

CHEM 20482 - Basic Organic Chemistry - Chapter 20 Review

Carboxylic Acid Derivatives

Structure & Nomenclature

R-C(=O)-Cl acyl chloride	change <i>-ic acid</i> to <i>-yl chloride</i>	Ex. $\text{CH}_3\text{C(O)Cl}$: acetyl chloride
R-C(O)-O-C(O)-R acid anhydride	change <i>acid</i> to <i>anhydride</i>	Ex. $\text{CH}_3\text{C(O)OC(O)CH}_3$: acetic anhydride
R-C(O)SR thioester	alkyl + change <i>-ic acid</i> to <i>-thiolate</i>	Ex. $\text{CH}_3\text{C(O)-SCH}_3$: methyl acetothiolate
R-C(O)OR' ester	alkyl + change <i>-ic acid</i> to <i>-ate</i>	Ex. $\text{CH}_3\text{C(O)-OCH}_3$: methyl acetate
R-C(O)NH₂ amide	change <i>-ic acid</i> to <i>-amide</i>	Ex. $\text{CH}_3\text{C(O)-NHCH}_3$: <i>N</i> -methylacetamide

Reactivity

For nucleophilic substitution reactions, the following order of reactivity is generally observed. You must know the mechanism for these reactions. (See textbook).

<i>Most reactive</i>	Molecule			<i>Least reactive</i>
RC(O)-Cl	RC(O)-O-C(O)R	RC(O)-SR	RC(O)-OR'	RC(O)-NR_2
acid chlorides	anhydrides	thioesters	esters & acids	amides
Cl^-	RCOO^-	SR^-	OR^- or OH^-	NH_2^- or NHR^- or NR_2^-
<i>Least basic</i>		Leaving Group		<i>Most basic</i>

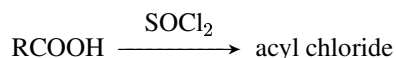
General Reactions

In general, reactions only work going from more reactive reactants to less reactive products

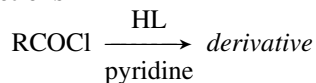
		<i>Reacts with:</i>			
RC(O)Cl	-	carboxylic acid → pyridine	alcohol → pyridine	water →	amine → base
RC(O)-O-C(O)R		-	alcohol → acid or base	water →	2 amine →
RC(O)OR'			-	water → acid or base	amine →
RCOOH	$\xrightarrow{\text{SOCl}_2}$		alcohol → acid or base	-	amine → Δ
$\text{RC(O)NR}'_2$				water, Δ → acid or base	-
		<i>To produce</i>			
		RC(O)Cl	RC(O)-O-C(O)R	RC(O)OR'	RCOOH
					$\text{RC(O)NR}'_2$

Acyl chlorides

Synthesis

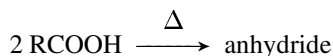


Reactions

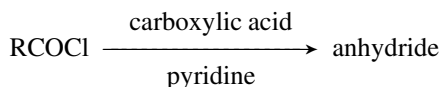


pyridine used to trap HCl by-product and deprotonate reactant

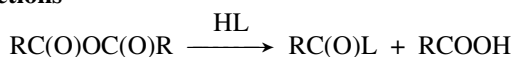
HL = acid (→ anhydride), thiol (→ thioether), alcohol (→ ester), water (→ acid), amine (→ amide).

Anhydrides**Synthesis**

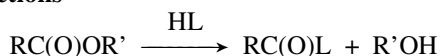
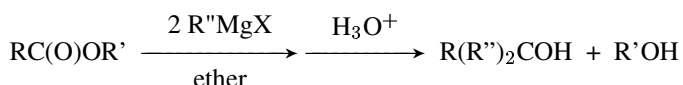
Best for diacids (to make cyclic product or acetic acid)



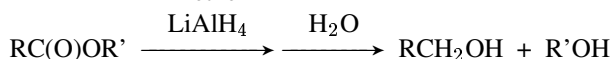
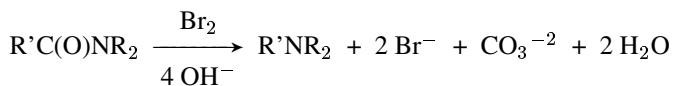
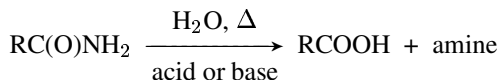
Only practical route for mixed anhydrides (different R groups)

ReactionsHL = thiol (\rightarrow thioester), alcohol (\rightarrow ester), water (\rightarrow acid), amine (\rightarrow amide)**Esters****Synthesis**

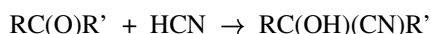
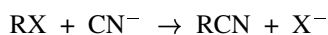
See above reactions. Most common route from carboxylic acid + alcohol. Mechanism for acid-catalyzed esterification discussed in detail in text, p.850-851 & 812-813. (Know this).

ReactionsHL = water (\rightarrow acid) or amine (\rightarrow amide)

(Two equivalents of Grignard required)

(NaBH₄ not reactive enough to reduce ester)**Amides****Synthesis**Can be prepared from any of above derivatives. **Lactams** (cyclic amides) can be prepared from intramolecular reactions. (See for example H.W. 20.35b).**Reactions**

Hoffman rearrangement

Nitriles**Synthesis**

cyanohydrin

Reactions