# Activation Of Carboxylic Acids

from chapter(s) _____ in the recommended text

## A. Introduction

## B. Reactivity

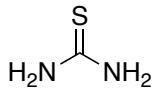
*poor* acylating agents because:

(i) hydroxide is a *mediocre*

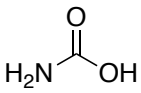
(ii) exists *as a carboxylate*.

*are* reactive to nucleophiles.

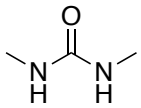
## C. Common Carboxylic Acids Derivatives



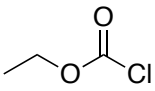
*thiourea*
***C***



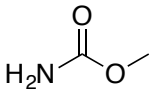
*carbamic acid*
***B***



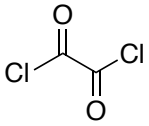
*N,N'-dimethylurea*
***C***



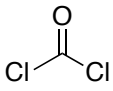
*ethyl chlorocarbonate*
***D***



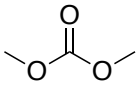
*methyl carbamate*
***E***



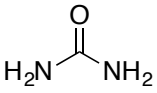
*oxalyl chloride*
***D***



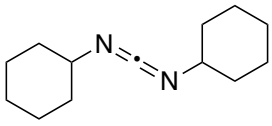
*phosgene*
***D***



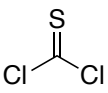
*dimethyl carbonate*
***A***



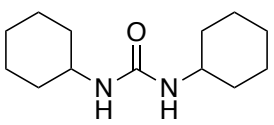
*urea*
***C***



*dicyclohexylcarbodimide (DCC)*
***E***



*thiophosgene*
***D***

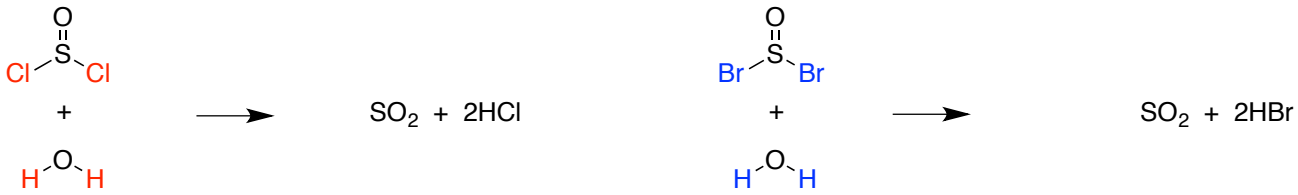


*N,N'-dicyclohexylurea*
***C***

## D. Activation Of Carboxylic Acids By Conversion To Acid Chlorides

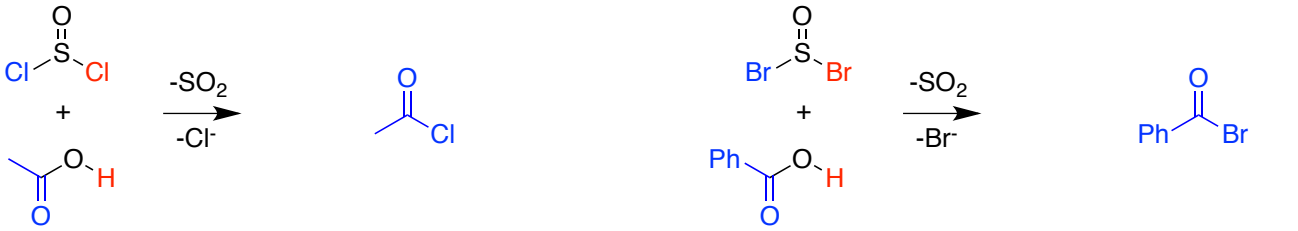
### Thionyl Halides: Excellent Dehydrating Agents

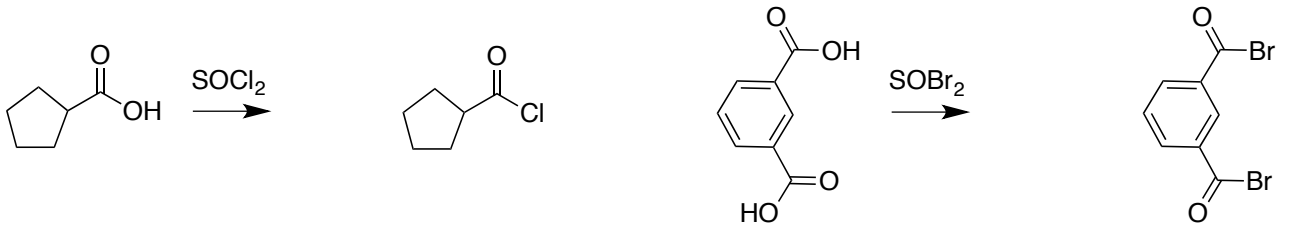
formula: $SOBr_2$

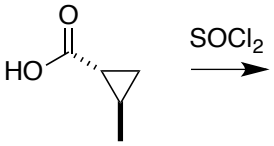


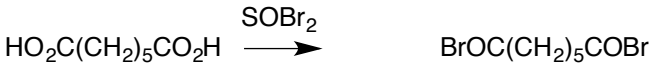

Thionyl Halide Plus Carboxylic Acid Gives Acid Halide, $SO_2$, And HX

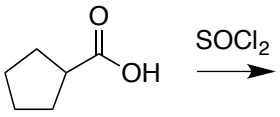
*acid halides*.



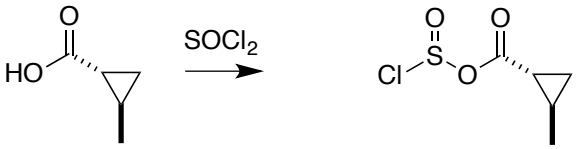





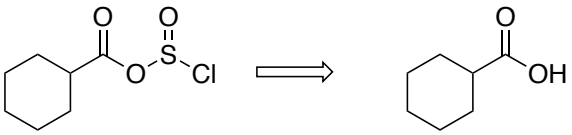



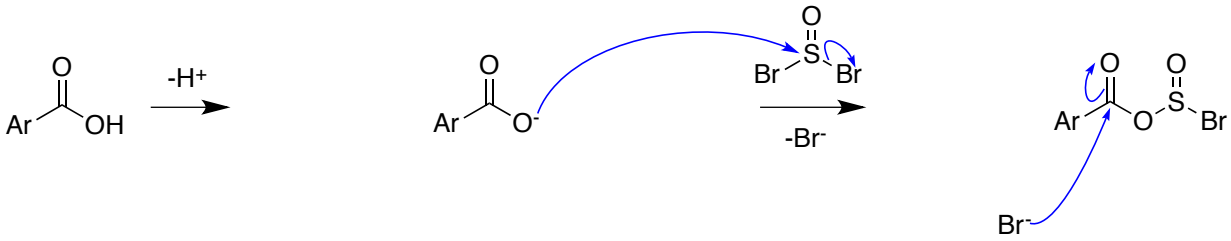




*sulfonyl anhydride intermediate*




*sulfonyl anhydride intermediate*






*carboxylate*

*sulfonyl anhydride intermediate*


*tetrahedral intermediate*

*carboxylic acid bromide*

## E. Activation By Forming Anhydrides

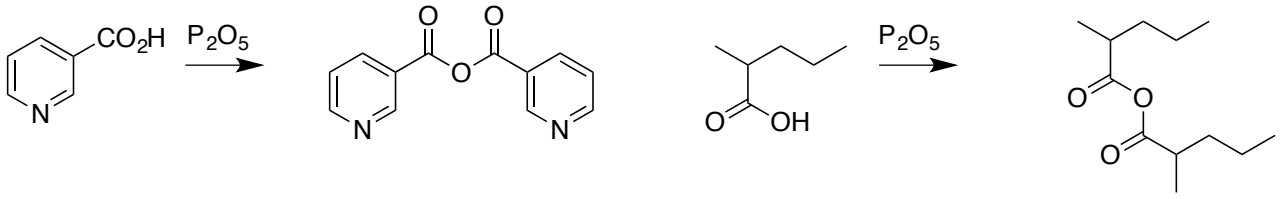
### Symmetrical Anhydrides

*2* molecules

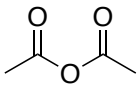
*1* molecule


*Symmetrical* anhydrides

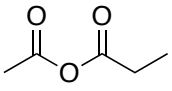
, but *unsymmetrical* ones




is *symmetrical*) and the *unsymmetrical* anhydride




*acetic anhydride*

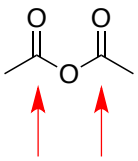


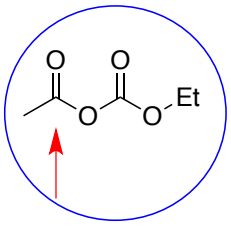

*anhydride from ethanoic and propionic acids*

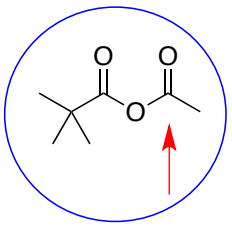
## Unsymmetrical And Mixed Anhydrides

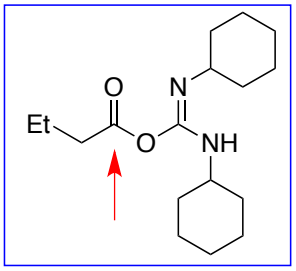
*2*
*unsymmetrical*.
*another type of acid*.

*are not*
that *can* be used
*eg*



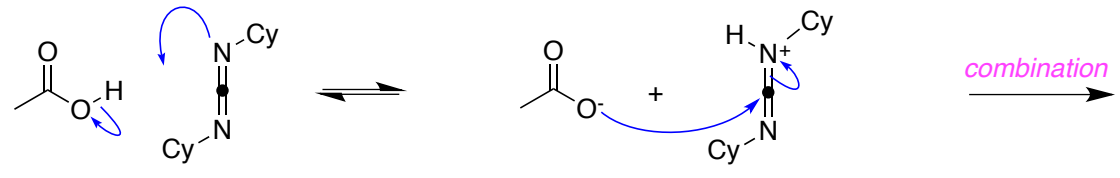



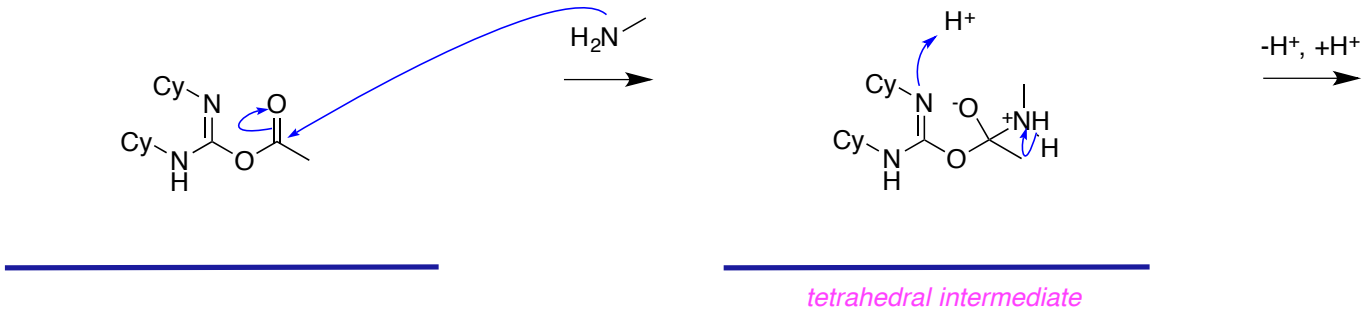

*draw arrows to most reactive carbonyl carbon(s), circle unsymmetrical anhydrides, and box those that are mixed*

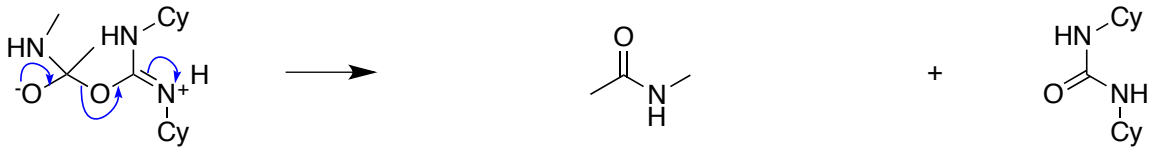
*different*,

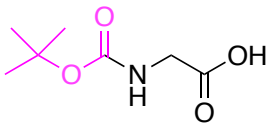
## Formation Of Unsymmetrical Anhydride Derivatives Using Carbodiimides

*urea*.

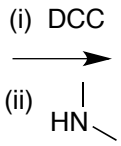


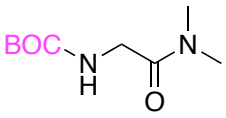



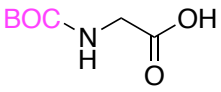



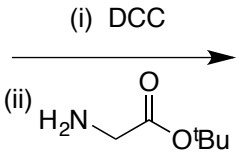


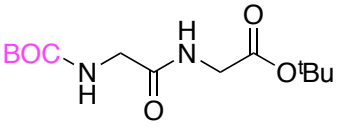
BOC
*tert*-ButylOxyCarbonyl

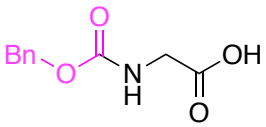


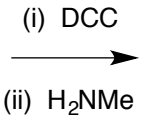


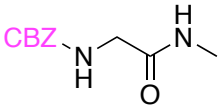


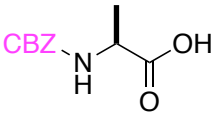



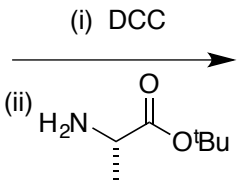


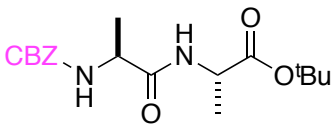
CBZ
CarboxyBenZyl





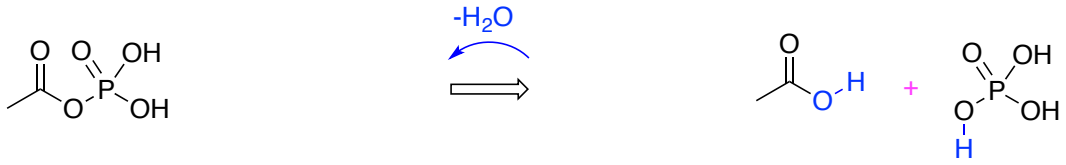


# F. Activation Of *Phosphate* Acids In Cells Via Phosphate Anhydrides

## Formation Of Mixed Anhydrides Of Phosphorus Acids

*mixed* anhydrides

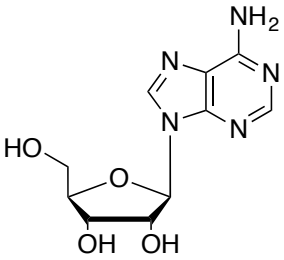



*acyl phosphate*

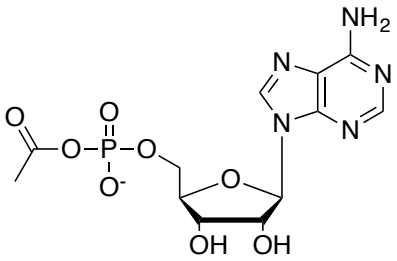
the *carbonyl* of
is a *better* leaving


*carboxylic and phosphoric acids*

*deprotonated*

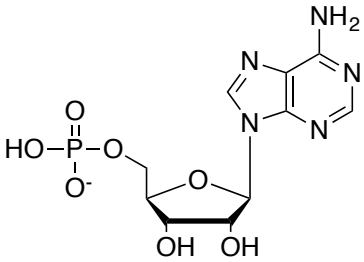


*adenosine*

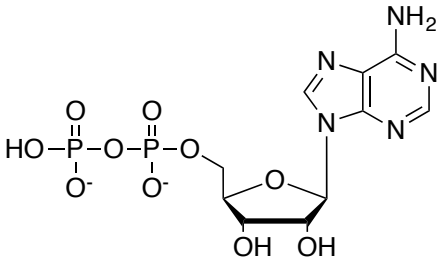


*acyl adenylate*

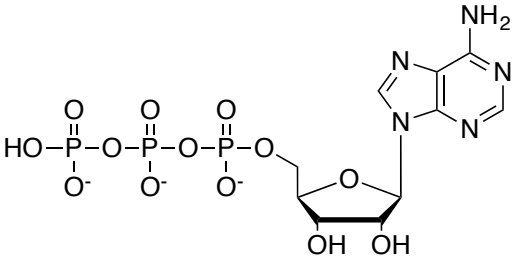
, *ADP / ATP*,



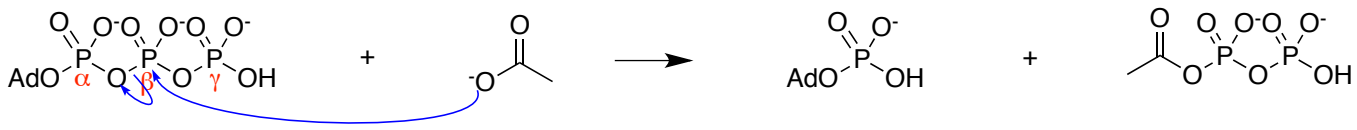
*AMP*



*ADP*



*ATP*




*AMP and acyl pyrophosphate*

$\beta$ phosphorus.
on the $\gamma$ phosphorus.

*repel* anionic
*faster* if encapsulated