# WILEY Organic Chemistry Third Edition

David Klein

#### **Chapter 15** Nuclear Magnetic Resonance Spectroscopy

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- Nuclear Magnetic Resonance (NMR) spectroscopy may be the most powerful method of gaining structural information about organic compounds
- **NMR** involves an interaction between electromagnetic radiation (light) and the **nucleus** of an atom
  - We will focus on C and H nuclei for analysis of organic compounds, for obvious reasons
  - The structure (connectivity) of a molecule affects how the radiation interacts with each nucleus in the molecule

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- Protons and neutrons in a nucleus behave as if they are spinning
- If an atom has an odd number of protons and/or odd number of neutrons, it will have net nuclear spin
- Examples:  ${}^{1}H$ ,  ${}^{13}C$ ,  ${}^{15}N$ ,  ${}^{19}F$ , and  ${}^{31}P$ .
- The spinning charge in the nucleus creates a **magnetic moment**
- Magnetic moment = magnetic field

• The **magnetic moment** exists perpendicular to the axis of nuclear spin



 If the normally disordered magnetic moments of atoms are exposed to an external magnetic field (B<sub>0</sub>), their magnetic moments will align with the field, or against the field:



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- $\beta$  spin state = opposing B<sub>0</sub>, higher energy spin state
- $\alpha$  spin state = aligned with B<sub>0</sub>, lower energy spin state



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• When an atom with an  $\alpha$  spin state is exposed to radio waves with just the right energy ( $\Delta E$ ), the **photons are absorbed** and **spin flips** to the  $\beta$  spin state





• The stronger the magnetic field, the greater the energy gap

**B**<sub>0</sub> causes electrons to circulate, inducing an opposing magnetic field (diamagnetism)

Nuclei then experience less B<sub>0</sub>, and are said to be shielded, requiring less energy to spin flip

Nuclei surrounded by less electron density are said to be deshielded



- The amount of radio wave energy necessary for the  $\alpha \rightarrow \beta$  energy transition depends on the electronic environment for the atom
- When the  $\alpha$  spins are flipped to  $\beta$  spins, **energy is absorbed**, and the atoms are said to be in **resonance**
- The use of the term, "resonance" here is totally different from when we are talking about electrons in molecular orbitals
- The amount of energy required for each <sup>1</sup>H to spin flip tells us about it's electronic environment, and thus the structure of the compound.

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- NMR requires a strong magnetic field (B<sub>0</sub>) and radio wave energy
- The strength of the magnetic field affects the energy gap



- The strong magnetic field is created when a high current is passed through a superconducting material at extremely low temperature (≈4 Kelvin)
- The greater the current, the greater the magnetic field
- **Pulsed Fourier-transform spectrometer**: a brief pulse of radio energy (all relevant wavelengths) is used to excite the sample
- Each of the atoms is excited and then relaxes, emitting energy
- The emitted energy is recorded as a **free induction decay (FID)**

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- The **FID** contains all of the information for each atom
- A mathematical treatment called a Fourier-transform separates the signals so an individual signal can be observed for each atom that was excited
- Often multiple FIDs are taken and averaged together
- Before analysis, NMR samples must be prepared neat or in a liquid solution (deuterated solvent) and placed in a small NMR tube
- The sample is placed into the magnetic field and the tube is spun at a high rate to average magnetic field variations or tube imperfections

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Deuterated solvents must be used (no H's)



Sample tube spins within the probe coils in the hollow bore at the center of the magnet.

Radio frequency (RF) generator and computer operating console.

Fourier transformation of the signal occurs in the computer.

the sample is generally at room temp when collecting the HNMR spectrum

#### 15.3 Characteristics of a <sup>1</sup>H NMR Spectrum

- NMR spectra contain a lot of structural information
  - Number of signals
  - Signal location (chemical shift)
  - Signal intensity (area under the signal)
  - Signal shape (splitting pattern)



- The number of signals in a 1H NMR spectrum indicates the number of different kinds of protons in a compound
- Identical protons are **chemically equivalent**. Such protons fall into the category of being either **homotopic** or **enantiotopic**
- Homotopic protons: if the molecule has an axis of rotational symmetry that allows one proton to be rotated onto the other without changing the molecule



• Another test for homotopic protons is to replace the protons one at a time with another atom



• If the resulting compounds are identical, then the protons that you replaced are homotopic

• Enantiotopic protons: if the molecule has a plane of reflection that makes one proton the mirror image of the other



- The replacement test is universal
- It will work to identify any equivalents protons whether they are homotopic or enantiotopic



• If the resulting compounds are enantiomers, then the protons that you replaced are enantiotopic

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- To determine if protons are equivalent, look for rotational symmetry.
- If none is found, then look for a plane of symmetry



• The replacement test produces diastereomers:



- These protons are called **diastereotopic**, and not chemically equivalent
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- If the protons are neither homotopic nor enantiotopic, then the are NOT chemically equivalent
- Consider the indicated H's below, in 2-butanol:



These protons cannot be interchanged by rotational symmetry or reflectional symmetry

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- There are some shortcuts you can take to identify how many signals you should see in the <sup>1</sup>H NMR
  - The 2 protons on a CH<sub>2</sub> group will be equivalent if there are NO chirality centers in the molecule
  - 2. The 2 protons on a  $CH_2$  group will NOT be equivalent if there is a chirality center in the molecule



- There are some shortcuts you can take to identify how many signals you should see in the <sup>1</sup>H NMR
  - 3. The 3 protons on any methyl group will always be equivalent to each other
  - 4. Multiple protons are equivalent if they can be interchanged through either a rotation or mirror plane

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#### 15.4 Variable Temperature NMR

Recall that cyclohexane chairs have 6 equatorial and 6 axial protons



- the axial and equitorial protons have different electronic environments
- Technically, there are two types of protons here, but only one signal is observed in the 1H NMR

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#### 15.4 Variable Temperature NMR

• At room temperature, the chair interconversion occurs rapidly



- The NMR is not fast enough to see the individual structures, so the average is observed (one signal)
- If the temperature was reduced to -100 °C, ring flipping is slow enough to observe two signals

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 In many NMR solvents, 1% TMS is added as an internal standard. The frequency of the protons in TMS is lower than that observed for most organic compounds



• The shift for a proton signal is calculated as a comparison to TMS

 $\delta = \frac{\text{observed Shift from TMS in hertz}}{\text{operating frequency of the instrument in hertz}}$ 

• For benzene on a  $\delta = \frac{2181 \text{ Hz}}{300 \text{ MHz instrument}} = 7.27 \times 10^{-6}$ 

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• The shift for a proton signal is calculated as a comparison to TMS

 $\delta = \frac{\text{observed Shift from TMS in hertz}}{\text{operating frequency of the instrument in hertz}}$ 

• For benzene on a 60 MHz instrument

$$\delta = \frac{436 \text{ Hz}}{60 \times 10^6 \text{ Hz}} = 7.27 \times 10^{-6}$$

• The Hz of the signal is different in different instruments, but the shift relative to TMS ( $\delta$ ) is constant

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• The shift for a proton signal is calculated as a comparison to TMS

## $\delta = \frac{\text{observed Shift from TMS in hertz}}{\text{operating frequency of the instrument in hertz}}$

• The shift relative to TMS ( $\delta$ ) is a dimensionless number, because the Hz units cancel out

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- Units for  $\delta$  are often given as ppm (parts per million), which simply indicates that signals are reported as a fraction of the operating frequency of the spectrometer
- Most <sup>1</sup>H signals appear between 0-10 ppm

- Early NMRs analyzed samples at a constant energy over a range of magnetic field strengths
- low field strength = downfield
- high field strength = upfield
- Shielded protons required a stronger external magnetic field to be excited at the same energy as deshielded protons.



- Current NMRs analyze samples at a constant field strength over a range of energies
- Shielded protons have a smaller magnetic force acting on them, so they have smaller energy gaps and absorb lower energy radio waves



- Alkane protons generally give signals around 1-2 ppm
- Protons can be shifted downfield when nearby electronegative atoms cause deshielding.



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• To predict chemical shifts, start with the standard ppm for the type of proton (methyl, methylene, or methine)



• Use table 16.1 to adjust the ppm depending on proximity to certain function groups

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• The effect on beta protons is about one-fifth the effect on alpha protons

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• Handbooks, or tables found online at credible websites, can be used for functional groups beyond table 15.1



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#### 15.5 Chemical Shift – Anisotropic Effects

 When the electrons in a pi system are subjected to an external magnetic field, they circulate and produce a magnetic field, causing diamagnetic anisotropy



• **Diamagnetic anisotropy** means that different regions of localized space has different magnetic strengths



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• The result of the **diamagnetic anisotropy** effect is similar to deshielding for aromatic protons. More magnetic field means more energy required to spin-flip the proton(s)



• Aromatic protons appear in the neighborhood of 7 ppm.

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• The result of the **diamagnetic anisotropy** effect is similar to shielding for protons *on the inside of* the pi system



[14] Annulene

- protons outside the ring: appear at 8 ppm
- Protons inside the ring: appear at -1 ppm.

 It is necessary to be familiar with the ppm values of these common types of protons

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 Checkpoint
 15.10

TABLE 15.2 CHEMICAL SHIFTS FOR PROTONS IN DIFFERENT ELECTRONIC ENVIRONMENTS					
TYPE OF PROTON		CHEMICAL SHIFT ( $\delta$ )	TYPE OF PROTON		chemical shift (δ)
Methyl	R—C <mark>H₃</mark>	~0.9	Alkyl halide	R-C-X R	2–4
Methylene	)⊂H₂	~1.2	Alcohol	R—O— <mark>H</mark>	2–5
Methine	— <mark>сн</mark>	~1.7	Vinylic	<sup>H</sup>	4.5–6.5
Allylic	<i>∕</i> ≁ <sup>H</sup>	~2	Aryl	H	6.5–8
Alkynyl	R— <b>≕</b> — <b>H</b>	~2.5	Aldehyde	R H	~ 10
Aromatic methyl	CH3	~2.5	Carboxylic acid	R O H	~12

- The **integration** (area) under the peak quantifies the relative number of protons giving rise to a signal
- A computer will calculate the area of each peak representing that area with a **step-curve**



- The computer operator sets one of the peaks to a whole number to let it represent a number of protons
- The computer uses the integration ratios to set the values for the other peaks



- Integrations represent numbers of protons, so you must adjust the values to whole numbers
- If the integration of the first peak is doubled, the computer will adjust the others according to the ratio



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<sup>15-42</sup> 

- The **integrations** are relative quantities rather than an absolute count of the number of protons
- Symmetry can also affect integrations



 3-pentanone has two kinds of protons. The relative integration value of the two signals would be 2:3



• The molecular formula (C₅H<sub>10</sub>O) must be known in order to know that the **absolute ratio is actually 4:6**, and not 2:3



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• Multiplicity (splitting pattern): the number of peaks in a given signal



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- Multiplicity results from magnetic affects that protons have on each other
- Consider protons H<sub>a</sub> and H<sub>b</sub>



 Since protons align with or against the external magnetic field, so there will be two different magnetic environments for H<sub>a</sub>:



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- Consider an example where there are two protons on the adjacent carbon
- Here, there are three possible environments for H<sub>a</sub>





 Now, consider a scenario where H<sub>a</sub> is split by three neighboring H<sub>b</sub> atoms:





- Table 15.3 shows how the multiplicity trend continues
- By analyzing the splitting pattern of a signal in the <sup>1</sup>H NMR, you can determine the number of equivalent protons on adjacent carbons



- The trend in table 15.3 also allows us to predict splitting patterns
- When there are "n" number of neighboring protons that are chemically equivalent, there will be how the n+1 peaks in the signal



- Remember **three key rules** for splitting:
  - Equivalent protons can not split one another because they resonate together
  - 2. To split each other, protons must be within a 2 or 3 bond distance



- Remember three key rules
  - 3. The n+1 rule only applies to protons that are all equivalent
  - The splitting pattern observed for the proton shown below will be more complex than a simple triplet



- Complex splitting will be discussed later in this section
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- The degree to which a neighboring proton will couple to its neighbor is called a **coupling constant**, or **J value**
- The *J* value is the distance between peaks of a splitting pattern measured in units of Hz
- protons splitting each other will have the same coupling constant

 $J_{ab} = J_{ba}$ 



- Higher field strength instruments will give better resolution between peaks, because the coupling constant is a smaller percentage of the overall Hz available.
- 300 MHz spectrometer avoids overlapping of peaks (right), compared to the 60 MHz spectrometer (left)



- Sometimes recognizable splitting patterns will stand out in a spectrum
- An isolated ethyl group gives a triplet and a quartet



The triplet and quartet must have the same coupling constant if they are splitting each other



#### Not an ethyl group

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 A peak with an integration equal to 9 suggests the presence of a *tert*butyl group

- An isolated isopropyl group gives a doublet and a septet
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- Complex splitting results when a proton has two different kinds of neighboring protons
- In the molecule shown, H<sub>b</sub> is split into a quartet by H<sub>a</sub> and into a triplet by H<sub>c</sub>



If J<sub>ab</sub> is much greater than J<sub>bc</sub> then the signal will appear as a quartet of triplets



 Complex splitting results when a proton has two different kinds of neighboring protons

If J<sub>bc</sub> is much greater than J<sub>ab</sub>, the signal will appear as a triplet of quartets

 If J<sub>bc</sub> is similar to J<sub>ab</sub>, then several lines may overlap, and the signal is called a multiplet



Πa

H<sub>a</sub>



• Splitting is not observed for some protons. Consider ethanol



• The protons bonded to carbon split each other, but the hydroxyl proton is not split

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 The hydroxyl proton and other labile or exchangeable protons undergo rapid exchange with trace amounts of acid. Show a reasonable mechanism



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• Such exchange blurs the shielding/deshielding affect of the neighboring protons giving a singlet that is often broadened

## 15.9 Using <sup>1</sup>H NMR to Distinguish between Compounds

• The three molecules below might be difficult to distinguish by IR of MS.



 They are easily distinguished with <sup>1</sup>H NMR because they do not have the same # of protons.

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### 15.10 Analyzing a <sup>1</sup>H NMR Spectrum

- With a given formula and <sup>1</sup>H NMR spectrum, you can determine a molecule's structure by a 5-step process
  - **1.** Calculate the degree of unsaturation or hydrogen deficiency index (HDI).
  - 2. Consider the number of NMR signals and integration (gives clues about the symmetry in the molecule)
  - **3.** Analyze each signal, and draw fragments consistent with each signal
  - 4. Assemble the fragments into a complete structure
  - 5. Verify the proposed structure is consistent with all of the spectral data
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- Because <sup>1</sup>H is by far the most abundant isotope of hydrogen, <sup>1</sup>H NMR signals are generally strong
- <sup>13</sup>C only accounts for about 1% of carbon atoms in nature, so a sensitive receiver coil and/or concentrated NMR sample is needed
- In <sup>1</sup>H NMR, shift, splitting, and integration are important
- In <sup>13</sup>C NMR, only the number of signals and the chemical shift will be considered

- In <sup>13</sup>C NMR, the <sup>1</sup>H-<sup>13</sup>C splitting is often so complex that the spectrum is unreadable
- To elucidate the <sup>13</sup>C spectrum and make it easier to determine the total number of <sup>13</sup>C signals, <sup>13</sup>C NMR are generally **decoupled**
- In the vast majority of <sup>13</sup>C spectra, all of the signals are singlets



#### 15.12 Chemical Shifts in <sup>13</sup>C NMR

- Compared to <sup>1</sup>H, <sup>13</sup>C atoms require a different frequency of energy to excite (resonate)
- Compared to the standard TMS, <sup>13</sup>C NMR signals generally appear between 220 and 0 ppm
- Each signal in a <sup>13</sup>C NMR spectrum represents a unique type of carbon
- Planes and axes of symmetry can cause carbon atoms to be electronically equivalent

#### 15.12 Chemical Shifts in <sup>13</sup>C NMR

 Note how symmetry affect the number of <sup>13</sup>C signals for these compounds:



#### 15.12 Chemical Shifts in <sup>13</sup>C NMR

 Like <sup>1</sup>H signals, chemical shifts for <sup>13</sup>C signals are affected by shielding or deshielding



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#### 15.13 DEPT <sup>13</sup>C NMR Spectroscopy

- <sup>13</sup>C spectra generally give singlets that do not provide information about the number of hydrogen atoms attached to each carbon
- Distortionless Enhancement by Polarization Transfer (DEPT) <sup>13</sup>C
  NMR provides information the number of hydrogen atoms attached to each carbon
- DEPT-90: Only CH signals appear
- DEPT-135: CH<sub>3</sub> and CH give (+) signals, and CH<sub>2</sub> give (-) signals

#### 15.13 DEPT <sup>13</sup>C NMR Spectroscopy

- DEPT-90: Only CH signals appear
- DEPT-135: CH<sub>3</sub> and CH = (+) signals, CH<sub>2</sub> = (-) signals



• Practice with SkillBuilder 15.10

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15.13 Magnetic Resonance Imaging (MRI)

MRI (Magnetic Resonance Imaging) instruments are essentially <sup>1</sup>H

- The body is analyzed rather than a sample in an NMR tube
- Different tissues have different concentrations of protons.

NMR spectrometers

- The MRI gives a 3D image of different tissues.
- Radio waves and magnetic field are very mild, so no side effects are experienced



Chris Bjornberg/Photo Researchers

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