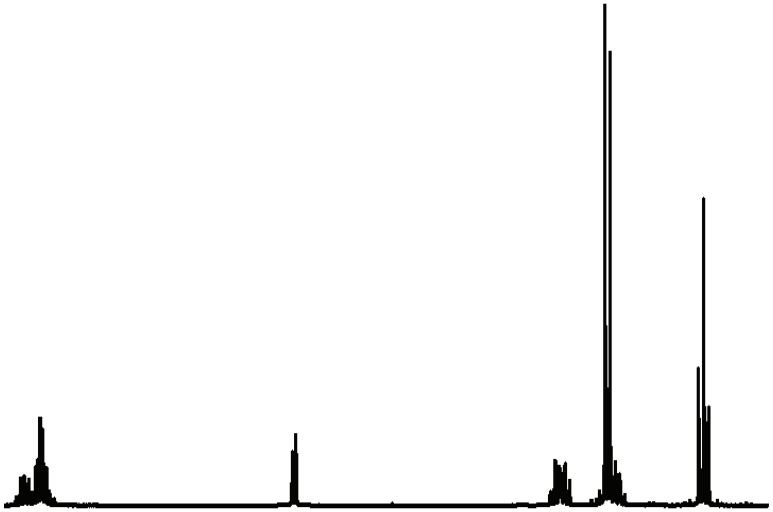
Organic Chemistry
NAT-BAS

Notes in Molecular Spectroscopy
NMR, IR, MS



Department of Science, Systems and Models,
Roskilde University, 2011

Simulated NMR spectra are made with the programs
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Contents

Introduction

The Laboratory course associated with the Nat-Bas Organic Chemstry course includes 3 lectures in spectroscopic identification of organic compounds. NMR spectroscopy is the main focus of these lectures, due to its excellence in providing easy to understand structural information about organic molecules. Other useful spectroscopic techniques are infrared (IR also referred to as vibrational spectroscopy), and mass spectroscopy (MS).

The current note extends Chapter 4 of the course book: Fox & White-sell: Organic Chemistry, 3rd ed., Jones & Bartlett Publ. 2004 (in the following referred to as F&W). The contents of this chapter give a good introduction to basics of both NMR-, IR-, and Mass-spectrometry. However, the text in F&W is too short to be sufficient for the practical use in the laboratory work. The purpose of the present note is to fill this gap.

The main focus is on NMR spectroscopy, and only on NMR of hydrogen atoms (also called ^{1}H-NMR or PMR). This type of NMR is probably the most powerful tool in structure determination of organic compounds. The powerful features of NMR are its resolution to atomic level, and its richness in information about molecular composition, intramolecular bonding, and structure. In this course, as in general, the task is not to read the structure out of the spectrum. That is impossible. Rather, spectra are used to verify or perhaps falsify a tentative molecular structure, or to determine which of a number of structures is in accordance with the spectrum.

Lecture 1

Read the following pages in F&W:
Page 166 (NMR-spectroscopy) to 168 and Figure 4.12

The NMR spectrum

For an introduction to the technique see F&W. The test compound is dissolved in a suitable solvent (see later) with an added internal standard tetramethylsilane, $(CH_3)_4Si$ (TMS). The sample is contained in a special glass tube. The tube is positioned in the magnetic field. The interpretation of ^1H NMR spectra is based on the following parameters:

1) Chemical shifts
2) Integrals
3) Spin-spin coupling constants
4) Peak shapes

In the first chapter we are dealing with chemical shifts and integrals.

Chemical shifts. The chemical shift occurs because the electrons shield the nucleus to a varying degree depending on the electron configuration. This means that each type of protons will have a different chemical shift (see spectrum of Figure 1). For convenience the chemical shifts are referenced to TMS. The chemical shifts are given in parts per million (ppm) and usually called δ. Using ppm enables one to use the same numbers irrespective of the instrument field strength and frequency used. The chemical shift is obtained by measuring the number of Hz the signal is shifted from TMS and divide by the operation frequency of the instrument (typically 300 MHz).
For the spectrum of phenylacetone (Fig. 1) we find for $CH_3C{=}O$ 630 Hz/300 * 10^6 = 2.1 ppm.
For the CH_2 signal 1080/300 * 10^6=3.6 ppm and for the phenyl protons 2160/300 * 10^6=7.2 ppm.

Having recorded the spectra of a large set of compounds we can now tabulate these values. This is for protons attached to carbons done in Tables 1-3. ^{1}H chemical shifts are typically found in the range 0-20 ppm.

Analyses of Table 1: Protons attached to an aliphatic carbon, reveal that the chemical shifts are slightly increasing going from CH_3 (methyl) to CH_2 (methylene) to CH (methine) and more importantly that the chemical shifts increase with increasing

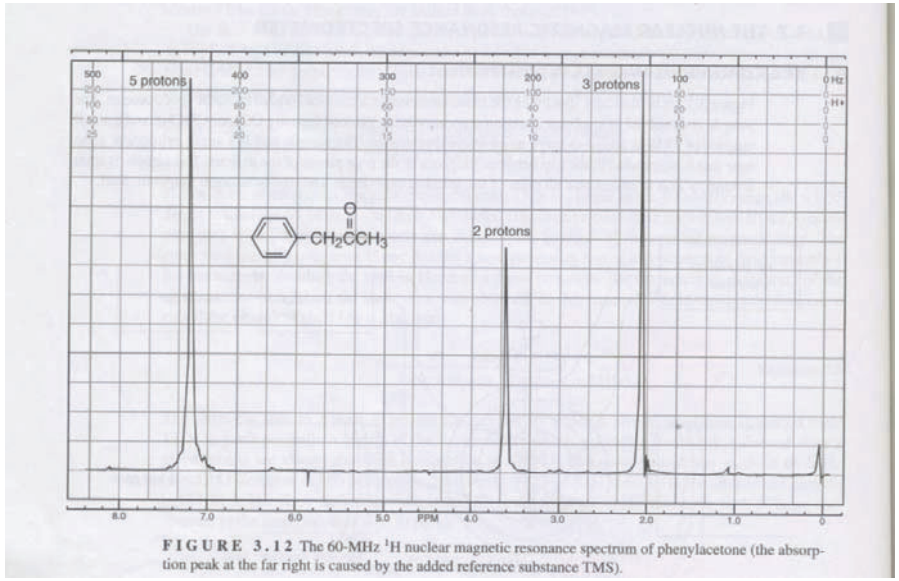


FIGURE 3.12 The 60-MHz ^{1}H nuclear magnetic resonance spectrum of phenylacetone (the absorption peak at the far right is caused by the added reference substance TMS).

Figure 1. The compound is phenylacetone and the solvent is chloroform-d (-d indicates that the solvent is deuteriated) also called $CDCl_3$.

The frequency axis is calibrated to 0.0 ppm at the TMS signal.

Spectrum is a very old type.

electronegativity of the first atom. Compare CH_3-CH_3 (0.9 ppm) with CH_3-S (2.1 ppm), CH_3-N (~2.3 ppm) and CH_3-O (~3.5 ppm). Notice also that even if the first atom is oxygen the values vary according to the particular functional group CH_3-OH (alcohol)(3.3),CH_3-OR (ether) (3.3 ppm), CH_3-OC=OR (ester) (3.7 ppm), CH_3-OAr (aromatic ether) (3.8 ppm).

From Table 2 it is seen that protons attached to double bonds have chemical shifts around 5.25 ppm, but the chemical shift can be as small as 3.7 ppm and as high as 8 ppm depending on the substituents and their positions.

For protons at triple bonds the chemical shifts fall in the range 1.8-3.1 ppm (Table 2).

For protons at aromatic carbons the value for benzene itself is 7.27 ppm. For substituted benzenes the chemical shifts vary according to type and position (Table 8). This will be treated in detail in lecture 2.

Aldehydes (Table 2) HC=O show a characteristic chemical shift just below 10 ppm.

For protons attached to oxygen, sulphur or nitrogen meaning typically alcohols, carboxylic acids, amines, thiols etc. values are given in Table 3. The ranges are seen to be very broad due to hydrogen bonding. Exchange is also an issue (see lecture 3). Resonances of protons that are involved in exchange are often broad.

2. Peak integrals.

The integral is the area of the peak. The *integral* is directly proportional to the number of equivalent hydrogens giving rise to that signal. This is used to determine the integer number of responsive H-atoms for each peak. In figure 2 we see that the integrals come as 3:2:5. The methyl group has 3 protons, the methylene group 2 and the phenyl group 5 (the complexity of the signal is not important).

How to obtain integrals? If the spectrum is computer generated the integrals are normally given below. Notice that the integrals normally not are normalized, but the numbers are in the ratio 3:2:5. Traditionally, integrals have been printed as an integral curve (see Fig. 2). The integrals are the distance from the horizontal line before the signal to the horizontal line after the line.

In this process, solvent peaks, TMS, and small signals from impurities should, of course, be disregarded.
If the number of protons is known (in Fig. 2 10H), the total integral (55.5+22+32.5= 110) can be set equal to the number of protons and the integral corresponding to one proton can be calculated as 110/10=11. If the number of protons is not known, the methyl signal at low frequency can quite often be used to determined the size of the integral for 3 protons (see Table 1 for position of methyl groups).
Example: Refer to Figure 2. The vertical jumps of the integration line for the 3 peaks are 55.5 divisions (signal at 7.2 ppm), 22 divisions (3.2 ppm), and 32.5 divisions (2.1 ppm). The signal at 2.1 ppm is assumed to be from a $-CH_3$ group. That is, 3 H-atoms make an increase of 32.5. 1 H-atoms is then 32.5/3 = 11 divisions. The 3.2 ppm signal then becomes 22/11 = 2 H-atoms, and the 7.2 ppm peak is 55/11 = 5 H-atoms.

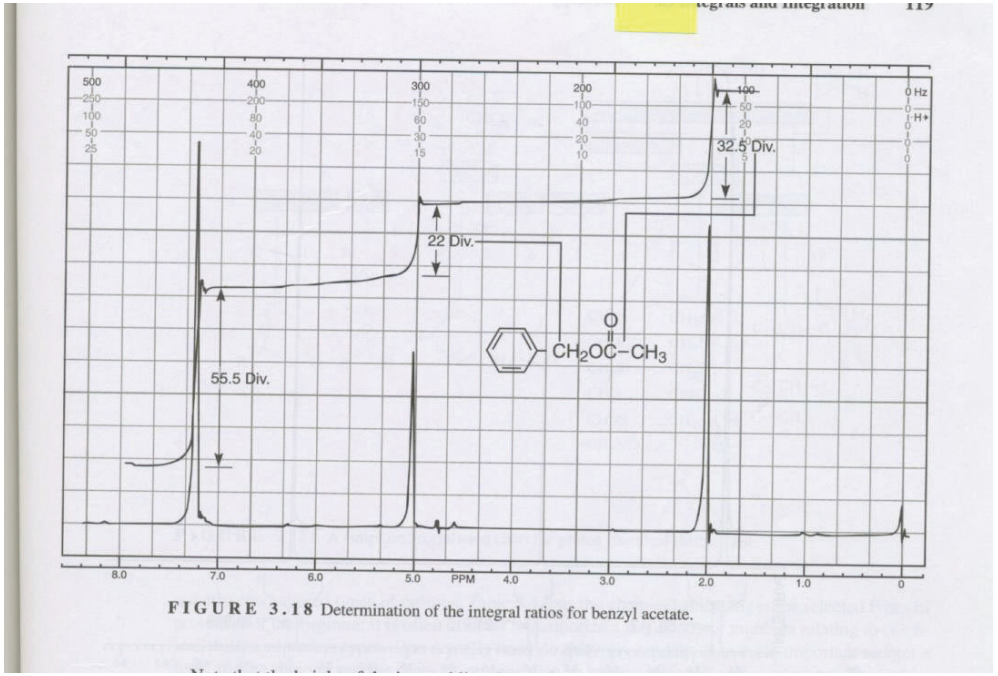


FIGURE 3.18 Determination of the integral ratios for benzyl acetate.

Figure 2. Integrals. Div = divisions = units

- Having learned about chemical shifts and integrals we can check our assignment by consulting Tables 1 to 3.
- Why is the signal at 3.2 ppm in Fig. 1 not predicted well? Or the one at 5.0 in Fig. 2?.

Notes:

1. The length in Hz of a 15 ppm long axis of a spectrum from a 300 MHz instrument is equal to $300 \cdot 10^{6} \cdot 15 \cdot 10^{-6} = 4500$ Hz. The end points are at frequencies 300,000,000.0 and 300,004,500.0 Hz, respectively.

NMR axes are traditionally oriented with increasing shifts (frequencies) towards the left hand side of the plot. The terms 'low field' (large ppm) and 'high field' or 'upfield' (small ppm) are traditional and still used.

Chemical shift tables

Table 1

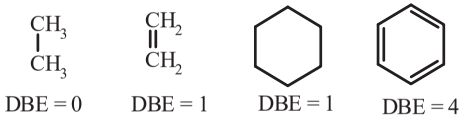
Typical chemical shifts in ppm of aliphatic H in various chemical environments

X	C**H**$_3$–X	R–C**H**$_2$–X	RR'C**H**–X
–R	0.9	1.4	1.5
–Ar	2.3	2.7	3.0
–C=C	1.6	2.3	###
–C–C=C	1.1	1.7	###
–C–N	1.1	1.4	###
–C–O	1.3	1.9	2.0
–CO–R	2.2	2.4	2.7
–CO–Ar	2.6	2.9	3.3
–CO–O–R	2.0	2.2	2.5
–CO–O–Ar	2.4	###	###
–OH	3.3	3.6	3.9
–O–R	3.3	3.4	3.7
–O–Ar	3.8	4.3	4.5
–O–C=C	3.8	3.7	###
–O–CO–R	3.7	4.1	4.8
–S	2.1	2.4	3.2
–N	2.3	2.5	2.8
–Cl	###	3.6	4.2
–Br	###	3.5	4.3
–I	###	###	4.3

R, R', aliphatic residues; Ar, aromatic residue. The shifts are approximate and will in most cases fit experimental values within ± 0.2 ppm.

Double Bond Equivalents (DBE).

DBE (also known as the degree of unsaturation) is the combined number of double bonds and ring closures in a molecule.



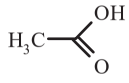
DBE can be calculated from the atom composition of the molecule

$$DBE = \tfrac{1}{2}(2n_C + 2 + n_N - n_H - n_{Hal})$$

Oxygen and sulphur have no influence on the calculation. For $C_2H_4O_2$ we calculate

$$DBE = \tfrac{1}{2}(2 \cdot 2 + 2 - 4) = 1$$

This molecule must contain one double bond or one ring closure. It may be acetic acid , but many other structures could also fit.



acetic acid

A more complicated molecule; C_3H_4NCl gives

DBE= 0.5(2*3+2-4+1-1) = 2

Appendix

HCN-analysis.

The HCN analysis provides the relative contents in per cent of the weight of elements H, C, and N. For example, you might get the numbers for your compound

C 41.12%;
H 6.75%;
N 0.00%;

These correspond to fractions $f_C = 0.4112$, $f_H = 0.0675$, and $f_N = 0.0$. The numbers do not add up to 100% in this case. The remaining 52.13% (f = 0.5213) consists of other elements than C, H, or N. These must be found experimentally. If experiments reveal no other elements, the remainder is assumed to be O.
Calculation of the stoichiometric composition is possible if a reasonably accurate molecular weight is available. Assume that Mw = 60 has been determined. The number of any atom kind (X) can be calculated from the formula

$$n_X = f_X \cdot Mw / M_X$$

where M_X is the atom mass of atom kind X.

$$n_C = 0.4112 \cdot 60 / 12 = 2.056 \approx 2$$
$$n_H = 0.0675 \cdot 60 / 1 = 4.050 \approx 4$$
$$n_O = 0.5213 \cdot 60 / 16 = 1.955 \approx 2$$

The composition is then $C_2H_4O_2$.

Table 2.
Chemical shifts of H on double and triple bonded C

Structure	δ/ppm range
C=C	
>C=C**H**	4.5-6.0
>C=C=C**H**	4.0-5.0
>C=C**H**–CO	5.8-6.7
–**H**C=C–CO–	6.5 - 8.0
–**H**C=C–O–	4.0-5.0
>C=C**H**–O–	6.0-8.1
–**H**C=C–N	3.7-5.0
C≡C	
–C≡C**H**	1.8-3.1
Aromatic	
Ar**H**	6.0 - 9.0
Aldehydes, formic acids and formamides	
R–C**H**O (aliphatic aldehydes)	9.4-10.0
Ar–C**H**O (aromatic aldehydes)	9.7- 10.5
–O–C**H**O (formic acids)	8.0-8.2
>N–C**H**O (formamides)	8.0-8.2

Table 3.
Typical chemical shifts of H bound to O, N, and S.

Structure	δ/ppm
Aliphatic amines, RNH_2, R_2NH	0.5-4.5
Aromatic amines, $ArNH_2$, ArNHR	3-6
Amides, RCONH, RCONHR	5-12
Aliphatic alcohols, R–OH	0.5-4.5
Phenols, Ar–OH	4.5-10
Phenols, Ar-OH hydrogen bonded	4.5-16
Carboxylic acids, RCOOH	9- 15
Imines, >C=N–OH	9- 12
Aliphatic thiols, R–SH	1 -2
Aromatic thiols, Ar–SH	3-4
H-bonded (>C =O...H–O–)	7-16

Further reading

This note is based on the following literature, which is recommended for further reading.

D. L. Pavia, G. M. Lampman and G. S. Kriz, Introduction to Spectroscopy, 3.ed.Brook/Cole, 2001.

D. H. Williams & I. Fleming, *Spectroscopic Methods in Organic Chemistry,* McGraw-Hill Book Co., 5 ed, 1995.

P. R. Young, *Practical Spectroscopy: The rapid interpretation of spectral data.* Books/Cole. Thomson learning, 2000

R. R. Ernst, G. Bodenhausen & A. Wokaun, *Principles of Nuclear Magnetic Resonance in One and Two Dimensions.* Oxford University Press. 1990.

J. K. M. Sanders & B. K. Hunter, *Modern NMR Spectroscopy,* Oxford University Press, 1989.

Exercise 4.

Compound **a** has the sum formula C_7H_8.

Calculate DBE (the number of double bond equivalents) see p. 41. The ^{1}H-NMR spectrum is shown below.

Write the structure formula for **a**.

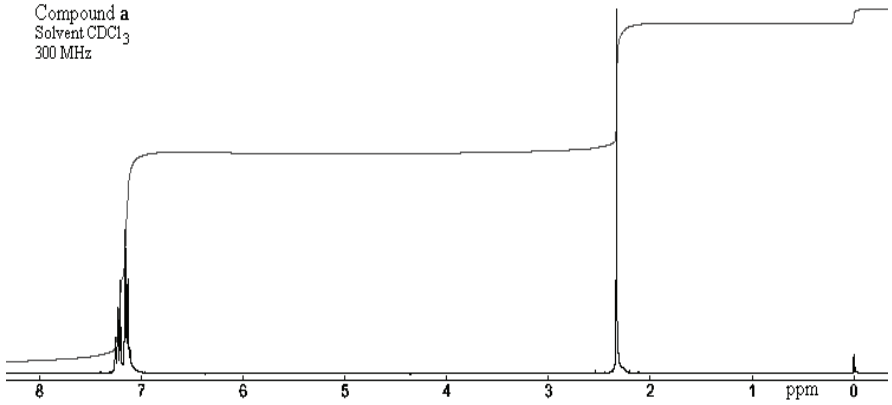


Table 4
Chemical shifts and multiplicity of
solvent signals for common NMR solvents.

Solvent	δ/ppm	Multiplicity
Acetic acid-d_4	2.05	singlet
.	11.5[a]	singlet
Acetone-d_6	2.05	quintet (1:2:3:2:1)[b]
Acetonitrile-d_3 (CD_3CN)	1.95	quintet (1:2:3:2:1)
Benzene-d_6	7.3	singlet
Chloroform-d ($CDCl_3$)	7.25	singlet
Cyclohexane-d_{12}	1.40	triplet (1:1:1)
Deuterium oxide (D_2O)	4.7[a]	singlet
Dimethylsulfoxide-d_6		
(DMSO-d_6)	2.5	quintet (1:2:3:2:1)
Dioxane-d_8	3.55	triplet (1:1:1)
Methanol-d_4	3.35	quintet (1:2:3:2:1)
.	4.8[a]	singlet
Dichloromethane-d_2		
(CD_2Cl_2)	5.35	triplet (1:1:1)
Toluene-d_8	2.3	quintet (1:2:3:2:1)
.	7.2	singlet
Trifluoro acetic acid-d	11.3[a]	singlet

Notes: a, Chemical shifts vary with temperature and solute concentration (H-bonded H); b, relative intensities of multiplet components. Note that the relative intensities are different from normal triplets and quintets. This is due to their origin from ^{2}J-coupling (J≈1.5 Hz) between ^{1}H and ^{2}H (D). D has spin 1.

Table 4a

Position of H_2O signals in different NMR solvents

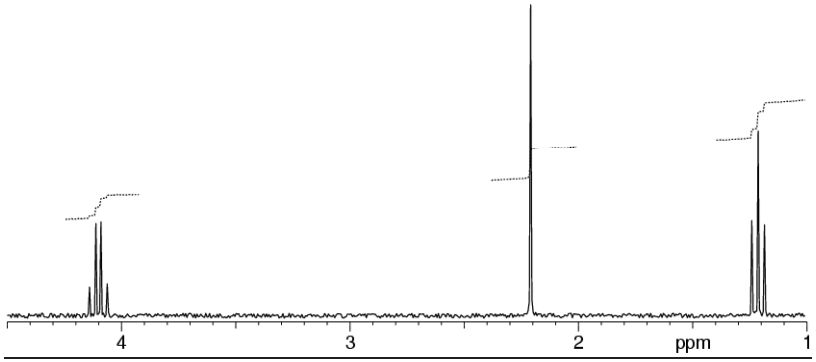
Acetone-d_6	2.85 ppm (broad)
Acetonitril-d_3	2.16 ppm
Benzene-d_6	0.50 ppm
Chloroform-d	1.54 ppm (broad)
Deuterium oxide (Heavy water)	4.82 ppm
Dichloromethane-d_2	1.52 ppm
Dimethylsulphoxide-d_6	3.32 ppm (broad)
Dimethylformamide-d_7	3.48 ppm
p-Dioxane-d_8	2.43 ppm
Pyridine-d_5	4.96 ppm
Tetrahydrofuran-d_8	2.23 ppm
Toluene-d_8	0.52 ppm

Exercise 3.

Which of the following formulae is consistent with the NMR-spectrum below? Full explanation is required. (Solvent is $CDCl_3$. The spectrum is recorded at 250 MHz.)

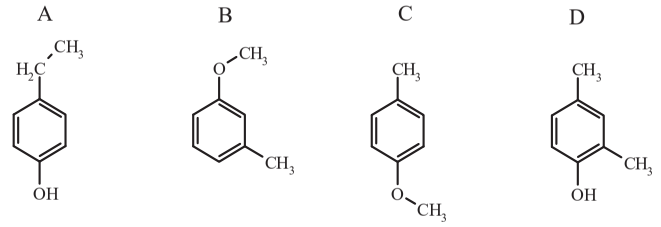
A Methyl propionate

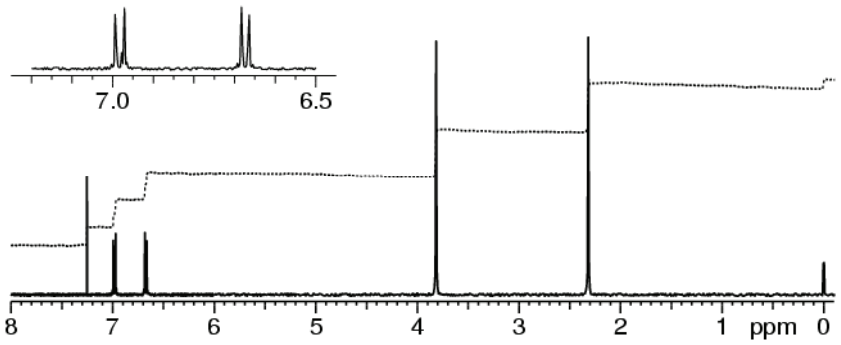
B Ethyl acetate



Exercise 2.

Which of the following formulae is consistent with the NMR-spectrum below? Explain fully. (The solvent is $CDCl_3$, and the spectrum is recorded at 300 MHz).





Solvent signals.

For the interpretation of the NMR spectrum, it is important to identify solvent signals and not to mistake them for signals from the sample. Chemical shifts and appearance of solvent signals from common NMR-solvents are listed in Table 4.

Solvents used to dissolve samples for NMR-spectroscopy usually are deuteriated to prevent the occurrence of very large signals from the solvent in the 1H NMR spectra. For example, if ordinary chloroform, $CHCl_3$, was used instead of $CDCl_3$, the H-atom in $CHCl_3$ would generate an NMR-peak several hundred-fold more intense than peaks from the sample. This could make the spectrum useless. The solvent signal is strongly reduced by replacing 99% or more H with D. D or ^2H, although still an NMR active nucleus, generates no signals in the frequency range for ^1H. The remaining peak intensity is due to incomplete replacement. For solvents with methyl groups, such as DMSO-d_6, the incomplete replacement of H for D results in a strangely shaped solvent peak. That is, a narrowly spaced quintet with component intensity ratios 1:2:3:2:1, unlike that expected from a Pascal triangle pattern (see F and w p. 177).
Another signal to watch for is that of water (see Table 4a).

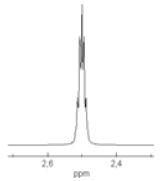


Figure 3. Solvent signal of DMSO-d_6

Lecture 2

Read intensively in F&W:
Page 174 (Spin-spin coupling) to 179 (Spin-spin decoupling)

Coupling constants.
Couplings are seen in the spectra as extra splittings. (see Fig. 1)

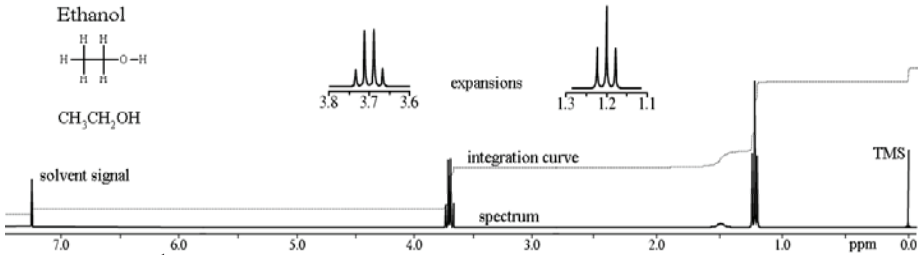


Figure 1. The ^{1}H-NMR-spectrum of ethanol dissolved in deuteriated chloroform (improved version of Figure 4.12 in F&W).

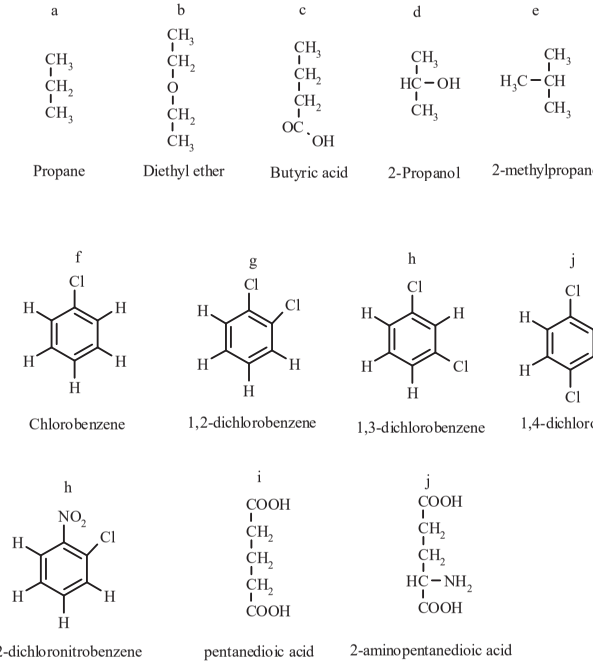
The couplings are transmitted through the bonds. We see primarily couplings through two bonds (Ha-C-Hb, Ha and Hb have different chemical shifts) or through three bonds (H-C-C-C-H). Couplings through two bonds we denote ^{2}J or geminal couplings (see Table 6). Couplings through three bonds we denote ^{3}J or vicinal couplings. See Table 7. Couplings constants are always given in Hz and as the name says, they are constants. Couplings over four or more bonds are typically seen in aromatic systems or other conjugated systems (see

Exercises in NMR

Exercise 1.

For each of the compounds below

a. Draw circles around groups of chemically shift equivalent H-atoms.
b. Suggest chemical shifts and relative intensities for the expected peaks in the ^{1}H-NMR spectrum.
c. Suggest the multiplicities of the peaks.

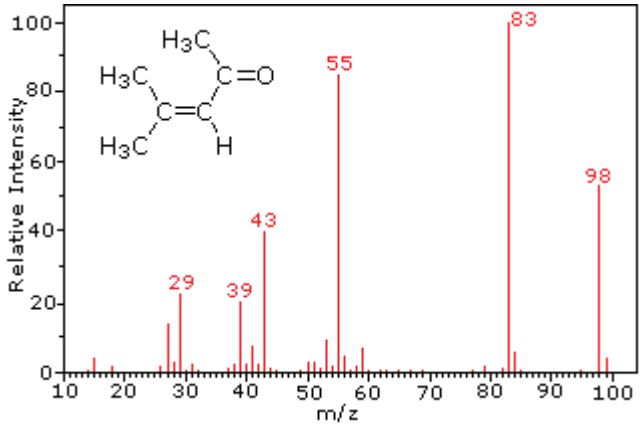


Mass Spectrometry.

The Molecular ion, or parent ion (M^+), is usually the one associated with the peak having the second highest m/z in the mass spectrum (sometimes named the **n** peak). The highest is the molecular ion of molecules with one ^{13}C, ^{2}H or other element isotope replacement, called the **n+1** peak. **n+2** -peaks may occur. However the latter are much less intense than the n peak.

The molecular ion is often of low intensity. Occasionally it is not observed because of very efficient fragmentation. Other methods must then be used to determine the molecular weight.

Analysis of fragmentation patterns is not part of Organic Chemistry (NAT-BAS).

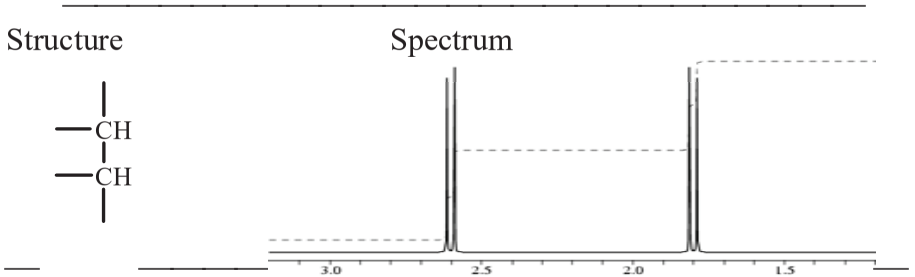


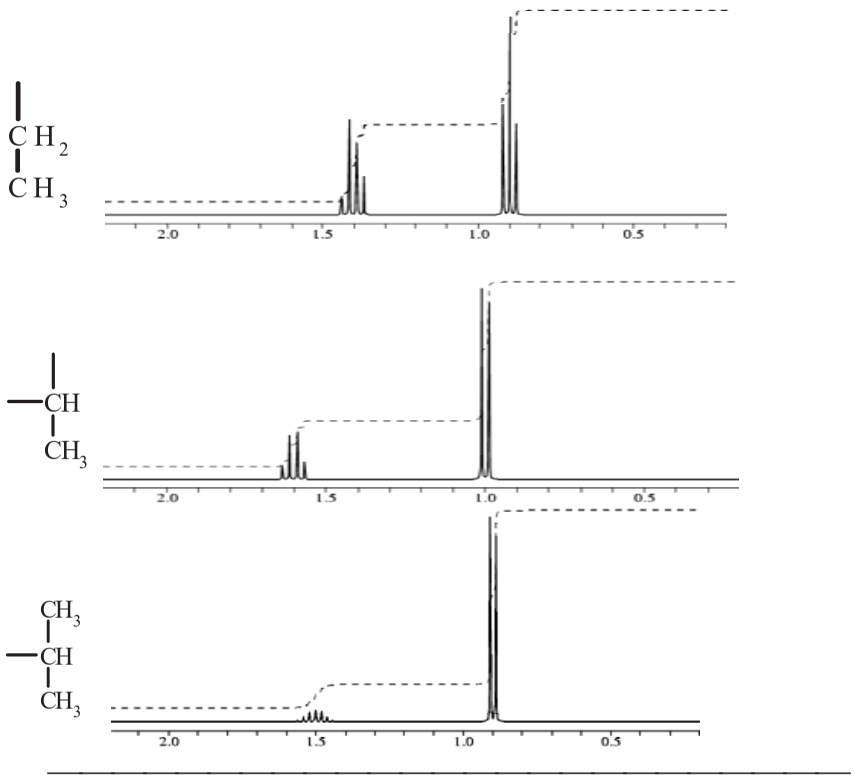
Typical mass spectrum. M+ = 98; M+1=99.

Table 8 for these so-called long-range couplings.
As we start analyzing coupling patterns Fig. 2 is very useful. The first spectrum is one proton coupling with one proton. This gives rise to a doublet (a doublet is two lines of equal height) and another doublet. If two protons couple with three we observe a quartet and a triplet (a quartet is four equally spaced lines, a triplet three lines). If one couples with three we see a quartet and a doublet. If one couple with six we observe a heptet (seven lines, look carefully for the two outer lines) and a doublet. From these observations we can formulate the so-called n+1 rule. The multiplicity (the number of lines of the signal) is one higher than the number of protons that it couples to (see below).

4. Spin-spin splitting
The n+1 rule. The rule is usually obeyed for H-atoms in saturated hydrocarbon skeletons. It fails if the coupling constants are not equal for all vicinal H-atoms. This occurs typically when rotation about the C-C bond is restricted, *e.g.* by ring closure. This topic will be further elaborated in Lecture 3. Figure 2 shows four examples of frequent molecular fragments and how their spectra are likely to appear.

Figure 2. Typical vicinal coupling patterns:





The Coupling Constant is the spacing between the lines in doublets, triplets, *etc.*. Unlike chemical shifts, coupling constants are measured in Hz. Since the coupling is unaffected by the external magnetic field, numbers in Hz are independent of the instrumental field strength.

The size of a coupling constants may be obtained from expanded plots (see Figure 1). Remember that, if the spectrum is measured at 300 MHz, then 1 ppm is 300 Hz.

Example: How large is the coupling constant (J) between H atoms in the CH_2 and CH_3 groups in ethanol? Refer to the expansion at 3.7 ppm in Figure 3 on page 14. Use a ruler. The 0.2 ppm long expanded axis measures 10.5 mm. One ppm (300 Hz) is then 10.5/0.2 = 52.5 mm. The distance between the outer peaks of the quartet approximately 3.1 mm and covers three J. J is then 300Hz * 3.1 mm / (52.5 mm * 3) = 5.9 Hz.

IR-spectra

Traditionally, IR-spectra are shown either as transmission or as absorption spectra. The contents are identical, but the appearance is different. The two modes are compared in Figure 11. All spectra in F&W are shown as absorption spectra, but with the absorbance axis inverted. This mode is unusual.

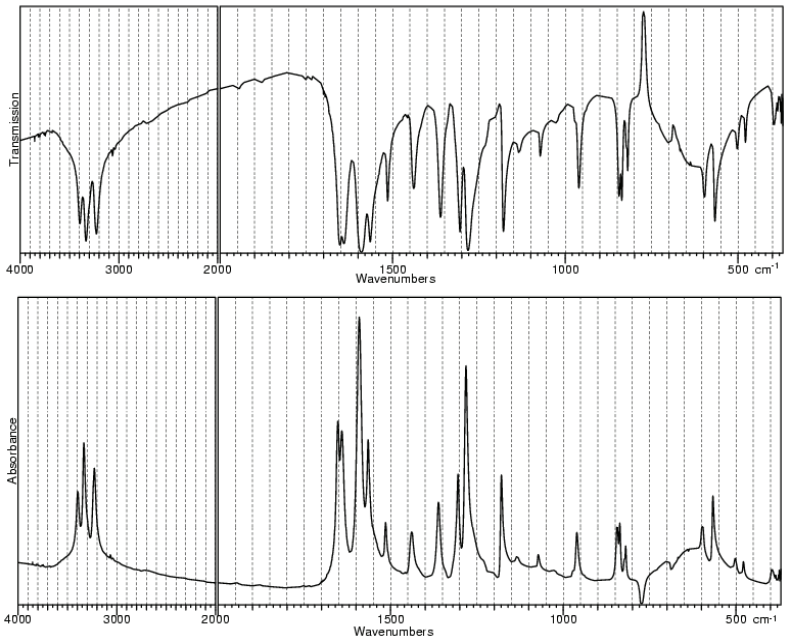
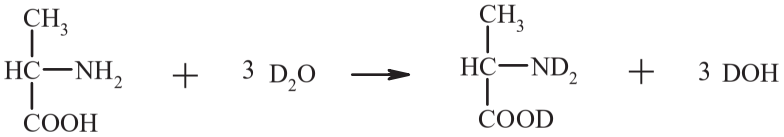


Figure 11: Transmission and absorption.

IR spectra are analyzed looking for so called group frequencies. C-H stretching vibrations, C=O stretching vibrations etc. Check Table 4.3 at page 190 of F.W. for more information.
Which functional groups are present in the IR spectrum?

H/D-replacement

In D_2O solution, *labile* H-atoms are replaced with D-atoms from the solvent. Labile H-atoms are those covalently bound to electronegative heavy atoms, such as O, N, and S.



Example:
Since D_2O is in large excess, the replacement is complete. This means that NMR-signals from NH, OH, SH, etc. are absent when the solvent is D_2O. The absent peak integral is instead found under the solvent (DOH) signal at 4.7-4.9 ppm. The total number of labile H-atoms in the sample can be estimated from the integral of the DOH signal .

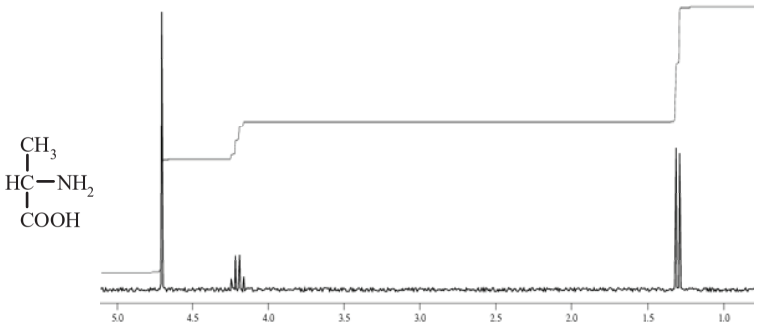


Figure 3. 300 MHz 1H-NMR spectrum of alanine (2-aminopropionic acid) dissolved in D_2O.

Using the n+1 rule predict the NMR spectrum of

a. $–CH_2-CH_2-$
b. the central CH_2 group of :
c. $–CH_2-CH_2-CH_2-$
d. $–CH_2-CH_2-CH_3$

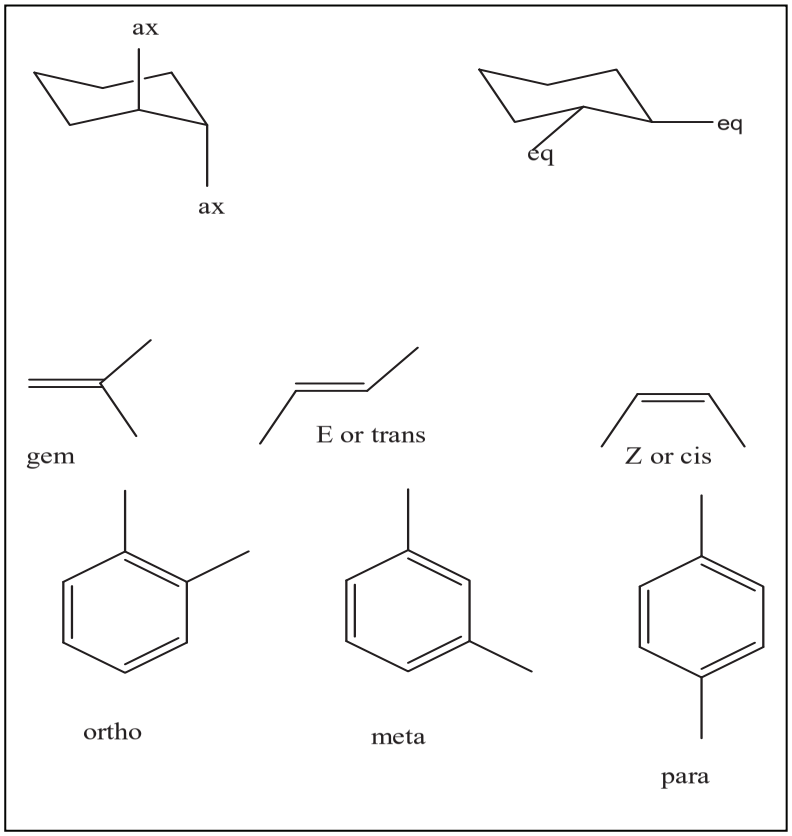
The intensities of the spin patterns follow Pascals triangle (see F and W p.177):

Singlet 1
Doublet 1:1
Triplet 1:2:1
Quartet 1:3:3:1
Pentet 1:4:6:4:1
Hextet ??? (**try!!**)
Heptet ???

When you have done the heptet, then you know why it is difficult to see the outer lines.

Magnitudes of coupling constants

A couple of situations are occurring very often:
$-CH_n-CH_n-$ (n= 1 to 3). Around a single bond we have free rotation and the ^3J coupling (vicinal coupling) is typically 6-7 Hz (See Table 6). Another situation is cyclic compounds in which the protons are locked. For cyclohexane we find for axial hydrogens ^3J = 8-14 Hz whereas for equatorial only 0-5 Hz. The vicinal coupling constant depends on the dihedral angle. For structures see next page.
For olefinic protons (protons at double bonds) the $^2J(H,H)$ coupling is rather small and sometimes even zero (Table 6). $^3J(H,H)$trans (trans means on opposite sites of the double bond, see next page) is large 12-18 Hz). $^3J(H,H)$cis is only 6-14 Hz.
For aromatic compounds we find $^3J(H,H)$ortho = 6-9 Hz, whereas $^4J(H,H)$meta = 1-3 Hz and $^5J(H,H)$para = 0-1 Hz. For ortho, metha and para (see next page).


ax
ax
eq
eq
gem
E or trans
Z or cis
ortho
meta
para

Exchange broadening

Hydrogen atoms bound to O, N, S usually show broad peaks, and absence of spin coupling to vicinal carbon bound H. The phenomenon responsible for this is called chemical exchange. It may heavily influence the peak shapes of labile hydrogen atoms, that is, as above, NH, OH and SH and is expected to be more predominant in solvents with good hydrogen bonding capability. Carboxyl (-COOH) groups may be broadened over several ppm-units. They may then be observed only as a slow increase on the integral line or not at all.

Line broadening and lack of spin coupling is explained by migration of the H-atoms from molecule to molecule between H-bond donor-acceptor pairs. Broadening and absence of spin coupling is expected when the residence time is in the millisecond range or shorter. The broadening may be affected by change in temperature, acidity, and solvent composition.

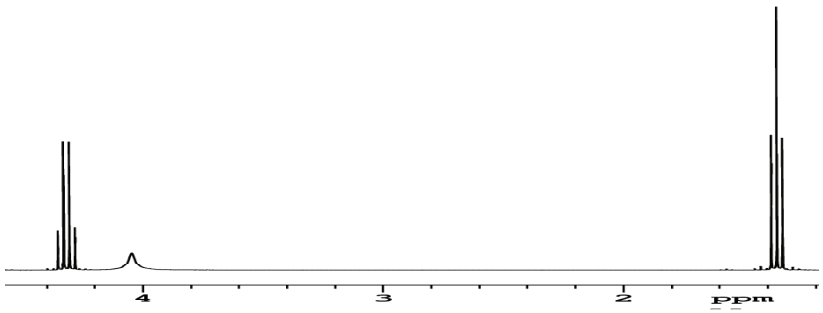


Figure 2: The aliphatic region of ethyl 3-aminobenzoate showing the contrast between the broad -NH_2 proton signal at 4.1 ppm and the sharp lines of the ethyl group.
See also the -OH signal at 1.5 ppm in the ethanol spectrum in Figure 1 of Lecture 1.

AX- versus AB-coupling.

The appearance of the spin-spin splitting is markedly influenced by the difference in chemical shift (measured in Hz) between the two signals. This is illustrated in Figure 3 for a system with two doublets. If they are far apart, the Pascal triangle patterns results. The spin system is called an AX-system. As the signals get closer together, the proximal components increase and the distal components decrease in intensity. It is then called an AB-system. When chemical shifts are identical, no splitting is seen, the involved protons are equivalent.

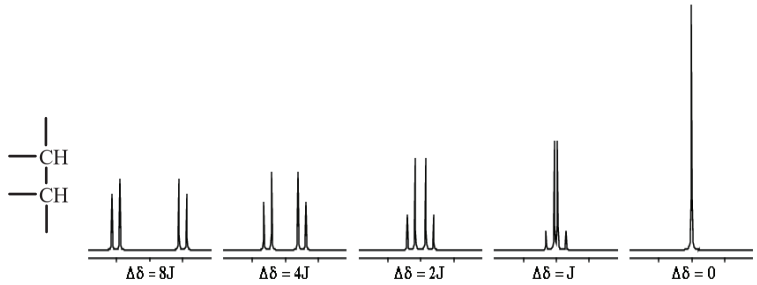


*Figure 3, A*ppearance of 2-spin system at different chemical shift distances. If the distance in Hz is larger than ten-fold the coupling constant, $\Delta\delta/J > 10$, then the simple splitting pattern is observed. The central components of the doublets increase intensity as the ratios gets smaller. When $\Delta\delta$ is zero, the two H-atoms are equivalent, and the coupling is not seen (see chapter on equivalence).

Geminal, Vicinal and Long Range Couplings

H-atoms bound to adjacent C-atoms are called *vicinal H-atoms*. The magnetic coupling between them is therefore called *vicinal coupling*. It passes through 3 covalent bonds, and the coupling constant is then denoted by the symbol ^3J. These are the couplings that give rise to the ordinary spin-spin-splitting in ^{1}H-NMR spectra.

Coupling between spins is a common phenomenon, and is not restricted to vicinal H-atoms. There is also couplings between H-atoms bound to the same C, called *geminal* coupling. These, however, are only seen if these H-atoms are not equivalent. An important example of this is in the case of *diastereotropic H-atoms* (see Lecture 3).

Long Range Coupling through 4 or 5 covalent bonds is seen in systems with *delocalized electrons*, such as aromatic systems or chains with conjugated double bonds, ^{4}J couplings may be strikingly apparent, and ^{5}J couplings may be visible.

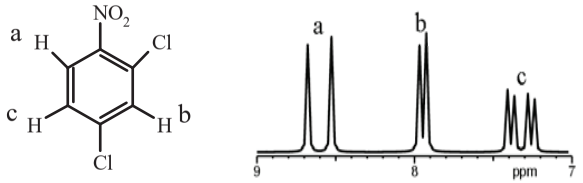


Figure 4: Long-range couplings in the aromatic ring of 2,5-dichloro nitrobenzene. H^a is split with an ordinary large vicinal (^{3}J) coupling (7 Hz) to H^c. H^b forms a narow doublet because of a 2 Hz ^{4}J-coupling (or 'meta-coupling') to H^c. (In the absence of long range coupling it would have formed a sharp singlet. H^c forms a complex multiplet due to splitting by unequal couplings. The expected ^{5}J coupling between H^a and H^b is not resolved. The spectrum is measured at 300 MHz.

Long range couplings may change the involved peaks into complex multiplets with a hairy appearance. This along with AB-style peak deformation (see above) can make it difficult to sort out the patterns. See Figs. 5 and 6.

Diastereotropic H-atoms

Complicated spectra are seen in cases where a –CH_2- is bound to a chiral center, as shown in the simulated spectrum below. A chiral center is typically a carbon with four different atom attached also called an asymmetric carbon. Such a situation is often found in aminoacids.

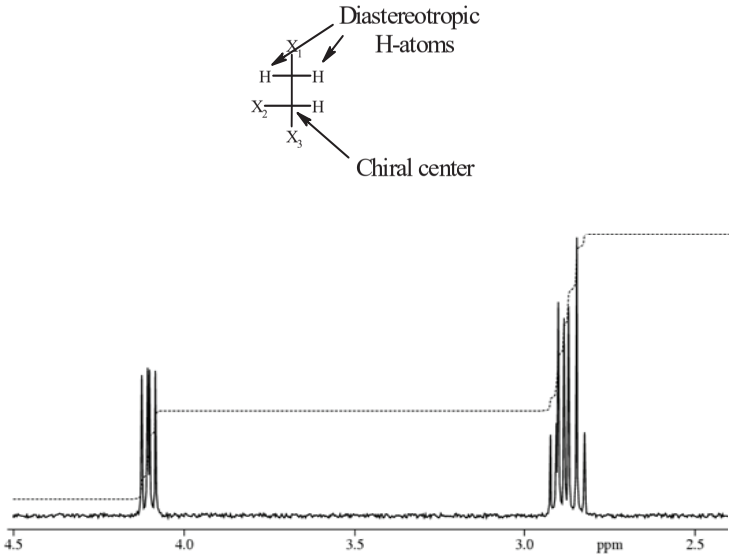


Figure 1: Expected splitting of H-atoms associated with an asymmetric carbon atom.

The H atoms of the –CH_2- in this case are non-equivalent, and their chemical shifts are different. The chemical shift difference depends on the rest of the molecule and may vary from almost none to a few tenth´s of a ppm. Consequently the large geminal coupling between them is displayed. Furthermore, their vicinal couplings to the H of the chiral –CH are different so that the Pascal triangle pattern is distorted. Together these effects lead to more or less distorted splitting pattern which is some times highly complicated.

Equivalence

Equivalent H-atoms are defined as H-atoms with the same chemical shift. *Which H-atoms in a formula can one expect to be equivalent?* Rules 1 and 2 are useful guides.

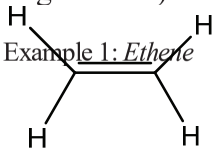
Rule 1: H-atoms, in structure of freely rotating single-bonds, are equivalent, if the trees of bond connections to all other atoms in the molecule are identical.

Consequently, H-atoms bound to the same C-atom (in methyl ($-CH_3$) and methylene ($-CH_2-$) groups) are expected to be equivalent. Also, symmetry related H-atoms in symmetric molecules are equivalent (3-pentanol examples in F&W, p 179).

There is one important exception from this rule. It is treated under the heading *Diastereotropic H-atoms.*

Rule 2: H-atoms in a ridgid structure (that is structure with double bonds or ring closures) are equivalent only if they are related by symmetry.

Example 1: *Ethene*

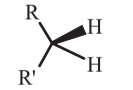


There are two mirror planes, one vertical, and one horizontal. Any of the four atoms can be reflected into any of the others by one or both mirror planes. That is, all four H-atoms are equivalent, and the NMR spectrum contains only one singlet.

If one H-atom is replaced by another group (as a phenyl-group to make styrene as in the example on p. 178 in F&W), then both mirror planes are canceled. That is, all the remaining three H-atoms are non-equivalent.

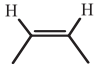
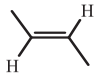
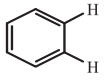
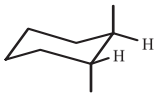
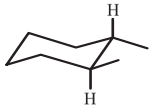
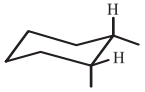
Example 2: *Benzene*:
There are at least 6 mirror planes. All H-atoms are equivalent

Table 5.
Geminal coupling constants

Structure	$^2J_{HH}$ (Hz) range
	-8…-18
	-11…-14
	-3…+3

The signs are not important for the kind af analysis that we do in this course. Concentrate on magnitudes.

Table 6 Vicinal coupling constants

Structure	$^3J_{HH}$ (Hz) range	typically
CH_3-CH_2-	6-8	7
CH_3-CH<	5-7	6
-CH_2-CH_2-	5-8	7
>CH-CH<	0-8	7
>C=CH-CH<	4-11	6
>C=CH-CH=C<	6-13	11
>CH-CHO	0-3	2
>C=CH-CHO	5-8	7
	0-12	8
	12-18	15
	6-9	
	0-5	
	8-14	
	0-7	

Lecture 3

Page 177 (Nonequivalent nuclei) - 182 (The NMR spectrometer)
Page 184 (Effect of Field strength) - 185 (Medical applications).
Read extensively:
Page 182 (The NMR spectrometer) - 185 Top

Now mastering analysis of ^{1}H NMR spectra other techniques may of course be useful as supplement. It is of importance to remember the results of the practical tests. Burning test, Beilstein test, solubility, test for halogens, test for aldehydes, ketones etc.
Two other spectroscopic techniques come also to mind:
IR-spectroscopy and Mass spectrometry. For these techniques read:

IR-spectroscopy.
Read extensively the following in F&W:
Page 188 (Infrared (IR) spectroscopy) to 190 (Characteristic absorptions).
Read intensively :
Page 190 (Characteristic absorptions of Functional groups) to 199 (Visible and Ultraviolet (UV) spectroscopy).

Mass spectroscopy (MS).
Read intensively:
Page 205 (Mass Spectrometry) to 206 (Fragmentation Patterns).

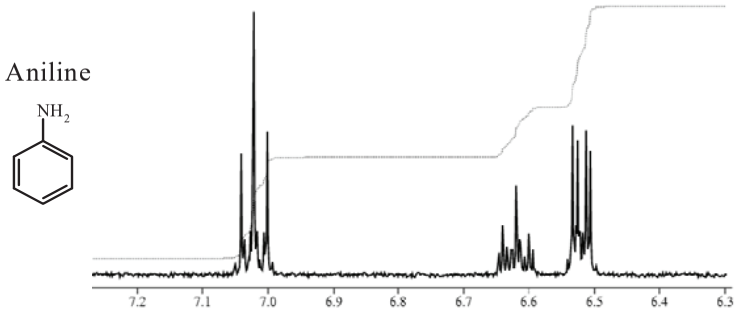


Figure 5: Aromatic region of the NMR spectrum of aniline

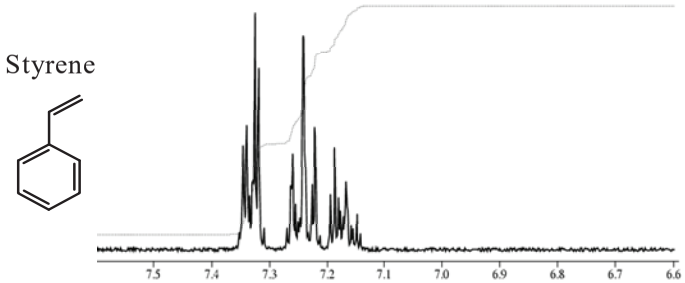
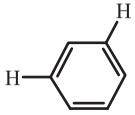
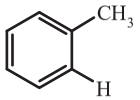


Figure 6: Aromatic region of the NMR spectrum of styrene

Table 7. Long-range coupling constants.

Structure	$^4J_{HH}$ (Hz)
-CH=C-CH<	0-3
-HC=C=CH-	4-6
HC=C-CH<	1 -3
	1 -3
	0.6 - 0.9

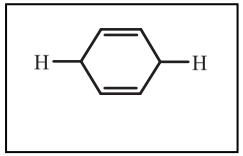
	$^5J_{HH}$ (Hz)
>CH-C=C-CH<	0-2
-HC=C=C-CH<	2-3
>CH-C≡C-CH<	1 -3
	0- 1
	8-10

Table 8

Substituent corrections (z_i) to chemical shifts (in ppm) for aromatic H in benzene (Equation 1 on p.25)

Substituent	ortho	meta	para
–H	0	0	0
$–CH_3$	-0.20	-0.12	-0.22
$–CH_2CH_3$	-0.14	-0.06	-0.17
$–CH=CH_2$	0.06	-0.03	-0.10
–Ar	0.37	0.20	0.10
–CHO	0.56	0.22	0.29
$–COCH_3$	0.62	0.14	0.21
–COOH	0.85	0.18	0.27
–OH	-0.56	-0.12	-0.45
$–O–CH_3$	-0.48	-0.09	-0.12
$–O–COCH_3$	-0.25	0.03	-0.13
$–NH_2$	-0.75	-0.25	-0.65
$–NO_2$	0.95	0.26	0.38
–F	-0.26	0.00	-0.04
–Cl	0.03	-0.02	-0.09
–Br	0.18	-0.08	-0.04
–I	0.39	-0.21	0.00

The substituent correction to the chemical shifts are highly reliable for mono substituted benzene. They are less reliable but still very useful for di- and tri-substituted benzene. For more complicated substituents use the substituent in the Table that looks alike. Example, CH_2OH use CH_2CH_3.

Exercise:

Calculate the chemical shifts for the three other H-atoms in 4-chlorobenzoic acid.

For more complete tables consult e.g.

D.H.Williams and I.Fleming, Spectroscopic Methods in Organic Chemistry, McGraw Hill.

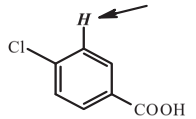
Substituent shifts

Chemical shifts of H-atoms in specified types of structure can be estimated with good accuracy by using empirical substituent shifts. This method is explained here for derivatives of benzene which is part of many of the unknown compounds in this course.

Remember that the six H-atoms in benzene itself are magnetically equivalent and form a sharp singlet (at 7.27 ppm). When one or more H-atoms are substituted, the chemical shifts of the remaining H atoms are changed and their equivalence is fully or partially lost. The change in chemical shift can be calculated by use of the substituent shifts listed in Table 4 (p 18), and Equation [1].

$$\delta_H = 7.27 + \sum_i z_i \qquad [1]$$

The index *i* in Eq. 1 runs over all positions in the ring, that is, the two *ortho*-positions, the two *meta*-positions, and the one *para*-position. The position here is relative to the H-atom, for which the chemical shift is to be calculated. Example: Calculate the chemical shift of the highlighted H-atom in 4-chlorobenzoic acid.



From the H-atom's point of view the Cl atom is in the *ortho*-position, and the COOH group is in the *meta*-position. The *ortho*-substituent shift of chlorine and the meta-shift for carboxyl is found in Table 8, are 0.03 and 0.18 ppm, respectively. All other positions are filled with H-atoms with zero substituent shifts. The estimated chemical shift from equation [1], δ_H, is then 7.27 + 0.03 + 0.18 = 7.48 ppm.