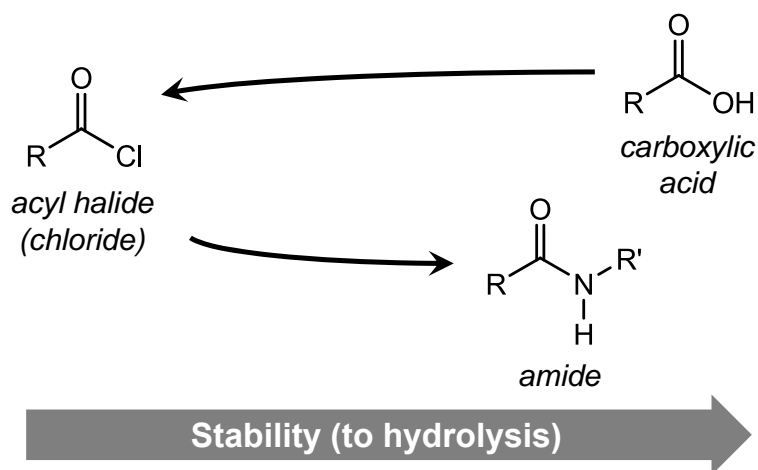


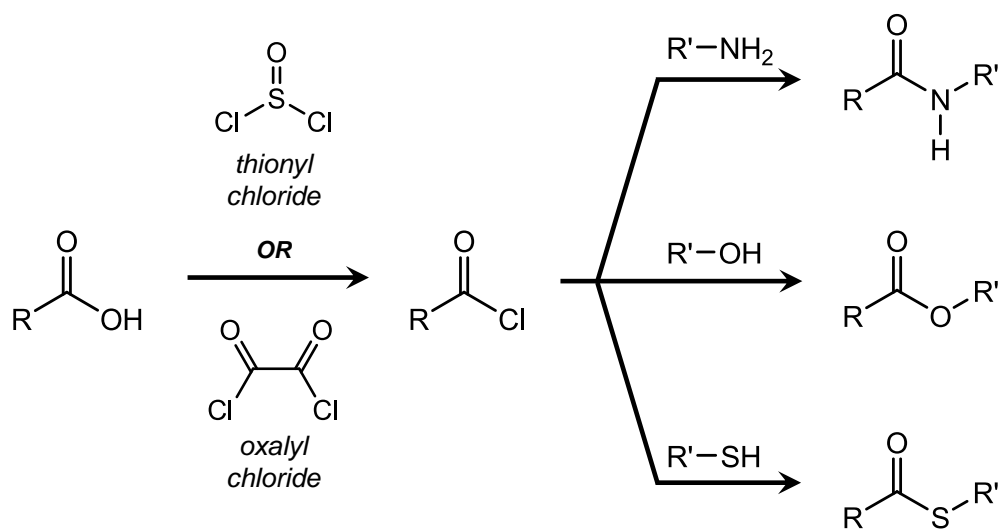
Exchanging Carboxylic Acid Derivatives

Often impractical to synthesize carboxylic acid derivatives by equilibrium reactions.

Solution: "Activate" acyl group first, by converting acid to a more reactive derivative.

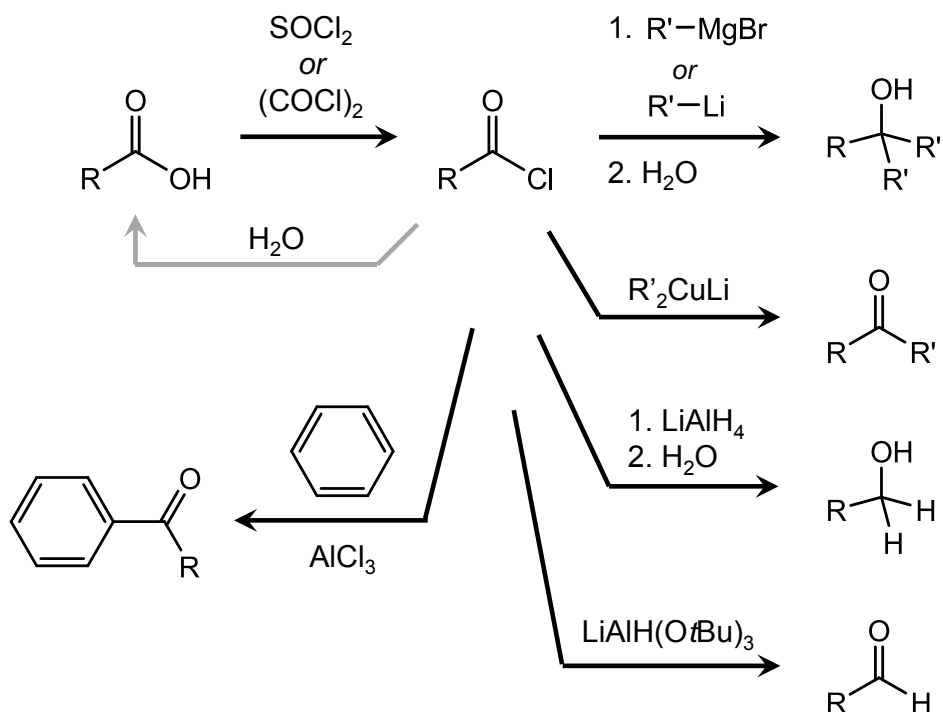


Acyl Halides as Acylating Agents

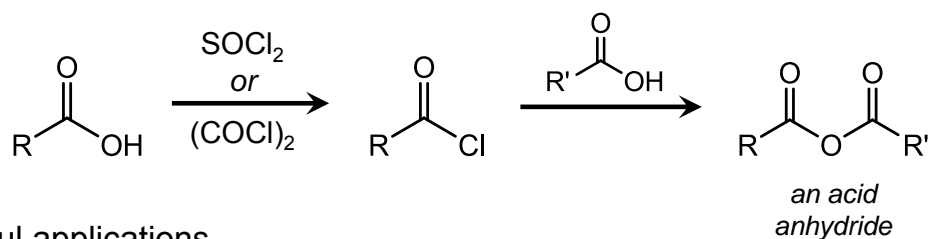


Acyl halides are so reactive, no acid/base catalyst necessary.

Reactivity of Acyl Halides

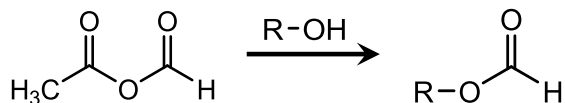


Acid Anhydrides



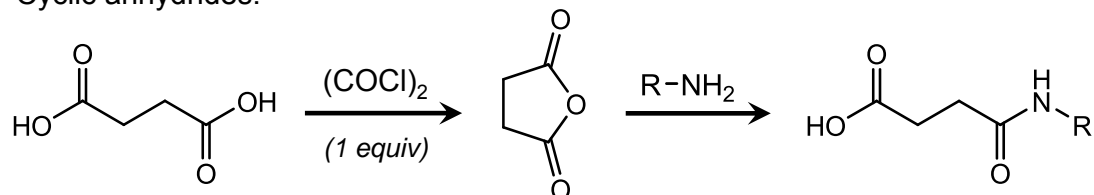
Useful applications

- Formylation. (*Formyl chloride unstable.*)



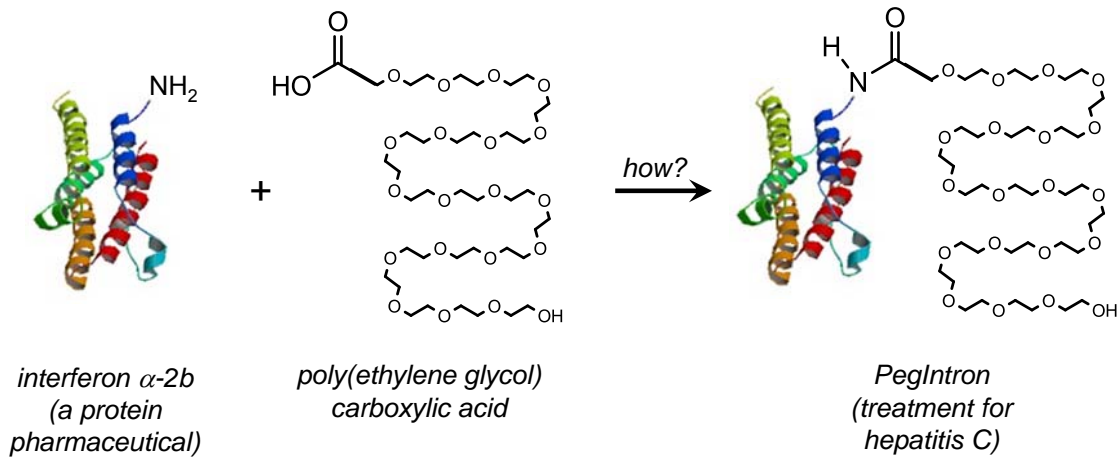
undergo same reactions as acyl halides.

- Cyclic anhydrides.



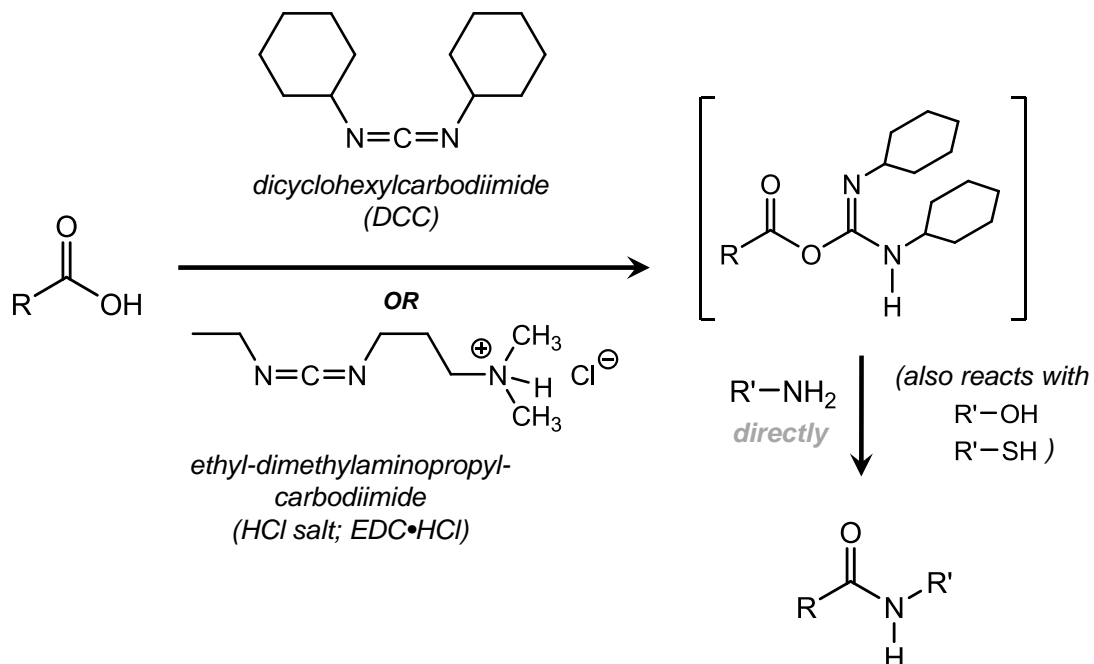
Acylation in Polar Media

For molecules that are only soluble in H₂O, can't use acyl halides.



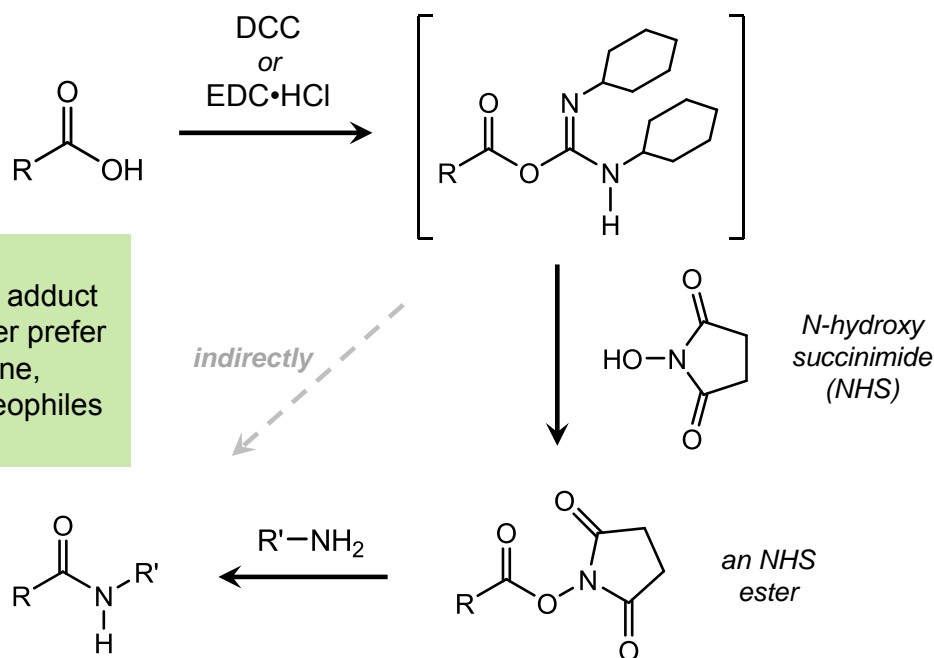
(Connecting polymer to protein increases circulation time of injected protein in blood.)

Carbodiimide Coupling of Nucleophiles and Carboxylic Acids

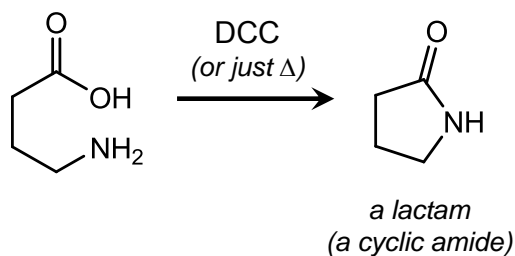
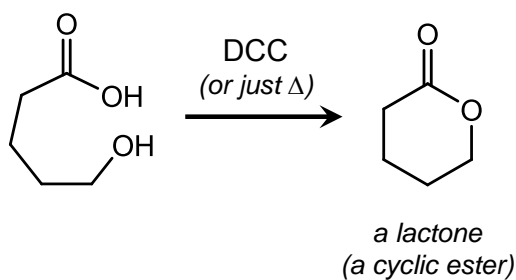


Indirect Coupling via NHS Esters

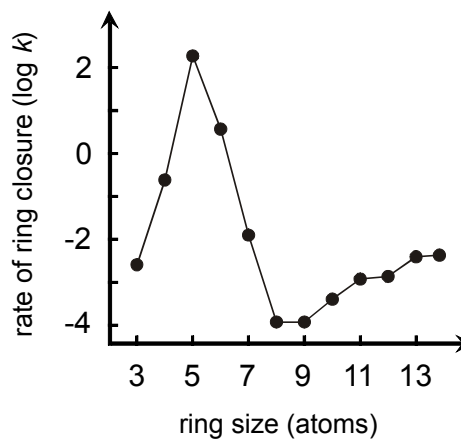
Key feature:
Carbodiimide adduct and NHS ester prefer stronger (amine, alcohol) nucleophiles over H₂O.



Lactones and Lactams



5-, 6-membered rings are easiest to make.



← ring strain → ← entropy cost of joining ends →