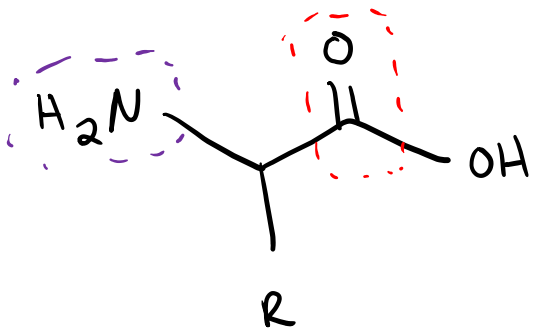
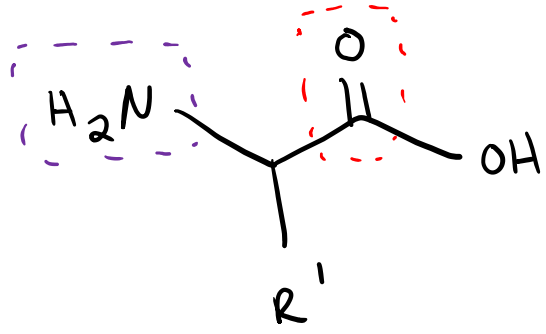
Peptide Synthesis

4/24/2023

Peptide Synthesis: Protecting Groups



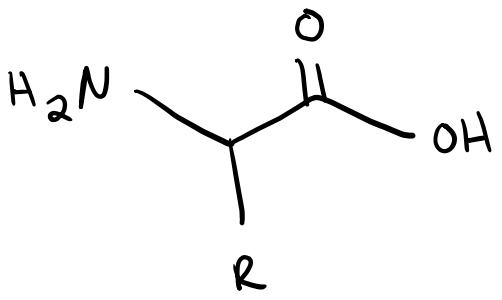


2 Electrophiles

2 nucleophiles

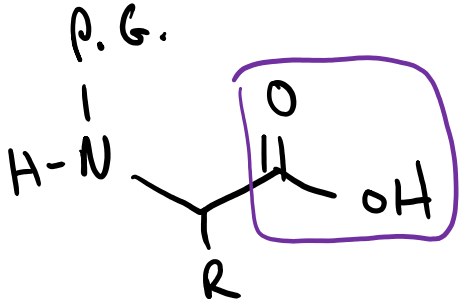
- need to control regiochem or get a mixture products

Strategy

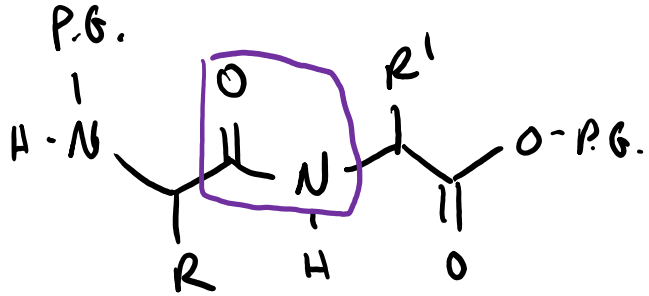


protect amine

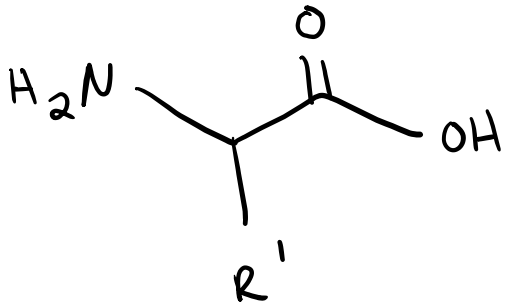
"protecting group"



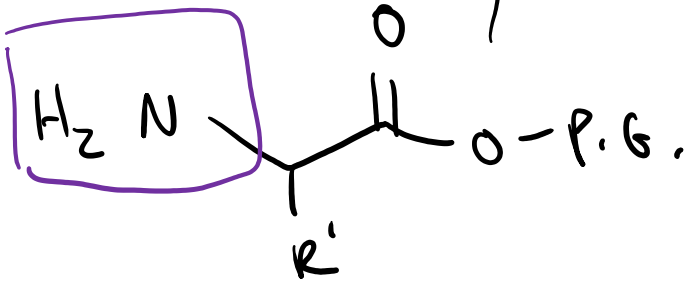
DCC

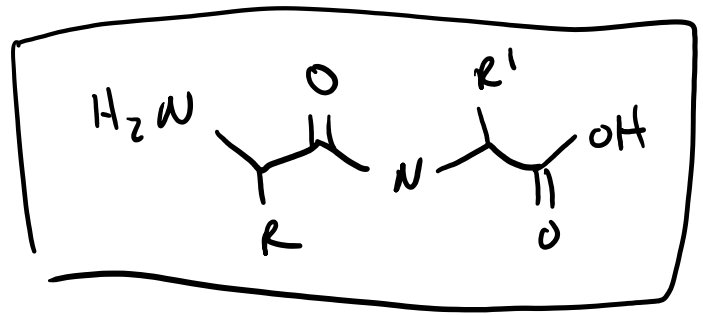


deprotect



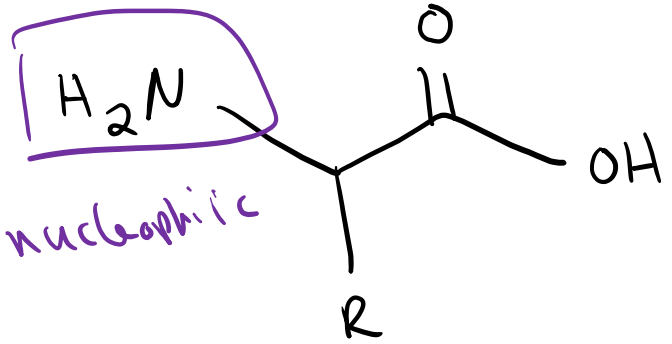
protect Carb. acid

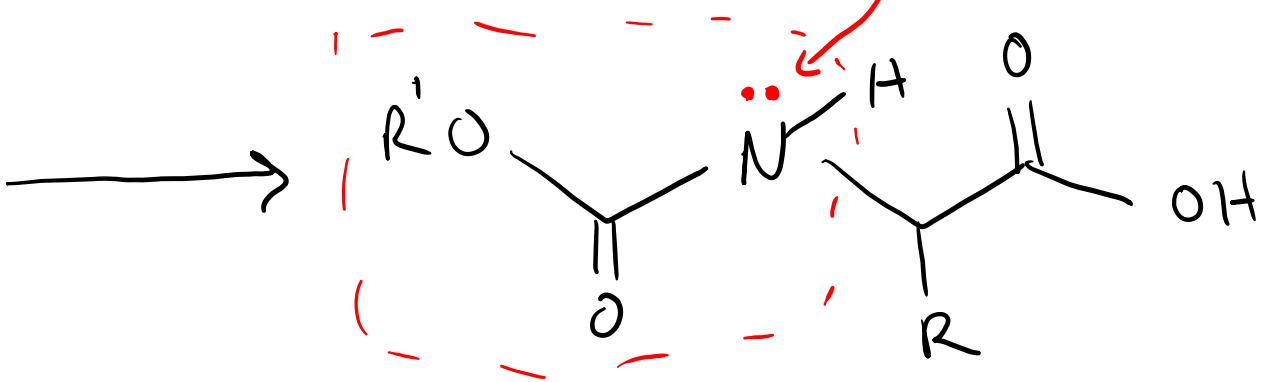




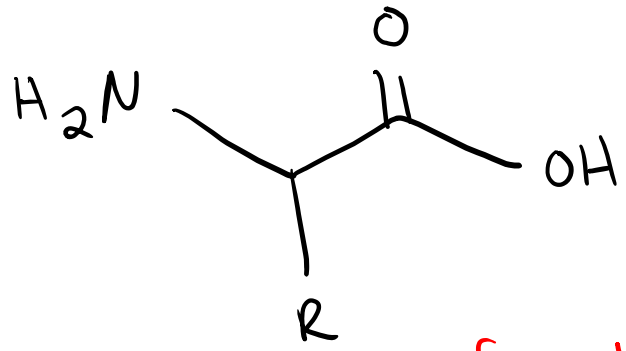
Protecting the Amine Group

General:

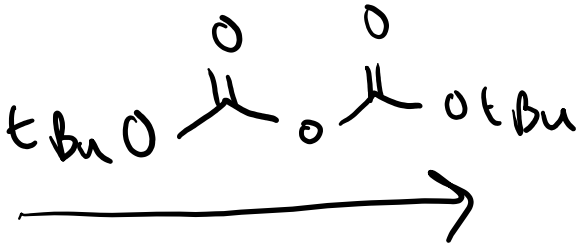




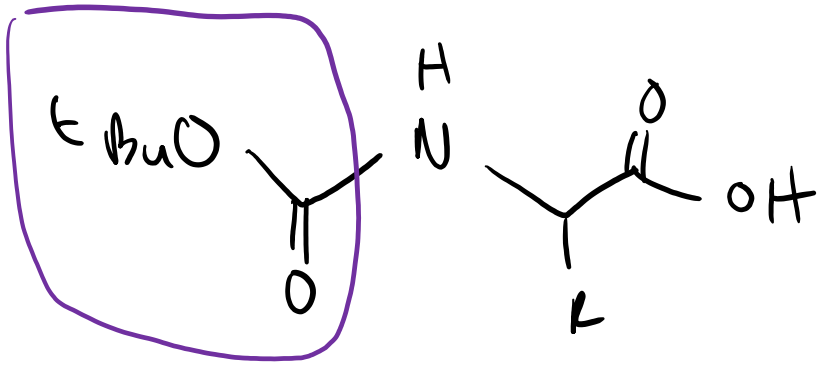
Using the "Boc" protecting group:



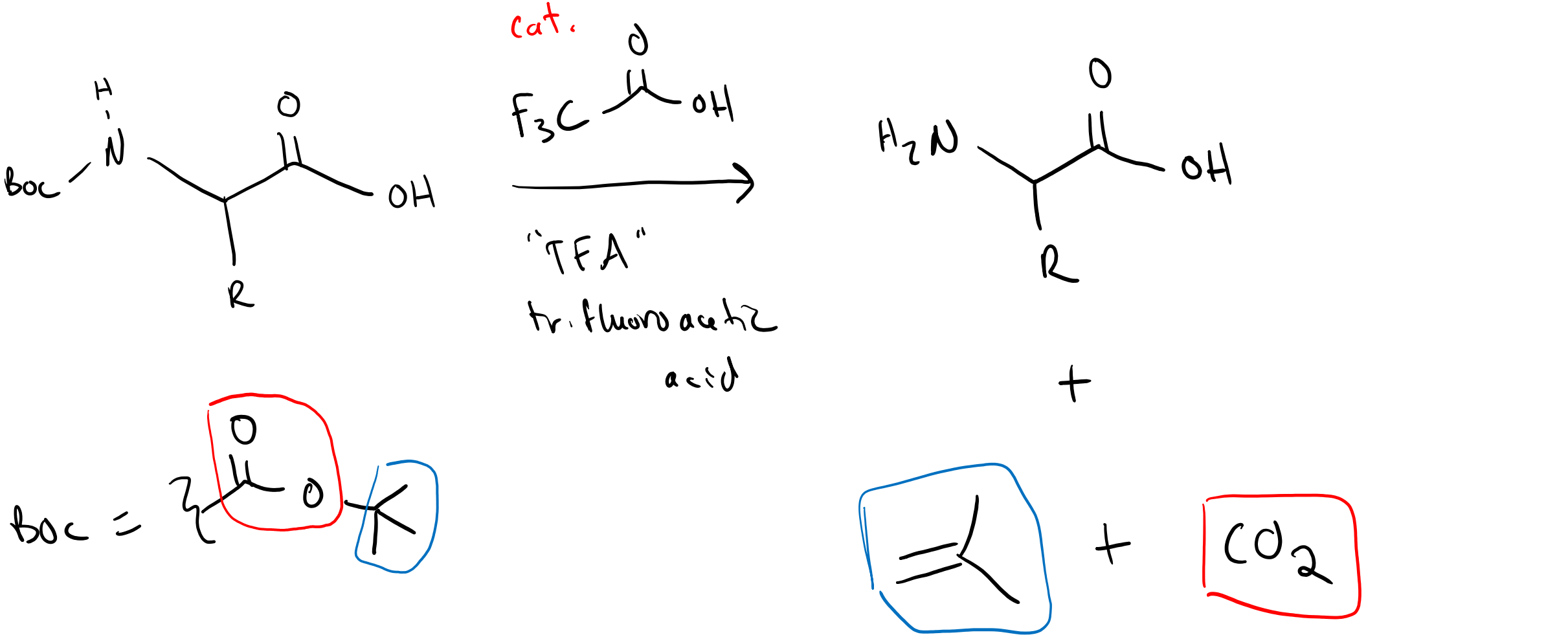
Ch. 20 - amide formation



"Boc"

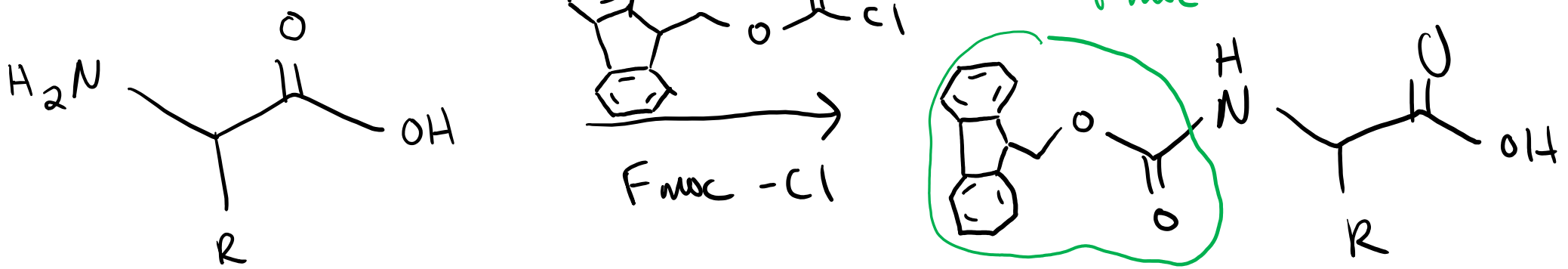


“Deprotecting” the Amine: Removing Boc



Amine Protection and Deprotection with "Fmoc"

protection



Mech. Ch. 20 amine + acid chloride → amide

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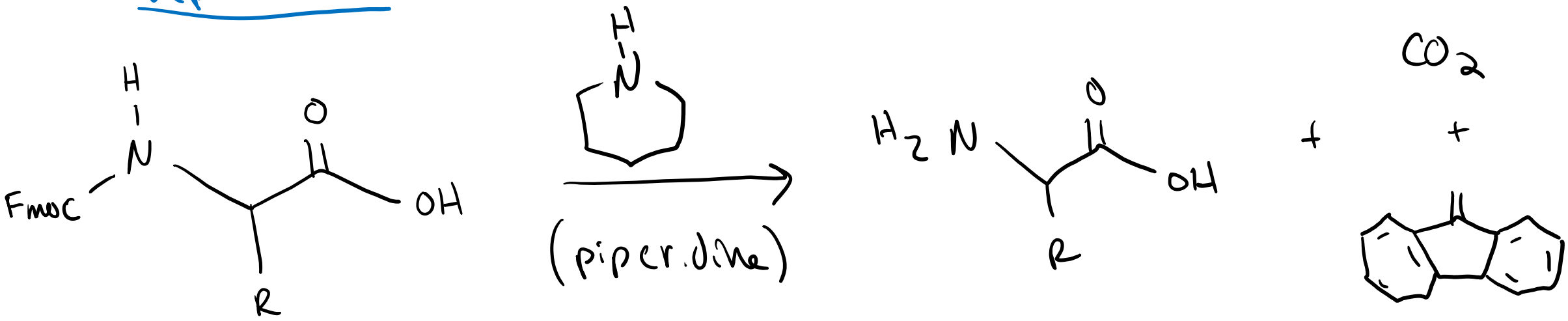
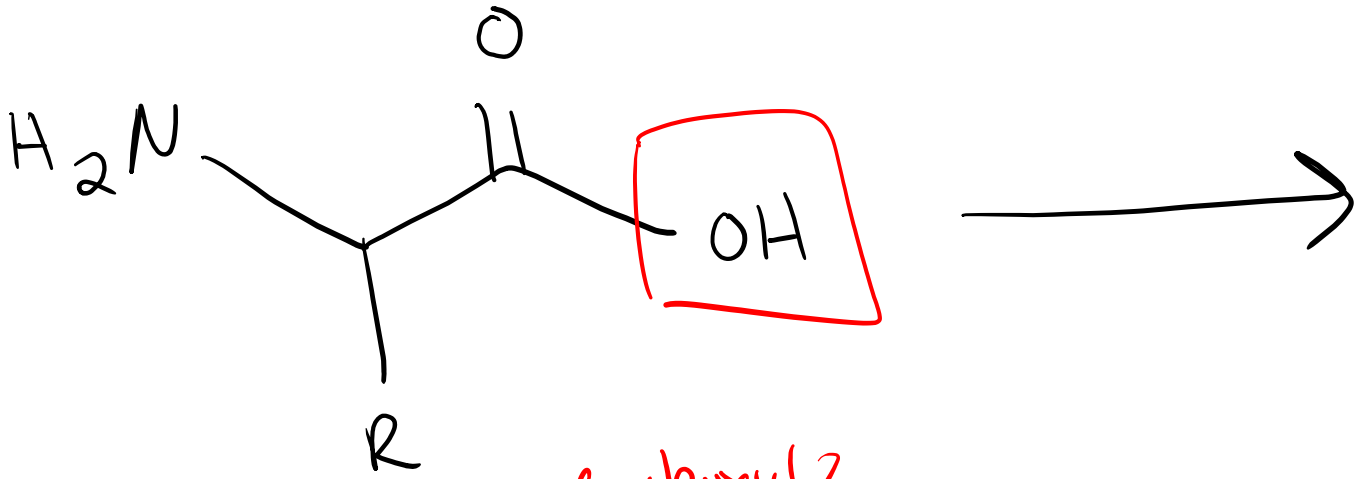
deprotection



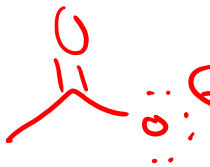
Protecting the Carboxylic Acid

(25.6)



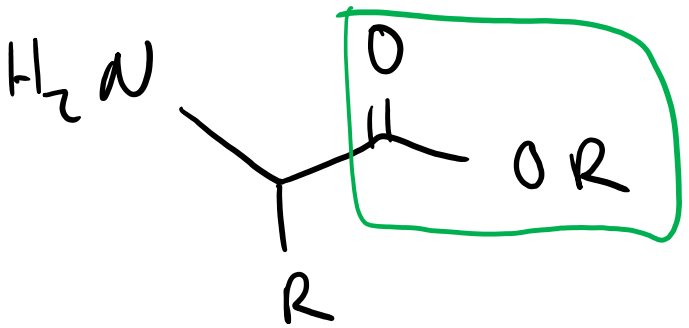
carboxylic acid

acidic!



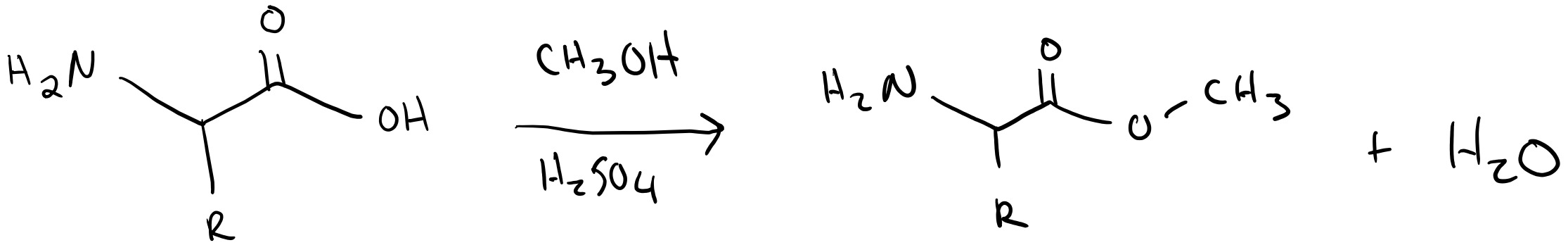
is what starts rxn w/ DCC.

ester

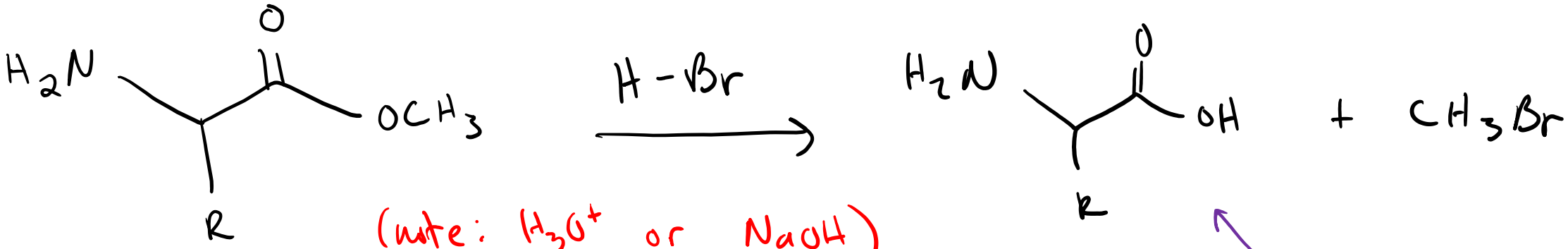


- not acidic!
- weak electrophile - won't be attacked by N
- won't attack DCC (no $-\ddot{O}:^{\ominus}$)

Protecting/Deprotecting the Carboxylic Acid: Methyl Ester

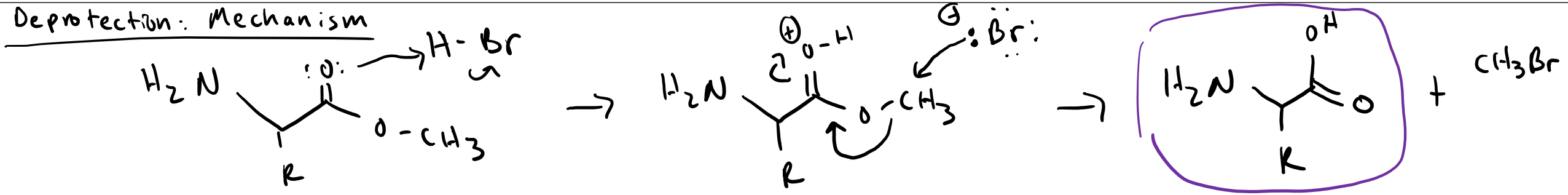


Fischer Esterification

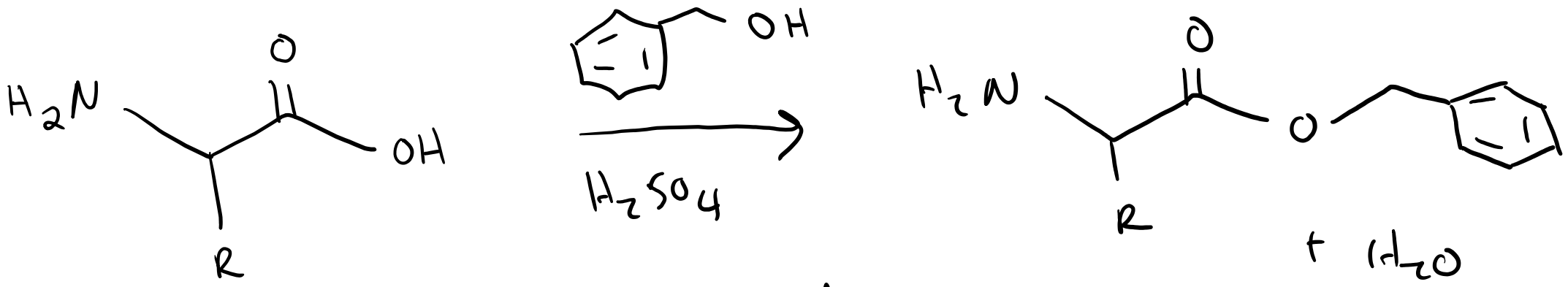


(note: H_3O^+ or NaOH)

Deprotection: Mechanism

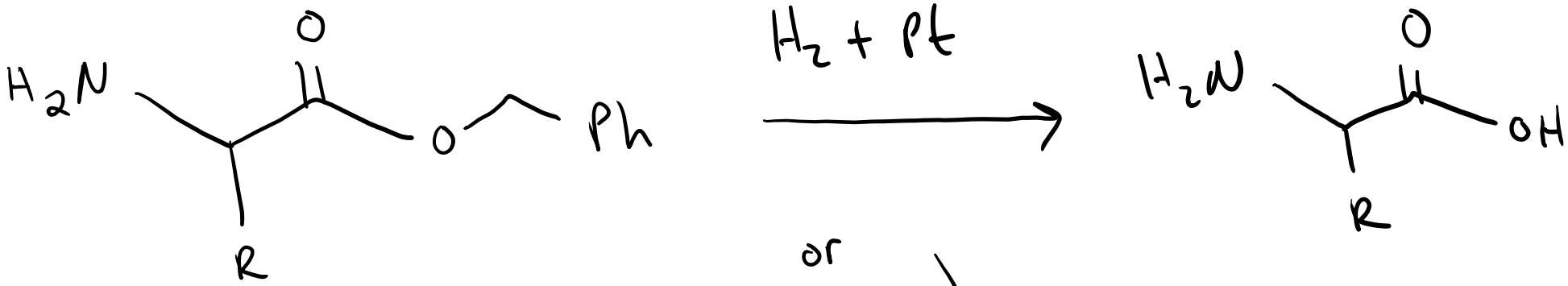


Protecting/Deprotecting the Carboxylic Acid: Benzyl Ester



Fischer Esterification

Deprotection

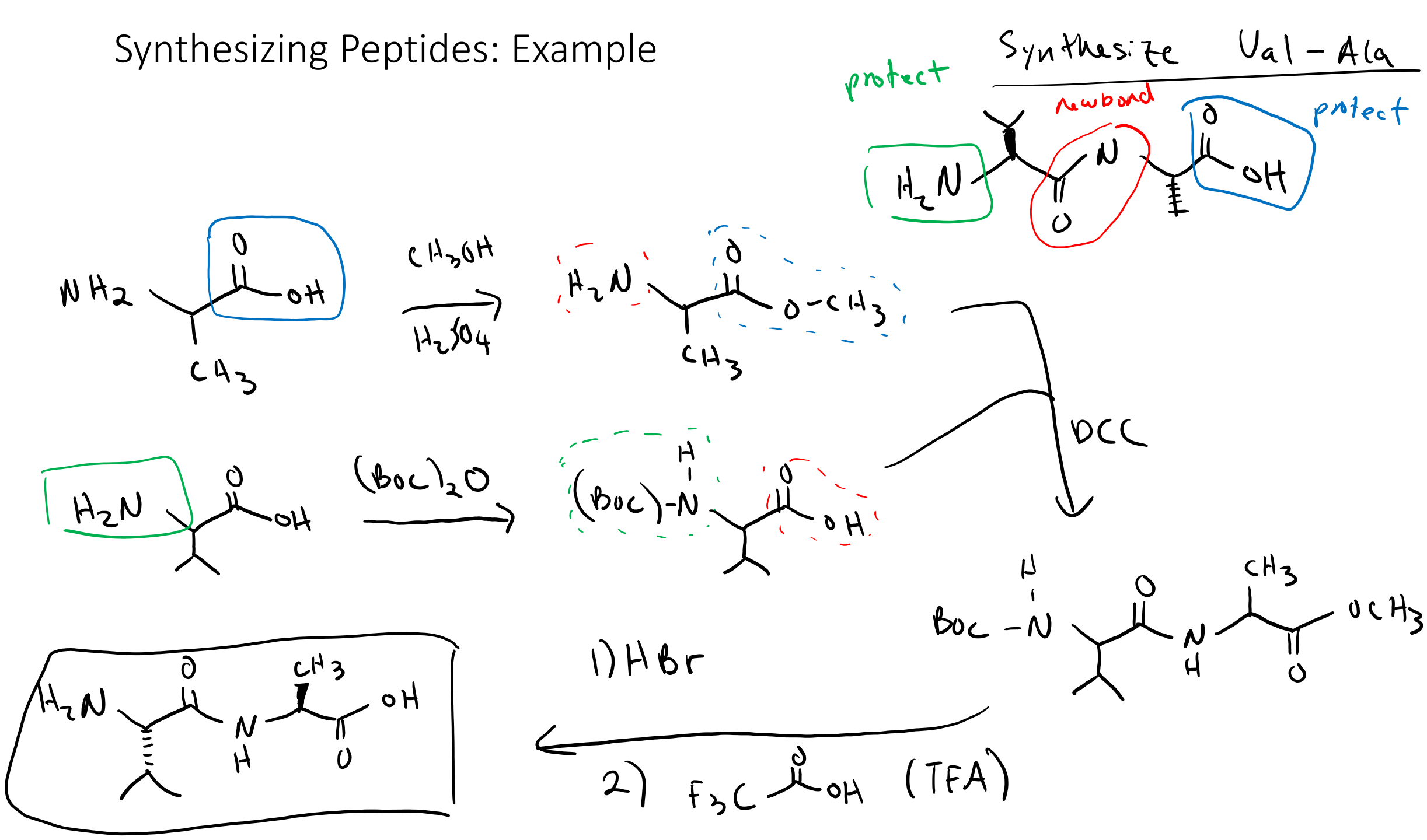


No mechanism

Synthesizing Peptides: General Strategy

1. Sketch peptide target
2. protect amine + carboxylic acid groups as needed
3. form peptide bond using DCC
4. deprotect as needed
5. repeat 2-4 as needed

Synthesizing Peptides: Example



Synthesizing Peptides: Example

Synthesize Phe - Ser - Cys