

Essentials in Carbohydrate Chemistry and Biochemistry

GlycoQuizz

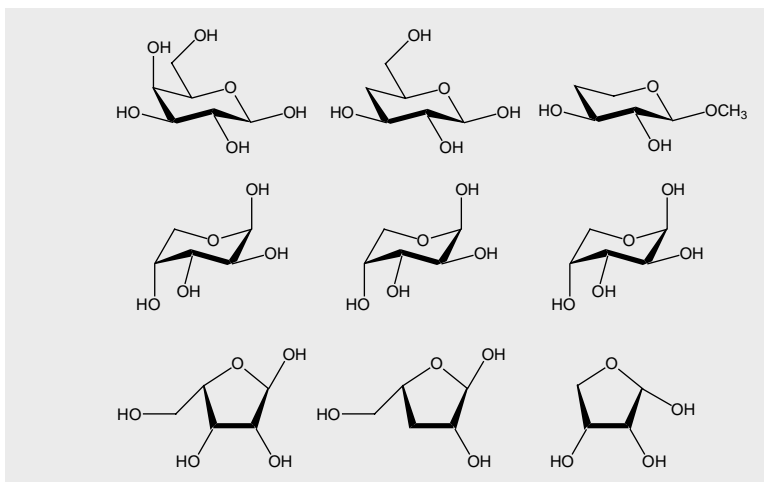
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Exercises and problems on glycosciences

1 Structures and stereochemistry of carbohydrates

- 1.1 Draw any aldohexose of the D-series in its open-chain form as Fischer projection.
Then draw the enantiomer of the chosen aldohexose and two diastereomers of it, one of the D-, the other of the L-series.
- 1.2 How many stereoisomers of the aldohexose, selected in exercise 2.1, are theoretically possible?
- 1.3 Select any aldopentose and explain, how its furanose and its pyranose form, respectively, are formed.
- 1.4 Take the pentopyranose, formed in exercise 2.3 and draw both of its anomeric forms in their more stable chair conformations.
- 1.5 Draw each of the following glycosides both in their more and less stable chair conformation: methyl α -D-mannopyranoside, methyl α -D-arabinopyranoside, methyl α -D-galactopyranoside, methyl β -L-galactopyranoside.
- 1.6 Draw D-erythrose in a stable cyclic form.
- 1.7 Draw arabinose in two different stereoisomeric forms.
- 1.8 Construct a case, where the anomeric forms of a cyclic hemiacetal are enantiomers.
- 1.9 How many stereocenters has a ketose with four carbon atoms?
- 1.10 How many stereoisomers of D-fructose are theoretically possible?
- 1.11 Draw D-sorbose and its mirror image as furanoses.
- 1.12 Exemplify the difference between an α - and a β -glycoside using Newman projection along the C1-C2 bond of the sugar ring.
- 1.13 Draw the structure of a compound which can formally be named as 1,3,4-trideoxy-arabinopyranose. Can this compound form an open chain form?
- 1.14 Explain, how the equilibrium between methyl α -D-mannoside and methyl β -D-mannoside can occur. Which glycoside is the more stable one and why?

- 1.15** Explain, why only two of nine stereoisomeric inositols (1,2,3,4,5,6-hexahydroxycyclohexanes) are chiral.
- 1.16** How many stereoisomeric L-alditols are possible?
- 1.17** Draw the structures of all possible stereoisomeric disaccharides consisting of two D-glucopyranose rings.
- 1.18** Explain the difference between starch and cellulose.
- 1.19** Determine whether the following molecules are D- or L-sugars.

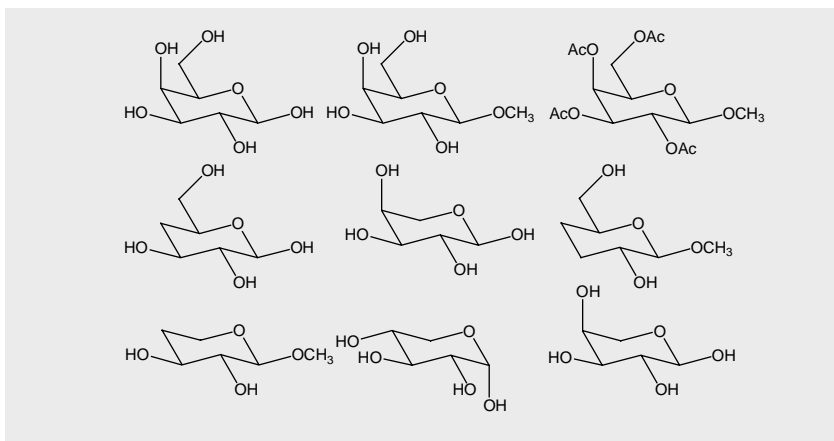


- 1.20** Explain the structural characteristics of cyclodextrins.
- 1.21** Name the dihedral angles, which are used to define oligosaccharide conformations.
- 1.22** Answer the following questions with either 'yes' or 'no' and determine, which of the following statements are correct and which are wrong:
- Is an anomeric mixture of methyl glucoside chiral?
 - A 1:1-mixture of a D-aldohexose and its L-form is not optically active.
 - Is the β -anomer of 2,3,4,6-tetra-O-acetyl-glucosylbromide stable?
 - Can 4-deoxy-D-arabinose form a stable cyclic hemiacetal? (If yes, draw its structure).
 - Can an octose form a stable cyclic hemiacetal? (If yes, propose a structure).
 - Are D-mannose and L-glucose stereoisomers?
 - Are D-gulose and L-glucose enantiomers?
 - All monosaccharides with D-configuration show a positive rotation value in polarimetry.
 - Is the equilibrium between the open-chain form of D-mannose and its pyranose form shifted to the open-chain form due to the axial position of the 2-hydroxyl group?

- D-Galactose and L-galactose have different melting points.
- Fructose is a disaccharide.
- Fucose is a disaccharide.
- Fructose and fucose are synonymous names for the same sugar.
- The anomeric mixture of a given aldohexose shows no optical activity.
- There are 32 stereoisomeric aldohexopyranoses.
- Solid, crystalline monosaccharides undergo mutarotation.
- Maltose and isomaltose are anomers.
- Proteoglycans are polysaccharides obtained by proteolytic degradation of natural products.
- Glycosides are acetals.
- Disaccharides are always reducing.
- A molecule is only called a carbohydrate, when all ring-positions are hydroxylated.
- Aldohexoses can be reduced to alditols.
- There are two enantiomeric forms of mannitol.
- The open-chain form of D-erythrose is a *meso* form.
- Galactosamine and galactosyl amine are synonymous names for the same molecule.
- Are L-fucose and L-rhamnose diastereomers?
- The 1C_4 conformation is preferred in L-glucose.
- Pectins consist of amino acids.
- Human milk contains only oligosaccharides formed from D-glucose.

2 IUPAC nomenclature of carbohydrates

2.1 Name the following carbohydrates according to IUPAC nomenclature.



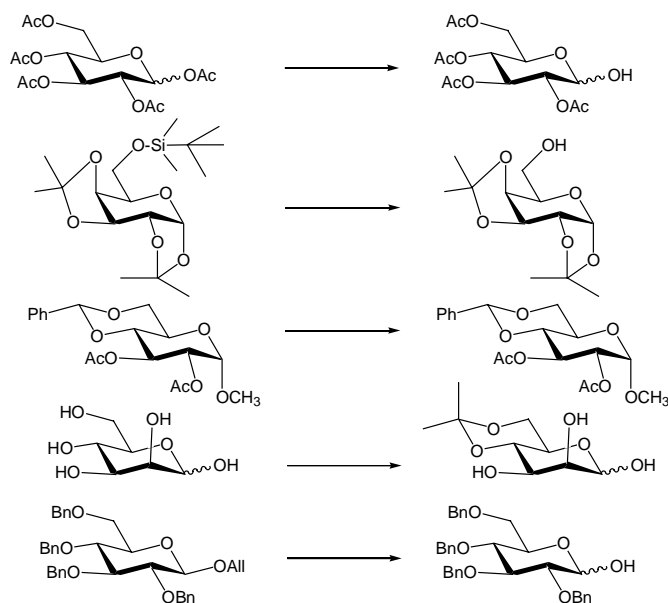
2.2 Draw the structures of the following glycosides:

- Ethyl α -D-glucopyranoside Ethyl β -D-glucopyranoside
- Ethyl α -L-glucopyranoside *p*-Nitrophenyl α -D-mannopyranoside
- Methyl β -D-ribofuranoside Methyl β -D-ribofuranoside
- 2-Aminoethyl α -L-6-deoxy-galactopyranoside
- 2-Amino-2-deoxy- α -D-galactose

3 Protecting group patterns

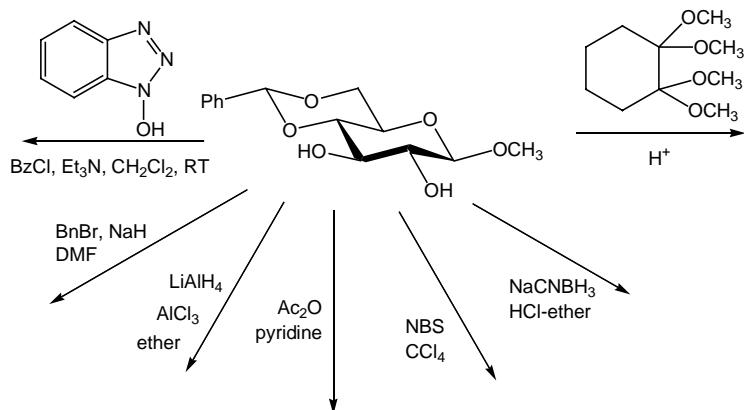
- 3.1 What is meant by 'orthogonal protection'? Give examples for orthogonal protecting groups.
- 3.2 Comment on the different reactivity of the hydroxyl groups of a sugar ring. List the hydroxyl groups in methyl α -D-galactoside according to increasing reactivity.
- 3.3 Which hydroxyl group of a glycoside is most readily regioselectively protected and why?
- 3.4 Would you choose an acetyl group for the reversible protection of an amino group? Suggest an alternative.

- 3.5** Acyl groups tend to migrate in contrast to ether protecting groups. Show, how $O \rightarrow N$ acyl group migration occurs.
- 3.6** Give an example, where an acetyl group migration has been utilized for the synthesis of a desired monosaccharide derivative.
- 3.7** Name three reagents, which can be used for isopropylideneation.
- 3.8** Suggest reagents which can be used in the following reactions:

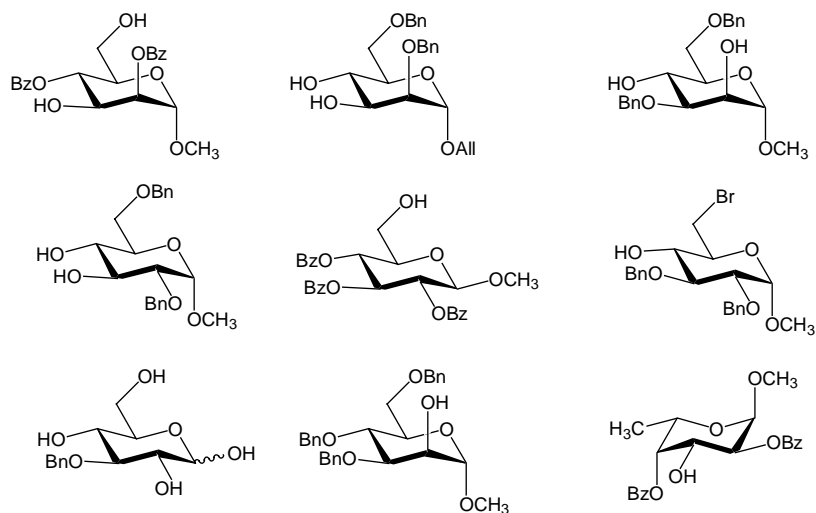


- 3.9** Which protecting groups are suited for the regioselective 6- O -protection of glycosides?
- 3.10** What is the levulinoyl group and how can it be cleaved?
- 3.11** Explain, how DMAP accelerates benzylation using benzoyl chloride.
- 3.12** How can an O -chloroacetyl group be cleaved selectively in the presence of O -acetyl groups?
- 3.13** Give examples of acyclic acetals, which can be used for the protection of OH groups.
- 3.14** Name two standard methods for the protection of vicinal diols.
- 3.15** Explain why benzylidene acetals form six-membered 1,3-dioxanes rather than 1,3-dioxolanes.

3.16 Complete the following scheme:



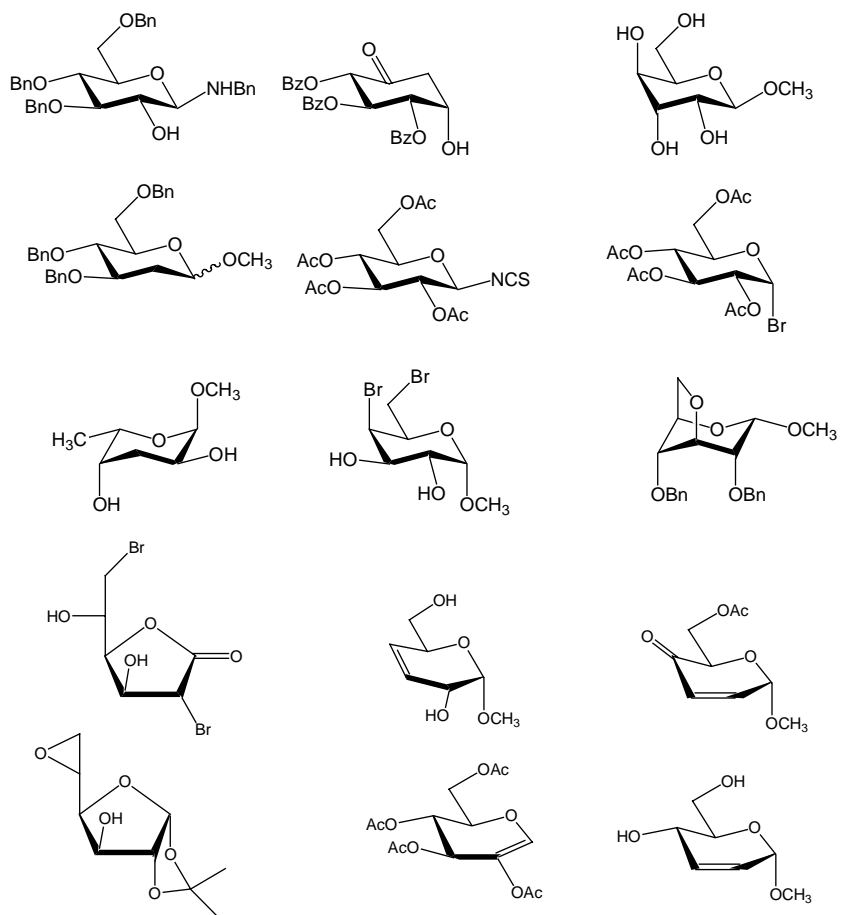
3.17 Suggest synthetic sequences to prepare the following protected saccharide derivatives either from the reducing sugar or from the respective glycoside:



4 Functionalization of monosaccharides

- 4.1 Name three methods for the activation of hydroxyl groups.
- 4.2 What is DAST, what is it used for?
- 4.3 Explain, how DMF together with methyl sulfonyl chloride can lead to the conversion of OH into Cl.
- 4.4 Name a method for the preparation of a sugar epoxide.
- 4.5 What is the general structure of a glycal and a hydroxyglycal?
- 4.6 What is the 'Payne rearrangement'?
- 4.7 Suggest a synthesis for 2-azido-2-deoxy-glucose.
- 4.8 How can deoxygenation of a hydroxyl group be achieved according to Barton and McCombie?
- 4.9 Explain the mechanism of the Staudinger ligation of glycosyl azides.
- 4.10 What is the 'Horton chloride'?
- 4.11 How can glycosyl thiols be prepared?
- 4.12 What can be achieved by 'azidonitration'?
- 4.13 Explain the mechanism of the 'Ferrier rearrangement'.
- 4.14 Explain the mechanism of the synthesis of tri-*O*-acetyl-glucal starting from the per-acetylated glycosyl bromide.
- 4.15 Show a method which allows conversion of a D-sugar into an L-sugar?
- 4.16 What can a Mitsunobu reaction be used for? Show an example.
- 4.17 Explain, why benzylidene acetals form six-membered 1,3-dioxanes rather than 1,3-dioxolanes.
- 4.18 How is D-mannono-1,4-lactone prepared?
- 4.19 What is the structure of nojirimycin?
- 4.20 How can glycosyl fluorides be prepared from 2-OH-unprotected methyl glycosides?

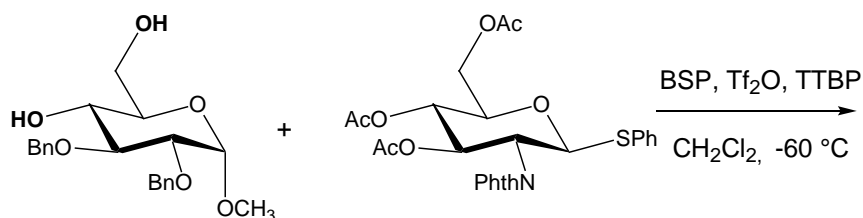
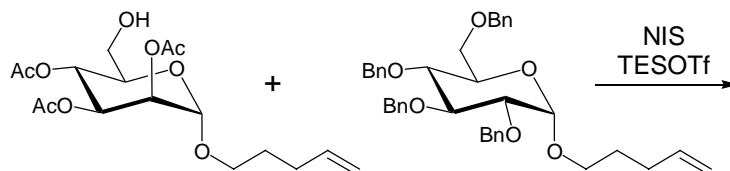
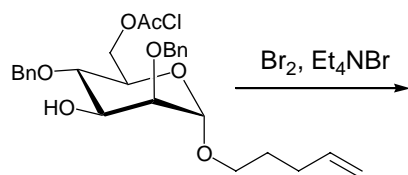
4.21 Suggest syntheses for the following saccharides:



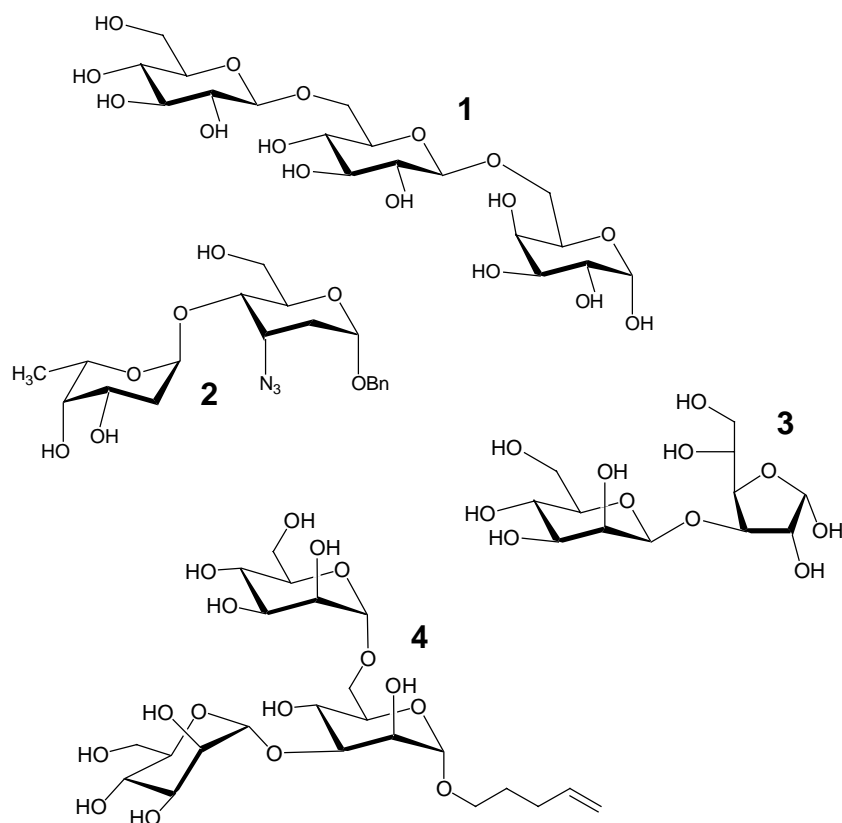
5 Glycoside synthesis

- 5.1** Perform two different retrosynthetic cuts with a glycoside and show the resulting glycosyl donor and acceptor synthons in each case.
- 5.2** Explain, which products can arise from the nucleophilic attack of an alcohol onto an acetoxonium ion.
- 5.3** Is it possible to use per-acetylated sugars as glycosyl donors? –If yes, draw an example.
- 5.4** Explain, why the synthesis of 1,2-*trans* glycosides can be a stereospecific reaction, whereas the synthesis of 1,2-*cis* glycosides cannot.
- 5.5** Explain the difference between glycosidation according to an S_N1 - and an S_N2 -type process.
- 5.6** How can the synthesis of 1,2-*cis* glucosides be achieved starting from glucosyl bromide?
- 5.7** Explain the effect, which can be exerted by acetonitril when used as the solvent in glycosylation reactions.
- 5.8** Which glycosyl halides can be used for glycoside synthesis? –Which of them is stable in the OH-unprotected form?
- 5.9** Explain, which rearrangement reaction a glycosyl trichloroacetimidate can undergo under the catalysis of Lewis acids.
- 5.10** Explain, how the stereoselective synthesis of β -mannosides can be achieved employing mannosyl bromides.
- 5.11** Explain the concept of 'intramolecular aglycon delivery'. –Draw an example.
- 5.12** Name two examples for glycosyl donors, which are stable enough to allow protecting group chemistry.
- 5.13** What is the 'armed-disarmed' concept, how can it be utilized?
- 5.14** Suggest a mechanism for Lewis-acid catalyzed isomerisation of glycosyl ortho-esters into the respective glycosides.
- 5.15** Which interconversions can be carried out with thioglycosides at the anomeric center?

- 5.16** What is DMDST? –How does this reagent effect activation of thioglycosides?
- 5.17** What is the mechanism of the activation of *n*-pentenyl glycosides as glycosyl donors?
- 5.18** Which side reaction does normally occur upon activation of 2-deoxy-2-acetamido glycosyl donors?
- 5.19** What is the principal problem in synthesis of 2-deoxy glycosides? –How can it be solved for 2-deoxy- α - and 2-deoxy β -glycosides?
- 5.20** Which types of enzymes can be used for glycoside synthesis?
- 5.21** How is ‘cofactor regeneration’ utilized in enzymatic glycoside synthesis?
- 5.22** What is meant by the term ‘glycosynthase’?
- 5.23** What are the advantages of oligosaccharide block synthesis?
- 5.24** Complete the following reactions:



- 5.25** Which principal approaches can you envisage to allow oligosaccharide synthesis in one-pot?
- 5.26** There are two principal approaches for the solid-phase synthesis of oligosaccharides: either the glycosyl donor or the glycosyl acceptor is attached to the solid support. Explain the differences and discuss advantages and disadvantages.
- 5.27** Explain, how glucosamine can be synthesized utilizing the Heyns rearrangement.
- 5.28** Explain a strategy for the synthesis of a glycosyl amino acid.
- 5.29** What is DMDO? –What is it used for?
- 5.30** Suggest syntheses for the following oligosaccharides (**1** to **4**):



6 Glycoconjugate structures and biosynthesis

- 6.1 Describe where oligosaccharides occur in cell membranes and how they can be attached.
- 6.2 Which carbohydrates are typical constituents of eukaryotic cell membranes?
- 6.3 Describe three principal possibilities which are used in nature to attach a carbohydrate to a protein.
- 6.4 Write up the structure of the core pentasaccharide which is common to all *N*-glycans.
- 6.5 Explain why all *N*-glycans have a core saccharide in common.
- 6.6 How are the *N*-glycans of glycoproteins divided into sub-groups?
- 6.7 Explain the biosynthesis of 5-*N*-acetylneuraminic acid (Neu5Ac).
- 6.8 In which cell organelle is CMP-Neu5Ac biosynthesized?
- 6.9 What is the difference between a glycosyl transferase and a glycosidase?
- 6.10 What are the substrates for glycosyl transferases?
–How are they biosynthesized?
- 6.11 What are the activated forms of mannose, galactose, L-fucose, and neuraminic acid from which the respective sugars are transferred to oligosaccharides catalyzed by the specific glycosyl transferases?
- 6.12 What is a 'GPI anchor'?
- 6.13 What is 'ceramide'?
- 6.14 What is the principal structure of a ganglioside?
- 6.15 Draw the structure of the glycosphingolipid which is named GM2.
- 6.16 Compare the structural diversity of oligosaccharides with that of proteins and oligonucleotides.
- 6.17 How does 'avidity' differ from the term 'affinity'?
- 6.18 What is the 'dolicholphosphate cycle'?
- 6.19 What is a glycosyl transferase of the 'Leloir type'?
- 6.20 What are the substrates of non-Leloir glycosyl transferases?
- 6.21 What is meant by 'trimming' and 'processing' of glycoconjugates?
- 6.22 What is a 'chaperone'?
- 6.23 How does quality control of *N*-glycoprotein biosynthesis occur?
- 6.24 What is meant by 'microheterogeneity' of glycoconjugates?

- 6.25 Do *O*-glycoproteins have a common core structure?
–How are they divided into sub-groups?
- 6.26 What does ‘LAM’ and what ‘LPS’ stand for?
- 6.27 Which organelles participate in *N*-glycoprotein biosynthesis?
- 6.28 What could be the function of a ‘flipase’?
- 6.29 Discuss, which parts of a protein are glycosylated; can more than one glycosylation site occur?
- 6.30 Discuss the different structural possibilities for amphiphilic glycoconjugates.
- 6.31 What is the structure of *N*-acetylmuramic acid, where does it occur?
- 6.32 Is it always a GalNAc residue which links the oligosaccharide moiety of *O*-glycoproteins to the peptide backbone?
- 6.33 What is the configuration of the double bond in sphingosine?
- 6.34 How is the large diversity of glycosphingolipids biosynthesized?

7 Glycobiology

- 7.1 What is a lectin? Distinguish the function of a lectin from that of an enzyme and an antibody. Give an example.
- 7.2 Today, there is a medication against Influenza (flu) available.
How do such drugs work, what is the target of the active molecule?
- 7.3 What is the molecular difference between the blood groups A, B and O?
- 7.4 What is the strategy to obtain a carbohydrate-based vaccine?
- 7.5 Explain the biosynthesis of 5-*N*-acetylneuraminic acid (Neu5Ac).
- 7.6 In which cell organelle is CMP-Neu5Ac biosynthesized?
- 7.7 What does the abbreviation sLe^X stand for? Write up (i) the full name, and (ii) the molecular formula.
- 7.8 Which modification has been made in the biosynthesis of neuraminic acid to allow the presentation of chemically altered neuraminic acid residues on the cell surface?
- 7.9 How do bacteria adhere to cell surfaces?
- 7.10 What does the abbreviation ‘CRD’ stand for?
- 7.11 Give a definition for the term ‘glycomimetic’.

- 7.12** What is the typical affinity of a carbohydrate ligand for its protein receptor as measured in e.g. ELISA?
- 7.13** What does 'ELISA' stand for? What is its purpose?
- 7.14** How does 'avidity' differ from the term 'affinity'?
- 7.15** What is characteristic for carbohydrate binding of so-called C-type lectins?
- 7.16** What does 'siglec' stand for?
- 7.17** What does 'CD' stand for?
- 7.18** What is meant by 'carbohydrate cluster effect'?
- 7.19** What is a 'glycodendrimer'?
- 7.20** How does the family of sialic acid molecules differ?
- 7.21** What is a 'glycochip'? What is it used for?
- 7.22** What monosaccharidic building blocks are found as constituents of the glycocalyx of a eukaryotic cell?
- 7.23** What distinguishes a glycoprotein of type 1 from that of type 2?
- 7.24** What is a 'glycopolymer'? How can it be synthesized?
- 7.25** What is a 'selectin'? How many different selectins are known?
- 7.26** What are carbohydrate vaccines?
- 7.27** What is meant by 'antiadhesion therapy'?
- 7.28** What does 'ROMP' stand for; how has it been used in glycobiology?
- 7.29** What are type 1 fimbriae?
- 7.30** How are senescent erythrocytes cleared from blood circulation?