Prof Ben Davis

THIRD YEAR ORGANIC CHEMISTRY - REVISION COURSE Lecture 2

MOLECULAR STRUCTURE 3: SPECTROSCOPIC ANALYSIS

Books: Williams and Fleming**, " Spectroscopic Methods in Organic Chemistry",**
Harwood and Claridge**, Organic Spectroscopy OCP**
Harwood and Moody**, Experimental Organic Chemistry, Ch 5**
Morrison and Boyd**, Organic Chemistry, 6th Edition, Chapter 17**
Claridge **High-Resolution NMR Techniques in Organic Chemistry**
A more advanced text bit very up to date and an excellent resource

A. MASS SPECTROMETRY

Analysis of compounds by mass spectrometry depends upon ionising a molecule, and then separating these ions by passage through a magnetic field; the ions are separated according to their *m/e* ratio. Ionisation can be achieved in various ways, *e.g.* by bombarding the sample with a beam of high energy electrons (**Electron Impact**), or by collisions with other charged ions such as CH_5^+ or NH_4^+ or even MeO^-(**Chemical Ionisation**) or **Electrospray**.

EI $M + e^- \longrightarrow M^+ + 2e^-$

EI generally leads to extensive fragmentation, giving a pattern of signals which can be used to deduce the structure of the compound, but also often means that the molecular ion signal is very weak or missing.

CI $M + CH_5^+ \longrightarrow MH^+ + CH_4$

$M + CH_3O^- \longrightarrow (M-H)^- + CH_3OH$

CI is that the ionisation process generates an ion which is less highly energetic and does not spontaneously collapse; thus, the molecular ion is often the base peak.
ES is milder still and even allows e.g. proteins to be examined.

Mass spectra allow the direct determination of molecular weight, since for most ions *e* = 1. Furthermore, decomposition of the compound under the ionising conditions generates fragment ions which are often diagnostic for various compound classes. The intensity of each of these peaks is a measure of the relative abundance of the ion responsible for the signal, which in turn depends on their relative stability, *e.g.*

$PhCH_2CH_3 \longrightarrow [PhCH_2CH_3]^{+\cdot} \longrightarrow$ $PhCH^+CH_3$ (25%) $PhCH_2^+$ (95%) Ph^+ (10%)

Extensive tables of common fragment ions are available in standard reference texts.

High resolution experiments (to 4DP (5-10ppm)) permit exact molecular composition to be verified, by comparison with the molecular mass calculated from the exact masses of the most abundant isotopes for the constituent atoms, e.g.

$Ph_2(CH_3)CH$ MW=$C_{14}H_{14}$ 182.2646 PhN=NPh MW=$C_{12}H_{10}N_2$ 182.2244

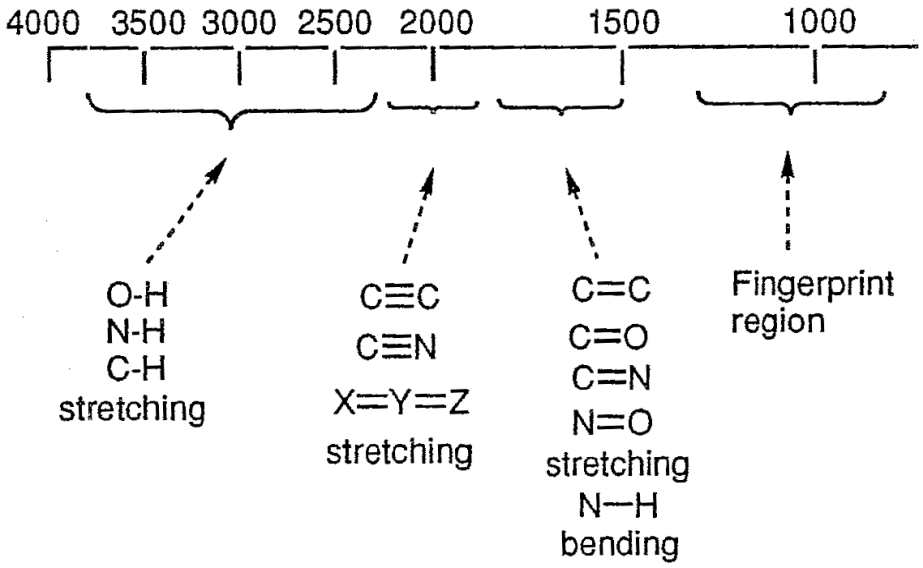
B. ELECTROMAGNETIC SPECTRUM

By irradiating molecules at different frequencies, we can gain different types of information about their structure, since these frequencies will bring in to resonance various modes of molecular motion, or electronic or nuclear excitation.

(i) . INFRA-RED SPECTROSCOPY

- Molecular vibrations as a source of bonding information - stretching and bending
- Measured in cm^{-1}
- Characteristic group frequencies for various functional groups, broadly governed by Hooke's Law, so resonance frequency is directly dependent on bond strength and inversely related to mass.

- Typical absorptions are:



- Absorption of common functional groups (cm^{-1})

Hydrocarbons

C-C	1500
C=C	1650
C≡C	2100
C-H	3000

Alcohols

O-H	3200-3600 (broad)
C-O	1100

Carbonyl

For RC(O)X, the more electronegative X, the higher the absorption frequency (thus, acid chlorides, anhydrides and esters absorb at a higher frequency than ketones). Conversely, the more electron releasing by resonance is X, the lower the frequency (this is because the C=O is weakened, i.e. has more single bond character and therefore is more near the "normal" C-O resonance at 1100):

RC(O)O(O)R	RC(O)Cl	RC(O)OR'	RCHO	RC(O)R	$RC(O)NR'_2$
1850	1800	1750	1740	1720	1690

• Conjugation to C=C lowers frequency by 15-40cm^{-1}

• Ring strain raises the frequency (smaller the ring, higher the frequency), but 6 membered rings show the normal frequency

• Hydrogen bonding to the C=O lowers frequency by about 50cm^{-1}

Complications arise from

- overtones (appear at twice the frequency of the fundamental)
- shifting, due to conjugation, electron withdrawal, strain (angle or Van der Waals) and hydrogen bonding . . . but these shifts can also be very useful for definitively assigning structure once they have been recognized.

(ii). ULTRAVIOLET/VISIBLE SPECTROSCOPY

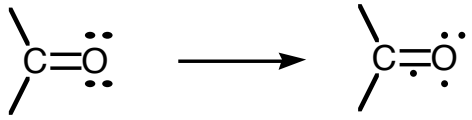
- Electronic transitions as a source of bonding information, since absorption of a photon leads to excitation of electrons from a ground state to an excited one;
- The wavelength (λ_{max}) of an absorption (in nm) can be used to deduce details of the structure of the chromophore. UV spectroscopy is most important in the structural analysis of compounds containing π electrons, and particularly highly conjugated systems;
- There are empirical rules available for predicting λ_{max} values;
- The absorption is governed by Beer-Lambert Law:

$$A = \log(I / I_0) = \varepsilon.c.l$$

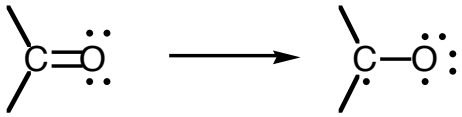
where I = transmitted light intensity
I_o = incident light intensity
c = concentration (M)
l = path length of cell (cm)
ε = molar extinction coefficient (usually in the range 0-10^5 , with <10^3 considered to be a weak absorption)

- The most frequently observed and therefore the most important transitions are the ones which involve loosely held *n* and π electrons
- Typical absorptions are:

n ----> π^*



π ----> π^*



(iii). NMR SPECTROSCOPY

In the presence of an applied magnetic field, nuclei can align themselves in $2I+1$ ways, where I is the nuclear spin; this is because nuclei can be considered to spin, and this circulation of charge generates a *magnetic moment*. For the most important nuclei, ^{1}H and ^{13}C, which have $I = 1/2$, this means that they can take up 2 orientations,

* aligned to the field (low E)
* opposed to the field (high E)

with the difference in energy given by

$$\Delta E = h\gamma B_0/2\pi$$

and number in each orientation is given by Boltzmann distribution $N\beta/N_\alpha = \exp(-\Delta E/kT)$

This difference is usually very small (1 in 10^5) and requires sensitive electronic detection; this makes the NMR technique insensitive compared to UV and IR. But the higher B_o, the bigger the $N\beta/N_\alpha$ difference, and the better sensitivity. The application of FT techniques also gives improved spectra, since successively acquired FIDs can be added.

A pulse of radio frequency radiation is applied, which disturbs the equilibrium ground state Boltzmann distribution; relaxation from this excited state emits radiation at right angles to the applied field, which is detected by a suitable RF receiver.

NMR Active Nuclei		NMR Inactive Nuclei
(I=1/2)	(I=3/2)	(I=0)
^{1}H (99.98%)	^{11}B(80%)	^{12}C (98.9%)
^{13}C (1.108%)	^{7}Li(93%)	^{16}O (99.96%)
^{19}F (100%)	^{35}Cl	
^{29}Si (4.70%)	^{79}Br	
^{31}P (100%)		

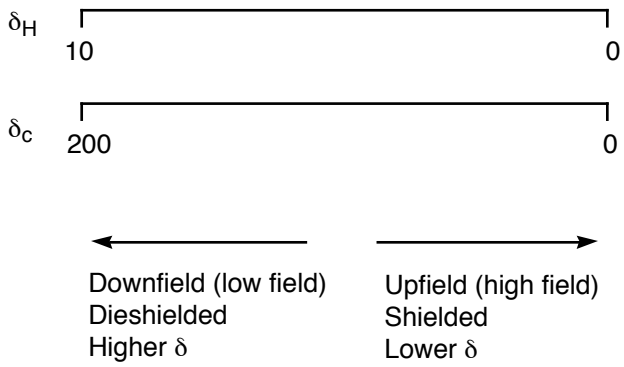
(a) Chemical Shift

The precise resonance frequency of any active nucleus is very sensitive to its surrounding magnetic environment; this is due largely to local variations in electron density, which of course creates a magnetic field. Thus the field experienced by any nucleus is given by the sum of the applied magnetic field and the local magnetic field. In practice, this means that different nuclei have (slightly) different resonance frequencies, allowing their individual identification.

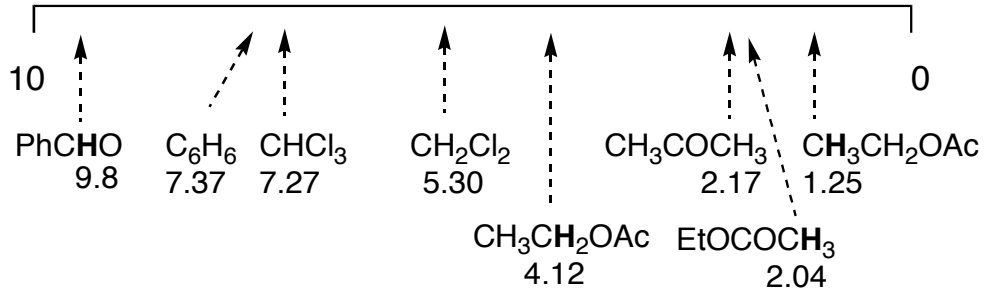
Because this difference is due to their chemical nature, we talk about the *chemical shift* of the relevant nuclei, which is defined as:

$$\delta = (\nu_S - \nu_{TMS}(Hz))/B_O(MHz)$$

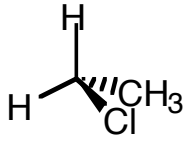
δ is essentially the resonance frequency relative to TMS (Me_4Si), which is a non-toxic, cheap and chemically inert reference. The conventional representation is:

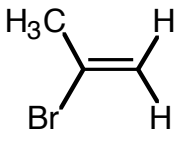
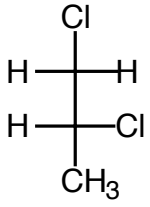


Some typical chemical shift values:



We say that nuclei with the same chemical shift are *chemically equivalent*. (this implies that they must also be stereochemically equivalent). If not, they can be

• *enantiotopic* or *prochiral* e.g.  (indistinguishable in achiral environment)

• *diastereotopic* e.g.  or 

Factors Affecting Chemical Shift

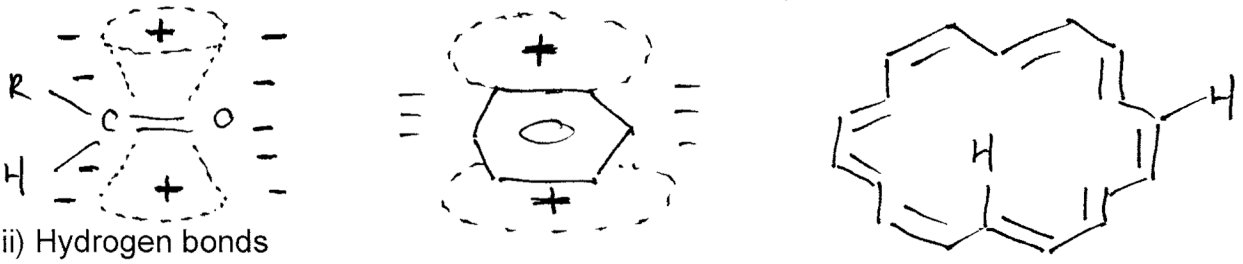
(i) Inductive effect

EWG deshield adjacent nuclei (i.e. shift downfield to higher δ)

ERG shield adjacent nuclei (i.e. shift upfield to lower δ)

(ii) Anisotropy

π-bonds can have large effects on chemical shift of adjacent nuclei, but this effect is highly directional (anisotropy) + = SHIELDING ; − = DESHIELDING



(iii) Hydrogen bonds

Hydrogen bonding results in deshielding of a proton (since its bonding electrons are now shared with a third atom), giving a downfield shift of the proton.

(iv) Solvent

Changing from CCl_4 or $CDCl_3$ to deuterated acetone, MeOH, or DMSO can have a noticeable effect on chemical shift, and C_6D_6 can have a very large effect on chemical shift of certain protons.

(b) Integration

The area under the resonance peak for any type of proton is directly proportional to the number of protons resonating at that frequency. However, this is not usually true in carbon NMR, hence these NMR are never routinely integrated.

(c) Coupling (First Order)

The signal given by any proton is influenced by its adjacent protons; splitting of the signal is caused by spin-spin coupling. A set of *n* equivalent protons will split the signal for its immediate neighbour (adjacent) protons into *n+1* peaks.

The splitting can be quantified as the coupling constant, expressed in Hz, which is independent of the applied field.

Nuclear Overhauser Effect

nOe spectra enable the identification of protons which are nearby in space.

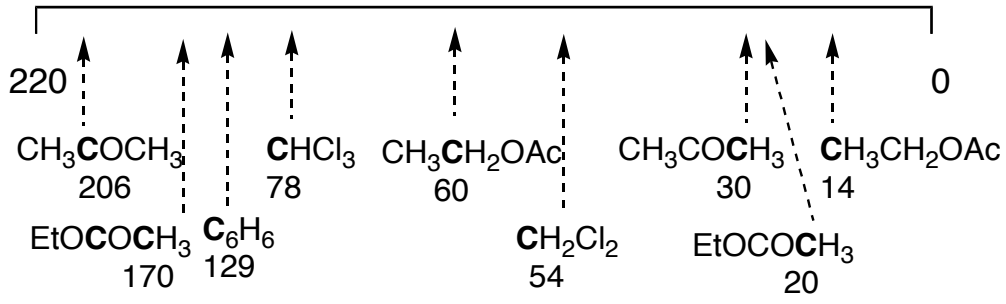
Two- Dimensional Techniques

COSY allows the assignment of ^3J coupled protons, and are plotted as 2D spectra; this plot is a contour plot, with the basic spectrum along the diagonal, and cross-peaks indicate peaks which are coupled

CARBON NMR

The isotope ^{13}C has an abundance of only 1.1%, but spectra can still be acquired, although longer acquisition times are needed. The parameters of the carbon NMR spectrum are similar to proton, and give much the same sort of information:

(a) Chemical shift gives an indication of the electronic environment of the nucleus; a rough rule is that the chemical shift of any carbon is about 20 times the magnitude of the chemical shift of its attached proton;



(b) The multiplicity of a carbon with *n* attached protons is *n+1*; however, carbon spectra are routinely run with off-resonance proton decoupling, so all peaks appear as singlets. The use of DEPT sequence allows the identity of each carbon resonance to be determined;

(c) Unlike proton NMR, however, integration of the signal is not an accurate indication of the numbers of nuclei resonating at any given frequency; this is a result of the way in which carbon spectra are routinely acquired.