Chemistry 2312 November 4, 2022

Honors Organic Chemistry Laboratory T. R. Hoye

Spectroscopies Worksheet #2

OPTIONAL

This is an exercise to give you an appreciation for the power of **two-dimensional** (or 2D) NMR spectroscopy, a relatively routine type of data that can be collected on modern spectrometers.

As I said in a lecture last week, I do not expect you to do this, but I suspect that there are some of you who might like to try your hand at portions of it to strengthen your NMR analysis skills. I plan to go through this worksheet as the topic of our class meeting on Thur, Nov 17th.

The spectra to consider here are all for **isomenthone**, but they have been recorded in benzene-d_6 rather than $CDCl_3$ because of the more favorable chemical shift dispersion observed for the proton resonances in benzene.

I have sent you an email message with the following publication; you likely will find it helpful to read it:

- a PDF titled "Intro to 2D NMR Tutorial J Chem Ed Ohio Northern 2016", which is a *J. Chem. Ed.* article introducing you to 2D spectroscopy.[1]

I have uploaded to the course website:

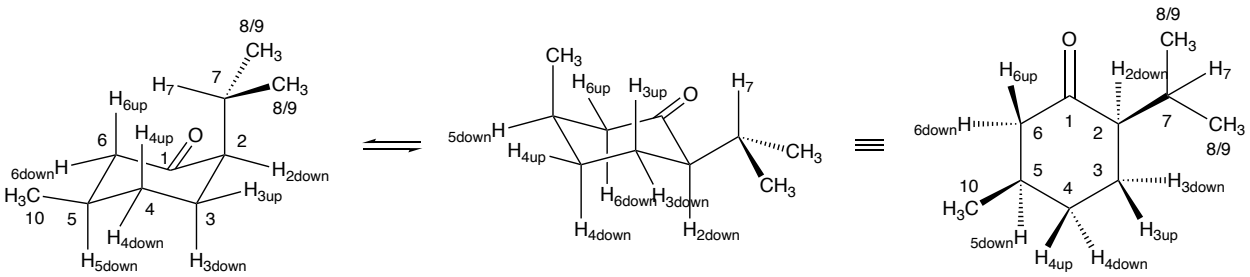
- an MNova file ("Isomenthone 2D Sneddon Complete Processed for Students.mnova") containing the following NMR data, each recorded in benzene-d_6 and from a 500 MHz spectrometer for better chemical shift dispersion of the proton resonances:

1. Proton (1D)
2. Carbon (1D)
3. COSY correlation spectroscopy (proton-proton coupling)
4. NOESY nuclear Overhauser enhancement spectroscopy (proton-proton, through space interaction)
5. HSQC heteronuclear *single* quantum coherence (C_α–H one-bond coupling)
6. HMBC heteronuclear *multiple bond* correlation [C_β–H (2-bond) or C_γ–H (3-bond) coupling]

[1] "Introducing 2D NMR Spectroscopy to Second-Year Undergraduate Chemistry Majors Using a Building-Up Approach", Anderson-Wile, A. M. *J. Chem. Educ.* **2016**, *93*, 699–703.

Below are the structures of the two principle chair conformations of isomenthone. (Recall that you have computed the energies of these conformational isomers, and the isopropyl rotamers within each, using molecular mechanics.)

The table below contains the proton and carbon chemical shifts, listed from largest to smallest δ values, from the 1D NMR spectra of isomenthone recorded in benzene-d_6. For many of the protons, coupling constant values from analysis of the multiplets is provided. (FYI, the singlet at δ 0.61 is the resonance of the protons in residual water in benzene.)



^{1}H Assignment (from the 1D ^{1}H spectrum) **^{13}C Assignment**

H	*J* (Hz)	ppm	multiplicity
Ha		2.13	dddd
Hb	9.3, 13.3	1.86	dd
Hc	8.3, 6.4	1.84	dsept
Hd	1.2, 5.1, 6.3, 8.3	1.82	dddd
He	4.6, 4.6, 8.8, 8.8, 6.7	1.66	ddddq
Hf		1.58	dddd
Hg	4.1, 5.1, 9.3, 13.9	1.43	dddd
Hh		1.27	ddddd
Hi	3.9, 8.5, 9.6, 13.6	1.11	dddd
H_3(j)	6.3	0.81	d
H_3(k)	6.3	0.76	d
H_3(l)	6.8	0.72	d

C	ppm
m	211.1
n	57.1
o	48.1
p	33.9
q	29.8
r	26.9
s	26.5
t	21.1
u	21.0
v	19.8

Chemical shift questions

1. What is the proton chemical shift of each of the six methylene protons? Which of the methylene protons are attached to the same carbon atom? What is the chemical shift of each of those three carbon atoms? (Hint: HSQC*)

H6a and H6b:	**C6:**
H3a and H3b:	**C3:**
H4a and H4b:	**C4:**

2. What is the proton chemical shift of each of the three methine protons (i.e., CHRR'R''), and what is the chemical shift of each of three carbons to which each of these protons is attached? (Hint: HSQC*)

H7:	**C7:**
H2:	**C2:**
H5:	**C5:**

3. There are three resonances for methyl groups; each is a doublet.

   • What is the proton chemical shift of the two methyl groups of the isopropyl moiety (Me^8 and Me^9)?

   δ = and ppm

   • Explain how you can determine these from the HMBC* spectrum.

   • Explain how you can determine these from the COSY* spectrum.

   • What is the chemical shift of the methine proton H_{5down}? δ = ppm

4. Explain how you can use the COSY spectrum to identify the chemical shift of H_7.

Coupling constant questions

1. The resonances for two of the additional protons each contains a coupling constant of ca. 1.2 Hz; what is the chemical shift of each of these? This small J value arises from long range (W or 4-bond) coupling. What is the assignment of each of these two protons?

2. What are the four J values of the dddd having a chemical shift of 2.13 ppm? Which proton gives rise to this resonance?

3. What are the four J values of the dddd having a chemical shift of 1.58 ppm? Which proton gives rise to this resonance?

4. What are the five J values of the ddddd having a chemical shift of 1.27 ppm? Which proton gives rise to this resonance?

2D questions

1. Protons attached to the carbons alpha to a carbonyl carbon typically show an HMBC, two-bond correlation cross-peak. Carbonyl carbons are typically among the farthest downfield in a ^{13}C NMR spectrum. From the HMBC spectrum, what are the chemical shifts of the protons attached to C2 and to C6?

2. The closest distance between two protons is typically those associated with a geminal pair of methylene protons. The intensity of nuclear Overhauser enhancements between two protons is very sensitive to the distance between two protons. Describe how you can identify the three pairs of methylene protons from the NOESY spectrum.

Full assignment question

In the table immediately below, provide the correct assignment of each resonance in each of the two spectra with the proton or carbon atom with which it is associated. Working interactively and iteratively with the different types of spectral data will be helpful as you work through this. There is a near infinite number of separate paths of logical analysis and deduction that can get you to the right answer set – not unlike a (e.g., NYTimes Sunday) crossword puzzle.

^{1}H Assignment (from the 1D ^{1}H spectrum)

H	H#	*J* (Hz)	ppm	multiplicity
Ha			2.13	dddd
Hb		9.3, 13.3	1.86	dd
Hc		8.3, 6.4	1.84	dsept
Hd		1.2, 5.1, 6.3, 8.3	1.82	dddd
He		4.6, 4.6, 8.8, 8.8, 6.7	1.66	ddddq
Hf			1.58	dddd
Hg		4.1, 5.1, 9.3, 13.9	1.43	dddd
Hh			1.27	ddddd
Hi		3.9, 8.5, 9.6, 13.6	1.11	dddd
H_3(j)		6.3	0.81	d
H_3(k)		6.3	0.76	d
H_3(l)		6.3	0.72	d

^{13}C Assignment

C	C#	ppm
m		211.1
n		57.1
o		48.1
p		33.9
q		29.8
r		26.9
s		26.5
t		21.1
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