Nuggets of Knowledge for Chapter 5 – Nuclear Magnetic Resonance Spectroscopy (NMR)
Chem 2310

I. Introduction to Spectroscopy

- What NMR does:
    - NMR spectroscopy exposes an organic compound to radio waves in the presence of a strong magnetic field. The radio waves cause transitions in the energy levels of the nuclei of the atoms.
    - The process by which this gives us a spectrum is quite complex; in this class we will focus on interpretation of spectra rather than understanding how the instrument works.
- What information NMR gives us:
    - Because the change takes place in the nucleus, the spectrum gives us information about the atoms in the compound.
    - This information can then be used to deduce the structure of the compound.
- Types of atoms that can be used:
    - Only atoms with odd (rather than even) mass numbers can be detected by NMR.
    - The most common atoms used are ^{1}H, or proton NMR, and ^{13}C NMR, since these atoms are the most common in organic compounds.
    - Of these two, proton NMR is by far the most common, and when no atom is specified, it is assumed to be proton NMR.
- What a spectrum looks like:
    - The x-axis is written at the bottom of the spectrum, from right to left. In proton NMR, the range is usually 0-10 ppm (but is sometimes expanded to 0-13 ppm). In ^{13}C NMR, the range is much larger, from 0-250 ppm.
    - Each signal on the NMR spectrum is called a peak. A peak may be a single spike, or a cluster of spikes. Each peak has three characteristics:
        - Where it falls on the x-axis, which is called the chemical shift. This tells us something about what other atoms are nearby.
        - The area covered by the peak, which is called the integration. This tells us how many atoms are creating this peak.
        - The number of spikes in the peak, which is called the splitting. This tells us how many hydrogen atoms are next to the ones creating the peak.

- All three pieces of information for each peak must be used together. There are three levels of expertise that you will be expected to master.
    - Initially, you will learn to assign hydrogens in a known compound to peaks in a spectrum.
    - Then, you will learn to sketch the spectrum of a known compound by using its structure.
    - Finally, you will learn to deduce the structure of an unknown compound from its spectrum.

II. Distinguishing Equivalent Hydrogens

- When considering the structure of a compound (either to assign its hydrogen atoms to the peaks on a spectrum, or to sketch the spectrum), the first thing to consider is which of the hydrogen atoms are equivalent.
- When two (or more) hydrogen atoms are in the same environment – that is, they have the same nearby atoms and the same neighboring hydrogen atoms – they are said to be equivalent.
    - Equivalent hydrogen atoms generate identical NMR peaks which exactly overlap, giving just one peak with more area. The additional area is proportional to how many equivalent hydrogen atoms there are.
- Rules of thumb:
    - Hydrogen atoms on the same carbon are nearly always equivalent (exceptions include hydrogen atoms on carbon-carbon double bonds).
    - Hydrogen atoms on different carbon atoms are usually not equivalent (exceptions occur when there are repeated elements in a compound).
- More exact rule:
    - If two hydrogens could each be separately replaced by another atom (say, a chlorine), and the same new compound results, then they are equivalent.

III. Chemical Shift

- The “0” on the chemical shift scale is set by a reference compound, tetramethyl silane (usually referred to as TMS). Chemical shift refers to how far a peak is “shifted” from this value.
- Toward 0 is defined as upfield, while away from 0 is define as downfield.

- There are several factors which allow you to predict the relative positions of two peaks:
    - Number of hydrogen atoms on the same carbon: The more hydrogen atoms there are on the same carbon, the farther upfield the peak will be.
        - This is a relatively small effect, but can differentiate between a CH_3, CH_2, or CH that are otherwise similar.
    - Nearby electronegative atoms: If an electronegative atom such as nitrogen, oxygen, or a halogen is near the hydrogen atom, this will cause the peak to be shifted downfield.
        - This effect is quite strong next to the electronegative atom, but falls off quickly the farther away the hydrogen atom is.
        - The more electronegative the atom, the further down the peak will be. Also, two electronegative atoms will shift the peak farther than one electronegative atom.
        - This is most useful for identifying hydrogens next to alcohols, amines, and alkyl halides, but can also be helpful for hydrogens next to ketones, aldehydes, esters, amides, and carboxylic acids.
    - Hybridization of the atom the hydrogen is attached to: Hydrogen atoms attached to sp^2 atoms are furthest downfield; hydrogens attached to sp^3 atoms are furthest upfield. Hydrogen atoms attached to sp atoms are in the middle.
        - This is most useful for identifying hydrogens attached to carbon-carbon double bonds.
    - Aromaticity: Hydrogens attached to aromatic rings are significantly further downfield than hydrogens attached to nonaromatic rings or chains.
        - This is a huge effect, and is very useful for identifying aromatic compounds.
    - Hydrogen bonding: The degree of hydrogen bonding causes the hydrogen atoms involved to shift. This will be affected by the concentration of the sample as well as the identity of the compound, causing these hydrogen atoms to appear in quite a large range.
        - This makes alcohol, amine, and amide hydrogens difficult to identify, as they can be in different places in different spectra of the same compound.
        - This can also affect the width of the peak, sometime making these peaks wider than usual.
- When two sets of nonequivalent hydrogen atoms have very similar chemical shifts, their peaks may overlap. When it is not possible to clearly distinguish one peak from another, they are considered together, even though they aren't actually equivalent.

- This most often occurs when several CH_2 groups are next to each other, but not close to any electronegative atoms, aromatic rings, sp^2 hybridized carbons, etc.

- The following is a list of ranges where hydrogen atoms often appear in relationship to other atoms and bonds. These ranges are guidelines, not hard and fast rules.

range	description
0.5-2.0 ppm	H's unaffected by other factors
1.0-5.0 ppm	H's on alcohols and amines (sometimes broad)
2.0-2.5 ppm	H's next to C=O's
2.5-3.0 ppm	H's next to amines
2.0-3.0 ppm	H's on C's next to aromatic rings
3.0-4.0 ppm	H's on carbons next to O or halogens
4.5-6.5 ppm	H's on C=C
6.5-8.5 ppm	H's on aromatic rings
7.5-9.5 ppm	H's on amides (sometimes broad)
9.0-11.0 ppm	H's on aldehydes
9.0-13.0 ppm	H's on carboxylic acids (often very broad)

- Chemical shifts that stand out include:
  - hydrogens on aromatic rings (around 7 ppm)
  - hydrogens on carbon-carbon double bonds (4-6 ppm)
  - carboxylic acid and aldehyde hydrogens (9-11 and 9-13 ppm)
  - alcohol and amine hydrogens if broad

IV. Integration

- When two hydrogen atoms are in exactly the same environment, they produce the same peak, and are said to be equivalent. The area under the peak is proportional to the number of hydrogen atoms that are contributing to that peak.

- The area under a peak can be computed mathematically and shown as the integration line on the spectrum.

  - The height of the peak (how tall it is) is not significant. A peak may be tall and thin, or broad and short, but still have the same area.

- The integration only has meaning when comparing two different peaks. The ratio of the integration of the two peaks gives the ratio of the number of hydrogen atoms giving rise to those peaks.

- The ratio of hydrogen atoms does not give the actual number of hydrogen atoms; for example, a ratio of 1:3 could be 1 and 3, or 2 and 6, or 3 and 9. The actual number must be determined from the structure of the compound.

- To compare the integration of the peaks in a spectrum, measure how far the line rises from where the peak begins to where it ends. It is helpful to extend the line horizontally with a ruler, then measure in mm.

V. Spin-spin Splitting

- When a hydrogen atom or set of equivalent hydrogen atoms is isolated from any other hydrogen atoms, its peak occurs as a single spike, called a singlet.

- When hydrogen atom or a set of equivalent hydrogen atoms has one or more hydrogen atoms that are not equivalent located one carbon away, they are said to be neighbors. This causes both peaks to be split into a cluster of spikes.

- Hydrogen atoms that are neighbors to each other are said to be splitting each other; they are also said to be coupled to each other.

    - The distance between the spikes will be the same for each group of hydrogen atoms that are coupled – it is called the coupling constant.

- The number of spikes in a peak is equal to the original spike plus one for each neighboring hydrogen atom.

    - A set of hydrogen atoms with one neighbor will be a doublet. The spikes will be approximately equal in height.

    - A set of hydrogen atoms with two neighbors will be a triplet. The middle spike will be about twice as high as the two outside spikes.

    - A set of hydrogen atoms with three neighbors will be a quartet. The two middle spikes will be about three times as high as the two outside spikes.

    - A set of hydrogen atoms with four neighbors will be a quintet. The spikes will have a 1:3:5:3:1 ratio of height.

    - A set of hydrogen atoms with five or more neighbors is called a multiplet, and the number of peaks is given in parenthesis, as in multiplet (6). The outside peaks are often so small they can't be seen, so it isn't always easy to tell how many there are.

- When two peaks are coupled together and also have chemical shifts that are close to each other, they appear to lean toward each other; that is, the spikes nearest each other get slightly taller.

- When two sets of hydrogen atoms are not equivalent, but the chemical shifts are so similar that their peaks overlap, the splitting is usually impossible to determine. In this case, it is simply labeled as a multiplet, with no number.

- The regular rules about neighbors get more complicated when a C=C is involved. The reason for this is that triplets, quartets, and so on are the result of two or more overlapping doublets. These doublets overlap because the coupling constants are equal. With C=C, the coupling constants are not equal, so the doublets separate out. This can be called complex splitting.

- Hydrogen atoms attached to oxygen or nitrogen do not usually participate in splitting with other hydrogen atoms. Rapid changes in hydrogen bonding causes the splitting to average out. It is possible to see this splitting if the sample is very dilute, and no water is present, so that very little hydrogen bonding occurs.

VI. Deuterium in NMR

- The most common isotope of hydrogen is ^{1}H, on which proton NMR is based. Deuterium, or ^{2}H, is a less common isotope of hydrogen, and is commonly designated by the symbol D. Like all isotopes, hydrogen and deuterium have similar chemical behavior. They form the same number of bonds, etc.

    - Deuterium is useful in NMR because it has a mass of 2, and therefore doesn't show up on an NMR spectrum.

    - If the compound you are taking an NMR of contains deuterium atoms, they will not appear on the NMR spectrum. They will not split regular hydrogen atoms, either.

- In order to prepare a sample for taking an NMR spectrum, it must be diluted by dissolving it in a solvent. If the solvent contained regular hydrogen atoms, its NMR spectrum would overwhelm the spectrum of the compound dissolved in it. To solve this problem, the solvents which are used have had all of the hydrogen atoms replaced by deuterium. These are called deuterated solvents.

    - The most common deuterated solvent is deuterated chloroform, $CDCl_3$. It will dissolve nonpolar and moderately polar compounds.

    - For polar compounds, deuterated dimethyl sulfoxide, DMSO-d_6, is used. It is more expensive, and more difficult to use because it easily absorbs water from the air.

- Deuterated solvents are never completely pure; they always contain a small amount of compounds with the regular type of hydrogen. These impurities show up as small peaks on the NMR spectrum. It is important to know what solvent has been used to take the spectrum so that you can eliminate these peaks from consideration as part of the compound.

    - $CHCl_3$ appears as a singlet at 7.25 ppm.

    - DMSO appears as a singlet at 2.5 ppm.

- The solvents or the compounds may also contain water, especially if the compound has the capacity to hydrogen bond. Water peaks must also be recognized and eliminated from

consideration as part of the compound. Because water undergoes extensive hydrogen bonding, it occurs in different places depending on the solvent you are using.

- When using $CDCl_3$ as the solvent, water appears as a singlet at 1.5 ppm. It is less common for spectra taken using this solvent to have a water peak, but it does happen.
- When using DMSO-d_6 as the solvent, water appears as a singlet at 3.35 ppm. Since the solvent itself absorbs water easily, most spectra taken using this solvent have a water peak.

- In addition to deuterated solvents, deuterated water, D_2O, is also useful in NMR. When a compound with an OH or NH is shaken with D_2O, the hydrogen atom in the compound is replaced by deuterium. This has the effect of removing this peak from the spectrum. This is often called D_2O exchange.
  - By comparing a spectrum taken before and after using D_2O, you can look for the peak that disappeared – that will be the OH or NH peak.
  - D_2O is also contaminated with DHO and H_2O, which appear at around 3.35 ppm, often a large peak.

VII. Carbon-13 NMR

- Carbon-13 NMR is not as useful as proton NMR. This is because only 1% of the carbon atoms in a compound are ^{13}C; the rest are ^{12}C, which does not appear on an NMR spectrum. This causes several consequences.
  - More concentrated samples are needed, or a longer time is needed to take a spectrum. A proton NMR takes about 10 seconds to run; a ^{13}C NMR can take anywhere from 2 hours to 24 hours to run, depending on the concentration of the sample.
  - The spectrum will contain more noise, making it more difficult to distinguish important peaks.

- Chemical shifts range from about 0-250 ppm.
  - 0-80 ppm: sp^3 carbon atoms
  - 65-85 ppm: carbon atoms triple bonded to carbon atoms
  - 100-160 ppm C=C in alkenes and aromatic rings
  - 110-130 ppm carbon atoms triple bonded to nitrogen atoms
  - 160-220 ppm C=O

- Integration is affected by the number of hydrogen atoms attached to the carbon, rather than just the number of carbon atoms creating the signal, so an integration line is not used.
    - CH_3's are tallest, CH_2's are next, then CH's, and finally C's with no hydrogens, which are very short and often hard to distinguish.
- Splitting between carbon atoms almost never occurs, because two ^{13}C atoms are almost never found in the same compound, let alone next to each other.
    - Splitting does occur between carbon and hydrogen atoms. However, this usually creates so much overlapping that steps are taking to eliminate this – this is called a proton-decoupled ^{13}C spectrum, and is the most common kind.
- The most useful piece of information that can be determined from a ^{13}C NMR spectrum is the number of non-equivalent carbon atoms in the compound. This can help to distinguish compounds which are symmetrical from those that aren't, for example.
- Deuterated chloroform is the most common solvent used. It gives a small triplet at 78 ppm.