Chapter 10. Ouellette, 2/e. Chemistry X402.

Ch 10. Aldehydes and ketones.

Skip: Sect 6, 9.

Ch 10 & 12 discuss compounds that contain the carbonyl group, >C=O. Ch 10 discusses compounds with "only" a carbonyl group; Ch 12 discusses more complex functional groups, consisting of both a carbonyl group plus another part. [Ch 11, in between, discusses a class of biochemicals that contains simple (Ch 10) carbonyl groups.]

> Reminder: Three separate one-page handouts that summarize some aspects of the "oxygen" chapters are attached to the Ch 8 handout.

⇒ **Practice quiz** posted at the web site: Ch 10. A quiz that will help you relate material from Ch 4-10. Challenging! Good practice for reviewing for the test.

Essays. Not assigned. As so often, they discuss interesting biological applications. The Essay on p 286, dealing with vision, is also an example of the biological role of a cis-trans isomerism at a C=C double bond; this is mentioned below in the note for Sect 9, a skipped section. Also see Computer resources.

Notes

> Students have asked… What does it mean if nothing is said about a particular section in this part of the chapter handout? The simple answer is that it doesn't mean anything, except that I didn't have anything to add. Skipped sections are noted explicitly, both at the top of the handout, and then near the end with some discussion. Other sections are covered. If I have nothing further to add, I may have no comment here.

Sect 1. Note the convention, p 268, of writing an aldehyde group as –CHO. –COH is incorrect; it would appear to be an alcohol.

Sect 3. Again, note the distinction between molecules that can serve only as H-bond donors, vs those that can serve as both H-bond donors and H-bond acceptors.

Sect 4. Skip the last sub-section, Reduction to a methylene group.

Sect 5. This is an overview introduction to several types of reactions discussed in later sections. The key idea is that one can add things across the C=O double bond. Further, in such reactions one needs to consider the polarity of both the adding reagent A-B and the C=O double bond; this is a major new issue, and we will go through it in detail in class. If you find the later subsections of Sect 5 difficult, leave them for now.

Sect 7-8. These sections are important, because of the relevance to sugars, as he notes (p 282). They are also fairly difficult.

> Many authors now avoid the terms ketal and hemiketal, using acetal and hemiacetal as broader terms that include both the aldehyde and ketone products. I think that is now IUPAC preference. I don't care much.

Important: the two reaction steps to make an acetal are quite different: the first step (to hemiacetal) is an addition reaction, whereas the second step (to acetal) is a substitution.

Sect 10. The top level idea is that the H "very near" to a carbonyl group (so-called α-hydrogens) are special. The keto-enol isomerization is one particular manifestation of this, and is relevant to biochem. Note that tautomers are a sub-class of isomers.

> You may want to go back and look at Section 4.5, as some background on the (non)-acidity of ordinary C-H bonds. In the Ch 4 handout, we mentioned that we would see a case of enhanced acidity of certain C-H bonds, near an O, in Ch 10.
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> Because of the keto-enol equilibrium, which usually favors the keto form, it is unusual to have an -OH directly at a C=C double bond. This was mentioned under "hydration of alkynes", p 121. (We didn't pay much attention to that; some of you might want to go back and read it in light of this new explanation.)

Sect 11. The aldol reaction is important in biochem. It is also useful in organic, as a way to make new C-C bonds. Formally, it is once again an addition reaction across a double bond. The A-B adding reagent is a C-H bond in this case. That is unusual; the special C-H bond is α to a carbonyl group. We won't go into the details, but be aware of it; we may mention it later.

> Some students, quite alertly, have questioned why the aldol reaction is referred to as a condensation. A proper condensation gives off a small molecule, such as H_2O (p 49). The aldol reaction, as described on p 289, does not give off H_2O. It really looks more like an addition reaction; in fact, some authors use the term aldol addition to refer to this reaction. As Ouellette notes on p 290, however, the aldol addition product readily dehydrates, and a common use of the aldol procedure includes this step; if you look at the overall reaction of aldol addition + dehydration, it does now look like a condensation.

Reaction summary. Most important are #1, 2, 5. #1 & 2 are not really new. The reaction shown in #5 has two steps; the first forms the hemiacetal, and you should know about that. You should also be aware of #7.

Suggested problems

For Models, #5 is most relevant. #1-4 are all closely related, and a little beyond us; try #1 if you want, but don't worry too much about it. Exercises: 21-26 are fairly advanced for us; try #25. 27-30 & 37-40 are on skipped sections. 47-52 are fairly advanced for us; maybe see if you can do one of them.

As usual, I encourage you to turn in a sampling of problems from various sections, especially those that give you trouble.

Overview of skipped sections

Sect 6. Reduction of carbonyl compounds to alcohols was in Sect 4, which is required. Sect 6 discusses other reactions that make alcohols, but with new C-C bonds being formed. Some use the Grignard reagent, introduced in Sect 9.4, which we skipped.

Sect 9. We discuss the addition of O compounds (alcohols) to carbonyls. We will skip the corresponding reaction of N compounds (amines). If you read this, note that the initial addition step is similar in both cases, but what happens after that is different. The (non-assigned) essay on p 286 in part makes use of this section; it also describes an important biological application of cis-trans alkene isomerism. (Imines are sometimes called Schiff bases, especially by biochemists.) Also see Computer resources.

Further reading

A Corma, Synthetic chemistry: Ship reverses out of bottle. Nature 425:356, 9/25/03. News. Zeolites are aluminosilicates, with well-defined pores. The pores are "designed" in by using various "structure-directing agents" (SDAs) during production. In some cases, this is very costly. This article discusses recent work using cyclic ketals as SDAs. The advantage? They are easily removed, by breaking them down with gentle acid treatment, once the zeolite is assembled.

I Kubo et al, Antibacterial activity of coriander volatile compounds against Salmonella choleraesuis. J Agric Food Chem 52:3329-3332, 6/04. Mexican salsa has antibacterial activity. One common ingredient in salsa is coriander (= cilantro). Here they report on antibacterial properties of volatile compounds from coriander. The active compounds are (2E)-alkenals, with (2E)-dodecenal the most active. They suggest that the activity of the compound is due to its action as a detergent, disrupting the cell membrane.

> Comment: Finding compounds in natural products with one or another biological activity is common. However, caution must be used in interpreting the results. For example, in this case, there is insufficient information -- so far -- on how important these coriander compounds are, compared to compounds from other ingredients, for the observed antibacterial activity of the salsa. Further, the fact that a compound has an activity when tested in the lab does not mean it would be therapeutically useful. For example, if one were possibly interested in the compounds tested here as antibiotics for human therapy, they would have to be tested in that way. (It is likely that they would not be so good: too volatile, and perhaps too toxic.) Thus, screens for natural products for activities may generate leads for the pharmaceutical industry, but most of those leads do not turn out to be useful.

J J Vollmer & J Rosenson, Chemistry of St John's Wort: Hypericin and hyperforin. J Chem Educ 81:1450, 10/04. Many functional groups here, some from Ch 10. Nice to browse.

J W Yang et al, A metal-free transfer hydrogenation: Organocatalytic conjugate reduction of α,β-unsaturated aldehydes. Angew Chem Int Ed 43:6660-2, 12/10/04. Their procedure is highly selective for reducing a C=C conjugated to a carbonyl group. The first step is actually imine formation, from addition of an amine across the carbonyl group (Sect 10.9), but the subsequent work-up regenerates the carbonyl group but reduces the conjugated C=C.

C A Taatjes et al, Enols are common intermediates in hydrocarbon oxidation. Science 308:1887, 6/24/05. An interesting article on the chemistry of combustion.

P Kukura et al, Structural observation of the primary isomerization in vision with femtosecond-stimulated Raman, Science 310:1006, 11/11/05. + News, p 980. Also see Computer resources, below.

M D Gordin, Facing the music: How original was Borodin's chemistry? J Chem Educ 83:561, 4/06. Alexander Borodin occupies a somewhat unusual niche: a professional chemist who also made a significant mark as a composer (perhaps best known for the opera Prince Igor). How important a chemist? Well, that is the subject of this article; since much of his work was with carbonyl compounds, the article is appropriate for this chapter. This article is perhaps most of interest to those who know of Borodin the composer, but it also provides some insight into the science of the era. For more about Borodin's dual career, see the Art & Music section of my web page Internet resources: Miscellaneous.

D Glindemann et al, The two odors of iron when touched or pickled: (skin) carbonyl compounds and organophosphines. Angew Chem Int Ed 45:7006-9, 10/27/06. It is a common observation that some metals smell, at least sometimes. Yet, it is also quite unreasonable that they smell, since they are non-volatile. This paper offers an explanation. Contact of metals such as iron and copper with human skin can lead to the production of volatile carbonyl compounds, which we can smell. They even suggest that the response has evolutionary significance, because it allows us to smell blood.

C-H Chen et al, Activation of aldehyde dehydrogenase-2 reduces ischemic damage to the heart. Science 321:1493, 9/12/08. The body metabolizes ingested alcohol in two oxidation steps, just as you would expect from the organic chemistry. The enzyme for the second step is aldehyde dehydrogenase (it removes 2 H, to form the acid). In this new work, in rodents, they show that activating this enzyme reduces heart damage following a "heart attack". They think this is due to reduced levels of an endogenous aldehyde. They suggest it may be possible to develop drugs that limit heart damage. Many people of east Asian descent have a defective form of this enzyme and are unusually sensitive to ethanol; they discuss the implications of their findings for such people.

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

"I Have Seen the Light! Vision and Light-Induced Molecular Changes."
How vision works, including the chemistry of the photoreceptor. That chemistry involves an aldehyde reaction, and also cis-trans isomerization. Includes good graphics, at molecular and biological levels. From R Casiday and R Frey of Washington Univ. Relates to Essay, p 286. Also see Kukura et al (2005), above.

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