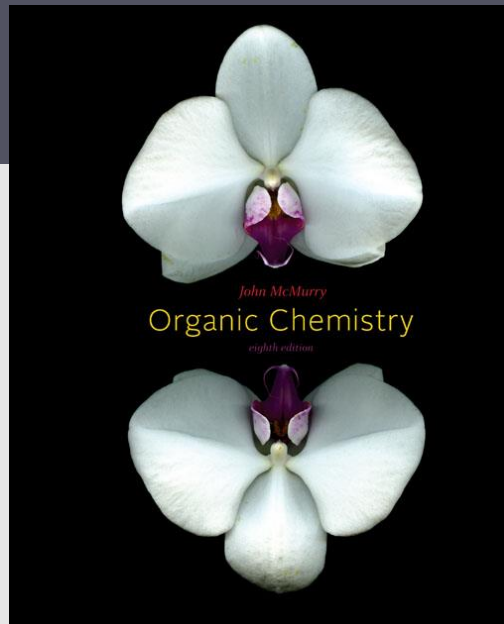


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Chapter 13

Structure Determination: Nuclear Magnetic Resonance Spectroscopy

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The Use of NMR Spectroscopy



- Used to map carbon-hydrogen framework of molecules
- Used to determine relative location of atoms within a molecule
- Most helpful spectroscopic technique in organic chemistry
- Depends on very strong magnetic fields

Why This Chapter?



- NMR is the most valuable spectroscopic technique used for structure determination
- More advanced NMR techniques are used in biological chemistry to study protein structure and folding

13.1 Nuclear Magnetic Resonance Spectroscopy

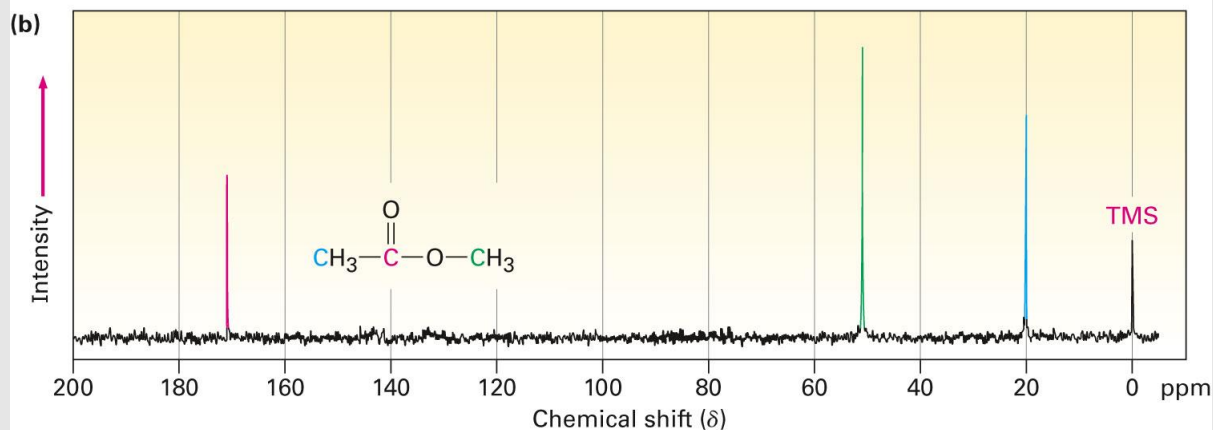
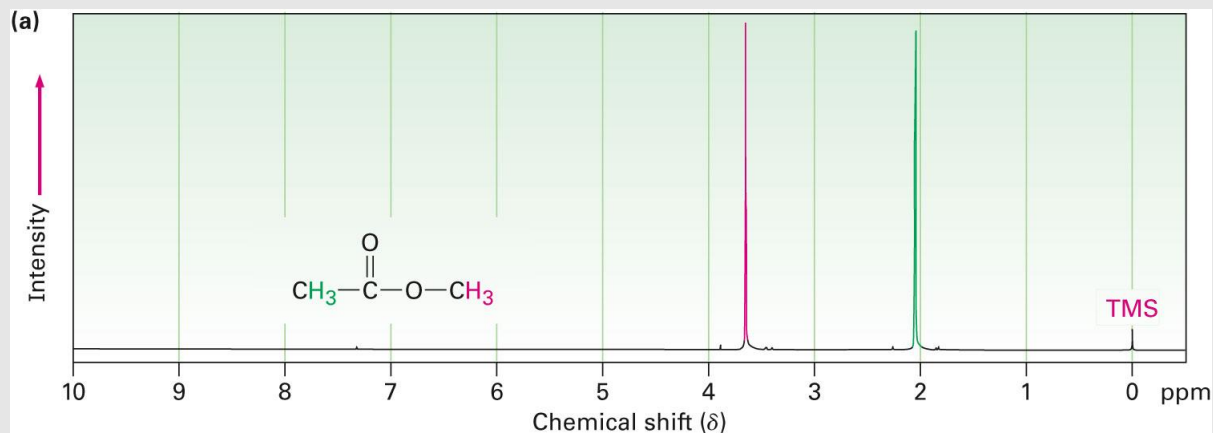


- ^1H or ^{13}C nucleus spins and the internal magnetic field aligns parallel to or against an aligned external magnetic field (See Figure 13.1)
- Parallel orientation is lower in energy making this spin state more populated
- Radio energy of exactly correct frequency (resonance) causes nuclei to flip into anti-parallel state
- Energy needed is related to molecular environment (proportional to field strength, \mathbf{B}) – see Figure 13.2

13.2 The Nature of NMR Absorptions



- Electrons in bonds **shield** nuclei from magnetic field
- Different signals appear for nuclei in different environments



The NMR Measurement

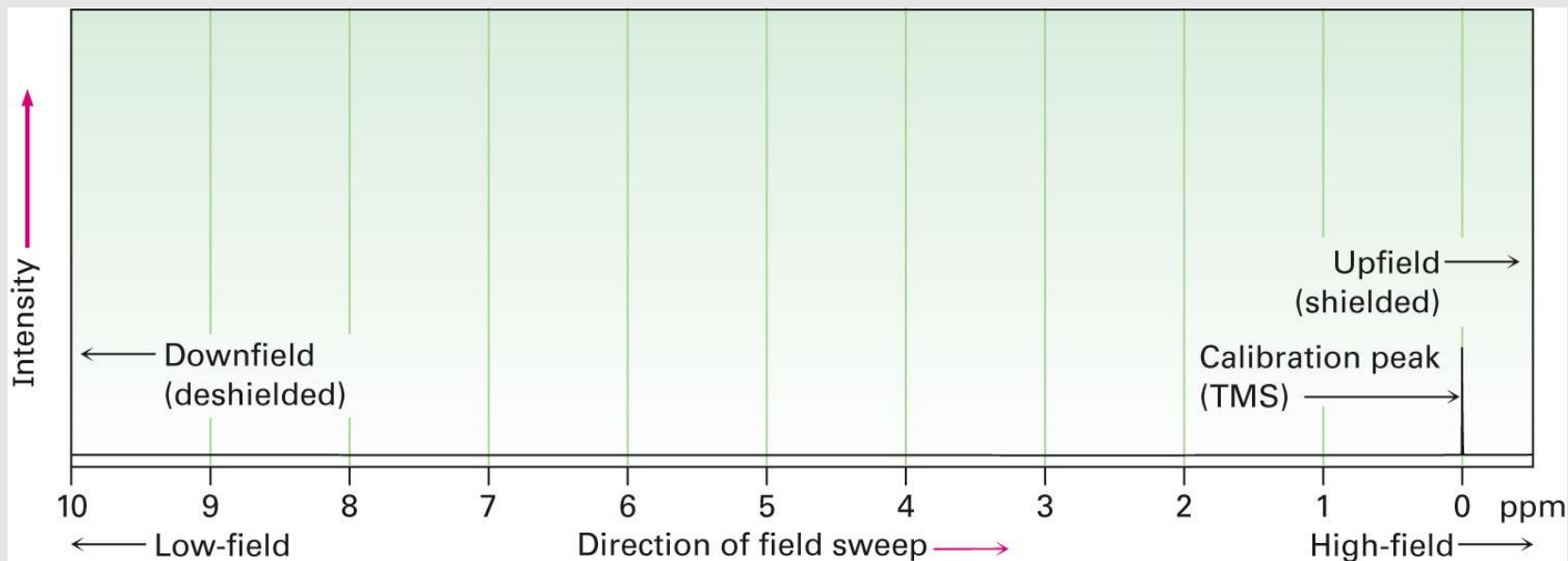


- The sample is dissolved in a solvent that does not have a signal itself and placed in a long thin tube
- The tube is placed within the gap of a magnet and spun
- Radiofrequency energy is transmitted and absorption is detected
- Species that interconvert give an averaged signal that can be analyzed to find the rate of conversion
- Can be used to measure rates and activation energies of very fast processes

13.3 Chemical Shifts



- The relative energy of resonance of a particular nucleus resulting from its local environment is called chemical shift
- NMR spectra show applied field strength increasing from left to right
- Left part is **downfield** is **upfield**
- Nuclei that absorb on upfield side are strongly shielded.
- Chart calibrated versus a reference point, set as 0, tetramethylsilane [TMS]



Measuring Chemical Shift



- Numeric value of chemical shift: difference between strength of magnetic field at which the observed nucleus resonates and field strength for resonance of a reference
 - Difference is very small but can be accurately measured
 - Taken as a ratio to the total field and multiplied by 10^6 so the shift is in parts per million (ppm)
- Absorptions normally occur downfield of TMS, to the left on the chart
- Calibrated on relative scale in **delta (δ) scale**
 - Independent of instrument's field strength

13.4 ^{13}C NMR Spectroscopy: Signal Averaging and FT-NMR



- Carbon-13: only carbon isotope with a nuclear spin
 - Natural abundance 1.1% of C's in molecules
 - Sample is thus very dilute in this isotope
- Sample is measured using repeated accumulation of data and averaging of signals, incorporating pulse and the operation of Fourier transform (FT NMR)
- All signals are obtained simultaneously using a broad pulse of energy and resonance recorded
- Frequent repeated pulses give many sets of data that are averaged to eliminate noise
- Fourier-transform of averaged pulsed data gives spectrum (see Figure 13-6)

13.5 Characteristics of ^{13}C NMR Spectroscopy

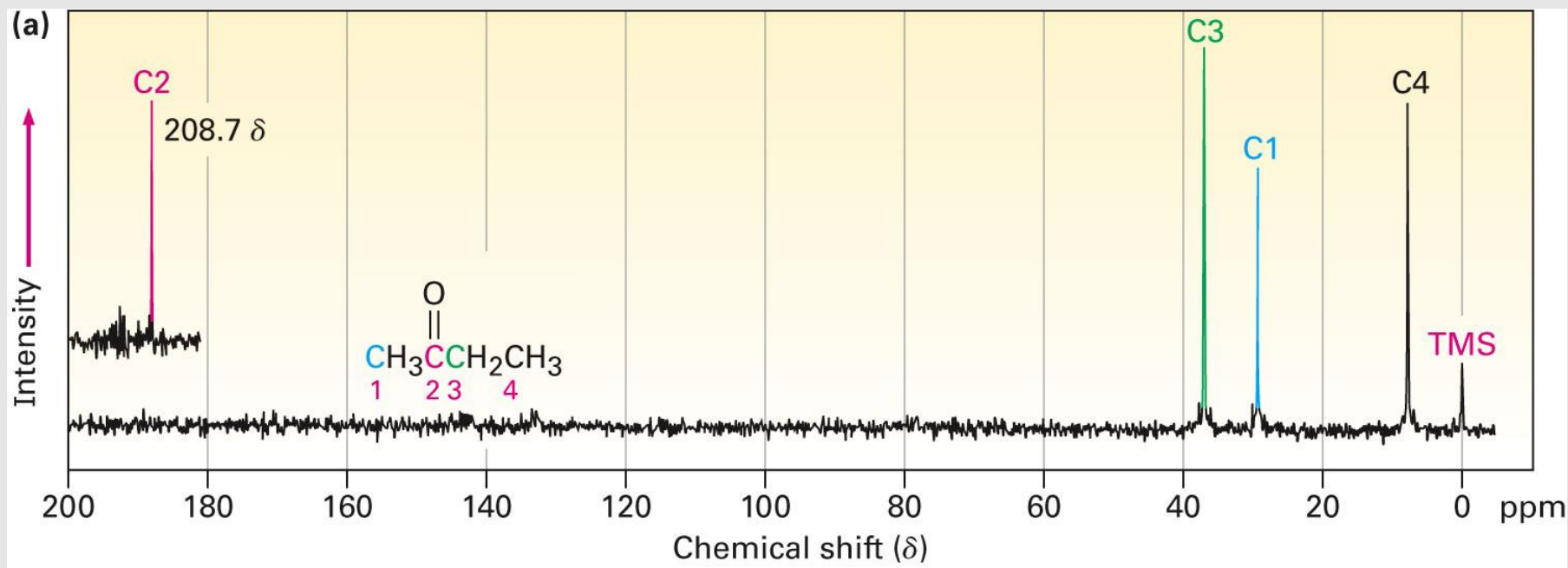


- Provides a count of the different types of environments of carbon atoms in a molecule
- ^{13}C resonances are 0 to 220 ppm downfield from TMS (Figure 13-7)
- Chemical shift affected by electronegativity of nearby atoms
 - O, N, halogen decrease electron density and shielding (“deshield”), moving signal downfield.
- sp^3 C signal is at δ 0 to 9; sp^2 C: δ 110 to 220
- C(=O) at low field, δ 160 to 220

Characteristics of ^{13}C NMR Spectroscopy (Continued)



- Spectrum of 2-butanone is illustrative- signal for $\text{C}=\text{O}$ carbons on left edge



13.6 DEPT ^{13}C NMR Spectroscopy

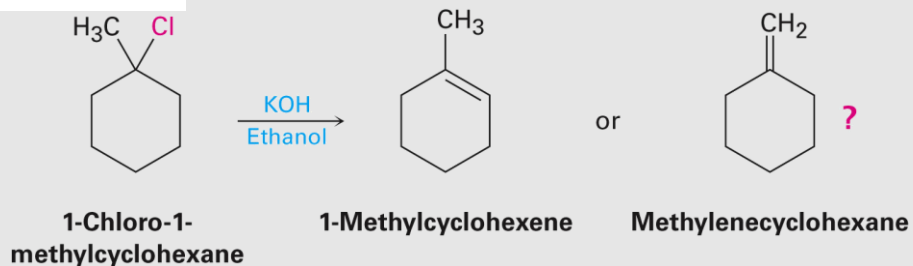
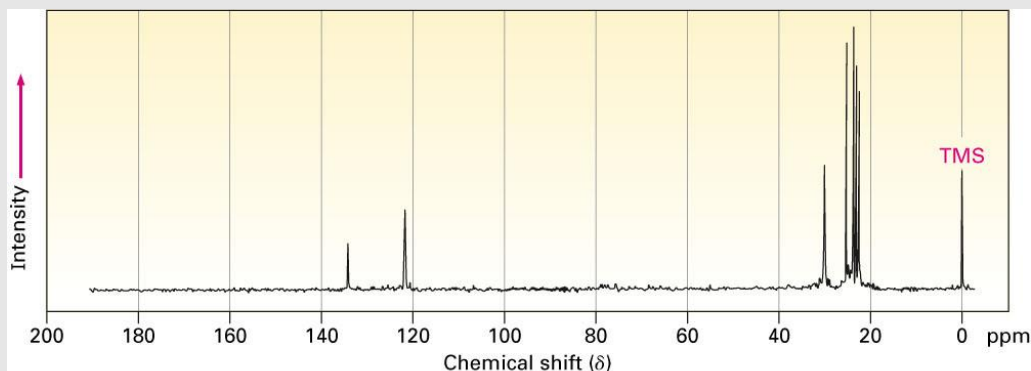


- Improved pulsing and computational methods give additional information
- **DEPT-NMR** (*distortionless enhancement by polarization transfer*)
- Normal spectrum shows all C's then:
 - Obtain spectrum of all C's except quaternary (broad band decoupled)
 - Change pulses to obtain separate information for CH_2 , CH
 - Subtraction reveals each type (See Figure 13-10)

13.7 Uses of ^{13}C NMR Spectroscopy



- Provides details of structure
- Example: product orientation in elimination from 1-chloro-methyl cyclohexane
- Difference in symmetry of products is directly observed in the spectrum
- 1-chloro-methylcyclohexane has five sp^3 resonances (δ 20-50) and two sp^2 resonances δ 100-150



13.8 ^1H NMR Spectroscopy and Proton Equivalence

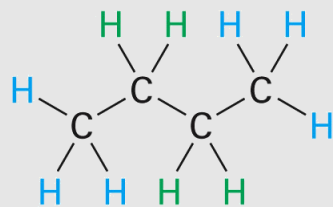


- Proton NMR is much more sensitive than ^{13}C and the active nucleus (^1H) is nearly 100 % of the natural abundance
- Shows how many kinds of nonequivalent hydrogens are in a compound
- Theoretical equivalence can be predicted by seeing if replacing each H with “X” gives the same or different outcome
- Equivalent H's have the same signal while nonequivalent are different
 - There are degrees of nonequivalence

Nonequivalent H's

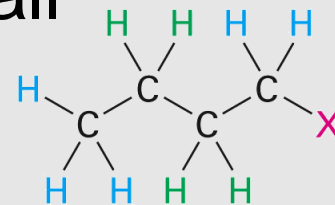


- Replacement of each H with “X” gives a different constitutional isomer
- Then the H's are in **constitutionally heterotopic** environments and will have different chemical shifts – they are nonequivalent under all circumstances

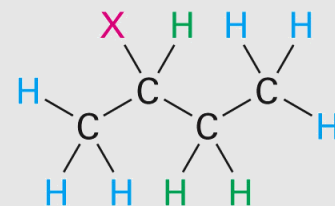


The $\text{-CH}_2\text{-}$ and -CH_3 hydrogens are **unrelated** and have different NMR absorptions.

Replace either
H or H with X



or

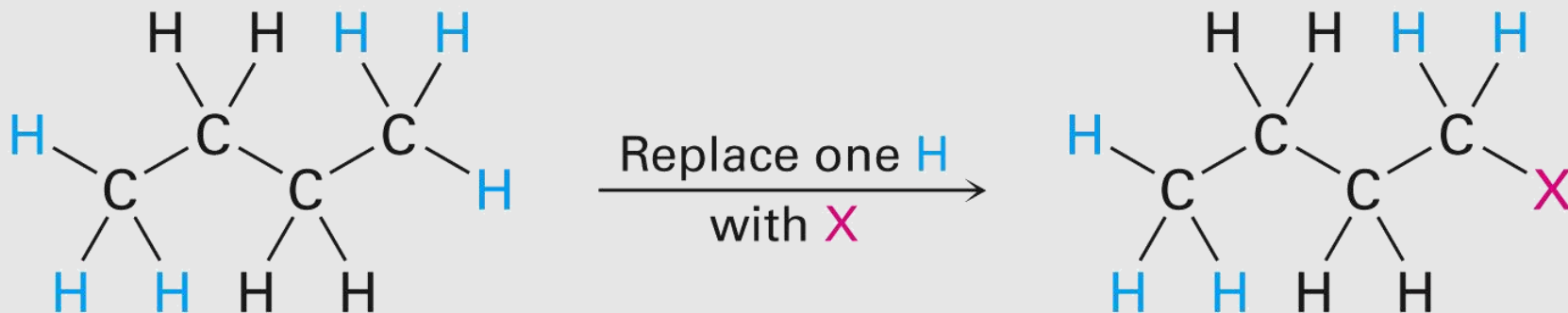


The two substitution products are **constitutional isomers**.

Equivalent H's



- Two H's that are in identical environments (**homotopic**) have the same NMR signal
- Test by replacing each with X
 - if they give the identical result, they are equivalent
 - Protons are considered **homotopic**



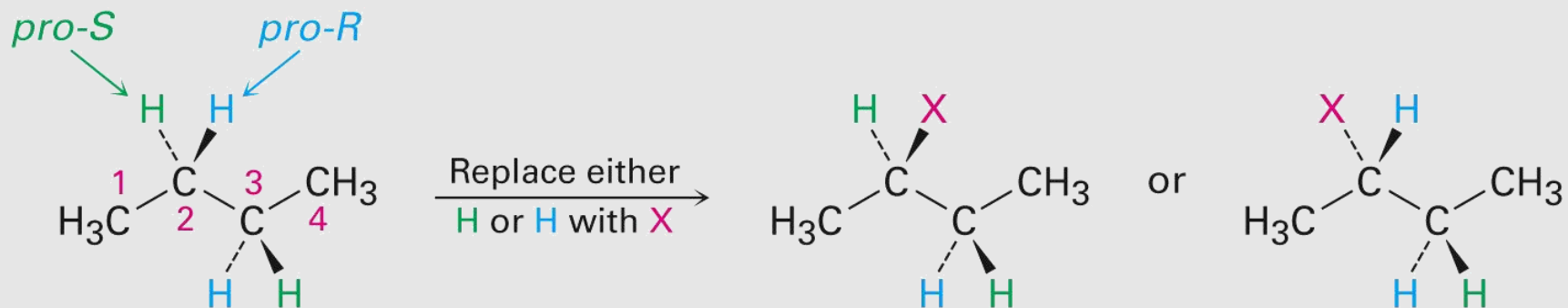
The six -CH₃ hydrogens are **homotopic** and have the same NMR absorption.

Only one substitution product is possible.

Enantiotopic Distinctions



- If H's are in environments that are mirror images of each other, they are **enantiotopic**
- Replacement of each H with X produces a set of enantiomers
- The H's have the same NMR signal (in the absence of chiral materials)



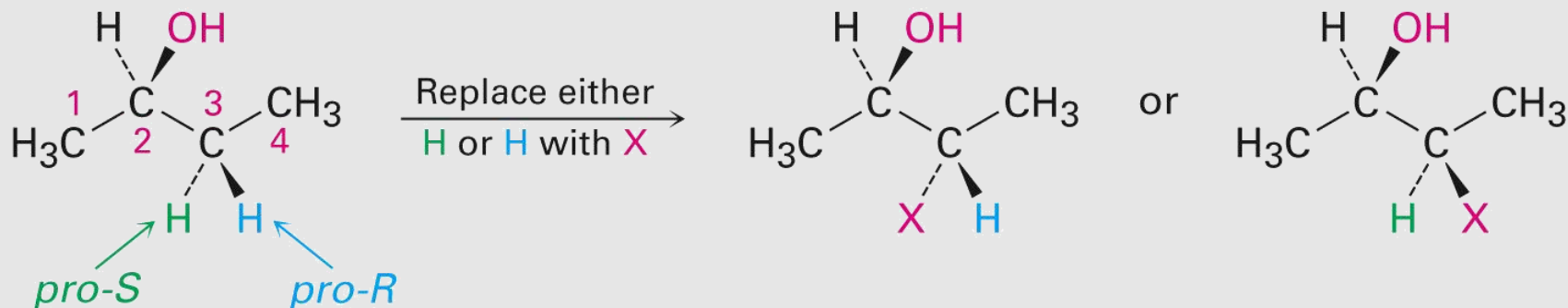
The two hydrogens on C2 (and on C3) are **enantiotopic** and have the same NMR absorption.

The two possible substitution products are **enantiomers**.

Diastereotopic Distinctions



- In a chiral molecule, paired hydrogens can have different environments and different shifts
- Replacement of a *pro-R* hydrogen with X gives a different diastereomer than replacement of the *pro-S* hydrogen
- **Diastereotopic hydrogens** are distinct chemically and spectroscopically



The two hydrogens on C3 are **diastereotopic** and have different NMR absorptions.

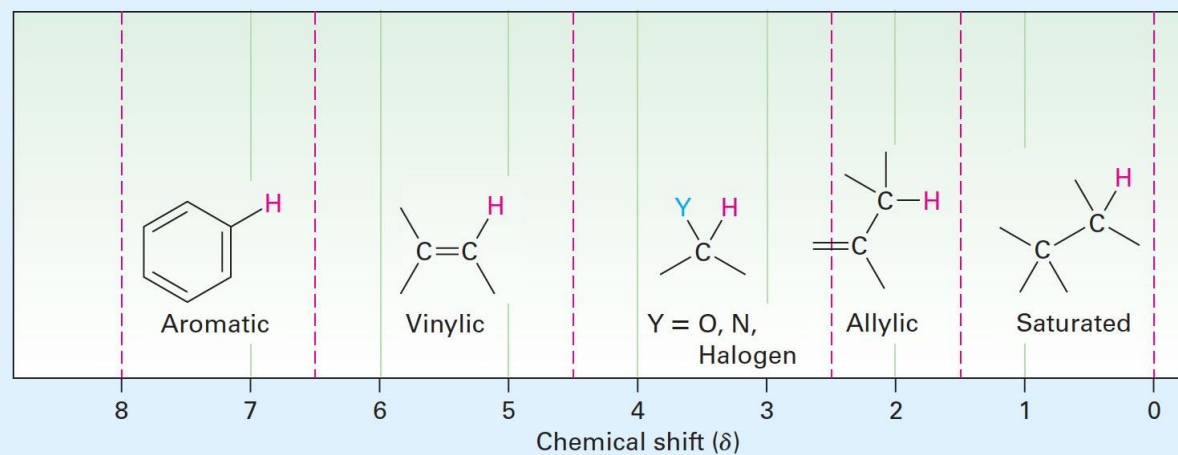
The two possible substitution products are **diastereomers**.

13.9 Chemical Shifts in ^1H NMR Spectroscopy



- Proton signals range from δ 0 to δ 10
- Lower field signals are H's attached to sp^2 C
- Higher field signals are H's attached to sp^3 C
- Electronegative atoms attached to adjacent C cause downfield shift

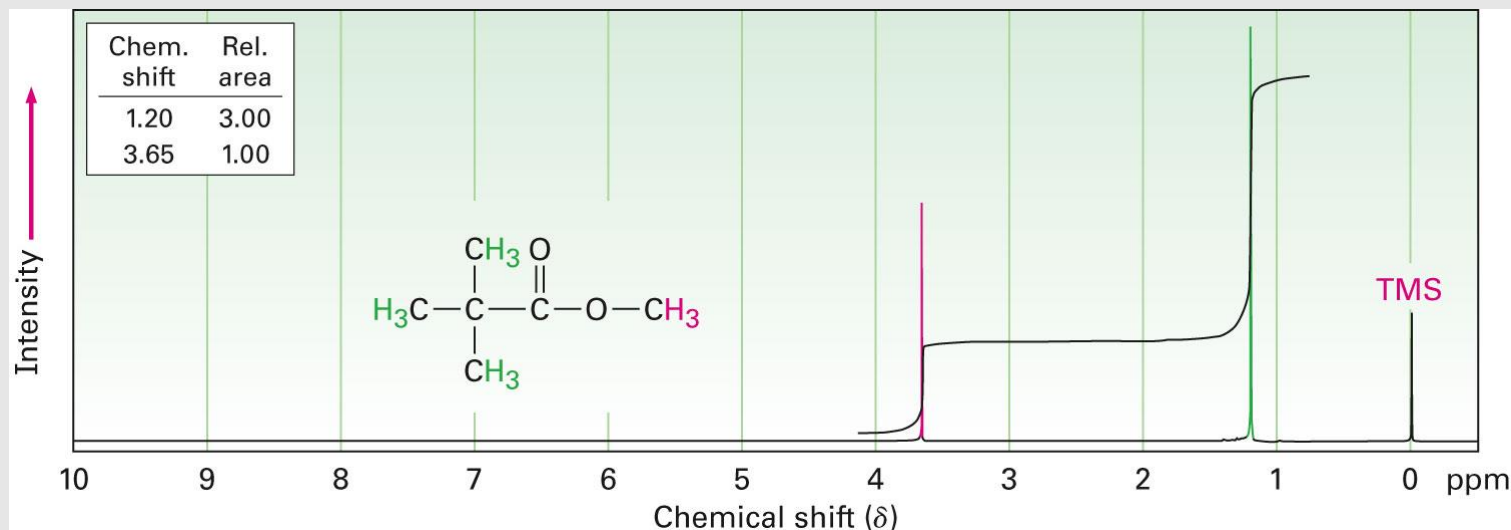
Table 13.2 Regions of the ^1H NMR Spectrum



13.10 Integration of ^1H NMR Absorptions: Proton Counting



- The relative intensity of a signal (integrated area) is proportional to the number of protons causing the signal
- This information is used to deduce the structure
- For example in ethanol ($\text{CH}_3\text{CH}_2\text{OH}$), the signals have the integrated ratio 3:2:1
- For narrow peaks, the heights are the same as the areas and can be measured with a ruler



13.11 Spin-Spin Splitting in ^1H NMR Spectra

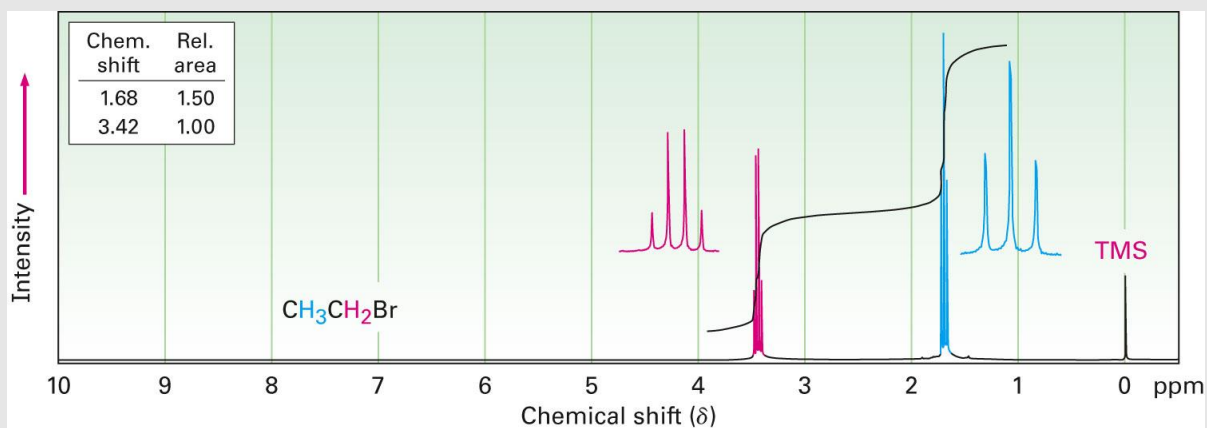
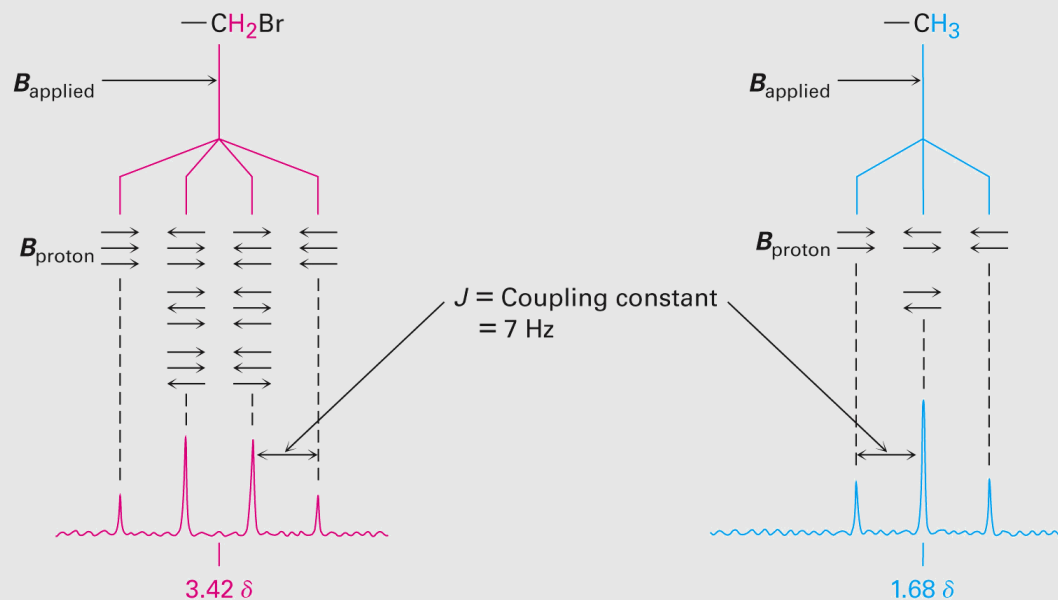


- Peaks are often split into multiple peaks due to interactions between nonequivalent protons on adjacent carbons, called **spin-spin splitting**
- The splitting is into one more peak than the number of H's on the adjacent carbon (“n+1 rule”)
- The relative intensities are in proportion to a binomial distribution and are due to interactions between nuclear spins that can have two possible alignments with respect to the magnetic field
- The set of peaks is a multiplet (2 = doublet, 3 = triplet, 4 = quartet)

Simple Spin-Spin Splitting



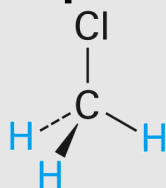
- An adjacent CH_3 group can have four different spin alignments as 1:3:3:1
- This gives peaks in ratio of the adjacent H signal
- An adjacent CH_2 gives a ratio of 1:2:1
- The separation of peaks in a multiplet is measured and is a constant, in Hz
 - J (coupling constant)



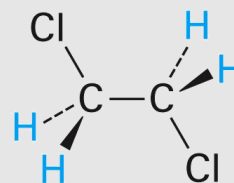
Rules for Spin-Spin Splitting



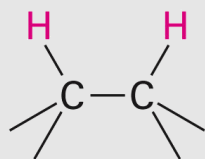
- Equivalent protons do not split each other
- The signal of a proton with n equivalent neighboring H's is split into $n + 1$ peaks
- Protons that are farther than two carbon atoms apart do not split each other



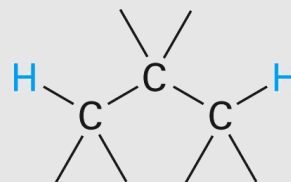
Three C-H protons are chemically equivalent; no splitting occurs.



Four C-H protons are chemically equivalent; no splitting occurs.



Splitting observed

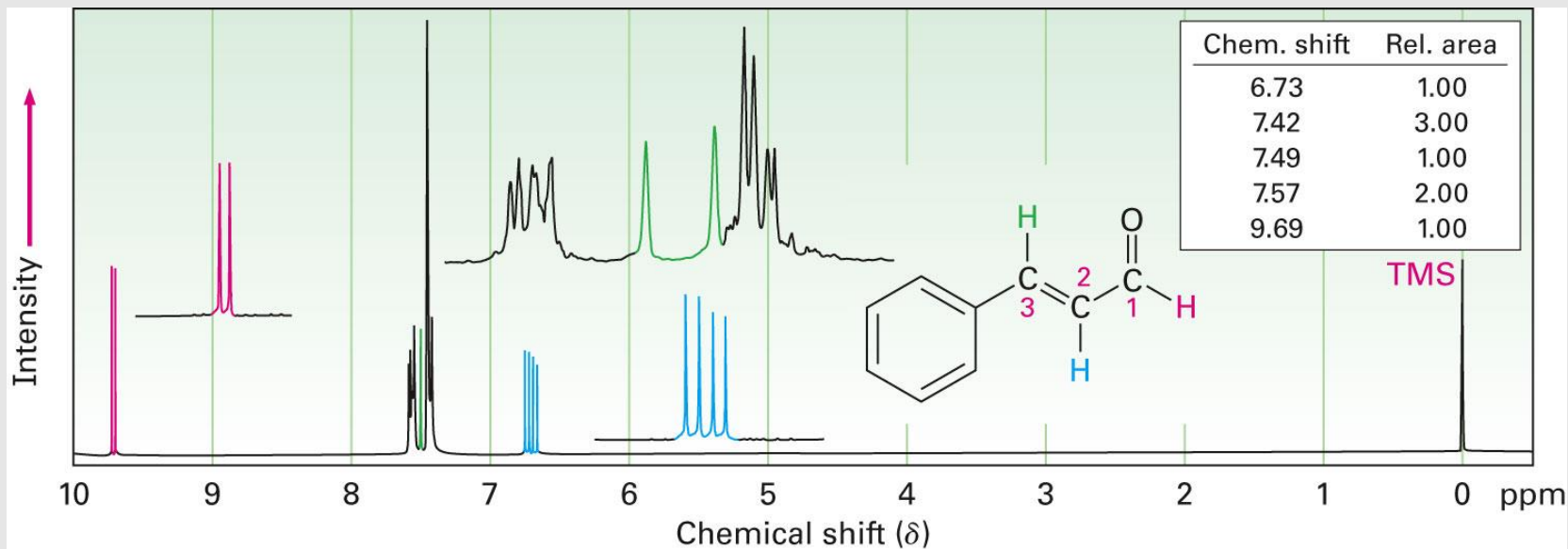


Splitting not usually observed

13.12 More Complex Spin-Spin Splitting Patterns



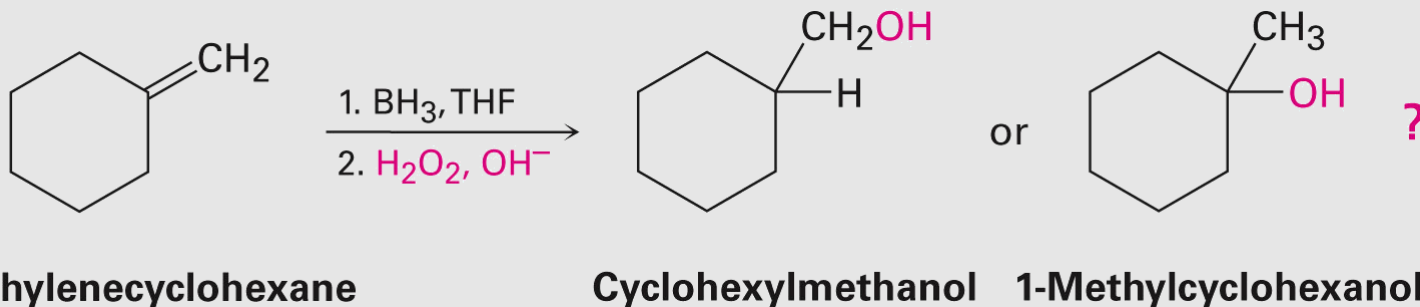
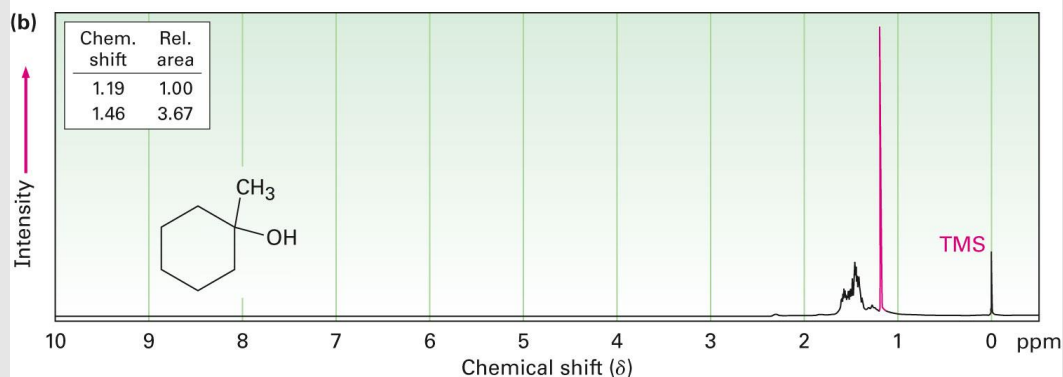
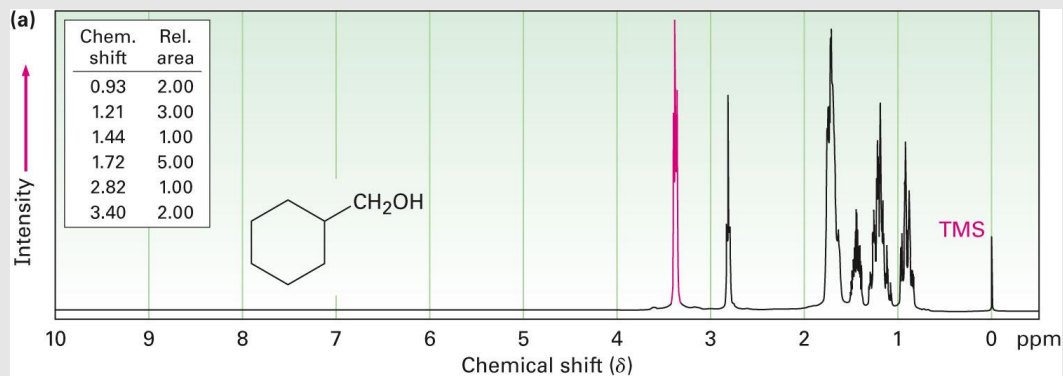
- Spectra can be more complex due to overlapping signals, multiple nonequivalence
- Example: *trans*-cinnamaldehyde



13.13 Uses of ^1H NMR Spectroscopy



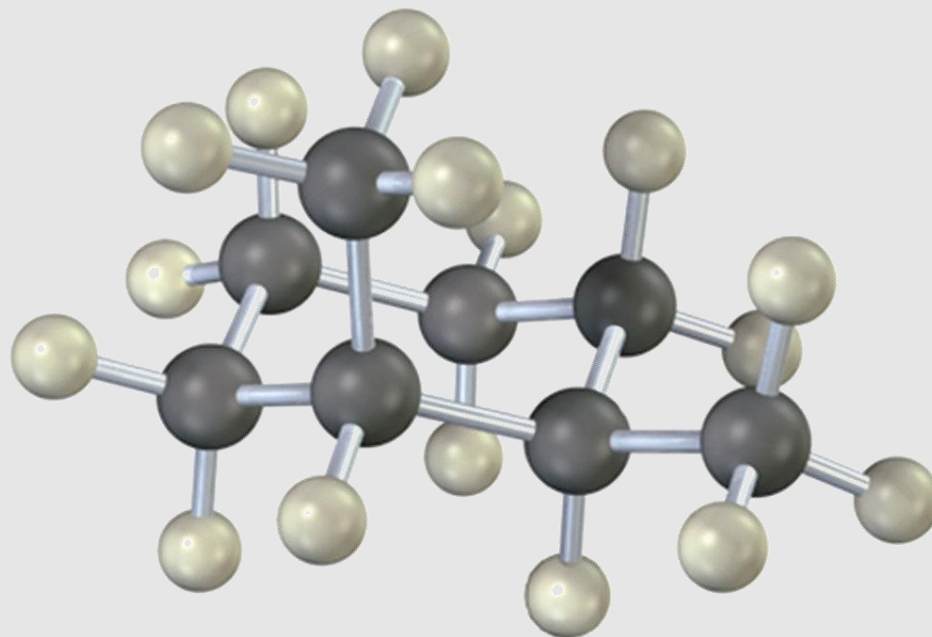
- The technique is used to identify likely products in the laboratory quickly and easily
- Example: regiochemistry of hydroboration/oxidation of methylenecyclohexane
- Only that for cyclohexylmethanol is observed



Let's Work a Problem



How many electronically nonequivalent kinds of protons and how many kinds of carbons are present in the following compound?



Answer



Since this compound is a 1,2-dimethylcyclohexane, it will have a plane of symmetry between the 1 and 2 positions of the compound. Therefore, it is a meso compound, and the plane of symmetry results in the presence of 4 equivalent protons, as well as 4 equivalent carbons