An Introduction to Carbohydrates

What is a **carbohydrate**? Why are carbohydrates important?

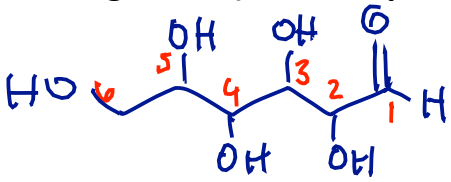
$C_n(H_2O)_m$ glucose $C_6H_{12}O_6$

sugars
- energy – starches,
- structure – cellulose, chitin
- DNA/RNA backbone

stereochemistry!

Draw the structures (*without* stereochemistry, for now) of the following carbohydrates. Where are each of these carbohydrates found in nature?

glucose (2,3,4,5,6-pentahydroxyhexanal)



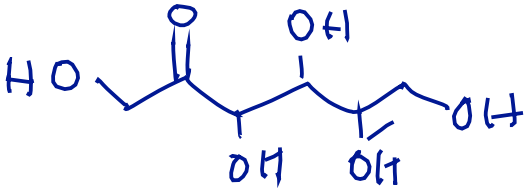
aldehyde

6-carbon sugars: hexoses

aldehyde : aldoses

aldohexose

fructose (1,3,4,5,6-pentahydroxyhexan-2-one)

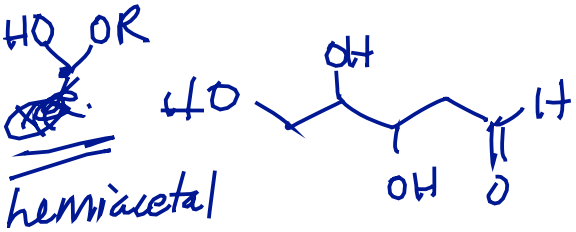


ketone

ketone sugars: ketose

ketohexose

2-deoxyribose (3,4,5-trihydroxypentanal)

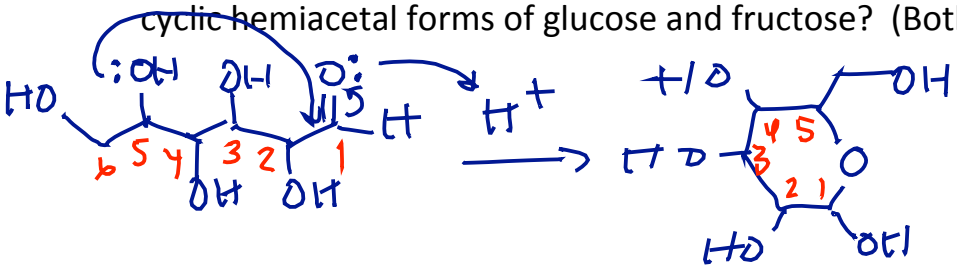


hemiacetal

5-carbon sugars: pentose

aldopentose

These *monosaccharides* usually exist as a more stable *cyclic hemiacetal*. What are the cyclic hemiacetal forms of glucose and fructose? (Both form 6-membered rings.)



sugars: monosaccharides

"pyranose" – 6-membered cyclic sugar

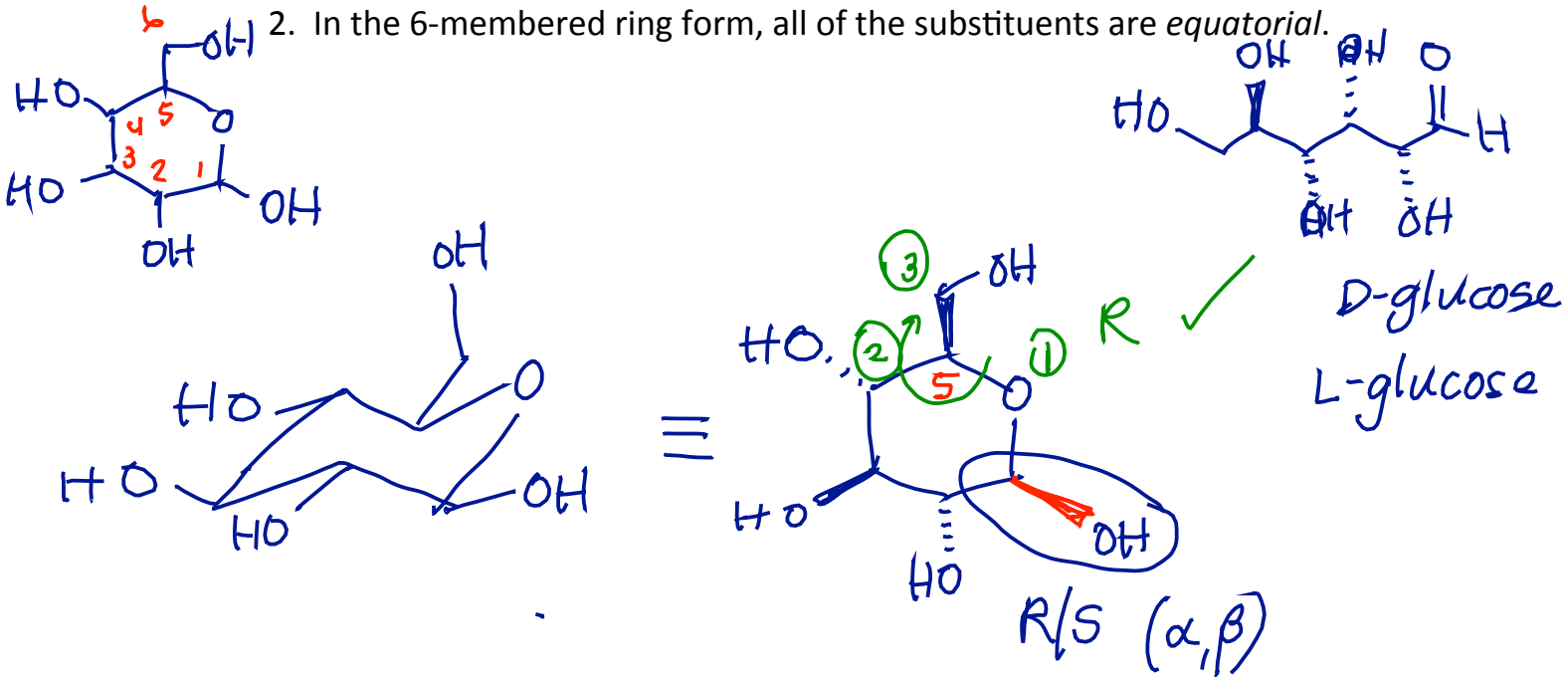
pyran

Reading: Section 24.1

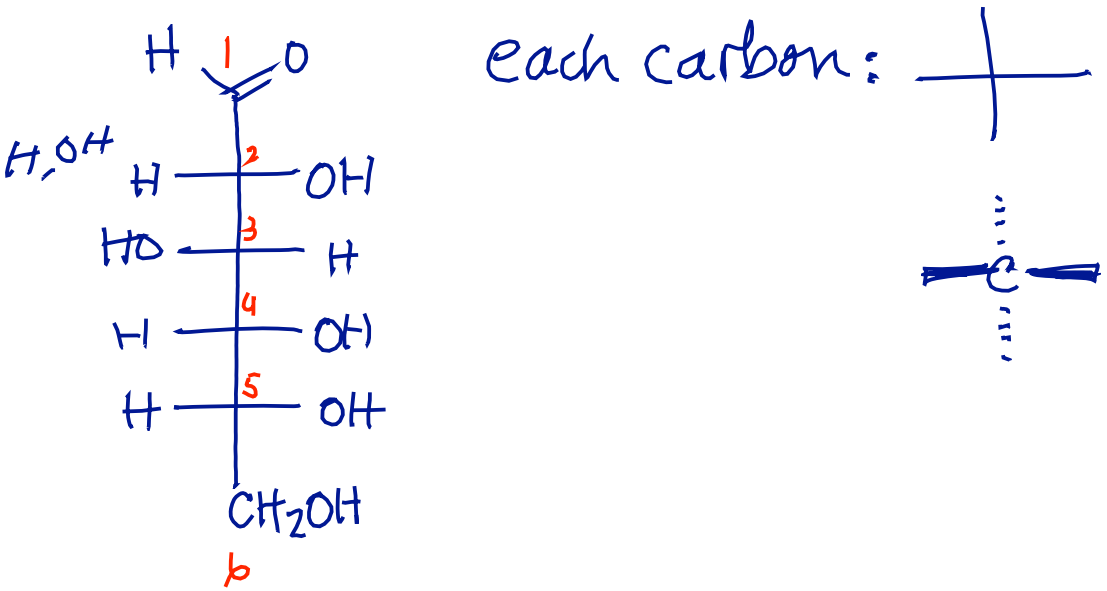
Stereochemistry of Carbohydrates

Let's figure out the stereochemistry of D-glucose by using the following facts:

1. The terminal carbon (#5) has the *R*-configuration.
2. In the 6-membered ring form, all of the substituents are *equatorial*.



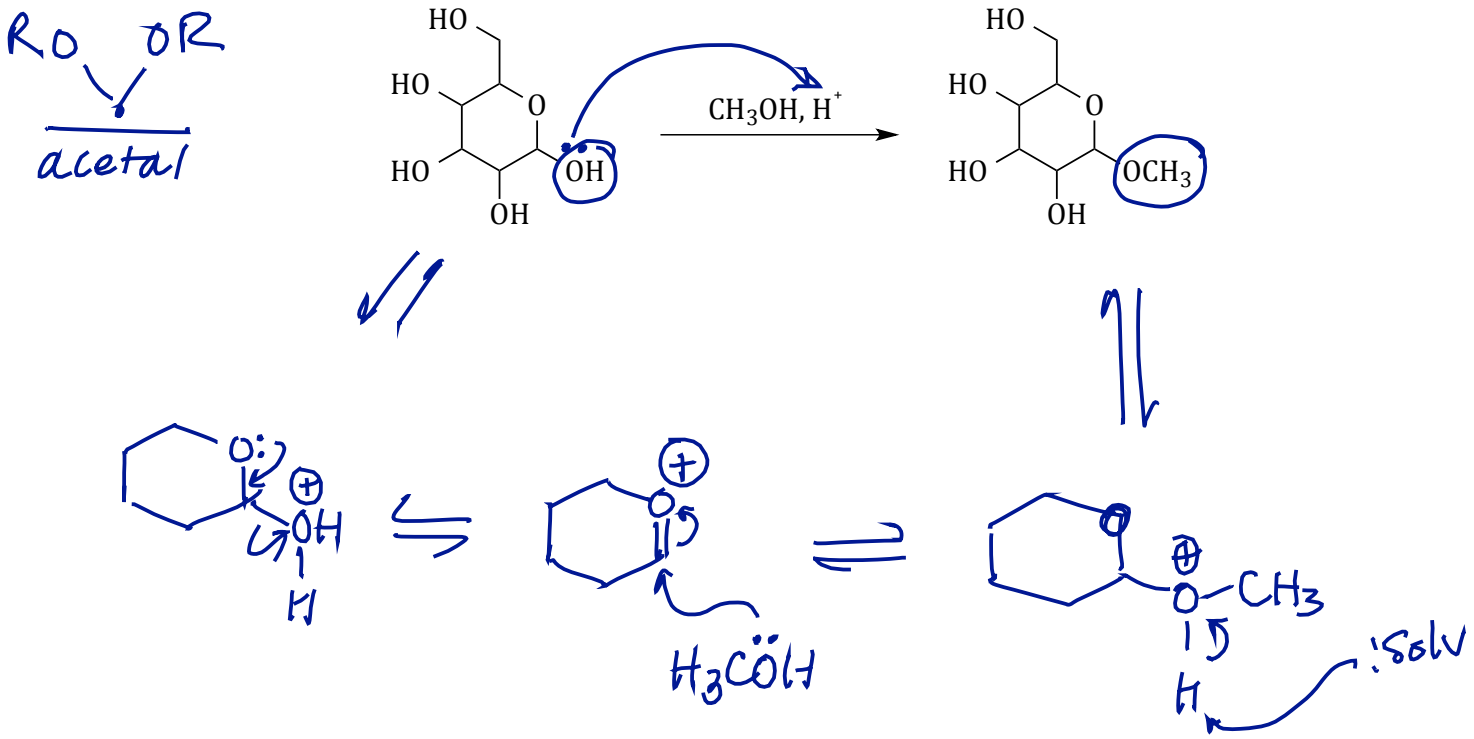
The stereochemistry of carbohydrates is often shown using a **Fischer projection**. Draw a Fischer projection that shows the correct stereochemistry of glucose.



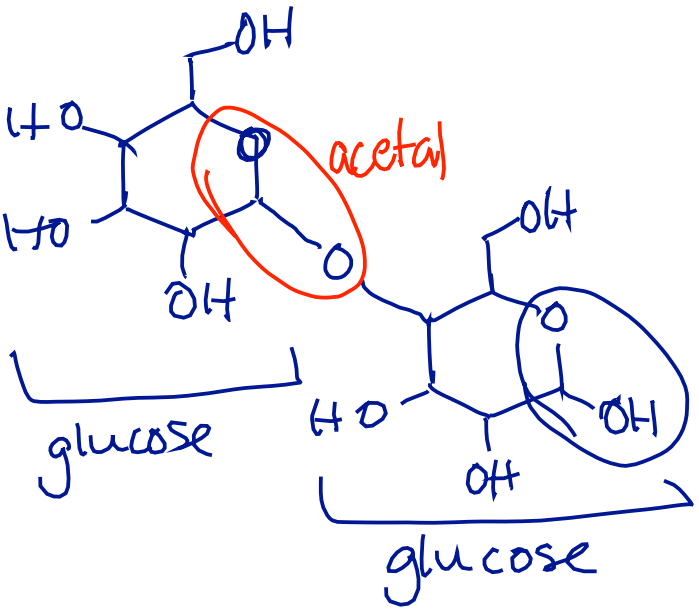
Reading: Sections 24.1, 24.2, 24.3

Acetals, Disaccharides, & Polysaccharides

Glucose will react with an alcohol to form an acetal. Provide a mechanism:



What if the alcohol is, in fact, merely the –OH group from *another* monosaccharide?



"maltose"

disaccharide

sucrose: glucose + fructose

lactose: glucose + galactose

oligosaccharide: "few"

polysaccharide: lots

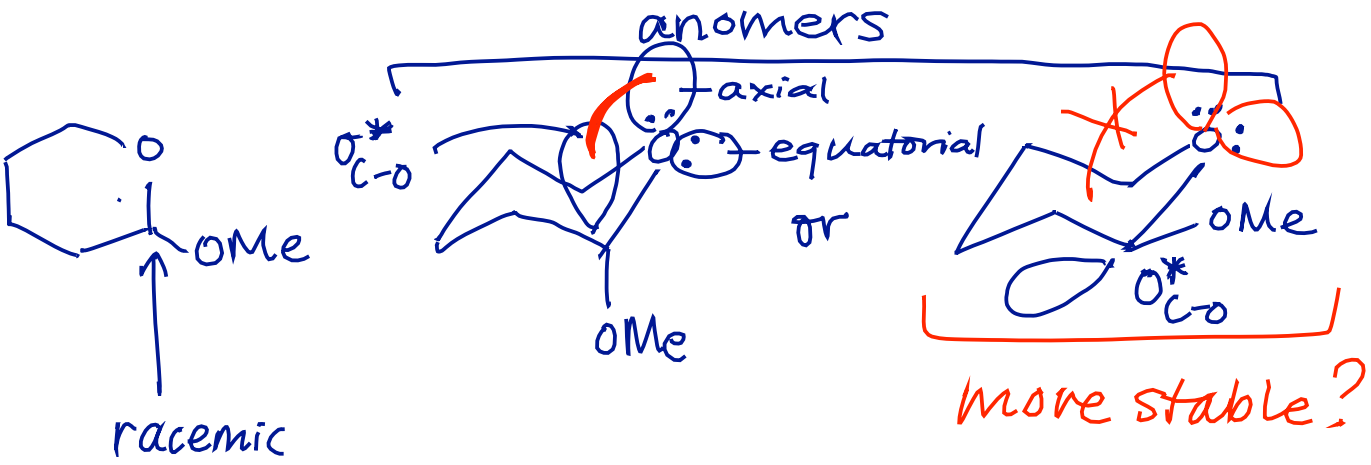
Reading: Sections 24.11

hemiacetal/acetal C called "anomeric carbon"

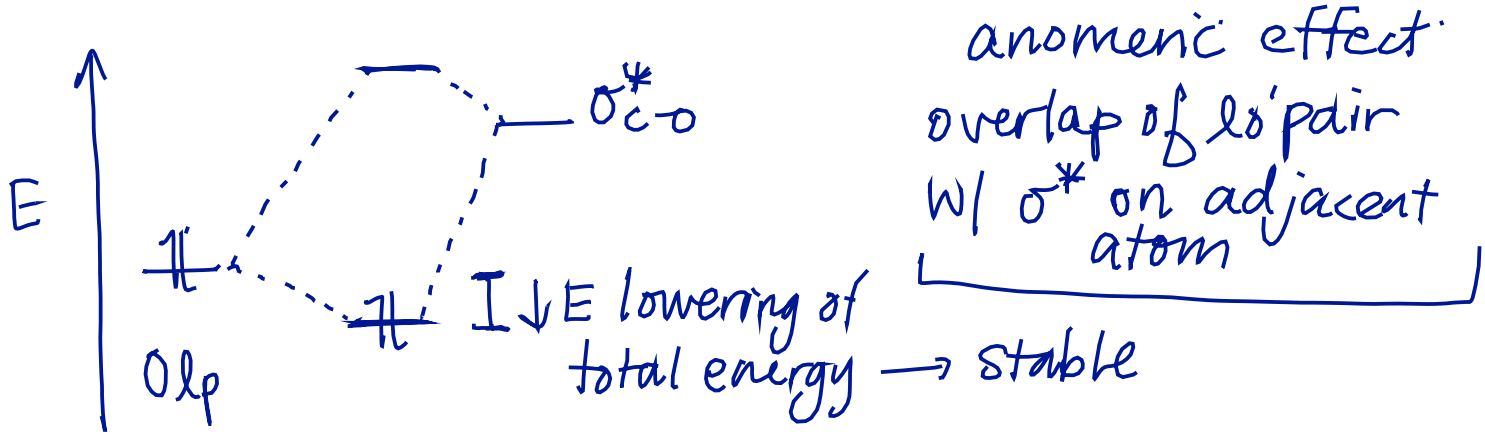
Week 5 July 21, 2014

The Anomeric Effect

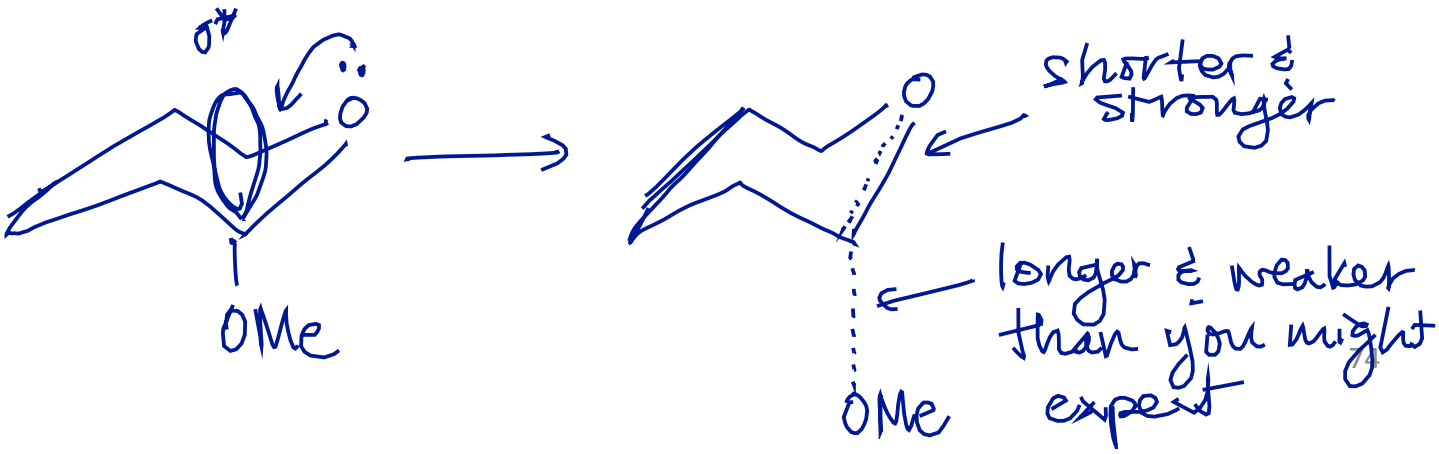
Consider the methyl acetal of glucose. There are two possible diastereomers of this compound at the acetal carbon. Draw these two structures. Which would you predict to be more stable?



It turns out that the most stable conformation actually has the –OMe group in an *axial* position. Why is this conformation more stable?



What are some other manifestations of this **anomeric effect**?



proteins: poly-amino acids

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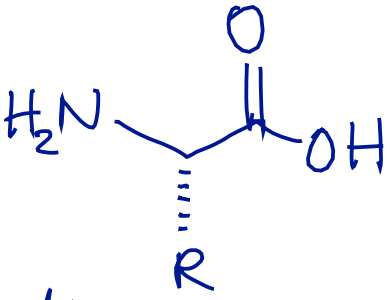
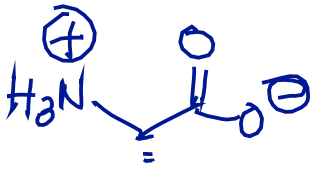
Amino Acids: Structure & Synthesis

Draw the structures of some **amino acids**. What is the pK_a of each of the functional groups in an amino acid? In what form will these amino acids be found at pH = 7?



pka's: $-COOH$ 5 → mostly deprotonated

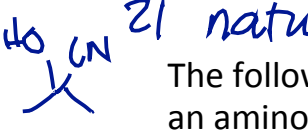
$-NH_3^+$ 9 → mostly protonated

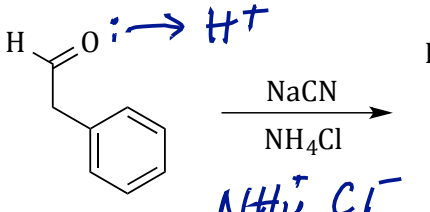


diff R groups:
21 natural amino acids

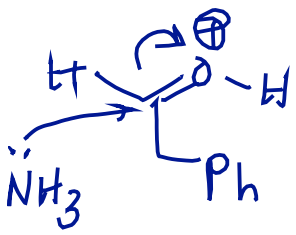
zwitterion
⊕/⊖ nonadjacent

The following procedure, known as the **Strecker synthesis**, is one way to synthesize an amino acid. Provide a curved-arrow mechanism.

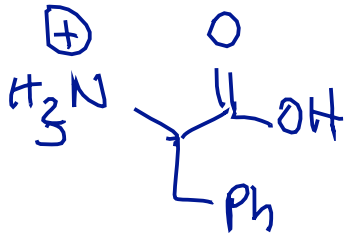


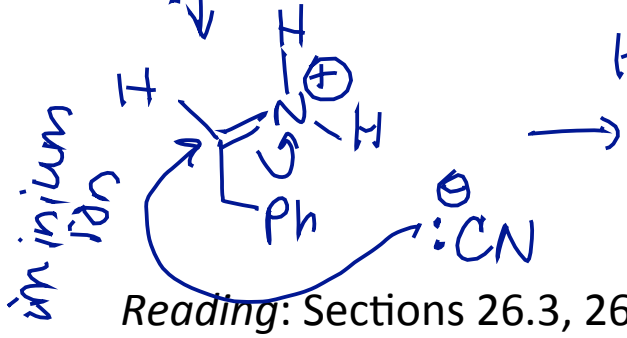


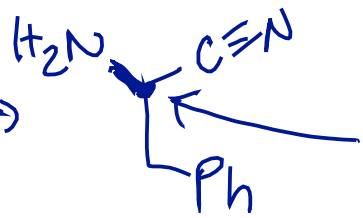
$NH_4^+ Cl^-$
$NH_3 + HCl$
buffer
pH~ 5



neutralize







racemic

H_3O^+, Δ

α-amino nitrile (cyanohydrin)

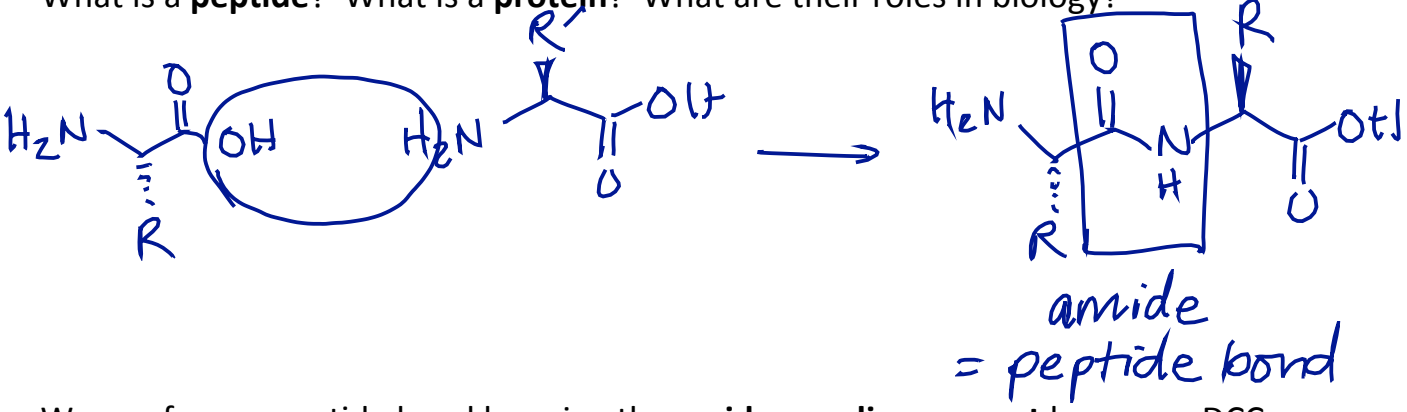
Reading: Sections 26.3, 26.4C

Week 5 July 21, 2014

The Structure of Peptides:
The peptide bond

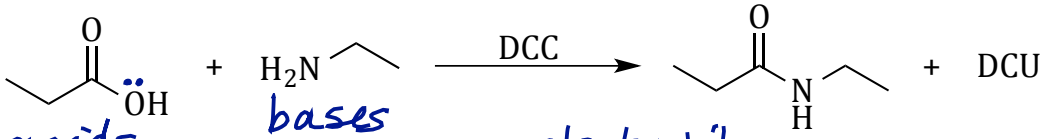
dipeptide

What is a **peptide**? What is a **protein**? What are their roles in biology?

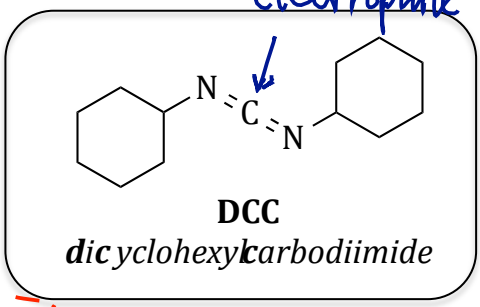


amide
= peptide bond

We can form a peptide bond by using the **amide coupling reagent** known as DCC. Provide a curved-arrow mechanism.

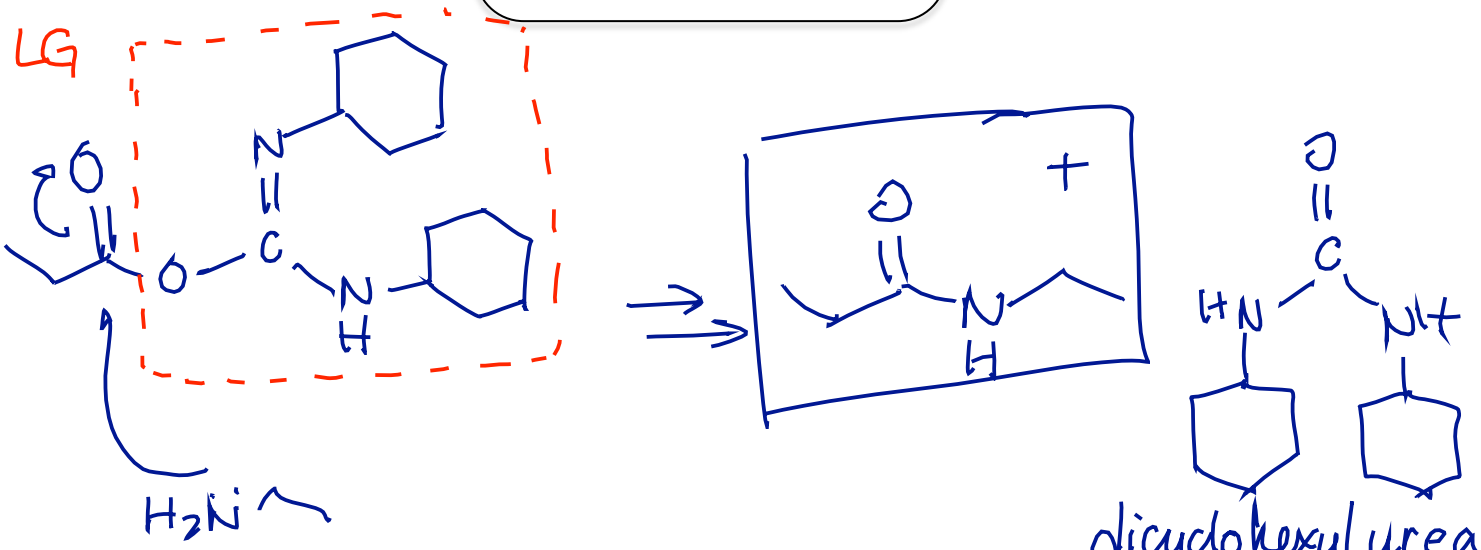


acids bases



electrophile

DCC
dic*yclohexyl****c****arbodiimide***



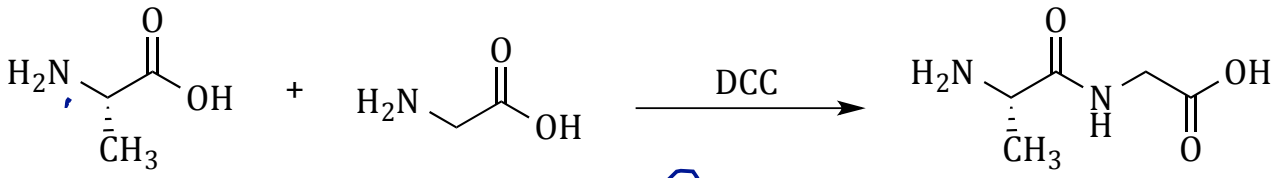
dicyclohexyl urea

Reading: Section 26.6

New rxn:

Synthesis of Peptides:
Protecting Groups

Why can't we use DCC to synthesize the following dipeptide?



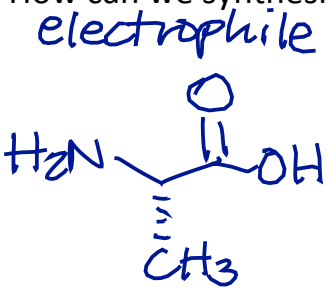
alanylglycine

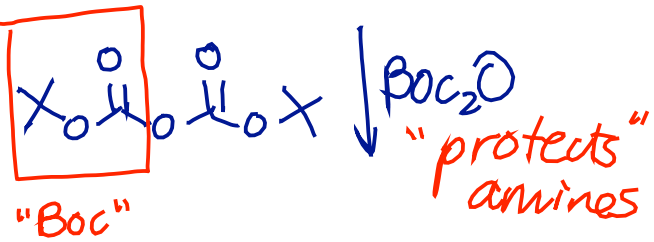
1) Which COOH react w/ DCC?
2) Which amine reacts?

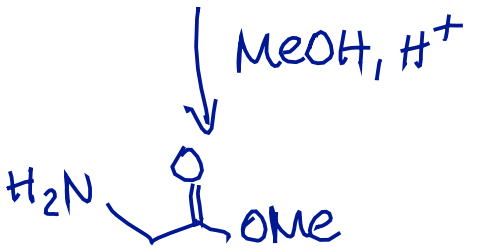
glycylalanine
alanylalanine
glycylglycine

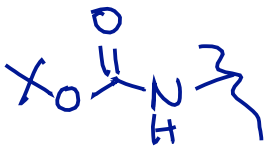
PROBLEM: indiscriminate coupling

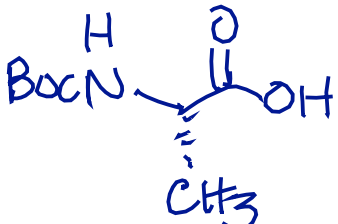
How can we synthesize that dipeptide using **protecting groups?**

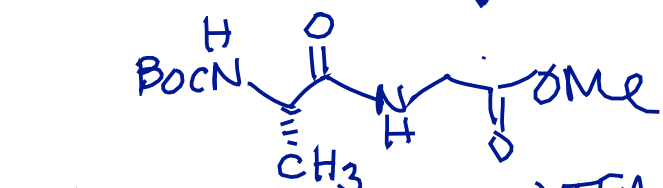


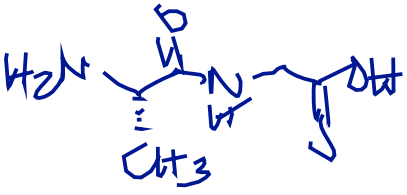












1) TFA (removes Boc)
2) OH^- (hydrolyze ester)
3) H^+ workup

Reading: Section 26.6

Nobel Prize: 1984

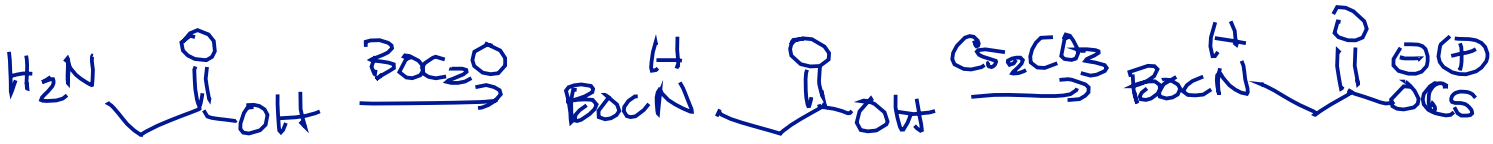
Merrifield

Week 5 July 21, 2014

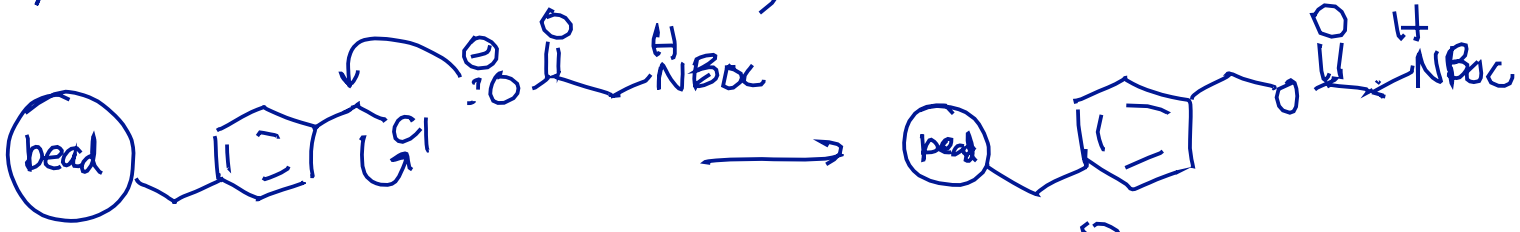
Synthesis of Peptides:
Solid-Phase Synthesis

Today, nearly all chemical synthesis of peptides is performed using *solid-phase synthesis*. Show how you can use solid-phase synthesis to synthesize alanylglycine.

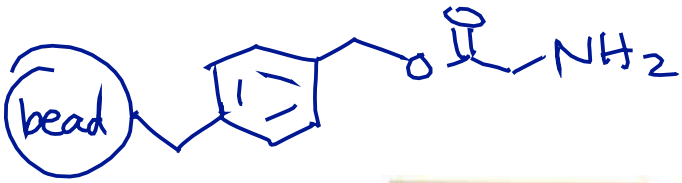
1) Start w/ "C-terminal" amino acid
→ Boc-protect (Boc_2O)
→ deprotonate carb. acid (Cs_2CO_3)



2) Attach to a "bead" (resin)

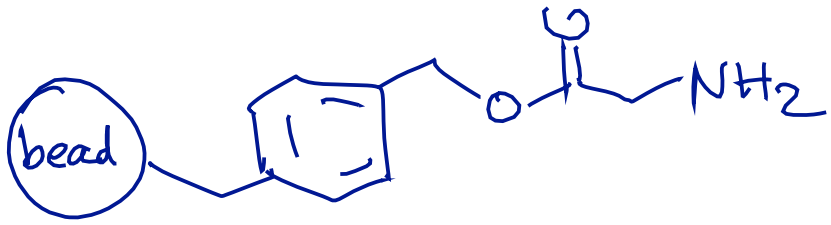


3) Remove Boc (TFA):

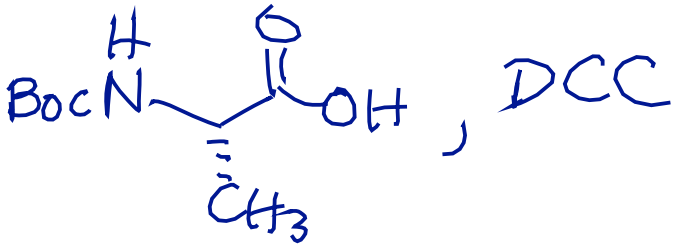


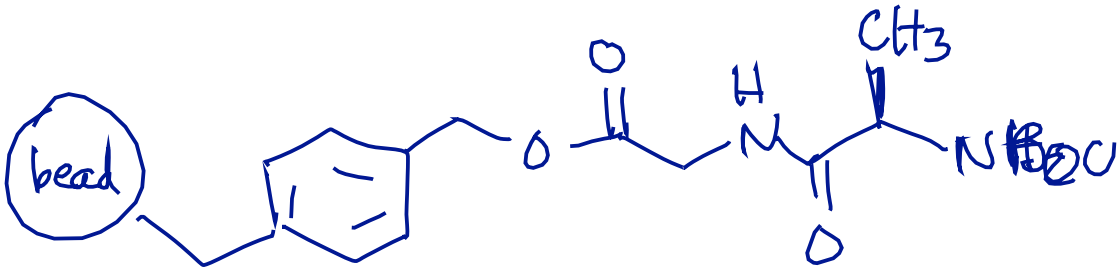
Even machines can do solid-phase synthesis!

Reading: Section 26.6



4) Add next AA (Boc-protected)



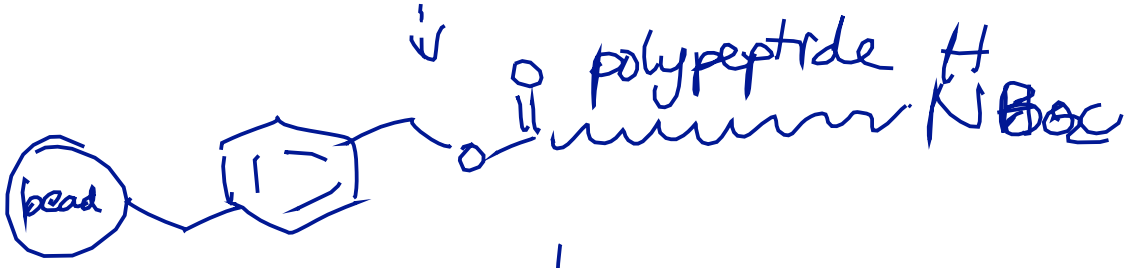


↓ deprotect (TFA), FILTER

↓ add next AA

5) Lather, rinse, repeat

↓



6) Remove from bead (also removes the last Boc)

↓ HF