

How Can You Solve Complicated Organic Structures.

Tools of the trade (for problems in these discussions):

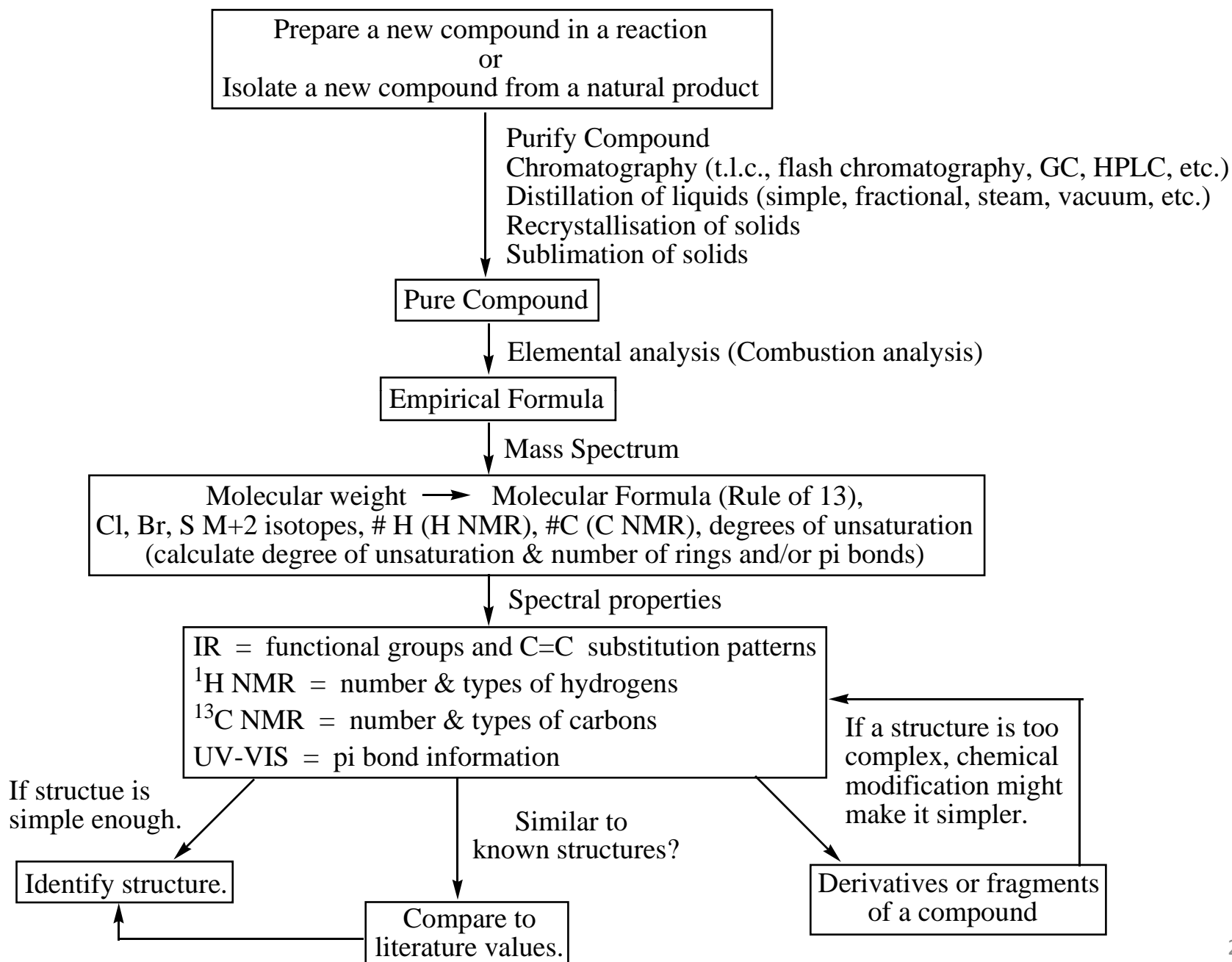
1. Limited MS data from atomic isotopes (M^+ , $M+1$, $M+2$, etc.), the number of protons in the H NMR and the number and types of carbons in the C NMR spectra, can help determine a formula, degrees of unsaturation, number of pi bonds and rings.
 2. IR information – helps decide what functional groups and alkene and aromatic substitution patterns are present. (uses bond stretching and bond bending vibrations)
 3. NMR information – provides the most useful information to determine the connectivity of the atoms (^1H , ^{13}C , DEPT, HETCOR/HSQC, COSY, HMBC).
 4. Mass Spectrometry from an organic chemist's perspective
 5. Additional structure problems to solve
-

As you go through these lectures, click the pause button when you want to think about what was just said or about how you would approach a proposed problem. After you have organized your thoughts, click 'continue'. Replay any parts you don't understand. Ask questions in the comments section if you need to. Please point out any significant errors you notice in the slides. Thanks.

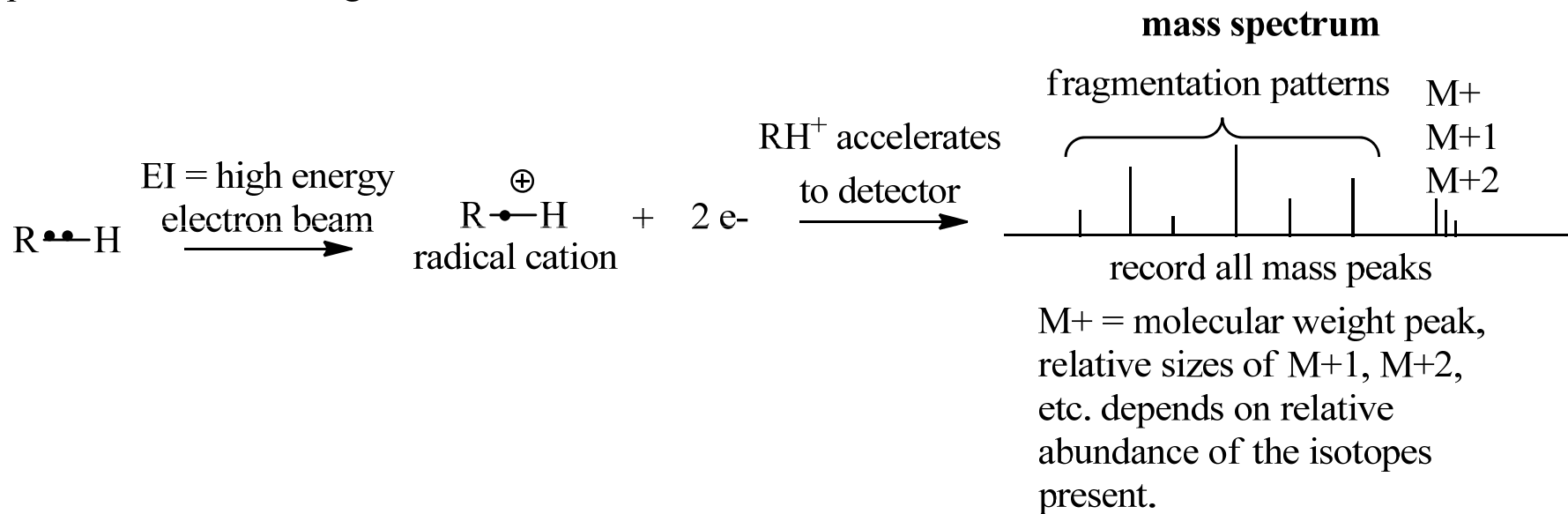
link to copies of slides:

http://www.cpp.edu/~psbeauchamp/pdf_videos/lecture_1_formulas.pdf

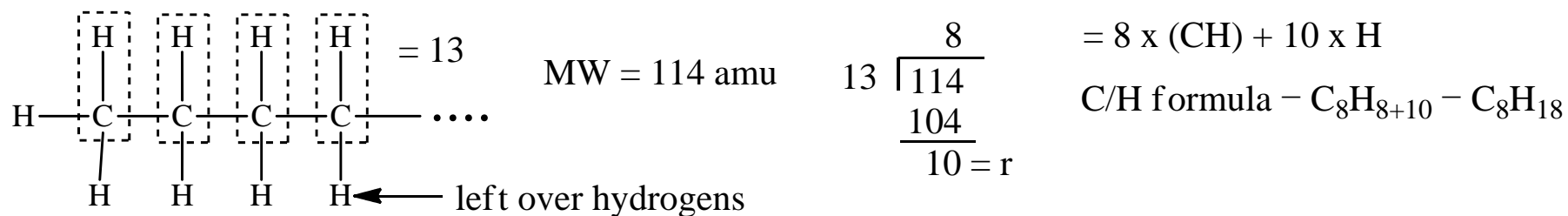
Common reasons and an approach to identify organic or biological structures.



Our first goal is to obtain a molecular weight which we can use to help us determine a molecular formula. the most common tool to do this is *mass spectrometry*. We don't say *spectroscopy* because *spectroscopy* implies that electromagnetic radiation is used in the technique. MS is different from the other routine spectroscopies (UV-Vis, IR, H and C NMR) in that absorption or emission of electromagnetic radiation (light) is *not* used. In MS, the sample (molecule) is ionized by a high energy electron beam in a process referred to as electron impact (EI). An electron is knocked out of a bonding molecular orbital (MO), forming a radical cation, RH^+ . The radical cation is accelerated to a detector where we can see its mass to charge ratio ($m/e =$ its molecular weight). We will refer to the molecular weight peak as the M^+ peak (molecular ion peak or parent peak). Because the energy of the electron beam is so great the molecule also fragments to smaller pieces, which can give additional clues about the molecular structure. Understanding fragmentation is not our purpose here, but the molecular weight can provide some possible formulas using the "Rule of 13". Also, in real MS, the M^+ peak is sometimes very small or even missing. There are ways around this, but we won't consider these complications in our discussions here. A separate lecture is planned for how an organic chemist views MS.



Using the molecular weight as a starting point, we can first assume only C and H are present. We can divide the molecular weight by 13 (= C + H amu) to determine how many CH units there are. The remainder will equal the number of left over hydrogen atoms and the C/H formula would be solved as follows.



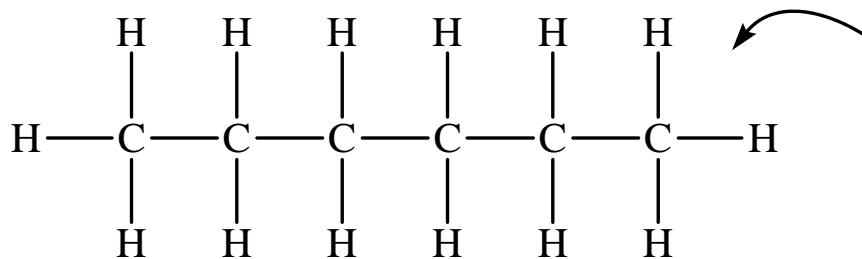
What if there was an oxygen atom? Oxygen has a mass of 16 so we would have to substitute out 16 amu from C and H (= C + 4H) to add in the mass of oxygen giving us a new formula of C₇H₁₄O. Two oxygen atoms (or one sulfur atom) would require a swap of 32 amu (= 2C + 8H for 2O or 1S) giving formulas of C₆H₁₀O₂ or C₆H₁₀S. Since an odd number of nitrogen atoms produces an odd molecular weight, our molecular weight (114 amu) would only allow zero nitrogens or two nitrogens (or another even number). A possible formula with two nitrogen atoms (28 amu) requires a switch of (2C + 4H) for N₂ producing C₅H₁₀N₂.

new possible formulas (even MW)	
only C & H	C ₈ H ₁₈ (even mass = 114 amu)
1xO = 1C + 4H	C ₇ H ₁₄ O (even mass = 114 amu)
2xO = 2C + 8H	C ₆ H ₁₀ O ₂ (even mass = 114 amu)
1xS = 2C + 8H	C ₆ H ₁₀ O ₂ (even mass = 114 amu)
2xN = 2C + 4H	C ₆ H ₁₄ N ₂ (even mass = 114 amu)

new possible formulas (odd MW = 115)	
only C & H	C ₈ H ₁₉
(odd mass = 115 amu, not possible)	
1xN = 1C + 2H	C ₇ H ₁₇ N
1xN + 1xO = 2C + 6H	C ₆ H ₁₃ NO

There is more information to be gained from our molecular formulas. The degree of unsaturation (also called hydrogen deficiency) will reveal the total number of pi bonds and/or rings present. This will prove very helpful to our goal of solving the chemical structure.

In a linear chain of carbons there are two bonding positions on every carbon, with two additional positions on the end carbons. This produces $(2n + 2)$ single bond positions on an alkane skeleton, where n is the number of carbons. This is the maximum number of bonding positions in any alkane, so when this number of single bonding groups are actually present, the formula is referred to as saturated (no more will fit). Count all of the hydrogen and the halogen atoms (F, Cl, Br, I) in the total number of atoms forming only one bond.

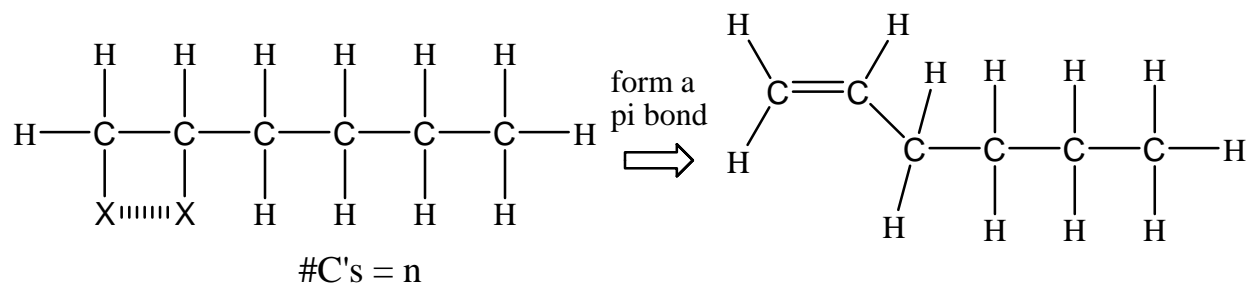


number of carbon atoms = n

Maximum bonding positions = $2n + 2$

This compound is referred to as saturated when the total number of single bonding groups equals the maximum number of bonded positions. All of the bonded atoms would be hydrogen atoms in an alkane. However, we will add halogen atoms in with hydrogen atoms because they all only form single bonds and occupy a single bonding position on the carbon skeleton.

What happens if there is a pi bond? The maximum number of single bonding groups (hydrogen and halogen atoms) is reduced by two for each pi bond.



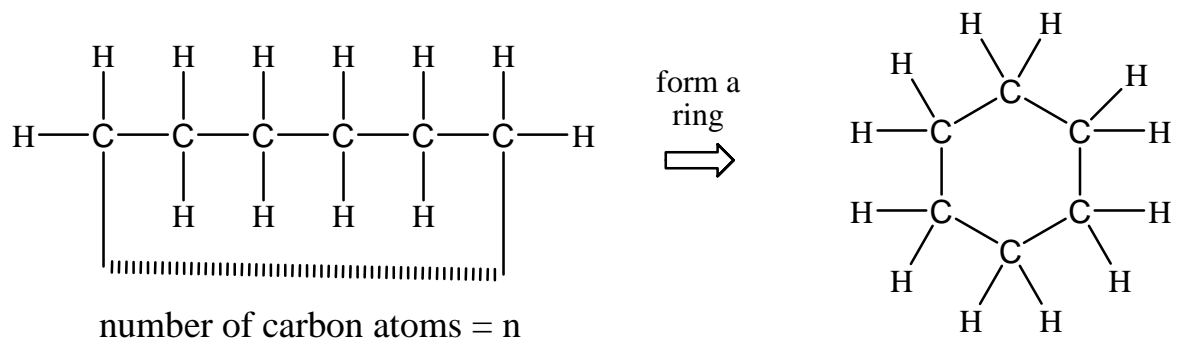
Maximum bonding positions on n carbon atoms = $2n + 2$

Actual number of bonding positions with one pi bond = $2n$

This structure is referred to as unsaturated because it has fewer than the maximum number of single bonding groups. Each pi bond represents one degree of unsaturation (1° unsaturation) and takes away two single bonding groups from the formula.

$$\text{Degree of unsaturation} = \frac{(2n + 2) - (2n)}{2} = \frac{2}{2} = 1 \text{ degree of unsaturation}$$

What happens if there is a ring? The maximum number of single bonded atoms is again reduced by two for each ring.



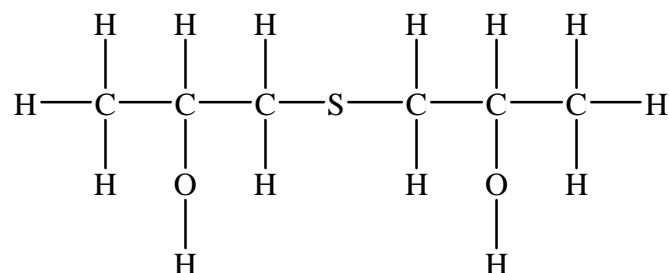
Maximum bonding positions on n carbon atoms = $2n + 2$

Actual number of bonding positions with one pi bond = $2n$

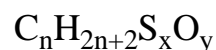
This structure is referred to as unsaturated because it has fewer than the maximum number of single bonding groups. Each ring represents one degree of unsaturation (1° unsaturation) and takes away two single bonding groups from the formula.

$$\text{Degree of unsaturation} = \frac{(2n + 2) - (2n)}{2} = \frac{2}{2} = 1 \text{ degree of unsaturation}$$

What happens if there is an oxygen atom added to the carbon skeleton? Since oxygen makes two bonds, the bond that it takes is replaced with the second bond that it forms. There is no change in the calculation no matter how many oxygen atoms there are, and we can ignore all oxygen atoms in our calculations. Divalent sulfur is similar to oxygen in this regard.



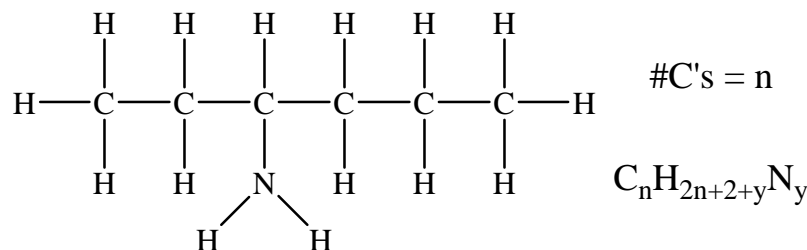
#C's = n



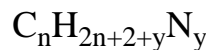
Maximum bonding positions on n carbon atoms = $2n + 2$

Oxygen atoms (or divalent sulfur), in any amount, do not change the above calculation. They merely act as spacer atoms. We just ignore them when calculating the degree of unsaturation.

What happens if there is a nitrogen atom? Since a nitrogen atom makes three bonds, the bond that it occupies on the carbon skeleton is replaced by two additional bonds and that produces a net increase of one bond per nitrogen atom.



#C's = n



Maximum bonding positions on n carbon atoms with nitrogen present = $2n + 2 + \#N$ atoms

Every single nitrogen atom will add an extra bonding position. Also, an odd number of nitrogen atoms (1,3,5...) will lead to an odd molecular weight.

$$\text{degrees of unsaturation} = \frac{\left(\begin{array}{l} \text{maximum number of} \\ \text{single bonding positions} \\ \text{on a carbon skeleton} \end{array} \right) - \left(\begin{array}{l} \text{actual number of} \\ \text{single bonding atoms} \\ \text{on a carbon skeleton} \end{array} \right)}{2}$$

$$= \frac{(2n + 2 + \# N) - (\text{single bond atoms})}{2}$$

(where n = the number of carbon atoms and # N is the number of nitrogen atoms and single bonding atoms = H and halogens) 7

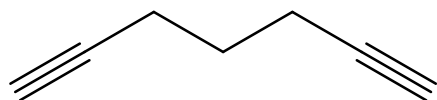
Problem - Determine the degrees of unsaturation for each of the following formulas. What combinations of pi bonds and rings are possible in each case? Is it possible for any of the following formulas to have an alkene, alkyne, carboxylic acid, ester, amide, nitrile, aromatic ring, ketone, aldehyde, ether, amine or alcohol? Try and draw some examples of such structures. Note that we cannot tell the difference between pi bond and ring unsaturation yet. ^{13}C NMR will allow us to make those distinctions (later).

- a. C_7H_8 b. $\text{C}_5\text{H}_{10}\text{O}$ c. $\text{C}_4\text{H}_8\text{O}_2$ d. $\text{C}_6\text{H}_{11}\text{N}$ e. $\text{C}_7\text{H}_{17}\text{NO}$
- f. $\text{C}_{10}\text{H}_9\text{ClN}_2\text{O}$ g. $\text{C}_9\text{H}_9\text{NO}_2$ h. $\text{C}_{12}\text{H}_8\text{Cl}_2$ i. $\text{C}_7\text{H}_5\text{N}$ j. $\text{C}_6\text{H}_{10}\text{SO}_4$

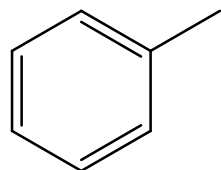
$$\text{degrees of unsaturation} = \frac{(2n + 2 + \# \text{ N}) - (\text{single bond atoms})}{2}$$

(where n = the number of carbon atoms and # N is the number of nitrogen atoms and single bonding atoms = H and halogens)

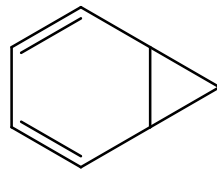
a. $\text{C}_7\text{H}_8 = 4^\circ$ unsaturation



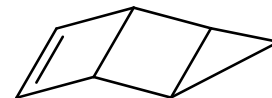
pi bonds rings
4 0



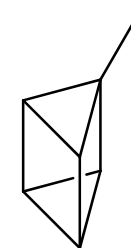
pi bonds rings
3 1



pi bonds rings
2 2

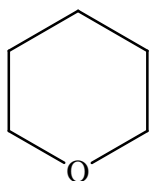


pi bonds rings
1 3

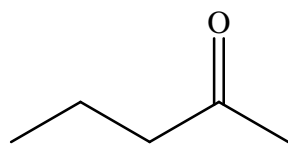


pi bonds rings
0 4

b. $\text{C}_5\text{H}_{10}\text{O} = 1^\circ$ unsaturation

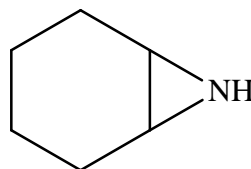


pi bonds rings
0 1

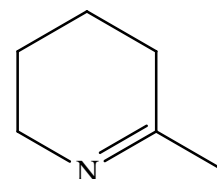


pi bonds rings
1 0

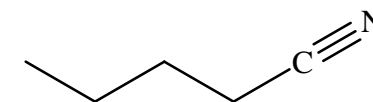
d. $\text{C}_6\text{H}_{11}\text{N} = 2^\circ$ unsaturation



pi bonds rings
0 2

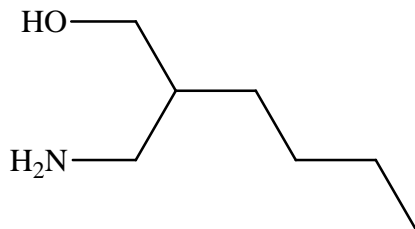


pi bonds rings
1 1



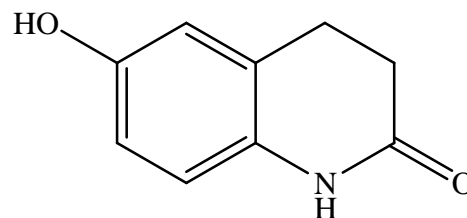
pi bonds rings
2 0

e. $\text{C}_7\text{H}_{17}\text{NO} = 0^\circ$ unsaturation



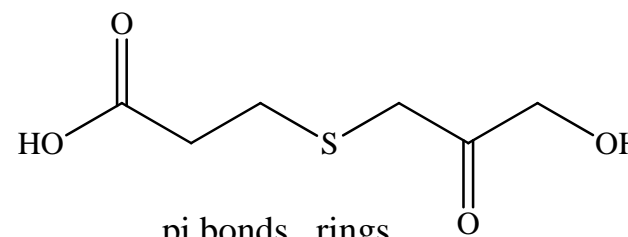
pi bonds rings
0 0

g. $\text{C}_9\text{H}_9\text{NO}_2 = 6^\circ$ unsaturation



pi bonds rings
4 2

j. $\text{C}_6\text{H}_{10}\text{SO}_4 = 2^\circ$ unsaturation



pi bonds rings 10
2 0

Let's return to our mass spec information. For now, we are only interested in the M+ peak and the smaller trailing peaks due to the presence of other higher mass isotopes of the atoms we commonly encounter in organic chemistry: H, C, N, O, Cl, Br and S. We will not include F, I and P in our problems. The lowest mass isotope of each of these elements is also the most abundant isotope. This is indicated by showing its abundance as 100% and the the percents of the higher mass isotopes (M+1, M+2, etc) as relative percents of the lowest mass isotope. These are shown below for the possible elements in our structure problems (first row). Also shown are some combinations of two of these elements (second row). We will use the M+, M+1, M+2, etc. peaks to reveal if S, Cl and/or Br is present in our structures. A few examples will show how this is done. All of this assumes an M+ peak is present and is large enough to see M+1, M+2, etc. This is common enough for small molecules, but not usually the case for larger molecules, using EI mass spectrometry. There are ways around this problem, but we won't consider them. In our problems, we assume M+, M+1, M+2, etc. are present.

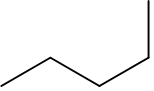
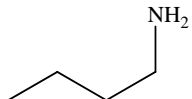
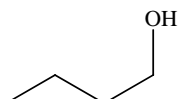
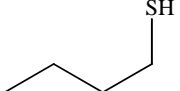
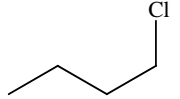
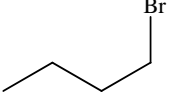
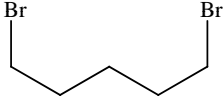
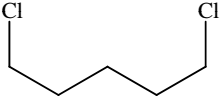
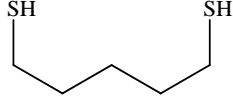
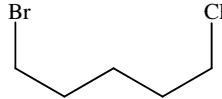
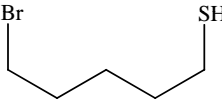
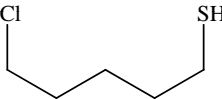


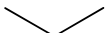

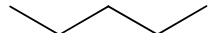
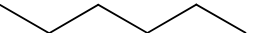
	H	C	N	O	Cl	Br	S
M+	100%	100%	100%	100%	100%	100%	100%
M+1	0.02%	1.1%	0.38%	0.04%	0%	0%	0.8%
M+2	0%	0%	0%	0.20%	32%	97%	4.5%
M+4	0%	0%	0%	0%	0%	0%	0%
	(Cl) ₂	(Br) ₂	(Br,Cl)	(S,Cl)	(S,Br)		
M+	100%	100%	100%	100%	100%		
M+1	0%	0%	0%	0.7%	0.7%		
M+2	64%	194%	129%	36%	102%		
M+4	10%	95%	31%	1.4%	4.4%		

Special points to note:

¹³C is about 1% of the ¹²C peak
¹⁵N is about 0.4% of the ¹⁴N peak
¹⁸O is about 0.2% of the ¹⁶O peak
³⁷C is about 32% of the ³⁵Cl peak
⁸¹Br is about 97% of the ⁷⁹Br peak
³³S is about 0.8% of the ³²S peak and
³⁴S is about 4.5% of the ³²S peak

The percents shown only consider the atom(s) shown and not other atoms that are part of a molecular formula.

Mass Spec Information can help decide how many C, N, Cl, Br and S atoms are present.

 <p>Chemical Formula: C_5H_{12} Exact Mass: 72.09 $M+ = 72.09$ (100.0%), $M+1 = 73.10$ (5.5%)</p>	 <p>Chemical Formula: $C_4H_{11}N$ Exact Mass: 73.09 $M+ = 73.09$ (100.0%), $M+1 = 74.09$ (4.7%)</p>	 <p>Chemical Formula: $C_4H_{10}O$ Exact Mass: 74.07 $M+ = 74.07$ (100.0%), $M+1 = 75.08$ (4.5%)</p>	 <p>Chemical Formula: $C_4H_{10}S$ Exact Mass: 90.05 $M+ = 90.05$ (100.0%), $M+1 = 91.05$ (5.1%), $M+2 = 92.05$ (4.6%)</p>	 <p>Chemical Formula: C_4H_9Cl Exact Mass: 92.04 $M+ = 92.04$ (100.0%), $M+1 = 93.04$ (4.3%), $M+2 = 94.04$ (32.0%), $M+3 = 95.04$ (1.4%)</p>	 <p>Chemical Formula: C_4H_9Br Exact Mass: 135.99 $M+ = 135.99$ (100.0%), $M+1 = 136.99$ (4.3%), $M+2 = 137.99$ (97.3%), $M+3 = 138.99$ (4.3%)</p>
 <p>$C_5H_{10}Br_2$ Exact Mass: 227.91 $M+ = 227.91$ (100.0%), $M+1 = 228.92$ (5.4%), $M+2 = 229.91$ (194.6%), $M+3 = 230.92$ (10.7%), $M+4 = 231.91$ (94.6%), $M+5 = 232.91$ (5.1%)</p>	 <p>$C_5H_{10}Cl_2$ Exact Mass: 140.02 $M+ = 140.02$ (100.0%), $M+1 = 141.02$ (5.5%), $M+2 = 142.01$ (63.9%), $M+3 = 143.02$ (3.5%), $M+4 = 144.01$ (10.2%)</p>	 <p>$C_5H_{12}S_2$ Exact Mass: 136.04 $M+ = 136.04$ (100.0%), $M+1 = 137.04$ (7.1%), $M+2 = 138.03$ (9.0%)</p>	 <p>$C_5H_{10}BrCl$ Exact Mass: 183.97 $M+ = 183.97$ (100.0%), $M+1 = 184.97$ (5.6%), $M+2 = 185.96$ (129.2%), $M+3 = 186.97$ (7.1%), $M+4 = 187.96$ (35.0%), $M+5 = 188.96$ (1.7%)</p>	 <p>$C_5H_{11}BrS$ Exact Mass: 181.98 $M+ = 181.98$ (100.0%), $M+1 = 182.98$ (6.3%), $M+2 = 183.97$ (101.8%), $M+3 = 184.98$ (5.6%), $M+4 = 185.97$ (4.4%)</p>	 <p>$C_5H_{11}ClS$ Exact Mass: 138.03 $M+ = 138.03$ (100.0%), $M+1 = 139.03$ (6.3%), $M+2 = 140.02$ (36.5%), $M+3 = 141.03$ (2.0%), $M+4 = 142.02$ (1.5%)</p>
 <p>CH_4 Exact Mass: 16.03 $M+ = 16.03$ (100.0%), $M+1 = 17.03$ (1.1%)</p>	 <p>C_2H_6 Exact Mass: 30.05 $M+ = 30.05$ (100.0%), $M+1 = 31.05$ (2.2%)</p>	 <p>C_3H_8 Exact Mass: 44.06 $M+ = 44.06$ (100.0%), $M+1 = 45.07$ (3.3%)</p>	 <p>C_4H_{10} Exact Mass: 58.08 $M+ = 58.08$ (100.0%), $M+1 = 59.08$ (4.4%)</p>	 <p>C_5H_{12} Exact Mass: 72.09 $M+ = 72.09$ (100.0%), $M+1 = 73.10$ (5.5%)</p>	 <p>C_6H_{14} Exact Mass: 86.11 $M+ = 86.11$ (100.0%), $M+1 = 87.11$ (6.5%)</p>

Notice that the $M+1$ percent is approximately the same as the number of carbon atoms in the formula.

Our approach to obtaining a molecular formula, degrees of unsaturation, pi bonds and rings will be as follows.

1. Determine if ^{35}Cl , ^{79}Br or ^{32}S are present (and how many) using the mass spec information listed above (M+2 peaks, etc.).
2. A proton count can be determined by using the proton integration from the H NMR. This will be given until H NMR is covered.
3. A carbon count can be estimated by dividing the M+1 mass spec peak by 1.1, since the ^{13}C isotope is 1.1% of the ^{12}C isotope. This can be confirmed by counting the number of carbon peaks in the proton decoupled ^{13}C NMR (taking into account any symmetry features). This will be given until ^{13}C is covered. A minor complication is that ^{33}S is 0.8% of ^{32}S and two ^{15}N is about 0.8% of ^{14}N . Both of these possibilities can appear as an extra carbon atom in a formula unless subtracted from the M+1 percent. An odd molecular weight indicates an odd number of nitrogen atoms (1, 3, etc.).
4. The total masses of any ^{35}Cl , ^{79}Br , ^{32}S (use the exact masses of the lower atomic mass isotopes), plus the total mass of hydrogen ($^1\text{H} = 1 \times n$) and carbon ($^{12}\text{C} = 12 \times m$) is subtracted from the exact mass, the M+ peak. This will leave a residual mass most likely composed of ^{14}N and/or ^{16}O . Usually, how many of each element becomes clear by inspection, looking for some combination of 14 and 16 to equal the residual mass. If you can't tell, start subtracting 14 until you come to a number divisible by 16.
5. Once all of the atoms are determined, one uses the formula to calculate the total degrees of unsaturation, which equals the total pi bonds and rings.
Maximum saturation # = $2(n) + 2 + \#\text{N}$, (where $n = \#$ of carbon atoms, and $\#\text{N} = \#$ of nitrogen atoms).
Unsaturation = $[(\text{maximum saturation \#}) - (\# \text{ of single bonding groups})] / 2$
6. Pi bonds are estimated from the chemical shifts in the ^{13}C NMR, looking for alkene, alkyne (possibly seen in the IR), aromatic, nitrile (easily seen in the IR) and C=O functionality. Certain types of pi bonds will not show up in the ^{13}C , such as N=O and N=N pi bonds (nitro, nitroso, diazo, azido, etc.). Most of these are rare for us, but the nitro ($-\text{NO}_2$) is common enough and can be seen in the IR spectrum (1550 cm^{-1} and 1350 cm^{-1}). The number of pi bonds is subtracted from the total degrees of unsaturation to find out how many rings are present.

The procedure described here is a good first step towards finding an unknown structure. Two examples are provided below. Having an IR and/or NMR data will give many additional clues to help decide what a structure is. We'll look at those techniques in our second and third topics.

Example 1 - finding a molecular formula and the number of pi bonds and rings

Mass spec data:

Exact Mass: 369.06

M+ = 369.06 (100.0%),

M+1 = 370.06 (17.7%),

M+2 = 371.06 (99.6%),

M+3 = 372.06 (17.2%),

An odd mass indicates
an odd number of nitrogen
atoms.

1. $M+ \approx M+2$ so bromine is present (Br exact mass = 79).
2. Proton count from ^1H NMR = 20 (given for now, until a H NMR is provided)
3. Carbon count from MS data = $(17.7)/(1.1) = 16$
Carbon count from ^{13}C NMR is 16 (given for now, until a C NMR is provided)
4. Total mass of $^{79}\text{Br} + 20 \text{H} + 16 \text{ }^{12}\text{C} = 291$
5. Residual mass = $369 - 291 = 78 = 64 + 14 = 4 \times \text{O} + 1 \times \text{N}$

Molecular formula = **$\text{C}_{16}\text{H}_{20}\text{BrNO}_4$**

6. Maximum single bonding positions = $2(16) + 2 + 1 = 35$
degrees of unsaturation = $[(35) - (21)] / 2 = 14 / 2 = 7$ degrees
7. ^{13}C NMR shows 6 x (=C) in alkene/aromatic region = 3 x (C=C)
and 1 x (C=O) for a total of 4 pi bonds. However, there are two absorptions in the IR
at 1550 and 1350 cm^{-1} , indicate that a nitro group might be present (N=O). That brings the
total pi bonds to 5. The number of rings = (total unsaturation) - (pi bonds) = $7 - 5 = 2$ rings

Example 2 - finding a molecular formula and the number of pi bonds and rings

Mass spec data:

Exact Mass: 414.13

M+ = 414.13 (100.0%),

M+1 = 415.13 (22.9%),

M+2 = 416.12 (40.0%),

M+3 = 417.13 (8.3%),

M+4 = 418.12 (1.5%),

An even mass indicates
no nitrogen atoms or an
even number of nitrogen
atoms.

1. M+2 = (M+) x (40.0%) so Cl (32%) and S (4.5%) are likely present (exact mass = 35+32 = 67).

Also M+4 = 1.5%, supports this conclusion. Sulfur also adds 0.8% to the M+1 peak.

2. Proton count from ^1H NMR = 27 (given for now, until a H NMR is provided)

3. Carbon count from MS data = $(22.9 - 0.8) / (1.1) = 20$ (subtract 0.8 for each sulfur atom present)

Carbon count from ^{13}C NMR is 20 (given for now, until a C NMR is provided)

4. Total mass of $^{35}\text{Cl} + ^{32}\text{S} + 27 \text{H} + 20 \text{ }^{12}\text{C} = 334$

5. Residual mass = $414 - 334 = 80 = 5 \times 16 = 5 \times \text{O}$

Molecular formula = **$\text{C}_{20}\text{H}_{27}\text{ClO}_5\text{S}$**

6. Maximum single bonding positions = $2(20) + 2 = 42$

degrees of unsaturation = $[(42) - (28)] / 2 = 14 / 2 = 7$ degrees

7. ^{13}C NMR shows 6 x (=C) in alkene/aromatic region = 3 x (C=C)

and 2 x (C=O) for a total of 5 pi bonds.

The number of rings = (total unsaturation) - (pi bonds) = $7 - 5 = 2$ rings