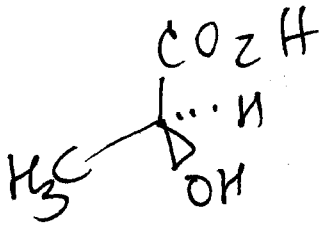
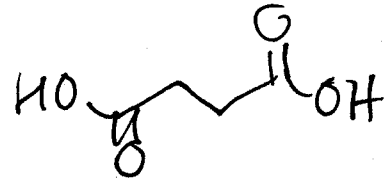
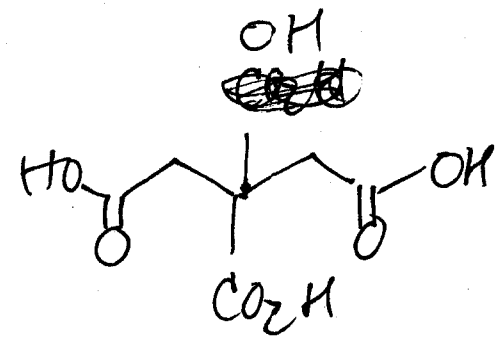
Acid chlorides + anhydrides — not found in nature (too reactive)



(S)(+) lactic acid

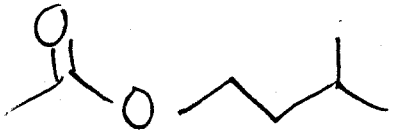


succinic acid

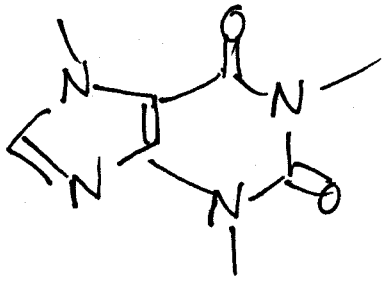


citric acid

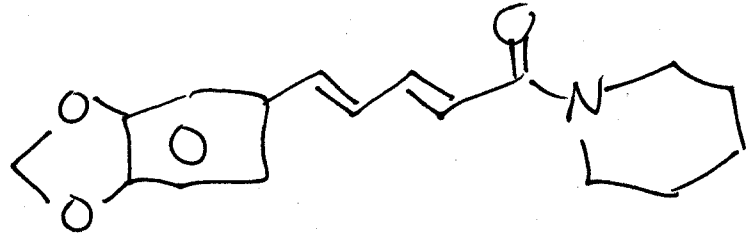
citric acid cycle



isopentyl acetate
bananas / pears

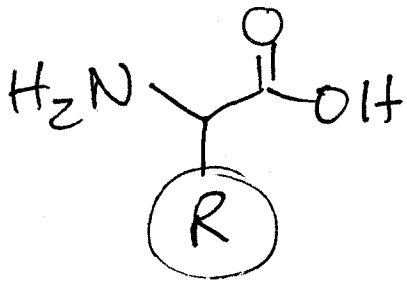


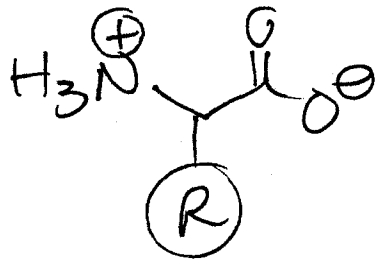
caffeine



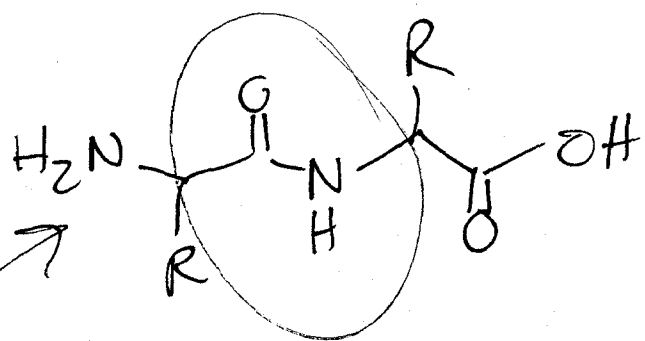
piperine
(black pepper)

Amino acids





zwitterion form

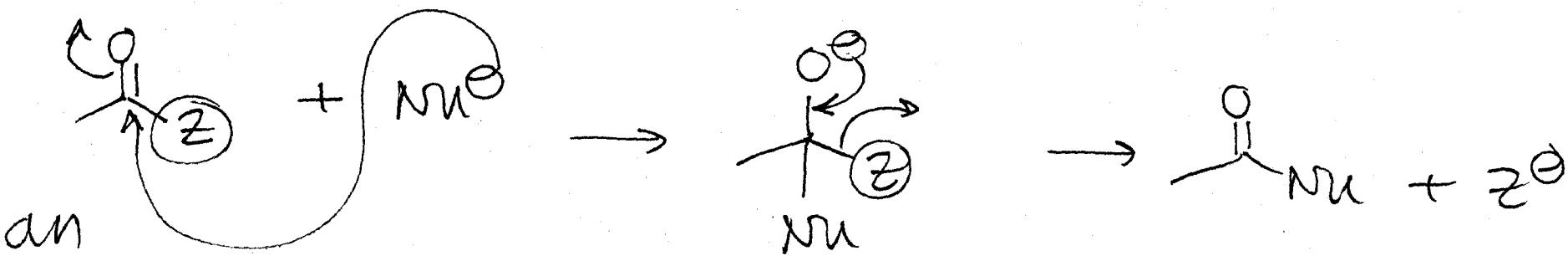


C-terminus

peptide bond (an amide)

N-terminus

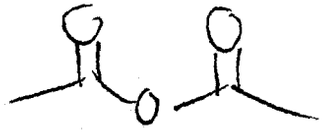
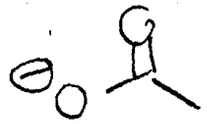
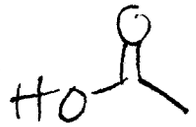
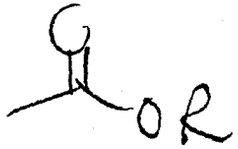
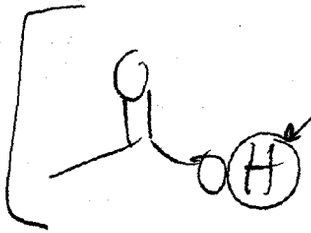
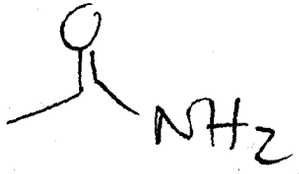
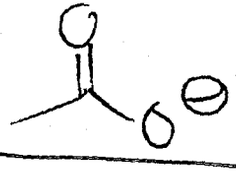
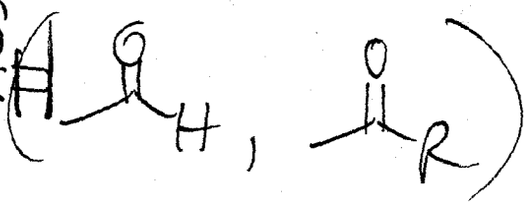
Acyl Substitution



an acyl compound

tetrahedral intermediate

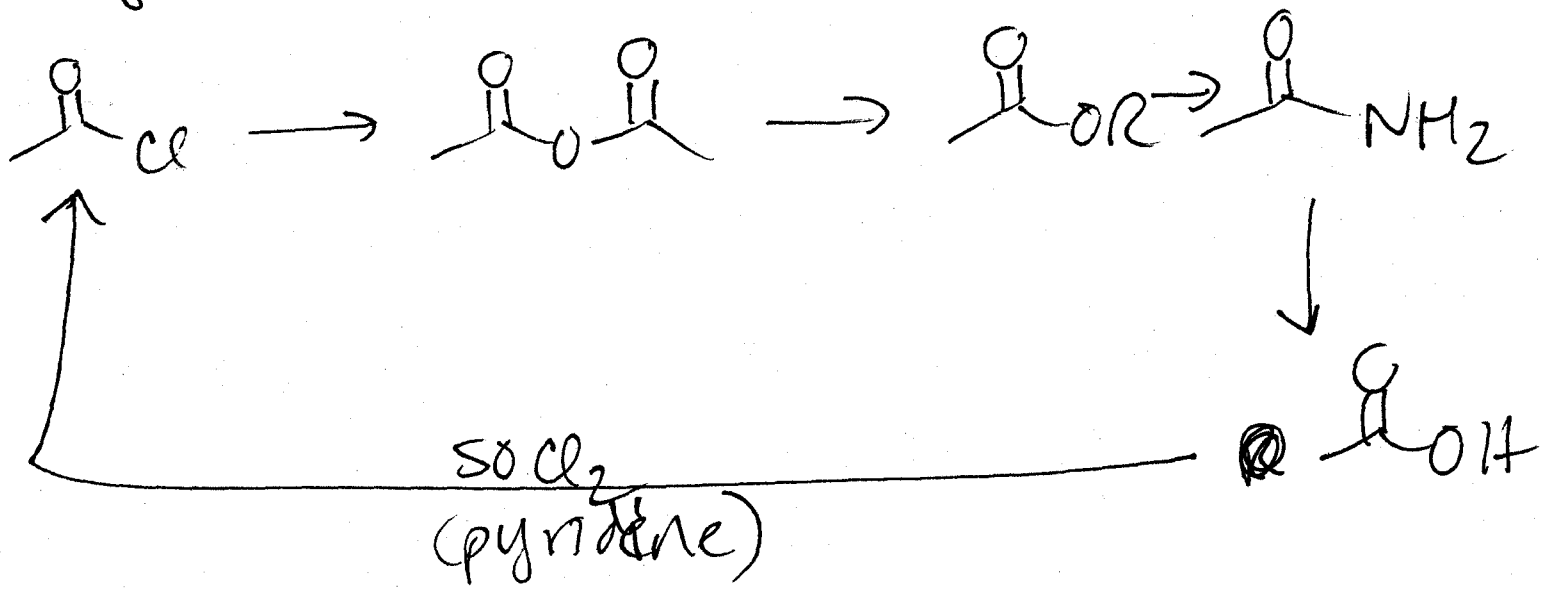
a new acyl compound

compound	Z (LG)	conj. acid	pka
	$Cl^{\ominus}$	HCl	-7
			3-5
	$^{\ominus}OR$	HOR	15-16
CLASS 7  problem-acidic H	$^{\ominus}OH$	H_2O	15.6
	$^{\ominus}NH_2$	NH_3	36
	O^{2-}	$HO^{\ominus}$	—
CLASS 	$H^{\ominus}$, $R^{\ominus}$	H_2, RH	~40 ~60

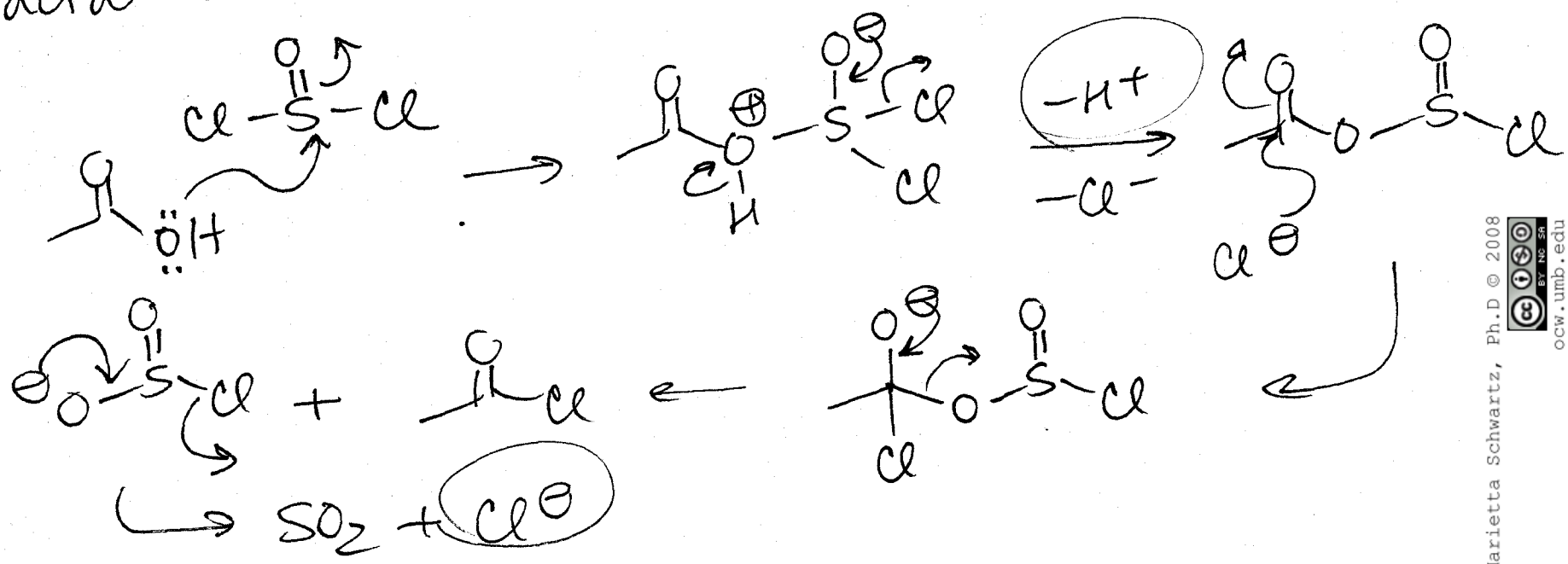
v. reactive

not so reactive

Reactivity cycle



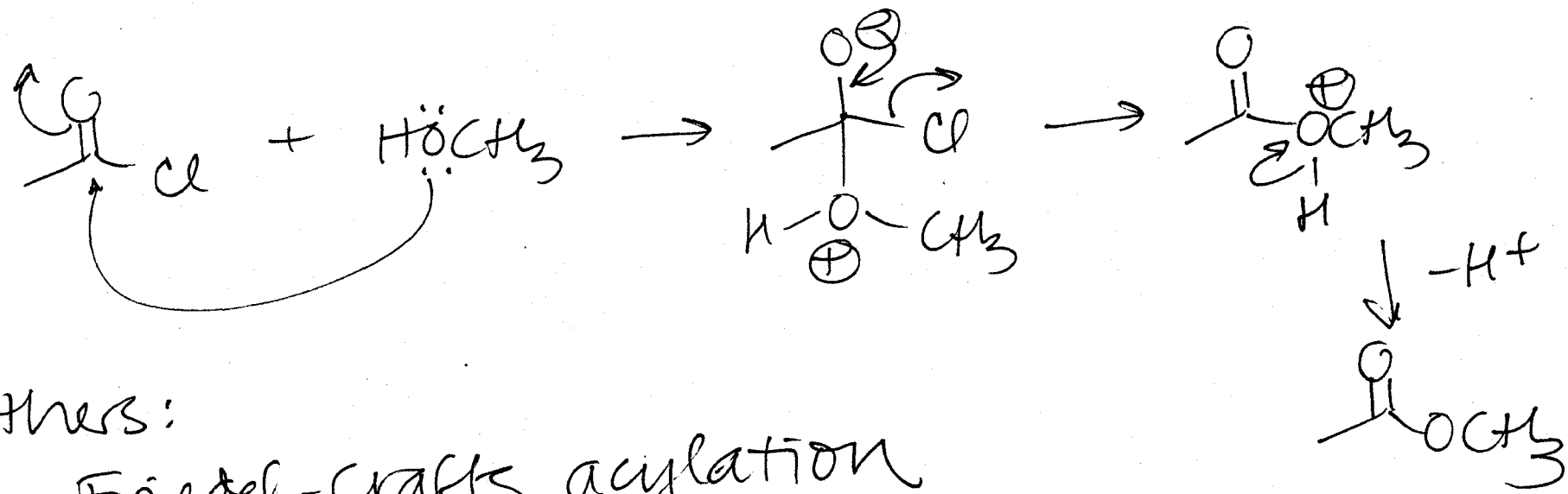
acid → acid chloride



Acid chlorides

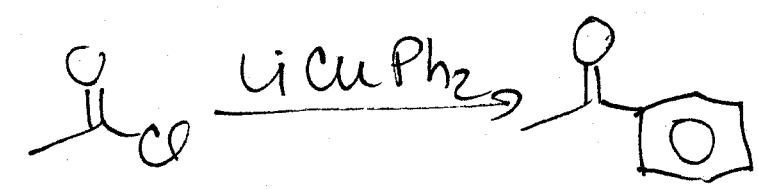
Add a nucleophile (acyl substitution)

- + carboxylic acid → anhydride
- + alcohol → ester
- + amine → amide
- + H_2O → carboxylic acid (hydrolysis)



Others:

- Friedel-Crafts acylation
- react w/ $LiCuR_2$ → ketone



Anhydrides

From: - acid chloride + carboxylic acid
- dehydration of diacids

Reactions:

acyl substitution

(+ carboxylic acid / H_3O^+ → different anhydr.)

+ alcohol / H_3O^+ → ester ← $^{\ominus}OR$

+ amine / Δ → amide

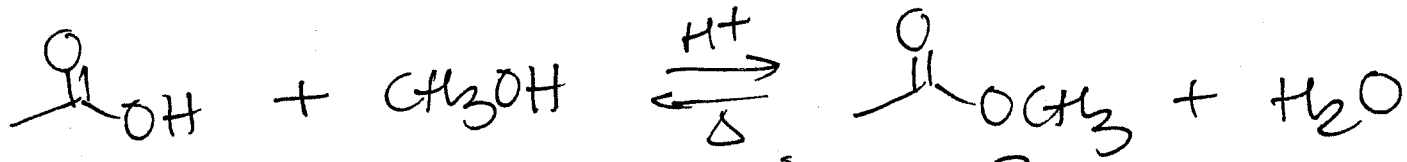
+ H_3O^+ / Δ → carboxylic acid

Friedel-Crafts acylation (most often with cyclic anhydrides)

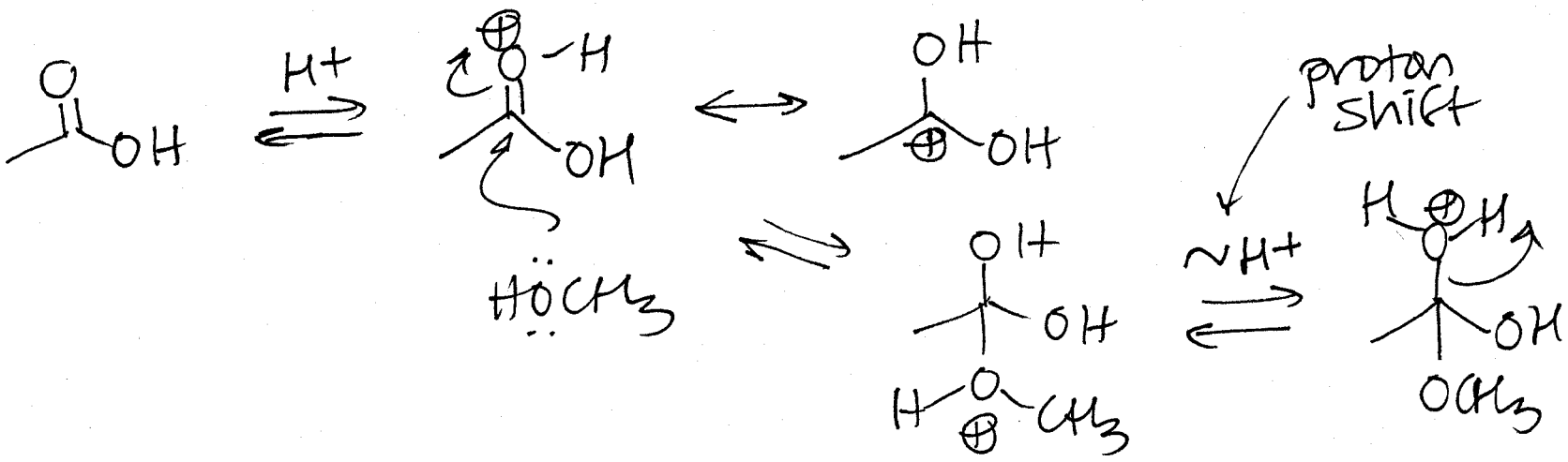
Esters

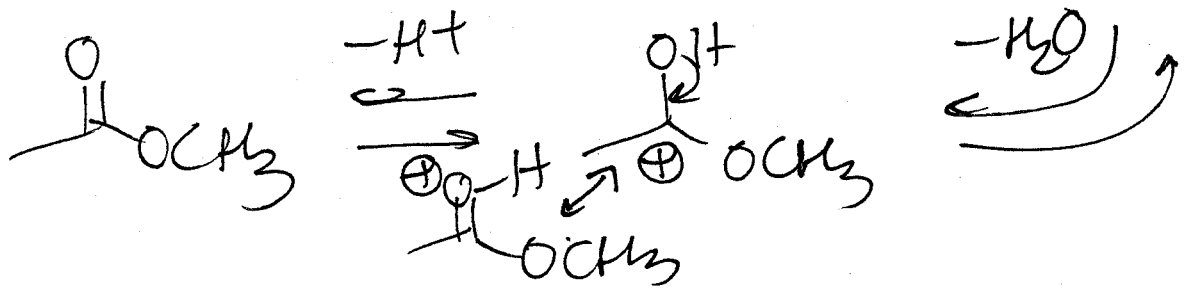
From: acid chloride + alcohol
anhydride + alcohol/H+ or $^{\ominus}OR$

Fischer esterification

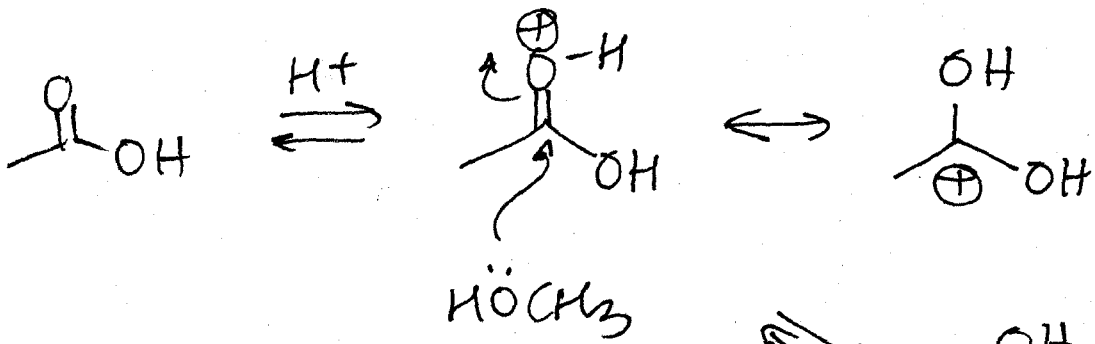


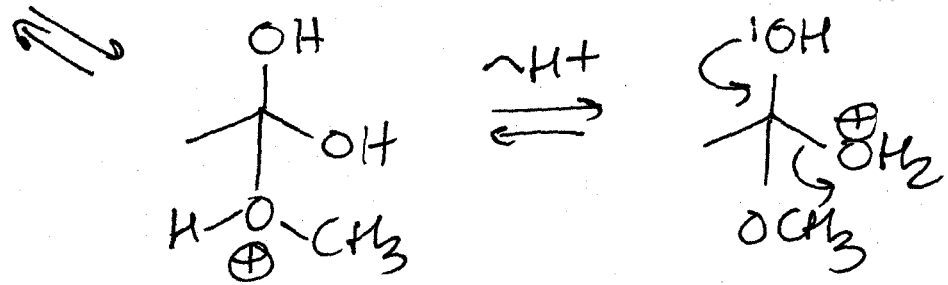
which way does it go?
* LeChatelier's Principle!





Fischer Esterification





Forward	Reverse
Protonate C=O	Protonate C=O
NU = ROH	NU = H_2O
shift proton	shift proton
loss of H_2O	loss of ROH
deprotonate	deprotonate