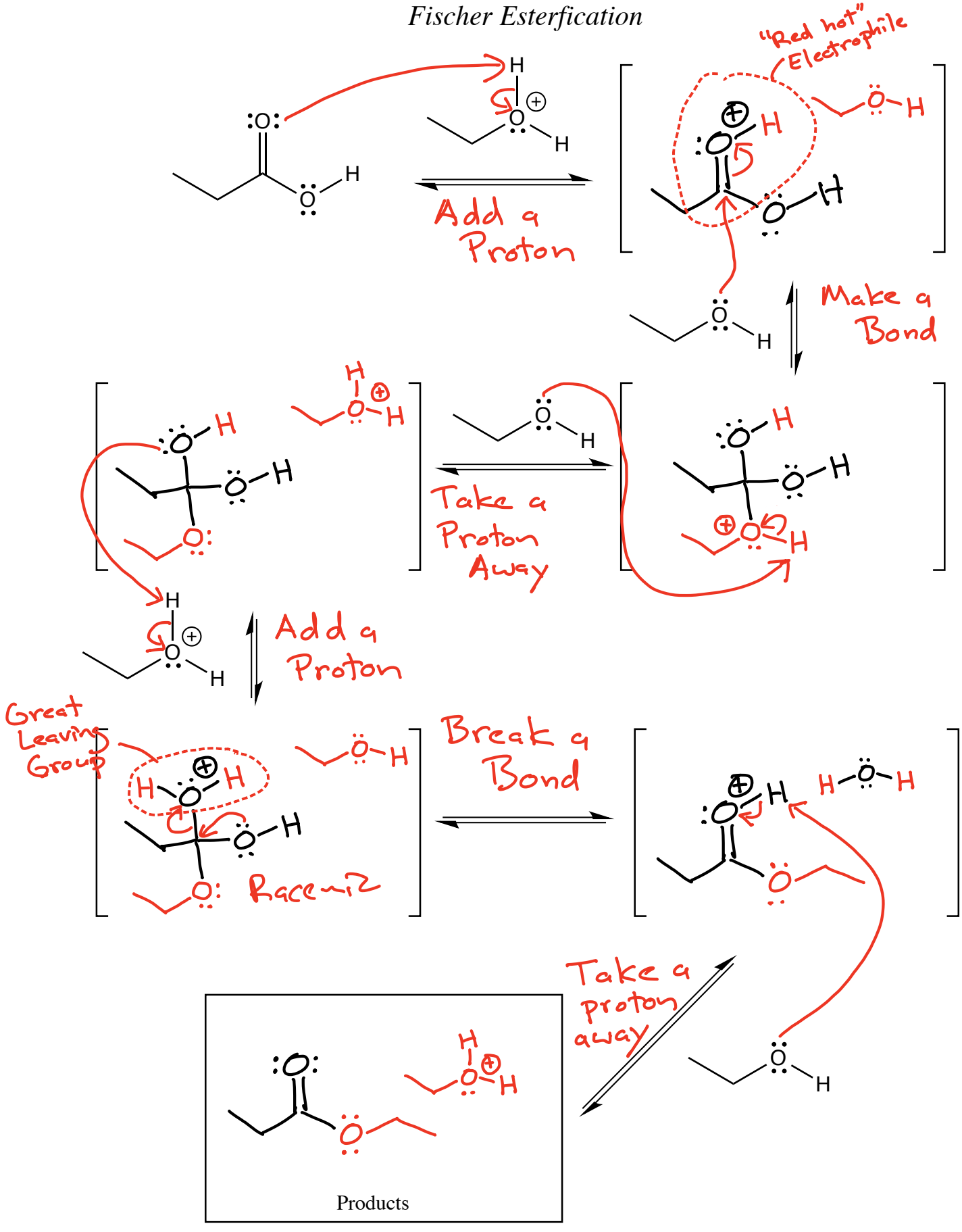
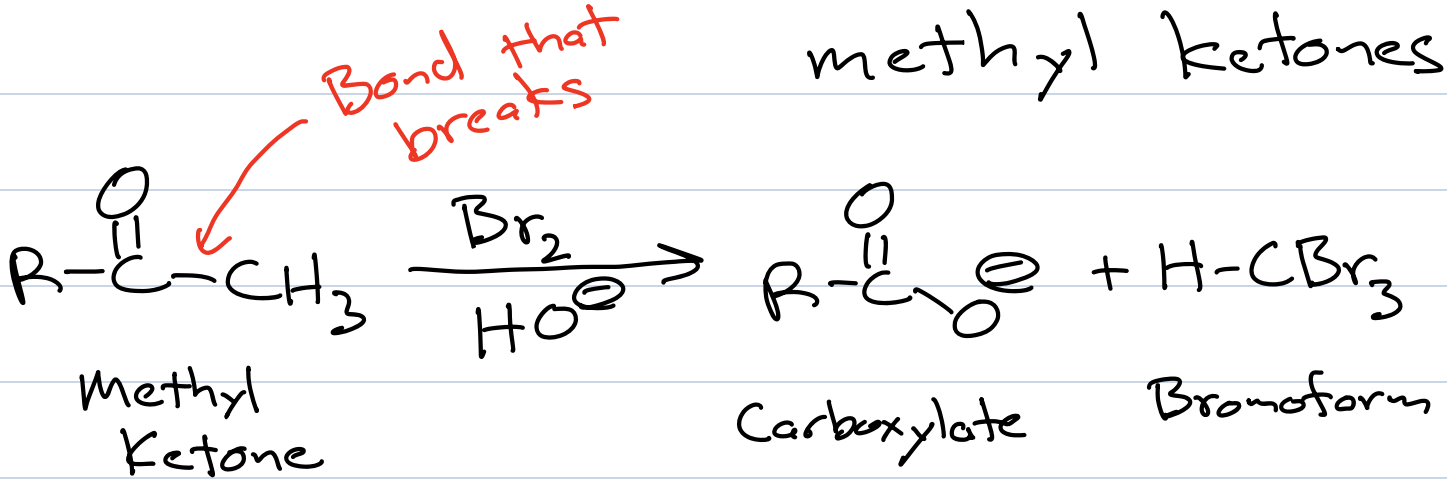
*Fischer Esterfication*



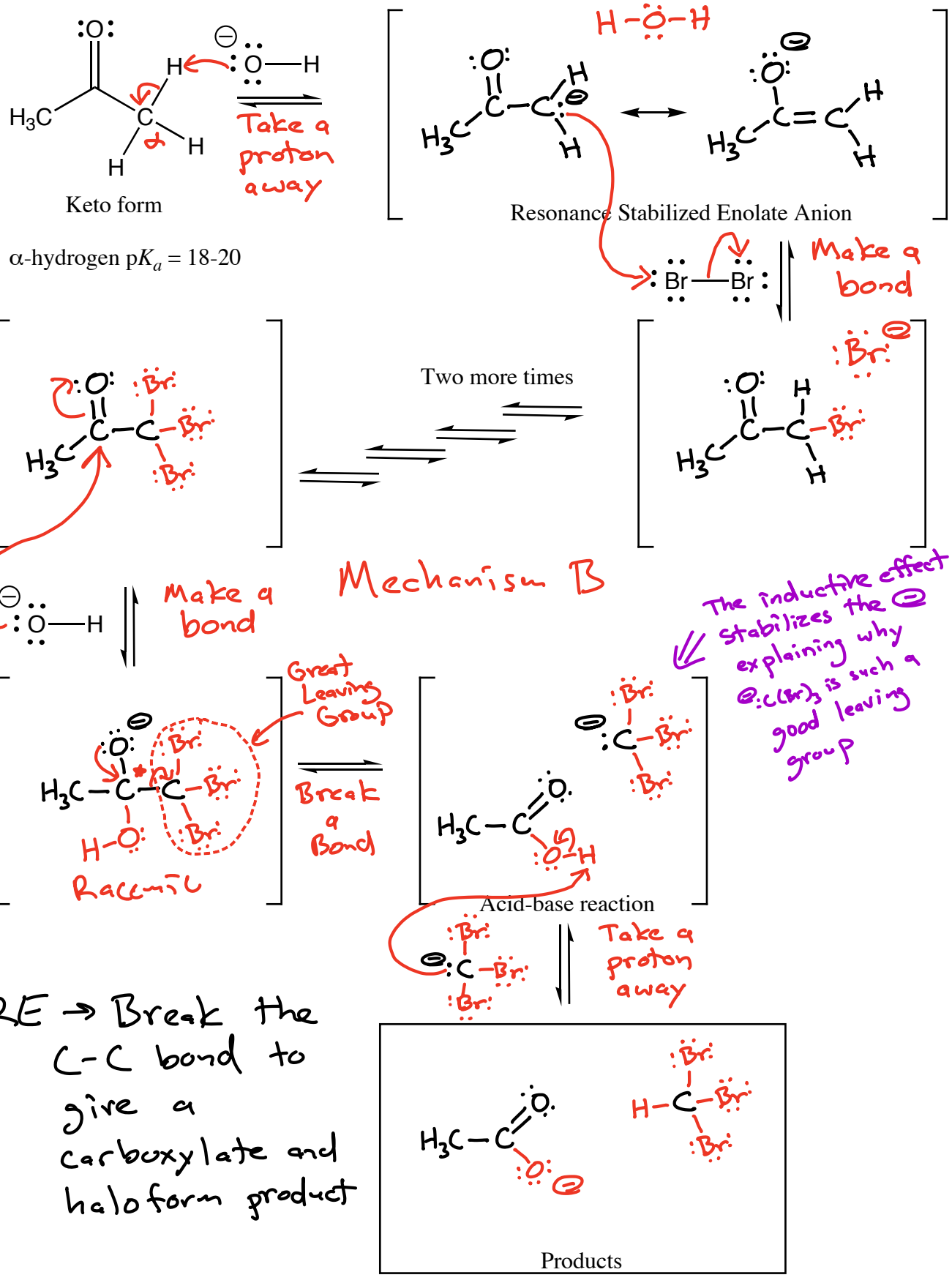
The haloform reaction → uses methyl ketones




Not that useful for synthesis, however the mechanism contains three elements that are important to second semester organic chemistry

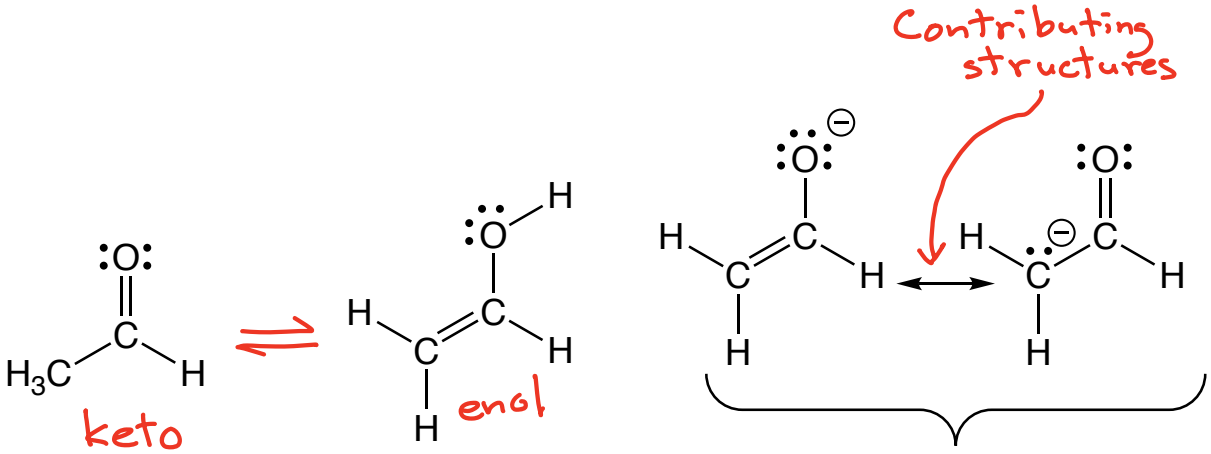
1) acidity of α-hydrogen
2) enolate nucleophile
3) Mechanism B

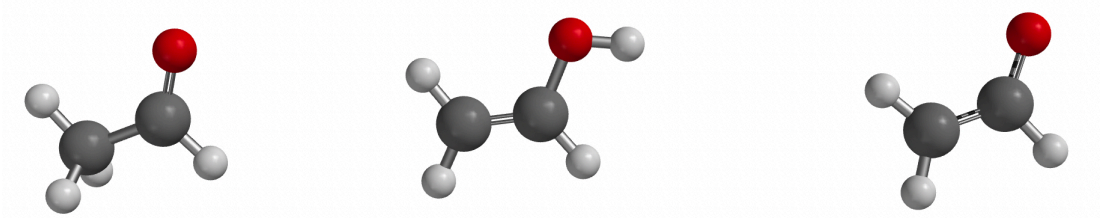
# *The Haloform Reaction*

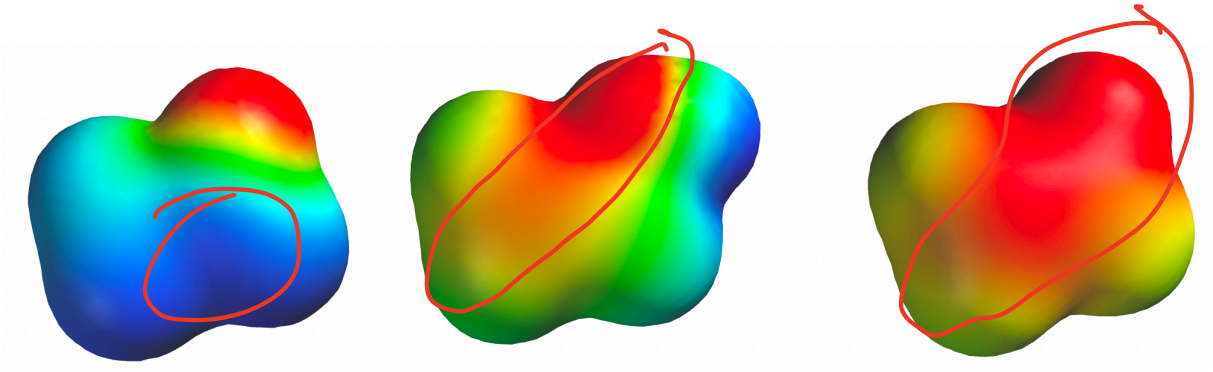



KRE → Break the C-C bond to give a carboxylate and haloform product

Be Careful: Do not confuse keto-enol equilibrium with enolate contributing structures!





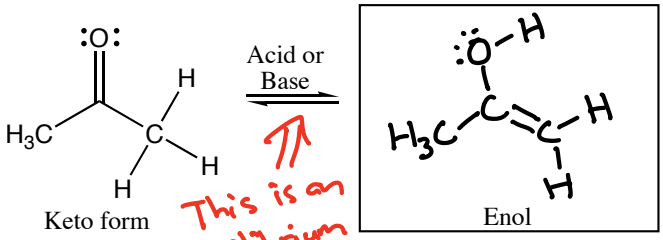
Electrophile

Nucleophile

Strong Nucleophile

*Keto-Enol Tautomerization vs. Enolate Resonance*

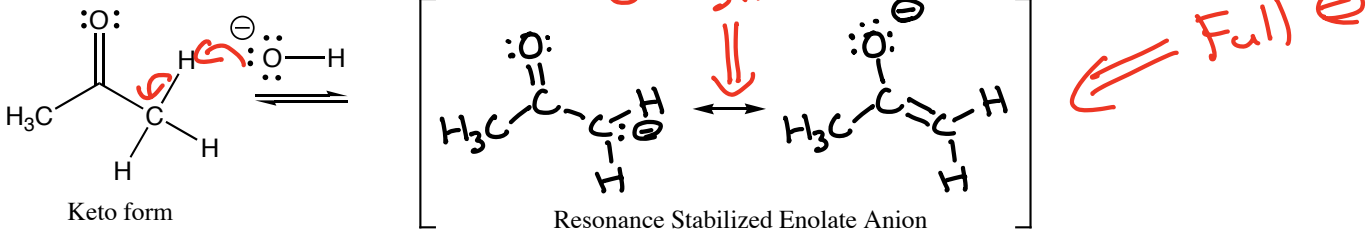
## *Keto-Enol Tautomerization*




This is an equilibrium

Both the keto and enol molecules are Neutral!

## *Enolate Resonance*




α-hydrogen p$K_a$ = 18-20

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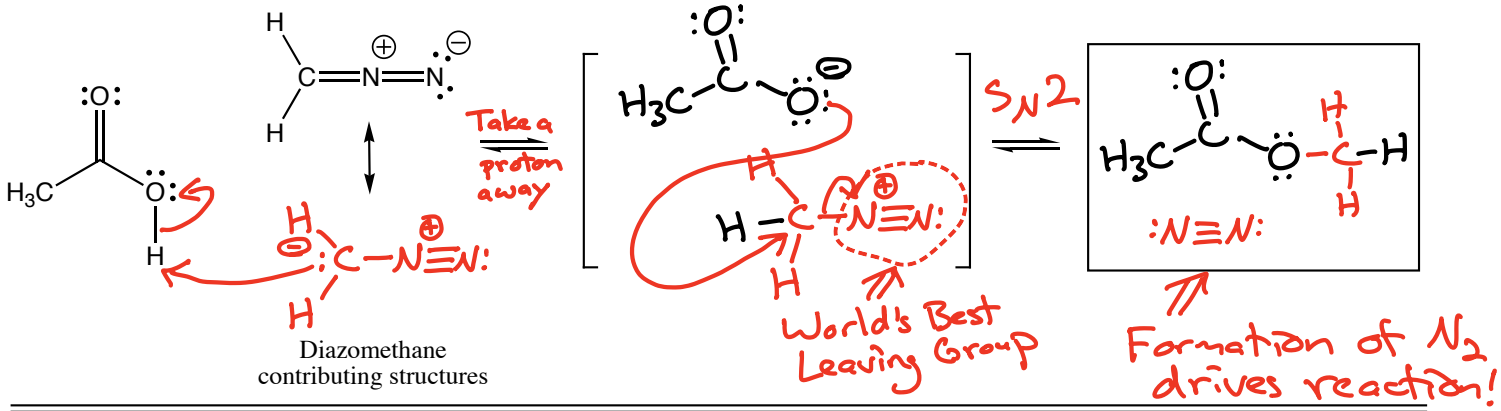
## *Diazomethane reaction*

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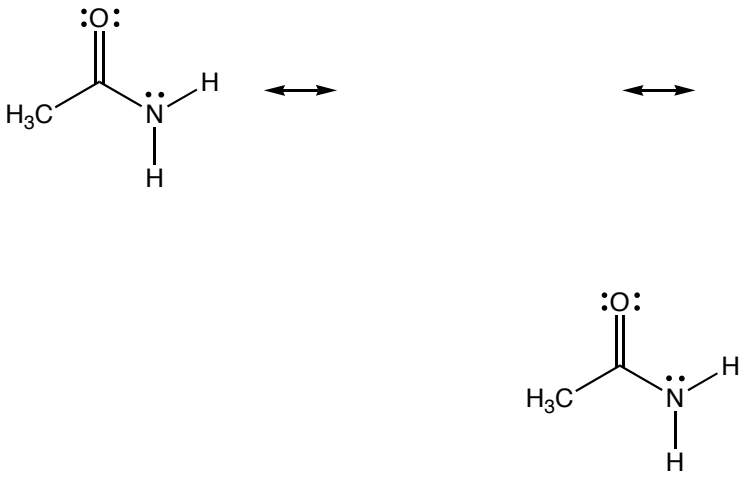
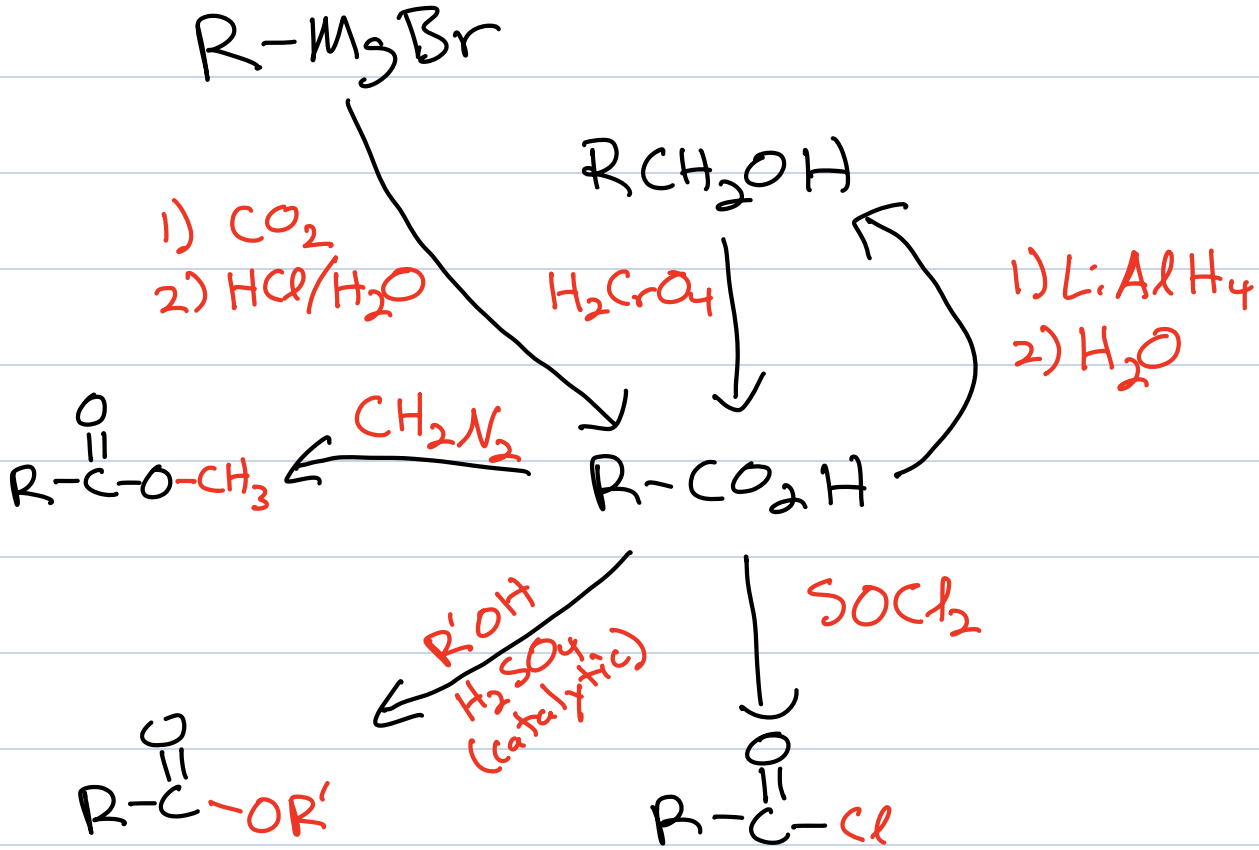
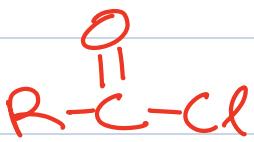
## *Amide Resonance VERY IMPORTANT!!!!!!*



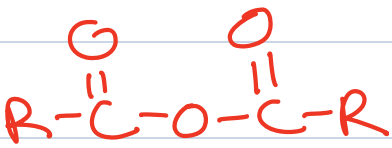
# Summary of Carboxylic Acid Reactions → So Far...



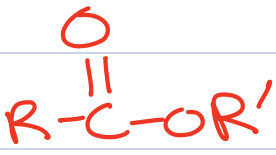
# Carboxylic Acid Derivatives



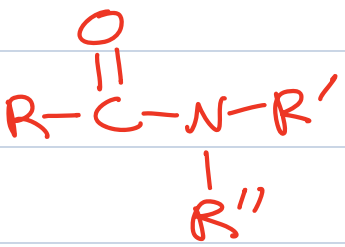
Acid Chloride



Anhydride

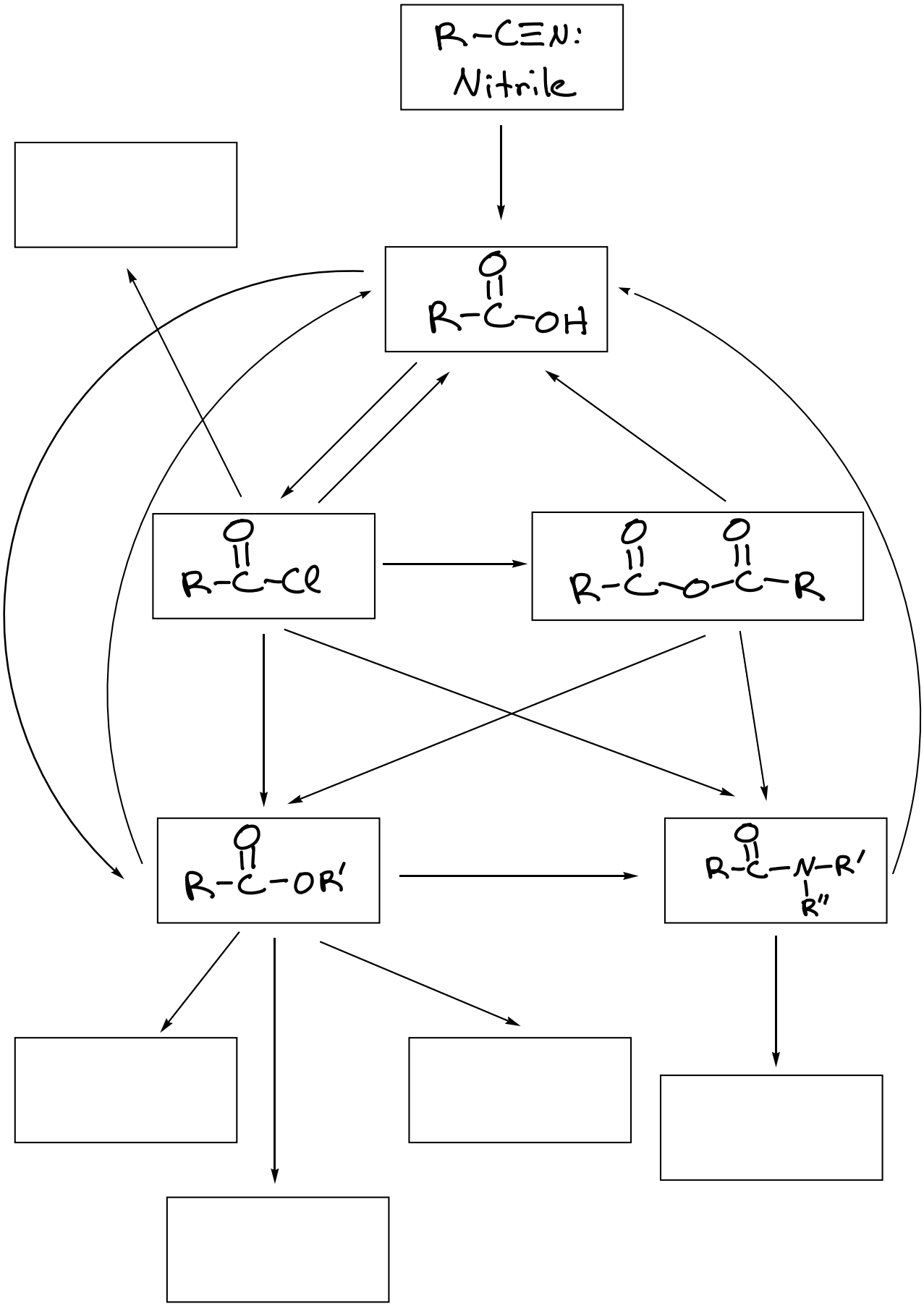


Ester



Amide

*Interconversion of Carboxylic Acid Derivatives*



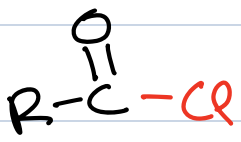
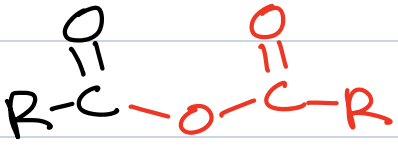
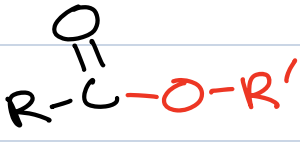
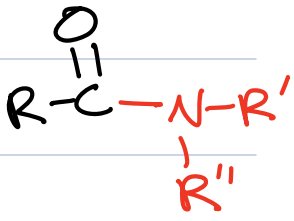
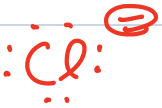
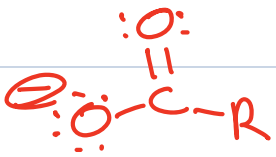
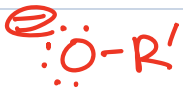
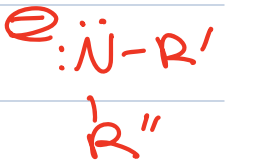
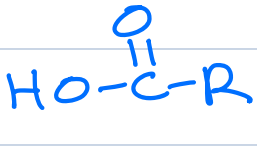
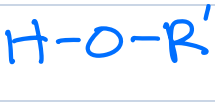
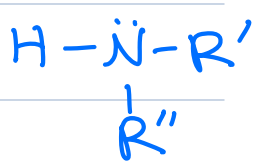
# Characteristic Reactions of Carboxylic Acid Derivatives

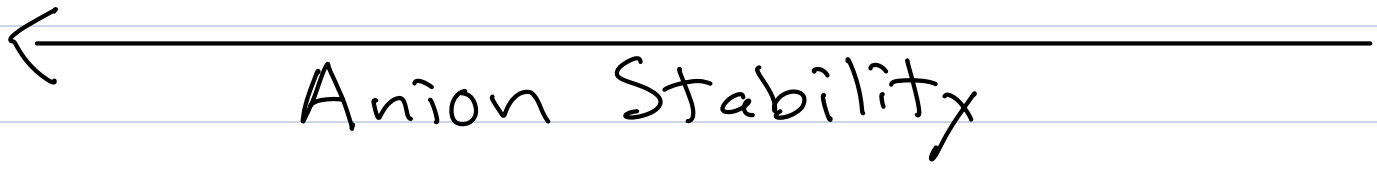
## Mechanism B

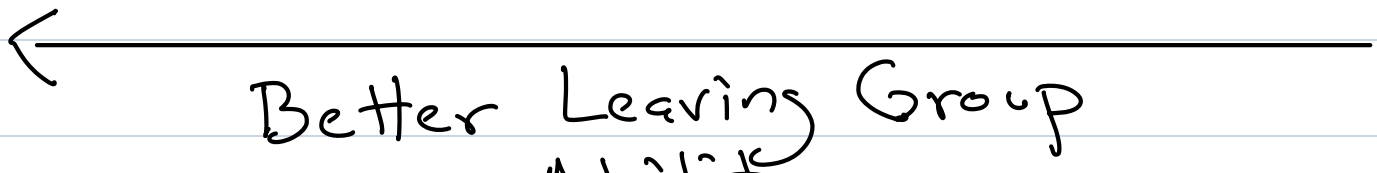
The key issue is leaving group ability

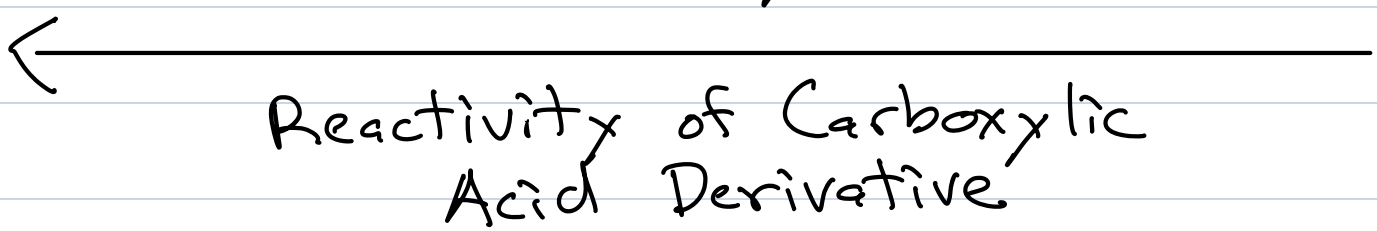
Both depend on anion stability

- The more stable the anion of the leaving group, the better the leaving group ability ⇒ the more reactive the carboxylic acid derivative
- The relative leaving group ability is correlated with the $pK_a$ of the leaving group conjugate acid

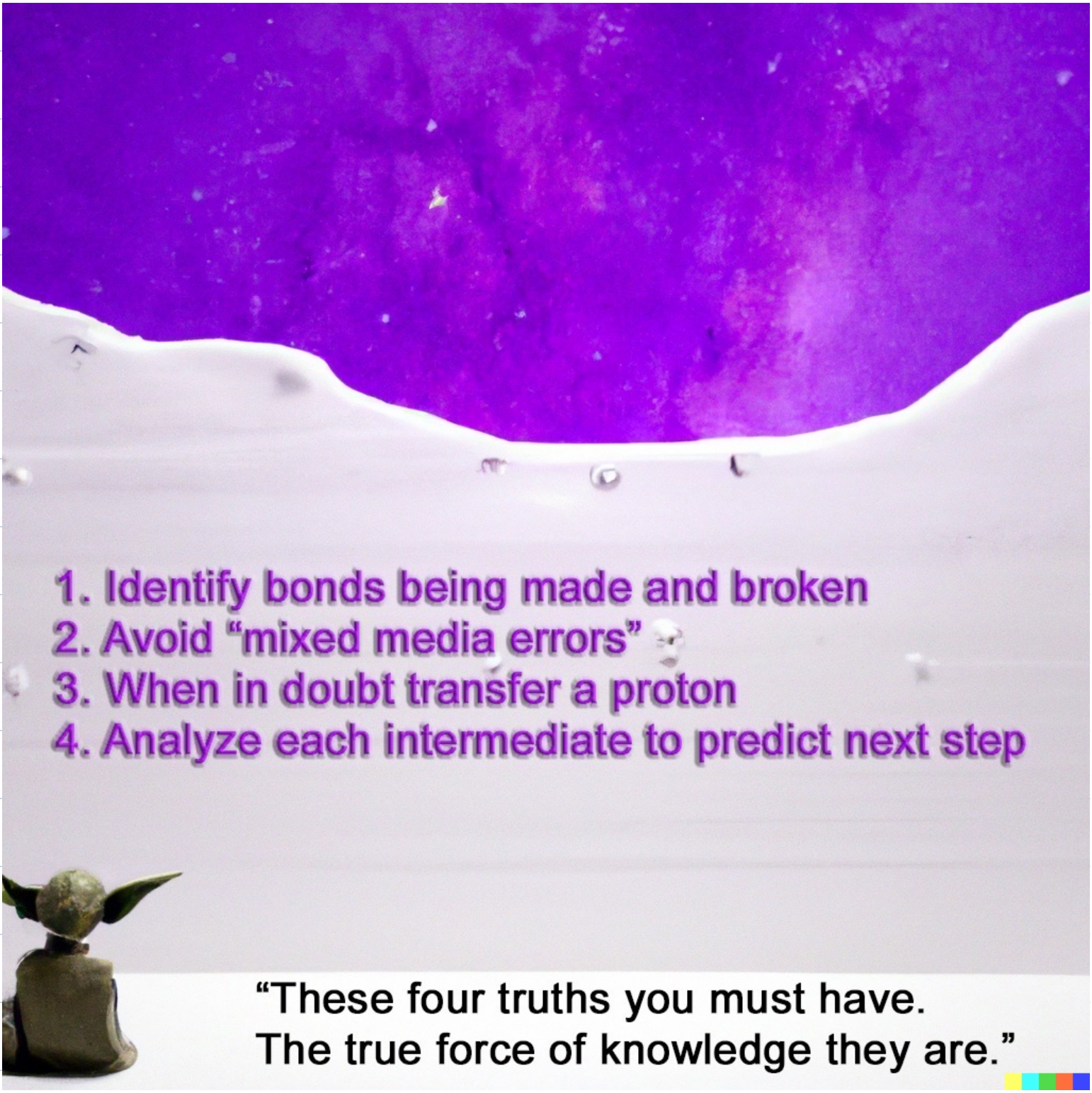
| | Acid Chloride | Anhydride | Ester | Amide |
|---|---|---|---|---|
| |  |  |  |  |
| Leaving Group |  |  |  |  |
| Conjugate Acid |  |  |  |  |
| $pK_a$ | -7 | 3-5 | 16 | 38 |




Think of carboxylic acid derivatives
$\Rightarrow$ C=O with a leaving group attached


1. Identify bonds being made and broken
2. Avoid “mixed media errors”
3. When in doubt transfer a proton
4. Analyze each intermediate to predict next step
“These four truths you must have.
The true force of knowledge they are.”