

CHEM 322
Laboratory Methods in
Organic Chemistry

Introduction to NMR
Spectroscopy

What structural information does NMR spectroscopy provide?

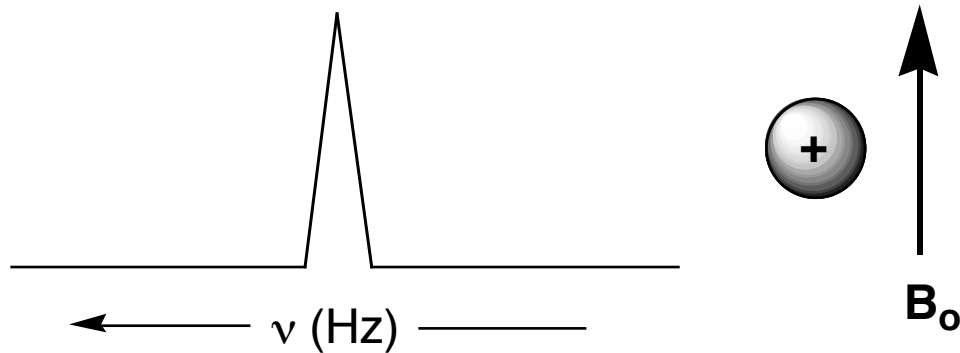
- 1) **Chemical shift** (δ) data reveals the molecular (functional group) environment of the observed nucleus.
- 2) Peak **integration** (area) is proportional to the relative number of nuclei giving rise to a signal.
- 3) **J-Coupling** provides H,H and C-13,H connectivity information (how nuclei are connected to each other).
- 4) The nuclear Overhauser effect (**NOE**) provides 3-D H,H spatial information.
- 5) Polarization transfer experiments (**DEPT**) provide C-13,H connectivity information.

Chemical Shift

Consider the general equation for resonance,

$$\nu_o = \gamma B_o / 2\pi$$

For a “bare” proton, the “effective” external field (B_{eff}) is equal to the “actual” applied field (B_o).

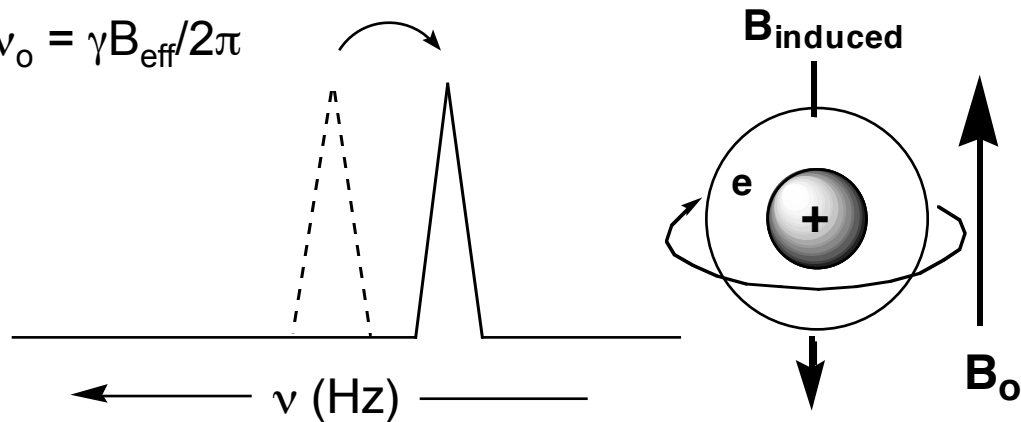


However, for protons surrounded by an electron cloud,

$$B_{\text{eff}} = B_o - B_{\text{ind}} \text{ or } B_o (1 - \sigma),$$

leading to a smaller ν_o for the resonance condition,

$$\nu_o = \gamma B_{\text{eff}} / 2\pi$$

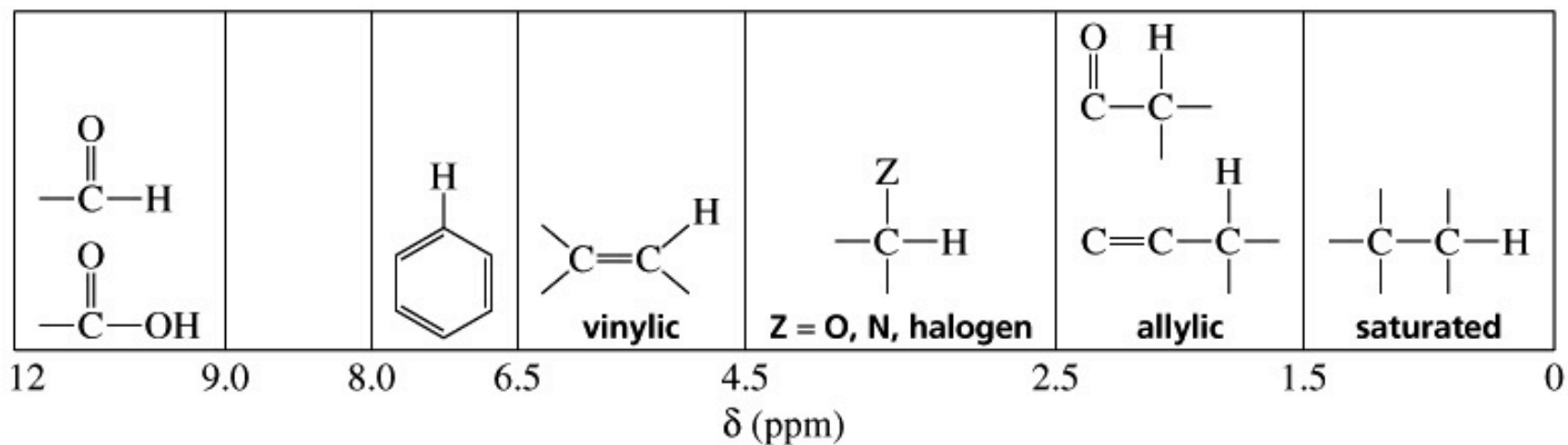


The proton is thus said to be “shielded” and its chemical shift is defined as

$$\delta = [(\nu_{\text{sample}} - \nu_{\text{reference}}) / \nu_{\text{reference}}] \times 10^6 \text{ (in ppm)}$$

relative to a “standard” such as $(\text{CH}_3)_4\text{Si}$ (TMS) where δ is defined as 0.00 ppm.

^1H NMR chemical shift ranges for important functional groups:



How many NMR signals are to be expected for a given structure?

Determine sets of chemical equivalent nuclei.

Nuclei are said to be **chemically equivalent** if they can be interchanged by

(1) a symmetry operation (reflection through a plane, rotation about an axis) or

(2) a fast ($k > 1000 \text{ sec}^{-1}$) intramolecular dynamic process (bond rotation, tautomerization).

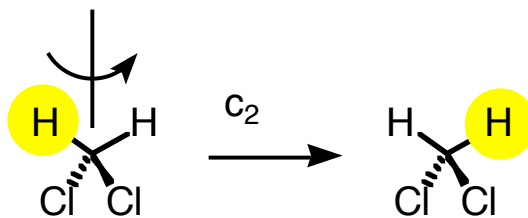
Chemically equivalent nuclei have the same chemical shift.

NMR-active nuclei are chemical shift equivalent if they are interchangeable through any symmetry operation (rotation, reflection, inversion) or by a rapid process.

Examples:

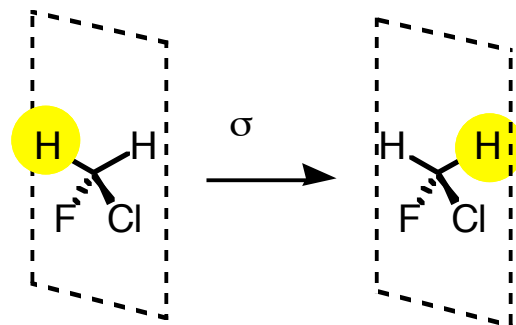
1. Interchange by rotation

Protons are **homotopic** and thus chemical shift equivalent in achiral and chiral solvents.



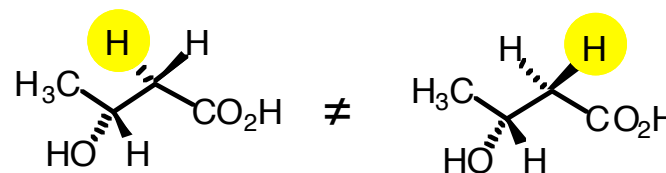
2. Interchange by reflection

Protons are **enantiotopic** and thus chemical shift equivalent in achiral solvents.



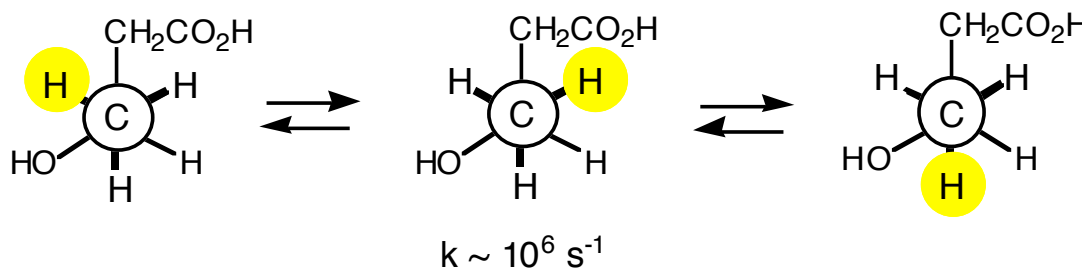
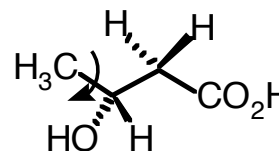
3. No interchange by symmetry

Methylene protons are **diastereotopic** and thus chemical shift nonequivalent except by coincidental signal overlap.

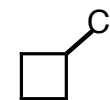
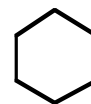
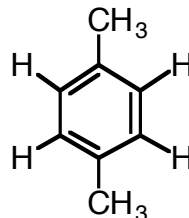
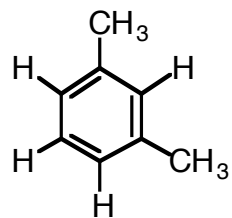
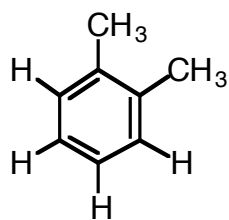
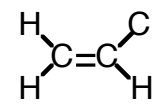
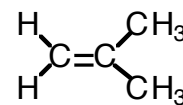
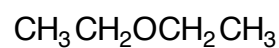
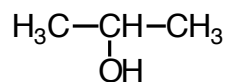
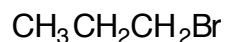


4. Interchange by rapid interconversion

Protons are chemical shift equivalent when the kinetics are fast on the NMR time-scale.



Predict the theoretical number of signals that could be observed in the ^1H and ^{13}C NMR spectra of the following compounds.



Integration of NMR Signals

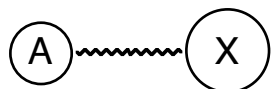
Since the number of absorption/relaxation events is proportional to the number of nuclei in a chemically equivalent set, the area under a signal is proportional to the relative number of those nuclei in the molecule. This is usually obtained by electronic integration.

For example, the ^1H NMR spectrum of ethyl chloride, $\text{CH}_3\text{CH}_2\text{Cl}$, would be comprised of two signals with an integrated area ratio of 3/2.

What will each NMR signal's splitting pattern be?

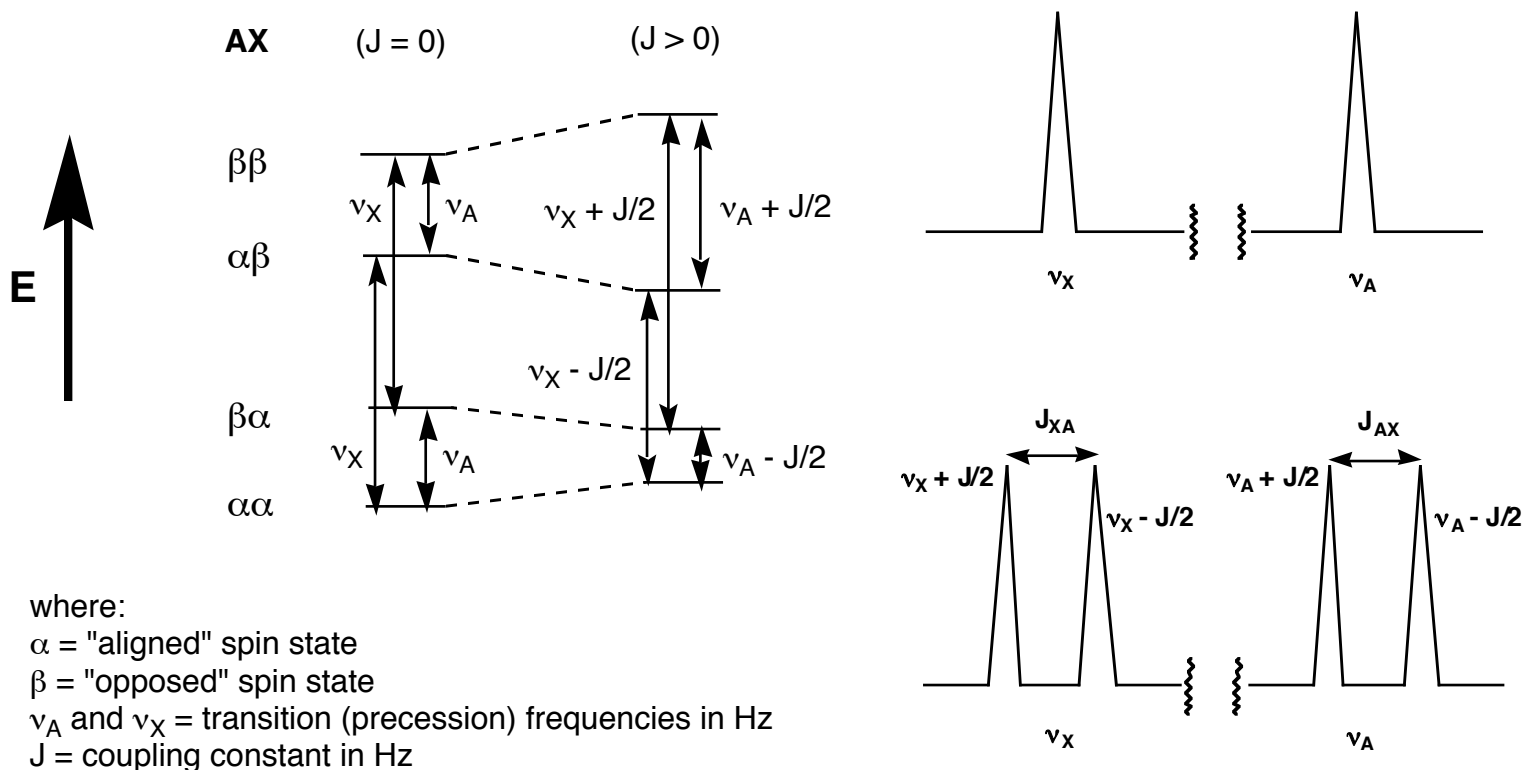
Spin-Spin or J-Coupling

Consider two sets of chemically equivalent nuclei "A" and "X" each having a nuclear spin of $\pm 1/2$. The NMR signal due to each will be mutually "split" by the "coupled" nucleus. In general, we will restrict ourselves to nuclei that are not separated by more than 3 bonds.



The splitting pattern can be predicted by applying the $N + 1$ Rule, where N is the number of equivalent nuclei coupled to the observed nucleus.

J-Coupling of an AX System with Spin of $\pm 1/2$ (^1H , ^{13}C , ^{19}F , ^{31}P)



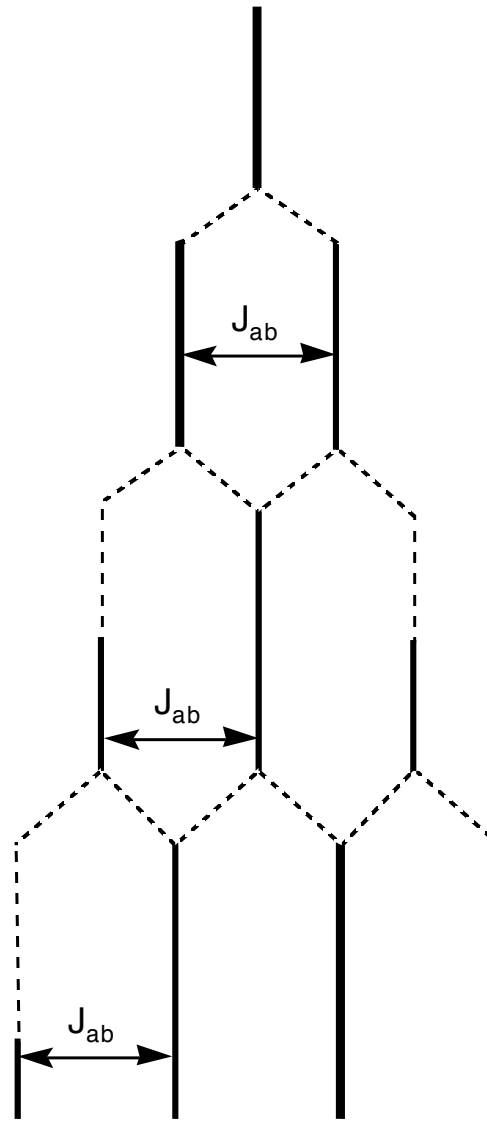
NMR Splitting Tree Diagrams

level 1: set H_a
no spin-spin coupling
 $N+1 = 1$
singlet (s)

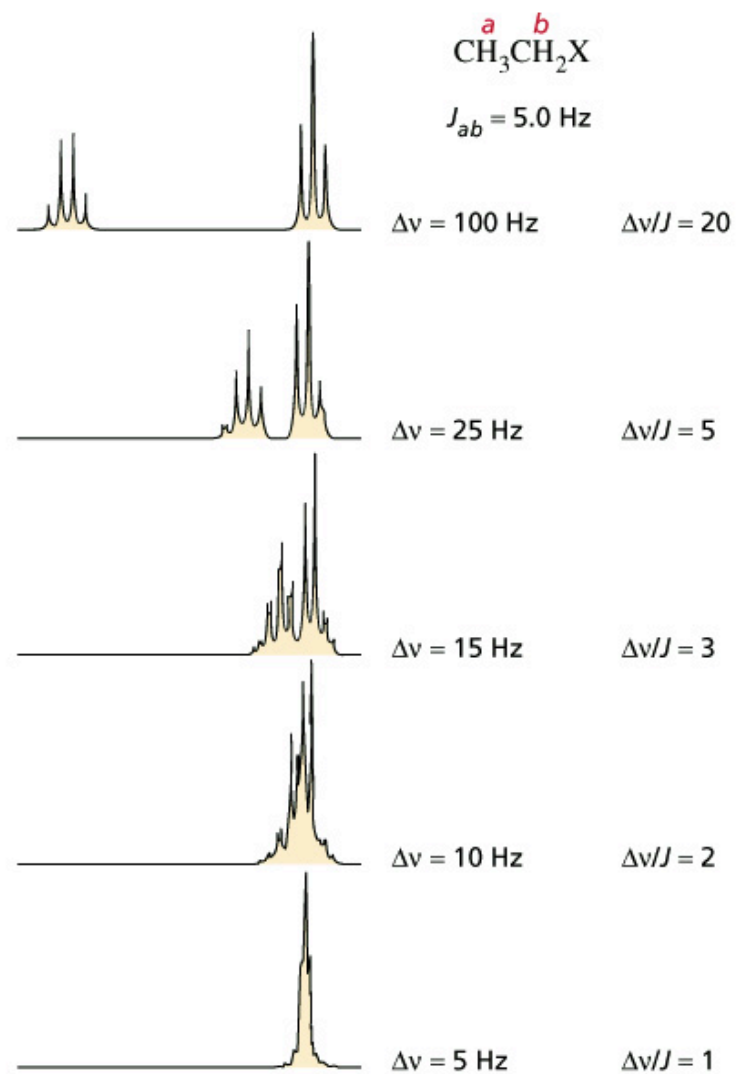
level 2: set H_a
coupled to H_b
 $N+1 = 2$
1:1 doublet (d)

level 3: set H_a
coupled to $2 \times H_b$
 $N+1 = 3$
1:2:1 triplet (t)

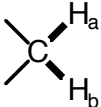
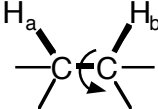
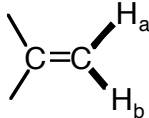
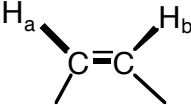
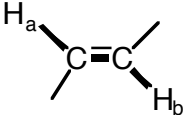
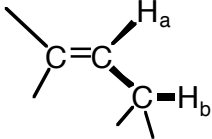
level 4: set H_a
coupled to $3 \times H_b$
 $N+1 = 4$
1:3:3:1 quartet (q)



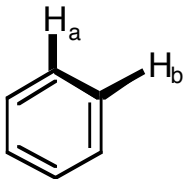
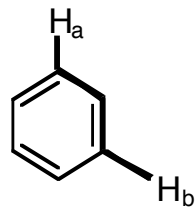
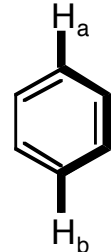
Second Order Effects ($\Delta\nu/J < 10$)



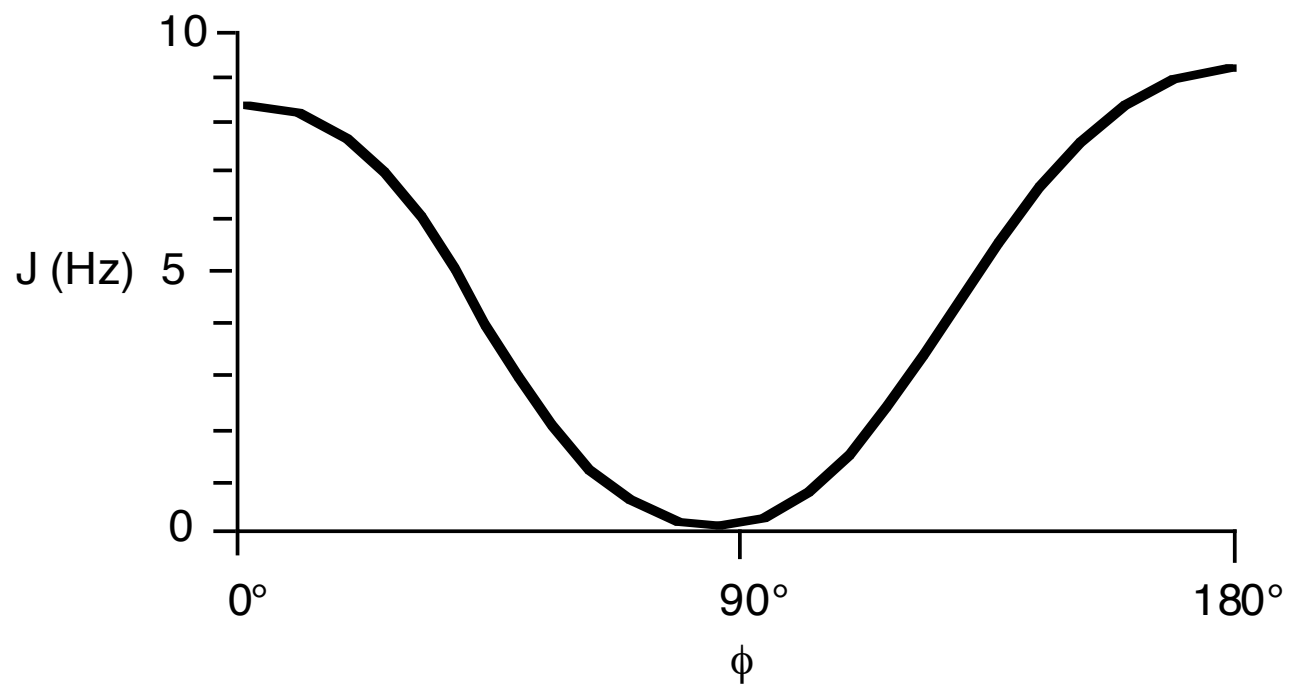
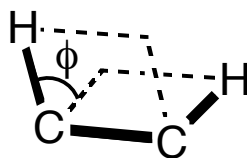
Spin-Spin Coupling Constants

Connection	Coupling-Type	J-value
	geminal (alkane)	12-15 Hz
	vicinal (alkane)	2-9 Hz*
	geminal (alkene)	0.5-3 Hz
	vicinal (cis-alkene)	7-12 Hz
	vicinal (trans-alkene)	13-18 Hz
	vicinal (allylic)	4-10 Hz

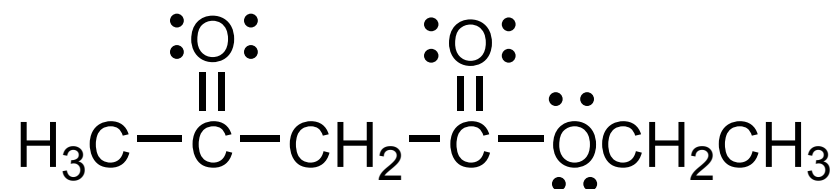
Spin-Spin Coupling Constants (Continued)

Connection	Coupling-Type	J-value
 A benzene ring with two adjacent protons labeled H _a and H _b .	ortho-aromatic	6-9 Hz
 A benzene ring with two protons labeled H _a and H _b separated by one carbon atom.	meta-aromatic	1-3 Hz
 A benzene ring with two protons labeled H _a and H _b opposite each other.	para-aromatic	0-1 Hz

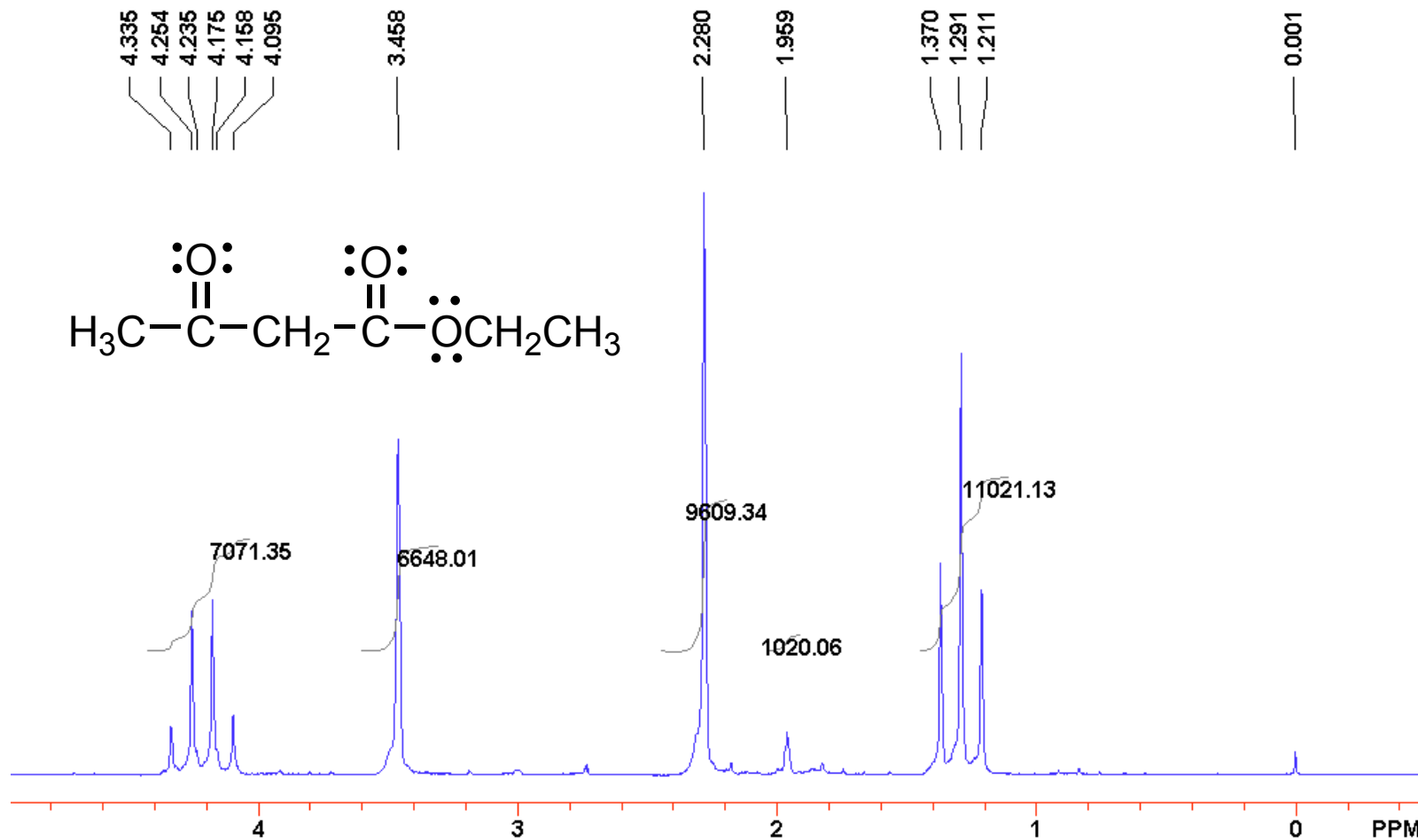
Karplus Curve for Estimating Vicinal Coupling Constants



In-Class Problem: Predict the ^1H NMR spectrum of ethyl acetoacetate.



300 MHz ^1H NMR spectrum of starting material:



Solvent: CDCl_3

300 MHz ^1H NMR spectrum of reaction aliquot after extractive workup:

