Nuclear Magnetic Resonance Spectroscopy
(Chapter 13, Loudon)
CCE Division Liquid NMR Facility

500 MHz NMR

Prof. John D. Roberts (1918-2016)
$^1$H NMR Spectrum of Methyl $t$-Butyl Ether
NMR Spectra of Ethanol

13.7 Characteristic Functional-Group NMR Absorptions
$^1$H NMR Spectrum of 2-Bromopropene

89.56 MHz

0.05 ml : 0.5 ml CDCl$_3$

<table>
<thead>
<tr>
<th>Marked Atom</th>
<th>Chemical Shift (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>5.540</td>
</tr>
<tr>
<td>B</td>
<td>5.346</td>
</tr>
<tr>
<td>C</td>
<td>2.294</td>
</tr>
</tbody>
</table>
Summary

Electron-poor environment
Deshielded
Higher $\delta$
"Downfield"

Electron-rich environment
Shielded
Low $\delta$
"Upfield"

Absorption Intensity

$\delta$, ppm

CDCl$_3$

Calibration peaks

TMS
Nuclear Magnetic Resonance Spectroscopy
(Chapter 13, Loudon)
The $^1$H NMR Spectrum

Proton NMR provides these types of information:

1. the number of sets of chemically equivalent and non-equivalent protons

2. the *number of protons* within each set (or their relative ratios)

3. the *chemical environments* of each set of protons (chemical shift)
Summary

Absorption Intensity

Electron-poor environment
Deshielded
Higher $\delta$
"Downfield"

Electron-rich environment
Shielded
Low $\delta$
"Upfield"

$\delta$, ppm

CDCl$_3$
Calibration peaks
TMS
Chemical Shift

The NMR Spectrum: Chemical Shift and Integral
NMR Spectra of Alkenes

- $B_i$ (induced field)
- $B_0$ (external applied field)
- Induced field $B_i$ opposes $B_0$ at the $\pi$ bond
- Induced $\pi$-electron circulation
- Induced field $B_i$ reinforces $B_0$ at the vinylic proton

13.7 Characteristic Functional-Group NMR Absorptions
The $^1$H NMR Spectrum

Proton NMR provides these types of information:

1. the number of sets of *chemically equivalent and non-equivalent protons*

2. the *number of protons* within each set (or their relative ratios)

3. the *chemical environments* of each set of protons (chemical shift)

4. the number of adjacent sets of protons or *connectivity*
$^1$H NMR spectra of 1-bromo-2,2-dimethylpropane and 1,1-dichloroethane
$^{1}H$ NMR spectrum of methyl propanoate
Coupling Constants Can Report on Stereochemical Relationships: *Cis* vs. *Trans*
Why Splitting Occurs

this combination can occur in two ways; therefore, it is twice as probable

\[ +\frac{1}{2} +\frac{1}{2}, \quad +\frac{1}{2} -\frac{1}{2}, \quad -\frac{1}{2} +\frac{1}{2}, \quad -\frac{1}{2} -\frac{1}{2} \]

possible spin combinations of the two neighboring \( b \) protons

splitting pattern of the \( a \) protons

13.4 The NMR Spectrum: Spin-Spin Splitting
Splitting Patterns

- The intensities of split signals have well defined ratios.

<table>
<thead>
<tr>
<th>Number of equivalent adjacent protons</th>
<th>Number of lines in splitting pattern (name)</th>
<th>Relative line intensity within splitting pattern</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>1 (singlet)</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>2 (doublet)</td>
<td>1 1</td>
</tr>
<tr>
<td>2</td>
<td>3 (triplet)</td>
<td>1 2 1</td>
</tr>
<tr>
<td>3</td>
<td>4 (quartet)</td>
<td>1 3 3 1</td>
</tr>
<tr>
<td>4</td>
<td>5 (quintet)</td>
<td>1 4 6 4 1</td>
</tr>
<tr>
<td>5</td>
<td>6 (sextet)</td>
<td>1 5 10 10 5 1</td>
</tr>
<tr>
<td>6</td>
<td>7 (septet)</td>
<td>1 6 15 20 15 6 1</td>
</tr>
</tbody>
</table>

13.4 The NMR Spectrum: Spin-Spin Splitting
Nuclear Magnetic Resonance Spectroscopy
(Chapter 13, Loudon)
Multiplicative Splitting: Spectrum of Styrene
Spectrum of 1-bromo-3-chloropropane

BrCH₂CH₂CH₂Cl

\[ J = 6.08 \text{ Hz} \quad J = 6.27 \text{ Hz} \quad J = 6.17 \text{ Hz} \]

13.5 Complex NMR Spectra
Spectrum of 1-iodopropane
Dynamic Systems: The Time Dependence of NMR

- Both diastereotopic protons can be observed if the rate of chair interconversion is reduced by lowering the temperature.

![Diagram of cyclohexane-$d_{11}$ with labeled protons](image)

Each spectrum at higher temperature:
- >-49 °C
- <=-60 °C
- <=-89 °C

Chemical shift: δ 1.62 δ 1.14
Fast Proton Transfers: NMR Spectra of Ethanol

13.7 Characteristic Functional-Group NMR Absorptions
H/D Exchange to Study Protein Structure

H/D Exchange

Dynamic regions exchange rapidly
Structured regions exchange slowly

Quench & Digest

Quenching locks in deuterium and unfolds the protein
Digestion localizes the information

©2013 David Weis
NMR of Other Nuclei

• Many other spin active nuclei may also be observed by NMR.

<table>
<thead>
<tr>
<th>Isotope</th>
<th>Relative sensitivity</th>
<th>Natural abundance, %</th>
<th>Observation frequency $\nu$, MHz*</th>
<th>Gyromagnetic ratio‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>$^1\text{H}$</td>
<td>(1.00)</td>
<td>99.98</td>
<td>300</td>
<td>26,753</td>
</tr>
<tr>
<td>$^{13}\text{C}$</td>
<td>0.0159</td>
<td>1.10</td>
<td>75</td>
<td>6728</td>
</tr>
<tr>
<td>$^{19}\text{F}$</td>
<td>0.834</td>
<td>100</td>
<td>282</td>
<td>25,179</td>
</tr>
<tr>
<td>$^{31}\text{P}$</td>
<td>0.0665</td>
<td>100</td>
<td>122</td>
<td>10,840</td>
</tr>
</tbody>
</table>

* At magnetic field $B_0 = 70,500$ gauss. ‡ In radians gauss$^{-1}$ s$^{-1}$ defined in Eq. 13.17.
Proton-Decoupled $^{13}$C NMR

\[ \text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Cl} \]

Chemical shift, ppm ($\delta$)
Chemical Shift in $^{13}$C NMR
$^1$H and $^{13}$C NMR Spectra of 1,2,2-trichloropropane
$^{13}$C NMR Spectrum of Ethyl Benzoate

25.16 MHz

0.5 ml : 1.5 ml CDCl$_3$

<table>
<thead>
<tr>
<th>ppm</th>
<th>Int.</th>
<th>标记碳</th>
</tr>
</thead>
<tbody>
<tr>
<td>166.54</td>
<td>194</td>
<td>1</td>
</tr>
<tr>
<td>132.80</td>
<td>410</td>
<td>2</td>
</tr>
<tr>
<td>130.62</td>
<td>244</td>
<td>3</td>
</tr>
<tr>
<td>129.57</td>
<td>1000</td>
<td>4</td>
</tr>
<tr>
<td>128.34</td>
<td>801</td>
<td>5</td>
</tr>
<tr>
<td>60.90</td>
<td>353</td>
<td>6</td>
</tr>
<tr>
<td>14.33</td>
<td>294</td>
<td>7</td>
</tr>
</tbody>
</table>
DEPT $^{13}$C NMR Spectrum of Citronellal
Magnetic Resonance Imaging

No harmful x-rays:
Magnets and radiowaves

Imaging of biological tissue
Detection of tumors
Visualization of brain function

Gadopentetic acid (OptiMark® Magnevist®)
Nuclear Magnetic Resonance Spectroscopy
(Chapter 13, Loudon)
Steps for Solving Structures

1. Write down the molecular formula, molecular mass (MS) & determine the unsaturation number if possible.

2. Identify functional groups or fragments (IR, NMR).

3. Determine the number of nonequivalent sets of protons or carbons ($^{1}H$ & $^{13}C$ NMR). Use the integrals and molecular formula to calculate how many protons or carbons correspond to each absorption.

4. Write out partial structures and possible complete structures.

5. Use spectra to confirm or disprove the proposed structure(s).
Practice Problem

The molecular formula for an unknown compound is $\text{C}_7\text{H}_{16}\text{O}_4$. Data for the $^1\text{H}$ NMR are shown below. What is the structure of the compound?

- $d$ 1.93 (t, $J = 6$ Hz)
- $d$ 3.35 (s)
- $d$ 4.49 (t, $J = 6$ Hz)
- Relative integral 1:6:1