MOLECULAR VOCABULARY

THE ART OF DRAWING ORGANIC COMPOUNDS

24+ SLIDES, 60-90 MINUTES
LEVEL: BASIC

SCRIPT FOR LECTURER
COMPLEMENTARY MATERIAL FOR STUDENTS

For instructions to better use this material go to page 33

IN THIS LECTURE:

The language of organic chemistry is graphical. Molecular structures contain the great majority of information required to understand their chemical properties and behavior. Badly drawn structures lead to bad chemistry, it is that simple. However, not one syllabus of mainstream universities we know of includes training in this area. This lecture is designed to satisfy this need for the beginner student.

WHY THIS TOPIC IS SO IMPORTANT

Just as musicians are able to actually listen to music when reading the notes on a pentagram, chemists extract reams of thoughts and conclusions from just looking at molecular structures on paper or computer screens.

On paper, organic chemistry relies chiefly on drawing structures and formulas. Written words do not. It is a graphical language not devoid of beauty. From simple molecules such as methane to extremely complex structures, chemical drawings are worth 10,000 words as the saying goes, may be more.

Although computer applications are great help in drawing molecular structures, frequently the organic chemist must resort to pen and paper to explain a concept to students or the boss of the company. Students and professionals need to have a good handle on this art or be exposed to ridicule.

An organic chemist unable to draw readable molecular structures might be said to be illiterate!

THE LANGUAGE OF ORGANIC CHEMICAL STRUCTURES

Slide -2: Copyright page
Slide -1: Menu

SLIDE 1: TITLE

SLIDE 2: LECTURE CONTENTS

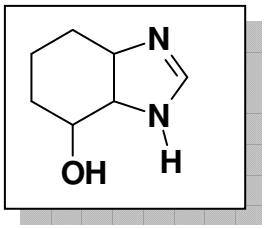
1. Molecules and rendering types: from the empirical formula to three dimensional structures
2. Aliphatics: Explicit hydrogens versus abbreviated line renderings
3. Branching in aliphatic compounds
4. Drawing aromatic compounds
5. Drawing alicyclic compounds and the problem of their non planarity, an introduction
6. A sophisticated example: cocaine

SLIDE 3: MAIN TYPES OF MOLECULAR RENDERINGS

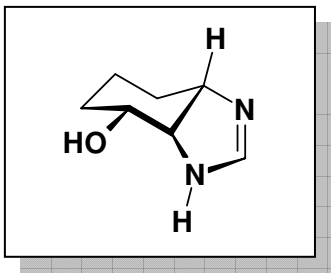
There are several styles to draw molecules, depending on what you want to say about them. Some of them express just their atomic composition. Others show the connectivity between atoms. Even others will give an indication of their distribution in three dimensional space while some specific renderings tell us about electronic densities and molecular orbitals.

The molecular formula showing only the atomic composition:
$C_7H_{12}N_2O$

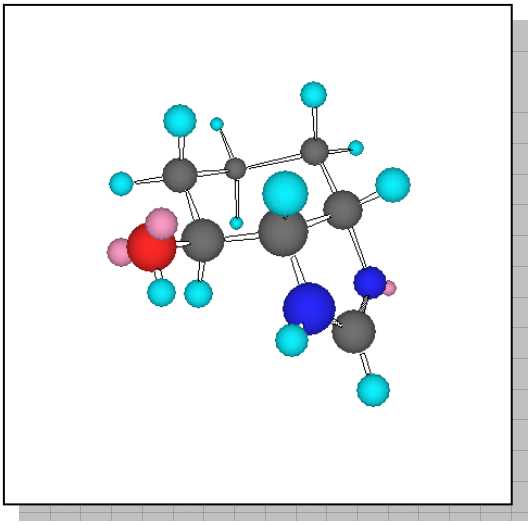
The line rendering showing abbreviated atomic connections:

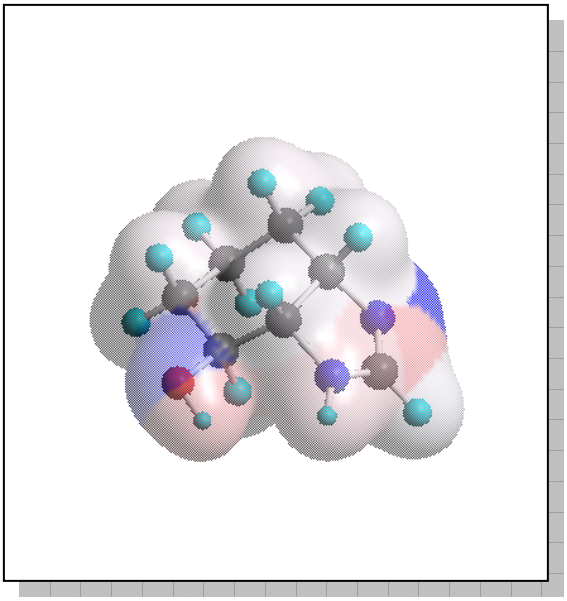


The line rendering in perspective, showing approximate spatial distribution of molecular components:



Molecular models of various types wheremore accurate spatial relationships of atoms, bonds and functionalities are seen. These models may be physical, made of plastic or wooden sticks and balls, or created with computer software





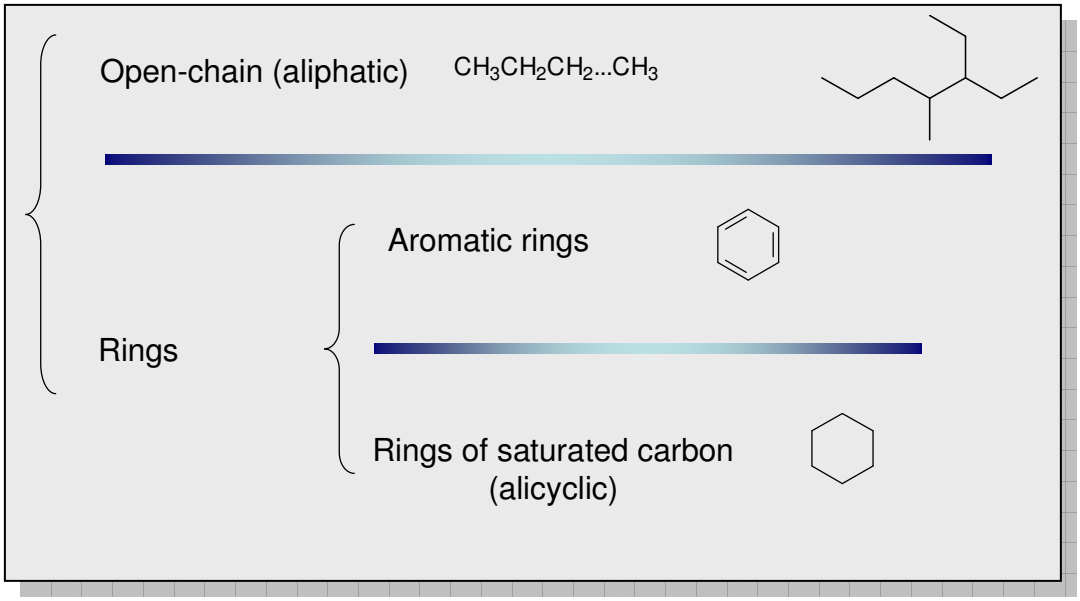
Various molecular properties can be calculated by computer means and rendered as surfaces of electron density and partial charge concentration. Here we see one such three-dimensional model in which partial charges may be seen as pink (negative) and blue (positive) areas depending on the position of heteroatoms in the molecule.

SLIDE 4: OPEN CHAIN AND CYCLIC CARBON ARRANGEMENTS

Step by step. First, you decide what you want to show in your drawing of a molecule. The most common parameters in the figure are *atoms and bonds* between them. Basically this means drawing a skeleton, as if this was the chassis of a vintage car. In most organic compounds this framework or backbone is made chiefly of carbon atoms, although it may also contain heteroatoms, N, O and S.

C-C-C---C or C-C-N-C---

There are two general types of frameworks: open chains with open ends, or aliphatic, and the cyclic structures were there is no beginning and no end. In turn, these cycles may be of two general types: aromatic like benzene, and alicyclic, made of saturated carbon. Each type has its drawing techniques.



Of course there are combinations of the two, cyclic structures with open ended side branches. These structures are drawn by combining the first two kinds.

SLIDE 5: BUILDING OUR FIRST MOLECULE

Just as a sample of this variety of possible renderings, let us see the many ways you can put on paper or computer screen a simple molecule: iso-butanol. Don't worry about nomenclature now. We will use this name, iso-butanol just to know who are we talking about.

The empirical formula is this: $C_4H_{10}O$

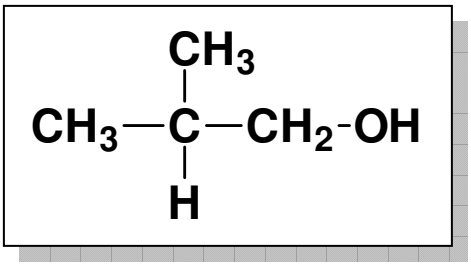
What does this formula say: only that there are four C, ten H and one O atom bonded together in a given manner in the molecule. This is the **atomic composition**. This is important information, but certainly not enough for the modern chemist. C in aliphatic compounds may

occur in four forms only: C, CH, CH_2 and CH_3. Our **group composition** in isobutanol is:

1 x CH, 1 x CH_2, 2 x CH_3 and 1 x OH

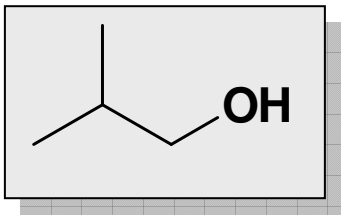
Now, let us develop a little this simple formula using the basic carbon units: C, CH, CH_2, or CH_3 depending on the number of hydrogens or other groups these carbons support. If you are to show only the constituent groups, *iso*-butanol will look like this:

But. adding bonds to these groups will convert you rendering into this:



This is certainly a more informative rendering. But it takes time to write down all these hydrogens and carbons. There is a way around this time consuming writing, the line-rendering.

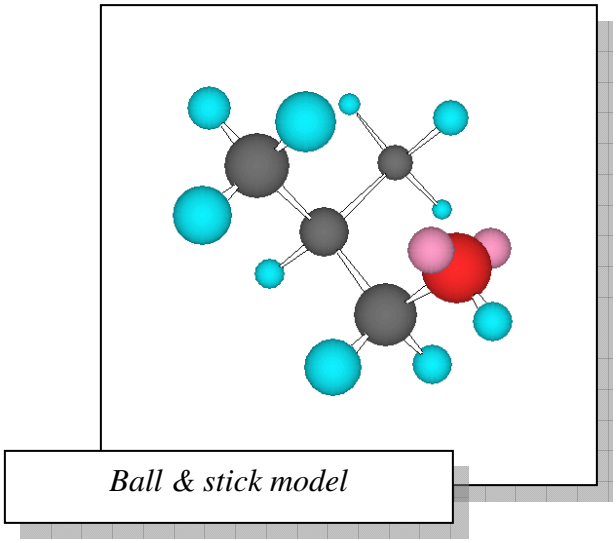
Lines will become bonds between carbons, whereas H on carbons will be ignored, we will assume they are there and fill up the invisible valences of C up to four. Remember this is just for C; heteroatoms N,O, S,P, Si etc and H on these other elements should all appear explicitly. *Iso*-butanol now looks like this:



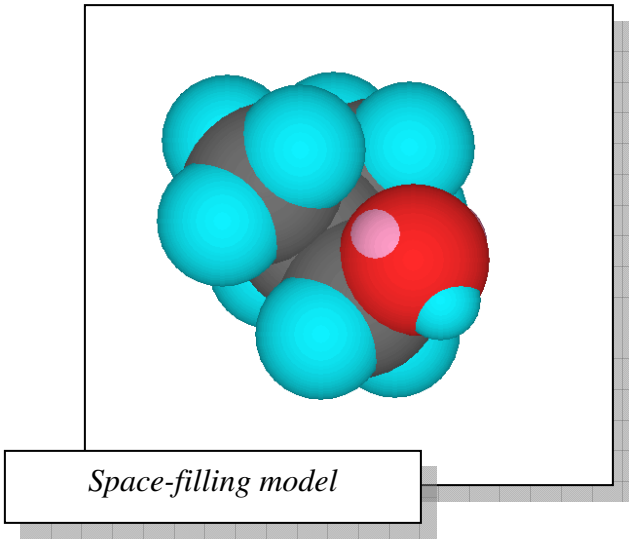
This is a a much cleaner view with all the information one needs to account for every atom and bond in the molecule.

SLIDE 6: THREE DIMENSIONAL RENDERINGS

Our next rendering shows the isobutanol molecule in space, using the ball and stick model and the space-filling model. Each color-coded sphere represents the Van der Waals volume of each atom. Hydrogen is in blue, carbon in grey and oxygen in red. The small pink-colored balls around oxygen represent the non bonding electrons.



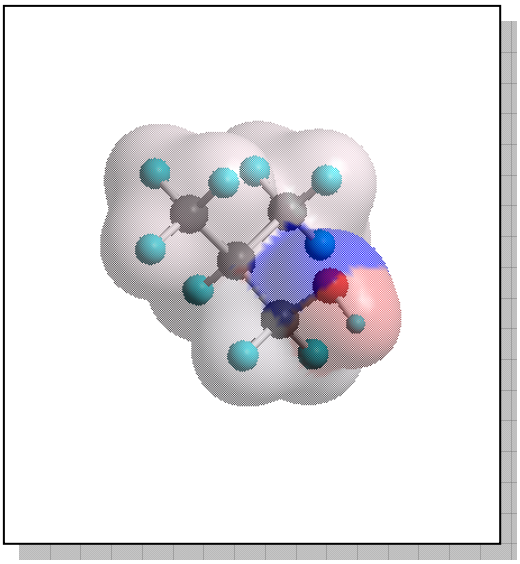
Ball & stick model



Space-filling model

It takes some time to identify all the molecular components of iso-butanol here, but it is a question of getting acquainted with it. Although it looks quite bulky and cumbersome, this sort of model is very useful to analyze intramolecular interference between substituents in a molecule, preferred conformations, docking places for other molecules, and how exposed or hidden are functional groups for chemical reaction.

SLIDE 7: 3-D SPECIAL CASES



Computational calculations give access to other informative models. In this example, the Hückel s showing partial electronic charges of iso-propanc been calculated and displayed here as a tran envelope.

Other calculations yield the shape of mo orbitals, something useful to have at hand at the t understanding the detailed mechanism of a reactio will use them throughout the course to pinpoint r centers and show how mechanisms operate.

There are other 3-D renderings for different sorts of compounds other than simple open chain substances like iso-butanol. As the course progresses you will get to know them in detail.

SLIDE 8: THE ABBREVIATED LINE RENDERING

Years ago it was customary to show all component atoms in organic compounds much in the same way it is done in inorganic materials. For example, in aliphatic hydrocarbons one has de empirical formula $C_xH_yZ_z$ This formula indicates the number of each element in the molecule, say $C_{24}H_{48}O_3$, a complex proposition *per se.*
When the structure of this formula is required, as it is generally done, the classical *condensed structure* is written as, for example:

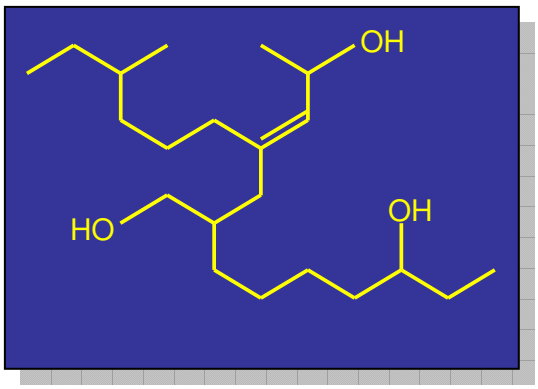
$CH_3CH_2CH(CH_3)CH(C_2H_5)CH$...

An exhausting exercise of futility.

Only small molecules like ethylene, methanol, acetaldehyde, acetic acid and the like are represented in their condensed renderings

$CH_2=CH_2$ **CH_3OH** **$CH_3C(O)H$** **CH_3COOH**

However, more complex molecules are much more conveniently drawn in the practical *linear abbreviated rendering*. This system allows one to draw literally any of the millions of organic compounds known in a clear and informative fashion.



Any student of organic chemistry needs to master this drawing capacity, interpret correctly molecular structures drawn by others and published in the chemical literature and use computer programs designed to perform this task cleanly.

SLIDE 9: THE MOLECULAR LINE RENDERING IN DETAIL.

THE OPEN CHAIN BACKBONE IN LINE ABBREVIATED FORM

We now turn to a step by step sequence to draw molecules on a piece of paper. Practical drawings of molecules depend on what you want to say about a compound. A good start is the *aliphatic* compounds, the open-chain carbon arrangements.

Suppose you started with a very simple chain: *n-pentane*: five carbons in a straight chain

We will draw this compound using the first three types of rendering: the molecular formula, the classical *condensed* rendering showing all atoms, and the *line abbreviated* drawing.

n-Pentane has 5 saturated carbons. You probably knew that they were saturated because there are n+2 hydrogen atoms, a total of 12 for the five carbons present. (***See lecture: How to estimate insaturation and oxidation level in organic compounds***) The empirical formula C_5H_{12} tells you that but not much else.

We need to learn about connections between atoms. Classical renderings convey this information by specifying each atom as groups: methyls (CH_3), methylenes (CH_2) and methynes (CH) with all hydrogen atoms included. This is the *condensed structure*

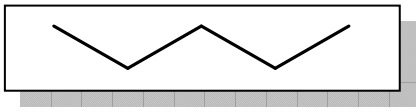
n-pentane**:** **$CH_3CH_2CH_2CH_2CH_3$**

and adding C-C bonds: **CH_3-CH_2-CH_2-CH_2-CH_3**

Really unnecessary and a bit cumbersome…

This is time consuming to write down and gives a cramped effect.

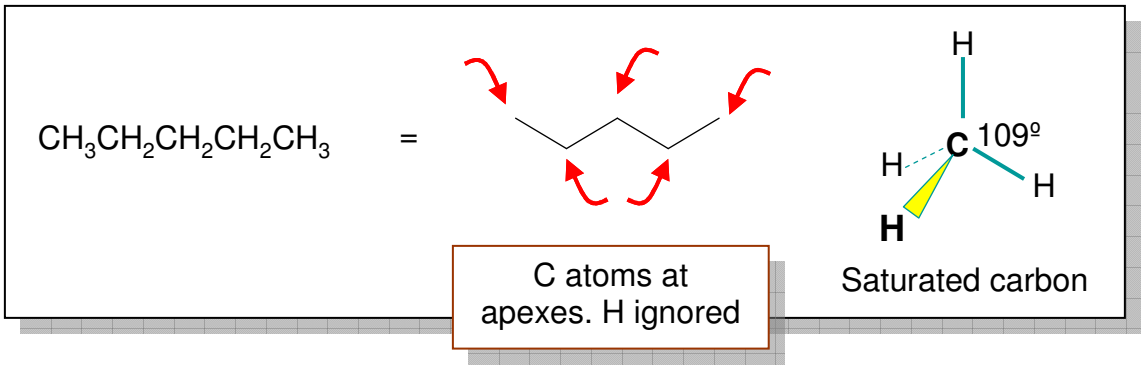
We will now proceed to build *n*-pentane in *line abbreviated form*. This rendering applied to *n*-pentane looks like this:



Simple, clean, fast…

It becomes evident that n-Pentane is a straight carbon chain. The first thing to realize is that carbon chains are not drawn as a straight line but in *angled segments*. There are various reasons for this.

At every joint of two segments representing bonds there is a carbon atom (red arrows below). If there was a straight line the joints would be invisible and no information about atoms would be there. Also, the angle between two segments is designed to show the true angled appearance of carbon chains, because you probably remember that the H-C-H bond angle of a saturated carbon is about 109º.



<u>SLIDE 10:</u> DRAWING ANALIPHATIC LONG CHAIN CARBINOL. QUIZ

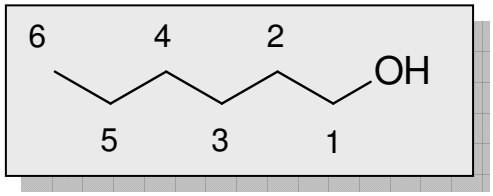
Lecturer: Brief quiz with 30 sec time limit.

Now you may want to try *n*-hexane-1-ol, a chain of six carbons with a OH unit at the end. Draw it in abbreviated form: You have 30 seconds…(*Click mouse to show clock and click again to start counting. Wait for students answer).*

(*Answer*) If you started with the classical writing you ended up with this:

$CH_3CH_2CH_2$ CH_2CH_2 CH_2OH
6 5 4 3 2 1

You may wish to identify each carbon atom with a sequential number starting from the one bonded to oxygen. In its abbreviated for it would look like this:



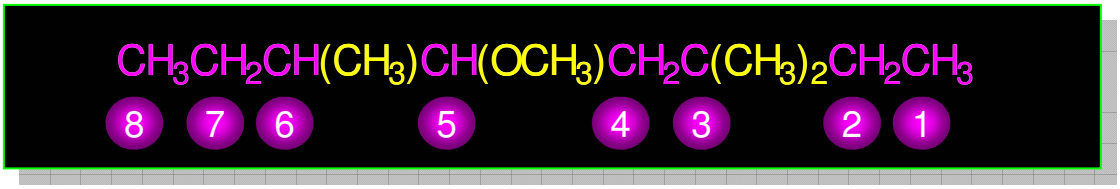
It is quite easy to correlate both number sequences.

This elementary example may seem very obvious to you, but this is just a first example. Very complex structures may be drawn using a series of steps

SLIDE 11 THE SYSTEMATICS BEHIND MORE COMPLEX BRANCHED ALIPHATICS

This first rather elementary example may seem very obvious to you, but this is just a first example. Very complex structures may be drawn using a series of steps

To show how each step is applied to a real molecule, let's use the following compound as an example. It is much more complex that *n*-pentane of *n*-hexanol.



One fundamental feature stands out:
The carbon building blocks (CH_3, CH_2, CH, C) (purple) appear interrupted by other blocks shown in parenthesis (yellow). These

yellow sections are substituents branching off from the carbon backbone at the C atom sitting by its *left*. OCH_3 for example is substituted on C5. The two CH_3 on the right sit on C3.

A bit of useful systematics needs be applied here for a correct rendering of this compound in abbreviated line form:

1) Identify the *longest* carbon chain which is composed by CH_3, CH_2, CH, and C without parenthesis. These are shown in purple above.
2) Assign numbers (purple balls) in sequence to these carbons. You may chose whichever direction, left to right or the opposite. For conventional reasons this is done from right to left because the most important heteroatom-containing substituent is frequently placed at the right end, defining the compound class. In this example we took C1 as the chain end which comes closer to the largest number of substituents (2 x CH_3) on the right.
3) As you may surmise, substituents on these carbons are not part of the main chain and appear within parenthesis.
4) Now you may draw angled lines defining the eight purple carbons, and place substituents on the corresponding carbon to the right of each as suggested above.

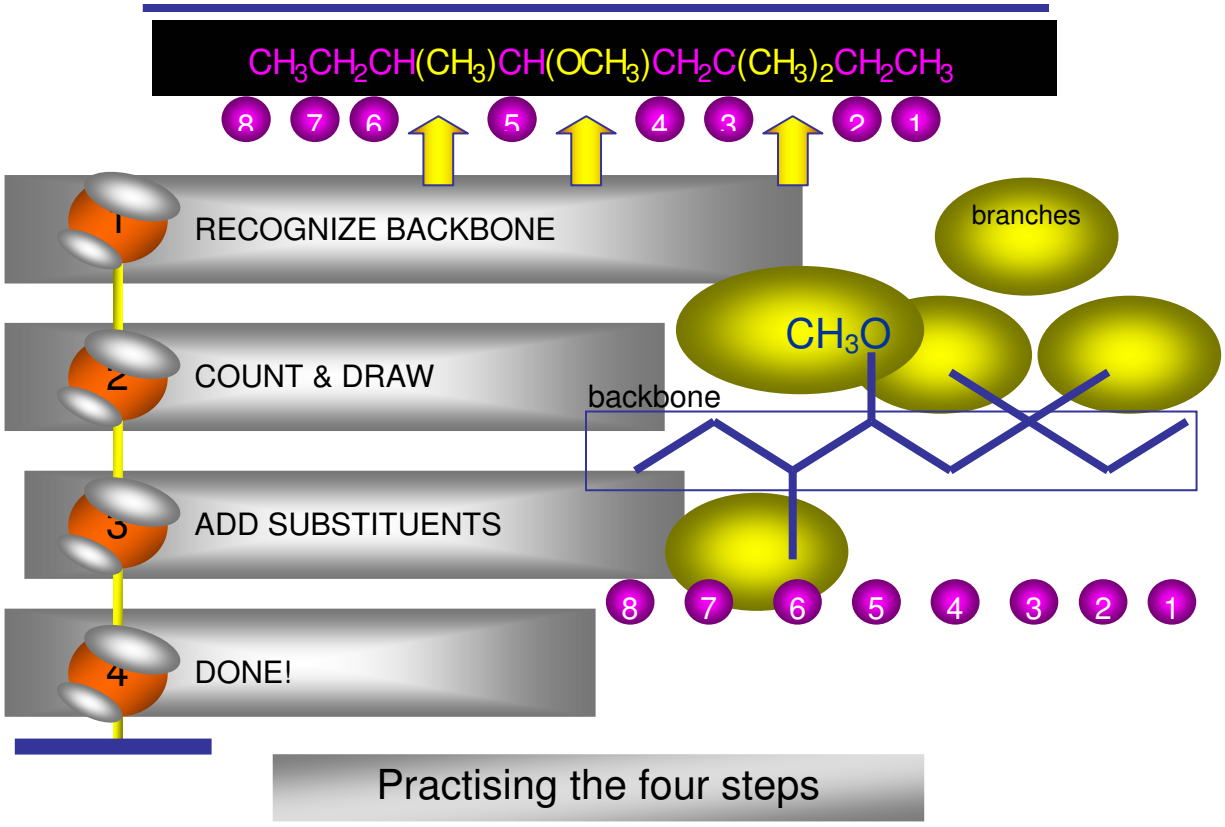
SLIDE 12: A MORE COMPLEX BRANCHED ALIPHATIC ALCOHOL

Lecturer: you may use this as a second quiz

Suppose you are presented with this formula, a $C_{12}H_{24}O$ compound, the same in the previous slide:

$CH_3CH_2CH(CH_3)CH(OCH_3)CH_2CH(CH_3)_2CH_2CH_3$

Take your time, 2-3 minutes to come with the right answer. It will give you an opportunity to handle the four steps shown

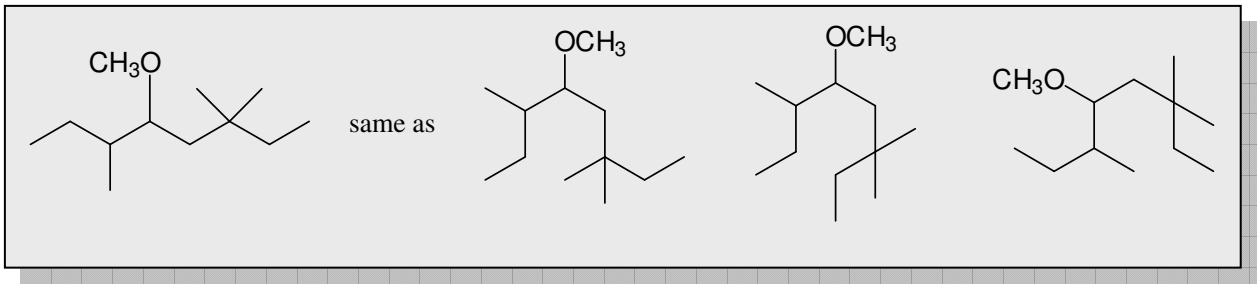


SLIDE 13: OTHER SHAPES

Organic chemists work frequently with rings, six-membered (and others as well), so it is also comfortable to see line structures in the shape of a pseudo six-member ring. It is just a matter of drawing the carbon skeleton using an imaginary hexagon template (*animation*)

The aliphatic ether we just drew in the previous exercise would look like the drawings below after twisting the bonds a little. Mind that

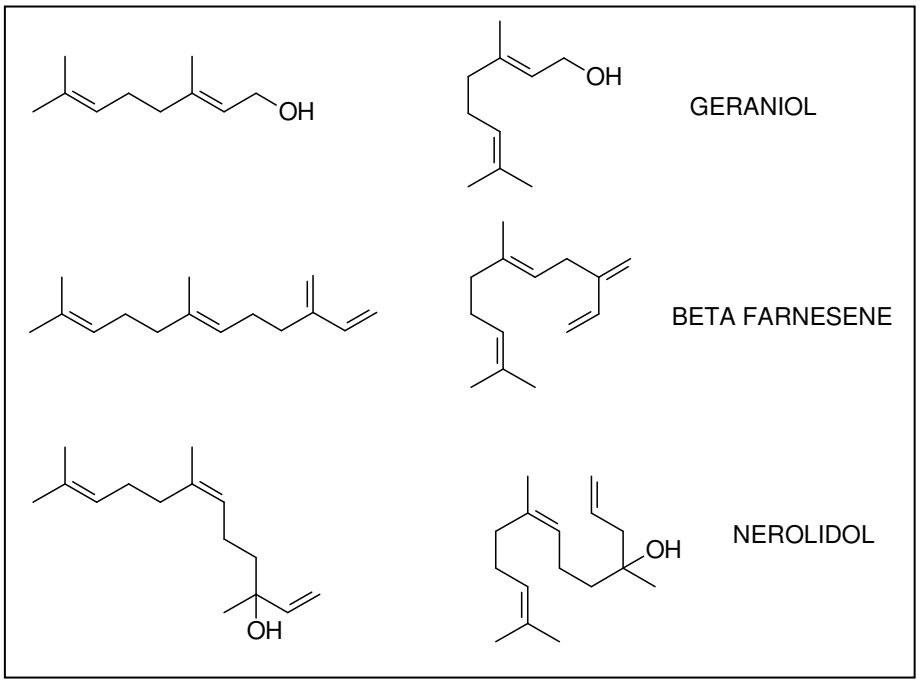
all structures represent exactly the same compound, but the ones to the right have been drawn using a six-membered ring template.



The abbreviated rendering not only is a lot easier to draw but also tells you right away the length of the carbon chain, its general distribution in space, the location of substituents and functional groups. It can still tell you other features like the stereochemistry of specific substituents but this topic will be left for a later chapter when the student becomes familiar with 3D structures abd stereochemistry.

SLIDE 14: THE PSEUDO SIX-MEMBERED RING, A USEFUL TOOL IN DRAWING NATURAL PRODUCTS

It is very common to use a sort of hexagon template to draw many alicyclic natural products, as is the case of the following monoterpenes found in flowers scents, leaf essential oils and bark substances. Most molecular attributes are shown clearly and fast by the line abbreviated renderings. A few examples: (*animation shows hexagon templates while drawing the molecular structures to the right*



SLIDE 15: BUILDING MORE COMPLEX ALIPHATICS

Lecturer: Quiz or class exercise:

We sill consider fitting in other common functional groups to the saturated hydrocarbon chain in the following two examples.

Try to transform the following two compounds into line renderings using what you know:

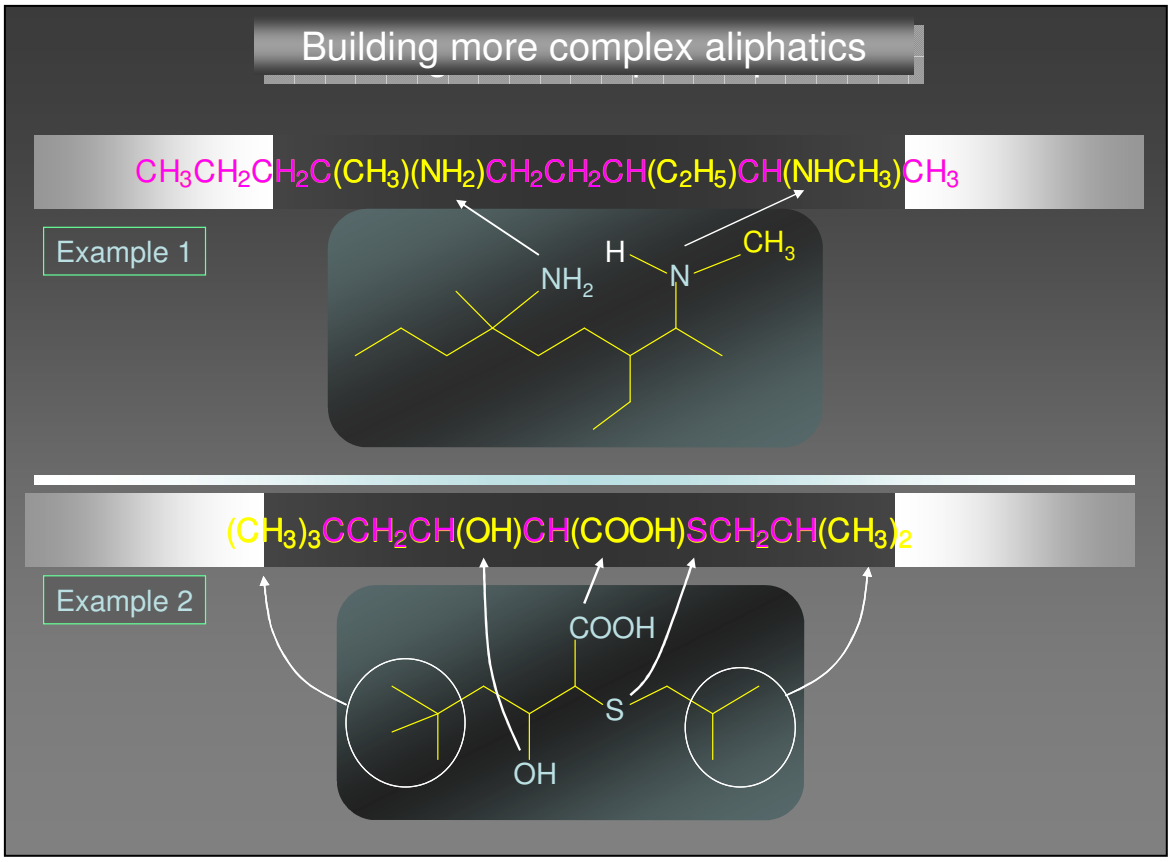
Example 1:

$CH_3CH_2CH_2C(CH_3)(NH_2)CH_2CH_2CH(C_2H_5)CH(NHCH_3)CH_3$

Example 2:

$(CH_3)_3CCH_2CH(OH)CH(COOH)SCH_2CH(CH_3)_2$

After working out the four said steps, which are shown stepwise in this slide animation, the end result should look like this:



SLIDE 16: DRAWING MULTIPLE BONDS IN ALIPHATICS

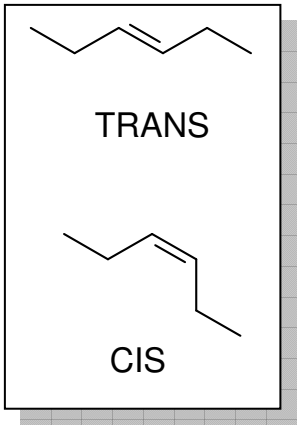
There are four kinds of multiple bonds in organic aliphatics:

C=C	C≡C	C=O	C≡N

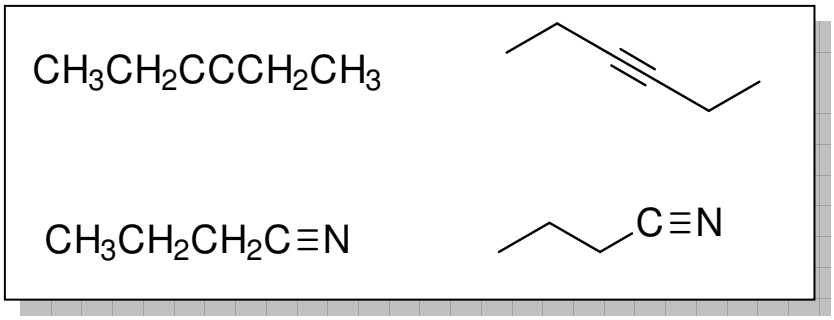
These blocks may be found anywhere along the chain. The first two are the only ones that may possibly form part of the straight backbone, the later two may only be substituents or constitute the end of the chain.

C=C, the archetype of *alkenes*, comes in two types, cis and trans or more correctly Z and E:

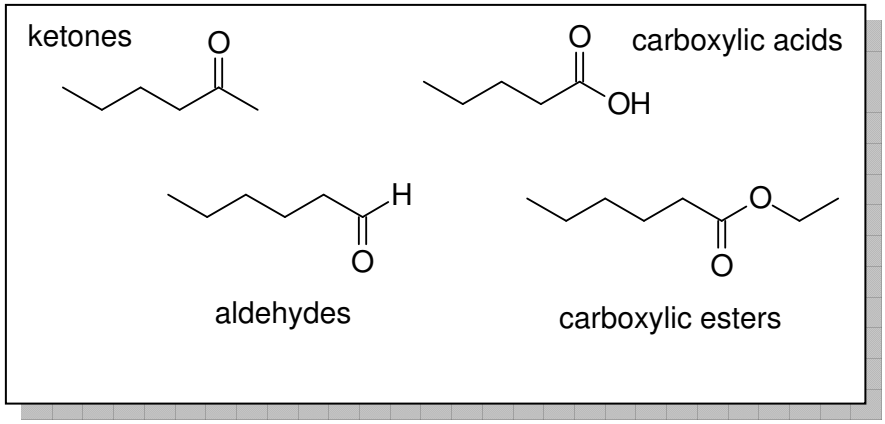
(This nomenclature will be reviewed in the chapter about alkenes)



C≡C which represent alkynes or acetylenes, are always straight as well as C≡N
These two may be collapsed together for the drawing purposes only



C=O Is a 'bent' group, so it is treated as the usual CH_2-CH_2... chain as follows:



Mind that aldehydes, carboxylic acids and carboxylic esters are *always* at the end of the carbon chain so they may be treated as functional groups attached to a given backbone carbon atom.

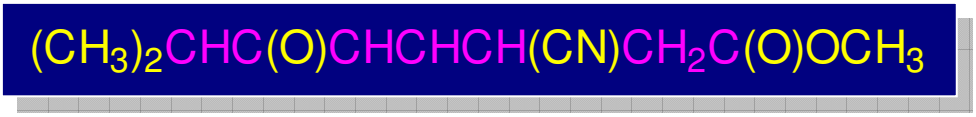
SLIDE 17: BUILDING FUNCTIONALIZED ALIPHATIC ALKENES

The multiple bond functions are easily inserted in the line abbreviated form according to the rules just reviewed
Let´s develop the following compound shown below in the expanded formula into a line abbreviated form:

$$(CH_3)_2CHC(O)CHCHCH(CN)CH_2C(O)OCH_3$$

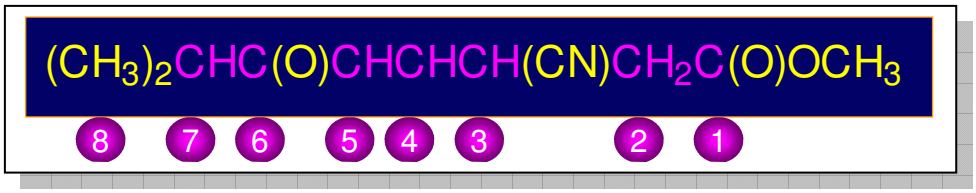
and follow the four step sequence.

1) Define the carbon backbone. Momentarily this is an arbitrary decision.- In this example the two methyls on the left end raise a small complication, because one of them may be treated as part of the main chain leaving the second methyl as a substituent, as one should do while determining the correct nomenclature for this compound (a later chapter). Conversely, the two methyls may be treated arbitrarily as substituents only for the purposes of building the line abbreviated drawing.
   A similar argument surrounds the $C(O)OCH_3$ on the right. It may be treated as a substituent [$COOCH_3$], or, more correctly the C(O) carbon may be taken as part of the backbone. Let us take the latter possibility.
   The backbone carbons are shaded in purple.



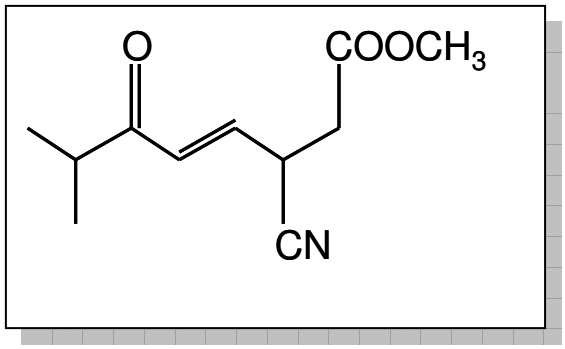
2) The purple carbons are numbered from right to left arbitrarily. Later in the chapter on nomenclature of aliphatic hydrocarbons we will see that the direction of numbering atoms is very important. Not for now, though.

To get closer to the real thing we have included one of the methyls at the right end as Carbon Nº 9 (C9) [part of the main chain or backbone].



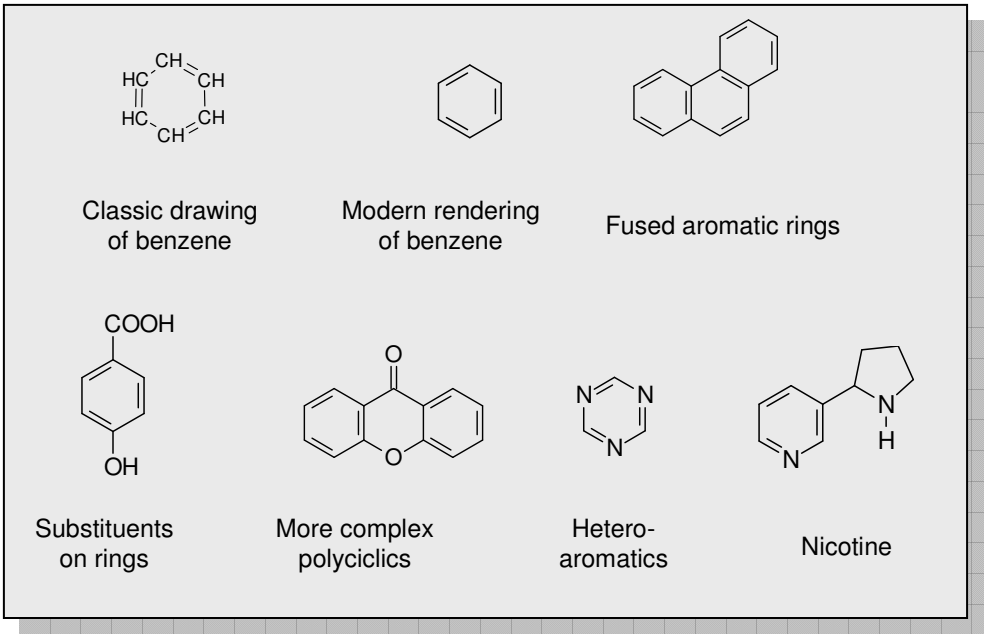
3) Functional groups stand out in parenthesis, and we mark them in yellow.
   However, notice that carbons C3-C4-C5 are not CH_2 but CH. If on C3 we have the fourth valence occupied by CN, in C4 and C5 one valence appears to be missing. Why? Well, there is an unsaturation here, a C=C which completes the fourth valence in both. Let us assume that this alkene is *trans*. Note that this information is not expressed in the simple expanded formula but will always be shown by the line abbreviated rendering
   .
4) We are now ready to draw the lines of the numbered carbons, and later add the functional groups (*animation*).

This compound is clearly created from a 8 carbon straight chain supporting four functional groups. Three of them are embedded in the chain (C=O, C=C and $COOCH_3$), while the fourth branches off from C2. We have also a methyl group treated as a substituent on C7.



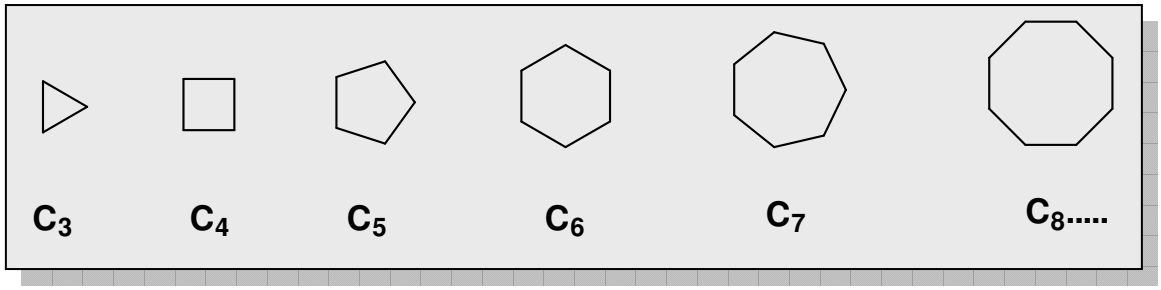
SLIDE 18: DRAWING AROMATICS

Aromatics are quite simple to draw. In the first part of the course you will find individual benzene rings and also fused aromatic rings into polycyclic compounds. So, the cumbersome explicit structure in which all atoms are shown with letters is not used any more; simply ignore all these letters except when a heteroatom replaces one or more hydrogens, or is a component of the ring. These rings are named heteroaromatics, which are of extreme importance to biochemistry and toxicology. Nicotine, one of the poisons in cigarette smoke is just one example.

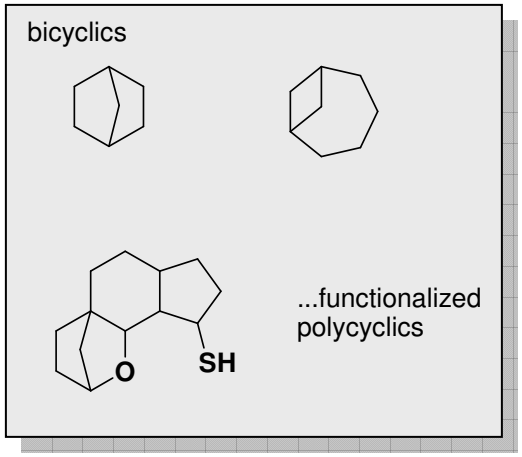


SLIDE 19: DRAWING ALICYCLICS

The alicyclic or ringed structures are easily drawn as regular polygons. These polygons of increasing size begin from the three-membered cyclopropanes up to cyclooctanes with eight carbons and beyond.



There are also internal bridges within rings that connect distant carbons with methylenes or other components as we see here. In the end, complex structures including hetero-atoms and several substituents may be drawn quickly and easily. It only takes the habit of doing this frequently and some basic ability for geometry.

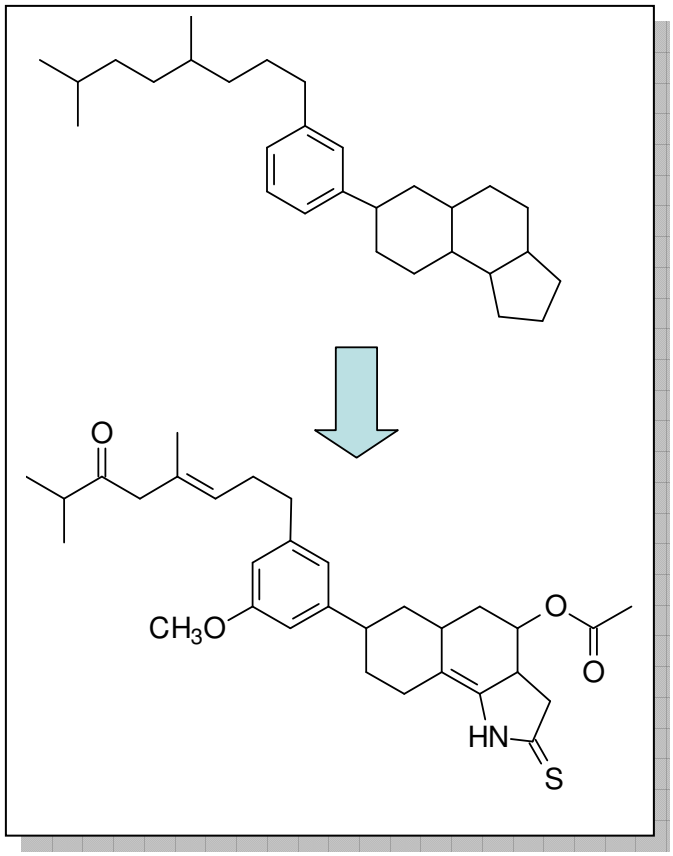


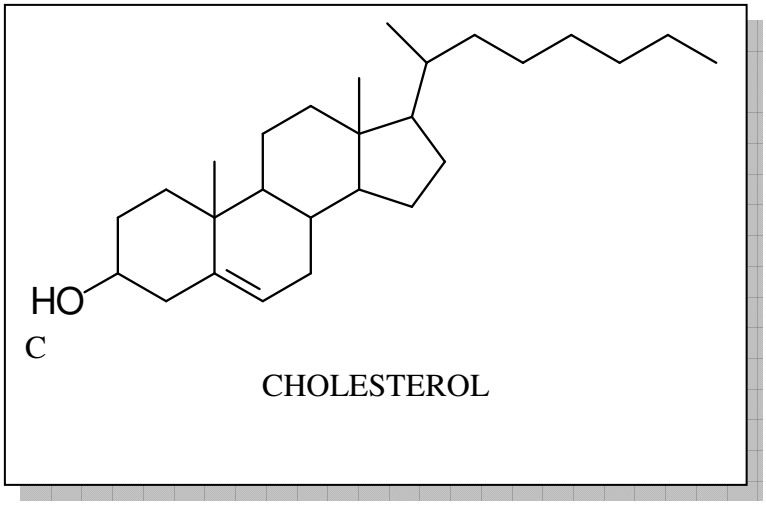
SLIDE 20:

Combinations of open chains and cyclic structures are of course possible. By now you probably grasped the idea that apparent bond angles as you draw them on paper are the more or less the same for both types of molecules, open-chain and cyclic for most rings (C5 and C6).

Your drawing begins with the carbon backbone, then you add functional groups at the right places and your rendering is complete.

However there is no indication yet of the position of some substituents relative to the molecular plane. This will be treated after considering that carbon molecules may be flat, two-dimensional structures and three dimensional combinations as well.



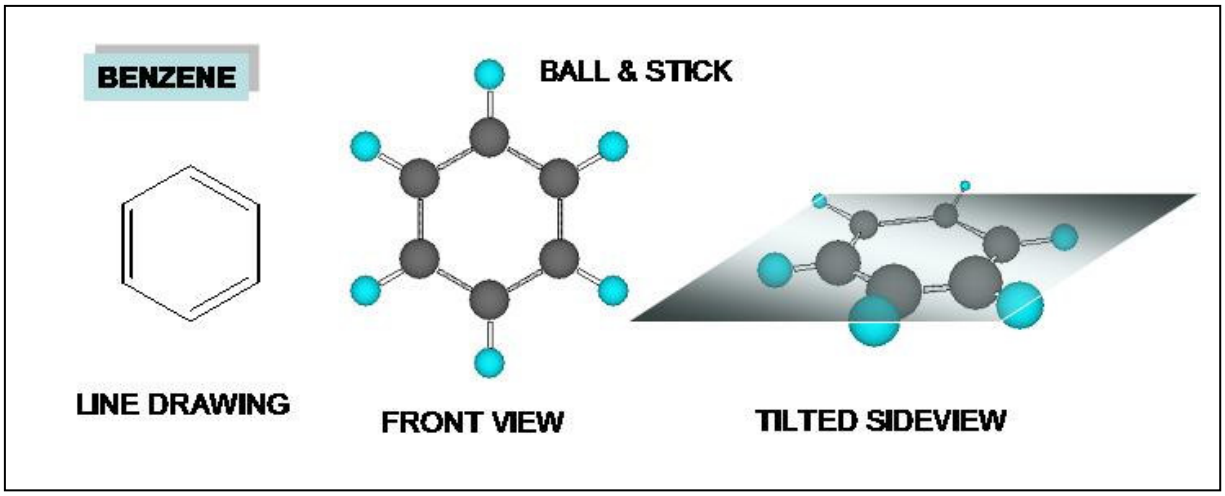


CHOLESTEROL

In this way you are able to represent quickly and cleanly relatively complex organic compounds such as cholesterol, an essential component of animal life for building steroidal hormones, bile acids for intestinal digestion, membrane construction and other tasks.

SLIDE 21: PLANAR MOLECULES: MOST AROMATICS

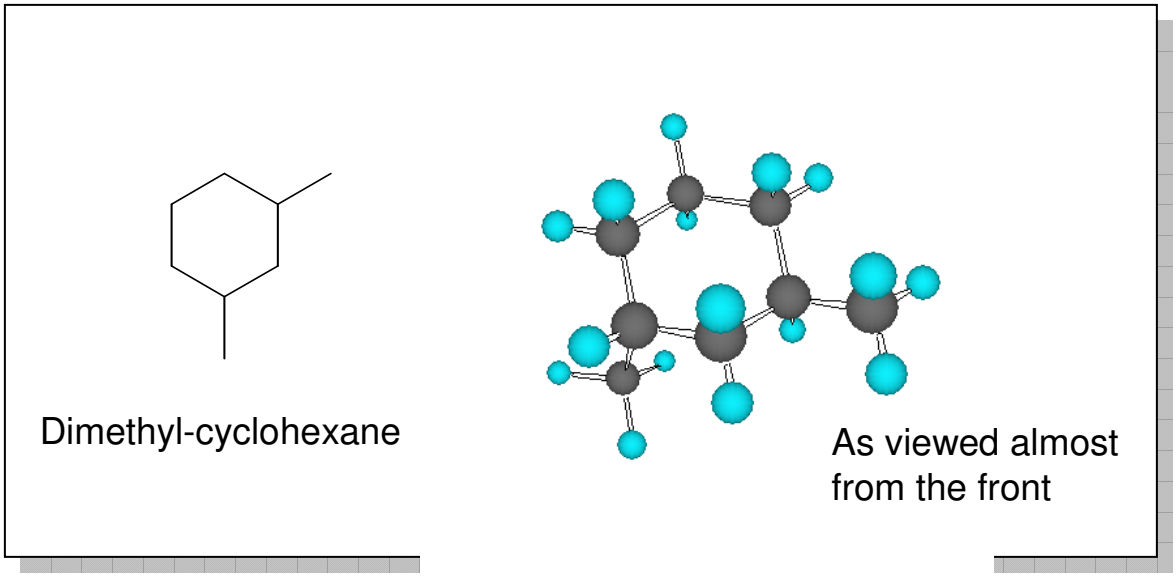
There is one more issue to consider: **the 3-dimensional shape of rings**. Aromatic compounds like benzene are planar. All atoms, C and H, share de same plane in space. To show this feature let's take benzene, draw it with all its hydrogens, now build a ball and stick model to see it in perspective, and tilt the model sidewise to see the profile of the molecule. All carbons and hydrogens fall in one single plane, the molecular plane. All other aromatic compounds accruing two or more rings are also planar.



SLIDE 22: ALICYCLIC NON-AROMATIC HYDROCARBONS: NON PLANAR STRUCTURES

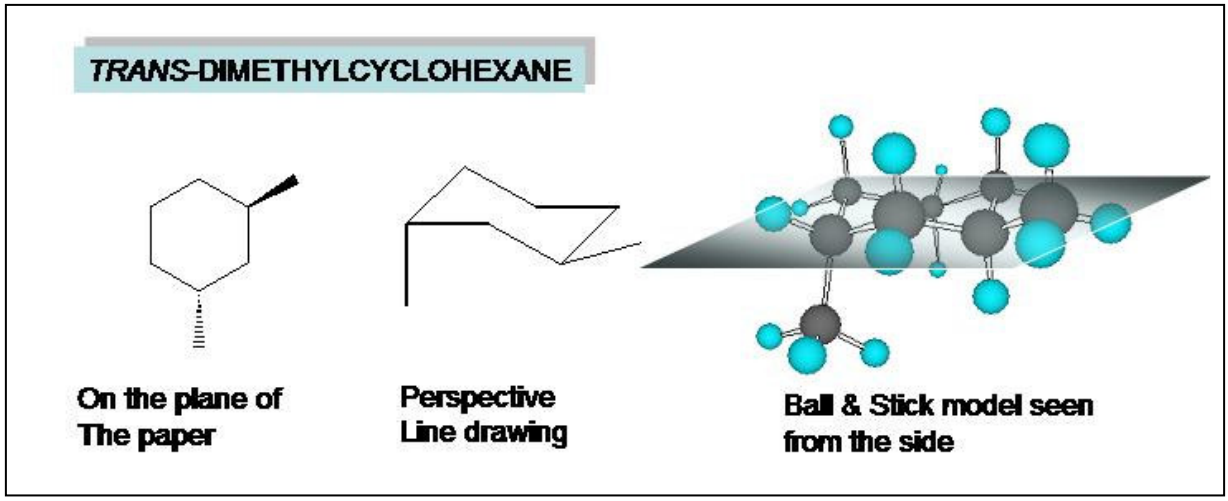
By contrast, ***cyclic structures of saturated carbons*** *are not planar.*

This is a bit complicated at the beginners' level. While this is a central topic in stereochemistry (*conformational analysis*), and we will postpone its discussion until then, it is convenient for you to at least be acquainted with this phenomenon at this point. If we perform the same tilting in cyclohexane the cyclic structure is not planar anymore. A first three dimensional view as seen from the front will begin to uncover this property:



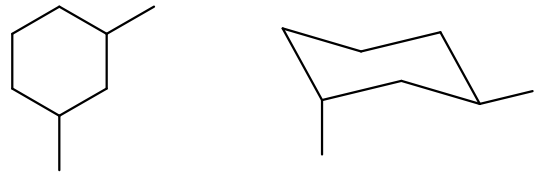
Let us start by drawing the conventional line abbreviated rendering of 1,3 dimethyl cyclohexane, as above. Apparently this is a flat structure as there is no indication of it being otherwise.

But if we proceed to tilt the structure (*animation*) as we did for benzene, you can see that some atoms will stick up or down from the molecular plane:



The cycle reminds you of a deck chair, which is indeed the name of this particular conformation of cyclohexane. The 3-dimensional *line drawing* would look like this:

:

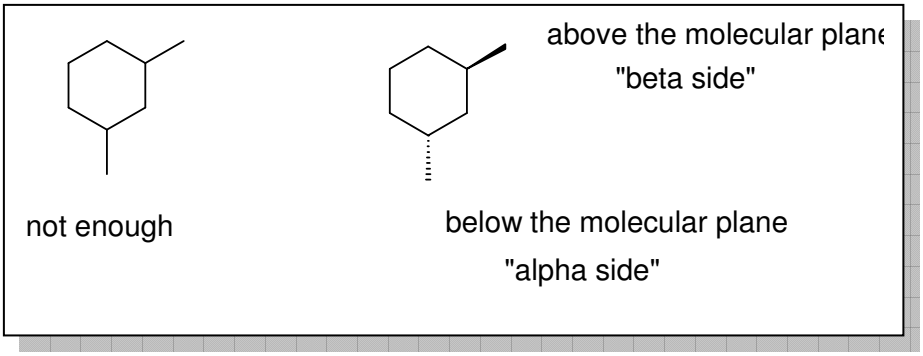


"flat" view

3-D view
a "chair"

This "chair form" is one of three different ways one can depict the cyclohexane ring in 3D. However, we will not care about this now and for the moment it will suffice to become acquainted with this flattened structure only.

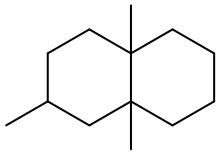
As a result, the positions of substituents relative to the molecular plane in cyclic structures of saturated carbons need to be defined in the flat view. The way to do this is simple enough: a solid line will show that the substituent, a methyl in this case, lays above the molecular plane, the **beta** side, whereas a dotted line indicates that it faces the underside, or **alpha** side, of the molecular plane.



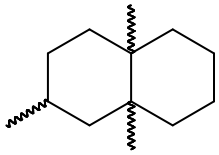
<u>SLIDE 23</u>: FUSED RINGS IN 3D

There is a whole lot to talk about this, but your proficiency will be bettered as you move forward to more advanced org chem chapters.

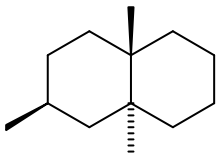
For the time being it is important to realize that when you draw a cyclic structure based on saturated carbons, you may wish to show whether substituents on all rings are below or above the molecular plane. You may leave them alone with the usual thin line, but you will limit your drawing without stereochemical definition.
There are three ways our:



you do not know
if positions are defined



you do know that
positions are not defined



you know every position
relative to the molecular
plane

As said, this kind of drawing requires further work which will be postponed until we reach the chapter on stereochemistry. It is unlikely that your lecturer will throw problems on this particular subject at this point. But if I were your lecturer, I would certainly ask you this…

Because I think it will be to your advantage if you become proficient in drawing molecules from now on. With a little bit of practice you will be writing complex structures in no time. Exercises at the end of this chapter will help you in becoming a proficient molecular drawer and expert chemical designer. You will be impressed by the impact this ability has on your audience and class mates.

SLIDE 24: COMPUTER SOFTWARE

Today there are excellent computer programs for drawing molecules fast and easy which correct mistakes, detect absurd bonds, display your compound in various rendering types, perform quantum mechanical calculations and show optimized structures in 3-D with bright colors. Interatomic distances, bond lengths and dihedral angles are calculated with accuracy, NMR and IR spectra are estimated along with several other properties. If this is great help for the organic chemist, you must also develop a good hand in drawing molecules on paper or a blackboard. This is the equivalent of hand-writing vs keyboard to write notes in class, a letter to a friend or a short business message.

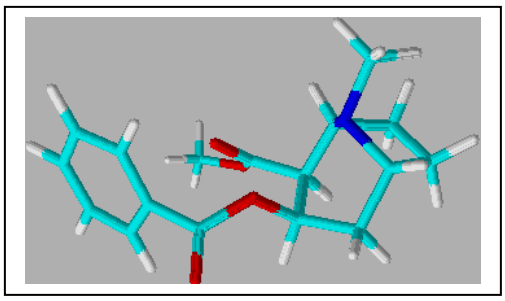
The time will come when you have to resort to your molecular drawing abilities while giving a lecture, a quick explanation to a student, or solving problems in a chemical plant; because *molecular drawing is the language of organic chemistry*.

ANEX A:

CONTEMPORARY MOLECULAR RENDERINGS: THE MOLECULE OF COCAINE

SLIDE A-1: TITLE

SLIDE A-2: WHAT IS COCAINE



Cocaine is a compound of the alkaloid family isolated from the leaves of the South American plant *Erythroxilon coca*. *Cocaine*, as you know, is an illegal drug in almost all countries of the world although the coca leaves are extensively used in the Andes of South America for medicinal purposes. About one third of the Bolivian coca leaf harvest is claimed to be exported to pharmaceutical and beverage industries in the US and Europe.

An extract of these leaves, once cocaine is taken out, is used in the manufacture of coca cola as a flavoring agent, and chewing a ball of coca is common among many Bolivian and Peruvian indians. Its juices give them strength and energy while reducing appetite.

Interestingly, these indians use organic chemistry to their advantage to avoid being stoned by cocaine. While chewing the leaves they roll a boll of lime in their cheeks. Lime is alkaline and alkaloids are

generally insoluble in alkaline medium, thus cocaine will not be extracted by saliva and remain within the leaf matrix. The key to this property is the tertiary amine.

Cocaine was first isolated by Frederick Gaedcke in 1855, in Germany. He named the white crystals *Erythroxiline*, because of the botanical name of the source plant: *Erythroxilon coca*. At the time all that was know of *Erythroxiline* was its empirical formula: $C_{17}H_{21}NO_4$, because tools for molecular structure determination were primitive. Just think: No one knew the molecular structure of benzene in 1855 (It was first proposed by Kekulé in 1866). Later on, as the molecular structure was elucidated by painful derivatization and comparison with compounds known at the time, and new reactions became known, the synthesis of *Erythroxiline* was finally achieved in 1898 by another German chemist, Richard Willstätter in 5 steps.

SLIDE A-3:
As we have seen, there are several ways to represent cocaine either on paper or on your computer screen. While the empirical formula tells nothing about the structure, the line abbreviated rendering shows the connections between atoms. This is what was known to Willstätter when he faced the difficult task of synthesizing cocaine at the turn of the 19th century.

Ever since Derek Barton, an outstanding British chemist, devised the so called *conformational analysis* of carbon rings in the late 1950's, it is possible to understand the 3-dimensional intimacies of molecular components as we see here. The methylamine unit stands above a casket-shaped seven membered ring. On this ring the carboxymethyl and benzoate groups stick out to the right of the molecule more or less on the molecular plane.

SLIDE A-4:

This arrangement is a bit complex. The line rendering of the 3 D structure, in all its usefulness, does not serve the purpose of showing the exact distribution of molecular components in space. To appreciate this feature you have to resort to molecular models. In addition to the ball and stick physical models that you can manipulate with your own hands, there is computer software available that allows you to create one such model on screen. Here is the result of the application of one such computer program, shown here nrom the same point of view of the line rendering we had before. It's still a bit confusing for beginners like you, but with practice you will come to get a good hold of this rendering.

Let us now clear up a bit the apparent confusion created by the ball and stick model on your screen. To do this we will observe cocaine's structure in sections, a technique we will be using many times in the course of these lessons. First the carbon ring backbone on the left. As you can see the gray balls representing carbon atoms in this ring stand up clearly with almost the same shape of the ring and spatial distribution conveyed by the line drawing. Protons on these carbons, shown here as blue spheres, obscure somewhat the ring. However, as you will understand later, it is important to determine the relative position of protons in a compound to better understand various properties, either chemical or spectroscopic.

On the other hand, the nitrogen atom which characterizes the alkaloid family of compounds, extends visibly from the top of this ring.

Now is the turn of substituents on the right hand side. The methyl ester group is easily recognized by the red balls of oxygens and the methyl group at the end.

Finally, the benzoate sticks out to the right in parallel to the ester. The benzene ring of the benzoate unit is seen almost from the edge. This particular conformation was built by the computer as the

minimum energy structure, meaning that repulsive interactions between neighboring atoms are the least possible. The program twisted the aromatic ring until these interactions were minimal.

Models like these are extremely useful in understanding various chemical and spectroscopic properties of compounds, and synthesis design. In addition, space-filling models of cocaine, not shown here for simplicity, and other bioactive compounds are of pivotal importance in determining the molecular mechanism by which they interact with active sites in cells and tissues. Nowadays this technique is used extensively in the design of new pharmaceuticals.

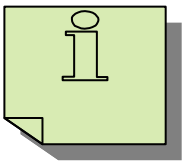
SLIDE A-5:

As we said before, there are still several other means of rendering molecular structures on paper or computer screen. We will come to these other forms as the course moves on. Suffice it to say for the time being that these other forms may acquire greatly sophisticated shapes. What we see here is an artistic rendering of the cocaine molecule which, in spite of its beauty, at present is perfectly useless from the chemical point of view. Drawings like these have been termed *non-photorealistic molecular renderings*. We will see one day however when similar drawings will express interesting molecular properties such as electromagnetic fields in and around the atomic sets, occupied molecular orbitals, fluctuations of electron density and the like. There is simply no end to what the future holds for us in organic chemistry and you may be part of this future if you work hard enough.

Slide 54 (END MENU)

This is the end of this presentation. I really hope you enjoyed it, at least as much as I took pleasure in making it for you. Now, you may proceed to either go back to the main menu, test yourself with the problems sheet, read and print this script so you may eventually have your own book on organic chemistry tailored to your specific needs, or even print a list of tables describing in brief terms the functional

groups we reviewed together just a moment ago. You my even want to have a second look at the list of the functional groups on screen. It is all up to you.



END

HOW TO USE THIS MATERIAL

The instructional materials of this lecture are:

1) This script
2) A set of interactive slides with advanced graphic features in Microsoft PowerPoint®
3) Action buttons for slide control
4) Embedded quizes
5) A problem sheet

SCRIPT

This scrip is just a suggested guide intended as an aid in the sequence of arguments of each slide, not a rigorous script to be followed word by word. Lecturer should provide his/her own personal language, ideas, examples, style and so forth based on these suggestions.

The script also contains information on the side: short old stories from the history of organic chemistry, curiosities, relevance of some compounds in industry and biology etc.

The script may be used as class complementary material for students by uploading it in a local network. It is designed as an organic chemistry text with illustrations, reaction schemes and many of the visuals shown in the slide show.

SLIDE SHOW

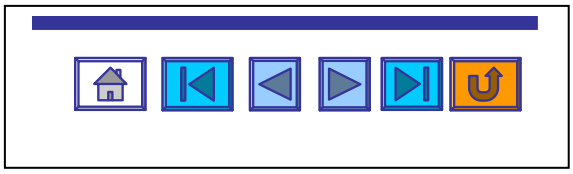
Slide numbers indicated in subtitles are those shown on the upper right corner of the actual slide. Generally they are TWO numbers BEHIND the actual slides in the PowerPoint sequence. Slide 1 is used for the mandatory copyrights page, lecture title appears on slide 2, and, slide 3 is for the lecture contents. The latter will be Slide 1.

Move forward images by left-clicking on mouse or using the arrows on the keyboard, but wait for animations to finish first for best visual impact and educational effect. Presentation of text, molecular renderings, equations and images have been designed and timed carefully to be shown with argument progress and not in overwhelming shots of data as in many slideshows. To take advantage of these highly educative effects, I strongly recommend lecturers to please become acquainted first with these visuals before class and control commands of each slide before presenting these lessons so they are in control of animations along their discussion

The flag marking the end of the last animation in each slide is a HEXAGON framing the slide number on the upper right corner, also showing the slide number.

ACTION BUTTONS

In various places along the slide show there are action buttons to travel to selected slides. Wiggle a little your mouse to activate the pointer and drive it to the selection button. The customary little 'hand' will appear, click on your selection and travel to that slide to jump back and forth as you wish.



At the lower right corner, most slides display a set of action buttons. These buttons allow you to move forward and backwards to: Content slide (menu), previous, next, first and last slides, or quit lesson altogether.

EMBEDDED QUIZES

Certain slides are prepared in a quiz format: there is a problem to be solved in class. In most instances there will be a clock shown on screen that the lecturer activates by clicking the mouse on the appropriate button (generally 30 secs. This will give students limited time to solve the proposed question. If the lecturer the lecturer deems this time too short, simply ignore the clock.

PROBLEM SHEET

There are many good sources available for study problems, to be sure. We have added a set of such problems that reinforce the particular subjects treated in this lecture.

Remember: Studying and using this material in class takes much less time than preparing the lesson from scratch, least of all using chalk and board or even web downloadable “fixed” and boring sets of cheap looking slides.