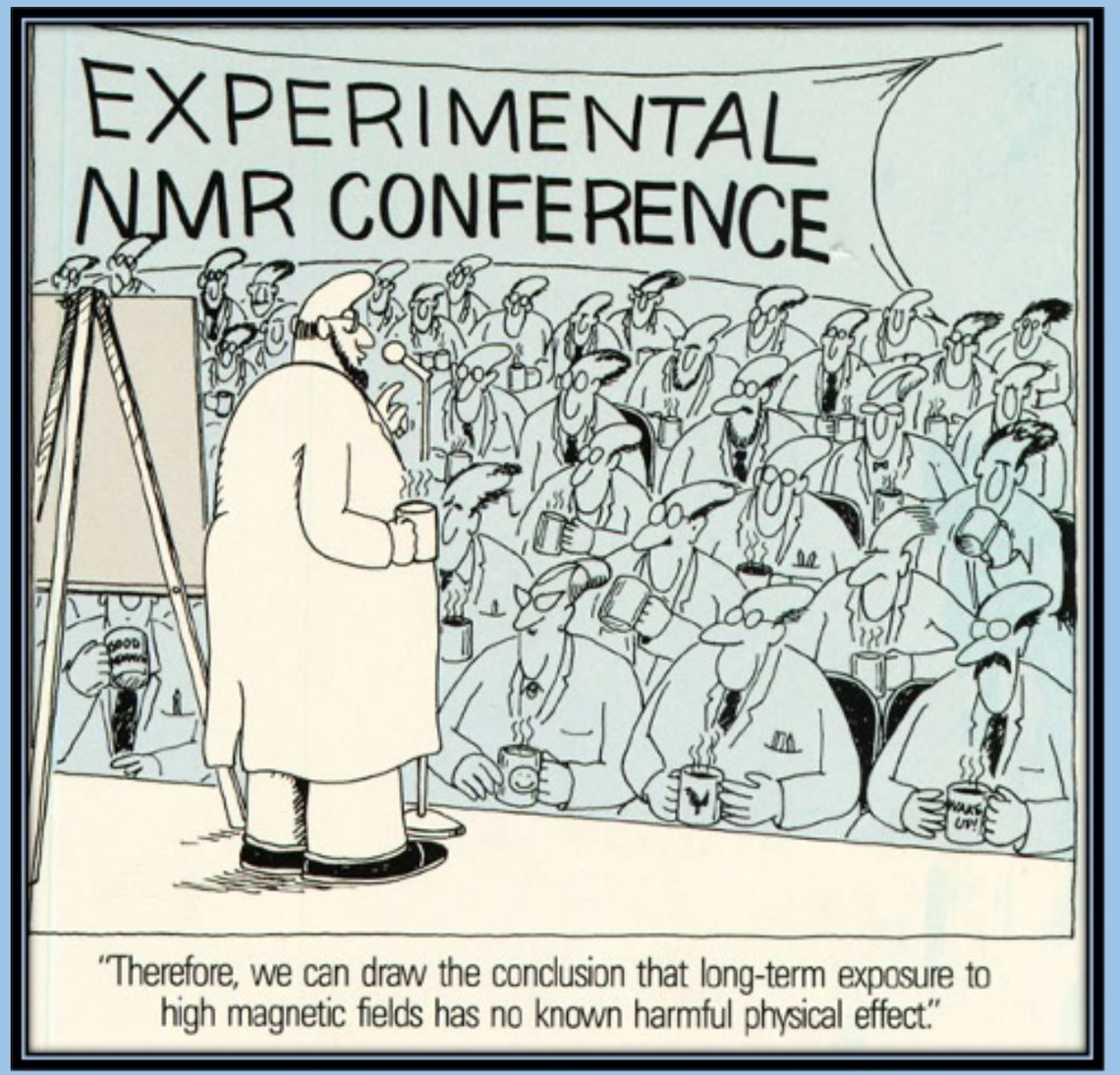
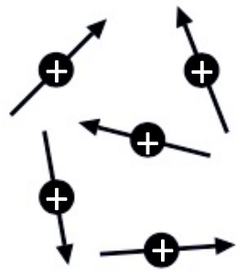
CHEM224

H^1-NMR Spectroscopy



The BASICS

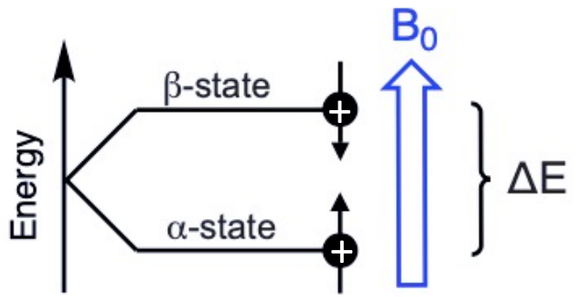
NMR Spectroscopy is a technique used to determine a compound's structure by manipulating the electromagnetism of the atomic nucleus. Because the **nucleus** is a spinning (+) charged particle, it generates its own magnetic field.



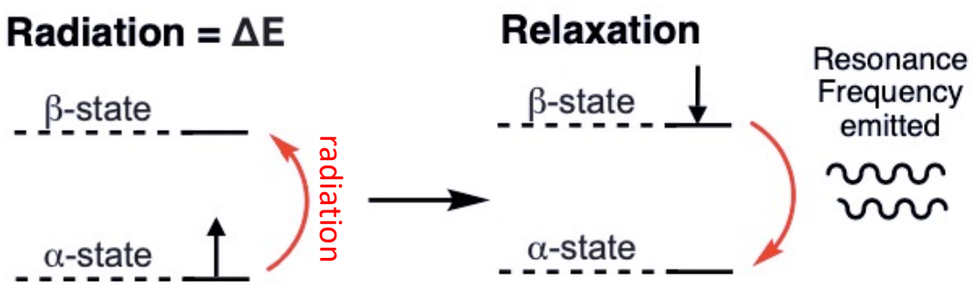
Random nuclear spins induce B fields random directions.

When an **external magnetic field** (B_0) is applied to the molecular nuclei, the spins (and their resultant fields) align themselves with or against B_0.

Aligning with B_0 results in a LOWER energy state (**α-state**), while aligning against the field results in a HIGHER energy state, (**β-state**).



As the nucleus relaxes and returns to the α-state, it releases electromagnetic energy that is transduced into an NMR spectrum. This flipping between α- to the β-state is known as **resonance**.



IMPORTANT NMR VOCAB

- **NMR Signal:** a peak that represents a particular bond in the structure
    - For H^1-HMR, each unique H bond will produce 1 NMR signal
    - For C^{13}-NMR, each unique C bond will produce 1 NMR signal
- **Chemical Shift** (δ) **:** the resonant frequency of a nucleus relative to a standard (e.g. TMS)
    - "where" the NMR signal occurs on the spectrum

    Note: the "ppm" value is reported relative to the spectrometer frequency
- **Shielding**: a ***decrease*** in chemical shift of a H^1 or C^{13} nucleus; feels ***weaker*** magnetic field
    - results in a **lower** ppm value (i.e. shifts right)
- **Deshielding**: an ***increase*** in chemical shift of a H^1 or C^{13} nucleus; feels ***greater*** magnetic field
    - results in a **higher** ppm value (i.e. shifts left)
- **Integration**: the measured area under a signal, which is used to determine the relative number of H's that produce that NMR signal
- **Splitting**: The shape of (or "number of peaks within") each signal, which is caused by the magnetic effect of *non*-equivalent neighboring hydrogen atoms.
    - Predictable according to the ***n+1*** **rule**

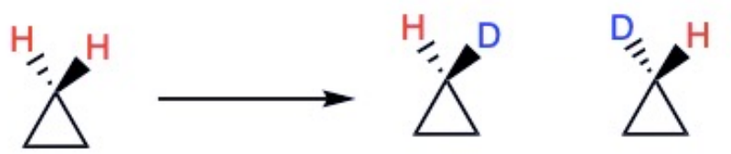
1. NUMBER OF SIGNALS

For H^1-NMR, the number of signals indicates the number of chemically unique protons.

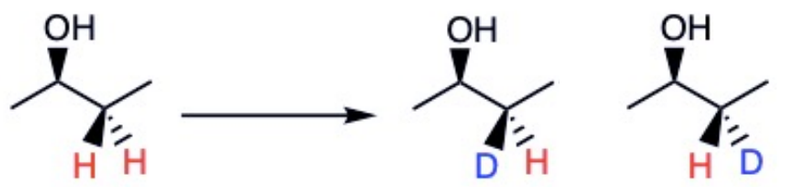
Chemically Equivalent H's → produce 1 signal
- **homotopic**: equivalence from rotational symmetry
- **enantiotopic**: equivalence from reflectional symmetry

Chemically Inequivalent H's → produce >1 signal
- **diastereotopic**: no equivalence from lack of symmetry

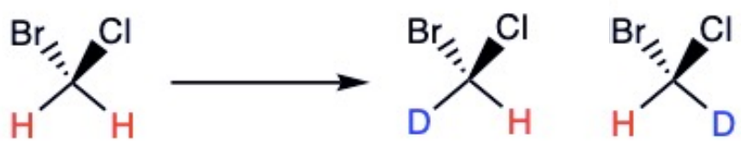
The relationship between two protons can be determined according to the **Replacement Test.**
To judge the equivalence of 2 vinylic H's, replace each H with a D one at a time and compare the compounds:



Identical (homotopic)



diastereomers (diastereotopic)

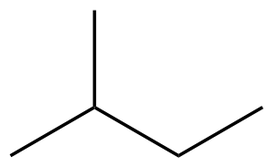


enantiomers (enantiotopic)

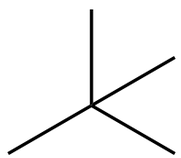
QUICK TIPS:
(1) Methyl groups are always homotopic.
(2) CH_2 groups are typically equivalent if there are no chiral centers present on the compound.
(3) 2 CH_2 groups are equivalent if there is a plane of symmetry.

PRACTICE: How many H^1-NMR signals will result from the following compounds?

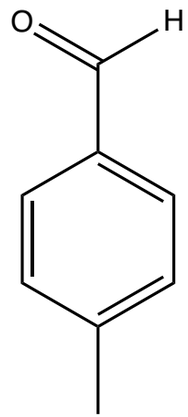
a)



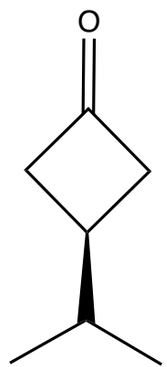
b)



c)



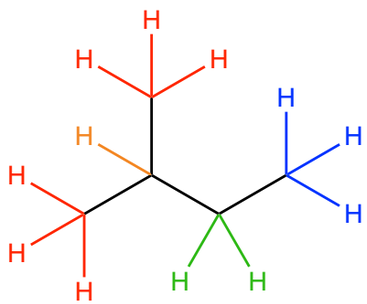
d)



ANSWER KEY

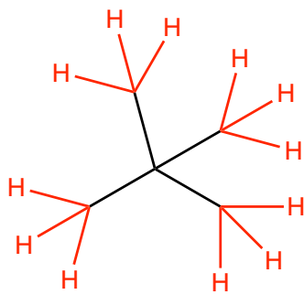
PRACTICE: How many H1-NMR signals will result from the following compounds?

a)



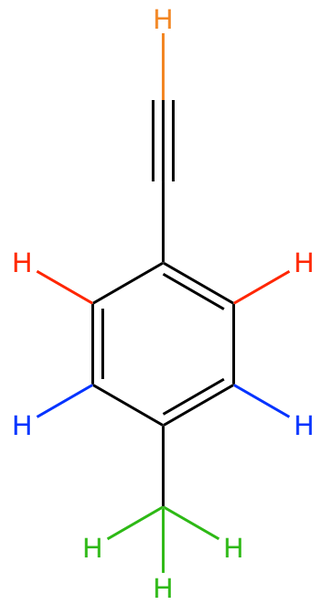
4 signals

b)



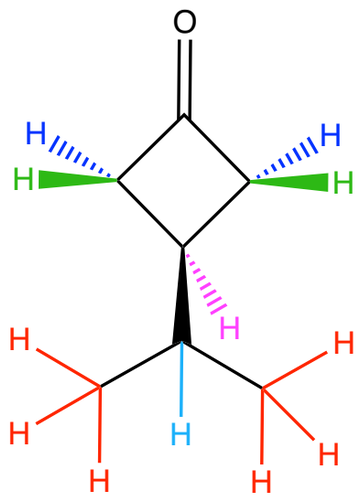
1 signal

c)



4 signals

d)



5 signals

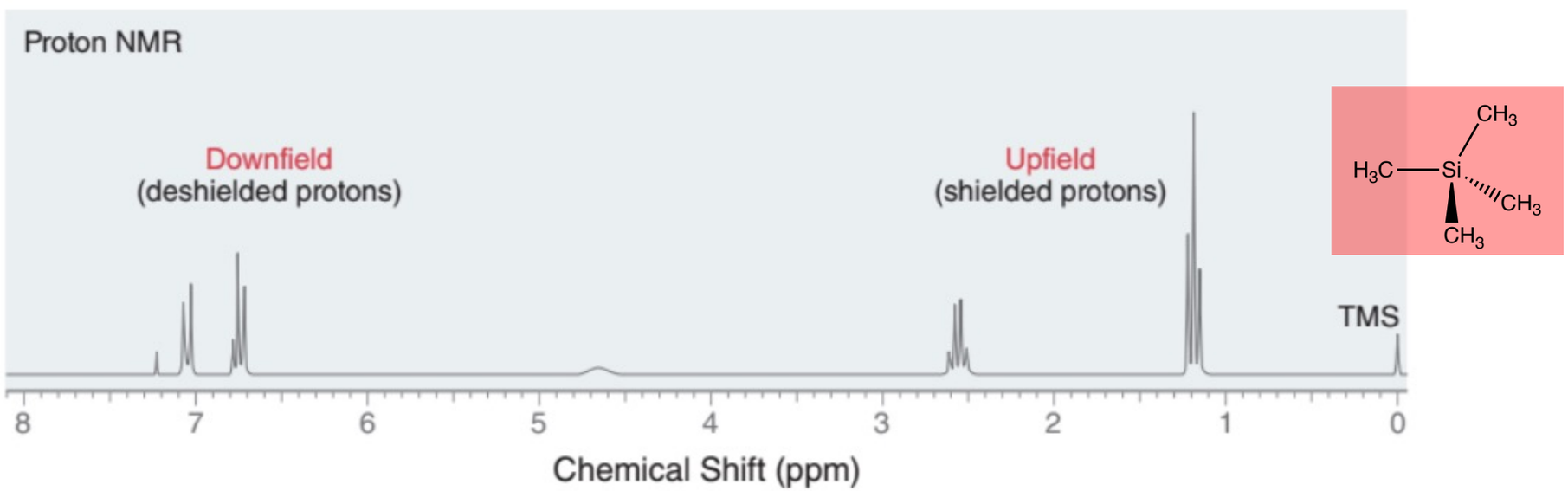
2. CHEMICAL SHIFT (δ)

The **location** of the signal on the spectrum, indicating the chemical environment of the H.

As each proton feels a different magnetic field based on its location and to which atoms it is bonded, certain signals will be shifted either **upfield** (shielded) or or **downfield** (deshielded).

Note: A well-shielded molecule is used as a standard (typically TMS), all other H signals are relative to the standard signal.

$$\delta = \frac{frequency\ of\ signal - frequency\ of\ reference}{spectrometer\ frequency} \times 10^6$$



2a. Calculating Chemical Shift

The chemical shift is described in ppm to remain **independent** from the spectrometer frequency

- To calculate shift, we must consider:
  - Frequency of Reference, ex. TMS (Hz), typically 0 Hz
  - Frequency of Specific H^1 (Hz)
  - Frequency of spectrometer (Hz)

$$\delta = \frac{frequency\ of\ signal - frequency\ of\ reference}{spectrometer\ frequency} \times 10^6$$

1. At what frequency would the chemical shift of chloroform ($CHCl_3$, δ = 7.28 ppm) occur relative to TMS on a spectrum recorded on a 300 MHz spectrometer?

2. What would be the chemical shift of a peak that occurs 655.2 Hz downfield of TMS on a spectrum recorded using a 90 MHz spectrometer?

3. A 1 GHz (1000 MHz) NMR spectrometer is being developed. At what frequency and chemical shift would chloroform occur?

ANSWER KEY

- The chemical shift is described in ppm to remain **independent** from the spectrometer frequency.
- To calculate shift, we must consider:
  - Frequency of Reference, ex. TMS (Hz)
  - Frequency of Specific H^1 (Hz)
  - Frequency of spectrometer (Hz)

$$\delta = \frac{frequency\ of\ signal - frequency\ of\ reference}{spectrometer\ frequency} \times 10^6$$

1. What would be the chemical shift of a peak that occurs 655.2 Hz downfield of TMS on a spectrum recorded using a 90 MHz spectrometer?

   The frequency of the standard is presumed to be 0 Hz. $\delta = \frac{655.2\ Hz - 0\ Hz}{90 \times 10^6\ Hz} \times 10^6 = \mathbf{7.28\ ppm}$

2. At what frequency would the chemical shift of chloroform ($CHCl_3$, δ = 7.28 ppm) occur relative to TMS on a spectrum recorded on a 300 MHz spectrometer?

   7.28 ppm $= \frac{frequency\ of\ signal - 0}{300 \times 10^6\ Hz} \times 10^6$ 7.28 ppm $= \frac{frequency\ of\ signal}{300}$

   $frequency\ of\ signal = (300\ Hz)(7.28)$

   $frequency\ of\ signal = \mathbf{2184\ Hz}$

1. A 1 GHz (1000 MHz) NMR spectrometer is being developed. At what frequency and chemical shift would chloroform occur?

   Because the shift is independent from the frequency of the spectrometer, the **shift remains at 7.28 ppm** .

   7.28 ppm $= \frac{frequency\ of\ signal - 0}{1000 \times 10^6\ Hz} \times 10^6$ 7.28 ppm $= \frac{frequency\ of\ signal}{1000\ Hz}$

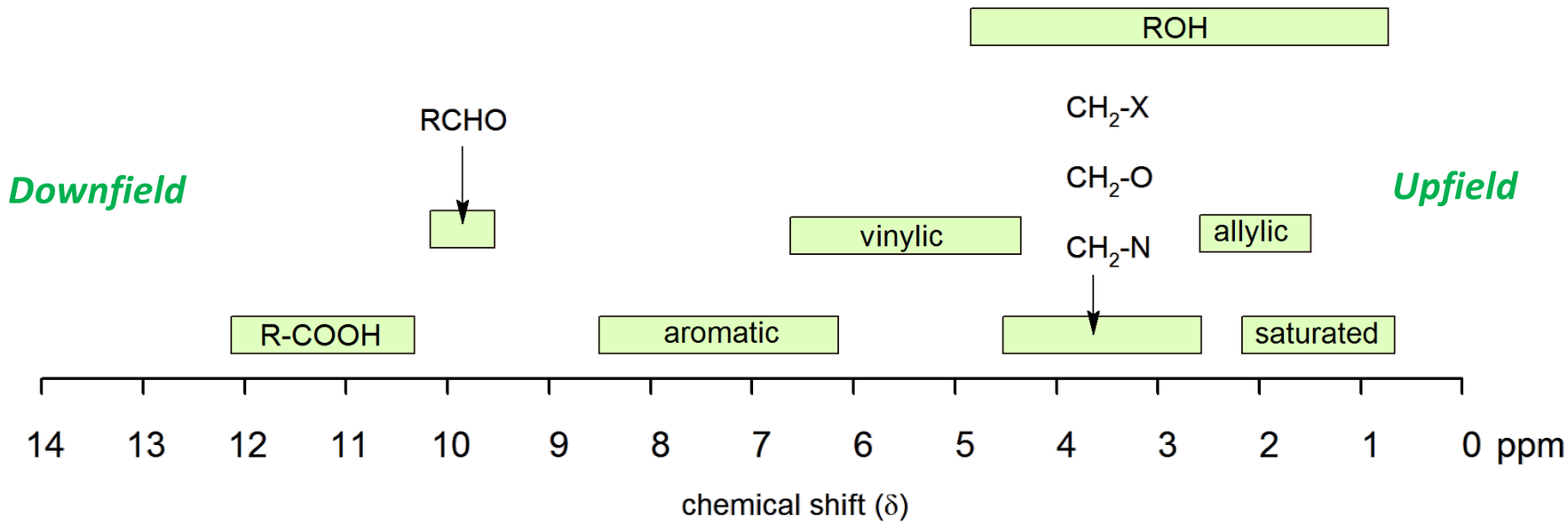
   $frequency\ of\ signal = (1000\ Hz)(7.28)$

   $frequency\ of\ signal = \mathbf{7280\ Hz}$

2b. CHARACTERISTIC SHIFTS

Certain C–H groups and functional groups have **characteristic shifts** that can help estimate the chemical shift.

Downfield shifts are due to the electron-withdrawing (i.e. deshielding) effect of atoms within the functional groups.



The **inductive effect** caused by the presence of electronegative atoms is most evident at the **α-position** and tapers off at the **β-position** (only 20% of the inductive effect results).

- The **γ**-position is unaffected.
- Multiple electronegative atoms produce an additive effect.

2c. ESTIMATING CHEMICAL SHIFT

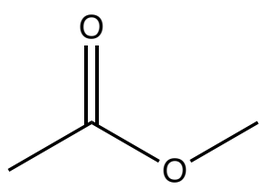
In the absence of inductive effects, benchmark values can be approximated by:

- the type of C–H bond
- any neighboring O or C=O

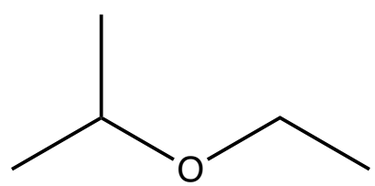
GROUP	ppm	GROUP	(α) ppm	(β) ppm
Methyl	+ 0.9	Ester O	+ 2.5	+ 0.5
Methylene	+ 1.2	Alcohol/Ether O	+ 3.0	+ 0.6
Methine	+ 1.7	Carbonyl	+ 1.0	+ 0.2

PRACTICE: Using the table above, estimate the chemical shift of the protons on the following compounds.

a)



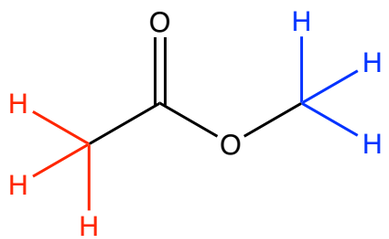
b)



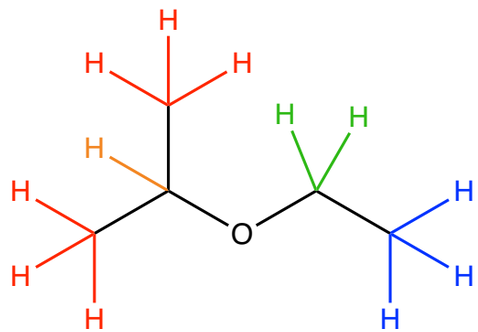
ANSWER KEY

PRACTICE: Using the table provided on the previous slide, estimate the chemical shift of the protons on the following compounds.

a)



b)



GROUP	ppm	GROUP	(α) ppm	(β) ppm
Methyl	+ 0.9	Ester O	+ 2.5	+ 0.5
Methylene	+ 1.2	Alcohol/Ether O	+ 3.0	+ 0.6
Methine	+ 1.7	Carbonyl	+ 1.0	+ 0.2

H signal: methyl + 0.9
α to carbonyl + 1.0
β to ester O + 0.5
2.4 ppm

H signal: methyl + 0.9
α to ester O + 2.5
β to carbonyl + 0.2
3.6 ppm

H signal: methyl + 0.9
β to ether O + 0.6
1.5 ppm

H signal: methine + 1.7
α to ether O + 3.0
4.7 ppm

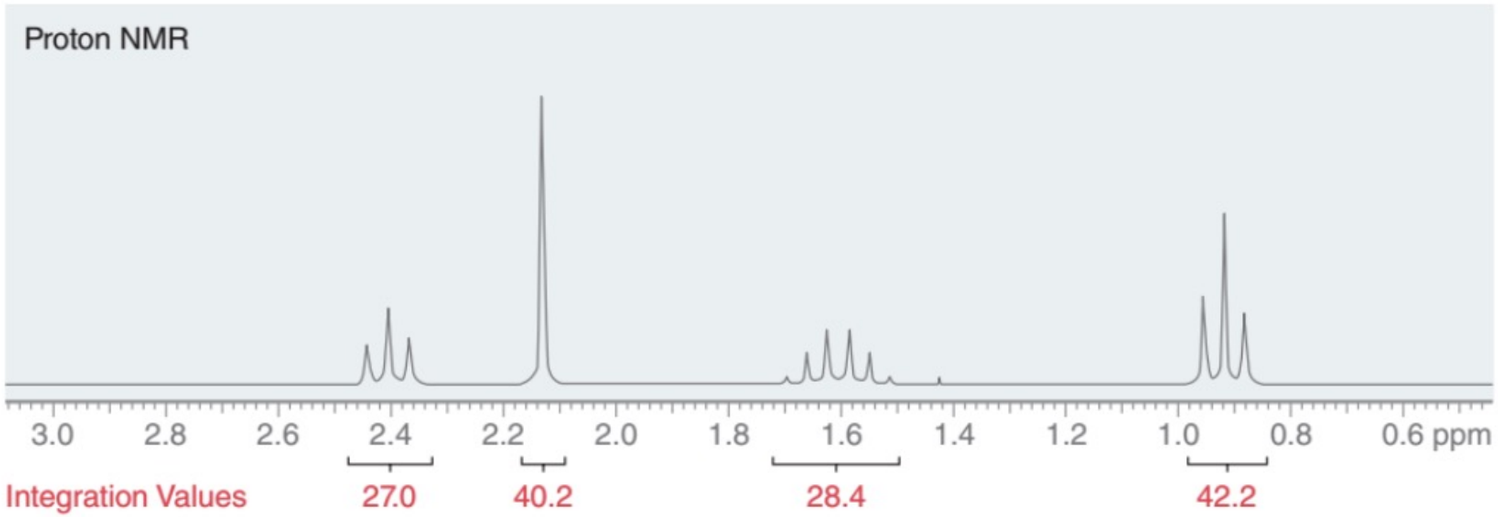
H signal: methylene + 1.2
α to ether O + 3.0
4.2 ppm

H signal: methyl + 0.9
β to ether O + 0.6
1.5 ppm

3. INTEGRATION

The **measured area** under a given signal; determines the relative number of H's that correspond to each signal.

Integration values are only useful when compared to each other. To use them, you must choose the smallest number and divide all the integration values by this number.



1. **Find smallest value.**
   The most deshielded value is
   the smallest: 27.0

2. **Divide all integrations by that value.**

$$\frac{27.0}{27.0} = 1.00 \qquad \frac{40.2}{27.0} = 1.49$$

$$\frac{28.4}{27.0} = 1.05 \qquad \frac{42.2}{27.0} = 1.56$$

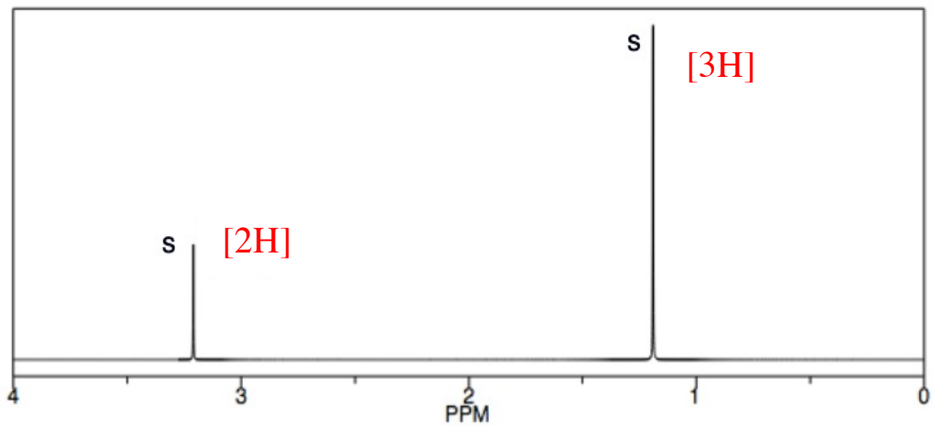
3. **Round values.**
   1.0 : 1.5 : 1.0 : 1.5

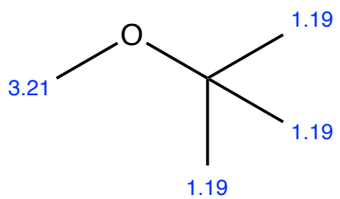
4. **Multiply to integers, if needed.**
   Having 1.5 H's is not possible, so all values must be multiplied x2.

   2 : 3 : 2 : 3

3a. INTEGRATION: Symmetry

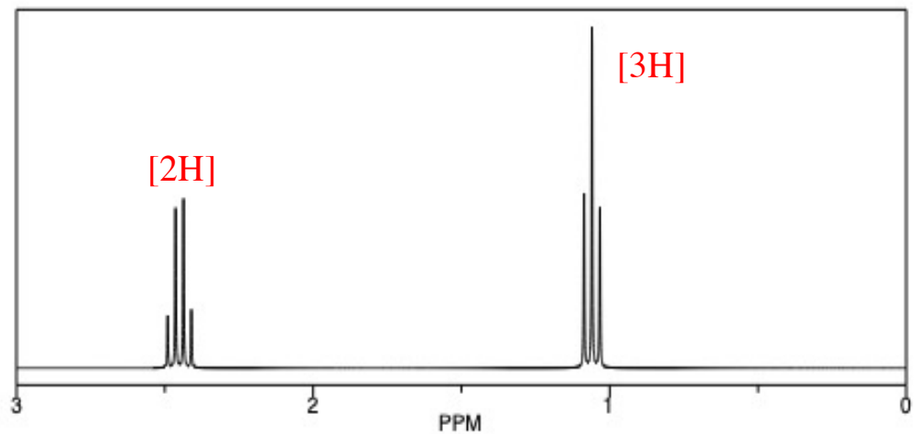
Integration ratios are only the *relative* number of H's that produce each signal. The compounds MTBE (*tert*-butyl methyl ether) and 3-pentanone represent this concept well.

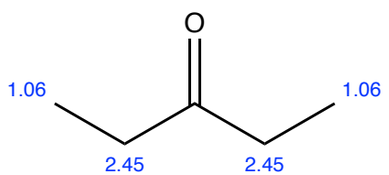




The spectrum indicates a 1 : 3 ratio, but there are not only 4 H's.

The ratio is relative to itself and can represent a 2 : 6 or even 3 : 9 ratio.





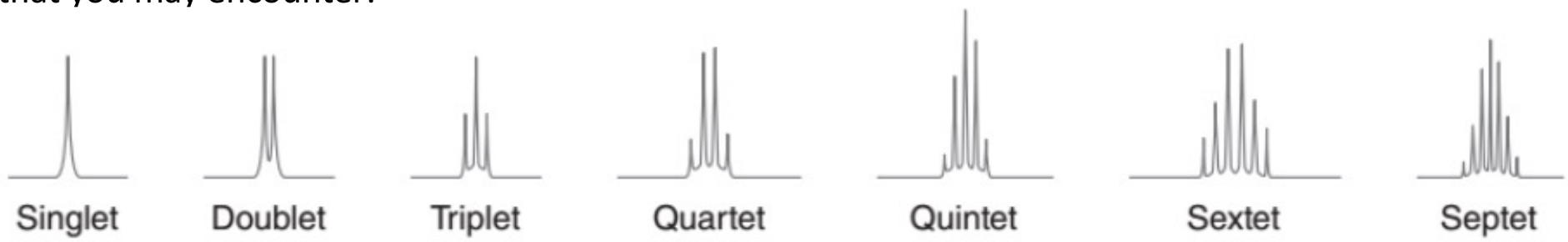
The spectrum indicates a 2 : 3 ratio, but there are not only 5 H's.

The ratio is relative to itself and represents a 4 : 6 ratio.

Note: **Symmetrical compounds** will only produce integration ratios representing half of the compound.

4. SPLITTING

The **shape of the signal** (i.e. number of peaks within the signal) is caused by the magnetic effect of *non*-equivalent neighboring hydrogen atoms. This splitting is predictable and follows a simple *n+1* rule. The following are the types of peaks that you may encounter:



Splitting occurs because a neighboring proton (2 to 3 bonds away from the proton in question) can experience two possible magnetic moments relative to the external magnetic field: aligning *with* it or *against* it.

Note: If there are no neighboring non-equivalent hydrogens (such as in MTBE), no splitting is observed.

This follows the ***n* + 1 rule**, with ***n* = the # of chemically-equivalent neighboring protons**.

4a. The *n + 1* Rule

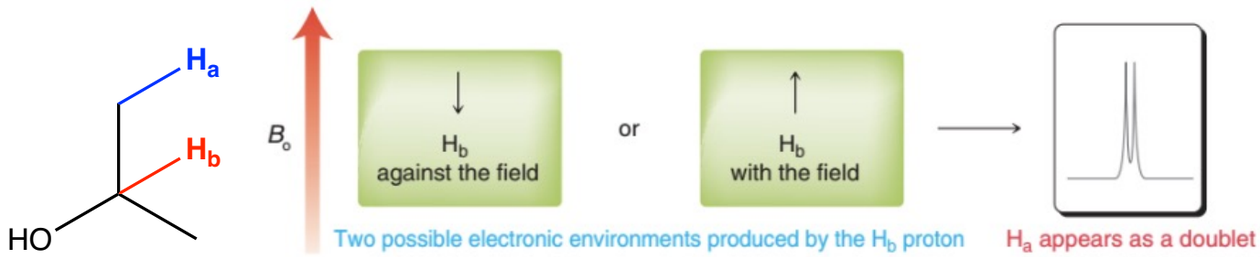
For a single H, its resultant magnetic field can be aligned either *with* or *against* the external magnetic field (B_0). Thus, two distinct magnetic moments are created: *with* B_0 or *against* B_0. Because the H nucleus is affected by both of its neighbor's magnetic moments, the signal splits into a **doublet.**

SPLITTING OF H_a

The only chemically-inequivalent neighbor is H_b (n = 1).

Note: H_a is <u>not</u> split by the other chemically-equivalent H_a protons.

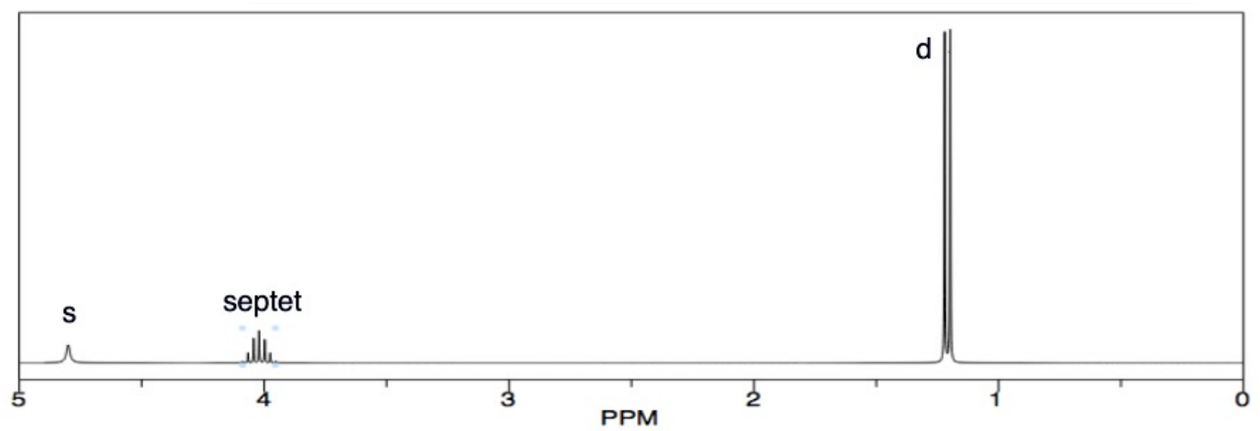
Splitting = n + 1 = 2 (doublet)



SPLITTING OF H_b

H_b is split by the 6 neighboring H_a protons (n = 6).

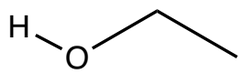
Splitting = n + 1 = 7 (septet)



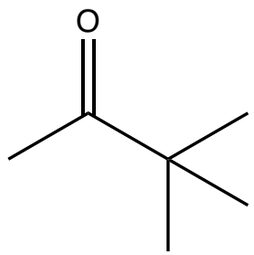
Note: Alcohol protons do not cause splitting because they are regularly exchanged with protic solvent.

PRACTICE: Determine the splitting patterns for each proton in the following compounds by determining the number of inequivalent neighboring protons and using the *n + 1* rule.

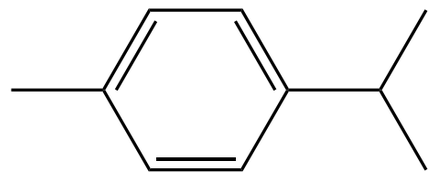
a)



b)

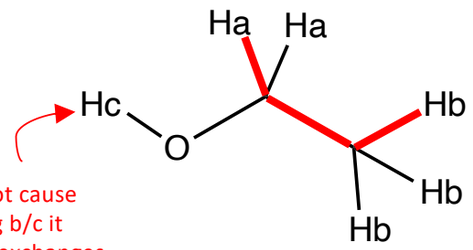


c)



ANSWER KEY

PRACTICE: Determine the splitting patterns for each proton in the following compounds by determining the number of unequivalent neighboring protons (within 2-3 bonds away) and using the *n + 1* rule.



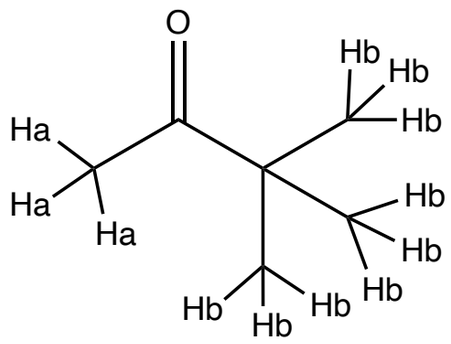
Does not cause splitting b/c it rapidly exchanges with other molecules of ethanol.

H_a signal – 3 H_b are 3 bonds away (n = 3)
Splitting = 3 + 1 = 4 (**quartet**), **2H**

H_b signal – 2 H_a are 3 bonds away (n = 2)
Splitting = 2 + 1 = 3 (**triplet**), **3H**

Pattern of **Ethyl** **:**

- quartet from 2H
- triplet of 3H

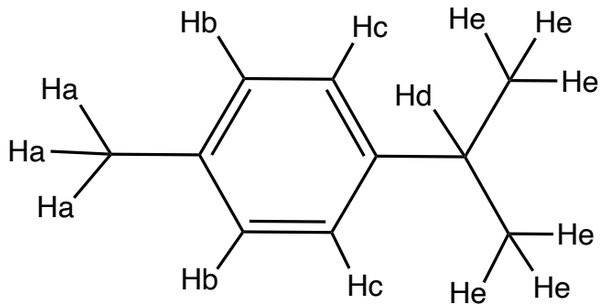


H_a signal – no chem-unequivalent neighbors within 2 to 3 bonds from H_a (n = 0)
Splitting = 0 + 1 = 1 (**singlet**), **3H**

H_b signal – no chem-unequivalent neighbors within 2 to 3 bonds from H_b (n = 0)
Splitting = 0 + 1 = 1 (**singlet**), **9H**

Pattern of **tert-Butyl** :

- singlet from 9H



H_a signal – 0 H's are 2-3 bonds away (n = 0)
Splitting = 0 + 1 = 1 (**singlet**), **3H**

H_b signal – **ortho**: 1 H_c is 3 bonds away (n = 1); (**d**)
meta: 1 H_b is 3 bonds away (no splitting)

H_c signal – **ortho**: 1 H_b is 3 bonds away (n = 1); (**d**)
meta: 1 H_c is 3 bonds away (no splitting)

Pattern of **para-sub. ring**:

- doublet, 2H
- doublet, 2H

H_d signal – 6 H_e are 3 bonds away (n = 6)
Splitting = 6 + 1 = 7 (**septet**), **1H**

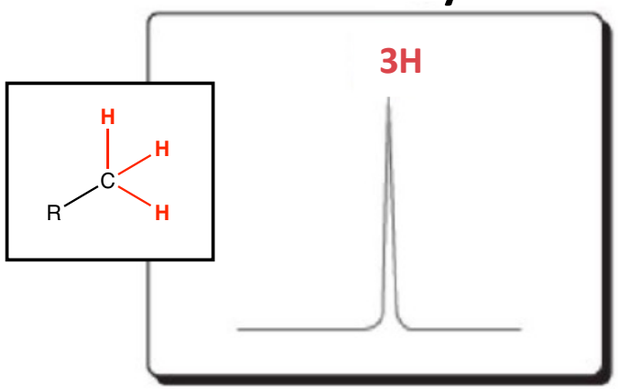
H_e signal – 1 H_d is 3 bonds away (n = 1)
Splitting = 1 + 1 = 2 (**doublet**), **6H**

Pattern of **isopropyl**:

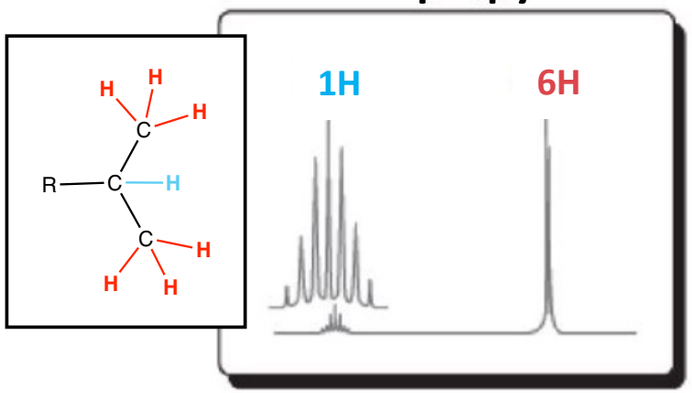
- septet, 1H
- doublet, 6H

4b. Common Patterns

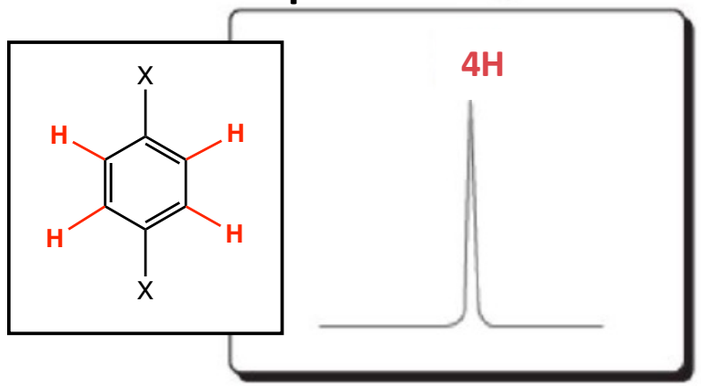
Methyl



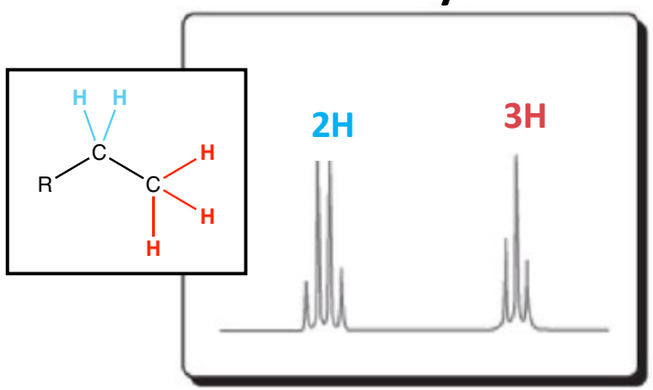
Isopropyl



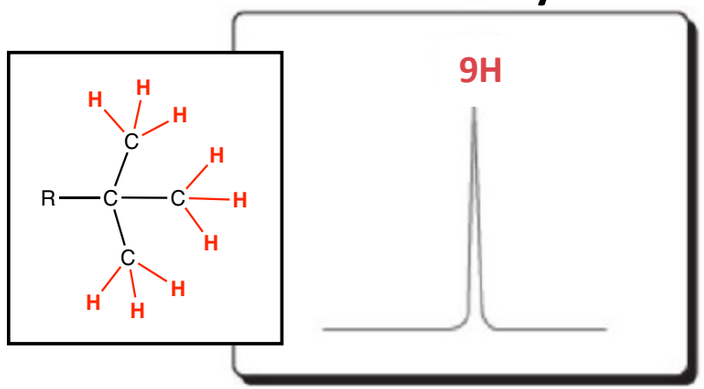
Symmetric para-substitution



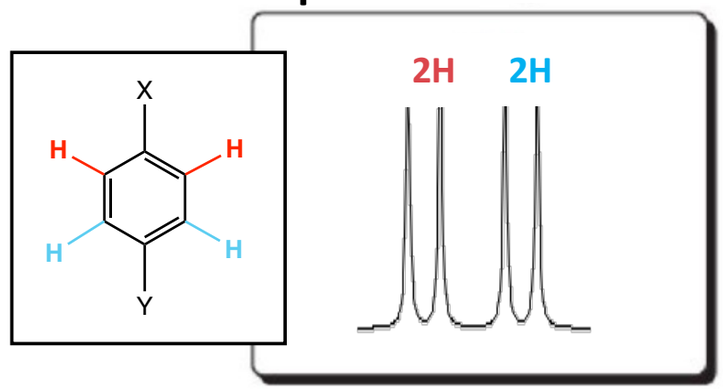
Ethyl



tert-Butyl

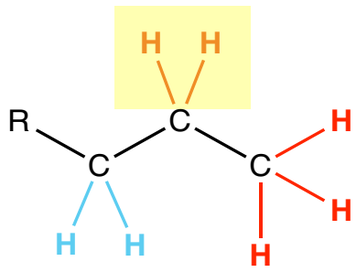


Asymmetric para-substitution



4b. Complex Splitting

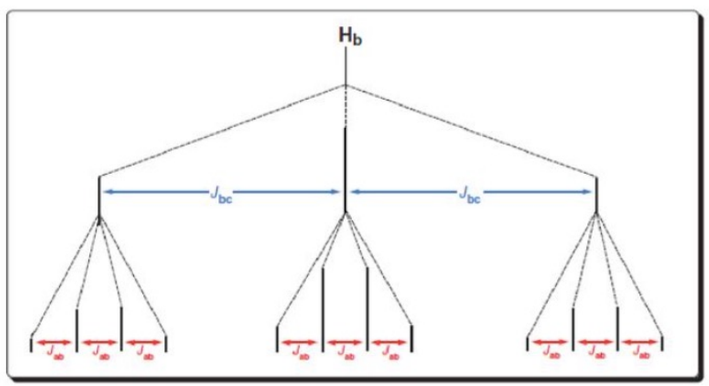
When there are multiple groups of inequivalent neighboring protons, complex splitting can occur.

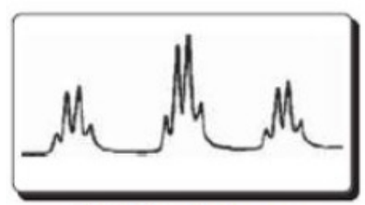


The yellow H's are split by two sets of H atoms.

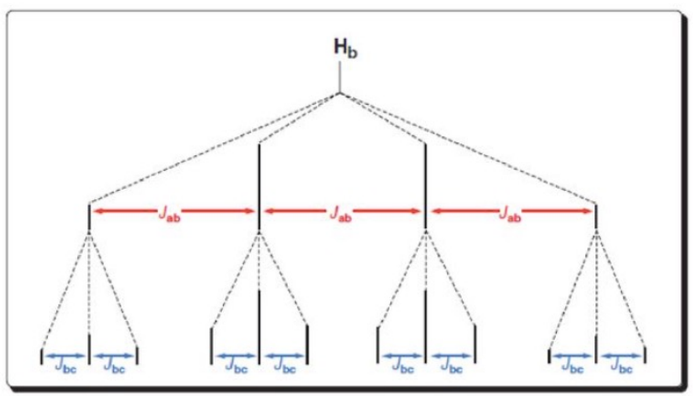
H signal – 3 H neighbors (n = 3)
Splitting = 3 + 1 = 4 (**quartet**)
– 2 H are neighbors (n = 2)
Splitting = 2 + 1 = 3 (**triplet**)

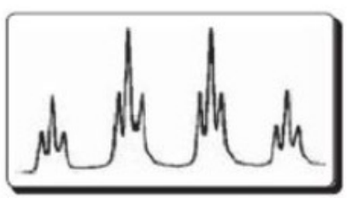
Which is it?
[2H, q] *or* [2H, t]



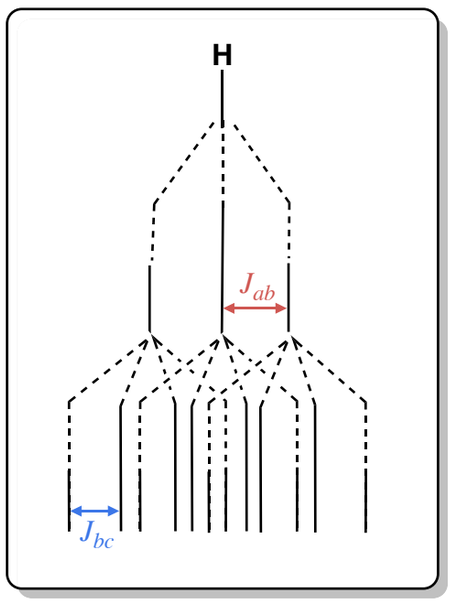


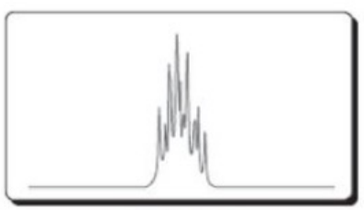
A triplet of quartets





A quartet of triplets

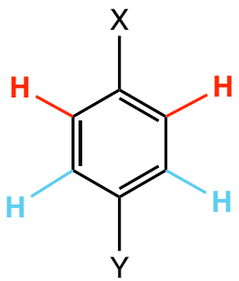




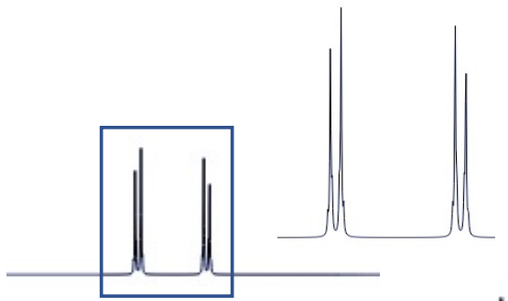
A multiplet

4c. Complex π Splitting: Aromatic H's

Calculating splitting patterns for aromatic H's must include ortho & meta splitting:

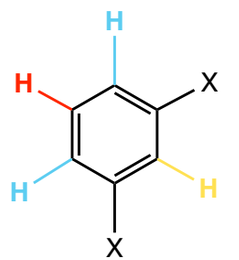


Asymmetric *para*-splitting

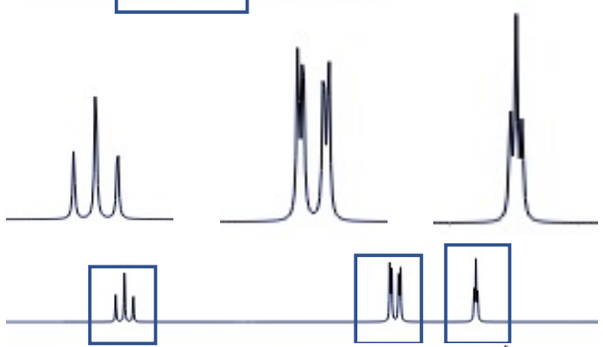


H – ortho: 1H
meta: no H's
(d)
(s)
doublet

H – ortho: 1H
meta: no H's
(d)
(s)
doublet



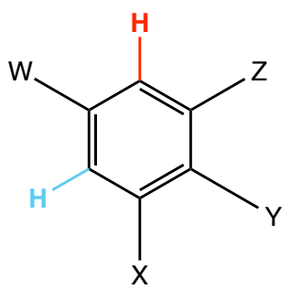
Symmetric *meta*-splitting



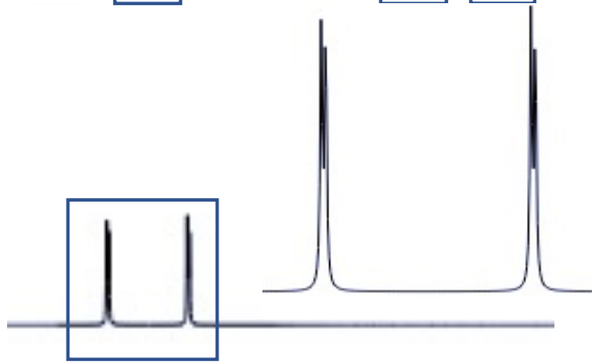
H – ortho: 2H
meta: no H's
(t)
(s)
triplet of singlets

H – ortho: 1H
meta: 1H
(d)
(d)
doublet of doublets

H – ortho: no H's
meta: 2H
(s)
(t)
singlet of triplets



Meta-Coupling of Aromatic H's

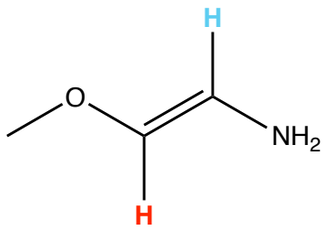


H – ortho: no H's
meta: 1H
(s)
(d)
singlet of doublets

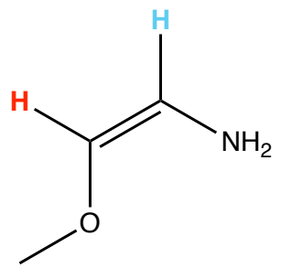
H – ortho: no H's
meta: 1H
(s)
(d)
singlet of doublets

4c. Complex π Splitting: Alkene H's

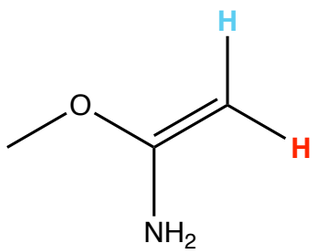
The position of vinylic H's affects the J-value and the results in characteristic trans, cis, and geminal splitting:



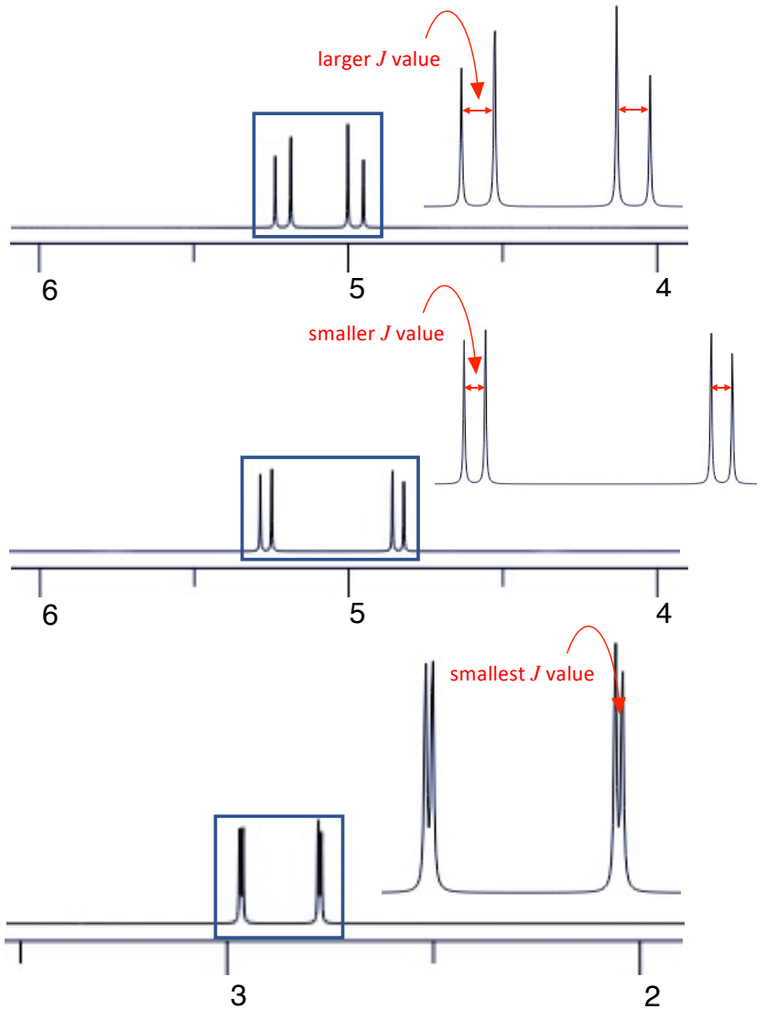
trans **alkene**



cis **alkene**



geminal alkene



Each alkene has only 2 H's, which only have each other as neighbors.

H – split by 1**H** (d)
H – split by 1**H** (d)

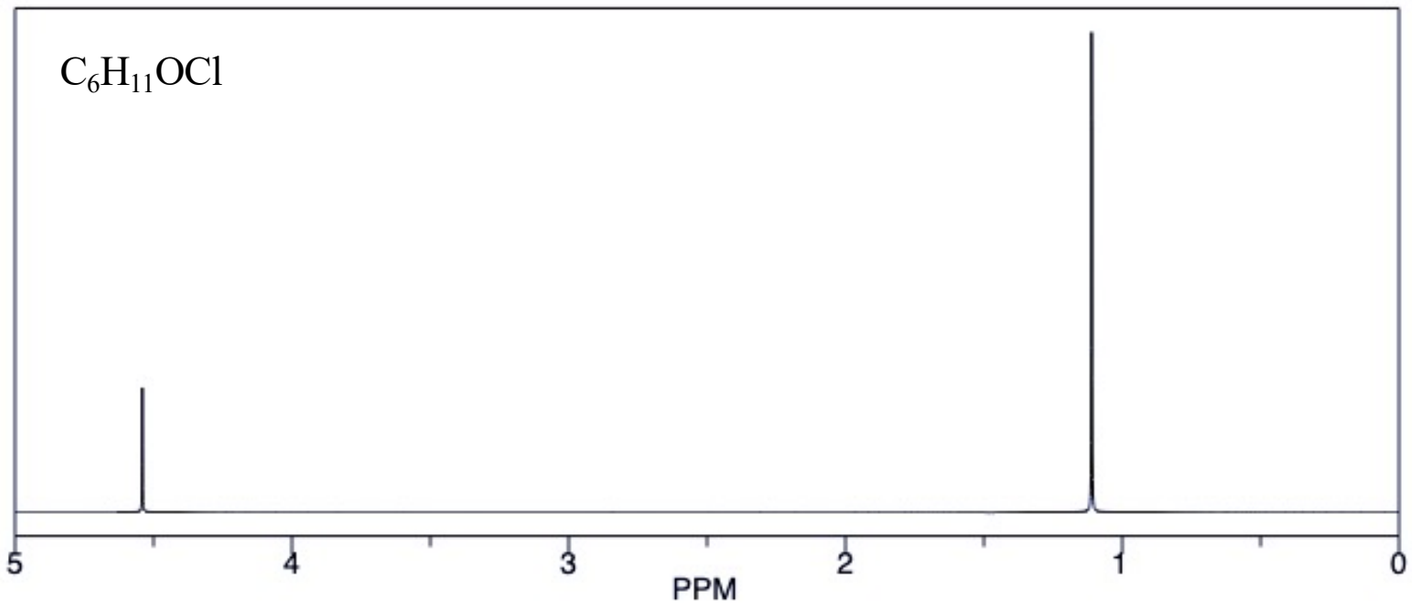
Thus, all signals are pairs of doublets.

The *J* values differ between alkenes, because the frequencies for each have different ranges:

Coupling	Range (Hz)	Typical (Hz)
Cis	6-14	10
Trans	11-18	16
Geminal	0-3	2

This observation is typically only useful when comparing spectra of isomeric alkenes.

PRACTICE 1: Use the following molecular formula and H^1-NMR spectrum to draw the compound.



STRATEGY: (1) If given molecular formula, calculate HDI.

– indicates # of π bonds and/or rings

(2) Calculate integration, if needed.

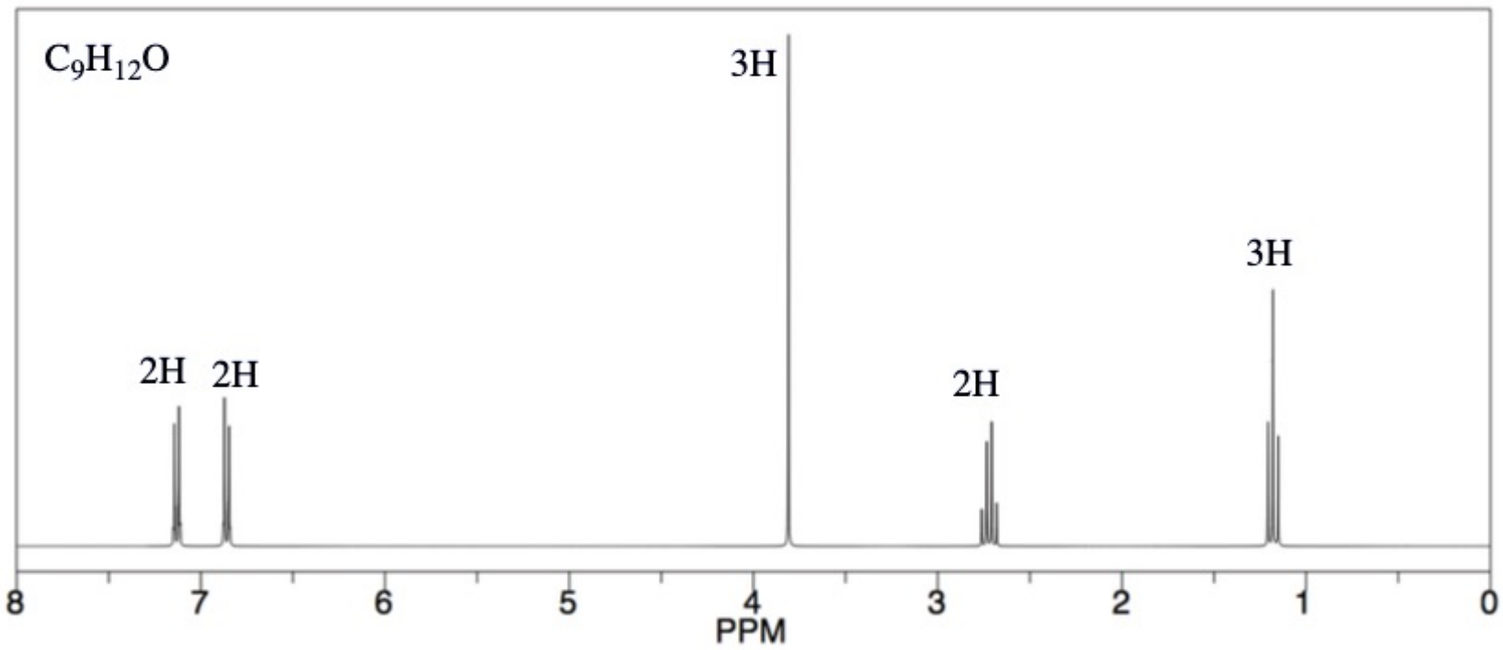
– reveals potential symmetry

(3) Analyze signals for common patterns.

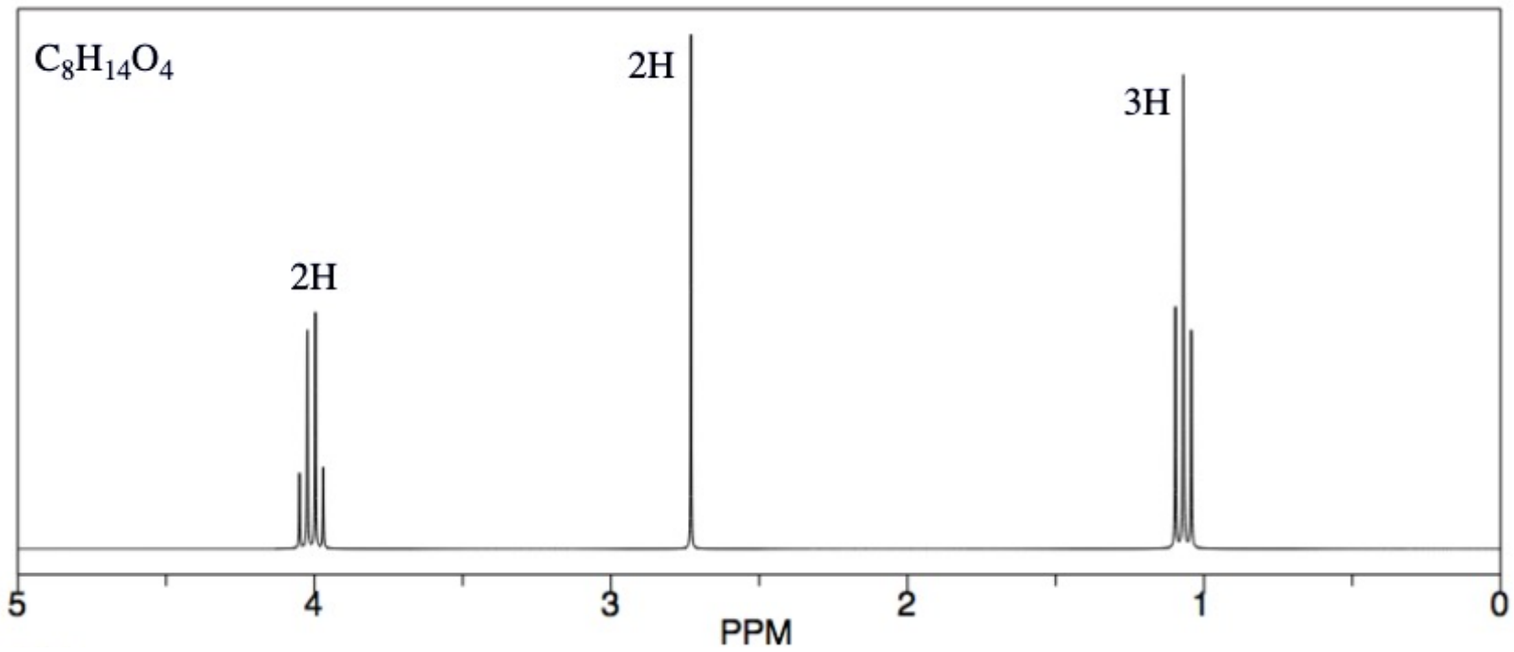
– draw consistent fragments

(4) Assemble fragments according to shifts.

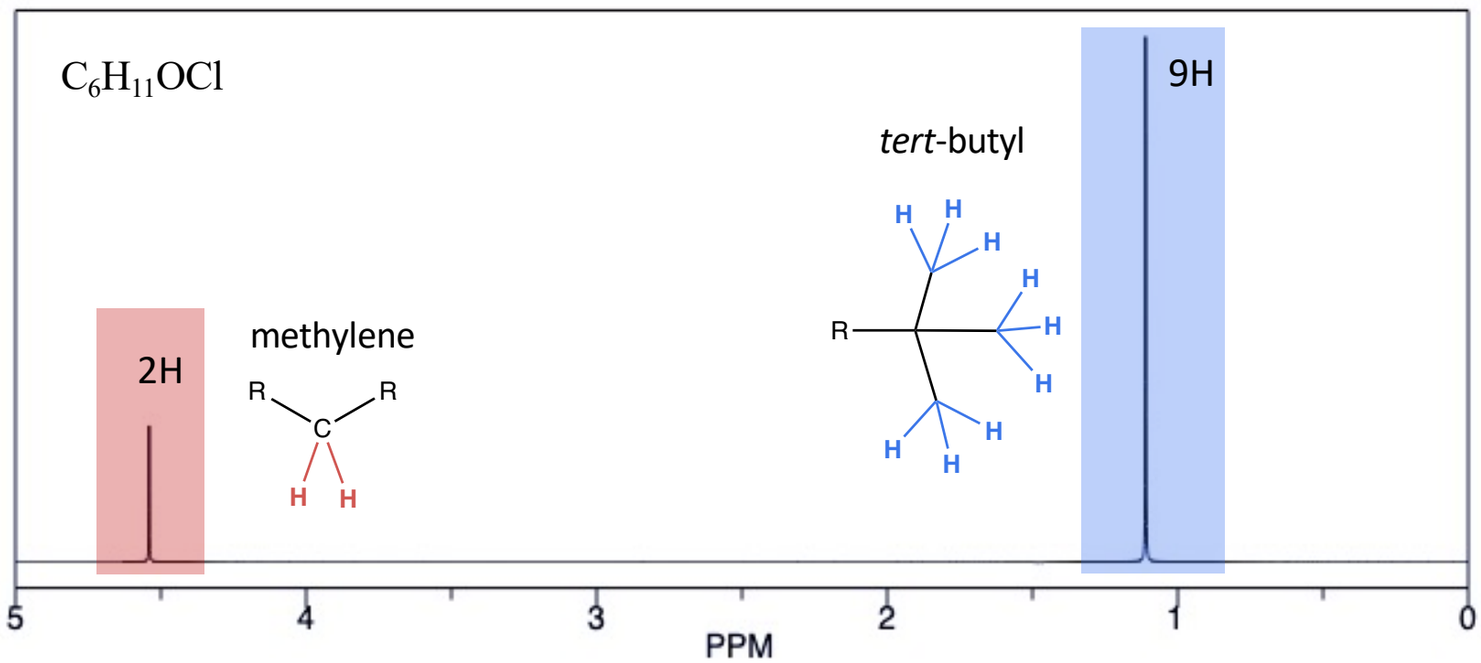
PRACTICE 2: Use the following molecular formula and H^1-NMR spectrum to draw the compound.



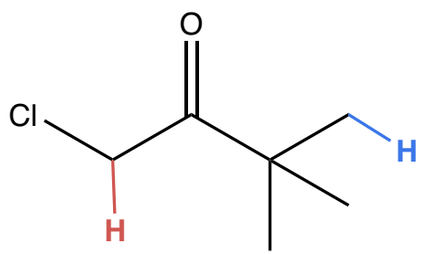
PRACTICE 3: Use the following molecular formula and H^1-NMR spectrum to draw the compound.



ANSWER KEY



ANSWER:



1-chloro-3,3-dimethylbutan-2-one

(1) Calculate HDI

$$HDI = \frac{2(6) + 2 - 11 - 1}{2} = 1$$

- Must have 1 π bond or 1 ring
- Presence of oxygen likely indicates carbonyl (C=O)

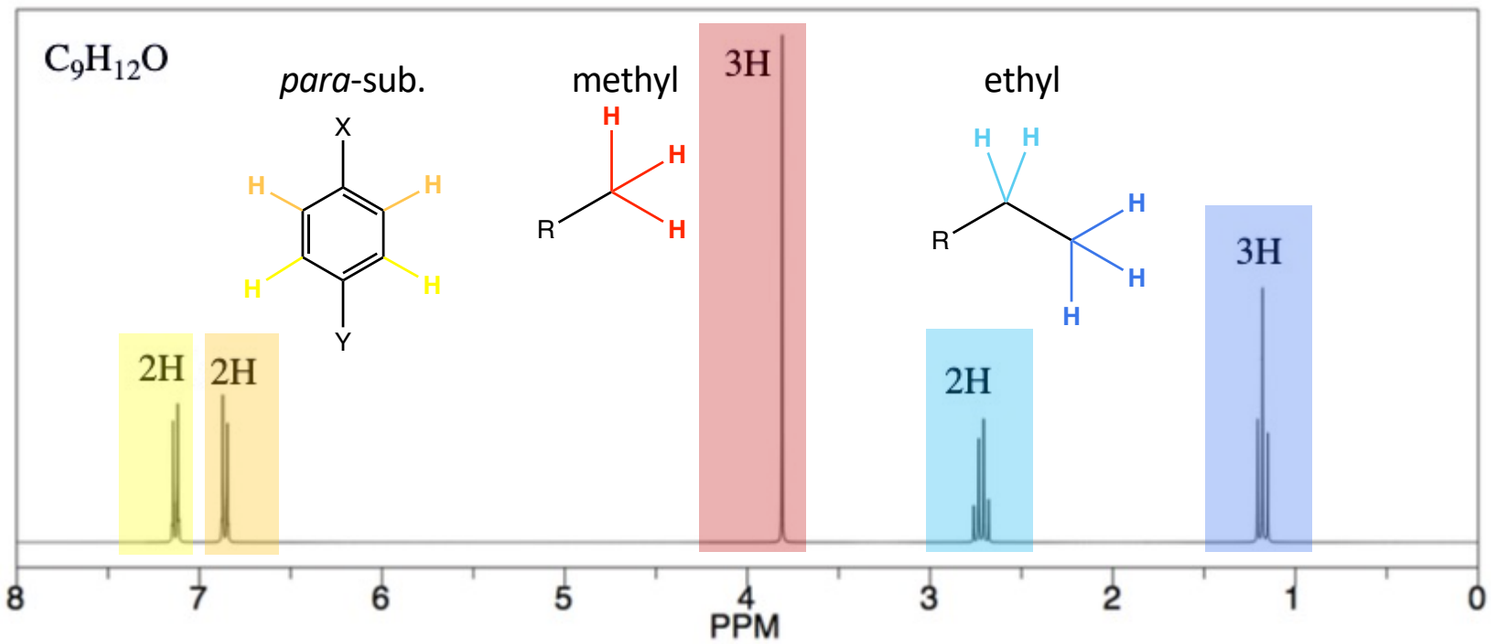
(2) *Integration given*

(3) Find fragment patterns

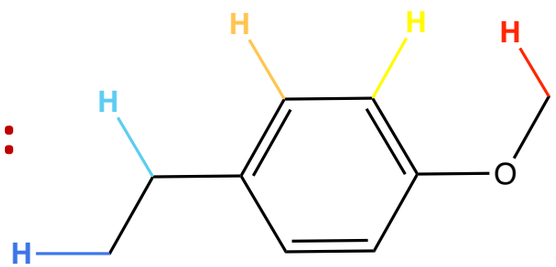
- methylene
- *tert*-butyl

(4) Deshielded CH_2 – next to Cl
Shielded t-Bu – away from Cl

ANSWER KEY



ANSWER:



1-ethyl-4-methoxybenzene

(1) Calculate HDI

$$HDI = \frac{2(9) + 2 - 12}{2} = 4$$

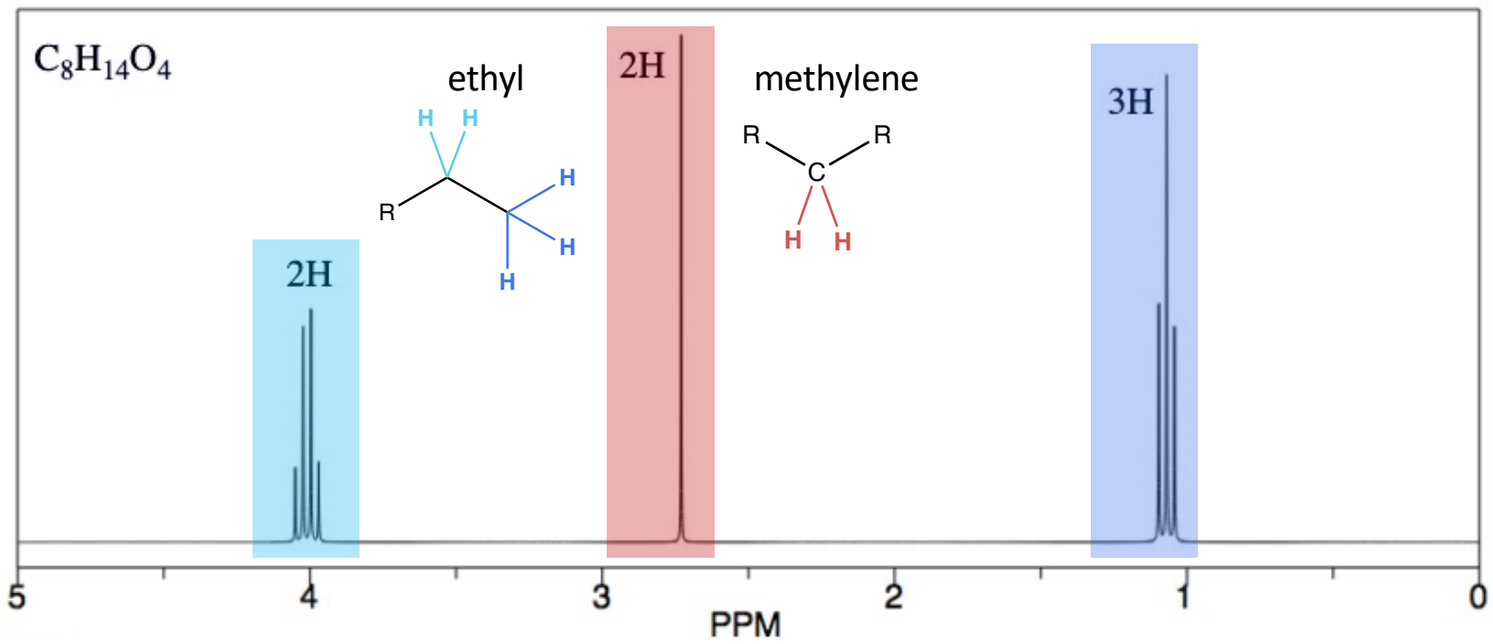
- Must have 4 DOUs
- Presence of peaks in aromatic region (6-8 ppm) indicate likely benzyl ring.

(2) *Integration given*

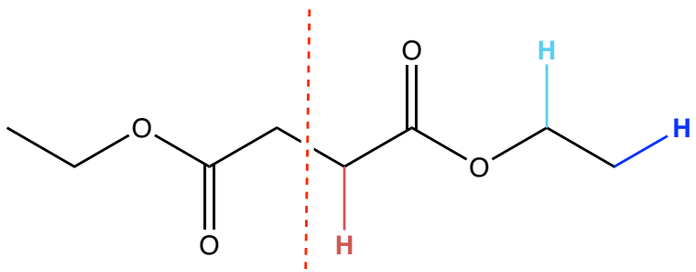
(3) Find fragment patterns
- ethyl
- methyl
- asymm. para-substitution

(4) Shielded Et – away from O
Deshielded Me – close to O

ANSWER KEY



ANSWER:



diethyl succinate

(1) Calculate HDI

$$HDI = \frac{2(8) + 2 - 14}{2} = 2$$

- Must have 2 DOUs
- Presence of 4 O's indicates a likelihood of 2 ester groups.

(2) Integration does <u>not</u> match molecular formula

- Molecule has 14 H's (only 7 shown)
- There must be 2 symmetric sides

(3) Find fragment patterns

- ethyl
- methylene

(4) Deshielded Et – closer to ester O
Shielded CH_2 – closer to ester C=O