Course Chem 345 Lecturer Gellman
Day Wed Date 5-4-2016
Notes Taken By KL Total # of Pages 5

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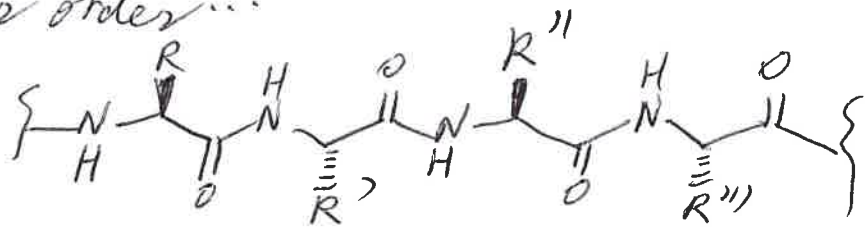
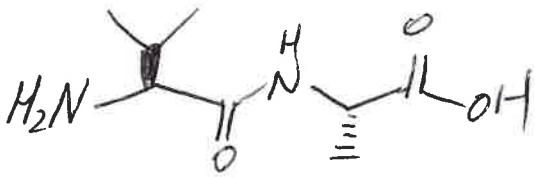
Review Sessions Today & Tomorrow 5-6 pm
B371

Recall: Challenge of sequence — specific peptide/protein synthesis — generate 2° amide bonds in proper order...

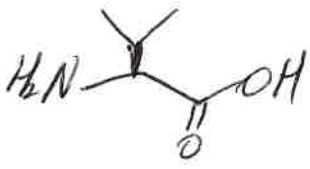


Biology: DNA → RNA → protein
↑
Ribosome

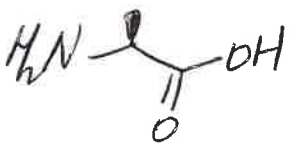
Chemical synthesis of peptides — use a "dipeptide" as example.



from

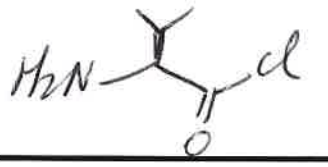


Valine



Alanine

Recall acid chlorides...

"  "

Self-reaction! ⇒ protect the amino group

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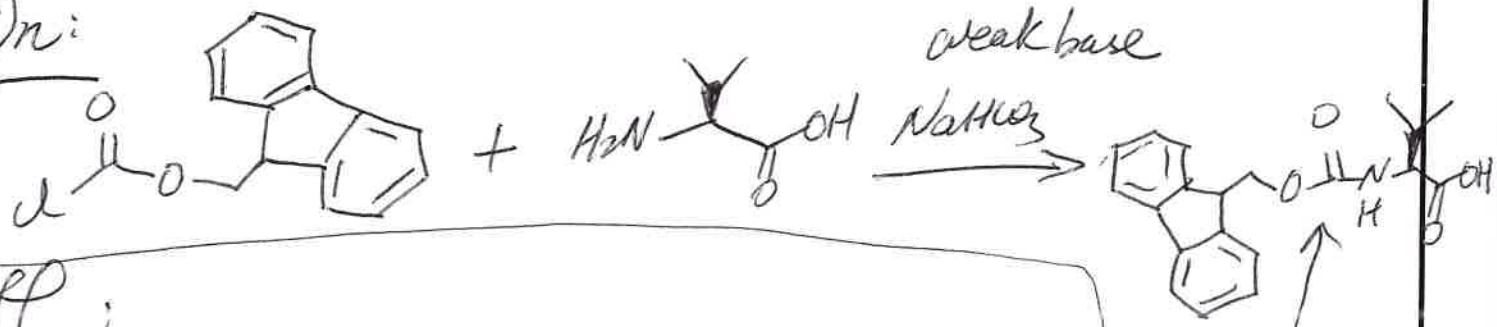
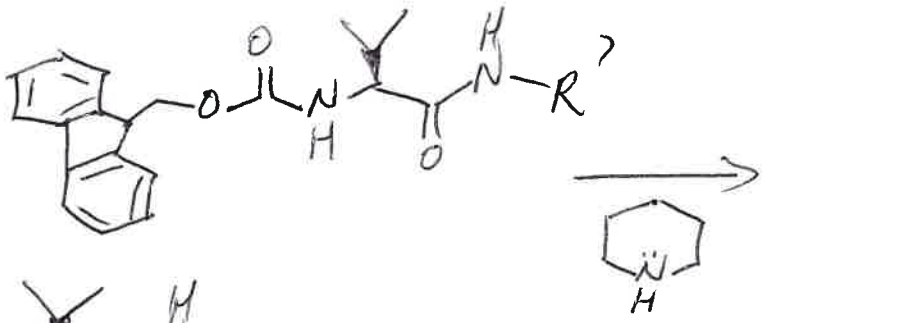
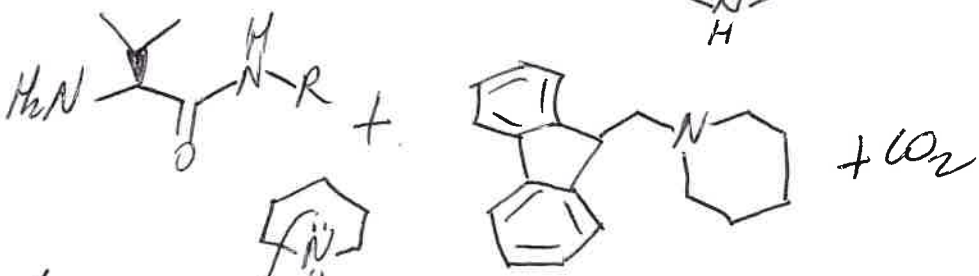
Example: Fmoc

On:

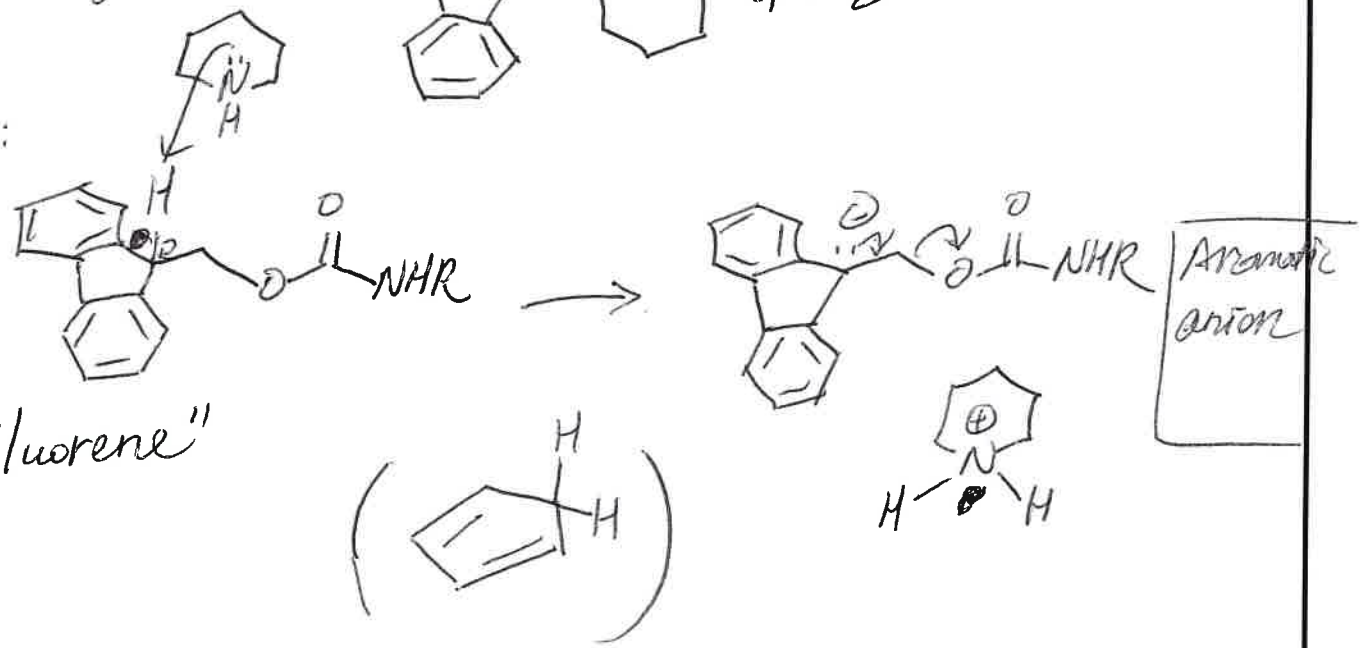


off:





Mech:



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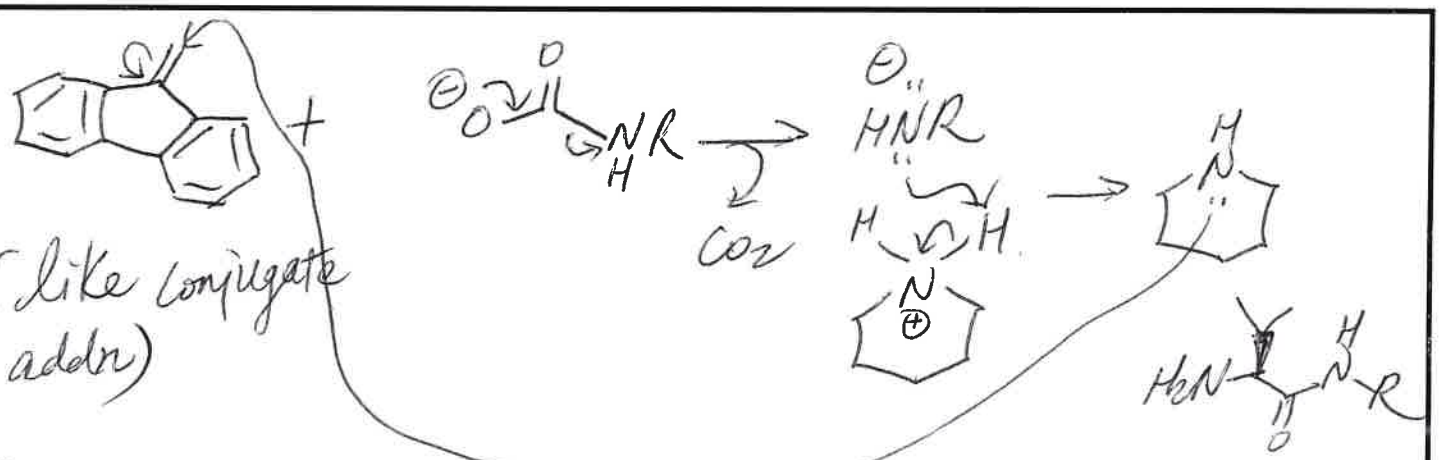


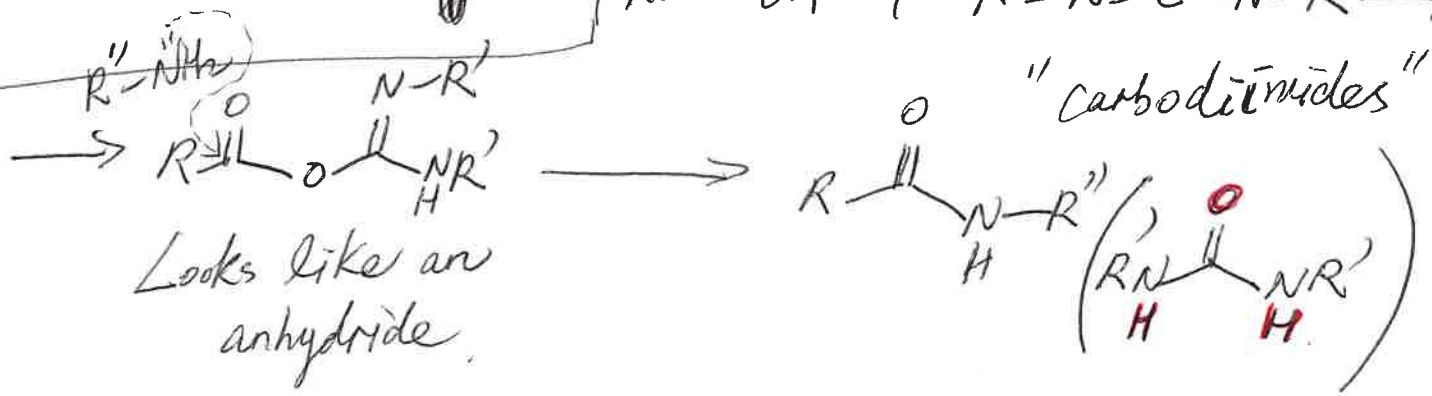
Can we use ...

"Fmoc-N(H)-CH(R)-C(=O)-Cl"

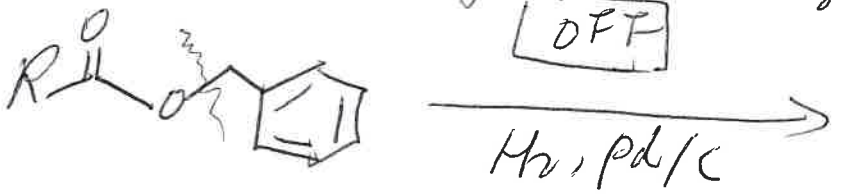
Not stable !!

Alternative way to render the carboxyl electrophilic (alternative to acid chloride)

$R-C(=O)-OH + R'-N=C=N-R' \rightarrow$ "carbodiimides"



Protect carboxylic acid groups as benzyl esters (urea)



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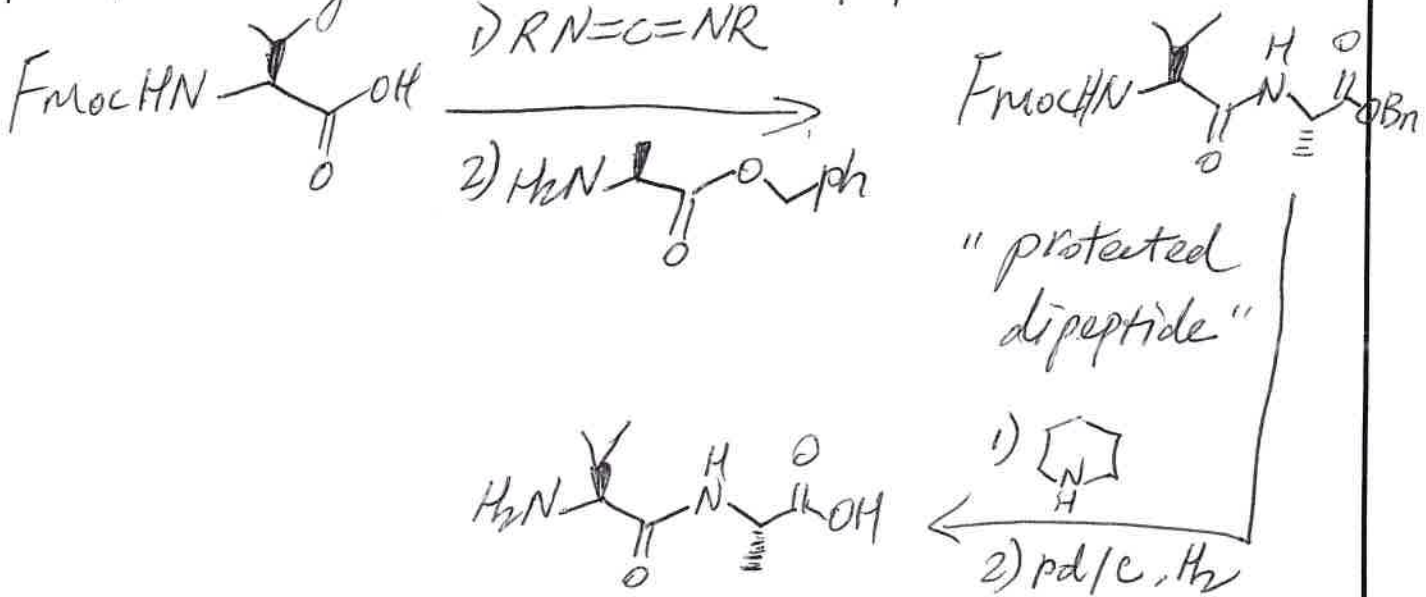
Put it all together to make dipeptide:



This process is "solution-phase" synthesis.

"Solid-phase" Synthesis
Growing polypeptide chain immobilized on a macroscopic material, "solid support"
Note: Yield really matters if synthesis requires 10's or 100's of steps.

Yield per residue	After 25 steps	After 50 steps
99%	80%	60%
96%	~40%	~15%

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Solid phase = polystyrene