

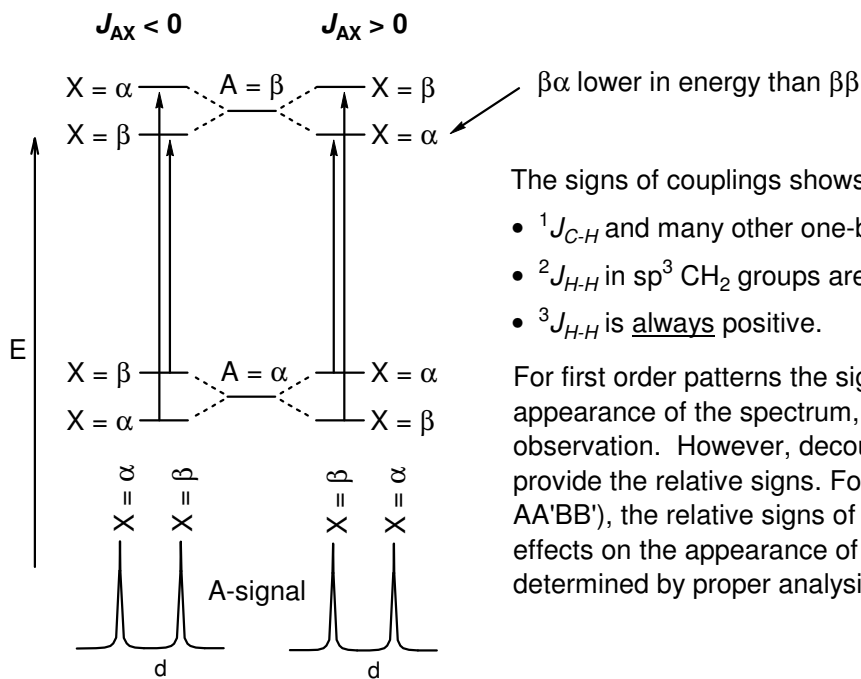
5.3 Spin-Spin Splitting: J -Coupling

There are two distinct types of magnetic interaction (coupling) between nuclei (A and X) with a non-zero spin - the direct interaction (dipole-dipole coupling: D) and the indirect or scalar coupling (spin-spin splitting: J). The direct interaction is about 1000 times as large as the scalar coupling (e.g. at 2 Å distance H-H dipolar coupling is ca 30,000 Hz). These direct couplings make the observation of high-resolution NMR spectra in solids and very viscous liquids difficult, and make NMR spectra in liquid crystals (where molecules are partially oriented, and the dipolar coupling is only partially averaged) very complex. In mobile isotropic liquids the random motion of molecules completely averages the dipolar coupling, so no direct effects are seen. There are however, indirect effects, such as the Nuclear Overhauser Effect (NOE) which have important consequences for NMR spectroscopy (see Sect. 8). In the following sections we will be concerned only with J coupling.

The scalar coupling J is a through-bond interaction, in which the spin of one nucleus perturbs (polarizes) the spins of the intervening electrons, and the energy levels of neighboring magnetic nuclei are in turn perturbed by the polarized electrons. This leads to a lowering of the energy of the neighboring nucleus when the perturbing nucleus has one spin, and a raising of the energy when it has the other spin. The J coupling (*always* reported in Hz) is field-independent (i.e. J is constant at different external magnetic field strength), and is mutual (i.e. $J_{AX} = J_{XA}$). Because the effect is usually transmitted through the bonding electrons, the magnitude of J falls off rapidly as the number of intervening bonds increases. Coupling over one (1J), two (2J) and three (3J) bonds usually dominates the fine structure of NMR spectra, but coupling across four (4J) and five (5J) bonds is often seen, especially through π bonds (double and triple bonds, aromatic carbons).

Sign of Coupling Constants

Coupling constants can be either positive or negative, defined as follows: coupling constants are positive if the energy of A is lower when X has the opposite spin as A ($\alpha\beta$ or $\beta\alpha$), and negative if the energy of A is lower when X has the same spin as A ($\alpha\alpha$ or $\beta\beta$).

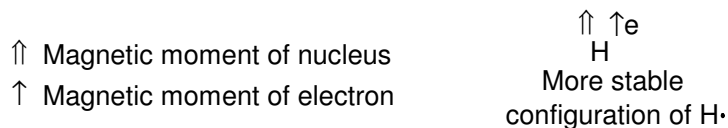


The signs of couplings shows some consistency.

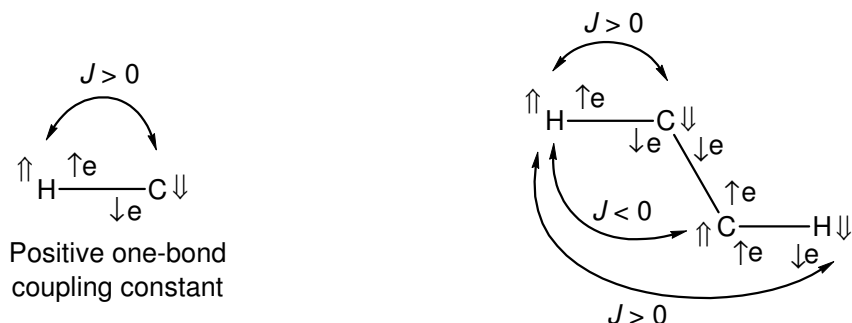
- $^1J_{C-H}$ and many other one-bond couplings are positive.
- $^2J_{H-H}$ in sp^3 CH_2 groups are negative, some others are positive.
- $^3J_{H-H}$ is always positive.

For first order patterns the signs of the couplings have no effect on the appearance of the spectrum, and so cannot be determined by observation. However, decoupling experiments (spin tickling) can provide the relative signs. For second-order patterns (e.g. ABX or AA'BB'), the relative signs of coupling constants often have dramatic effects on the appearance of the spectrum, and relative signs can be determined by proper analysis of the multiplets.

Mechanism of spin polarization: It is known from spectroscopy of the hydrogen radical ($\text{H}\cdot$) that the more stable orientation has the angular momentum vectors of the nucleus and the electron antiparallel. Since the gyromagnetic ratio of the nucleus is positive, and that of the electron is negative, this means that the magnetic vectors are parallel.

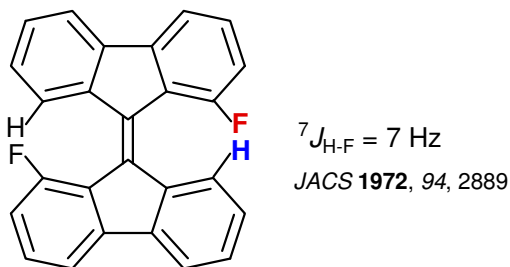


For the Fermi contact mechanism of spin-spin coupling (there are other mechanisms), the bonding electrons for a $\text{H}\text{-}^{13}\text{C}$ fragment will become polarized as shown, so that the more stable orientation of the ^{13}C -nucleus will be down, when the proton is up. This corresponds to a positive one-bond C-H coupling.

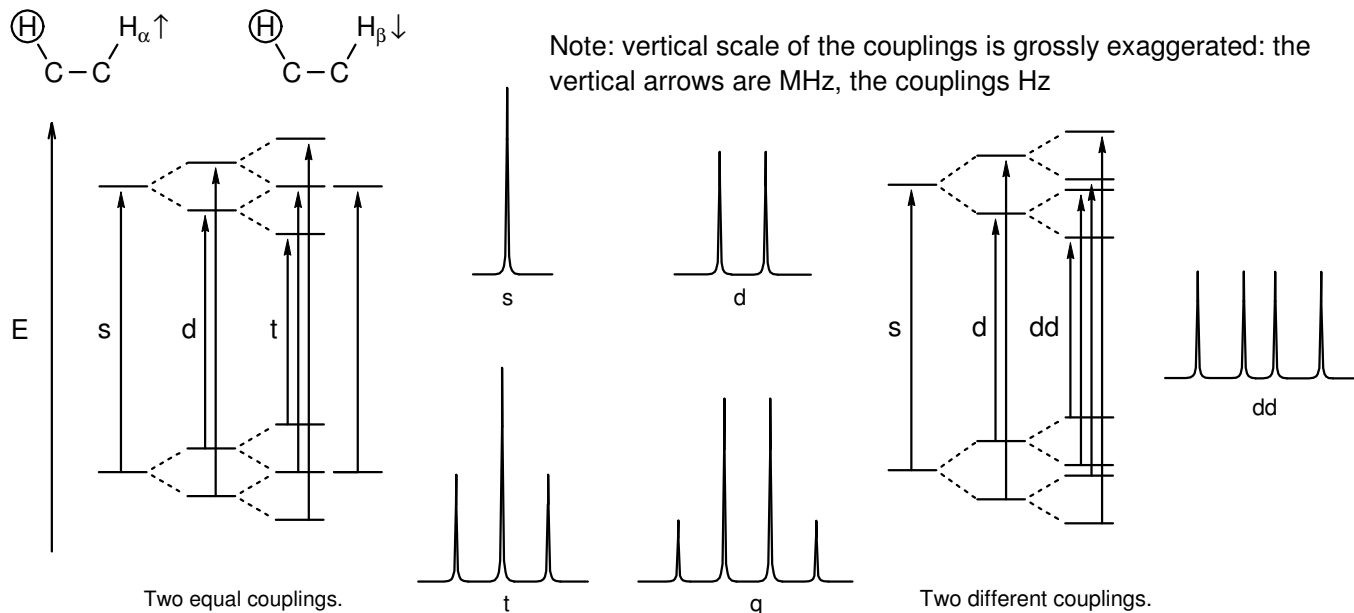


If we continue down the bond sequence, the polarization of the C-H electrons will cause polarization of the C-C electron pair. Again, parallel spins are the more stable orientation (triplets are more stable than singlets -- Hund's rule). Thus the two-bond coupling (2J) is predicted to be negative, and the three-bond coupling (3J) positive. This alternation of signs is often (but by no means always) seen.

The principal mechanism for J -coupling is through bond polarization, but there are situations where a through-space effect seems to be operative. These occur in molecules where spin 1/2 nuclei are forced into close proximity. For example, in the compounds below, there is a substantial H - F J coupling even though the H and F are separated by many bonds, where normally coupling is small or undetectable.

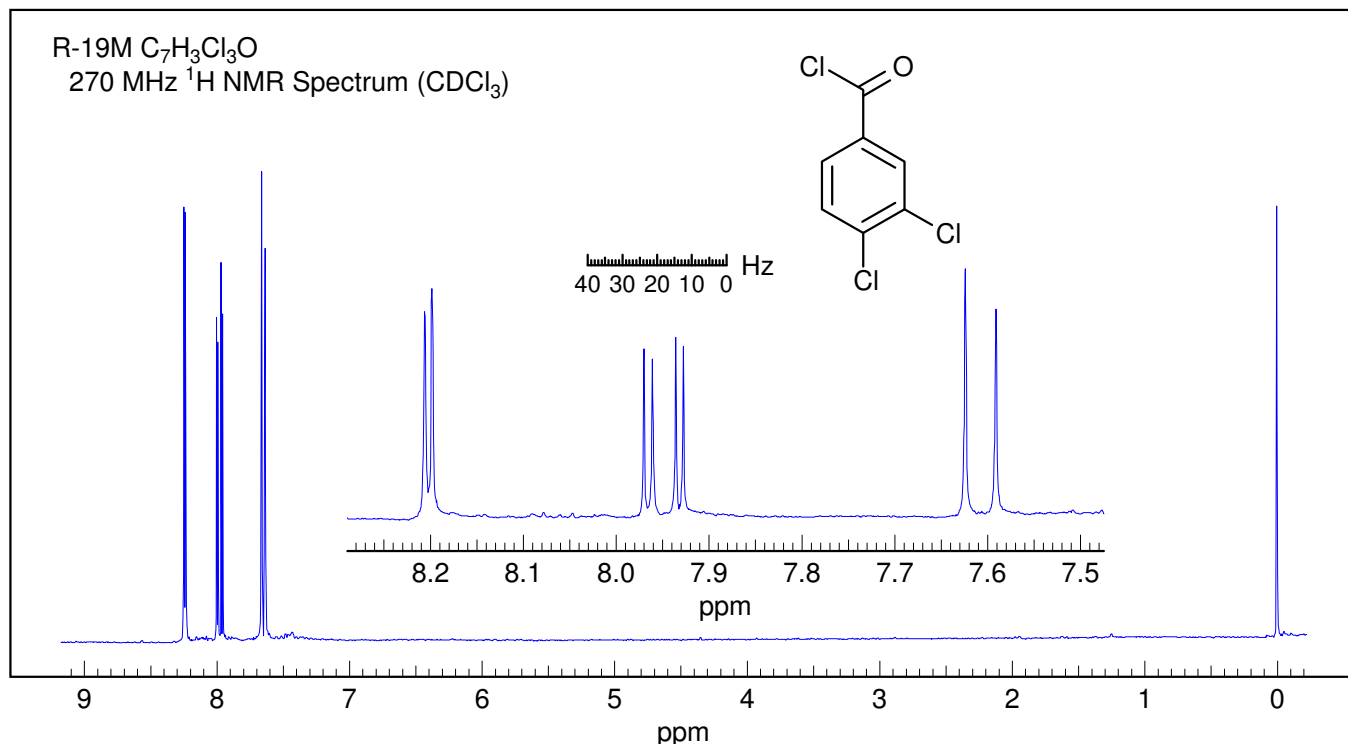


A depiction of the perturbation of energy levels of a nucleus A by a neighboring **magnetic** nucleus X is shown below (spin-spin splitting). The principal magnetic nuclei are other protons, the 100% abundant spin $\frac{1}{2}$ nuclei ^{19}F and ^{31}P , and some spin 1 or greater (quadrupolar) nuclei such as ^{14}N , ^2H , ^{11}B , and ^{12}B . Although Br, Cl, and I all have isotopes with spin $>\frac{1}{2}$, coupling is not seen because of relaxation effects. This will be discussed in more detail in Section 7.

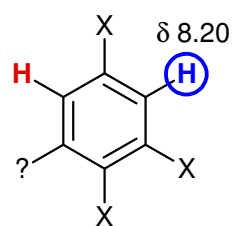


Two Different Couplings to one Proton

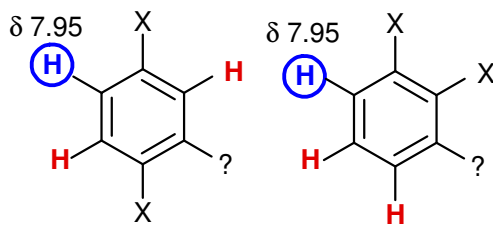
Consider the NMR spectrum of 3,4-dichlorobenzoyl chloride below.



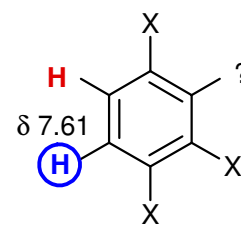
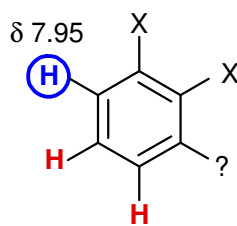
The proton-proton couplings in benzene are typically 7-9 Hz for J_{ortho} , 2-3 Hz for J_{meta} and <1 Hz for J_{para} . The substitution pattern can be derived from examination of each of the three aromatic protons. For example, the doublet at δ 8.2 with $J = 2.5$ Hz is interpreted as follows: this proton has no protons ortho to it, and only one proton meta to it. Structure **A** summarizes the information. For the doublet of doublets at δ 7.95 ($J = 8.5, 2.3$ Hz), formed by coupling of one proton to both an ortho and a meta proton, the two structures **B** and **C** are possible. The doublet at δ 7.6 ($J = 8.5$ Hz) defines the substitution pattern of structure **D**. In each case the position marked by ? is undefined since the para coupling is usually too small to resolve.



J ca 2 Hz
one meta H only

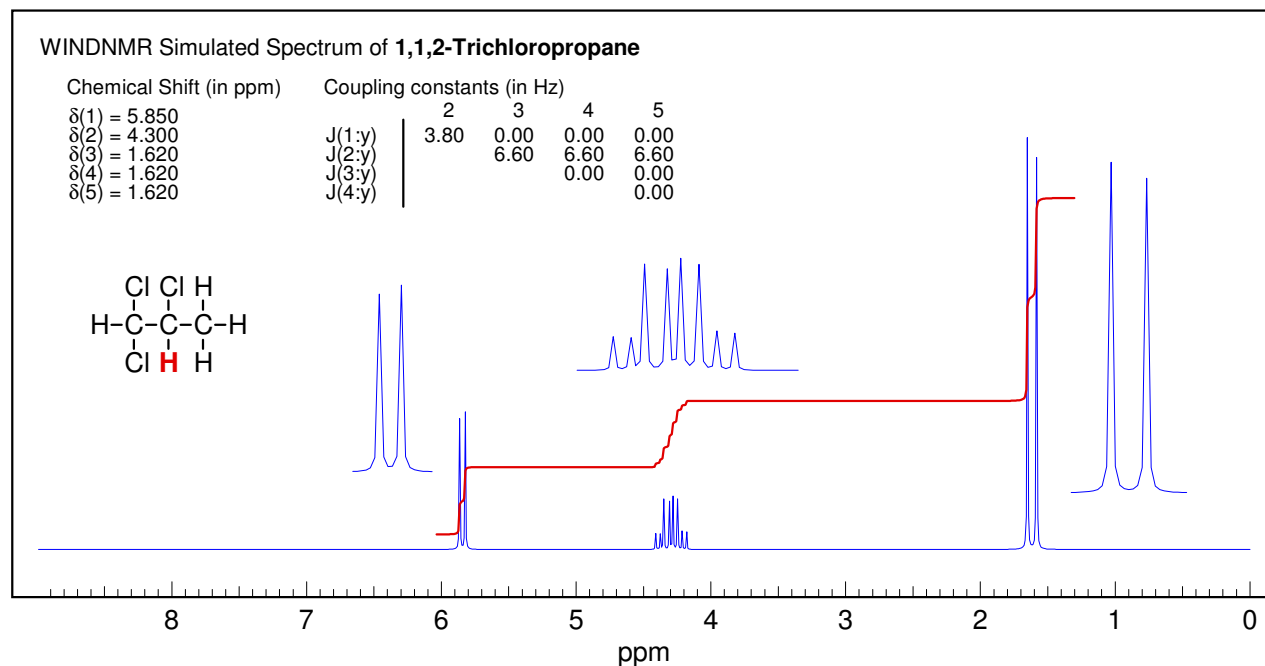


J ca 2 and 8 Hz
one ortho and one meta H

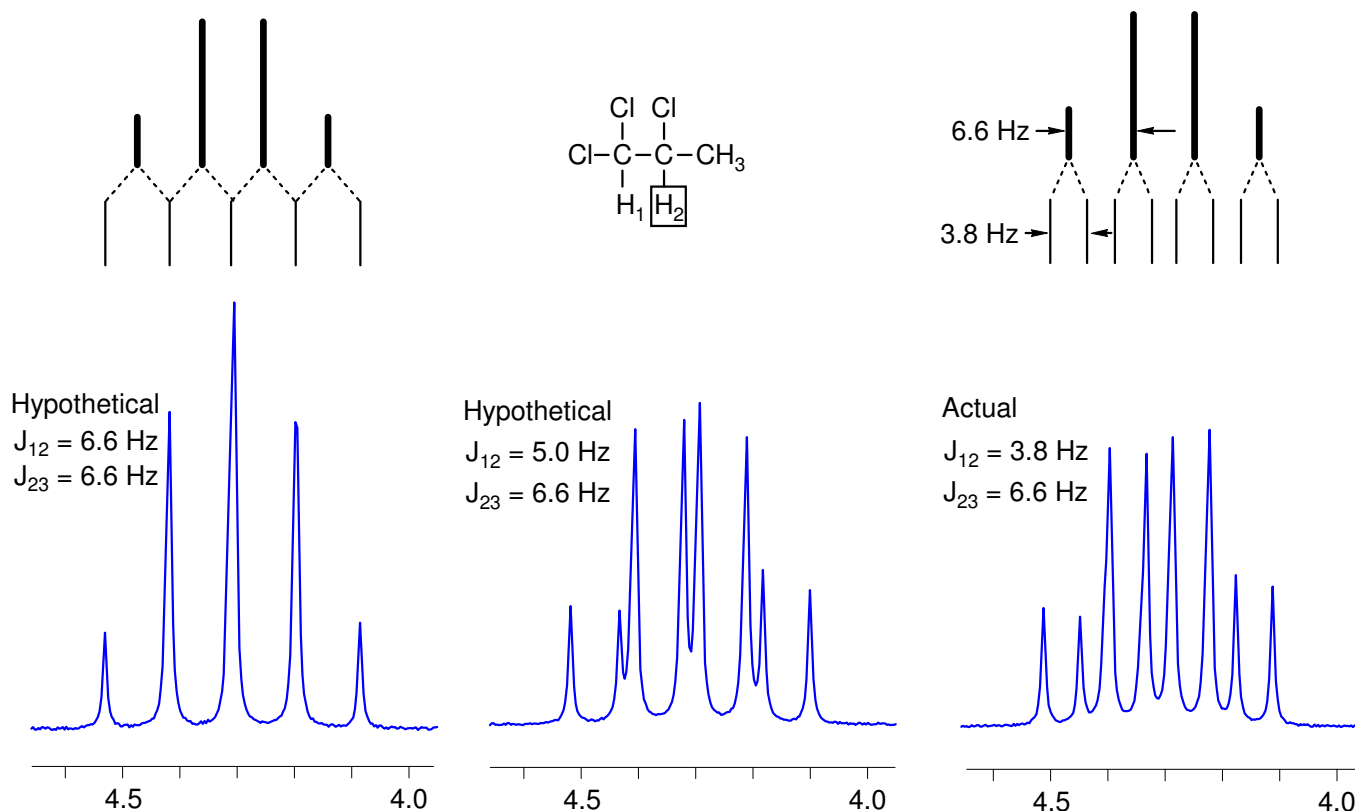


$J = 8$ Hz
one ortho H

A slightly more complicated case is 1,1,2-trichloropropane. A simulated spectrum is shown below.



The C-2 proton is coupled to one proton at C-1 and three protons of the methyl group at C-3. Naively, one might expect a *pentet* (p), as shown in the left spectrum below. Although pentets are, in fact, often observed in such situations, this occurs only if J_{1-2} and J_{2-3} are identical. When they are not (as is actually the case in this example), then we get a *quartet of doublets* (qd). It is customary to quote the larger coupling first (q) and then the smaller coupling (d). A proper text description of the multiplet is: δ 4.30, 1H, qd, $J = 6.6, 3.8$ Hz.



Exercise: what would a dq, $J = 6.6, 3.8$ Hz look like?

First Order Coupling Rules

1. Nuclei must be chemical shift nonequivalent to show obvious coupling to each other. Thus the protons of CH_2Cl_2 , $\text{Si}(\text{CH}_3)_4$, $\text{Cl-CH}_2\text{-CH}_2\text{-Cl}$, $\text{H}_2\text{C}=\text{CH}_2$ and benzene are all **singlets**. Equivalent protons are still coupled to each other, but the spectra do not show it. There are important exceptions to this rule: the coupling between shift equivalent but magnetically inequivalent nuclei can have profound effects on NMR spectra - see Sect. 5.7

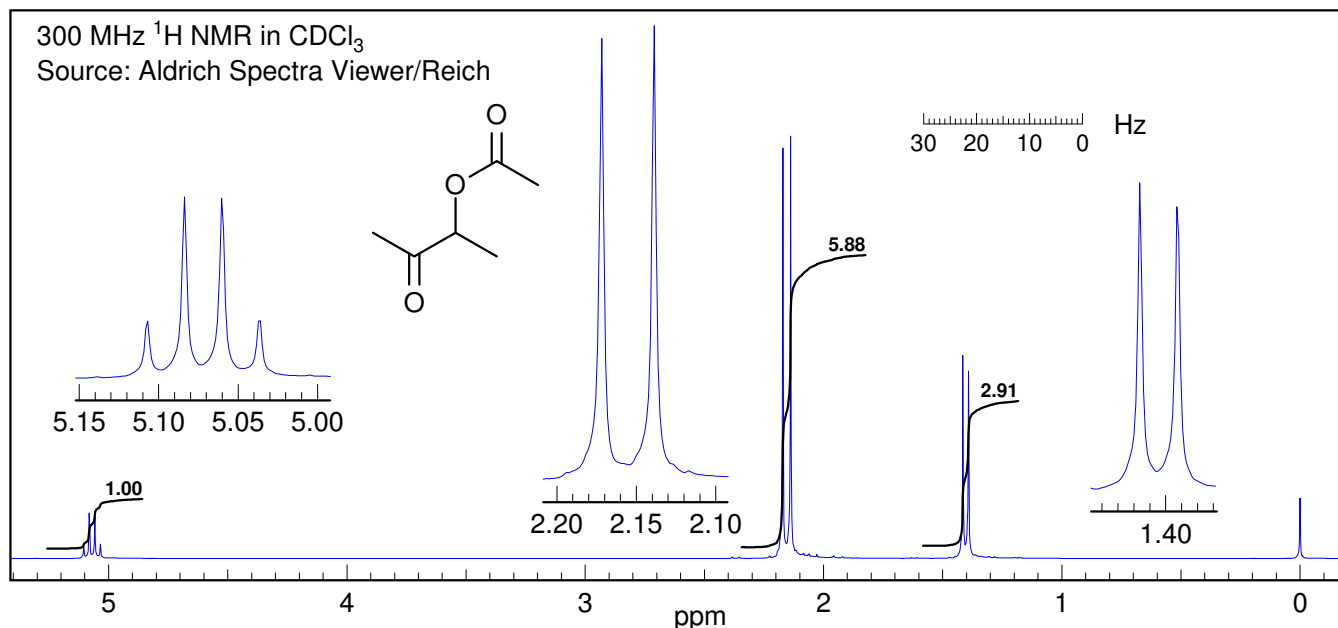
2. J coupling is **mutual**, i.e. $J_{\text{AB}} = J_{\text{BA}}$ **always**. Thus there is never just one nucleus which shows J splitting - there must be two, and they must have the same splitting constant J . However, both nuclei need not be protons - fluorine (^{19}F) and phosphorus (^{31}P) are two other common nuclei that have spin $\frac{1}{2}$ and 100% abundance, so they will couple to all nearby protons (the other 100% spin $\frac{1}{2}$ nuclei are ^{89}Y , ^{103}Rh and ^{169}Tm). If these nuclei are present in a molecule, there are likely to be splittings which are present in only one proton multiplet (i.e. not shared by two multiplets).

3. Two closely spaced lines can be either chemically shifted or coupled. It is not always possible to distinguish J from δ by the appearance of the spectrum (see Item 4 below). For tough cases (e.g. two closely spaced singlets in the methyl region) there are several possibilities:

- decouple the spectrum
- obtain it at a different field strength (measured in Hz, coupling constants are field independent, chemical shifts are proportional to the magnetic field)
- measure the spectrum in a different solvent (chemical shifts are usually more solvent dependent than coupling constants, benzene and chloroform are a good pair of solvents).

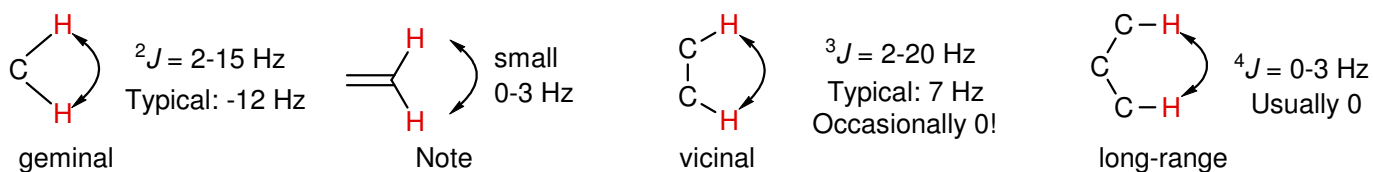
For multiplets with more than two lines, areas, intensities, symmetry of the pattern and spacing of the lines generally make it easy to distinguish chemical shift from coupling.

For a simple example see the spectrum of 3-acetoxy-2-butanone below. Here it is pretty easy to identify one of the doublets as the 4-methyl group, the other "doublet" (with a separation of 9 Hz, which could easily be a coupling) actually corresponds to the two $\text{CH}_3\text{C}(=\text{O})$ groups.

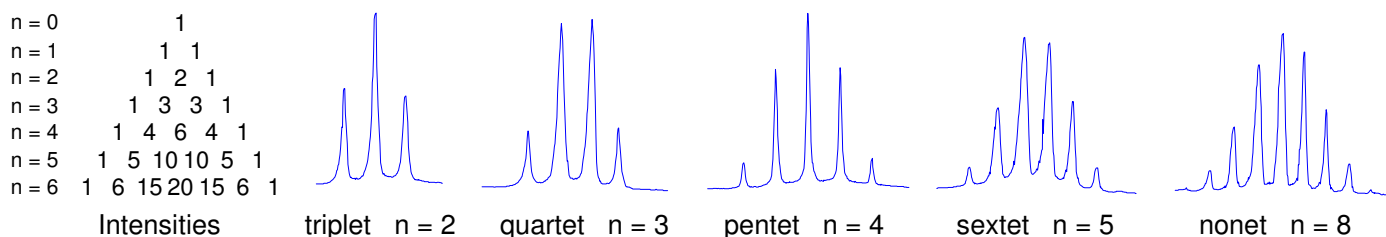


4. Chemical shifts are usually reported in δ (units: ppm) so that the numeric values will not depend on the spectrometer frequency (field-independent units), coupling constants are **always** reported in **Hz** (cycles per second). Chemical shifts are **caused** by the magnetic field, couplings are **field-independent**, the coupling is inherent in the magnetic properties of the molecule. However, all calculations on NMR spectra are done using Hz (or, more precisely, radians per sec).

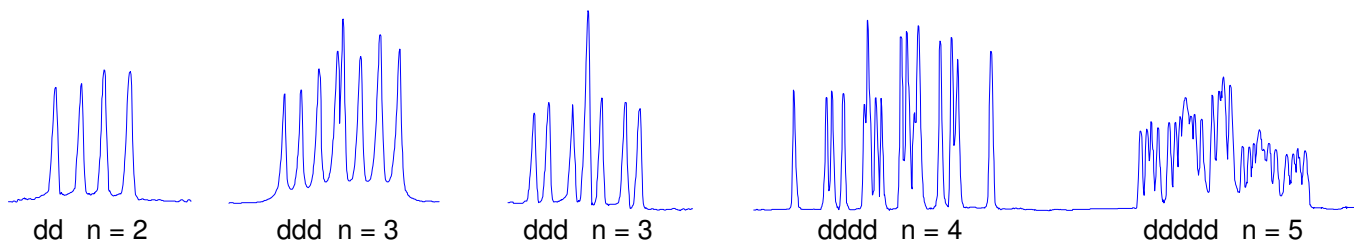
5. Protons two (2J , geminal) or three bonds (3J , vicinal) apart are usually coupled to each other, more remote protons (4J , 5J) **may** be if geometry is right, or if π -systems (multiple bonds) intervene. Long range couplings (4J or greater) are usually small, typically <0.5 Hz, but up to 3 Hz in some cases where there are intervening π bonds.



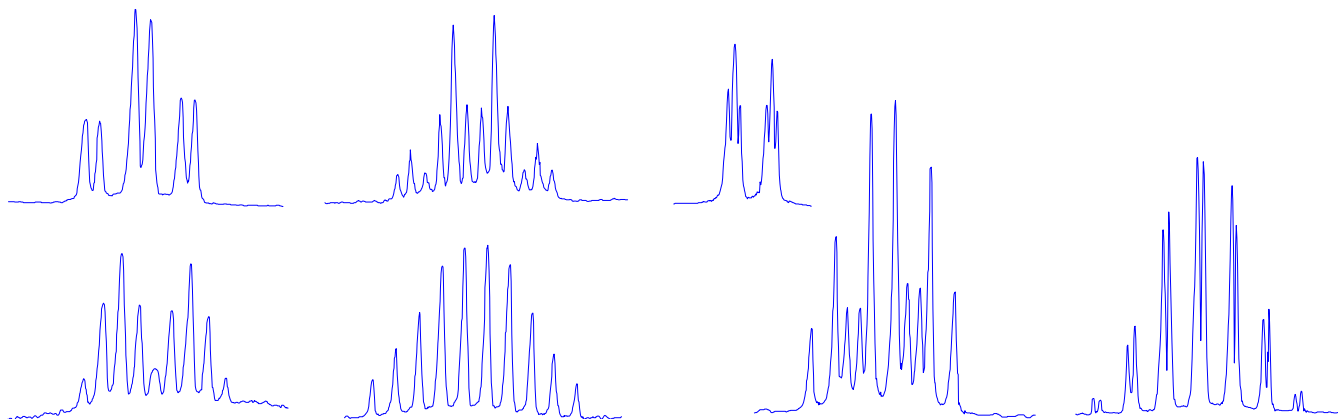
6. Multiplicity for first order patterns follows the "doubling rule". If **all couplings to a particular proton are the same** there will be $2n+1$ lines, where l is the spin and n is the number of neighboring nuclei ($n + 1$ for 1H $l = 1/2$). The intensities will follow Pascal's triangle.



7. If **all couplings are different**, then the number of peaks is 2^n for 1H , and the intensities are 1:1:1:1... Thus a proton coupled to two others by different couplings gives a **dd** (doublet of doublets, see Figure). This pattern is **never** called a quartet. As the number of couplings gets larger, accidental superpositions of lines will sometimes occur, so that the 1:1:1... intensity ratio no longer applies. The intensities are also often distorted by leaning effects (see AB/AX patterns), as seen in several examples below.



8. More typically, **some of the couplings are the same, others different**, so get a variety of patterns. In favorable cases, these patterns can be analyzed and all couplings extracted. The number and size of couplings (J -values) provide important structural information.



Second Order Effects

Protons or groups of protons form simple multiplets only if the chemical shift differences between the protons ($\Delta\nu$) are large compared to the coupling constants between them (J). If $\Delta\nu / J$ (all in **Hz**) is <5 then **second order** effects appear (see 5-HMR-9) which complicate the analysis.

Rules for Analyzing First Order Multiplets

A **first order multiplet** can be expected when **both** of the following criteria are met:

First, the chemical shift of the observed proton must be far away from any of the protons it is coupled to (far away means $\Delta\nu \gg J$). In practice, multiplets can be treated in a first order fashion if $\Delta\nu > 3J$, although the substantial leaning distortions can complicate analysis. The leaning will have almost completely disappeared by the time $\Delta\nu = 10J$.

Second, if more than one proton is coupled to the observed one, then these protons must not be "strongly coupled." In other words, if they are coupled to each other **and** very close in chemical shift then the observed proton multiplet may not yield true coupling constants on analysis, even though it looks first order. See the section on Virtual Coupling.

Structure of First Order Multiplets. The fundamental rule governing multiplet intensities for spin 1/2 nuclei with all couplings identical is Pascal's triangle (n = number of equivalent couplings). A very characteristic and diagnostic intensity relationship is that between the first and second lines - the intensity ratio is $1/n$, where n is the number of equivalent coupling partners.

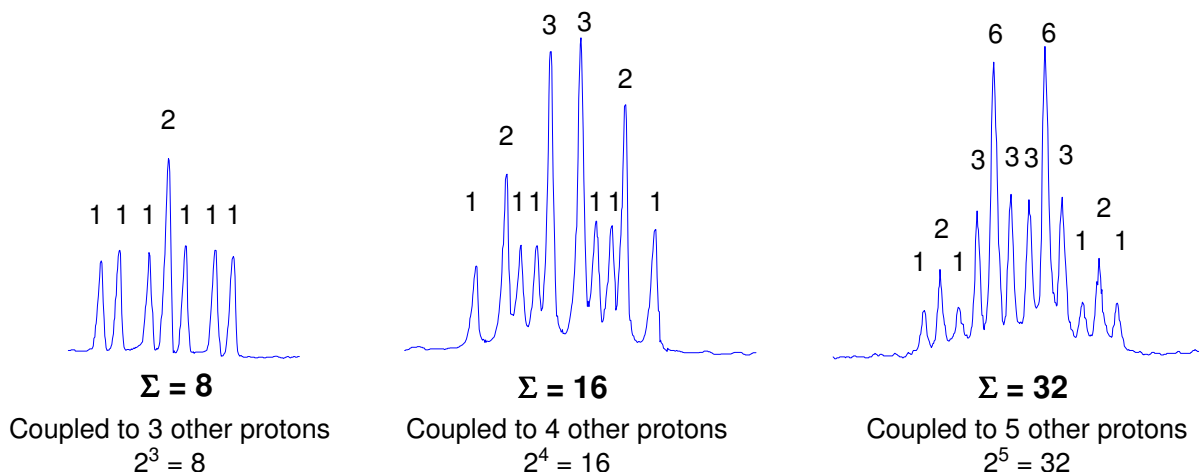
n	2ⁿ	Multiplet Intensities - Pascal's triangle
0	1	1 Singlet (s)
1	2	1 1 Doublet (d)
2	4	1 2 1 Triplet (t)
3	8	1 3 3 1 Quartet (q)
4	16	1 4 6 4 1 Pentet
5	32	1 5 10 10 5 1 Sextet
6	64	1 6 15 20 15 6 1 Septet
7	128	1 7 21 35 35 21 7 1 Octet
8	256	1 8 28 56 70 56 28 8 1 Nonet

A first order multiplet consists of the *product* (not the sum) of several such multiplets. In other words, a single line will first be split into one of the symmetrical multiplets (1:1 d, 1:2:1 t, 1:3:3:1 q, etc), then each line of this multiplet will be again split into d, t, q, or higher multiplet.

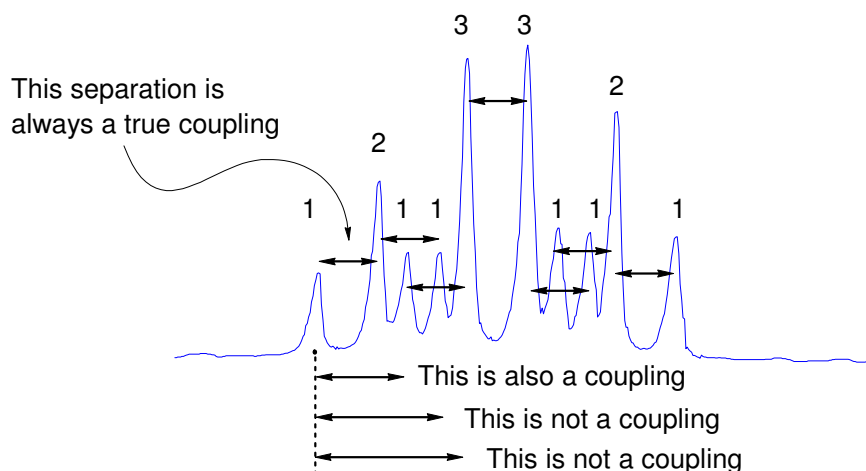
Recognizing a First Order Multiplet.

1. All truly first order multiplets are *centrosymmetric* - there is a mirror plane in the middle (in real spectra, this is usually not strictly true because of *leaning* and other distortions). However, the reverse is not true: not all symmetrical multiplets are first order.

2. If the small outermost peaks are assigned intensity 1, then all other peaks must be an integral multiple intensity of this one (1x, 2x, 3x, 4x in height), and the total intensity of all peaks must be a power of 2 (2, 4, 8, 16, 32, etc). The intensity of each of the two outermost lines is $1/2^n$ of the total multiplet intensity, where n is the number of protons which are coupled with the proton signal being analyzed. *There can be no lines smaller than the outermost one.* Note, however, that if n is large, the outermost peaks may not be distinguishable from noise. Intensity assignments and determination of n cannot be easily made for such multiplets



3. There is a strict regularity of spacing in a first order multiplet: if you have correctly identified a coupling constant *J*, then *every* peak in the multiplet must have a partner *J* Hz away to the left or to the right of it.



4. Most first order multiplets integrate to a single proton, a few may be 2 or 3 protons in area. It is rare to have more than 3 protons, unless there is symmetry in the molecule (e.g., $(\text{CH}_3)_2\text{CH-}$ gives a 6-proton doublet for the methyl groups). Thus a 4-proton symmetrical multiplet is usually not a first-order pattern (it is more likely to be the very common **AA'BB'** pattern).

5. The symmetry and intensities of an otherwise first-order multiplet can be distorted by *leaning* effects (see Section 5-HMR-9). Many such multiplets can still be correctly analyzed by first-order techniques, but you have to mentally correct for the intensity distortions. However, the coupling constants extracted may not be perfectly accurate.

• **Analyzing a First Order Multiplet.** First order multiplets are analyzed by constructing a reverse coupling tree, by "removing" each of the couplings in turn, starting with the smallest.

1. "Take out" the smallest couplings first. The separation between the two lines at the edge of the multiplet is the smallest coupling. Each time you remove a coupling you generate a new, simpler multiplet, which can then be analyzed in turn. Remember that *each line of the multiplet participates in each coupling*.

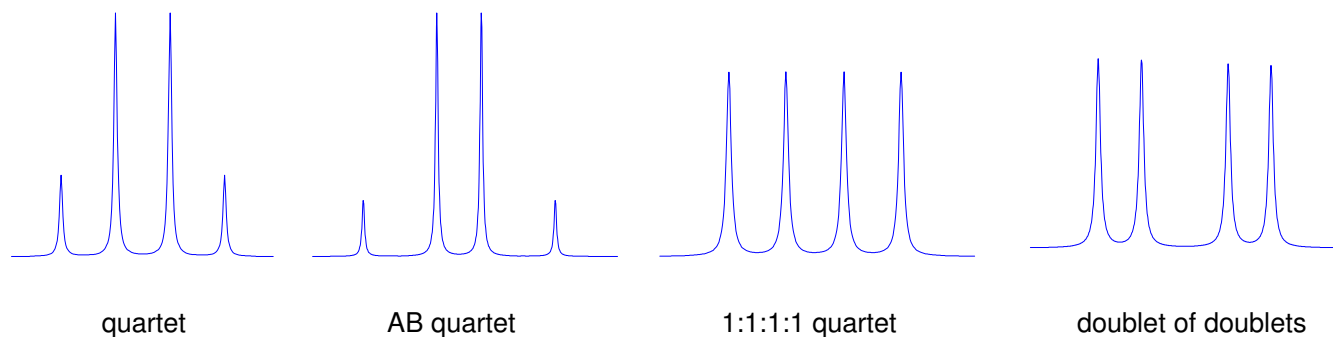
2. Watch line intensities (i.e., peak areas or peak heights) carefully--when you "take out" a coupling, the intensities of the newly created lines should be appropriate (i.e., each time you "take out" a coupling, also "take out" the proper intensity). When a coupling has been taken out completely, all intensity should be accounted for. Keep track of your analysis by using a "coupling tree".

3. The couplings may be removed one at a time as doublets, or as triplets, quartets and higher multiplets. The intensity ratio of the first two lines signals the number of protons involved in the coupling: 1:1 means there is only one proton, 1:2 means that there are 2 protons (triplet), etc. Be especially careful to keep track of intensities when you "take out" triplets (1:2:1) or quartets (1:3:3:1). Each time you completely remove a coupling you generate a new simpler multiplet which follows first order rules, and can be analyzed in turn.

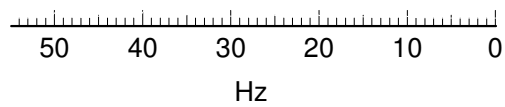
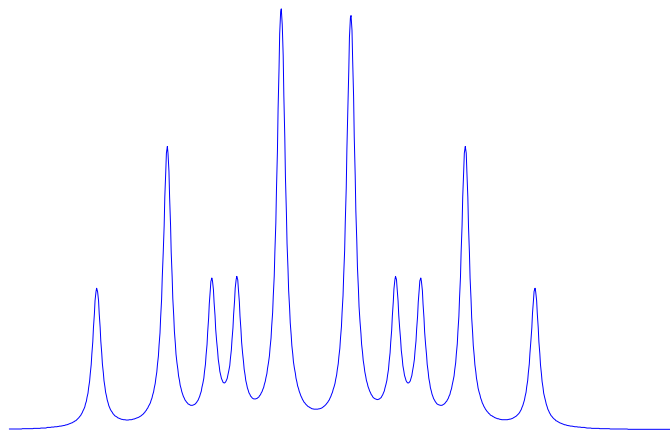
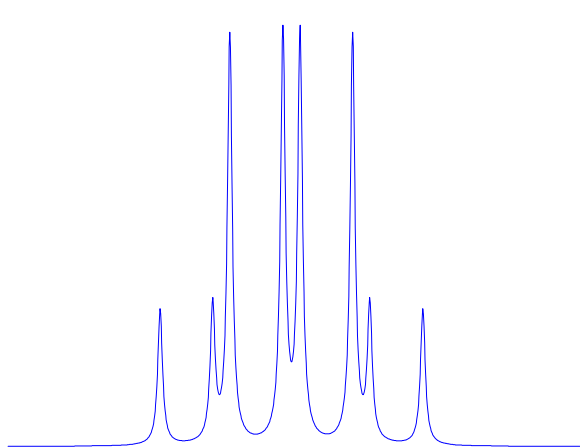
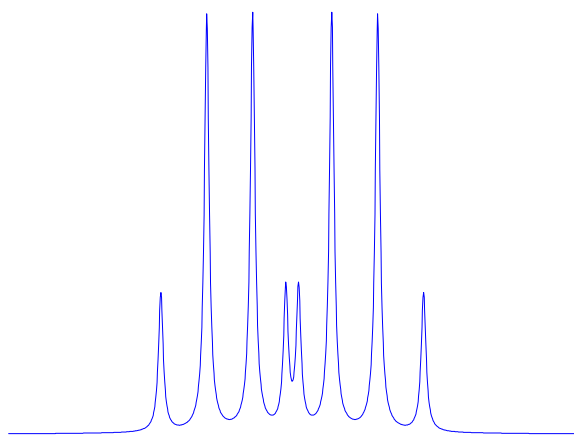
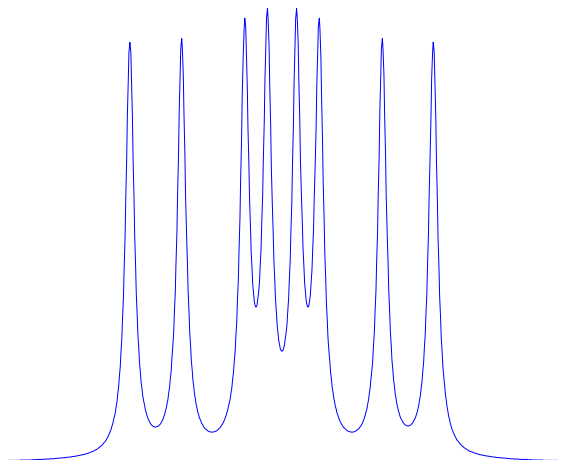
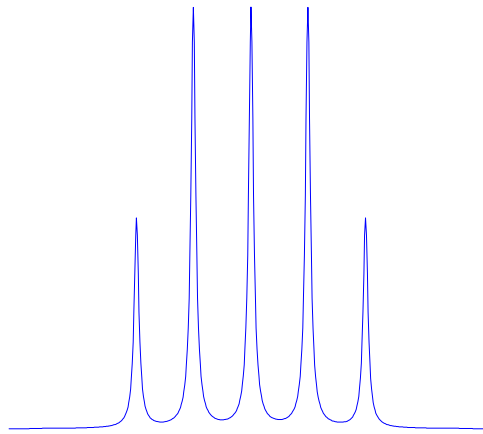
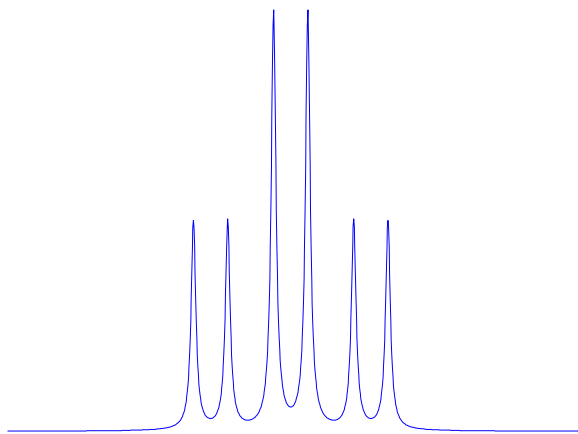
When you have finished your analysis, all peaks and all intensity in the multiplet must be accounted for. You can check the analysis as follows: the separation of the two outermost peaks of the multiplet is the sum of all the J s (i.e., for a dt, $J = 8, 3$ Hz the outermost lines are separated by $8 + 3 + 3 = 14$ Hz).

Reporting a First Order Multiplet. Multiplets are reported starting with the largest coupling, and the symbols must be in the order of the reported numbers: δ 2.10, 1H, qt, $J = 10, 6$ Hz means: a single proton q of 10 Hz, t of 6 Hz with a chemical shifts of 2.10 ppm.

Quartets. Keep clear in your mind the distinction between a simple q (one proton equally coupled to 3 others, with an intensity 1:3:3:1), an ABq (2 protons coupled to each other, see Section 5-HMR-10), and the quartet formed by coupling with a spin 3/2 nucleus (e.g., ^7Li , intensity 1:1:1:1, see Sect 7-MULTI-2). Only the first of these should be referred to by just a "q" symbol. The early NMR literature (and even modern novices) sometimes call doublets of doublets "quartets" (there are four lines, after all). Don't do this.



Practice Multiplets



First Order Analysis

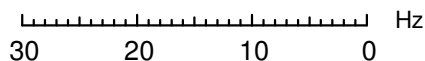
The separation between the first and second lines is the smallest coupling in the multiplet (J_1). They are in an intensity ratio of 1:1, so that coupling appears only once (i.e., it is a *doublet* splitting).

"Remove" the first coupling. Keep track of line intensities, and draw a child multiplet with positions at the center of each doublet. Each unit of line intensity can only be used once, and all line intensity must be accounted for

Repeat the process - the first and second lines now represent the next largest coupling J_2 . Remove this in turn, and repeat the process until you get a singlet

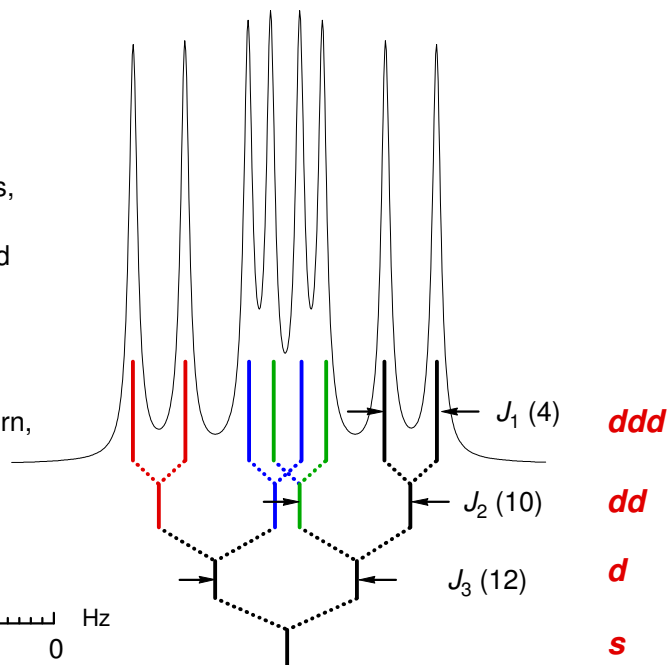
Report the couplings in order of size (reverse of the analysis): J_3, J_2, J_1

This is ddd, $J = 12, 10, 4$ Hz



$\Sigma = 8$ (3 couplings present)

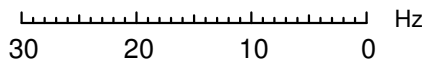
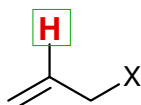
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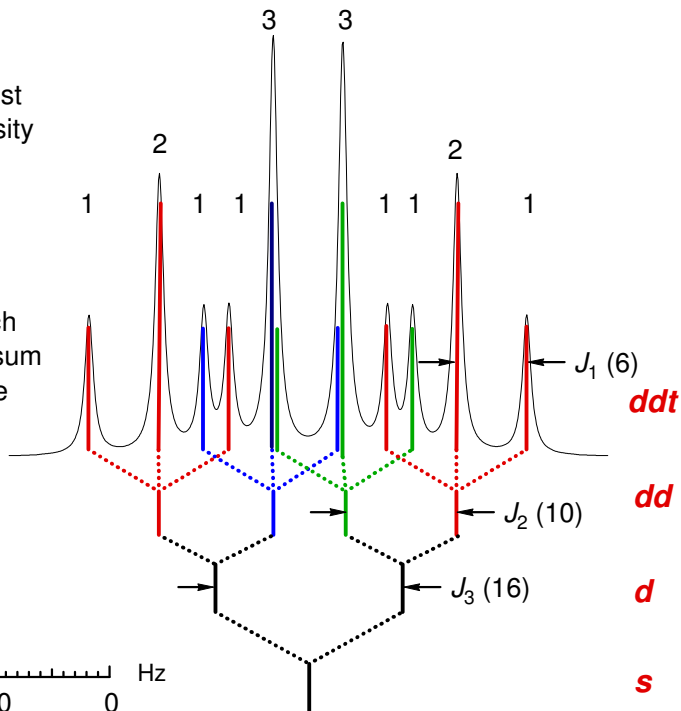
As always, the separation of the first two lines is the smallest coupling in the multiplet (J_1). However, they are in an intensity ratio of 1:2, so this coupling appears twice (i.e., it is a *triplet* splitting).

"Remove" the triplet coupling. Keep track of line intensities, and draw a child multiplet with positions at the center of each triplet. Note that the central two lines of intensity 3 are the sum of two lines - one of intensity 1 and the other intensity 2. The new multiplet is a *dd*, which can be solved in turn.

This is a ddt, $J = 16, 10, 6$ Hz - typically the way the central vinyl protons of an allyl group appears:



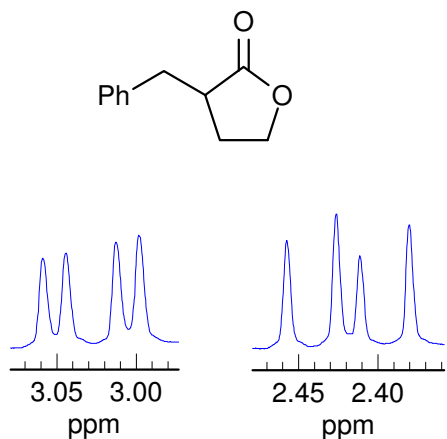
$\Sigma = 16$ (4 couplings present)



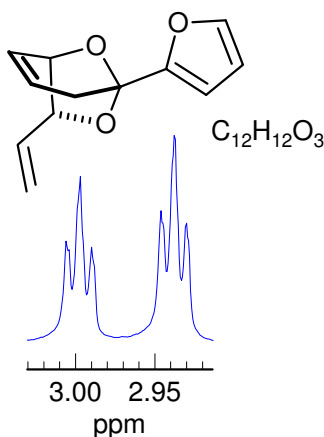
Simple Multiplets

Exercise: Assign the protons where structure and chemical shift scale are given
 Note the leaning in most of the multiplets, indicating that the coupled partner is not too far away.

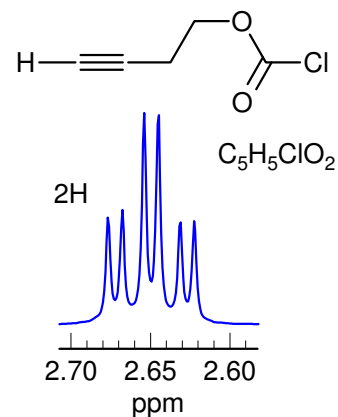
Doublet of doublets (dd)



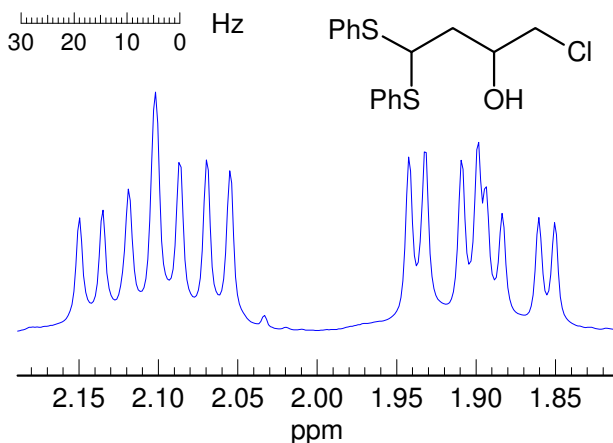
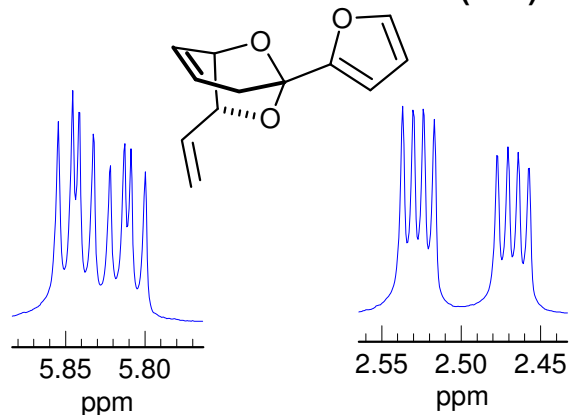
Doublet of triplets (dt, td)



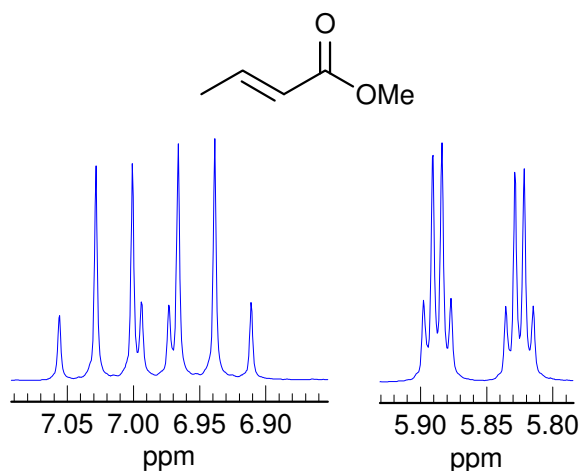
Triplet of doublets (td)



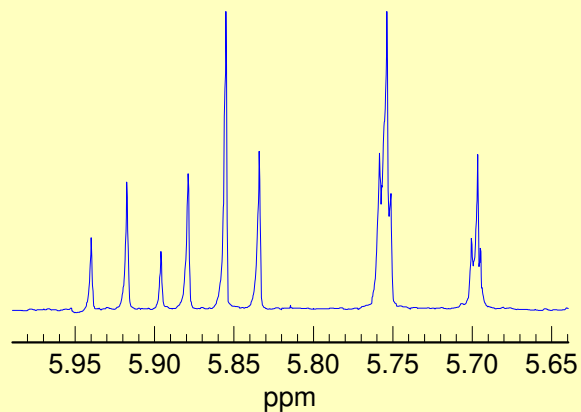
Doublet of doublet of doublets (ddd)



Doublet of quartets (dq)



Exercise: The multiplet below integrates to two protons. Using the chemical shift and coupling identify the structural fragment.

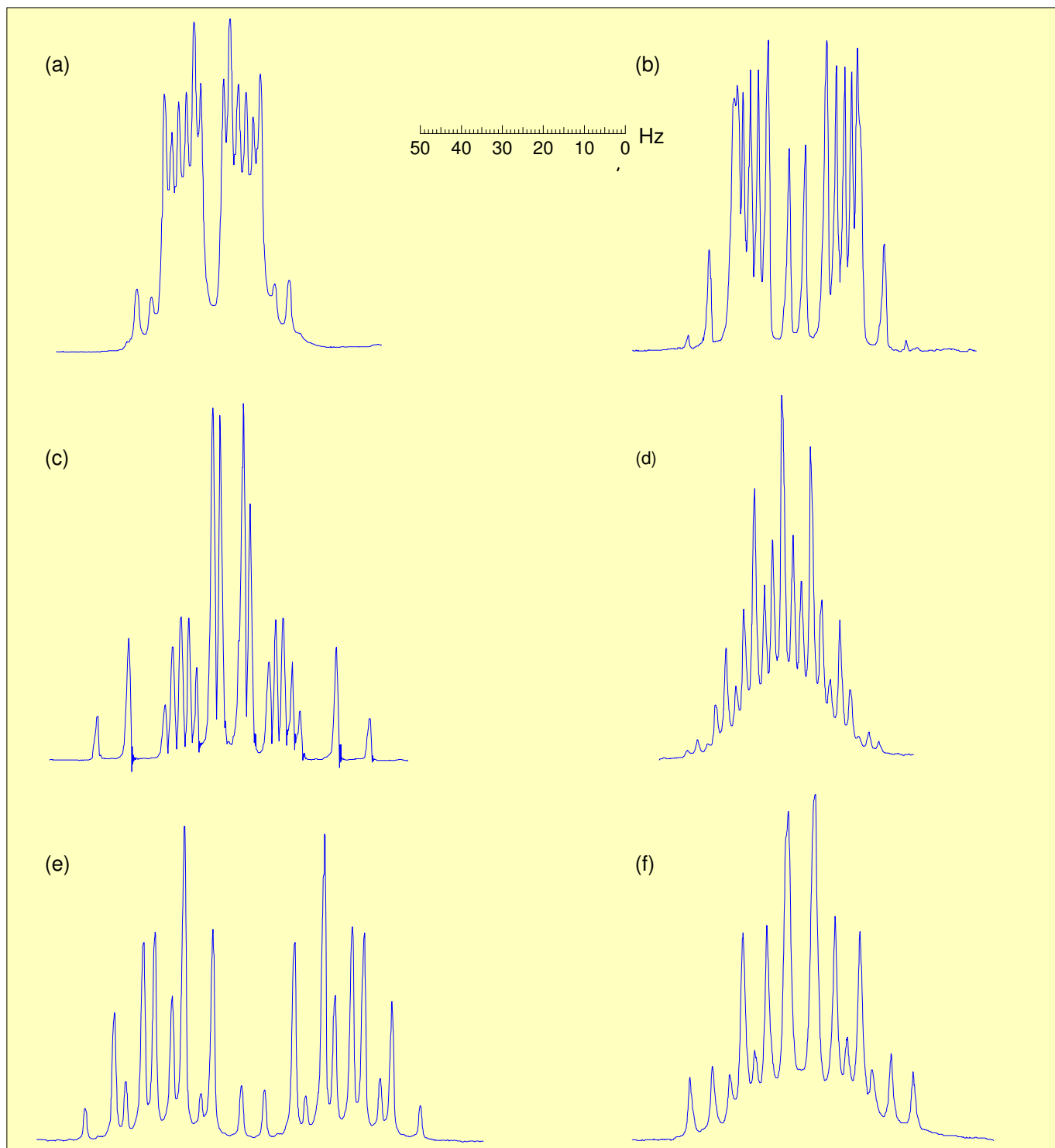


Symmetrical Multiplets which are NOT First Order

Exercise: Only ONE of the multiplets below is first order, find it. A second one is almost first order, but ultimately can be ruled out because of a very subtle line position inconsistency.

Some criteria to use:

- Pattern must be centrosymmetric (true of all of these)
- Intensity of lines - patterns must be repeated, especially examine outer lines
- Be wary if #H > 1, especially if 4H
- Consider size of possible couplings



5-HMR-3.14 Measurement of Coupling Constants

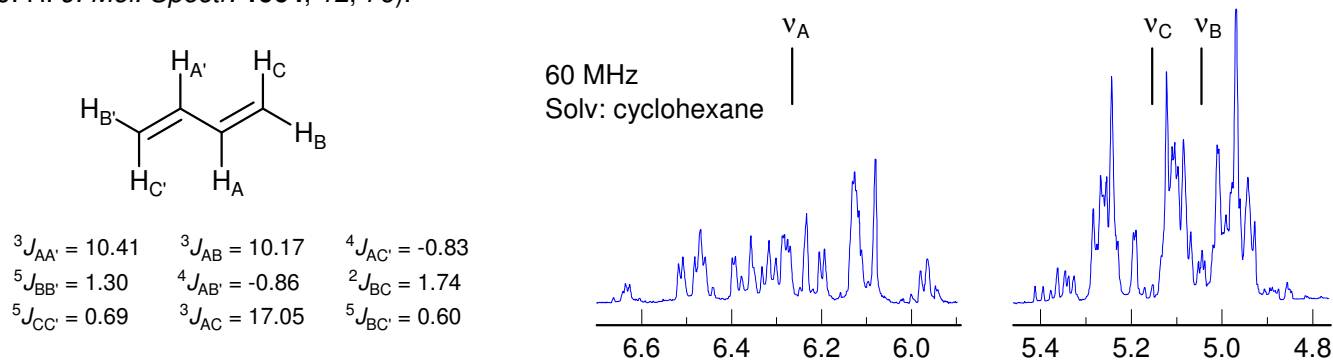
The accurate measurement of J coupling constants requires that the multiplets be correctly analyzed. In the following pages are described techniques for performing such analyses. The procedures are summarized below.

For first order multiplets a simple "coupling tree" analysis as described in Section 5-HMR-3.9 can directly yield coupling constants within the accuracy of the digital resolution of the spectrum. This includes AB spectra, where J_{AB} can be measured directly. See Section 5-HMR-7 for a description of the ABC... (Pople) nomenclature for spin systems.

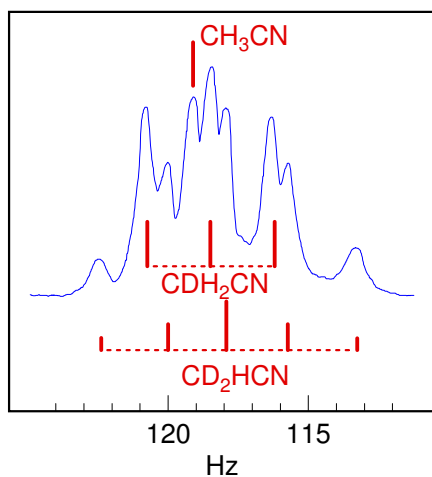
For AB_2 spectra both the coupling constant J_{AB} and the chemical shifts can be obtained by simple arithmetic manipulations, provided that line assignments can be made correctly. For ABX spectra J_{AB} is accurately measurable by inspection. An approximate analysis, which treats the peaks as AMX, will give values for J_{AX} and J_{BX} that will be in error by varying amounts, depending on the relative size of J_{AB} and ν_{AB} (the smaller ν_{AB} the larger the error), and the relative size of J_{AX} and J_{BX} . To get accurate values for the J_{AX} and J_{BX} coupling constants a proper ABX analysis as described in Section 5-HMR-12 is required.

For many simple compounds the symmetry is such that protons are homotopic or enantiotopic, and no coupling constants can be measured directly (e.g., the 2J coupling in methane or dichloromethane; the ortho, meta, and para couplings in benzene; the cis, trans and gem couplings in ethylene, etc). For such compounds the following techniques are used to measure J_{HH} :

Analysis of Complex Spin Systems. In molecules where the chemical shift-equivalent protons are of the AA' type (part of an $AA'XX'$, $AA'X_3X_3'$ or similar system), complete analysis of the coupling system can, in favorable circumstances, give the value of $J_{AA'}$. An example is 1,3-butadiene, an $AA'BB'CC'$ system in which all protons are coupled to all other ones. Analysis of the complex NMR spectrum gave, among numerous others, values for the following couplings between chemical shift equivalent nuclei: $^3J_{AA'}$, $^5J_{BB'}$ and $^5J_{CC'}$ (Hobgood, R. T., Jr.; Goldstein, J. H. *J. Mol. Spectr.* **1964**, *12*, 76).



Isotopic Substitution. Replacing one of the protons by deuterium (or even tritium) breaks the symmetry of the coupled system and allows measurement of J_{HD} (or J_{HT}). The value of J_{HH} can then be calculated from the gyromagnetic ratios. In the example below, the 60 MHz NMR spectrum of a mixture of undeuterated (s), monodeuterated (1:1:1 triplet, the spin of D is 1, see Sect. 7-MULTI-2) and dideuterated (1:2:3:2:1 quintet) acetonitrile is shown. Note the isotopic shifts (Grant, D. M.; Barfield, M. *JACS* **1961**, *83*, 4727)



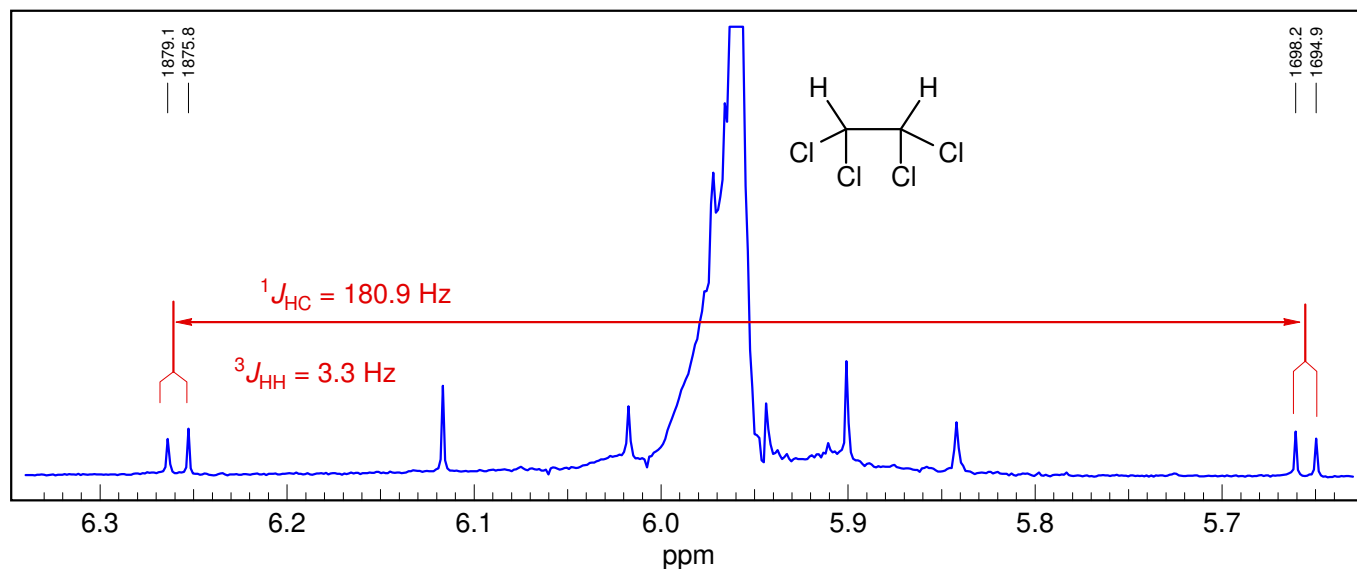
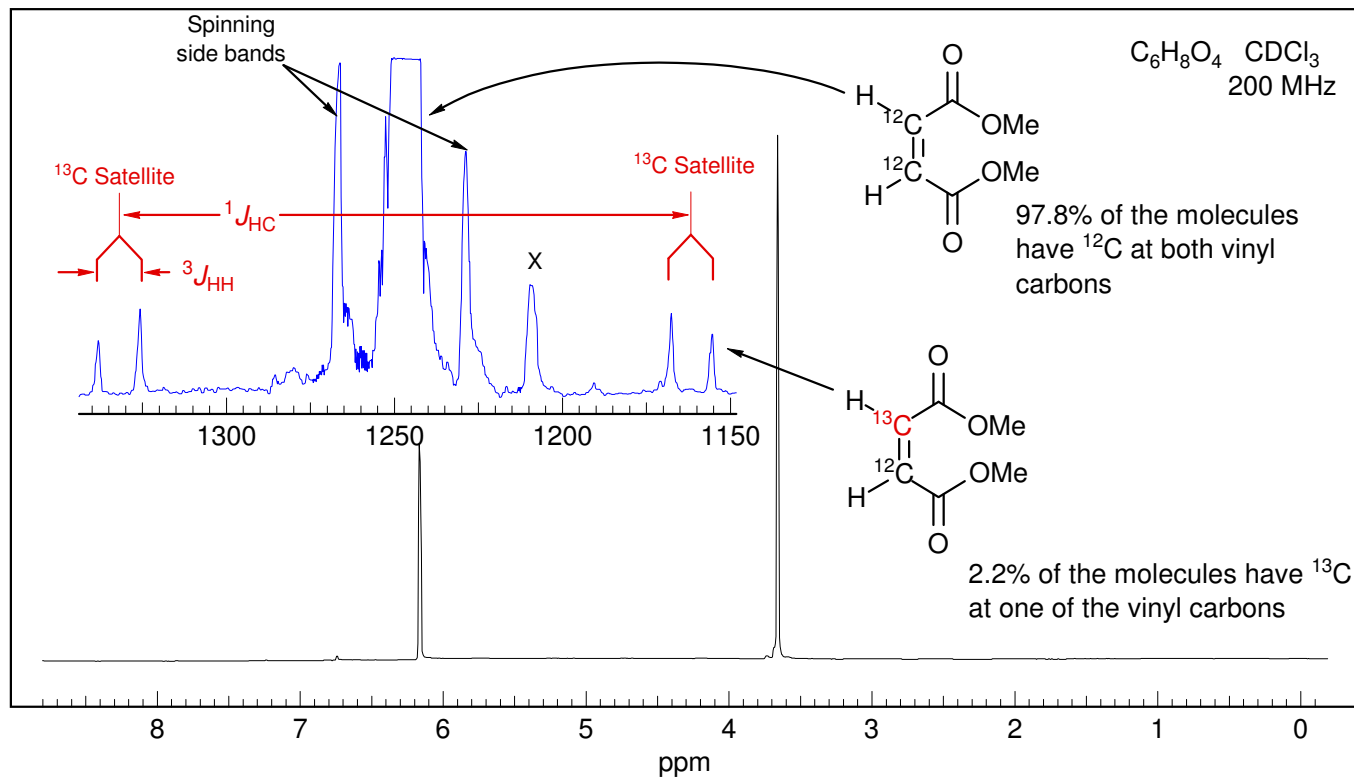
$$\frac{J_{HH}}{J_{HD}} = \frac{\gamma_H}{\gamma_D} = 6.488$$

$$J_{HH} = 6.488 \times J_{HD}$$

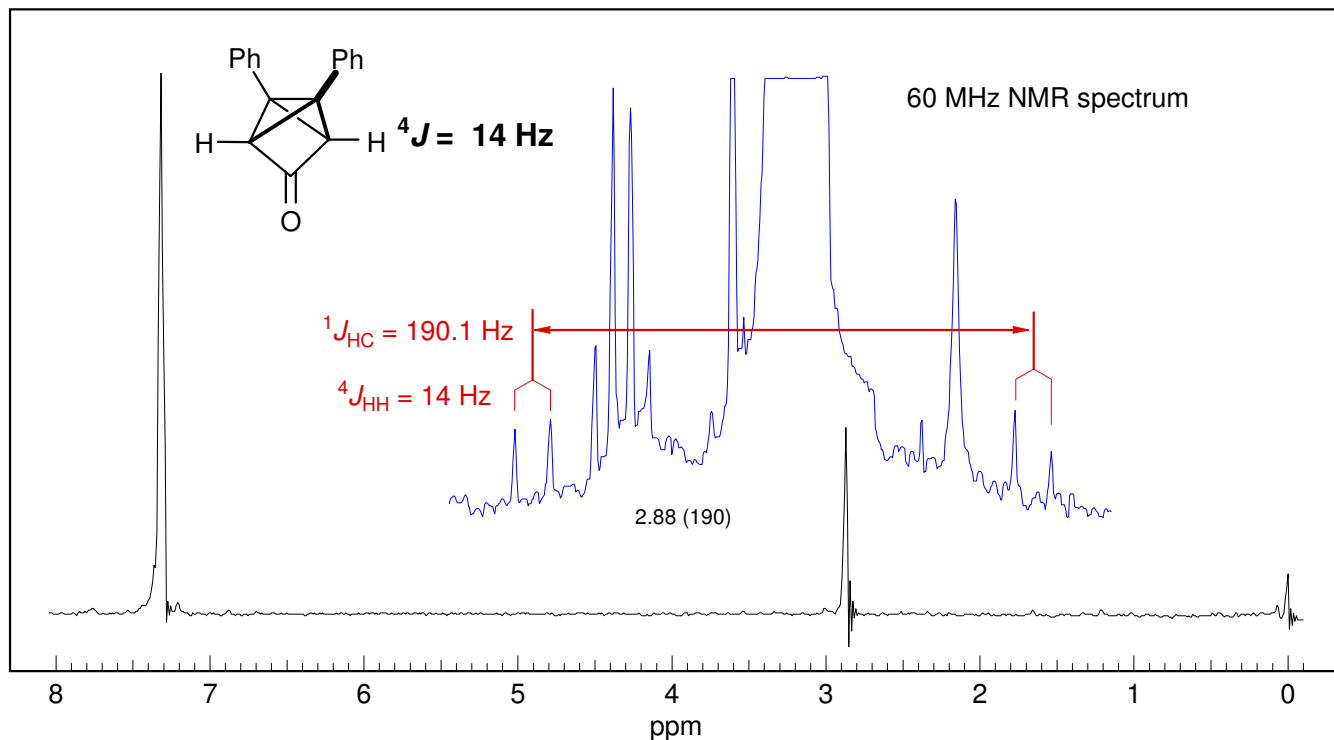
$$J_{HD} (\text{CH}_2\text{D-CN}) = 2.58 \text{ Hz}$$

$$J_{HH} (\text{CH}_3\text{-CN}) = 16.75 \text{ Hz}$$

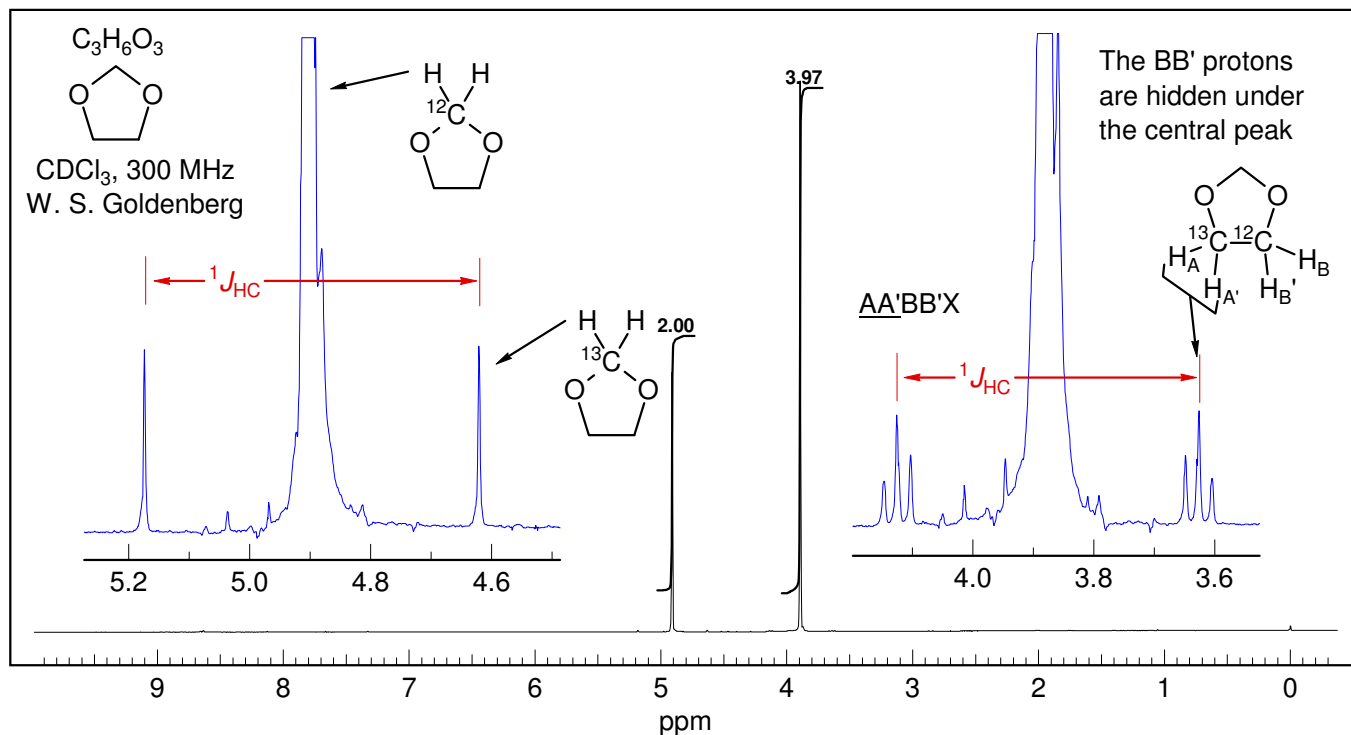
Analysis of ^{13}C Satellite Spectra. Vicinal couplings between homotopic or enantiotopic protons $^3J_{\text{HH}}$ can often be obtained by analysis of the ^{13}C satellites. The ^1H NMR signal for the vinyl protons of dimethyl maleate is a singlet. However, the ^{13}C satellites are doublets, with a splitting that is equal to $^3J_{\text{HH}}$. In effect, the A_2 spin system of the ^{12}C isotopomer has become an ABX pattern in the mono- ^{13}C labelled compound, where X is the ^{13}C nucleus, and A and B are the two vinyl protons, one on ^{13}C and the other on ^{12}C .



Below is an example of the measurement of a $^4J_{\text{HH}}$ in a symmetric tricyclic system using the ^{13}C satellite method (Masamune, *S. J. Am. Chem. Soc.* **1964**, *86*, 735)



For systems of the X-CH₂-CH₂-X type, the mono- ^{13}C isotopomer is an AA'BB'X pattern (X = ^{13}C), which can be solved to obtain $J_{\text{AA}'}$ (= $J_{\text{BB}'}$) as well as J_{AB} and $J_{\text{AB}'}$. Note that when both protons are on the same carbon the value 2J cannot be determined by this method. Thus for the O-CH₂-O signal, the ^{13}C satellites are singlets.

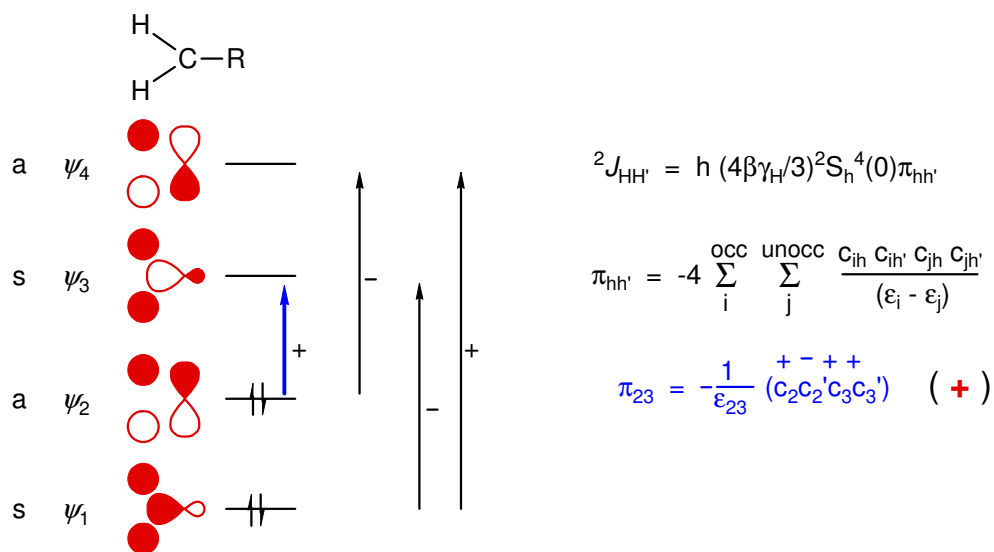


5.4 Geminal Proton-Proton Couplings ($^2J_{H-H}$)

Two-bond H-H couplings (Review: *Tet*, **1969**, 25, 4681) vary in a complicated way with structure, and they can only be understood if both magnitude and sign is taken into account. Some extreme examples are given below.



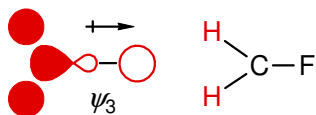
Most 2J couplings fall into two well-defined groups. For unstrained sp^3 CH_2 protons with innocuous substituents, the coupling is typically around -12 Hz, whereas the 2-bond coupling of sp^2 (vinyl) protons is much smaller, typically 2 Hz. The molecular orbital perturbation theory of Pople and Bothner-By (*J. Chem. Phys.* **1965**, 42, 1339) predicts the electronic effects of substituents on these coupling constants based on the interaction between filled and empty orbitals of the CH_2 fragment. Excitation between orbitals of the same symmetry has a negative effect on J , between orbitals of opposite symmetry has a positive effect. The $1/E$ term is largest for the HOMO-LUMO transition, so coupling effects are dominated by the $\psi_2 \psi_3$ transition. Substituents which reduce the energy gap between ψ_2 and ψ_3 (i.e. raise ψ_2 or lower ψ_3) will increase the size of $1/E$ and thus have a (+) effect on the coupling, whereas those which increase the energy gap (i.e. lower ψ_2 or raise ψ_3) will have a (-) effect. There are also changes in the orbital coefficients which affect the magnitude of the coupling.



σ -Acceptor substituents (electronegative atoms like F, O, N) interact mainly with ψ_3 and ψ_1 because of symmetry restrictions. The most important effect is to lower ψ_3 , and thus have a (+) effect on the coupling, whereas σ -donor substituents like Si or other metals will raise ψ_3 and thus have a (-) effect.

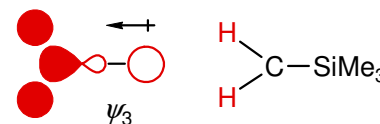
σ -Acceptor

$^2J_{\text{H-H}}$ coupling becomes more **positive**

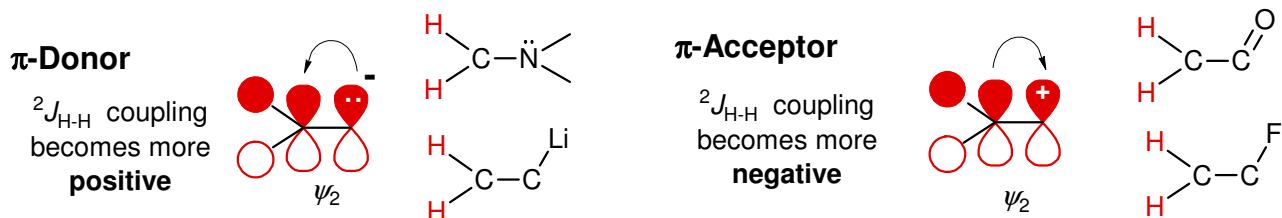


σ -Donor

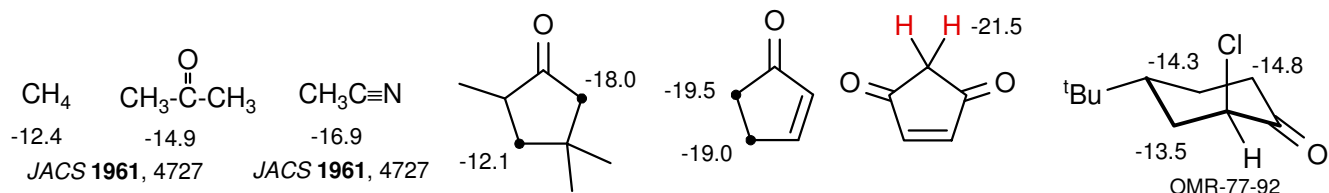
$^2J_{\text{H-H}}$ coupling becomes more **negative**



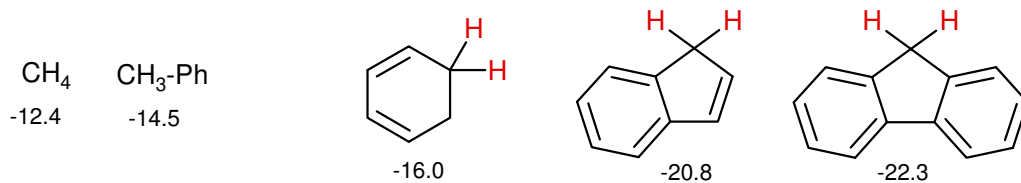
Remarkably, π -donors and acceptors have the opposite effect -- symmetry requires that these will interact mainly with ψ_2 . Thus π -donor substituents (directly attached atoms with lone pairs, or adjacent electron rich bonds) will raise ψ_2 , and result in a (+) effect, and π -acceptor substituents (carbonyl groups and related functions, or adjacent electron poor bonds) will lower ψ_2 and have a (-) effect.



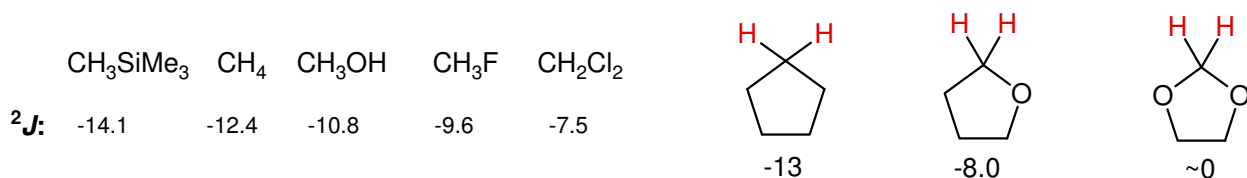
Gem coupling in Saturated Carbons (sp^3): In acyclic and unstrained ring systems the gem coupling is typically from -10 to -13 Hz. Substituents will change these couplings as described above: when the CH_2 group is substituted with a π -acceptor like a carbonyl or cyano group, the coupling becomes more negative, i.e. larger in magnitude, ranging from -16 to -25 Hz. This is a reliable and important effect which can help with structure assignments.



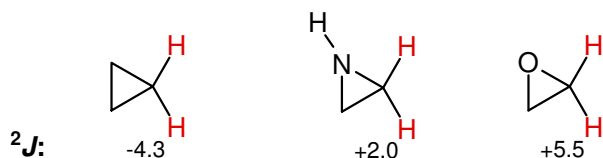
Conjugating aryl, alkene and alkyne substituents also make the coupling more negative.



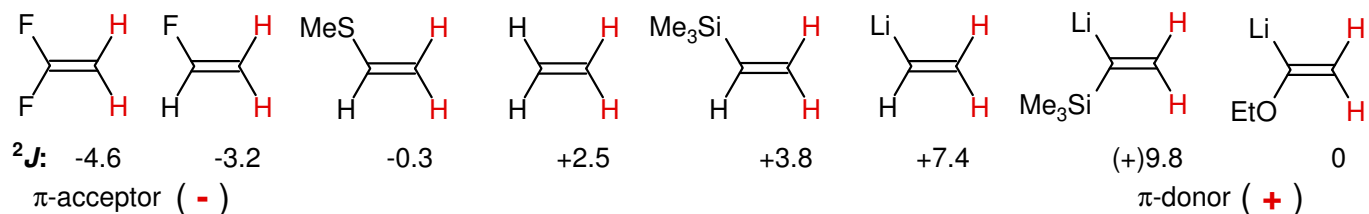
Substituents like the halogens, alkoxy and amino groups are both σ -acceptors and π -donors. Both are (+) effects, so the couplings become more positive (i.e. smaller numbers), in some cases they are close to zero.



Ring strain has a (+) effect on gem coupling. Thus in cyclopropane the coupling has increased from -12 to -4 Hz. The additional (+) effects of oxygen bring the coupling to +5.5 in ethylene oxide

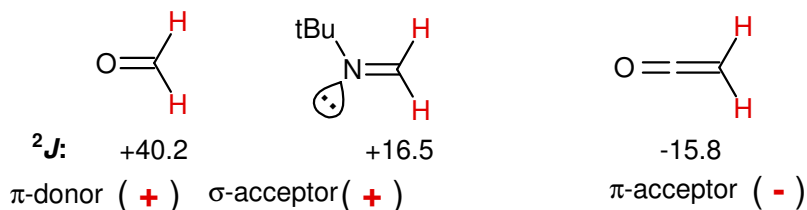


Gem coupling in Unsaturated Carbons (sp^2): The gem coupling in ethylene itself is +2.5 Hz, and most terminal alkenes have small couplings in the range of 1-3 Hz. Electronegative substituents (F, O) on the double bond behave as π -acceptors, with a (-) effect on the coupling, which can become close to zero for weakly accepting substituents (as in methyl vinyl sulfide). Electropositive substituents on the neighboring carbon (Si, Li) behave as π -donors with a (+) effect on the coupling. For α -trimethylsilylvinyl lithium both substituents have a (+) effect, and result in an exceptionally large coupling, whereas in α -ethoxyvinyl lithium the two substituents have opposite effects, and the coupling was too small to observe.

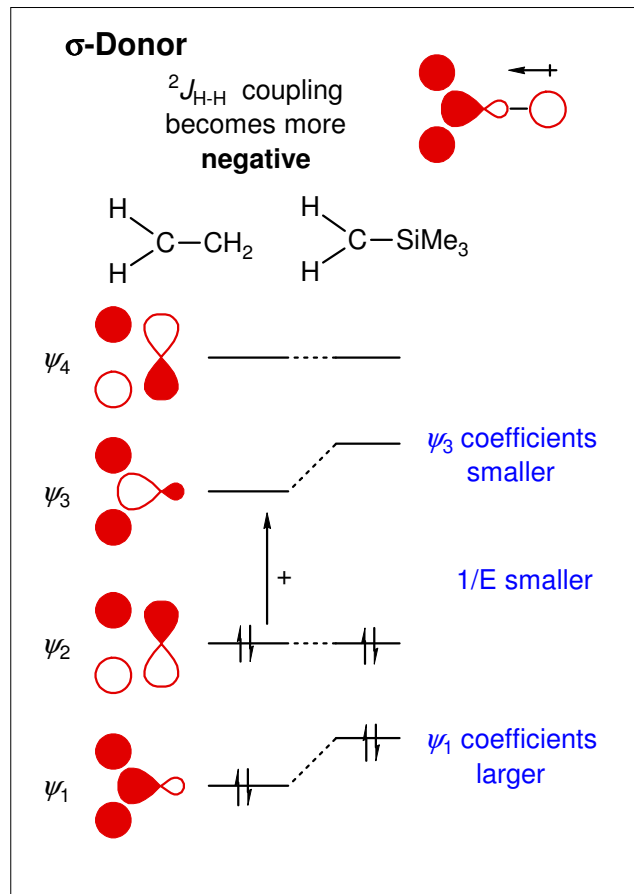
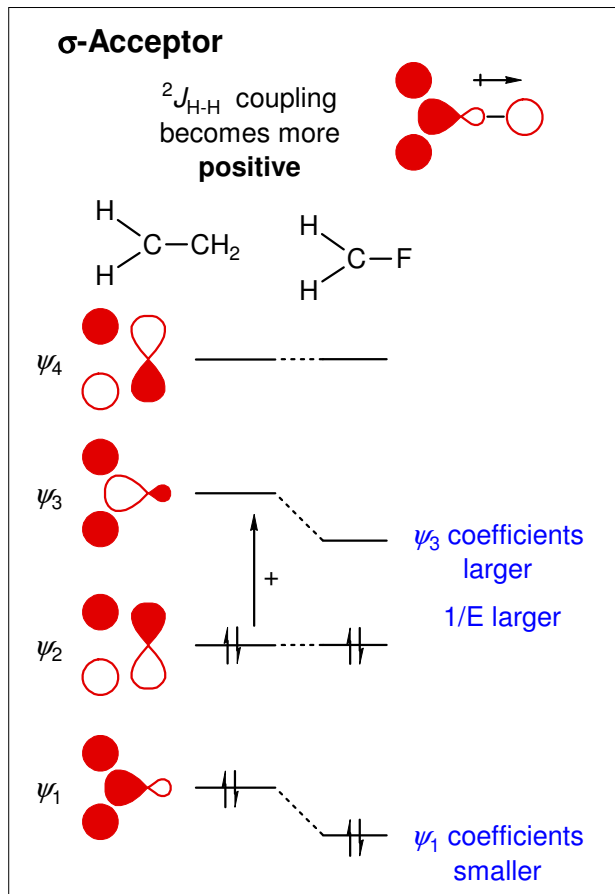
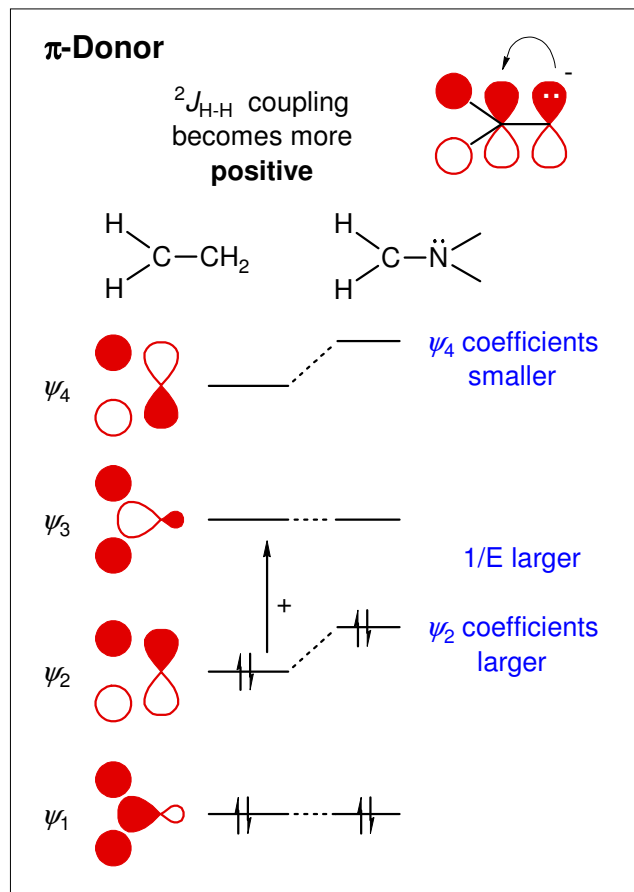
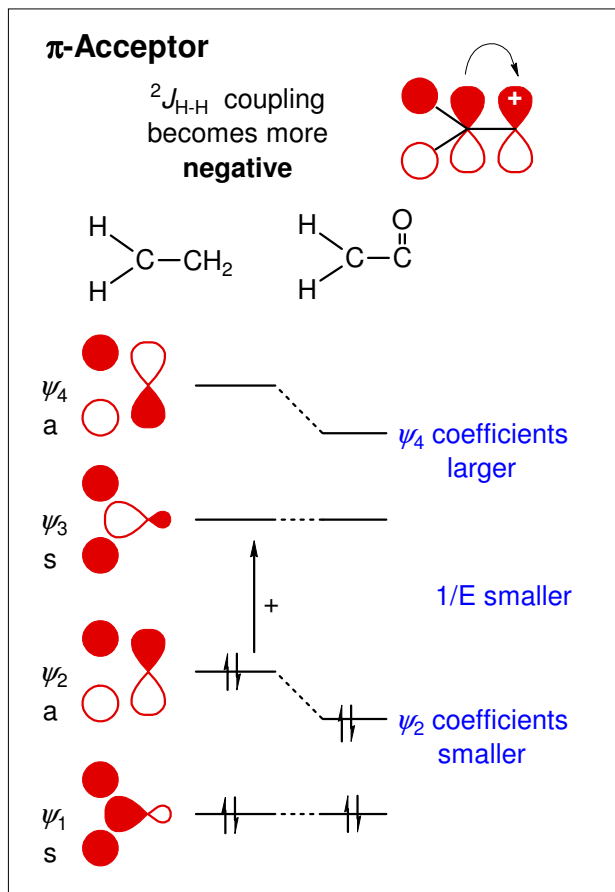


The large positive coupling in formaldehyde, and large negative coupling in ketene can be understood in these terms as well. For formaldehyde the oxygen substituent behaves as a strong σ -acceptor as well as a strong π -donor from the π -lone pair, both (+) effects, rendered especially large because of the short bond distance. Imines also show large positive 2J .

In a similar vein, for ketene the carbonyl substituent behaves as a strong π -acceptor, giving an usually large negative coupling.



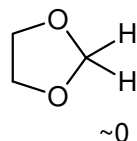
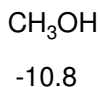
Geminal Coupling - Electronic Effects



Geminal Proton-Proton Couplings Summary ($^2J_{H-H}$)

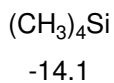
Geminal couplings between protons vary widely in sign and magnitude. There are both positive and negative substituent effects on the coupling, as summarized below. The remarkable feature is that σ and π acceptors have opposite effects on the coupling, as do σ and π donors.

Inductive σ -Acceptor +

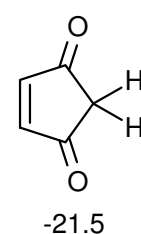
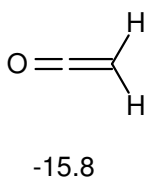
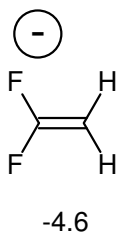
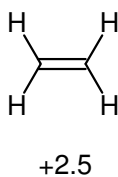


Oxygen and fluorine substituents are also π -donors

Inductive σ -Donor -

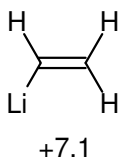


π -Acceptor -

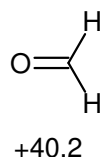


Gem-coupling constants of protons α to carbonyl groups are unusually large

π -Donor +

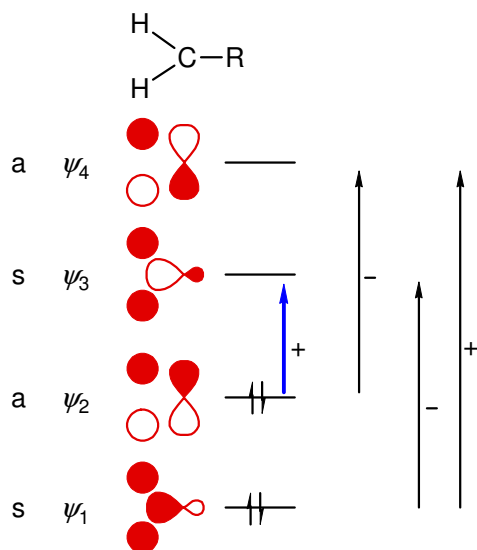
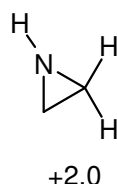
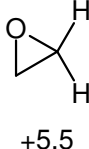
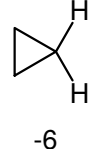
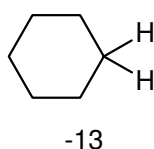


Gem-coupling of vinyl protons is usually small (<3 Hz). The coupling can be both positive or negative, and is sometimes too small to detect.



The oxygen in formaldehyde is both a π donor and a σ -acceptor - both positive effects.

High s-Character +



$$^2J_{HH'} = h (4\beta\gamma_H/3)^2 S_h^4(0) \pi_{hh'}$$

$$\pi_{hh'} = -4 \sum_i^{\text{occ}} \sum_j^{\text{unocc}} \frac{C_{ih} C_{ih'} C_{jh} C_{jh'}}{(\epsilon_i - \epsilon_j)}$$

$$\pi_{23} = -\frac{1}{\epsilon_{23}} (+ - + +)$$

Excitation between orbitals of the same symmetry has a negative effect on J , between orbitals of opposite symmetry has a positive effect.

The $1/E$ term is largest for the HOMO-LUMO transition, so coupling effect are dominated by the $\psi_2 \psi_3$ transition.

Pople, Bothner-By *J. Chem. Phys.* **1965**, *42*, 1339

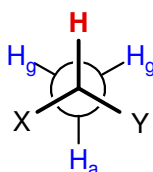
5.5 Vicinal Proton-Proton Coupling $^3J_{\text{HH}}$

The single most useful H-H coupling relationship is that between vicinal protons. The size of $^3J_{\text{H-H}}$ is predictable and provides detailed information about the spatial orientation between the two protons. Almost all $^3J_{\text{HH}}$ values are positive (a rare exception is the -2 Hz $^3J_{\text{H-H}}$ in *cis*-1,2-difluoroethylene), but their magnitude varies widely (from close to 0 Hz up to 25 Hz) depending on structural and conformational details.

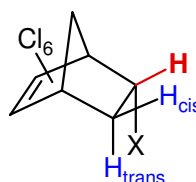
Three-Bond Coupling across Single Bonds. In acyclic systems with small conformational preferences, vicinal couplings are generally in the range 6-8 Hz, with electronegative substituents causing smaller J values (see the Pauling electronegativities **E** in the graphic). Note in particular the reduced 3J for protons on carbons bearing oxygen substituents (as well as F), which is seen for all types of 3-bond couplings (Review: Bothner-By *Adv. Magn. Reson.* **1965**, *1*, 195.)

CH ₃ -CH ₂ -X			
X	3J	E	Ref.
Li	8.9	-1.0	<i>TL</i> 1963 , 767
SiEt ₃	8.0	1.9	
H	8:0		<i>CJC</i> 1963 , 41,2114
I	7.45	2.5	
Br	7.33	2.8	
CH ₃	7.26	2.5	<i>CJP</i> 1960 , 32, 67
Cl	7.23	3.1	
NEt ₂	7.13	3.0	<i>JPC</i> 1964 , 68, 3430
OEt	6.97	3.5	<i>JPC</i> 1964 , 68, 3430
OH	6.97	3.5	<i>JCP</i> 1956 , 25, 362
F	6.9	4.0	<i>JACS</i> 1961 , 83, 4473
⁺ OEt ₂	4.7		<i>JACS</i> 1959 , 81, 3826

For a methyl group, the observed coupling is the average of the three couplings, since these will be fully averaged by methyl rotation:



$$^3J_{\text{obs}} = \frac{J_g + J_g + J_a}{3} = \frac{4 + 4 + 13}{3} = 7$$

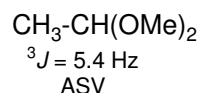
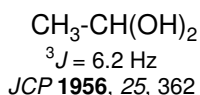
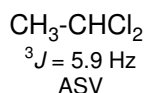
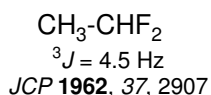


JACS **1962**, 84,516

X	J_{trans}	J_{cis}	E ^a
H	3.81	9.73	
CN	4.6	9.3	2.49
CO ₂ H	4.4	8.5	2.60
C ₆ H ₅	4.2	8.9	2.75
Cl	3.2	8.0	3.25
OH	2.4	7.4	3.43
OAc	2.5	7.7	3.80

^a *JCP* **1961**, **34**, 1099

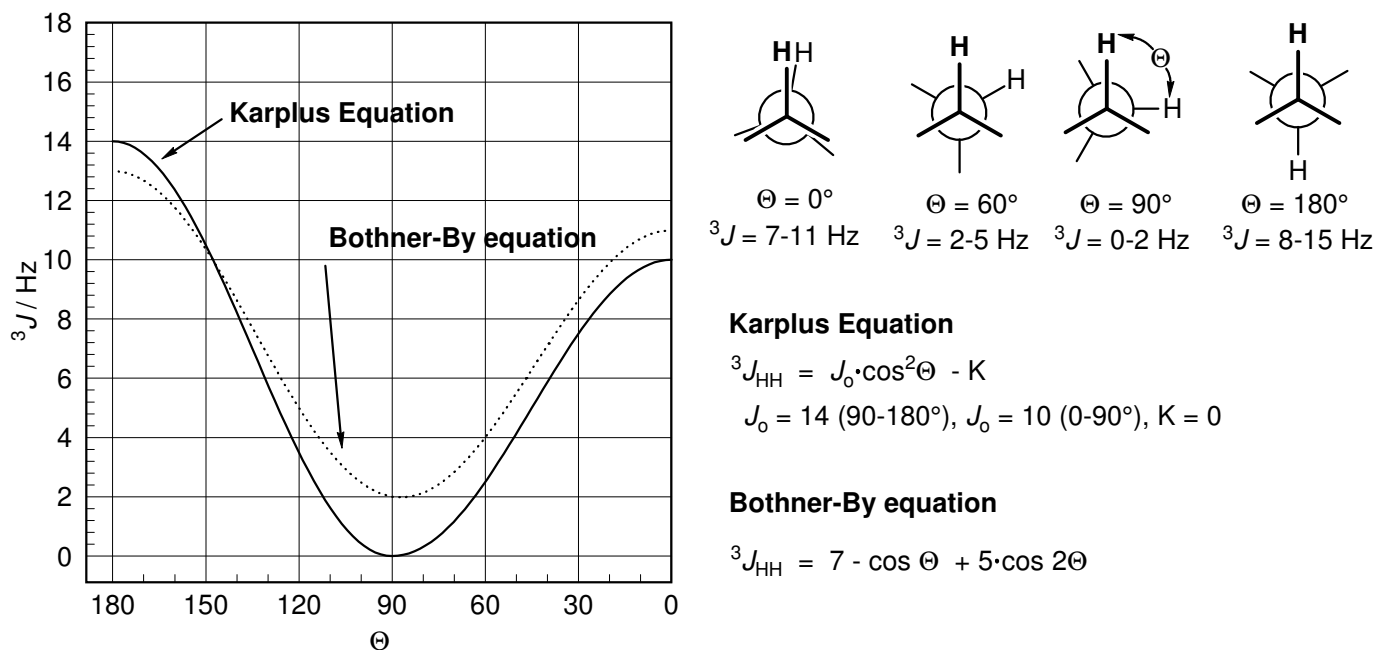
When there are two electronegative substituents the vicinal coupling is reduced further:



The Karplus Equation

The Karplus equation is based on the observation, supported by theoretical considerations, that vicinal H-H couplings will be maximal with protons with 180° and 0° dihedral angles (anti or eclipsed relationship results in optimal orbital overlap) and that coupling will be minimal (near 0) for protons that are 90° from each other. The equation gives us approximate values for $^3J_{\text{HH}}$ as a function of dihedral angle between the protons. It should be remembered, however, that this relationship strictly applies only in unstrained hydrocarbon systems, and that electronegative substituents and ring constraints may cause substantial perturbations (in both positive and negative directions) to the values predicted by this equation. Nevertheless, the Karplus curve (together with more complicated variants) is the mainstay of conformational analysis for all ring systems, and has generally proved reliable if care is taken. The constants J_0 and K are used to correct for substituent effects in more sophisticated uses of the Karplus equation, different J_0 values are also used for the 0 to 90° and the 90 to 180° sections of the curve.

The Bothner-By equation provides an empirical "Karplus" curve that does not require different J_0 values for the 0-90 vs 90-180° sections:



A convenient graphical form of the Karplus relationship is given in Figure 5.5.1 below. Here two curves, separated by 120° , represent the predicted coupling constants for a proton H_1 coupled to an adjacent methylene group (H_{cis} and H_{trans}), as a function of the dihedral angle.

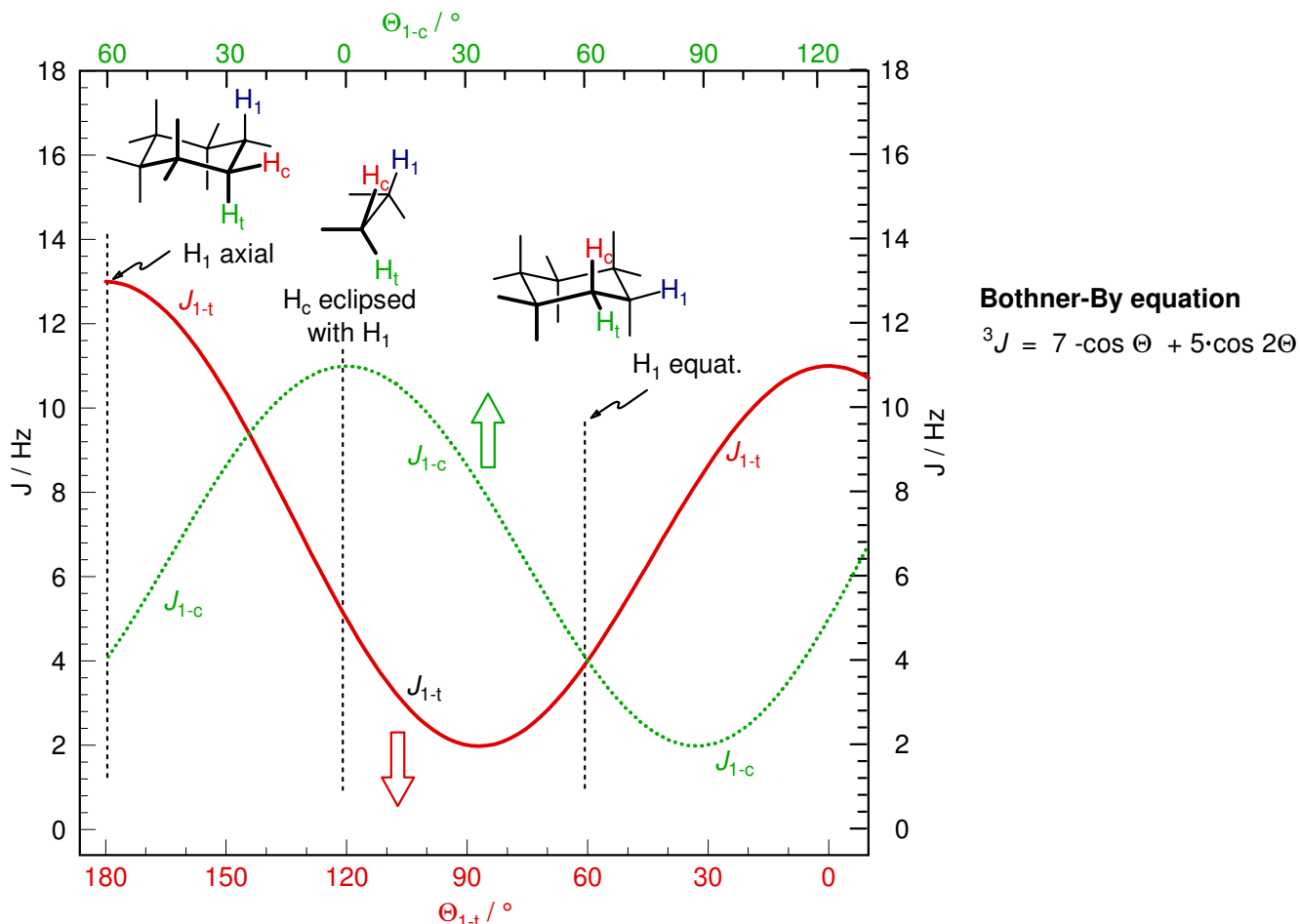
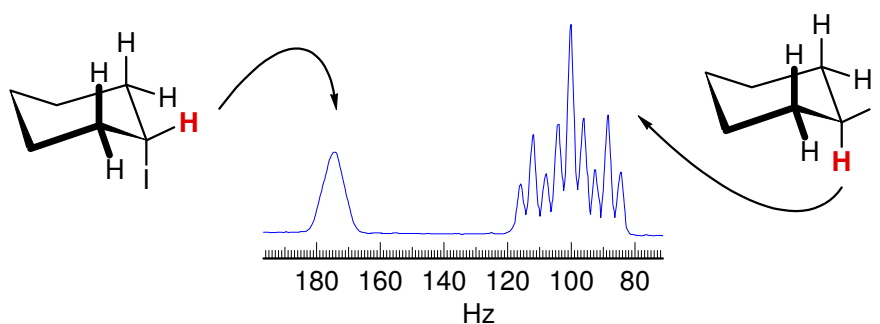


Figure 5.5.1. Double Karplus Curve for Vicinal coupling in Cycloalkanes.

5.5.3 Determination of Stereochemistry in Cyclic Compounds Using $^3J_{\text{HH}}$

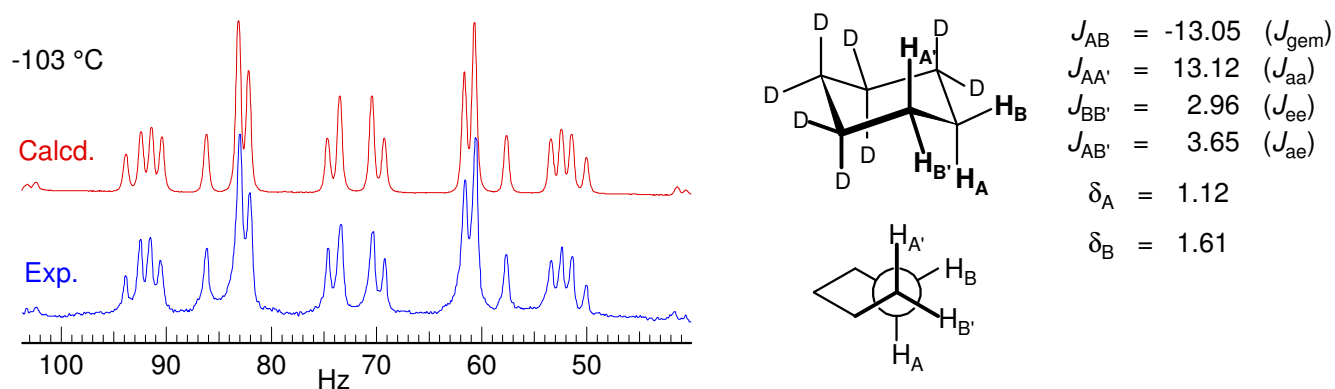
Cyclohexanes. It is often straightforward to establish stereochemical relationships among substituents, provided that the spectrum can be analyzed. In chair cyclohexanes, the relationship among vicinal protons is restricted to the narrow regions for $\Theta_{1-c} = 40-60^\circ$ on Figure 5.5.1 (i.e. to the left of the $\text{H}^1\text{-eq}$ crossing point at 60° , and to the right of the $\text{H}^1\text{-ax}$ point). These regions correspond to flattening of the cyclohexane, which is energetically easy. The opposite distortion ($\Theta_{1-c} = 60-85^\circ$) cannot occur to any significant extent. J_{aa} is usually much larger (9-12 Hz) than J_{ee} or J_{ea} (each usually 3-4 Hz).

Below is reproduced the 100 MHz NMR signal of the H^1 proton of iodocyclohexane at -80°C (from F. R. Jensen, C. H. Bushweller, Beck *JACS* **1969** *91*, 344, 3223). Under these conditions the ring inversion is slow on the NMR time scale, and separate signals are seen for the two conformational isomers. The couplings are not always this well resolved, but the axial proton multiplet will almost invariably be much wider than the equatorial one (remember that the separation of the outer two lines of a first order multiplet is the sum of all the coupling constants). At room temperature, the ring inversion will be fast on the NMR time scale, so an average spectrum will be observed. It will look much like that of the axial proton, since the equatorial isomer is the major one.



Axial and equatorial conformations of iodocyclohexane at equilibrium, -80°C (60 MHz)

The coupling constants in cyclohexane itself were determined by analysis of the $\text{AA}'\text{BB}'$ pattern of 1,1,2,2,3,3,4,4-octadeuteriocyclohexane at -103°C (Garbisch, *J. Am. Chem. Soc.* **1968**, *90*, 6543). The bottom spectrum (deuterium decoupled) is the experimental one, the top one is a simulation with the parameters listed.



The spectra of iodocyclohexane and cyclohexane itself also illustrate another feature common to many axial and equatorial cyclohexane protons: the chemical shift of the axial proton is usually **upfield** of the equatorial one, in the case of cyclohexane by 0.5 ppm.

The near identity of the magnitudes of the gem ($^2J_{\text{AB}} = -13.05$ Hz) and axial-axial ($^3J_{\text{AA}'} = 13.12$ Hz) couplings seen in cyclohexane is a common feature of substituted chair cyclohexanes and half-chair cyclohexenes. Note that the couplings do have opposite signs, although this is not detectable in first-order spectra. In molecules with electronegative substituents (e.g. pyranose sugars) the vic axial-axial couplings are smaller than these, with typical values between 8 and 11 Hz.

In an idealized cyclohexane, J_{ee} and J_{ae} would be identical, since each corresponds to a dihedral angle of 60° . However, cyclohexanes are typically slightly flattened, presumably due to axial-axial repulsions. This moves the dihedral angle for J_{ee} to slightly higher than 60° , hence smaller coupling, and that of J_{ae} to slightly below 60° , resulting in larger coupling (see the shaded areas in Figure 5.5.2). The dihedral angle in cyclohexane itself is 57° , and this leads to the slightly smaller value for J_{ee} ($J_{BB'} = 2.96$) compared to J_{ae} ($J_{AB'} = 3.65$). Similar effects are also commonly seen in substituted cyclohexanes which are conformationally homogeneous, especially if there are axial substituents of any size. If the flattening is substantial, J_{ee} can become too small to detect (as is the case for some bicyclo[3.3.1]nonanes with $\Theta_{1-t} = 90^\circ$), and J_{ae} can become substantially larger than the normal values of 3-4 Hz, reaching values of 5 or even 6 Hz. Thus you cannot always rely on getting an exact count of vicinal neighbors to a proton from its multiplicity.

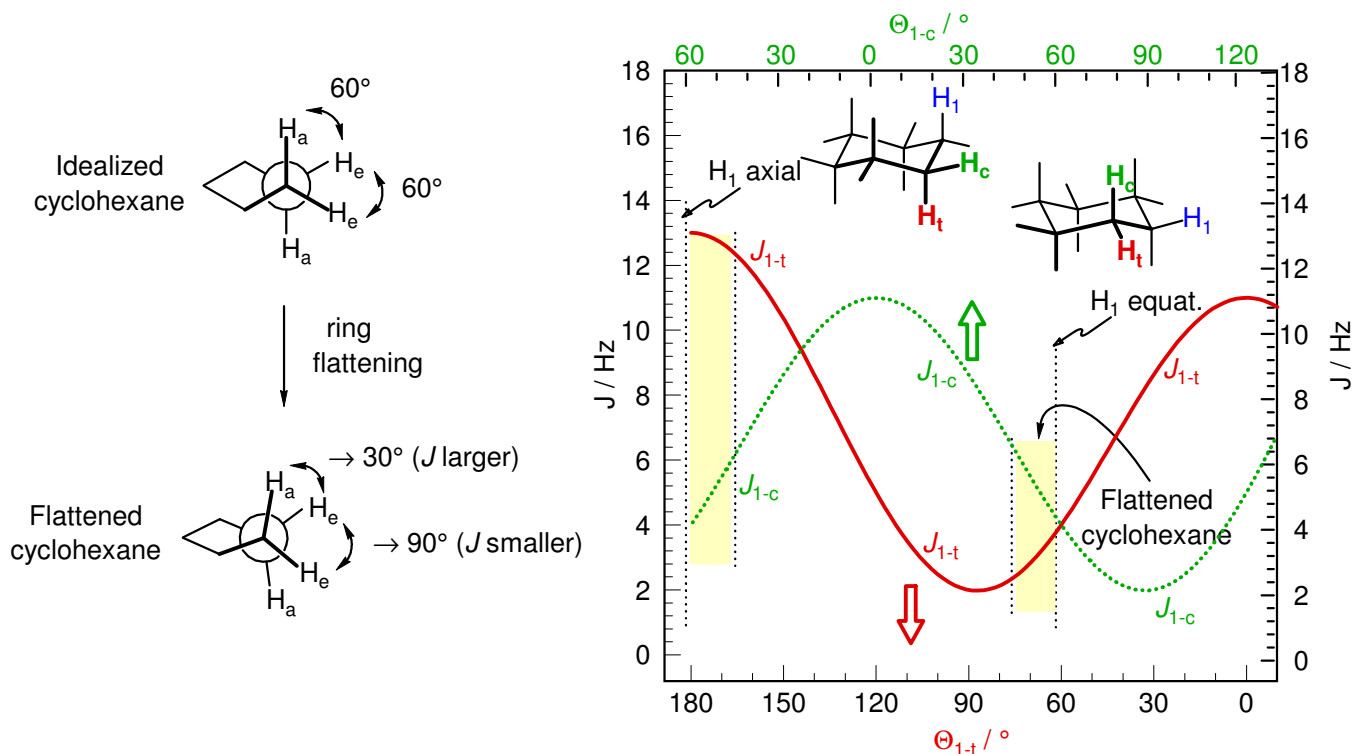
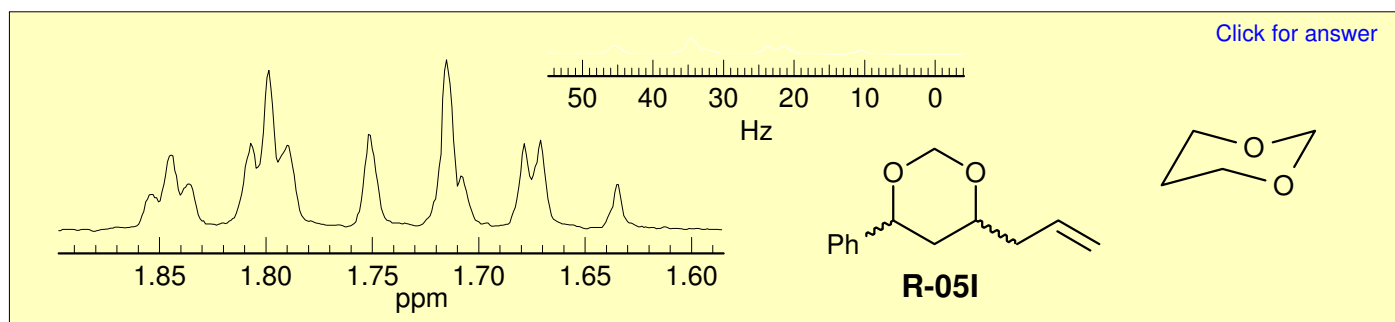


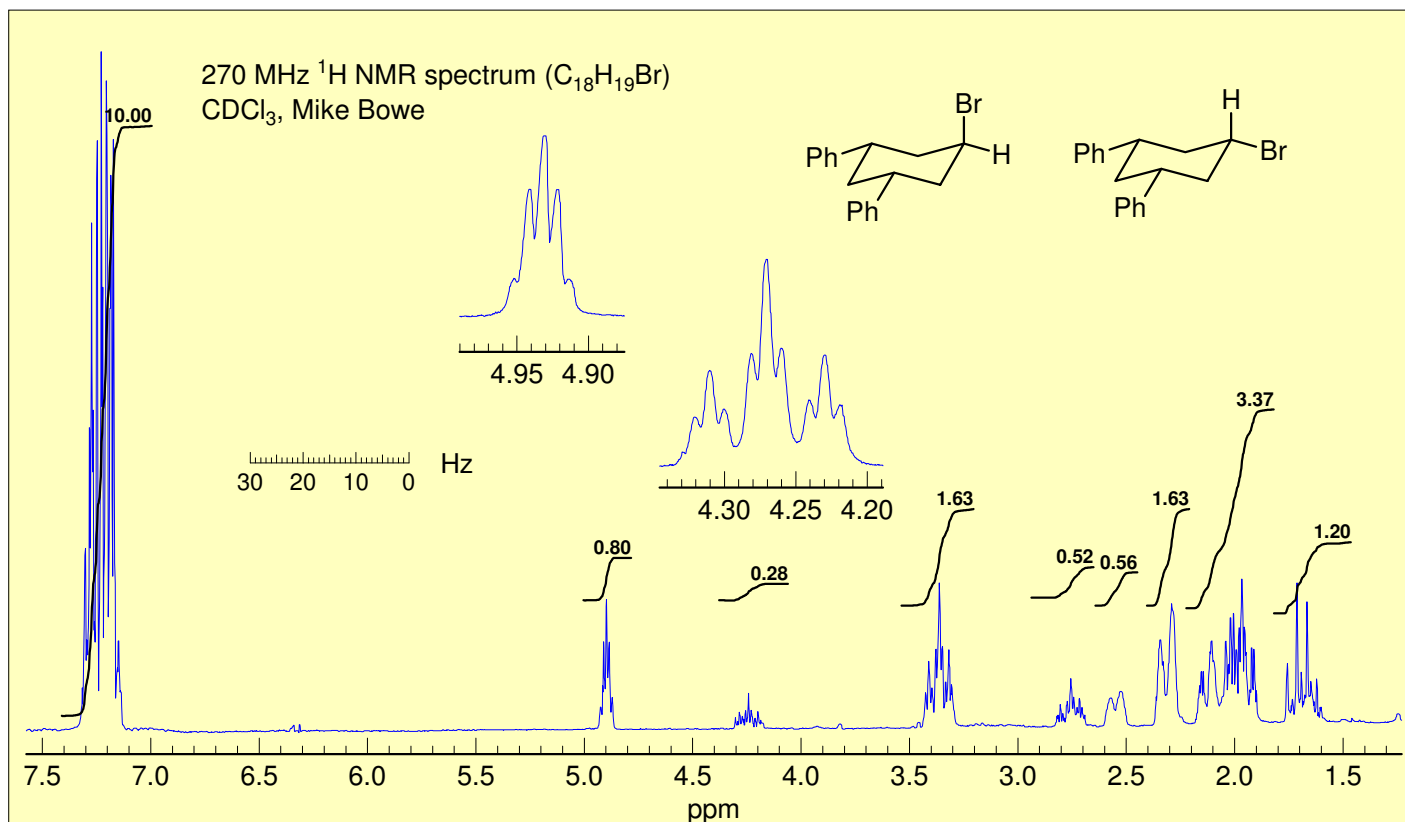
Figure 5.5.2. Karplus Curve (using the Bothner-By equation: $^3J = 7 - \cos \Theta + 5 \cdot \cos 2\Theta$) for vicinal coupling in cycloalkanes. The shaded area represents the conformational space of chair cyclohexanes, showing ring flattening.

The near identity of J_{ee} and J_{ea} has the unfortunate consequence that the couplings to an equatorial proton do not provide information about the *stereochemistry* of neighboring protons (i.e. whether they are axial or equatorial) although they will usually provide a *count* of the vicinal neighbors.

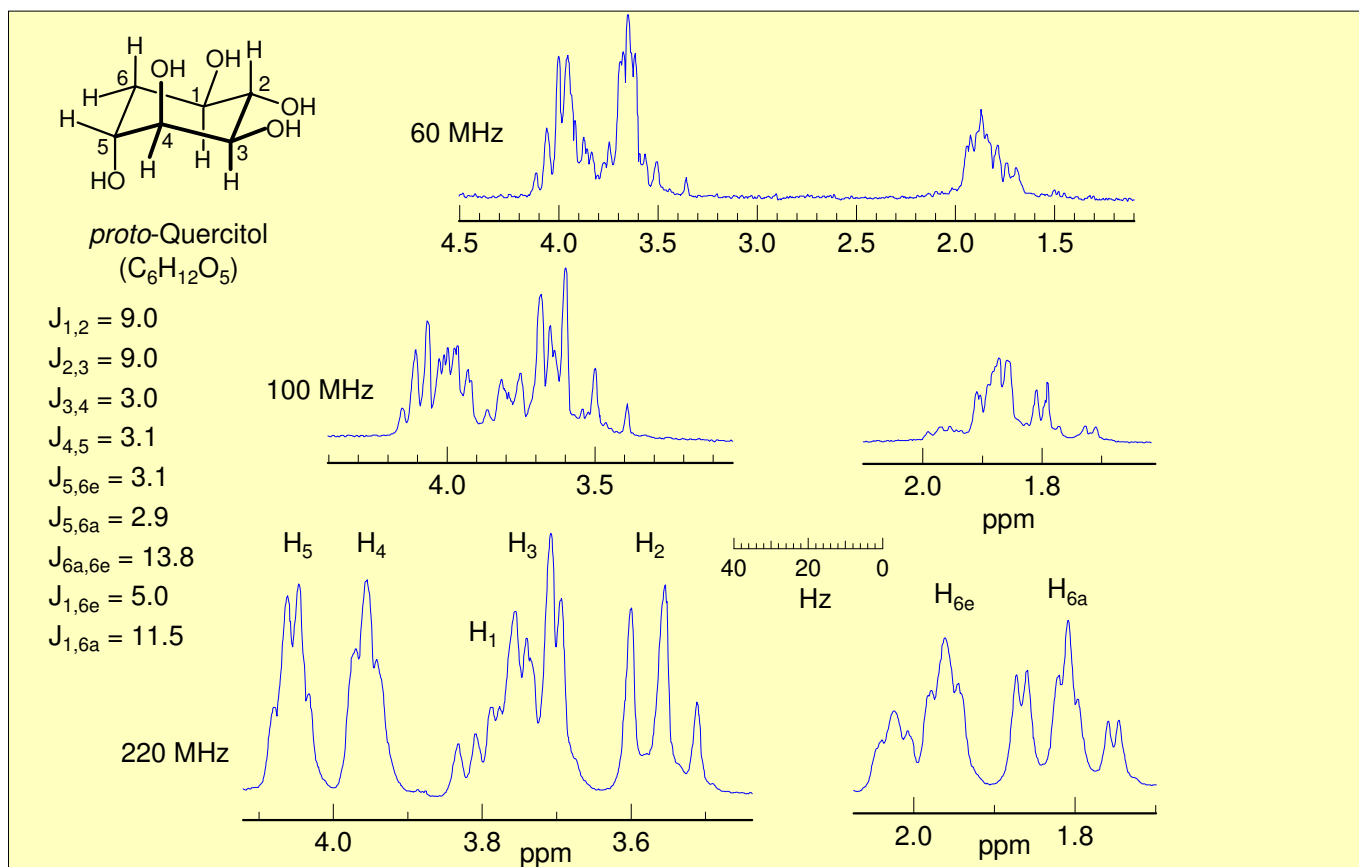
Exercise (R-05I). The multiplet below corresponds to two of the protons of compound **R-05I** ($C_{13}H_{16}O_2$). Analyze and assign the multiplet, report couplings and δ values, and determine the stereochemistry and conformation of the compound (add appropriate substituents and protons to the structure on the right). Briefly explain your reasoning.



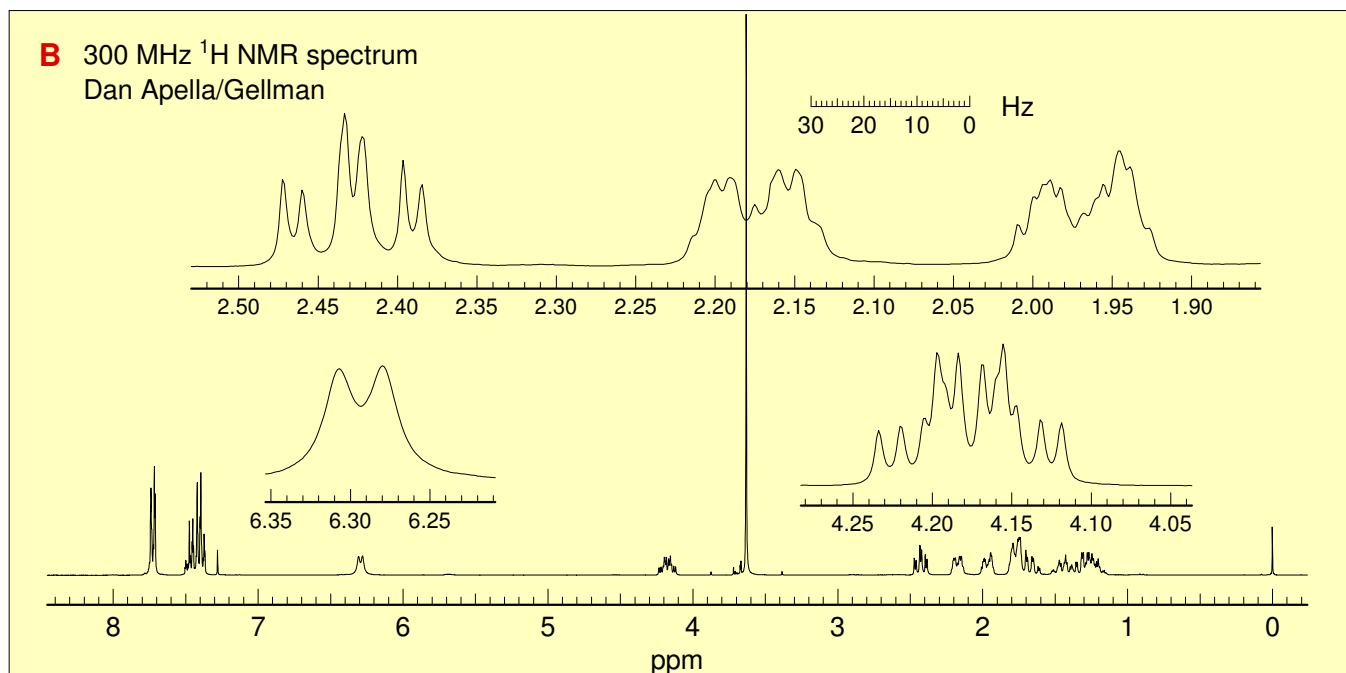
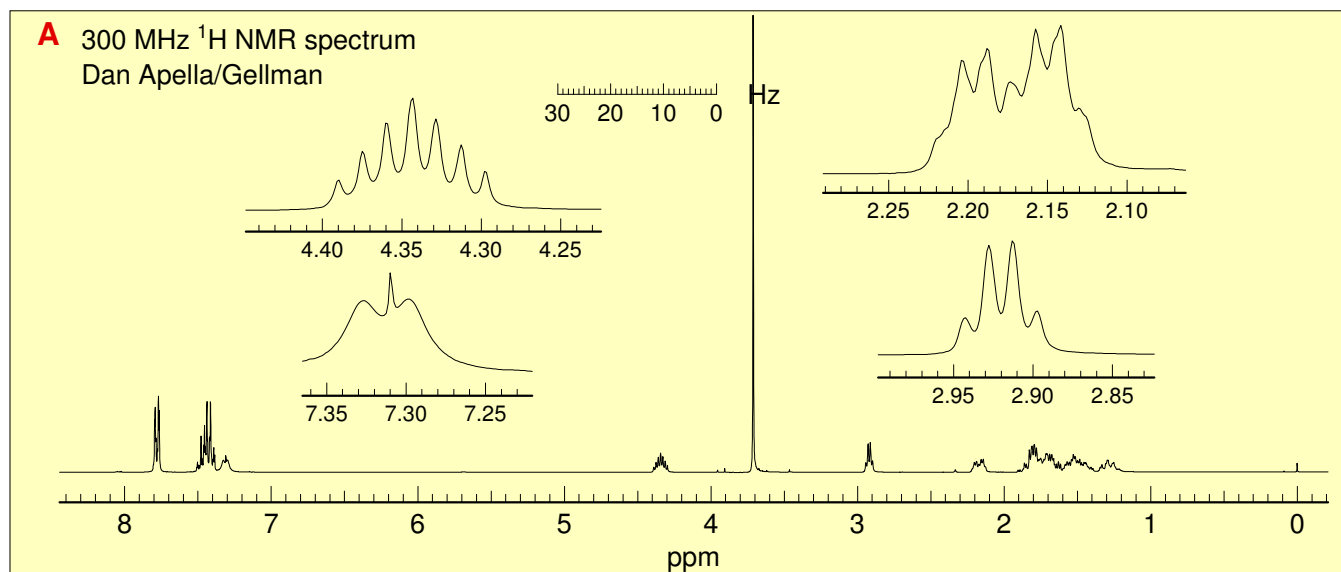
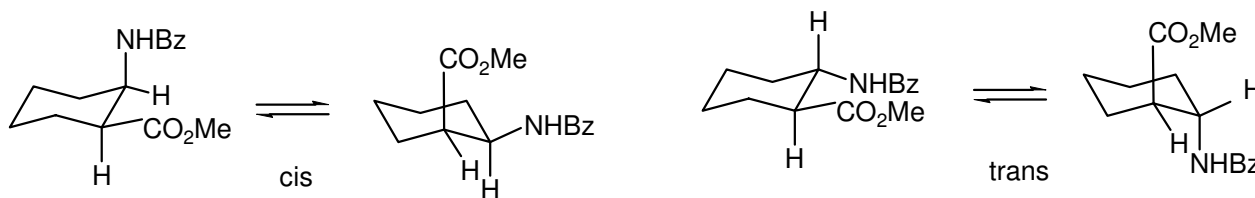
Exercise: Analyze the NMR spectrum of the mixture of 3,5-diphenylbromocyclohexanes below (assign signals):



Exercise: Examine the 220 MHz spectrum of proto-quercitol reproduced below, and analyze the couplings and chemical shifts (McCasland, G. E.; Naumann, M. O.; Durham, L. J., *J. Org. Chem.* **1968**, *33*, 4220).

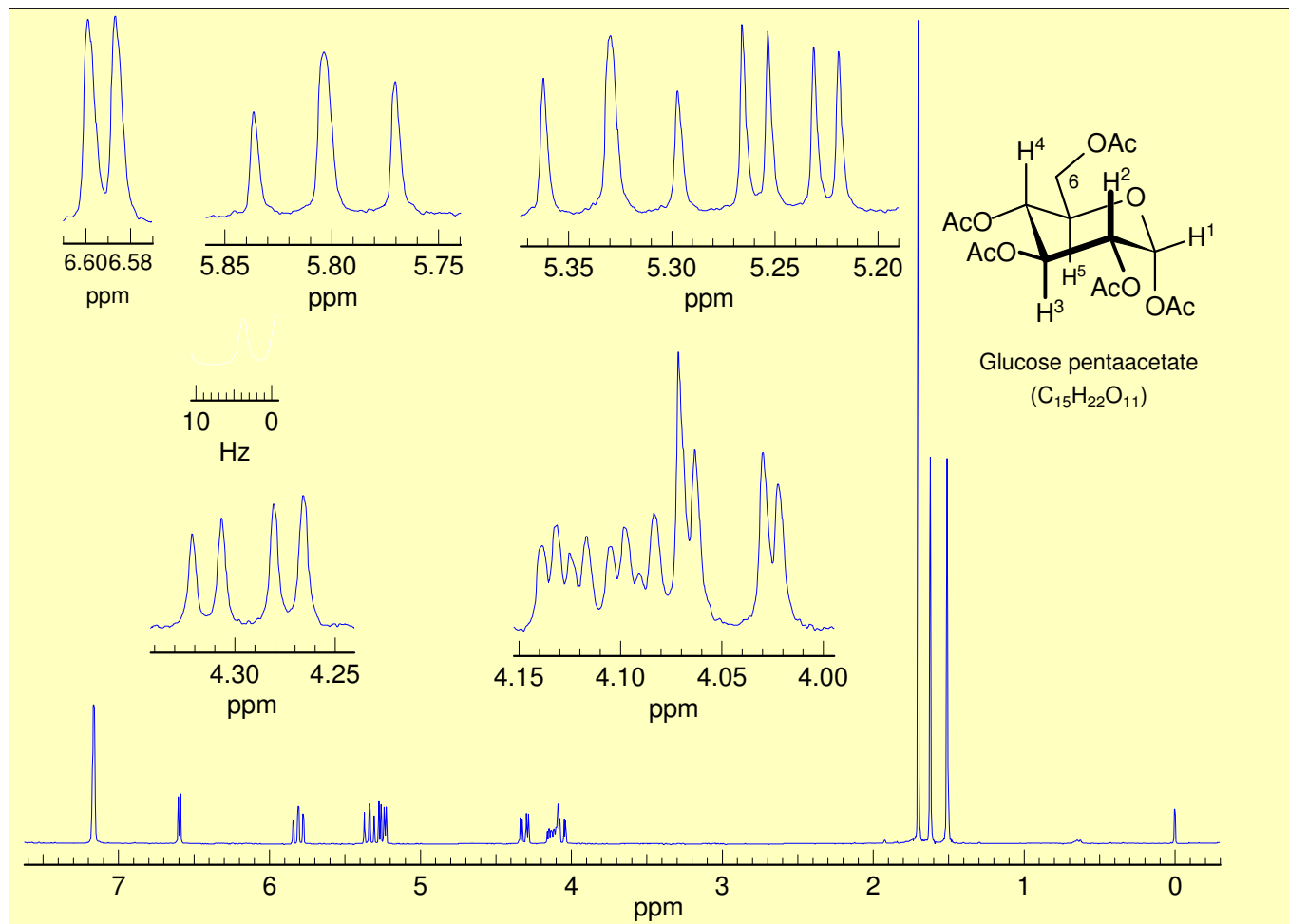


Exercise: The ^1H NMR spectra of two isomers of methyl 2-(N-benzoylamino)cyclohexanecarboxylate are shown below. Determine which isomer corresponds to spectrum A and B, and which conformation is the major one for each. Focus on an assignment and complete analysis of the three downfield protons corresponding to the N-H, α -carbomethoxy and α -aminobenzoyl protons.

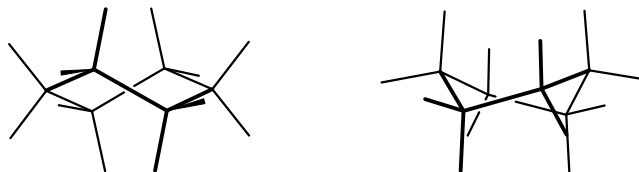


The pyranose (6-membered ring) forms of pentose and hexose sugars provide many examples where vicinal proton coupling constants allow complete assignment of stereochemistry. Analyze the ^1H NMR spectrum of glucose pentaacetate reproduced below, assuming that you don't know the stereochemistry. Analysis of this type always begin with the specific assignment of one or more of the protons, either from chemical shift information or the number of couplings. In this example, the best place to start is H^1 , which can be recognized both from its chemical shift (at δ 6.6), as well as from the fact this it will be the only proton in the molecule coupled to just one other proton.

Exercise: Examine the 300 MHz spectrum of glucose pentaacetate reproduced below. Assume you don't know the stereochemistry and use the spectrum to assign it at each carbons.

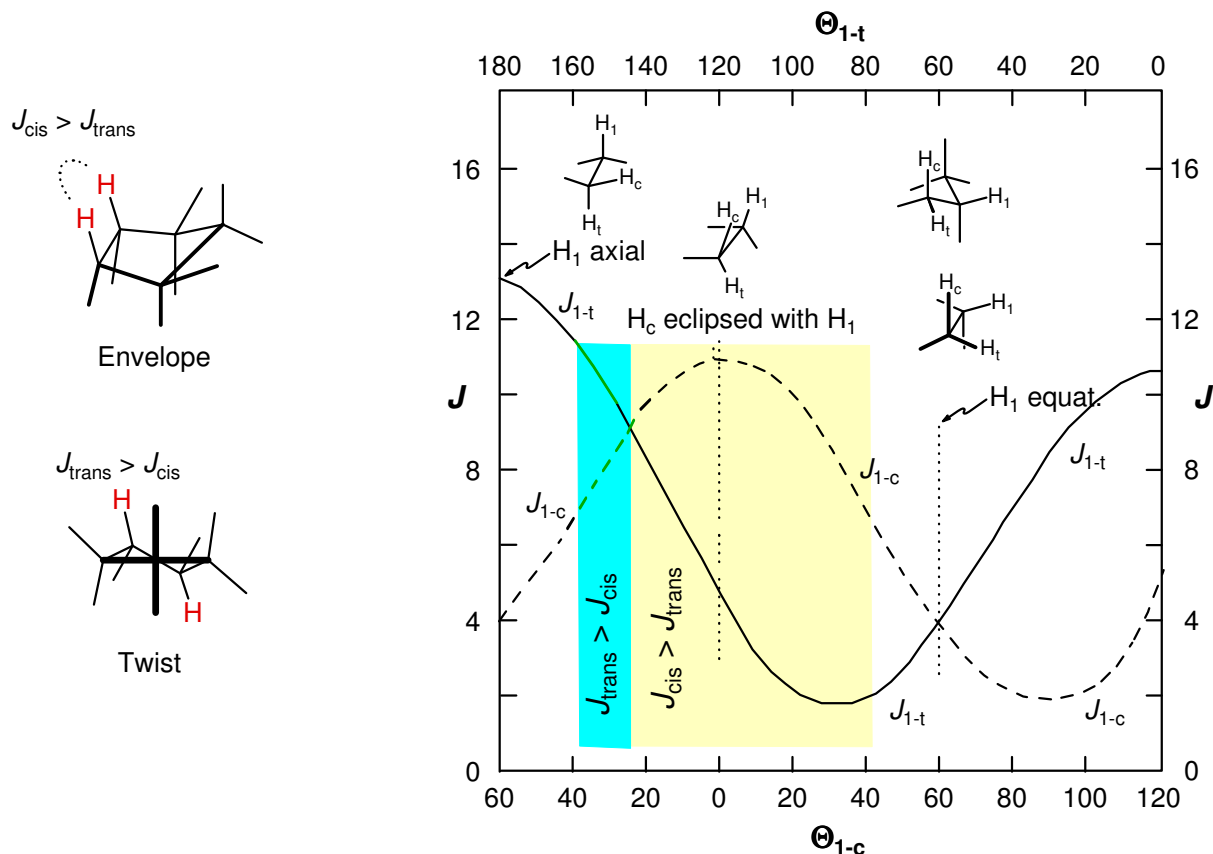


Boat Conformations. In boat and twist-boat cyclohexanes there are multiple conformations, each of which have available several C-C-C-C dihedral angles. In an idealized twist-boat there are four kinds of hydrogens, with eight dihedral angle relationships (ca 30, 30, 50, 50, 70, 90, 150, 170 degrees). In addition, there are six different twist boats possible for a multiply-substituted cyclohexane so stereochemical assignments are very difficult. Cyclohexanes in twist-boat conformations are quite rare, since twist-boat cyclohexane is ca 5 kcal higher in energy than the chair form. They are commonly seen only in bicyclic structures, or in 6-membered rings with multiple heteroatoms or those containing multiple sp^2 carbons. Even cyclohexanes with a tert-butyl groups forced to be axial can adopt modestly distorted chair conformations.



Twist-boat cyclohexane

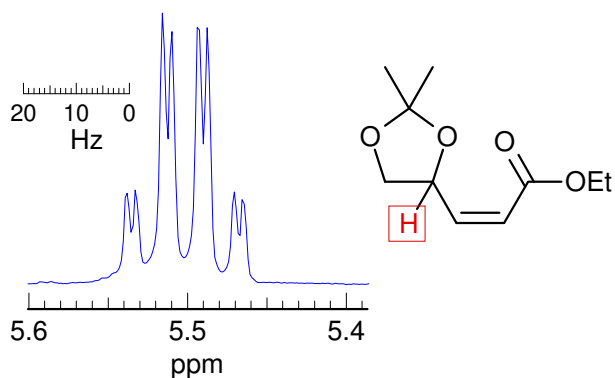
Cyclopentanes. The conformational analysis of substituted cyclopentanes is much more complicated than that of cyclohexanes. The energy differences between various envelope and twist conformations in five-membered rings are generally small, and there are as many as ten different envelope and ten different twist conformations, and each conformation has multiple dihedral angle relationships. Several of the 20 possible conformations may be populated in an individual structure. Thus the vicinal couplings in 5-membered rings are highly variable. For cyclopentanes in envelope conformations $J_{cis} > J_{trans}$ in the flat part part of the envelope, whereas in twist conformations the tendency is for $J_{trans} > J_{cis}$. In general, no firm assignments of stereochemistry can be made using the size of couplings alone unless a specific substitution pattern or heterocyclic system has been carefully investigated, or if substitution patterns allow prediction of the conformation.



Inspection of the double Karplus curves indicates a significant difference between the typical behavior of adjacent CH_2 groups in cyclohexanes and cyclopentanes. In a chair cyclohexane only one of the four vicinal couplings can be large (> 7 Hz), whereas in a cyclopentane it is common for 2 or even 3 of the 3J couplings to be large.



In most cyclopentanes, the C-C-C-C dihedral angles are significantly smaller than the 60° found in cyclohexanes. *Cis* protons will tend to have H-C-C-H dihedral angles close to 0° , and *trans* near 120° . The *cis* couplings (8-10 Hz) are usually larger than *trans* (2-9 Hz). However the Karplus curves for cyclopentane have a region where the *cis* and *trans* lines cross (Figure above, at ca 20° dihedral angle), so there is a small region where $J_{trans} > J_{cis}$. There are also cases where *cis* and *trans* couplings are identical, as on the compound below, where the allylic proton is a quartet of doublets, arising from accidental equivalence of three vicinal couplings.

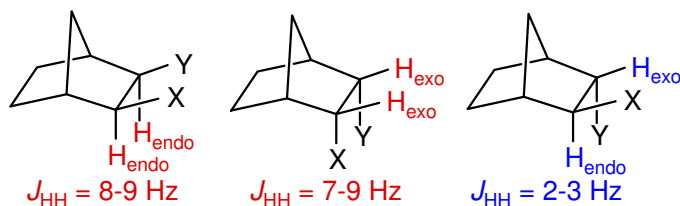


The three vicinal couplings to the allylic hydrogen (cis and trans in the 5-membered ring, and the coupling to the vinyl H) are accidentally equivalent.

This signal provides a word of warning about jumping to conclusions during the interpretation of coupling patterns - most would assume that the proton responsible for this multiplet is definitely coupled to a methyl group and one other proton by a small coupling.

If the ring puckering is strong enough, then $J_{trans} > J_{cis}$. In bicyclo[2.2.1]heptanes the endo-endo and exo-exo 3J are always greater than endo-exo couplings. Thus stereochemical relations among vicinal protons in 5-membered rings cannot be reliably determined by simply measuring coupling constants, except in cases where the substitution pattern of the specific ring system has been carefully investigated. For example, in the benzodihydrofurans below, changing the size of the substituent R causes a reversal in the size of J_{cis} and J_{trans} .

In rigid cyclopentanes, $J_{cis} > J_{trans}$

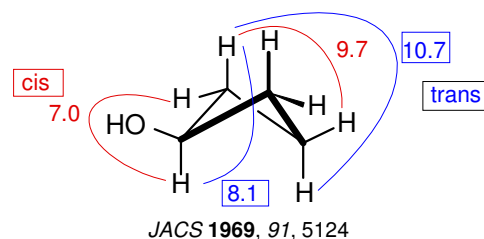


R =	Me	Et	iPr
$^3J_{cis}$	7.2	6.4	4.8
$^3J_{trans}$	6.8	7.1	8.4

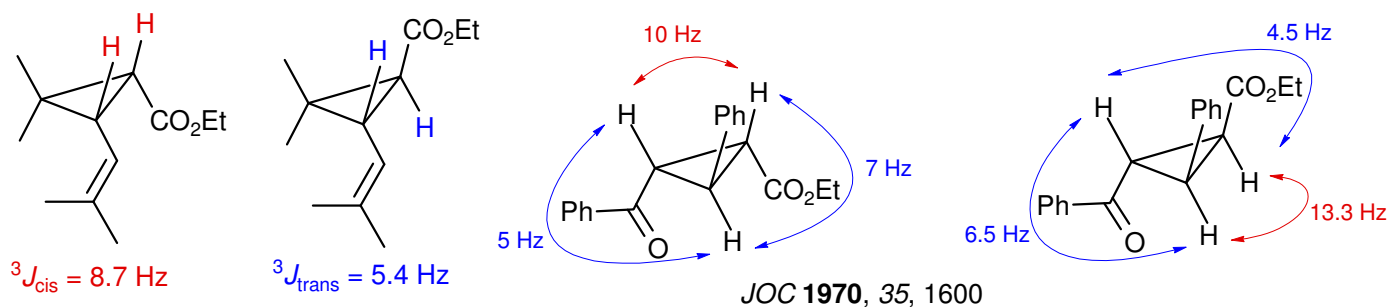
Cyclobutanes. Cyclobutanes are even flatter than cyclopentanes, so that cis couplings are almost always larger (6-9 Hz) than trans (2-8). However, if structural features which promote strong puckering of the ring such as a trans ring fusion, large or electronegative substituents are present, then trans couplings can become larger than cis, as shown for *cis*-1,3-dibromocyclobutane and cyclobutanol below.

$^3J_{cis}$	10.4	7.1	4.7	10.0	6.9
$^3J_{trans}$	4.9	8.8	1.8	6.4	4.6

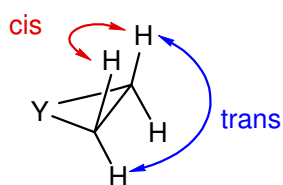
JACS 1969, 91, 5124



Cyclopropanes. Dihedral angles in cyclopropanes are rigidly fixed by the geometry of the ring system. We therefore find that J_{cis} (7-10 Hz) is always larger than J_{trans} (2-6 Hz), and this can be reliably used for structure assignment.



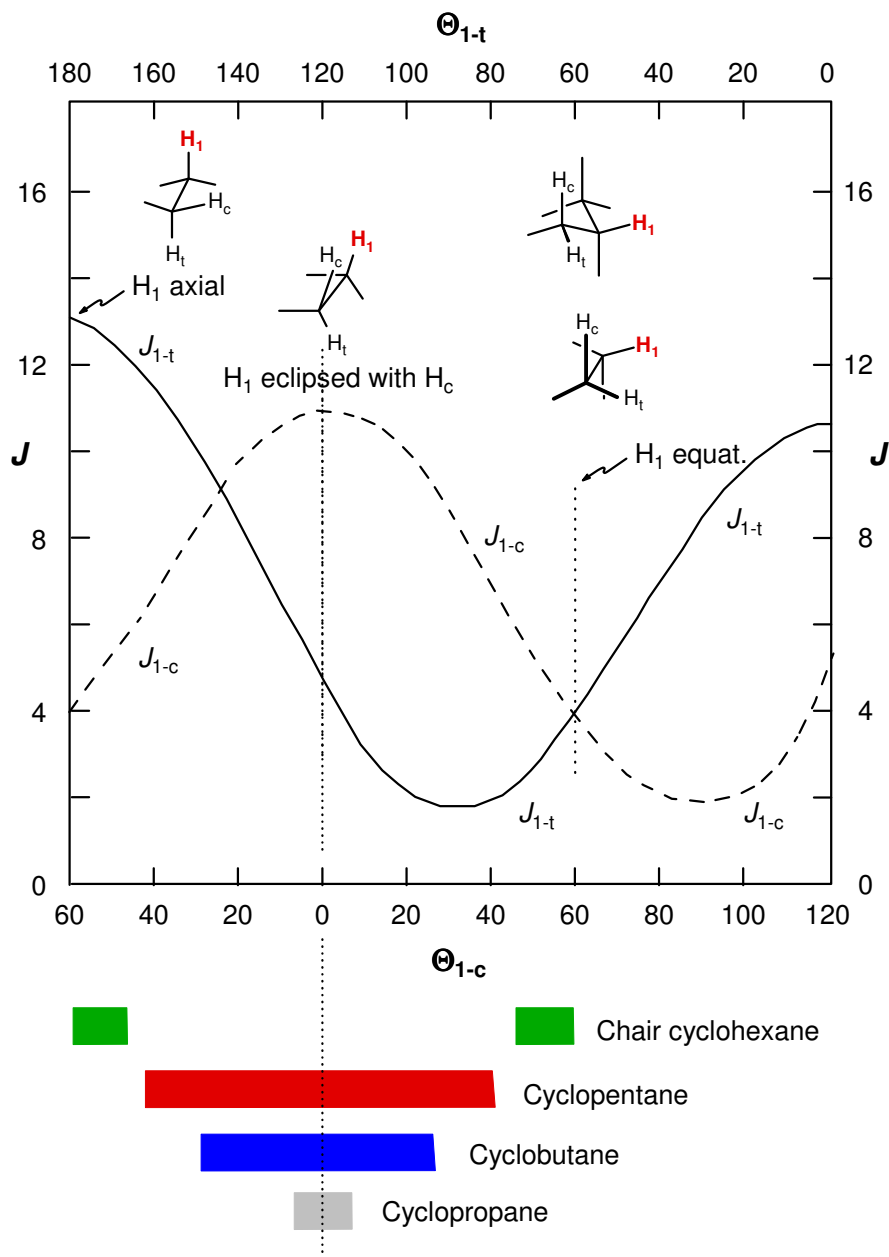
The same relationship holds for the 3-membered ring heterocycles, although the range of observed couplings is wider.



Y =	CH ₂	O	NH	S	S=O
$^3J_{\text{cis}}$	9.0	4.45	6.3	7.15	11.5
$^3J_{\text{trans}}$	5.6	3.1	3.8	5.65	10.5

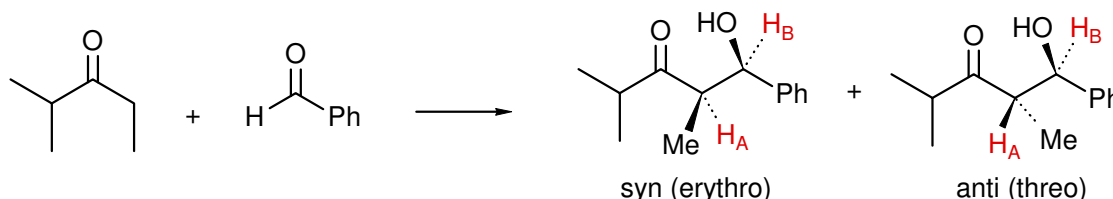
Tet. Lett **1970**, 2877

Summary: On the double Karplus curve below are indicated the dihedral angles and hence the cis and trans 3-bond couplings that can be observed for various rings. Chair cyclohexanes are conformationally well defined, with a relatively small range of 3J couplings possible ($J_{\text{eq-eq}}$ and $J_{\text{eq-ax}}$ typically 3-4 Hz, and $J_{\text{ax-ax}}$ typically 8-13 Hz). With 5 and 4 membered rings a wider range of couplings are seen depending on the extent and type of puckering present. Cis couplings will typically be larger than trans couplings. Unfortunately for both cyclopentanes and (less commonly) cyclobutanes, J_{trans} can occasionally be larger than J_{cis} for pseudoaxial protons, if the conformation places the dihedral angle to the left of the crossing point at ca 20° . For such systems both J_{trans} and J_{cis} will be relatively large (8-10 Hz). Cyclopropanes are rigid, and J_{cis} (eclipsed, $\Theta = 0^\circ$) is always greater than J_{trans} ($\Theta = 120^\circ$). With this in mind, the appearance of only well defined large (ca 10 Hz) and small (ca 3 Hz) in a CH coupled vicinally to one or more CH_2 groups is quite characteristic of cyclohexanes. Cyclopentanes and cyclobutanes, on the other hand, tend to more frequently have intermediate size couplings (5-9 Hz), and often nearly equal and large coupling to cis and trans vicinal neighbors.

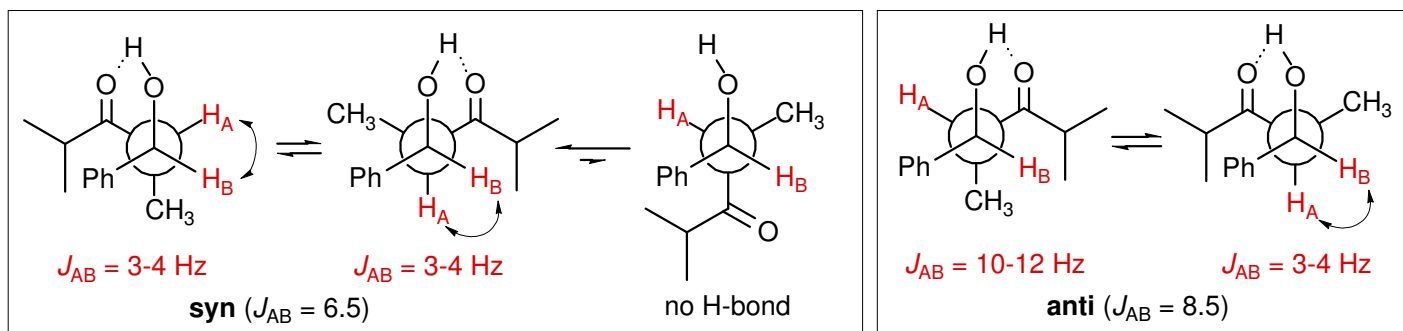


5.5.10 Acyclic Stereochemistry using $^3J_{\text{HH}}$

The use of 3J for conformational analysis in acyclic systems can be more difficult than within rings because of the larger number of conformations typically possible (Review: "Determination of Relative Configuration in Organic Compounds by NMR Spectroscopy and Computational Methods" Bifulco, G.; Dambruoso, P.; Gomez-Paloma, L.; Riccio, R. *Chem. Rev.*, 2007, 107, 3744 DOI: 10.1021/cr030733c). Basically, a single coupling constant cannot usually distinguish which of two diastereomers might be present since there are 3 possible staggered conformations for each diastereomer, two of which will typically have very similar predicted coupling constants for a pair of vicinal protons. Assignments become possible only when one can make some reliable predictions on which conformation predominates. One such situation is encountered with the diastereomeric products of an aldol condensation, as shown below:



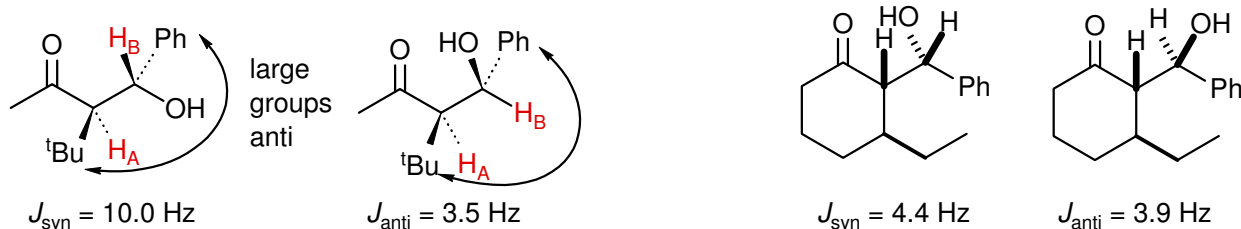
In non-polar media, a hydrogen bond between OH and the carbonyl group is expected. Since in the *syn* isomer both hydrogen bonded conformations have a gauche relationship between H_A and H_B , we expect a smaller 3J for the *syn* isomer than for the *anti*, where one of the H-bonded conformations has an anti relationship between H_A and H_B (Stiles-House rule: Stiles *J. Am. Chem. Soc.* **1964**, 86, 3337; House *J. Am. Chem. Soc.* **1973**, 95, 3310; Heathcock, *JOC*, **1980**, 45, 1066; Mukaiyama *JACS*, **1974** 96, 7503).



Syn		Anti		$J_{\text{syn}} < J_{\text{anti}}$			
				J_{syn}	J_{anti}	δ_{syn}	δ_{anti}
				2.5	9.0	5.40	4.83
				6.0	6.5	3.51	4.00
				6.1	9.5	3.50	3.65

Note that the chemical shift of the $\text{CH}(\text{OH})$ proton is not a reliable indicator of stereochemistry.

This method will only work if the intramolecular hydrogen bonded conformations are the principal ones for both diastereomers. Thus it sometimes fails in situations where the α and/or β -substituent is large, as in the α -t-Bu aldols below. Here gauche interactions destabilize the hydrogen bonded six-membered ring of the *syn* isomer, leading to a large coupling because of a high population of the non-hydrogen-bonded conformation with t-Bu and Ph anti periplanar in the *syn* isomer (Heng, Simpson, Smith *J. Org. Chem.* **1981**, *46*, 2932). Similarly, in more complicated systems additional conformational constraints can overwhelm the hydrogen bond effect. For example a 3-alkyl substituent in a cyclohexanone aldol has $J_{syn} > J_{anti}$ (Kitamura, Nakano, Miki, Okada, Noyori *J. Am. Chem. Soc.* **2001**, *123*, 8939).

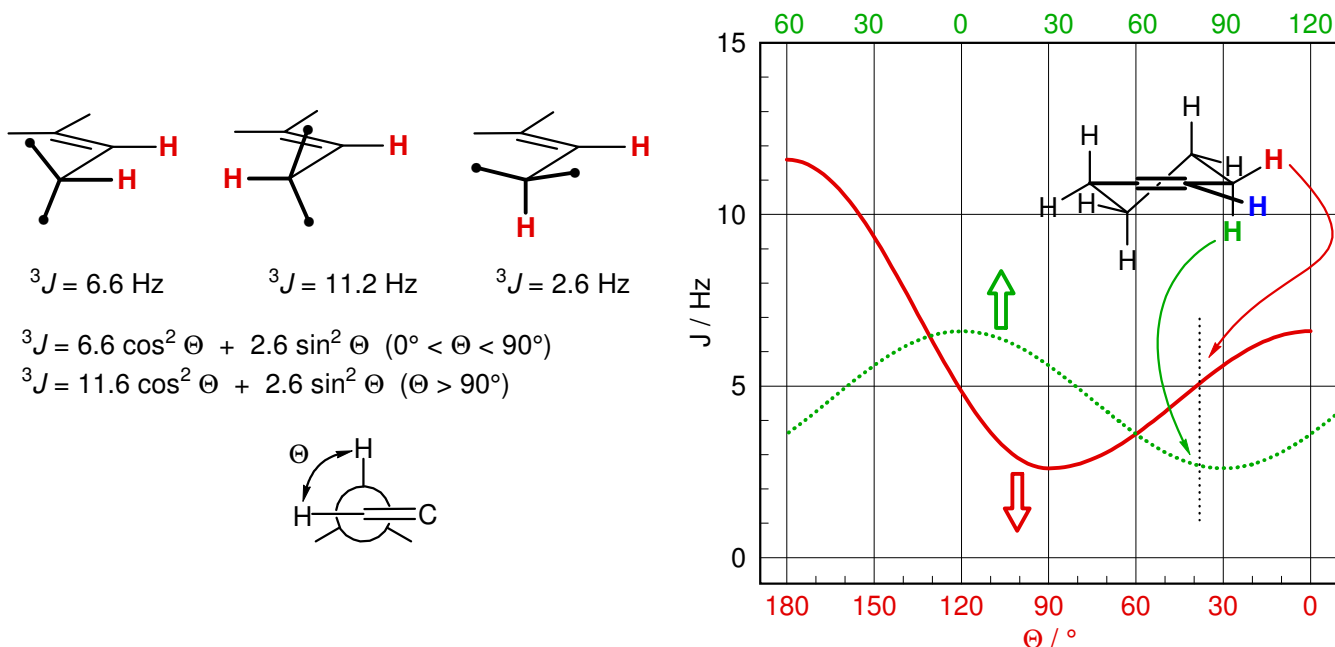


For use of ^{13}C shifts to assign stereochemistry see: Heathcock, *J. Org. Chem.*, **1979**, 4294.

Conformations of CH_2 Chains. Adjacent CH_2 groups in acyclic molecules ($\text{X-CH}_2\text{-CH}_2\text{-Y}$) typically show apparent triplets, or higher multiplets if X and/or Y contain vicinal protons coupled to the CH_2 groups. These are actually AA'BB' or AA'XX' systems, and thus are inherently non-first order. It turns out that if X and Y are sterically small, then the gauche conformation is sufficiently populated (anti/gauche ca 3:1) that nearly equal J_{AX} and $J_{AX'}$ are seen, leading to the apparent triplets. If X and/or Y is sterically large, then more complicated patterns are seen. See Sect. 5.15.

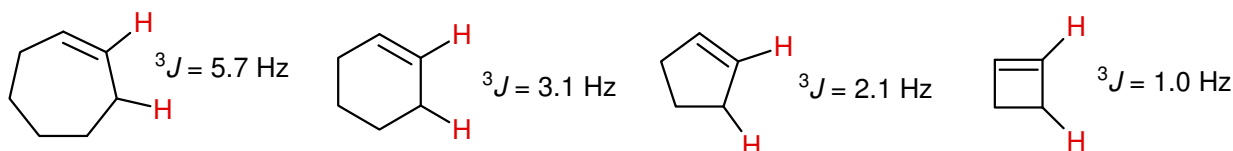
5-HMR-5.12 Allylic 3J

Couplings of vinyl hydrogens to vicinal protons across single bonds follow Karplus relationships similar to those of other vicinal couplings. The size of J is maximal at dihedral angles of 180° and 0° , and minimal when the C-H bonds are perpendicular ($\Theta = 90^\circ$), although the coupling does not go to 0.

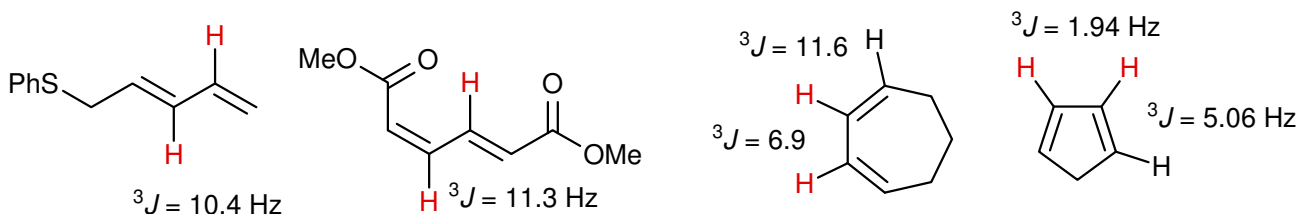


In acyclic systems without strong conformational restrictions, rotational averaging produces couplings of 5-8 Hz, very similar to those observed in aliphatic chains.

For cyclic olefins, the 3J coupling decreases as the ring size gets smaller. In cyclohexenes the couplings of an adjacent CH_2 group to the vinyl hydrogens are typically 4-5 Hz for the equatorial H, and 1-3 Hz for the axial H, as shown in the figure above. In cyclohexene itself the average of these is observed.

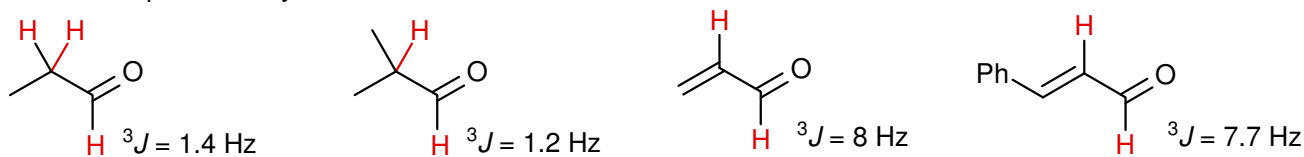


Dienes: The central 3J coupling in acyclic dienes is typically 10 Hz, very similar to the $^3J_{\text{cis}}$ across double bonds, provided that steric effects do not prevent the diene from achieving a near planar conformation. The coupling is again reduced in cyclic dienes, both because the dihedral angle is now 0° instead of 180° , and because of inherent reduction in the coupling because of angle distortions.



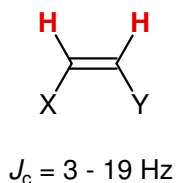
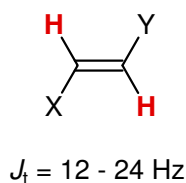
Aldehydes: In unconjugated aldehydes the 3J coupling is typically small (1-3 Hz). The coupling becomes considerably larger in conjugated aldehydes like acrolein, where the dihedral angle will be either 0° or 180° to maximize overlap of the π systems.

37-03



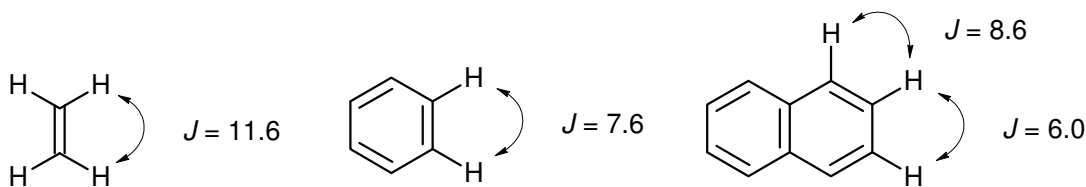
5-HMR-5.13 Olefinic 3J

The cis and trans couplings across a double bond are very reliable indicators of stereochemistry. With virtually no exceptions, $^3J_{\text{trans}} > ^3J_{\text{cis}}$, typical values are 17 and 10 Hz. However, the ranges do overlap for very strong electron donating (J increases) and withdrawing groups (J decreases).

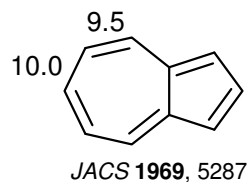
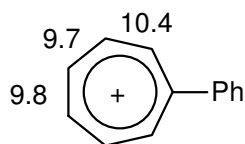
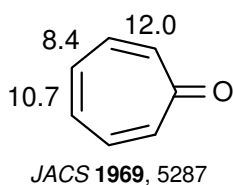


X	J_c	J_t	E_x
Li	19.3	23.9	-1.0
SiMe ₃	14.8	20.4	1.9
H	11.6	19.1	2.1
CO ₂ H	10.4	17.2	
OMe	7.0	14.3	3.5
F	4.7	12.7	4.0

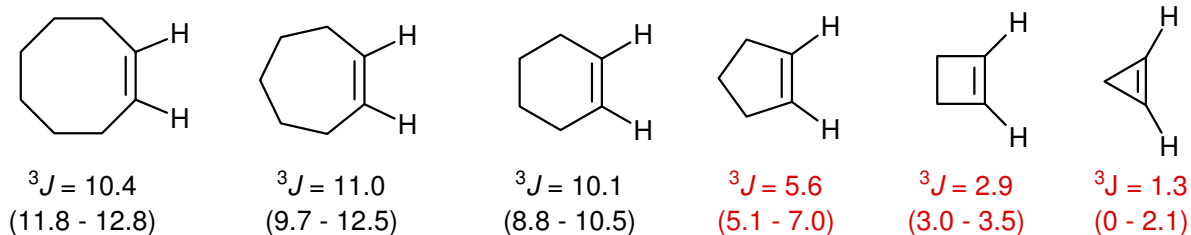
The coupling varies with π bond order. Thus the cis coupling in benzene and other aromatic six and larger membered rings is typically below 10 Hz (one empirical equation is: $^3J = 8.65 \cdot (\pi \text{ bond order}) + 1.66$):



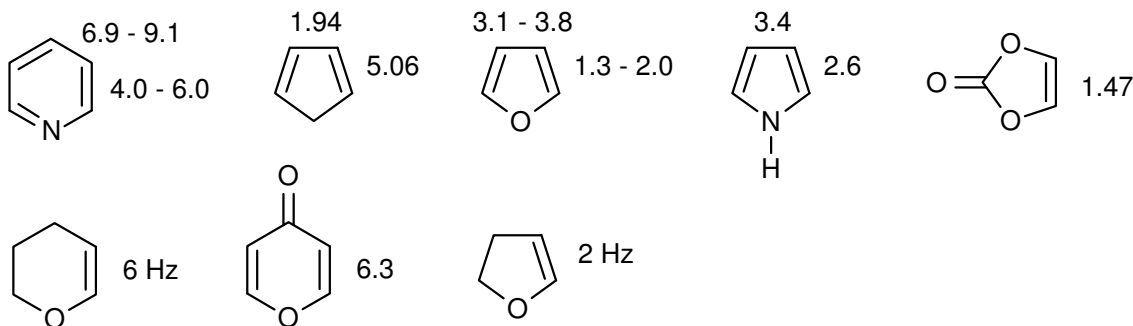
The tropone shows larger bond-alternation effects than the aromatic tropylium ion or the azulene.



Cycloalkenes smaller than cyclohexene show substantially reduced 3J values (*Chem. Rev.* 1977, 77, 599). Thus cyclopentenes can be easily distinguished from cyclohexenes and larger rings if this coupling can be identified.

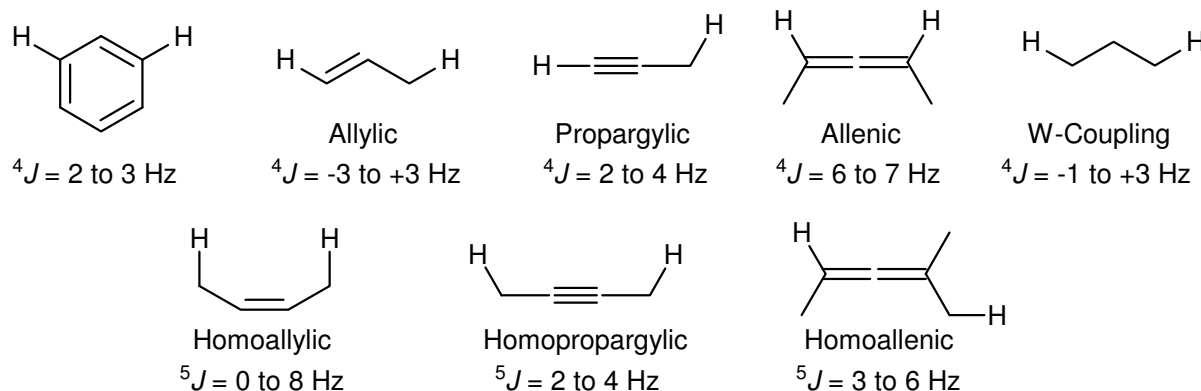


Heterocycles also generally have smaller 3J values than hydrocarbon systems.

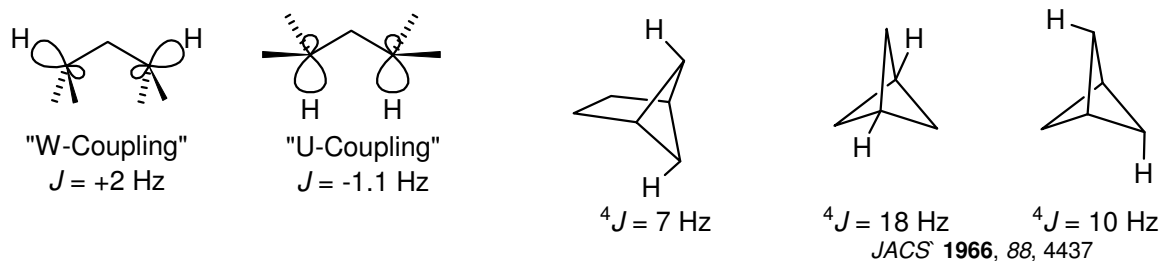


5.6 Long-Range (4J and higher) Proton-Proton Couplings

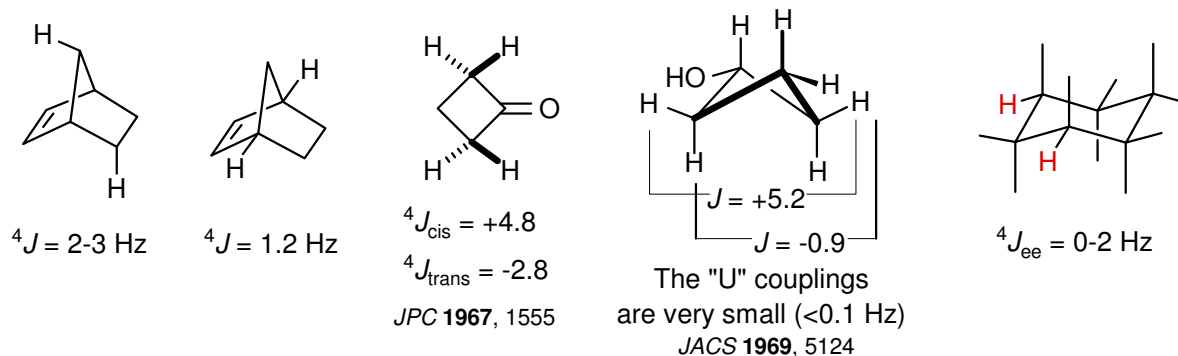
Proton-proton couplings over more than three bonds are usually too small to detect easily (< 1 Hz). However, there are a number of important environments where such couplings are present, and can provide useful structural information. Coupling across π -systems are the most frequently encountered 4J couplings: the meta-coupling in aromatic compounds, and the 4-bond allylic, propargylic and allenic couplings. 4-Bond couplings across saturated carbons (sp^3) or heteroatoms are rarer, and are usually seen only in cyclic compounds when there is a favorable geometric alignment along the H-C-C-C-H chain ("W-Coupling"). Longer range couplings (5J and higher) are also observed, particularly in acetylenes and allenes (Chem. Rev. 1977, 77, 599).



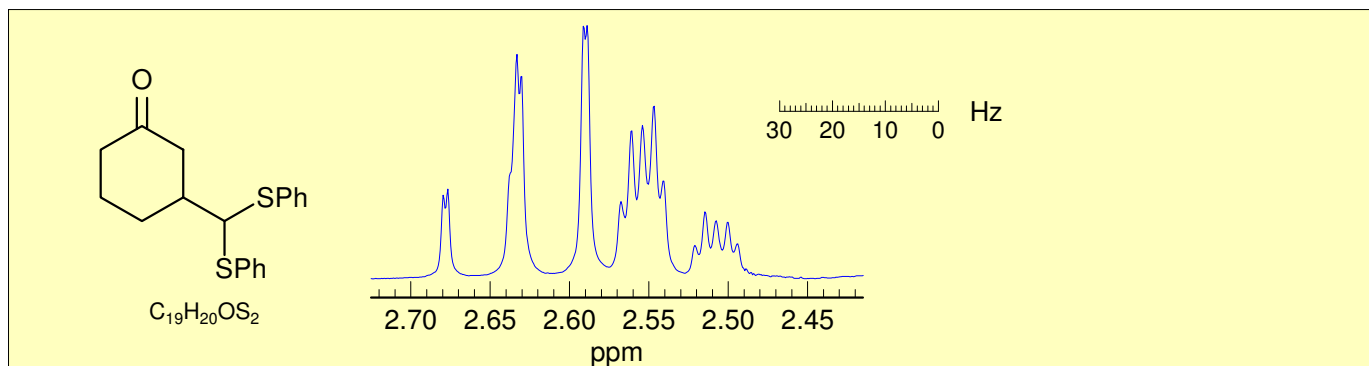
W-Coupling in Saturated Systems. Normally long-range couplings across saturated carbons (or O and N) are too small to detect easily (< 1 Hz). However, if there is proper orbital alignment between C-H bonds and the intervening C-C bonds then 4-bond and higher couplings can be observed. The most favorable alignment is the W arrangement of the connecting bonds ("W-coupling"), in which the H-C-C and C-C-H fragments are close to coplanar in an anti-arrangement. Thus coupling between 1,3-equatorial protons in cyclohexanes is frequently seen. However, couplings across U-shaped HCCC fragments can also sometimes be detected. Long-range couplings can become quite large in rigid strained bicyclic ring systems and/or when there are multiple coupling pathways available.



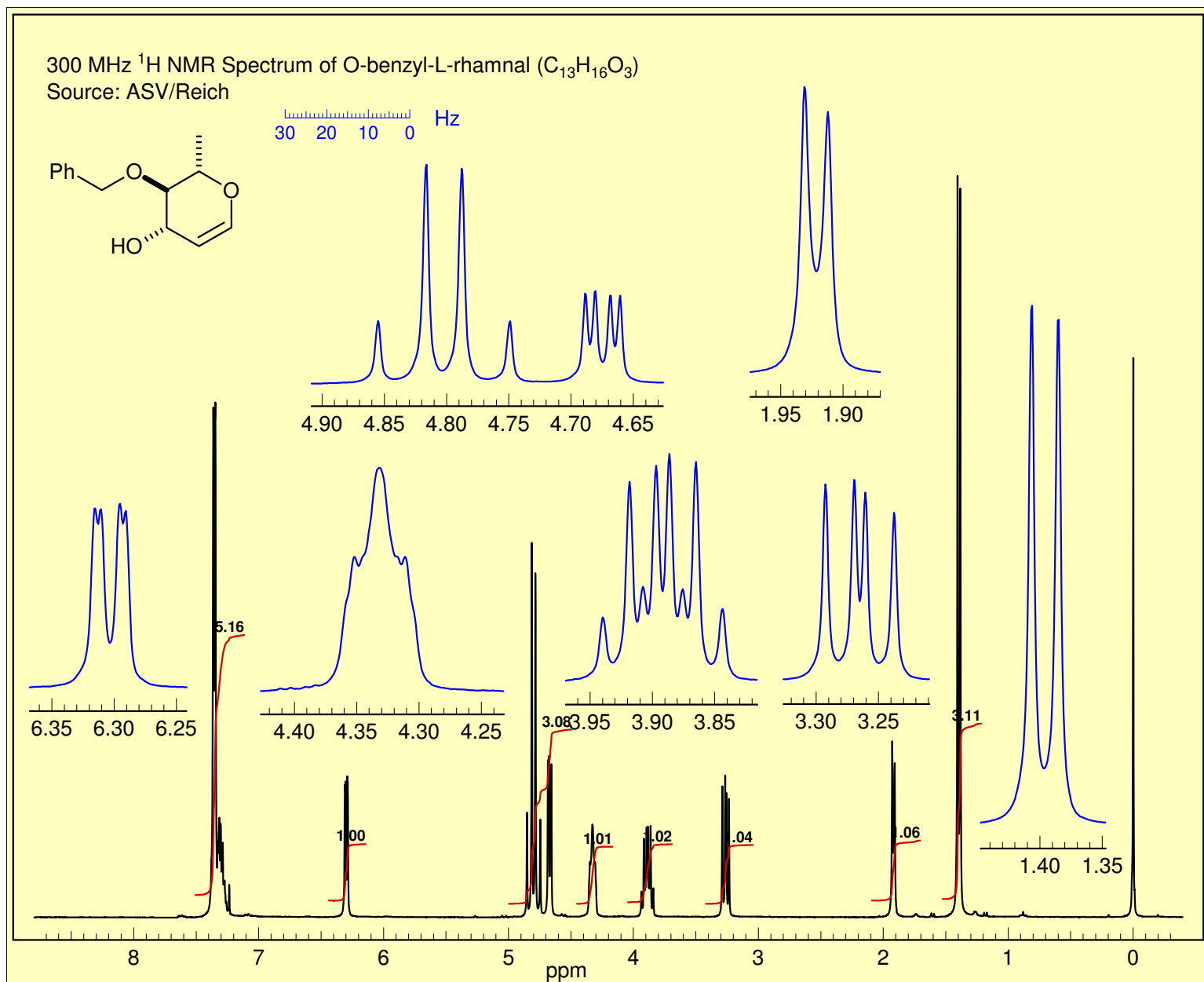
Do not expect to see such large long-range couplings in unstrained (5,6,7-membered) rings.



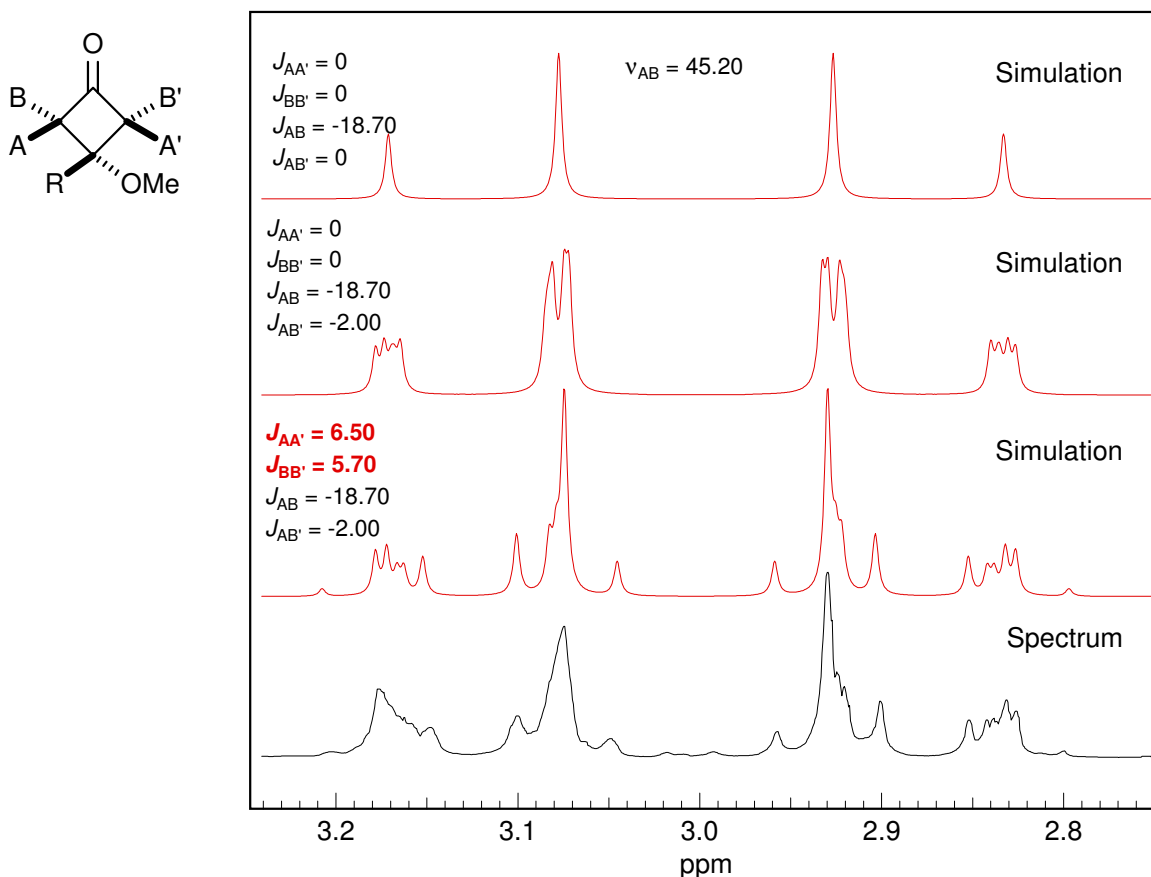
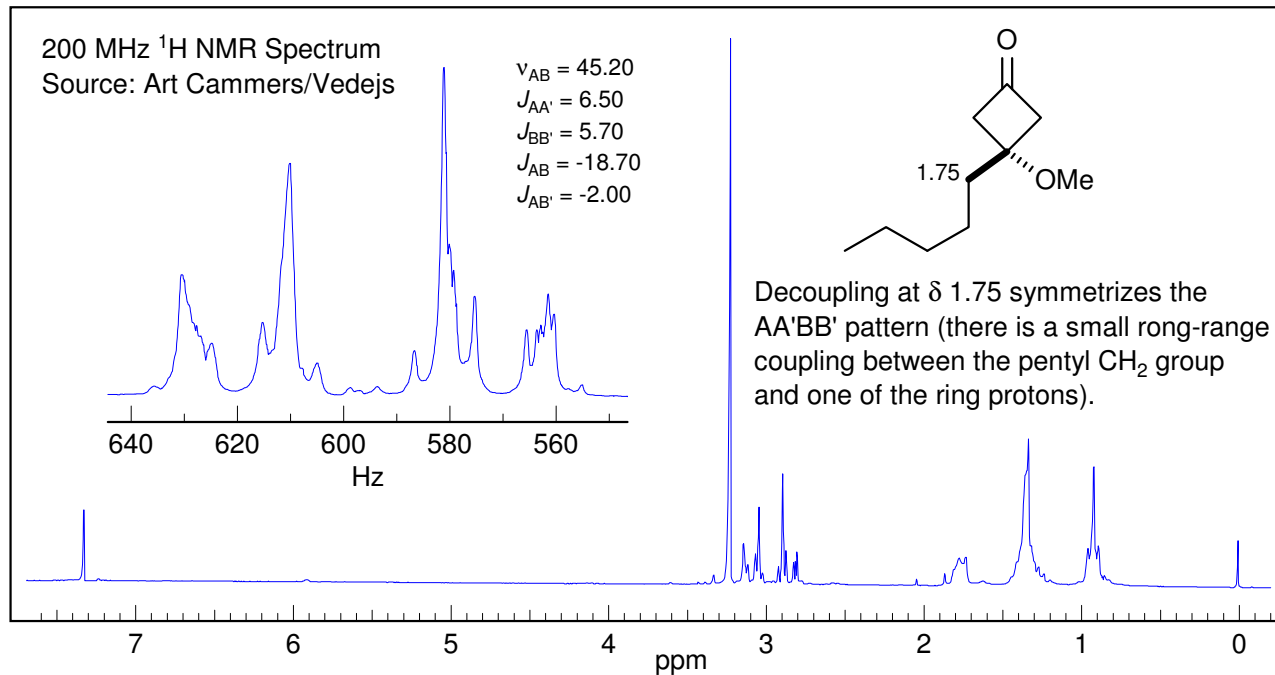
Exercise: Examine the 300 MHz spectrum of two of the protons of 3-bis(phenylthio)methylcyclohexanone reproduced below. Assign the protons and analyze the couplings (Sikorski/Reich).



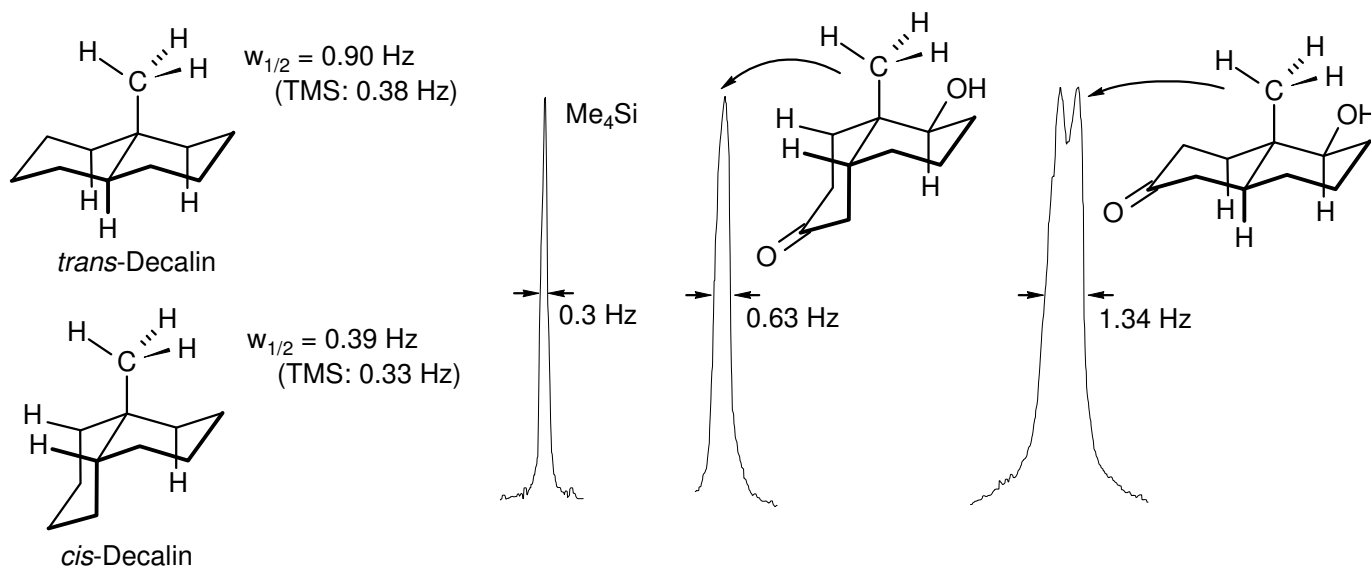
Exercise: Examine the 300 MHz 1H NMR spectrum of O-benzyl rhamnal below. Assign all protons, and extract couplings



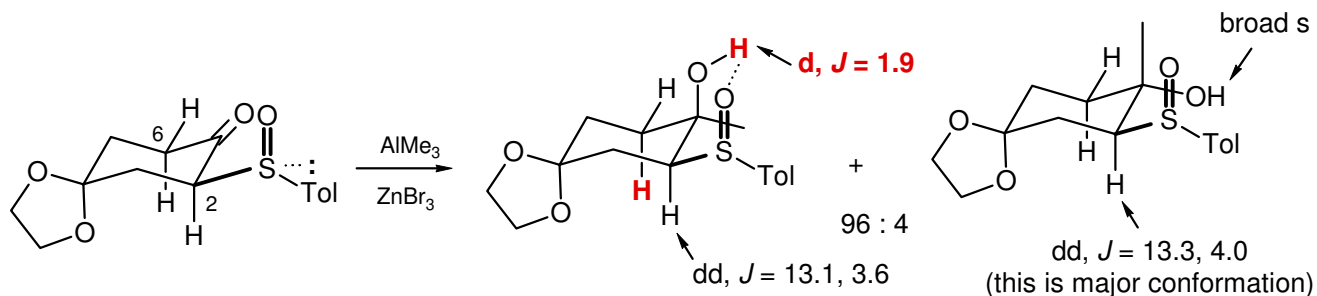
Cyclobutanes generally show substantial cross-ring 4J couplings, with $^4J_{\text{cis}}$, which has the proper orientation for a W-coupling, greater than $^4J_{\text{trans}}$. In fact, $J_{\text{cis}} > 0$ and $J_{\text{trans}} < 0$ in almost all cases (A. Gamba, R. Mondelli *Tetrahedron Lett.* **1971**, 2133), so this coupling can be used to assign stereochemistry in cyclobutanes. The figure below illustrates the effect of the long range couplings in a cyclobutanone (a simple **AB** quartet would be expected if there were no long-range couplings - top simulation). An **AA'BB'** simulation gives the parameters shown on the figure. The pattern is not completely centrosymmetric because there is a small long-range coupling from the side-chain CH_2 (δ 1.75) to one of the cyclobutane protons.



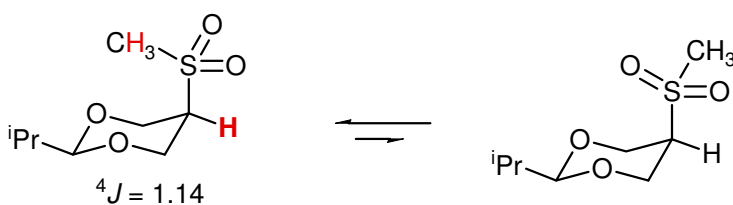
Stereochemistry of cis/trans Decalins. A useful application of long range couplings for the assignment of ring-fusion stereochemistry in decalin ring system bearing an angular methyl group has been developed (Williamson, K. L.; Howell, T.; Spencer, T. A. *J. Am. Chem. Soc.* **1966**, *88*, 325). In the trans-decalins, there are usually several ideal W-pathways for long range coupling between the methyl group and axial protons. In cis-decalins, there are fewer or no such pathways. Thus in a pair of cis/trans isomers, the methyl group in the trans isomer will usually be broader (or will actually show splitting), whereas the cis isomer will have a sharper (unsplit) methyl group.



W-Coupling Across Heteroatoms. In conformationally well-defined systems significant 4J couplings can be seen to OH and other XH protons. In the example below, the long-range W-coupling between the OH proton and the axial proton at C⁶ was used to assign configuration to the major isomer formed in the reaction. In the minor isomer the OH proton was not detectably coupled. The well-defined cyclohexane $^3J_{\text{ax-ax}}$ and $^3J_{\text{ax-eq}}$ at C² in both isomers shows that the ring-flip isomer shown predominates (Bueno, A. B.; Carreno, M. C.; Ruano, J. L. G. *Tetrahedron Lett.* **1995**, *36*, 3737).

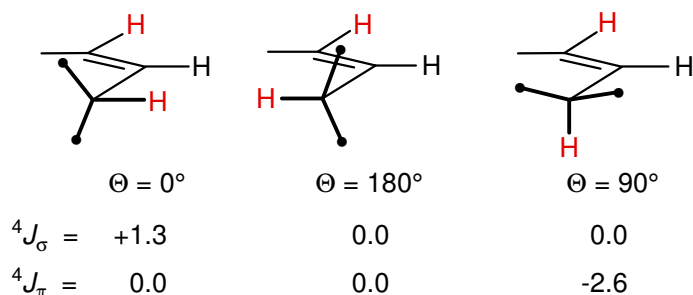


In a related system, the observation of an unusually large 4J across the sulfone sulfur was interpreted in terms of the conformation shown, in which the methyl group is over the ring, rather than alternative conformations in which the sulfone oxygen is over the ring (Kaloustian, M. K.; Dennis, N.; Mager, S.; Evans, S. A.; Alcudia, F. Eliel, E. L. *J. Am. Chem. Soc.* **1976**, *98*, 956-965).



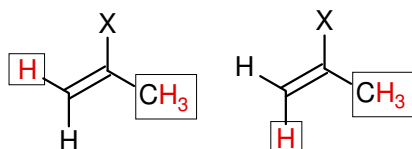
Allylic Coupling. 4-Bond coupling of vinyl to allylic hydrogens is usually easily observable. We can think of the coupling as having two components, the usual W-coupling transmitted through the σ -system, which is positive and is maximized for the *trans* proton when the allylic C-H bond is in the plane of the vinyl C-H group ($\Theta = 0^\circ$, $J > 0$), and a π -component, which is negative, and whose magnitude is maximized when the allylic C-H bond is perpendicular to the double bond ($\Theta = 90^\circ$, $J < 0$) (Garbisch, *J. Am. Chem. Soc.* **1964**, *86*, 5561). The positive σ -contribution added to the larger negative π -contribution normally results in a numerically slightly smaller (negative) coupling to the *trans* vinyl proton, but the effect is small, and not reliable enough for the unambiguous determination of double bond stereochemistry (note the marked entry below in which $J_{\text{trans}} > J_{\text{cis}}$) (Barfield, M.; Chakrabarti, B. *Chem. Rev.* **1969**, *69*, 757).

Allylic Coupling (4J)



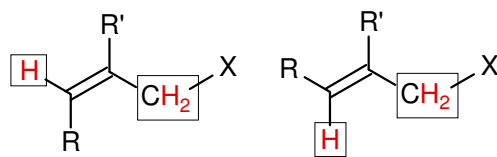
$$^4J = 1.3 \cos^2\Theta - 2.6 \sin^2\Theta \quad (\Theta = 0 - 90^\circ)$$

$$^4J = 2.6 \sin^2\Theta \quad (\Theta = 90 - 180^\circ)$$



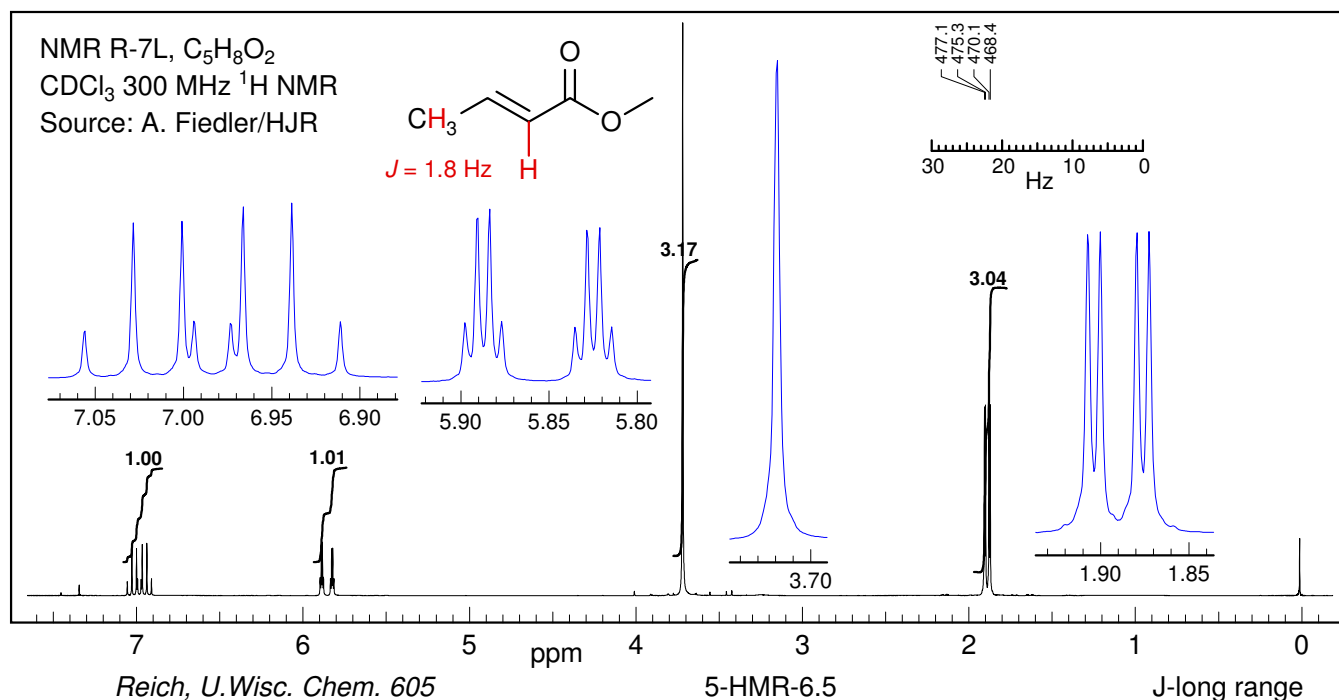
X = CH ₃	-1.25	-1.25
X = Cl	-0.7	-1.3
X = Ph	-0.8	-1.5

Can one distinguish E and Z isomers?

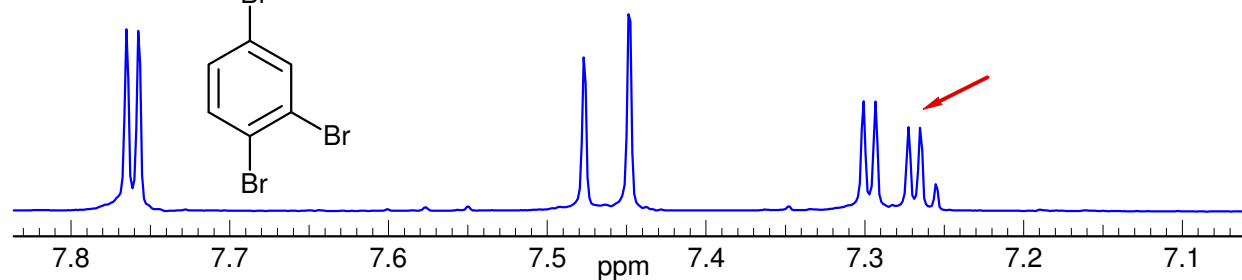
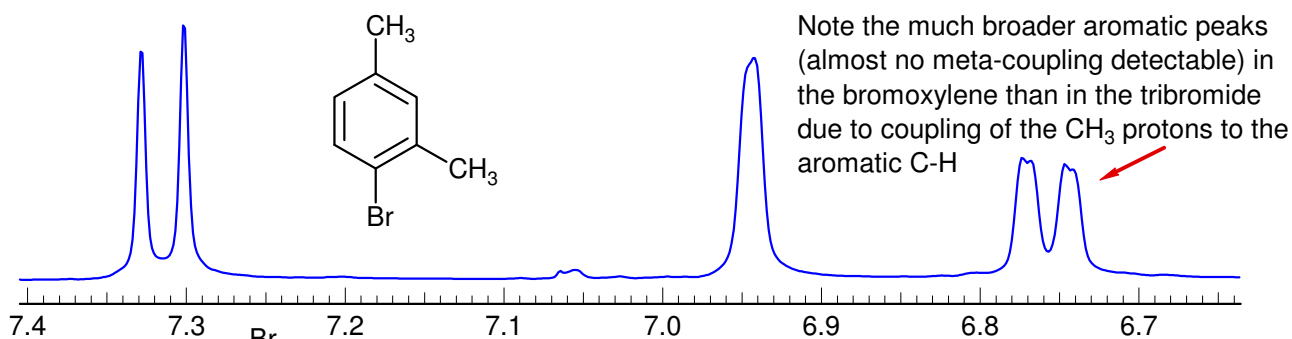
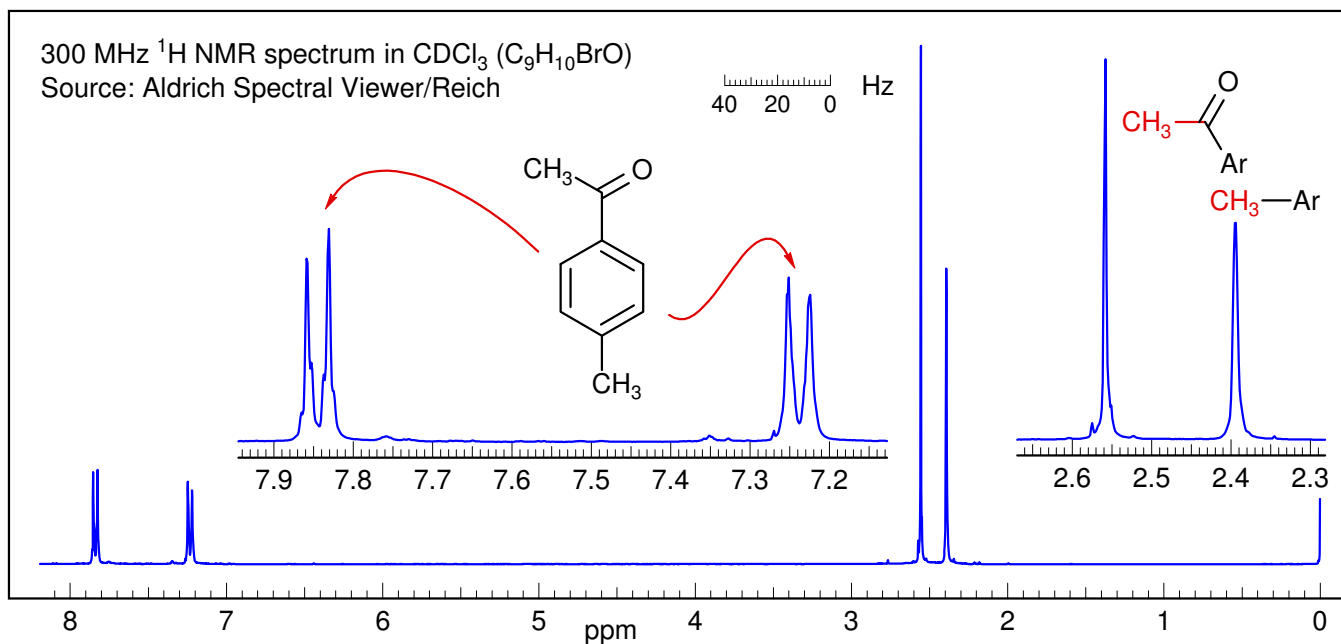


	J_{trans}	J_{cis}
X = CH ₃	-1.2	-1.7
X = Cl	-0.93	-1.41
X = OH	-1.25	-1.55
X = Ph	-1.47	-1.47
X = CH=CH ₂	-1.50	-1.30

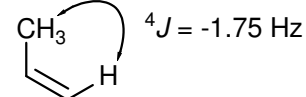
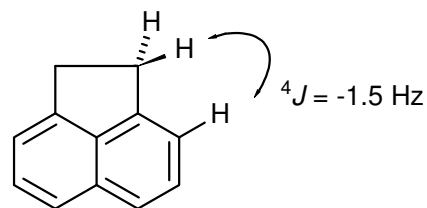
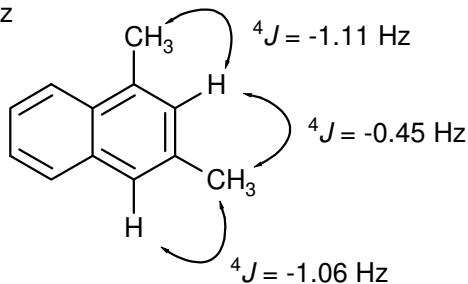
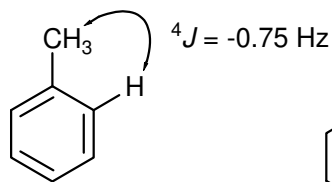
A typical example of allylic coupling is shown by methyl crotonate, where the 4J between the CH₃ and the α -CH is 1.8 Hz.



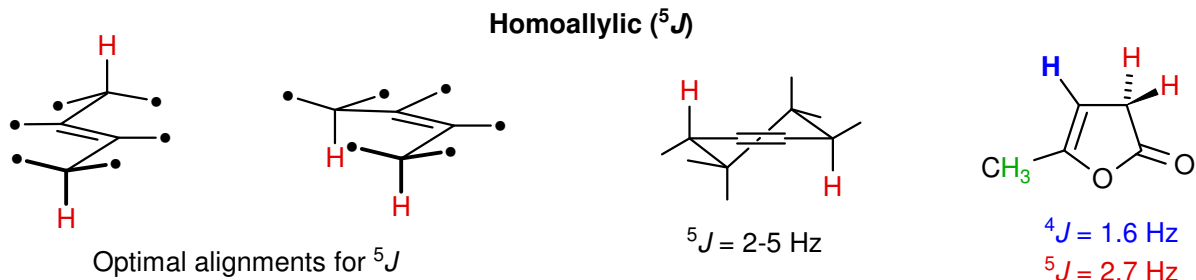
Benzylic Coupling. Coupling between benzyl protons and ortho hydrogens on aromatic rings are typically <1 Hz, and thus often not resolved, but almost always cause significant broadening of both the aromatic and benzyl protons. This can be clearly seen in the spectrum of p-methylacetophenone below, where the Ar-CH₃ is wider and thus noticeably shorter than the C(=O)-CH₃, and the protons ortho the CH₃ are broader than those ortho to the acetyl group. The coupling is related to π -bond order, so it is usually smaller than allylic coupling.



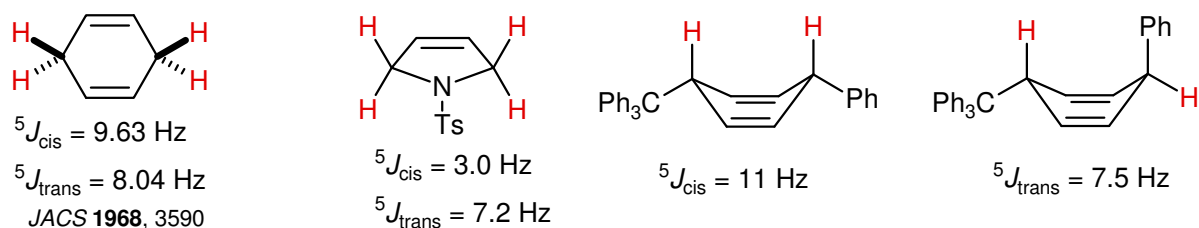
Benzylic Coupling (⁴J)



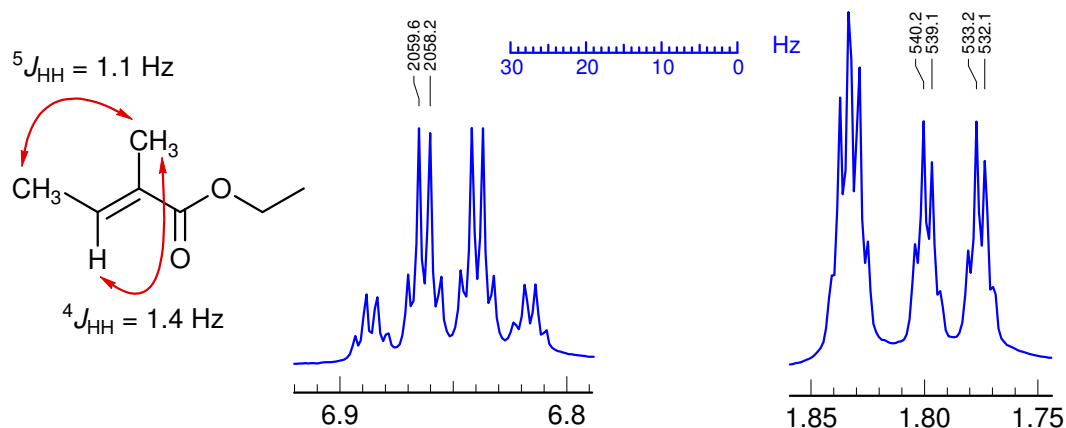
Homoallylic Coupling. Couplings across 5 bonds are unusual, but can be seen under favorable circumstances. Coupling is optimal when both C-H bonds are aligned with the π -orbital of an intervening double bond (perpendicular to the plane of the double bond). Especially large long-range couplings are seen for 1,4-cyclohexadienes and related structures where there are two paths for the coupling.



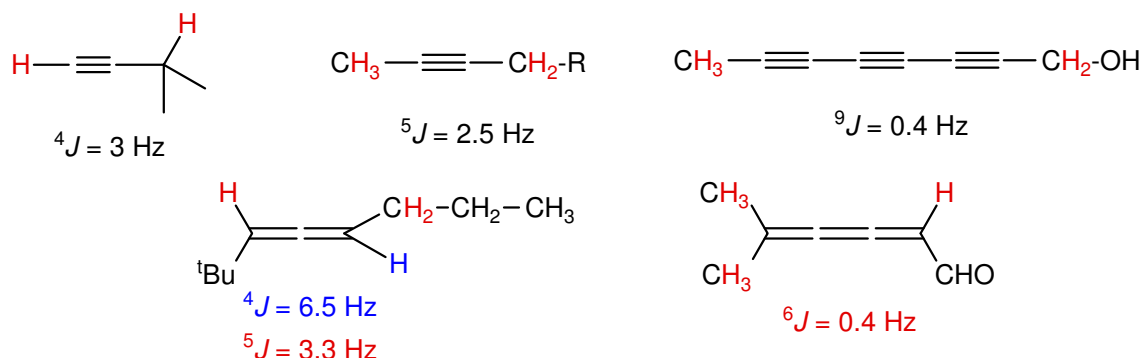
Some extreme examples of large homoallylic coupling:



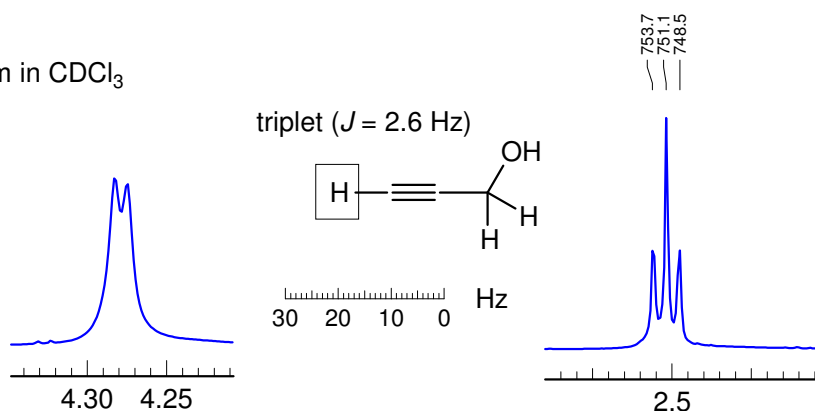
A typical example of homoallylic as well as allylic coupling is shown below:



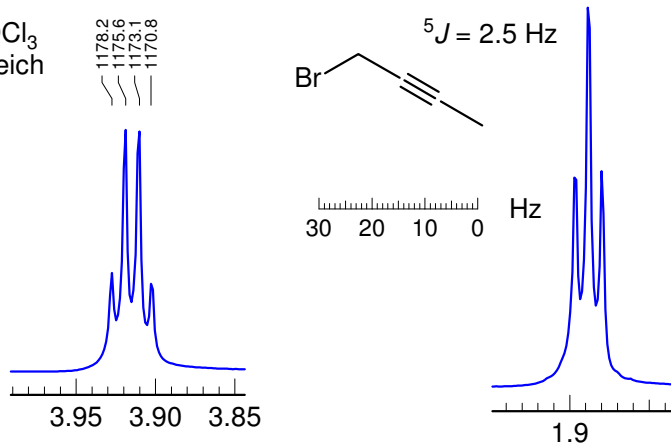
Long range Couplings in Acetylenes and Allenes. No special structural features are required to observe 4- and 5-bond couplings across acetylenes and allenes - such couplings are always present. Even couplings across 5, 6, and more bonds are detected across polyacetylene or cumulene chains



R-22B $\text{C}_3\text{H}_4\text{O}$
 300 MHz ${}^1\text{H}$ NMR spectrum in CDCl_3
 Source: ASV/Reich



R-22I ($\text{C}_4\text{H}_5\text{Br}$)
 300 MHz ${}^1\text{H}$ NMR spectrum in CDCl_3
 Source: Aldrich Spectra Viewer/Reich



Long range couplings like this are also observed across nitrogen as in the nitrilium ion below:

