Application of ^{1}H NMR in medicine: Magnetic Resonance Imaging (MRI):

Magnetic resonance imaging (MRI)—NMR spectroscopy in medicine—is a powerful diagnostic technique.

The "sample" is the patient, who is placed in a large cavity in a magnetic field, and then irradiated with RF energy.

Because RF energy has very low frequency and low energy, the method is safer than X-rays or computed tomography (CT) scans that employ high- frequency, high-energy radiation that is known to damage living cells.

Living tissue contains protons (especially the H atoms in H_2O) in different concentrations and environments.

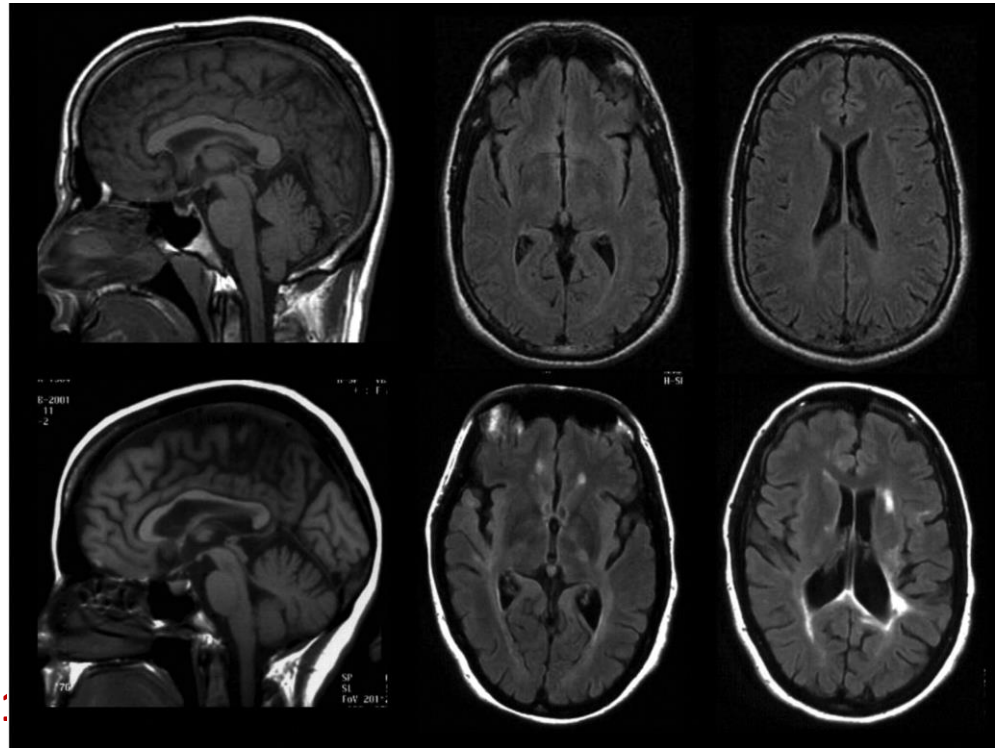
When irradiated with RF energy, these protons are excited to a higher energy spin state, and then fall back to the lower energy spin state.

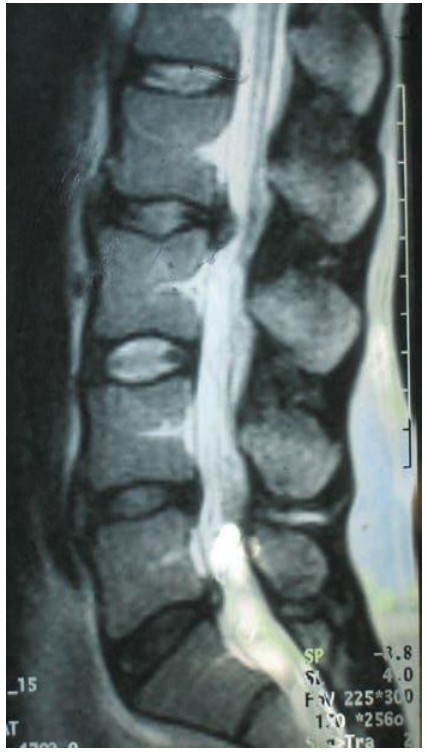
Application of ^{1}H NMR in medicine: Magnetic Resonance Imaging (MRI):

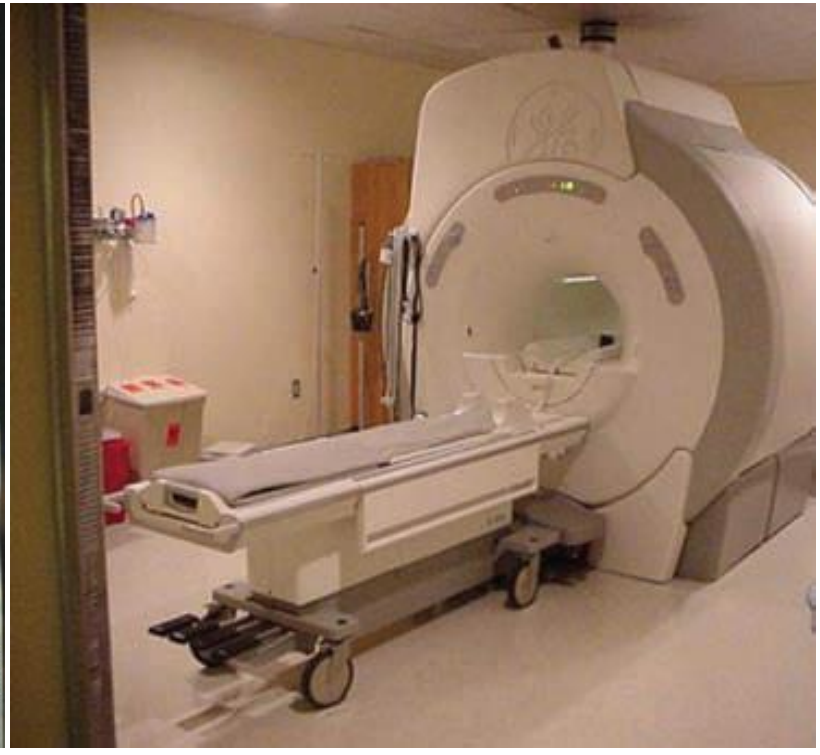
These data are analyzed by a computer that generates a plot that delineates tissues of different proton density.

MRIs can be recorded in any plane.

Moreover, because the calcium present in bones is not NMR active, an MRI instrument can “see through” bones such as the skull and visualize the soft tissue underneath.





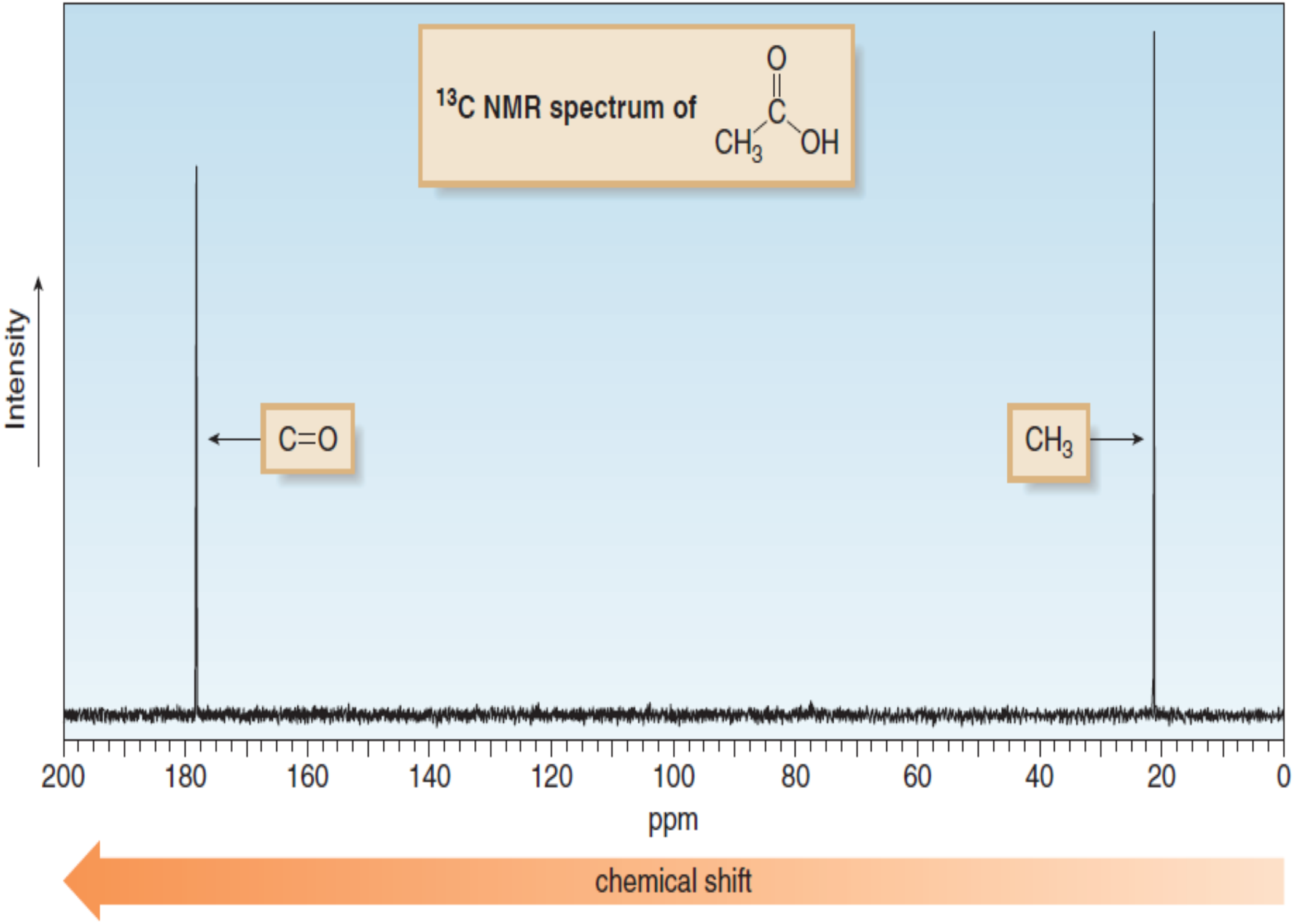


^{13}C NMR Spectroscopy:

- ^{13}C NMR spectroscopy is also an important tool for organic structure analysis.
- The physical basis for ^{13}C NMR is the same as for ^{1}H NMR.
- When placed in a magnetic field, B_0, ^{13}C nuclei can align themselves with or against B_0.
- More nuclei are aligned with B_0 because this arrangement is lower in energy, but these nuclei can be made to spin flip against the applied field by applying RF radiation of the appropriate frequency.
- ^{13}C NMR spectra, like ^{1}H NMR spectra, plot peak intensity versus chemical shift, using TMS as the reference signal at 0 ppm.

^{13}C NMR Spectroscopy:

- ^{13}C occurs in only 1.1% natural abundance, however, so ^{13}C NMR signals are much weaker than ^{1}H NMR signals.
- To overcome this limitation, modern spectrometers irradiate samples with many pulses of RF radiation and use mathematical tools to increase signal sensitivity and decrease background noise.
- ^{13}C NMR spectra are easier to analyze than ^{1}H NMR spectra because signals are not split.
- ***Each type of carbon atom appears as a single peak.***
- As shown in the next slide, the spectrum of acetic acid (CH_3COOH) illustrates the general features of a ^{13}C NMR spectrum.


^{13}C NMR spectrum of
O
C
CH_3
OH
Intensity
C=O
CH_3
200
180
160
140
120
100
80
60
40
20
0
ppm
chemical shift

^{13}C NMR Spectroscopy:

- **Why aren't ^{13}C signals split by nearby carbon atoms?**
- Splitting occurs when two NMR active nuclei (like two protons) are close to each other.
- Because of the low natural abundance of ^{13}C nuclei (1.1%), the chance of two ^{13}C nuclei being bonded to each other is very small (0.01%), and so no carbon–carbon splitting is observed.
- A ^{13}C NMR signal can also be split by nearby protons.
- This ^{1}H– ^{13}C splitting is usually eliminated from a spectrum, however, by using an instrumental technique that decouples the proton–carbon interactions, so that every peak in a ^{13}C NMR spectrum is a singlet.
- Two features of ^{13}C NMR spectra provide the most structural information: the number of signals observed and the chemical shifts of those signals.

^{13}C NMR: Number of Signals

The number of signals in a ^{13}C spectrum gives the number of different types of carbon atoms in a molecule.

Carbon atoms in the same environment give the same NMR signal, whereas carbons in different environments give different NMR signals.

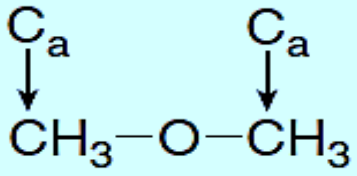
The ^{13}C NMR spectrum of acetic acid (CH_3COOH) has two signals because there are two different types of carbon atoms:

- The C of the CH_3 group and
- The C of the carbonyl (C=O).

- Because ^{13}C NMR signals are not split, the number of signals equals the number of lines in the ^{13}C NMR spectrum.

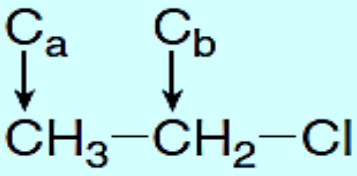
^{13}C NMR: Number of Signals

Thus, the ^{13}C NMR spectra of dimethyl ether, chloroethane, and methyl acetate exhibit one, two, and three lines, respectively, because these compounds contain one, two, and three different types of carbon atoms.



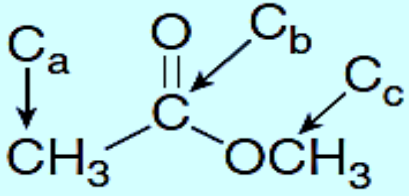
dimethyl ether

1 ^{13}C NMR signal
Both C's are equivalent.



chloroethane

2 ^{13}C NMR signals



methyl acetate

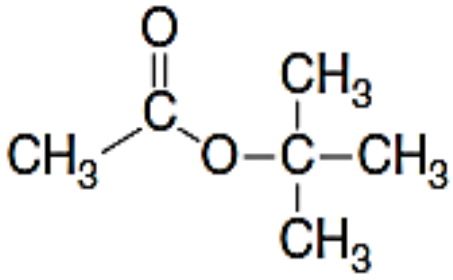
3 ^{13}C NMR signals

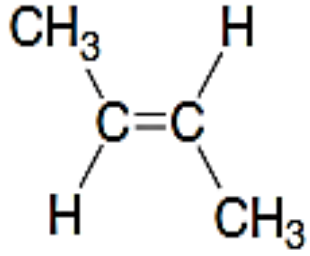
In contrast to what occurs in proton NMR, peak intensity is not proportional to the number of absorbing carbons, so ^{13}C NMR signals are not integrated.

^{13}C NMR: Number of Signals Sample Problem

How many lines are observed in the ^{13}C NMR spectrum of each compound?

a. $CH_3CH_2CH_2CH_2CH_3$

b. 

c. 

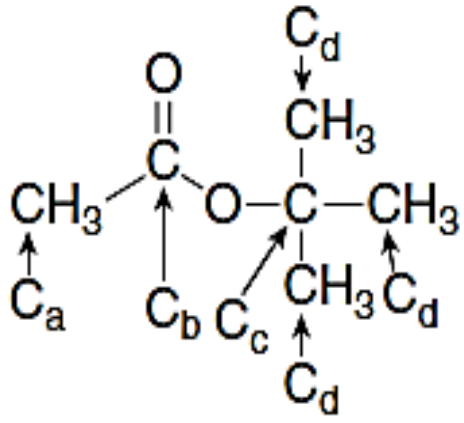
Solution

The number of different types of carbons equals the number of lines in a ^{13}C NMR spectrum.

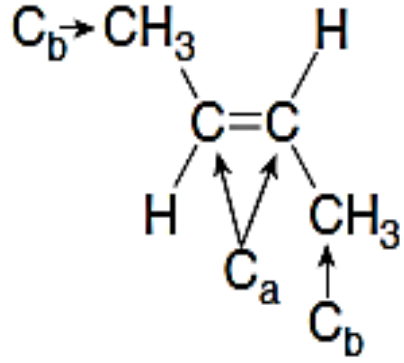
a. $CH_3CH_2CH_2CH_2CH_3$

C_a C_b C_c C_b C_a

3 types of C's
3 ^{13}C NMR signals

b. 

4 types of C's
4 ^{13}C NMR signals

c. 

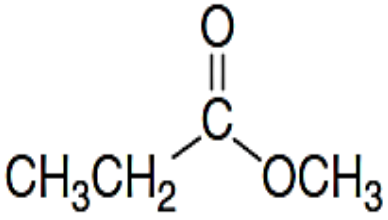
2 types of C's
2 ^{13}C NMR signals

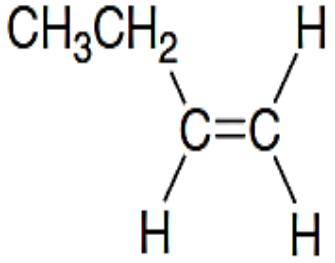
^{13}C NMR: Number of Signals Sample Problem

How many lines are observed in the ^{13}C NMR spectrum of each compound?

a. $CH_3CH_2CH_2CH_3$

c. $CH_3CH_2CH_2{-}O{-}CH_2CH_2CH_3$

b. 

d. 

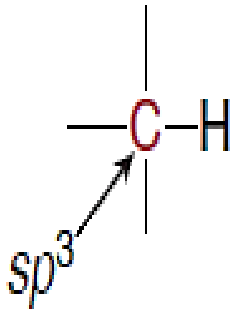
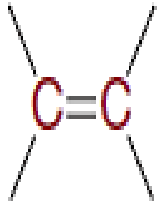
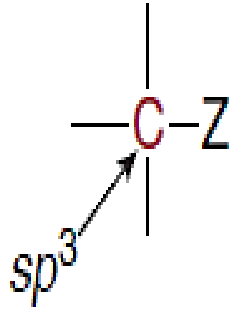
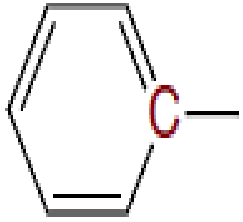
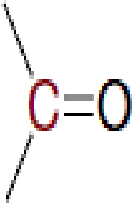
Draw all constitutional isomers of molecular formula $C_3H_6Cl_2$.

a. How many signals does each isomer exhibit in its ^1H NMR spectrum?

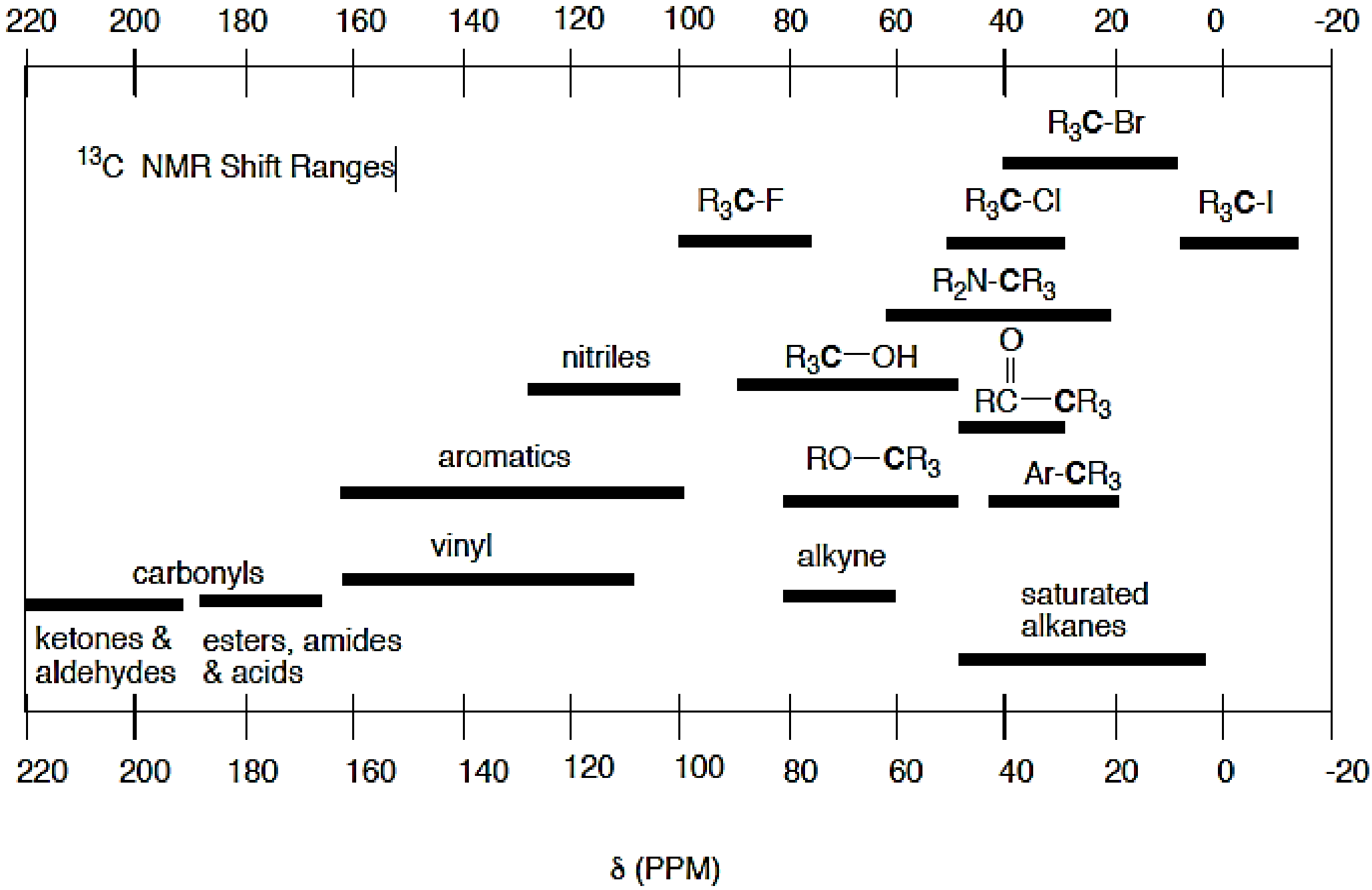
b. How many lines does each isomer exhibit in its ^{13}C NMR spectrum?

c. When only the number of signals in both ^1H and ^{13}C NMR spectroscopy is considered, is it possible to distinguish all of these constitutional isomers?

Common ^{13}C Chemical Shift Values

Type of carbon	Chemical shift (ppm)	Type of carbon	Chemical shift (ppm)
	5–45		100–140
 Z = N, O, X	30–80		120–150
—C≡C—	65–100		160–210

Chemical Shift Range of ^{13}C

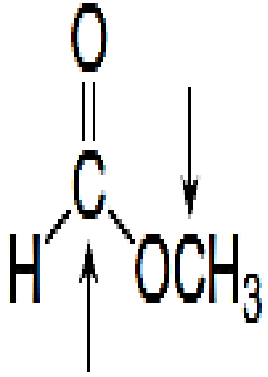


Common ^{13}C Chemical Shift Values: Sample Problem

Which of the indicated carbon atoms in each molecule absorbs farther downfield?

a. $CH_3CH_2OCH_2CH_3$

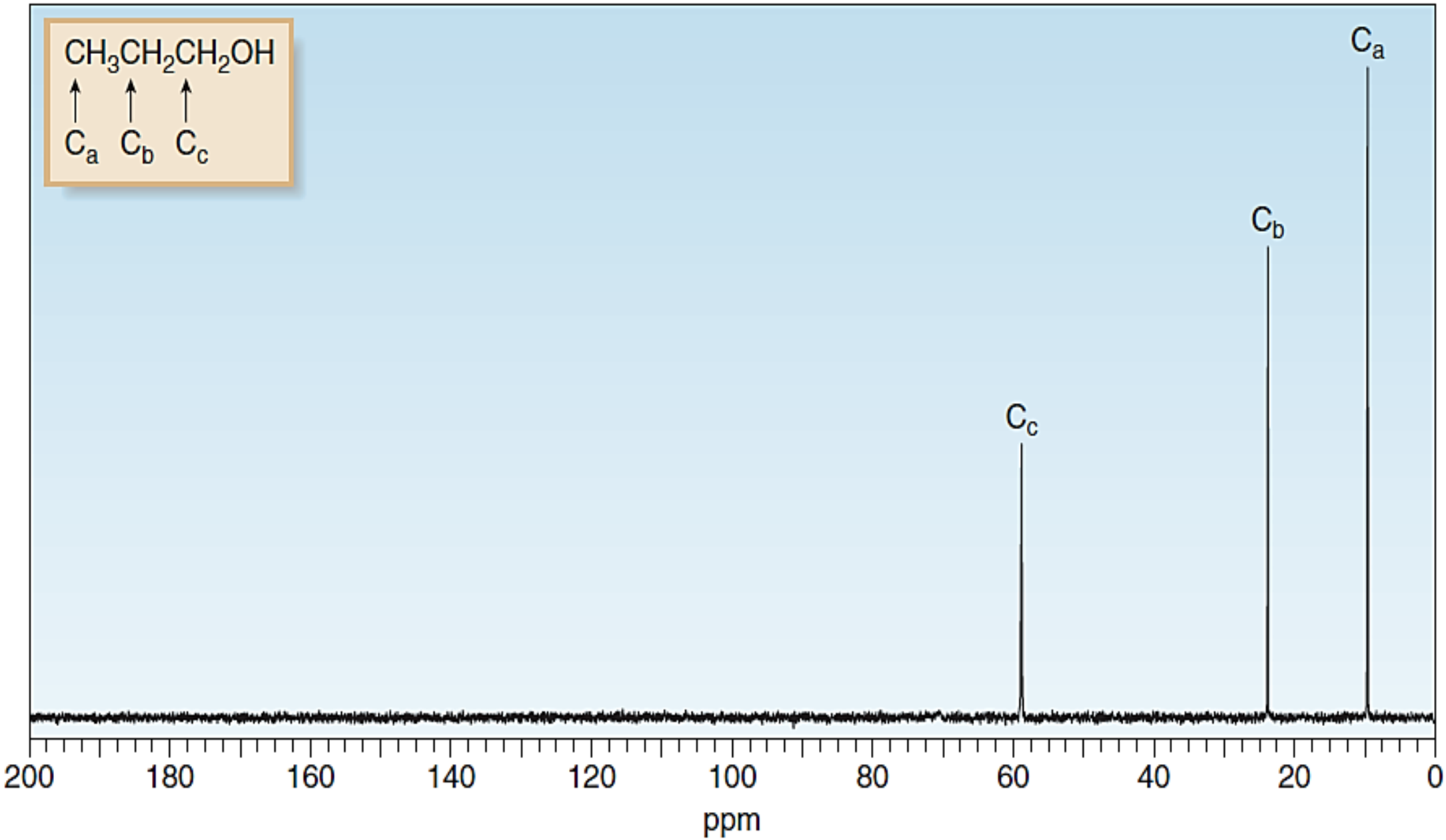
b. $BrCH_2CHBr_2$

c. 

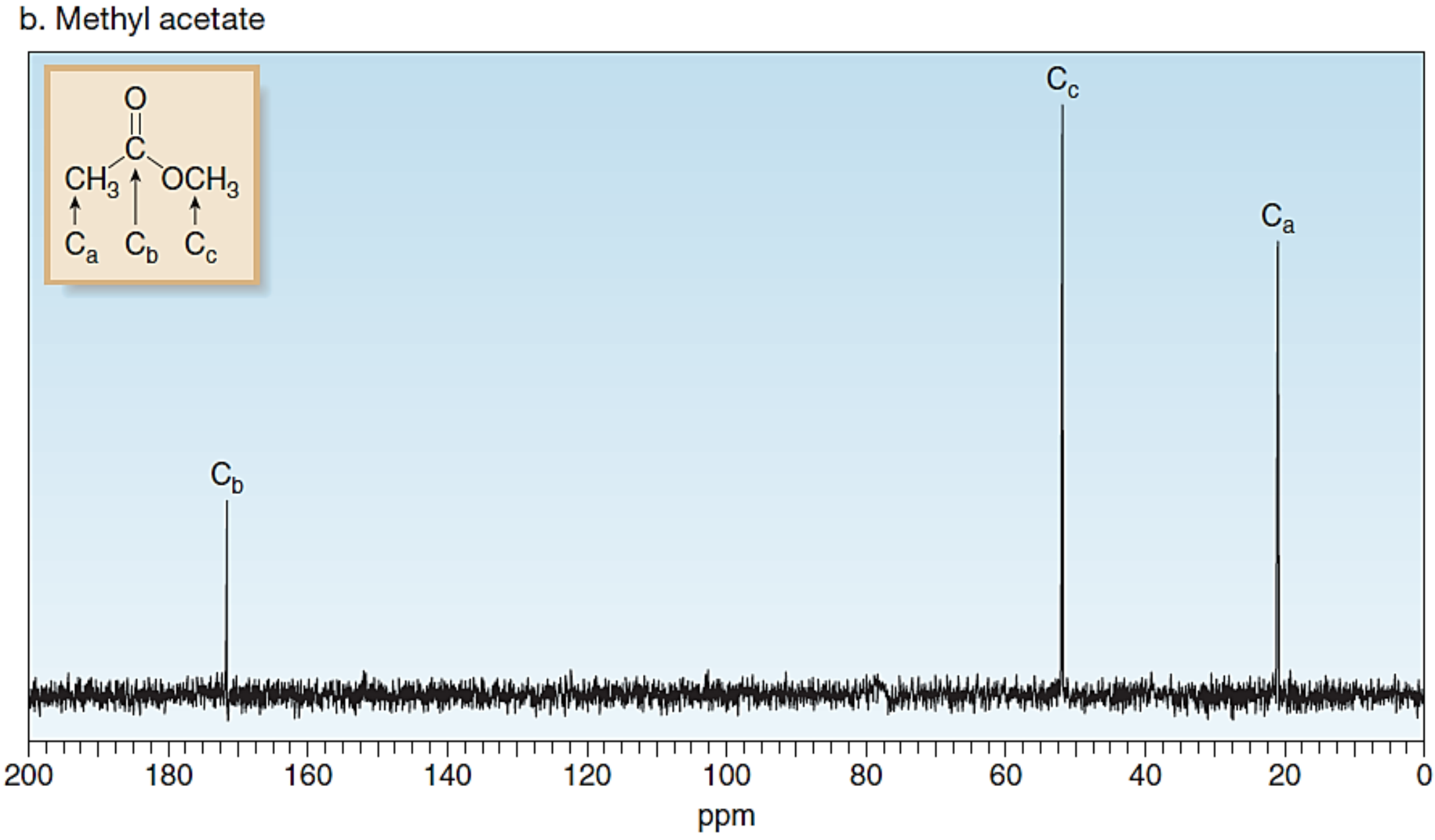
d. $CH_3CH{=}CH_2$

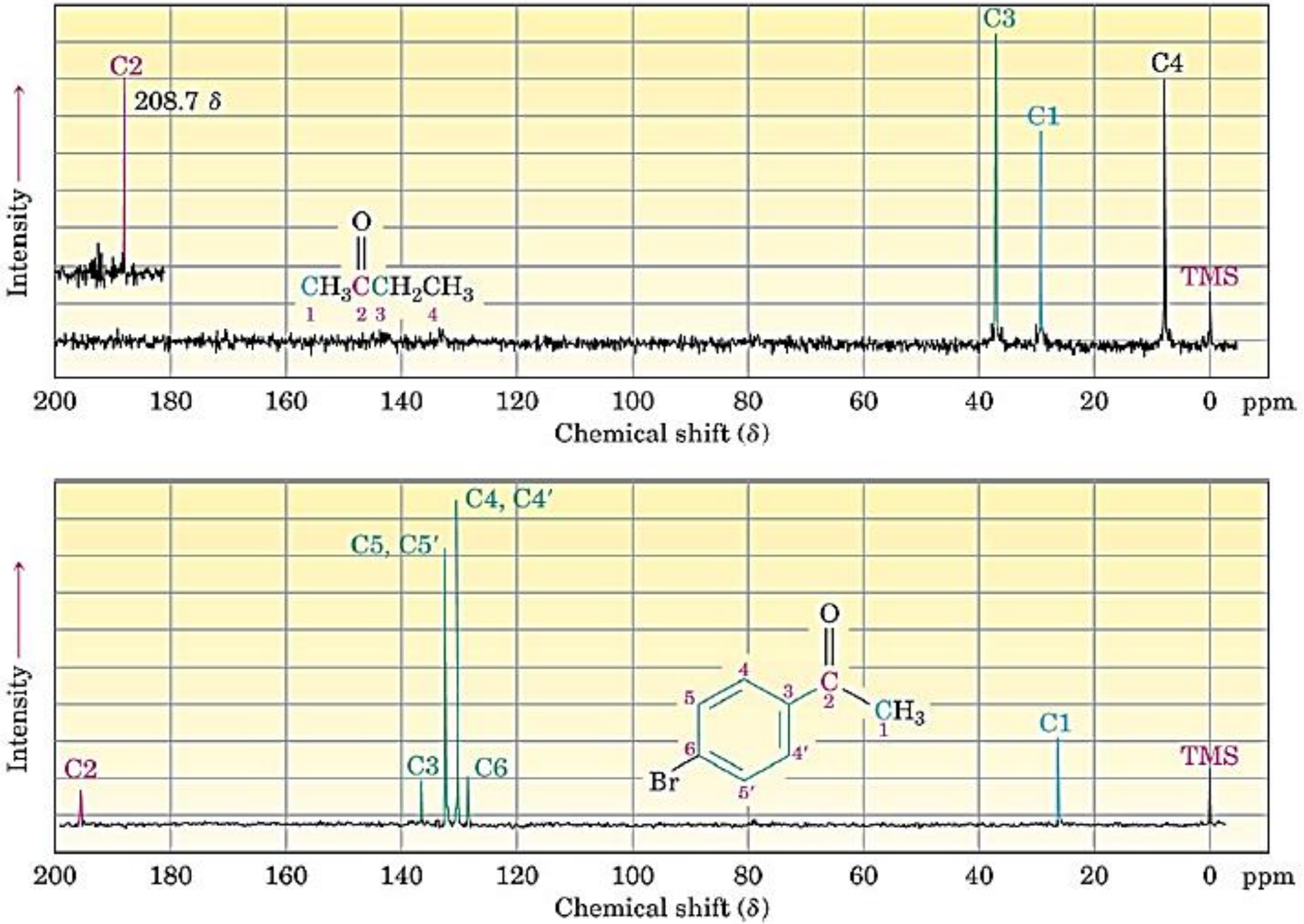
Representative ^{13}C NMR spectra

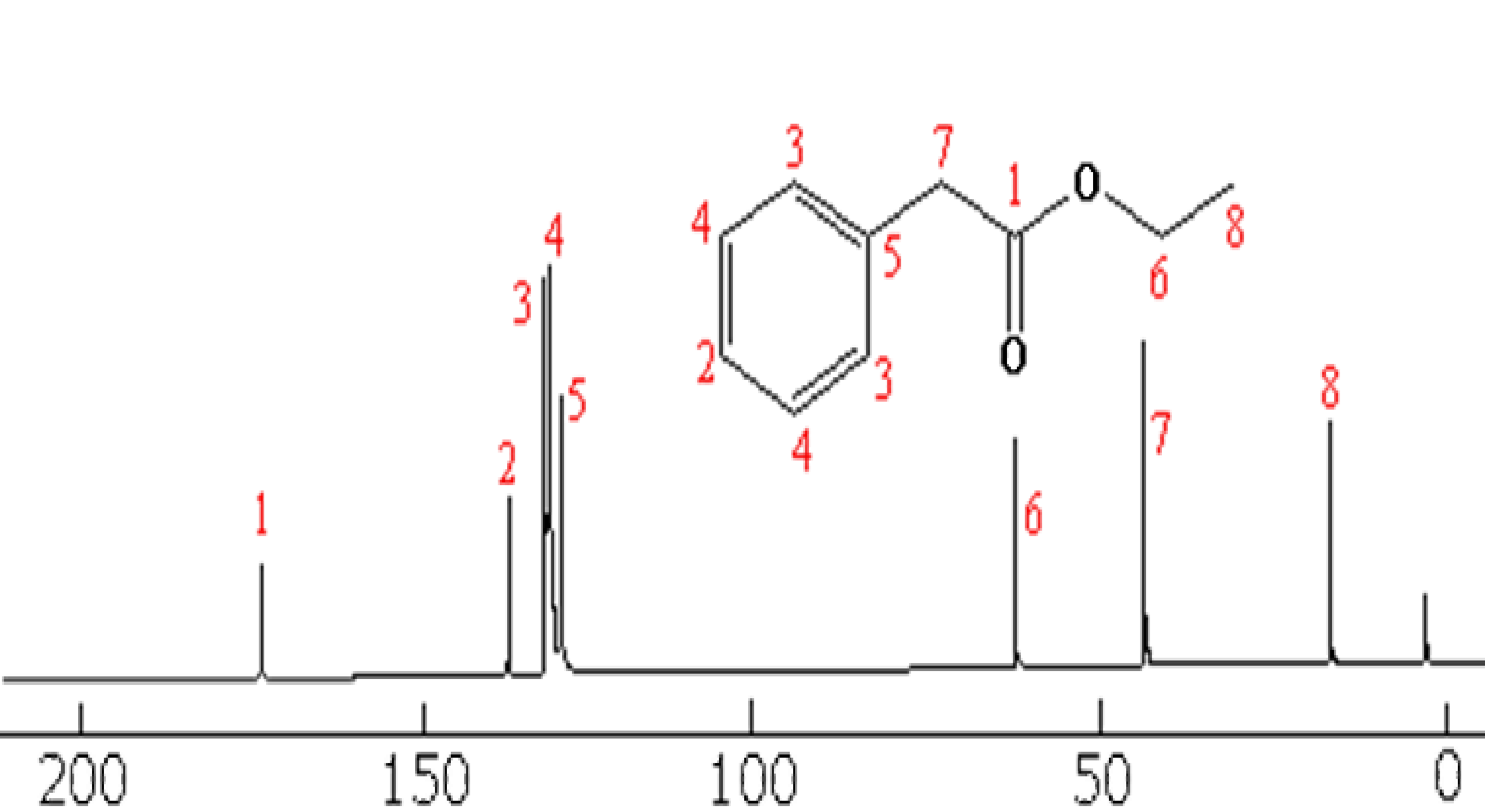
a. 1-Propanol



Representative ^{13}C NMR spectra



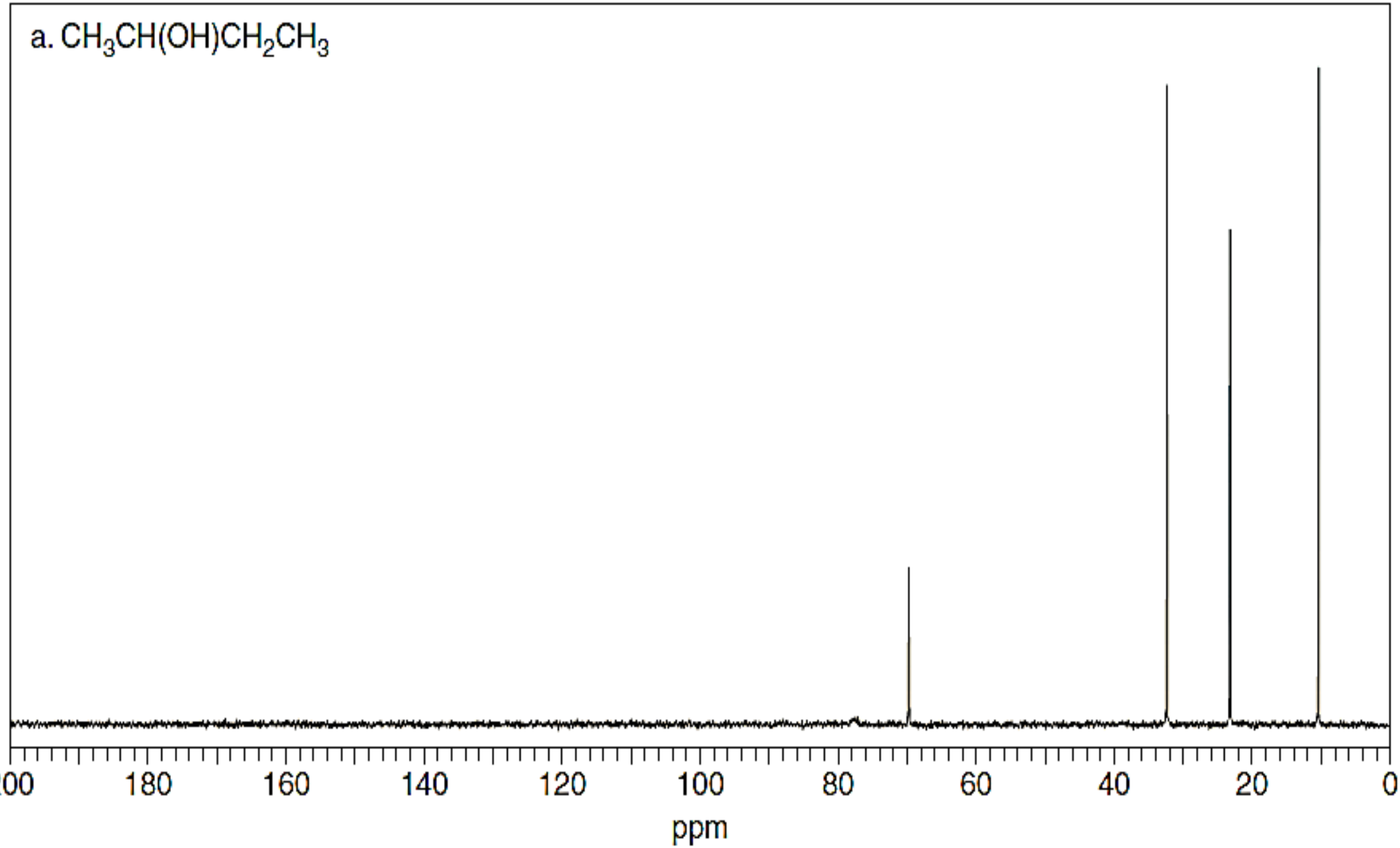

C2
208.7 δ
C3
C4
C1
TMS
O
CH3CCH2CH3
1 2 3 4
Intensity
200 180 160 140 120 100 80 60 40 20 0 ppm
Chemical shift (δ)
C4, C4′
C5, C5′
C2
C3
C6
C1
TMS
Br
CH3
Intensity
200 180 160 140 120 100 80 60 40 20 0 ppm
Chemical shift (δ)



13/03/2018

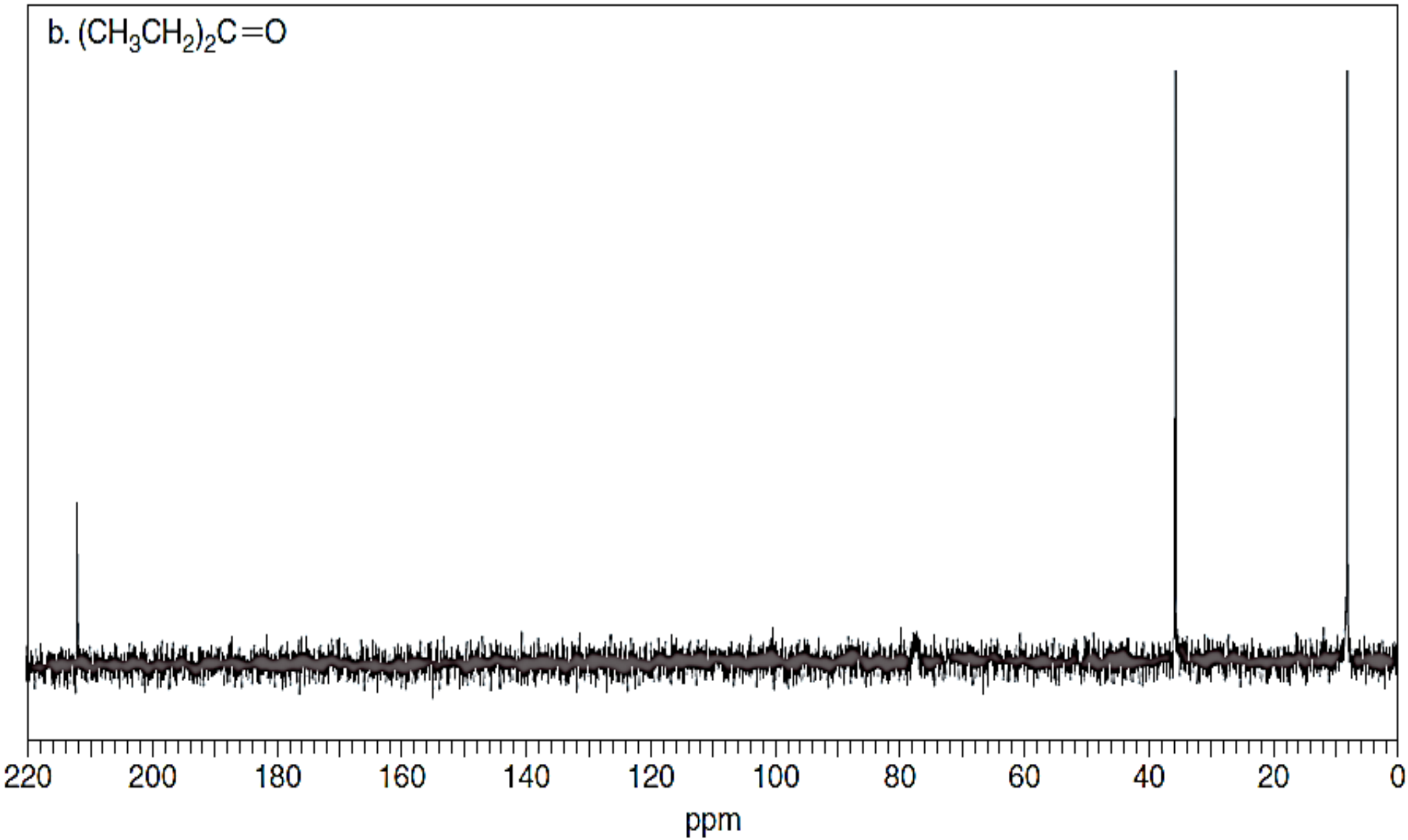
^{13}C NMR spectra: Sample Problem

Identify the carbon atoms that give rise to each NMR signal.



^{13}C NMR spectra: Sample Problem

Identify the carbon atoms that give rise to each NMR signal.

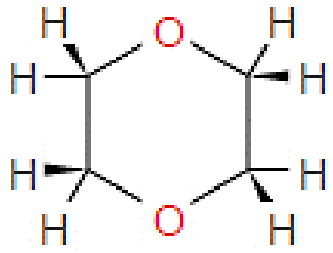


^{13}C NMR spectra: Sample Problem

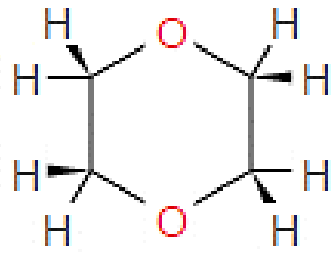
A compound of molecular formula $C_4H_8O_2$ shows no IR peaks at 3600–3200 or 1700 cm^{-1}. It exhibits one singlet in its ^1H NMR spectrum at 3.69 ppm, and one line in its ^{13}C NMR spectrum at 67 ppm. What is the structure of this unknown?

Draw the structure of a compound of molecular formula C_4H_8O that has a signal in its ^{13}C NMR spectrum at > 160 ppm. Then draw the structure of an isomer of molecular formula C_4H_8O that has all of its ^{13}C NMR signals at < 160 ppm.

^{1}H NMR



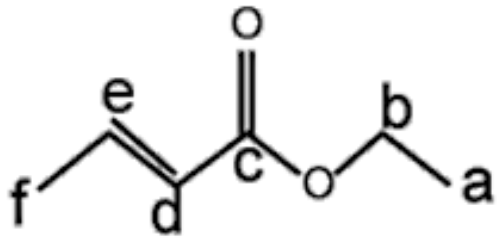
13C NMR spectra

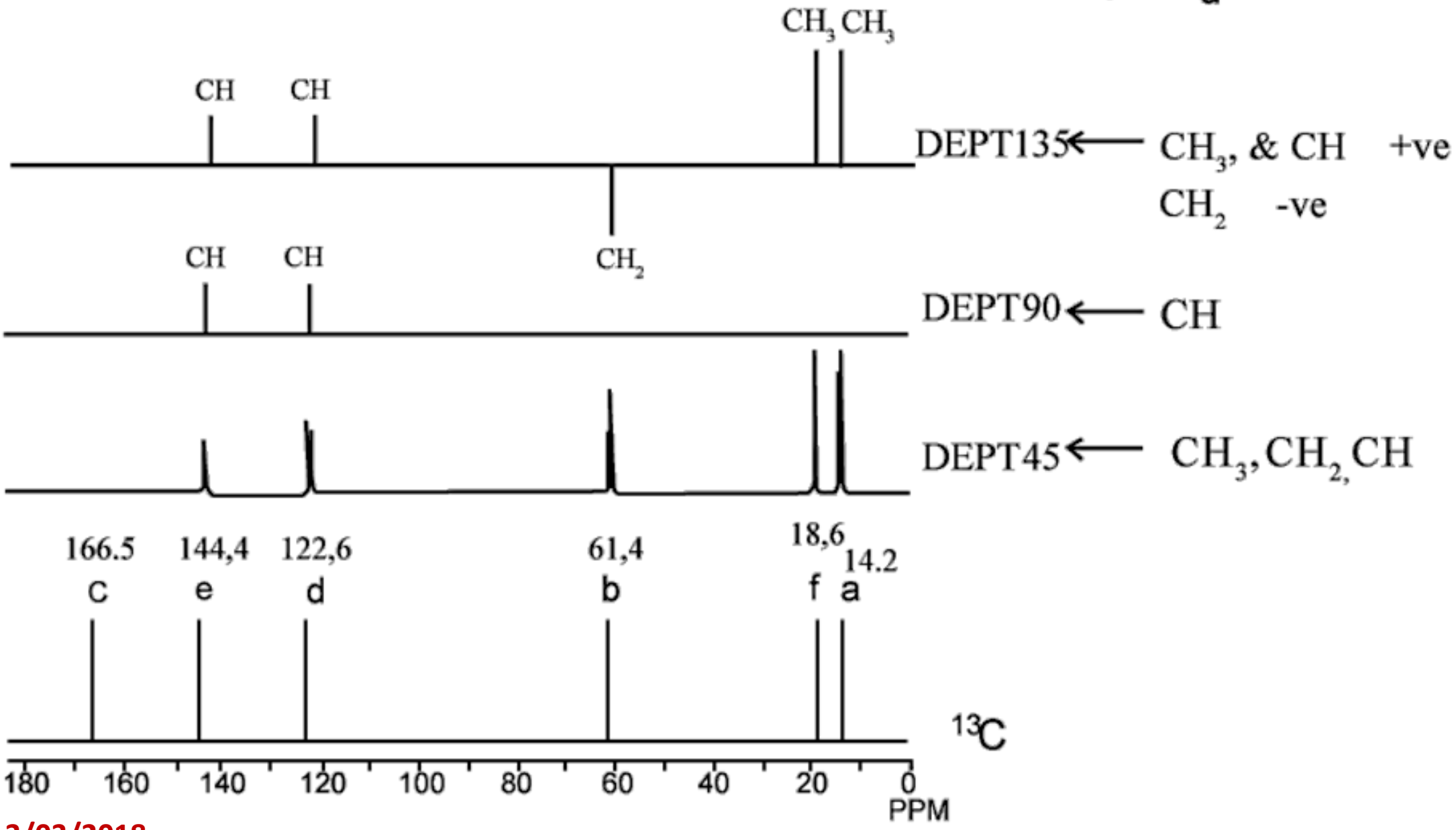


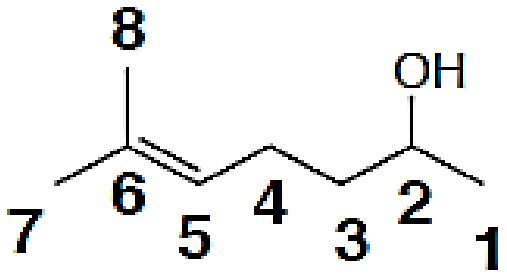
DEPT spectra:
(Distortionless Enhancement by Polarization Transfer)

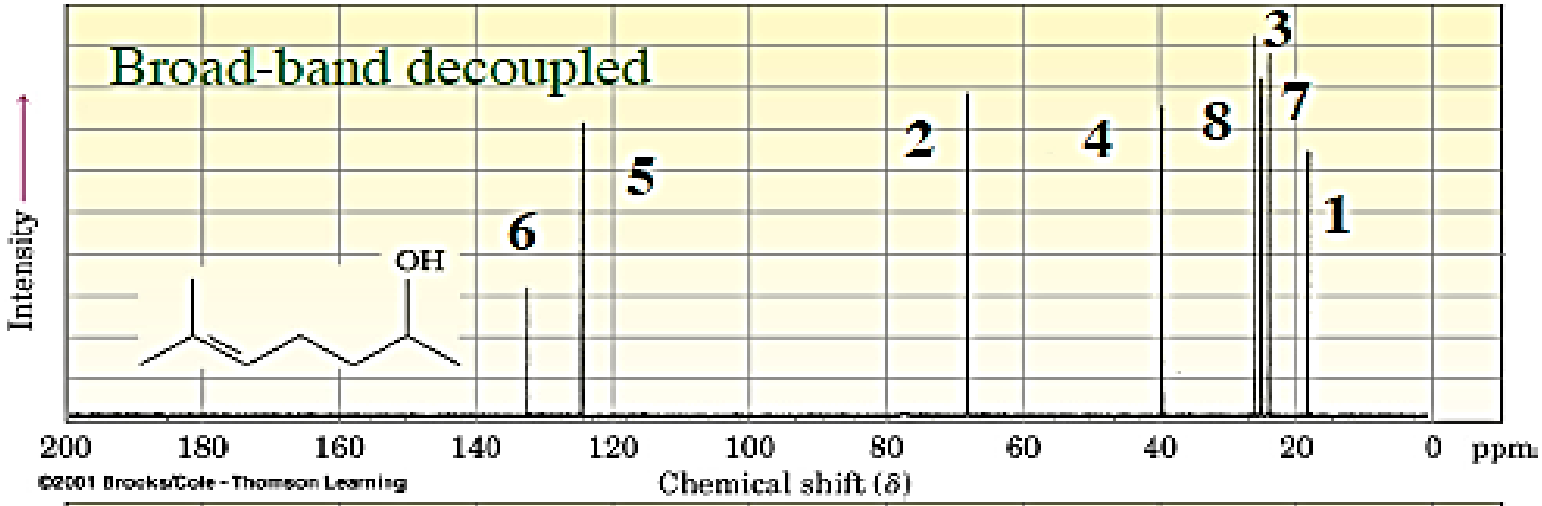
- A modern ^{13}C-NMR spectra that allows you to determine the number of attached hydrogens.
- Run: broad-band decoupled spectra
  - DEPT-45: CH's, CH_2's, and CH_3's give positive resonances.
  - DEPT-90: only CH's show up.
  - DEPT-135: CH's and CH_3's give positive resonances CH_2's give negative resonances

Distortion less Enhancement by Polarization Transfer






8
OH
7
6
5
4
3
2
1


Broad-band decoupled
Intensity
OH
6
5
2
4
8
3
7
1
200
180
160
140
120
100
80
60
40
20
0
ppm
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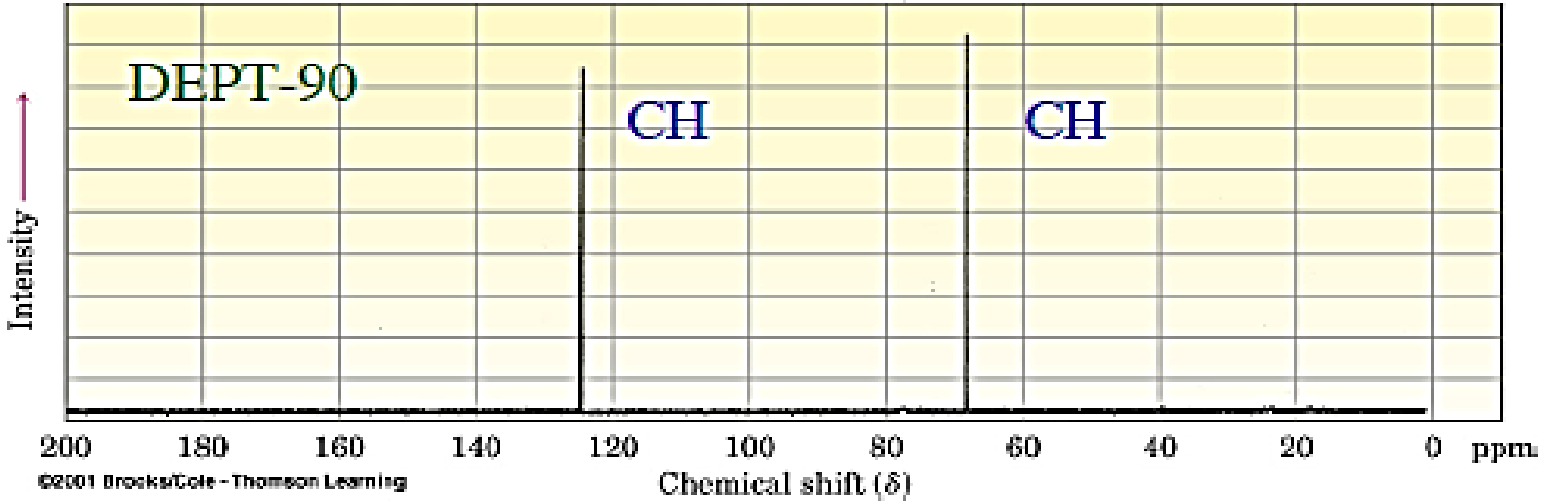
Chemical shift (δ)


DEPT-90
Intensity
CH
CH
200
180
160
140
120
100
80
60
40
20
0
ppm
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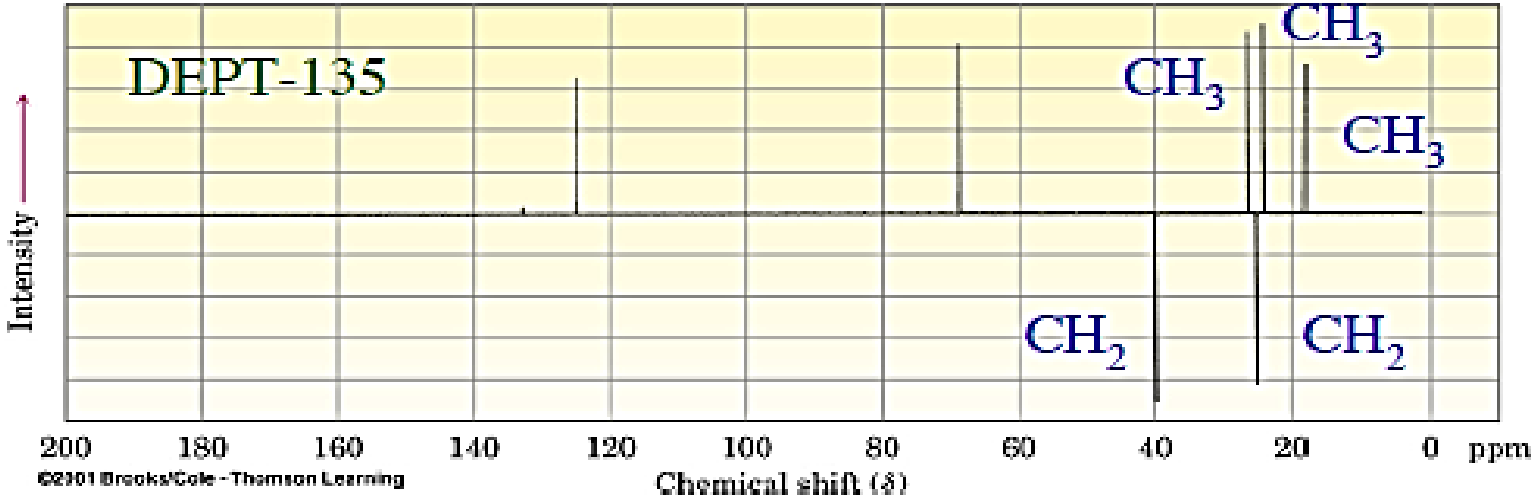
Chemical shift (δ)


DEPT-135
Intensity
CH3
CH3
CH3
CH2
CH2
200
180
160
140
120
100
80
60
40
20
0
ppm
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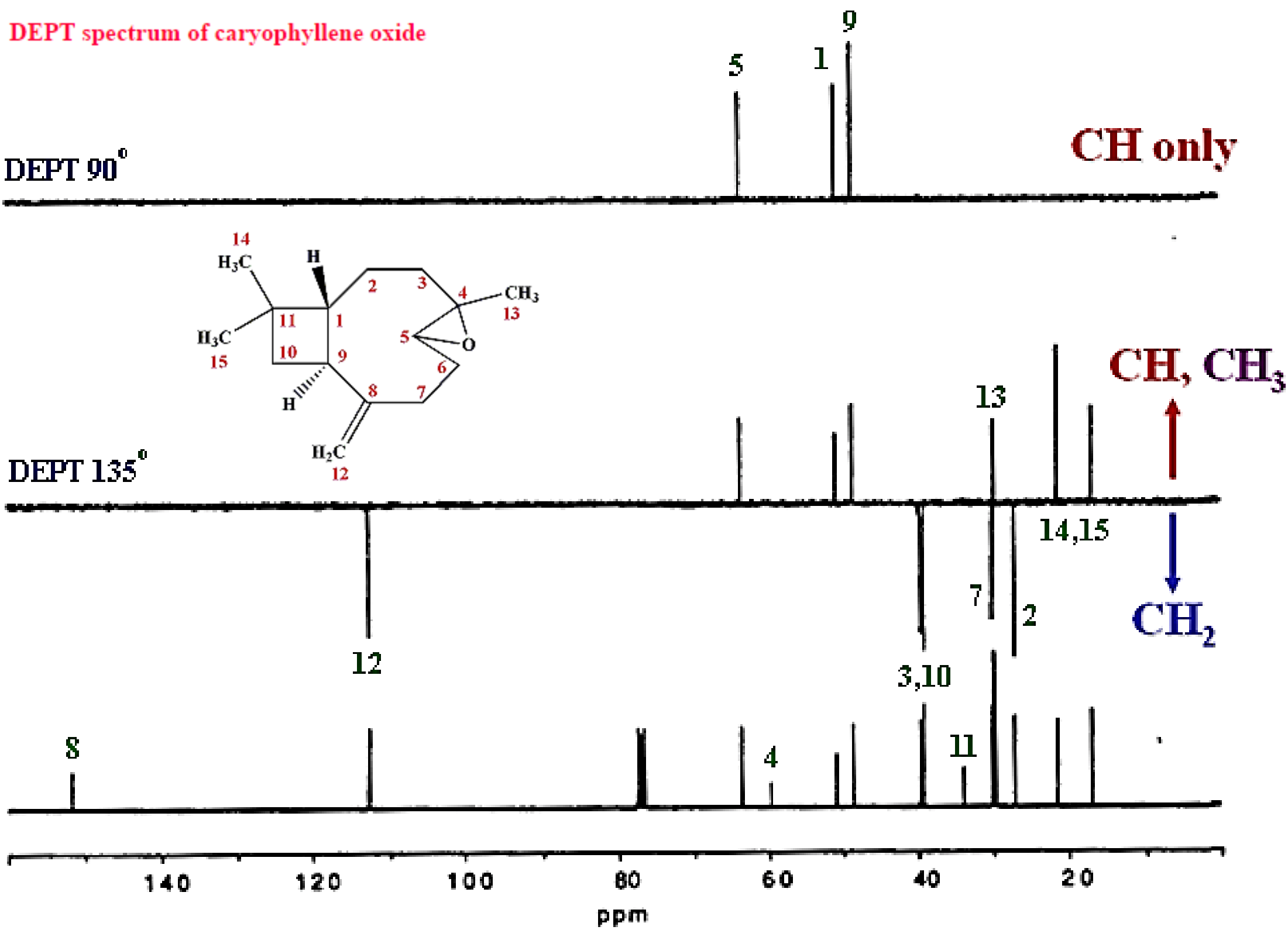
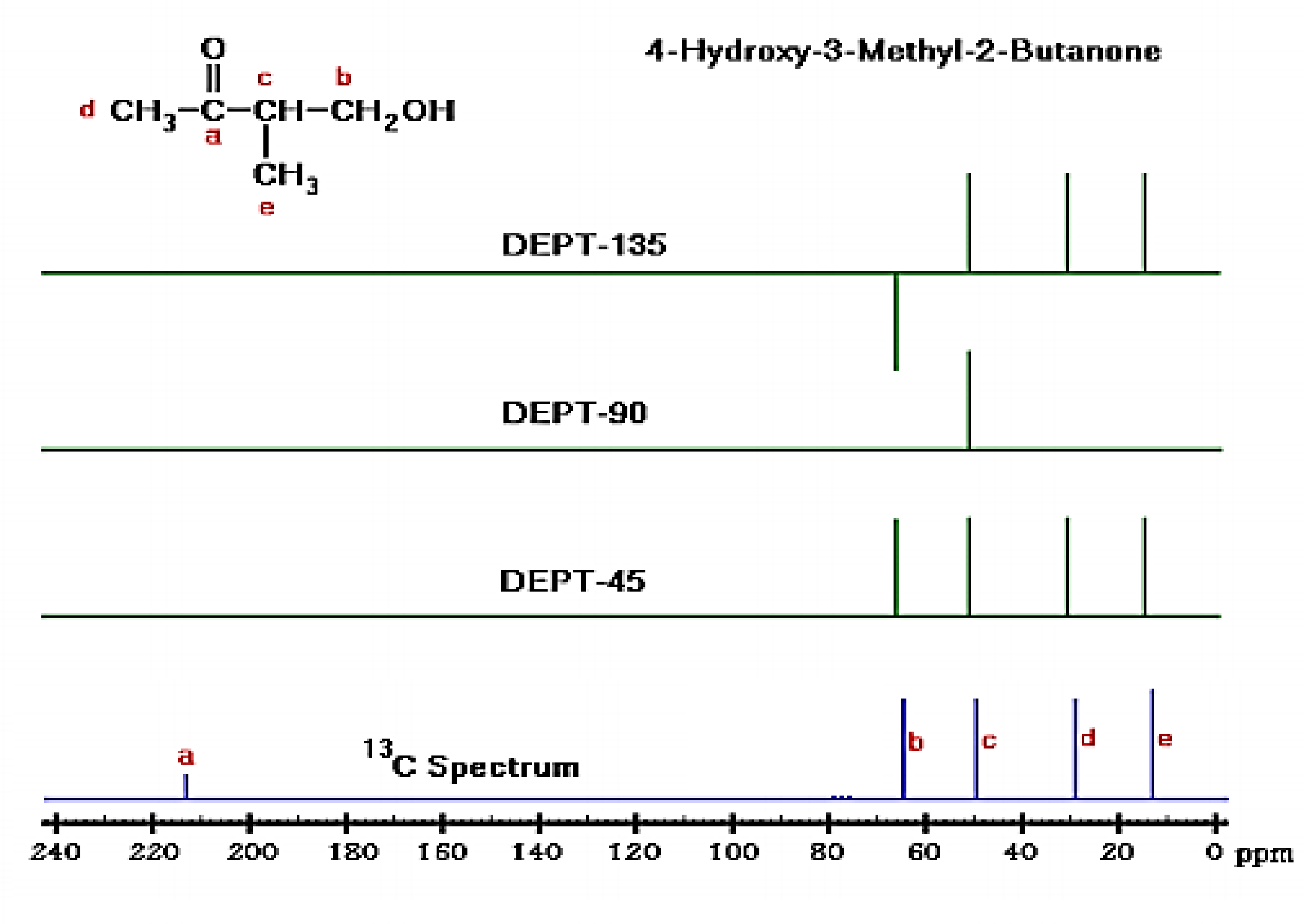
Chemical shift (δ)

DEPT spectrum of caryophyllene oxide




4-Hydroxy-3-Methyl-2-Butanone
O
c
b
d CH3–C–CH–CH2OH
a
CH3
e
DEPT-135
DEPT-90
DEPT-45
a
13C Spectrum
b
c
d
e
240
220
200
180
160
140
120
100
80
60
40
20
0 ppm

References:

1. Spectrometric Identification of Organic Compounds by Silverstein, Bassler and Morrill;
2. 2. Applications of absorption spectroscopy of organic compounds by Dyer JR.
3. 3. Organic Chemistry by McMurry; 5thed; Thomason learning CA, USA 2000.
4. http://memberfiles.freewebs.com/83/18/101361883/documents/merge4.pdf
5. http://www.mhhe.com/physsci/chemistry/carey/student/olc/ch13nmr.html
6. http://www.dbt.univr.it/documenti/OccorrenzaIns/matdid/matdid928241.pdf
7. http://www.chem.ualberta.ca/~htaube/B/2HMWK/hmwk02ans.pdf
8. http://chemwiki.ucdavis.edu/Core/Physical_Chemistry/Spectroscopy/Magnetic_Resonance_Spectroscopies/Nuclear_Magnetic_Resonance/NMR%3A_Experimental/NMR%3A_Interpretation/Pascal%E2%80%99s_Triangle
9. https://ibrevision.files.wordpress.com/2014/06/chemistry-option-a.pdf
10. http://www.cem.msu.edu/~reusch/OrgPage/nmr.htm
11. https://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/nmr/nmr1.htm
12. http://cbc.arizona.edu/rss/nmr/manuals/aptdept.pdf
13. http://orgspectroscopyint.blogspot.com/p/13-c-nmr.html
14. https://web.chemdoodle.com/demos/simulate-nmr-and-ms/
15. http://www.nmrdb.org/new_predictor/index.shtml?v=v2.34.2