Week 1

Review and Intro to NMR

1.1 Introduction and Review

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1.2 Chapter 9: Nuclear Magnetic Resonance and Mass Spectroscopy

From Solomons et al. (2016).

- **Nuclear magnetic resonance spectrum**: A graph that shows the characteristic energy absorption frequencies and intensities for a sample in a magnetic field. *Also known as* **NMR spectrum**.

- The chemical shift of a signal gives important clues about molecular structure.

Type of Proton	Chemical Shift (δ, ppm)	Type of Proton	Chemical Shift (δ, ppm)
1° Alkyl, RCH_3	0.8–1.2	Alkyl bromide, RCH_2Br	3.4–3.6
2° Alkyl, RCH_2R	1.2–1.5	Alkyl chloride, RCH_2Cl	3.6–3.8
3° Alkyl, R_3CH	1.4–1.8	Vinylic, $R_2C=CH_2$	4.6–5.0
Allylic, $R_2C=CR-CH_3$	1.6–1.9	Vinylic, $R_2C=CRH$	5.2–5.7
Ketone, $RCOCH_3$	2.1–2.6	Aromatic, ArH	6.0–8.5
Benzylic, $ArCH_3$	2.2–2.5	Aldehyde, RCOH	9.5–10.5
Acetylenic, $RC\equiv CH$	2.5–3.1	Alcohol hydroxyl, ROH	0.5–6.0[*]
Alkyl iodide, RCH_2I	3.1–3.3	Amino, $R-NH_2$	1.0–5.0[*]
Ether, $ROCH_2R$	3.3–3.9	Phenolic, ArOH	4.5–7.7[*]
Alcohol, $HOCH_2R$	3.3–4.0	Carboxylic, RCOOH	10–13[*]

[*]The chemical shifts of these protons vary in different solvents and with temperature and concentration.

Table 1.1: Approximate proton chemical shifts.

- "In ^{13}C NMR spectroscopy, signal area is not relevant in routine analyses" (Solomons et al., 2016, p. 396).

- **Coupling**: The magnetic effect of nonequivalent hydrogen atoms that are within 2 or 3 bonds of the hydrogens producing the signal that splits individual **signals** into multiple **peaks**. *Also known as* **signal splitting**, **signal multiplicity**.

- **Vicinal** (hydrogens): Hydrogens on adjacent carbons.

- **Geminal** (hydrogens): Hydrogens bonded to the same carbon.

  - Coupling occurs between geminal hydrogens in chiral/conformationally restricted molecules, specifically diastereotopic hydrogens.

- Interpreting NMR spectra:

  1. Count the number of signals in the spectrum to determine how many distinct proton environments there are in the molecule.
  2. Use chemical shift tables (such as Table 1.1) to correlate the chemical shifts of the signals with possible structural environments.
  3. Determine the relative area of each signal, as compared with the area of other signals, as an indication of the relative number of protons producing the signal.
  4. Interpret the splitting pattern for each signal to determine how many hydrogen atoms are present on carbon atoms adjacent to those producing the signal and sketch possible molecular fragments.
  5. Join the fragments to make a molecule in a fashion that is consistent with the data.

- The external magnetic field causes the σ (and π, if applicable) electrons in the viscinity of each proton to circulate, producing a small local magnetic field that can serve to either increase or decrease the external magnetic field experienced by the proton.

  - Increasing the effective field causes a larger chemical shift (it takes a higher energy photon/less magnetic field to induce a spin flip).
  - Decreasing the effective field causes a smaller chemical shift (it takes less energy/more magnetic field to induce a spin flip).

- **Shielded** (proton): A proton for which the induced local magnetic field opposes the external magnetic field to a relatively large degree.

- **Deshielded** (proton): A proton for which the induced local magnetic field opposes the external magnetic field to a relatively small degree (or even reinforces the external magnetic field).

  - For example, the π electrons of benzene circulate in such a way that the external magnetic field at the aromatic hydrogens is *augmented*.

- "Chemically equivalent protons are chemical shift equivalent in ^{1}H NMR spectra" (Solomons et al., 2016, p. 403).

- **Homotopic** (atoms): A set of atoms on some molecule such that replacing different ones with the same group gives the same compound.

  - For example, the six hydrogens of ethane are homotopic since replacing any of them with chlorine (for instance) gives the same compound: chloroethane.
  - Homotopic hydrogens are chemical shift equivalent.

- **Heterotopic** (atoms): A set of atoms on some molecule such that replacing different ones with the same group gives different compounds.

  - For example, in chloroethane, the CH_2 hydrogens are heterotopic to the CH_3 hydrogens since replacing the former yields 1,1-dichloroethane and replacing the latter yields 1,2-dichloroethane.
  - Heterotopic atoms are *not* chemical shift equivalent.

- **Enantiotopic** (atoms): Two atoms on some molecule such that replacing different atoms with the same group gives enantiomers.

  - Example: The CH_2 hydrogens of bromoethane.

– Enantiotopic atoms are chemical shift equivalent, except possibly when the compound in question is dissolved in a chiral solvent.

- **Diastereotopic** (atoms): Two atoms on some molecule such that replacing different atoms with the same group gives diastereomers.

  – Example: The CH_2 hydrogens of 2-butanol.

  – Diastereotopic atoms are *not* chemical shift equivalent (the asymmetry of the chirality center ensures this), except possibly by coincidence.

- **Coupling constant**: The separation in hertz between each peak of a signal. *Denoted by $\boldsymbol{J}$.*

  – On the order of $6 - -8\,\text{Hz}$.

- The reciprocity of coupling constants: The coupling constants of coupled atoms are the same.

  – In more complicated molecules, noting that two signals have the same coupling constant means the protons to which they correspond are likely coupled.

- **Dihedral angle** (between vicinal groups): The angle between viscinal groups as seen on the Newman projection through the bond connecting their parent atoms. *Denoted by $\boldsymbol{\phi}$.*

- **Karplus correlation**: The dependence of the coupling constant on dihedral angles.

  – Discovered by Martin Karplus of Harvard.

  – Useful for identifying cyclohexane conformations, and thus for determining which conformation is lower energy.

- An NMR spectrometer is a camera with a relatively slow shutter speed, in that it blurs pictures of rapidly occurring molecular processes.

- Examples of rapid processes that occur in organic molecules.

  – Chemical exchanges cause spin decoupling.

    ■ Consider ethanol.
    ■ Based on its structure, we'd predict that the signal corresponding to the hydroxyl proton would be a triplet.
    ■ However, it only appears as a triplet in very pure ethanol, where **chemical exchange** is slower due to the reduction in impurity-assisted chemical exchange catalysis common in normal ethanol.
    ■ Rapid chemical exchange means that neighboring protons don't have enough time to couple; thus, the hydroxyl proton appears as a singlet in relatively impure ethanol.
    ■ Occurs in the ^{1}H NMR spectra of alcohols, amines, and carboxylic acids; the signals of OH and NH protons are normally unsplit and broad.
    ■ "Protons that undergo rapid chemical exchange. . . can be easily detected by placing the compound in D_2O. The protons are rapidly replaced by deuterons, and the proton signal disappears from the spectrum" (Solomons et al., 2016, p. 413).

  – Conformational changes.

    ■ If, for example, we could isolate staggered bromoethane, the CH_3 hydrogens would be split into two signals, as the one anti-periplanar hydrogen is in a different chemical environment from its two geminal neighbors.
    ■ But we can't, so all three CH_3 hydrogens contribute to one peak.

- **Chemical exchange**: The swapping of identical atoms between molecules.

- **Exchangeable proton**: A proton that can engage in rapid chemical exchange.

- We now switch gears to ^{13}C NMR spectroscopy.

- Although ^{13}C does not occur naturally with nearly the same frequency as ^{12}C, it is important for its application to NMR spectroscopy.

- Simplifications from ^{1}H NMR spectroscopy.

  - Each distinct carbon produces one signal in a ^{13}C NMR spectrum.
  - Splitting of ^{13}C signals into multiple peaks is not observed in routine ^{13}C NMR spectra.

- No (technically just very little) carbon-carbon coupling since coupling only occurs for adjacent carbons and only 1 in 100 carbon atoms is ^{13}C (1.1 % natural abundance).

- Carbon-proton coupling can occur, however, splitting ^{13}C signals into multiplets.

- **Broadband proton decoupled** (spectrum): A ^{13}C NMR spectrum in which ^{1}H-^{13}C coupling is eliminated by choosing instrumental parameters to decouple the proton-carbon interactions. *Also known as* **BB proton decoupled**.
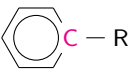
- Shielding and deshielding works the same way.

Type of Proton	Chemical Shift (δ, ppm)
1° Alkyl, RCH_3	0–40
2° Alkyl, RCH_2R	10–50
3° Alkyl, RCHR_2	15–50
Alkyl halide or amine, R_3CX (X = Cl, Br, NR$'_2$)	10–65
Alcohol or ether, R_3COR'	50–90
Alkyne, RC≡R$'$	60–90
Alkene, $R_2C=R'$	100–170
Aryl, C − R	100–170
Nitrile, RC≡N	120–130
Amide, RCONR$'_2$	150–180
Carboxylic acid or ester, RCOOR$'$	160–185
Aldehyde or ketone, RCOR$'$	182–215

Table 1.2: Approximate carbon-13 chemical shifts.

- In addition to the TMS peak, ^{13}C spectra have a $CDCl_3$ solvent peak at δ 77.

- **DEPT ^{13}C NMR spectrum**: A ^{13}C NMR spectrum that indicates how many hydrogen atoms are bonded to each carbon, while also providing the chemical shift information contained in a broadband proton-decoupled ^{13}C NMR spectrum. *Also known as* **distortionless enhancement by polarization transfer**.