OC2

Synthesis
–
Introduction to Protecting Groups

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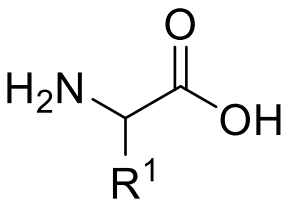
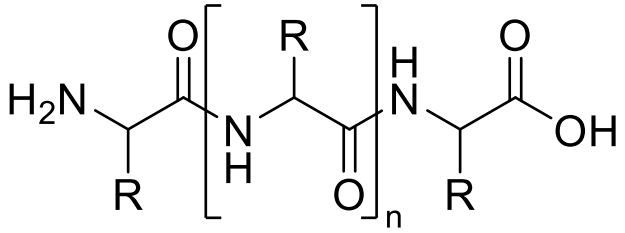
Peptide Synthesis – Protecting Groups

Peptides are made up of many amino acids joined together:

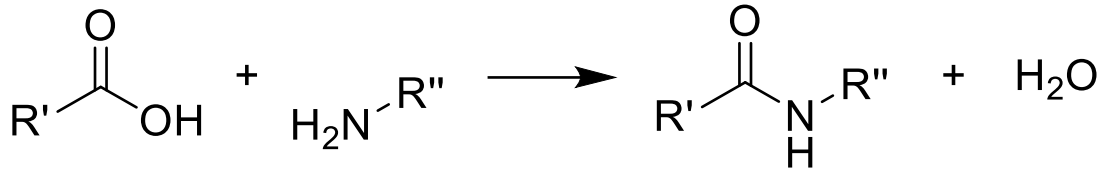


amino acid

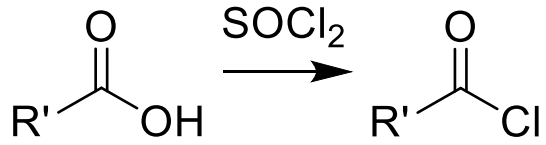


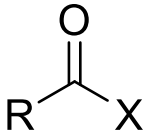
peptide

Amide bond formation:

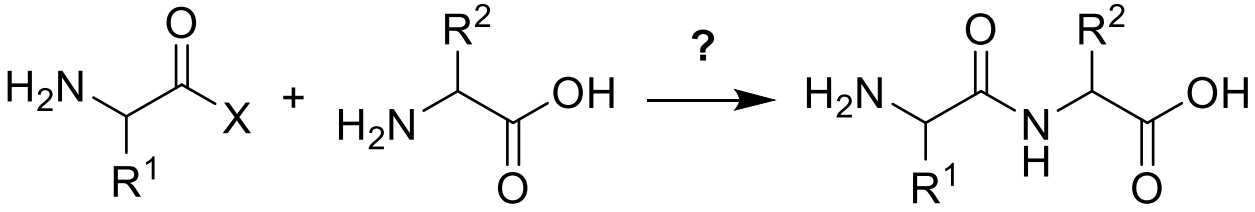


e.g. acid chloride:

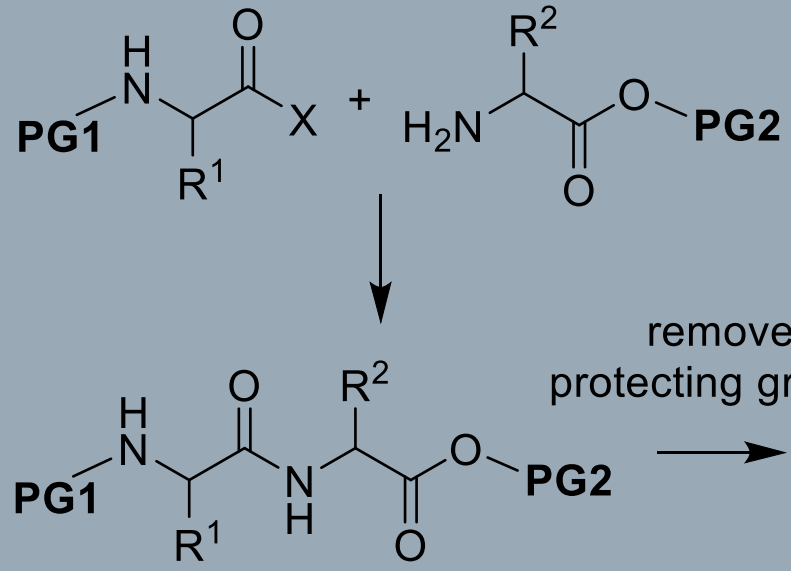


Consider  to be the activated form of a carboxylic acid.

For peptide synthesis there is a problem:

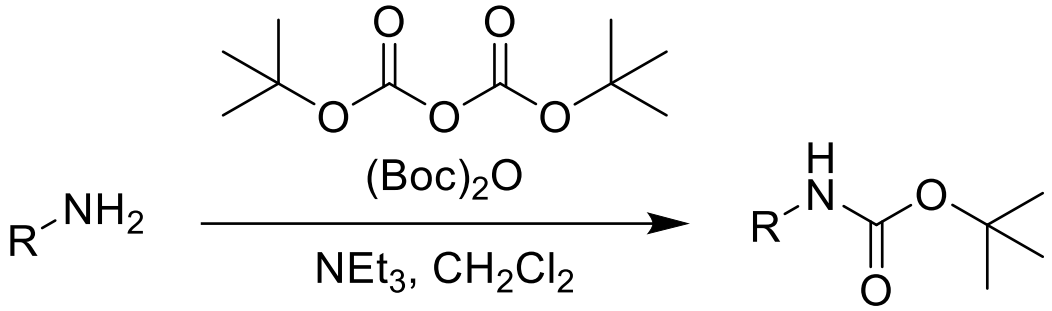


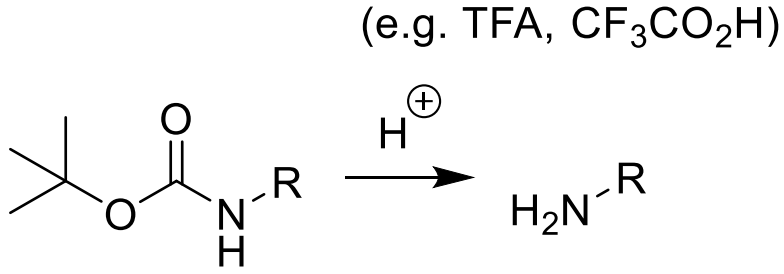
Solution: use protecting groups



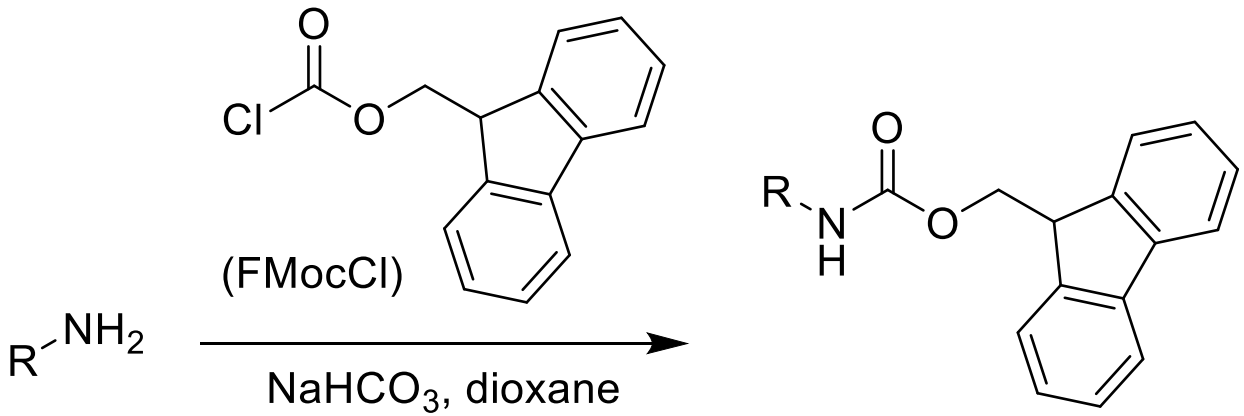
Protecting Groups for Amines

- **Boc-group:** stable to most things except extreme heat and strong acids

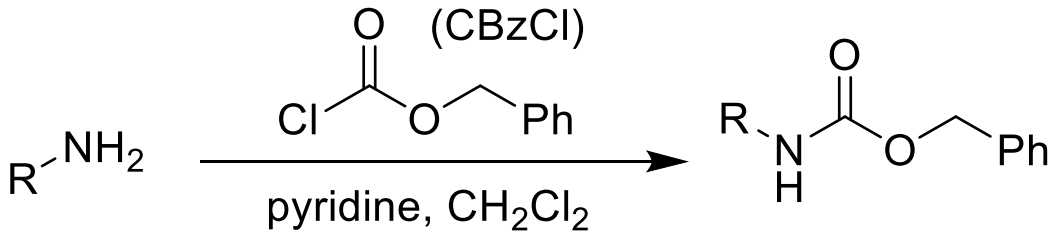




- **FMoc-group:** stable to all but basic conditions

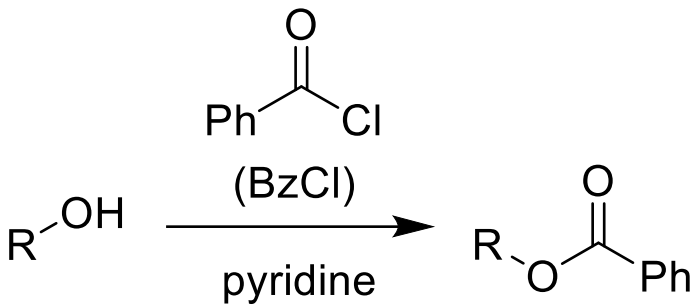


- **CBz-group:** stable to most things

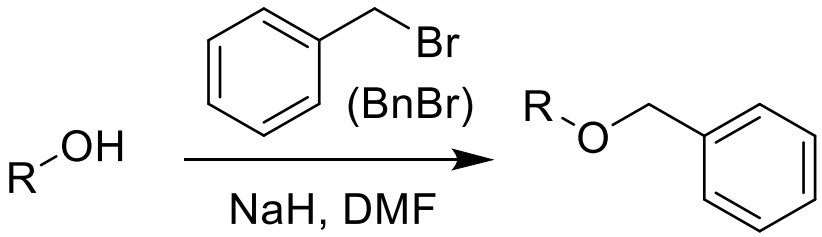


Protecting Groups for Alcohols

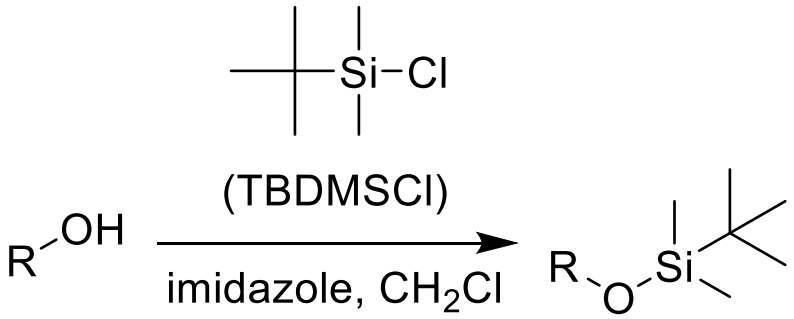
- **Bz-group:** stable to acid



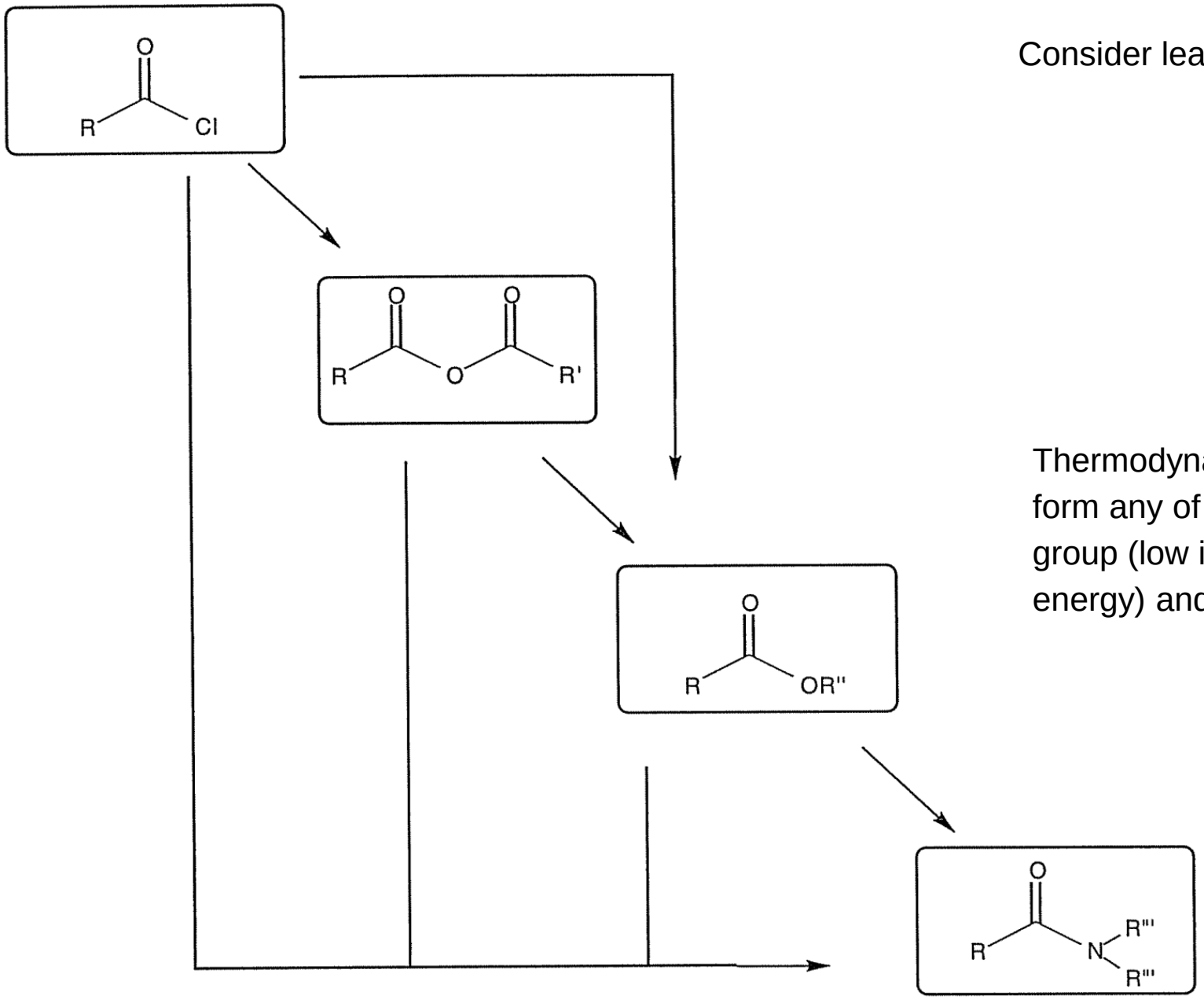
- **Bn-group:** stable to most things



- **TBDMS-group:** stable to most things (except some acids)



Interconversion

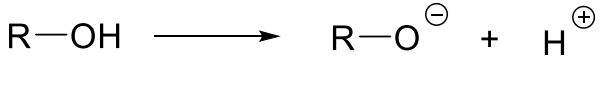
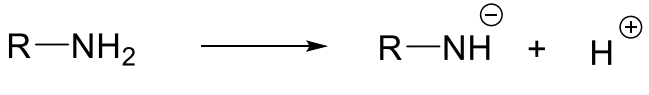
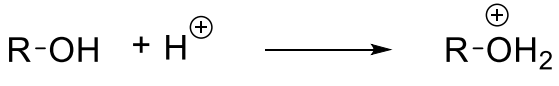
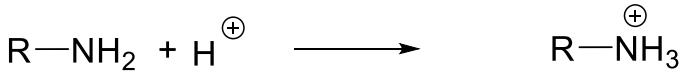
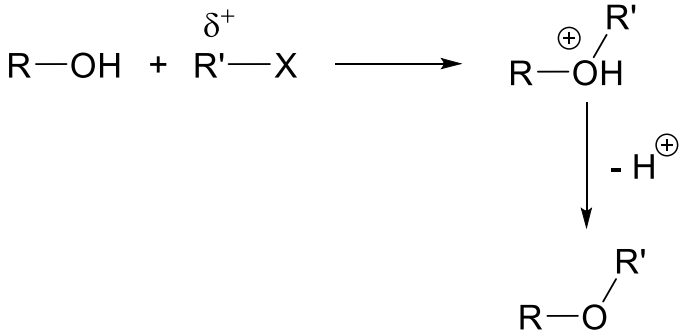
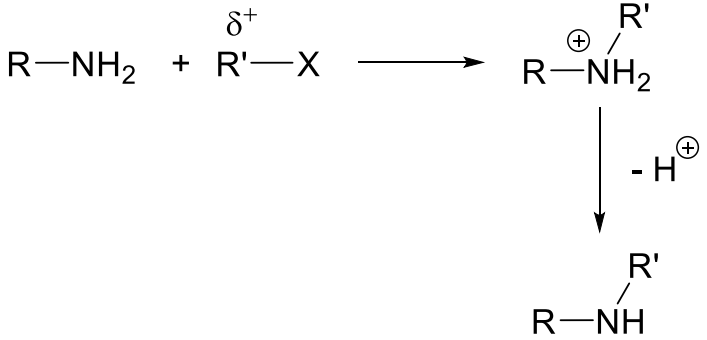
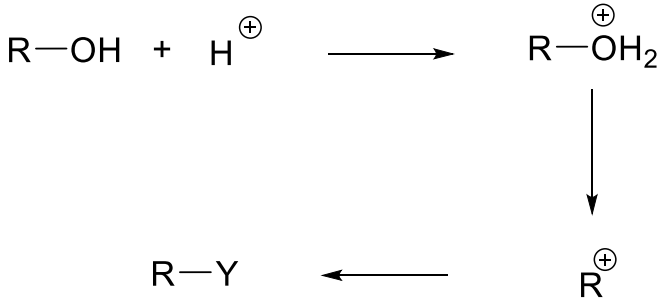


Consider leaving group abilities:

	pKa
R^-	R-H
R_2N^-	R_2N-H
RO^-	RO-H
RCO_2^-	RCO_2-H
Cl^-	Cl-H

Thermodynamically one can therefore react acid chloride to form any of the other derivatives since Cl^- is a good leaving group (low in energy). Amines are good nucleophiles (high in energy) and can convert any derivative to amides:

Properties of Amines compared to Alcohols

	R—OH	**R—NH_2**
as acid:	 pK_A (H_2O) = 15.7	 pK_A (NH_3) = 38
as base:	 pK_B (H_2O) = 15.7	 pK_B (NH_3) = 4.8
as nucleophile:		
as electrophile:		very rare

What’s next?

Revisions