# Week 2

# Spectrometry

## 2.1 Office Hours (Snyder)

1/17:

- Does cyclohexane only have one $^{13}$C NMR signal, and only one $^{1}$H NMR signal?
  - 1 singlet for $^{13}$C.
  - 1 singlet for $^{1}$H.
  - We don't integrate carbon.
  - We only integrate to compare things.
  - We won't have to deal with cyclohexane conformations wrt. NMR on any test.
- What do we need to know about the Karplus correlation?
  - We won't need it for problems.
  - It's useful, but we've got other things to worry about.
- Do chemists/when do chemists run $^{13}$C NMR experiments with all carbons isotopically carbon-13?
- Is the reason we don't integrate carbon because the placing of the carbon-13s is random? Would the proportions not still be representative?
- For $^{1}$H NMR, feel free to draw in the hydrogen atoms on the line-angle structure.
- Multiplying $n+1$ of different types of neighbors (e.g., if a hydrogen has 3 neighboring hydrogens to one side and 2 neighboring hydrogens to the other side, it has a maximum of $(3+1)(2+1) = 12$ peaks in its signal).
  - The multiplication analysis applies only to chains that are completely different.

## 2.2 NMR

1/18:

- With a 1400 MHz NMR spectrometer, we can see 3D structure.
- Goes over an example of sketching a $^{13}$C spectrum, DEPT 90, and DEPT 135 spectrum for a given molecule.
- You can flip groups in a problem, but you have to be consistent.
  - If you have closely spaced peaks in a sketch, be consistent with identifying a certain peak as CH, $CH_2$, or $CH_3$. But it doesn't matter which of the peaks you identify which way.
- There can be variation in signal height, but we won't discuss this.

- Transition to $^{1}$H NMR spectroscopy.
- A typical $^{13}$C NMR experiment takes 1-2 hours (for about 5 mg of material) to build appropriate peaks since there are so few $^{13}$C atoms interspersed.
  - On a strong field machine, though, a $^{1}$H spectrum can be done in seconds.
- $^{1}$H NMR offers better resolution with respect to some functional groups than $^{13}$C NMR.
  - Aldehydes and carboxylic acids will be clearly resolved.
  - Benzenes and alkenes will be better separated, too.
- Goes over typical chemical shifts (see Table 1.1).
- Goes over an example of sketching a $^{1}$H spectrum.
- Neighboring spins parallel to the magnetic field increase ppm (deshielding).
- Introduces the coupling constant $J$.
- Splitting can happen in $^{13}$C spectra, but it can't be observed on the time scale on which we measure.
- Terminology: Singlet, doublet, triplet, quartet, pentet, and sextet.
- Multiple neighbors? Multiply!
  - If you have 3 neighbors on one side and 2 on the other, for instance, you will have $(3+1)(2+1) = 12$ peaks.
  - Note that this is our predicted value — due to overlap, we may see fewer, but we will always go with the predicted value in this class.
- Count neighbors even on non-carbon atoms.
- Hybridization.
  - Don't get bothered by the hybridization of parent carbons if it doesn't restrict conformations. For example, the $sp^2$ carbon in an aldehyde behaves the same as any other parent carbon.
  - Do worry about hybridization if it makes hydrogens nonequivalent. In 1-butene for example, the two terminal hydrogens on the alkene are nonequivalent.
    - We will not worry about multiplicity due to this effect, though the rules are similar to what we've seen.
- Benzenes.

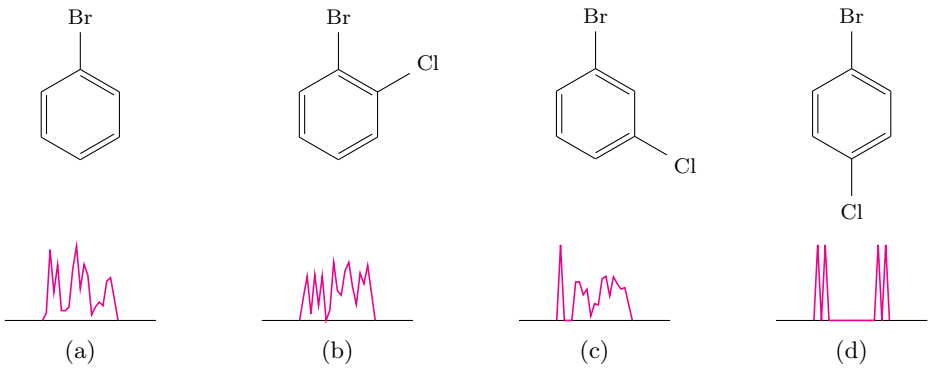
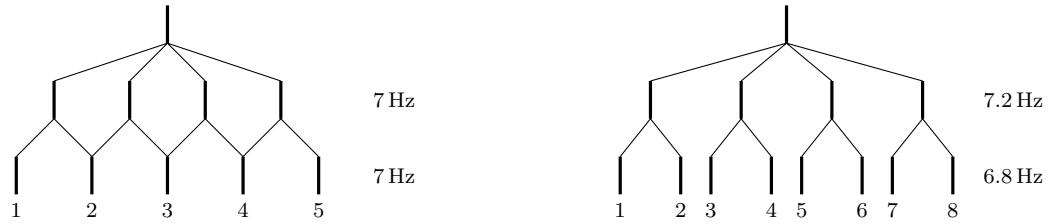



Figure 2.1: Benzenes in $^{1}$H NMR spectroscopy.

  - We can predict a bunch of splitting and peaks, but often there is so much overlap that we more just get a jagged blob (see Figures 2.1a and 2.1b).
  - If you can find a clear singlet, perhaps separated a bit from the rest, integration can tell you how many substituents you have (see Figure 2.1c).
  - The pattern in Figure 2.1d is a dead giveaway for para substituents.
- Alkene coupling constants.
  - *cis*-alkenes typically have $J = 6 - 10\,\text{Hz}$.
  - *trans*-alkenes typically have $J = 12 - 18\,\text{Hz}$.
  - These are identifiable, diagnostic signals.
- Enantiomers are identical in NMR experiments.
  - Remember that all of their physical properties are the same (including the various forms of spectroscopy) except optical rotation.

## 2.3 Mass / IR Spectrometry

1/20:
- Solomons et al. (2016) says to add (not multiply) in the $n + 1$ rule for multiple types of neighboring hydrogens.
  - What accounts for this inconsistency is the **Pascal approach**.
  - Solomons et al. (2016) assumes that the coupling constants in the NMR instruments we use will be equal for both neighboring groups. This leads to overlap in the second splitting.
    - This is often a good assumption, but not always.
  - The multiplicative approach gives you the maximum number of signals you might see.
    - You will often see more signals on better machines, i.e., ones that can distinguish coupling constants to decimal places instead of just whole numbers.
- **Pascal approach**: A mode of analysis in which we explicitly draw splitting of NMR peaks.




(a) Additive rule. (b) Multiplicative rule.

Figure 2.2: Pascal approach.

  - The analyses in Figure 2.2 refer to a hydrogen with three neighbors to one side and one to the other (thus we split into $3 + 1 = 4$ peaks and then again into $1 + 1 = 2$ subpeaks per peak).
  - Notice how in Figure 2.2a, a less sensitive instrument displays peak overlapping and thus an additive rule works, while in Figure 2.2b, a more sensitive instrument resolves individual peaks.
  - Dr. Snyder always wants us to use the multiplicative rule on homeworks and tests.
- Reconstructs meta-bromomethylbenzene from its NMR spectrum.
- How spectroscopy is used in modern research.

  - X-ray crystallography was the first type of spectroscopy on the scene, being able to identify the position of every atom save hydrogen. Yet it was restricted to crystalline solids.
  - NMR is kind of the holy grail of today.
  - How we extract chemicals from natural materials: We look for things that are stationary (because they have to be able to repel things through chemical means). Then we dry them, grind them down, and add an organic solvent.
  - We then rotavap and use column chromatography.
- Mass spectrometry is a destructive process, but you only need a very tiny amount.
- Goes over theory of EI and hexane as an example.
  - Note that after EI, ions are accelerated around a corner where they bend in proportion to their mass to charge ratio (heavier ions bend less; ions with more charge bend more).
- We want to train our eyes to pick out the most dominant signals in a mass spectrum.
- A pattern of $-14, -14, -14$ is indicative of a linear alkane that's losing a $CH_2$ group each time.
- Alcohols will either have $\alpha$-cleavage or dehydration.
- We should be able to detect bromine and chlorine.
- $m/z = 77$ is a dead giveaway for a phenyl cation.
- Now IR spectroscopy.
- Misc. IR notes.
  - Tighter bonds vibrate faster (e.g., C≡C > C=C > C−C).
  - Bonds that are more polar also have higher wave numbers.
  - Esters usually have higher carbonyl stretches than ketones.
  - Putting a double bond next to a ketone lowers it's stretching frequency due to resonance detracting from the double bond character of the C=O bond.
  - Sometimes you can tell benzene because it has a smaller C−H peak.
  - Hydroxyl groups in alcohols, carboxylic acids, and phenols have different peaks, properties, and reactivity.
- IR summary.
  - A great tool to determine functional groups on small molecules.
  - Non-destructive.
  - You should be able to understand why each bond is positioned at a specific wavenumber range, learn that range, and then be able to identify all of the following functional groups from an individual IR spectrum.
    - Carbonyls (aldehydes, ketones, esters, carboxylic acids).
    - Alkynes.
    - Nitriles/cyanides.
    - Alcohols.
    - Primary and secondary amines.

## 2.4 Chapter 9: Nuclear Magnetic Resonance and Mass Spectroscopy

*From Solomons et al. (2016).*

1/18:

- **Mass spectrometry**: The formation of ions in a mass spectrometer followed by separation and detection of the ions according to mass and charge.
- **Mass spectrum**: A graph that on the $x$-axis represents the formula weights of the detected ions, and on the $y$-axis represents the abundance of each detected ion.

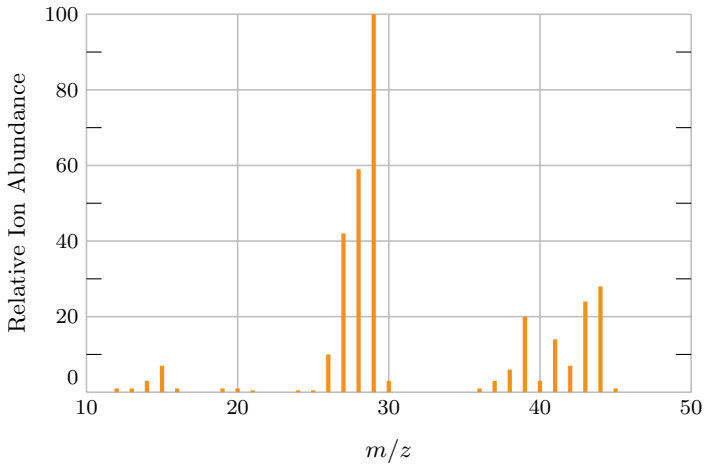



Figure 2.3: The mass spectrum of propane.

  - The $x$-axis is labeled $m/z$ where $m$ is mass and $z$ is charge.
  - The examples Solomons et al. (2016) consider all have $z = +1$, so the $x$-axis in them effectively represents the formula weight of each detected ion.
- **Base peak**: The tallest peak in a mass spectrum.
  - Usually caused by an easily formed fragment of the original compound.
  - Relative ion abundance on the $y$-axis is either expressed as a percentage of the base peak or directly as the number of detected ions.
  - The base peak in Figure 2.3 corresponds to the $C_2H_5{}^+$ ion, $m/z = 29 = 2 \cdot 12 + 5 \cdot 1$.
- **Molecular ion**: The ion with the formula weight of the original compound.
  - One of the higher value $m/z$ peaks.
  - Usually not the base peak.
- Small peaks having $m/z$ values 1 or 2 higher than the formula weight of the compound are due to $^{13}C$ and other isotopes.
- **Electron impact**: A method for ionizing molecules in a mass spectrometer by placing the sample under high vacuum and bombarding it with a beam of high-energy electrons. *Also known as* **EI**.
  - The energy of the electrons is in the range of 70 eV or $6.7 \times 10^3$ kJ/mol.
  - The incoming electrons ionize the molecules to molecular ions, which are radical cations since they have a +1 charge and an unshared electron.
- Note that there are ionization methods other than EI, but it is the most common.

- Localizing the radical and charge along the structure.

(a) Propane. (b) Methanol. (c) Trimethylamine. (d) 1-Butene.

Figure 2.4: Molecular ions.

  - The choice of where we localize the radical/charge is often arbitrary (esp. with hydrocarbons).
  - However, "as we might expect, ionization potentials indicate that in [the] formation of radical cations, the nonbonding electrons of nitrogen, oxygen, and halogen atoms, and the $\pi$ electrons of alkenes and aromatic molecules, are held more loosely than the electrons of carbon-carbon and carbon-hydrogen $\sigma$ bonds" (Solomons et al., 2016, p. 425).
  - Thus, "when a molecule contains oxygen, nitrogen, or a $\pi$ bond, we place the odd electron and charge at a nitrogen, oxygen, halogen, or $\pi$ bond. If resonance is possible, the radical cation may be delocalized" (Solomons et al., 2016, p. 425).

- Three important principles.
  1. The reactions that take place are all unimolecular since the pressure is kept so low.
  2. Single-barbed arrows denote the movement of single electrons.
  3. The relative ion abundances give key information about the structures of the fragments produced and their original locations in the molecule.

- Fragmentation by cleavage at a single bond.
  - When such a process happens in a molecular ion, a cation and a radical are produced, although only the cation will be detected by the positive ion mass spectrometers we're considering.
  - Each cleavage can happen in two ways (since one fragment will take the radical and the other will take the positive charge).
  - The path that produces the more stable carbocation will occur more rapidly.
    - Notice the difference in relative ion abundance between the secondary $CH_3CH_2^+$ ($m/z = 29$) and the primary $CH_3^+$ ($m/z = 15$) in Figure 2.3.

- When drawing cleavage reactions, use brackets and delocalization; when drawing cleavage mechanisms, use localization.

- Chain branching increases the likelihood of cleavage at a branch point because a more stable carbocation can result.

- Examples of fragmentation to form resonance-stabilized cations.
  1. Alkenes ionize and frequently undergo fragmentations that yield resonance-stabilized allylic cations.

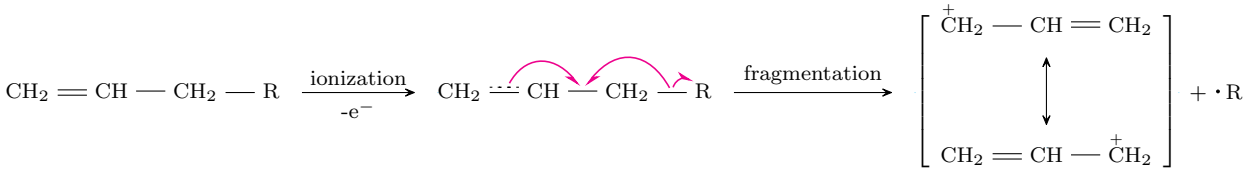


Figure 2.5: Resonance fragmentation: Alkenes.

2. Carbon-carbon bonds next to an atom with a lone pair usually break readily because the resulting carbocation is resonance stabilized.

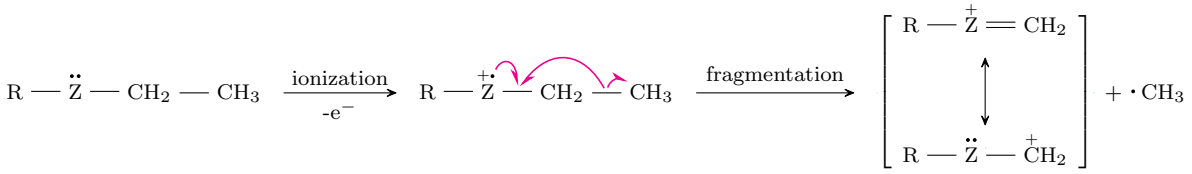



Figure 2.6: Resonance fragmentation: Lone pairs.

3. Carbon-carbon bonds next to the carbonyl group of an aldehyde or ketone break readily because resonance-stabilized ions called **acylium ions** are produced.

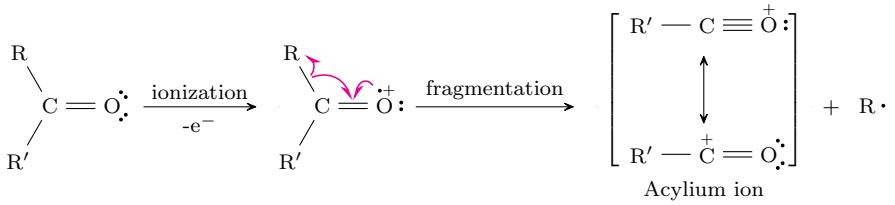
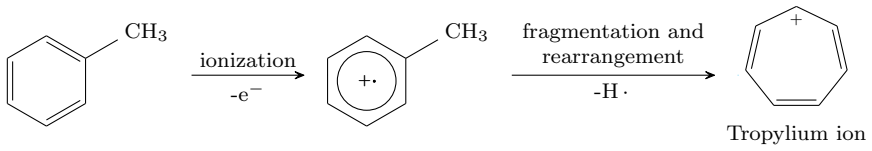


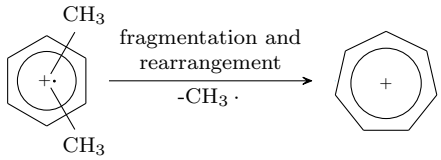

Figure 2.7: Resonance fragmentation: Carbonyls.

   – Note that either the C–R or the C–R′ bond could break.

4. Alkyl substituted benzenes ionize by loss of a $\pi$ electron and undergo loss of a hydrogen atom or methyl group to yield the relatively stable **tropylium ion**. This fragmentation gives a prominent peak (sometimes the base peak) at $m/z = 91$.




(a) Losing a hydrogen radical.




(b) Losing a methyl radical.

Figure 2.8: Resonance fragmentation: Alkyl-substituted benzene rings.

5. Monosubstituted benzenes with other than alkyl groups also ionize by loss of a $\pi$ electron and then lose their substituent to yield a phenyl cation with $m/z = 77$.

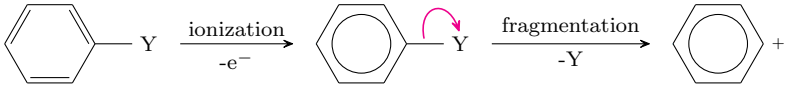



Figure 2.9: Resonance fragmentation: Monosubstituted benzene rings with nonalkyl groups.

   – Y is a halogen, nitro group, acyl group, nitrile group, etc.

- Fragmentation by cleavage of two bonds leads to a new radical cation and a neutral molecule.
  1. Alcohols frequently show a peak at $M^{+\cdot} - 18$. This corresponds to the loss of a molecule of water.

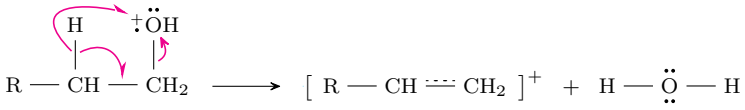


Figure 2.10: Fragmentation: Loss of $H_2O$.

  2. Carbonyl compounds with a hydrogen on their $\gamma$ carbon undergo a fragmentation called the McLafferty rearrangement.

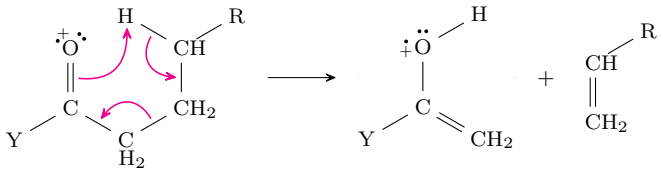


Figure 2.11: Fragmentation: McLafferty rearrangement.

     - Y may be an alkyl, hydride, ether, hydroxyl, etc.
  3. There are also often peaks corresponding to the elimination of other small molecules.

- Isotope effects:
  - The presence of $^{13}C$ will provide a small peak at $M^{+\cdot} + 1$.
  - "In the mass spectrum for a sample containing chlorine, we would expect to find peaks separated by two mass units, in an approximately 3 : 1 (75.5% : 24.5%) ratio for the molecular ion or any fragments that contain chlorine" (Solomons et al., 2016, p. 432).
  - "In the mass spectrum for a sample containing bromine, we would expect to find peaks separated by two mass units in an approximately 1 : 1 ratio (50.5% : 49.5% $^{79}Br$ to $^{81}Br$)" (Solomons et al., 2016, p. 433).
  - In a molecule containing two bromine atoms, for example, we'll see peaks at $M^{+\cdot}$, $M^{+\cdot} + 2$, and $M^{+\cdot} + 4$ in a 1 : 2 : 1 ratio.