

CHEM / BCMB 4190/6190/8189

Introductory NMR

Lecture 4

Chemical Shift:

In a diamagnetic molecule, the effective magnetic field (B_{eff}) is always less than the applied magnetic field (B_0).

$$B_{\text{eff}} = B_0 (1 - \sigma)$$

σ – the shielding constant is independent of magnetic field strength.

New Resonance Condition:

$$\nu_1 = \gamma(1 - \sigma)B_0/2\pi$$

the reduction in B_0 is determined mainly by the distribution of electron density.

Chemical shifts are greatly affected by substituents which specifically influence this distribution.

How does it happen?

1. Through bonds.
2. Through Space.

Reference Compounds and the δ scale:

Internal Standard (example TMS):

$$\delta = \frac{\nu_{\text{sample}} - \nu_{\text{reference}}}{\nu_{\text{reference}}} \times 10^6$$

$$\delta = \Delta\nu / \text{observing frequency} \times 10^6$$

$$\delta (\text{TMS}) = 0$$

δ is independent of the magnetic field strength.

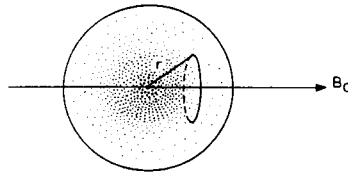
Influence of Charge density on Shielding:

B_0 induces an electron current in the electron shell and this causes an opposing field at the position of the nucleus.

For Hydrogen atom (1 electron):

$$B_{\text{eff}} = B_0 - 4\pi e^2 B_0 / 3M_e c^2 \int r \rho(r) dr$$

$\rho(r)$ describes the electron density as a function of the distance r from the nucleus



Electron currents in a magnetic field.

$$\sigma = \frac{4\pi Z e^2}{3M_e c^2} \int_0^{\infty} r \rho(r) dr$$

Z = Atomic number

Reality:

- electron distribution about a nuclei in a molecule do not display spherical symmetry.
- Larmor precession of the electron system about the field direction is now impeded by presence of other nuclei.
- Need a second term to describe effect of non-spherical charge distribution.

Since this will not adequately define σ it is referred to as σ_{dia} for the diamagnetic shielding term.

σ_{para} is a second term introduced to take into account non-spherical charge distribution.

It is a magnetic moment opposing that of the diamagnetic component

σ_{para} turns out to be very complicated and only have exact calculations for model compounds. But.....

$$\sigma_{\text{para}} \propto 1/\Delta E$$

ΔE is the average electronic excitation energy.

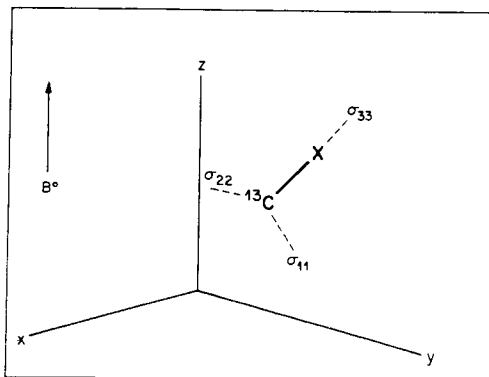
For Hydrogen ΔE is large so σ_{para} is small.

For heavier atoms ΔE is smaller so σ_{para} is larger

But σ_{para} is always less than σ_{dia} .

Chemical Shift Anisotropy:

σ is dependent on its orientation relative to the magnetic field B_0 .



The principal values of the carbon-13 screening tensor, σ_{11} , σ_{22} , and σ_{33} , represented along three mutually perpendicular axes in a laboratory frame for a molecule containing a ^{13}C -X bond. One of these axes, corresponding to σ_{33} , is shown as coinciding with the ^{13}C -X bond, although in general it is not necessary that any of the axes coincide with chemical bonds.

In solution this is averaged out as the result of rapid tumbling so

$$\sigma = (\sigma_{11} + \sigma_{22} + \sigma_{33})/3$$

What effects Shielding at a particular nucleus?

- A. Local diamagnetic currents about the nucleus (σ_{dia})
- B. Local paramagnetic currents about the nucleus (σ_{para})
- C. Current flowing in distant groups (σ_{others})

^1H NMR: the B-component is small but C-component can be significant.

^{13}C NMR: the B-component is also significant because of low lying excited states.

Inductive Effects in ^1H NMR:

- A. Electronegative groups cause deshielding of nuclei near them.
- B. This effect falls off as the number of intervening bonds increases.
- C. The correlation is by no means exact!!!!

For methyl groups (CH_3R) it is simple:

$\text{CH}_3\text{I} = 2.16 \text{ ppm}$

$\text{CH}_3\text{Br} = 2.68 \text{ ppm}$

$\text{CH}_3\text{Cl} = 3.05 \text{ ppm}$

$\text{CH}_3\text{F} = 4.26 \text{ ppm}$

\uparrow EN of R you \downarrow shielding.

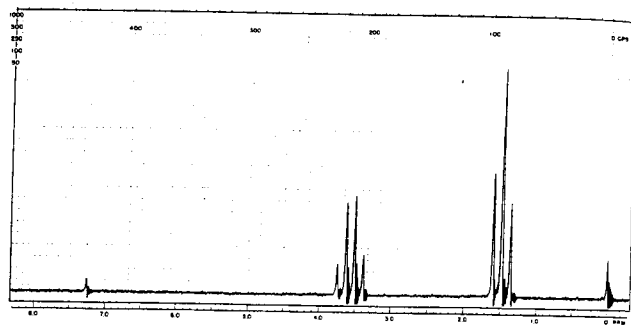
For ethyl groups ($\text{CH}_3\text{CH}_2\text{R}$) it is more complicated:
In general with $\text{CH}_3\text{CH}_2\text{R}$:

At CH_2 position as \uparrow EN of R you \downarrow shielding but not as rapidly as with corresponding methyl groups.

At CH_3 position at \uparrow EN of R you \downarrow shielding but to a lesser degree.

Fine but if $\text{R}=\text{X}$:

The shielding of the CH_3 protons increases with increasing EN of the halide.



11 Ethyl chloride
 $\text{C}_2\text{H}_5\text{Cl}$

(a) (b)
 $\text{CH}_3\text{CH}_2\text{Cl}$

Sweep offset: — ppm
Freq. response: — cps
Sweep time: 2.50 sec
Spec. amp: — %

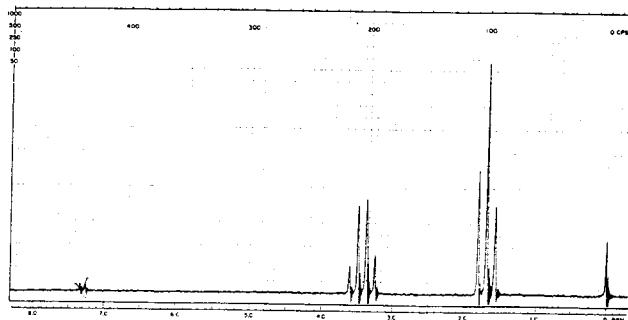
ASSIGNMENTS
a 1.48
b 3.52
c —
d —

10 Ethyl bromide
 $\text{C}_2\text{H}_5\text{Br}$

(a) (b)
 $\text{CH}_3-\text{CH}_2-\text{Br}$

Sweep offset: — ppm
Freq. response: — cps
Sweep time: 2.50 sec
Spec. amp: — %

ASSIGNMENTS
a 1.67
b 3.35
c —
d —

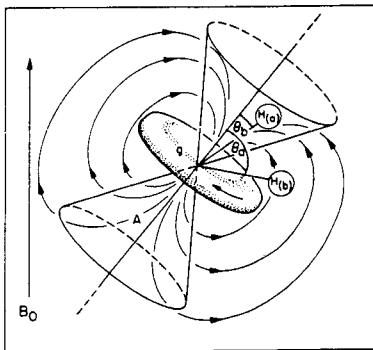


Shielding by Magnetically Anisotropic Groups:

1. General:

Chemical bonds are usually magnetically anisotropic so they have different susceptibilities along three directions.

In the case of axially symmetric charge distribution this can be easily explained with two susceptibilities:



The shielding region about an electron grouping g , which has cylindrical but not spherical symmetry. Protons $H_{(a)}$ and $H_{(b)}$ are in the shielding and deshielding zones, respectively, the nodal surface of zero shielding being the double cone.

$$\bar{\sigma}_n = (\chi_{\parallel} - \chi_{\perp}) (1 - 3\cos\Theta)/3r^3 4\pi$$

$\bar{\sigma}_n$ – depends on geometry and susceptibilities, not the nuclide being observed.

$$\bar{\sigma}_n = 0 \text{ when } \Theta = 54.7^\circ$$

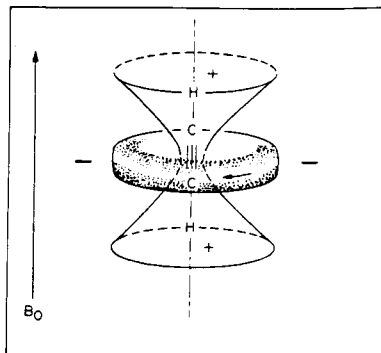
Acetylenes:

Classic example: by usual criteria of bond hybridization and acidity, there should be a progressive deshielding of protons from ethane, ethylene and acetylene.

Ethane = 1.96 ppm

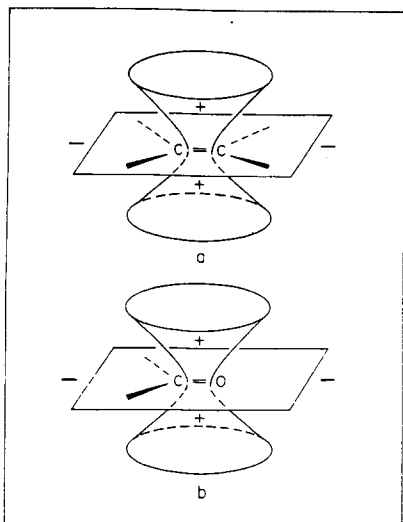
Ethylene = 5.84 ppm

Acetylene = 2.88 ppm

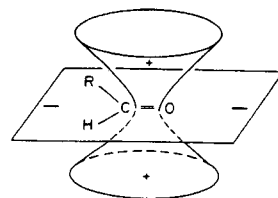


The shielding zone about an acetylenic bond.

Other Examples:



The shielding region about an olefinic double bond (a) and a carbonyl double bond (b).

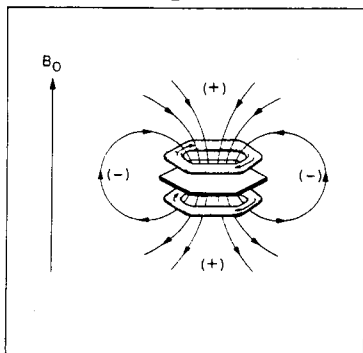


Shielding of the aldehydic proton.

Ring Current Effects:

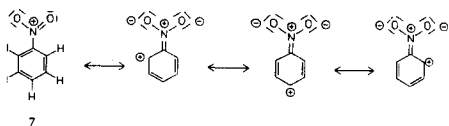
Protons on aromatic rings resonate at unexpectedly low fields.

Due to circulation of π -electrons in the plane of the ring giving enhanced diamagnetic susceptibility in a direction perpendicular to the ring:

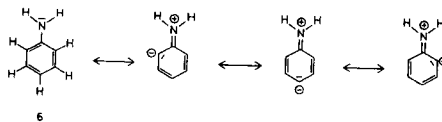


Mesomeric effects of aromatic substituents:
- stronger at ortho and para positions

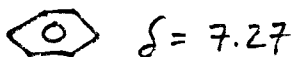
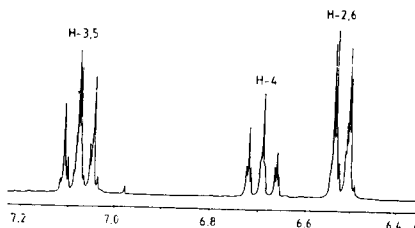
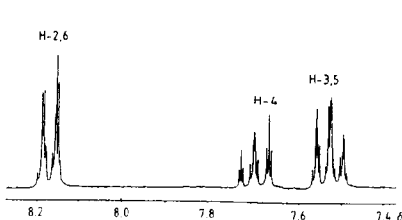
If there is an increase electron density in ring +M and if there is a decrease electron density there is a -M.



Scheme II



Scheme I



Electric Field effects(σ_e):

There are intramolecular electric fields associated with groups like carbonyls and nitros.

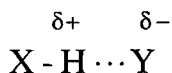
Protonation can also produce an electric field effect.

Hydrogen Bonding and solvents (σ_H):

Protons that are hydrogen bonded have particularly low shielding values.

They are effected dramatically by:

- concentration
- temperature



The hydrogen bond tends to draw H towards Y and repel the X-H bonding electrons towards X resulting in reduced electron density around Y.

Chemical Shift:

$$B_{\text{eff}} = B_0 (1 - \sigma)$$

$$\sigma = \sigma_{\text{dia}} + \sigma_{\text{para}} + \sigma_{\text{N}} + \sigma_{\text{R}} + \sigma_{\text{e}} + \sigma_{\text{i}}$$

N- magnetic anisotropy of neighboring groups.

R- ring current effects in arenes.

e- electric field effect.

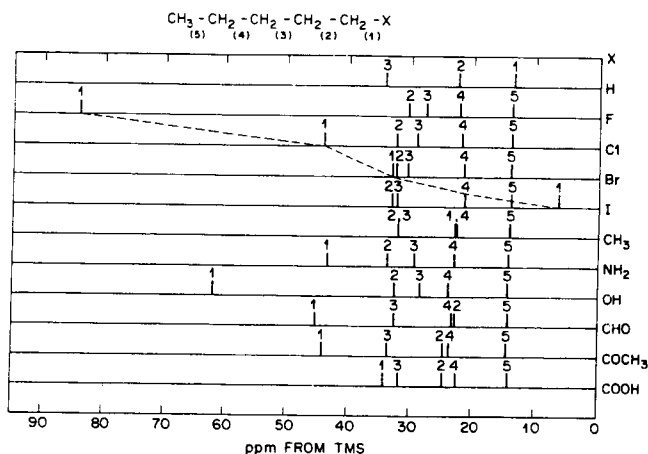
i- effects of intermolecular interactions.

¹³C Chemical Shifts:

- covers 200 ppm range
- TMS is used as internal standard as with ¹H chemical shifts to establish δ scale.
- Greater variability is attributed to the fact that there is greater electron density about the nuclei.
- σ_{para} has a more significant role due to existence of low-lying excited states.
- There is not a lot of other information in ¹³C spectrum.
- More spread out than the ¹H spectrum so sometime trickier to figure out.

Inductive Effects:

- Should propagate down the chain with alternating effect, decreasing as the third power of the distance.
- This prediction is not borne out!



Schematic carbon-13 spectra illustrating the transmission of inductive effects in straight-chain aliphatic compounds. All spectra are represented as proton-decoupled so that carbon resonances appear as singlets.

- C_1 shows the expected effect for halogens but something strange going on with Iodine.
- Effect with Iodine explained as “heavy atom effect” associated with large number of electrons which will greatly alter σ_{dia} .
- C_2 shielding is independent of EN but always deshielding.
- C_3 effect is always shielding relative to H substitution?!

¹³C Shielding in hydrocarbons:

- ¹³C chemical shifts are very sensitive to molecular structure and geometry as well as from substituent effects.

¹H in hydrocarbons – 2 ppm range

¹³C in hydrocarbons – 50 ppm range

α, β, and γ effects:

i) α effect

- deshielding effect of $\sim 9 \pm 1$ ppm

α -Effect in ¹³ C Shielding			
	structure	ppm from TMS	α -effect ppm
(a)		- 2.1	—
(b)		5.9	8.0
(c)		16.1	10.2
(d)		25.2	9.1
(e)		27.9	2.7

- crowding becomes a problem with neopentane.

ii) β -effect

- similar to that produced by α carbons.
- Effect is reduced if carbon of interest is branched.

β -Effect in ^{13}C Shielding

	structure	ppm from TMS	β -effect ppm
(a)	$^{\alpha}\text{CH}_3 - \text{C} - ^{\alpha}\text{CH}_3$	5.9	—
(b)	$^{\alpha}\text{CH}_3 - \text{C} - ^{\alpha}\text{CH}_2 - \beta\text{CH}_3$	15.6	9.7
(c)	$^{\alpha}\text{CH}_3 - \text{C} - ^{\alpha}\text{CH} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \end{matrix}$	24.3	8.7
(d)	$^{\alpha}\text{CH}_3 - \text{C} - ^{\alpha}\text{C} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \\ \downarrow \beta\text{CH}_3 \end{matrix}$	31.5	7.2
(e)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \text{C} - ^{\alpha}\text{CH}_3$	16.1	—
(f)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \text{C} - ^{\alpha}\text{CH}_2 - \beta\text{CH}_3$	25.0	8.9
(g)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \text{C} - ^{\alpha}\text{CH} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \end{matrix}$	31.8	6.8
(h)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \text{C} - ^{\alpha}\text{C} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \\ \downarrow \beta\text{CH}_3 \end{matrix}$	36.7	4.9
(i)	$\begin{matrix} ^{\alpha}\text{CH}_3 \\ ^{\alpha}\text{CH}_3 \end{matrix} \searrow \text{C} - ^{\alpha}\text{CH}_3$	25.2	—
(j)	$\begin{matrix} ^{\alpha}\text{CH}_3 \\ ^{\alpha}\text{CH}_3 \end{matrix} \searrow \text{C} - ^{\alpha}\text{CH}_2 - \beta\text{CH}_3$	29.9	4.7
(k)	$\begin{matrix} ^{\alpha}\text{CH}_3 \\ ^{\alpha}\text{CH}_3 \end{matrix} \searrow \text{C} - ^{\alpha}\text{CH} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \end{matrix}$	34.1	4.2
(l)	$\begin{matrix} ^{\alpha}\text{CH}_3 \\ ^{\alpha}\text{CH}_3 \end{matrix} \searrow \text{C} - ^{\alpha}\text{C} \begin{matrix} \nearrow \beta\text{CH}_3 \\ \searrow \beta\text{CH}_3 \\ \downarrow \beta\text{CH}_3 \end{matrix}$	38.1	4.0

iii) γ -effect

- this is shielding rather than deshielding!

γ -Effect in ^{13}C Shielding

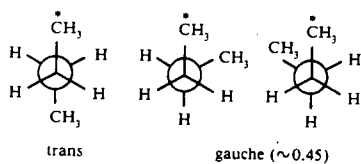
	structure	ppm from TMS	γ -effect ppm
(a)	$^{\alpha}\text{CH}_3 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH}_3$	15.6	—
(b)	$^{\alpha}\text{CH}_3 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH}_2 - ^{\gamma}\text{CH}_3$	13.2	- 2.4
(c)	$^{\alpha}\text{CH}_3 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH} \begin{matrix} \nearrow ^{\gamma}\text{CH}_3 \\ \searrow ^{\gamma}\text{CH}_3 \end{matrix}$	11.3	- 1.9
(d)	$^{\alpha}\text{CH}_3 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{C} \begin{matrix} \nearrow ^{\gamma}\text{CH}_3 \\ \rightarrow ^{\gamma}\text{CH}_3 \\ \searrow ^{\gamma}\text{CH}_3 \end{matrix}$	8.8	- 2.5
(e)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH}_3$	25.0	
(f)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH}_2 - ^{\gamma}\text{CH}_3$	22.6	- 2.4
(g)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{CH} \begin{matrix} \nearrow ^{\gamma}\text{CH}_3 \\ \searrow ^{\gamma}\text{CH}_3 \end{matrix}$	20.7	- 1.9
(h)	$^{\alpha}\text{CH}_3 - ^{\alpha}\text{CH}_2 - \overset{\text{I}}{\overset{ }{^{\alpha}\text{CH}_2}} - ^{\beta}\text{C} \begin{matrix} \nearrow ^{\gamma}\text{CH}_3 \\ \rightarrow ^{\gamma}\text{CH}_3 \\ \searrow ^{\gamma}\text{CH}_3 \end{matrix}$	18.8	- 1.9

Possible explanations for deshielding:

- 1) non-bonded steric interactions.
- 2.) mediated via attached protons.
- 3.) Correlation with electronegativity.

Scheme 1

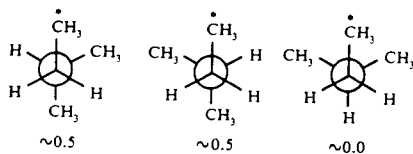
Butane:



C^{*} shielding
vs. propane

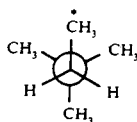
-2.4 ppm
or
5.3 ppm
per contact

2-Methylbutane:



-4.3 ppm
or
~4.3 ppm
per contact

2,2-Dimethylbutane:



-6.8 ppm
or
~3.4 ppm
per contact

iv) δ -effects

- very small $\sim 0.3 - 0.5$

v) ϵ -effects

- still detectable but ~ 0.1

Grant and Paul incremental system for alkanes:

$$\delta_i = -2.3 + 9.1n_\alpha + 9.4n_\beta - 2.5n_\gamma + 0.3n_\delta + 0.1n_\epsilon + \sum S_{ij} \quad (6-4)$$

where:

δ_i = chemical shift of the carbon nucleus of interest

n = numbers of carbon atoms in the α -, β -, γ -, δ - and ϵ -positions relative to this nucleus

S_{ij} = steric correction terms taking account of branching.

Example: 2-methylbutane (6)

C-1: $n_\alpha = 1$, $n_\beta = 2$, $n_\gamma = 1$

Steric corrections: primary with adjacent tertiary $\rightarrow -1.1$
 $S_{ij} = -1.1$

$$\delta(\text{C-1}) = -2.3 + (9.1 \times 1) + (9.4 \times 2) - (2.5 \times 1) - 1.1 = 22.0$$

C-2: $n_\alpha = 3$, $n_\beta = 1$

Steric corrections: 1. tertiary with adjacent primary $\rightarrow 0$
 2. tertiary with adjacent secondary $\rightarrow -3.7$
 $S_{ij} = -3.7$

$$\delta(\text{C-2}) = -2.3 + (9.1 \times 3) + (9.4 \times 1) - 3.7 = 30.7$$

C-3: $n_\alpha = 2$, $n_\beta = 2$

Steric corrections: 1. secondary with adjacent tertiary $\rightarrow -2.5$
 2. secondary with adjacent primary $\rightarrow 0$
 $S_{ij} = -2.5$

$$\delta(\text{C-3}) = -2.3 + (9.1 \times 2) + (9.4 \times 2) - 2.5 = 32.2$$

C-4: $n_\alpha = 1$, $n_\beta = 1$, $n_\gamma = 3$

Steric corrections: primary with adjacent secondary $\rightarrow 0$
 $S_{ij} = 0$

$$\delta(\text{C-4}) = -2.3 + (9.1 \times 1) + (9.4 \times 1) - (2.5 \times 2) = 11.2$$

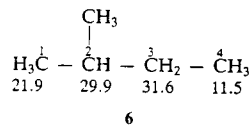


Table 6-4.

Steric correction factors $S_{ij}^{(1)}$ for estimating ^{13}C chemical shifts in branched alkanes by the method of Ref. [5].

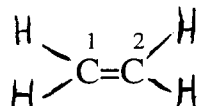
$i \backslash j$	primary	secondary	tertiary	quaternary
primary	0	0	-1.1	-3.4
secondary	0	0	-2.5	-7.5
tertiary	0	-3.7	-9.5	-15.0
quaternary	-1.5	-8.4	-15.0	-25.0

i = observed nucleus; j = neighbor nucleus

Alkenes:

$\delta \approx 100\text{-}150$ ppm

ethene = 123.5 ppm



- substituents reduce C^1 shielding (except Br, I and CN) and increase C^2 shielding.
- C^1 is a combination of inductive effects but also mesomeric effect.
- Some large β -effects can be accounted by mesomeric effects.



Table 2-9.

^{13}C chemical shifts of mono-substituted ethylenes.



X	$\delta(\text{C}^1)$	$\delta(\text{C}^2)$
H	123.5	123.5
CH_3	133.4	115.9
$\text{CH}=\text{CH}_2$	137.2	116.6
C_6H_5	137.0	113.2
F	148.2	89.0
Cl	125.9	117.2
Br	115.6	122.1
I	85.2	130.3
OCH_3	153.2	84.1
OCOCH_3	141.7	96.4
NO_2	145.6	122.4
CN	108.2	137.5

Arenes:

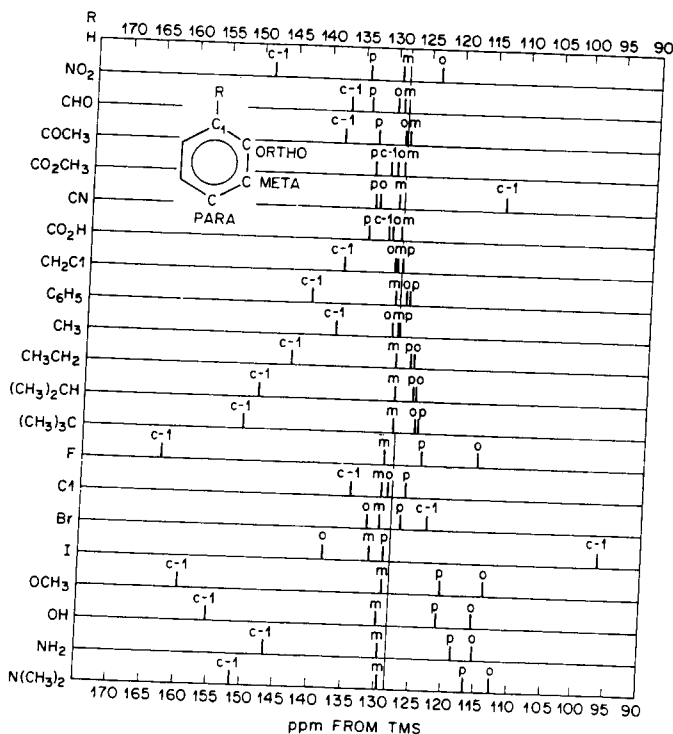
Benzene $\delta = 128.5$

Substituted $\delta = 100-150$ ppm

Effects: $C_1 > C_{ortho}^{2,6} > C_{para}^4 > C_{meta}^{3,5}$

C^1 is responsive to inductive effects

Mesomeric structures yield ^+M and ^-M effects.



¹H Signal Intensities:

- area under the curve is proportional to the number of protons (Integration)

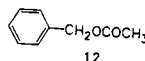
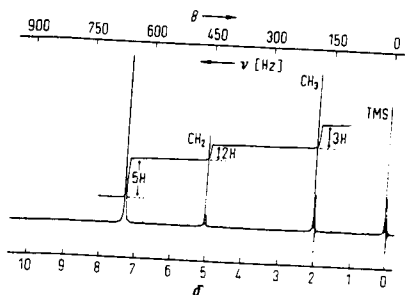


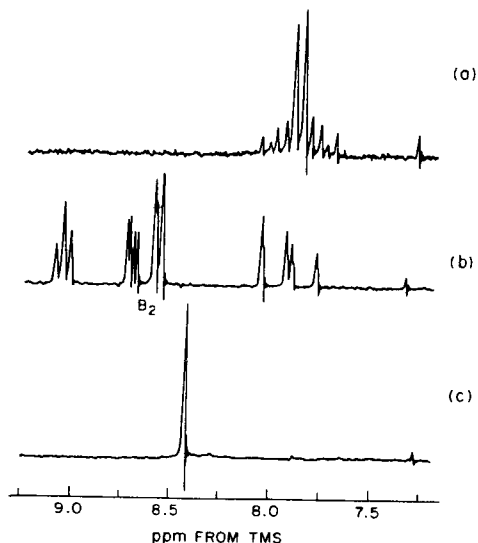
Figure 1-28.
90 MHz ¹H NMR spectrum of
benzyl acetate (**12**) with integrat-
ed curve.

¹³C Signal Intensities:

- areas are distorted due to low natural abundance and sensitivity.
- if decoupled signals are proportional to the number of directly bonded hydrogen atoms.

Relationship Between the Spectrum and Molecular Structure:

- 1) Equivalent nuclei have the same resonance frequency.
- 2) Coupling between equivalent nuclei is not seen in first order spectra.



60 MHz proton spectra in CCl_4 solution of (a) *o*-dinitrobenzene; (b) *m*-dinitrobenzene; (c) *p*-dinitrobenzene.

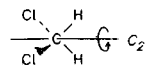
Chiral Molecules:

Enantiomers: give identical NMR spectra

Diastereomers: give different NMR spectra

The case of CH_2 :

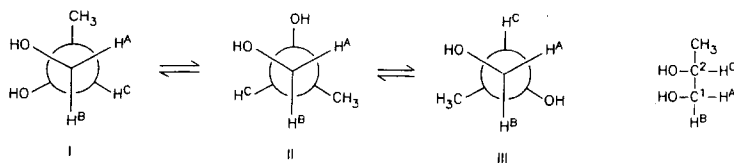
Homotopic: two fold axis of symmetry (C_2), protons are equivalent



Enantiotopic: two protons appear equivalent in the NMR but they are not (prochiral).



Diastereotopic: two protons are not equivalent in NMR.



for H^A :

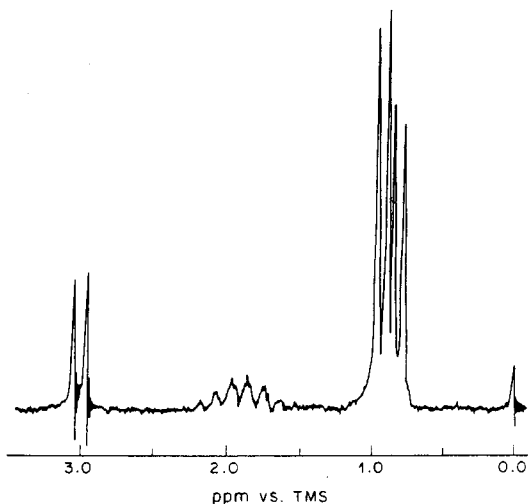
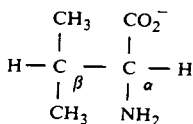
$OH, CH_3/H, H(\delta_1)$ $OH, OH/H, CH_3(\delta_2)$ $OH, H/H, OH(\delta_3)$

for H^B :

$H, H/OH, OH(\delta_4)$ $H, CH_3/OH, H(\delta_5)$ $H, OH/OH, CH_3(\delta_6)$

$$\bar{\delta}_A = x_I \delta_1 + x_{II} \delta_2 + x_{III} \delta_3$$

$$\bar{\delta}_B = x_I \delta_4 + x_{II} \delta_5 + x_{III} \delta_6$$



Proton spectrum of L-valine (15% solution in D_2O , 2M in NaOD, 60 MHz); separate doublets for each methyl group appear at 0.90 and 0.83 ppm.