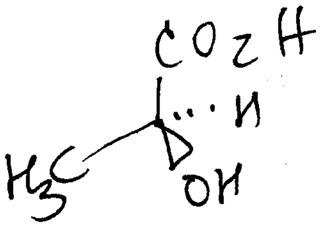
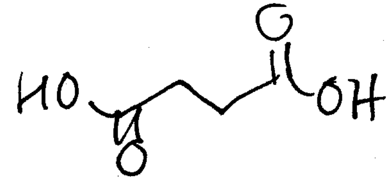
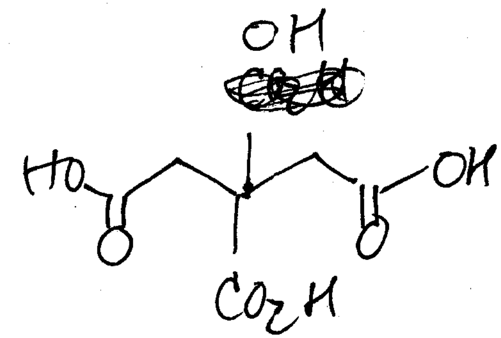
Acid chlorides + anhydrides — not found in nature (too reactive)



(S)(+) lactic acid

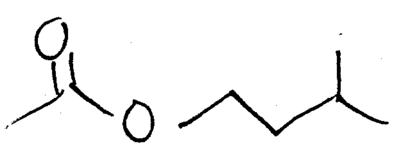


succinic acid

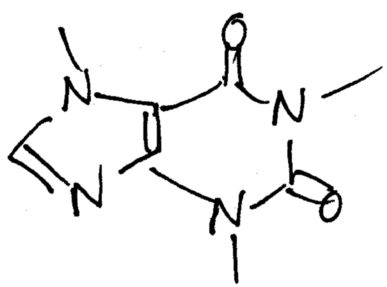


citric acid

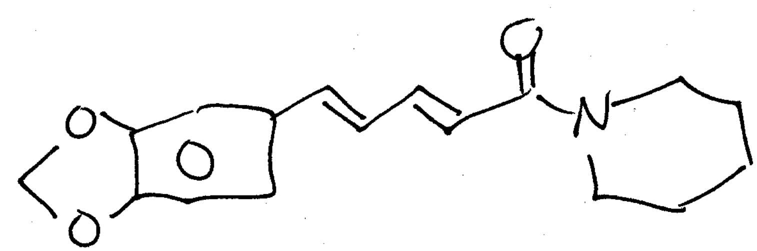
citric acid cycle



isopentyl acetate
bananas / pears

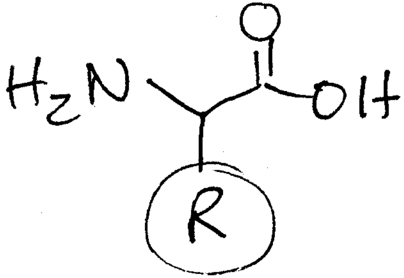


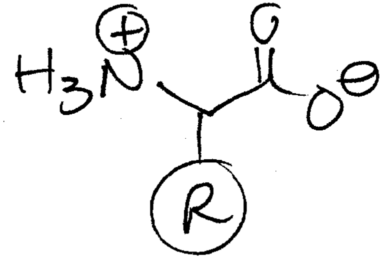
caffeine



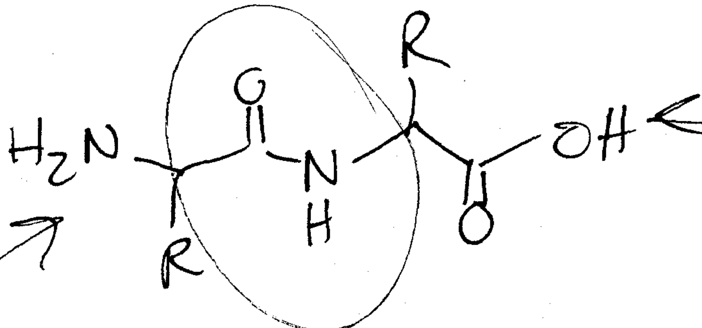
piperine
(black pepper)

Amino acids





zwitterion form

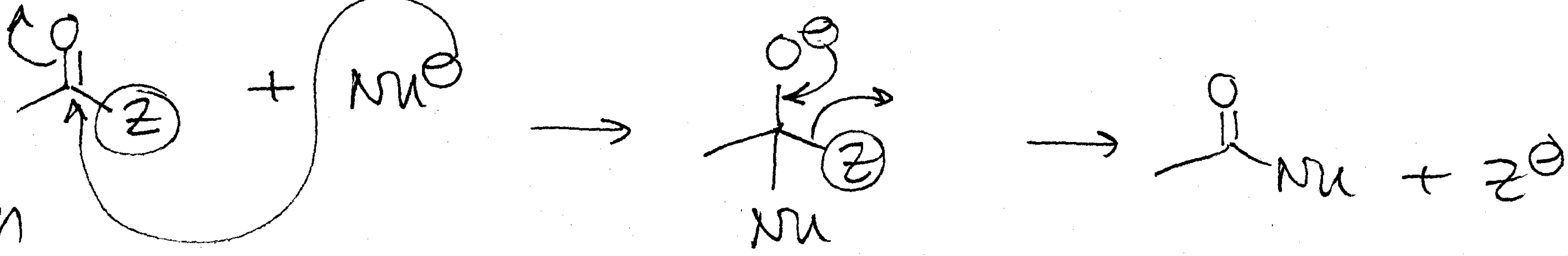


peptide bond
(an amide)

N-
terminus

C-terminus

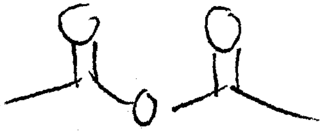
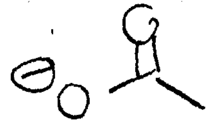
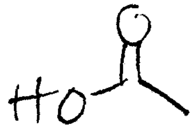
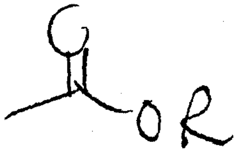
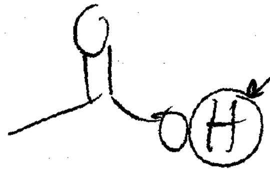
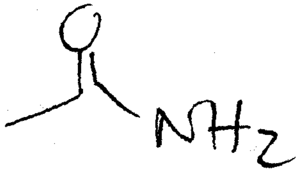
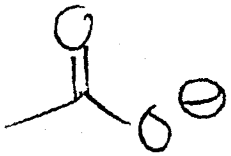
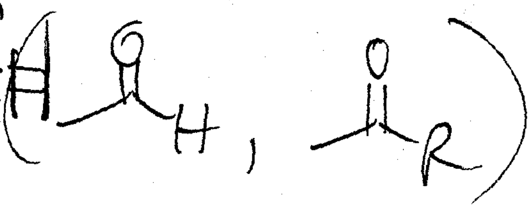
Acyl Substitution



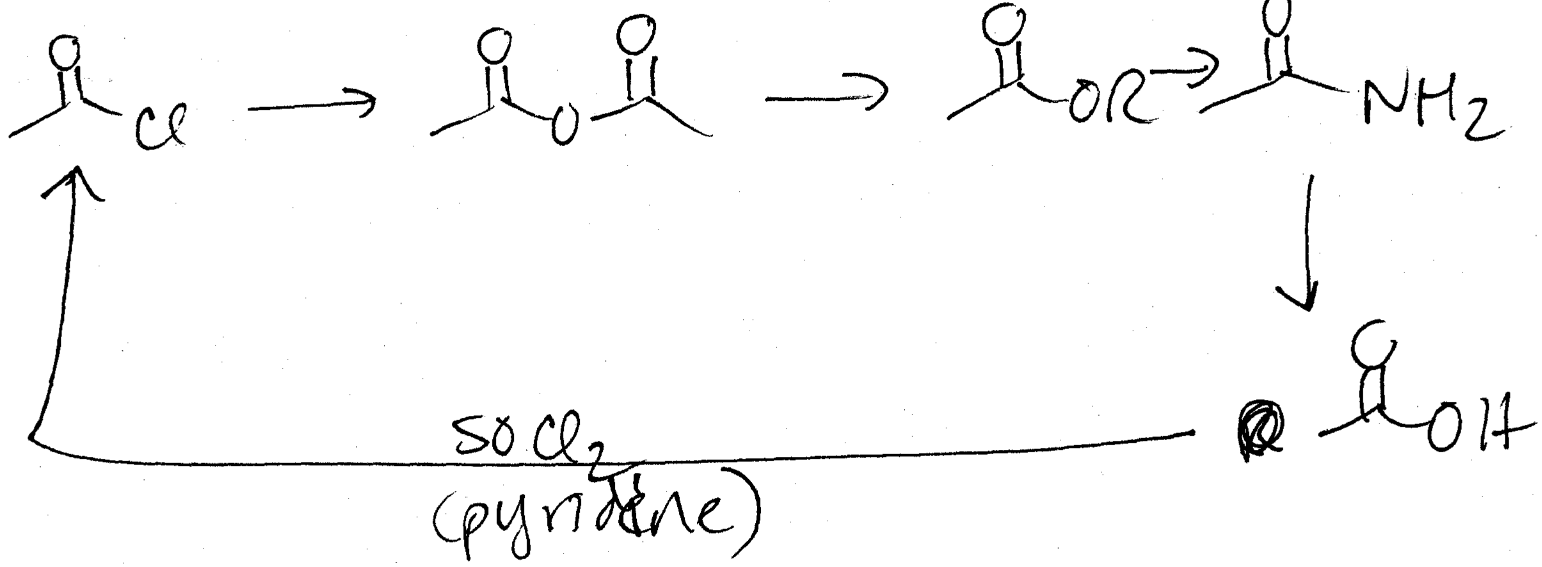
an acyl compound

tetrahedral intermediate

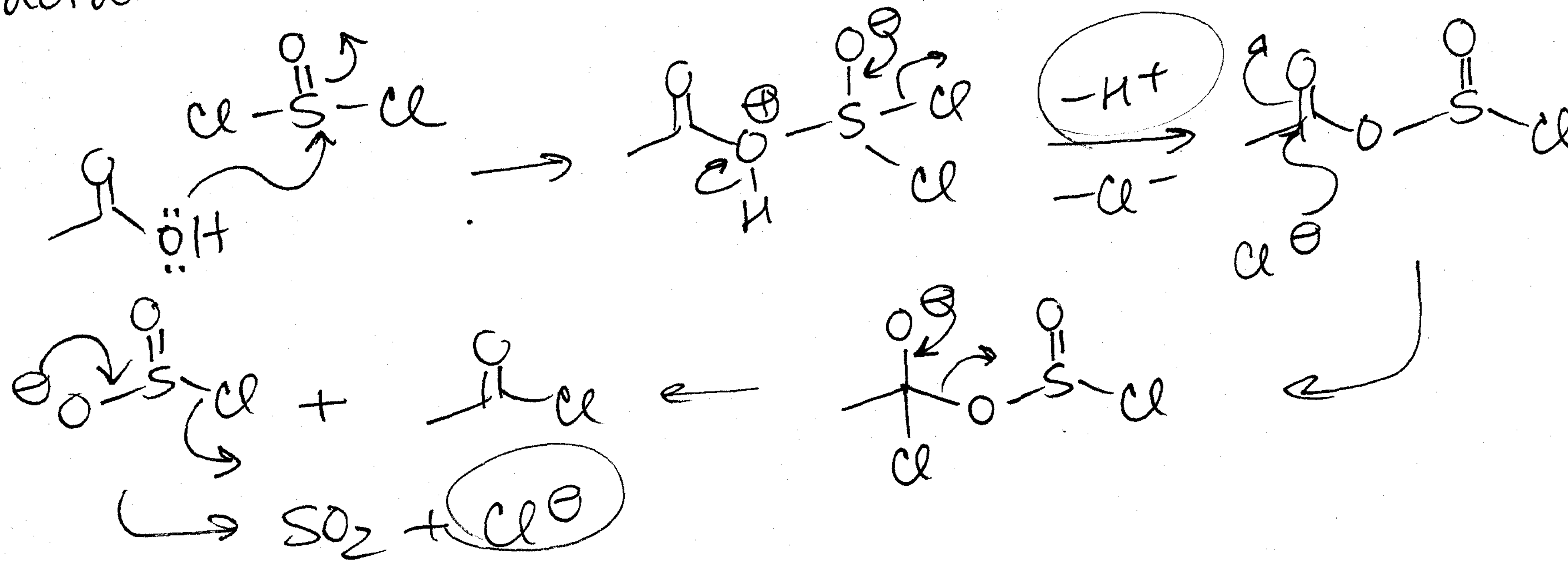
a new acyl compound

compound	Z (LG)	conj. acid	pKa	
	$Cl^{\ominus}$	HCl	-7	v. reactive
			3-5	
	$^{\ominus}OR$	HOR	15-16	
CLASS I  problem-acidic H	$^{\ominus}OH$	H_2O	15.6	
	$^{\ominus}NH_2$	NH_3	36	not so reactive
	O^{2-}	$HO^{\ominus}$	—	
CLASS II 	$H^{\ominus}$, $R^{\ominus}$	H_2, RH	~40 ~60	

Reactivity cycle



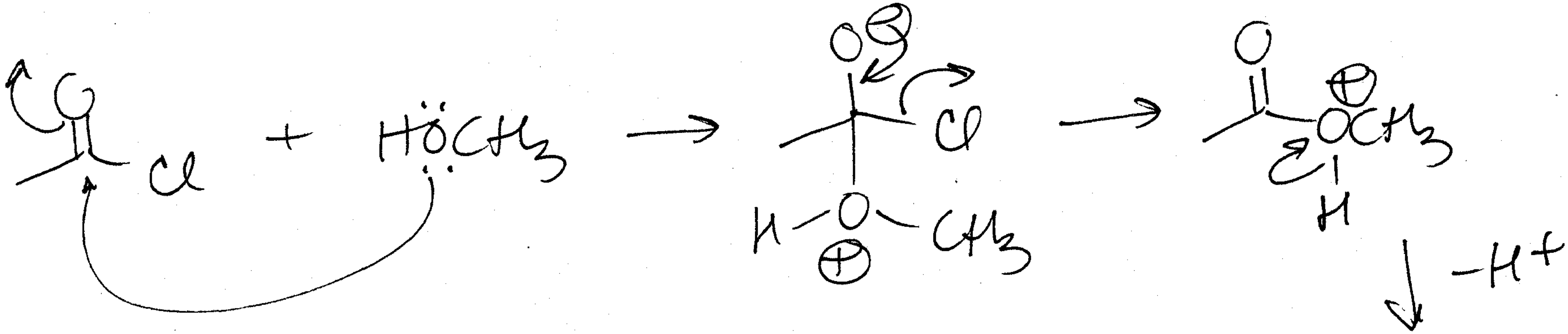
acid → acid chloride

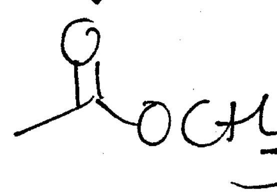


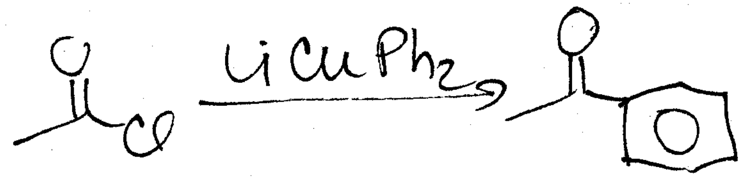
Acid chlorides

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 anhyd.)

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

+ amine / Δ → amide

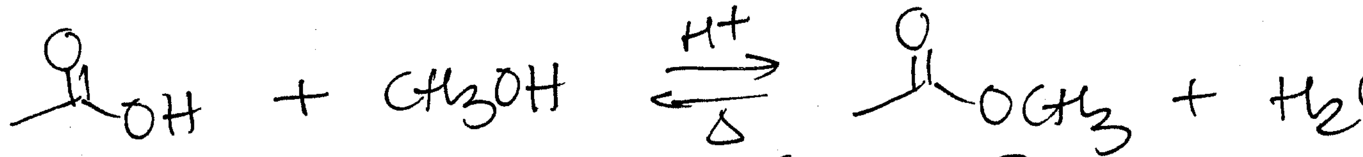
+ H_3O^+ / Δ → carboxylic acid

Friedel-Crafts acylation (most often with cyclic anhydrides)

Esters

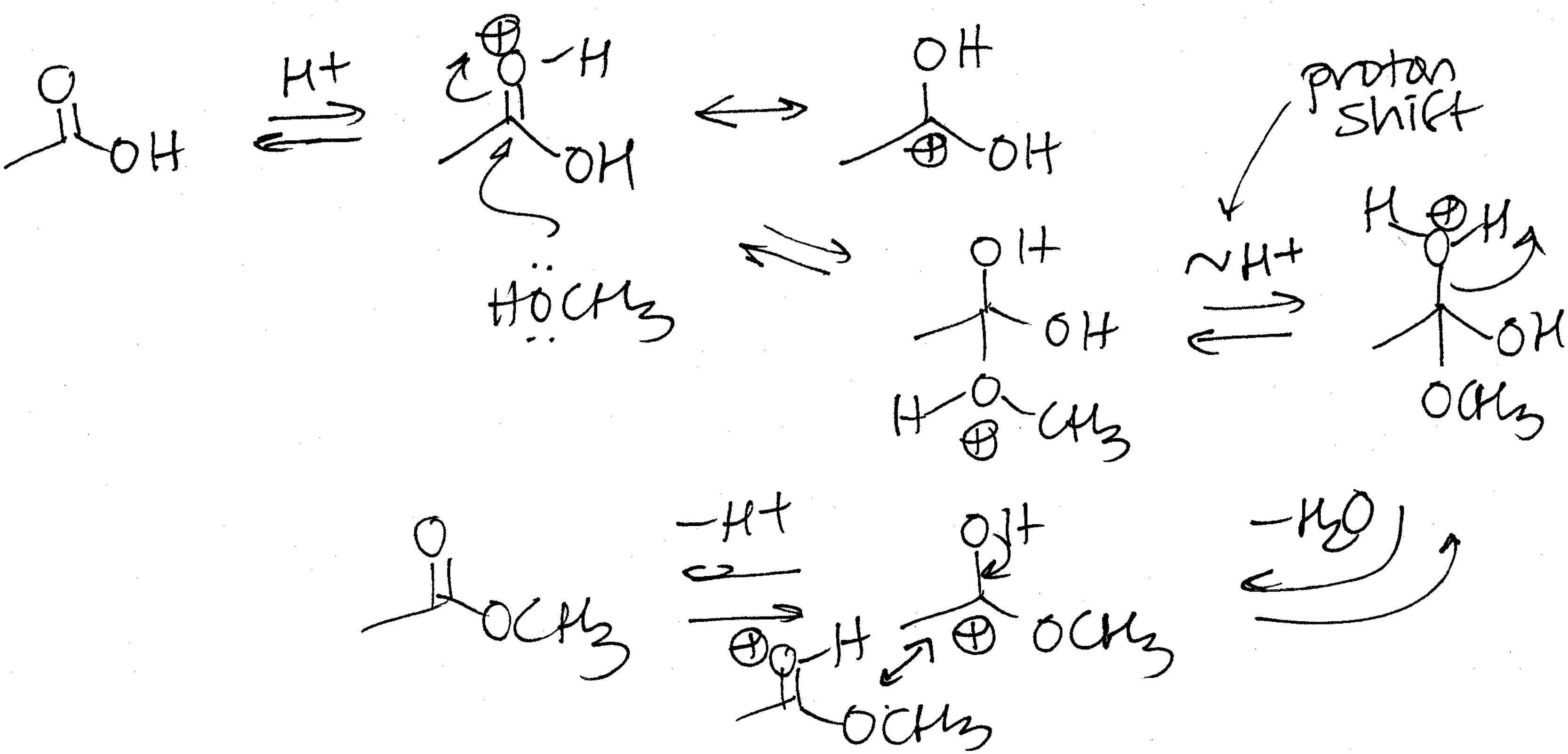
From: acid chloride + alcohol
anhydride + alcohol/H^+ or $^{\ominus}OR$

Fischer esterification

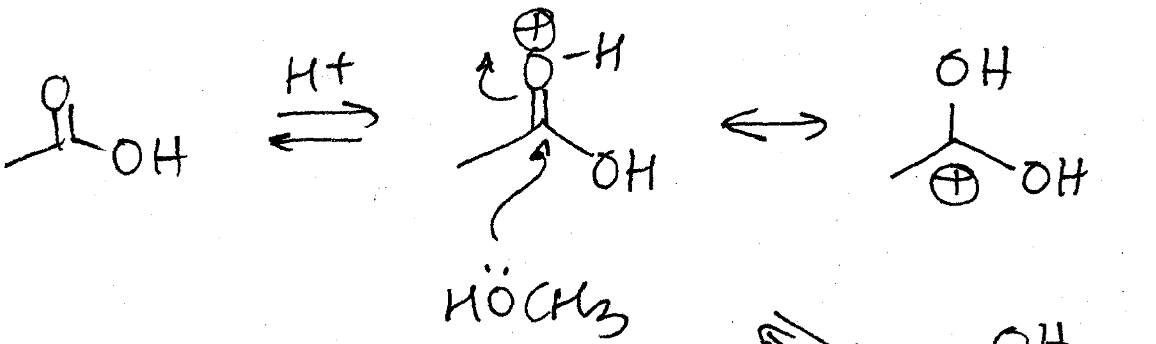


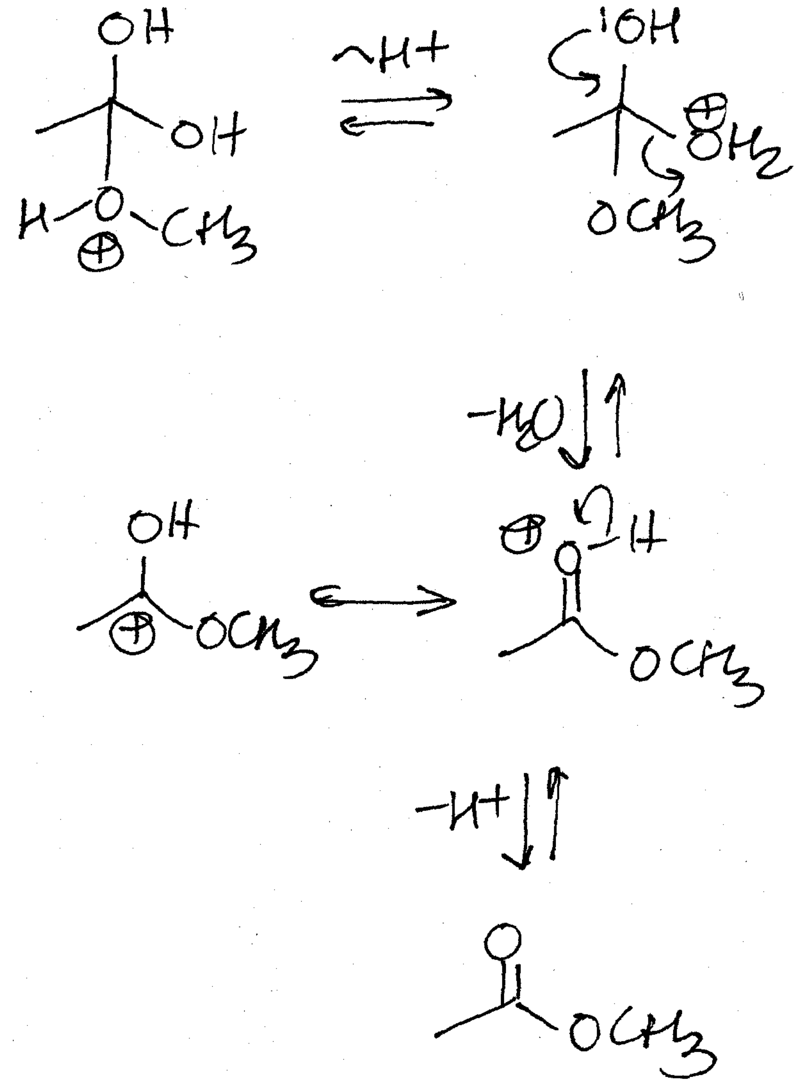
which way does it go?

* Le Chatelier's Principle!



Fischer Esterification





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