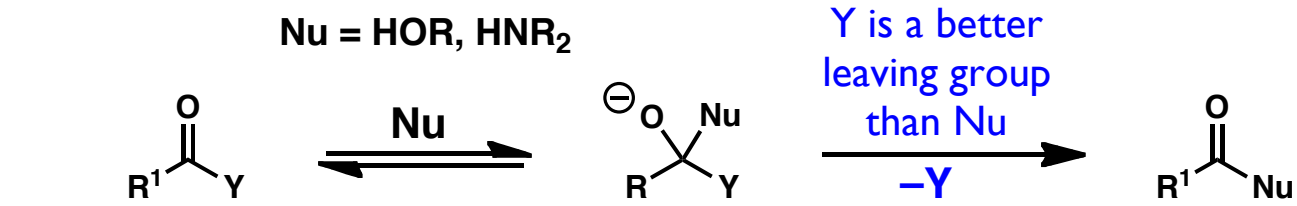
From Last Time: Nucleophilic *Substitution* at the Carbonyl

Guide to addition/elimination reactions

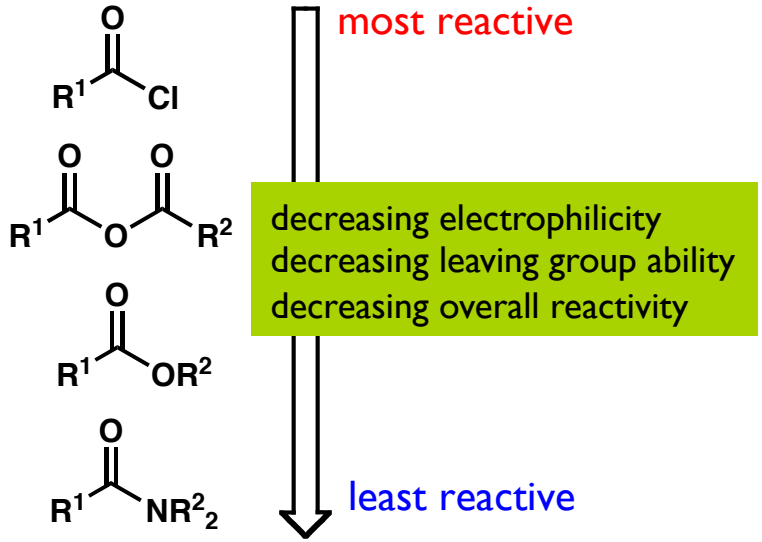
- note: HOR, HNR_2 are relatively weak nucleophiles



Must meet the following 3 conditions for reaction to occur:

- Y must be a better leaving group than Nu (otherwise the reverse reaction will dominate)
- Nu must be nucleophilic enough to attack $R^1C(O)Y$
- $R^1C(O)Y$ must be electrophilic enough to react with Nu

reactions proceed down the hierarcy of carboxylic acid derivatives



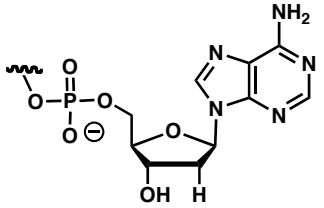
Understanding Biology on a Chemical Level

transcription

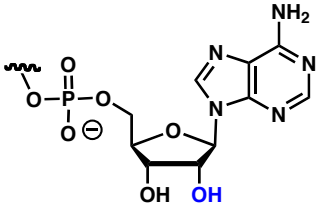
translation

DNA → RNA → protein

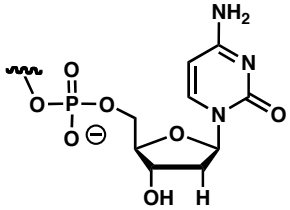
2'-deoxyadenosine-5'-phosphate



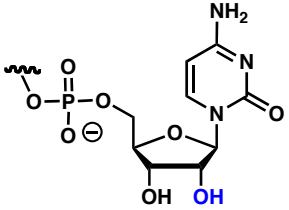
adenosine-5'-phosphate



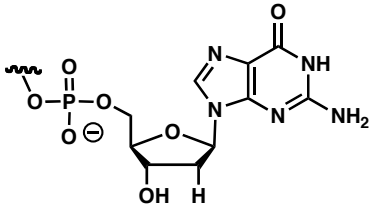
2'-deoxycytidine-5'-phosphate



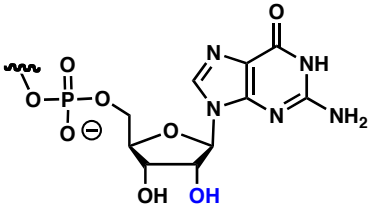
cytidine-5'-phosphate



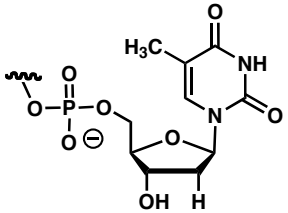
2'-deoxyguanosine-5'-phosphate



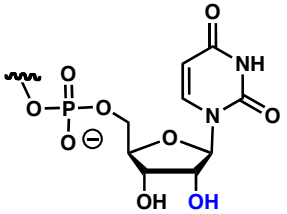
guanosine-5'-phosphate

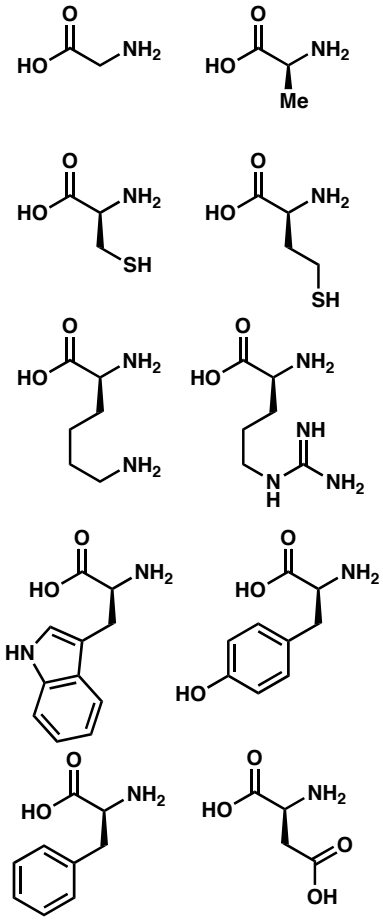


2'-deoxythymidine-5'-phosphate



uradine-5'-phosphate

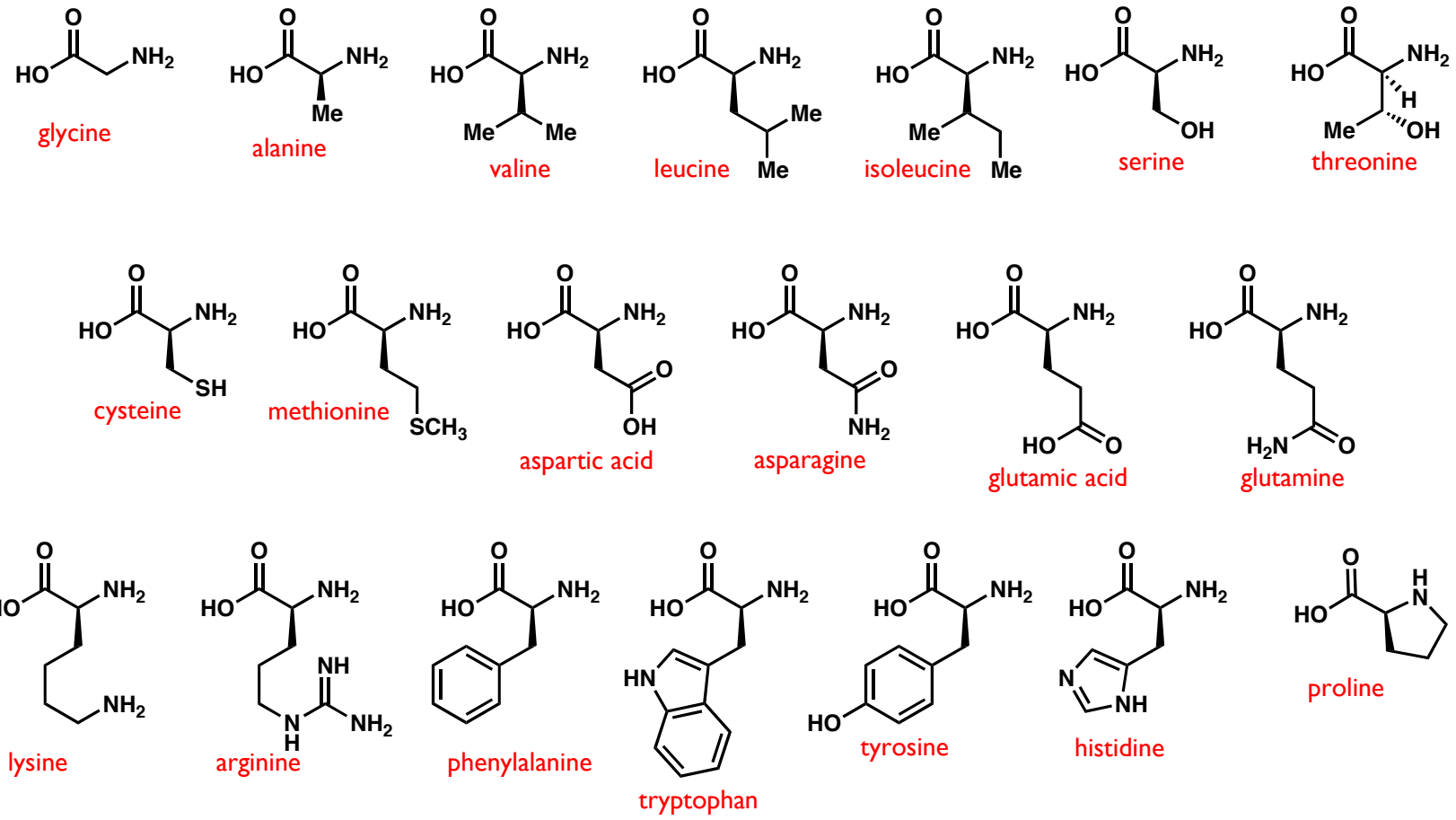




(plus 10 more)

Proteins are Amino Acid Polymers

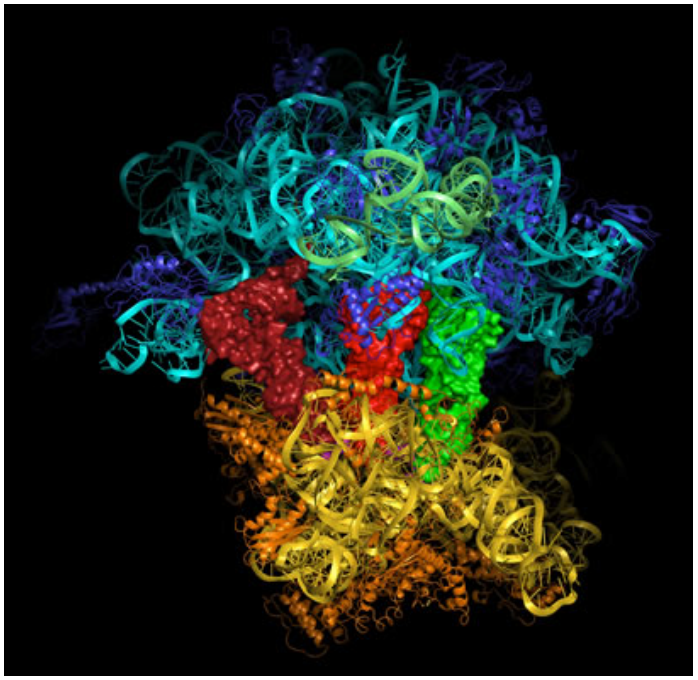
there are twenty canonical amino acids



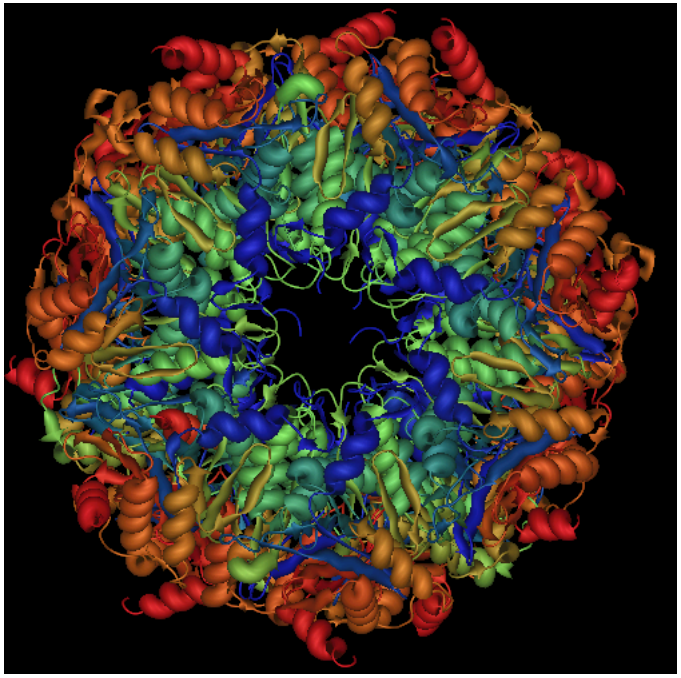
Proteins are Amino Acid Polymers

amino acids are both nucleophiles *and* electrophiles

ribosomes: RNA and protein assemblies that make new proteins



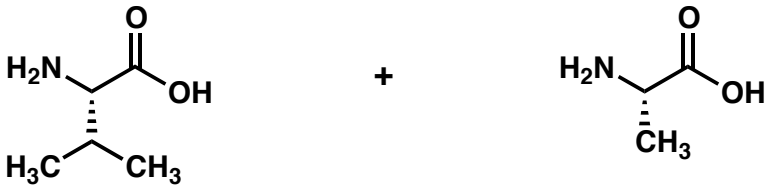
proteasomes: proteins that catalyze the degradation of other proteins



Peptide Synthesis: In the Laboratory

amino acids are both nucleophiles *and* electrophiles

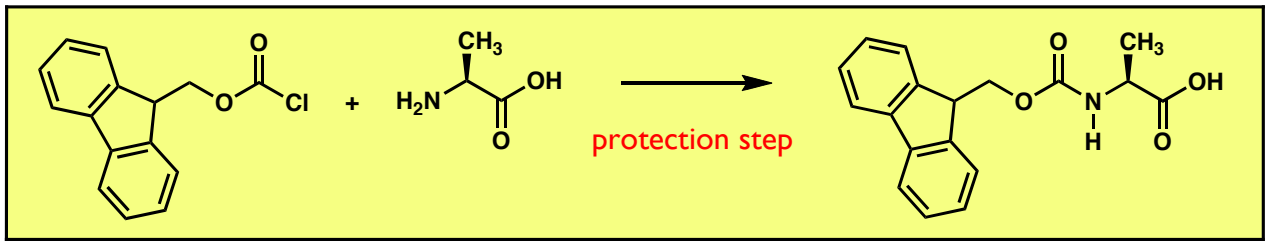
- chemists use "peptide coupling" reactions



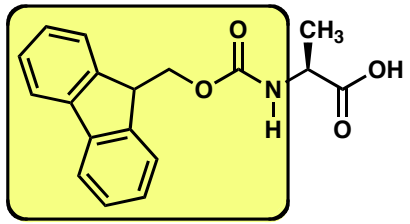
Blocking Groups are Known as "Protecting Groups"

the Fmoc protecting group for amines: generates a less nucleophilic 'carbamate'

- added to nitrogen by an acylation reaction
- cleaved from nitrogen using base

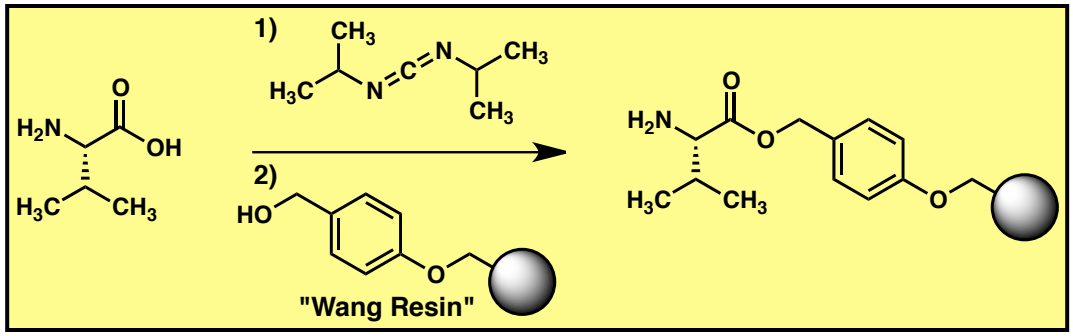


N-Fmoc-alanine



Amino Acids can be Attached to Resins by Ester Linkages

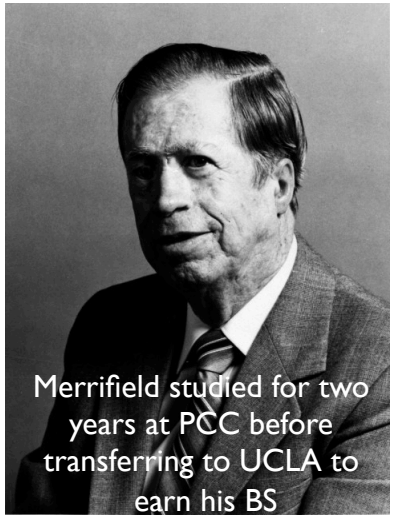
- amino acid is added to resin by esterification reaction
- diisopropyl carbodiimide is used to generate ester under mild conditions

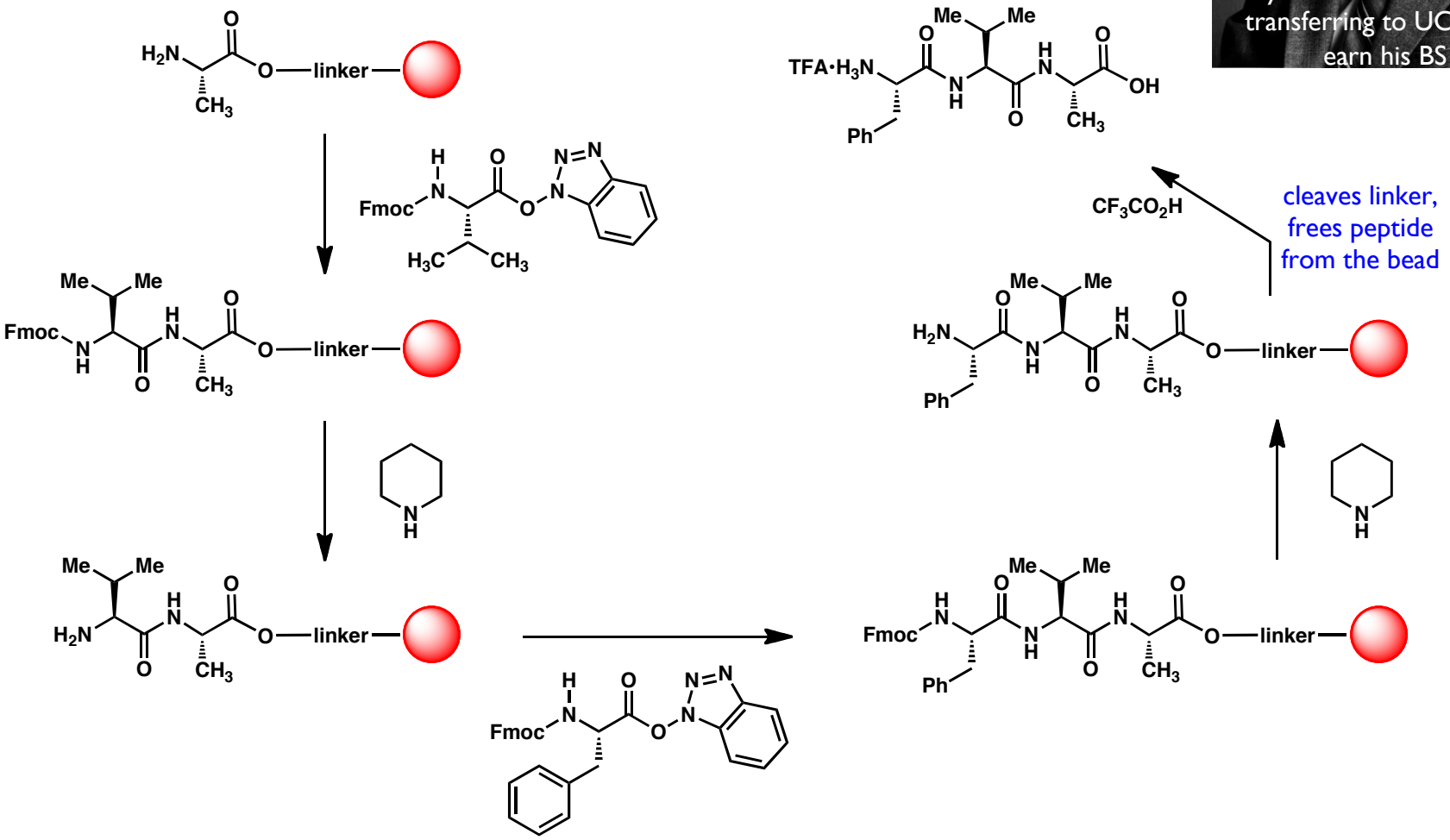


The Merrifield Peptide Synthesis

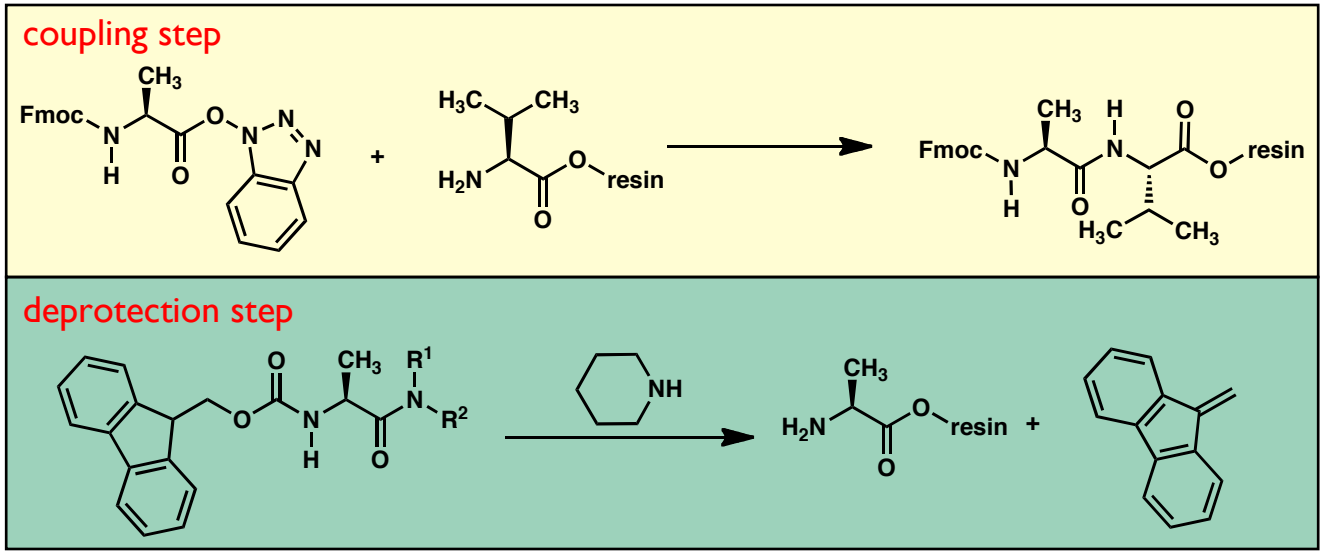
Robert Bruce Merrifield: won Nobel Prize in Chemistry in 1984 for the development of "solid phase" peptide synthesis.

- substrates are appended to a polystyrene bead; simplifies purification
- it works so well, it can be automated and performed by a machine



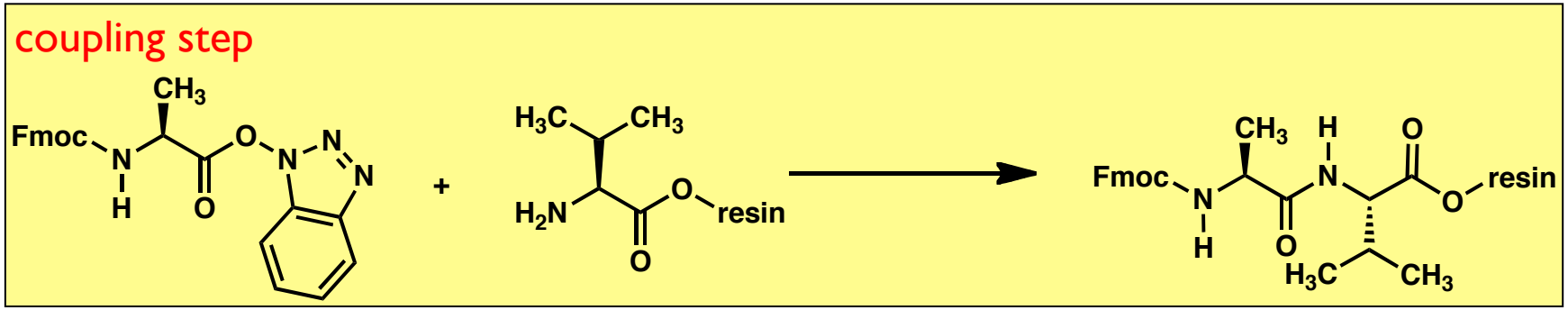


The Chemistry of Peptide Synthesis

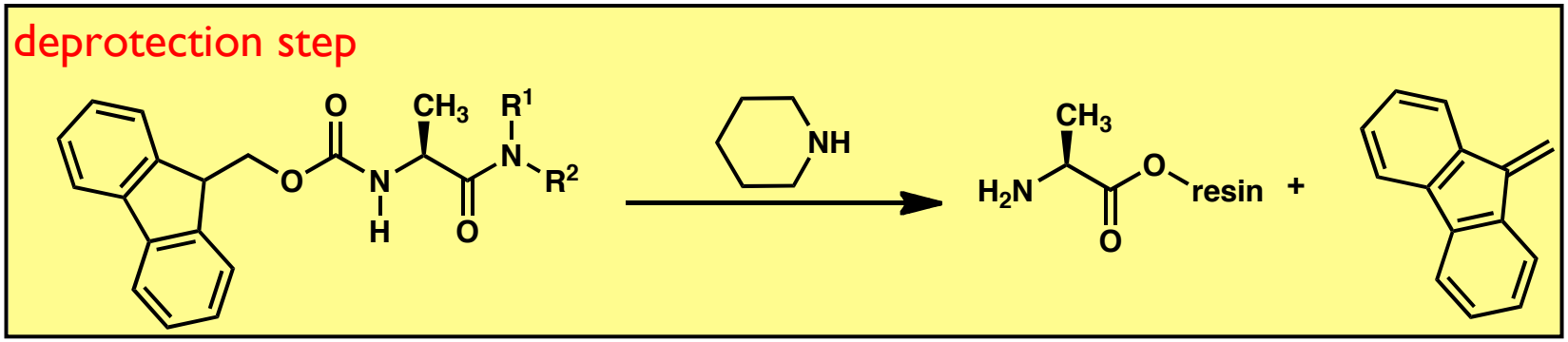


What are the mechanisms for these reactions?

Mechanism of Amide Bond Formation



Mechanism of Fmoc-Deprotection



what is the mechanism for this reaction?