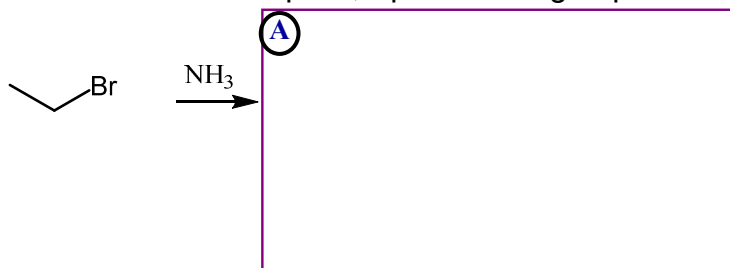
Like esters, amides can undergo hydrolysis to form carboxylic acids or carboxylates. The amides are much less reactive to the initial nucleophilic addition step, so these reactions require higher temperatures and/or longer reaction times than do other hydrolysis reactions, but mechanistically it is quite similar:

Notes

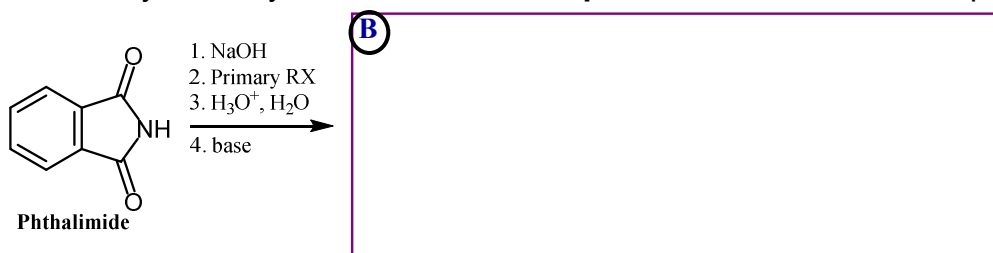
Lesson VI.12. Amide Formation, Amide Hydrolysis and the Gabriel Synthesis

Gabriel Synthesis

Preparation of primary amines from alkyl bromides is very useful; however, if one uses ammonia as the nucleophile, up to four R groups can add to N:



The Gabriel Synthesis yields 1° amines from **phthalimide** over a few steps:

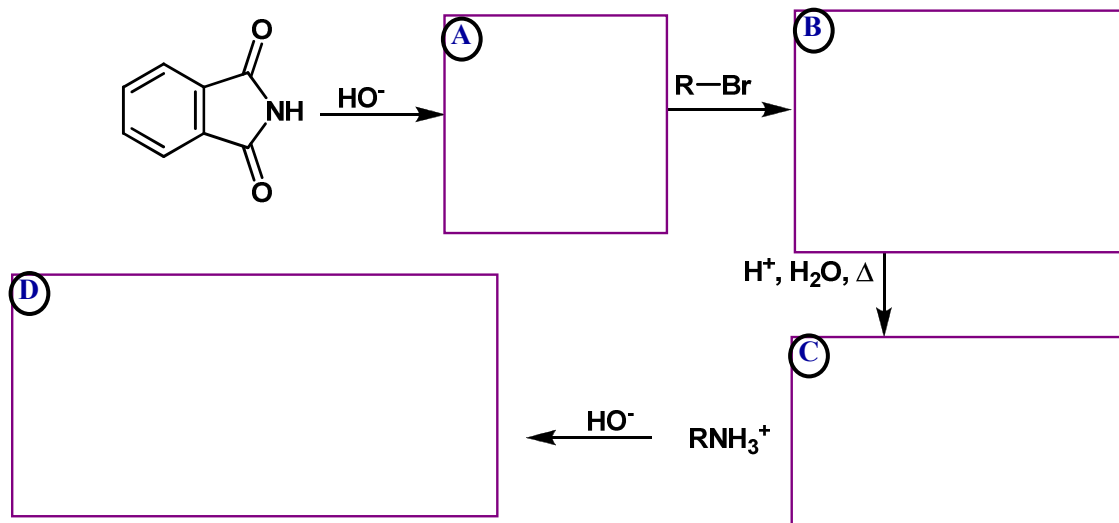


What is the mechanism for the Gabriel Synthesis?

Notes

Lesson VI.12. Amide Formation, Amide Hydrolysis and the Gabriel Synthesis*Gabriel Synthesis*

The Gabriel Synthesis yields 1° amines by protecting two sites of the N for the S_N2 reaction, then deprotection by acid hydrolysis:



Notes