Chapter 11. Ouellette, 2/e. Chemistry X402.

Ch 11. Carbohydrates

Skip: none; we will cover the entire chapter.

Also read, for review as needed: Sect 2.6, and possibly 2.10, on chemical equilibria. The key point of immediate relevance is Le Chatelier's principle. This will help you with the equilibrium between linear and cyclic forms of the sugars. It has implications for the ability to oxidize the aldehyde group, even though most of the sugar is in the cyclic hemiacetal form, with no free aldehyde group.

Essays: Not assigned, but here are some notes about them, since I suspect you will want to at least browse them. (You are not responsible for the Essays or for these notes about them.)

- p 320. Although the title focuses on lactose, it actually discusses the metabolism of other sugars, too. An important issue is the inability of some people to metabolize one or another sugar. Distinguish lactose intolerance, an inability to break a disaccharide into its monosaccharide components, and galactosemia, the inability to properly metabolize a particular common monosaccharide. In the former case, the non-broken disaccharide simply accumulates, causing an osmotic imbalance, and also allowing for some undesirable bacterial metabolism later in the digestive tract. A similar effect occurs with some other oligosaccharides, including some from beans. The commercial product Beano is analogous to the Lactaid shown on p 319; check labels and you will see that each contains an enzyme to break down di- or oligo-saccharides to individual sugars. In contrast, in galactosemia a normal monosaccharide is improperly metabolized, and actually leads to accumulation of an intermediate that is toxic.
- p 323. Along with the biology story here, this Essay introduces more types of sugar derivatives. Note the amino-sugars; the amino group (p 19) will be formally introduced in Ch 14. The amino group of amino-sugars is often acetylated (p 21), as shown here. Chitin, of lobster shells and insect skeletons, is similar to cellulose, except that the 2 position of the sugar has been modified with an N-acetylamino group. The Essay also shows a "deoxy" sugar (fucose). Another deoxysugar is 2-deoxyribose, the "D" of DNA (p 448, bottom). For more about the blood groups, see Rose et al (2005), below.

⇒ A **practice quiz** for Ch 11 is at the web site. It includes some practice with chirality as well as with carbohydrates.

Notes

I do not expect you to know the individual sugars (although I do urge you to learn the structure of the most important sugar). What is important is to see how the sugars are related. This extends to the derivatives. Note that many of the derivatives involve oxidation or reduction of one group in the sugar. (A copy of Table 11.1 will be attached to the next test.)

Sect 2. Note that an L-sugar is the enantiomer of the corresponding D-sugar (p 301, bottom).

Sect 3. Both Fischer and Haworth projections are useful ways to draw sugar structures in 2D. However, converting between them is not particularly easy. If you have models, you can try it.

But you are not responsible for doing this interconversion. I will give you the sugars in Fischer form, and will also give you one in Haworth form. These serve as reference points. Example 11.5 is a nice illustration of this.

Sect 5-8. General comments about reactions of sugars. Some of these reactions are "chemical" and some are "biochemical". Of course, biochemical reactions are chemical, but the emphasis is different. For example, the easiest place for a chemist to oxidize a sugar is at the aldehyde position, giving the -onic acid; this follows from what you have learned about the reactivity of the various groups. On the other hand, the 6-oxidation product, the -uronic acid, is more common biologically. How can this be? Because cells have an enzyme that provides the specificity, so that the oxidation reaction occurs at a particular position. Ch 6 (e.g. Fig 6.11) introduced the idea that enzymes distinguish enantiomers. Now, we see that enzymes recognize specific positions within a molecule. The big issue is that the reactions that actually occur in complex biological systems are controlled by enzymes, which provide specificity. Most enzymes are proteins, and we will discuss proteins in Ch 15. In the Metabolism section that follows, we will look at properties of enzymes.

Sect 5. A short version of this section might say… sugars are aldehydes, and they act like it.

Sect 7 & 8 give a nice juxtaposition of chemical vs biochemical aspects of a single story. Both involve glycosides (= acetals of sugars), and the basics of that are the same in both sections. Sect 7 deals with glycosides from simple alcohols, such as might be made in an org chem lab. Sect 8 deals with natural disaccharides, which are glycosides of a second sugar molecule.

The Reaction summary emphasizes the organic reactions of sugars; you could usefully make your own version of this, including or even focusing on the biochemical reactions.

As usual, discussions of mechanism are "advanced".

Suggested problems

The Models exercises are quite good; you may be able to do some of them, such as #3, without actually making a model. All of the Exercises are good practice; do a good sampling of them. For Haworth structures, I suggest you do them by comparison with the given Haworths; trying to convert from Fischer to Haworth is harder.

Errata

p 326, #11 part c and all parts of #12. The answer section shows the starting sugar, not the answer.

p 328, #41a. The structure shown is incorrect. The -OH on the glycosidic C should be -H.

Further reading

D Ringe, Bacterial behaviour: Function by serendipity. Nature 415:488, 1/31/02. News. Boron is an essential nutrient, in trace quantities, for plants; it is also toxic to most organisms. The essential role for boron has been elusive, but it is known that borate interacts with sugars. (Boric acid, a weak acid, is H_3BO_3.) In the work discussed here, they study a signaling system between bacterial cells. They were actually studying the receptor for the signal system, but quite accidentally found the signaling molecule bound to it. That signaling molecule is a borate ester of a sugar. They also note recent work showing a role for borate in plant cell wall structures, also involving interactions with carbohydrates. Also see Ricardo et al (2004).

T Swager, Polymer light-emitting devices: Light from insulated organic wires. Nature Materials 1:151, 11/02. News. Discusses use of small cyclic oligosaccharides, called cyclodextrins, threaded onto the polymer LEDs, as insulation for the polymer wires.

A T Fazleabas & J J Kim, Development: What makes an embryo stick? Science 299:355, 1/17/03. News. Attachment (implantation) of the embryo to the uterine wall is a complex process. Here they discuss work on the importance of hormonally-induced sugar residues on the surface of the cells of the uterine wall as a key part of the recognition process. More about sugars on cell surfaces in Ch 13 (and other items below).

C J Phelps et al, Production of α-1,3-galactosyltransferase-deficient pigs. Science 299:411, 1/17/03. Pigs are considered a potential good source of organs for transplantation to humans. However, there is an immunological problem, involving cell-surface sugars. Turns out that the problem has been identified, and pigs lacking it have been made. Also see Hamilton et al (2006).

M Jarvis, Chemistry: Cellulose stacks up. Nature 426:611, 12/11/03. News. Cellulose is the most prevalent organic chemical on earth, largely in its role as a structural material in plants. In fact, cellulose is unusual among the carbohydrates in being insoluble in water. The simple view of the insolubility of cellulose is that the chains line up just right so as to allow extensive interchain hydrogen bonding. The non-uniformity of ordinary cellulose has made structural studies difficult. But the work reported here uses better crystals, and reports more details. Of particular interest is the possible role of C-H hydrogens in the hydrogen bonding network. Although we normally say that the C-H bond does not have $H^{\delta+}$, we now realize from the discussion of H alpha to a carbonyl group that this is a simplification.

A Ricardo et al, Borate minerals stabilize ribose. Science 303:196, 1/9/04. See Ringe (2002), above, for some background. Here they show that borate stabilizes sugars, including ribose, against chemical degradation. They suggest this might have implications for the pre-biotic origin of ribose, hence of RNA.

G Brumfiel, Cell biology: Just add water. Nature 428:14, 3/4/04. News feature. Freezing and freeze-drying of cells are useful procedures -- for long term storage of blood cells and egg cells, and for lab work. However, survival of cells through these processes is often poor. High concentrations of the disaccharide trehalose may be helpful, though learning to use it seems to be a challenge in itself. They are now able to make freeze-dried blood products, which should be useful to the military.

M Kawakubo et al, Natural antibiotic function of a human gastric mucin against Helicobacter pylori infection. Science 305:1003, 8/13/04. They show that the carbohydrate chains of mucins (glycoproteins) produced by cells deep in the gastric mucosa (mucous membranes) inhibit infection by Helicobacter. It is possible, then, that these mucins are responsible for the normally low level of Helicobacter infection in that area.

N L Rose et al, Glycosyltranferases A and B: Four critical amino acids determine blood type. J Chem Educ 82:1846, 12/05. Good overview of the AB blood type system (p 323), including history, and enzymatic and genetic basis. Also see Liu et al (2007).

K Keegstra & J Walton, Plant science: β-Glucans--Brewer's bane, dietician's delight. Science 311:1872, 3/31/06. News. β-Glucan is a general term for beta-linked polymers of glucose; several -- including cellulose -- are present in various types of plant cell walls. The term is also used specifically to refer to a type of mixed 1,3- and 1,4-linked polymer found in the barley used in brewing. The work discussed here reveals a key enzyme to make this polymer; it is part of a family of enzymes related to cellulose synthase.

J L Fantini et al, Popping popcorn kernels: Expanding relevance with linear thinking. J Chem Educ 83:414, 3/06.

P H Tsang et al, Adhesion of single bacterial cells in the micronewton range. PNAS 103:5764, 4/11/06. Bacteria stick to things; some of them stick very well. In fact, the ability of bacteria to grow attached to things, including other bacteria, is an emerging field of study. Here they study the adhesive holdfast of Caulobacter crescentus, a type of bacteria often involved in bio-fouling of surfaces. They developed new methods to measure the strength of this unusually strong attachment, which is due to a poorly-characterized polysaccharide.

R F Service, Chemistry: Sugary recipe boosts grow-your-own plastics. Science 312:1861, 6/30/06. This news story discusses recent work on a new process for converting fructose into a compound that would be useful as a precursor for making plastics. Although they argue for the improvements they have made, it remains to be seen whether this will be practical (including cost-efficient). Comment: The use of bio-feedstocks to replace petroleum-based fuels is sometimes criticized as an "improper" diversion of food resources. That criticism is less applicable to the use of bio-feedstocks for making industrial chemicals (petrochemicals), because the amounts needed are, relatively, quite small here.

D R Burton & R A Dwek, Immunology: Sugar determines antibody activity. Science 313:627, 8/4/06. News. A discussion of the role of the sugars that are attached to antibody molecules. Little is understood at this point, but some evidence suggests relevance to rheumatoid arthritis.

S R Hamilton et al, Humanization of yeast to produce complex terminally sialylated glycoproteins. Science 313:1441, 9/8/06. The listing for Phelps et al (2003) introduces the point that organisms vary in how they glycosylate proteins -- and that this is immunologically important. Yeast is a convenient host for making proteins. Here they modify yeast so that therapeutic human proteins made in yeast are glycosylated to look like human proteins. Doing this required making 18 genetic changes in the yeast.

D W Ball, Concentration scales for sugar solutions. J Chem Educ 83:1489, 10/06. You know about molarity and percent by weight. How about degrees Brix or degrees Baumé? Those are two examples of special units that have been developed in industries using concentrated sugar solutions. A little applied chemistry here. Anyone making maple syrup?

S A Tishkoff et al, Convergent adaptation of human lactase persistence in Africa and Europe. Nature Genetics 39(1):31, 1/07. The textbook Essay on Metabolism of lactose intolerance was noted above. Infant humans can hydrolyze lactose -- the key sugar in milk. In general, adult humans lose this ability. However, some groups of humans retain the ability to use lactose; these are groups where milk continues to be important. The paper here analyzes the genetics of lactase persistence -- the retention of the enzyme to hydrolyze lactose -- in diverse populations. They show that four populations they study have different mutations leading to lactase persistence. They thus suggest that this trait has arisen multiple times due to selective pressure under specific “local” conditions.

J Finkelstein, Glycochemistry & glycobiology. Nature 446:999, 4/26/07. Introduction to a Nature Insight feature series. Articles include: Chemical glycosylation in the synthesis of glycoconjugate antitumour vaccines; Unusual sugar biosynthesis and natural product glycodiversification; Cycling of O-linked beta-N-acetylglucosamine on nucleocytoplasmic proteins; Glycan-based interactions involving vertebrate sialic-acid-recognizing proteins; Heparan sulphate proteoglycans fine-tune mammalian physiology; Exploiting the defensive sugars of HIV-1 for drug and vaccine design; Synthesis and medical applications of oligosaccharides.

Q P Liu et al, Bacterial glycosidases for the production of universal red blood cells. Nature Biotechnology 25:454, 4/07. See Rose et al (2005) for general background. Group O blood lacks the A and B antigens; O blood can be used as a donor for people of any AB type. Here, Liu et al report a way to treat blood cells to remove A and B antigens -- thus effectively converting them into O cells suitable for donation to a person of any AB type. (This is not a new idea, but previous attempts have been unsuccessful.)

A A Weiss & S S Iyer, Glycomics aims to interpret the third molecular language of cells. Microbe 2:489, 10/07. Microbe is free online; a link for this item is posted on my web page for organic/biochem Internet resources. A nice overview, written for a general audience, of the role of carbohydrates on cell surfaces. The sugars are found as part of glycolipids and glycoproteins (more about these in later chapters, on lipids and proteins). Many receptors for viruses and toxins involve sugar residues -- hence the connection to microbiology. The article discusses influenza virus and botulinum toxin among the examples where the sugar residues are key in determining the specificity of the agent.

J Novembre et al, Adaptive drool in the gene pool. Nature Genetics 39:1188, 10/07. News. Salivary amylase is the first enzyme that helps us digest starch -- in the mouth. Humans in societies with high starch consumption have more salivary amylase -- and more copies of the gene for it -- than humans in societies with low starch consumption. This suggests that natural selection has been occurring in humans for this trait, and also supports the emerging idea that copy number variation is important. They also note limited data supporting the same correlation with other primates. My web site includes a link to a BBC news story about this work.

B Lieberman, Human evolution: Details of being human. Nature 454:21, 7/3/08. A "news feature", highlighting the career of Ajit Varki, at UC San Diego. Varki has spent much of his career working on the differences in glycosylation between humans and other animals. His focus is on a class of sugar derivatives called sialic acids, based on a 9-carbon amino sugar derivative neuraminic acid. One issue is whether the amino group carries an acetyl group or a glycolyl group. The latter requires one additional step, converting the $-CH_3$ group of acetyl to a $-CH_2OH$ group. Humans lack the enzyme for that step. This small difference has consequences -- including for immune system recognition, and the specificity of different malarial parasites. It is not discussed in this article, but differences in sialic acid are also responsible for differences in cell specificity of bird vs human influenza viruses.

A A Fushan et al, Allelic polymorphism within the TAS1R3 promoter is associated with human taste sensitivity to sucrose. Current Biology 19:1288, 8/11/09. The protein TAS1R3 is a membrane protein that is involved in recognition of the sweet taste. Here, they show that natural variation in how much people make of this protein is correlated with their sensitivity of tasting sweetness. Thus we are beginning to understand, at the molecular level, not only how we detect sweetness but why people vary in their ability to do so.

K R Walters, Jr., et al, A nonprotein thermal hysteresis-producing xylomannan antifreeze in the freeze-tolerant Alaskan beetle Upis ceramboides. PNAS 106:20210, 12/1/09. As the title suggests, previously characterized biological anti-freezes were all proteins. Now, a polysaccharide is found that plays the role.

Computer resources (See web page for details and links.)

An interesting story of the development of an **artificial sweetener**, using an uncommon and unmetabolized sugar. The article also discusses the sweetness of **L-sugars**; these might be suitable as artificial sweeteners, but are not economically practical.

Electricigenic bacteria -- bacteria that can couple their electron transport directly to an external electrode, and thus can serve as the basis of a microbial fuel cell. One possible application is the use of waste organics, including sugars, to make electricity. One of the examples most studied is the genus Geobacter (a genus that does not itself use sugar). I list a web site focusing on Geobacter, and a link to the following related article: D Lovley, Microbial energizers: Fuel cells that keep on going. Microbe 1:323, 7/06.

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