

DEFINITIONS

1. A spin system consists of sets of nuclei that "interact (spin couple) among each other but do not interact with any nuclei outside the spin system. It is not necessary for all nuclei within a spin system to be coupled to all the other nuclei"⁴ in the spin system. The spin system definition requires that spin systems be "insulated" from one another: e.g., the ethyl protons in ethyl isopropyl ether constitute one system, and the isopropyl protons another.
2. A set of nuclei consists of chemical shift equivalent nuclei.
3. If nuclei ~~are interchangeable~~ by a symmetry operation or a rapid mechanism they are chemical shift equivalent; that is, they have exactly the same chemical shift under all achiral conditions. The interchange by a symmetry operation may occur in any reasonable conformation of the molecule. A rapid mechanism means one that occurs faster than once in about 10^{-3} seconds.
4. Nuclei are magnetically equivalent if they couple to all other nuclei in the spin system in exactly the same way. Chemical shift equivalence is presupposed.

CHEMICAL SHIFT EQUIVALENCE

The symmetry operations are: rotation about a symmetry axis (C_n), reflection at a center of symmetry (i), reflection at a plane of symmetry (σ), or higher orders of rotation about an axis followed by reflection in a plane normal to this axis (S_n). The symmetry element (axis, center, or plane) must be a symmetry element for the entire molecule. The term "interchange" will be clarified by the examples below. Chemical shift equivalent protons are given the same letter of the alphabet in the Pople notation (i.e., placed in a set as described above) and if magnetically nonequivalent are distinguished by primes such as A, A', A'' . c.c.

Although it is of no consequence unless a chiral solvent is used, note that only those protons that are interchangeable through an axis of rotation are completely identical

homotopic

protons, whereas those that are interchangeable through other symmetry operations are enantiotopic, i.e., nonsuperimposable mirror images. Noninterchangeable protons are termed diastereotopic. Identical protons are chemical shift equivalent in any environment, chiral or achiral. Enantiotopic protons are chemical shift nonequivalent only in a chiral solvent. Diastereotopic protons are not chemical shift equivalent in any environment, although they may fortuitously absorb at the same position.

Protons *a* and *b* in trans-1,2-dichlorocyclopropane are chemical shift equivalent, as are the protons *c* and *d* (Figure 32). The molecule has an axis of symmetry passing through C_1 and bisecting the C_1-C_2 bond. Rotation of the molecule by 180° around the axis of symmetry interchanges proton H_a for H_b and H_c for H_d . If the protons were not labeled, it would not be possible to tell if the symmetry operation had been performed merely by inspecting the molecule before and after the operation.

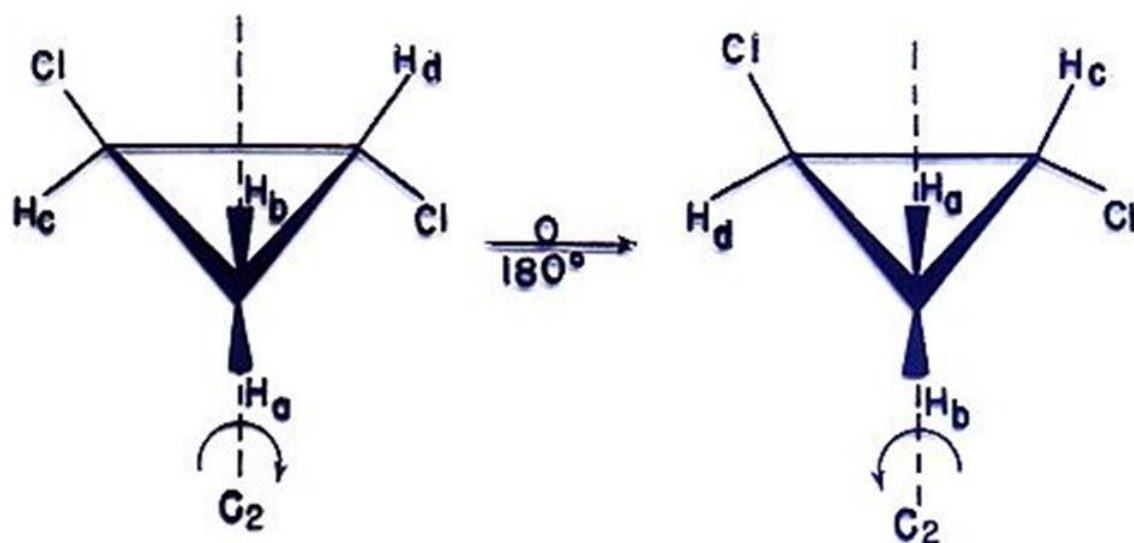


Fig. 32.

Trans-1,2-Dichlorocyclopropane showing axis of symmetry and effect of rotation around the axis.

An interesting situation occurs in a molecule such as 1,3-dibromo-1,3-diphenylpropane which has a methylene group between two centers of optical activity (Figure 33).

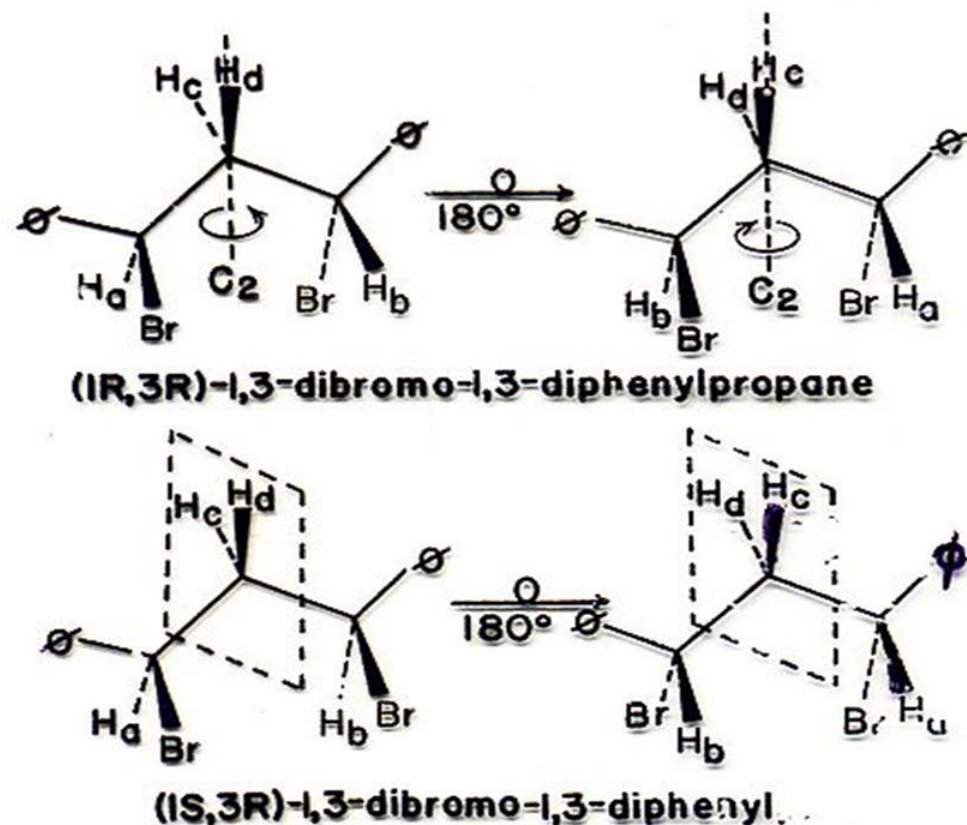


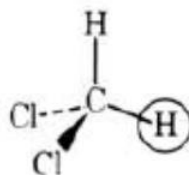
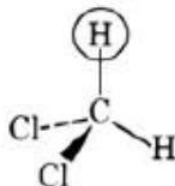
Fig. 33.

Two isomers of 1,3-dibromo-1,3-diphenylpropane. In the (1R, 3R) isomer, H_a and H_b are chemical shift equivalent, as are H_c and H_d . In the (1S, 3R) isomer, H_a and H_b are chemical shift equivalent, but H_c and H_d are not.

Test for Chemical Shift Equivalence

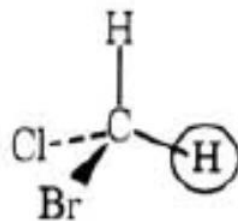
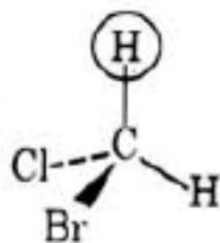
Suppose the question is: Must these two hydrogens atoms have the same, or may they each have a different, chemical shift: must they necessarily be chemical shift equivalent or not? To answer the question, build two molecular models of the compound and distinguish by some tag or marker one of the hydrogen atoms in the first model and the other hydrogen atom in the second model. Now compare the two models. There can be four possible results.

1) The two models will be *identical*. If this is the case, the two hydrogen atoms will necessarily be chemical shift equivalent in any solvent: achiral, racemic, or chiral. If this is the result, the two hydrogen atoms may be said to be “equivalent.” An example of this would be the hydrogen atoms of dichloromethane

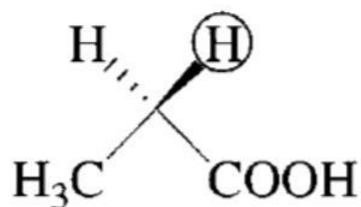
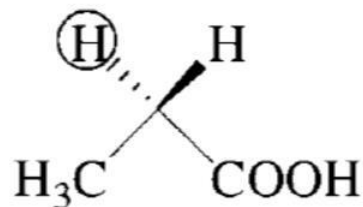


Homomeric models
Homotopic atoms

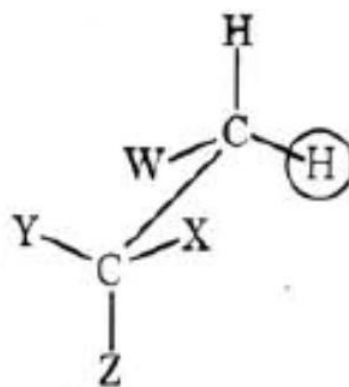
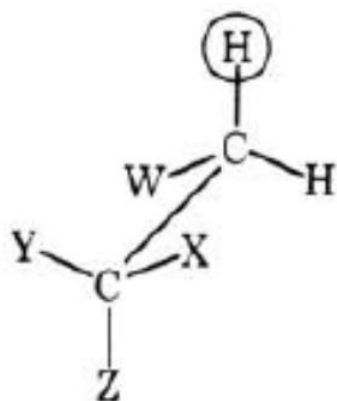
2) The two models will be *enantiomers*. If this is the case, the two hydrogen atoms will necessarily be chemical shift equivalent in an achiral or racemic solvent. If a chiral solvent is used, the two hydrogen atoms will not necessarily be chemical shift equivalent. If the models are enantiomers, the two hydrogen atoms are said to be *enantiotopic*.³ An example of this would be the hydrogen atoms of bromochloromethane



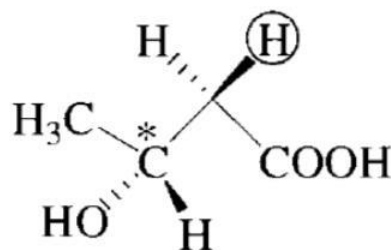
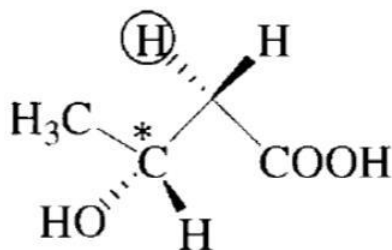
Enantiomeric models
Enantiotopic atoms

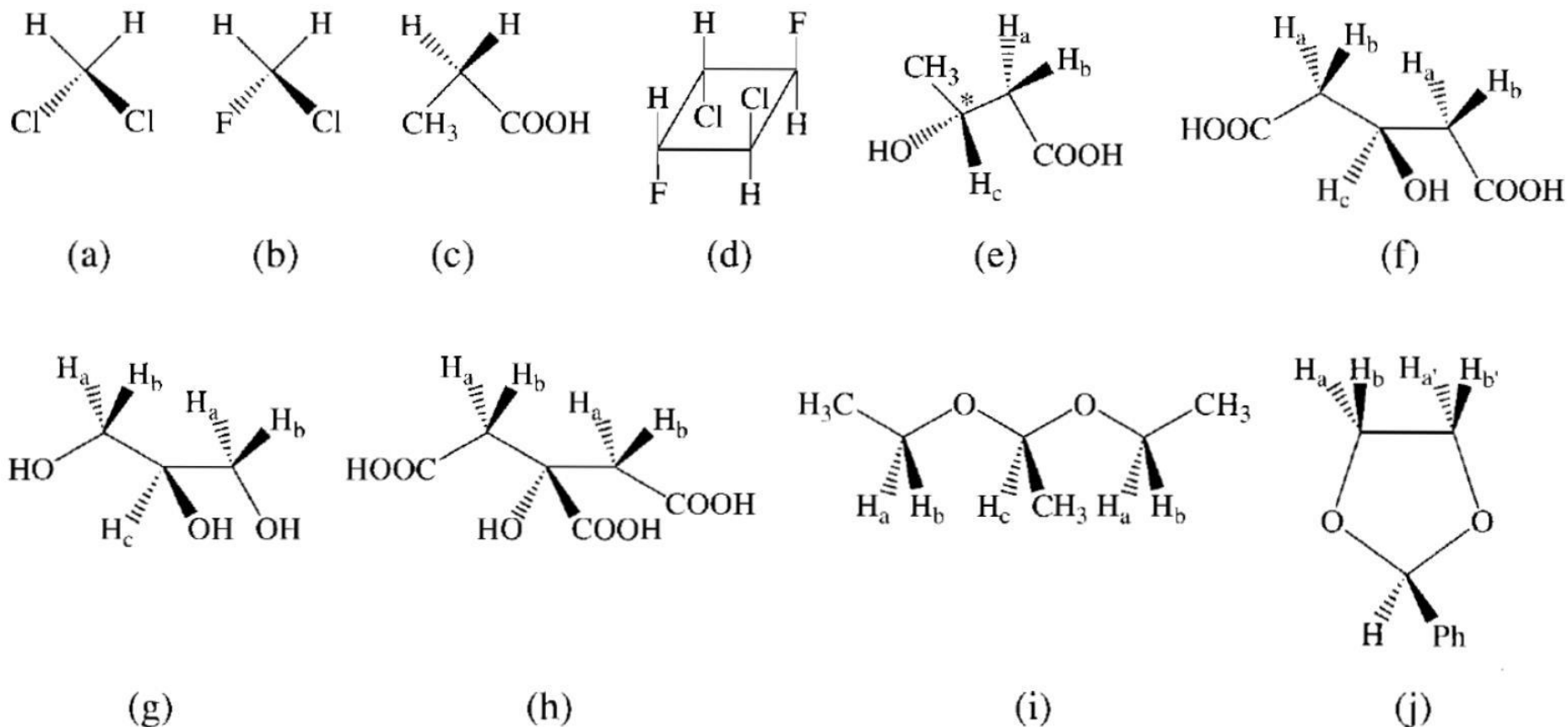


3) The two models will be *diastereomers*. If this is the case, the two hydrogen atoms will not necessarily be chemical shift equivalent in any solvent. If the models are diastereomers, the two hydrogen atoms are said to be *diastereotopic*.³ An example of this would be the methylene protons of a molecule containing a chiral center, such as WCH_2-CXYZ



Diastereomeric models
Diastereotopic atoms





a. Homotopic protons

b, c. Enantiotopic protons

d. Enantiotopic protons

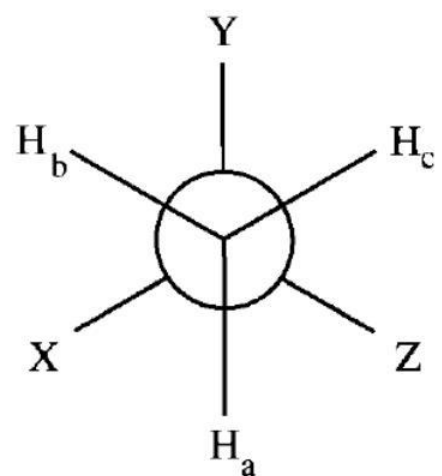
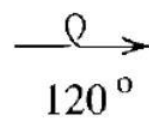
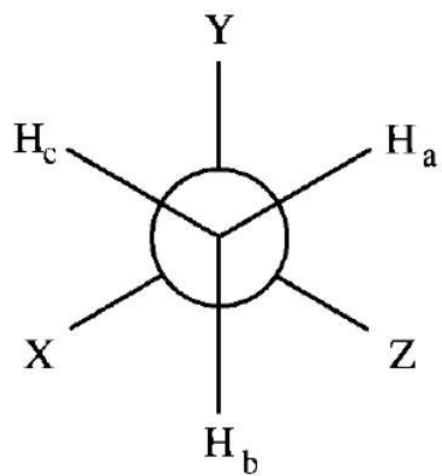
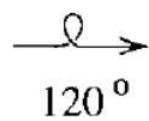
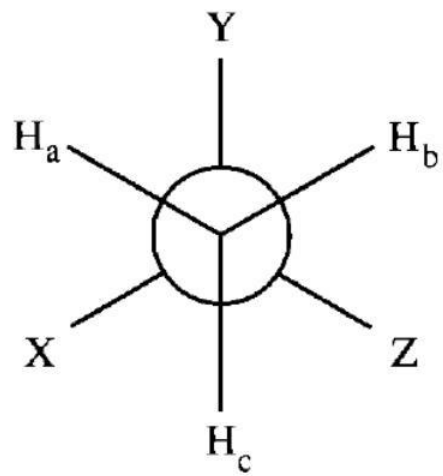
e. Diastereotopic protons in a chiral molecule

f, g, h, i, j Diastereotopic protons in achiral molecules

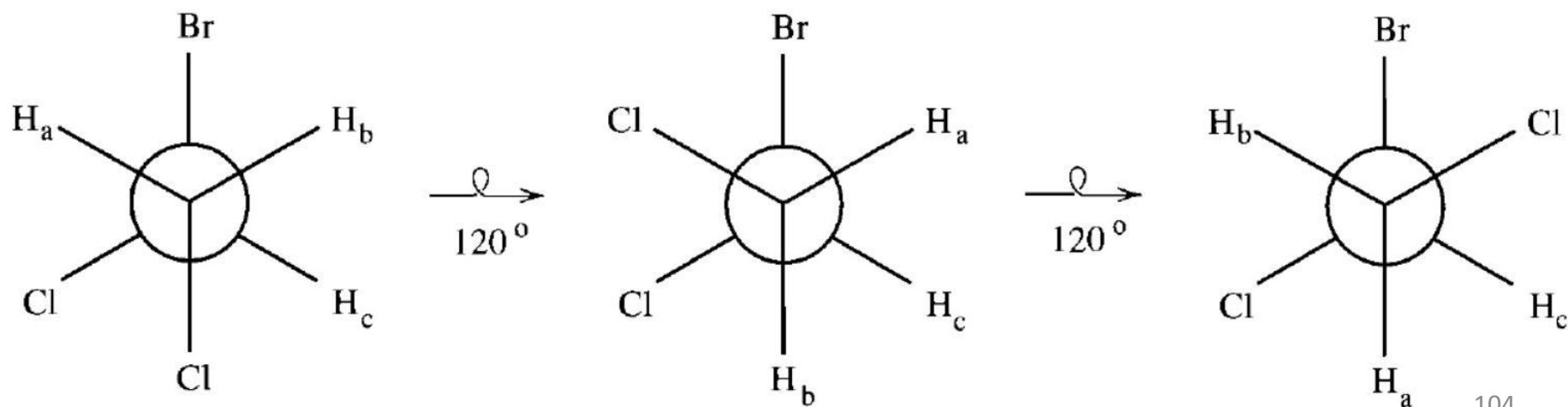
3.8.3.4 Interconversion Around the Single Bonds of Chains

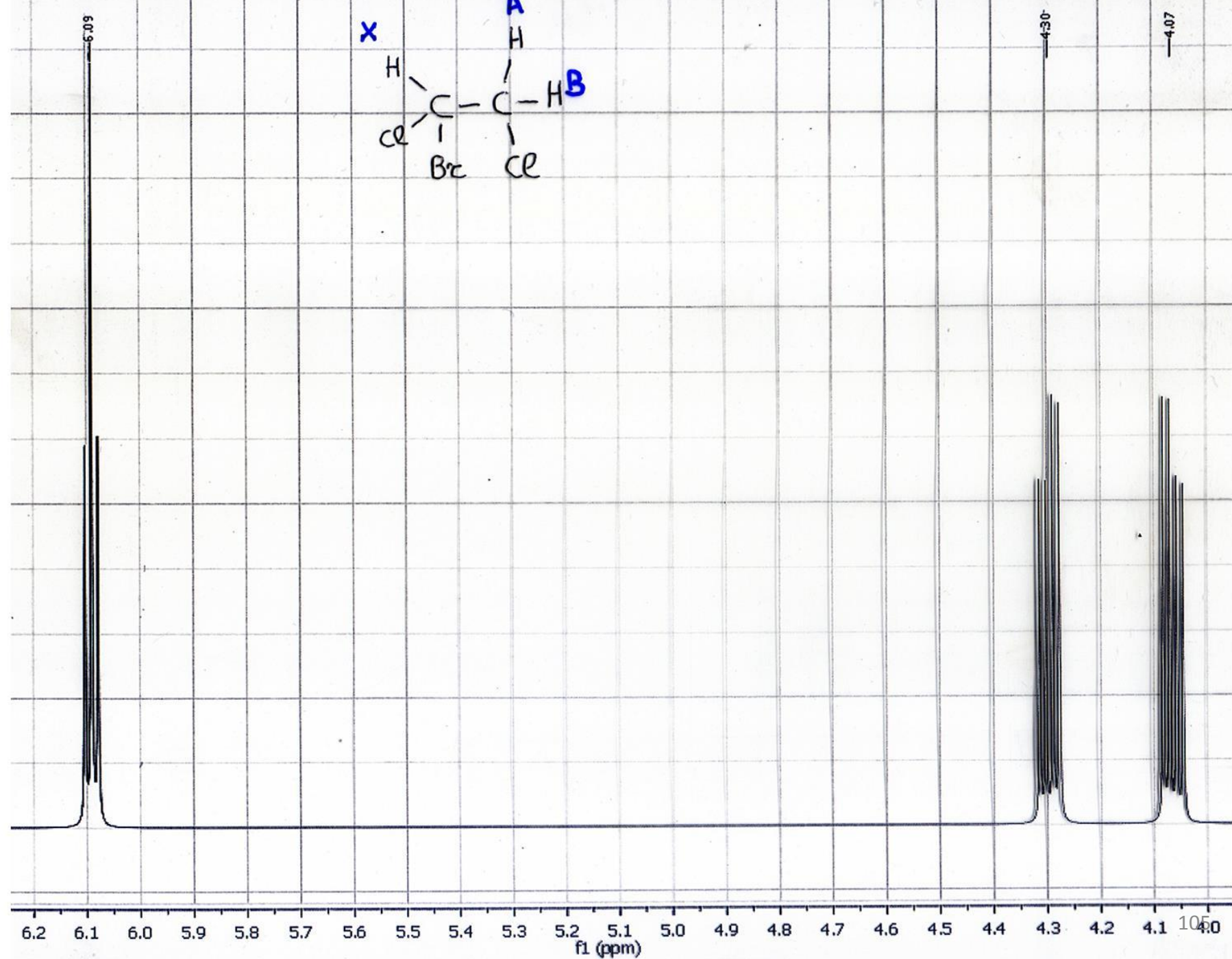
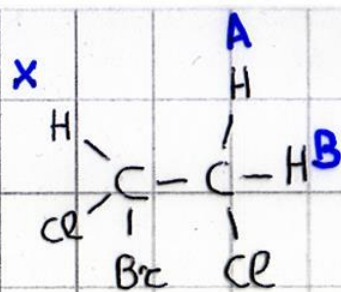
Chemical shift equivalence of protons on a CH_3 group results from rapid rotation around a carbon-carbon single bond even in the absence of a symmetry element. Figure 3.46a shows Newman projections of the three staggered rotamers of a molecule containing a methyl group attached to another sp^3 carbon atom having four different substituents, that is, a chiral center. In any single rotamer, none of the CH_3 protons can be interchanged by a symmetry operation. However, the protons are rapidly changing position. The time spent in any one rotamer is short ($\sim 10^{-6}$ s), because the energy barrier for rotation around a C—C single bond is small. The chemical shift of the methyl group is an average of the shifts of the three protons. In other words, each proton can be interchanged with the others by a rapid rotational operation. Thus, without the labels on the protons, the rotamers are indistinguishable.

In the same way the three rotating methyl groups of a *t*-butyl group are chemical shift equivalent except for rare steric hindrance. Both the methyl group and the *t*-butyl group are described as “symmetry tops.”

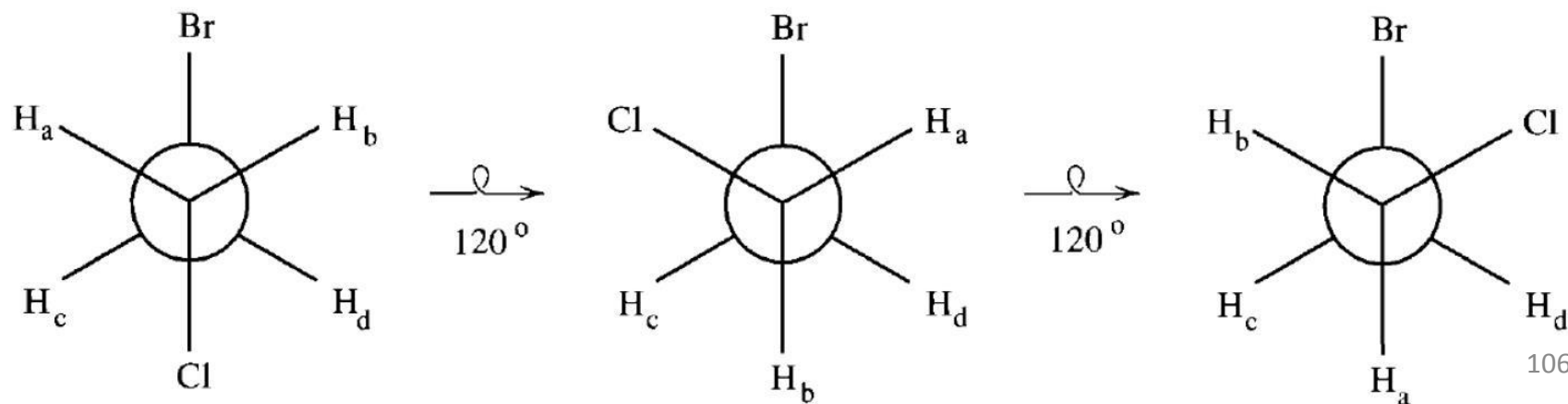


Consider a methylene group next to a chiral center, as in 1-bromo-1,2-dichloroethane (Figure 3.46c). Protons H_a and H_b are not chemical-shift equivalent since they cannot be interchanged by a symmetry operation in any conformation; the molecule has no simple axis, plane, center, or alternating axis of symmetry. Although there is a rapid rotation around the carbon-carbon single bond, the CH_2 protons are not interchangeable by a rotational operation; the averaged chemical shifts of H_a and H_b are not identical. An observer can detect the difference before and after rotating the methylene group: the protons in each rotamer are diastereotopic. The system is ABX.



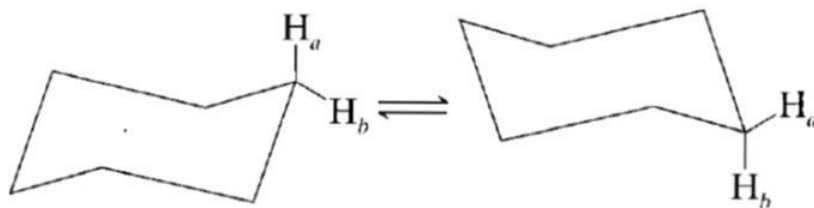


The staggered rotamers of 1-bromo-2-chloroethane (Figure 3.46b) are distinguishable. However, in the *anti* rotamer, H_a and H_b are chemical-shift equivalent (enantiotopic) by interchange through a plane of symmetry, as are H_c and H_d ; thus, there are two sets of enantiotopic protons. In neither of the *gauche* rotamers is there a symmetry element, but H_a and H_b , and H_c and H_d , are chemical-shift equivalent by rapid rotational interchange between two enantiomeric rotamers. Now we have one chemical shift for H_a and H_b in the *anti* rotamer, and a different chemical shift for H_a and H_b in the *gauche* rotamers. By rapid averaging of these two chemical shifts, we obtain a single chemical shift (i.e., chemical shift equivalence) for H_a and H_b , and of course for H_c and H_d .



In general, if protons can be interchanged by a symmetry operation (through a plane of symmetry) in one of the rotamers, they are also chemical-shift equivalent (enantiotopic) by rapid rotational interchange.

Interconversion Around the Single Bonds of Rings Cyclohexane at room temperature exists as rapidly interconverting, superposable chair forms.



An axial proton becomes an equatorial proton and vice versa in the interconverting structures, and the spectrum consists of a single “averaged” peak. As the temperature is lowered, the peak broadens and at a sufficiently low temperature two peaks appear—one for the axial protons, one for the equatorial protons. In other words, at room temperature, the axial and equatorial protons are chemical-shift equivalent by rapid interchange. At very low temperatures, they are not chemical-shift equivalent; in fact, in each “frozen” chair form, the protons of each CH_2 group are diastereotopic pairs, but at room temperature, the rate of chair interconversion is sufficiently high to average the chemical shifts of these geminal protons.

Methylcyclohexane exists at room temperature as a rapidly interconverting mixture of axial and equatorial conformers. These conformers are not superposable, and at low temperatures a spectrum of each conformer exists.

In a fused cyclohexane ring, such as those of steroids, the rings are “frozen” at room temperature and the axial and equatorial protons of each CH_2 group are not chemical-shift equivalent.

MAGNETIC EQUIVALENCE

Magnetic equivalence presupposes chemical shift equivalence. To determine whether chemical shift equivalent nuclei are magnetically equivalent, one determines whether they are coupled equally to each nucleus (probe nucleus) in every other set in the spin system. This is done by examining geometrical relationships. If the bond distances and angles from each nucleus in relation to the probe nucleus are identical, the nuclei in question are magnetically equivalent. Magnetically nonequivalent nuclei in a set are designated by primes (e.g., AA').

Consider the protons a, b and c, d in p -fluoronitrobenzene (Figure 36). Protons a and b are chemical shift equivalent by interchange through an axis or plane of symmetry. Protons a and b are coupled to nucleus F through the same bond distances and angles. However, protons a and b are coupled to proton c (or d) with different geometry. Thus, protons a and b fail the test for magnetic equivalence. Protons c and d are treated in the same way and are also found not to be magnetically equivalent. The system is $AA'BB'X$.

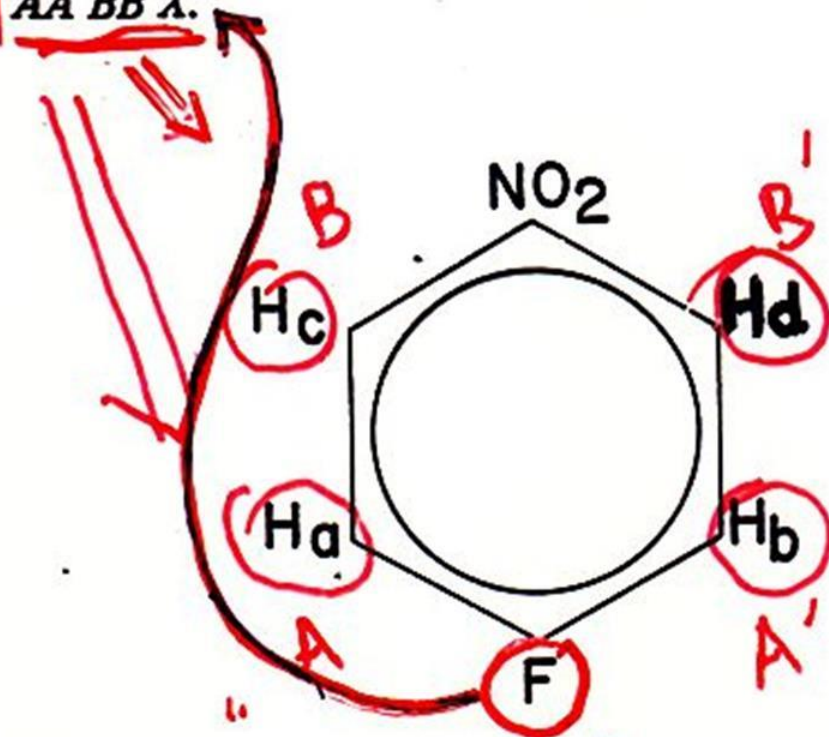
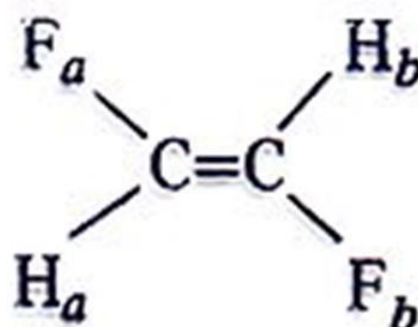
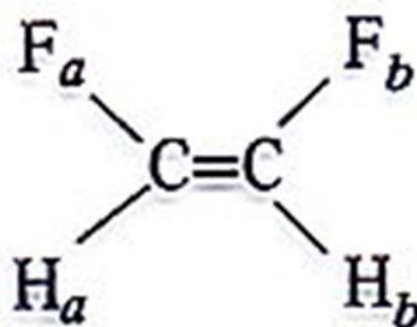
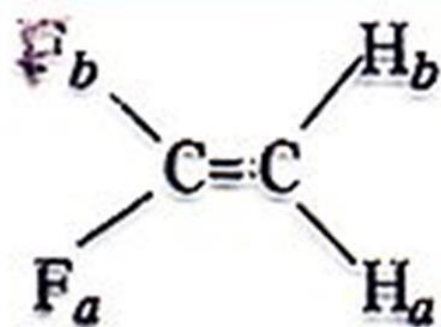


Fig. 36. p -Fluoronitrobenzene.

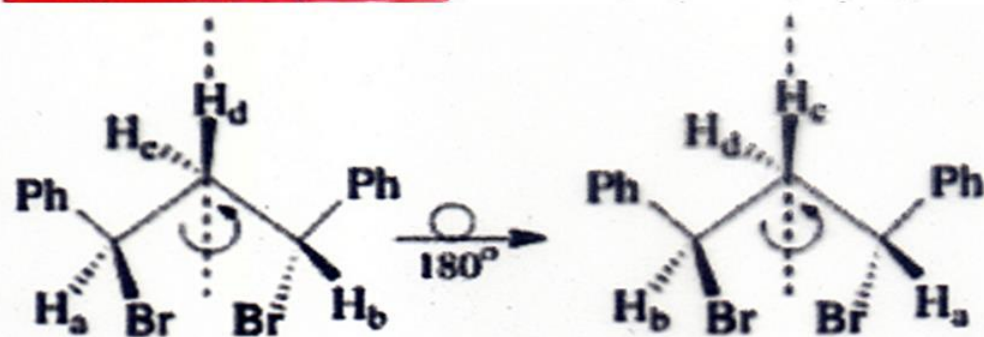
We propose a somewhat more practical definition and test for magnetic equivalence: two chemical shift equivalent protons are magnetically equivalent if they are symmetrically disposed with respect to each nucleus (probe) in any other set in the spin system. This means that the two protons under consideration can be interchanged through a reflection plane passing through the probe nucleus and perpendicular to a line joining the chemical shift equivalent protons. Note first that this plane is not necessarily a molecular plane of symmetry. Note also that the test is valid in any reasonable molecular conformation. ←

The three isomeric difluoroethylenes furnish additional examples of chemical shift equivalent nuclei that are not magnetically equivalent.

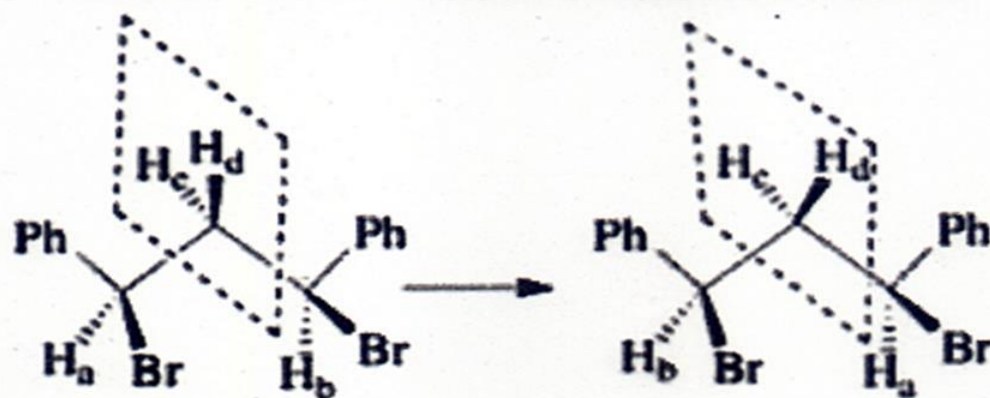


In each case, the protons H_a and H_b and fluorines F_a and F_b comprise sets (of chemical shift equivalent nuclei) that are not magnetically equivalent.

Note that in the (1R,3R)-compound of Figure 33, H_a and H_b are not magnetically equivalent (since they do not identically couple to H_c); H_c and H_d also are not magnetically equivalent since $J_{cb} \neq J_{db}$ and $J_{da} \neq J_{ca}$. Observe also that in the 1S,3R compound of Figure 33, $J_{ad} = J_{bd}$ and $J_{ac} = J_{bc}$; thus, in this molecule H_aH_b are magnetically equivalent.



(1R,3R)-1,3-Dibromo-1,3-diphenylpropane



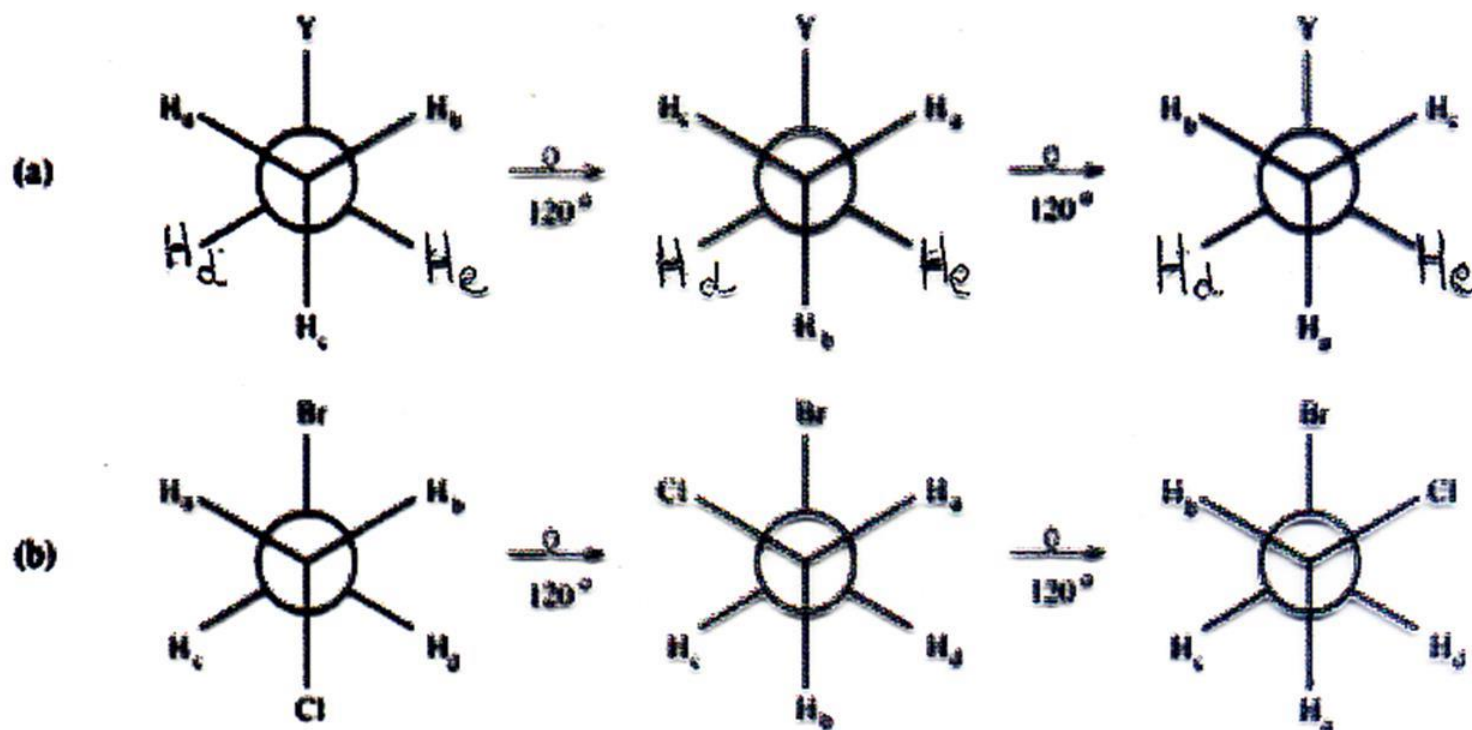
(1S,3R)-1,3-Dibromo-1,3-diphenylpropane

FIGURE 3.56 Two isomers of 1,3-dibromo-1,3-diphenylpropane. In the (1R,3R)-isomer, H_a and H_b are chemical-shift equivalent, as are H_c and H_d . In the (1S,3R)-isomer, H_a and H_b are chemical-shift equivalent, but H_c and H_d are not.

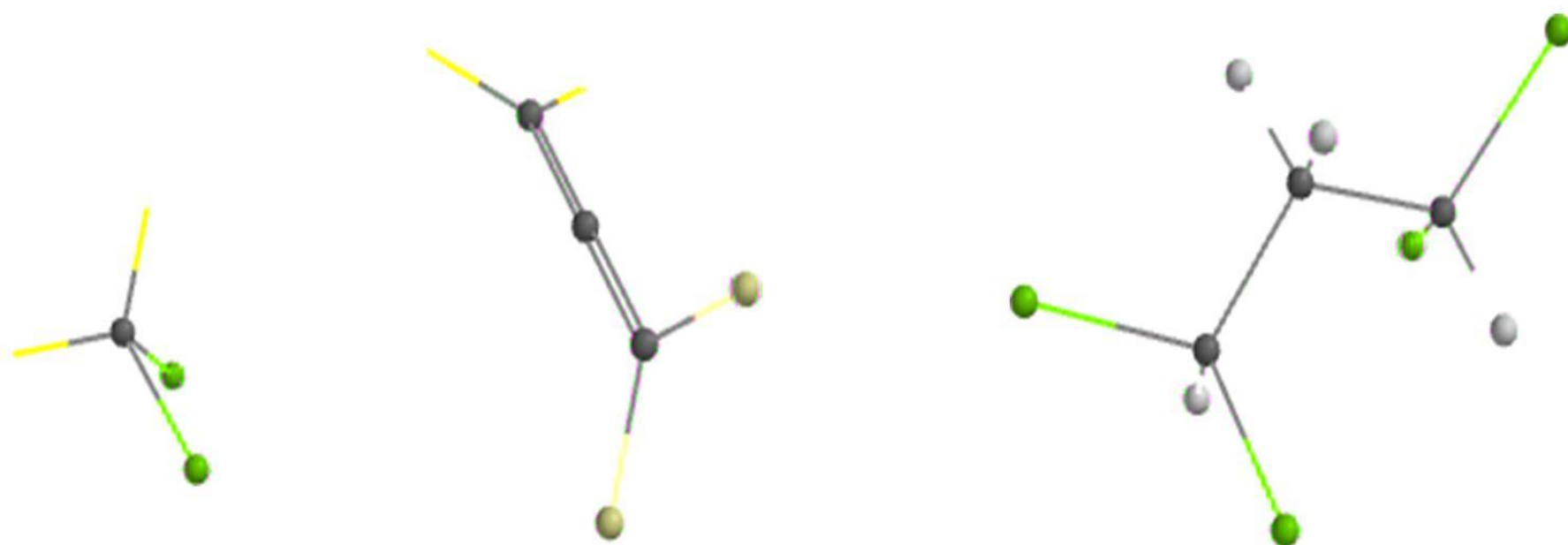
The question of magnetic equivalence in freely rotating methylene groups of aliphatic compounds becomes complex. The following assignments illustrate the nuances involved (if substituents Y and Z cause large chemical shift differences, the AMX designation is used instead of ABC):

$\text{CH}_3\text{CH}_2\text{Y}$	A_3B_2
$\text{ZCH}_2\text{CH}_2\text{Y}$	$AA'BB'$
$\text{YCH}_2\text{CH}_2\text{CH}_2\text{Y}$	$AA'BB'AA'$
$\text{CH}_3\text{CH}_2\text{CH}_2\text{Y}$	$A_3BB'CC'$
$\text{ZCH}_2\text{CH}_2\text{CH}_2\text{Y}$	$AA'BB'CC'$
$\text{YCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Y}$	$AA'BB'B''B'''A''A'''$
$\text{ZCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Y}$	$AA'BB'CC'DD'$

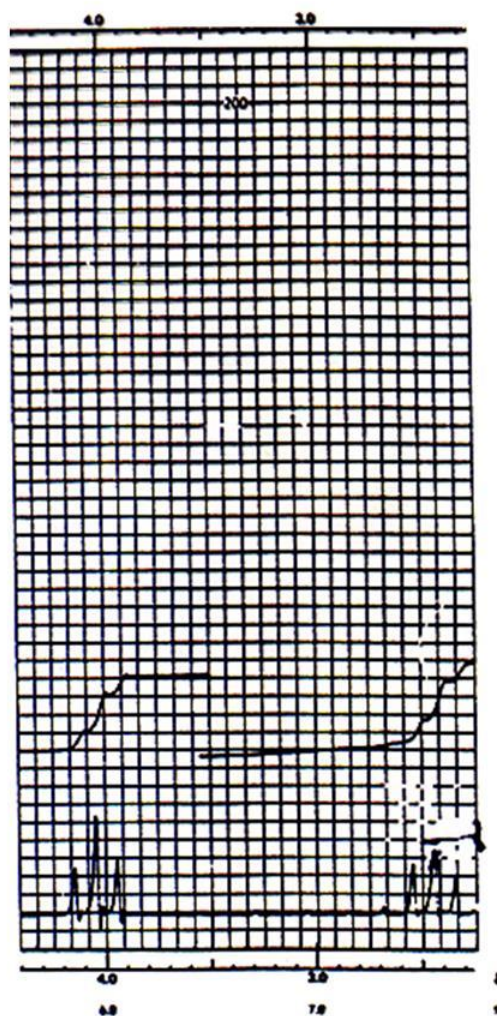
Methyl protons are magnetically equivalent by rotational averaging of the couplings to an adjacent methylene group whose protons are also magnetically equivalent if there is no other coupling involved. Averaging by rotation is valid since the rotational conformers are equivalent, thus equally populated. In ZCH_2CH_2Y , however, the population of the *anti* conformer is probably different from those of the enantiomeric *gauche* conformers, and rotational averaging is not valid.



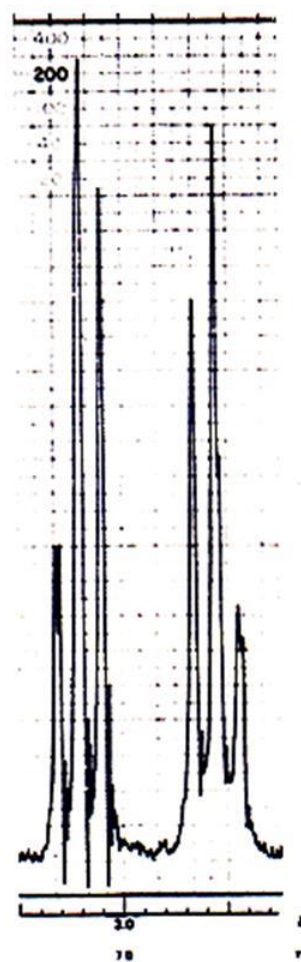
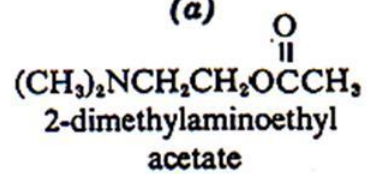
As pointed out by Ault : "True A_2X_2 systems are quite rare (examples include difluoromethane, 1,1-difluoroallene, and 1,1,3,3-tetrachloropropane), and most systems which are described as A_2X_2 systems should really be classified as $AA'XX'$ systems."



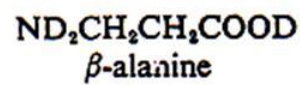
$AA'XX'$ systems often give deceptively simple A_2X_2 spectra; the spectrum of 2-dimethylaminoethyl acetate (Figure 37a) is a case in point. Figure 37 shows the progressive distortions as $AA'XX' \rightarrow AA'BB'$ (i.e., $\Delta \nu/J$ decreases) in compounds of type ZCH_2CH_2Y . As the absorptions move closer together, the inner peaks increase in intensity, additional splitting occurs, and some of the outer peaks disappear in the baseline noise. The general appearance of symmetry throughout aids recognition of the type of spin system involved. At the extreme, the two methylene groups become chemical shift equivalent and a single A_4 peak results.



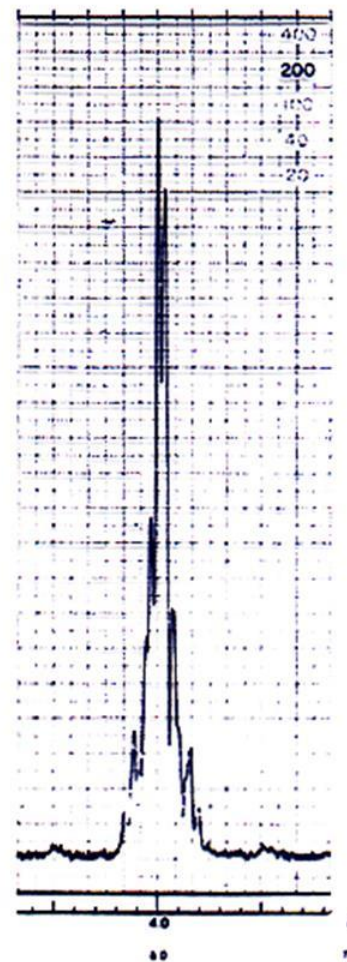
(a)



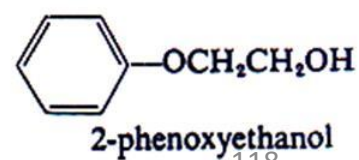
(b)



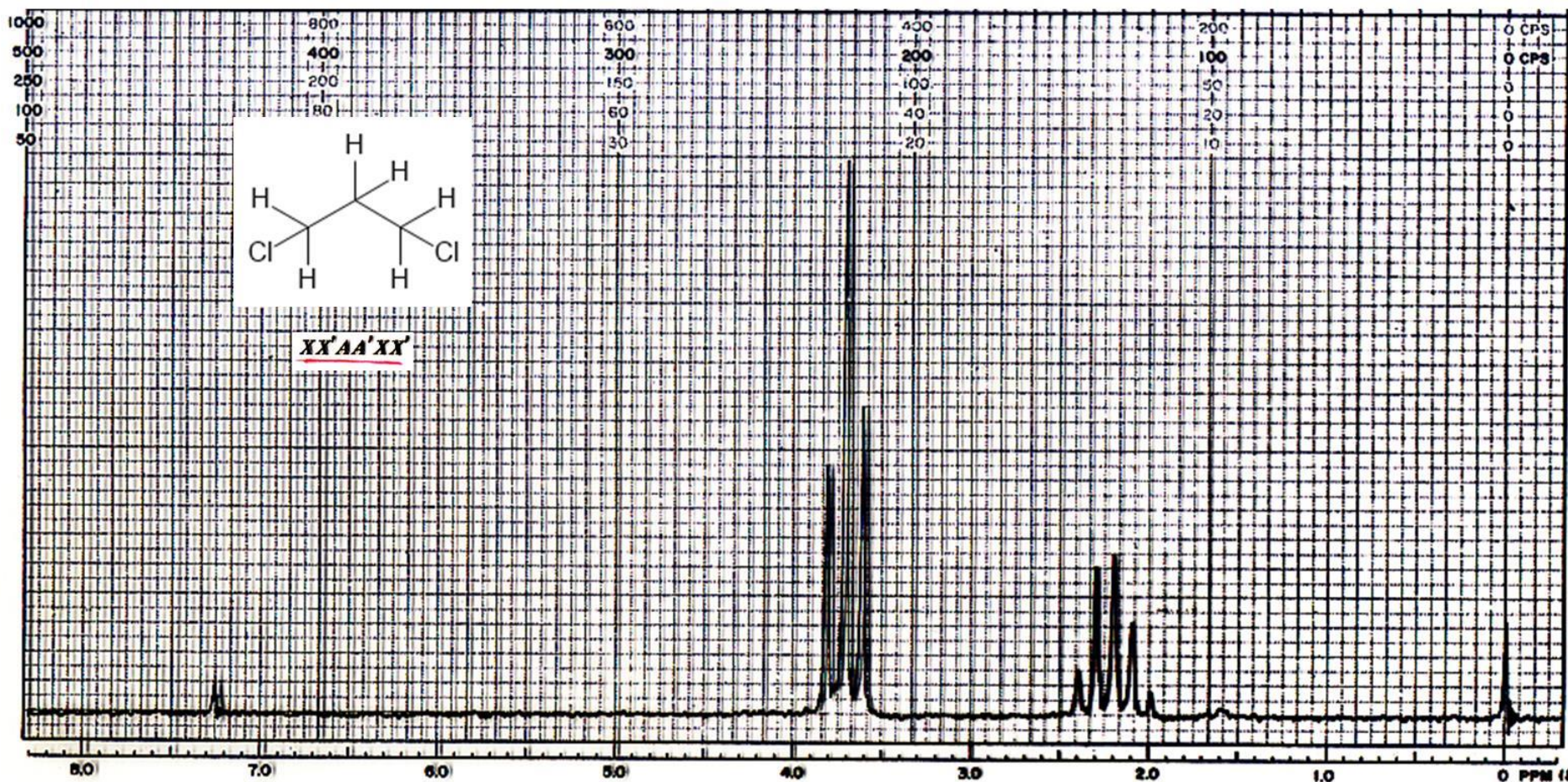
(c)



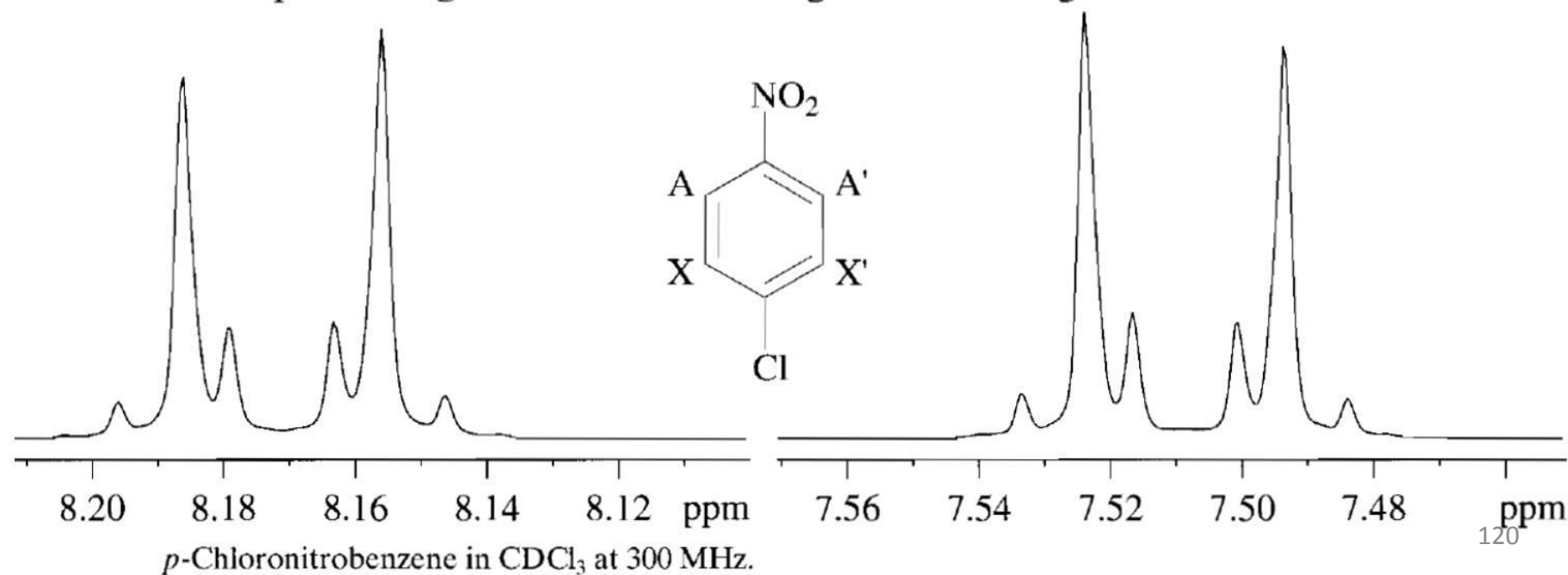
(d)



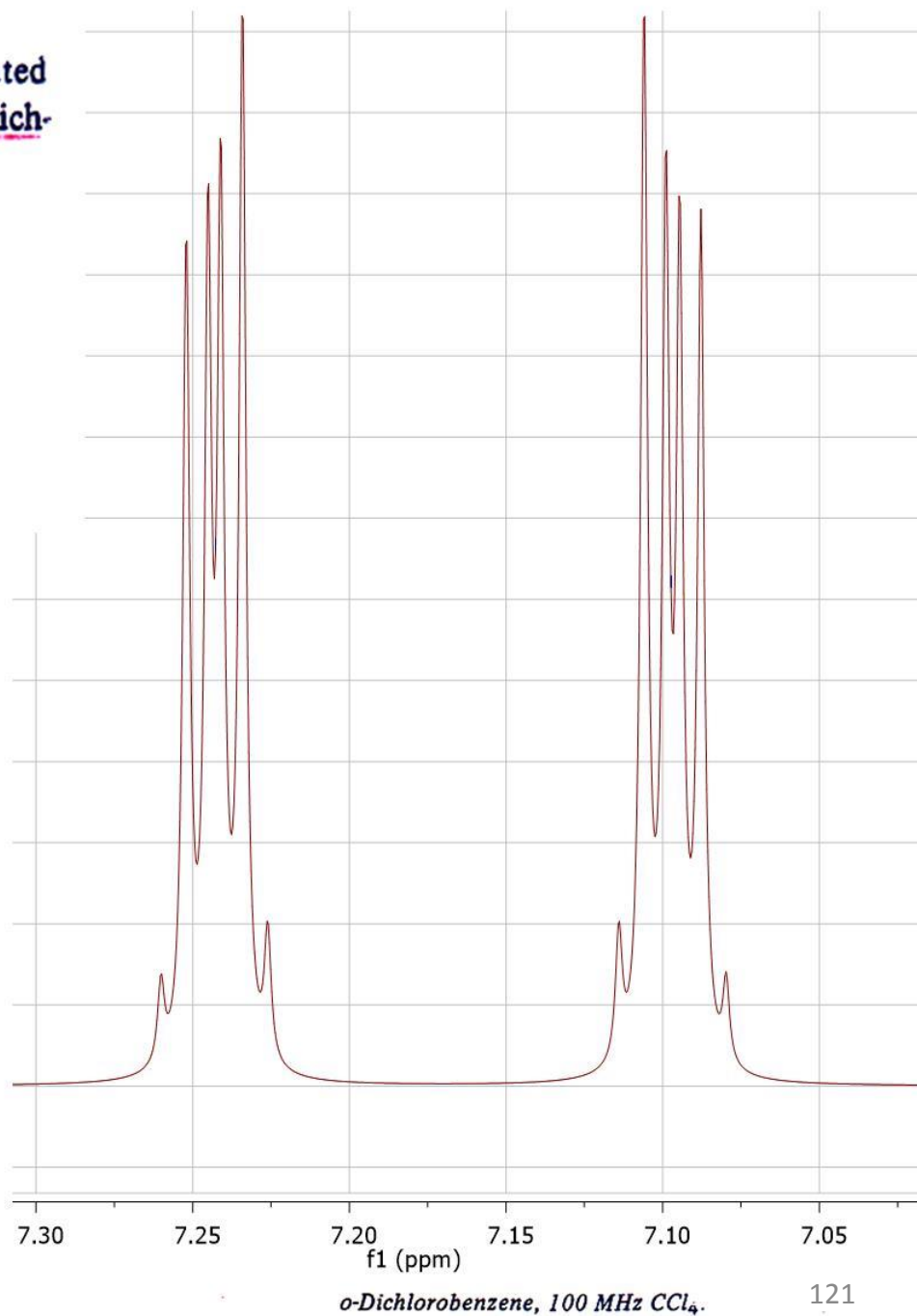
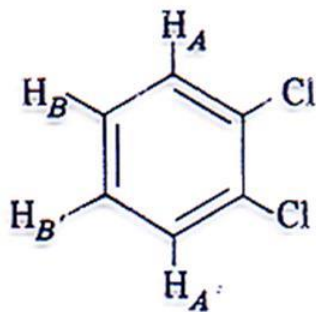
Although 1,3-dichloropropane is properly described as ~~XX~~AA'XX system, it also presents a deceptively simple spectrum (Figure 40) that resembles an A₂X₄ system: triplet and quintuplet



Consider the protons in *p*-chloronitrobenzene (see Figure 3.47). There is an axis of symmetry (through the substituents) that provides two sets of chemical-shift-equivalent protons presumably A₂ and X₂. However, neither the two A protons nor the two X protons are magnetically equivalent, and the correct labeling is AA' and XX'. This is not a first-order spin system and is written in the Pople notation as AA'XX'. These multiplet patterns do not conform to first-order intensity patterns in the Pascal triangle (Figure 3.32) nor do the distances (in Hz) between the peaks correspond to coupling constants. Spectra such as these do not become first-order spectra regardless of the strength of the magnetic field.

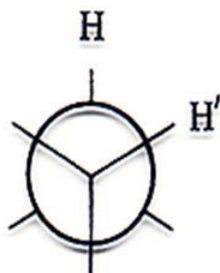


The aromatic protons of symmetrically *o*-disubstituted benzenes also give $AA'BB'$ spectra. An example is *o*-dichlorobenzene (Figure 39).



VICINAL AND GEMINAL COUPLING IN RIGID SYSTEMS

Coupling between protons on vicinal carbon atoms in rigid systems depends primarily on the dihedral angle ϕ between the $\text{H}-\text{C}-\text{C}'$ and the $\text{C}-\text{C}'-\text{H}'$ planes. This angle can be visualized by an end-on view of the bond between the

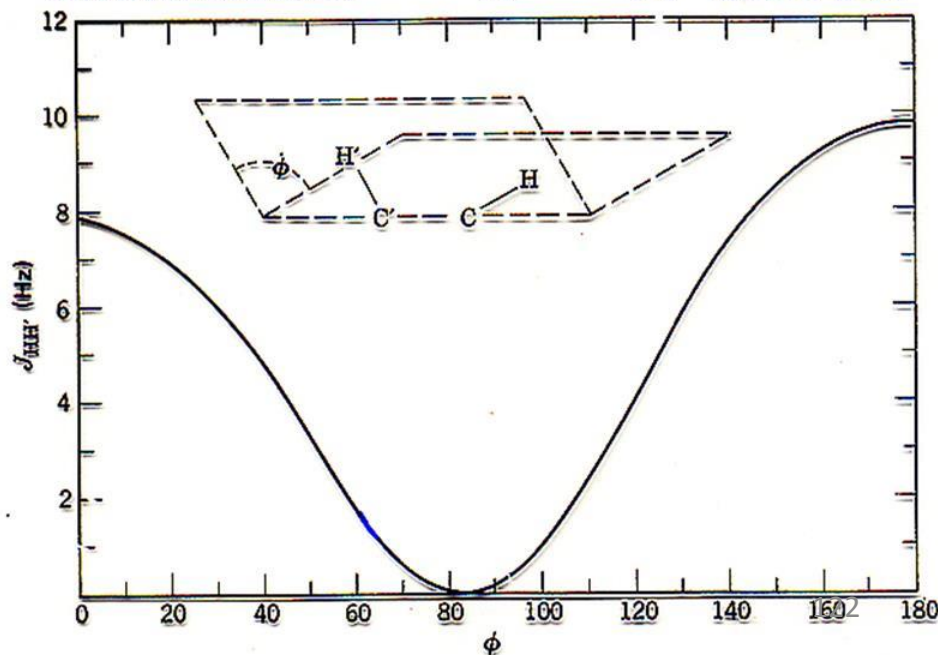


vicinal carbon atoms and by the perspective in Figure 46 in which the calculated relationship between dihedral angle and vicinal coupling constant²⁸ is graphed. Karplus emphasizes

that his calculations are approximations and do not take into account such factors as electronegative substituents, the bond angles θ ($\angle \text{H}-\text{C}-\text{C}'$ and $\angle \text{C}-\text{C}-\text{H}'$), and bond lengths. Deductions of dihedral angles from measured

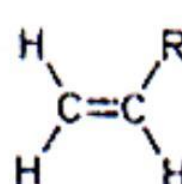
coupling constants are safely made only by comparison with closely related compounds. The correlation has been very useful in cyclopentanes, cyclohexanes, carbohydrates, and bridged polycyclic systems. In cyclopentanes, the observed values of about 8 Hz for vicinal *cis* protons and about 0 Hz for vicinal *trans* protons are in accord with the corresponding angles of about 0° and about 90° , respectively. In substituted or fused cyclohexane rings, the following relations obtain:

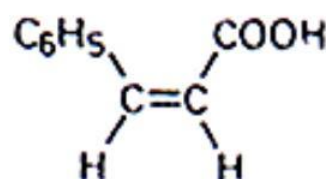
	Calc. J	Observed J (Hz)
axial-axial	9	8-14 (usually 8-10)
axial-equatorial	1.8	1-7 (usually 2-3)
equatorial-equatorial	1.8	1-7 (usually 2-3)



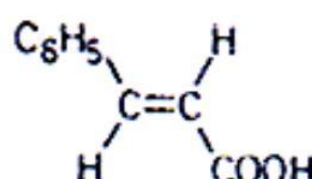
A modified Karplus equation can be applied to vicinal coupling in olefins. The prediction of a larger *trans* coupling ($\varphi = 180^\circ$) than *cis* coupling ($\varphi = 0^\circ$) is borne out.

$J(E)(\Phi = 180^\circ)$ is always larger than $J(Z)(\Phi = 0^\circ)$

 108		$J(Z)$	$J(E)$
	R = H	11.6	19.1
	R = C ₆ H ₅	11.5	18.6
	R = OCH ₃	6.7	14.0
	R = F	4.7	12.8



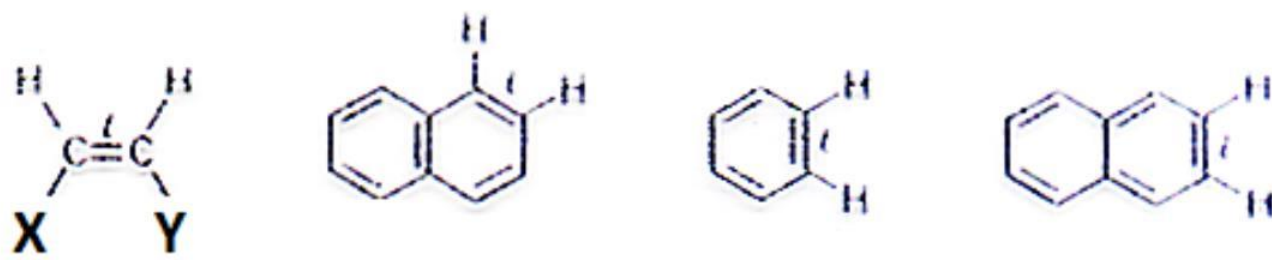
$$J(Z) = 12.3 \text{ Hz}$$



$$J(E) = 15.8 \text{ Hz}$$

In small rings or rigid bicyclic systems like norbornane the J coupling of cis-protons can however be larger than that of *trans*-protons. For cyclopropane J_{cis} is about 8 and J_{trans} about 5 Hz.

If, as in the cases of olefins or aromatics, there is no possibility of the dihedral angle varying (rotation about the C—C bond) then J reduces with increasing bond length l and increasing bond angle α .



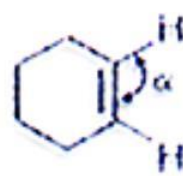
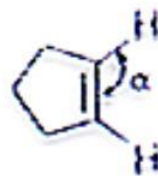
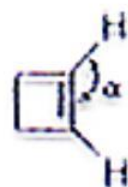
$J : 11.6 \text{ Hz}$

8.3 Hz

7.56 Hz

6.9 Hz

increasing distance l →
decreasing π -bond order



$J : 1.3 \text{ Hz}$

2.8 Hz

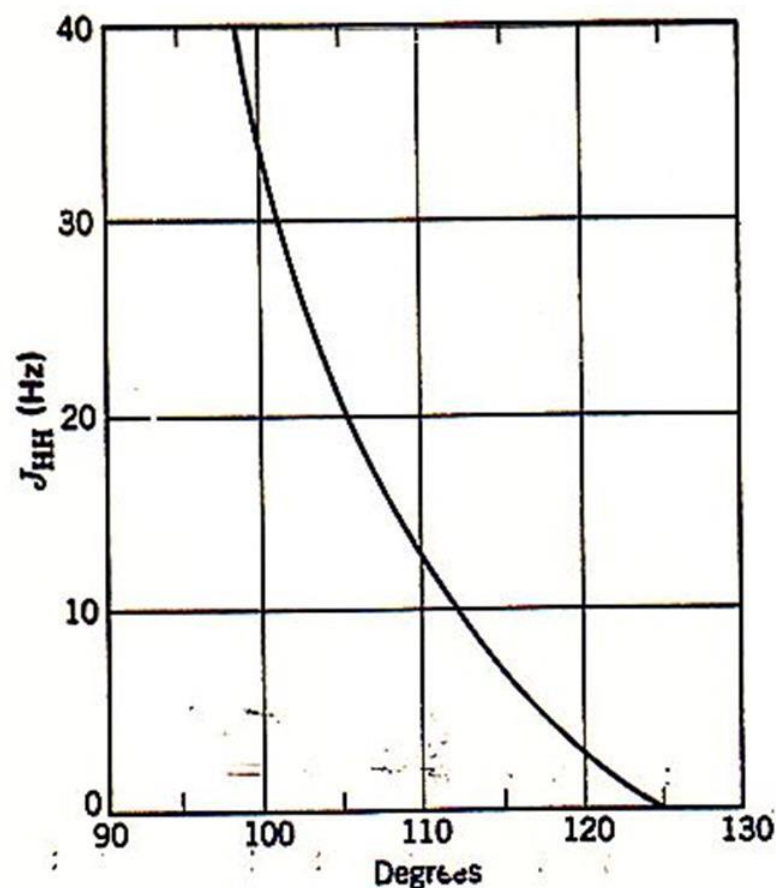
5.1 Hz

8.8 Hz

← increasing angle α

The calculated relationship³² between the H—C—H angle of geminal protons is shown in Figure 47. This relationship is quite susceptible to other influences and should be used with due caution. However, it is useful for characterizing methylene groups in a fused cyclohexane ring (approximately tetrahedral, $J \sim 12$ to 18), methylene groups of a cyclopropane ring ($J \sim 5$), or a terminal methylene group ($J \sim 0$ to 3).

methylene to a chiral



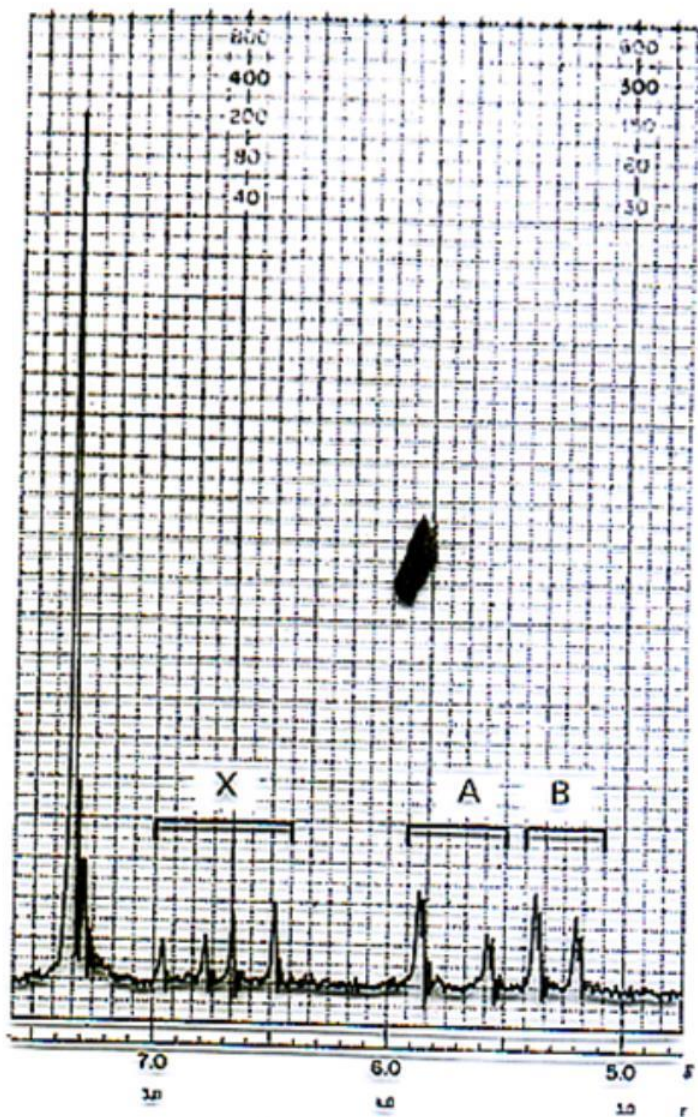
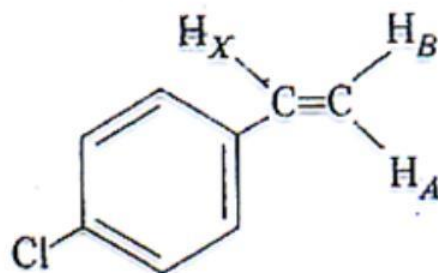
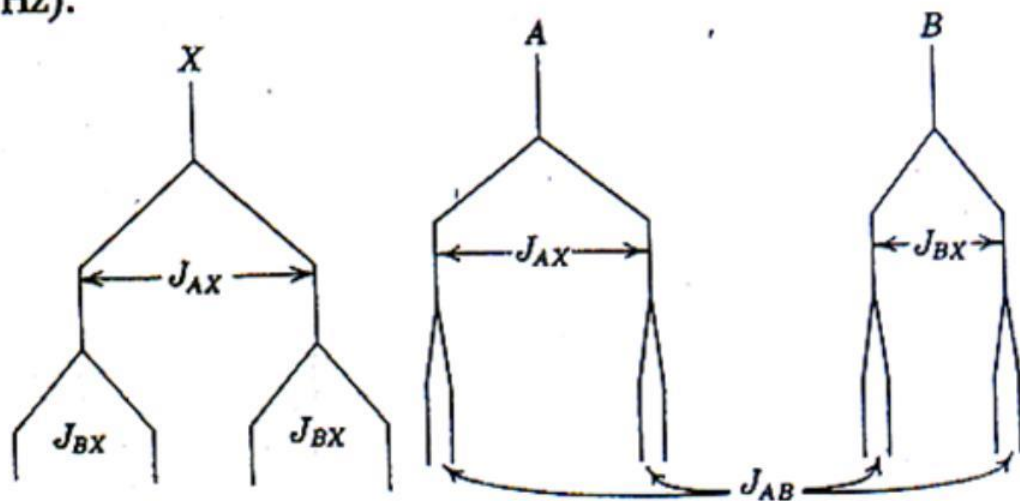


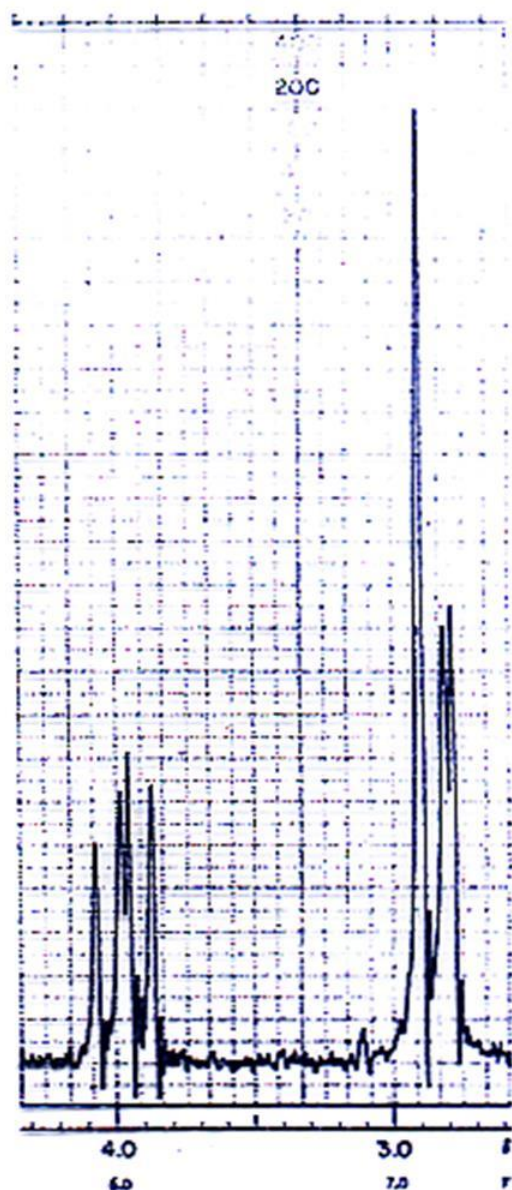
Fig. 41.
p-Chlorostyrene, 60 MHz.



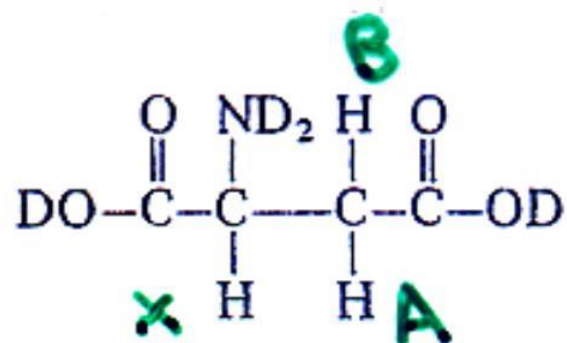
A: κίνηση
αναντ.

Protons A and B are not chemically equivalent. Proton A ($\delta \sim 5.70$) is deshielded about 25 Hz, compared with proton B, because of its relative proximity to the ring. Proton X ($\delta \sim 6.70$) is strongly deshielded by the ring, and is split by proton A ($J \sim 18$ Hz) and by proton B ($J \sim 11$ Hz). The A proton is split by the X proton ($J \sim 18$ Hz) and by the B proton ($J \sim 2$ Hz). The B proton is split by the X proton ($J \sim 11$ Hz) and by the A proton ($J \sim 2$ Hz).





Aspartic acid in D_2O ,

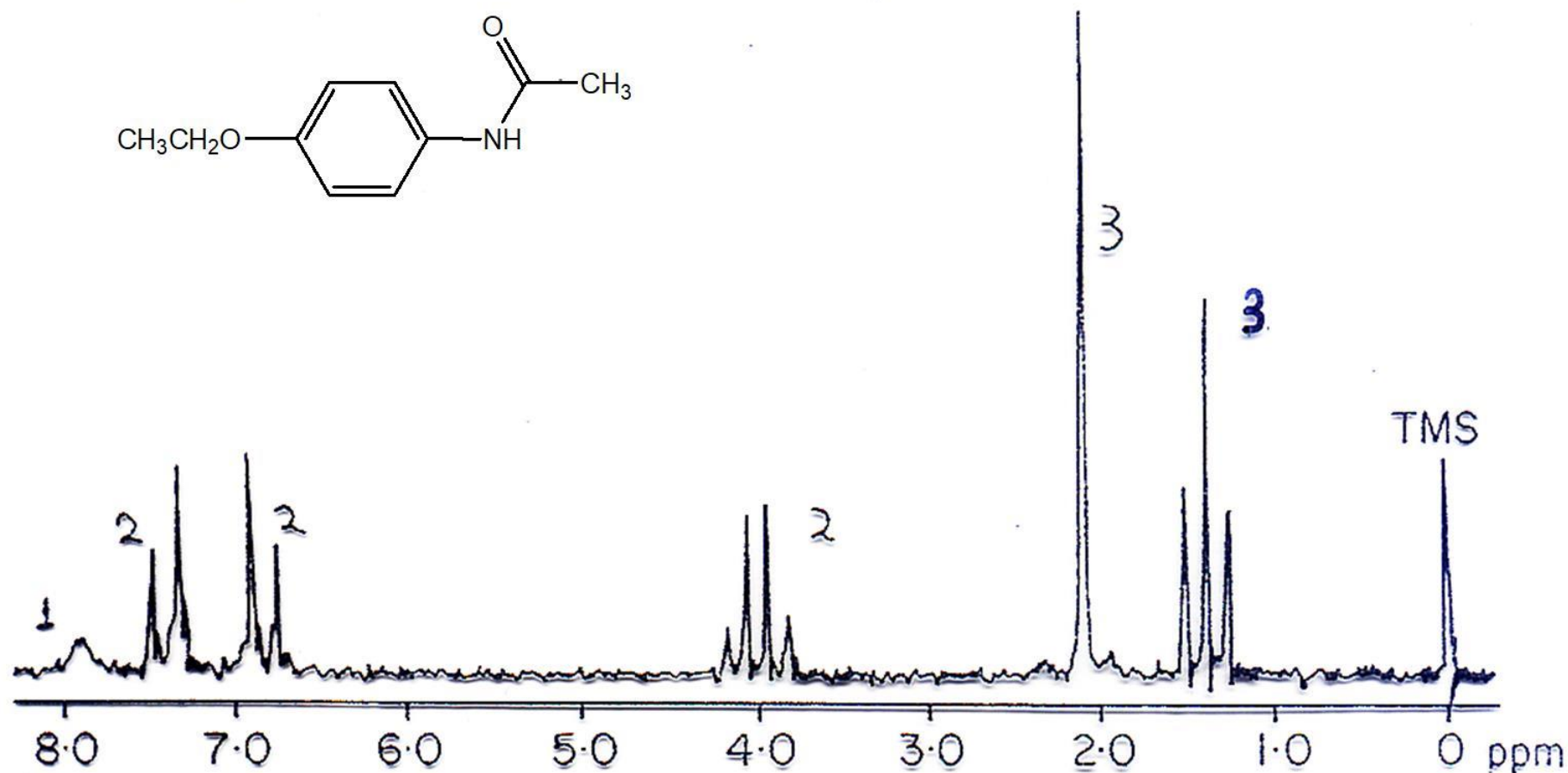
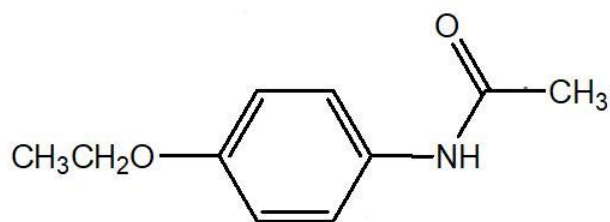


Index of Unsaturation

In the course of this book we are going to be solving many problems like the one in Example 6.7. Here is a little "trick" to make the process a little easier. Whenever you encounter a molecular formula $C_cH_hN_nO_oX_x$ (where X represents halogen: F, Cl, Br, or I), begin by calculating its **index of unsaturation (IOU)** from the equation

$$IOU = \frac{1}{2} [2c + 2 + n - (h + x)]$$

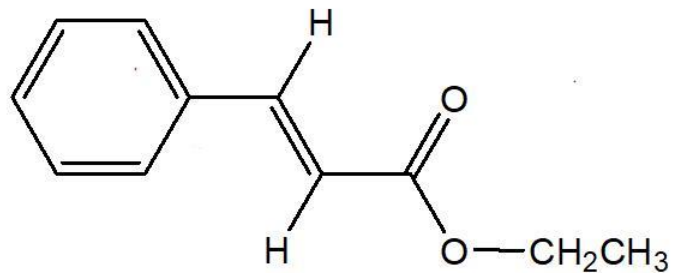
This equation derives from the normal valencies of (number of bonds to) atoms of carbon, nitrogen, hydrogen, and halogen (4, 3, 1, and 1, respectively) in molecules where all valences are satisfied (divalent atoms such as oxygen and sulfur do not appear in the equation). The IOU tells us how many rings plus π bonds there must be in any legitimate isomer with that molecular formula. Recall that a double bond is usually pictured as one cylindrically symmetric σ bond and one π bond between two parallel p orbitals. A triple bond consists of one σ bond and two π bonds. The IOU, therefore, is very useful in quickly eliminating from consideration any structures that do not possess the correct number of rings plus π bonds. Thus, the IOU of C_2H_3N (Example 6.7) is $[2(2) + 2 + 1 - 3]/2 = 2$, so the correct structure must have either two rings or one ring and one π bond (i.e., one double bond) or two π bonds (two double bonds or one triple bond). The $CH_3C \equiv N$ molecule fits in the last category.



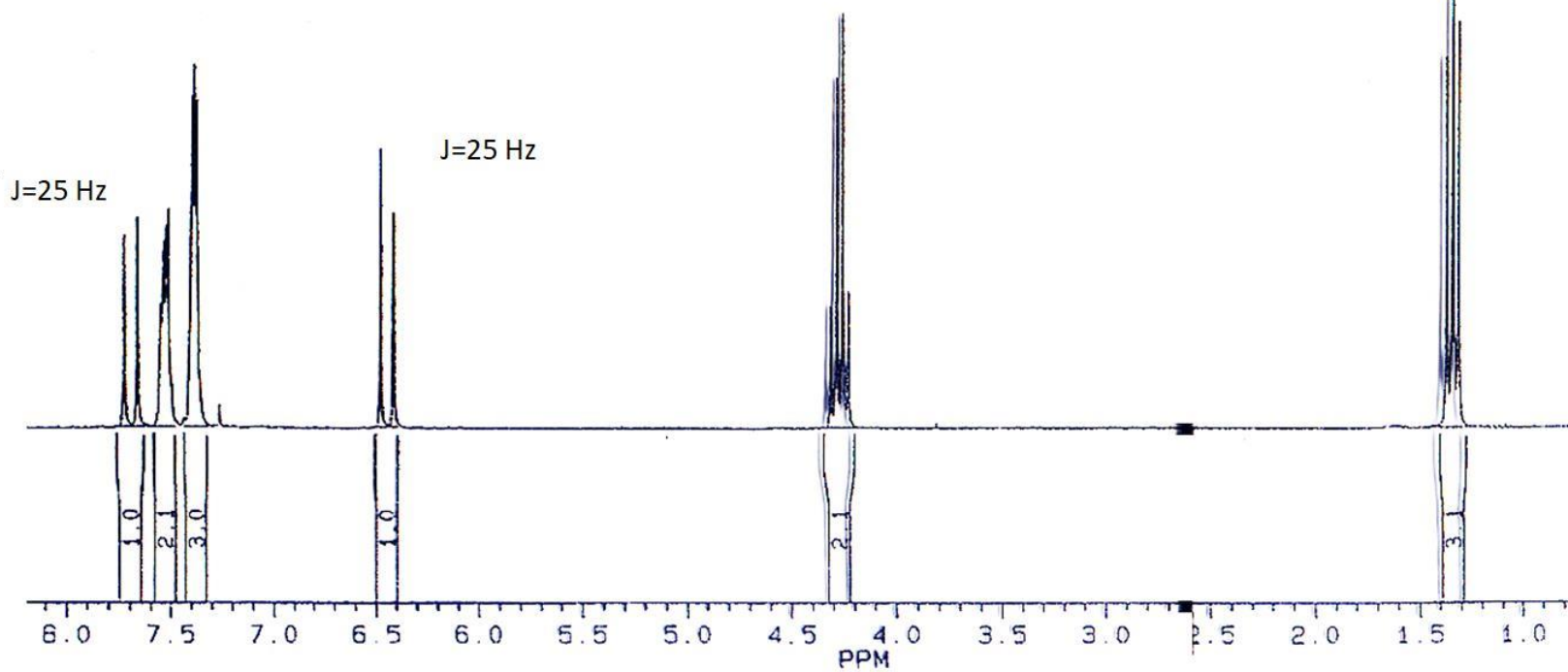
The n.m.r. spectrum of $\text{C}_{10}\text{H}_{13}\text{NO}_2$.

$$\text{IOU} = \frac{2C + 2 + N - (H + X)}{2} = \frac{20 + 2 + 1 - 13}{2} = 5$$

$$\text{IOU} = \frac{2C+2+N-(H+X)}{2} = \frac{22+2-12}{2} = 6$$



$\text{C}_{11}\text{H}_{12}\text{O}_2$



The 250-MHz ^1H spectrum

7.1 ^{13}C CHEMICAL SHIFTS REVISITED

In Chapter 6 we developed an understanding of the relationships between the molecular environment of a hydrogen atom and the chemical shift of its nucleus. Now let us see if the same approach of base values plus substituent parameters [Eq. (6.5b)] will allow us to predict ^{13}C chemical shifts. Recall from Sections 2.1 and 2.2 that ^{13}C (like ^1H) has a nuclear spin of $\frac{1}{2}$ but undergoes resonance at a much lower frequency than ^1H because of the lower magnetogyric ratio of ^{13}C . Also, the low natural abundance and low relative sensitivity of ^{13}C (Table 2.1) require that the signal-averaged pulsed-mode technique (Section 3.4) be used for data collection. Remember that TMS (its carbon signal now) still defines the zero point of our chemical shift scale and that ^{13}C chemical shifts span a range of about 250 ppm. And finally, unless otherwise noted, all ^{13}C spectra discussed in this chapter are proton decoupled (Section 5.5).

7.2 TETRAHEDRAL (sp^3 HYBRIDIZED) CARBONS

Take a moment to review the ^{13}C spectra of toluene in Section 5.4. How would you go about predicting the ^{13}C chemical shift of the methyl group in toluene? The logical base value is the ^{13}C chemical shift of methane (which, it turns out, is $\delta -2.3$, Table 7.1), to which we add the ^{13}C substituent parameter of a phenyl ring connected directly to the methyl carbon ($\Delta\delta = 23$, Table 7.2). The predicted value, therefore, is $\delta 20.7$, in excellent agreement with the observed value of $\delta 21.4$. Table 7.1 lists ^{13}C chemical shifts for a number of common alkanes and cycloalkanes, to be used as base values. Table 7.2 gives the substituent parameters for many common substituent groups as a function of their proximity to the carbon of interest (α = one-bond separation, β = two-bond separation, γ = three-bond separation). Notice once again that the

(de)shielding effect of a substituent tends to decrease as the number of intervening bonds increases. In fact, most groups exert a modest shielding effect (shown by the negative value of $\Delta\delta$) on the γ carbon.

TABLE 7.1 ^{13}C Chemical Shifts for Common Alkanes and Cycloalkanes^a

Name	Structure	C1 ^b	C2	C3
Methane	CH_4	-2.3		
Ethane	CH_3CH_3	5.7		
Propane	$\text{CH}_3\text{CH}_2\text{CH}_3$	15.8	16.3	
Butane	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_3$	13.4	25.2	
Pentane	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	13.9	22.8	34.7
Hexane	$\text{CH}_3\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$	14.1	23.1	32.2
Cyclopropane	Cyclo-(CH_2) ₃	-3.5		
Cyclobutane	Cyclo-(CH_2) ₄	22.4		
Cyclopentane	Cyclo-(CH_2) ₅	25.6		
Cyclohexane	Cyclo-(CH_2) ₆	26.9		
Cycloheptane	Cyclo-(CH_2) ₇	28.4		
Cyclooctane	Cyclo-(CH_2) ₈	26.9		

TABLE 7.2 ^{13}C Substituent Parameters ($\Delta\delta$, ppm)^a

X	Terminal X $\text{X}-\text{C}_\alpha-\text{C}_\beta-\text{C}_\gamma$			Internal X $\text{C}_\gamma-\text{C}_\beta=\text{C}_\alpha(\text{X})-\text{C}_\beta-\text{C}_\gamma$		
	α	β	γ	α	β	γ
-F	68	9	-4	63	6	-1
-NO ₂	63	4	—	57	4	—
-OR	58	8	-4	51	5	-4
-OC(=O)R	51	6	-3	45	5	-3
-OH	48	10	-5	41	8	-5
-NR ₂	42	6	-3	—	—	—
-NHR	37	8	-4	31	6	-4
-C(=O)Cl	33	—	—	28	2	—
-Cl	31	11	-4	32	10	-4
-C(=O)H	—	31	-2	0	—	-2
-C(=O)R	30	1	-2	24	1	-2
-NH ₂	29	11	-5	24	10	-5
-N ⁺ H ₃	26	8	-5	24	6	-5
-C(=O)O ⁻	25	5	-2	20	3	-2
-Phenyl	23	9	-2	17	7	-2
-C(=O)NH ₂	22	—	-0.5	2.5	—	-0.5
-C(=O)OH	21	3	-2	16	2	-2
-CH=CH ₂	20	6	-0.5	—	—	—
-C(=O)OR	20	3	-2	17	2	-2
-Br	20	11	-3	25	10	-3
-SR	20	7	-3	—	—	—
-SH	11	12	-4	11	11	-4
-CH ₃	9	10	-2	6	8	-2
-C≡C-H	4.5	5.5	-3.5	—	—	—
-C≡N	4	3	-3	1	3	-3
-I	-6	11	-1	4	12	-1

TABLE 7.5 ^{13}C Chemical Shift Ranges of Carbonyl Compounds

Compound class	Structure	δ (ppm)
Ketone	$\text{R}-\text{C}(=\text{O})-\text{R}$	195–220
Aldehyde	$\text{R}-\text{C}(=\text{O})-\text{H}$	190–200
Carboxylic acid	$\text{R}-\text{C}(=\text{O})-\text{OH}$	170–185
Carboxylate ester	$\text{R}-\text{C}(=\text{O})-\text{OR}$	165–175
Anhydride	$\text{R}-\text{C}(=\text{O})-\text{O}-\text{C}(=\text{O})-\text{R}$	165–175
Amide	$\text{R}-\text{C}(=\text{O})-\text{NR}_2$	160–170
Acid halide	$\text{R}-\text{C}(=\text{O})-\text{X} (\text{X} = \text{Cl}, \text{Br}, \text{I})$	160–170
Carbon monoxide	CO	183.4
Carbon dioxide	CO_2	124.8

In addition to their characteristic downfield positions, carbonyl carbons can also be recognized by their relatively low intensity. Except in the case of a formyl carbonyl [one attached directly to a hydrogen, $-\text{C}(=\text{O})\text{H}$], there are no hydrogens attached to carbonyl carbons, so their signal cannot benefit from NOE enhancement. Carbonyl carbons also tend to have longer T_1 relaxation times than many other carbons, another cause of lower intensities in a signal-averaged pulsed-mode spectrum (Section 5.4.1).

The nuclear Overhauser effect is the enhancement of intensity of an NMR signal generated by one nucleus when it is near another nonequivalent nucleus being simultaneously irradiated. We will discuss this effect in more detail later (Chapter 12), but for now, here is its most significant result: Among carbons with otherwise similar molecular environments (e.g., tetrahedral), the more hydrogens directly attached to a given carbon, the more intense will be its signal. This fact helps us assign the phenyl ring carbon signals to the various positions in toluene. The weakest signal (at δ 137.6) must correspond to the carbon lacking hydrogens, the one bearing the methyl group. Each of the remaining ring carbons has a single hydrogen attached, but there are two equivalent ortho carbons, two equivalent meta carbons, and only one para carbon. The second weakest signal at 125.6 ppm can therefore be assigned to the para carbon. The remaining two signals are harder to assign, especially since their relative intensity depends on the exact parameters of the pulse sequence (see Table 5.2). We will learn more in Chapter 7 about assigning such signals, but it turns out that the δ 128.5 signal results from the meta carbons, while the δ 129.2 signal is due to the ortho carbons. Empirically, we notice that the closer a ring carbon is to the methyl group, the farther downfield its signal occurs.

Finally, notice that the signal for the methyl carbon, with three hydrogens directly attached, is slightly *less* intense than the signal for the para carbon (with one hydrogen attached). This is because the molecular environment of the methyl carbons involves sp^3 hybridization (four single bonds), while the phenyl ring carbons are all sp^2 hybridized (two single bonds and one aromatic double bond). These differences in bonding environment (and the associated changes in relaxation times) more than offset the Overhauser enhancement factor.

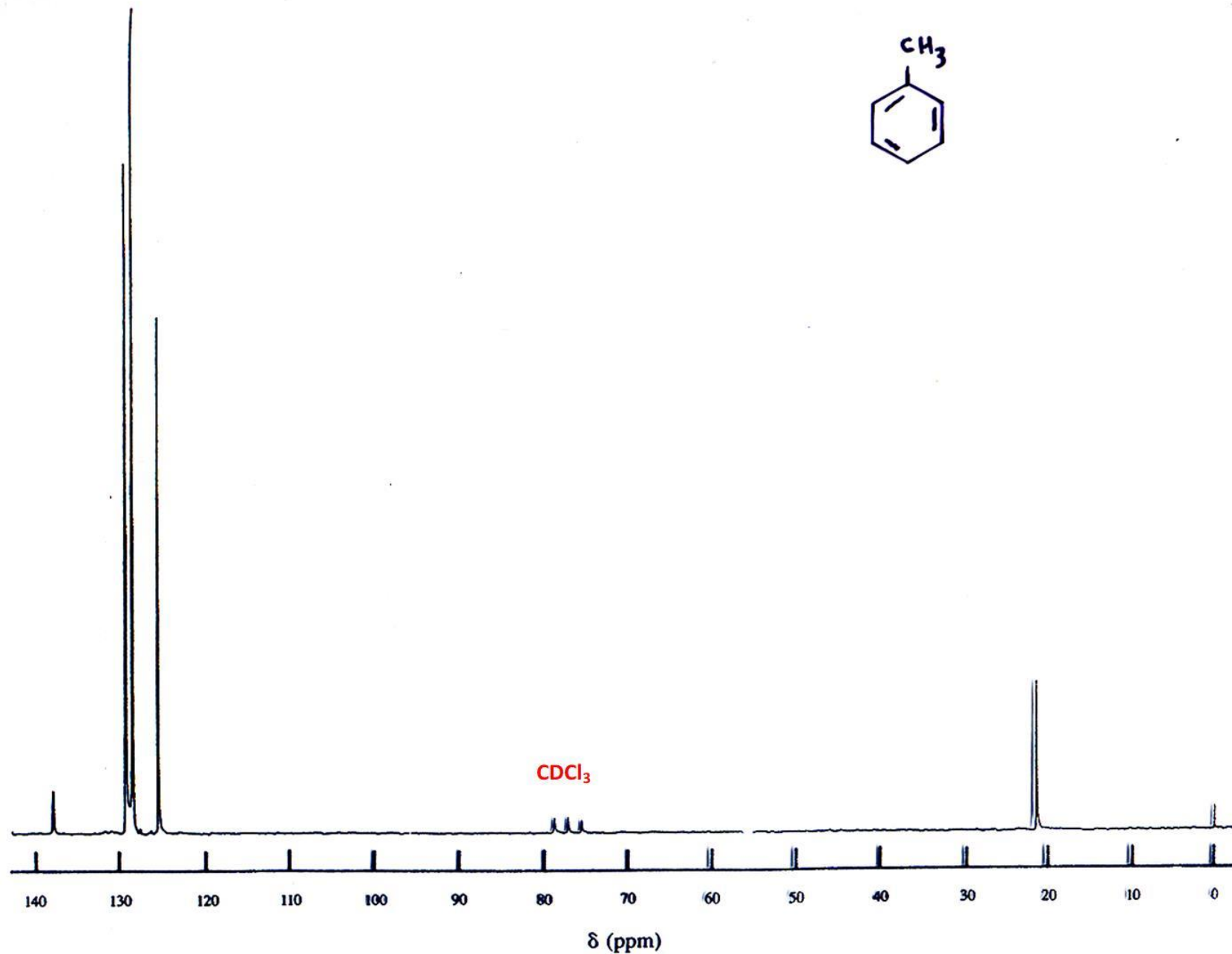
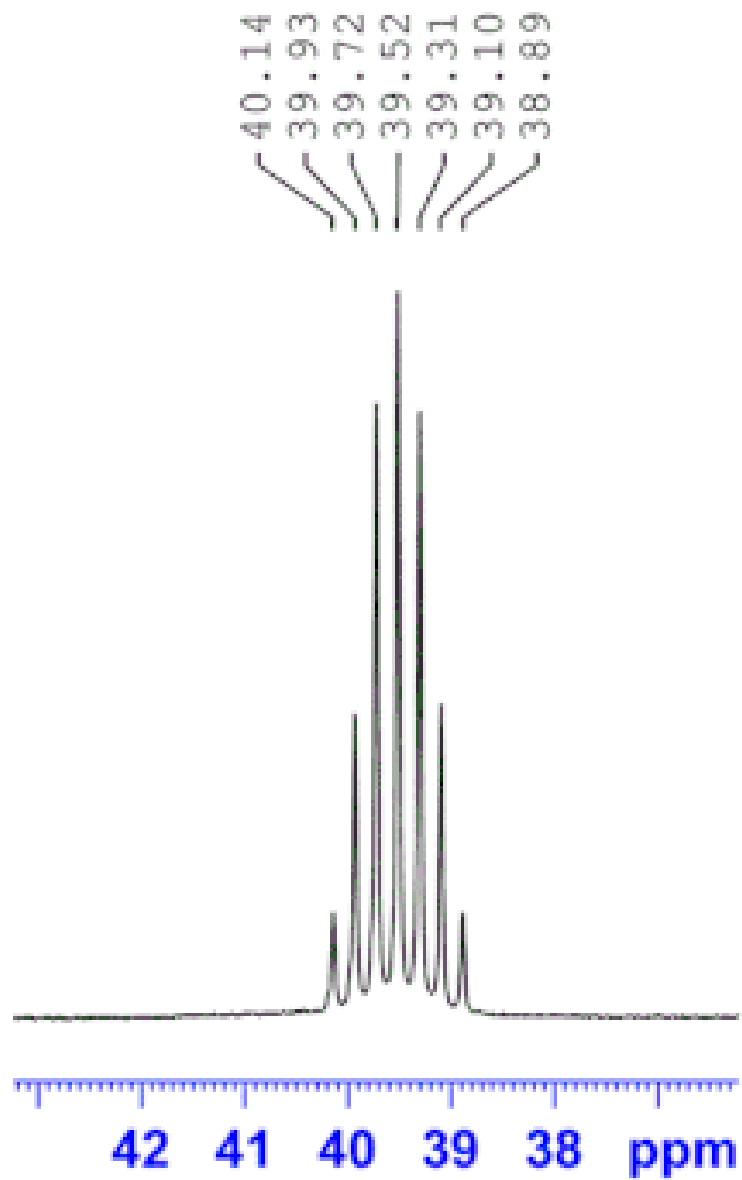
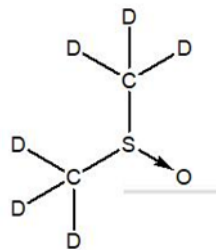


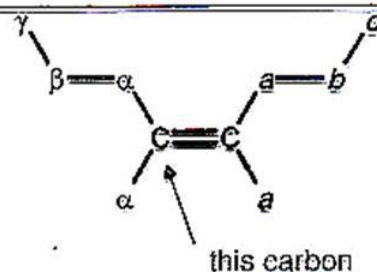
Figure 5.5. The 20.1-MHz ^{13}C spectrum of toluene.



We will treat molecules with vinyl carbons as derivatives of ethylene ($\text{H}_2\text{C}=\text{CH}_2$, Section 6.3), whose ^{13}C signal appears at δ 123.3.¹ To this base value, we will apply $\Delta\delta$ corrections (Table 7.3) for substituents according to their location with respect to the carbon of interest.

TABLE 7.3 Vinyl Carbon Substituent Parameters ($\Delta\delta$, ppm)^{a,b}

ethylene δ : 123.3

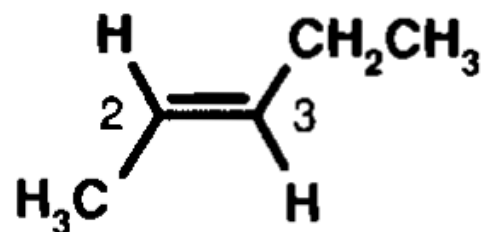


X	α	β	γ	a	b	c
-R	10.6	7.2	-1.5	-7.9	-1.8	-1.5
-OR	29	2	—	-39	-1	—
-OC(=O)R	18	—	—	-27	—	—
-C(=O)R	15	—	—	6	—	—
-Phenyl	12	—	—	-11	—	—
-C(=O)OR	6	—	—	7	—	—
-C(=O)OH	4	—	—	9	—	—
-OH	—	6	—	—	-1	—
-Cl	3	-1	—	-6	2	—
-Br	-8	0	—	-1	2	—
-C \equiv N	-16	—	—	15	—	—
-I	-38	—	—	7	—	—

^aData from refs. 1 and 4. R = alkyl.

^bWhen a group is in the b (or β) position, X_a (or X_α) is assumed to be carbon; when a group is in the c (or γ) position, both X_a and X_b (or X_α and X_β) are assumed to be carbon.

■ **EXAMPLE 7.7** Predict the chemical shift of the two vinyl carbons in *trans*-2-pentene:



- **Solution:** Carbon 2 has alkyl carbon substituents at positions α , a , and b . Therefore, $\delta_2 = \delta(\text{C}_2\text{H}_4) + \Delta\delta(\text{R}, \alpha) +$

$$\Delta\delta(R, a) + \Delta\delta(R, b) = 123.3 + 10.6 + (-7.9) + (-1.8) = 124.2$$

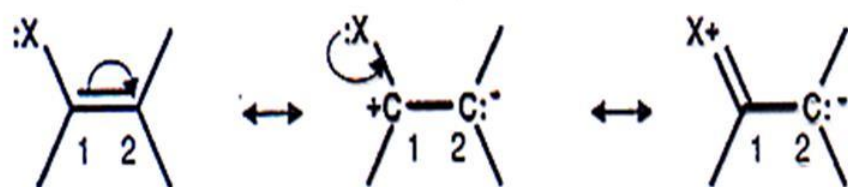
Similarly,

$$\begin{aligned}\delta_j &= \delta(C_2H_4) + \Delta\delta(R, \alpha) + \Delta\delta(R, a) + \Delta\delta(R, \beta) \\ &= 123.3 + 10.6 + (-7.9) + 7.2 = 133.2\end{aligned}$$

The observed values are δ 123.7 and 133.3, respectively. \square

Table 7.3 includes substituent parameters for several heteroatom-containing substituents. Notice that there is a very large difference between the $\Delta\delta$ value for a group located at the α position and the value for the same group at the β position. This is because the π electrons in the carbon-carbon double bond interact directly through resonance with many of these substituents, causing substantial shielding when at the α position and deshielding when at the β position, or vice versa.

For example, an atom X with an unshared pair of electrons (e.g., $X = \text{OR}, \text{NR}_2, \text{S}$, or halogen) can donate the pair to (i.e., share it with) the π system, as shown in the resonance structures below. This interaction increases the electron density at carbon 2 (thereby shielding it), while decreasing the electron density on carbon 1 and X (deshielding them):



Conversely, if atom X has an empty p -type valence orbital (e.g., $X = \text{C}=\text{O}, \text{C}\equiv\text{N}, \text{NO}_2$), it can withdraw a pair of electrons from the π bond, significantly deshielding carbon 2 while shielding X:

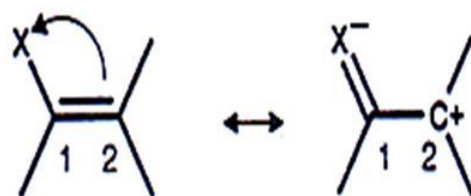
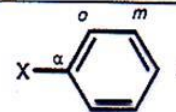


TABLE 7.4 Aromatic Substituent Parameters ($\Delta\delta$, ppm)Benzene: 128.5

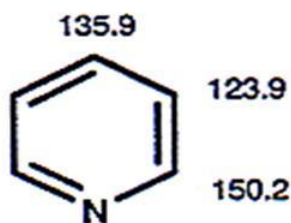
Aromatic Carbons

In the case of aromatic carbons, we will use as our base value the ^{13}C chemical shift of benzene (Example 4.3), δ 128.5. Notice that aromatic carbons appear slightly downfield of vinyl carbons, just as aromatic hydrogens appear downfield of vinyl hydrogens (Sections 6.3 and 6.5). Table 7.4 lists substituent parameters for a number of aromatic substituents as a function of proximity to a given carbon. Observe how, for many of these groups, their effect alternates back and forth from deshielding to shielding as the number of intervening bonds increases. This is a consequence of the changing balance between competing inductive and resonance effects of the substituent as a function of location.

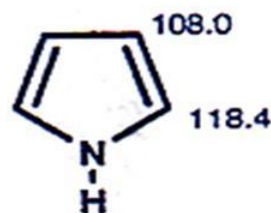
X	α	<i>o</i> (Ortho)	<i>m</i> (Meta)	<i>p</i> (Para)
-F	35.1	-14.3	0.9	-4.5
-OCH ₃	31.4	-14.4	1.0	-7.7
-OPh	29.0	-9.4	1.6	-5.3
-OH	26.6	-12.7	1.6	-7.3
-OC(=O)CH ₃	22.4	-7.1	-0.4	-3.2
-N(CH ₃) ₂	22.4	-15.7	0.8	-11.8
-C(CH ₃) ₃	22.2	-3.4	-0.4	-3.1
-CH(CH ₃) ₂	20.1	-2.0	0	-2.5
-NO ₂	19.6	-5.3	0.9	6.0
-NH ₂	19.2	-12.4	1.3	-9.5
-CH ₂ CH ₃	15.6	-0.5	0.0	-2.6
-S(O) ₂ NH ₂	15.3	-2.9	0.4	3.3
-Si(CH ₃) ₃	13.4	4.4	-1.1	-1.1
-CH ₂ OH	13.3	-0.8	-0.6	-0.4
-phenyl	12.1	-1.8	-0.1	-1.6
-NHC(=O)CH ₃	11.1	-9.9	0.2	-5.6
-SCH ₃	10.2	-1.8	0.4	-3.6
-CH ₃	9.3	0.7	-0.1	-2.9
-CH=CH ₂	9.1	-2.4	0.2	-0.5
-C(=O)Ph	9.1	1.5	-0.2	3.8
-C(=O)H	8.2	1.2	0.6	5.8
-C(=O)CH ₃	7.8	-0.4	-0.4	2.8
-CH ₂ OC(=O)CH ₃	7.7	0	0	0
-Cl	6.4	0.2	1.0	-2.0
-N=C=O	5.7	-3.6	1.2	-2.8
-C(=O)Cl	4.6	2.9	0.6	7.0
-C(=O)OH	2.9	1.3	0.4	4.3
-CF ₃	2.6	-3.1	0.4	3.4
-SH	2.3	0.6	0.2	-3.3
-C(=O)OCH ₃	2.0	1.2	-0.1	4.8
-Br	-5.4	3.4	2.2	-1.0
-C(=O)CF ₃	-5.6	1.8	0.7	6.7
-C \equiv CH	-5.8	6.9	0.1	0.4
-C \equiv N	-16.0	3.6	0.6	142 4.3
-I	-32.2	9.9	2.6	-7.3

Heteroaromatic Compounds

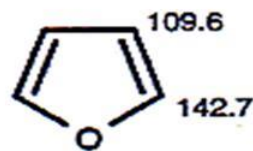
As was true for the hydrogens attached to heteroaromatic rings and polycyclic aromatic hydrocarbons (Section 6.5), the carbons of such rings also appear in the aromatic region. Some examples are given below,¹ and these can be used as base values when calculating chemical shifts for substituted derivatives of these compounds:



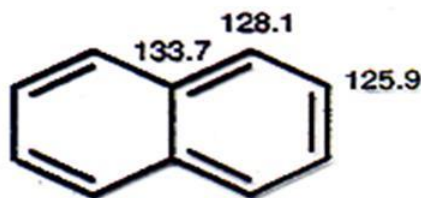
pyridine



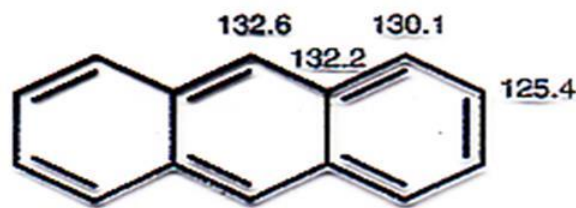
pyrrole



furan



naphthalene



anthracene

TRIPLY BONDED CARBONS

Recall (Section 6.4) that hydrogens attached to triply bonded carbons (*acetylenic* hydrogens) are unusually shielded because of the magnetic field anisotropy in the region of the triple bond. Exactly the same is true of acetylenic carbons themselves. Triply bonded (*sp*-hybridized) carbons usually appear in the δ 70–90 region, significantly upfield of typical vinyl and aromatic carbons. This is a region of the spectrum where relatively few other types of carbons are found. Acetylenic carbons are classified as either *terminal* (if they have a hydrogen directly attached) or *internal* (if they have a carbon attached). Signals for internal acetylenic carbons are usually downfield of and less intense than the signals for terminal ones. This is because of the deshielding effect of the carbon substituent (Table 7.2) and the absence of the intensity-increasing NOE (Section 5.4.1) due to the attached hydrogen.

Another important triply bonded carbon is the one in a cyano group ($-\text{C}\equiv\text{N}$). Because of the higher electronegativity (and hence deshielding effect) of the nitrogen, cyano carbons occur downfield of acetylenic carbons, usually around δ 115–120. And remember: With no hydrogens attached, they usually give fairly weak signals.

MISCELLANEOUS UNSATURATED CARBONS

There is a host of less common functional groups that involve unsaturated (i.e., multiply bonded) carbon and appear in the same downfield region of the ^{13}C spectrum as carbonyls, for example, the central (sp hybridized) carbon of an allene linkage ($\text{C}=\text{C}=\text{C}$). Such carbons give very weak signals

(why?) in the δ 200–215 region. The two outer carbons, by contrast, are more shielded than typical vinyl carbons (Section 7.4) and appear in the δ 75–95 range. Table 7.6 lists some additional examples.

SUMMARY OF ^{13}C CHEMICAL SHIFTS

The range of ^{13}C chemical shifts is shown graphically in Figure 7.2. This is a useful place to start when trying to identify an unknown compound from its ^{13}C spectrum. But remember that these ranges represent only generalizations and that certain combinations of substituents will cause a carbon signal to show up outside the confines of its "normal" region.

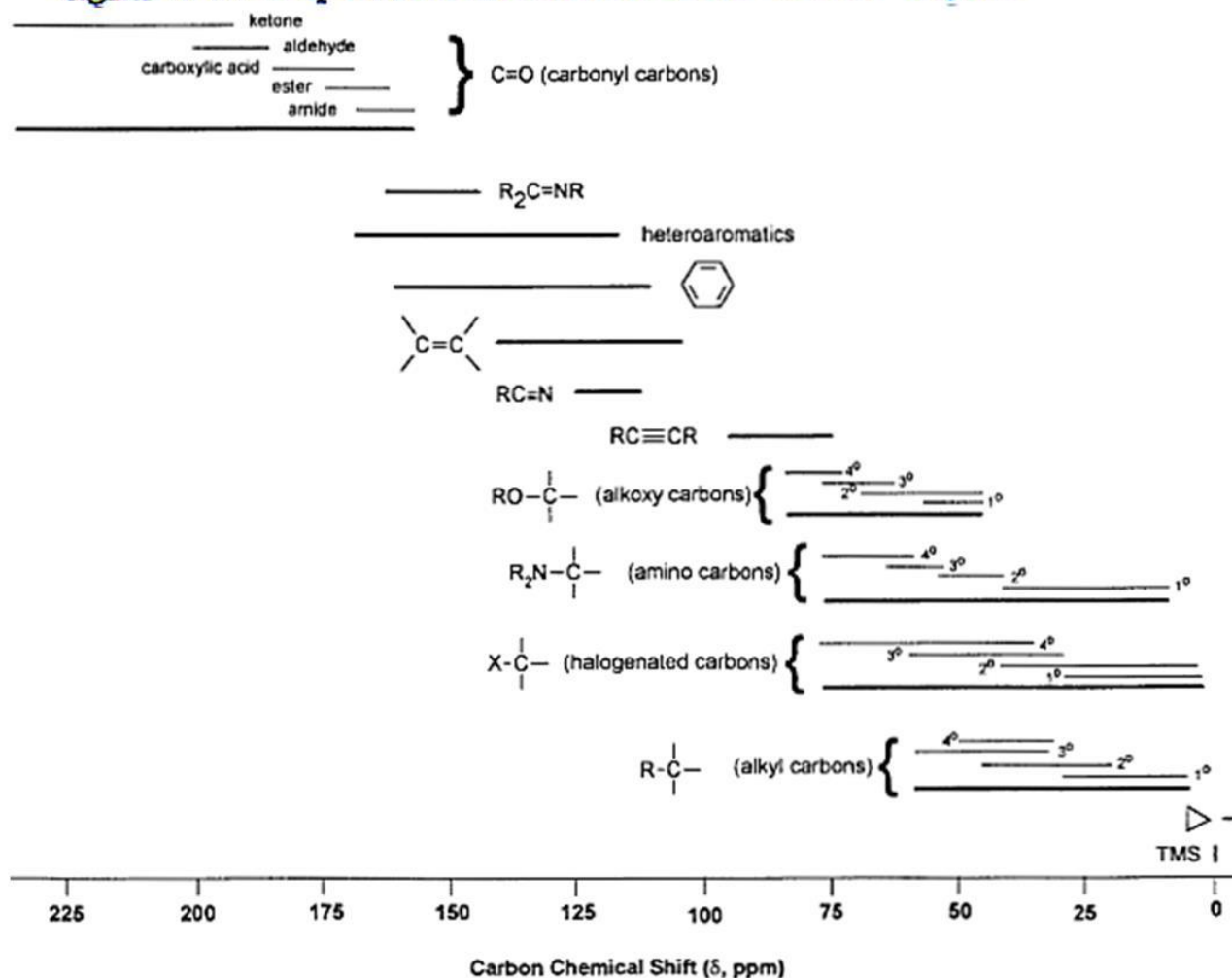


Figure 7.2. Pictorial representation of the ^{13}C chemical shift ranges for various classes of carbons.

Notice the similarity of Figure 7.2 with the corresponding one for hydrogen chemical shifts (Figure 6.8). This parallel behavior is because *in general* (there are exceptions) a carbon and the hydrogens attached directly to it both experience similar shielding and deshielding effects of neighboring substituents. To demonstrate the validity of this assertion, Figure 7.3 shows a plot of ^1H chemical shifts for 335 different hydrogens versus the ^{13}C chemical shifts of the carbons to which they are directly bonded.⁷ The linear relationship, expressed by Eqs. (7.1a) and (7.1b), exhibit a correlation coefficient of 0.95 over a wide variety of molecular environments:

$$\delta_{\text{H}} = 0.0479\delta_{\text{C}} + 0.472 \quad (7.1a)$$

$$\delta_{\text{C}} = 20.9\delta_{\text{H}} - 9.85$$

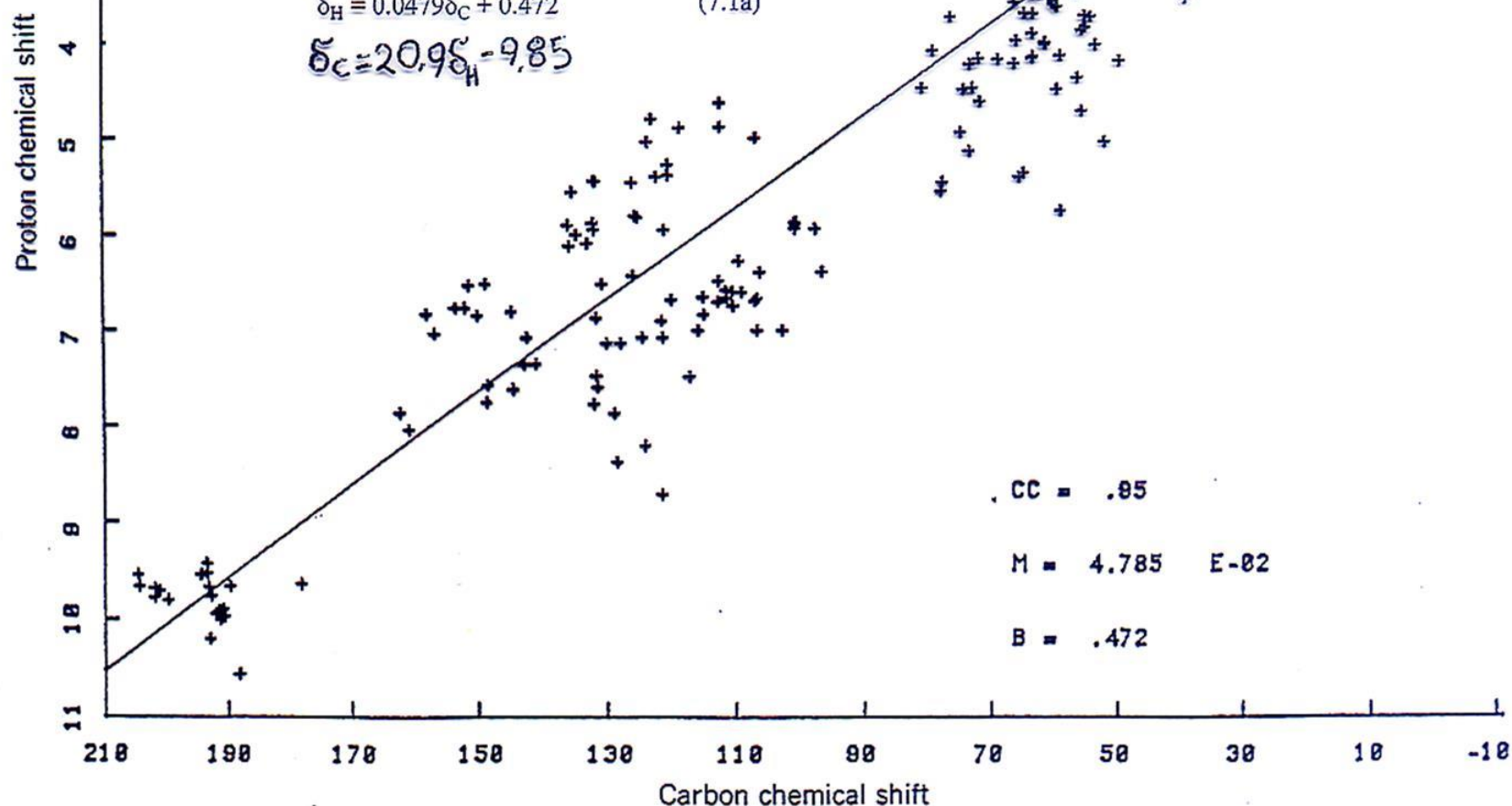


Figure 7.3. Graphical comparison of ^1H chemical shifts of C-H hydrogens versus the ^{13}C chemical shift of the attached carbon.

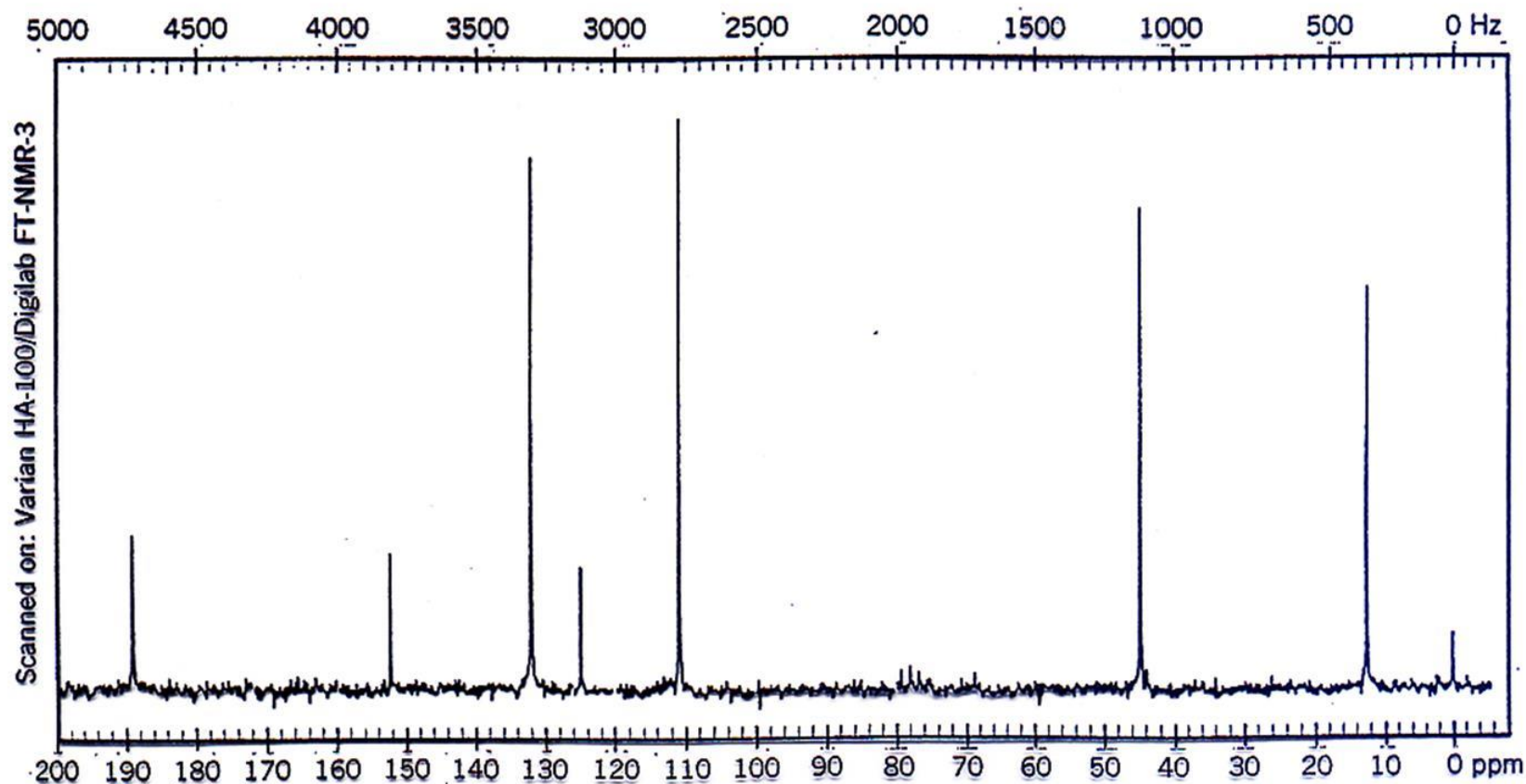
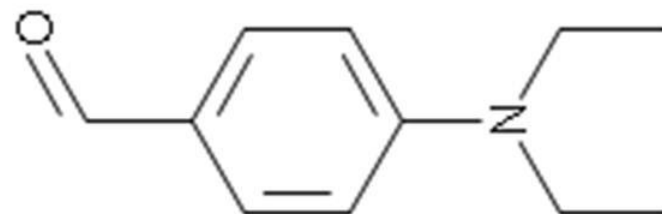


Figure 7.8. The 20-MHz ^{13}C spectrum of $\text{C}_{11}\text{H}_{15}\text{NO}$. © Sadtler Research Laboratories, Division of Bio-Rad Laboratories, Inc. (1983).

$$\text{IOU} = \frac{2C + 2 + N - (H + X)}{2} = \frac{22 + 2 + 1 - 15}{2} = 5$$

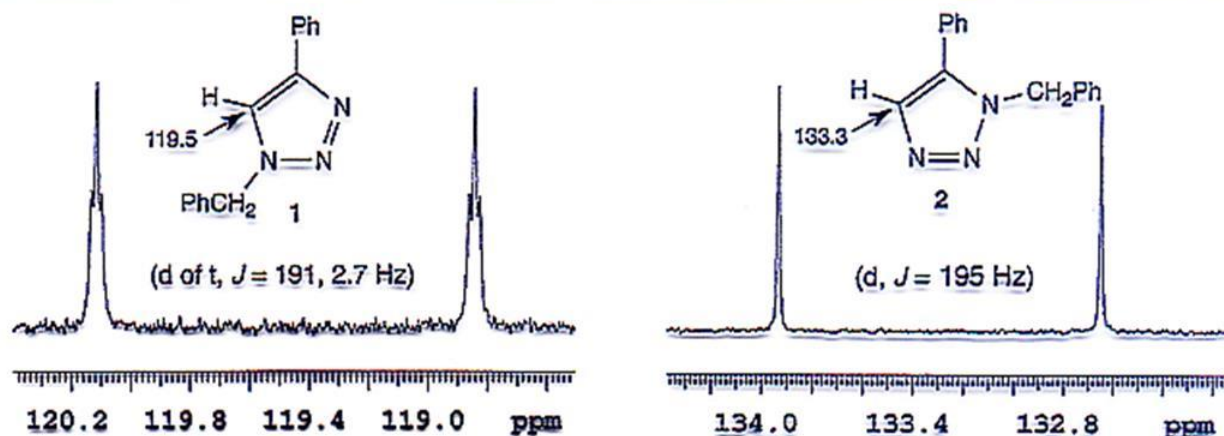


Method for Assigning Structure of 1,2,3-Triazoles

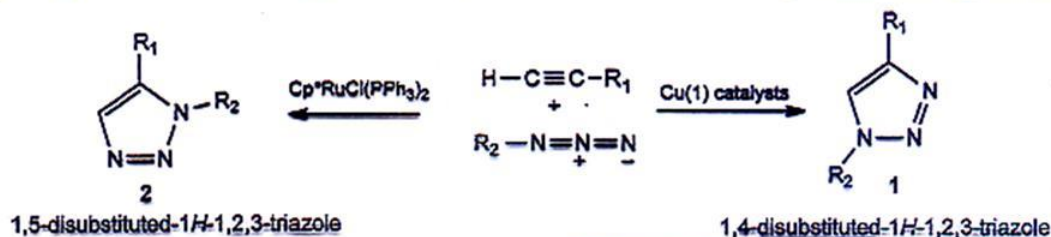
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Supporting Information



ABSTRACT: 1,4-Disubstituted-1H-1,2,3-triazoles 1 can easily be distinguished from the isomeric 1,5-disubstituted-1H-1,2,3-triazoles 2 by simple one-dimensional ^{13}C NMR spectroscopy using gated decoupling. The C_5 signal of 1 appears at $\delta \sim 120$ ppm, while the C_4 signal of 2 appears at $\delta \sim 133$ ppm. Computational studies also predict the upfield shift of C_5 of 1 relative to C_4 in 2.



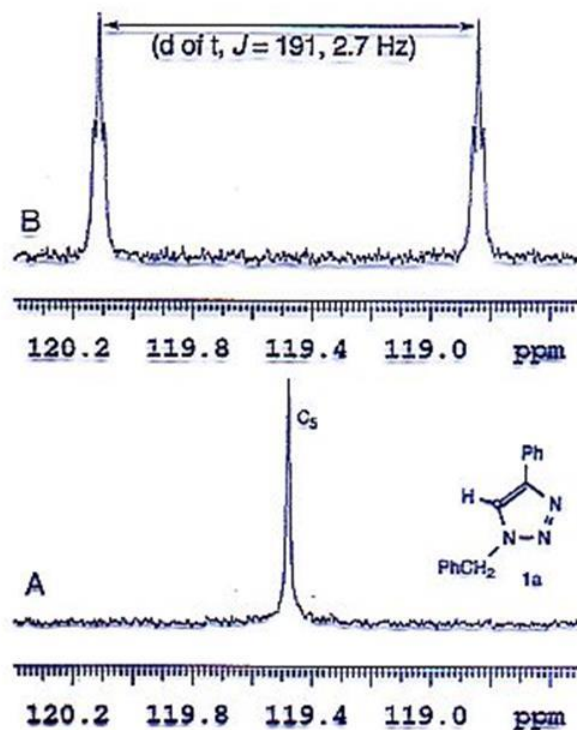


Figure 1. (A) Expanded ^{13}C NMR of **1a**. (B) ^1H coupled ^{13}C NMR of **1a**.

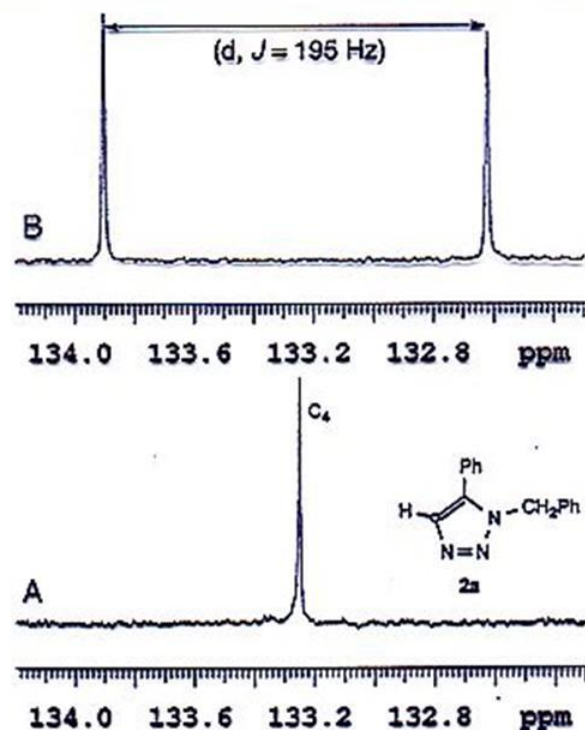


Figure 2. (A) Expanded ^{13}C NMR of **2a**. (B) ^1H coupled ^{13}C NMR of **2a**.