

Welcome to Organic II

Organic chemistry II, CHM 2211, section 2

Spring, 2008

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Tools for Structure Determination

Infrared Spectroscopy – Ch. 2 Nuclear Magnetic Resonance and Mass Spectrometry: Ch. 9

Identification of functional groups

Classical methods were “wet” chemistry

An alkene decolorizes bromine

An aldehyde gives a metallic silver mirror when treated with alkaline silver nitrate

Larger molecules are cleaved into small fragments, for example, by ozonolysis, and fragments identified

Modern methods are instrumental

1. Require much less sample
2. Can detect some functional groups when several are present
3. Fast
4. More accurate
5. Easily linked to data bases

Spectroscopy

Study of the interaction of energy with matter

When energy is applied to matter, it may be

1. Transmitted without change
2. Reflected without change
3. Absorbed
4. Emitted
5. Cause a chemical change

Spectroscopy is used to elucidate the structure of a molecule

◆ Infrared (IR) Spectroscopy (Chapter 2)

- Infrared energy causes bonds to stretch and bend
- Useful for identifying functional groups in a molecule

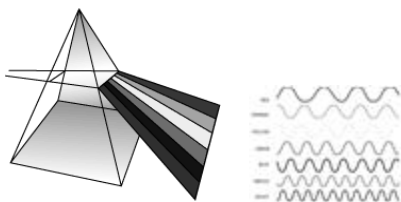
◆ Nuclear Magnetic Resonance (NMR)

- Energy applied in a strong magnetic field causes absorption by the nuclei of some elements (H and C-13)
- Used to identify connectivity of atoms in a molecule

◆ Mass Spectrometry (MS)

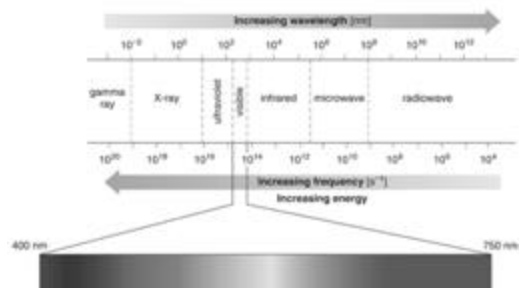
- Molecules are converted to ions
- The ions formed may remain intact (M^+), or they may fragment
- The mixture of ions is sorted by mass/charge ratio (m/z)
- Molecular weight and chemical formula may be derived from the unfragmented M^+ and $M+1$ ions
- Molecular structure may be deduced from the fragment ions

Light = travels in waves
Length of wave determines perceived color



Shorter wave length = higher frequency (more crests per second)

Light is only a small portion of the
Electromagnetic Spectrum



Basic Principle of Spectroscopy

- ◆ Energy in molecules is quantized
- ◆ Energy E is absorbed only when the frequency ν matches the Energy Gap
- ◆ $E = h\nu$
- ◆ $h = \text{Planck's constant } (1.58 \times 10^{-34} \text{ cal}\cdot\text{s})$



Molecular vibrations are quantized and fall in the infrared range

Regions of Organic Spectroscopy

- ◆ X-ray – collision with atoms produces patterns that can be analyzed with computers to get molecular shapes
- ◆ UV/VIS – determines spacing of electron levels, useful for conjugated molecules
- ◆ Infrared (IR) – determined by molecular vibrations, useful for functional groups
- ◆ Radiofrequencies (NMR) – Lowest energy, observes nuclear and electron spins, useful for specific environments of nuclei

Infrared Spectroscopy- overview

An Instrumental Method for Detecting Functional Groups

- ◆ Electromagnetic radiation in the infrared range is absorbed by a molecule at certain characteristic frequencies
 1. The bonds behave like tiny springs connecting the atoms
 2. As energy is absorbed by the bonds, they vibrate faster
 3. The bonds can absorb energy and vibrate faster only when the added energy is of a particular resonant frequency
 4. The frequencies of absorption are very characteristic of the type of bonds contained in the sample molecule

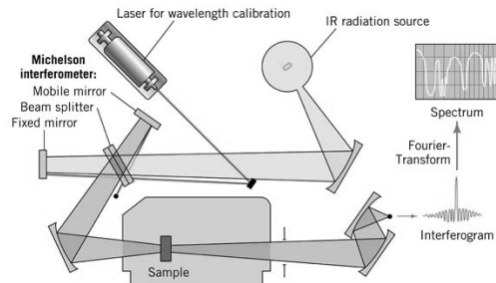
Infrared Spectrometer

Detects the frequencies absorbed by the sample molecule
Light of all IR frequencies is transmitted to the molecule and certain frequencies are absorbed
The absorption frequencies are specified as wavenumbers in units of reciprocal centimeters (cm^{-1})

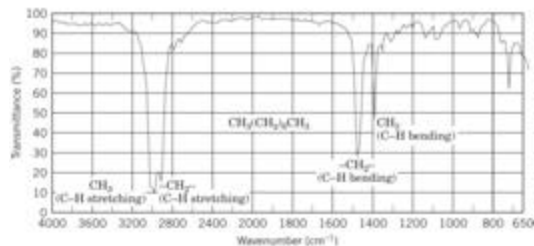
$$\bar{\nu} = \frac{1}{\lambda} \quad (\text{with } \lambda \text{ in cm})$$

- The spectrum is a plot of frequency on the horizontal axis versus strength of absorption on the vertical axis
- Higher wavenumbers (cm^{-1}) = more energy needed to stretch bonds

Schematic View of IR Spectrometer



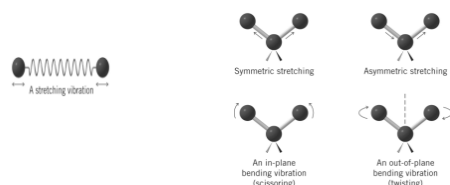
Example: IR of Octane



Higher energy

Lower energy

Various stretching and bending vibrations are induced by the absorption of infrared



The actual relative frequency of vibration can be predicted

Bonds with lighter atoms vibrate faster than those with heavier atoms

GROUP	BOND	FREQUENCY RANGE (CM ⁻¹)
Alkyl	C—H	2853–2962
Alcohol	O—H	3590–3650
Amine	N—H	3300–3500

Stronger bonds require more energy to stretch

BOND	FREQUENCY RANGE (CM ⁻¹)
C≡C	2100–2260
C≡N	2220–2260
C=C	1620–1680
C=O	1630–1780

C-C and C-O single bonds are less useful, but occur around 1000 cm⁻¹

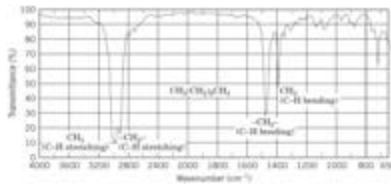
Two major application of IR

- ◆ Fingerprint for a molecule
 - The variety of bonds produces a mixture of vibrations and overtones which is often unique
- ◆ Specific functional groups
 - Generally only certain peaks are interpreted in the IR
 - Those peaks that are large and above 1400 cm⁻¹ are most valuable

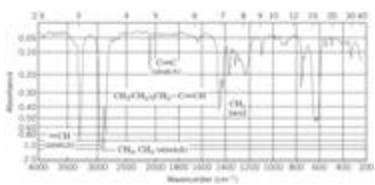
Hydrocarbons

- ◆ The C-H stretching region is from 2800-3300 cm⁻¹
- ◆ Characteristic of the type of C-H bond
- ◆ If C-H bond has more s character, it is shorter and stronger and vibrates at higher frequency
 - C-H bonds at sp centers appear about 3300 cm⁻¹
 - C-H bonds at sp² centers appear about 3080 cm⁻¹
 - C-H bonds at sp³ centers appear at about 2800-3000 cm⁻¹
- ◆ C-C bond stretching frequencies are only useful for multiple bonds
 - C-C double bonds give peaks at 1620-1680 cm⁻¹
 - C-C triple bonds give peaks at 2100-2260 cm⁻¹
 - These peaks are absent in symmetrical double and triple bonds

Octane

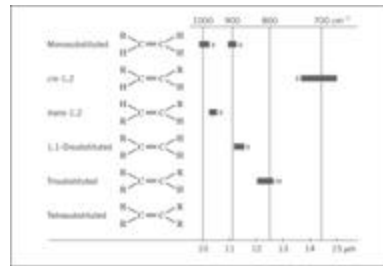


1-hexyne

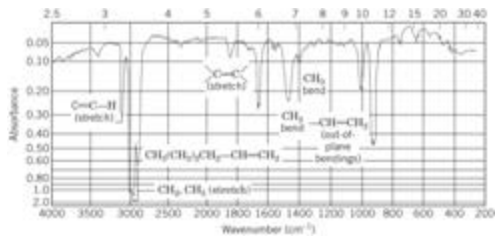


Alkenes

➔ The CH bending vibration peaks located at 600-1000 cm⁻¹ can be used to determine the substitution pattern of the double bond

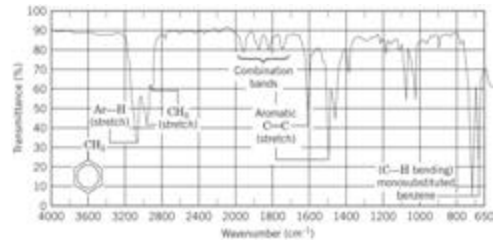


Example: 1-hexene



Aromatic Compounds

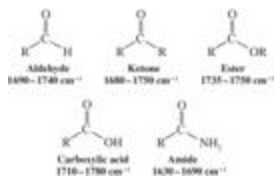
➔ The C-C bond stretching gives a set of characteristic sharp peaks between 1450-1600 cm⁻¹
 ➔ Substitution pattern shown between 650 and 1000 cm⁻¹



Carbonyl groups – very characteristic frequency

◆ carbonyl group gives a strong peak which occurs at 1630-1780 cm⁻¹

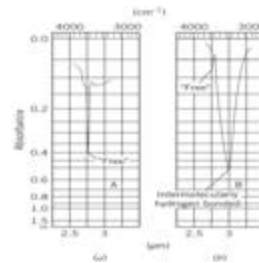
The exact location depends on the actual functional group



Alcohols

• The O-H stretching absorption is very characteristic

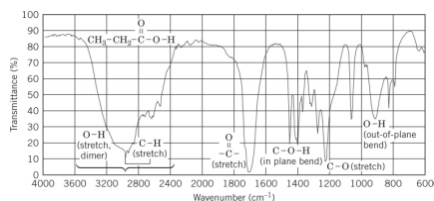
- In very dilute solutions, hydrogen bonding is absent and there is a very sharp peak at 3590-3650 cm⁻¹
- In concentrated solutions, the hydroxyl groups hydrogen bond to each other, giving a broad and large peak occurs at 3200-3550 cm⁻¹



Carboxylic Acids

The carbonyl peak at $1710-1780\text{ cm}^{-1}$ is very characteristic
The presence of both carbonyl and O-H stretching peaks is a good indication of the presence of a carboxylic acid

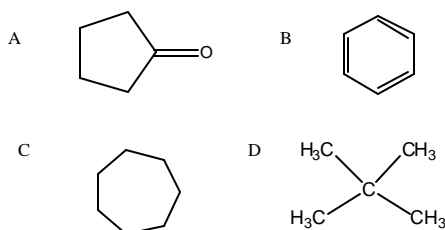
- Example: propanoic acid



Amines and Amides

- ◆ Dilute solution of 1° and 2° amines give sharp peaks at $3300-3500\text{ cm}^{-1}$ for the N-H stretching
 - 1° amines give two peaks
 - 2° amines give one peak
 - 3° have no N-H bonds and do not absorb in this region
- ◆ More concentrated solutions of amines have broader peaks
- ◆ Amides have amine N-H stretching peaks and a carbonyl peak

Which will have a strong absorption at 1730 cm^{-1} ?



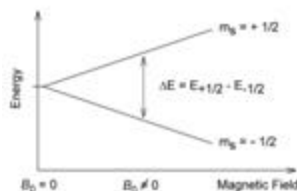
Six most useful IR frequencies

Frequency	Appearance	bond	Functional group
>3200	strong, broad	OH	Alcohol, carboxylic acid
>3200	medium	NH, spC-H	Amine, amides, terminal alkyne
~3100	weak to medium	sp ² C-H	alkene
2100-2300	sharp	Triple bond	Alkyne, nitrile
~1700	very strong, sharp	C=O	Ketone, aldehyde, acid, ester, amide
~1650	medium	C=C	Alkene, benzene ring

Region of $1000-700\text{ cm}^{-1}$ useful to identify substitution pattern of an alkene or substituted benzene ring

Nuclear Magnetic Resonance (NMR) Spectroscopy

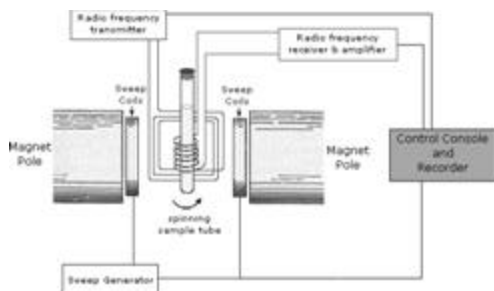
- ◆ The spinning nuclei of protons (^1H) and carbon-13 (^{13}C), and certain other elements and isotopes, behave as tiny bar magnets
- ◆ When placed in a magnetic field, the energies of two spin states become separated and we can do spectroscopy
- ◆ Spacings are tiny so absorb in radio frequency range
- ◆ Precise frequencies depends on the chemical environments



Nuclear Magnetic Resonance (NMR) Spectroscopy

- ◆ Continuous-Wave (CW) NMR Spectrometers
 - The older type of NMR spectrometer
 - The magnetic field is varied as the electromagnetic radiation is kept at a constant frequency
 - Different nuclei absorb the electromagnetic energy based on their chemical environment and produce peaks in different regions of the spectrum

Continuous-Wave (CW) NMR Spectrometer

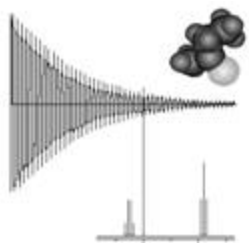


Scan by varying either the frequency or magnetic field

Fourier Transform (FT) NMR Spectrometers

- ◆ The sample is placed in a constant, very strong magnetic field
- ◆ The sample is irradiated with a short broad pulse of radio frequency energy that excites all nuclei at once
- ◆ The resulting signal contains information about all of the absorbing nuclei at once
- ◆ This signal is converted to a spectrum by a Fourier transformation
- ◆ FT NMR allows signal-averaging, which leads to enhancement of real spectral signals versus noise
- ◆ The strong, superconducting magnets used in FTNMR spectrometers lead to greater sensitivity and much higher resolution than continuous wave instruments

FT signal to conventional signal



Information from NMR

1. Number of signals
2. Intensity of each signal
3. Position of each signal
4. Splitting of each signal

Special effects such as long range molecular interactions or rate dependence may also be useful

Nuclear Magnetic Resonance Spectroscopy

Figure 15.15 An MRI image of the neck

An MRI instrument is especially useful for visualizing soft tissue. In 2002, 60 million MRI procedures were performed. The 2003 Nobel Prize in Physiology or Medicine was awarded to chemist Paul C. Lauterbur and physicist Sir Peter Mansfield for their contributions in developing magnetic resonance imaging.

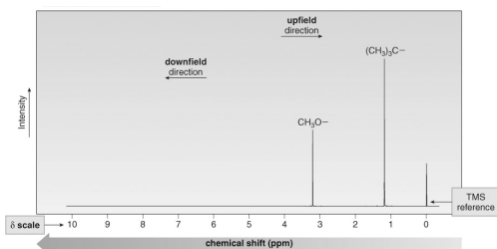


A: Spinal cord compression from a herniated disc
B: Spinal cord (would not be visualized with conventional X-rays)

Peak Positions in NMR Spectra – the Chemical Shift

- ◆ Nuclei in different chemical environments in a molecule will absorb at slightly different frequencies
- ◆ The position of the signals in the spectrum is called the “chemical shift”
- ◆ There are two reasons for differences in the magnetic environment for a proton
 1. The magnetic field generated by electrons circulating around the nucleus giving the signal
 2. Local magnetic fields generated by electrons elsewhere in the molecule

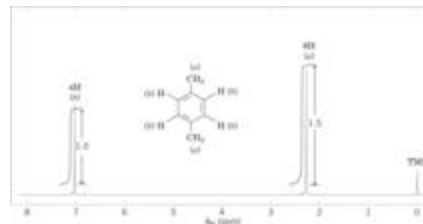
Proton NMR of Methyl t-butyl ether



Lower field
Deshielded

High field
Shielded

Proton NMR of 1,4-dimethylbenzene

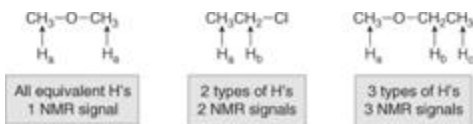


Lower field
Deshielded

High field
Shielded

Information

- Number of signals = number of unique H's
- Intensity of signal = proportional to the number of such H's.



Intensity ratios:

1:1

3:2

3:2:3

The Origin of NMR Signals

- The nuclei of certain elements and isotopes have spin states that are quantized
- ^1H has a spin quantum number $I = 1/2$ and has allowed spin states of $+1/2$ or $-1/2$
- Other nuclei with $I = 1/2$ are ^{13}C , ^{19}F and ^{31}P and these also respond to an external magnetic field
- Nuclei with $I = 0$ do not have spin (^{12}C and ^{16}O) and do not respond to an external magnetic field

How many 1H signals?

A. 1

B. 2

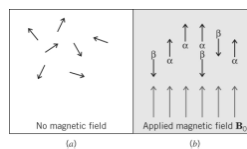
C. 3

D. 4

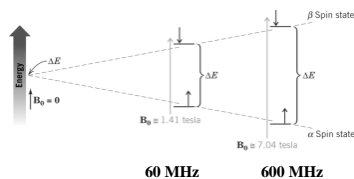
Same question for cyclohexene

The Origin of NMR Signals

- The nuclei of NMR-active nuclei behave like tiny bar magnets
- In the absence of an external magnetic field these bar magnets are randomly orientated
- In an external magnetic field they orient either with (a spin state) or against (b spin state) the magnetic field

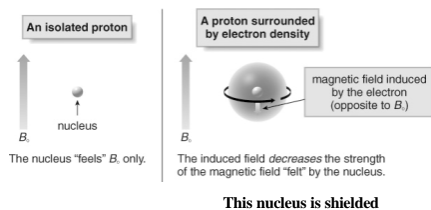


- Nuclei aligned with the magnetic field are lower in energy than those aligned against the field
- The nuclei aligned with the magnetic field can be flipped to align against it if the right amount of energy is added (ΔE)
- The amount of energy required depends on the strength of the external magnetic field
 - ➔ The stronger the external magnetic field, the higher the radio frequency energy required to flip the nuclear spin



Position of the Signal - Shielding and Deshielding

- ◆ Absorption frequency depends on the total magnetic field and therefore electron density around a nucleus
- ◆ High electron density around a nucleus *shields* the nucleus from the external magnetic field



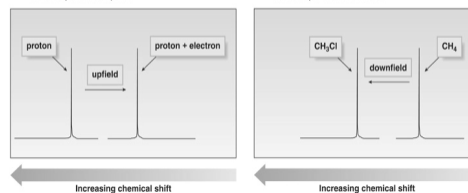
Shielding and Deshielding

- ◆ Shielding requires a higher magnetic field to bring the nucleus into resonance - the signals are upfield in the NMR spectrum
 - ➔ Lower electron density around a nucleus *deshields* the nucleus from the external magnetic field
 - ➔ Deshielding causes absorption of energy at lower frequencies - the signals are downfield in the NMR spectrum



Shielding and Deshielding

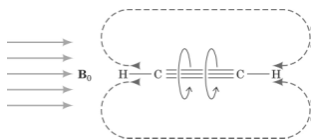
- (a) Shielding effects
- An electron shields the nucleus.
 - The absorption shifts upfield.
- (b) Deshielding effects
- Decreased electron density deshields a nucleus.
 - The absorption shifts downfield.



Electron withdrawing groups (Cl, O) pull electrons away, reduce the shielding, and thus shift signals downfield

Circulation of p electrons leads to a local induced magnetic field

- ◆ The induced field can reinforce or diminish the external field sensed by a proton (depending on the location of the proton), causing deshielding or shielding, respectively
- ◆ Alkene and aromatic ring hydrogens are deshielded by the circulation of p electrons.
- ◆ A terminal alkyne hydrogen is shielded by the circulation of p electrons.



◆ Position of signal – the Chemical Shift

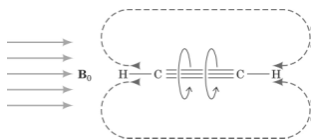
- ◆ Chemical shifts are measured in relation to the internal reference tetramethylsilane (TMS)
 - The protons of TMS are highly shielded, well away from other proton signals and a sharp single peak
 - TMS (tetramethylsilane) $\text{Si}(\text{CH}_3)_4$
- ◆ The δ scale for chemical shifts is independent of the magnetic field strength of the instrument (whereas the absolute frequency depends on field strength)

$$\delta = \frac{(\text{observed shift from TMS in hertz}) \times 10^6}{(\text{operating frequency of the instrument in hertz})}$$

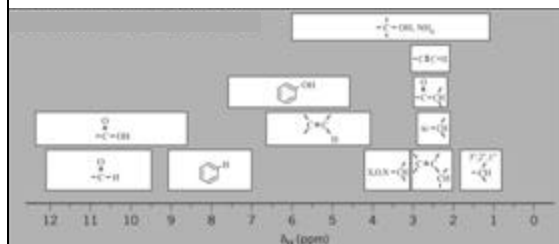
- ◆ Thus, the chemical shift in δ units for protons on benzene is the same whether a 60 MHz or 300 MHz instrument is used

Circulation of p electrons leads to a local induced magnetic field

- ◆ The induced field can reinforce or diminish the external field sensed by a proton (depending on the location of the proton), causing deshielding or shielding, respectively
- ◆ Alkene and aromatic ring hydrogens are deshielded by the circulation of p electrons.
- ◆ A terminal alkyne hydrogen is shielded by the circulation of p electrons.



Typical Range for ¹H NMR chemical shifts

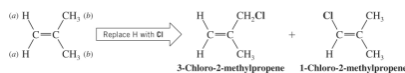


Closer Look at Equivalent and Nonequivalent Protons

- ◆ To predict the number of signals, must determine how many sets of protons are in unique environments

◆ Homotopic Hydrogens

- Hydrogens are chemically equivalent or homotopic if replacing each one in turn by the same group would lead to an identical compound



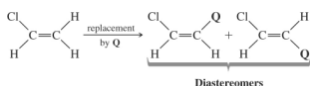
Enantiotopic Hydrogens

- ◆ If replacement of each of two hydrogens by some group leads to enantiomers, those hydrogens are enantiotopic
 - In the absence of a chiral influence, enantiotopic hydrogens have the same chemical shift and appear in the same signal



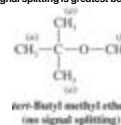
Diastereotopic Hydrogens

- ◆ If replacement of each of two hydrogens by some group leads to diastereomers, the hydrogens are diastereotopic
 - ★ Diastereotopic hydrogens have different chemical shifts and will give different signals



Signal Splitting: Spin-Spin Coupling

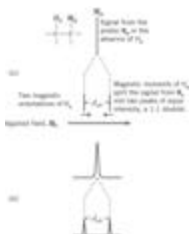
- ◆ The signal from a given proton will be split by the effect of magnetic fields associated with protons on adjacent carbons
- ◆ Characteristic peak patterns result from signal splitting that are related to the number of protons on adjacent carbons
 - ★ The effect of signal splitting is greatest between atoms separated by 3 or fewer bonds



- ★ Signal splitting is not observed between homotopic or enantiotopic protons (CH₃CH₃, no signal splitting)

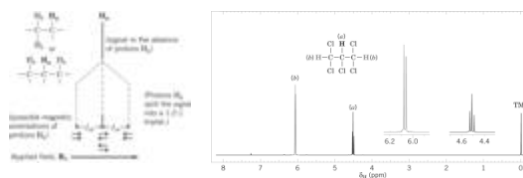
- ◆ Signal splitting occurs only when two sets of protons have different chemical shifts (i.e., are not chemical shift equivalent)

- ➔ The magnetic field sensed by a proton (H_a) being observed is affected by the magnetic moment of an adjacent proton (H_b)
 - * A proton (H_b) can be aligned with the magnetic field or against the magnetic field, resulting in two energy states for H_b .
 - * The observed proton (H_a) senses the two different magnetic moments of H_b as a slight change in the magnetic field; one magnetic moment reinforces the external field and one subtracts from it.
 - * The signal for H_a is split into a doublet with a 1:1 ratio of peak areas.
 - * The magnitude of the splitting is called the coupling constant J_{ab} and is measured in Hertz (Hz).

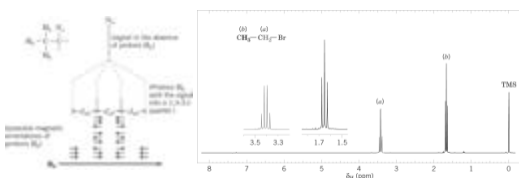


- When two adjacent protons H_b are coupled to H_a , there are four possible combinations of the magnetic moments for the two H_b s

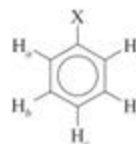
- ➔ Two of these combinations involve pairings of magnetic moments that cancel each other, causing no net displacement of signal
- ➔ One combination of magnetic moments reinforces and another subtracts from the applied magnetic field
- ➔ H_a is split into a triplet having a 1:2:1 ratio of signal areas



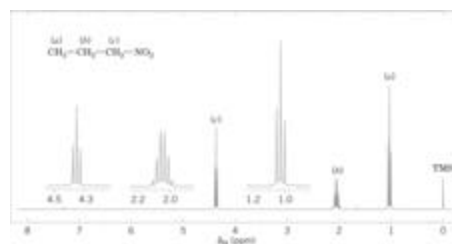
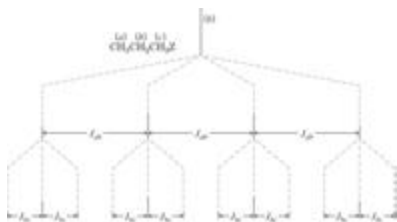
- ➔ When three adjacent protons are coupled to H_a , there are 10 possible combinations of the magnetic moments for the H_b s
- * Four unique orientations exist and so H_a is split into a quartet with intensities 1:4:6:4:1



- ➔ The general rule for splitting is that if there are n equivalent protons on adjacent atoms, these will split a signal into $n + 1$ peaks
- ➔ Coupled peaks have the same coupling constants J
 - * Comparison of coupling constants can help with the analysis of complex spectra
- ➔ Several factors complicate analysis of NMR spectra
 - * Peaks may overlap
 - * Spin-spin coupling can be long-range (i.e., more than 3 bonds)
- ➔ Splitting patterns in aromatic groups can be confusing
 - * A monosubstituted aromatic ring can appear as an apparent singlet or a complex pattern of peaks



- ➔ Much more complex splitting can occur when two sets of adjacent protons split a particular set of protons
- ➔ In the system below, H_a is split by two different sets of hydrogens: H_b and H_c
 - * Theoretically H_a could be split into a triplet of quartets (12 peaks) but this complexity is rarely seen
 - * The spectrum of 1-nitropropane shows splitting of H_a into only 6 peaks



High-Resolution Mass Spectrometry

- Low-resolution mass spectrometers measure m/z values to the nearest whole number
- High-resolution mass spectrometers measure m/z values to three or four decimal places
- The high accuracy of the molecular weight calculation allows accurate determination of the molecular formula of a fragment
- Example:

➔ One can accurately pick the molecular formula of a fragment with a nominal molecular weight of 32 using high-resolution MS



- The exact mass of certain nuclides is shown below

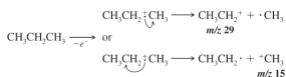
Isotope	Mass	Isotope	Mass
^1H	1.00783	^{19}F	18.9984
^2H	2.01410	^{35}S	31.9721
^{12}C	12.00000 (std)	^{37}S	33.9715
^{13}C	13.00336	^{39}S	33.9679
^{14}N	14.0031	^{40}Ca	34.9689
^{15}N	15.0001	^{42}Ca	36.9659
^{16}O	15.9949	^{81}Br	78.9183
^{17}O	16.9991	^{82}Br	80.9163
^{18}O	17.9992	^{127}I	126.9045

Fragmentation

- In EI mass spectrometry the molecular ion is highly energetic and can break apart (fragment)
- Fragmentation pathways are predictable and can be used to determine the structure of a molecule
- The processes that cause fragmentation are unimolecular
- The relative ion abundance is extremely important in predicting structures of fragments

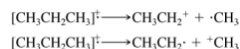
1. Fragmentation by Cleavage at a Single Bond

- Cleavage of a radical cation occurs to give a radical and a cation but only the cation is observable by MS
- The fragmentation proceeds to give mainly the most stable carbocations
 - ➔ In the spectrum of propane the peak at 29 is the base peak (most abundant) 100% and the peak at 15 is 5.6%

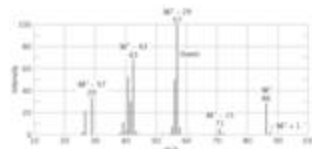


Writing the Fragmentation Equations

- The M^+ ion is usually formed by loss of one of its most loosely held electrons
- Nonbonding electrons on nitrogen and oxygen, and p electrons in double bonds are common locations for an electron to be lost (*i.e.*, where the remaining unshared electron in M^+ resides)
- In molecules with only C-C and C-H bonds, the location of the lone electron cannot be predicted and the formula is written to reflect this using brackets

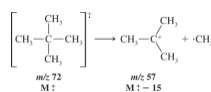
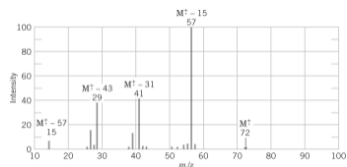


The spectrum of hexane



Spectrum of neopentane

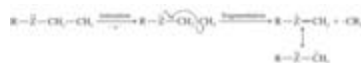
- Fragmentation of neopentane shows the propensity of cleavage to occur at a branch point leading to a relatively stable carbocation
- The formation of the 3° carbocation is so favored that almost no molecular ion is detected



- ◆ Carbocations stabilized by resonance are also formed preferentially
 - Alkenes fragment to give resonance-stabilized allylic carbocations

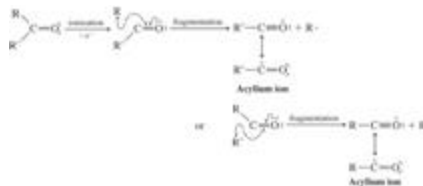


- ◆ Carbon-carbon bonds next to an atom with an unshared electron pair break readily to yield a resonance stabilized carbocation
 - Z=N, O, or S R may be H

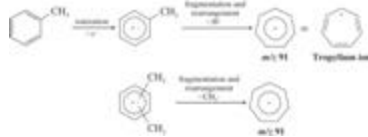


where Z = N, O, or S, R may also be H

- ◆ Carbon-carbon bonds next to carbonyl groups fragment readily to yield resonance stabilized acylium ions



- ◆ Alkyl substituted benzenes often lose a hydrogen or alkyl group to yield the relatively stable tropylium ion

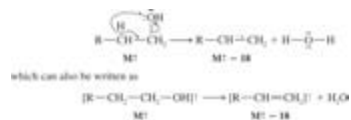


- ◆ Other substituted benzenes usually lose their substituents to yield a phenyl cation



- Fragmentation by Cleavage of 2 Bonds

- ◆ The products are a new radical cation and a neutral molecule
- ◆ Alcohols usually show an M⁺-18 peak from loss of water



- ◆ Cycloalkenes can undergo a retro-Diels Alder reaction (section 13.11) to yield an alkadienyl radical cation



- ◆ Carbonyl compounds can undergo a *McLafferty Rearrangement*
- * Y may be R, H, OH, OR etc.

