18/11/2024

Excellent!

Jigsaw 4E

1. [Keeler Sections 8.3 and 8.11] Two ^{1}H-^{1}H 2D spectra of ibuprofen are shown below.

   a. Explain the difference between the TOCSY and COSY experiments. Which spectrum corresponds to which experiment? How do you know?

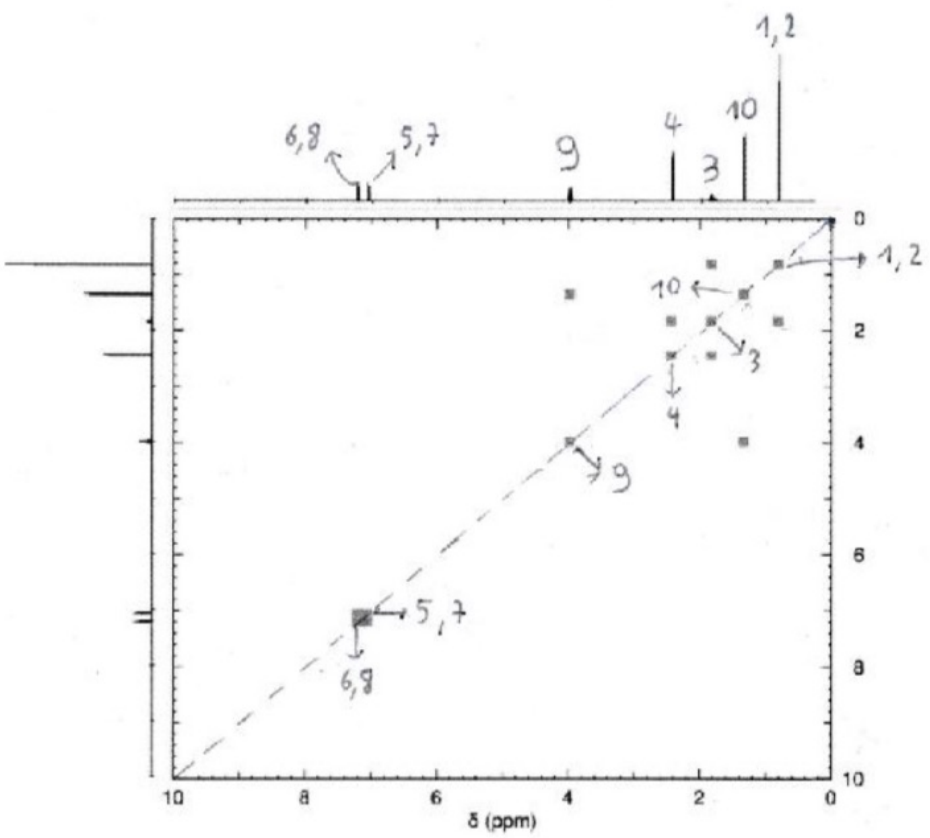
The COSY and TOCSY experiments are 2D NMR experiments used to analyze correlations between 1H-1H nuclei within a molecule.

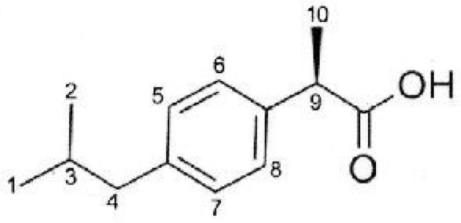
While COSY experiments reveal direct couplings between protons through scalar couplings up to 3 bonds and symmetry along diagonal, TOCSY experiments provide correlations for protons within the same spin system, including both direct and indirect couplings across multiple bonds via an extended 3-coupling network.

As observed, the second spectrum contains additional points on either side of the diagonal, reflecting indirect couplings across more than 3 bonds. This key feature indicates that it corresponds to the TOCSY experiment. Furthermore, the first spectrum is symmetric along the diagonal, a characteristic trait of the COSY experiment, which confirms its identification as such.

Good! (Note that the TOCSY experiment *should* also be symmetric along the diagonal, it's just that the given TOCSY spectrum is experimental, and experiments =/= theory)

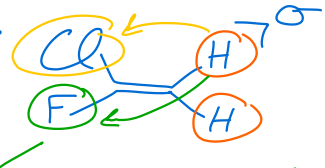
   b. Assign the spectra.





Exercise 2:

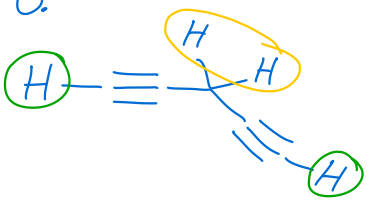
a.



→ Different coupling

- The 2 protons are chemically equivalent
  - → Same linkage
  - → Same chemical environment
- The 2 protons are not magnetically equivalent
  - → Do not have the same spin-spin coupling w/ all other nuclei as different configuration

b.



The 2 protons in yellow and the 2 protons in green:

- are chemically equivalent due to symmetry
- are magnetically equivalent as they have the same spin-spin coupling w/ all other nuclei

The protons are neither chemically nor magnetically equivalent for a green and a yellow proton as they have different linkage and chemical environment.

Correct, assuming that all C in the system are 12C (non-NMR active). If one or more of the C are 13C, the terminal 1H would no longer be magnetically equivalent to each other (the central 1H are still magnetically equivalent to each other)

Great work!

NMR Jigsaw 4E

October 2024

1 Exercise 1

The difference between COSY and TOCSY is the following:

- COSY identifies scalar couplings and bonds of protons that are directly coupled in the system
- TOCSY extends the analysis to all the connections/bonds of all protons inside of the spin system. In other words, it is an "extended" version of COSY.

This information allows us to deduce that, of the two graphs below, the first is COSY and the second is TOCSY. We can use the first or the second to assign the molecule. We'll use the first since it only gives information on the more direct bonds inside the molecule.
We can use this information to correlate the chemical information from the representation of the molecule, alongside the properties of COSY graphs seen in Jigsaw 3, to assign the number from the molecule to peaks on the graph:

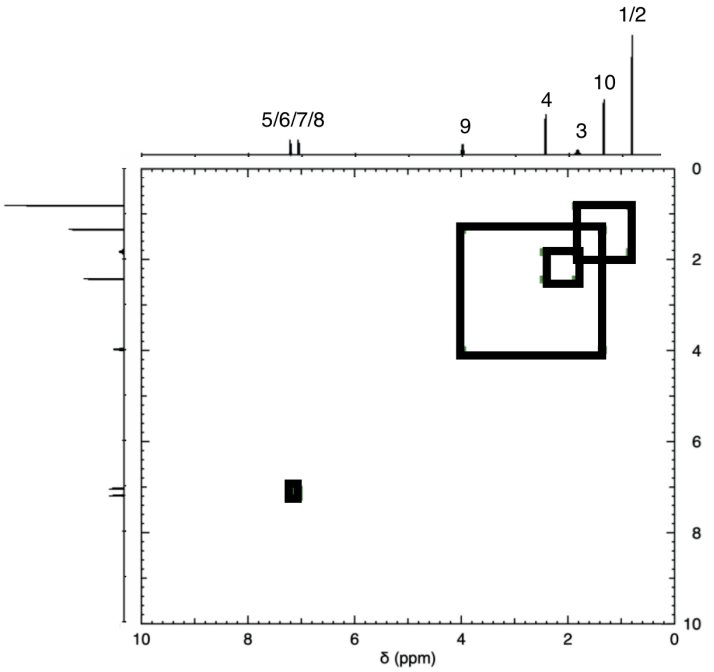


Figure 1: COSY Pulse Sequence

We proceed iteratively in the following fashion:

- We can first assert that the rightmost peak is a methyl group, as those are among the most strongly shielded thus yielding the lowest ppm values. The methyl groups in the graph are 1/2 (they both are chemically equivalent and so have the same PPM value).
- We can then leverage the fact that COSY cross-peaks shows couplings between linked protons. We draw the square (see graph) and can deduce that the 3rd peak corresponds to something connected to 1/2: 3
- We can also safely assert that the leftmost two peaks correspond to the 5/6/7/8 protons: these are protons on the benzene aromatic ring. Aromatic protons typically have higher PPM values due to deshielding effects (most notably from the aromatic π-electrons).

Great explanations!

- What remains is now the 2nd and the 4th peak, corresponding to 9 and 10, which are linked. 9 has the higher ppm-value, as it is attached to other groups, such as a carbonyl and a hydroxyl, which will deshield it whereas 10 will experience a weaker deshielding effect thus giving it a weaker PPM. The 2nd peak is thus 10 and the 4th 9.

2 Exercise 2

As seen in Hore Section 3.3, we define two protons as chemically equivalent if they possess the same chemical shifts. They are magnetically equivalent if chemical shifts and the same scalar couplings

1-Chloro-1-fluoroethene is chemically equivalent: while the chemical shifts are equivalent throughout, the asymmetry of the molecule yields differing J-couplings throughout

$HC{\equiv}C{-}CH_2{-}C{\equiv}CH$ is magnetically equivalent: there are similar chemical shifts and the symmetry of the molecule yields similar couplings throughout the molecule's protons

"similar" isn't enough, they need to be exactly identical
— see explanations on other set of solutions