Homotopic Hydrogens

- Hydrogens are chemically equivalent or homotopic if replacing each one in turn by the same group would lead to an identical compound.
If replacement of each of two hydrogens by some group leads to enantiomers, those hydrogens are enantiotopic.
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.

Diastereomers
Vinyl Protons

diastereotopic

\[
\text{H}^a
\quad \text{C} = \text{C} \quad \text{CH}_2\text{Br}
\]

\[
\quad \text{H}^b
\quad \text{H}
\]

\[
\text{H}^a
\quad \text{C} = \text{C} \quad \text{CH}_2\text{Br}
\]

\[
\quad \text{H}^b
\quad \text{H}
\]

\[
\text{H}^b
\quad \text{C} = \text{C} \quad \text{H}
\]

\[
\quad \text{H}^a
\quad \text{H}
\]

\[
\text{Z}
\quad \text{C} = \text{C} \quad \text{CH}_2\text{Br}
\]

\[
\quad \text{H}^b
\quad \text{H}
\]

\[
\text{H}^a
\quad \text{C} = \text{C} \quad \text{CH}_2\text{Br}
\]

\[
\quad \text{H}^a
\quad \text{H}
\]

\[
\text{Z}
\quad \text{C} = \text{C} \quad \text{H}
\]

\[
\quad \text{H}^b
\quad \text{H}
\]

\[
\text{diastereomers}
\]
Integração
The area under a peak is proportional to the number of protons that generate the peak.

Integration = determination of the area under a peak

Not only does each different type of hydrogen give a distinct peak in the NMR spectrum, but we can also tell the relative numbers of each type of hydrogen by a process called integration.
Benzyl Acetate

The integral line rises an amount proportional to the number of H in each peak.

METHOD 1

integral line

The simplest ratio of the heights is:

55 : 22 : 33 = 5 : 2 : 3
Benzyl Acetate (FT-NMR)

Actually:

\[
\begin{align*}
58.117 / 11.3 &= 5.14 \\
21.215 / 11.3 &= 1.90 \\
33.929 / 11.3 &= 3.00
\end{align*}
\]

METHOD 2

digital integration

Modern instruments report the integral as a number.

Integrals are good to about 10% accuracy.
SPIN-SPIN SPLITTING

**Bonded to the same carbon: two bonds between protons**

\[
\text{H}_1 \text{C}_2 \text{H}_1
\]

spin-spin splitting is normally observed (if nonequivalent)

**Bonded to adjacent carbons: three bonds between protons**

\[
\text{H}_1 \text{C}_2 \text{H}_3
\]

spin-spin splitting is normally observed (this is the most common case)
**Peak:** the units into which an NMR signal is split; doublet, triplet, quartet, etc.

**Signal splitting:** splitting of an NMR signal into a set of peaks by the influence of neighboring nonequivalent hydrogens

**(n + 1) rule:** if a hydrogen has \( n \) hydrogens nonequivalent to it but equivalent among themselves on the same or adjacent atom(s), its \(^1\text{H}-\text{NMR} \) signal is split into \((n + 1)\) peaks
Signal Splitting \((n + 1)\)

For these hydrogens, \(n = 1\); their signal is split into \((1 + 1) = 2\) peaks; a doublet

For this hydrogen, \(n = 3\); its signal is split into \((3 + 1) = 4\) peaks; a quartet
**Problem**: predict the number of $^1$H-NMR signals and the splitting pattern of each

(a) \( \text{CH}_3 \text{CCH}_2 \text{CH}_3 \)

(b) \( \text{CH}_3 \text{CH}_2 \text{CCH}_2 \text{CH}_3 \)

(c) \( \text{CH}_3 \text{CCH( CH}_3 \text{)}_2 \)
Signal coupling: an interaction in which the nuclear spins of adjacent atoms influence each other and lead to the splitting of NMR signals

Coupling constant \((J)\): the separation on an NMR spectrum (in hertz) between adjacent peaks in a multiplet;
- a quantitative measure of the influence of the spin-spin coupling with adjacent nuclei
1,1,2-Tribromoethane
Origins of Signal Splitting

- \( H_a \) signal

\[ \text{Spin-spin coupling} \]

\[ J_{ab} \]

- \( H_b \) signal

\[ \text{Spin-spin coupling} \]

\[ J_{ab} \]
$H_b$ in 1,1,2-Tribromoethane
THE TRIPLET IN $^1\text{H}$ NMR

$H_a$ splits into a 1:2:1 triplet peak

$H_b$ can both be parallel, anti-parallel

$H_a$ is coupled to $H_b$ and $H_b$

or one parallel and one anti-parallel

$\therefore H_a$ splits into a 1:2:1 **triplet** peak
$H_a$ in 1,1,2-Tribromoethane

- Chemical shift of $H^a$
- Spins of $H^b$ protons: $H^b$ protons reinforce field or $H^b$ protons oppose field

$B_0$
Origins of Signal Splitting

- C - C -
  Hₐ  Hₐ

Spin-spin coupling

One Hₐ atom

- C - C -
  Hₐ  Hₐ

Spin-spin coupling

Two equivalent Hₐ atoms

- C - C - Hₐ -
  Hₐ  Hₐ

Spin-spin coupling

Three equivalent Hₐ atoms

Observed splitting in signal of Hₐ

1 : 1

1 : 2 : 1

1 : 3 : 3 : 1

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The Quartet in $^1$HMR

- Proton splits into $n+1$
- $n = \#$ adjacent H's
- Quartet 1:3:3:1
- Shielded/deshielded
- Chemical Shift

proton splits into n+1
quartet 1:3:3:1
n = \# adjacent H's
$\text{CH}_3\text{CH}_2\text{OCH}_3$
• Pascal’s Triangle
  ○ as illustrated by the highlighted entries, each entry is the sum of the values immediately above it to the left and the right
because splitting patterns from spectra taken at 300 MHz and higher are often difficult to see, it is common to retrace certain signals in expanded form

$^1$H-NMR spectrum of 3-pentanone; scale expansion shows the triplet quartet pattern more clearly
Equivalent Protons do not Couple

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

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

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• **Coupling constant (J):** the distance between peaks in a split signal, expressed in hertz
  - the value is a quantitative measure of the magnetic interaction of nuclei whose spins are coupled

<table>
<thead>
<tr>
<th>Coupling Constant (J)</th>
<th>Chemical Structure</th>
<th>Peak Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>8-11 Hz</td>
<td><img src="image1.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>8-14 Hz</td>
<td><img src="image2.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>0-5 Hz</td>
<td><img src="image3.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>0-5 Hz</td>
<td><img src="image4.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>6-8 Hz</td>
<td><img src="image5.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>11-18 Hz</td>
<td><img src="image6.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>5-10 Hz</td>
<td><img src="image7.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>0-5 Hz</td>
<td><img src="image8.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
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<tr>
<td>0-5 Hz</td>
<td><img src="image9.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
<tr>
<td>8-11 Hz</td>
<td><img src="image10.jpg" alt="Chemical Structure" /></td>
<td>Ha-Hb</td>
</tr>
</tbody>
</table>
Coupling of nuclear spins is mediated through intervening bonds

- H atoms with more than three bonds between them generally do not exhibit noticeable coupling
- for H atoms three bonds apart, the coupling is referred to as vicinal coupling

Diagram: 
- C-C
- Ha  Hb
- Vicinal coupling

H_a  H_b

J_{ab}  J_{ab}
an important factor in vicinal coupling is the angle $\alpha$ between the C-H sigma bonds and whether or not it is fixed

coupling is a maximum when $\alpha$ is 0° and 180°; it is a minimum when $\alpha$ is 90°
This observation was quantified by Martin Karplus, who determined that the experimental data best fit the following equation:

\[ ^3J_{HH} = A + B \cos \alpha + C \cos 2\alpha \]

*Where A, B, and C are empirically determined constants*

This observation showed the variation of coupling constant with dihedral angle, \( \alpha \).
thus far, we have concentrated on spin-spin coupling with only one other nonequivalent set of H atoms

more complex splittings arise when a set of H atoms couples to more than one set H atoms

a tree diagram shows that when \( H_b \) is adjacent to nonequivalent \( H_a \) on one side and \( H_c \) on the other, the resulting coupling gives rise to a doublet of doublets.
if $H_c$ is a set of two equivalent $H$, then the observed splitting is a doublet of triplets
More Complex Splitting Patterns

- because the angle between C-H bond determines the extent of coupling, bond rotation is a key parameter
- in molecules with relatively free rotation about C-C sigma bonds, H atoms bonded to the same carbon in CH₃ and CH₂ groups generally are equivalent
- if there is restricted rotation, as in alkenes and cyclic structures, H atoms bonded to the same carbon may not be equivalent
- nonequivalent H on the same carbon will couple and cause signal splitting
- this type of coupling is called geminal coupling
More Complex Splitting Patterns

- In ethyl propenoate, an unsymmetrical terminal alkene, the three vinylic hydrogens are nonequivalent.
More Complex Splitting Patterns

- A tree diagram for the complex coupling of the three vinylic hydrogens in ethyl propenoate.
More Complex Splitting Patterns

- Complex coupling in flexible molecules
  - coupling in molecules with unrestricted bond rotation often gives only \( m + n + 1 \) peaks
  - that is, the number of peaks for a signal is the number of adjacent hydrogens + 1, no matter how many different sets of equivalent H atoms that represents
  - the explanation is that bond rotation averages the coupling constants throughout molecules with freely rotation bonds and tends to make them similar; for example in the 6- to 8-Hz range for H atoms on freely rotating \( sp^3 \) hybridized C atoms
More Complex Splitting Patterns

- simplification of signal splitting occurs when coupling constants are the same
More Complex Splitting Patterns

- an example of peak overlap occurs in the spectrum of 1-chloro-3-iodopropane
- the central CH$_2$ has the possibility for 9 peaks (a triplet of triplets) but because $J_{ab}$ and $J_{bc}$ are so similar, only $4 + 1 = 5$ peaks are distinguishable
Depending on the symmetry of a molecule, otherwise equivalent hydrogens may be

- homotopic
- enantiotopic
- diastereotopic

The simplest way to visualize topicity is to substitute an atom or group by an isotope; is the resulting compound

- the same as its mirror image
- different from its mirror image
- are diastereomers possible
Homotopic atoms or groups have identical chemical shifts under all conditions.

Dichloromethane (achiral)

Substitution does not produce a stereocenter; therefore hydrogens are homotopic.
**Enantiotopic groups**

- Enantiotopic atoms or groups have identical chemical shifts in achiral environments.
- They have different chemical shifts in chiral environments.

Substitution produces a stereocenter; therefore, hydrogens are enantiotopic. Both hydrogens are prochiral; one is pro-R-chiral, the other is pro-S-chiral.
Stereochemistry & Topicity

- Diastereotopic groups
  - H atoms on C-3 of 2-butanol are diastereotopic
  - Substitution by deuterium creates a chiral center
  - Because there is already a chiral center in the molecule, diastereomers are now possible

- Diastereotopic hydrogens have different chemical shifts under all conditions

2-Butanol (chiral) → Chiral

Substitute one H on CH₂ by D
The methyl groups on carbon 3 of 3-methyl-2-butanol are diastereotopic

- if a methyl hydrogen of carbon 4 is substituted by deuterium, a new chiral center is created
- because there is already one chiral center, diastereomers are now possible

protons of the methyl groups on carbon 3 have different chemical shifts
Stereochemistry and Topicity

- $^1$H-NMR spectrum of 3-methyl-2-butanol
  - the methyl groups on carbon 3 are diastereotopic and appear as two doublets
1,1-Dichloroethane

CH$_3$CHCl$_2$

1,1-dichloroethane contains two types of hydrogen atoms, so we see two sets of peaks, a doublet at 2.1 ppm and a quartet at 5.9 ppm.
Ethyl benzene
Methyl Isopropyl Ketone

$\text{CH}_3^b$ $\text{CH}^c$ $\text{C} -$ $\text{CH}_3^a$

$\delta$ (ppm)
1-Nitropropane

\[
\text{CH}_3\text{—CH}_2\text{—CH}_2\text{—NO}_2
\]
Differentiate using $^1$H NMR

(a) $\text{CH}_3\text{CH}≡\text{CHCH}_2\text{CH}_3$ and $\text{H}_2\text{C}\text{CHCH}_2\text{CH}_3$

(b) $\text{CH}_3\text{CH}_2\text{OCH}_2\text{CH}_2\text{CH}_3$ and $\text{CH}_3\text{OCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$

(c) $\text{CH}_3\text{COCH}_2\text{CH}_3$ and $\text{CH}_3\text{CH}_2\text{CCH}_3$

(d) $\text{H}_2\text{C}≡\text{C}($$\text{CH}_3)$\text{CCH}_3$ and $\text{CH}_3\text{CH}≡\text{CHCCH}_3$

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Coupling Constants (J values)

- **C=C** (free rotation) 7 Hz\(^a\)
- **C=C** (cis) 10 Hz
- **C=C** (trans) 15 Hz
- **C=C** (geminal) 2 Hz
- **C=C** (allylic) 6 Hz

\(^a\) The value of 7 Hz in an alkyl group is averaged for rapid rotation about the carbon–carbon bond. If rotation is hindered by a ring or bulky groups, other splitting constants may be observed.
Para Nitrotoluene
Bromoethane

\[ \text{Quartet due to coupling with } \text{CH}_2\text{Br} \]
\[ \delta = 3.42 \]

\[ J = \text{Coupling constant} = 7 \text{ Hz} \]

\[ \text{Triplet due to coupling with } \text{CH}_3 \]
\[ \delta = 1.68 \]
para-Methoxypropiophenone
Styrene
$H_a$ splitting in Styrene

“Tree” Diagram

δ 6.6

chemical shift of $H_a$

$J_{ac} = 11$ Hz

$J_{ab} = 17$ Hz

$J_{ac} = 11$ Hz
In the system below, Hb is split by two different sets of hydrogens: Ha and Hc.

- Theoretically, Hb could be split into a triplet of quartets (12 peaks) but this complexity is rarely seen in aliphatic systems.
Why go to a higher field strength?

δ0.50
δ0.75
$\delta 0.50 \text{ (t, 2H, J=10)}$

$\delta 0.75 \text{ (t, 2H, J=10)}$