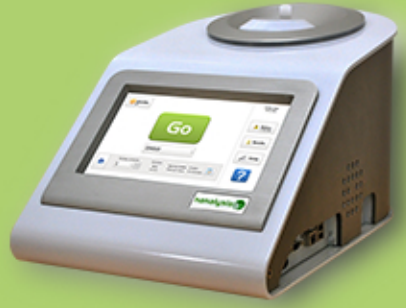
NMReady

Unknown Identification by ^{1}H NMR Spectroscopy

The incorporation of instrumentation into undergraduate laboratories has been shown to increase students understanding of both fundamental and practical characterization techniques.

The NMReady™ benchtop spectrometer offers an accessible, portable, affordable option with a modern, network accessible, easy-to-use interface that can be easily incorporated into teaching laboratories.



www.nanalysis.com
info_nanalysis@nanalysis.com
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Introduction:

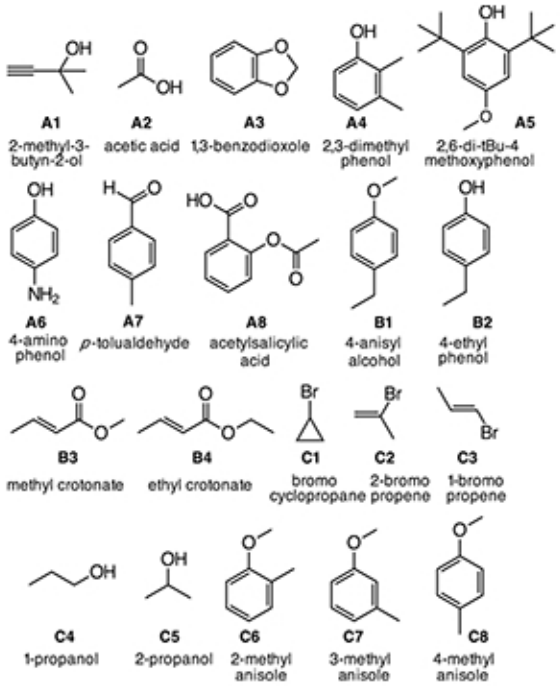
Nuclear Magnetic Resonance (NMR) was discovered in the 1940's by physicists investigating the magnetic properties of atomic nuclei. It wasn't long until synthetic chemists realized how valuable this spectroscopic technique could be for structural elucidation, especially when paired with supplemental techniques such as infrared (IR) spectroscopy.

Before NMR, the characterization of unknowns was a lengthy process requiring numerous, sequential tests (*e.g.*, melting point/boiling point, solubility, derivatization) whereas NMR is:
1) fast - data can be measured within minutes.
2) non-destructive - structure not damaged in the experiment.
3) indicative of the connectivity within a molecule not just about the molecule as a whole.

The following experiment can be used in conjugation with traditional unknown identification experiments or as a stand-alone experiment to highlight the diversity of a synthetic chemists' toolbox.

Preparation:

Select unknowns from below list, place them in vials labelled with an identifier (*e.g.*, A1, B2, C3). These are divided into 3 categories: *(i)* 'A' - simple; *(ii)* 'B' - coupled; and *(iii)* 'C' - constitutional isomers. Provide students with information about molecular weight (MW) & characteristic IR peaks. Lay out NMR tubes, caps, 1 mL syringes (or pasteur pipettes & bulbs) and *d*-$CHCl_3$. Students will be assigned 4 unknowns: 1'A', 1'B' & 2'C'.



Students' Procedure:

In partners, obtain 4 assigned unknowns (A, B & 2C). Record unknown numbers & accurately describe each compound. For each sample, prepare 1.0 mL of a 0.5 M solution in *d*-$CHCl_3$. Transfer ~0.7 mL of this solution into an NMR tube. Cap the tube & place it in the provided sample warmer for a minimum of 1 minute.

	Molecular Weight (MW in g/mol)	Important IR Frequencies (cm^{A-1})
Class A - Structure proposed primarily on δ & integration		
1	84.10	3303, 2120
2	60.10	2937, 1617
3	122.10	1152, 1126
4	122.20	3262
5	236.40	3688, 2911, 1113
6	109.13	3352, 3301, 3058 1614
7	120.20	1677
8	180.20	3006, 1693, 1606, 1096
Class B - Structure proposed on δ, integration & multiplicity		
1	138.20	3826, 1034, 1007
2	122.16	3200
3	100.10	1680, 1649, 1040
4	114.10	1662, 1649, 1103
Class C - δ, integration & multiplicity to distinguish structural isomers		
1	121.00	547
2	121.00	1637, 547
3	121.00	1626, 499
4	60.10	3333
5	60.10	3345
6	122.20	1062
7	122.20	1056
8	122.20	1043

Measure a 8 scan ^{1}H NMR spectrum for each unknown with a spectral width of 12 ppm, 2k points, & a scan delay of 2 sec. Work up your spectra (*i.e.*, phase, baseline correct, reference, integrate & peak pick). Save each spectrum in the form YYMMDD_initials_unknown identifier and print a copy to hand in with your final report.

Students' Discussion:

1) For each spectrum describe each resonance by filling out the following data table with chemical shift (location of the peak center), the relative integration, & multiplicity (designated by a letter *e.g.*, q = quartet).

Unknown	Chemical Shift (δ) (ppm)	Integration	Splitting Pattern (m)	Coupling Constant $^zJ_{H-H}$ (Hz)	Assignment

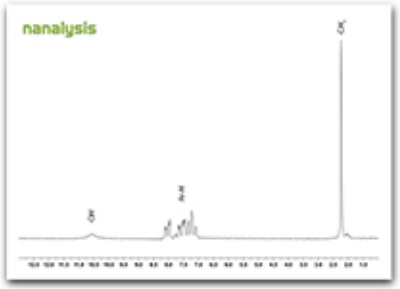
2) Assign each resonance to a chemical building block (*e.g.*, $-CH_3$, $-CH_2-$, -CH=CH-).
3) Propose a molecular structure, connecting your building blocks. Be sure each atom's octet is satisfied.
4) Provide the IUPAC name of your structure
5) In a few sentences explain how multiplicity aided your building block identification.
6) Report the data in the form of: δ XX.XX (m, integration, $^zJ_{H-H}$, assignment).

Key Concepts:

NMR sample preparation, NMR data collection, NMR Spectroscopy, structure elucidation

Example Discussion:

Class 'A' was chosen to illustrate how much information can be obtained by δ & integration. See example of acetylsalicylic acid below:



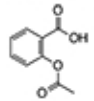
1 & 2)

Unknown	Chemical Shift (δ) (ppm)	Integration	Splitting Pattern (m)	Coupling Constant $^2J_{H-H}$ (Hz)	Assignment
A8	10.51	1	broad s	n/a	-O*H*
	8.22-7.01	5	multiplet (m)	n/a	Ar-*H*
	2.25	3	singlet (s)	n/a	-C*H*$_3$

3) C=O, C-O also present in molecular structure

4) MW = 180.2 - C (12 x 7) - H (1 x 9) - O (16) = 71 remaining

71 = C (12 x 2) - O (16 x 3) = 0 So: $C_9H_9O_4$

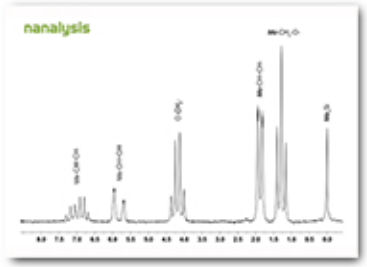
5) 

6) 2-acetoxybenzoic acid

7) Due to the phenomenon of multiplicity, coupled or not, a spectrum still contains information about structural connectivity. A singlet means there are no *I* = 1/2 neighbours.

8) δ 10.51 (s, 1H, -O*H*); 8.22-7.01 (m, 5H, Ar-*H*); 2.25 (s, 3H, -C*H*$_3$) ppm.

Class 'B' requires students to use δ, integration & multiplicity to determine the unknowns' structure. Below is a worked example of ethyl crotonate:



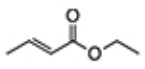
1 & 2)

Unknown	Chemical Shift (δ) (ppm)	Integration	Splitting Pattern (m)	Coupling Constant $^2J_{H-H}$ (Hz)	Assignment
B4	7.03	1	m	n/a	-C*H*=CH-
	5.83	1	d of q	15.6 & 1.8	-CH=C*H*-
	4.18	2	q	7.1	-O-C*H*$_2$-
	1.88	3	d of d	6.8 & 1.4	-CH-C*H*$_3$
	1.28	3	t	7.1	-CH$_2$-C*H*$_3$

3) Also C=O, C-O and -C=C-

4) MW = 114.10 - C (12 x 5) - H (1 - 10) - O (16) = 28 remaining

28 = C (12 x 1) - O (16 x 1) = 0 So: $C_6H_{10}O_2$

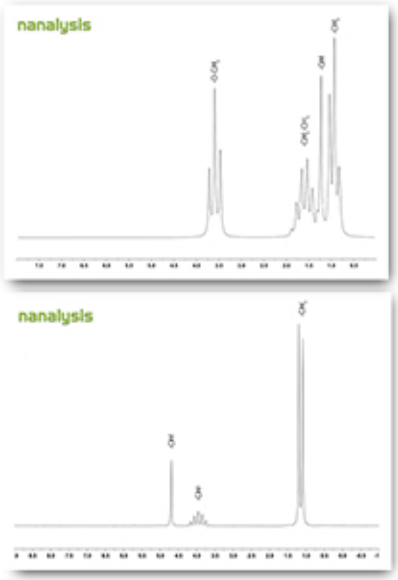
5) 

6) 2-butenoic ethyl ester

7) Vicinal & geminal couplings lay out the nearest neighbour & next nearest neighbour for additional connectivity information.

8) δ 7.03 (m, 1H, -C*H*=CH-); 5.83 (dq, 1H, $^2J_{H-H}$ = 15.6, $^3J_{H-H}$ = 1.8, -CH=C*H*-); 4.18 (q, 2H, $^2J_{H-H}$ = 7.1, -C*H*$_2$-); (dd, 3H, $^2J_{H-H}$ = 6.8, $^3J_{H-H}$ = 1.4, -C*H*$_3$); 1.28 (t, 3H, $^2J_{H-H}$ = 7.1 -C*H*$_3$) ppm.

Class 'C' illustrates how easily NMR can differentiate constitutional isomers, especially when compared with traditional chemical methods.

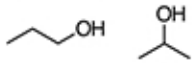


1 & 2)

Unknown	Chemical Shift (δ) (ppm)	Integration	Splitting Pattern (m)	Coupling Constant $^2J_{H-H}$ (Hz)	Assignment
C4	3.63	2	t	7.5	-OC*H*$_2$-
	1.98-1.26	2	m	7.5	-C*H*$_2$-
	1.67	1	s	n/a	-O*H*
	0.97	3	t	7.5	-C*H*$_3$
C5	4.69	1	s	n/a	-O*H*
	3.69	1	septet	6.6	-C*H*(CH$_3$)$_2$
	1.15	6	d	6.6	-CH(C*H*$_3$)$_2$

3) -OH is present in the structure & this can be seen in NMR

4) MW = 60 - C (12 x 3) - H (1 x 8) - O (16) = 0 so: C_3H_8O

5) 

6) C4 = *n*-propanol, C5 = *iso*propanol

7) Due to the symmetry differences in the molecules and the predicted connectivity the two samples are highly distinguishable despite having the same molecular weight and functional groups.

8) C4: δ 4.69 (s, 1H, -O*H*); 3.69 (septet, 1H, $^3J_{H-H}$ = 6.6, -C*H*(CH$_3$)$_2$); 1.15 (d, 6H, $^3J_{H-H}$ = 6.6, -CH(C*H*$_3$)$_2$) ppm.

C5: δ 3.53 (t, 2H, $^3J_{H-H}$ = 7.5, -OC*H*$_2$); 1.98-1.26 (m, 2H, $^3J_{H-H}$ = 7.5, -C*H*$_2$); 1.67 (s, 1H, -O*H*), 0.97 (t, 3H, $^3J_{H-H}$ = 7.5, -C*H*$_3$) ppm.

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References:

1) Carey, F. A. "Organic Chemistry" 5th Ed., McGraw Hill: Toronto, **2003**

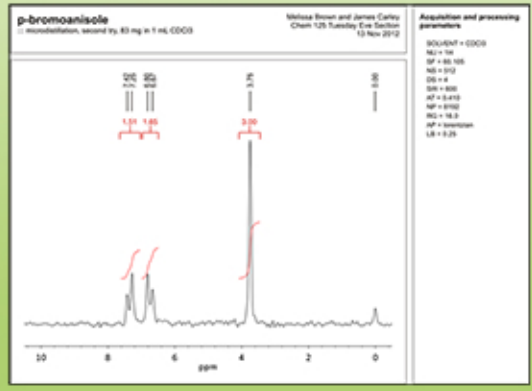
2) Silverstein, R. M.; Webster. F. X.; Kiemle, D. J., "Spectrometer Identification of Organic Compounds" 7th Ed., John Wiley & Sons, Inc: USA, **2005**

3) McClusky, J. V. *J. Chem. Educ.* **2007**, *84*, 983

4) Personal communication with Dr. Pullarkat Appukuttan Sumod, Mr. Jonathan Wong & chemistry staff at Nanyang Technological University

Data Accessibility:

NMReady outputs to a networked drive and has a print option. Students can process and print in third party software, like Mestrelab™, or use the NMReady directly. An example of data to be incorporated into a lab report processed and printed directly from the NMReady is presented below:



For additional ideas of how to incorporate the NMReady™ benchtop spectrometer into undergraduate laboratories please see:

1) Interpretation of ^{1}H NMR Spectra
2) Synthesis of Aspirin
3) Aldol Condensation
4) Biodiesel

available at:

www.nanalysis.com/experiments.html