Chemical shifts

Discovered in 1950 by Proctor and Yu based on solution ^{14}N NMR studies of NH_4NO_3

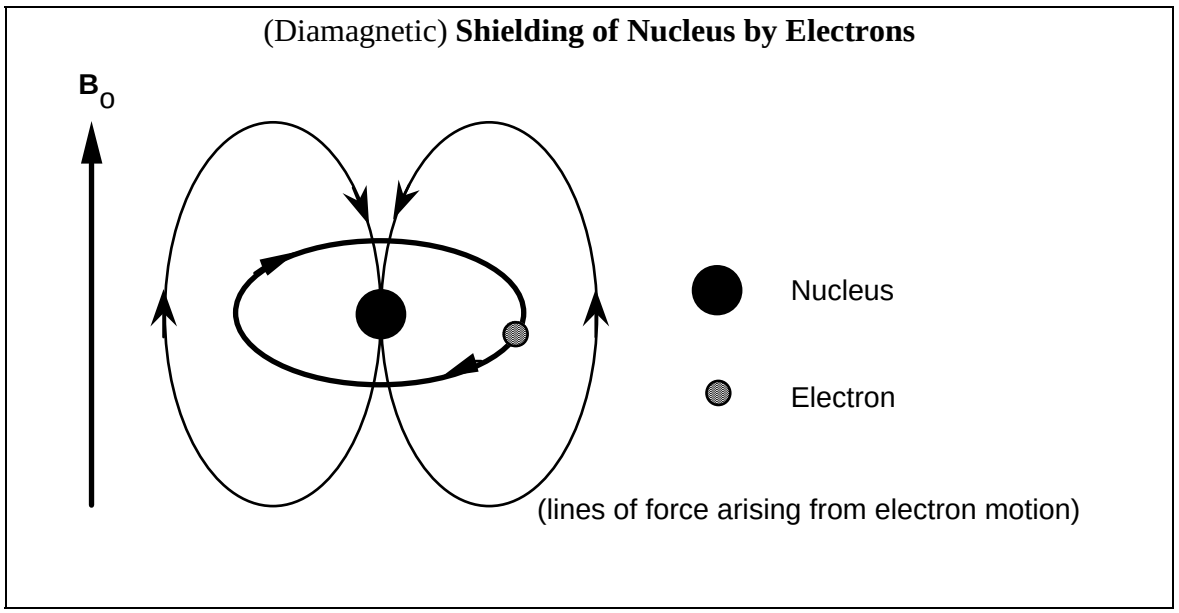
^{1}H chemical shifts

Empirical correlations between chemical shifts and structure

Typical ^{1}H chemical shift values.

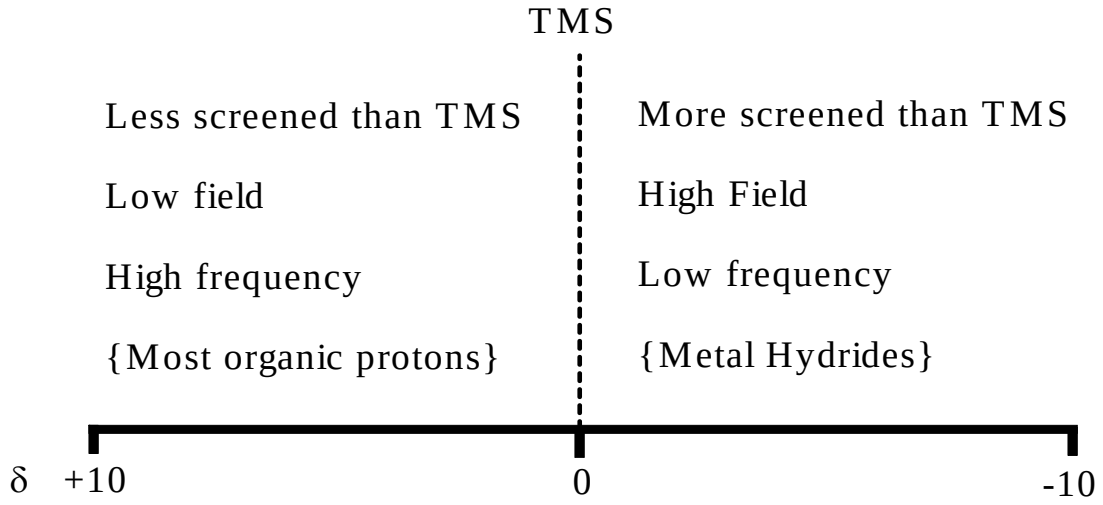
Proton	δ / ppm	Proton	δ / ppm
Aldehyde	9.5 - 10.5	C**H**$_3$ attached to double	
Aromatic	6.5 - 8.2	bonds/aromatics	1.8 - 2.5
Alkene	4.5 - 6.1	Methyl (C**H**$_3$–CO–)	1.8 - 2.7
Alkyne	2.0 - 3.2	Methylene (C**H**$_2$–O–)	~3.6 - 4.7
Acetal	4.5 - 6.0	Methylene (C**H**$_2$– R_1R_2)	~1.3
Alkoxy	3.4 - 4.8	Methine (C**H**–$R_1R_2R_3$)	~1.5
Methyl (C**H**$_3$–R)	~0.9	Cyclopropane	0.22
N-methyl	3.0 - 3.5	Me_4Si (TMS)	0.0
Methoxy	3.3 - 3.8	Metal hydride	–5 to –20

The influence of the electron density at the proton

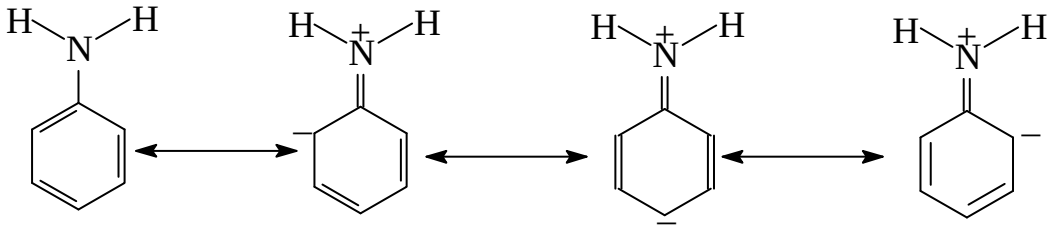


The applied magnetic field, B_0, induces circulations in the electron cloud surrounding the nucleus such that a magnetic moment μ, opposed to B_0, is produced (Lenz's law). Nuclei in a region of high electron density are more shielded from the applied field than those in regions of lower electron density. If inductive effects present in a molecule reduce the electron density in the hydrogen 1s orbital, dishielding (shift to higher frequencies) is expected.

	CH_3**F**	CH_3**Cl**	CH_3**Br**	CH_3**I**	CH_3**H**
δ(CH_3)	**4.13**	**2.84**	**2.45**	**1.98**	**0.13**
Electonegativity (Pauling)	**4.0**	**3.0**	**2.8**	**2.5**	**2.1**

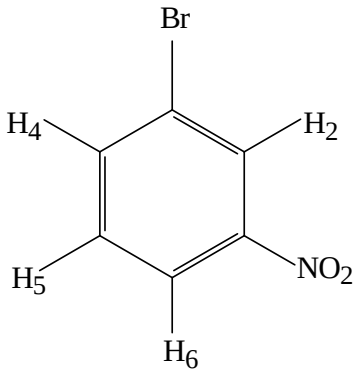


Substituents, such as OR or NR_2, can act both as an electron withdrawing group (due to electronegativity, thus causing a shift to higher frequencies) and as a donor of lone pairs (if double bonds are present, thus causing a shift to lower frequency). Mesomeric effects can be used to explain the shielding observed in aromatic compounds, such as aniline, in which the protons in the *ortho* and *para* positions are more strongly shielded than in the *meta* position:



Inductive substituent effects are approximately *additive*.

For 3-bromonitrobenzene:



$\delta(H_2)=7.27+0.22+0.95=8.44$

$\delta(H_4)=7.27+0.22+0.33=7.82$

$\delta(H_5)=7.27-0.13+0.17=7.31$

$\delta(H_6)=7.27-0.03+0.95=8.19$

Chemical shifts increments (in ppm) for substituted benzenes

Substituent	*Ortho*	*Meta*	*Para*
NO_2	0.95	0.17	0.33
CHO	0.58	0.21	0.27
COCI	0.83	0.16	0.3
COOH	0.8	0.14	0.2
$COOCH_3$	0.74	0.07	0.2
$COCH_3$	0.64	0.09	0.3
CN	0.27	0.11	0.3
C_6H_5	0.18	0	0.08
CCl_3	0.8	0.2	0.2
$CHCl_2$	0.1	0.06	0.1
CH_2Cl	0	0.01	0
CH_3	-0.17	-0.09	-0.18
CH_2CH_3	-0.15	-0.06	-0.18
$CH(CH_3)_2$	-0.14	-0.09	-0.18
$C(CH_3)_3$	0.01	-0.1	-0.24
CH_2OH	-0.1	-0.1	-0.1
CH_2NH_2	0	0	0
F	-0.3	-0.02	-0.22
CI	0.02	-0.06	-0.04
Br	0.22	-0.13	-0.03
I	0.4	-0.26	-0.03
OCH_3	-0.43	-0.09	-0.37
$OCOCH_3$	-0.21	-0.02	-
OH	-0.5	-0.14	-0.4
p-$CH_3C_6H_4SO_3$	-0.26	-0.05	-
NH_2	-0.75	-0.24	-0.63
SCH_3	-0.03	0	-
$N(CH_3)_2$	-0.6	-0.1	-0.62

For multiple substitution the influence of each additional substituent is slightly less:

CH_4 **0.23** CH_3Cl **3.05** CH_2Cl_2 **5.33** $CHCl_3$ **7.26** ppm

Magnetic anisotropy effects

Chemical bonds are regions of high electron density and therefore can create local magnetic fields. Electrons within bonds are not usually able to circulate freely and so the chemical shift will depend on the orientation of the nucleus with respect to the bond.

Diatomic molecule A-B: the external field B_0 induces a magnetic moment μ_A, which is proportional to the magnetic susceptibility, χ_A, of A with components $\mu_A(x)$, $\mu_A(y)$, and $\mu_A(z)$ in a Cartesian coordinate system. Its contribution to the shielding of B is given by:

$$\Delta\sigma = 1/4\pi \sum_{i=x,y,z} \chi_A(i)\,(1 - 3\cos^2\theta(i)) / r^3$$

θ - the angle between the direction of μ_A and the A-B bond direction.

r - the distance between A and B.

In solution, the molecules are rapidly reorienting and the resulting net contribution is zero if A is magnetically *isotropic*: $\chi_A(x)=\chi_A(y)=\chi_A(z)$. For the magnetically anisotropic group A [$\chi_A(x)\neq\chi_A(y)\neq\chi_A(z)$]:

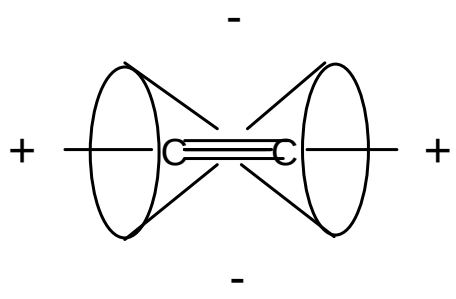
$$\Delta\chi = \chi_{//} - \chi_{\perp} = \chi_A(z) - 1/2\,[\chi_A(x)+\chi_A(y)]$$

The contribution to the chemical shift of individual protons is then determined by

$$\Delta\sigma = 1/3\,\Delta\chi\,(1 - 3\cos^2\theta) / 4\,\pi\,r^3$$

[typical values of $\Delta\chi$: $\Delta\chi_{C\text{-}H} = 90$, $\Delta\chi_{C\text{-}C} = 140$, $\Delta\chi_{C\equiv C} = -340 \times 10^{-36}$ m^3/molecule]

Generally, the results of the above equation are graphically represented by shielding cones, nodal planes ($\Delta\sigma = 0$) of which is fixed at the "magic angle" of 54.7°:

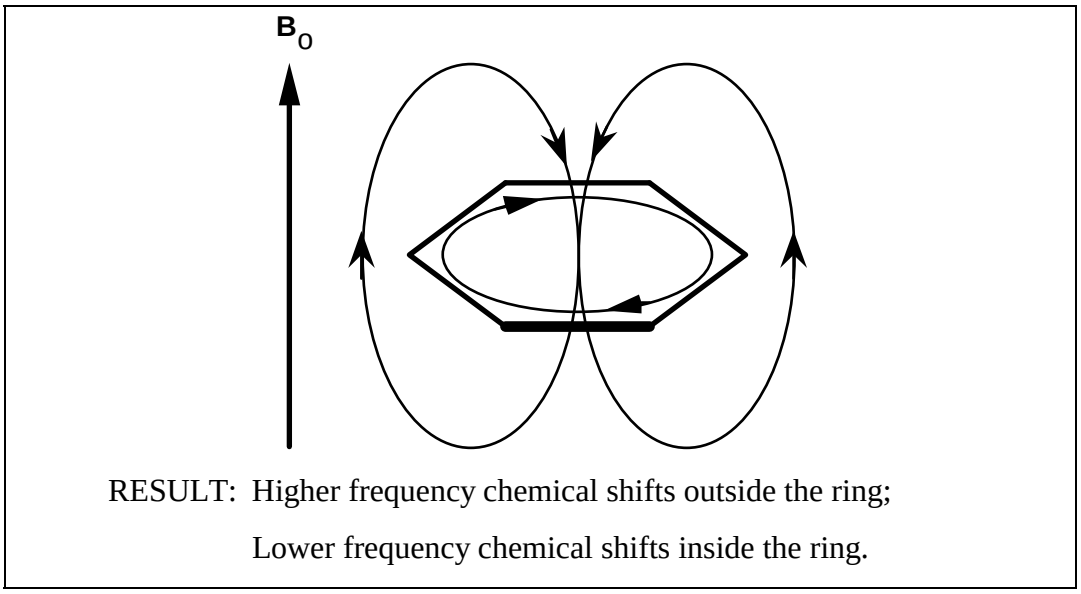


The ring current effect in cyclic π-systems

An aromatic molecule can be visualised as a current loop where π-electrons are free to move on a circle formed by the σ framework. A ring current is induced under the influence of the external magnetic field B_0. The secondary magnetic field resulting from this current supports the external magnetic field outside the ring and opposes the magnetic field inside the ring. As a result:

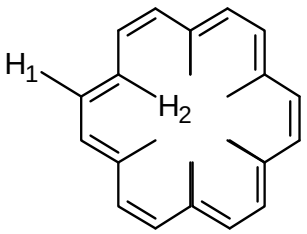
(i) protons in the molecular plane and outside the ring resonate at higher frequencies;

(ii) protons above or below the ring resonate at lower frequencies.



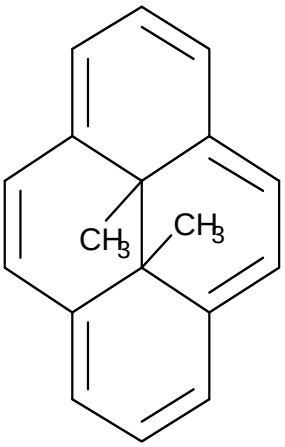
RESULT: Higher frequency chemical shifts outside the ring;
Lower frequency chemical shifts inside the ring.

In large unsaturated ring systems where the number of π-electrons satisfies the Hückel rules (4n + 2), effects are found which again indicate the existence of a ring current:



H_1 + 8.9 ppm

H_2 - 1.8 ppm



CH_3 - 4.25 ppm

The opposite ring current behaviour is observed for anti-aromatic ring systems.

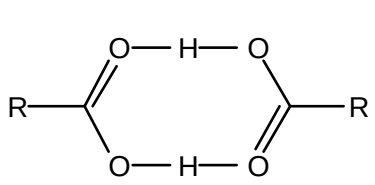
Chemical shifts through hydrogen bonding

In general, the formation of H-bonds leads to significant shifts to higher frequency. However, no distinct region of chemical shifts can be assigned to the resonances of exchangeable protons since the position of the corresponding signals strongly depends on the medium (e.g., solvent, concentration) and temperature. The ^1H resonance in H_2O is usually observed around 4.8 ppm due to hydrogen bonding, whereas the protons in a very dilute solution of H_2O in $CDCl_3$ resonate at 1.5-1.6 ppm (at 0.3-0.4 ppm in C_6D_6). The H-D exchange can cause signals from OH/NH/SH protons to disappear from the ^1H NMR spectrum, thereby helping with assignments.

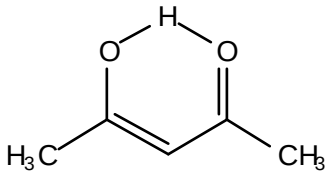
Typical ^1H chemical shift ranges for OH and NH protons

		δ / ppm
-OH	Alcohols	1-5
	Phenols	4-10
	Acids	9-13
	Enols	10-17
-NH	Amines	1-5
	Amides	5-6.5
	Amido groups in peptides	7-10

Examples of strong hydrogen bonds



δ = 9-15 ppm



δ = 15.4 ppm

Other factors

Solvent

The changes in ^1H resonance frequency affected by the solvent are usually smaller than 1 ppm. Complications caused by solvent effects can be avoided by using "inert" solvents (carbon tetrachloride, cyclohexane). On the other hand, strong solvent effects can be used in order to "simplify" the spectrum: if an aromatic solvent such as benzene is used, then this will solvate areas of low electron density and, due to ring current effects, this can change chemical shifts by as much as 1 ppm.

Temperature

The chemical shift difference between the resonance signals in the ^{1}H NMR spectrum of a sample of liquid methanol is temperature dependent and is used for the purpose of accurate temperature calibration: as the temperature rises, the extent of H-bonding diminishes, and the resonance for the hydroxyl proton moves to low frequency, towards the resonance signal of the methyl protons.

Unpaired electrons. Shift reagents

The interaction between electron and nuclear spin manifests itself as the hyperfine splitting of the signal in ESR experiments. In NMR experiments this interaction leads to a shift of the signal to higher or lower frequency relative to the signal of the same proton in the diamagnetic compound (*contact shift*). Paramagnetic impurities significantly accelerate the spin-lattice relaxation of protons and cause severe line-broadening.

The effects of paramagnetic *lanthanide shift reagents* can be used to simplify the ^{1}H NMR spectra. A lanthanide shift reagent is an octahedral complex of a lanthanide element (Eu, Dy, Pr, Yb) with a ligand chosen to make the complex soluble in NMR solvents, and this is dissolved in a solution of the compound. The lanthanides are capable of assuming higher coordination numbers than 6 so that if the organic molecule possesses a suitable coordination site (generally, any atom with an available lone pair) it can interact with the complex. This produces a pseudocontact shift of the protons of the organic molecule.

^{13}C chemical shifts

Since the organic chemist is interested primarily in the molecular carbon skeleton, a ^{13}C NMR spectrum yields structural information much more directly than a proton spectrum: quaternary carbons, as those of many functional groups (CN, C=O, C=NR), are detectable. In some cases, ^{13}C NMR easily distinguishes between groups that might otherwise be confused, e.g. cyanide (110-120 ppm) and isocyanide (135-150 ppm).

Typical ^{13}C chemical shift values of hydrocarbons.

CH_3-	10-30 ppm	$=CR_2$	130-150 ppm
R_3C-, R_2CH, RCH_2	25-50 ppm	Alkyne	70-85 ppm
$=CH_2$	105-120 ppm	Ar-H	115-130 ppm
=CH	110-140 ppm	Ar-C	130-150 ppm

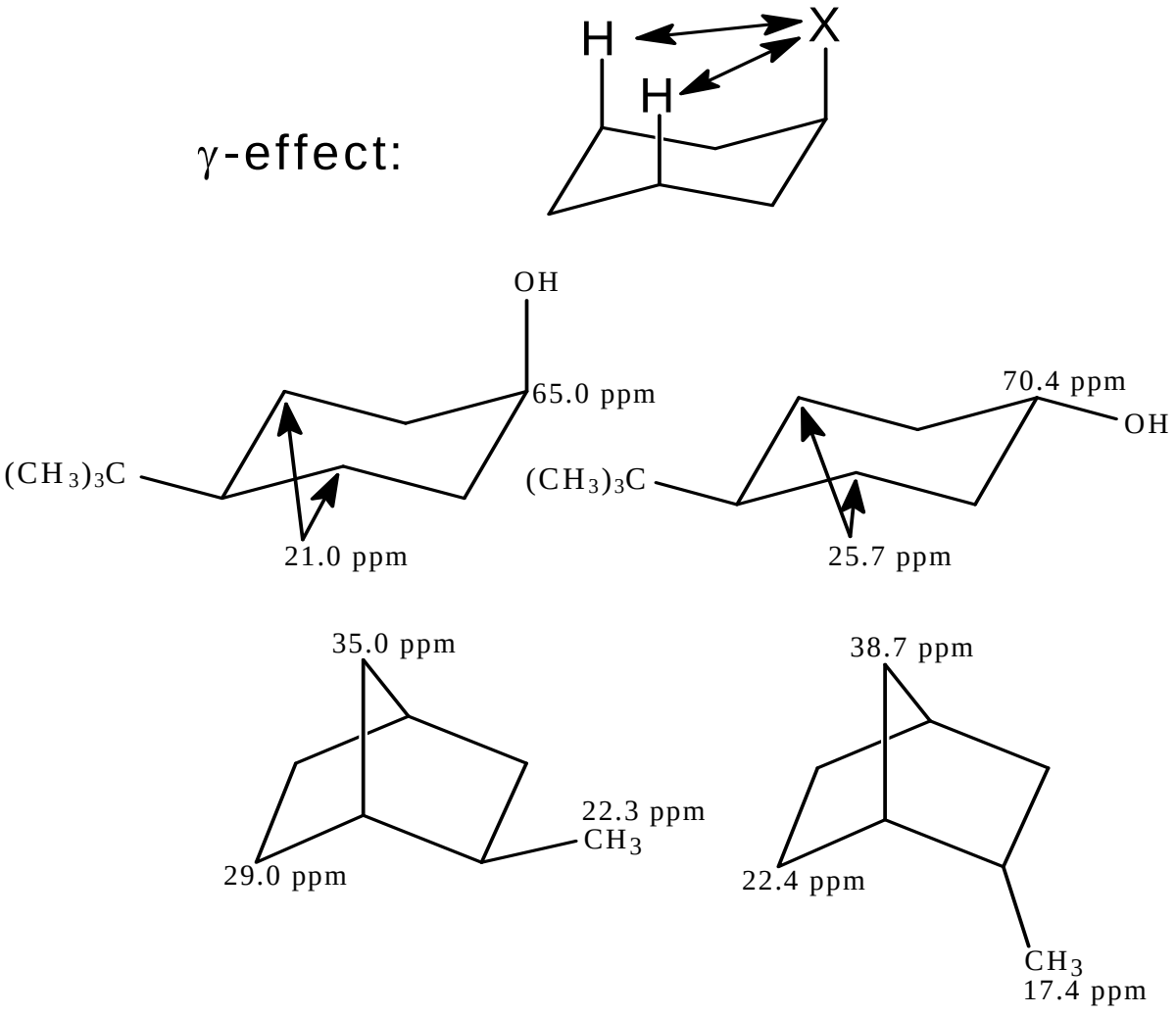
Typical ^{13}C chemical shift values of carbons bonded to oxygen.

Ketones	200-210 ppm	Acetals	90-110 ppm
Aldehydes	190-200 ppm	R_3C-O	70-85 ppm
Conjugated C=O	180-200 ppm	R_2HC-O	60-80 ppm
Carboxylic acids	170-180 ppm	RH_2C-O	45-65 ppm
Carboxylic esters	160-170 ppm	H_3C-O	50-60 ppm
Phenols (C_1)	150-160 ppm	Epoxides	40-60 ppm
Furans (C_2)	140-150 ppm		

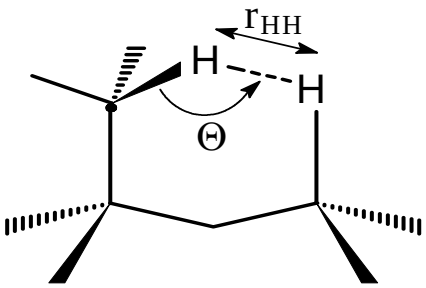
Reference book: E. Breitmaier and G. Bauer, ^{13}C-NMR-Spektroskopie, Thieme Verlag, Stuttgart 1977.

Steric effects

^{13}C chemical shifts are sensitive to molecular geometry. Carbons separated by several bonds strongly influence each other if they are spatially close.



Upfield shifts are observed in all cases where the stereochemistry leads to van der Waals interactions of the type indicated above. In rigid molecules this effect can be as large as 10 ppm. Smaller γ effects are observed if there is free rotation about the C–C bonds. For X=CH_3:

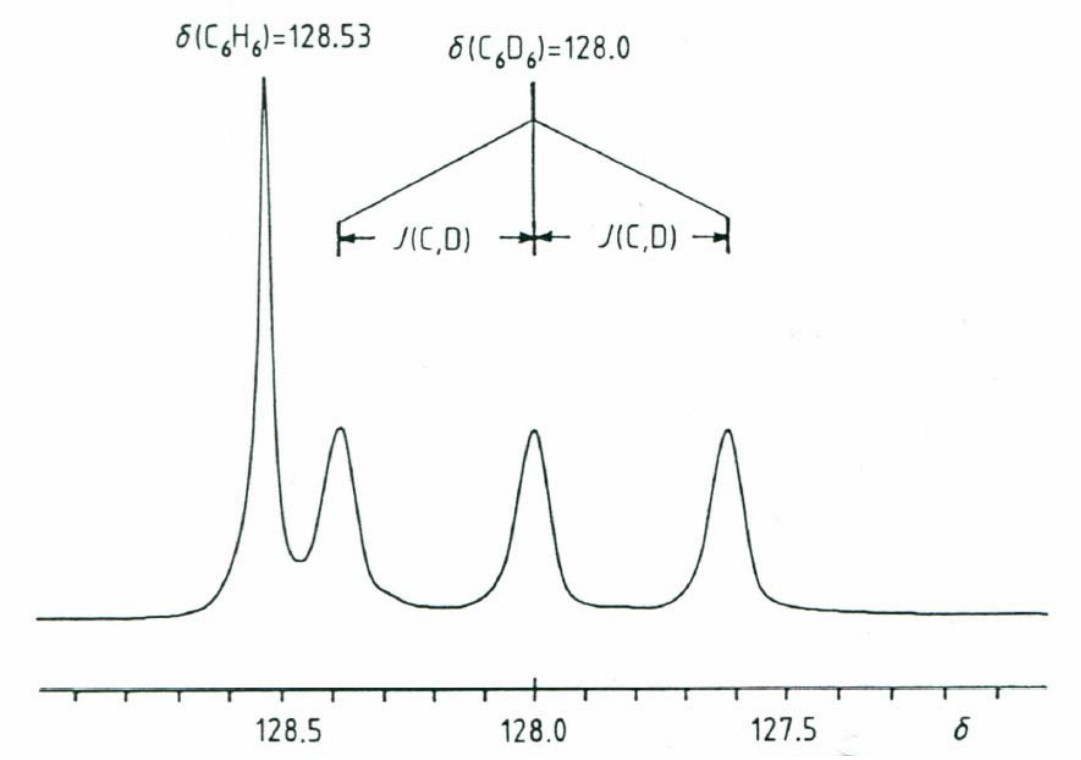


$\Delta\delta_{st} \sim F_{HH}(r) \cos \Theta$ {$F_{HH}(r)$ - the repulsive force between the protons}

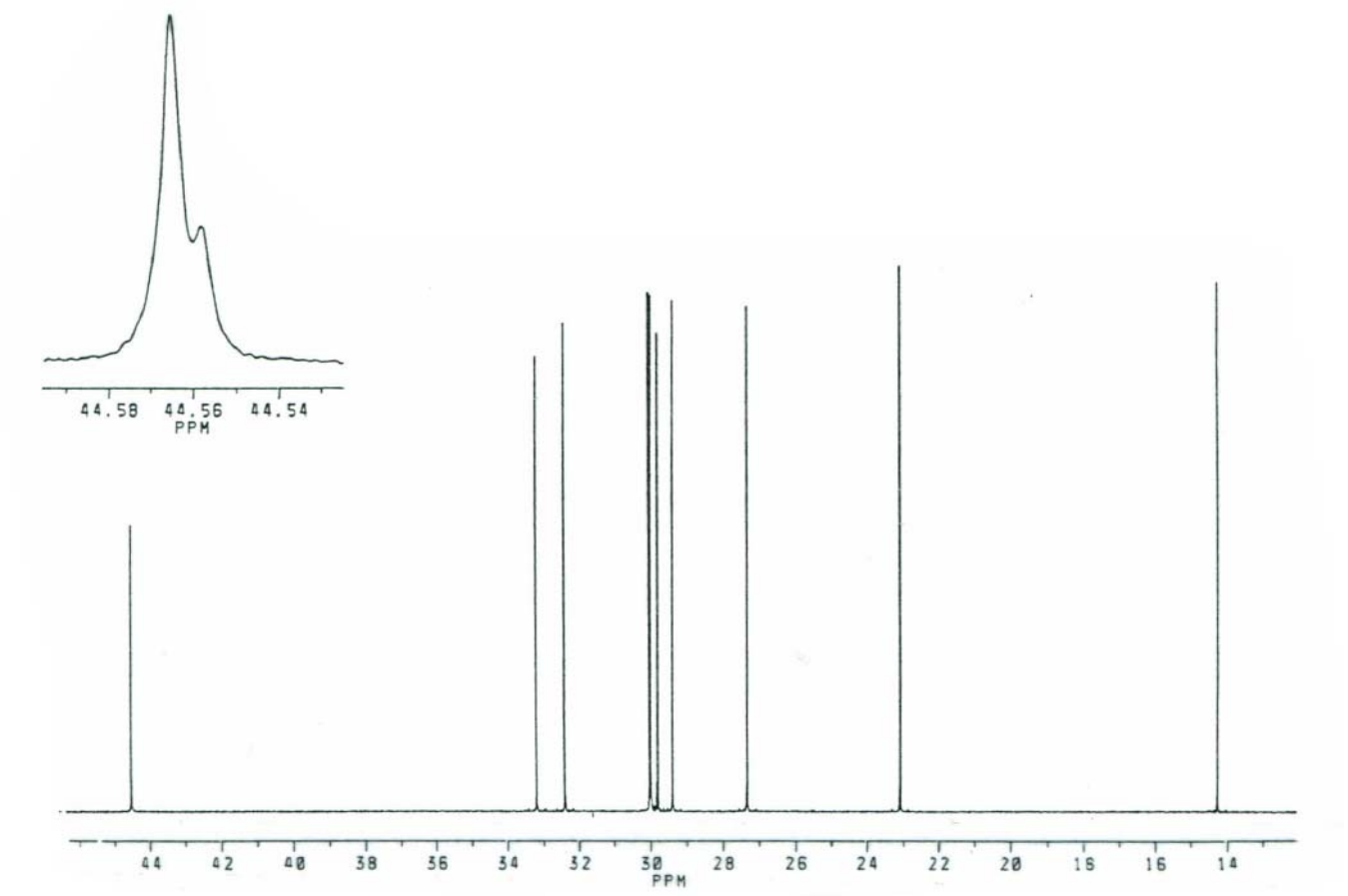
Depending on Θ, $\Delta\delta_{st}$ can have positive or negative values.

Isotope effects

The direct isotope effect arises from the fact that the vibrational properties of two isotopomers differ, leading to different degrees of nuclear shielding. For $^1H/^2H$ exchange the isotope effect is relatively large owing to the large ratio of the isotope masses; other pairs of isotopes give rise to much smaller effects (of the order of ppb (parts per billion)). The heavier isotopomer generally corresponds to a less positive value of chemical shift.



A 62.9 MHz proton-decoupled ^{13}C NMR spectrum of a mixture of 10% C_6H_6 and 90% C_6D_6. A 1:1:1 triplet is observed for C_6D_6 because of the ^{13}C-^{2}H coupling (^{1}J(C,D)=24.55 Hz). The isotope shift is 33.3 Hz (0.53 ppm).



A proton-decoupled ^{13}C spectrum of 1-chlorodecane in $CDCl_3$ at 295 K. The signal for C-1 attached to Cl (see upper trace) is split into a 3:1 doublet by the $^{35/37}Cl$ isotope effect.

Other nuclei

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

σ - the shielding constant, generally, can be represented as a sum of two components: diamagnetic, σ_{dia}, and paramagnetic, σ_{para}:

$\sigma=\sigma_{dia} + \sigma_{para}$

σ_{dia} represents the contribution from local diamagnetic electron currents at the site of the nucleus; σ_{para} reflects anisotropic, nonspherical local electron circulations.

For heavier nuclei, the chemical shift is usually the only spectral parameter available. The range of chemical shifts is generally much greater than for ^{1}H and ^{13}C. The paramagnetic contribution to the chemical shift becomes significant and is often dominant. Intra- and intermolecular effects, expressed in ppm, are similar in magnitude to those in ^{1}H NMR spectroscopy, but when considered in relation to the total shifts are less important.

Many elements allow the possibility of observing two or more different isotopes and in principle it does not matter which isotope is chosen for chemical shift measurements, since the values of δ are the same except for some very small isotope effects. In practice, one chooses the isotope which has most favourable nuclear properties.

For the heavier nuclei we are often only interested in the number of different sites present. Thus, the number of NMR peaks present (not the actual chemical shift values), is often of interest. There is rarely any overlap between peaks for heavy spin-½ nuclei due to their large chemical shift ranges.

88 nuclei (74% of nuclei with spin) have spins greater than $^{1}/_{2}$. These are known as quadrupolar nuclei. For most of these, the interaction with electric field gradients provides a very fast relaxation pathway, resulting in broad peaks, and so it is rare to be able to record high-resolution spectra (^{2}H and ^{11}B being exceptions). This relaxation mechanism depends on the local symmetry at the nucleus under investigation, and a highly symmetrical site will give a narrow peak (e.g., ^{14}N in NH_4^+ or ^{95}Mo in $Mo(CO)_6$). Many sites of chemical interest are not highly symmetric and the peaks often become too broad to detect.

Nuclei	Spin	Nat. abun. %	CS range/ppm	Standard
^{11}B	3/2	80.42	200	$BF_3(OEt_2)$
^{15}N	1/2	0.37	1000	CH_3NO_2
^{17}O	5/2	0.037	900	H_2O
^{19}F	1/2	100	1300	$CFCl_3$
^{27}Al	5/2	100	450	$Al(H_2O)_6^{3+}$
^{29}Si	1/2	4.7	600	$Si(CH_3)_4$
^{31}P	1/2	100	>300	85% H_3PO_4
^{119}Sn	1/2	8.56	>3000	$Sn(CH_3)_4$
^{195}Pt	1/2	33.8	14000	Na_2PtCl_6