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.
- 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.

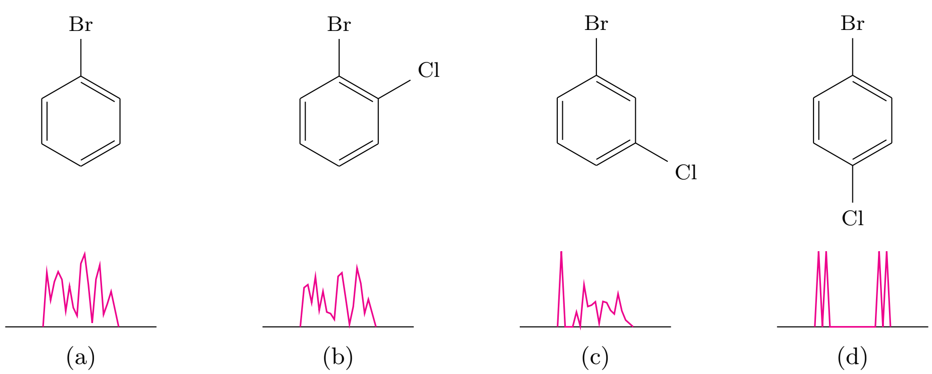


Figure 2.1: Benzenes in ^{1}H NMR spectroscopy.

  - 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 $J = 6 - 10\,\mathrm{Hz}$.
  - *trans*-alkenes typically have $J = 12 - 18\,\mathrm{Hz}$.
  - 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 Chapter 9: Nuclear Magnetic Resonance and Mass Spectroscopy

From Solomons et al. (2016).

- **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.

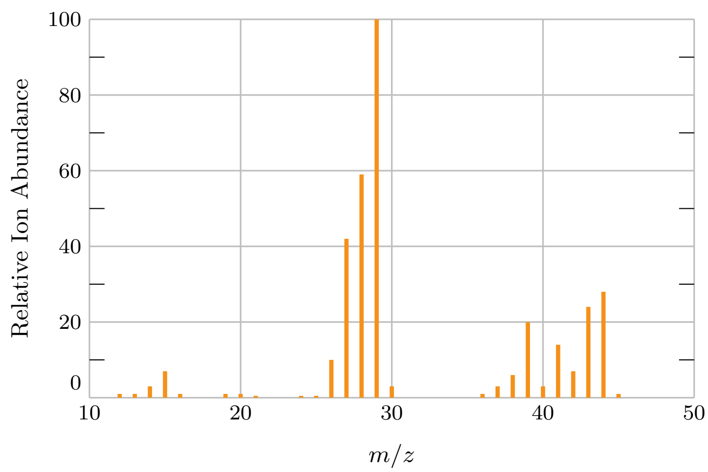


Figure 2.2: The mass spectrum of propane.

  - 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.
  - 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.
  - Usually an easily formed fragment of the original compound.
  - The base peak in Figure 2.2 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 6.7×10^3 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.

$[CH_3CH_2CH_3]^{\cdot +}$

(a) Propane.

$CH_3 - \overset{\cdot +}{\underset{\cdot\cdot}{O}}H$

(b) Methanol.

$CH_3 - \overset{\displaystyle CH_3 \atop |}{\underset{\cdot +}{N}} - CH_3$

(c) Trimethylamine.

$CH_2 \overset{\cdot +}{-} CHCH_2CH_3$

(d) 1-Butene.

Figure 2.3: 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 π electrons of alkenes and aromatic molecules, are held more loosely than the electrons of carbon-carbon and carbon-hydrogen σ bonds" (Solomons et al., 2016, p. 425).
  - Thus, "when a molecule contains oxygen, nitrogen, or a π bond, we place the odd electron and charge at a nitrogen, oxygen, halogen, or π 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 2.2.
- 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.

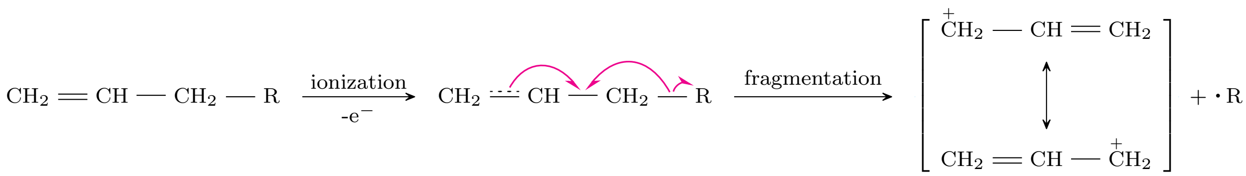


Figure 2.4: Resonance fragmentation: Alkenes.

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

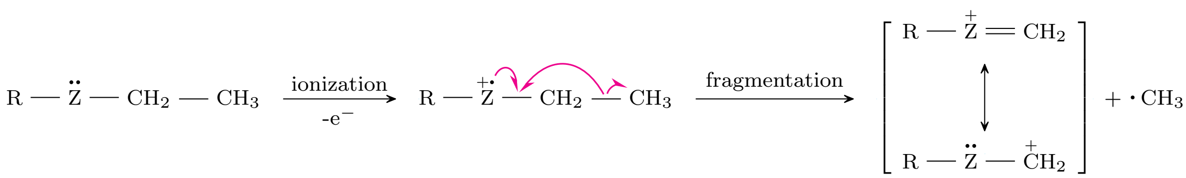
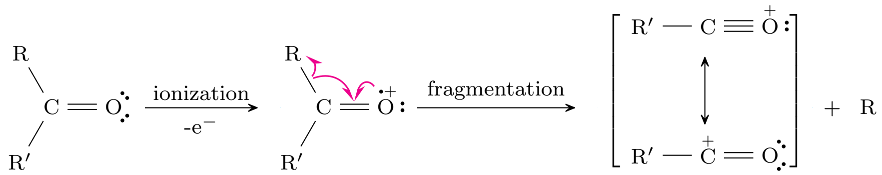


Figure 2.5: Resonance fragmentation: Lone pairs.

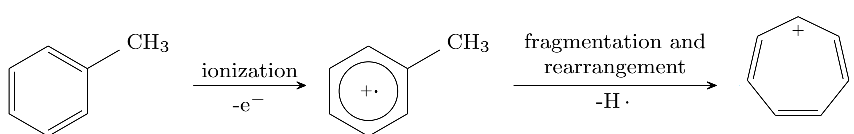
  3. Carbon-carbon bonds next to the carbonyl group of an aldehyde or ketone break readily because resonance-stabilized ions called **acylium ions** are produced.



Acylium ion

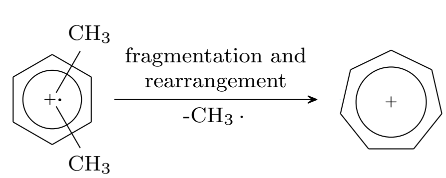
Figure 2.6: Resonance fragmentation: Carbonyls.

     – Note that either the C−R or the C−R′ bond could break.
  4. Alkyl substituted benzenes ionize by loss of a π 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 $m/z = 91$.



Tropylium ion

(a) Losing a hydrogen radical.



(b) Losing a methyl radical.

Figure 2.7: Resonance fragmentation: Alkyl-substituted benzene rings.

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

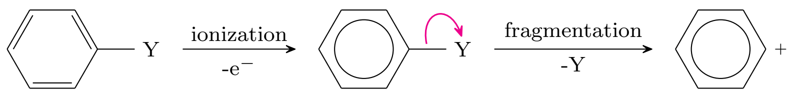


Figure 2.8: Resonance fragmentation: Monosubstituted benzene rings with nonalkyl groups.

   - 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.

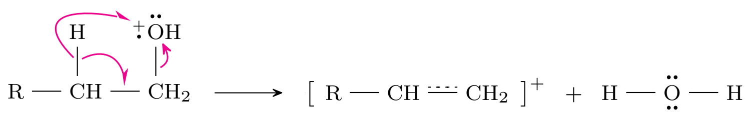


Figure 2.9: Fragmentation: Loss of H_2O.

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

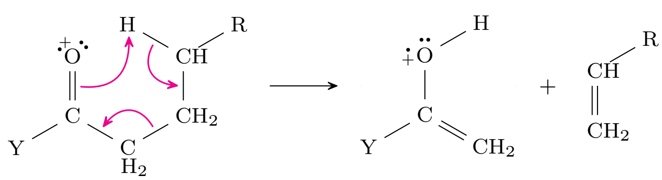


Figure 2.10: Fragmentation: McLafferty rearrangement.

   - 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.