Course 345 Instructor Gellman
Day Wed Date 5/7/2014
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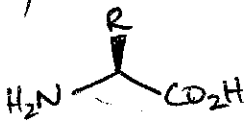
PLEASE COMPLETE NOTES IN INK AND DO NOT STAPLE.

Peptides / proteins

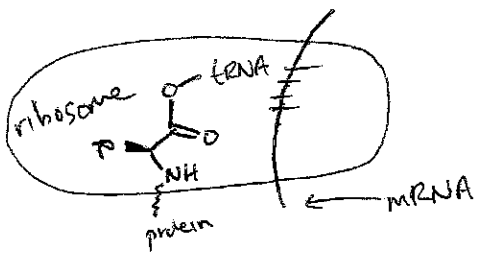
- Proteins are polymers of α-amino acids linked by amide bonds

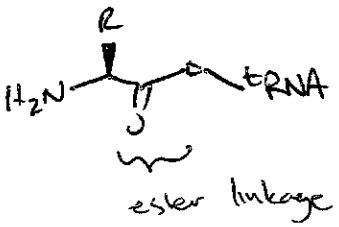


~20 common amino acids

* Sequence information for proteins is stored in DNA.

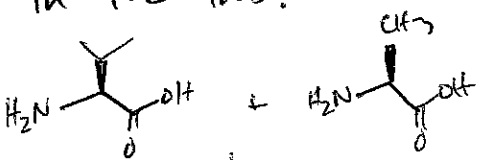
DNA $\xrightarrow{\text{transcription}}$ mRNA $\xrightarrow{\text{translation}}$ protein





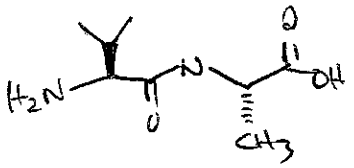
- How to synthesize protein/peptides in the lab?

1) Protecting groups



Acid chloride + amines ⟶✗ amides

-spontaneous side rxns



- Have to use protecting groups for the amine.

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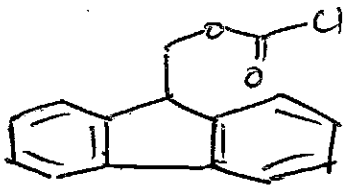
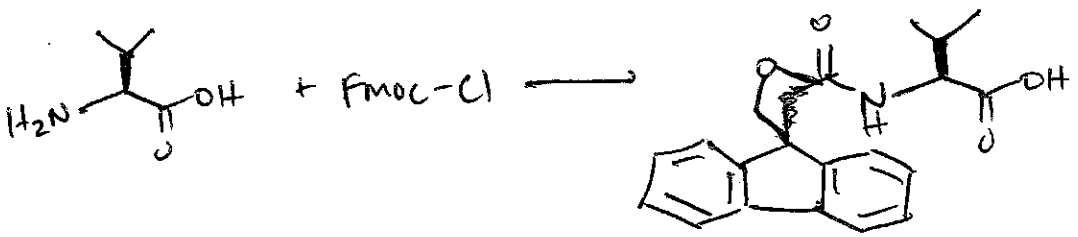
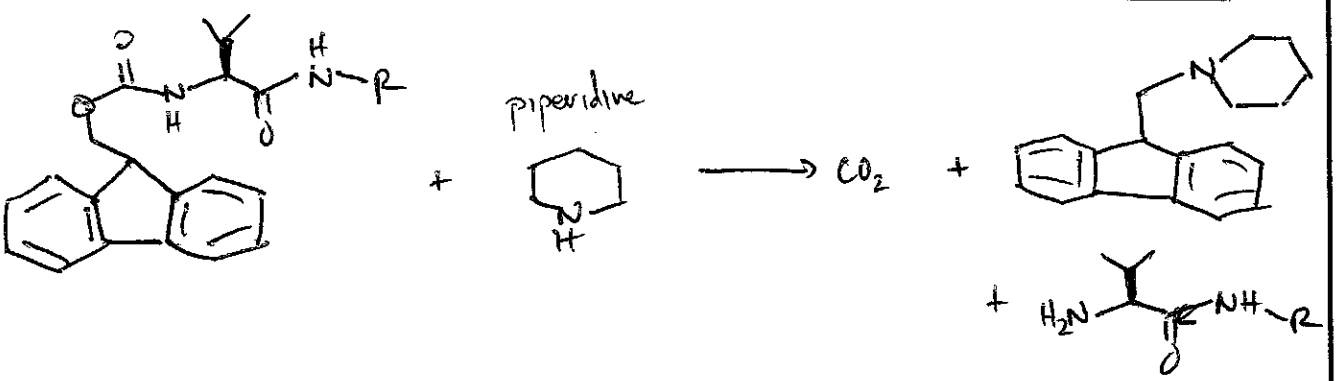
·1 protecting group- Fmoc



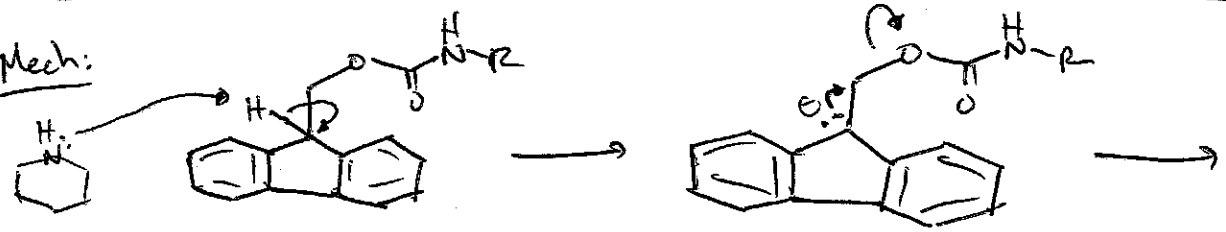
Fmoc Cl



Fmoc-protected valine



Mech:



stable carbanion due to aromatic res.

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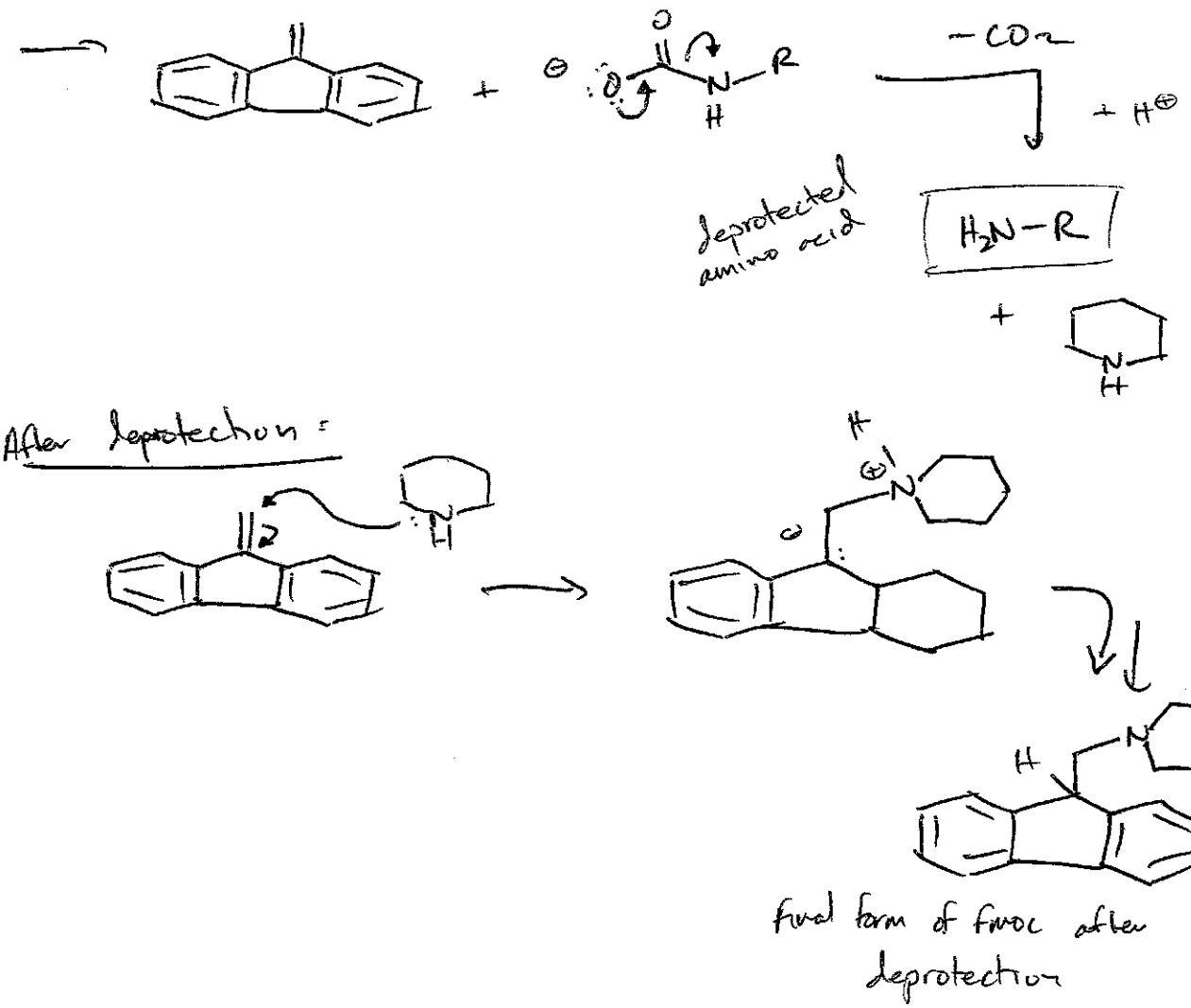

final form of Fmoc after deprotection

* Problem: need a way to couple amines with carboxylic acids that avoids use of acid chlorides (too reactive). Need other way to activate $R\overset{O}{\overset{\|}{C}}-OH$.

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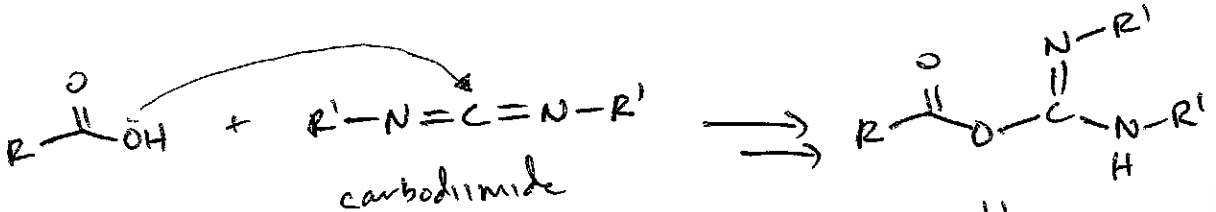
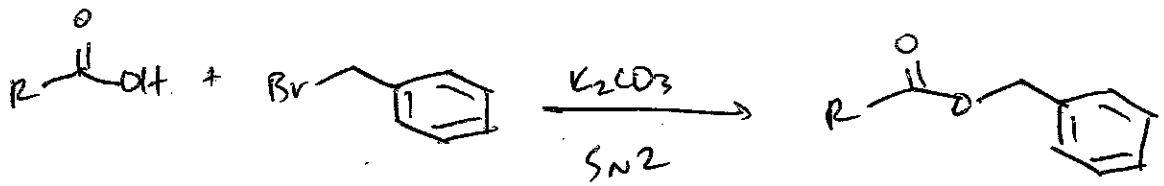
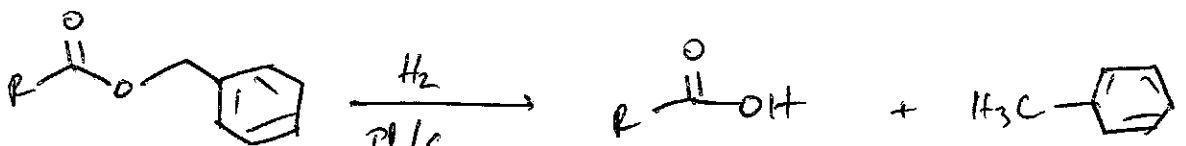
Solution: carbodiimides



- In order for this product to react selectively with the amine and not  , need to protect the acid

* Mask carboxylic acid with benzyl ~~ether~~ ester





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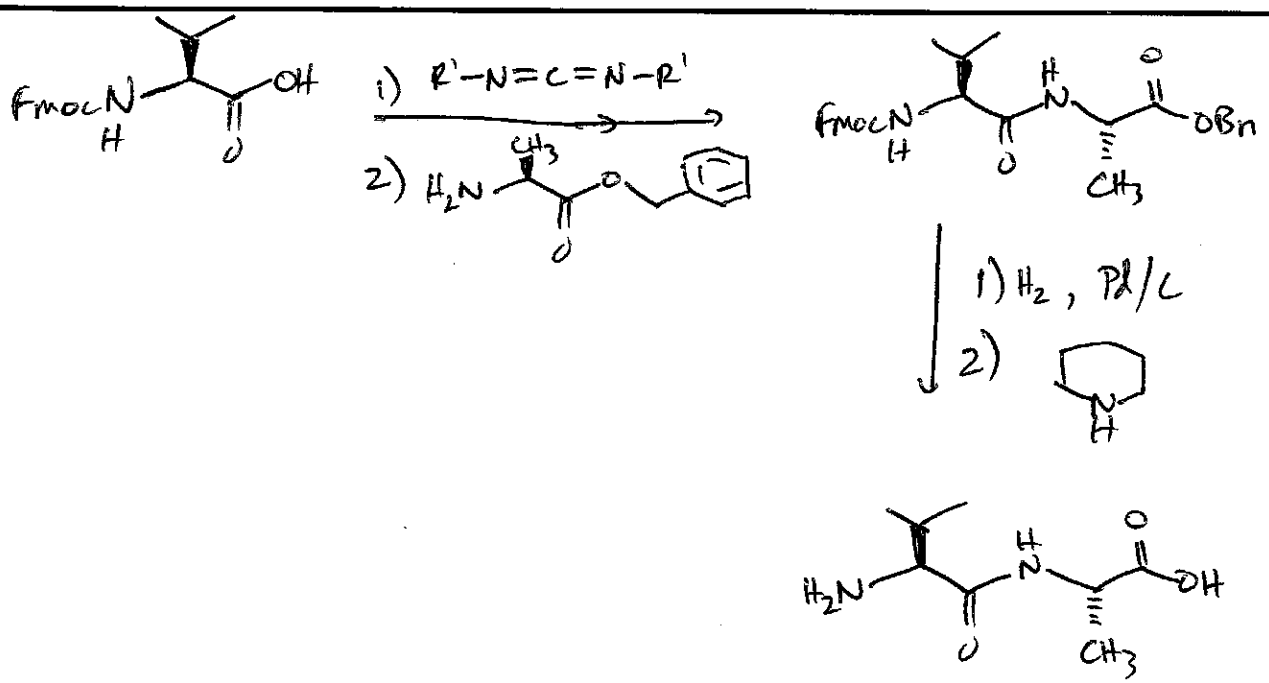

• Considering multi-step rxns:

Yield per amide bond	Yield over 25 steps	Yield over 50 steps
99 %.	80 %.	60 %.
96 %.	40 %.	15 %.