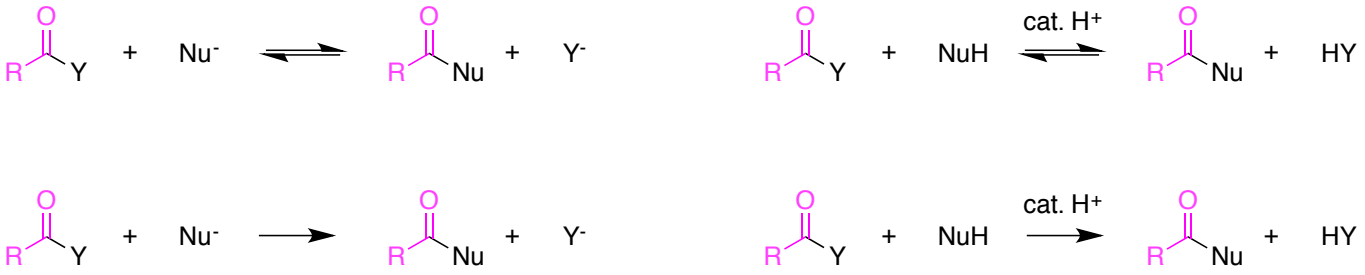
Reactivities Of Acylation Agents

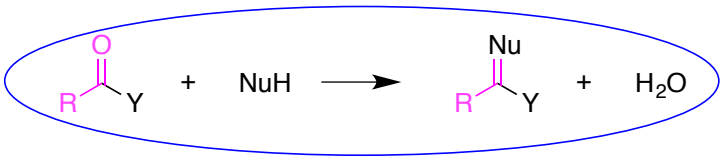
from chapter(s) _____ in the recommended text

A. Introduction

B. Acylation Reactions

RCO

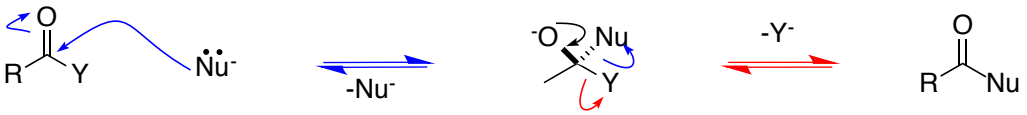




C. pH Dependence

Acylations Under Basic Conditions

readily receive
displaced



does
good
(*eg* OMe^-)
bad
(*eg* Cl^-).

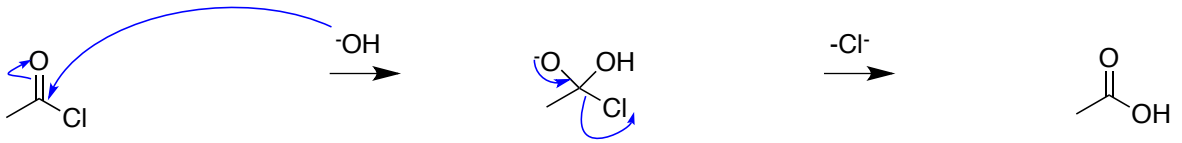
Cl^-, NO_3^-, HSO_4^-, H_2O, Br^- (add some more)

Me_2N^-, HO^-, HS^-, ^-OMe, CN^- (add some)

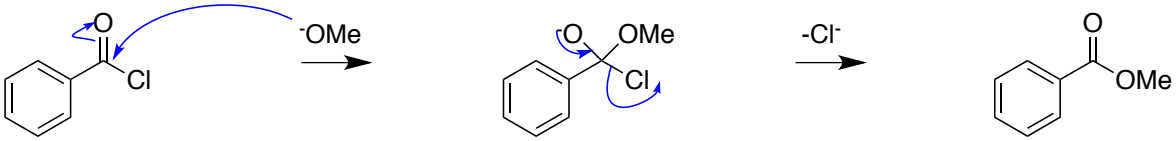
most

tetrahedral

moderately
more



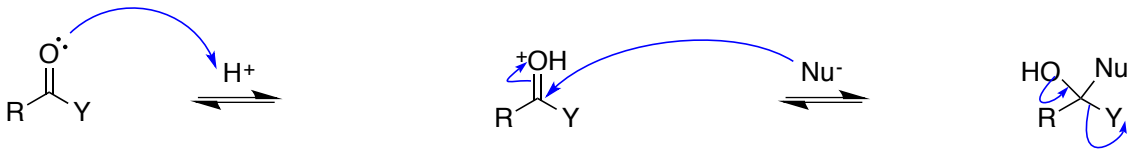
ethanoyl chloride *tetrahedral intermediate* *ethanoic acid*

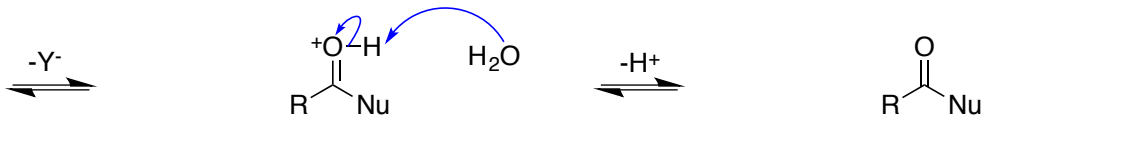


benzoyl chloride *tetrahedral intermediate* *methyl benzoate*

Acylations Under Acidic Conditions

increases





D. Reactivities Of Acylation Agents

Chemical Intuition

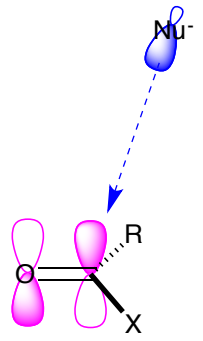
unreactive.
reactive
activate
reactive

cannot
less
more

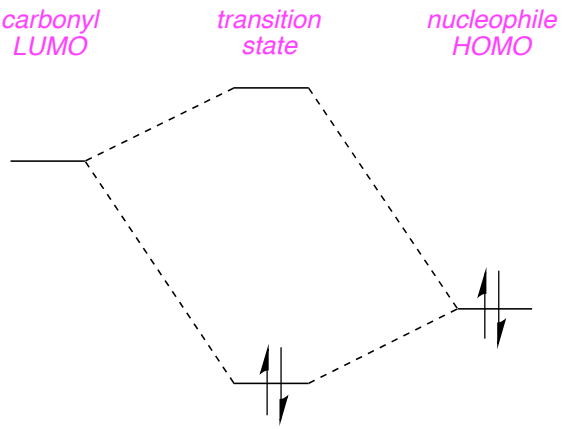
retard
unfavorable
faster

Molecular Orbital Description Of Acylation

a



b



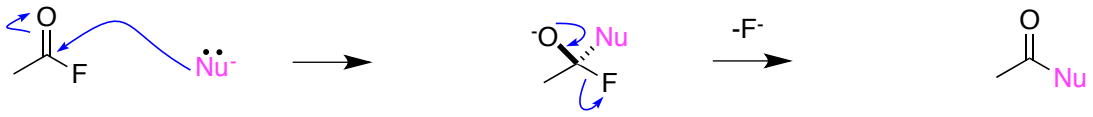
increase
lower its LUMO energy.
reactive
low energy LUMOs.
more stable
less reactive

high
good

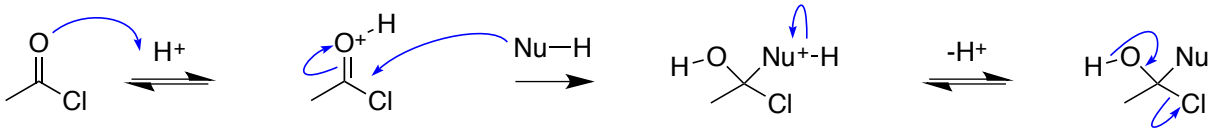
lower
excellent

Relative Reactivities Of Functional Groups In Acylation Reactions

Carbonyl Halides (Acid Halides) Are Hot



basic



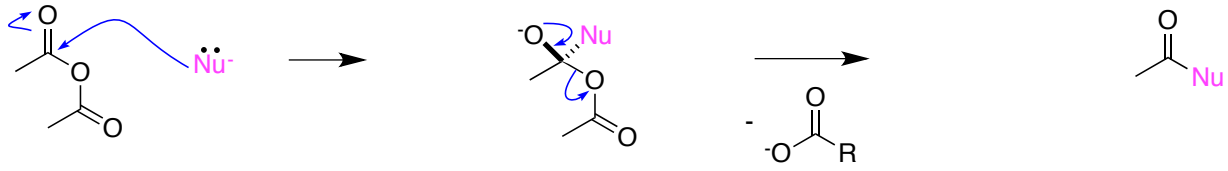
acid conditions.

Carboxylic Acid Anhydrides Are Very Reactive

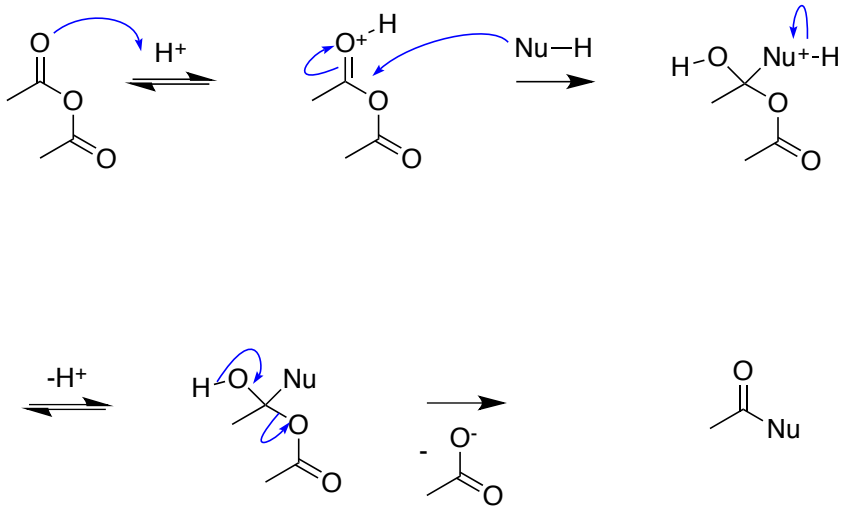
lower

excellent leaving groups.

under basic conditions .....



under acidic conditions .....



2 carboxylic

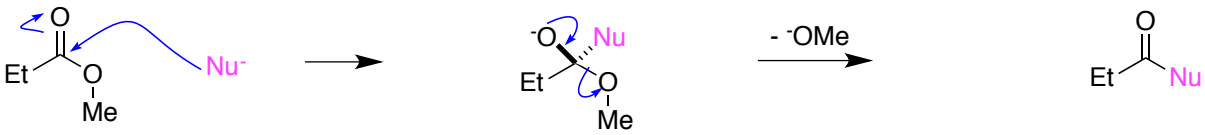
an electrophile

carboxylate leaving group.

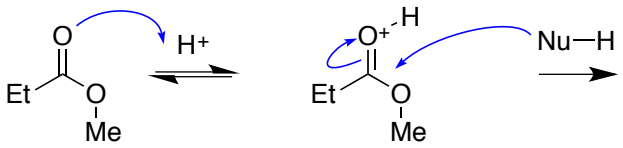
Esters Are Not Very Reactive

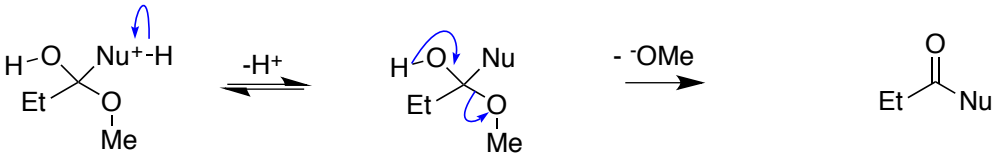
raises
inferior

under basic conditions .....



under acidic conditions .....





ester hydrolysis
transesterification

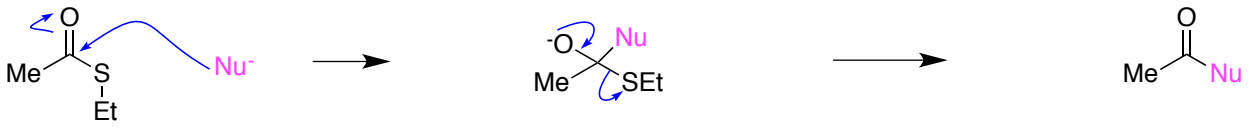
do not tend

Thioesters, Gentle Chemoselective Acylating Agents

better

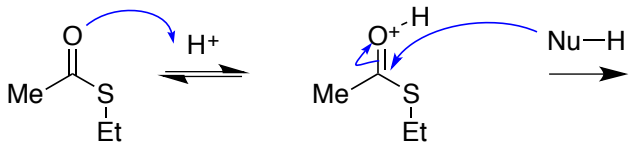
less

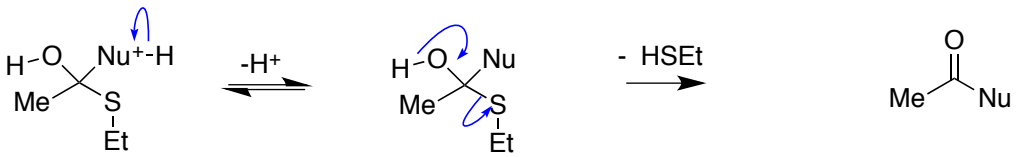
under basic conditions .....



tetrahedral intermediate

under acidic conditions .....





do tend to

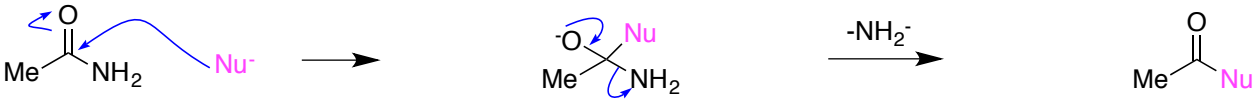
Amides, Poor Acylating Agents

worse

poor

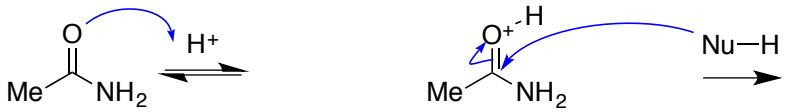
more

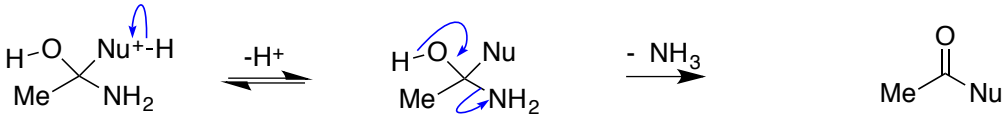
under basic conditions .....



tetrahedral intermediate

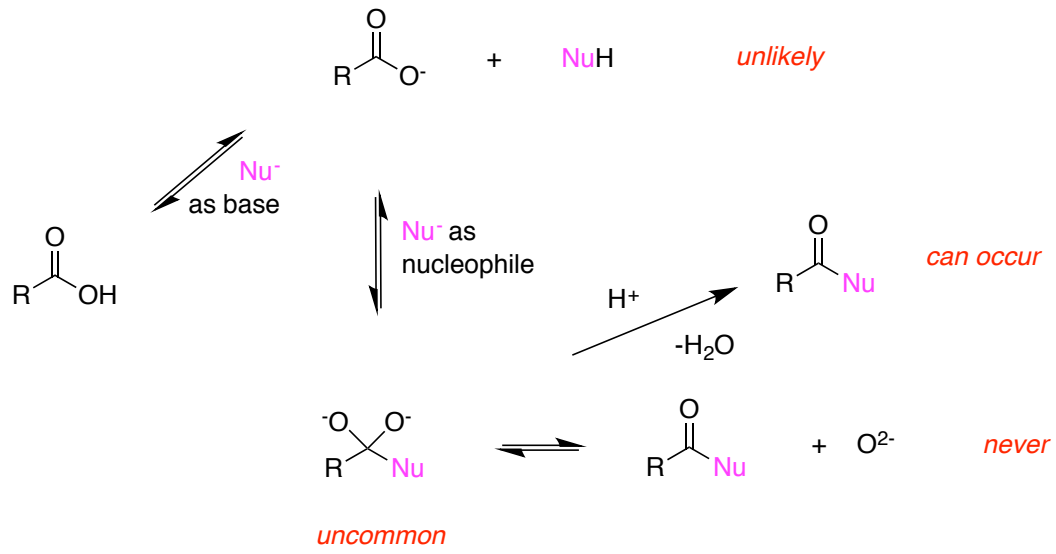
under acidic conditions .....





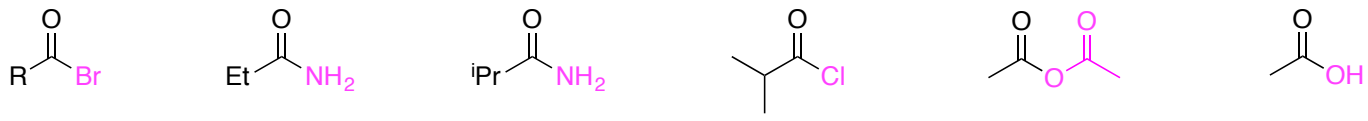
Carboxylic Acids Are Not Acylating Agents

(pKa = *3 – 5*

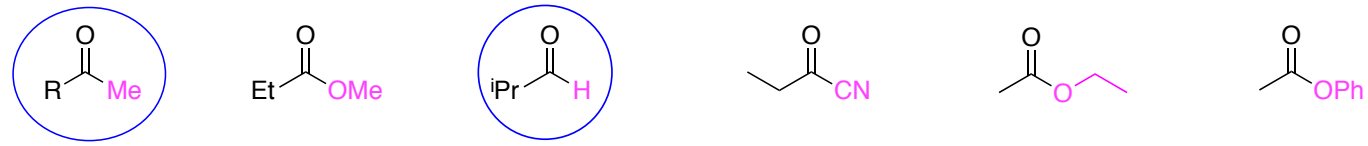


extremely basic and a very *poor*

Synopsis



E *I* *I* *E* *E* *I*



I *SS* *I* *E* *SS* *SS*

cannot

X = OAc OMe O^- NH_2 Cl OPh

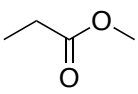
Cl OAc OPh OMe NH_2 O^-

most reactive *least reactive*

Nu =  ^-Me ^-OH $^-NH_2$ ^-Cl NH_3 OH_2

^-Me $^-NH_2$ ^-OH  ^-Cl NH_3 OH_2

most reactive *least reactive*



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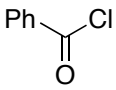
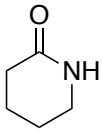


1

3



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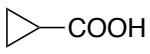

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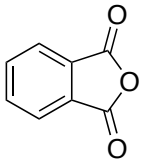

2