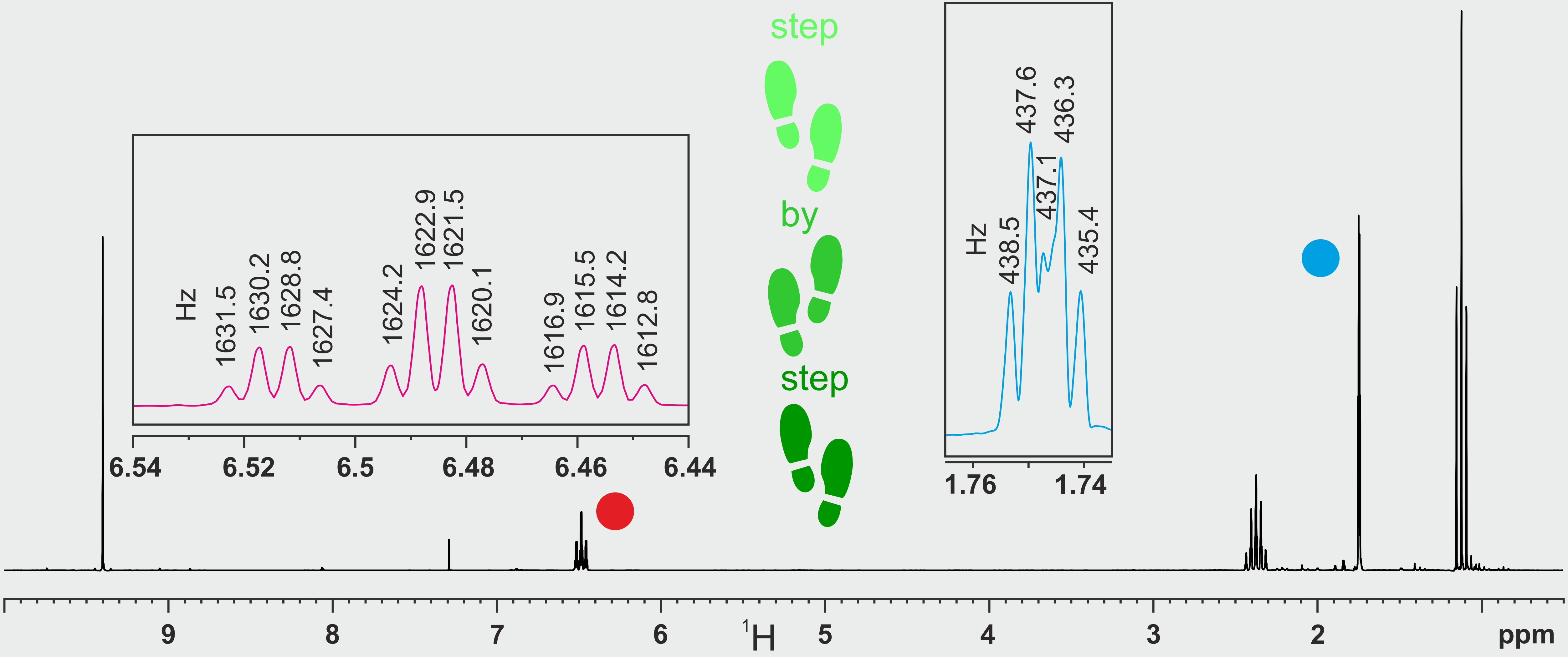
Exercise plus Solution – Quick PDF overview

It is recommended to use this PDF version only for a quick overview of the NMR challenge. All animations of the PowerPoint version are missing, under certain circumstances quality deficiencies may also occur.
The higher quality PowerPoint files are freely available for download at any time.



Problem of the Month:

February 2020

Get the constitution.

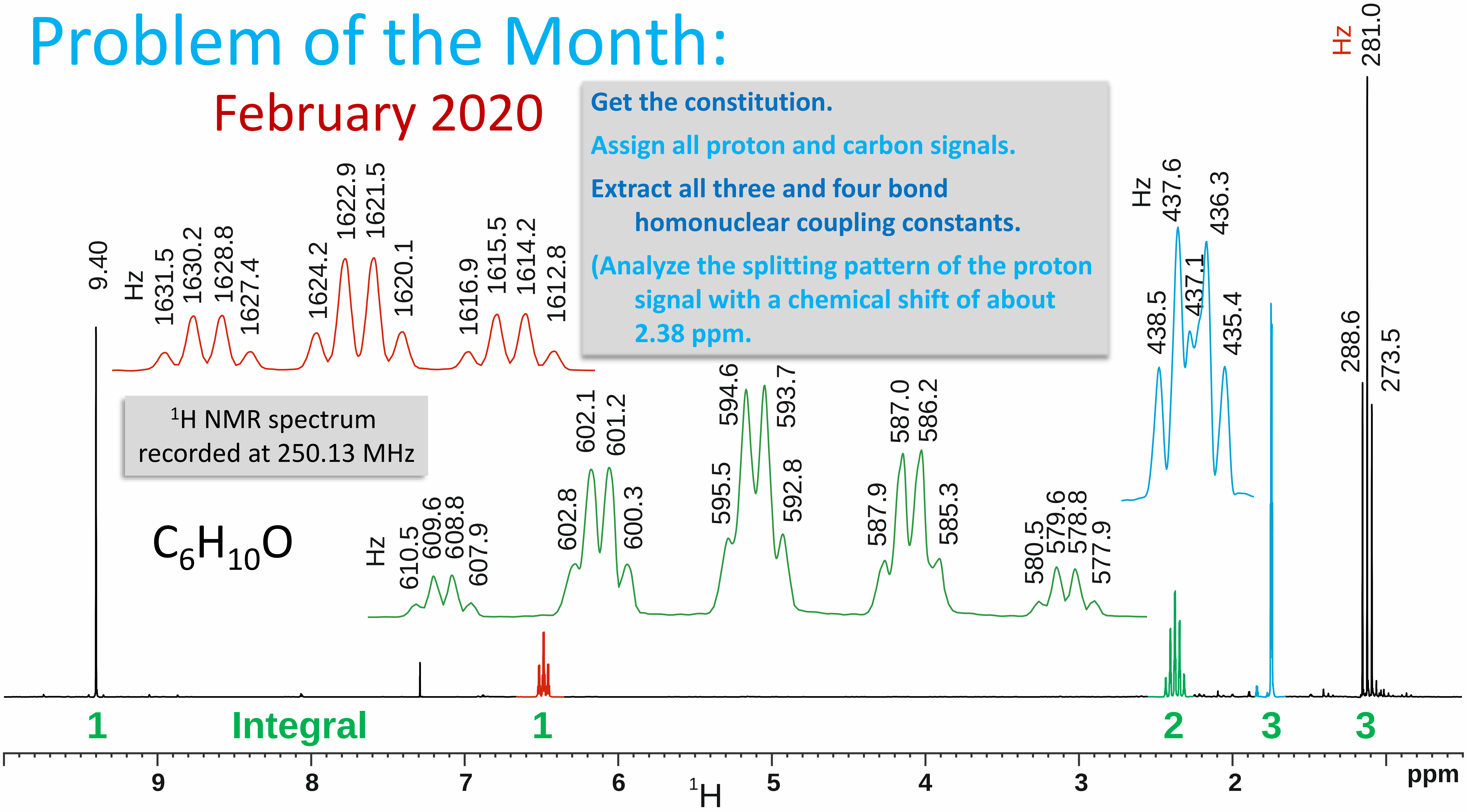
Assign all proton and carbon signals.

Extract all three and four bond homonuclear coupling constants.

(Analyze the splitting pattern of the proton signal with a chemical shift of about 2.38 ppm.

^{1}H NMR spectrum recorded at 250.13 MHz

$C_6H_{10}O$



$^1H/^{13}C$-HSQC
recorded at 250.13/62.90 MHz

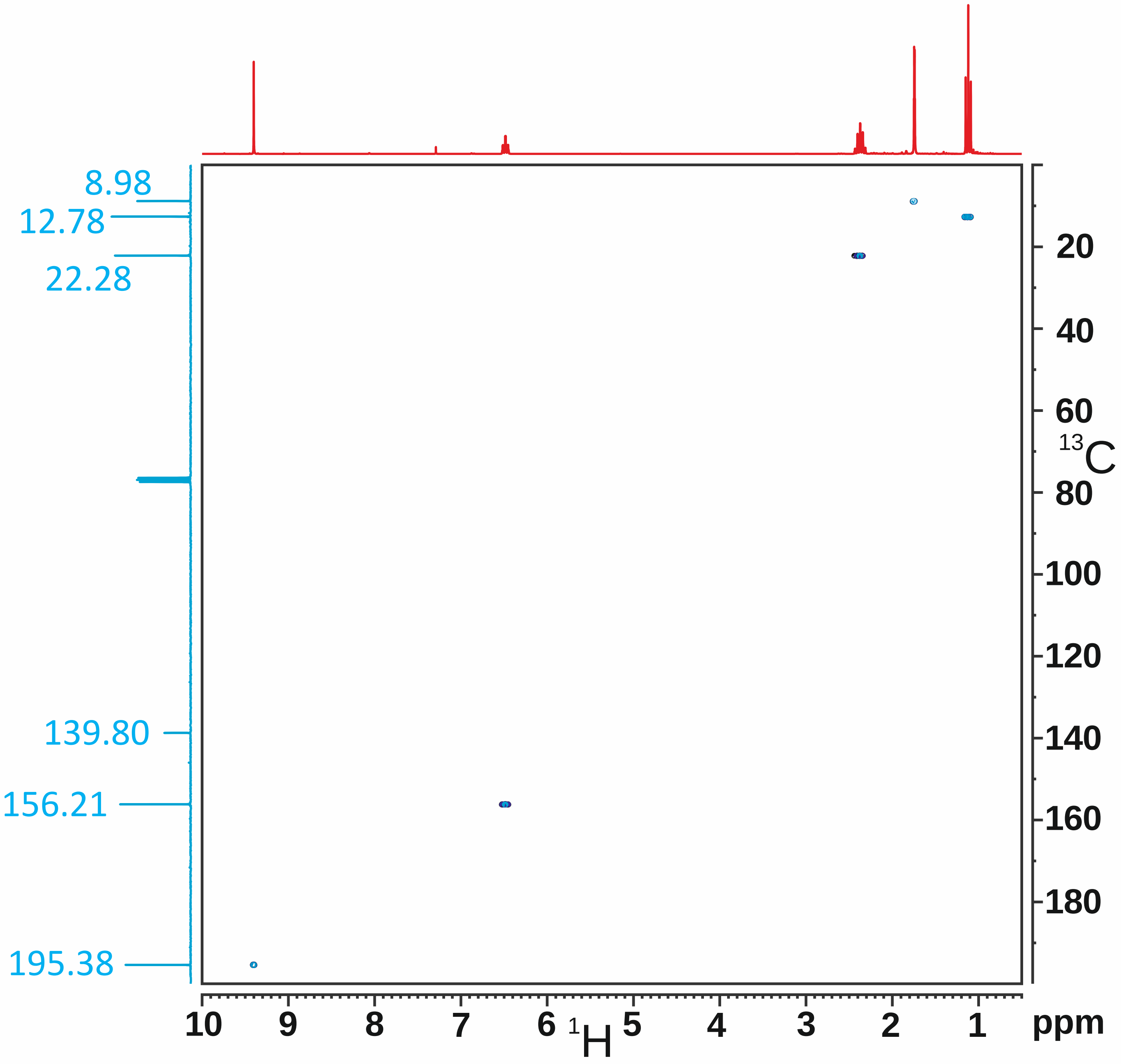
The f_1 projection contains all six carbon signals of the compound.

There is no separate one dimensional carbon spectrum given.

Hints

It's always helpful to calculate the degree of unsaturation (DBE) from the molecular formula.

The HSQC is usually the best method to find all or at least most of the building blocks

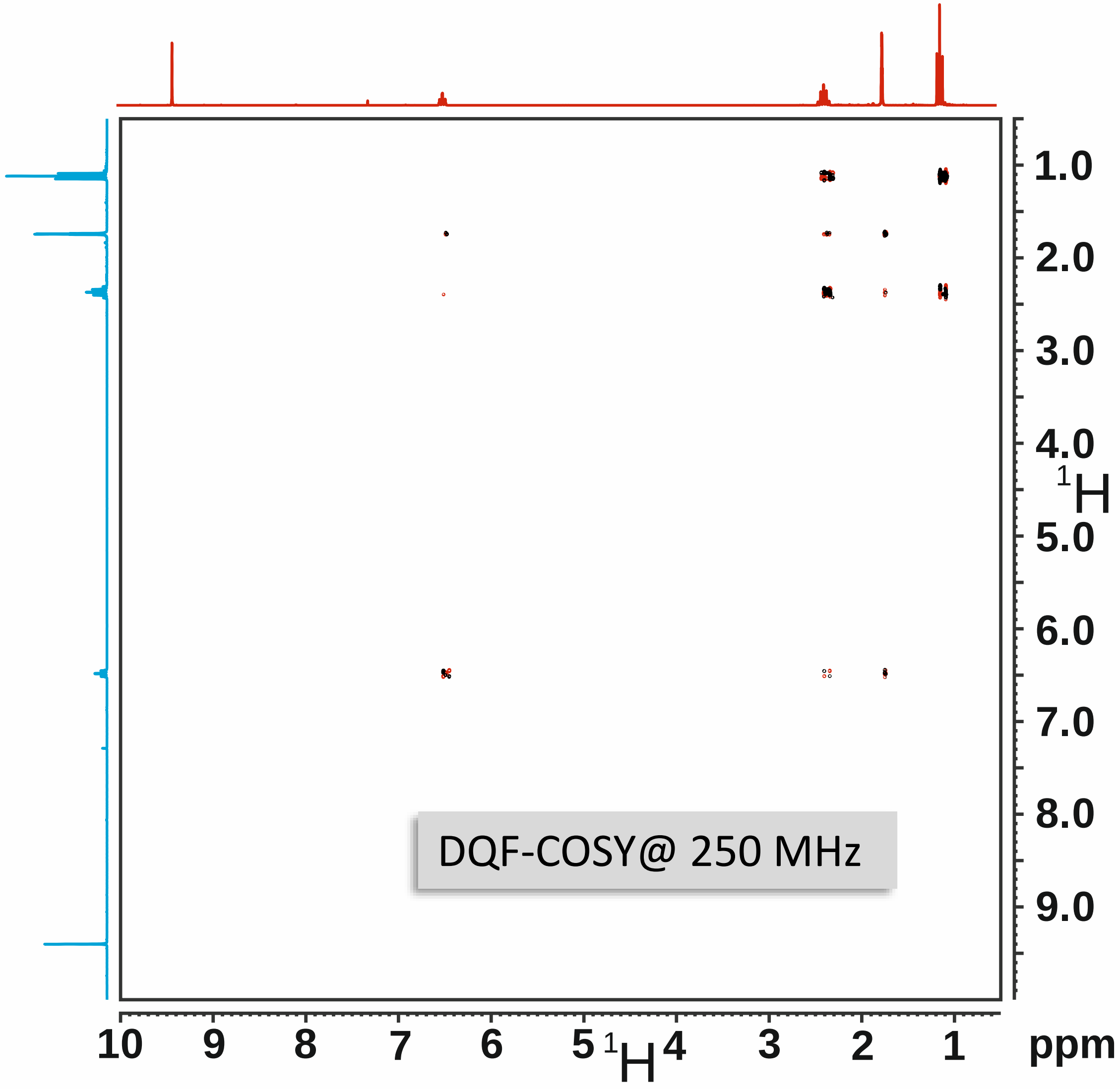


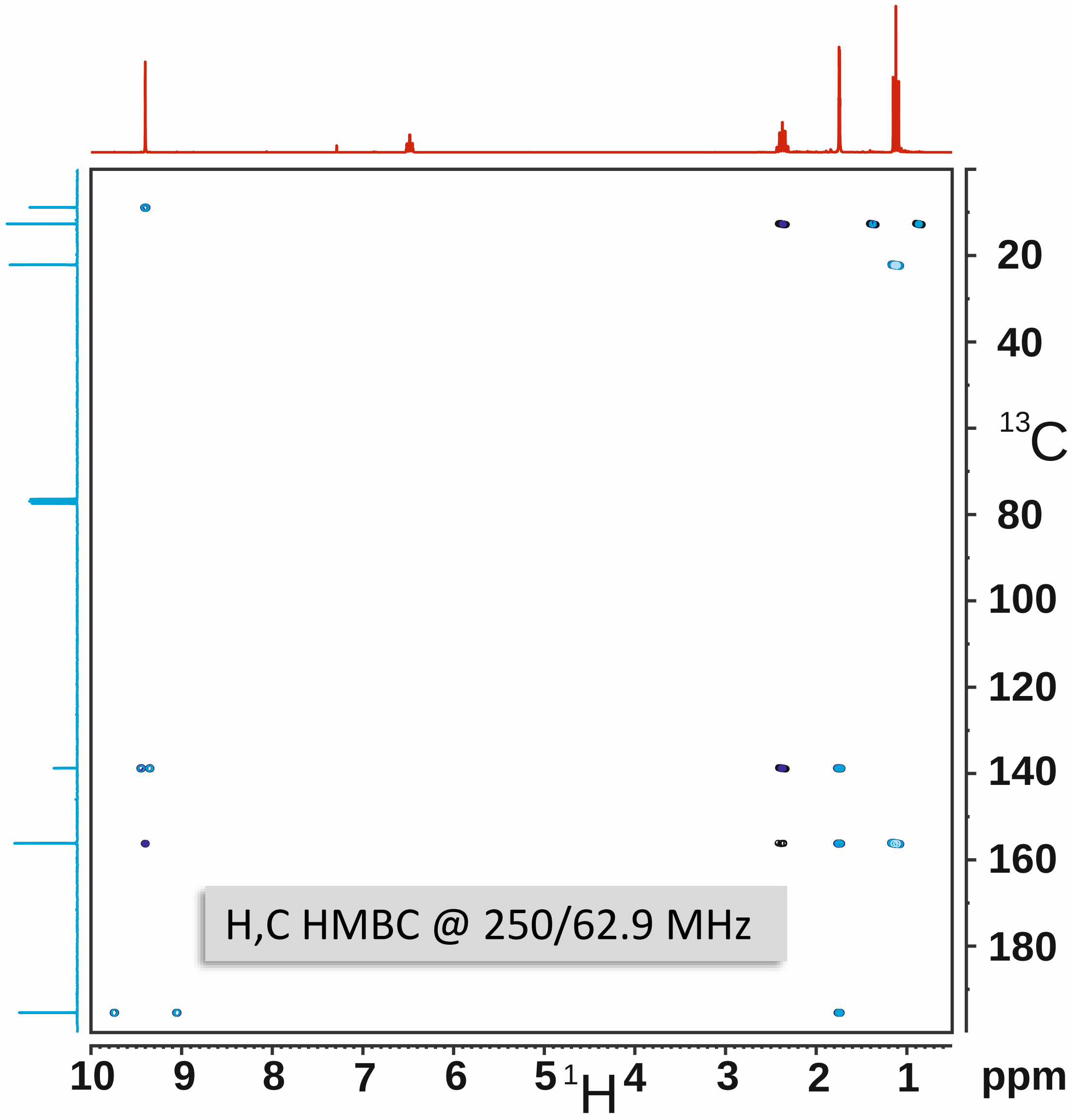
Hint

Cross peaks might indicate a coupling path across two, three, four or even more bounds.

This HMBC is not really necessary

Use it to check your result


DQF-COSY@ 250 MHz


H,C HMBC @ 250/62.9 MHz

Problem of the Month:

February 2020

Solution

Basics

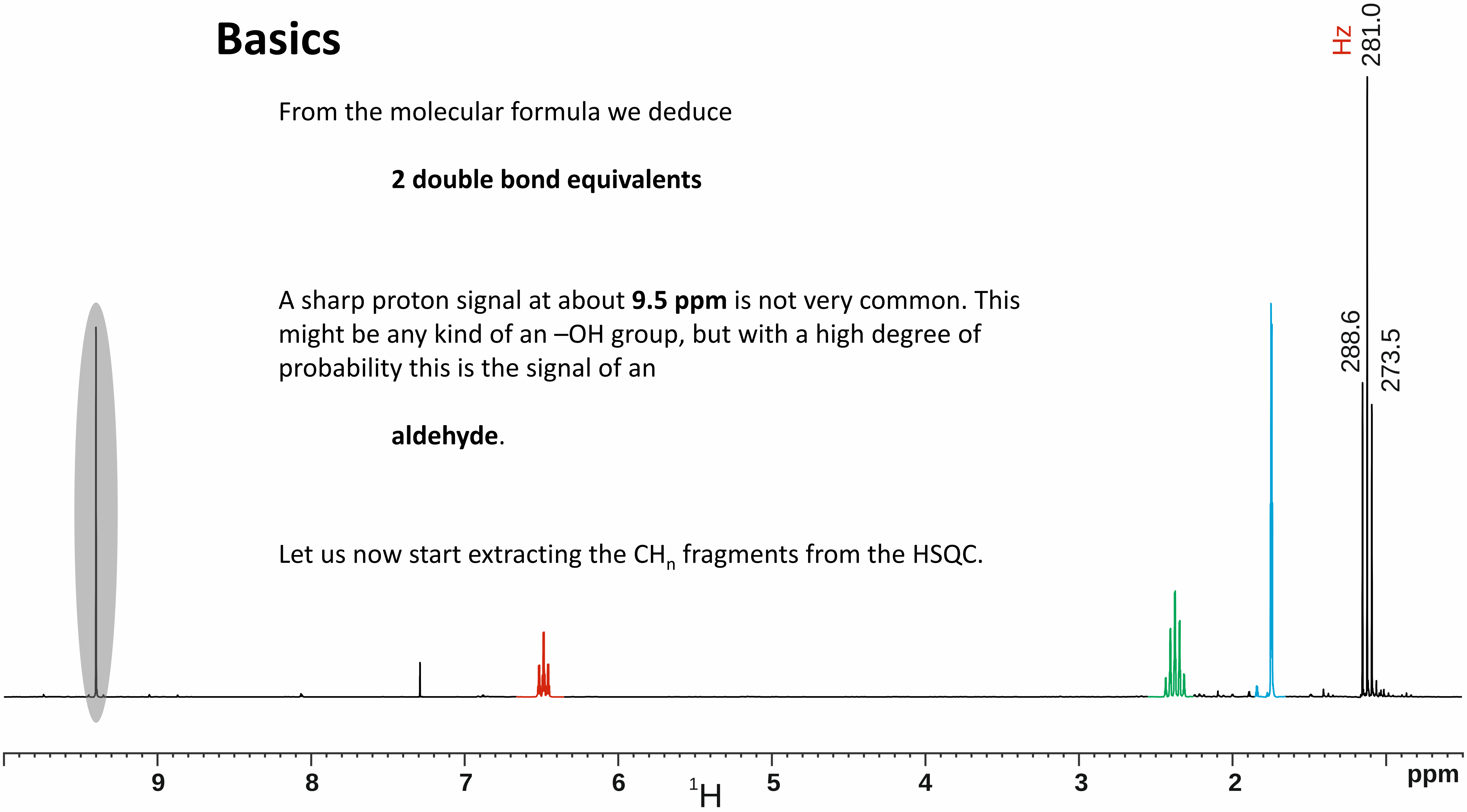
From the molecular formula we deduce

2 double bond equivalents

A sharp proton signal at about **9.5 ppm** is not very common. This might be any kind of an –OH group, but with a high degree of probability this is the signal of an

aldehyde.

Let us now start extracting the CH_n fragments from the HSQC.

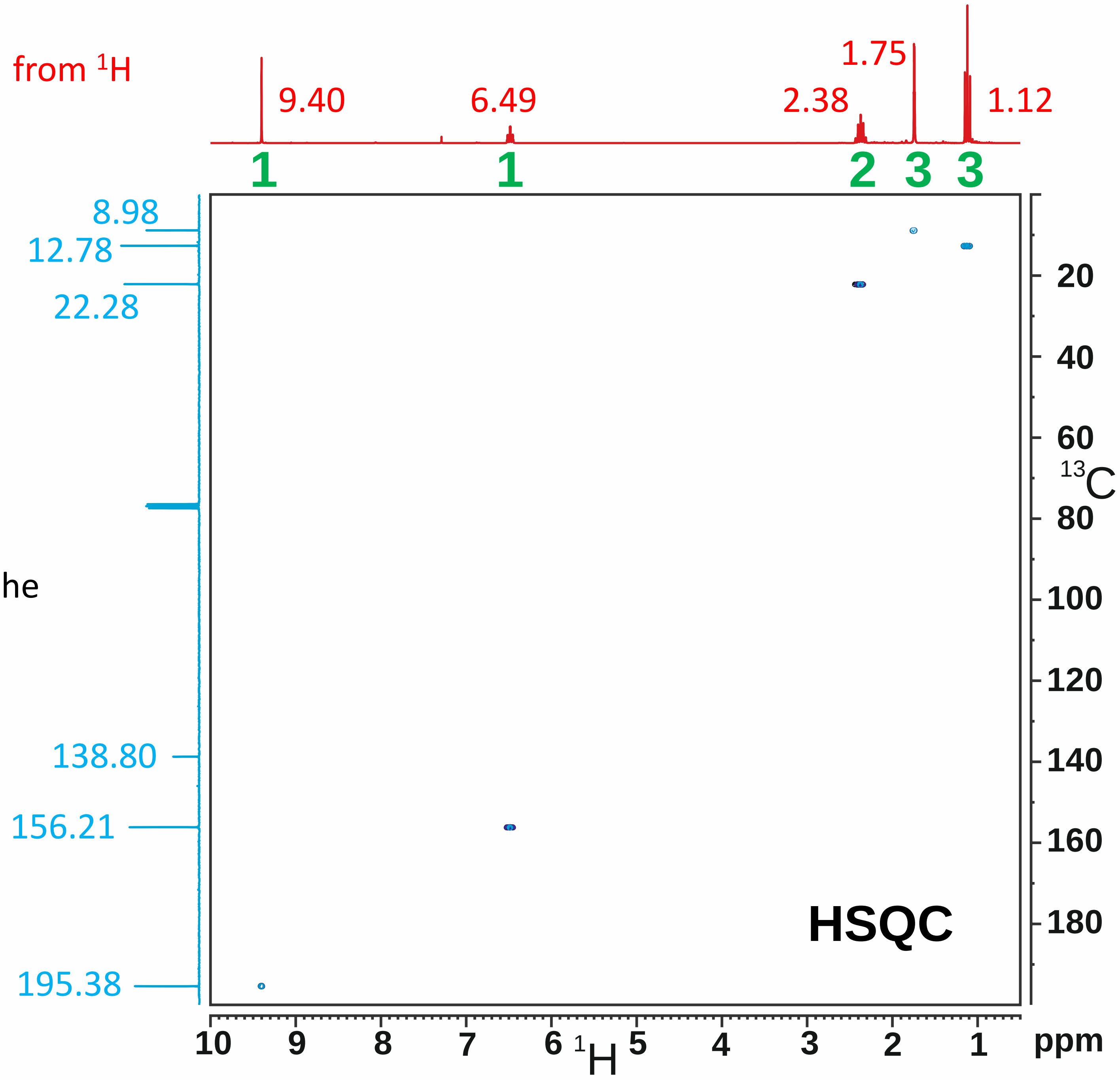


Building blocks

CH_n-fragments

It is very easy to evaluate an HSQC. The sensitivity, of course, is less than the sensitivity of a one dimensional proton spectrum but much higher than a one dimensional carbon spectrum. Therefore, the measurement of a HSQC is always recommended, if possible.

As additional data for the proton projections we need the chemical shifts and integrals from the one dimensional proton spectrum.



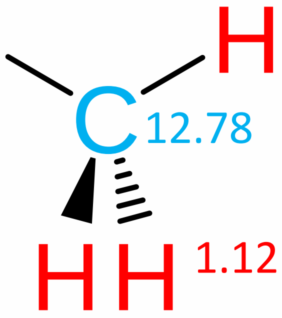
Building blocks

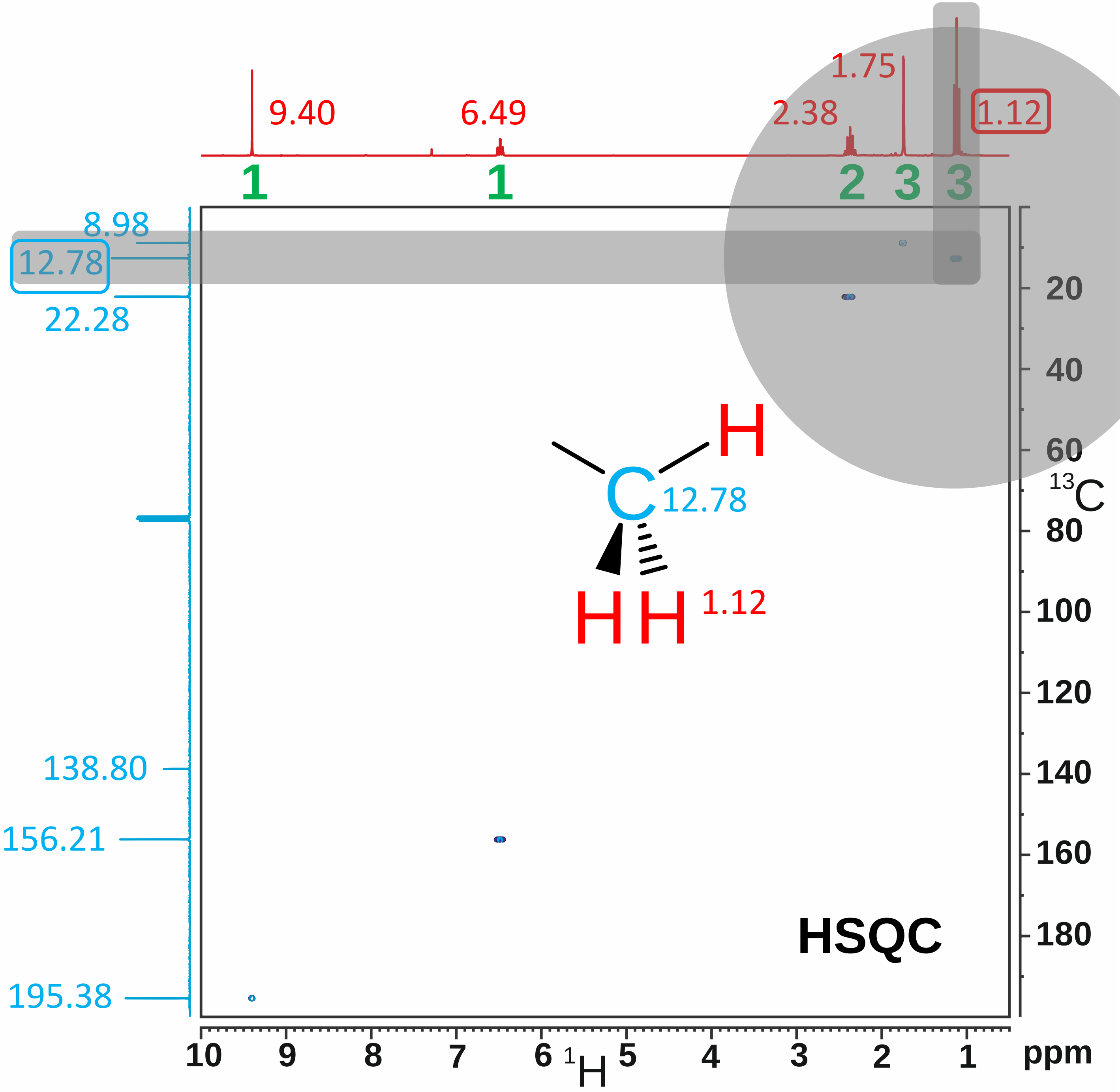
CH_n-fragments

Because we have one carbon signal for each of the six carbon atoms of the molecular formula, every cross peak in the HSQC is the result of a CH_n group.

There is no symmetry at all.

Let us start.

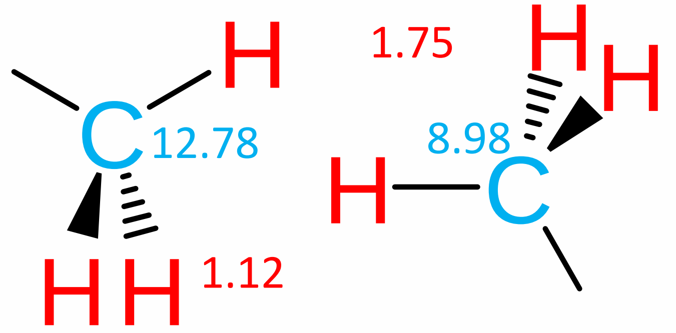


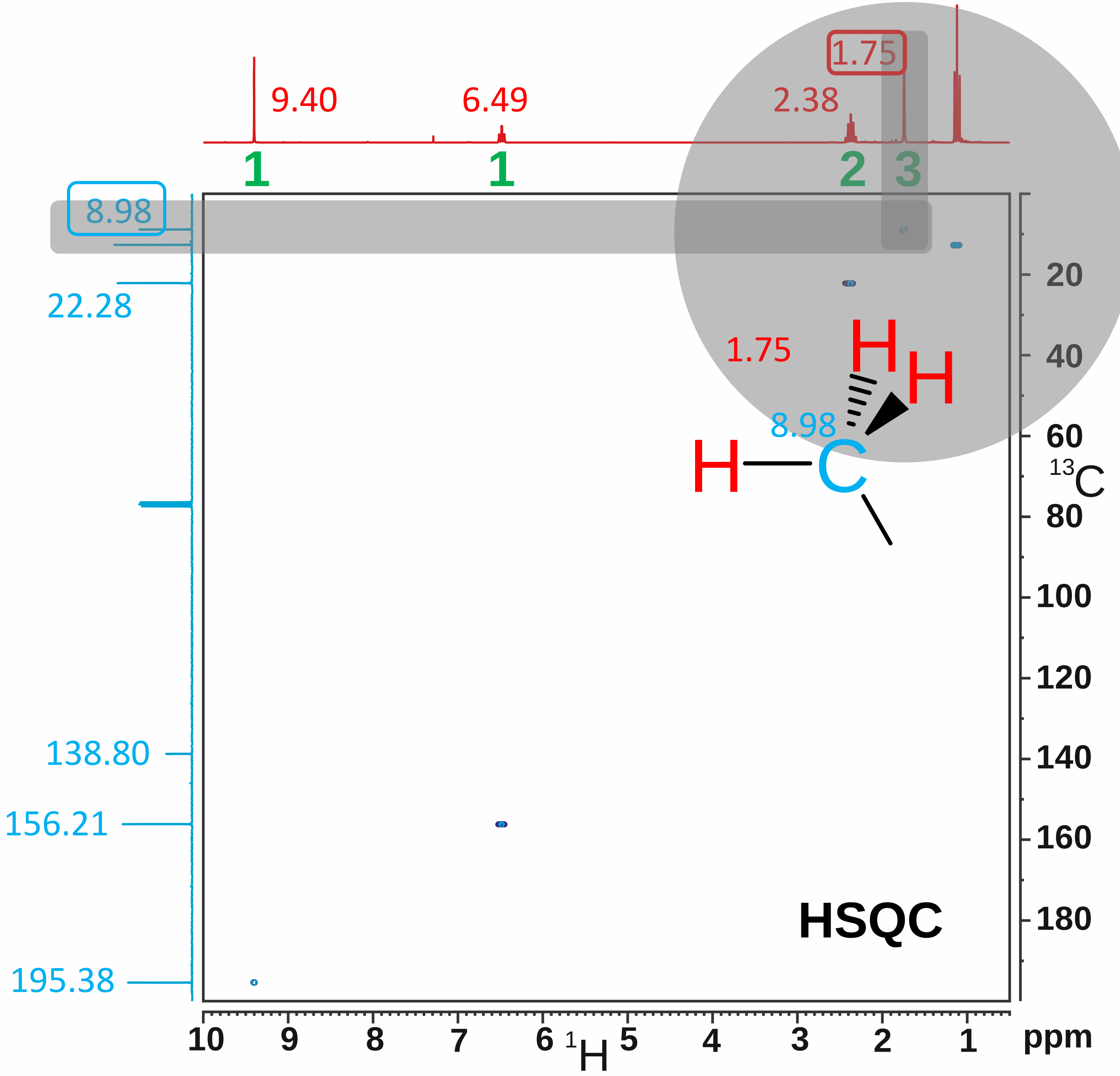


Building blocks

CH$_n$-fragments

There is one more methyl group.

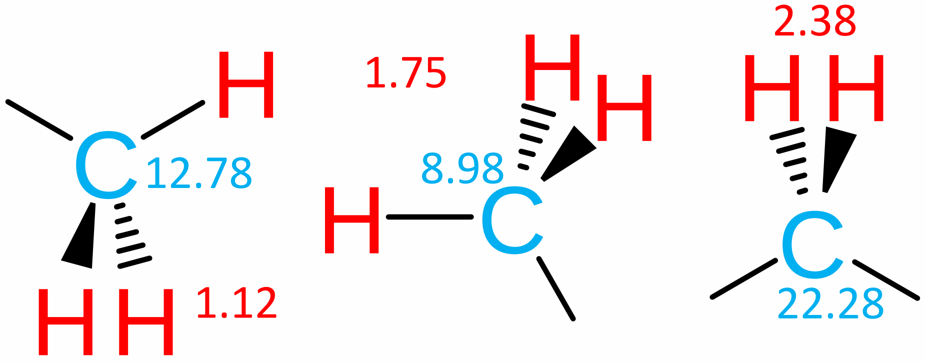


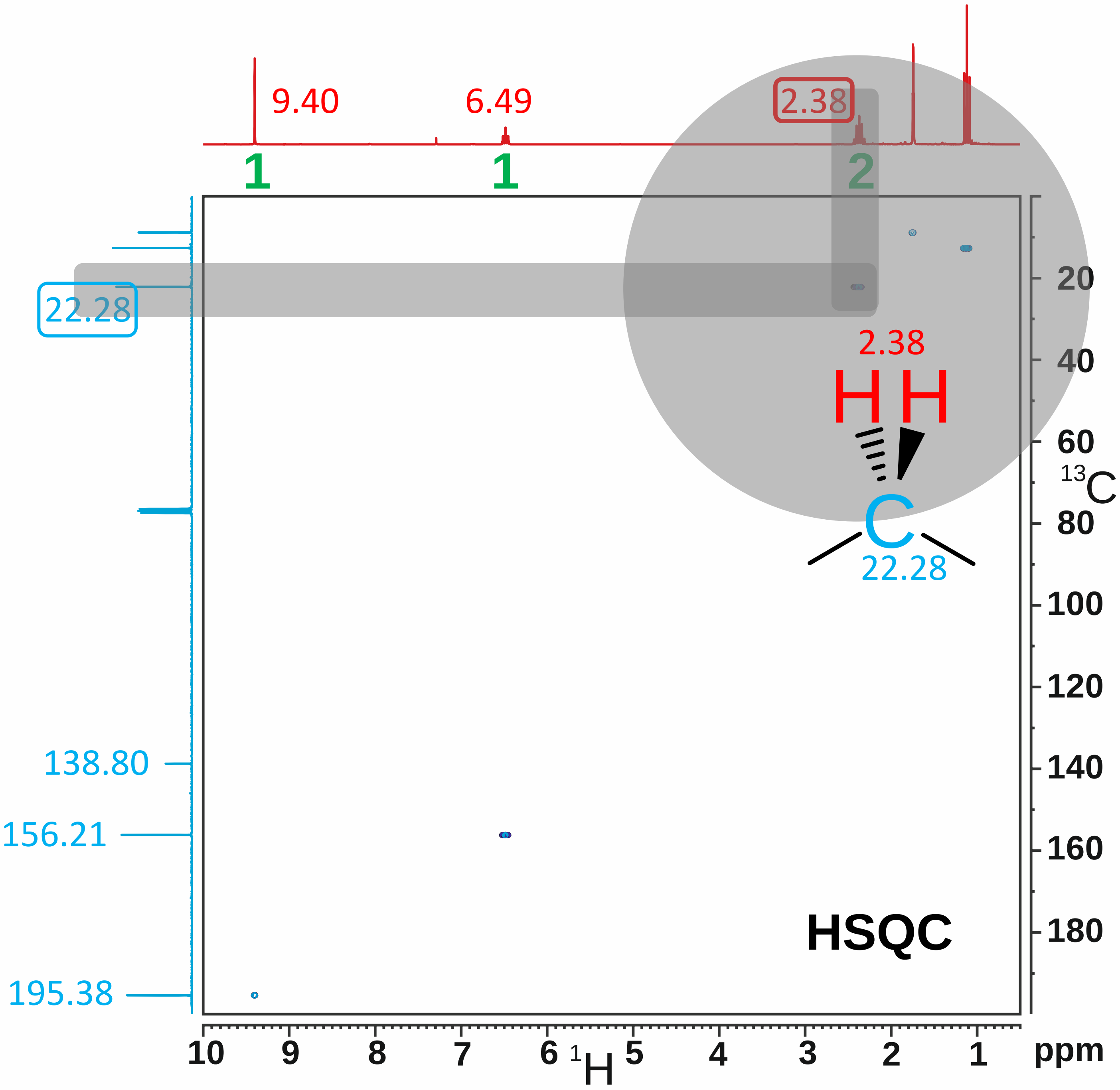


Building blocks

CH$_n$-fragments

The next cross peak belongs to a CH$_2$ group.

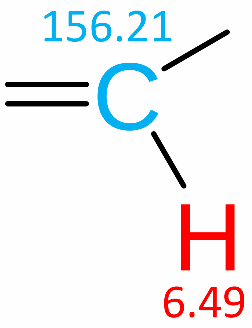


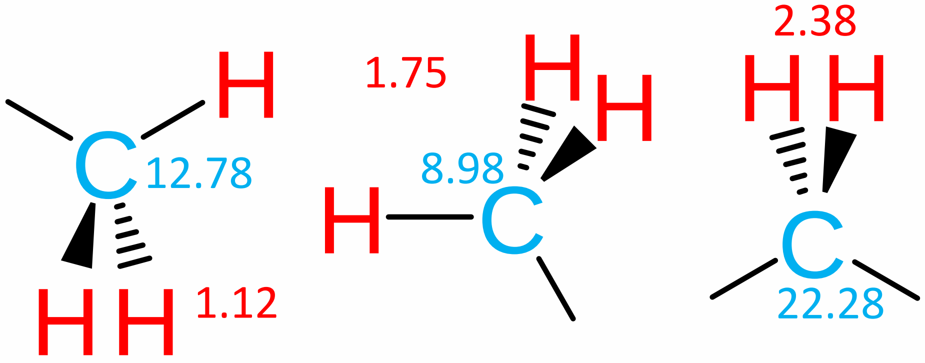


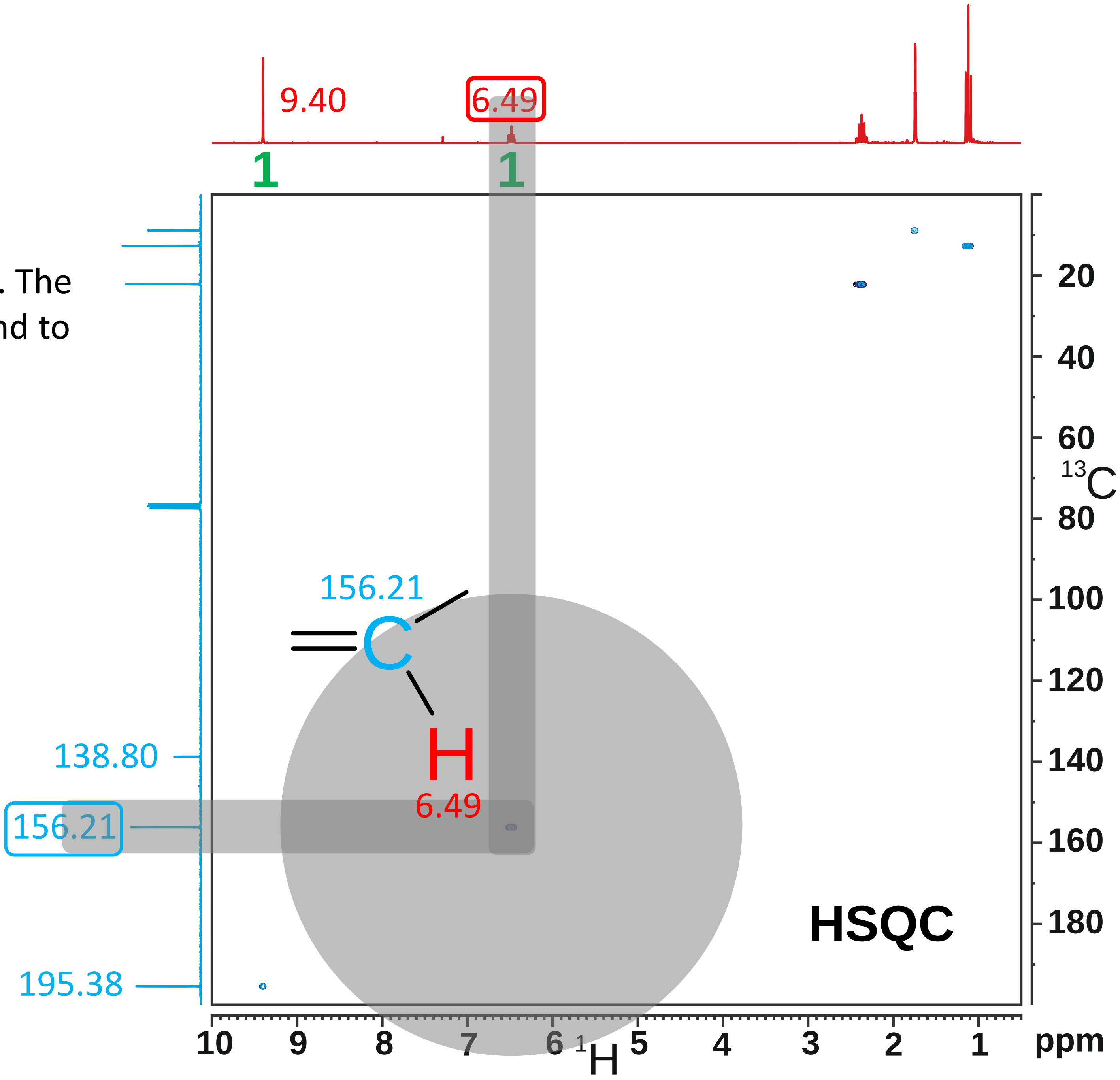
Building blocks

CH_n-fragments

In the next two fragments, the carbon is sp^2 hybridized. The chemical shifts of both the carbon and the proton bound to the carbon are very characteristic of sp^2 hybridization.



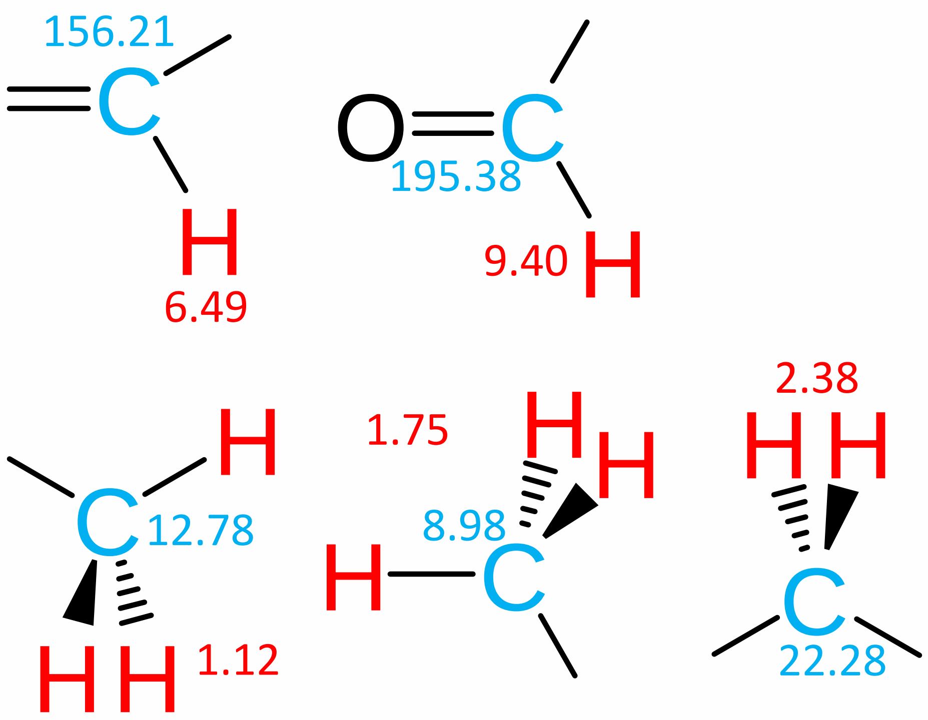


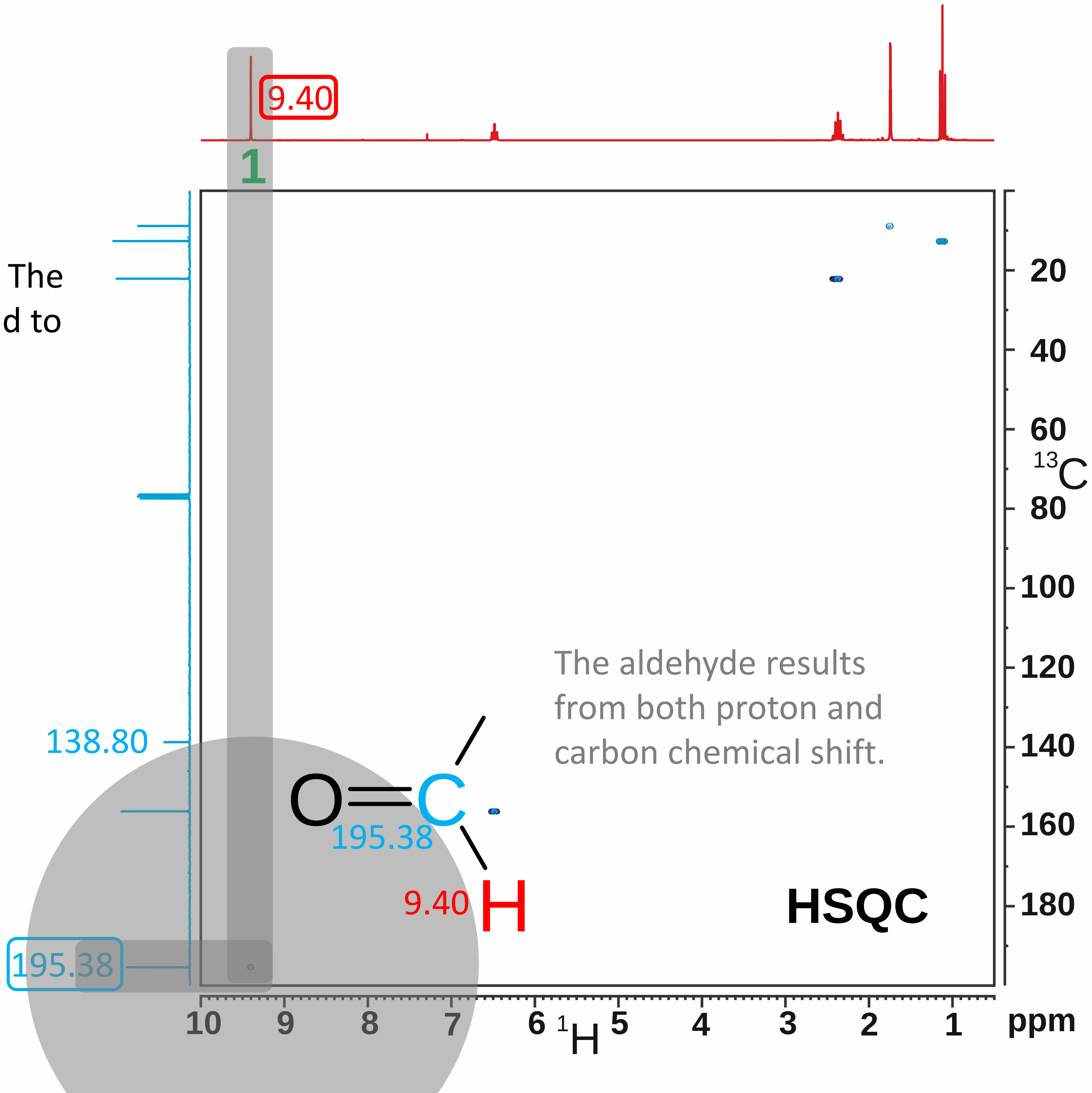


Building blocks

CH$_n$-fragments

In the next two fragments, the carbon is sp^2 hybridized. The chemical shifts of both the carbon and the proton bound to the carbon are very characteristic of sp^2 hybridization.





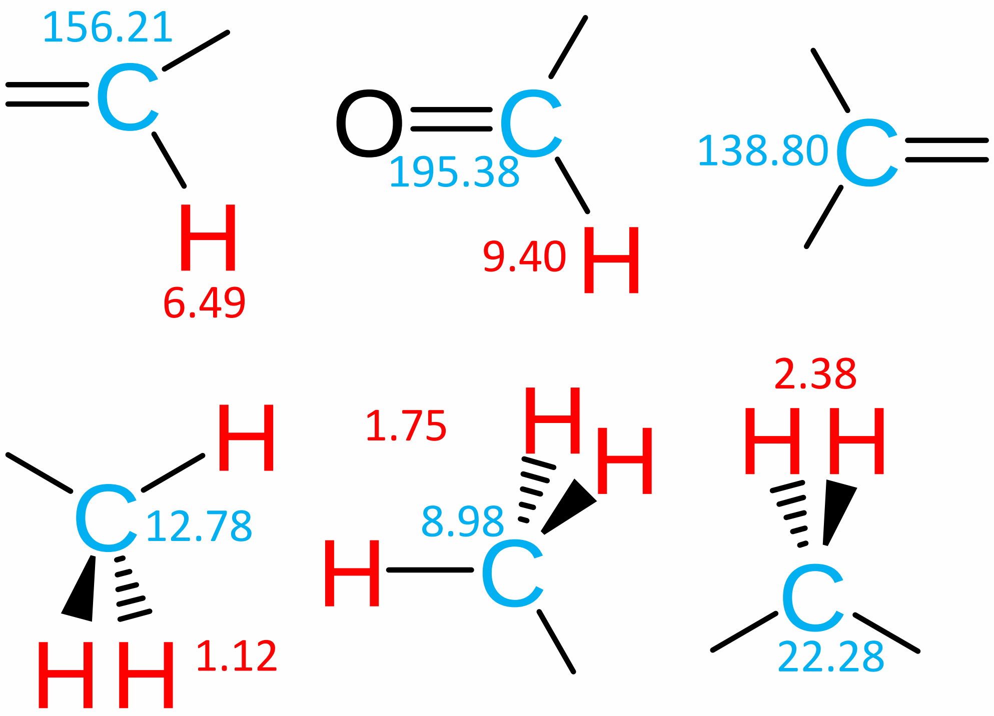
The aldehyde results from both proton and carbon chemical shift.

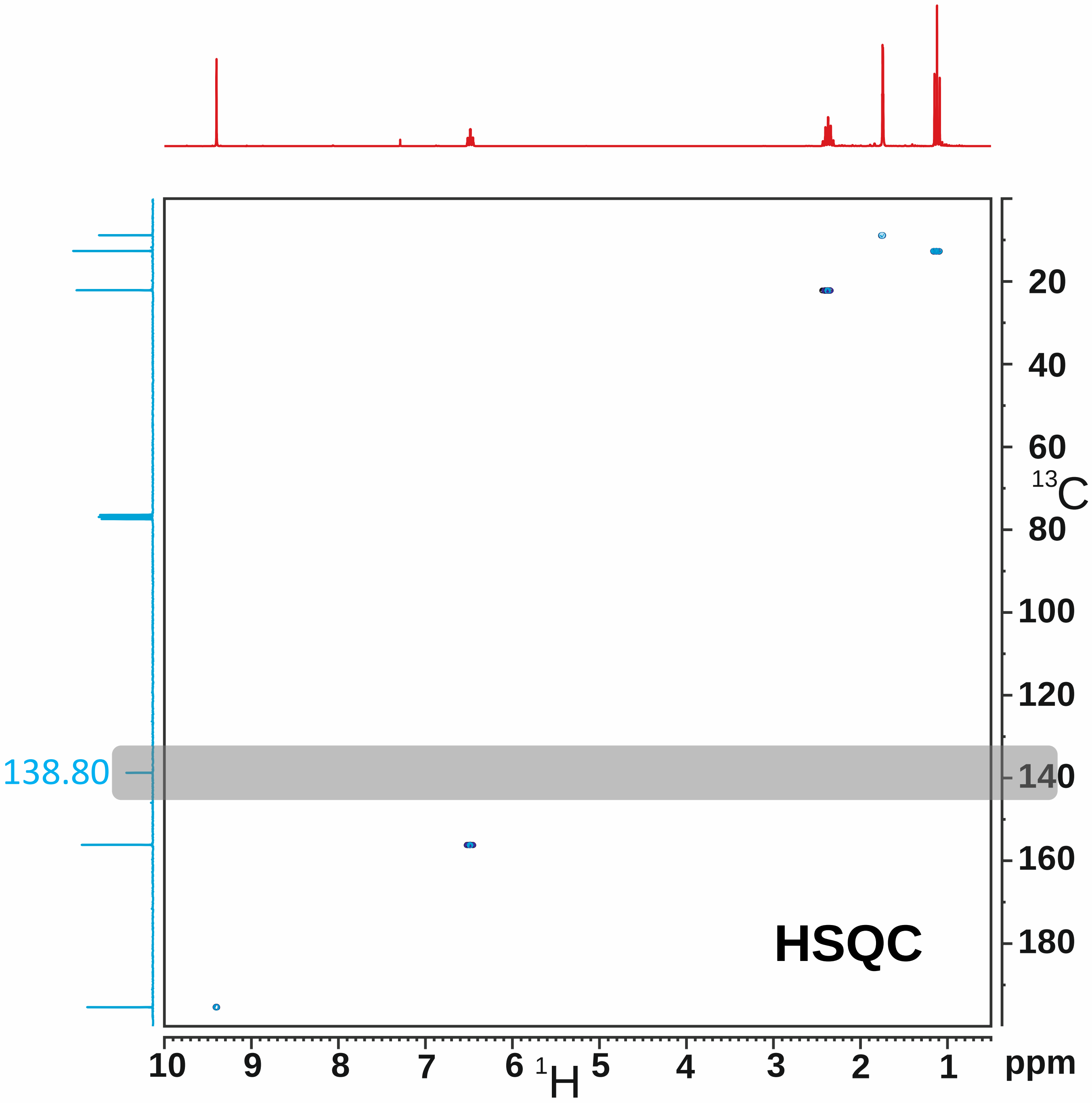
Building blocks

CH_n-fragments

There is no HSQC cross peak for the carbon signal at 138.80 ppm.
That‘s fine.

molecular formula - $C_6H_{10}O$
found so far - $C_5H_{10}O$
missing - **C**

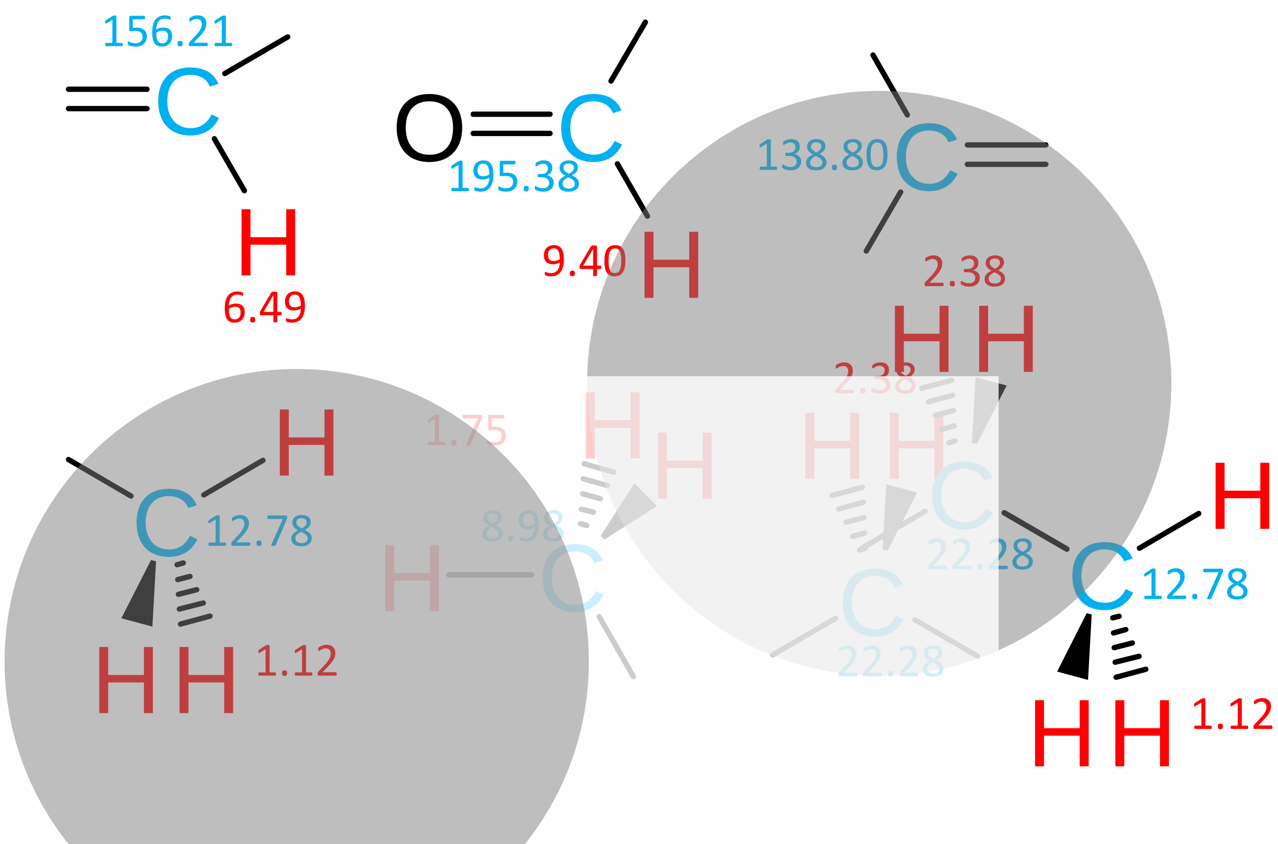


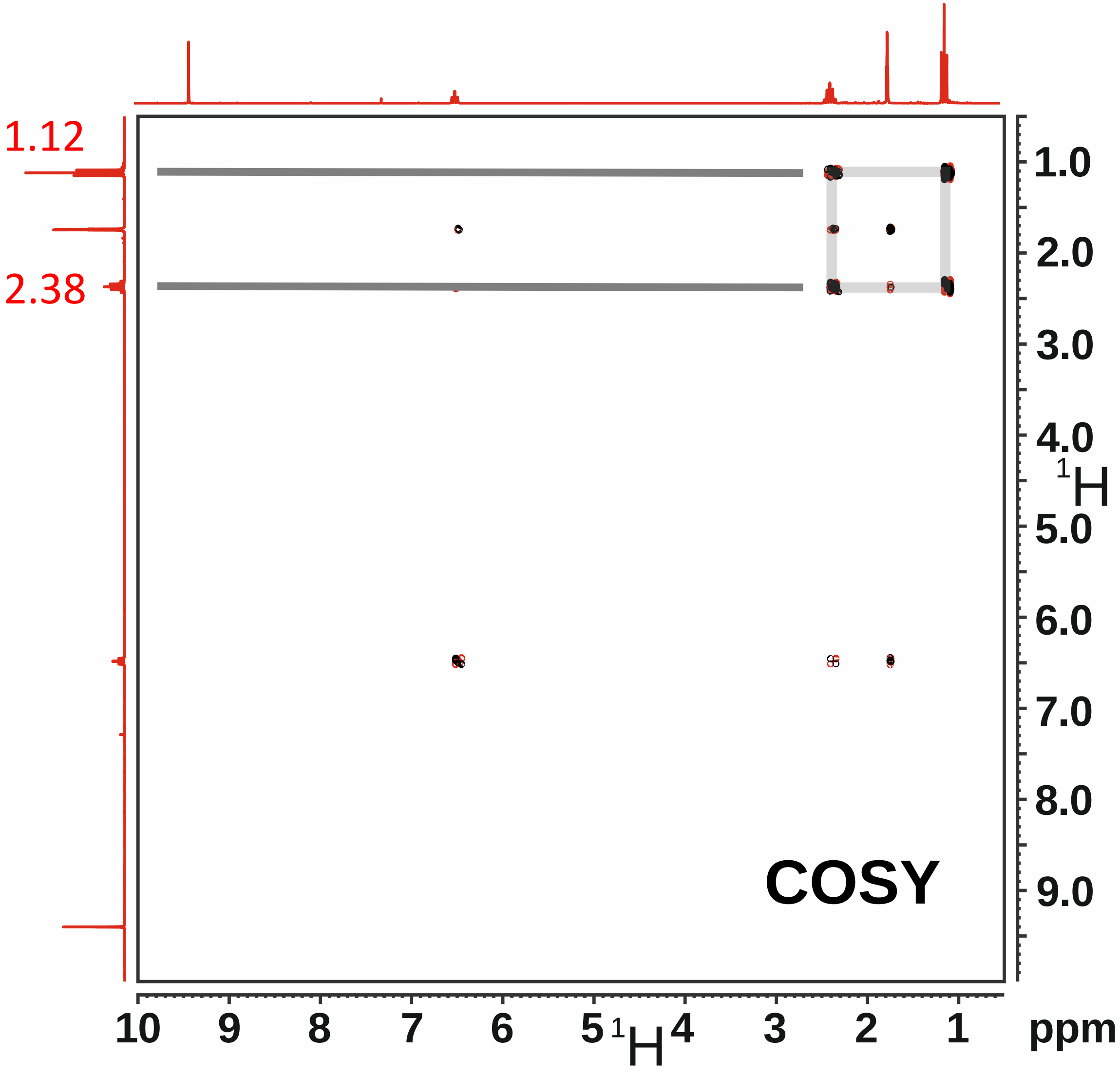


Linking the fragments

Because protons are part of nearly each of the fragments, the best way to connect the fragments is the COSY.

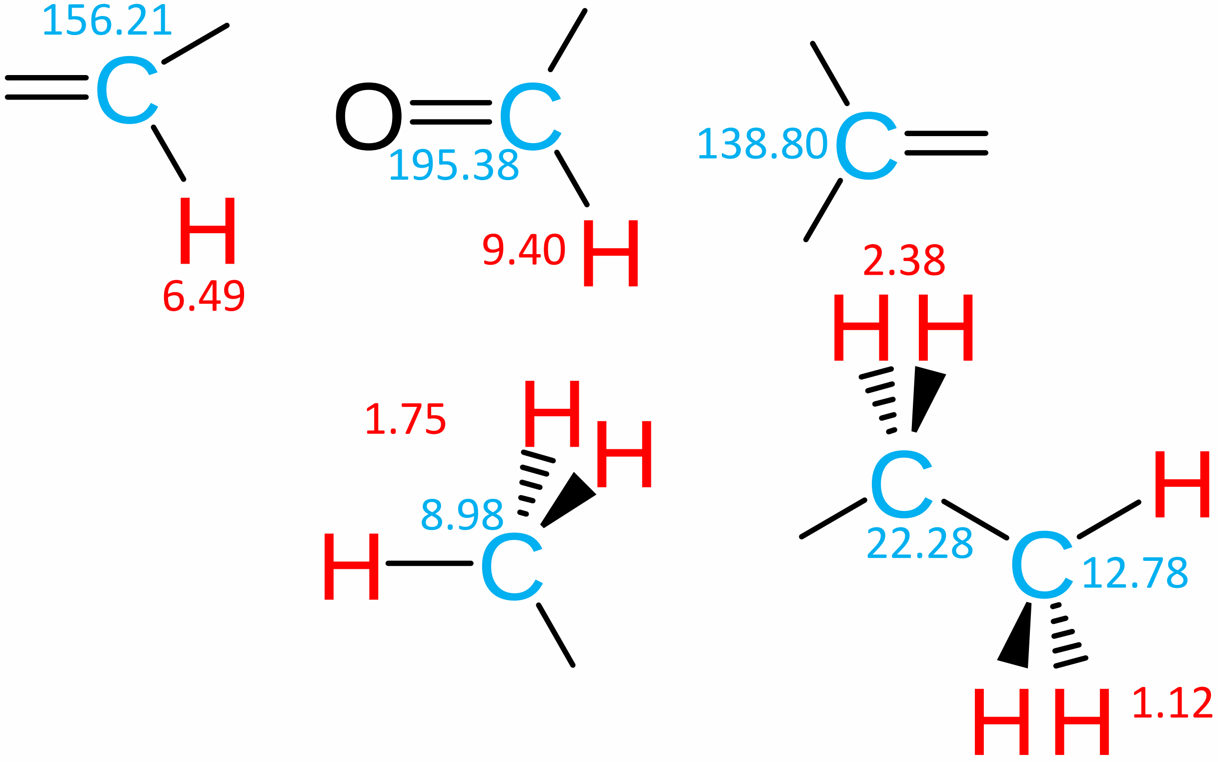
The first connectivity is easily visible.

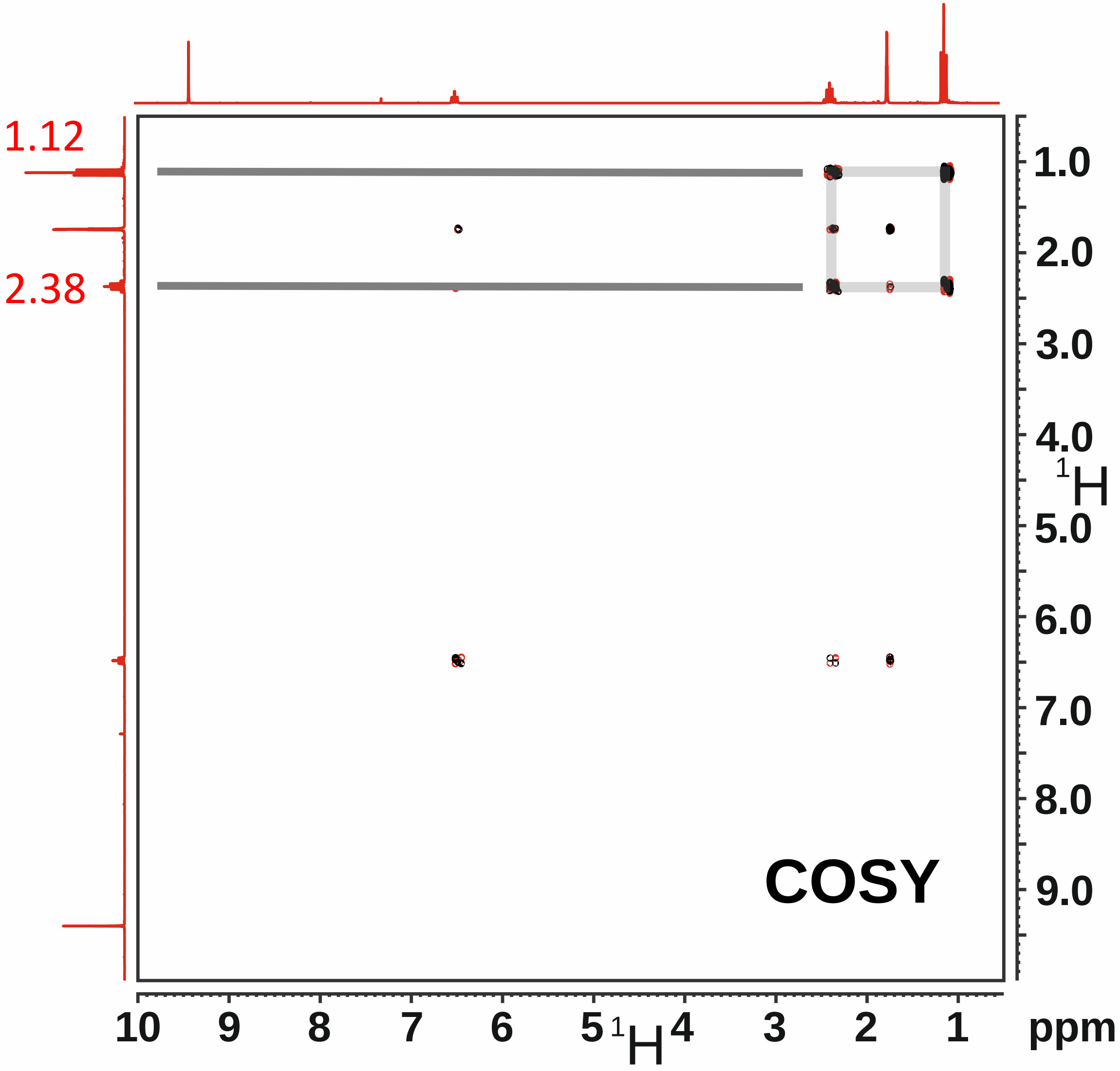




Linking the fragments

The next connectivity seems to be clear.



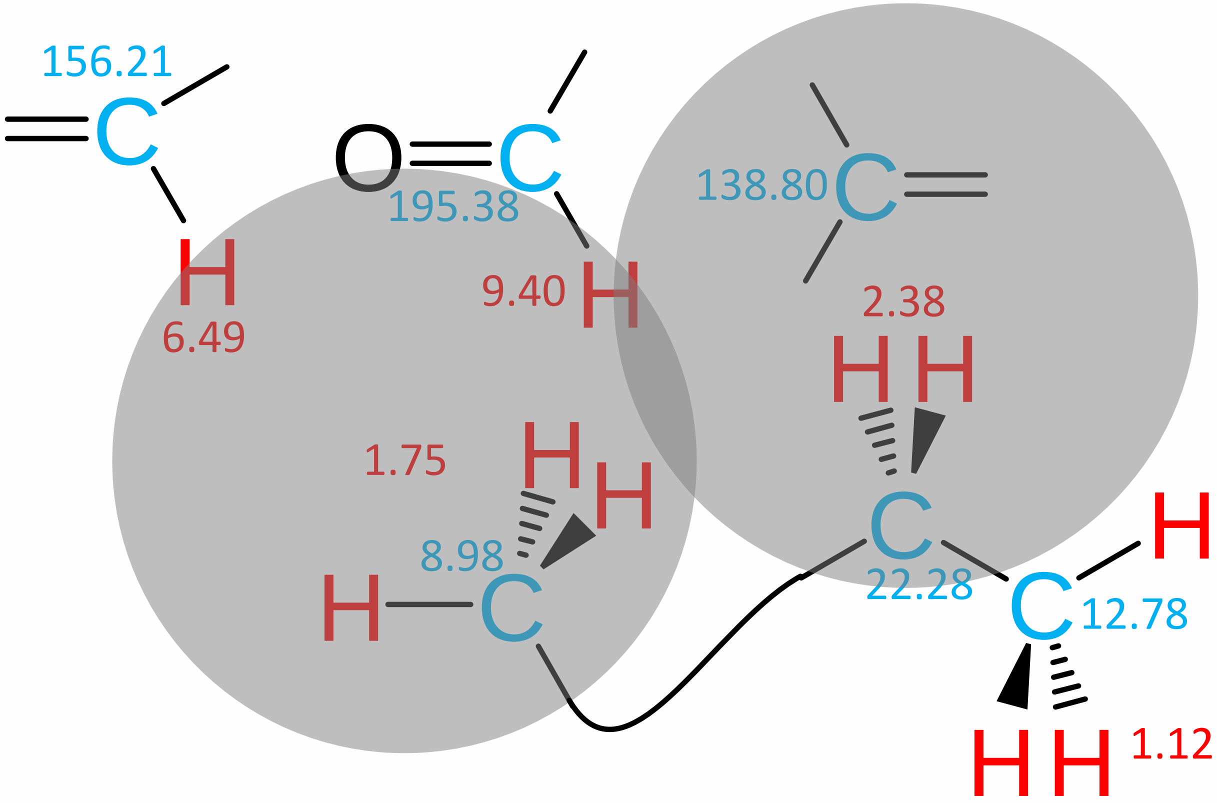


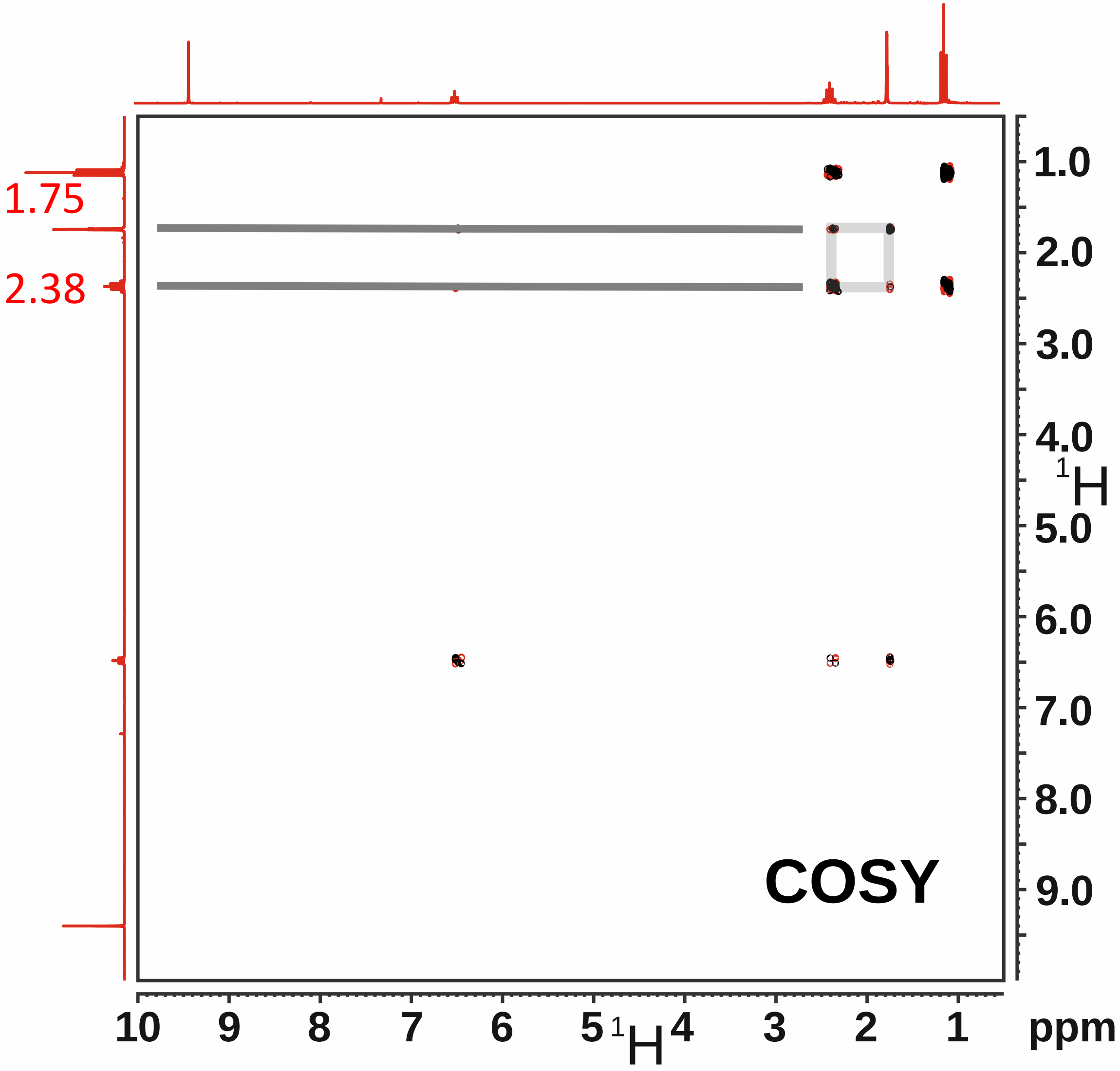
Linking the fragments

The next connectivity seems to be clear.

But this would finally result in propane.

That is impossible, because we would then have at least two molecules and furthermore there would have to be a proton multiplet with 6 protons.

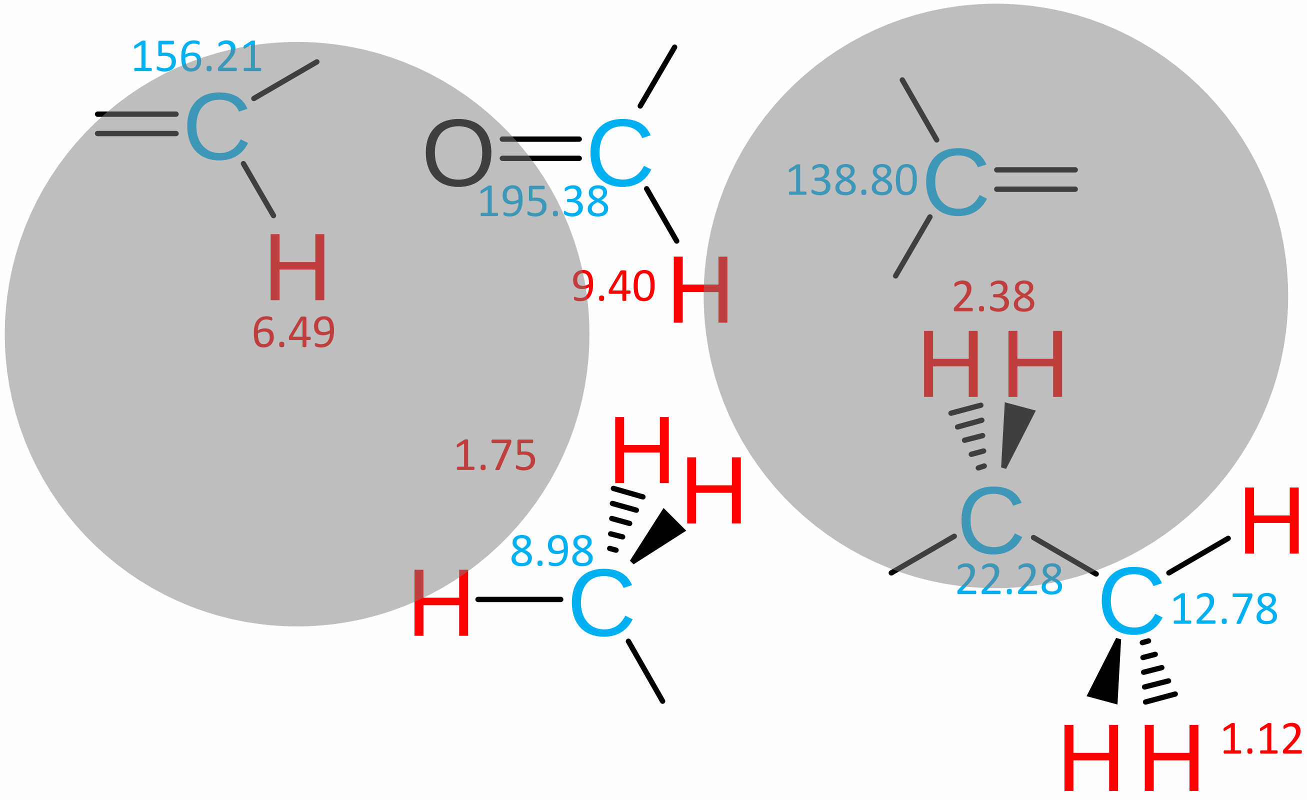


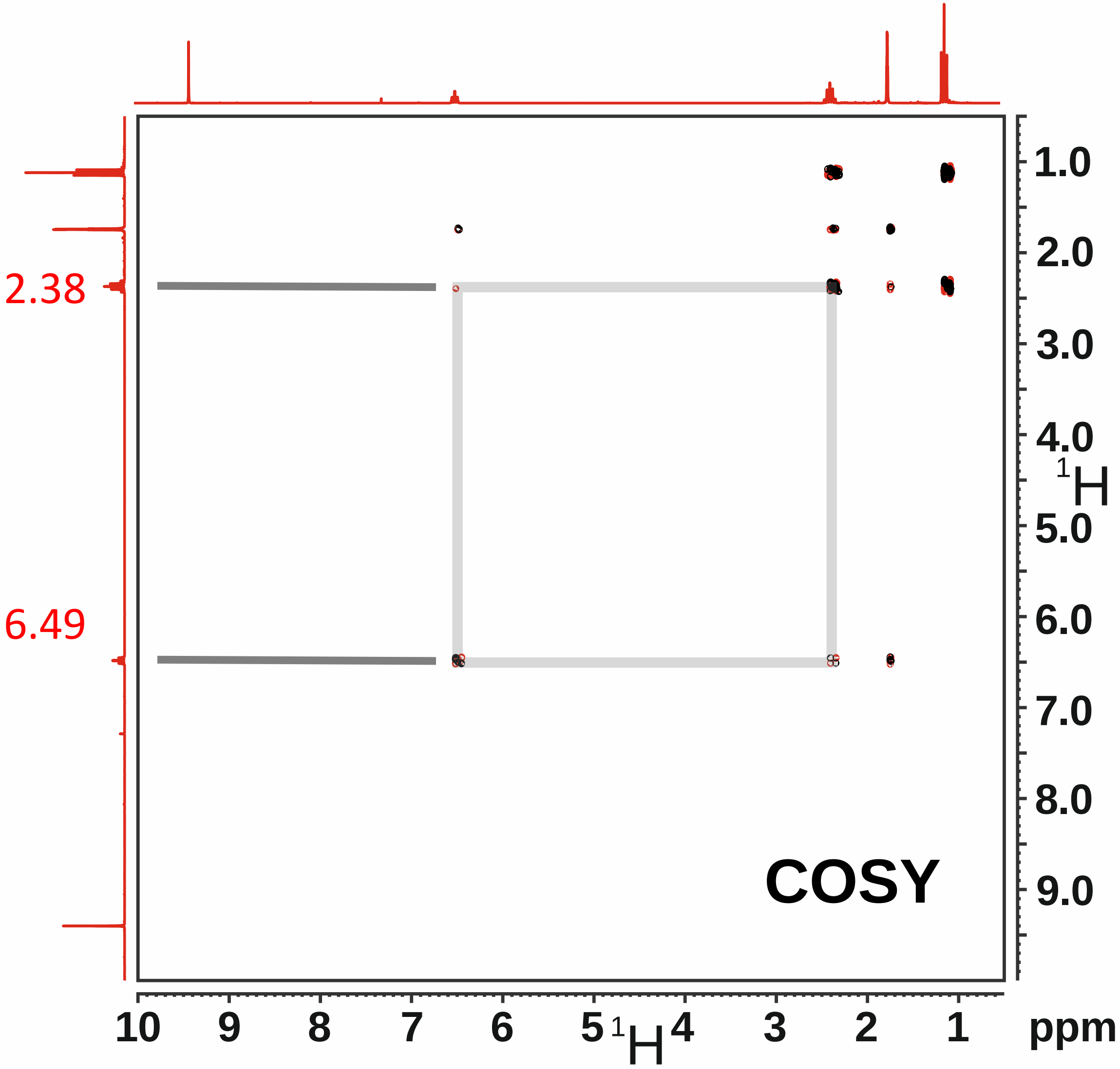


Linking the fragments

But …?

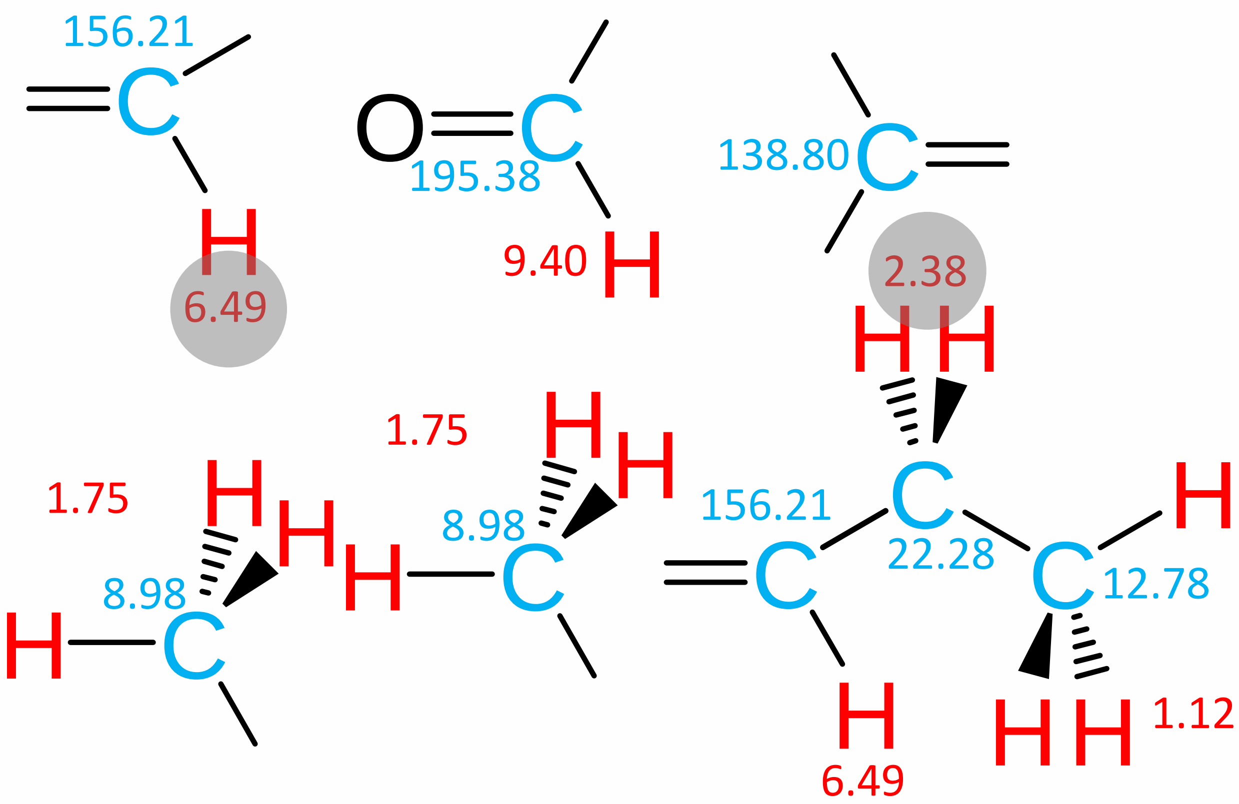
There is another correlation between the protons with the chemical shifts of 2.38 ppm and 6.49 ppm.

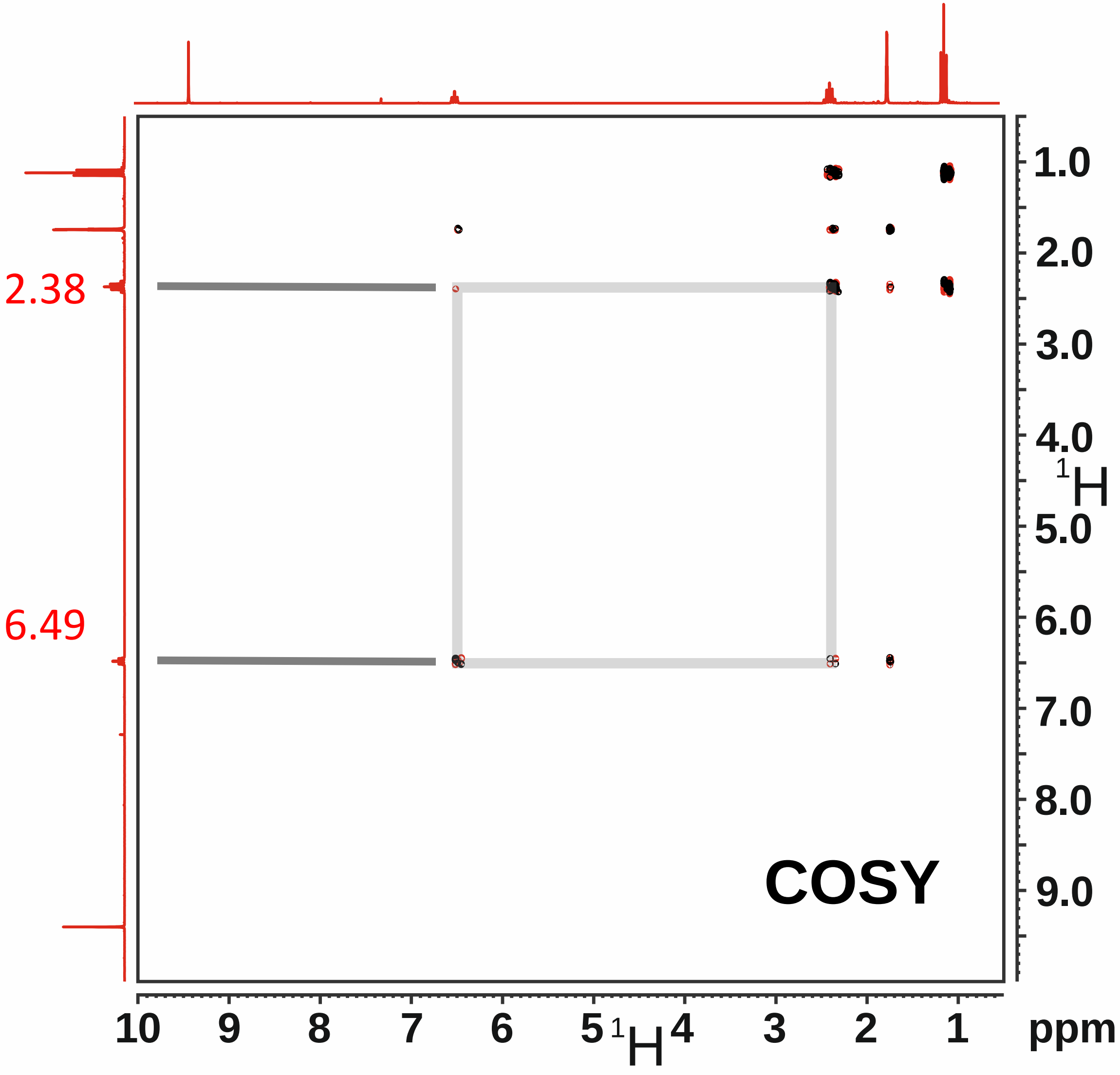




Linking the fragments

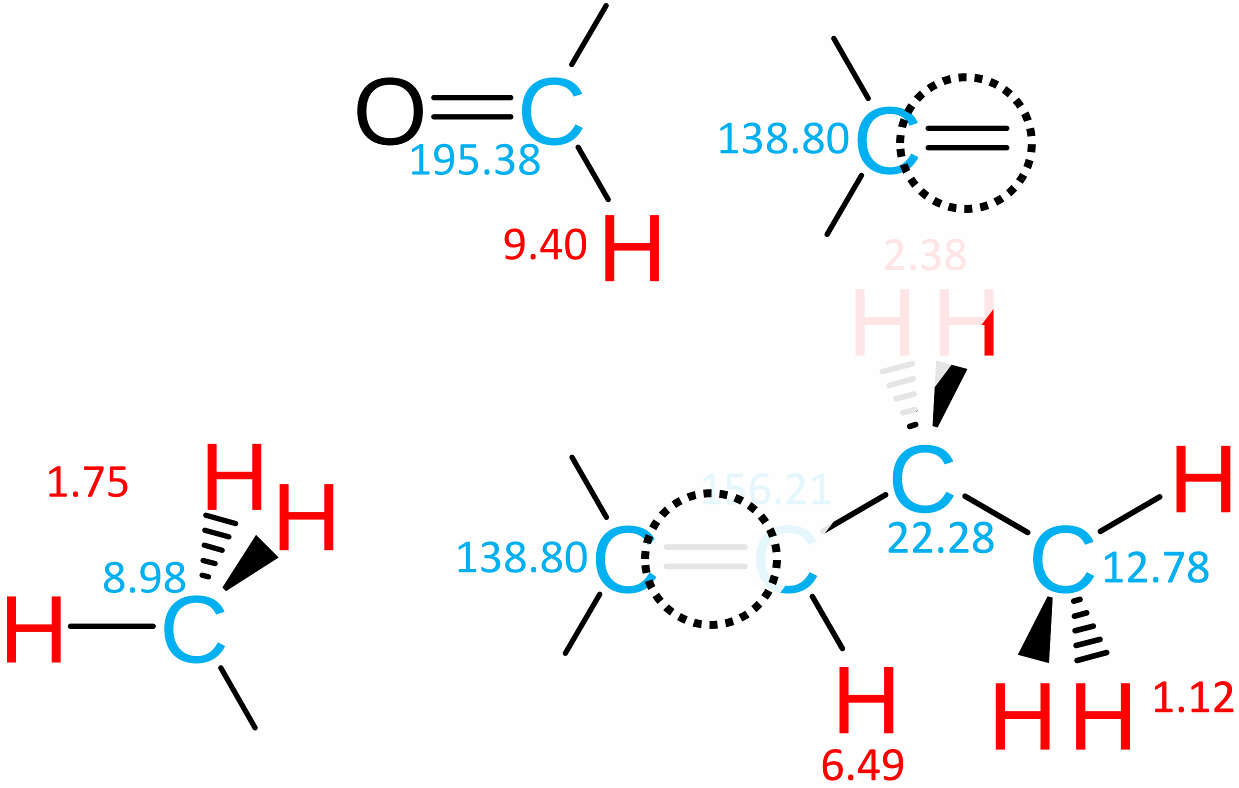
Let us connect the corresponding fragments.

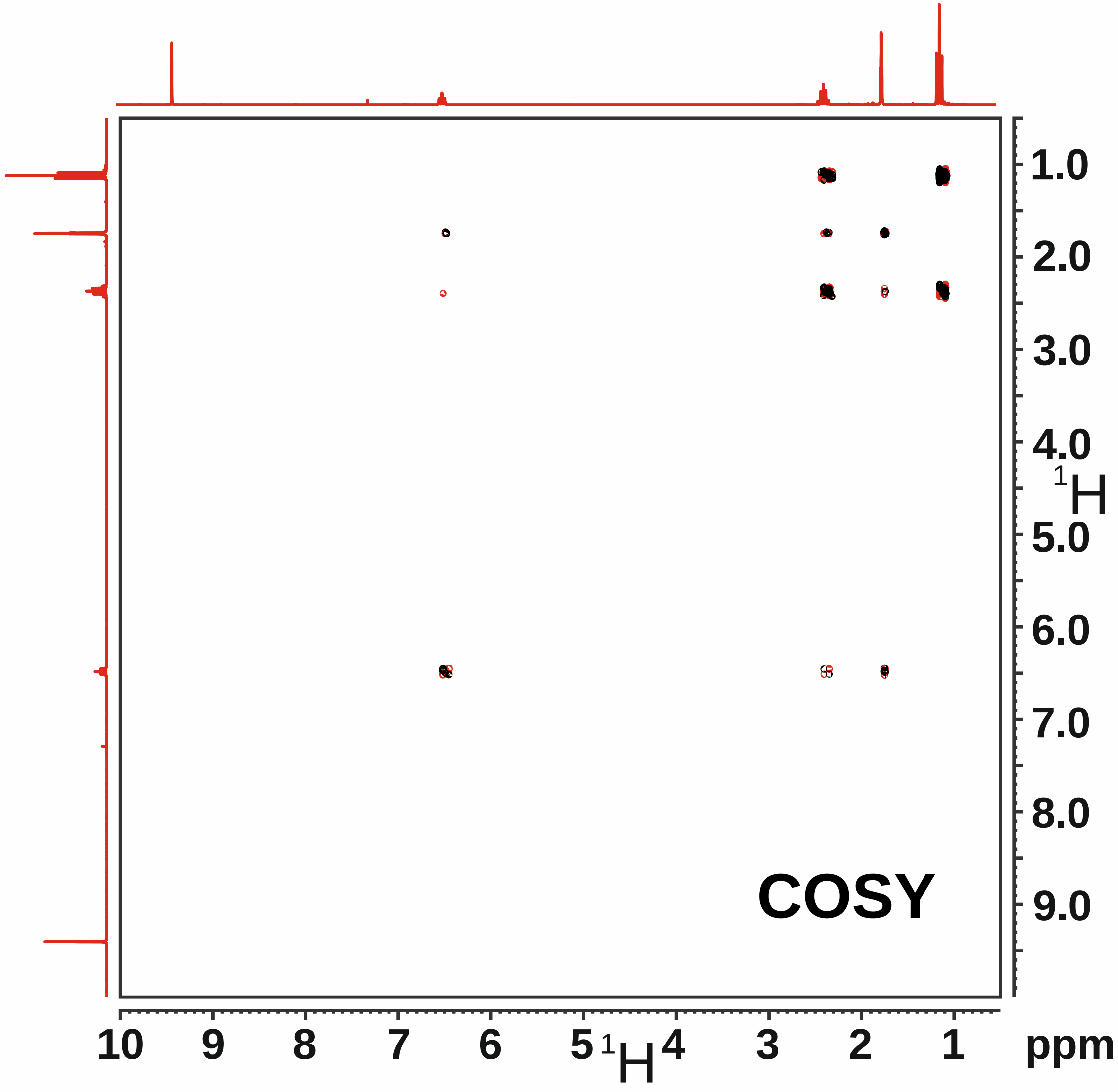




Linking the fragments

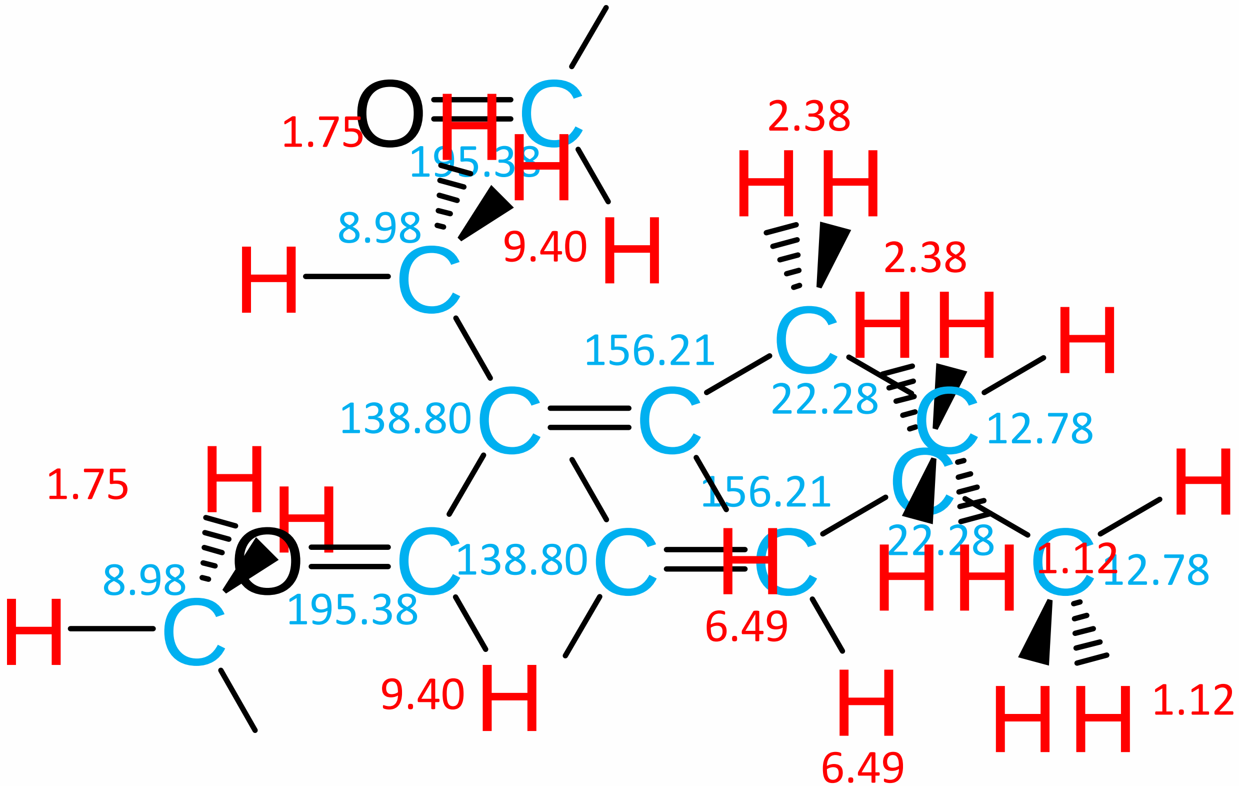
To get the next connectivity, we don‘t need any COSY peak. There is only one possibility.

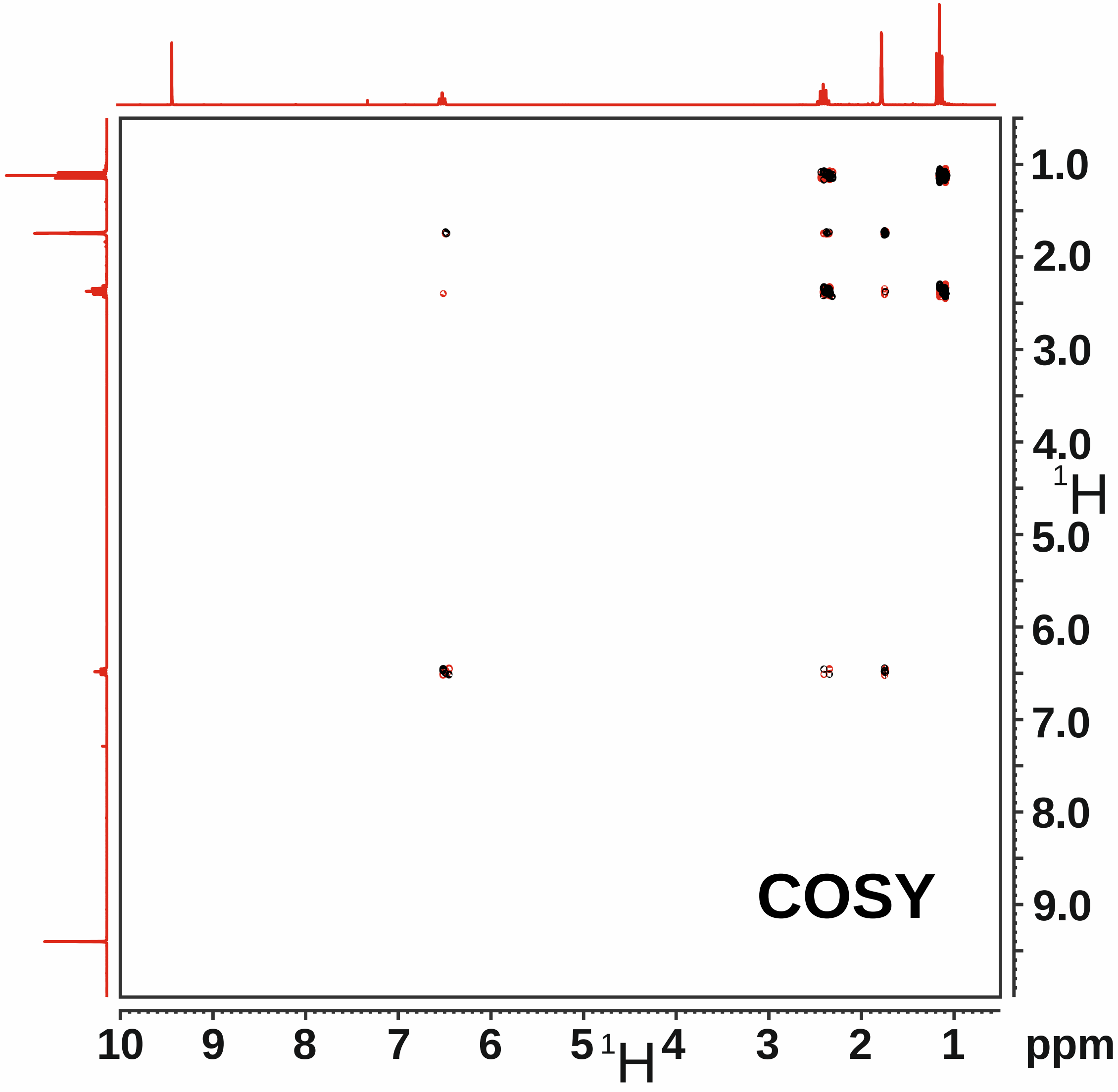




Linking the fragments

Now there is only one remaining possibility to connect the three pieces.

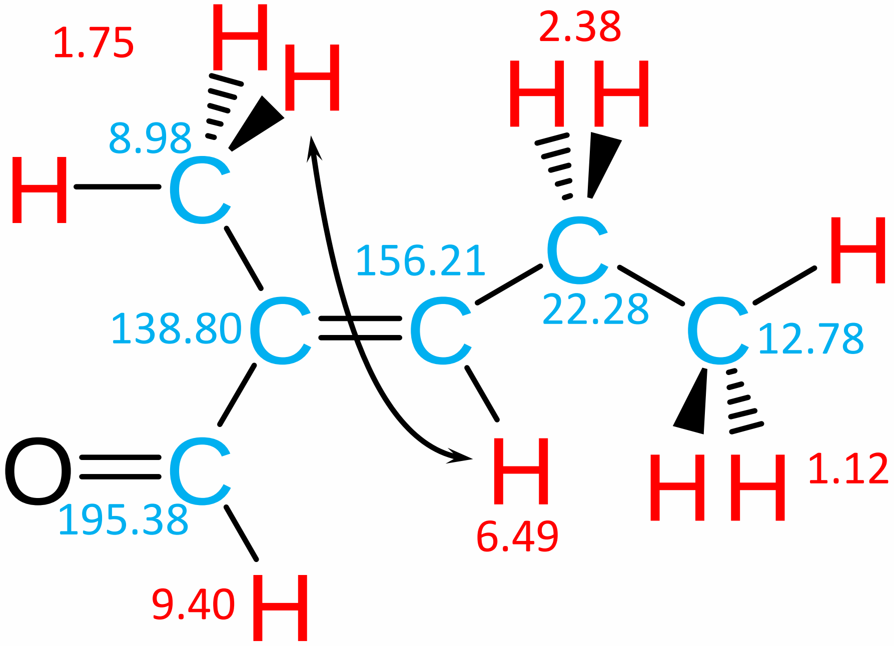


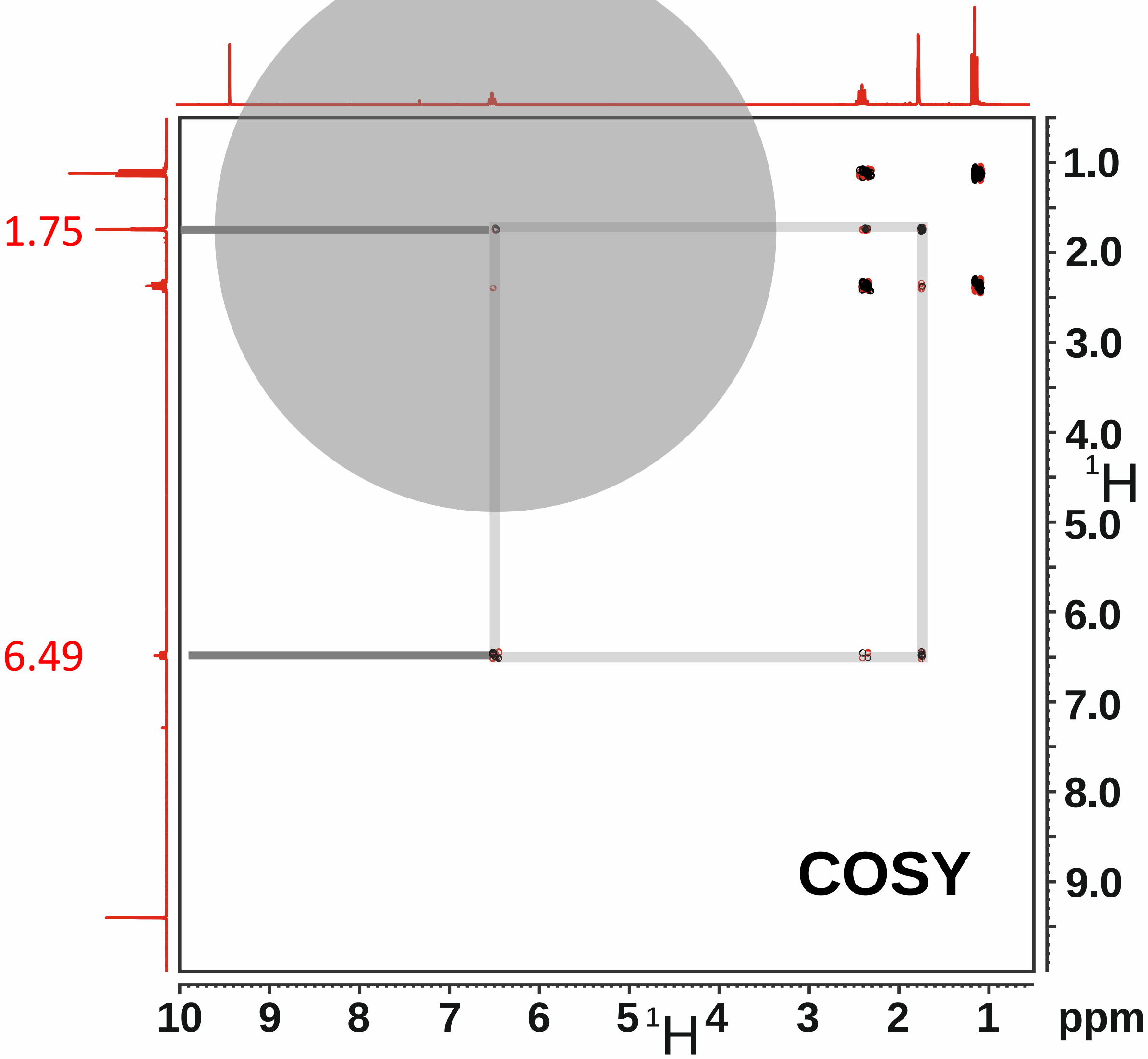


Two open questions

1. What is the reason for this cross peak?

We have found one four bond correlation. Such four bond correlations are not infrequently observed as soon as π electrons are part of the coupling pathway.

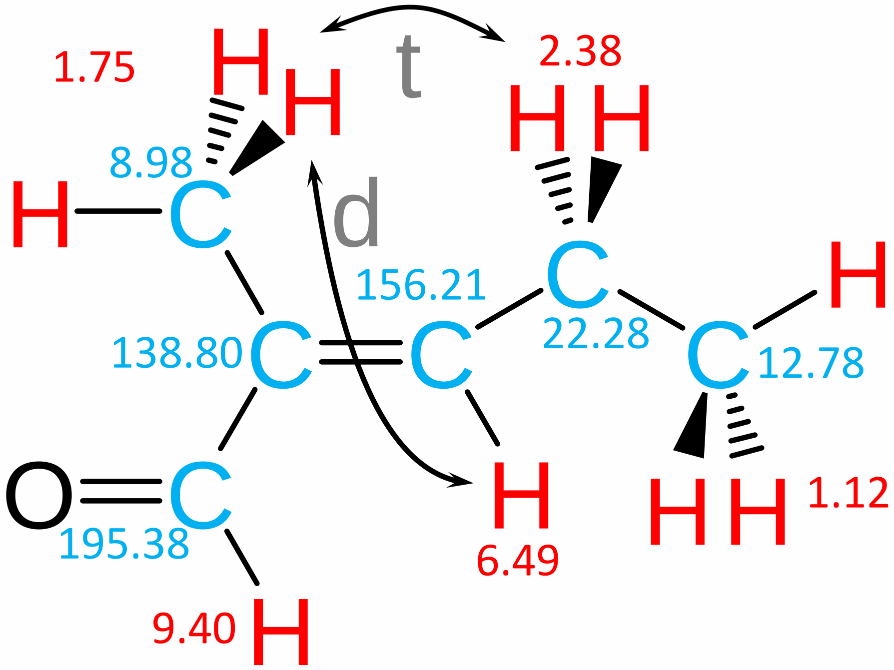


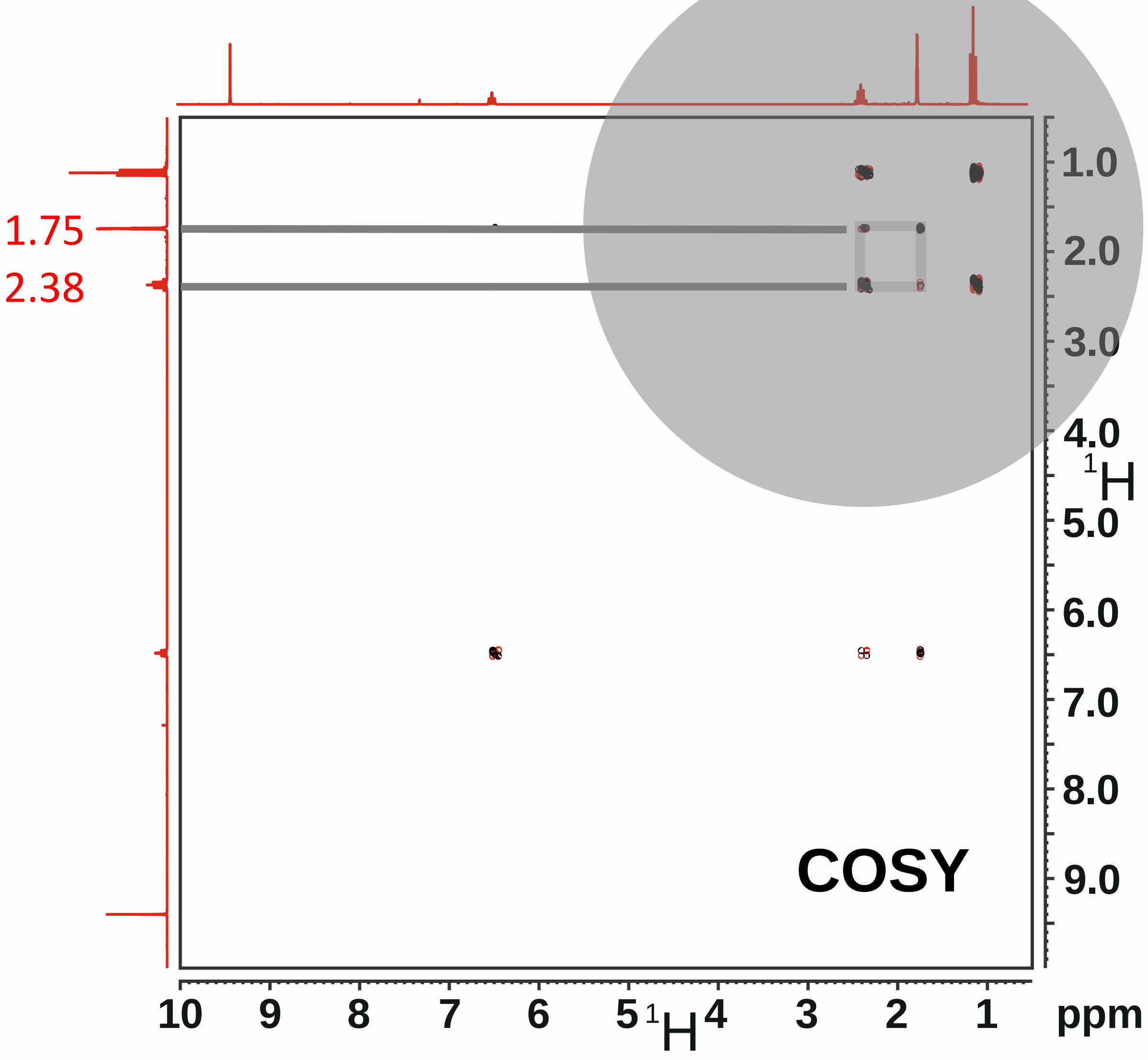


Two open questions

2. And where does this cross peak come from? Please remember, we already tried to use this cross peak in error.

We have found a five bond correlation! These are not very common. The methyl group at 1.75 ppm should appear as a doublet of triplets due to both long range couplings.



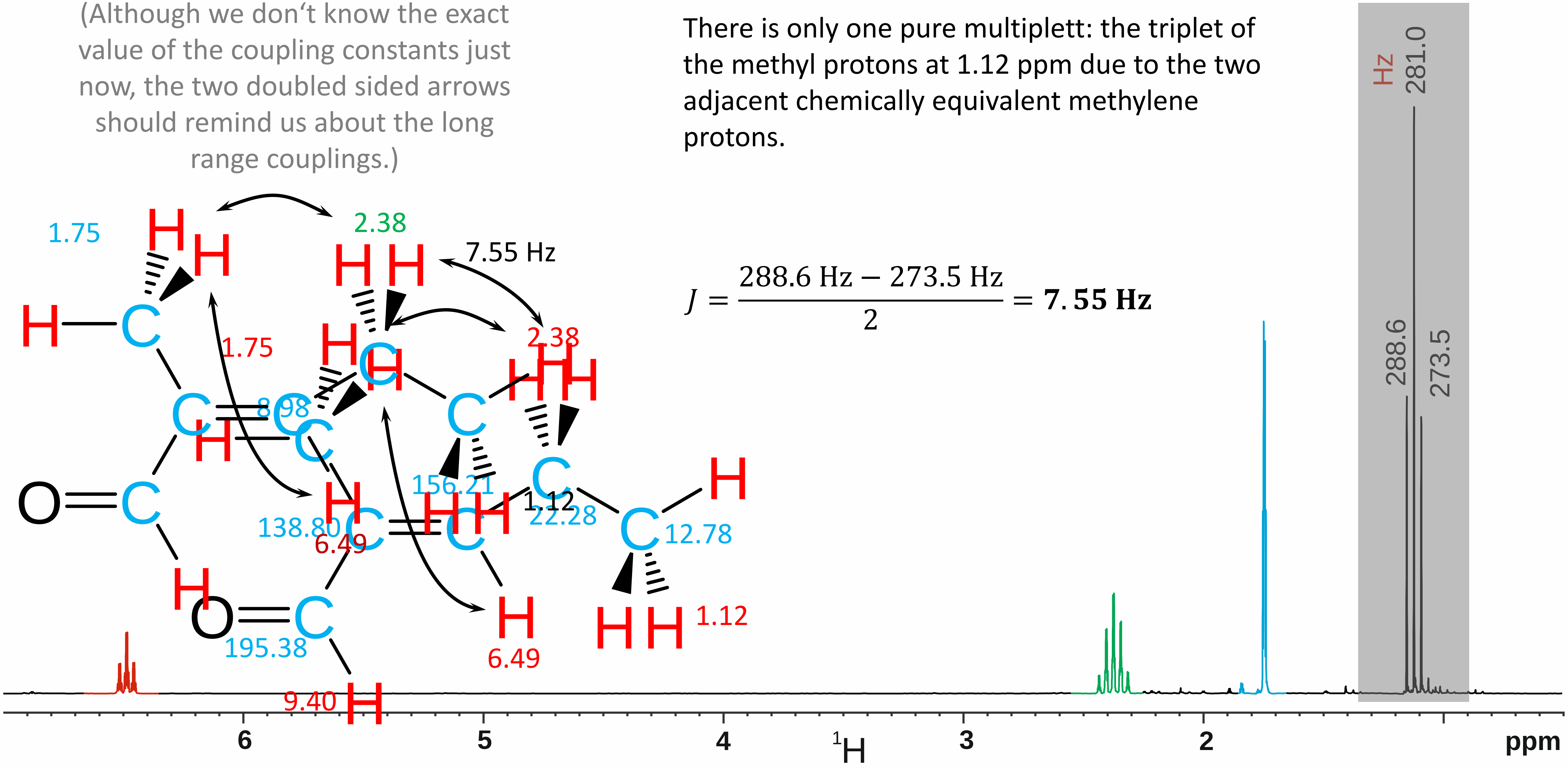


Coupling constants

(Although we don‘t know the exact value of the coupling constants just now, the two doubled sided arrows should remind us about the long range couplings.)

There is only one pure multiplett: the triplet of the methyl protons at 1.12 ppm due to the two adjacent chemically equivalent methylene protons.

$$J = \frac{288.6\ \text{Hz} - 273.5\ \text{Hz}}{2} = \mathbf{7.55\ Hz}$$

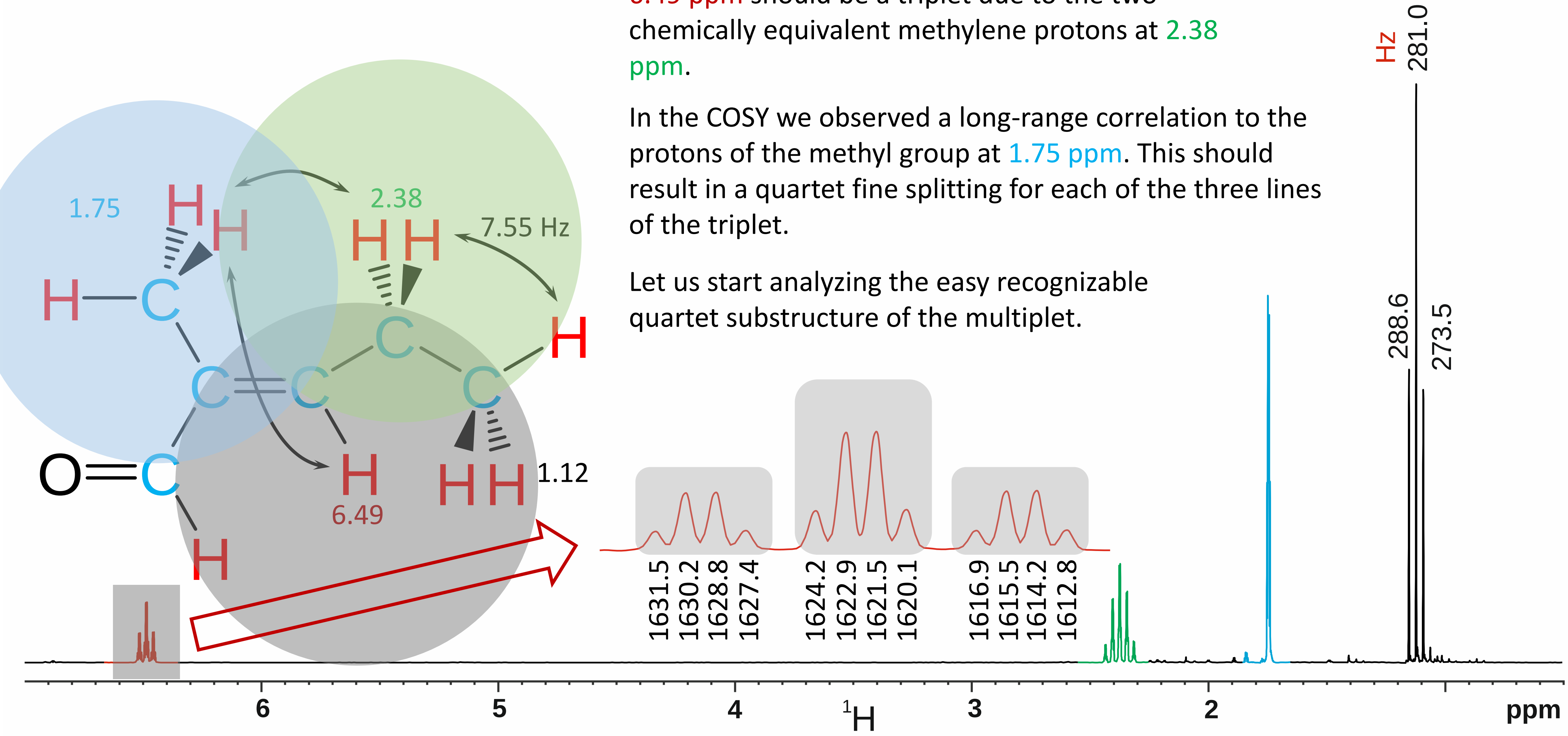


Coupling constants

The primary structure for the proton multiplet at 6.49 ppm should be a triplet due to the two chemically equivalent methylene protons at 2.38 ppm.

In the COSY we observed a long-range correlation to the protons of the methyl group at 1.75 ppm. This should result in a quartet fine splitting for each of the three lines of the triplet.

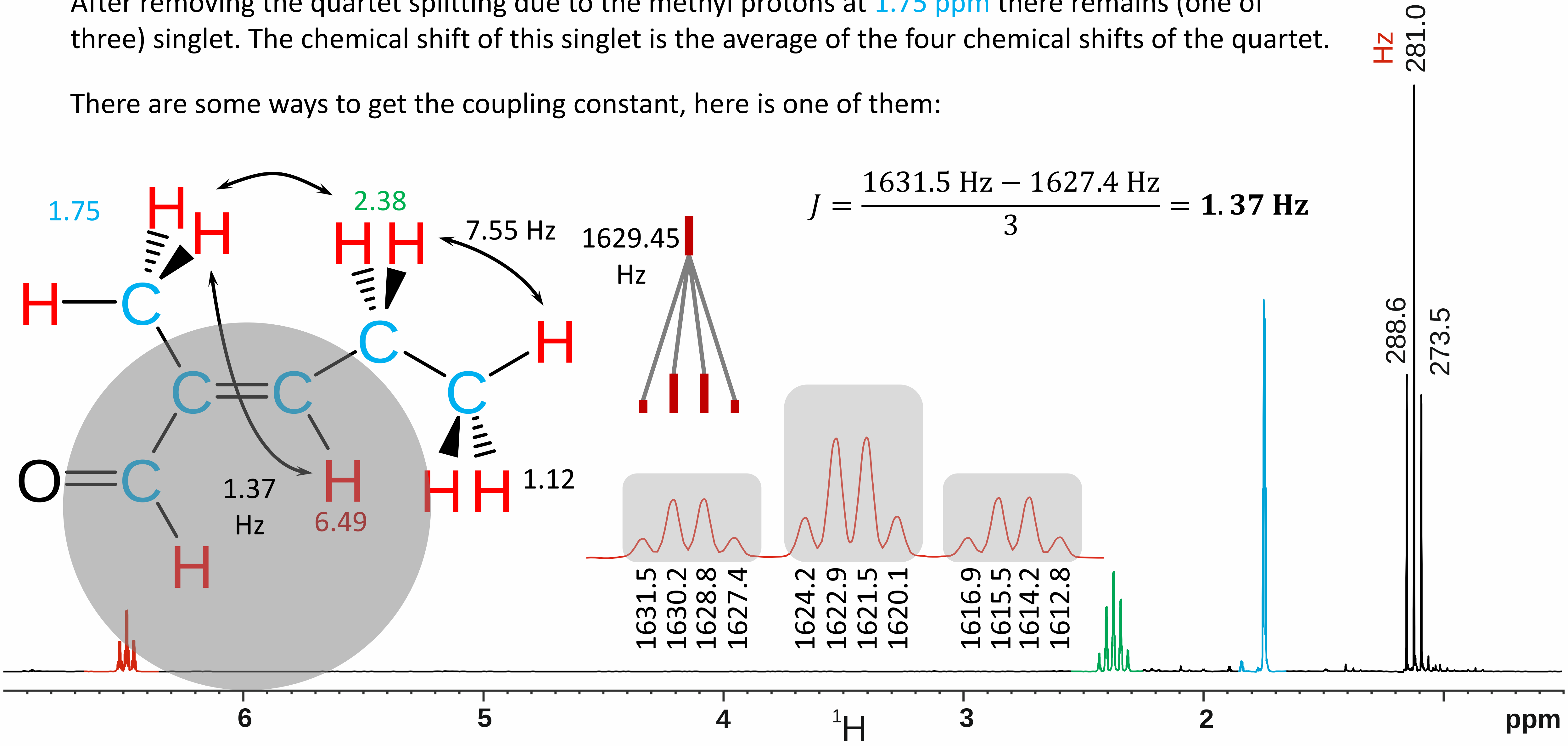
Let us start analyzing the easy recognizable quartet substructure of the multiplet.



Coupling constants

After removing the quartet splitting due to the methyl protons at 1.75 ppm there remains (one of three) singlet. The chemical shift of this singlet is the average of the four chemical shifts of the quartet.

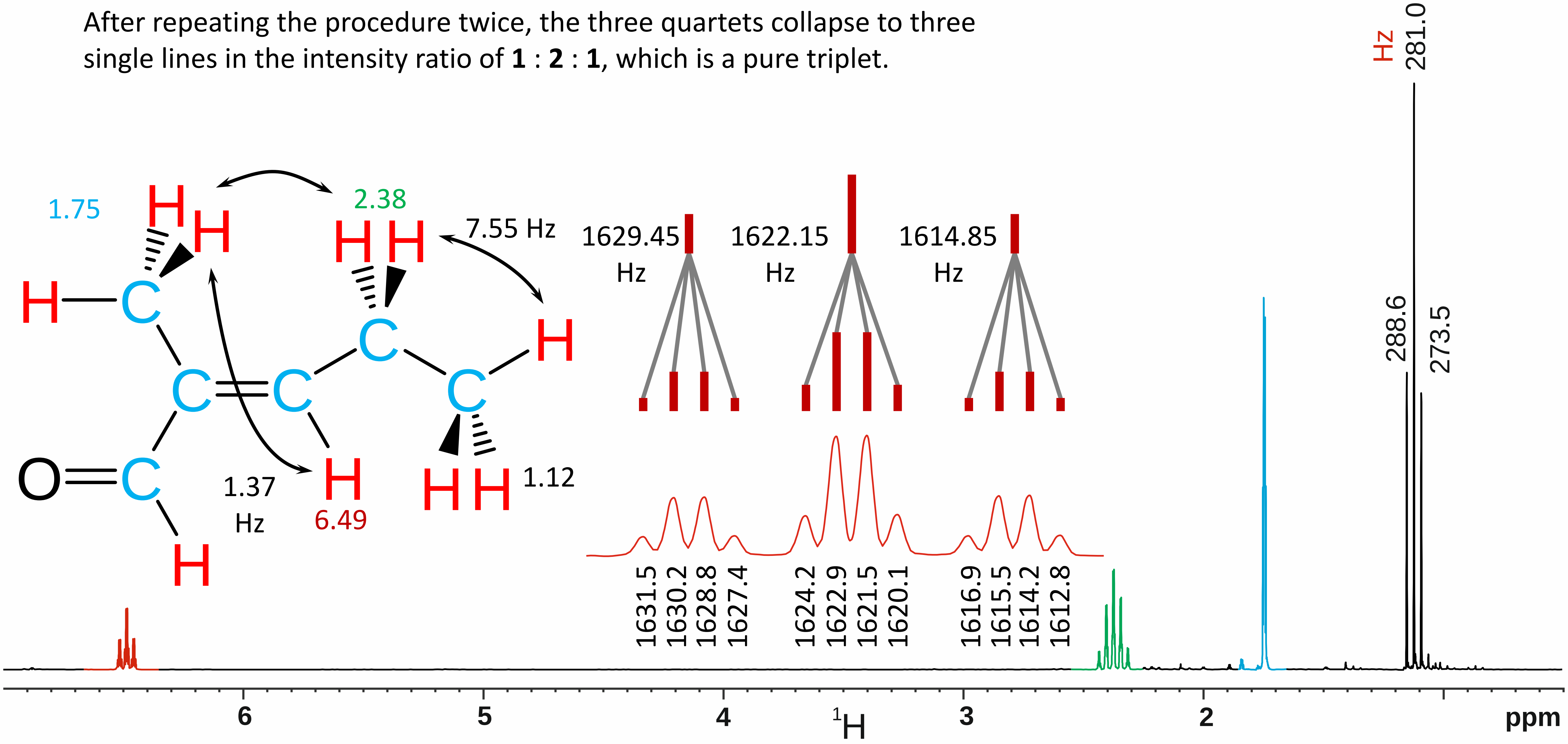
There are some ways to get the coupling constant, here is one of them:



$$J = \frac{1631.5\ \text{Hz} - 1627.4\ \text{Hz}}{3} = \mathbf{1.37\ Hz}$$

Coupling constants

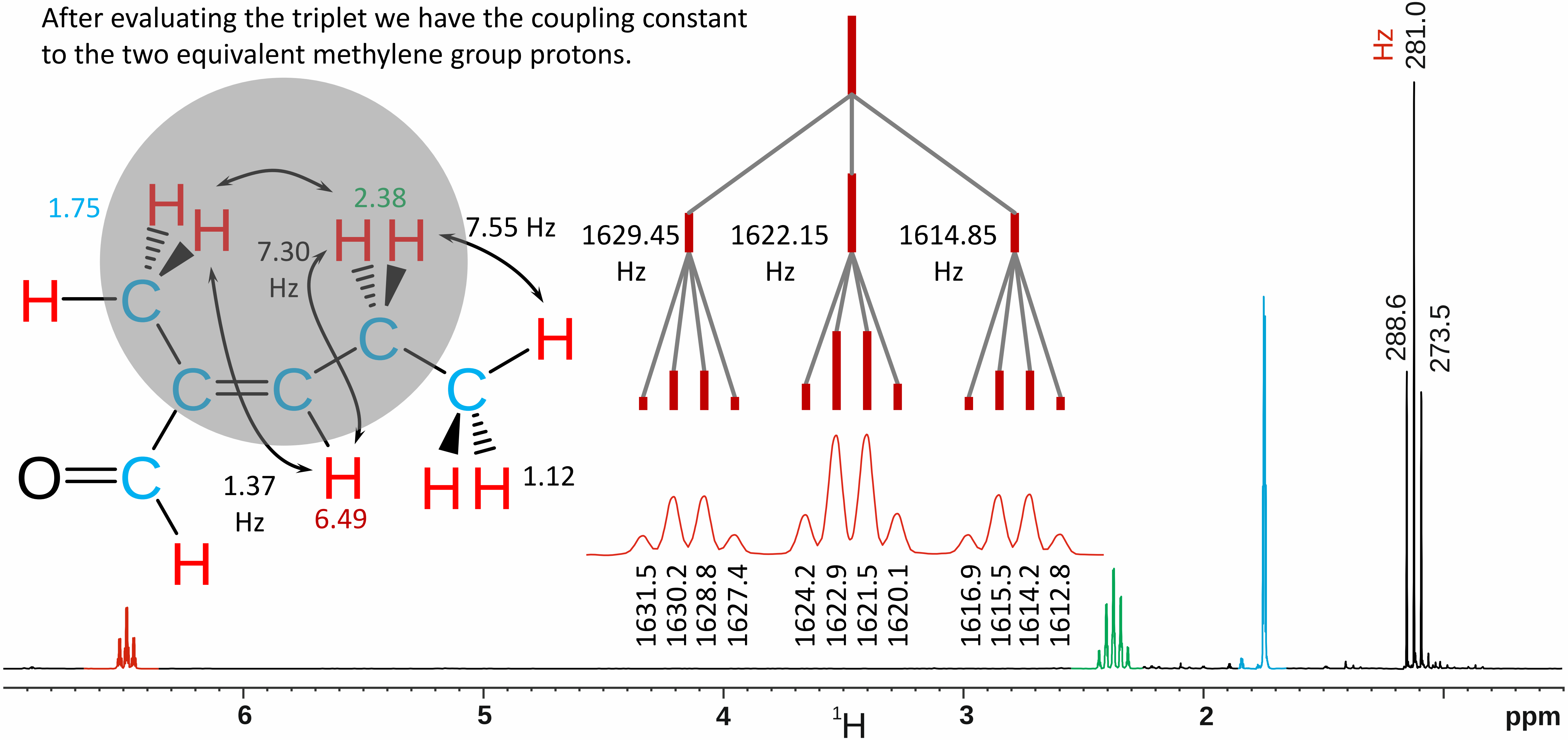
After repeating the procedure twice, the three quartets collapse to three single lines in the intensity ratio of **1** : **2** : **1**, which is a pure triplet.



Coupling constants

$$J = \frac{1629.45\ \text{Hz} - 1614.85\ \text{Hz}}{2} = \mathbf{7.30\ Hz}$$

After evaluating the triplet we have the coupling constant to the two equivalent methylene group protons.

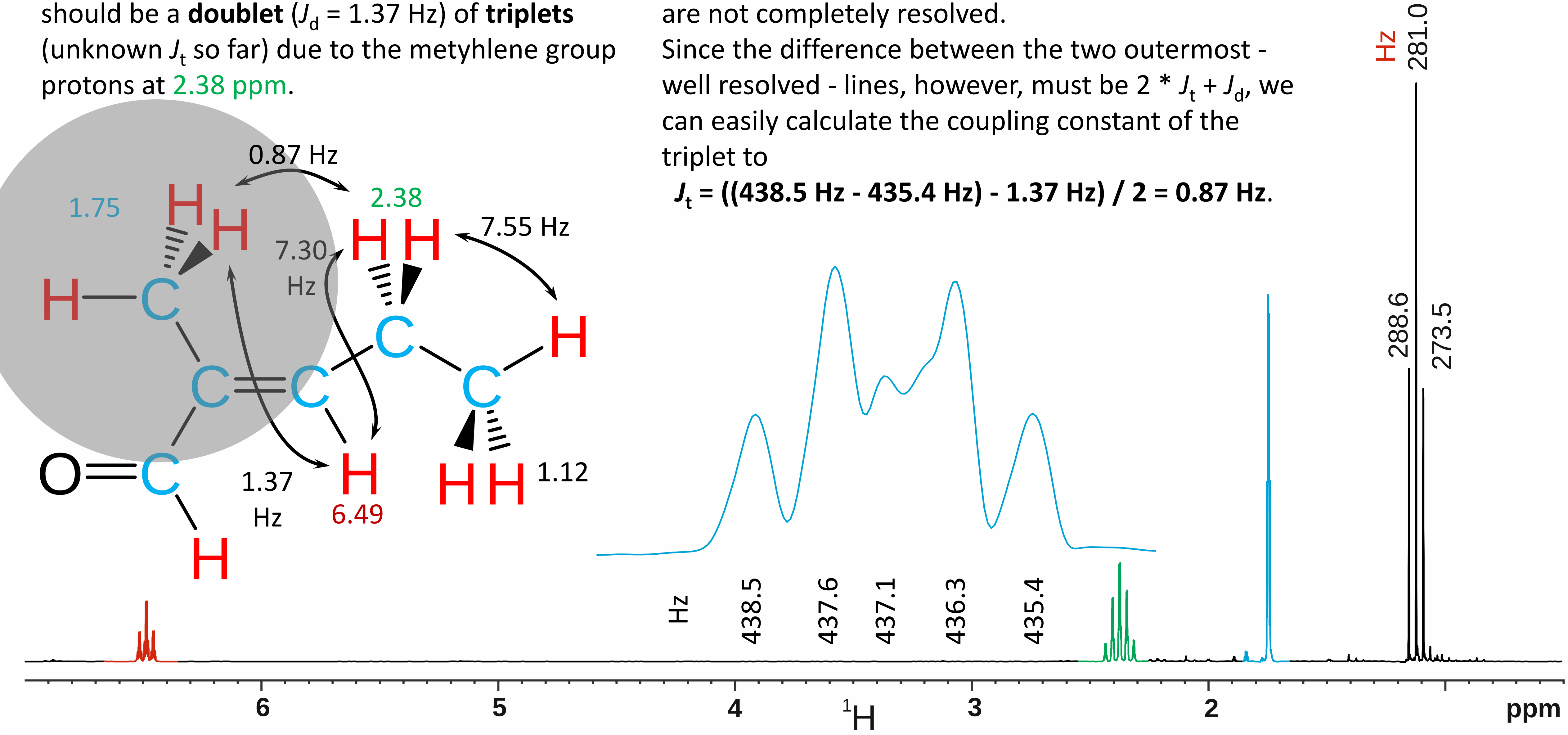


Coupling constants

The multiplet of the methyl group at 1.75 ppm should be a **doublet** (J_d = 1.37 Hz) of **triplets** (unknown J_t so far) due to the metyhlene group protons at 2.38 ppm.

The multiplet apparently consists of 6 lines, but they are not completely resolved.
Since the difference between the two outermost - well resolved - lines, however, must be 2 * J_t + J_d, we can easily calculate the coupling constant of the triplet to

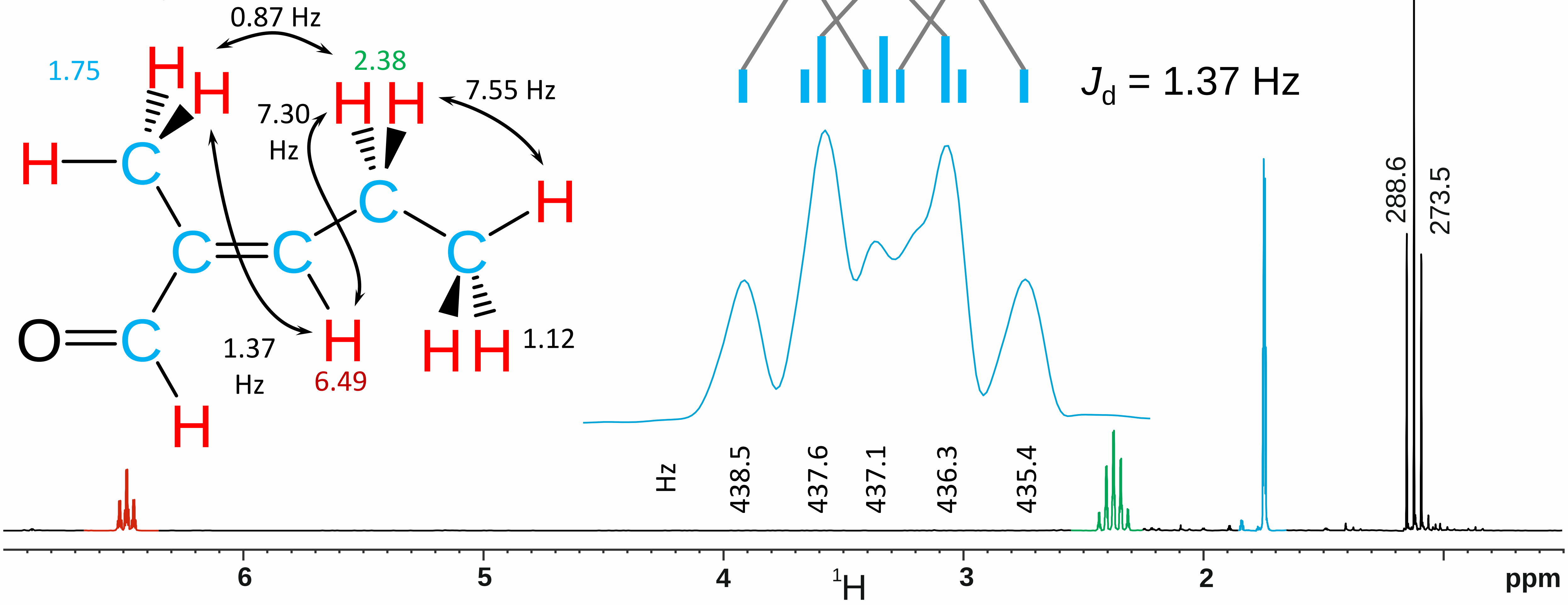
$$\boldsymbol{J_t = ((438.5\ \text{Hz} - 435.4\ \text{Hz}) - 1.37\ \text{Hz}) / 2 = 0.87\ \text{Hz}}.$$



Coupling constants

Let us try to simulate the multiplet with the somewhat overlapping lines using the two coupling constants.

Please don‘t expect 100% perfection. Perfection would require to sum over 6 lorentzian lines.



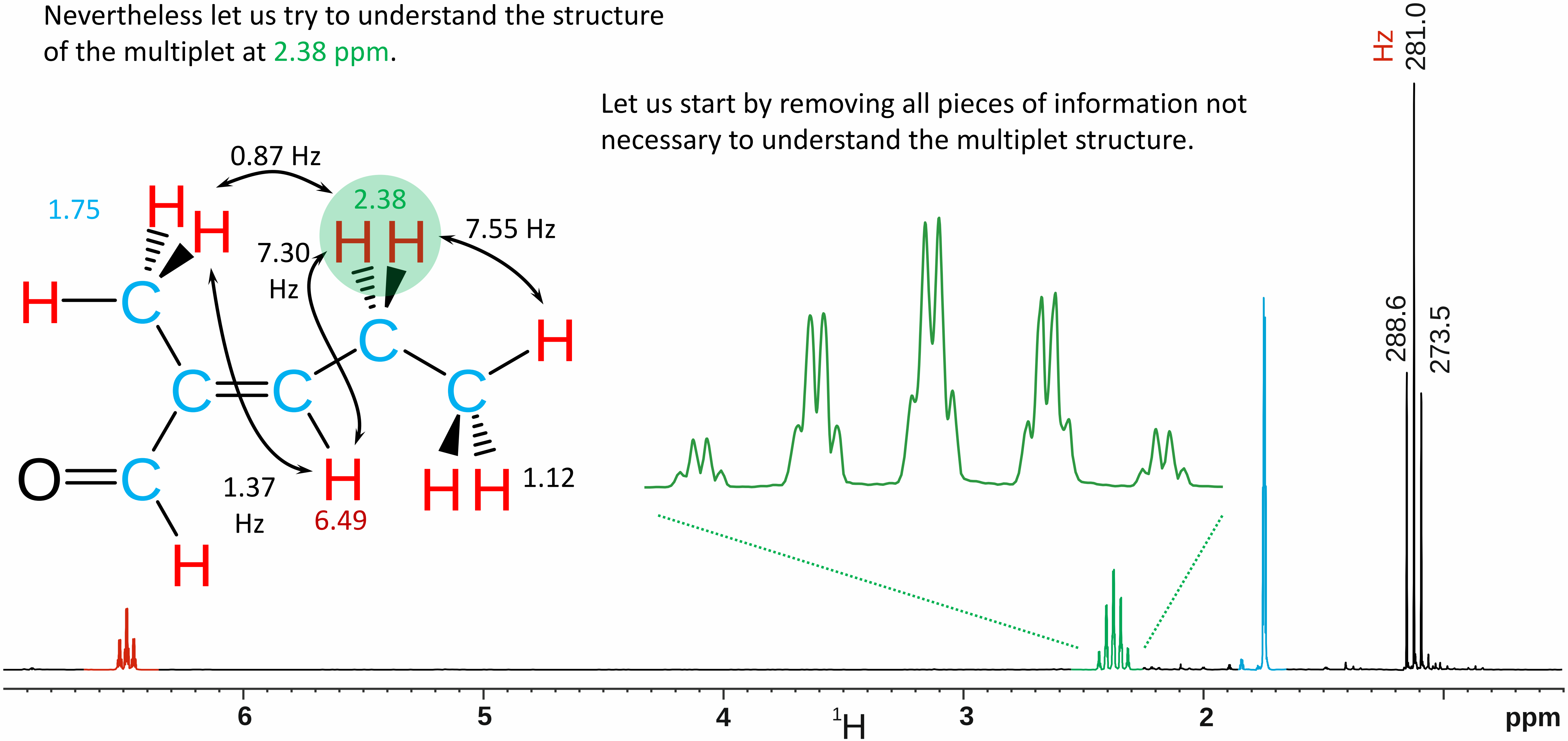
$J_t = 0.87$ Hz

$J_d = 1.37$ Hz

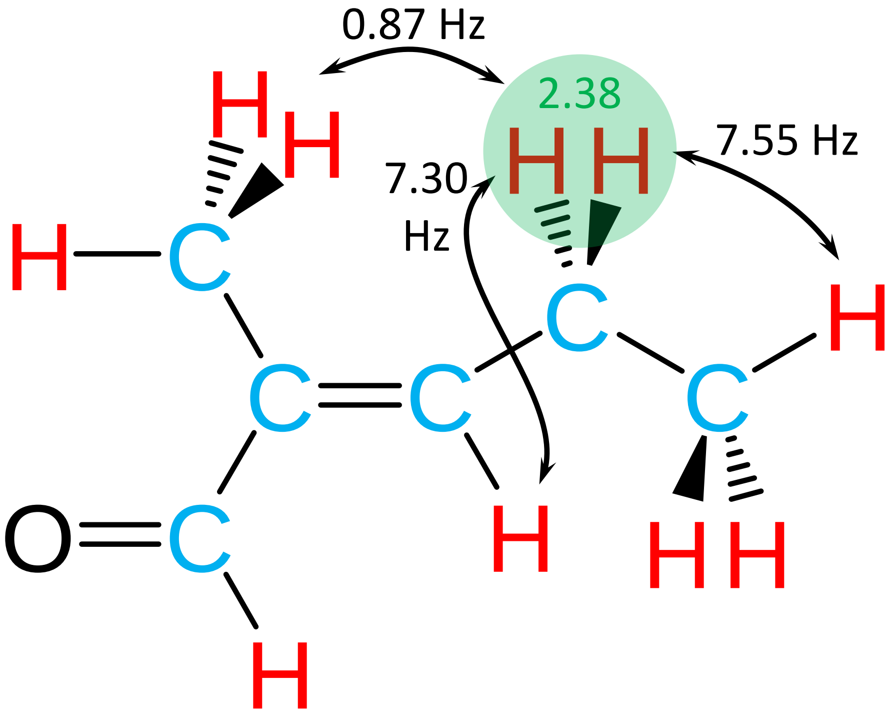
Coupling constants

Everything is finished now.
Nevertheless let us try to understand the structure of the multiplet at 2.38 ppm.

Let us start by removing all pieces of information not necessary to understand the multiplet structure.



Coupling constants



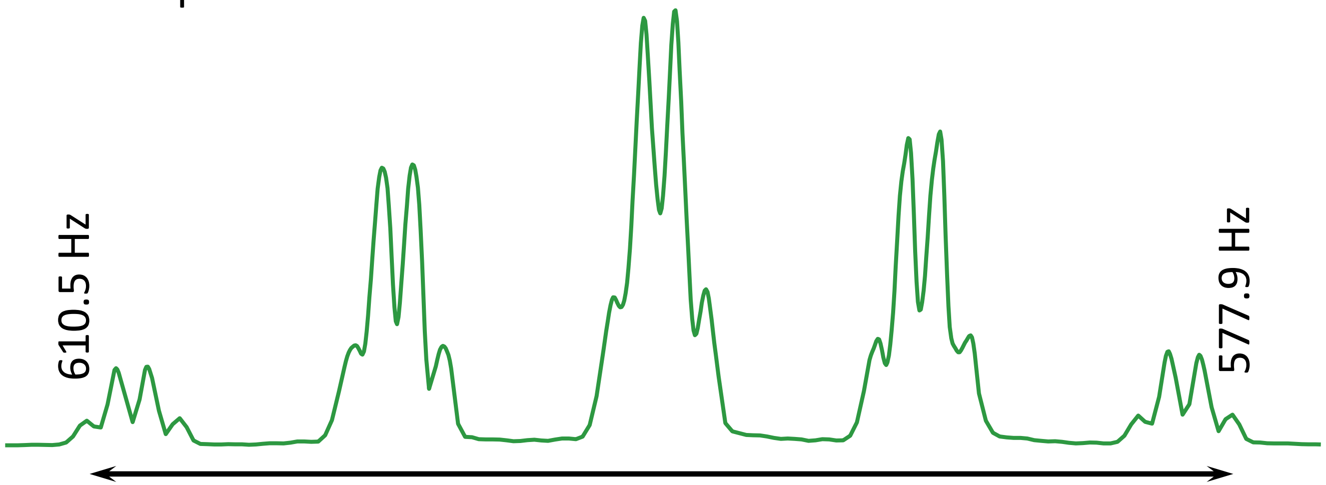
As a first check the frequency difference between the two outmost lines should be

$$\Delta\nu = 3 * 0.87\ \mathrm{Hz} + 7.30\ \mathrm{Hz} + 3 * 7.55\ \mathrm{Hz} = \mathbf{32.56\ Hz}$$

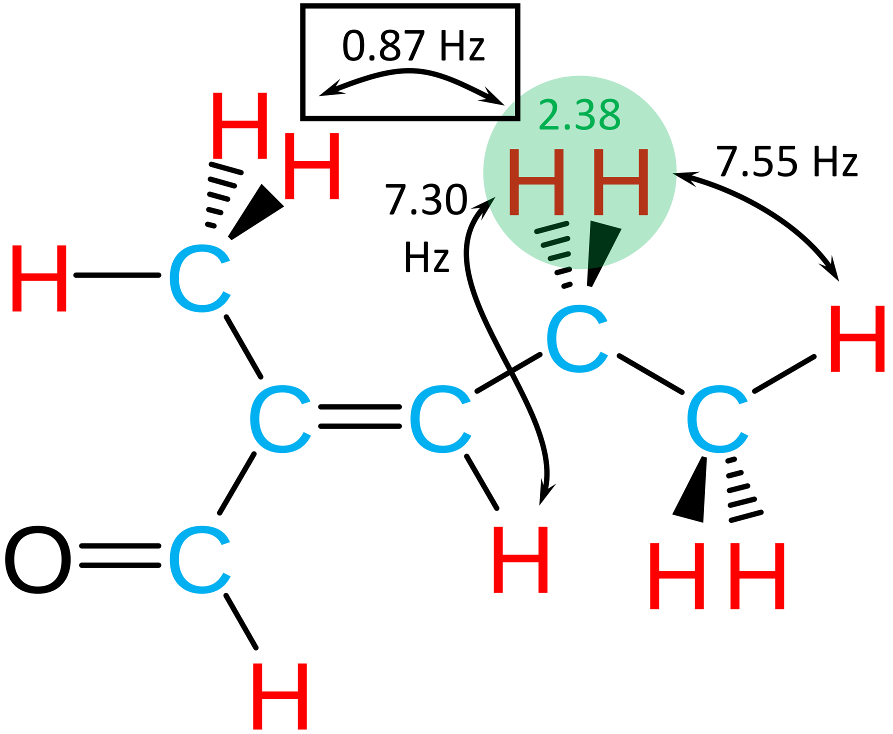
We have

$$610.5\ \mathrm{Hz} - 577.9\ \mathrm{Hz} = \mathbf{32.6\ Hz},$$

which is perfect.



Coupling constants

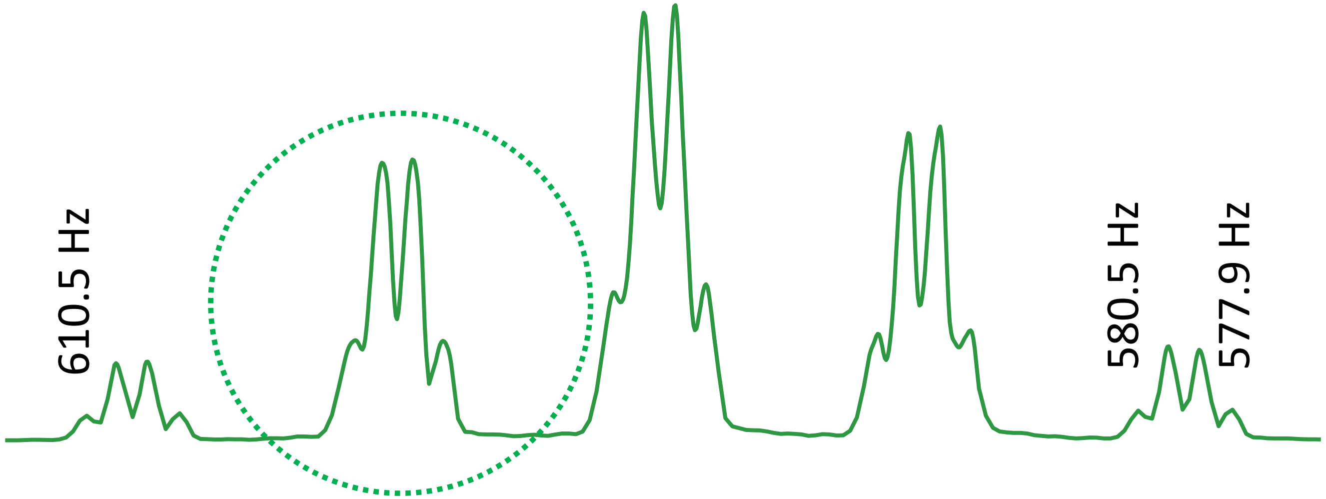


A quartet with a small coupling constant is visible 5 times. This should be due to the five bond coupling pathway. Let us check.

$$J = \frac{580.5\ \mathrm{Hz} - 577.9\ \mathrm{Hz}}{3} = \mathbf{0.87\ Hz}$$

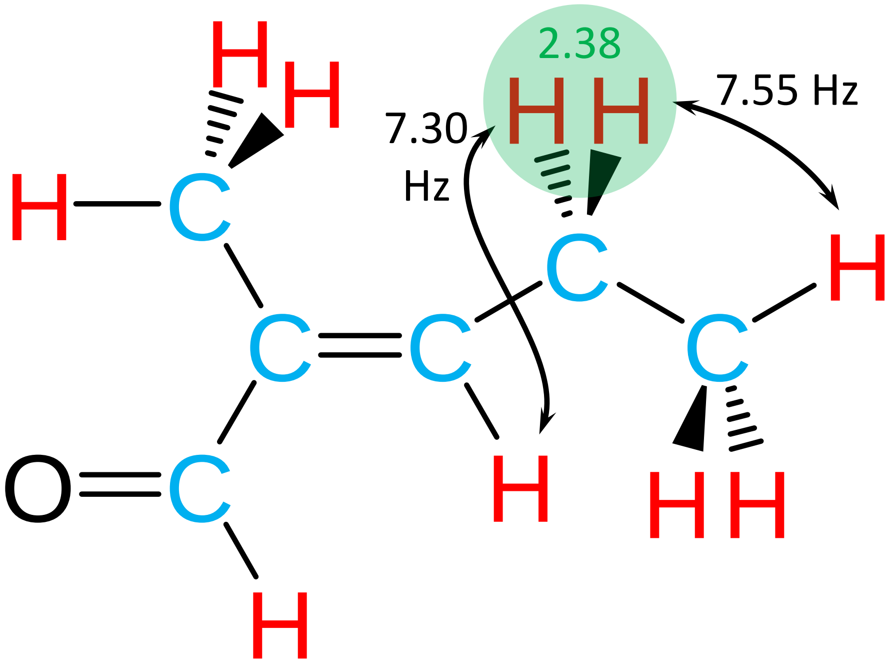
If we average five times over the four lines of each quartet there remains 5 „lines“ in the integral ratio of about

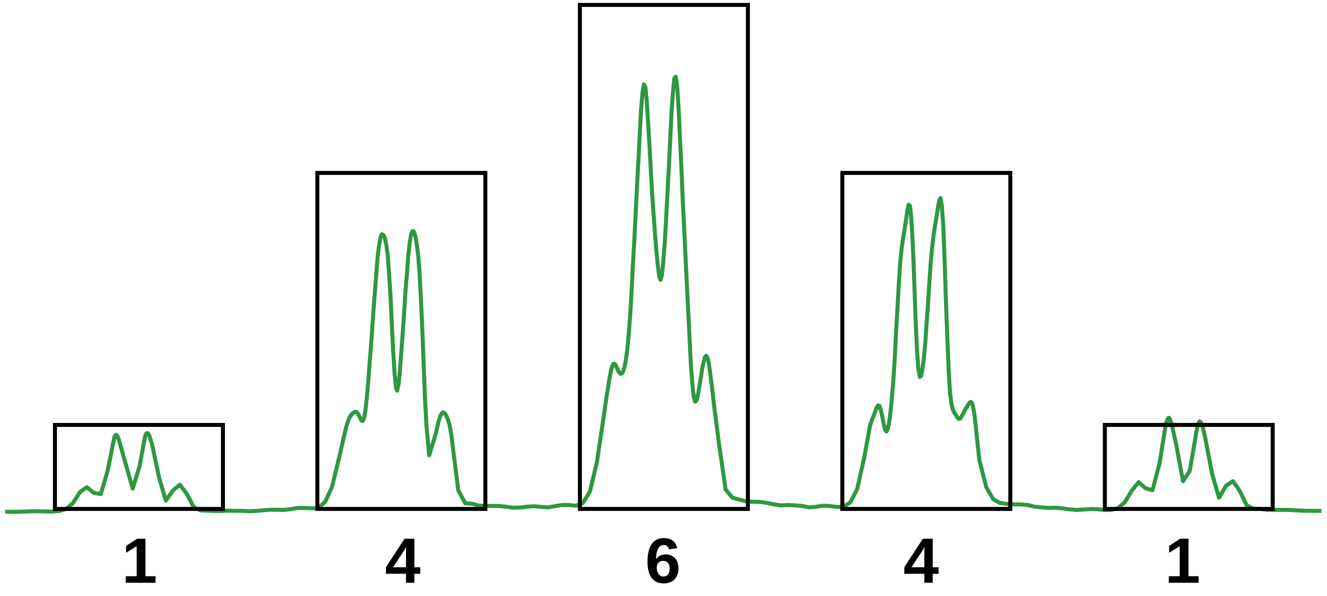
1 : 4 : 6 : 4 : 1.



Coupling constants

Of course that cannot be a quintet. It is a **doublet** (7.30 Hz) of **quartets** (7.55 Hz). Due to the very similar coupling constants some lines strongly overlap.

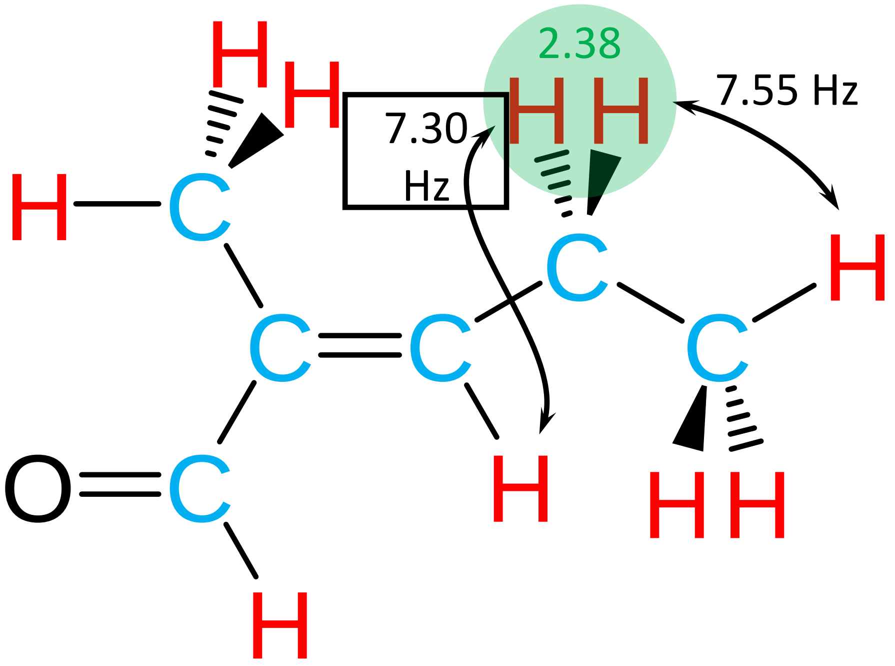


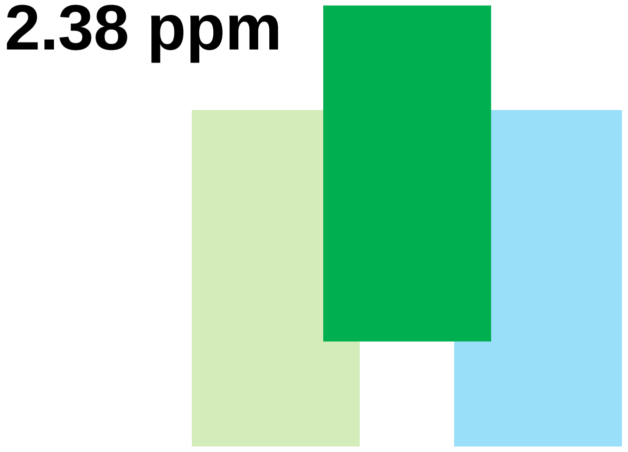


Coupling constants

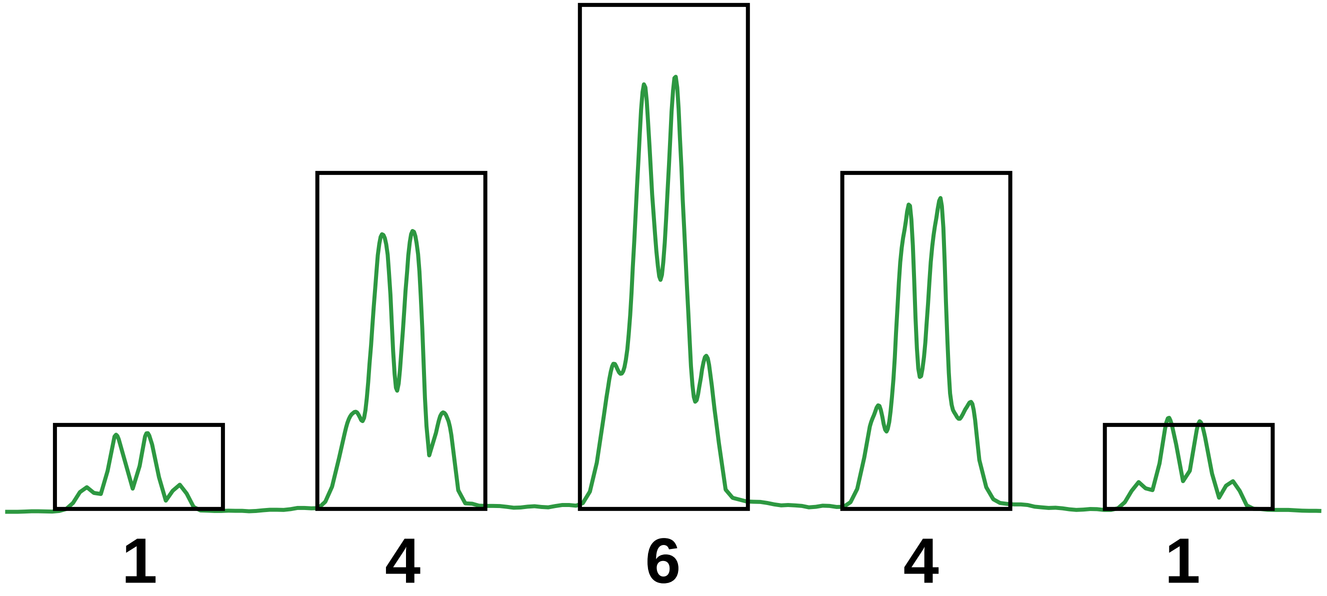
Let us simulate the multiplet pattern of the signal at 2.38 ppm step by step.

We start with the doublet splitting with a coupling constant of **7.30 Hz**.





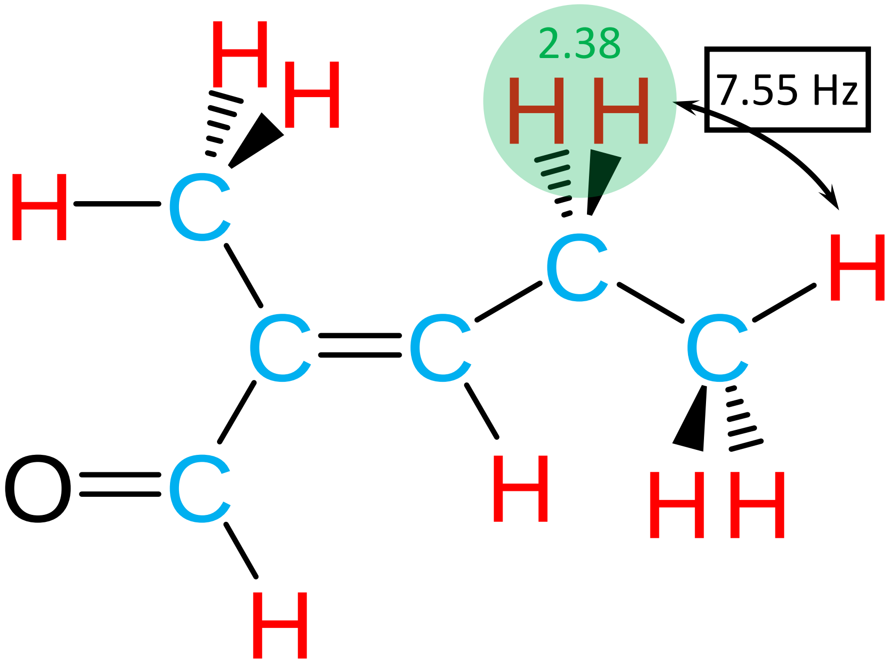
We use slightly different colous for the two lines to better see the overlapping in subsequent slides.

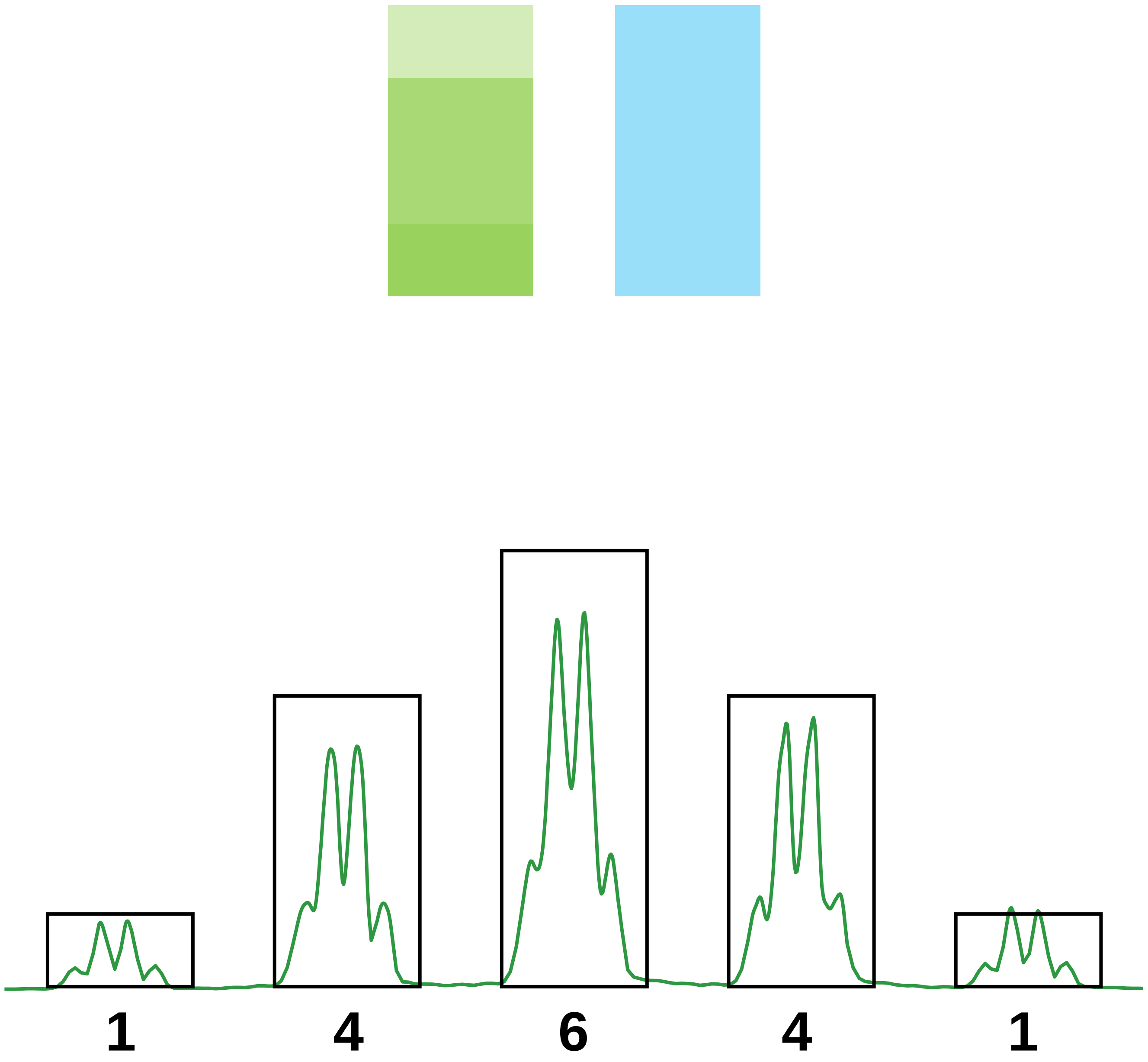


Coupling constants

Now both lines should split into an quartet by a coupling constant of **7.55 Hz**.

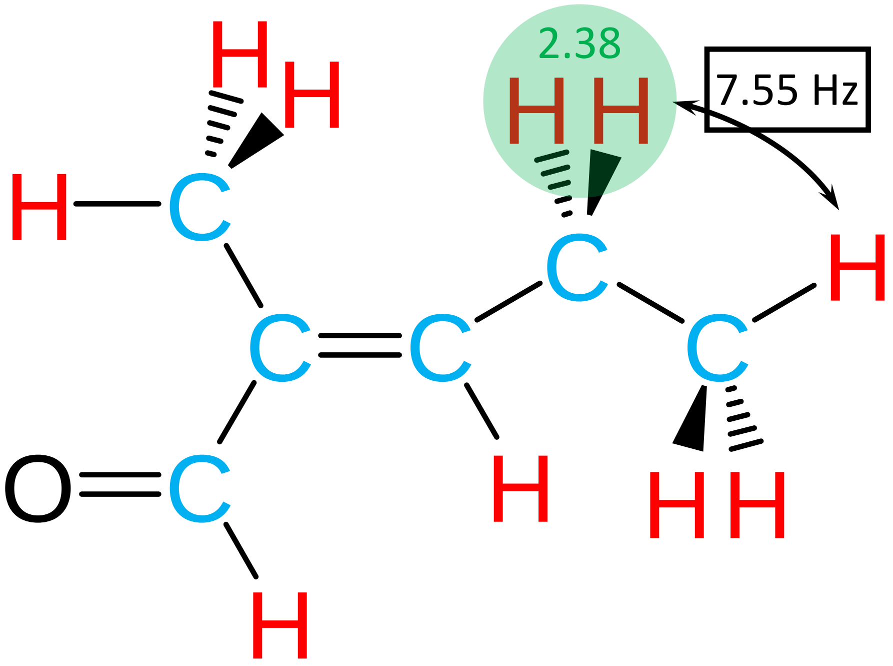
Let us start with the left line.

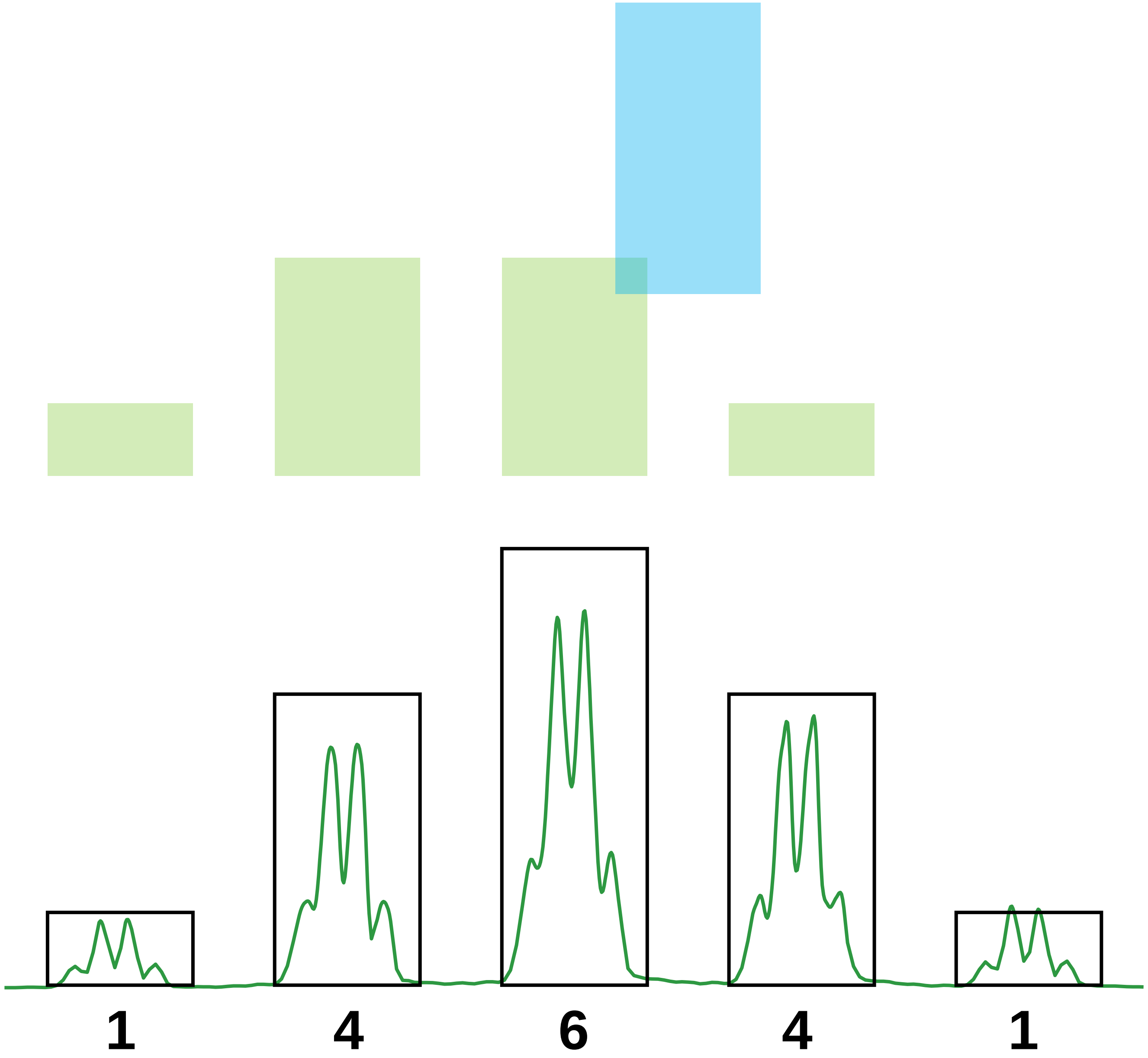




Coupling constants

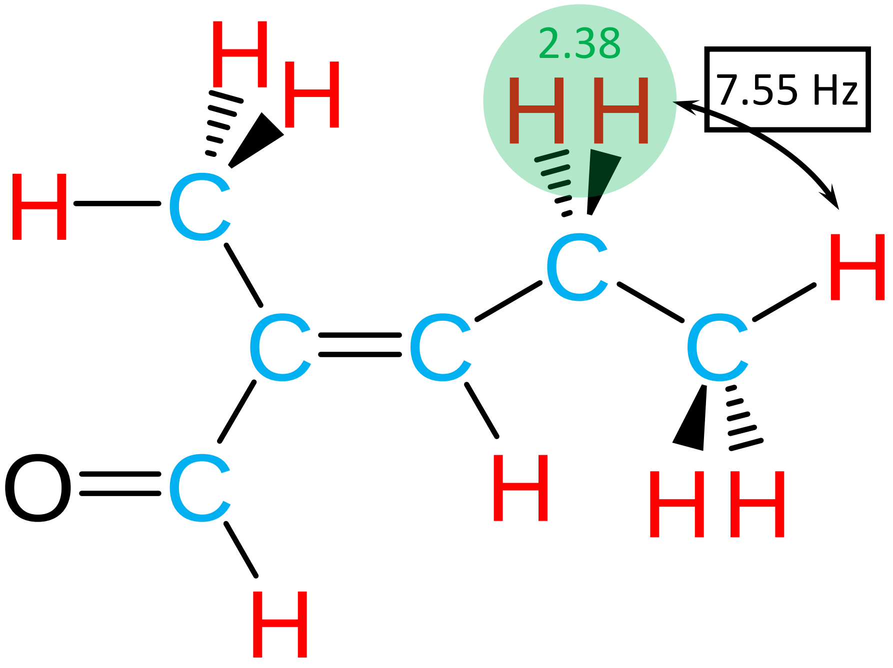
These four lines are the first part of our „quintet“.

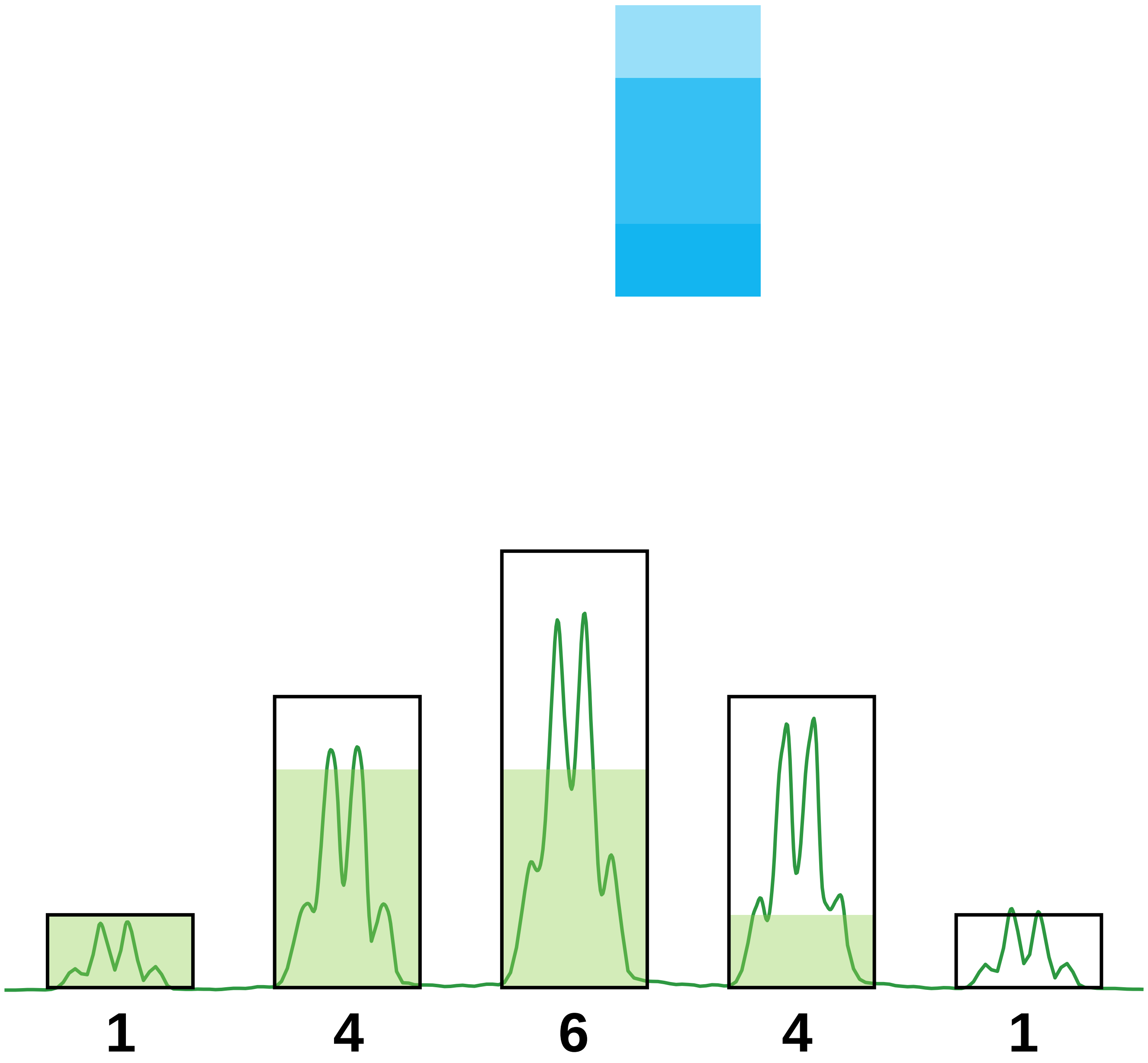




Coupling constants

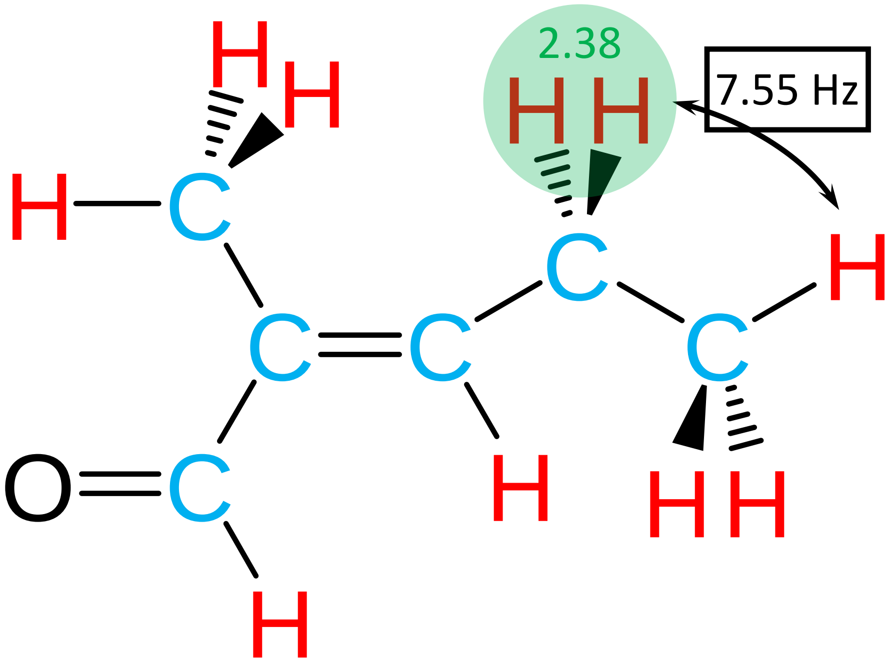
Let us repeat the quartet splitting with the second line of the doublet.

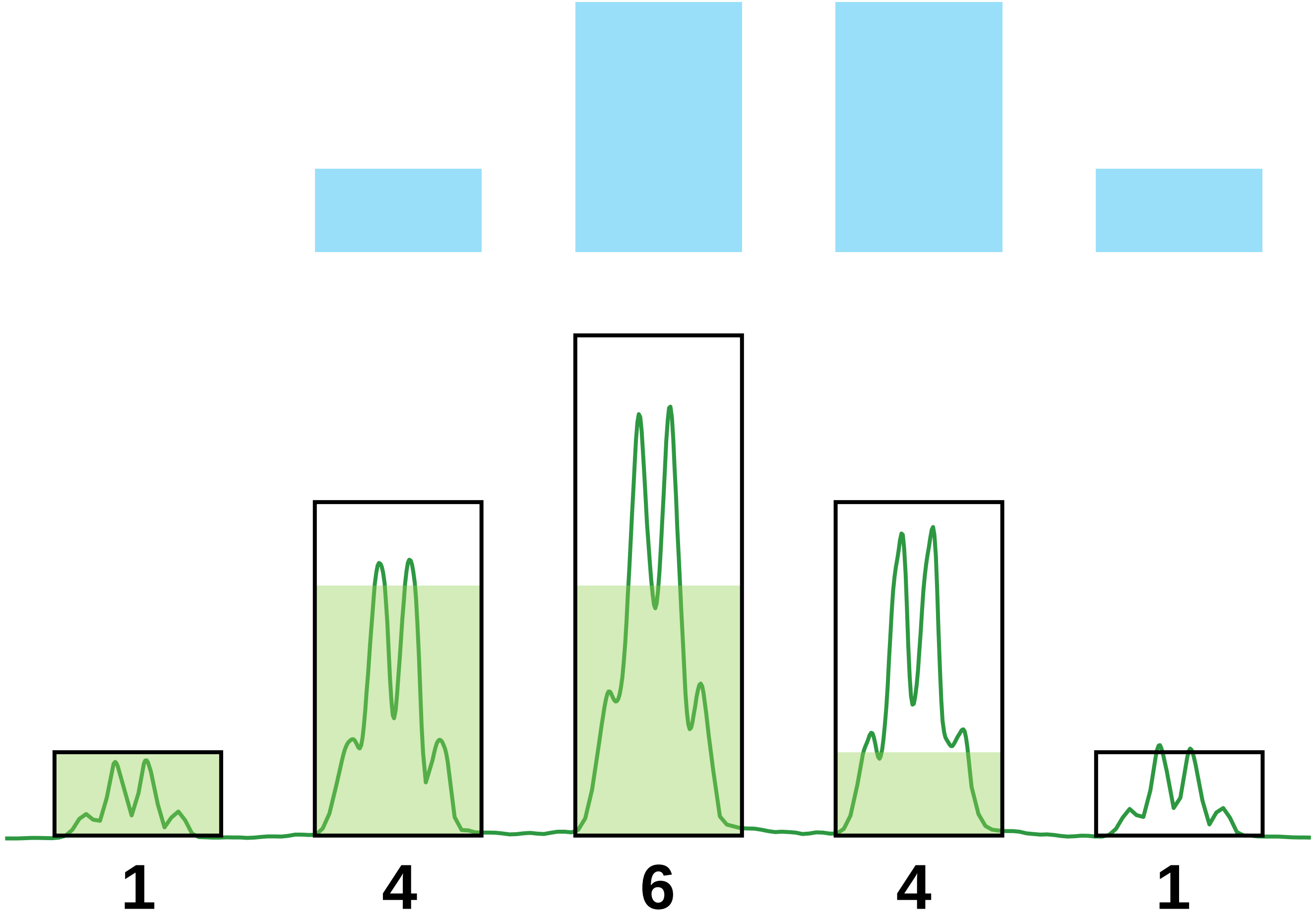




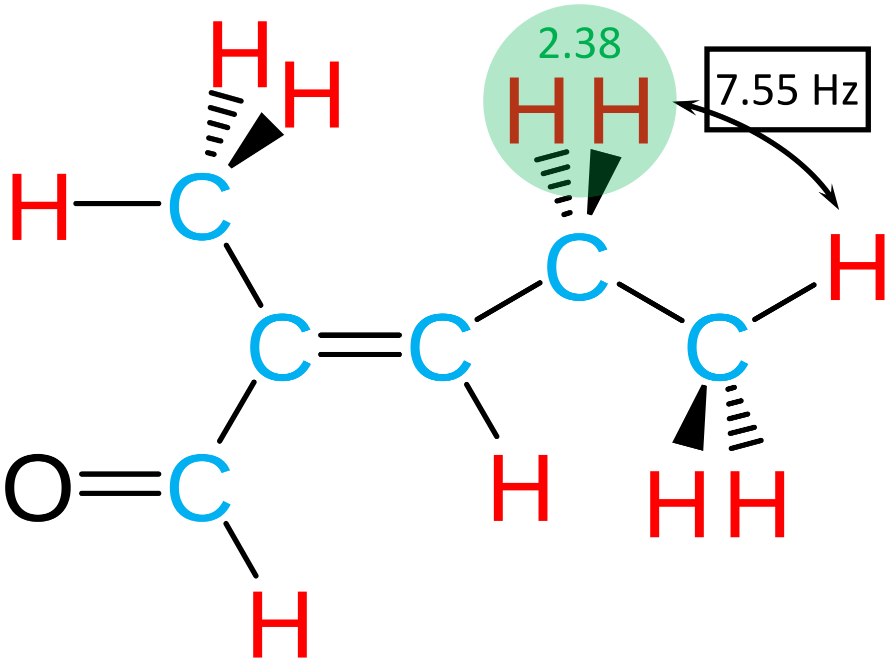
Coupling constants

If we add these four lines to the existing four lines finally we get our pseudo quintet.

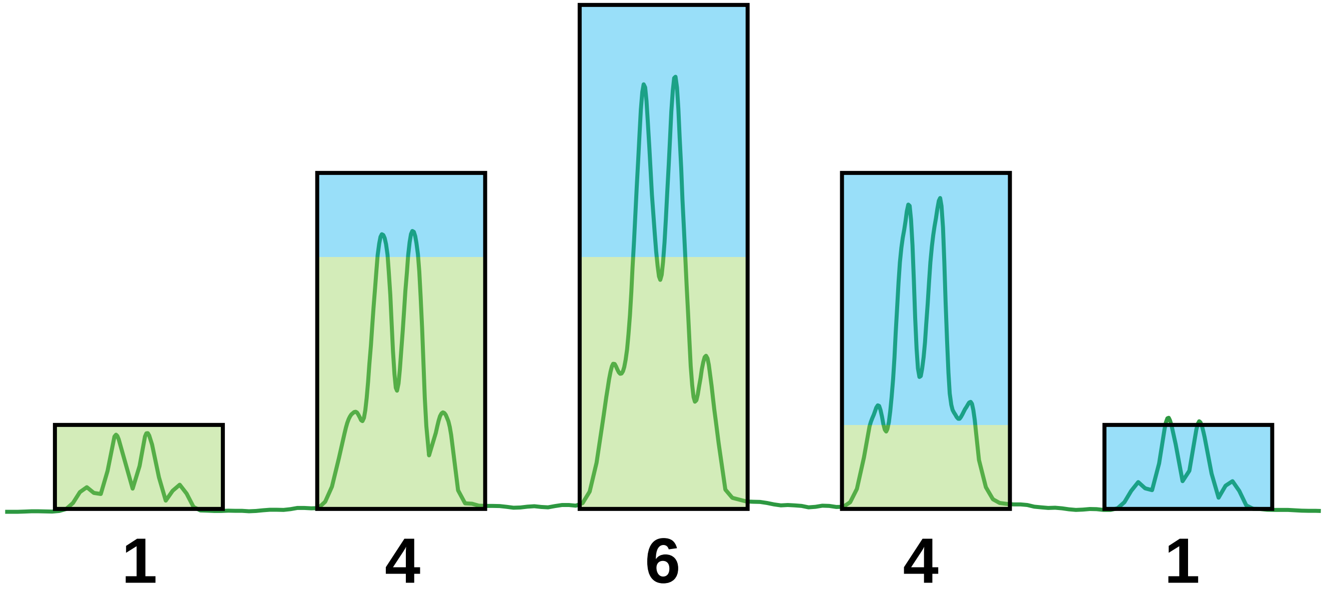




Coupling constants

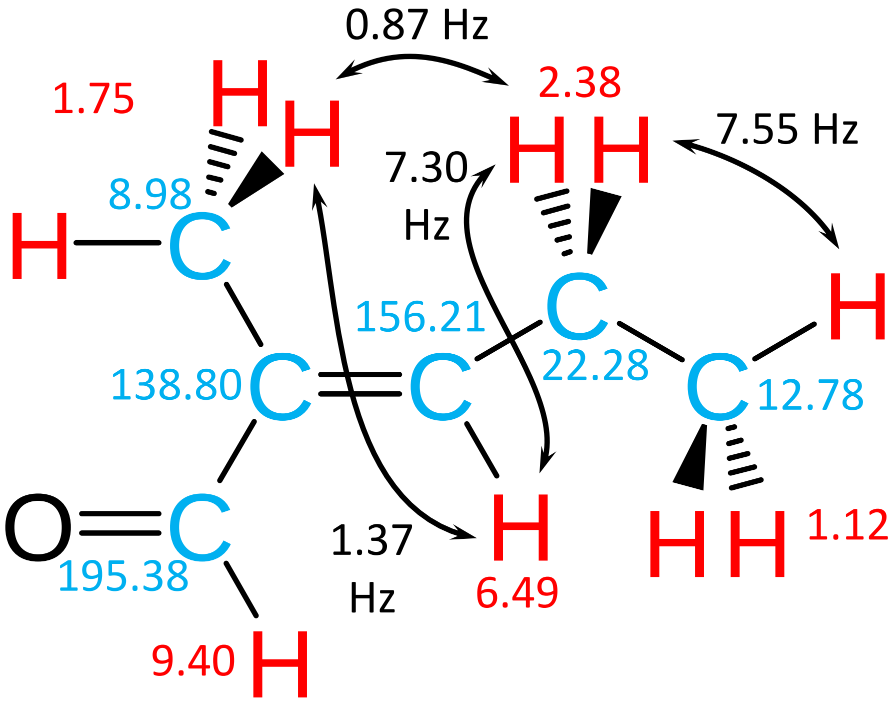


There is not a perfect proportionality between line intensities (heights) and integrals, due to the slightly different coupling constants. As a result of these tiny differences the lines of the quartet substruture in the center of the pseudo quintet are a little bit broader (and hence the intensity slightly smaller than expected) than the same substructure lines at the two outmost lines. The integrals for the pseudo quintet, however, remain in the expected 1 : 4 : 6 : 4 : 1 ratio.

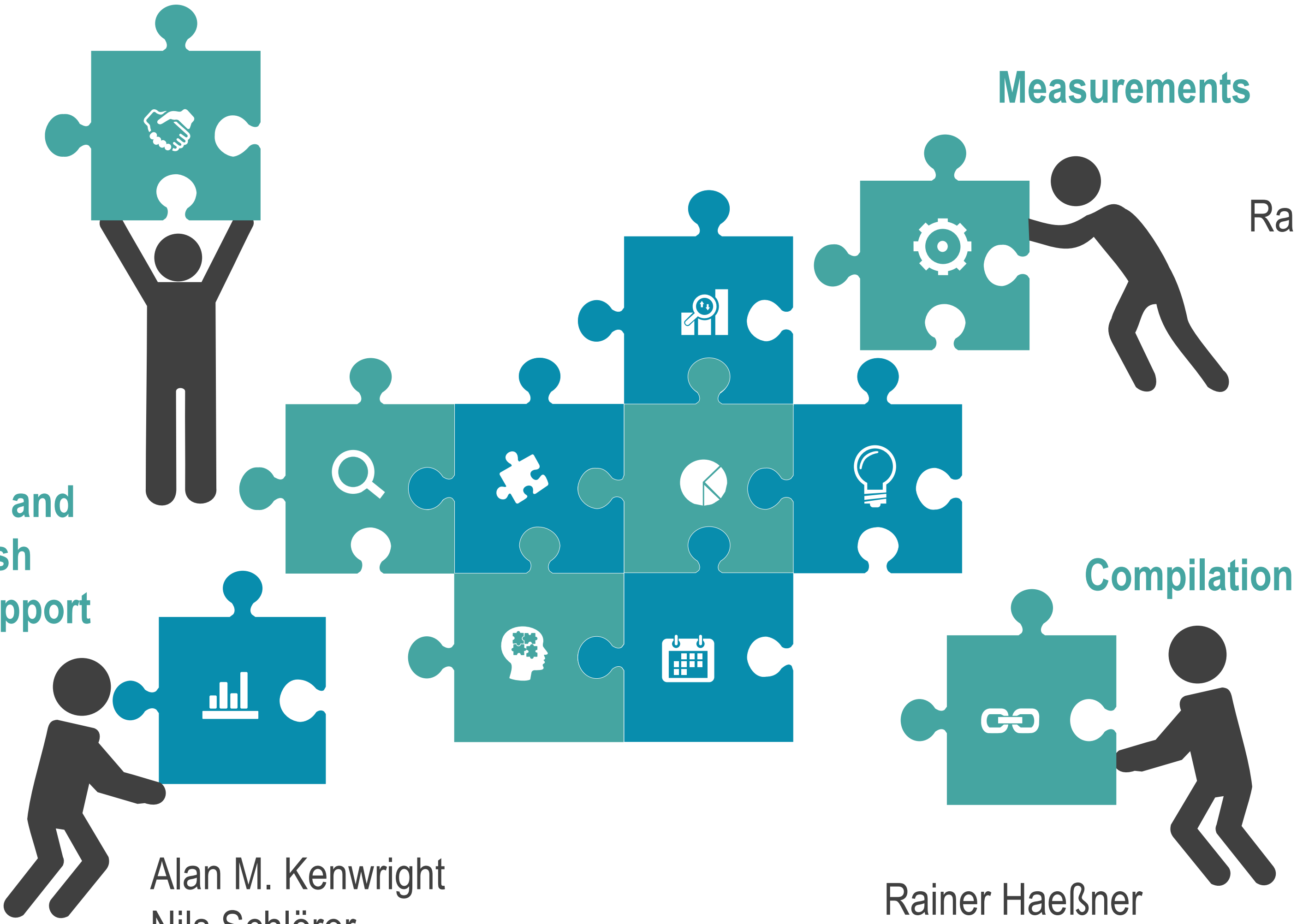


Complete solution

Using the available data it is not possible to determine the configuration around the double bond.



Contributions



Spectrometer time

TU Munich

Measurements

Rainer Haeßner

Discussions and native English language support

Alan M. Kenwright
Nils Schlörer

Compilation

Rainer Haeßner