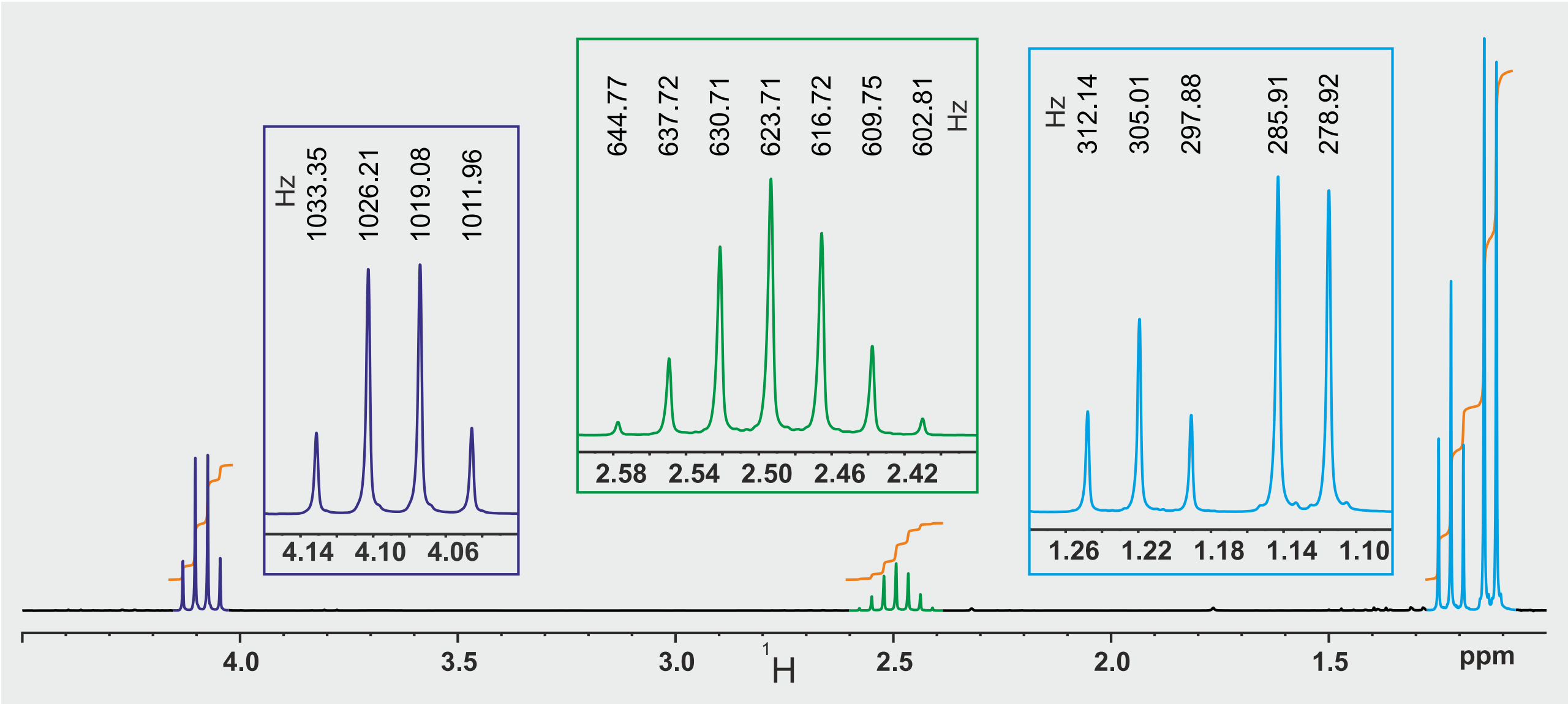
Exercise plus Solution – Quick overview

It is recommended to use this 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.

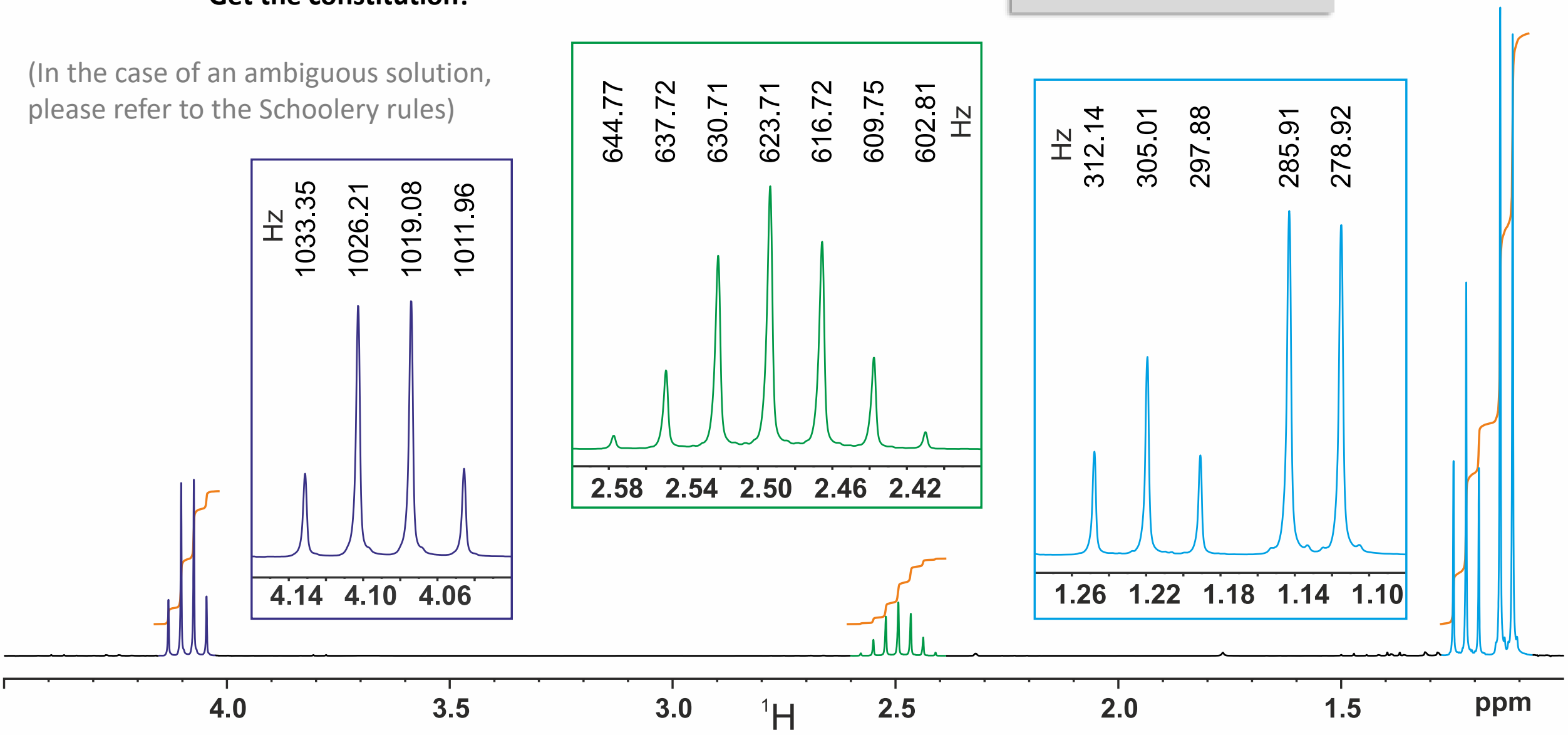


$C_6H_{12}O_2$ measured in $CDCl_3$

Get the constitution!

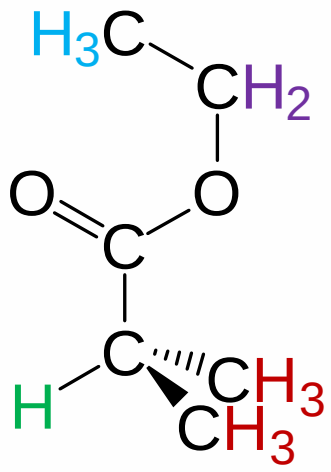
(In the case of an ambiguous solution, please refer to the Schoolery rules)

^{1}H NMR spectrum recorded at 250.13 MHz



Solution at a glance

There is no step by step solution available so far.



Solution at a glance

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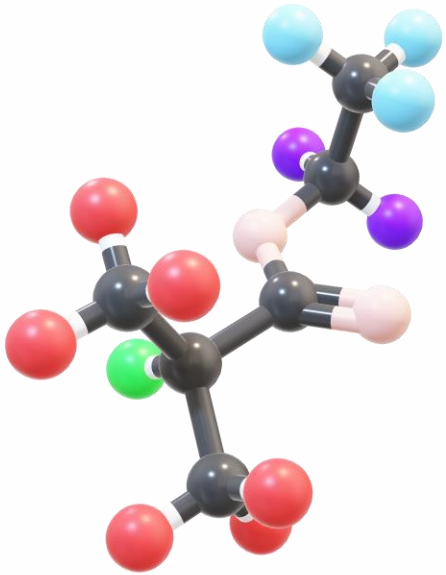


Isobutyric acid ethyl ester

1 DBÄ

Basics

Double bond equivalents, number of signal groups, integration

Solution

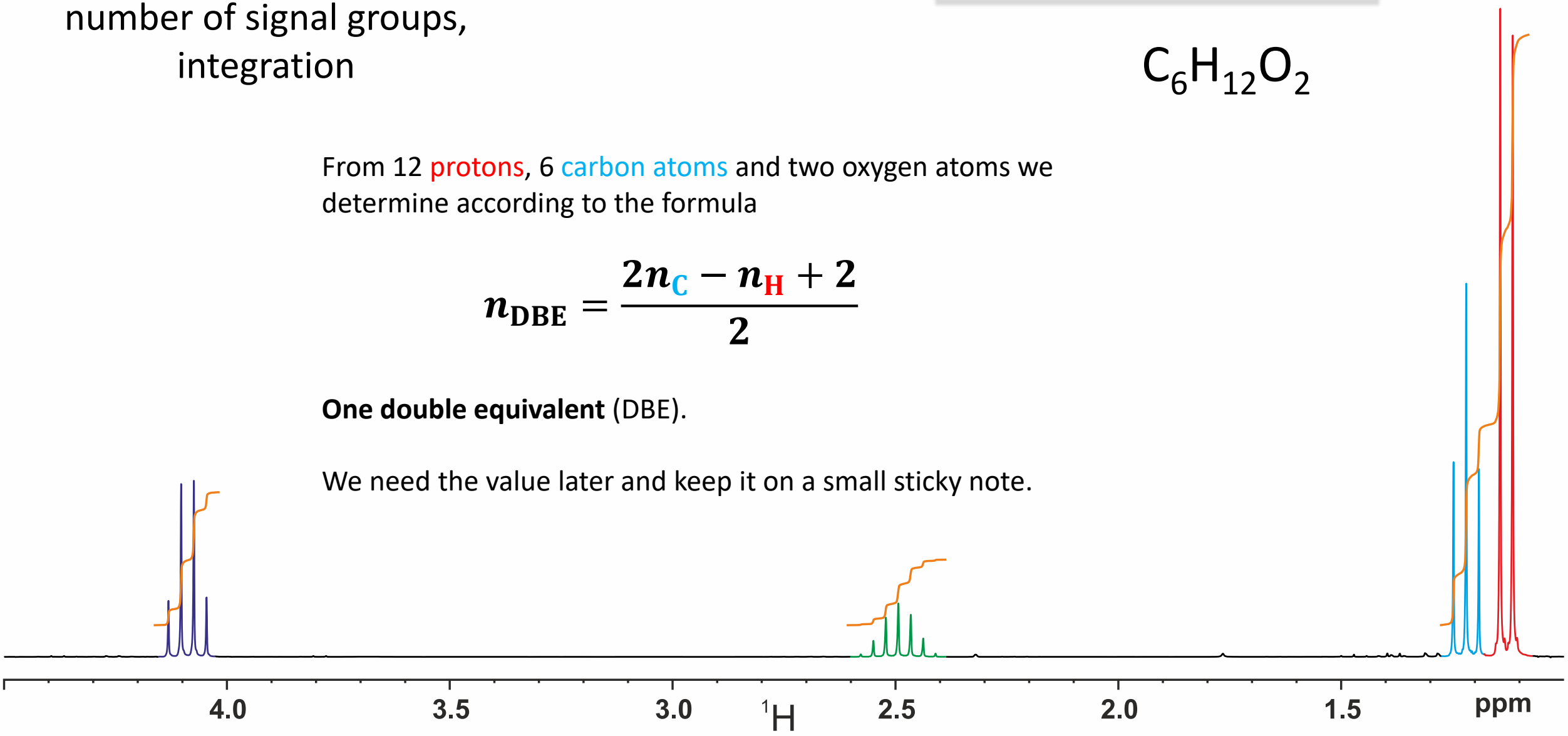
$C_6H_{12}O_2$

From 12 protons, 6 carbon atoms and two oxygen atoms we determine according to the formula

$$n_{DBE} = \frac{2n_C - n_H + 2}{2}$$

One double equivalent (DBE).

We need the value later and keep it on a small sticky note.



Basics

Double bond equivalents,
number of signal groups,
integration

1 DBÄ

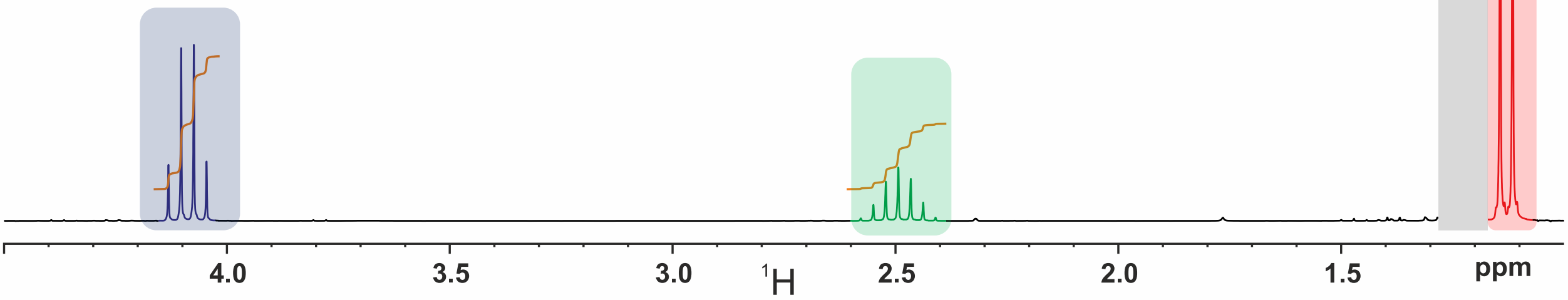
Solution

$C_6H_{12}O_2$

Two signal groups are easy to recognise.

With the colour marking made here, the two high-field signal groups are also easy to recognise.
Not having this aid, it sometimes helps to partially hide spectral ranges that are close together.

A doublet is now clearly visible.



Basics

Double bond equivalents, number of signal groups, integration

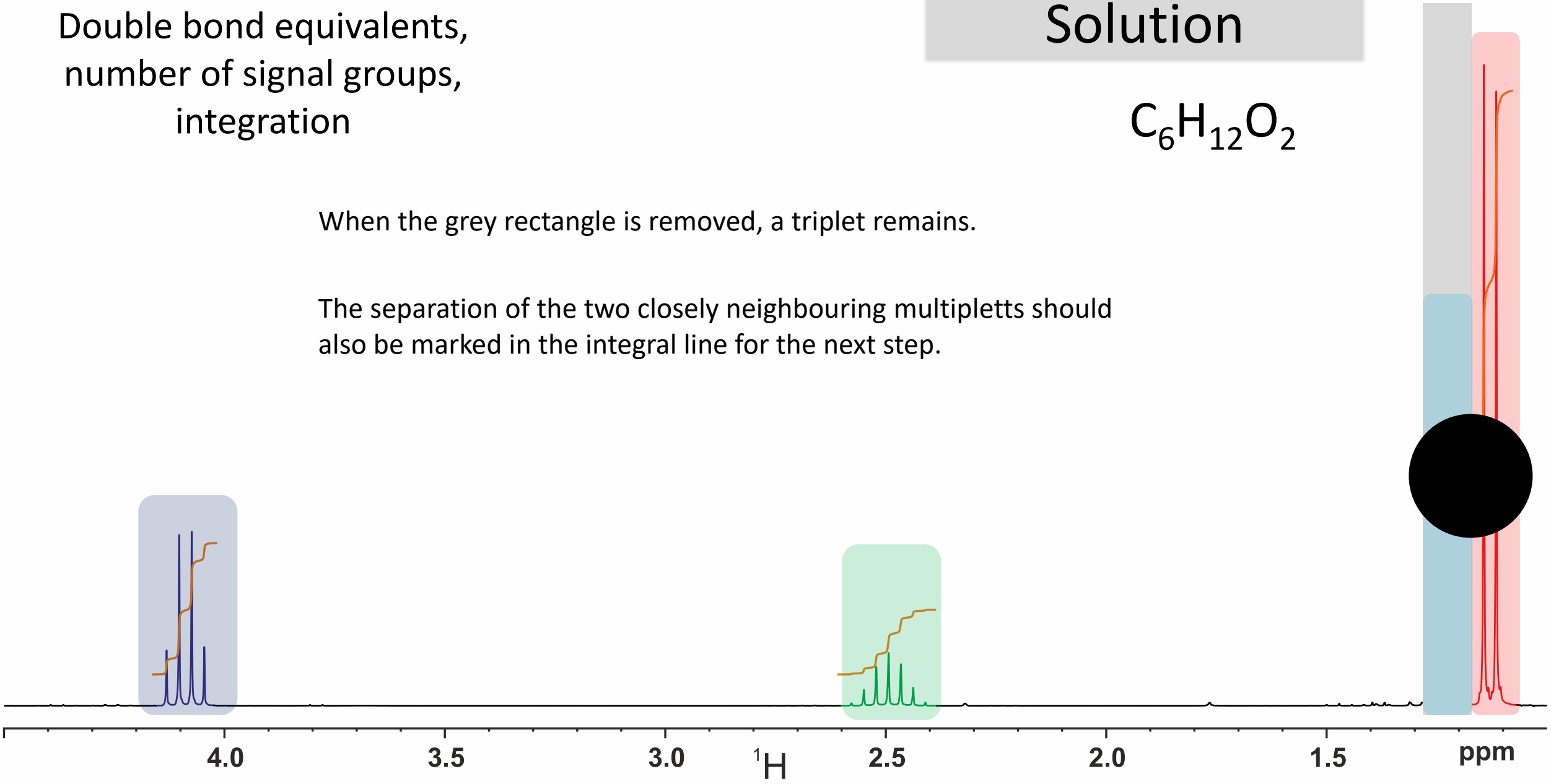
1 DBÄ

Solution

$C_6H_{12}O_2$

When the grey rectangle is removed, a triplet remains.

The separation of the two closely neighbouring multipletts should also be marked in the integral line for the next step.



Basics

Double bond equivalents, number of signal groups, integration

$C_6H_{12}O_2$

1 DBÄ

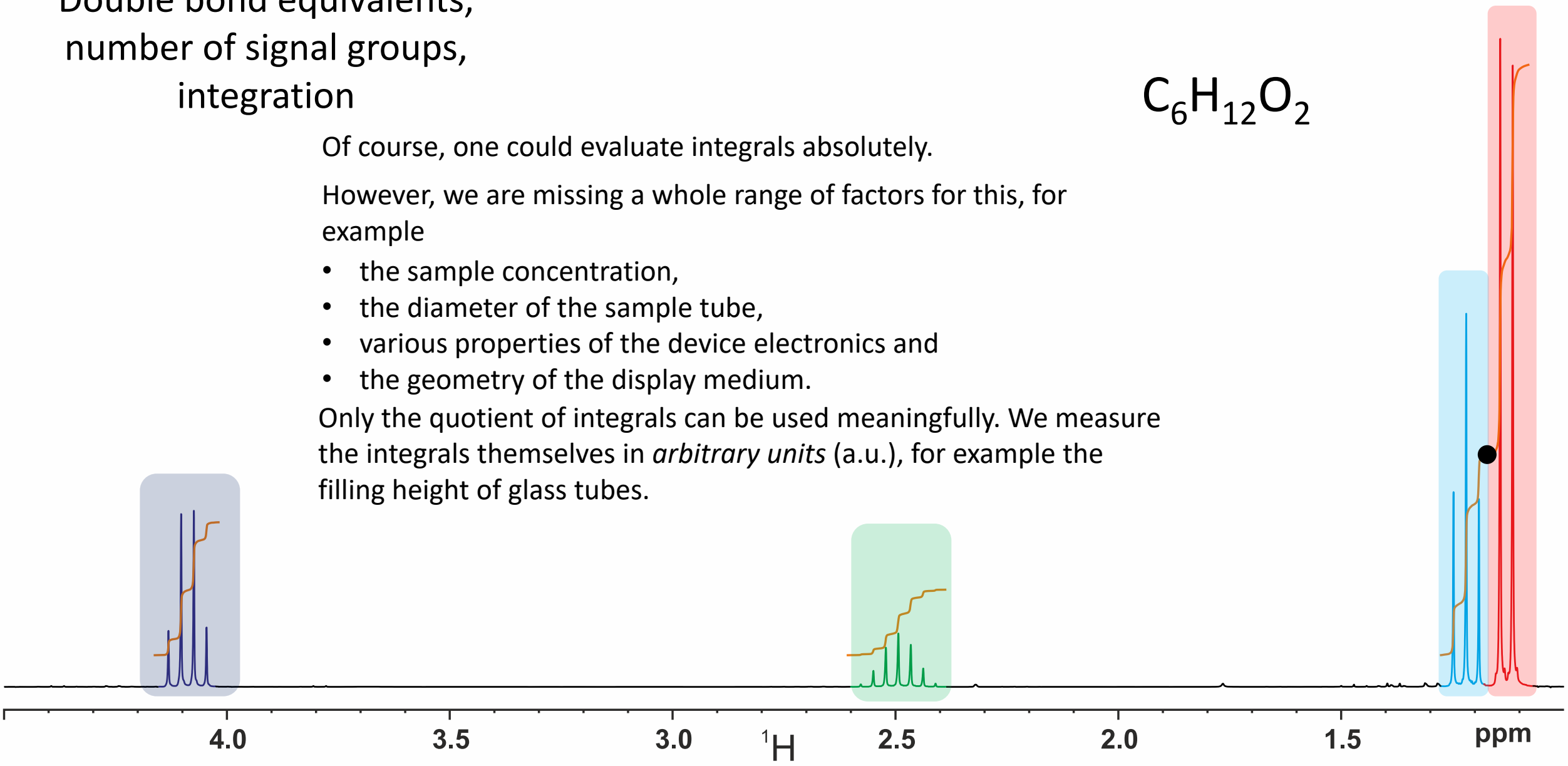
$C_6H_{12}O_2$

Of course, one could evaluate integrals absolutely.

However, we are missing a whole range of factors for this, for example

- the sample concentration,
- the diameter of the sample tube,
- various properties of the device electronics and
- the geometry of the display medium.

Only the quotient of integrals can be used meaningfully. We measure the integrals themselves in *arbitrary units* (a.u.), for example the filling height of glass tubes.



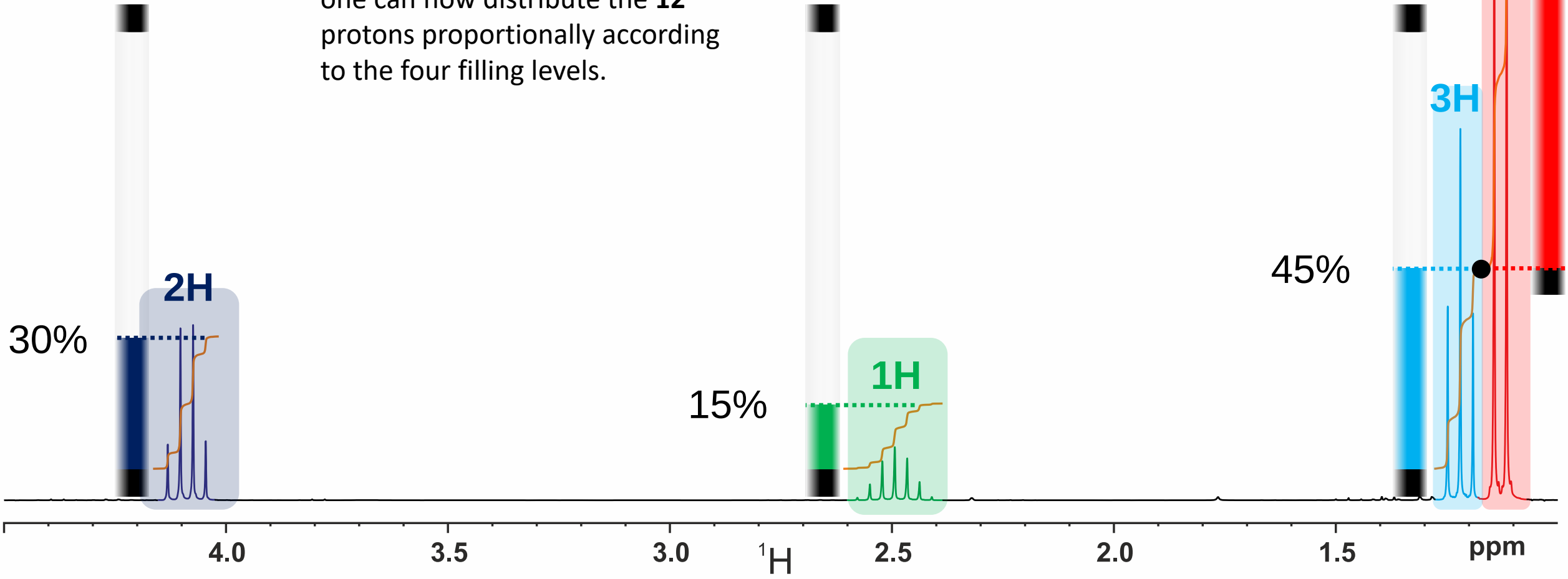
Basics

Double bond equivalents, number of signal groups, integration

$C_6H_{12}O_2$

1 DBÄ

Using the simple rule of three, one can now distribute the **12** protons proportionally according to the four filling levels.



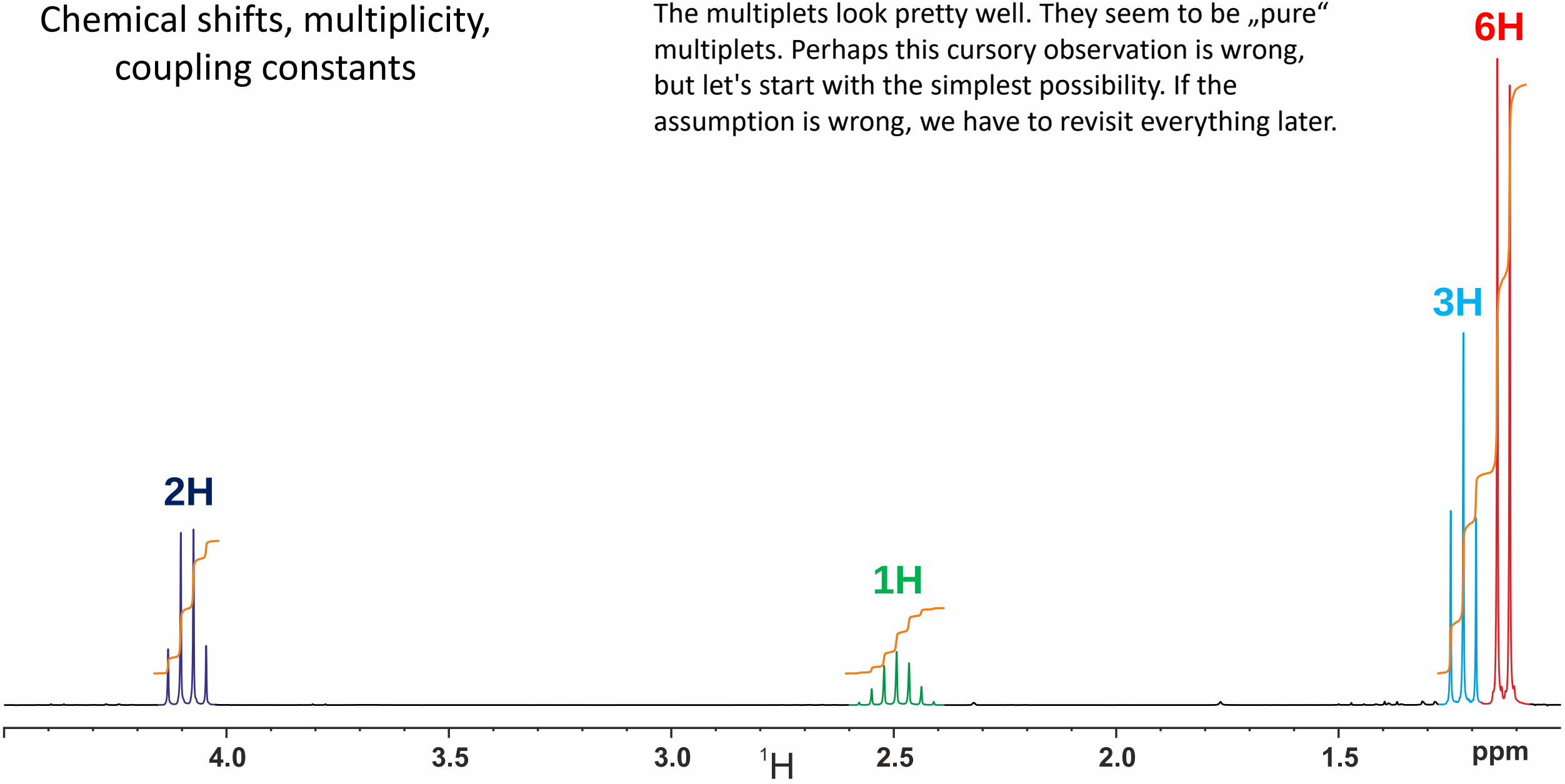
NMR parameters

Chemical shifts, multiplicity, coupling constants

$C_6H_{12}O_2$

1 DBÄ

The multiplets look pretty well. They seem to be „pure“ multiplets. Perhaps this cursory observation is wrong, but let's start with the simplest possibility. If the assumption is wrong, we have to revisit everything later.



NMR parameters

Chemical shifts, multiplicity, coupling constants

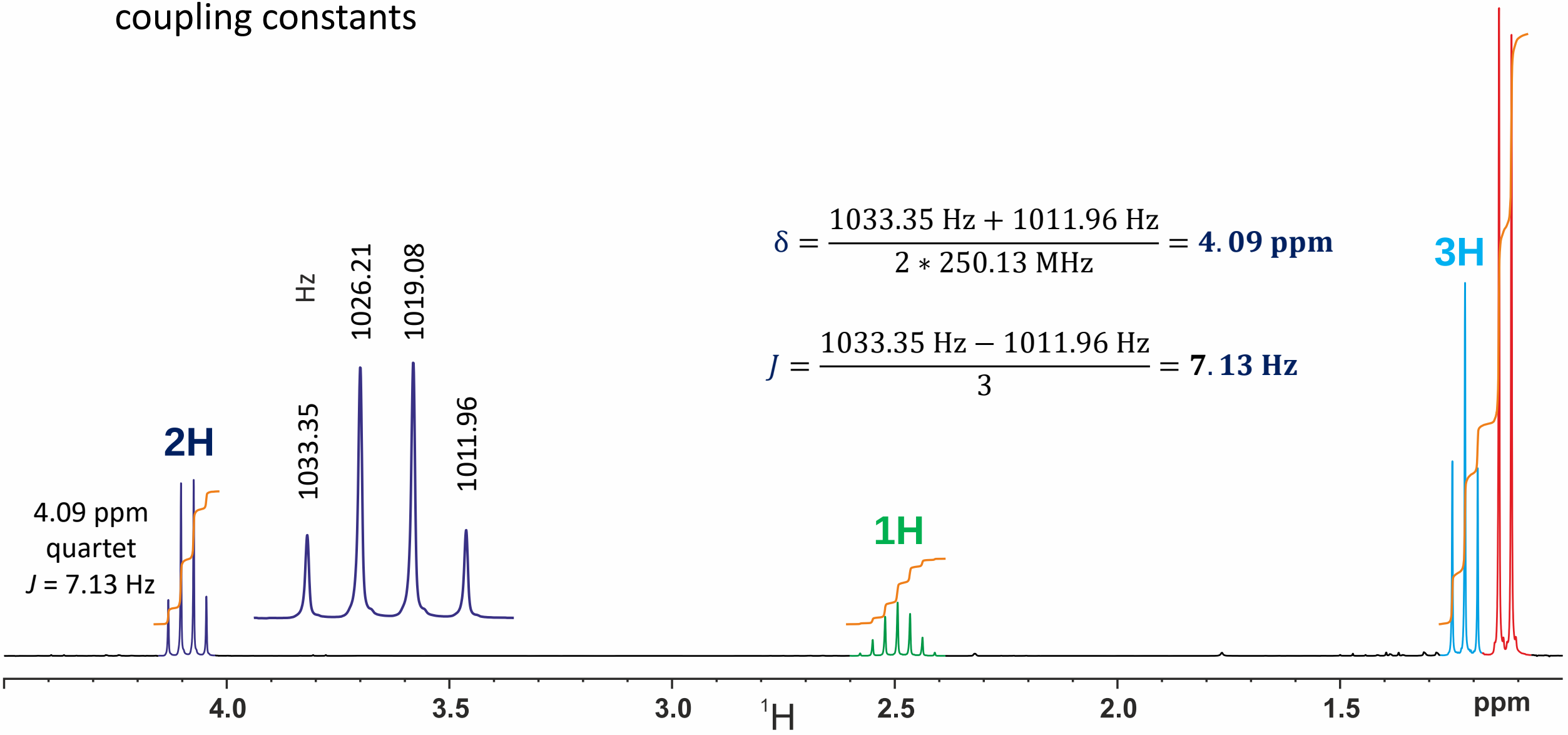
$C_6H_{12}O_2$

1 DBÄ

Let's start with the quartet at deepest field.

$$\delta = \frac{1033.35\ \text{Hz} + 1011.96\ \text{Hz}}{2 * 250.13\ \text{MHz}} = \mathbf{4.09\ ppm}$$

$$J = \frac{1033.35\ \text{Hz} - 1011.96\ \text{Hz}}{3} = \mathbf{7.13\ Hz}$$



NMR parameters

Chemical shifts, multiplicity, coupling constants

$C_6H_{12}O_2$

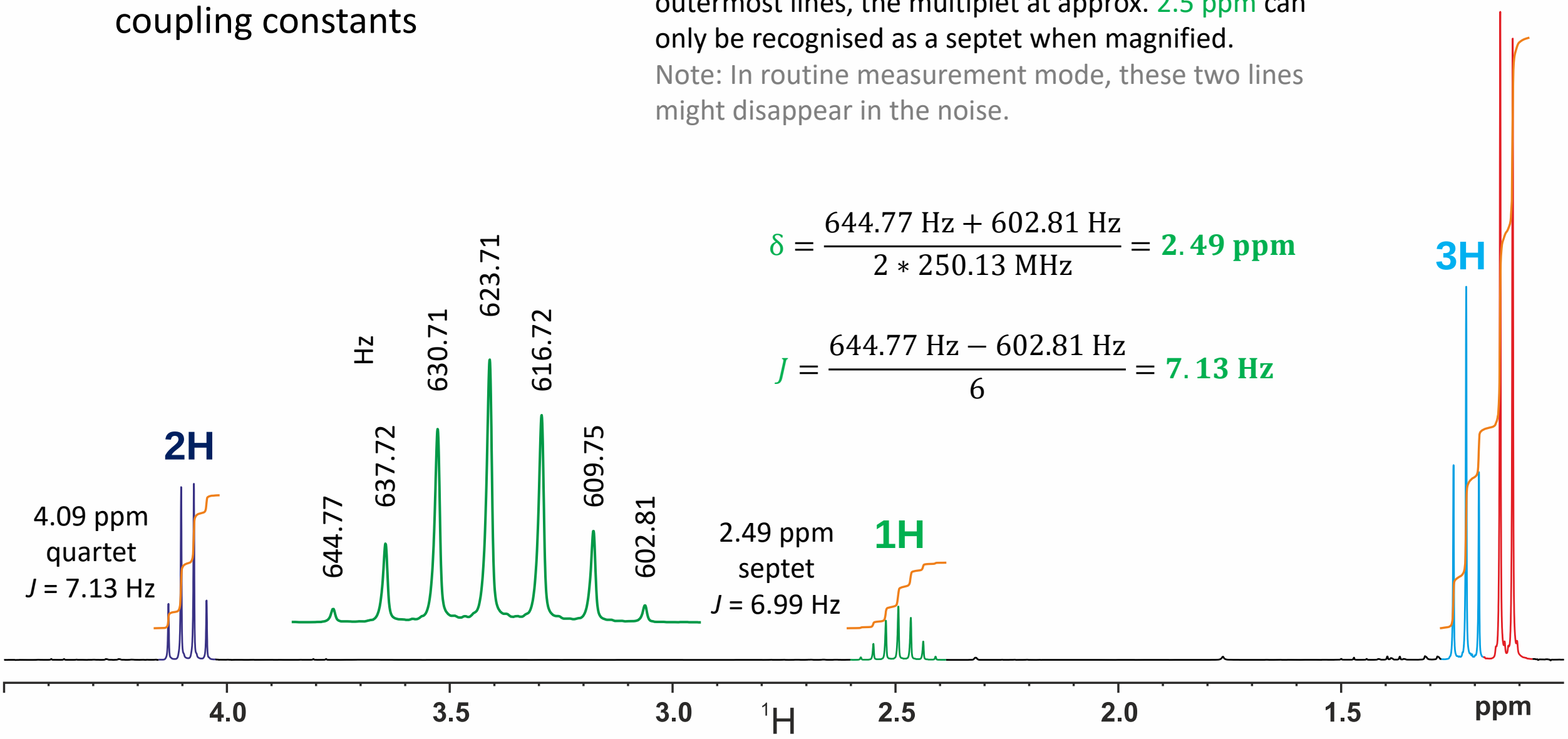
1 DBÄ

Because of the very weak intensity of the two outermost lines, the multiplet at approx. 2.5 ppm can only be recognised as a septet when magnified.

Note: In routine measurement mode, these two lines might disappear in the noise.

$$\delta = \frac{644.77\ \text{Hz} + 602.81\ \text{Hz}}{2 * 250.13\ \text{MHz}} = \mathbf{2.49\ ppm}$$

$$J = \frac{644.77\ \text{Hz} - 602.81\ \text{Hz}}{6} = \mathbf{7.13\ Hz}$$



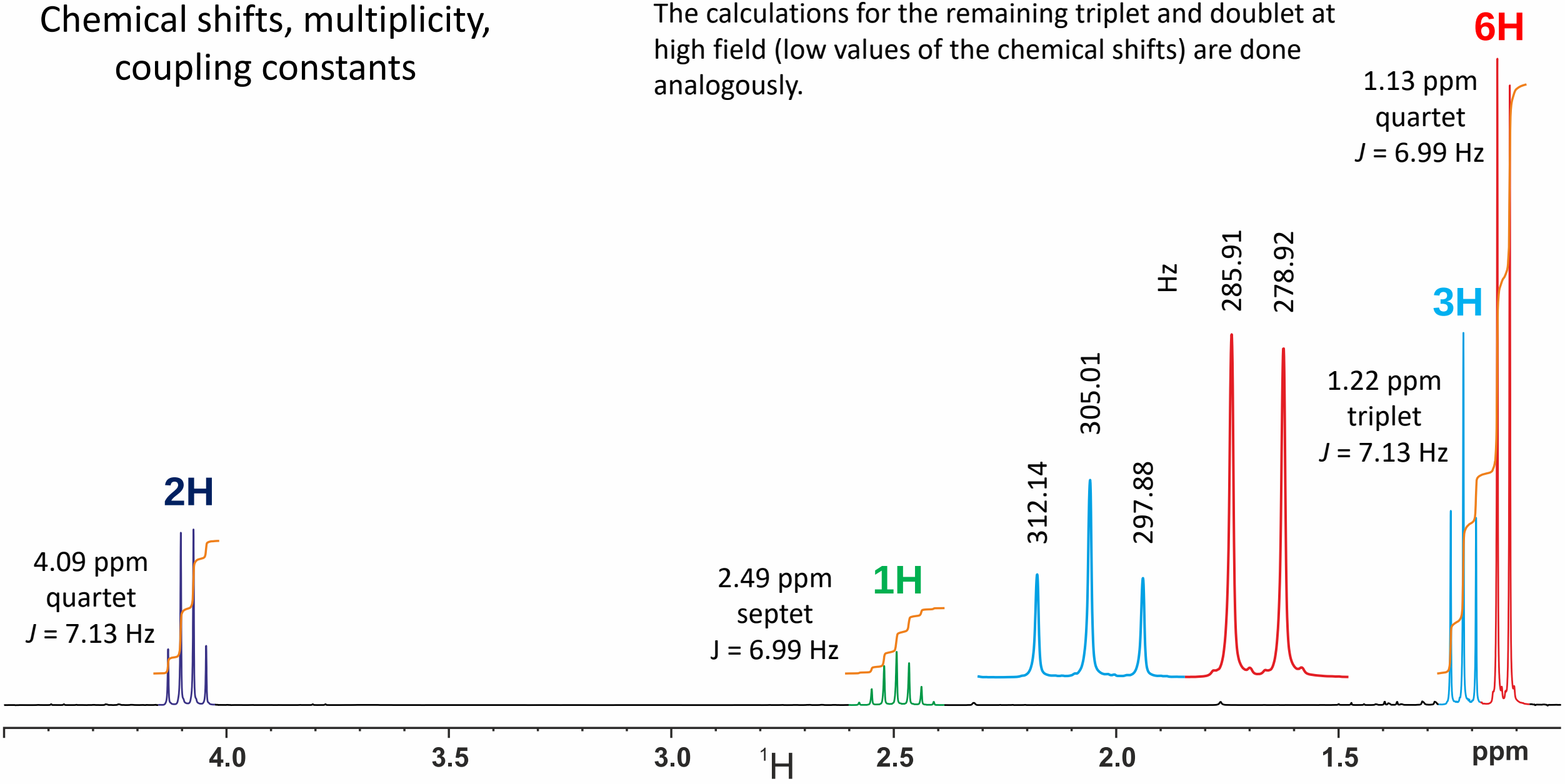
NMR parameters

Chemical shifts, multiplicity, coupling constants

$C_6H_{12}O_2$

1 DBÄ

The calculations for the remaining triplet and doublet at high field (low values of the chemical shifts) are done analogously.



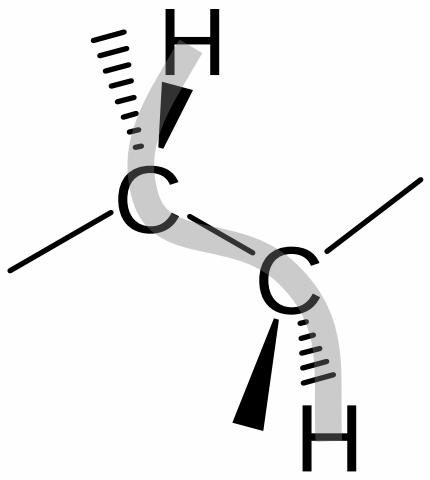
Building blocks

$C_6H_{12}O_2$

1 DBÄ

In each of the four multipletts, the coupling constant – independent of the multiplicity – is about 7 Hz.

A coupling constant of 7 Hz is very common. This is a coupling via three bonds (technical term: *vicinal coupling*) along the chain **H – C – C – H** under the condition of a free rotation around the **C – C** single bond.



Building blocks

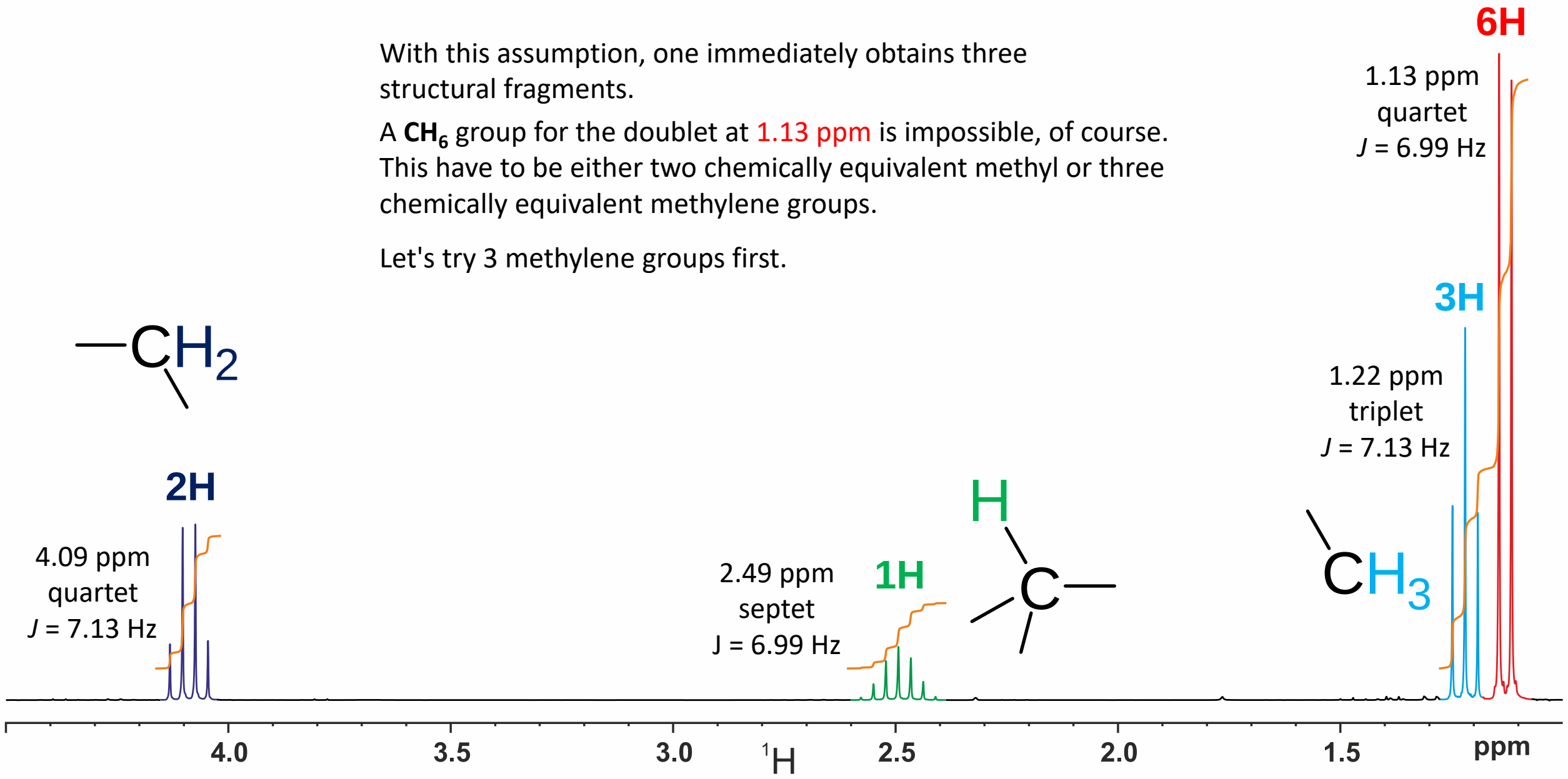
$C_6H_{12}O_2$

1 DBÄ

With this assumption, one immediately obtains three structural fragments.

A **CH_6** group for the doublet at 1.13 ppm is impossible, of course. This have to be either two chemically equivalent methyl or three chemically equivalent methylene groups.

Let's try 3 methylene groups first.



Building blocks

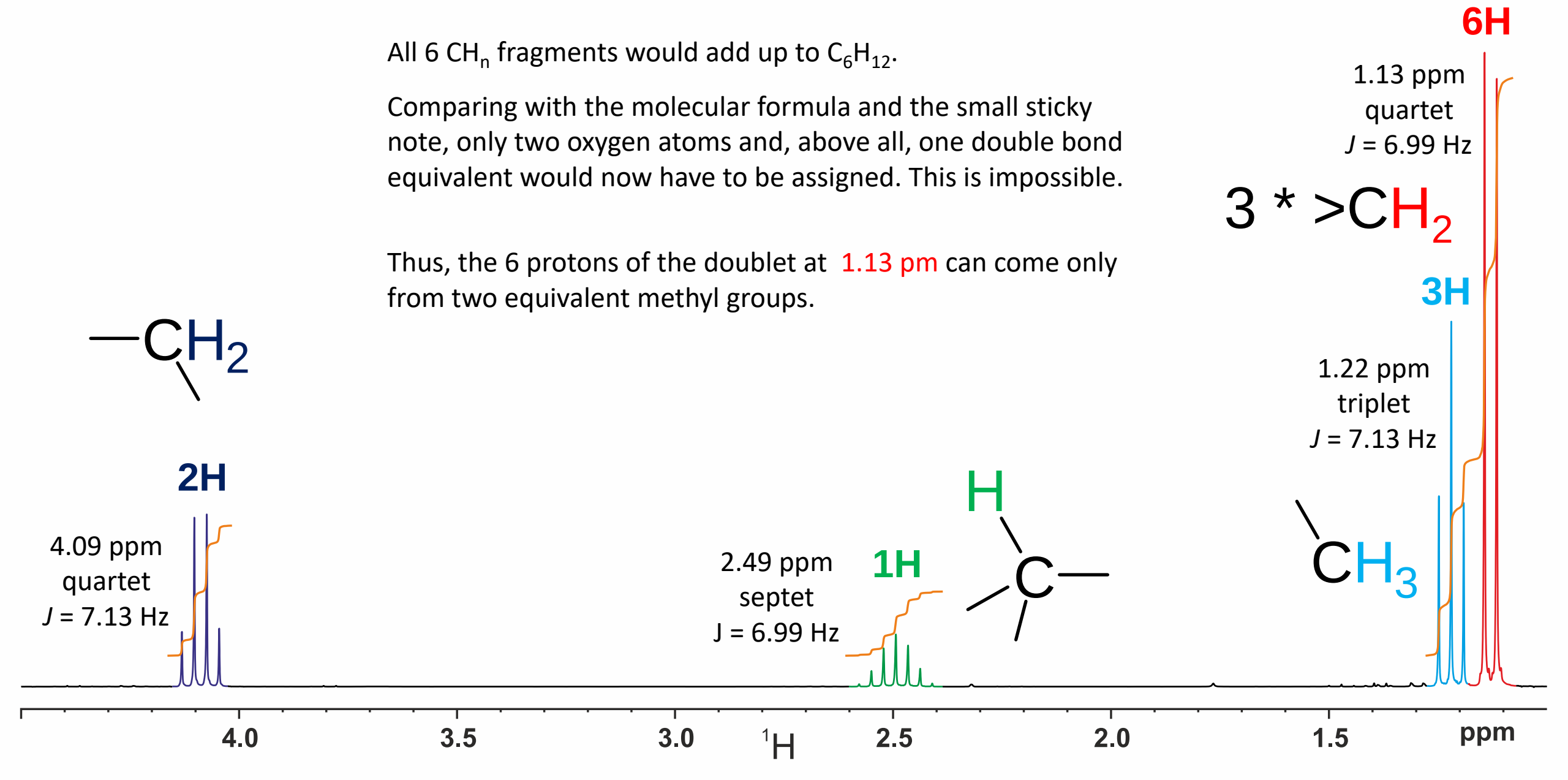
$C_6H_{12}O_2$

1 DBÄ

All 6 CH_n fragments would add up to C_6H_{12}.

Comparing with the molecular formula and the small sticky note, only two oxygen atoms and, above all, one double bond equivalent would now have to be assigned. This is impossible.

Thus, the 6 protons of the doublet at 1.13 pm can come only from two equivalent methyl groups.

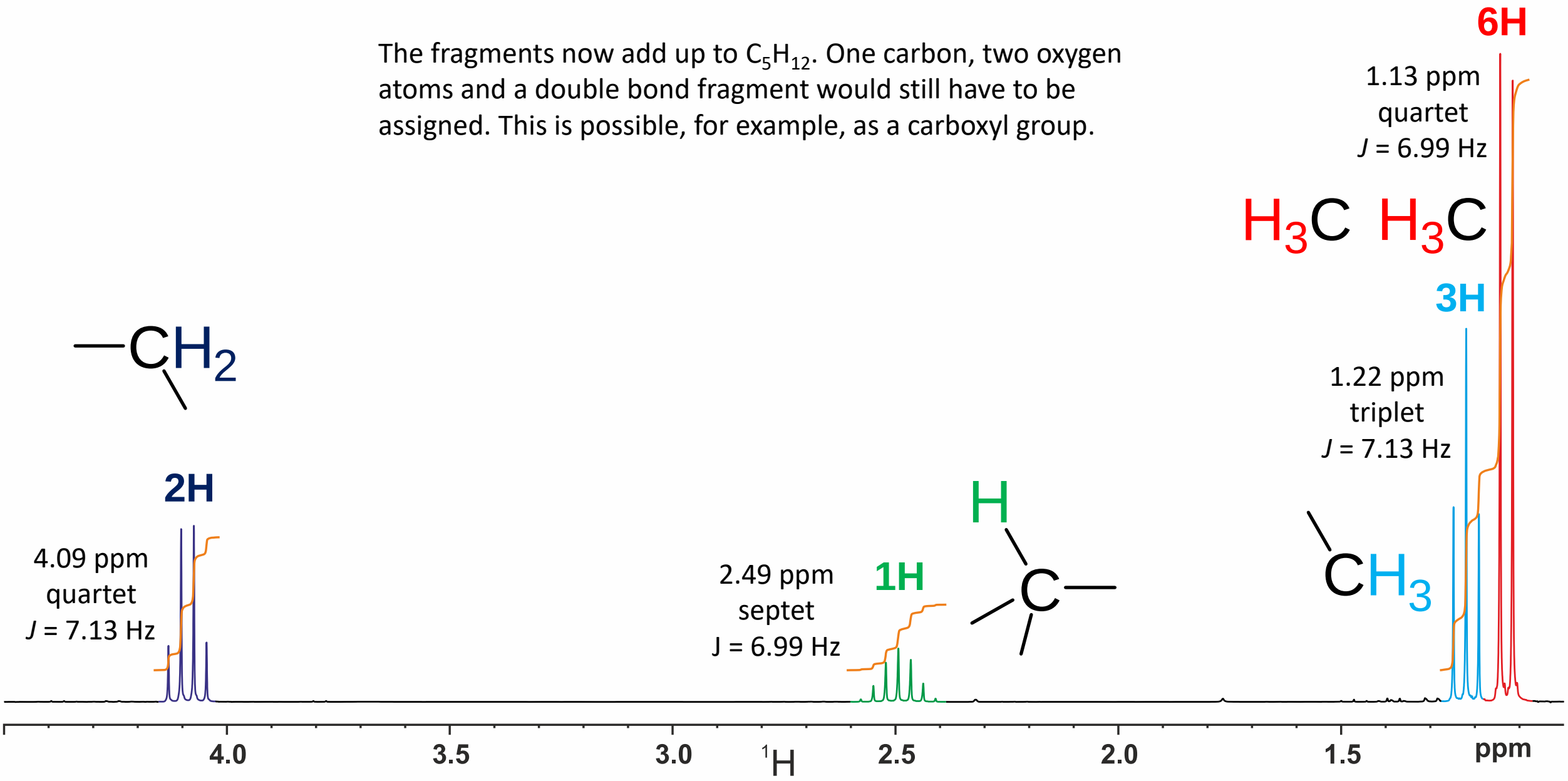


Building blocks

$C_6H_{12}O_2$

1 DBÄ

The fragments now add up to C_5H_{12}. One carbon, two oxygen atoms and a double bond fragment would still have to be assigned. This is possible, for example, as a carboxyl group.



Building blocks

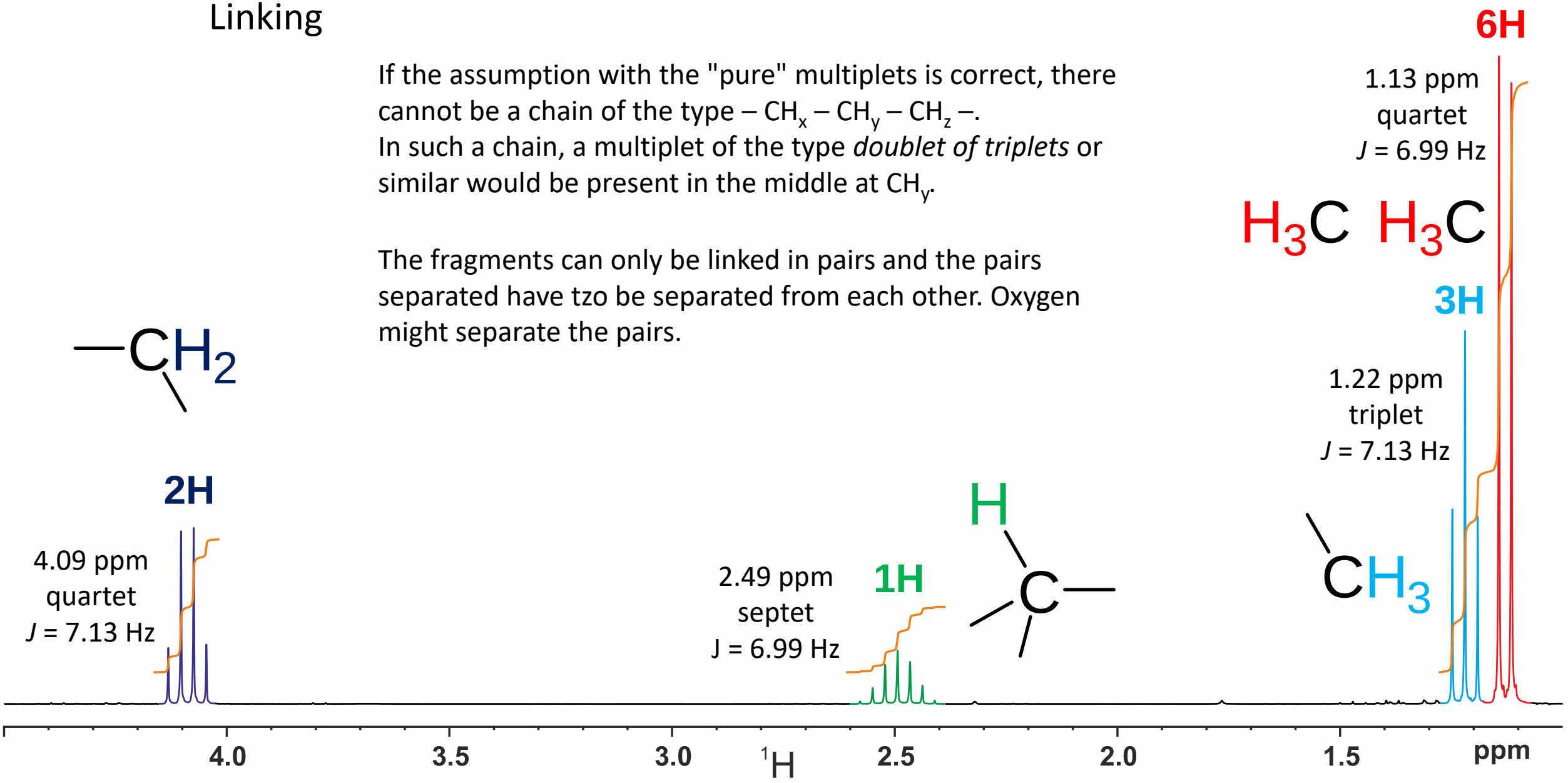
Linking

$C_6H_{12}O_2$

1 DBÄ

If the assumption with the "pure" multiplets is correct, there cannot be a chain of the type – CH_x – CH_y – CH_z –.
In such a chain, a multiplet of the type *doublet of triplets* or similar would be present in the middle at CH_y.

The fragments can only be linked in pairs and the pairs separated have tzo be separated from each other. Oxygen might separate the pairs.



Building blocks

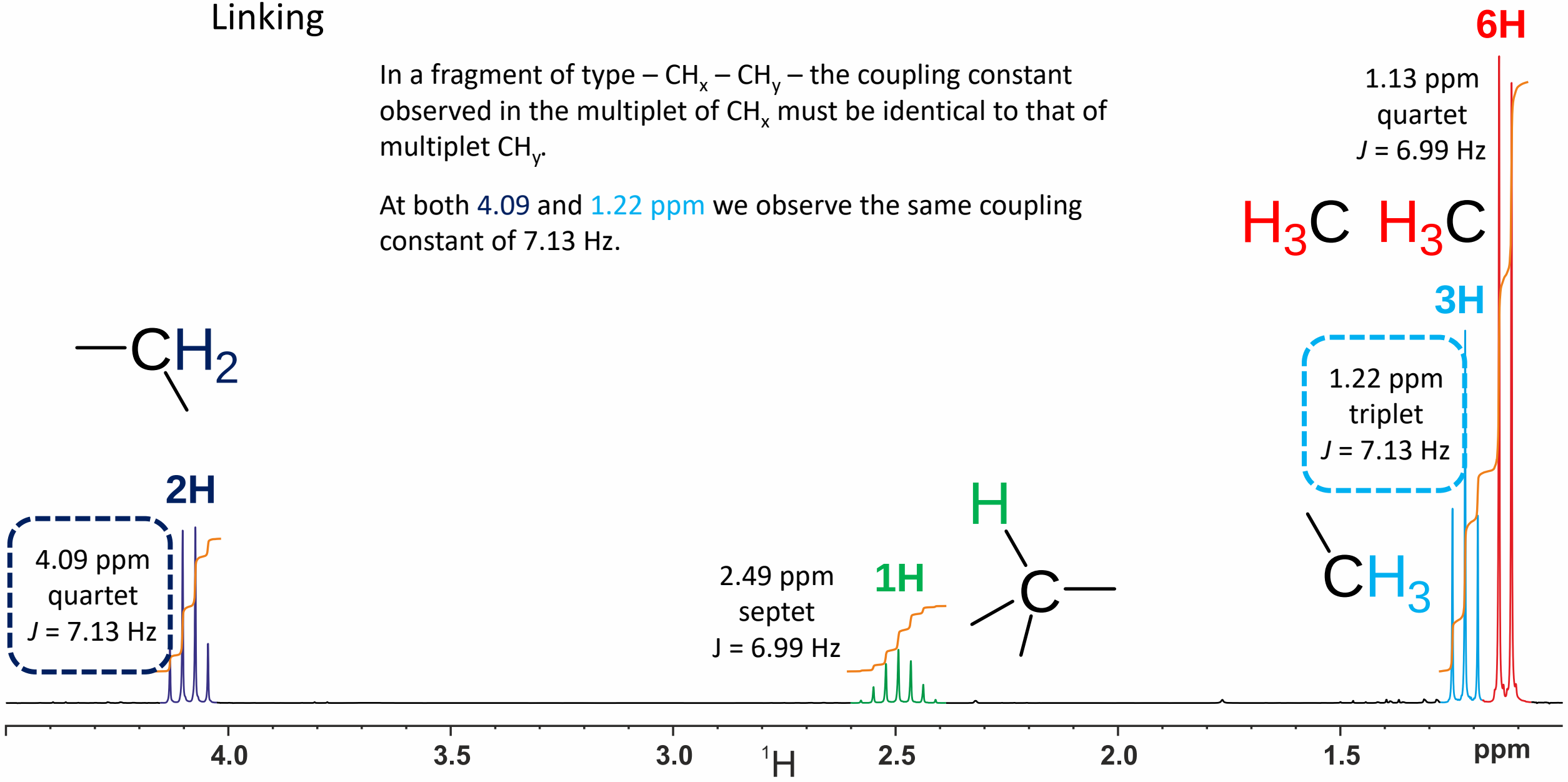
Linking

$C_6H_{12}O_2$

1 DBÄ

In a fragment of type – CH_x – CH_y – the coupling constant observed in the multiplet of CH_x must be identical to that of multiplet CH_y.

At both 4.09 and 1.22 ppm we observe the same coupling constant of 7.13 Hz.



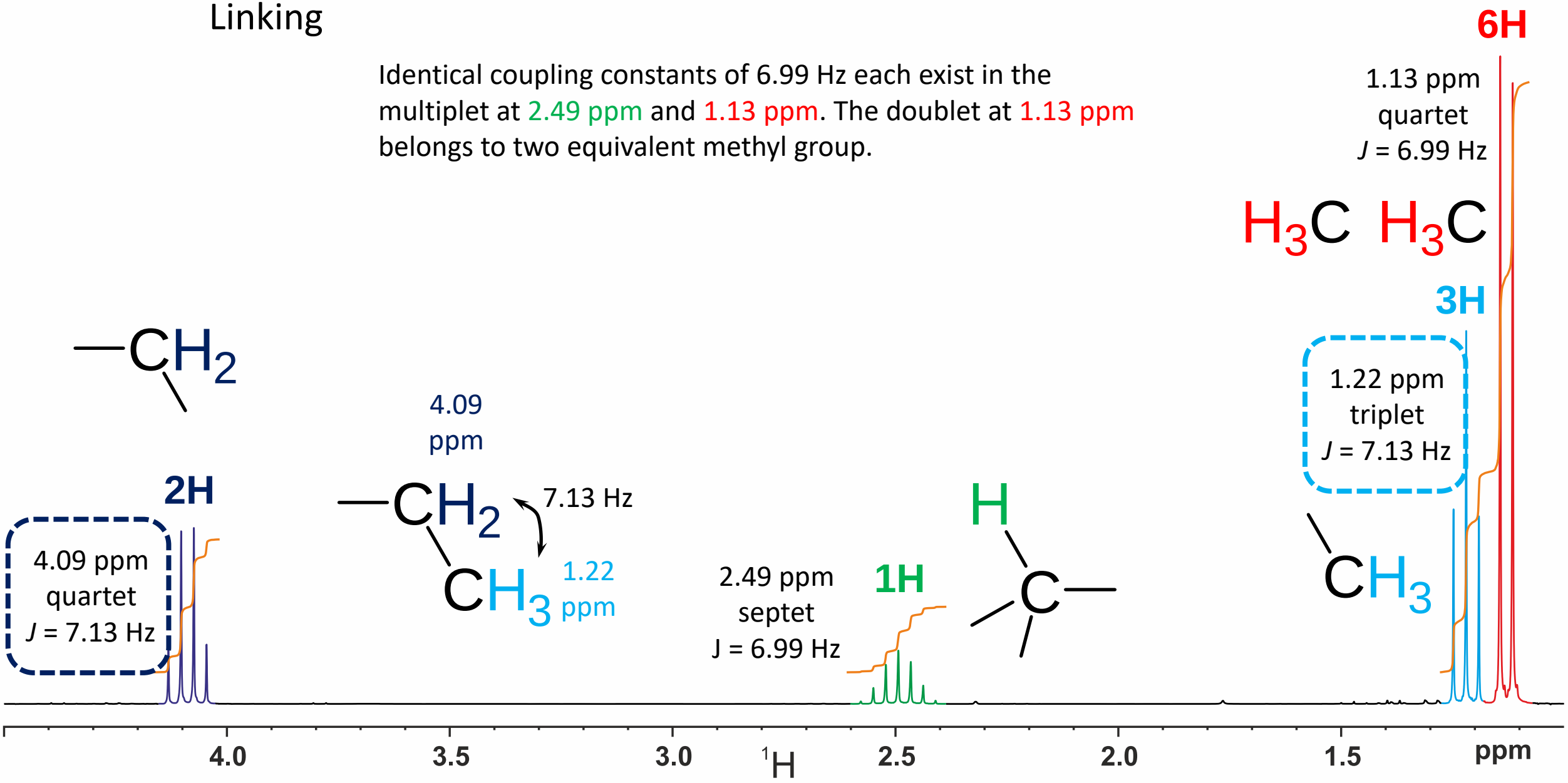
Building blocks

Linking

$C_6H_{12}O_2$

1 DBÄ

Identical coupling constants of 6.99 Hz each exist in the multiplet at 2.49 ppm and 1.13 ppm. The doublet at 1.13 ppm belongs to two equivalent methyl group.



Building blocks

Linking

$C_6H_{12}O_2$

1 DBÄ

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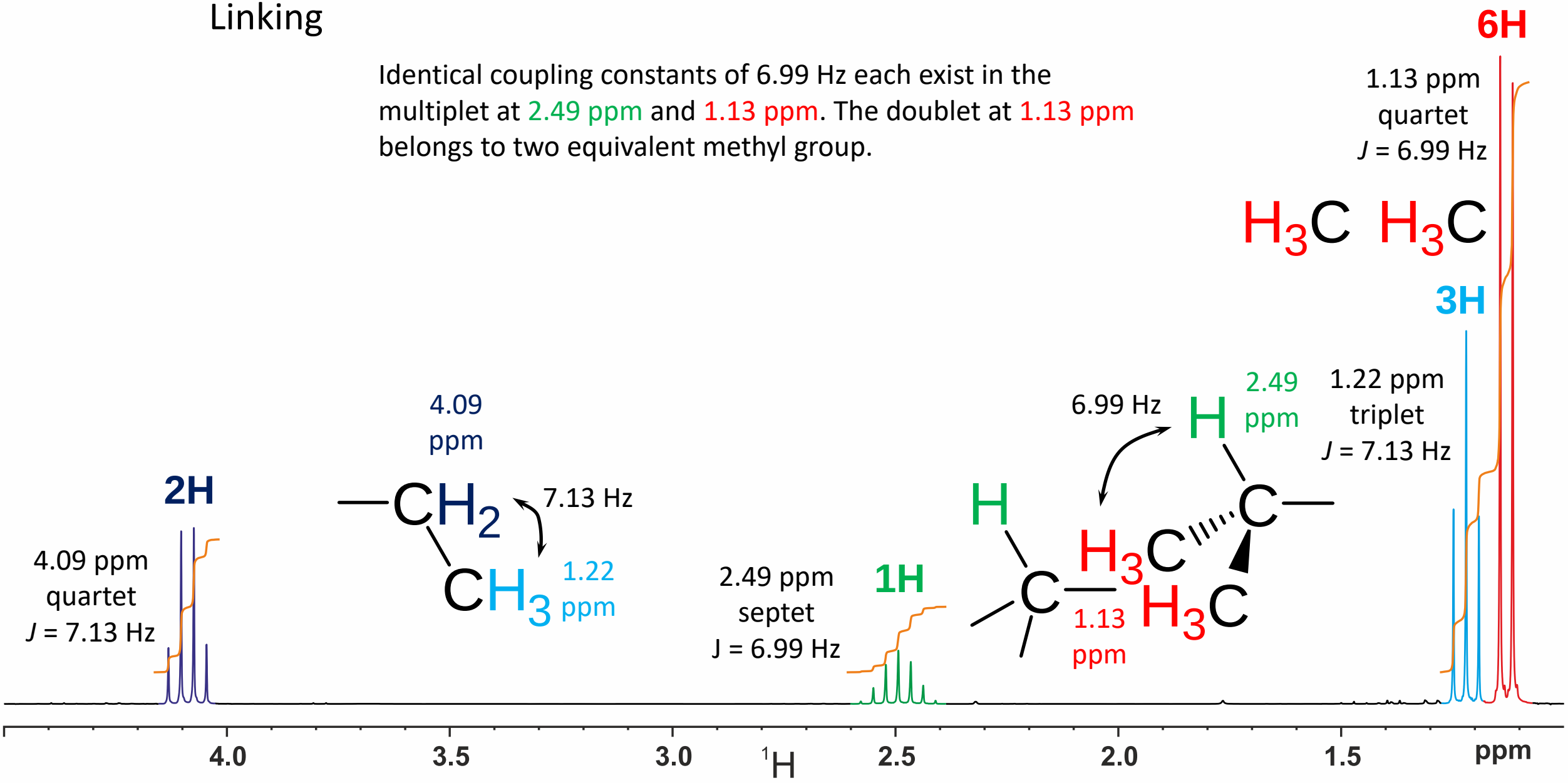


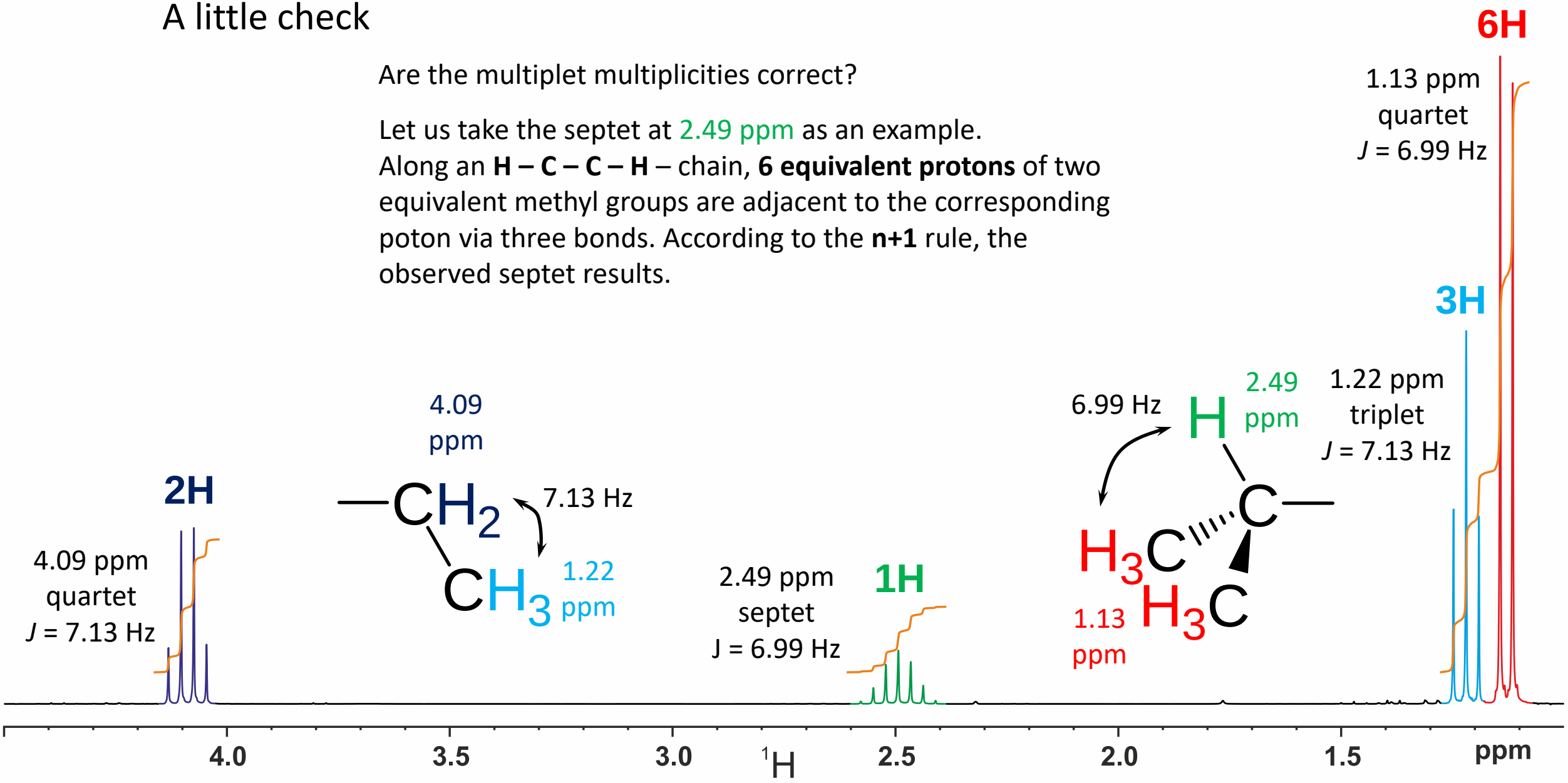
Building blocks

A little check

$C_6H_{12}O_2$ 1 DBÄ

Are the multiplet multiplicities correct?

Let us take the septet at 2.49 ppm as an example.
Along an **H – C – C – H** – chain, **6 equivalent protons** of two equivalent methyl groups are adjacent to the corresponding poton via three bonds. According to the **n+1** rule, the observed septet results.



Finalisation

$C_6H_{12}O_2$

1 DBÄ

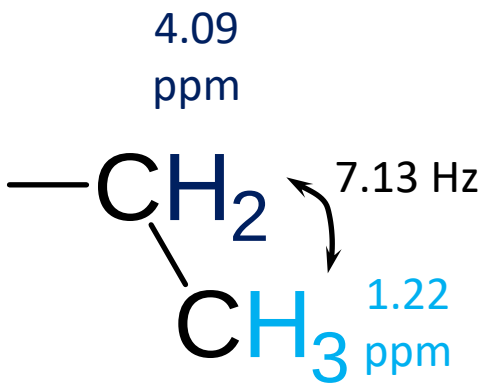
Two possibilities

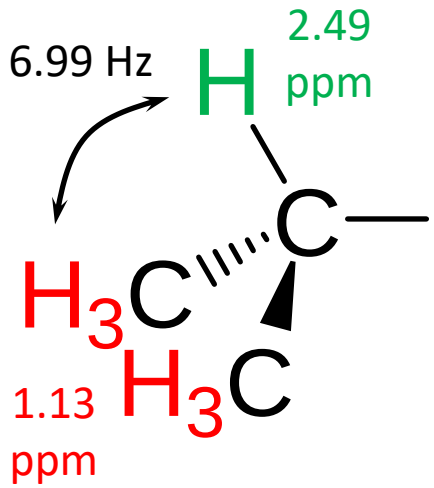
The isopropyl and ethyl groups add up to C_5H_{12}.

Missing:

- one carbon atom,
- two oxygen atoms, and
- one double bond equivalent.

This is a carboxylic group that has to be placed between the two fragments. Let's rearrange these two fragments a little bit.





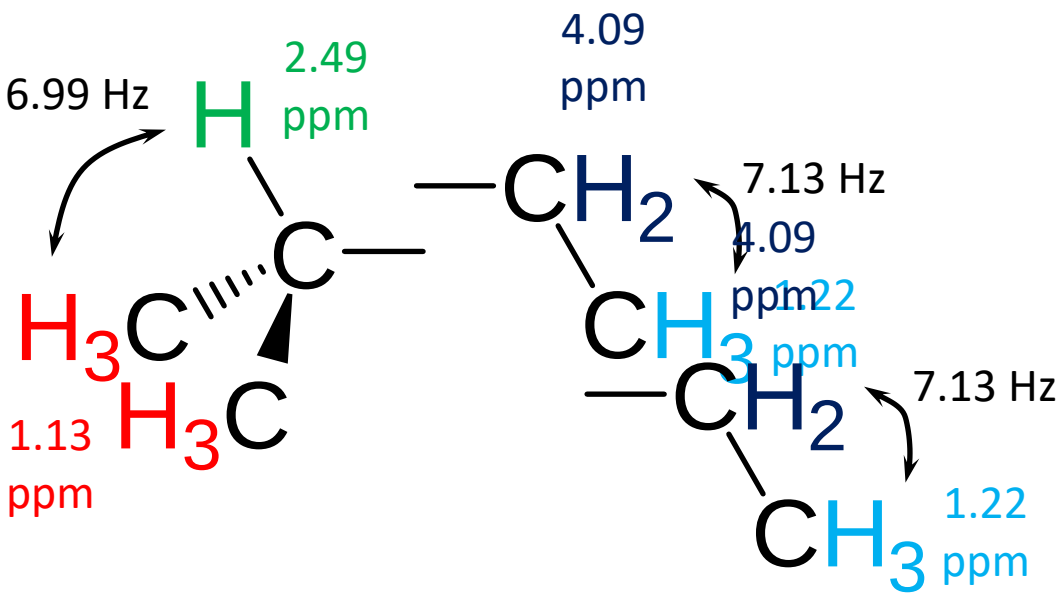
Finalisation

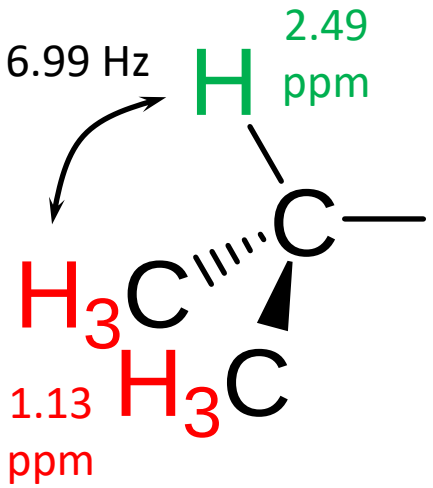
Two possibilities

$C_6H_{12}O_2$

1 DBÄ

And now we can tentatively insert the carboxylic group.





Finalisation

Two possibilities

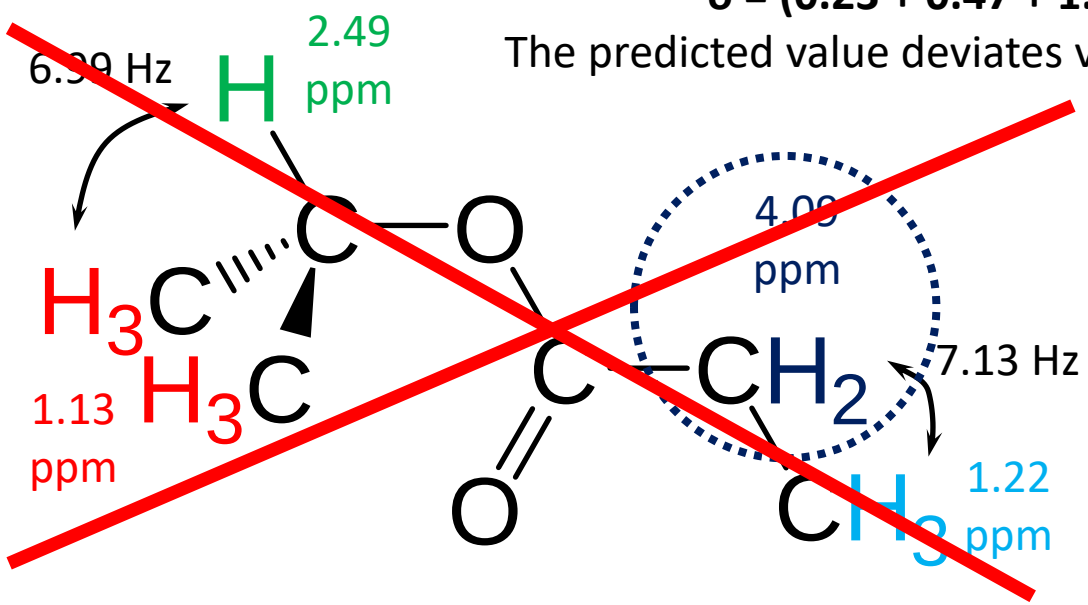
Is this structure correct? There are no measurement available that could directly confirm the chosen connectivity.

The expected chemical shift of methylene protons can be estimated quite well with the help of a simple calculation. A search for *Schoolery's rule* should quickly show the simple calculation method.

For the methylene protons in propionic acid methyl ester shown here, the estimation results in

δ = (0.23 + 0.47 + 1.55) ppm = 2.25 ppm

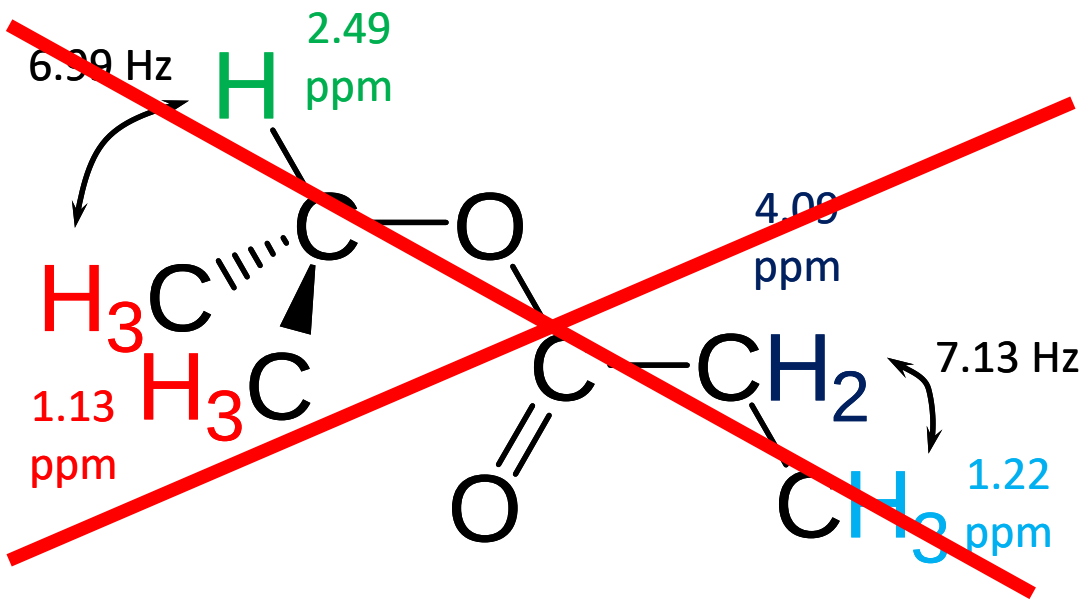
The predicted value deviates very strongly from the measured value.



Finalisation

Two possibilities

Let us duplicate our structure …

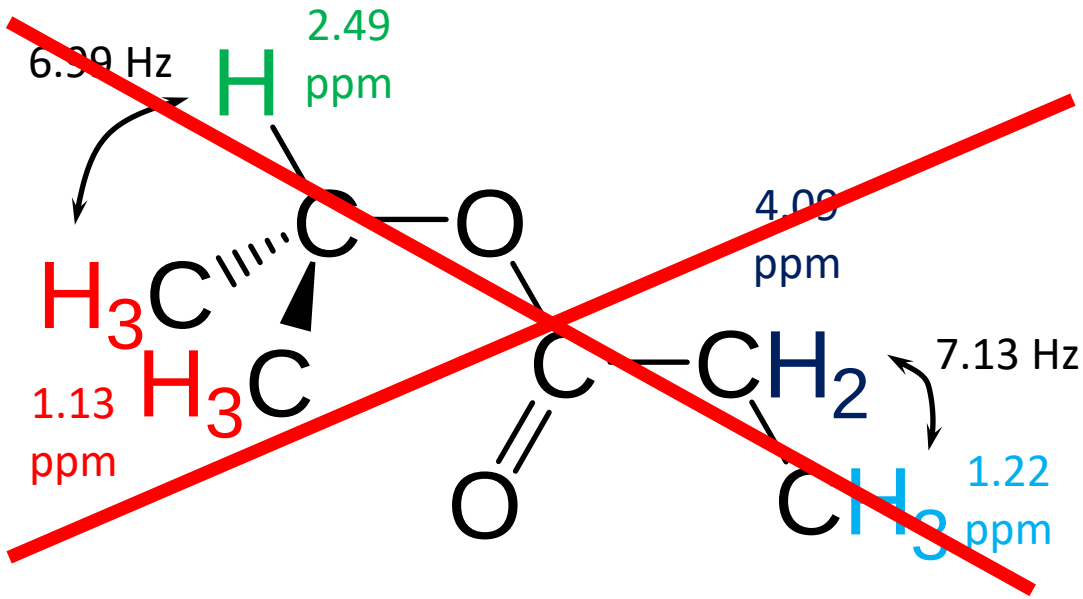


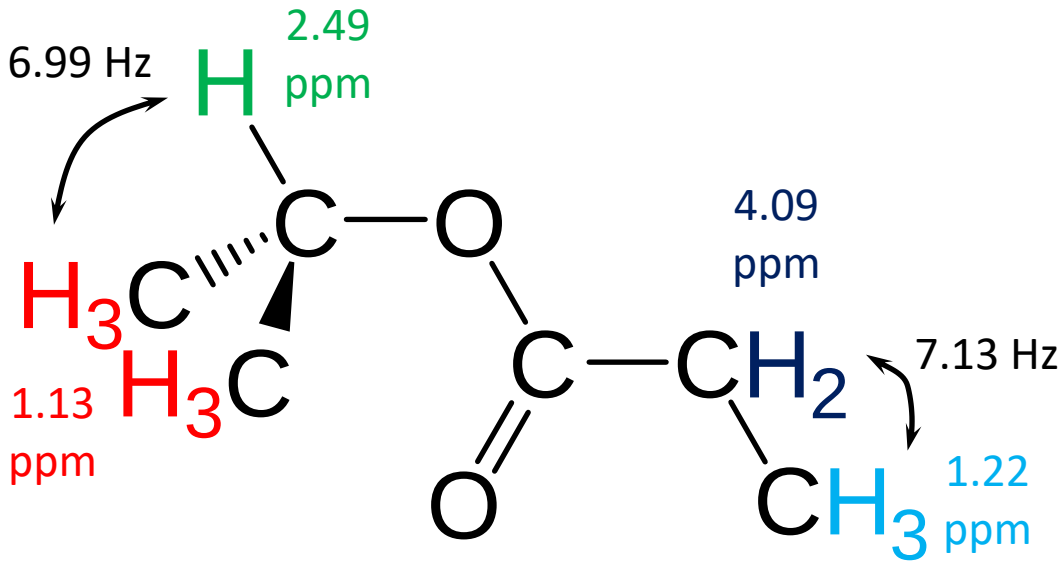
Finalisation

Two possibilities

… and invert the carboxylic group.

Using some minor cosmetics …



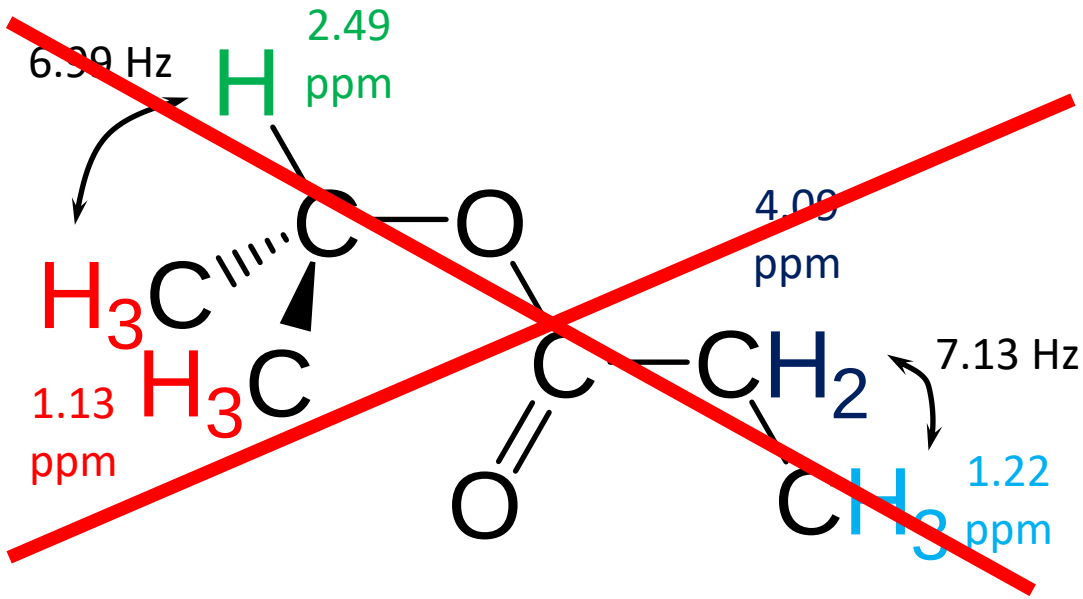


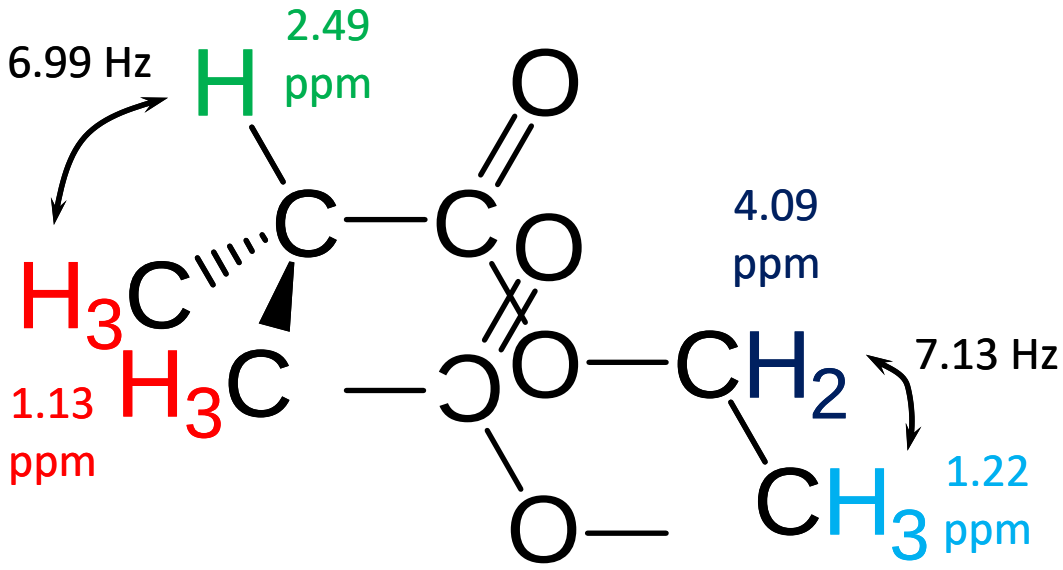
Finalisation

Two possibilities

… all bonds are in place and ...

… the carbon atom symbol is the right way up again.





Finalisation

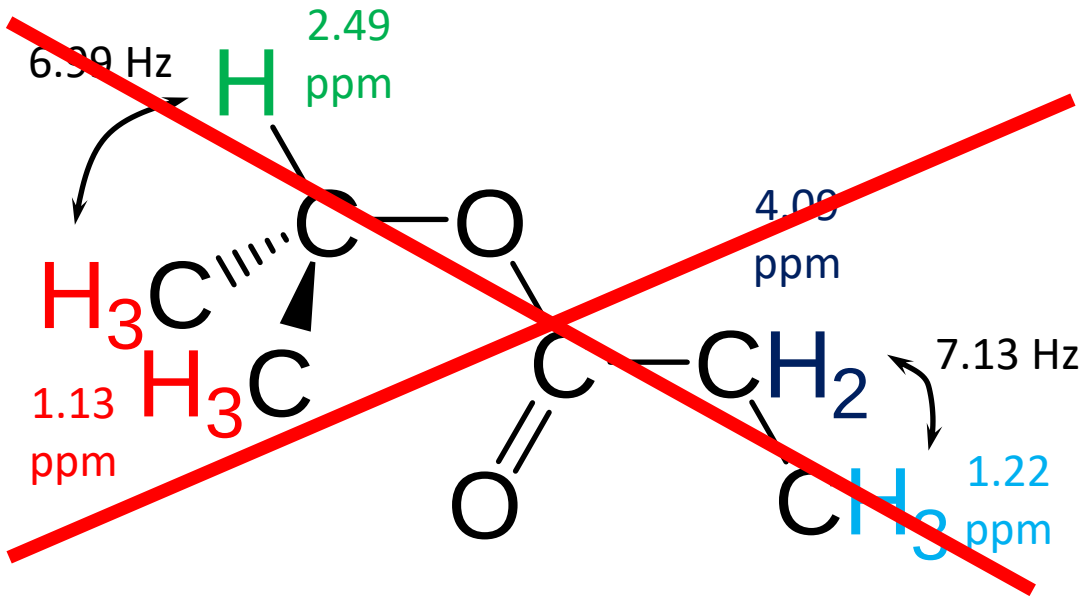
Two possibilities

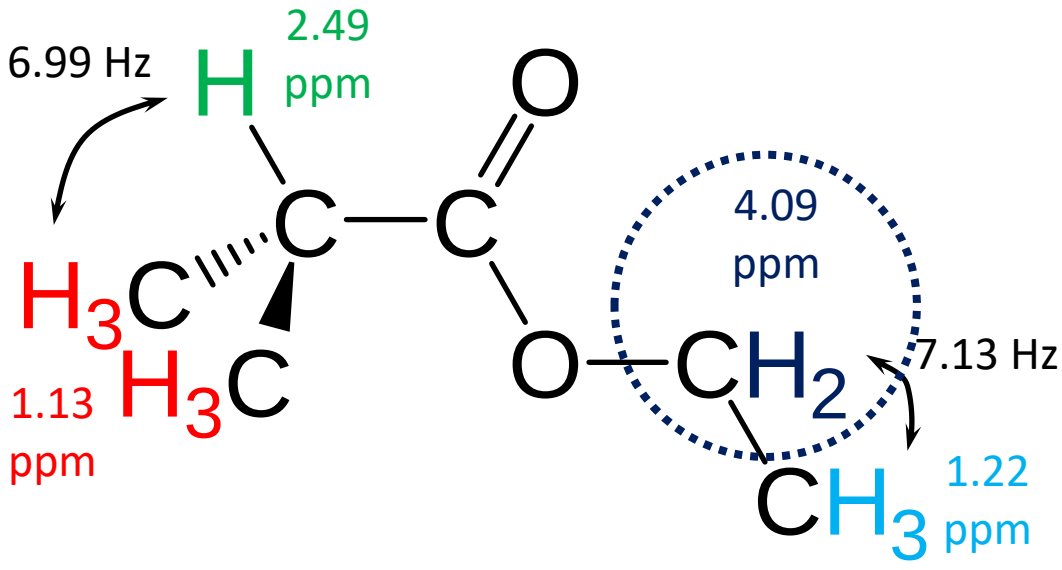
And what about the prediction of the chemical shifts for the protons of the methylene group now?

This time the estimation gives

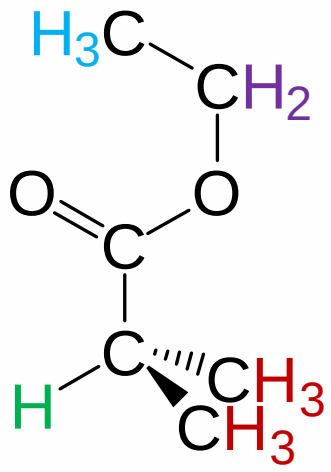
δ = (0.23 + 0.47 + 3.13) ppm = 3.83 ppm

Not absolutely perfect, but much better than before for the left structure.





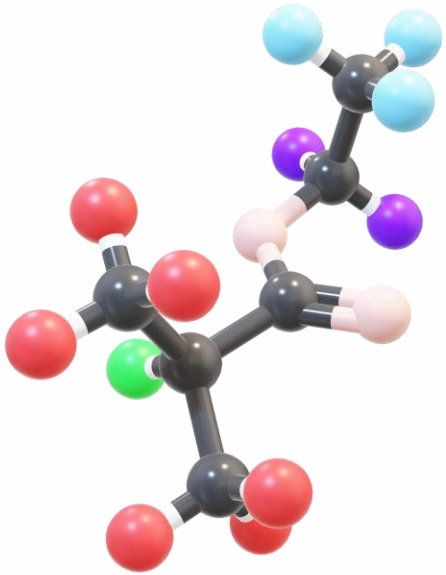
Summary


H3C
CH2
O
O
C
C
H
CH3
CH3

Hz
1033.35
1026.21
1019.08
1011.96
644.77
637.72
630.71
623.71
616.72
609.75
602.81
312.14
305.01
297.88
285.91
278.92
4.14
4.10
4.06
2.58
2.54
2.50
2.46
2.42
1.26
1.22
1.18
1.14
1.10
4.0
3.5
3.0
2.5
2.0
1.5
ppm
1H

Summary

(Feel free to turn the 3D structure)



Isobutyric acid ethyl ester

Contributions

Spectrometer time

TU Munich

Measurements

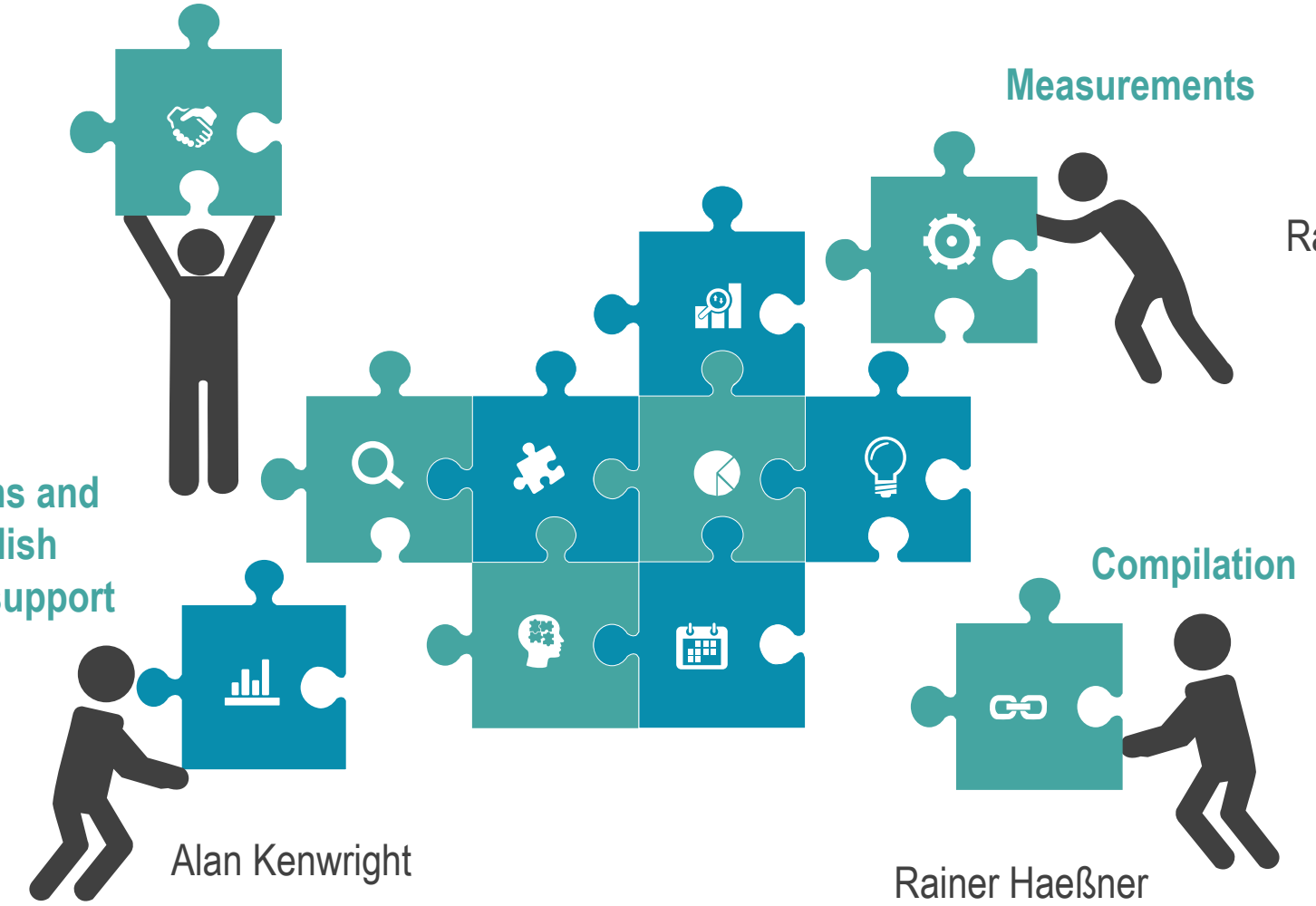
Rainer Haeßner

Discussions and native English language support

Alan Kenwright

Compilation

Rainer Haeßner



More exercises …