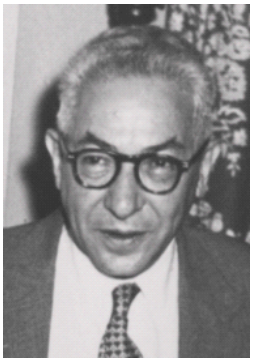
Fig. 10-1



Isidor Rabi (1898-1988)
http://nobelprize.org/nobel_prizes/physics/laureates/1944/rabi-bio.html

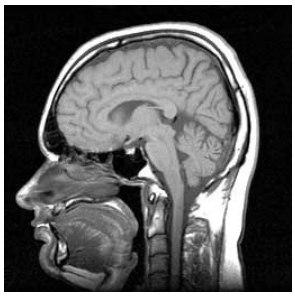
Experiment 10

IDENTIFICATION OF ORGANIC UNKNOWNS. II

Text Topics and New Techniques

Stereochemistry, polarimetry and interpretation of nmr spectra.

Fig. 10-2
MRI of human head



Discussion and Techniques

Experiment 7 provided experience with the use of the physical properties (density, boiling point, refractive index) and infrared spectroscopy to determine the identity of an unknown. This week, another very valuable method for identifying an organic compound, nuclear magnetic resonance spectroscopy, will be added to the resources available. Two physicists, F. Bloch and E.M. Purcell received the Nobel Prize in Physics, in 1952, for the first experimental observations of nmr. Prof. R.R. Ernst received the Nobel Prize in Chemistry, in 1991, for the development of nmr techniques. However, it was the work of physical-organic chemists like John Roberts at the California Institute of Technology who made nmr an organic chemist friendly tool. Thanks to the creativeness and ingenuity of Paul Lauterbur, Peter Mansfield, Raymond Damadian, Bill Edelstein and others, a modified nmr technique called mri (magnetic resonance imaging) is now a powerful tool for medical diagnosis. Lauterbur and Mansfield shared the Nobel Prize in Medicine for their contributions to this field. For more information, see:
http://www.isbe.man.ac.uk/personal/dellard/dje/history_mri/history%20of%20mri2.htm
http://en.wikipedia.org/wiki/Magnetic_resonance_imaging

Nmr spectroscopy provides substantial information about the presence of functional groups and more importantly, the structures and the carbon backbones of compounds. Like ir, nmr also involves the absorption of energy. The transitions for nmr involve inversion of nuclear spin. The energy required for a spin inversion is much less than the energy required to activate electronic (uv and visible) and vibrational (ir) transitions and falls in narrow regions of the microwave energy portion of the electromagnetic spectrum. The particular region depends on the type of nucleus. The first requirement for observation of a spin inversion is that the nucleus must have a spin. ^{1}H and ^{13}C have spins but ^{12}C does not. Therefore the first two nuclei are candidates for nmr but the latter is not. Other nuclei besides ^{1}H and ^{13}C are studied using nmr but ^{1}H and ^{13}C are the two routinely and most commonly used for the analysis of organic compounds.

Because of the energies involved in ir transitions, almost all of the molecules at room temperature are in their lowest vibrational energy states. For nmr, the situation is considerably different. The two spin energy states, aligned with and against the field, have such a small energy difference (microwave region) that the two states are almost equally populated. The nmr must be a very sensitive instrument to be able to detect the slight excess of molecules that move up in energy compared to those that go down. Second, ir spans an energy region of about 4000 to 400 cm^{-1} or about a ten-fold change in energy. For ^{1}H nmr, the transitions take

place in a very narrow section of the microwave region that involves a change of only about 20 parts per million or about 0.002% change in energy. Because of the extreme sensitivity and resolution needed, an nmr instrument must be constructed according to very high specifications. To make sure that the magnetic field is as homogeneous as possible and the same strength field is experienced by all the molecules, the sample tube has a very small diameter (4.2 mm i.d.) and the tube spins rapidly (20 Hertz) to average out field strength differences while scans are being performed.

Magnets for nmr instruments come in a varying sizes from the equivalent of 60 mega-Hertz to several hundred mega-Hertz. Since the energy of the transitions are reported as ratios, all instruments give transition energies at the same positions that do not depend on the field strength. However, the coupling which appears in the spectrum as the splitting patterns does change appearance with field strength. The coupling does not depend on the field strength and the splitting patterns appear to get squashed together in the instruments with stronger magnets. However, the splitting can be easily observed by expansion of the axis. Just be careful when comparing spectra run on a 60 or 90 mega-Hertz instrument with Internet spectra run on a 300 mega-Hertz instrument. Unless accompanying expanded portions of the spectrum are included, the splitting will be difficult to observe and compare to a spectrum run on a 60 mega-Hertz instrument.

For a discussion of the interpretation of nmr spectra, please refer to your organic chemistry textbook or to one of the Internet sites below with hotlinks available at the ***Organic Chemistry Directory***:
Organic Chemistry Directory - http://murov.info/orgchem.htm

http://www.chem.ualberta.ca/~orglabs/Interactive%20Tutorials/hnmr/HNMRmain.html
http://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/spectro.htm
http://www.nd.edu/~smithgrp/structure/workbook.html
http://organicchemistryreview.com/spectroscopy.html
http://www.shu.ac.uk/schools/sci/chem/tutorials/
http://www.colby.edu/chemistry/NMR/NMR.html
http://www.science-and-fun.de/1hbuch/english/
http://www.kayelaby.npl.co.uk/toc/#3_8
http://www.wfu.edu/~ylwong/chem/nmr/h1/
http://w3.chem.ucla.edu/~webspectra/
http://www.ch.ic.ac.uk/local/organic/nmr.html

The brief discussion here is only intended to present some of the most important features.

Chemical shifts. There are three basic types of information present in an ^{1}H spectrum. The chemical shift provides some information about which functional groups are or are not present. The table on the next page gives an abbreviated list of ^{1}H and ^{13}C chemical shifts. The pK_a values are included for informational purposes only. As chemical shifts are due to shielding by electrons, electronegative atoms such as halogens, oxygen and nitrogen cause downfield shifts. It is particularly important to notice that aromatic hydrogens are in the 6.5 to 8.5 δ region and it is generally possible by inspection to determine if the molecule is aromatic. Other notable absorptions are the regions 2.1 - 2.6 δ for hydrogens α to a carbonyl (common for methyl ketones such as acetone), 3.3 - 4 for hydrogens on carbons singly bonded to an oxygen (common for alcohols, ethers and esters), 4.6 - 5.7 for alkenes, 9.5 - 10 for aldehydic hydrogens and 10 -13 for carboxyl hydrogens.

Splitting patterns are the result of coupling with adjacent hydrogens. When there is coupling to hydrogens on one side of the carbon only, there will be n + 1 lines present (n = # of identical hydrogens). In other words, for a compound like CH_3CH_2Cl, the signals for the methyl hydrogens will be split into 3 lines (2 + 1) by the adjacent methylene group and the methylene will be split into 4 lines by the adjacent methyl group. If there are hydrogens on both sides of a carbon, the splitting will be more complex and a multiplet usually results. Common patterns when there are only 2 kinds of hydrogen coupling include the triple-quartet indicative of an ethyl, 2 doublets indicative of -CH-CH-, a doublet and a quartet indicative of $-CH-CH_3$, two triplets indicative of $-CH_2-CH_2-$ and a doublet and a multiplet (a septet but usually the outer lines are two weak to observe) indicative of isopropyl.

Selected ^{1}H and ^{13}C Chemical Shifts and pK_a values

Type of proton	^{1}H δ (ppm)	^{13}C δ (ppm)	pK_a
R **C**H_3	0.8 - 1.0	10 - 40	50
R**C**H_2R	1.2 - 1.4	15 - 55	50
R_3**C**H	1.4 - 1.8	20 - 60	50
R**C**OCH_3	2.1 -2.6	180 - 215	18 - 20
R**C**OOH, R**C**OOR, R**C**ONH_2		160 - 185	24 - 25 (α hydrogens)
Ar**C**H_3	2.2 - 2.6		41
sp**C**H	2.5 - 3.1	65 - 85	25
-O**C**H_3, O-**C**	3.3 - 4.0	40 - 80	
R**C**H_2Cl (or Br)	3.4 - 3.8	25 - 80	
vinylic (sp^2**C**H)	4.6 - 5.7	100 - 150	44
ArH	6.5 - 8.5	110 - 160	43
aldehyde**CH**	9.5 - 10	180 - 215	
RO**H**	0.5 - 5.5*		15 - 18
ArO**H**	10.5 - 12.5*		10 - 11
N**H**	0.4 - 2*		36 - 40
ArNH_2	3.4 - 4.2*		
COO**H**	10 - 13*		3 - 5
H_2SO_4			-9
HCl			-7
HNO_3			-1.3
H_3PO_4			2.1
H_2O			15.7

*variable depending on concentration and solvent

Integration. The third piece of information in the nmr spectra is the integration. The relative integrations give the ratios of the number of hydrogens that have caused each signal. By considering the chemical shift, the splitting and the integration, it is possible to determine considerable structural information about the molecule and often can be used to determine the overall structure. Once possible structures have been determined using nmr and other information, it is possible to confirm identity by comparing the spectrum to a spectrum in a collection. For collections of nmr spectra, refer to pages 9 and 10 of the ***Chemistry Resources*** section of this text.

^{13}C. For ^{13}C spectra, chemical shifts provide most of the easily obtainable information. The spectra are usually run in a way that eliminates coupling and it is not a routine procedure to obtain integrations. However, the chemical shifts are much bigger than with proton chemical shifts and the information can considerably facilitate structure determinations. For example, note that carbonyl carbons are around 200 δ and usually discernible in the spectrum. Carbon as can be noted from the atomic mass for carbon in the periodic table (12.011 g/mol), contains only 1% ^{13}C. This means that the instrument must be even more sensitive than for proton resonance. Part of this is usually accomplished by performing many scans and having the computer average the scans. This helps to minimize the contributions from noise. Generally it also means that ^{13}C scans have to be on pure or concentrated samples. In addition to containing ^{1}H spectra, both the NIMC site and Aldrich contain many ^{13}C spectra.

Solvent. Pure liquids are sometimes ok but high viscosity results in broad signals. ^{1}H spectra are usually run in 10 to 20% solutions. Solvent selection is limited, however, by the desirability to avoid solvents having hydrogens. CCl_4 and $CDCl_3$ are probably the two most commonly used solvents for nmr. Handle CCl_4 with extreme care because of its potential health hazards (suspected carcinogen). Deuterochloroform ($CDCl_3$) is similar in price to CCl_4 and because of some polarity is often a better solvent and is considered less hazardous. The deuterium does not resonate in the light hydrogen region. Another relatively inexpensive deuterated solvent is heavy water (D_2O) but water is a poor solvent for most organic compounds. Many other deuterated solvents are available but unfortunately are not nearly as inexpensive as $CDCl_3$.

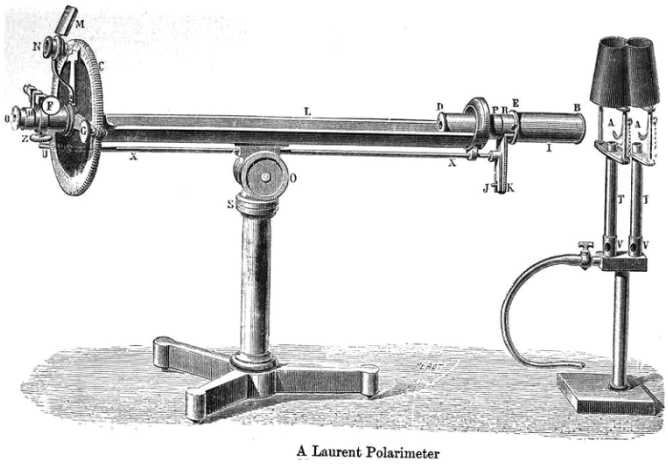
For ^{13}C, samples are usually run neat (pure). For solids, carbon tetrachloride or deuterochloroform are used but it is necessary to take into account that each has a carbon that will give a signal.

TMS. As it is very difficult to determine the absolute energy of a transition, a standard is usually added to the nmr tube and the chemical shifts are determined in ppm (δ) relative to the standard. Tetramethylsilane is an excellent choice for this purpose for both ^{1}H and ^{13}C spectra. TMS has many hydrogens but they are all identical and they absorb at high energy where very few other protons absorb. For ^{13}C spectra, TMS is also a good standard as it has 4 identical carbons that absorb at high energy out of the region of most other carbon absorptions. TMS is inert and very volatile so it is fairly easy to remove it from the sample after running it if it is important to recover the sample. Other compounds such as chloroform can also be used especially if a second point is needed to calibrate the range of the scan.

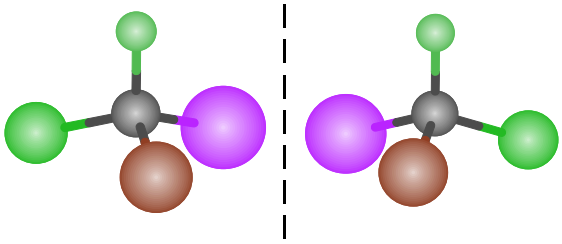
Polarimetry. The second unknown in this experiment is chiral. By far, the most common origin of chirality in organic compounds is a carbon with 4 different groups attached. When there is only one carbon with 4 different groups attached, the molecule will have a non-superimposable mirror image. The two possible stereoisomers are called enantiomers. Except for two characteristics, enantiomers have the same properties. However, enantiomers rotate the plane of plane polarized light in equal but opposite directions and they interact with other chiral molecules differently. The extent of light rotation is measured with an instrument called a polarimeter. To illustrate the different ways enantiomers interact with other chiral molecules, consider the amino acids that are linked together in protein. All but the simplest one, glycine, are chiral. Virtually all naturally occurring amino acids on earth have only one of the two possible configurations. Since we don't have the enzyme required for metabolizing the enantiomeric set of amino acids, we could not survive on a diet containing only the enantiomeric amino acids.

Analyzer - fixed polarizer
rotatable polarizer light source

Fig. 10-3 polarimeter tube compartment



A Laurent Polarimeter



Procedure

This experiment involves the analysis of two liquid unknowns. The possible list of unknowns for the unknown will be a slightly expanded version of the list used in ***Experiment 7***. You will be given several milliliters of a liquid unknown that will be one of the following:

aromatic hydrocarbons

t-butylbenzene
ethylbenzene
isopropylbenzene
toluene
1,3,5-trimethylbenzene
p-xylene

ether

anisole

ketones

2-butanone
cyclohexanone
2-heptanone
3-heptanone
2-hexanone
3-hexanone
3-methyl-2-butanone
5-methyl-3-heptanone
5-methyl-2-hexanone
4-methyl-2-pentanone
2-octanone
2-pentanone
3-pentanone

acetophenone
propiophenone

alcohols

1-butanol
2-butanol
1-hexanol
2-hexanol
2-methyl-1-butanol
3-methyl-1-butanol
2-methyl-2-butanol
2-methyl-1-pentanol
4-methyl-2-pentanol
1-pentanol
2-pentanol

esters

butyl acetate
t-butyl acetate
ethyl acetate
ethyl butanoate
ethyl pentanoate
ethyl propanoate
isobutyl acetate
isobutyl propanoate
isopropyl acetate
isopropyl butanoate
methyl butanoate
methyl isobutanoate
methyl pentanoate
propyl propanoate
propyl acetate

ethyl benzoate
methyl benzoate

Unknown II. Using the instructions in the *Techniques* section of this experiment and ***Experiment 7***, determine the boiling point, density, refractive index, ir and nmr (^{1}H and ^{13}C if available) spectra of your unknown. Use the spectra coupled with the physical properties and chemical resources to deduce the identity of your compound and who else in the class has the same unknown.

Liquids x and y. For the second unknown, you will need a partner. Two liquids, x and y will be available in the laboratory. You will determine the physical properties, ir and nmr spectra and the optical rotation of one of the two liquids and your partner will do the same measurements on the other liquid. In addition you should carefully smell both of the liquids and try to describe any similarities and/or differences in their odors. For the optical rotation measurements, polarimeter tubes already full with x and y should be available. Compare all the measurements, the spectra and the odors of x and y and comment on the relationship of x and y. Although the goal of this part of the experiment is the comparison and not identification of x and y, determine as much as you can about the structure of x and y from the spectra and identify them if possible.

Reference

Murov, S. L.; Pickering, M. *J. Chem. Educ.*, **1973**, *50*, 74.

Prelaboratory Preparation - *Experiment 10*

List all the goals of the experiment.

Observations

Report all relevant observations.

Conclusions

This section should include the following:

1. Were the goals of the experiment achieved? Explain your answer.
2. What was the identity of your unknown. Carefully explain the evidence.
3. Who else had the same unknown? Carefully explain the evidence.
4. Compare all the information obtained about x and y. What was the relationship, if any, between the two compounds?
5. Report any structural conclusions you can come to about x and y as well as their identities if possible.
6. Comment on the usefulness of ir and nmr for determining structures of your unknown and x and y.