7.3: Two Dimensional Homonuclear NMR Spectroscopy

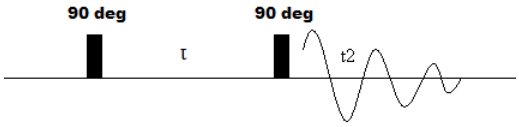
Learning Objectives

- Understand what correlation spectroscopy is and why it is used
- Learn about different types of homonuclear 2-D NMR spectroscopy

The previous sections have discussed one-dimensional NMR techniques, but for particularly complicated molecules it is hard to get the full picture of what is happening. Two-dimensional NMR spectra provide more information about a molecule than one-dimensional NMR spectra in these situations. In this section, homonuclear 2-D NMR spectroscopy is going to be considered and what is meant by homonuclear is looking at the correlation of the same nuclei in a molecule.

Correlation Spectroscopy (COSY)

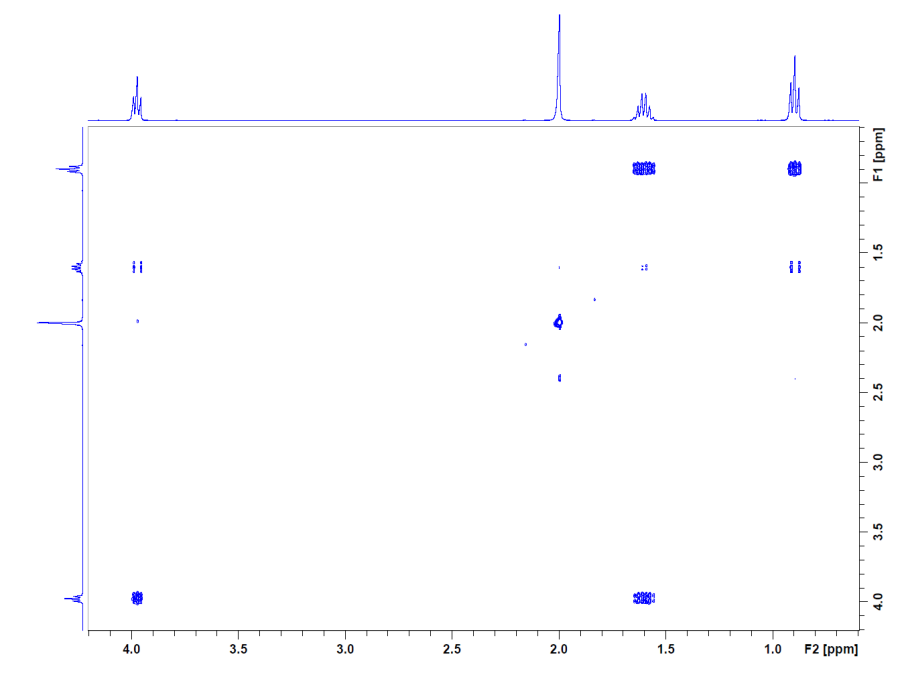
The most basic form of 2-D NMR is the COSY (COrrelation SpectroscopY) experiment. This experiment looks at ^{1}H coupling to ^{1}H through bonds typically 3 bonds away. It relies on the J-coupling to provide spin-spin correlation to indicate which protons are close to each other on the cross peak. In a ^{1}H-^{1}H COSY experiment, the pulse sequence consists of proton pulses separated by the required evolution period (t_1), and the acquisition period (t_2). The evolution period is systematically incremented during the repeated pulse sequences. Specifically, it consists of a 90^o RF pulse followed by an evolution time and an additional 90^o pulse (shown below). The resulting oscillating magnetization (symbolized by decaying the sinusoidal curve) is then acquired during t_2.



A COSY takes a 1-D ^{1}H NMR and spreads it across two dimensions, which means the peaks are spread out into an array. The spectra of COSY give rise to cross peaks (off diagonal) for all protons that have spin-spin coupling. This means that the peaks off the diagonal are coupled protons. The purpose of a COSY is to determine which protons are coupled to what other protons in the molecule through bonds. In the example below, you will use a simpler molecule, propyl acetate, to understand how to read a COSY and what information you can glean from it.

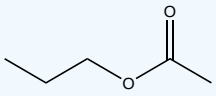
Example 7.3.1

The COSY spectrum for propyl acetate is below:



Assign all of the correlations for propyl acetate and indicate the coupling as geminal, vicinal, or long range.

Solution

The structure of propyl acetate 

From the chapter on 1-D ^{1}H NMR spectroscopy, the methyl group attached to the carbonyl will be a singlet. It does not have any neighboring carbons to couple with. The other hydrogens will have coupling neighbors, so while you may only need 1-D ^{1}H NMR to correlate the coupling hydrogens, this knowledge will help flesh out how to read a COSY.

First, the COSY is set out in an array and spread across two dimensions. The peaks are displayed on the axis. In the above spectrum, it is the same proton spectrum for propyl acetate on each of the axis because it is a homonuclear experiment where you look at the same nuclei. The peaks are then plotted against each other. There peak at 3.9 ppm on both axis, so there is a data point at (3.9, 3.9). This is repeated with all the peaks, which ends up being a diagonal. This information along the diagonal is the same information from the 1-D ^{1}H NMR.

The points of interest are those not along the diagonal or the cross peaks. These peaks inform about which hydrogens are coupled to what other hydrogens. There is a cross peak at (0.9, 1.6). There is also a cross peak at (1.6, 0.9) because these protons are coupled to each other and if you recall coupling is reciprocal. The peak at 0.9 ppm corresponds to the methyl group with a neighboring -CH_2- and the 1.6 ppm peak is the -CH_2- with the neighboring methyl group. However, the peak at 1.6 ppm has another cross peak (1.6, 3.9), which indicates that it is also coupled to the -CH_2- on the other side. And of course, there is a cross peak at (3.9, 1.6) since the coupling goes both ways.

All the cross peaks have now been identified and the bonding between these hydrogens is all vicinal coupling.

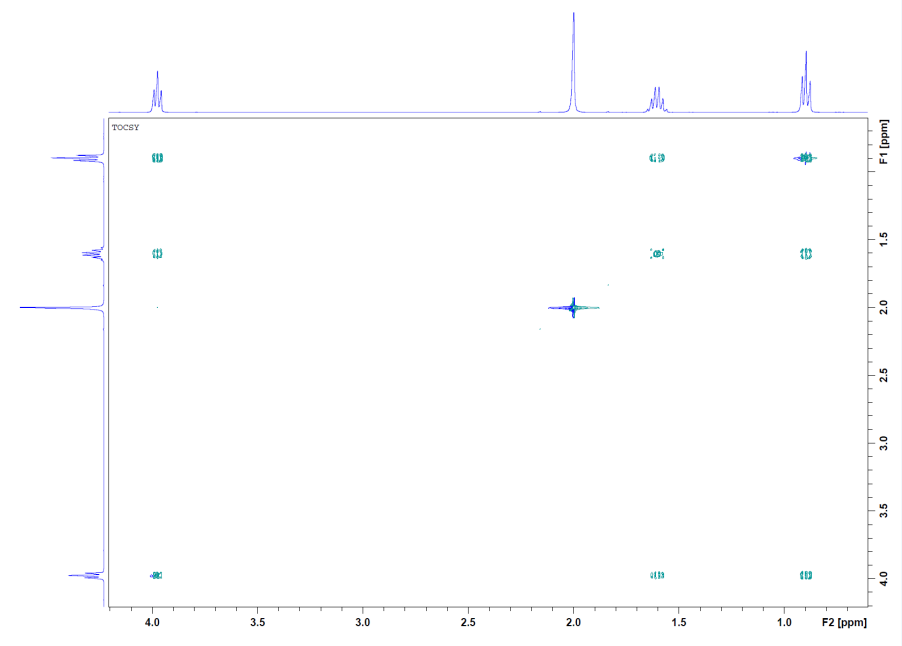
Total Correlation Spectroscopy (TOCSY)

The next type of ^{1}H to ^{1}H correlation spectroscopy is TOtal Correlation SpectroscopY (TOCSY). In this type of coupling, the information obtained creates correlations between all protons within a given spin system. A molecule can have just one spin system or hundreds in more complex systems. The goal in TOCSY is to transfer the magnetization beyond directly coupled spins. This is not just looking at geminal and vicinal correlations as in COSY, but the entire spin system. The pulse sequence is similar to COSY, but in TOCSY, a mixing period is added to the pulse sequence. This allows the magnetization to be relayed from one spin to its neighbor to its neighbor throughout the entire spin system. The longer this mixing period, the further out the transfer of

magnetization can travel with the goal being the entire spin system. The spectra of TOCSY give rise to cross peaks for all protons that are part of a coupled spin network. TOCSY spectra display the entire chain of protons, each coupled to the next.

Example 7.3.2

Below is the TOCSY of propyl acetate:



Does what you know of the structure of propyl acetate match what the TOCSY is indicating?

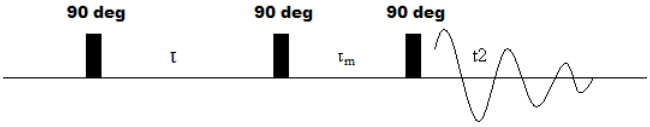
Solution

YES! Remember that TOCSY tells information about the entire spin system. As a reminder, a spin system includes nuclei where spin-spin interaction exists between them. In propyl acetate, this is the chain where the hydrogens are coupled. Just like in COSY, the peaks that show up along the diagonal in a TOCSY is the same information as a ^{1}H NMR spectrum and it is the cross peaks that inform about the chain of connection. The peak at 2.0 ppm has no cross peaks since it is a methyl group with no neighboring hydrogens. The other peaks are much more interesting. There is a cross peak at (0.9, 1.6) just like in COSY. This is because those protons are coupled to each other. There is also a cross peak at (1.6, 0.9) again because the reciprocality of how coupling works. However, there is a new cross (0.9, 3.9) because the methylene at 3.9 ppm is coupled to the methylene at 1.6 ppm. For the 1.6 ppm methylene, there are two cross peaks (1.6, 0.9) and (1.6, 3.9) like in COSY because it is coupled to those protons. Then in the 3.9 ppm methylene, there is again two cross peaks (3.9, 0.9), which is new from COSY and (3.9, 1.6), which was the same as COSY. The cross peak (3.9, 0.9) appears for the same reason the cross peak (0.9, 3.9) appeared when looking at the 0.9 ppm peak because the methylene at 1.6 ppm is coupled to the 0.9 ppm methyl group. The TOCSY does corroborate what we know about the connectivity of propyl acetate.

Nuclear Overhauser Effect (NOE) Correlation Spectroscopy

Thus far, only the coupling of nuclei through bonds has been considered. In this type of coupling, the magnetization of nuclei affect those closely bound to them through the electrons that make up those bonds. This is not the only type of coupling that occurs. Coupling directly between nuclei that are in close spatial proximity to each other also occurs. This is called the Nuclear Overhauser Effect (NOE), and it arises when the spin relaxation of nuclei A is felt by nearby nuclei B, stimulating a corresponding change in magnetization in B. In a typical NMR spectrum, the interference of electrons makes this coupling undetectable. However, a sample can be decoupled to “neutralize” the bond coupling through electrons, allowing the space coupling of the NOE to be detected. This is called NOESY (Nuclear Overhouser Effect SpectroscopY) and is another type of homonuclear NMR. The purpose of NOESY is to determine which signals arise from protons athar are close to each other in space, even if they are not bonded. NOESY can be very useful for looking at stereochemistry and 3-D structure.

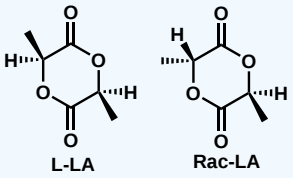
Like COSY, the first step is a 90^o pulse followed by a variable evolution time. Unlike COSY, however, pulse two actually consists of two 90 degree pulses separated by a short delay. The first pulse converts the bulk magnetization from the transverse plane to the z-plane, eliminating the effect of electron-aided bond coupling. Then, during the $\tau\tau_m$, there is cross relaxation between spatially adjacent nuclei. Finally, the last 90 degree pulse converts the space coupling of nuclei into an observable transverse magnetization, which can be detected during t_2.The pulse sequence for a NOESY NMR experiment is depicted below.



Just like in COSY, the peaks that show up along the diagonal in a NOESY is the same information as a ^{1}H NMR spectrum and it is the cross peaks that inform about the through space relationships. The cross peaks correlate the spin of one nuclei to that illuminated by the source spin (other nuclei) if nearby. In the example below, you will use a simpler molecule, propyl acetate, to understand how to read a NOESY and what information you can glean from it.

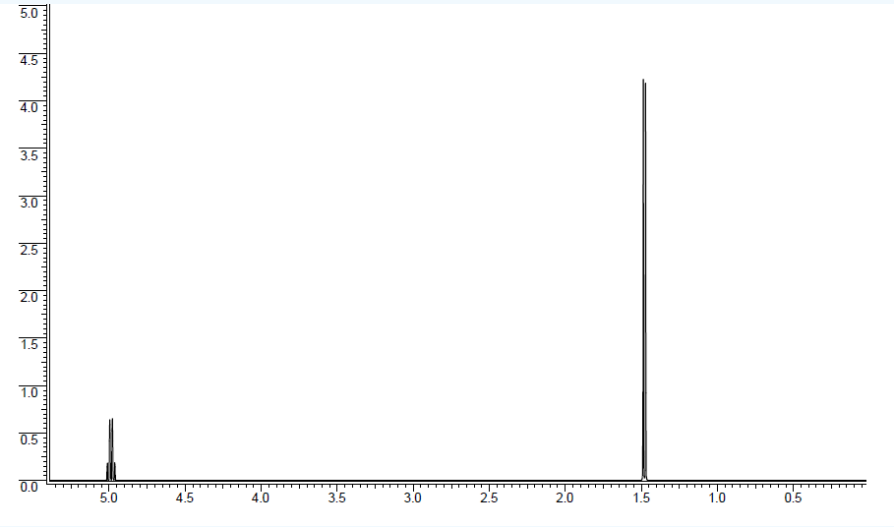
Example 7.3.3

Lactide is a product of the fermentation of corn and soybeans; it can be polymerized to make a sort of brittle plastic, PLA. PLA is used for food packaging because it can be composted in industrial and municipal waste management sites. However, there are three isomers of lactide (D-lactide, L-lactide, and Rac-lactide). L-lactide and Rac-lactide are depicted below:

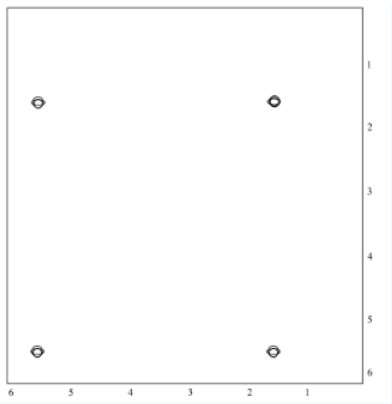


Using the spectral data, do you have L-lactide, or rac-lactide?

^{1}H NMR:



NOESY:



Solution

rac-Lactide is the diastereomer L-lactide (or D-lactide). It has different physical properties, including different NMR spectra. We could carefully compare the spectrum below to reported spectra for rac-LA and L-LA (or D-LA) to see which isomer we have. On the other hand, we could just look at the NOESY spectrum. In rac-LA, the methyl on one end of the molecule is on the same face of the ring as the hydrogen on the other end. NOESY would allow us to see that through-space relationship. We wouldn't see it in L-LA or D-LA, since the two methyl groups are on the same face. Just like in a COSY spectrum, all of the peaks that show up along the diagonal of a NOESY spectrum are simply the ones we would see in a regular ^{1}H spectrum. The peaks that show up off the diagonal tell us about through-space relationships. In this case, the relationship between the methyl hydrogen and the alpha hydrogen suggest we have a sample of rac-LA.

? Exercise 7.3.1

The magnetic effect of which type of particle must be removed from an NMR experiment in order to observe an NOE?

Answer

Electrons.

? Exercise 7.3.2

What type of information do you get from:

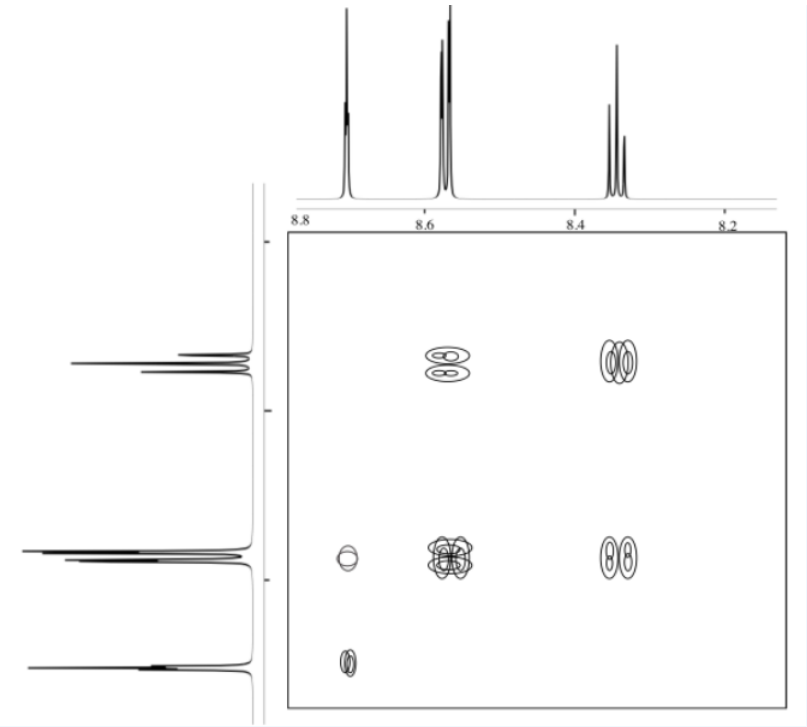
1. COSY?
2. NOESY?
3. TOCSY?

Answer

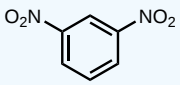
1. COSY gives information on which spins are coupled to each other through bonds.
2. NOESY determines which signals arise from protons that are close to each other in space, even if not bonded.
3. TOCSY creates correlations between all the protons within a spin system (not just geminal and vicinal coupling as in COSY).

? Exercise 7.3.3

The following COSY spectrum is for an isomer of dinitrobenzene. Which isomer is it?



Answer



: meta isomer

References

Silverstein, R.M, Webster, F.X, and Kiemle D.J. Spectrometric Identification of Organic Compounds. 7th ed. John Wiley & Sons, Inc. 2005.

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