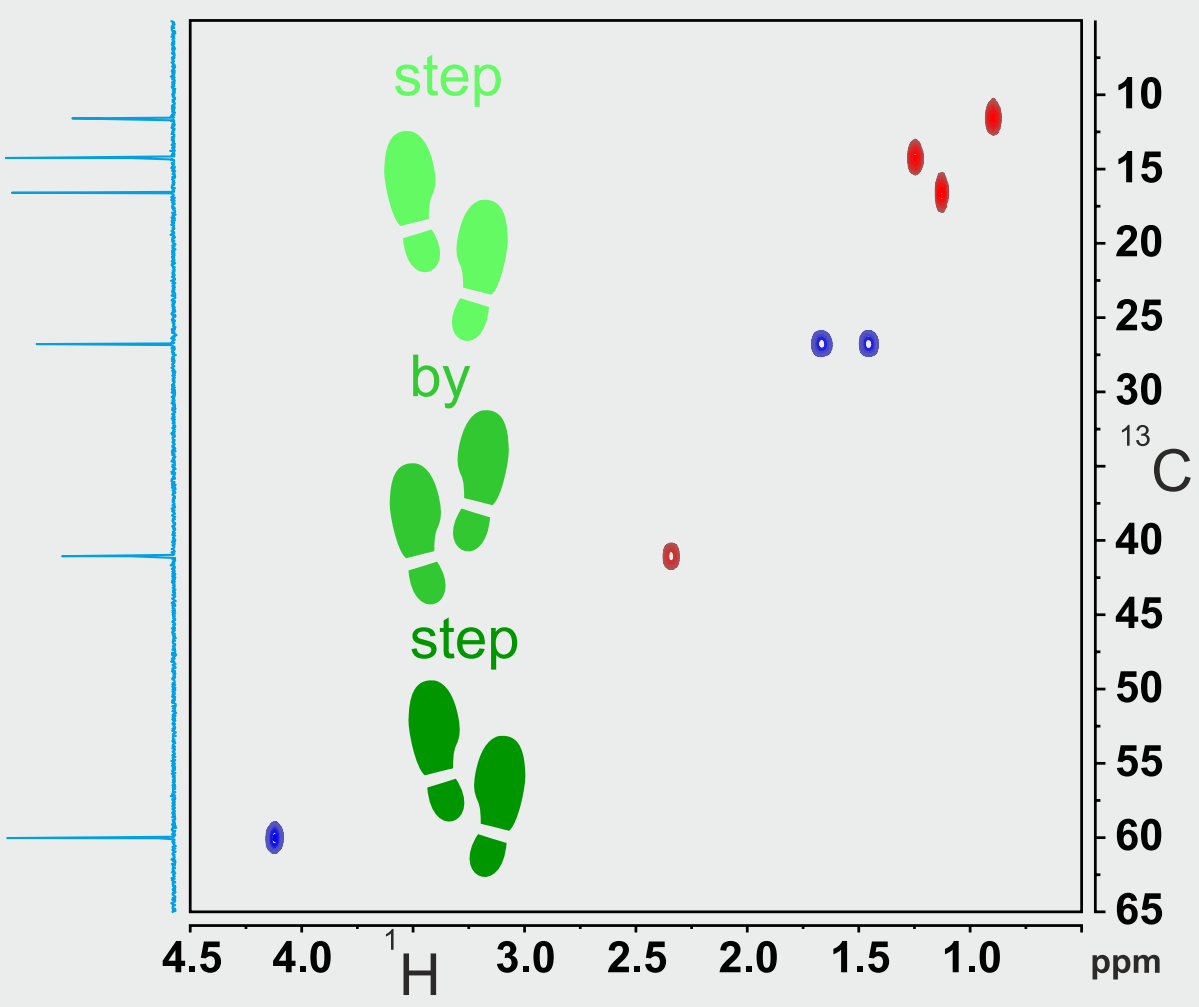
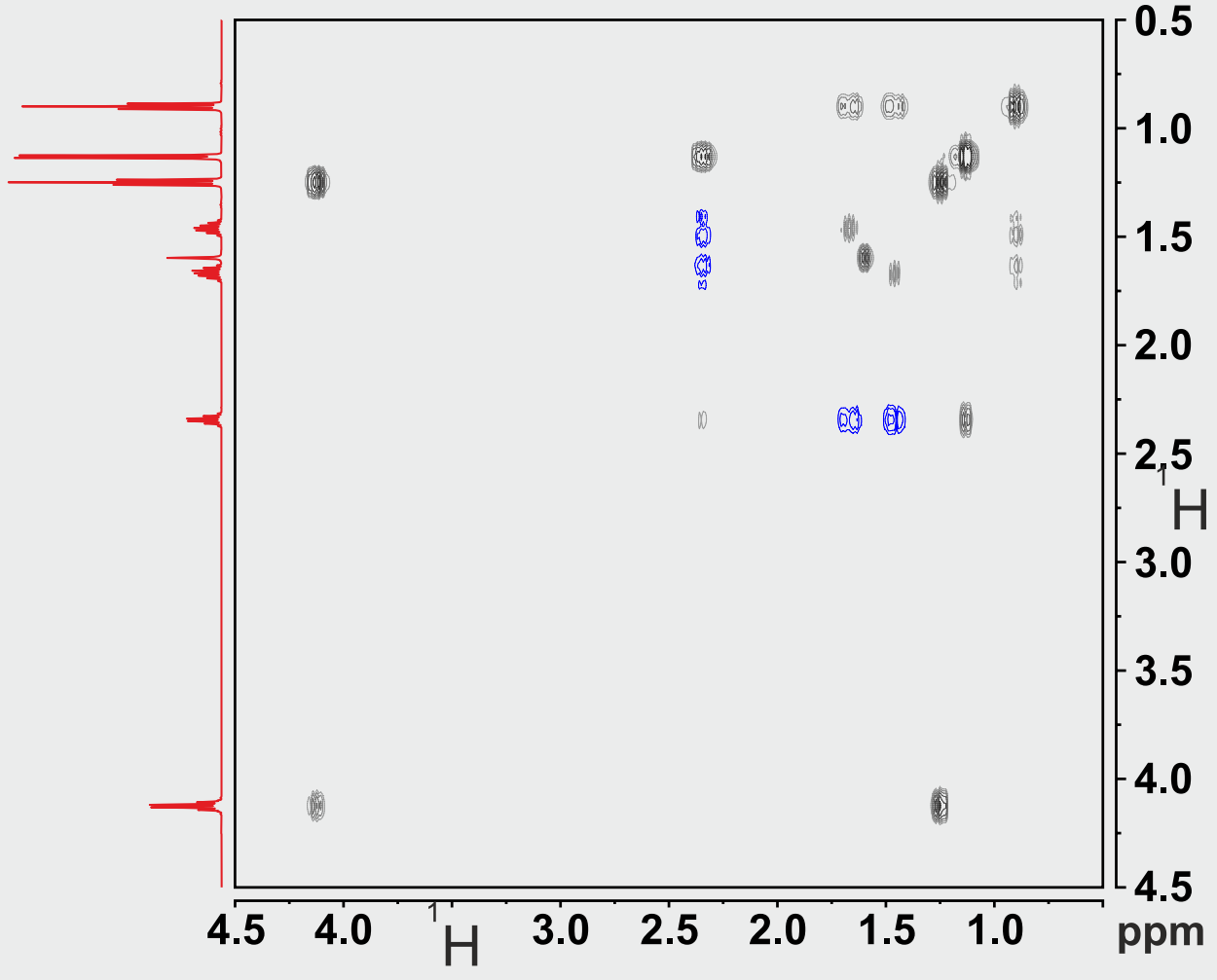
# Exercise plus Solution – Quick PDF overview

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.



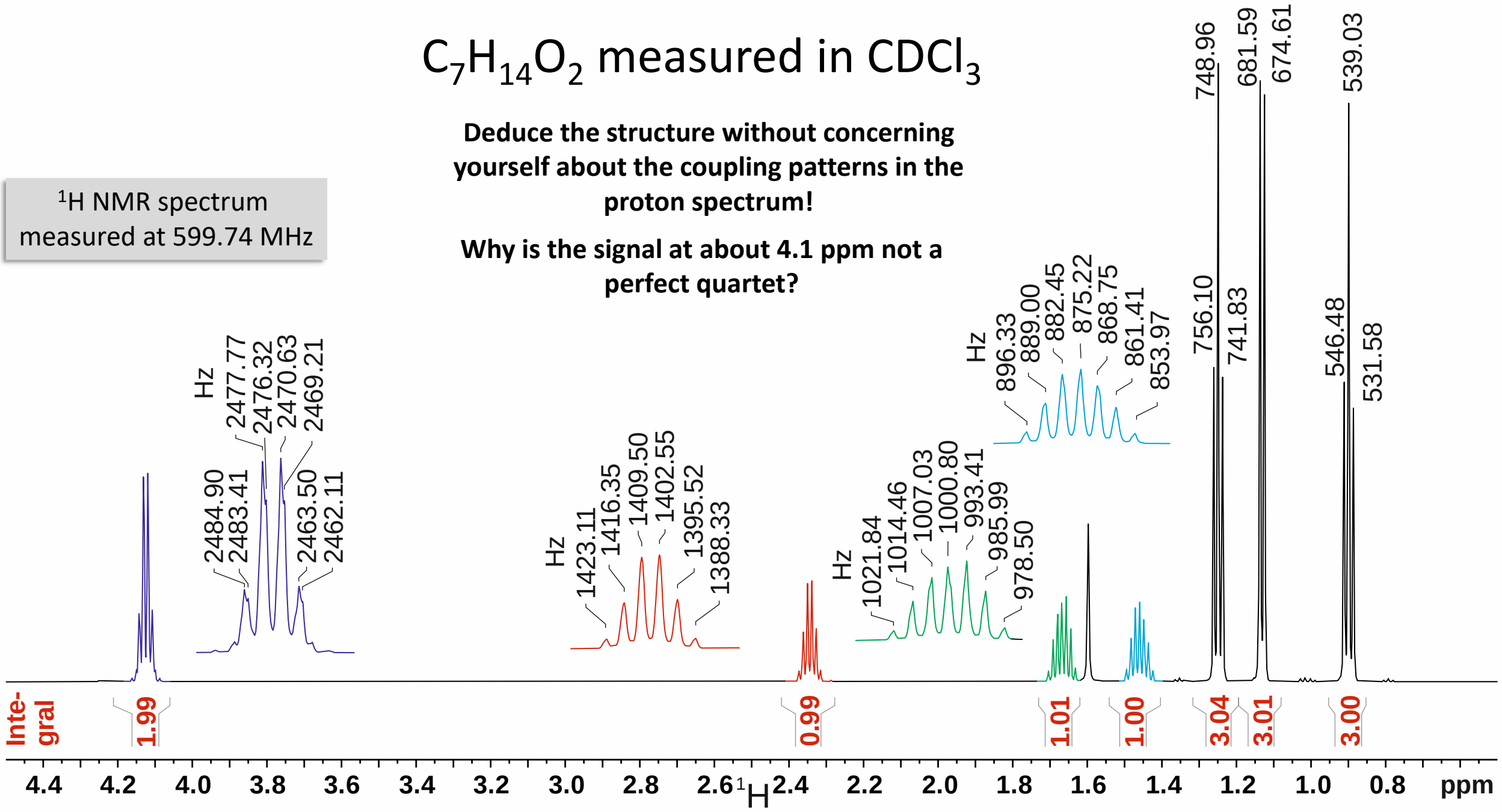



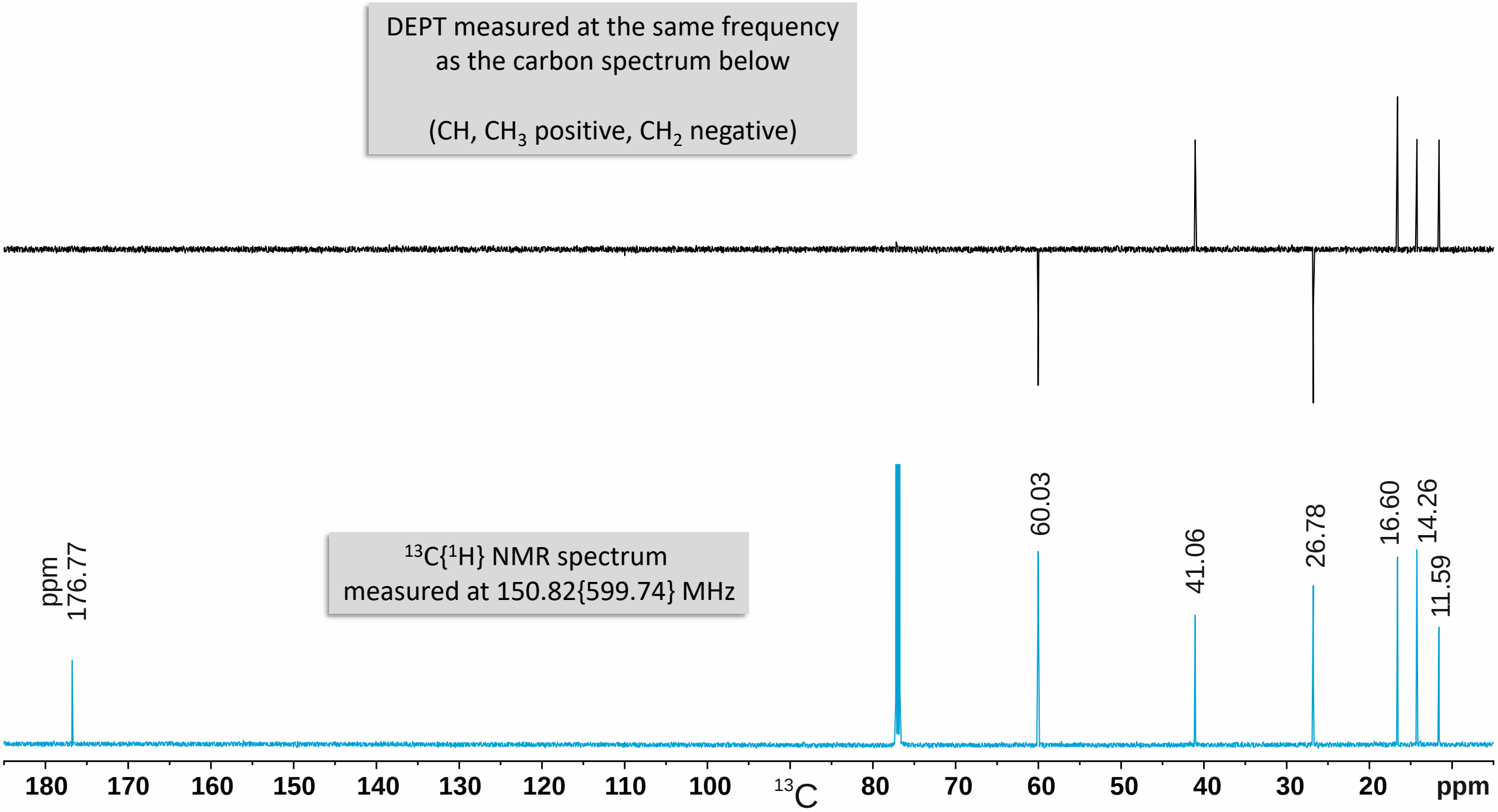
# $C_7H_{14}O_2$ measured in $CDCl_3$

**Deduce the structure without concerning yourself about the coupling patterns in the proton spectrum!**

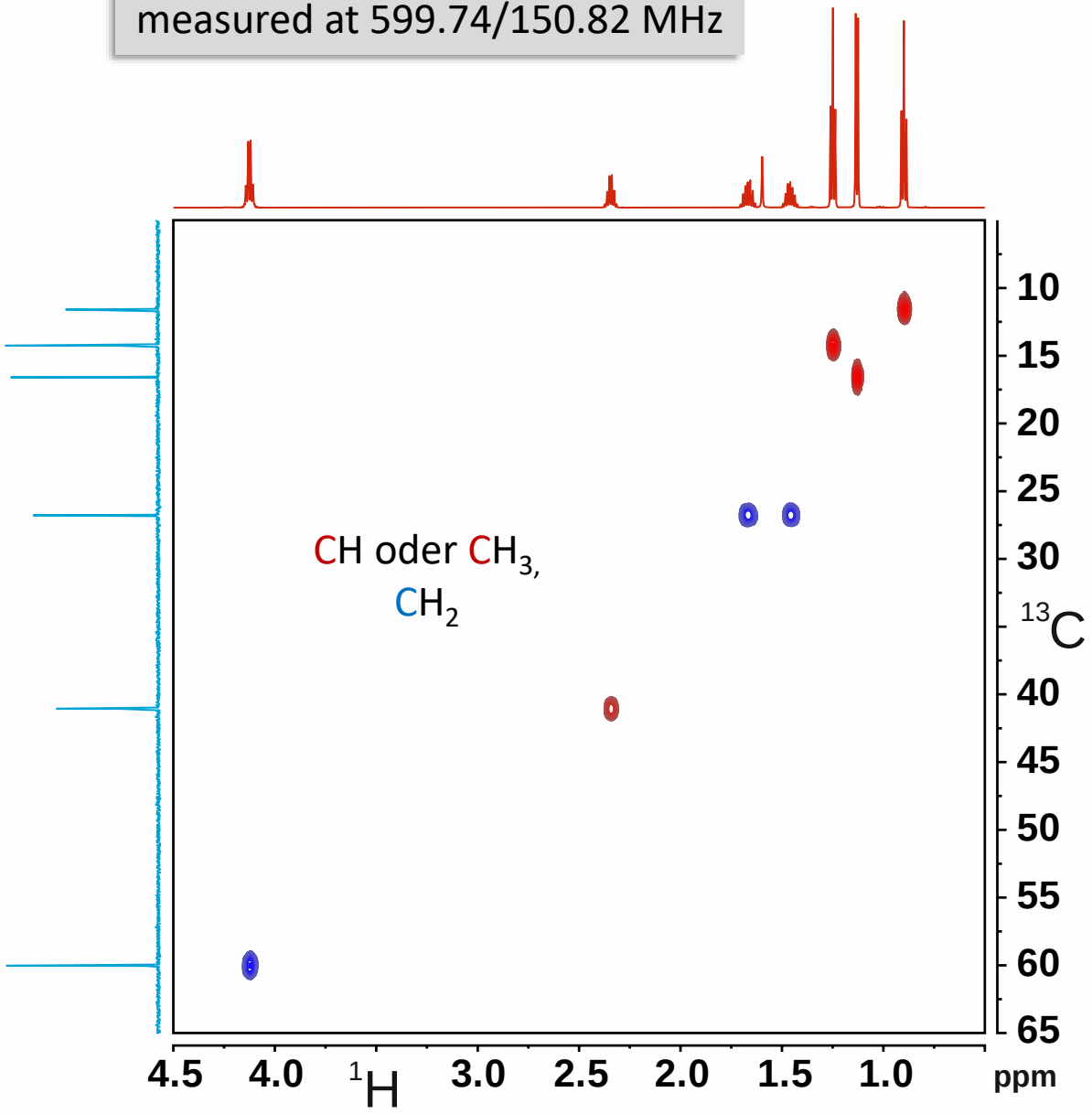
**Why is the signal at about 4.1 ppm not a perfect quartet?**

$^1$H NMR spectrum measured at 599.74 MHz

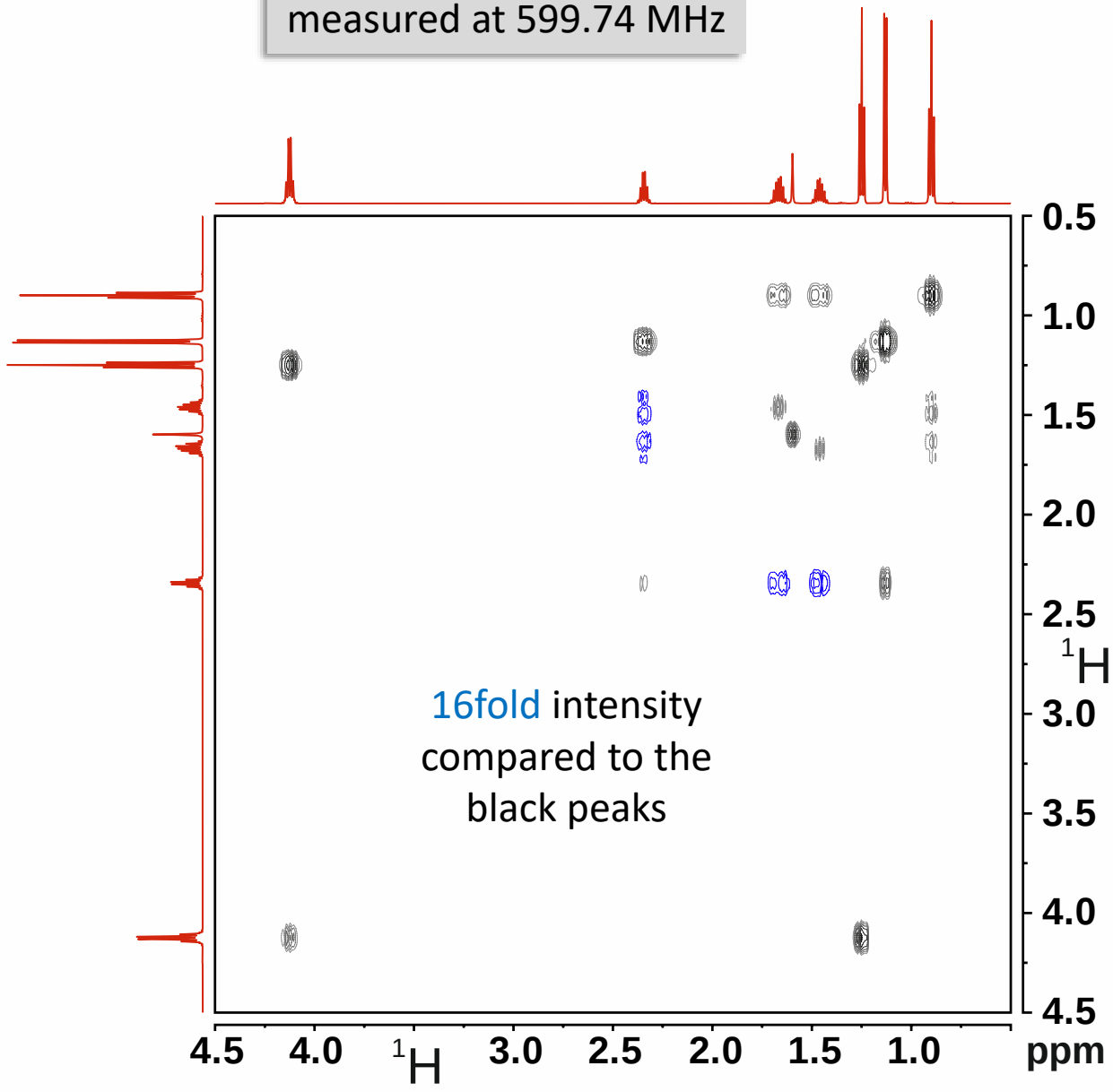



DEPT measured at the same frequency as the carbon spectrum below
(CH, CH3 positive, CH2 negative)
13C{1H} NMR spectrum measured at 150.82{599.74} MHz
ppm
176.77
60.03
41.06
26.78
16.60
14.26
11.59
180
170
160
150
140
130
120
110
100
13C
80
70
60
50
40
30
20
ppm

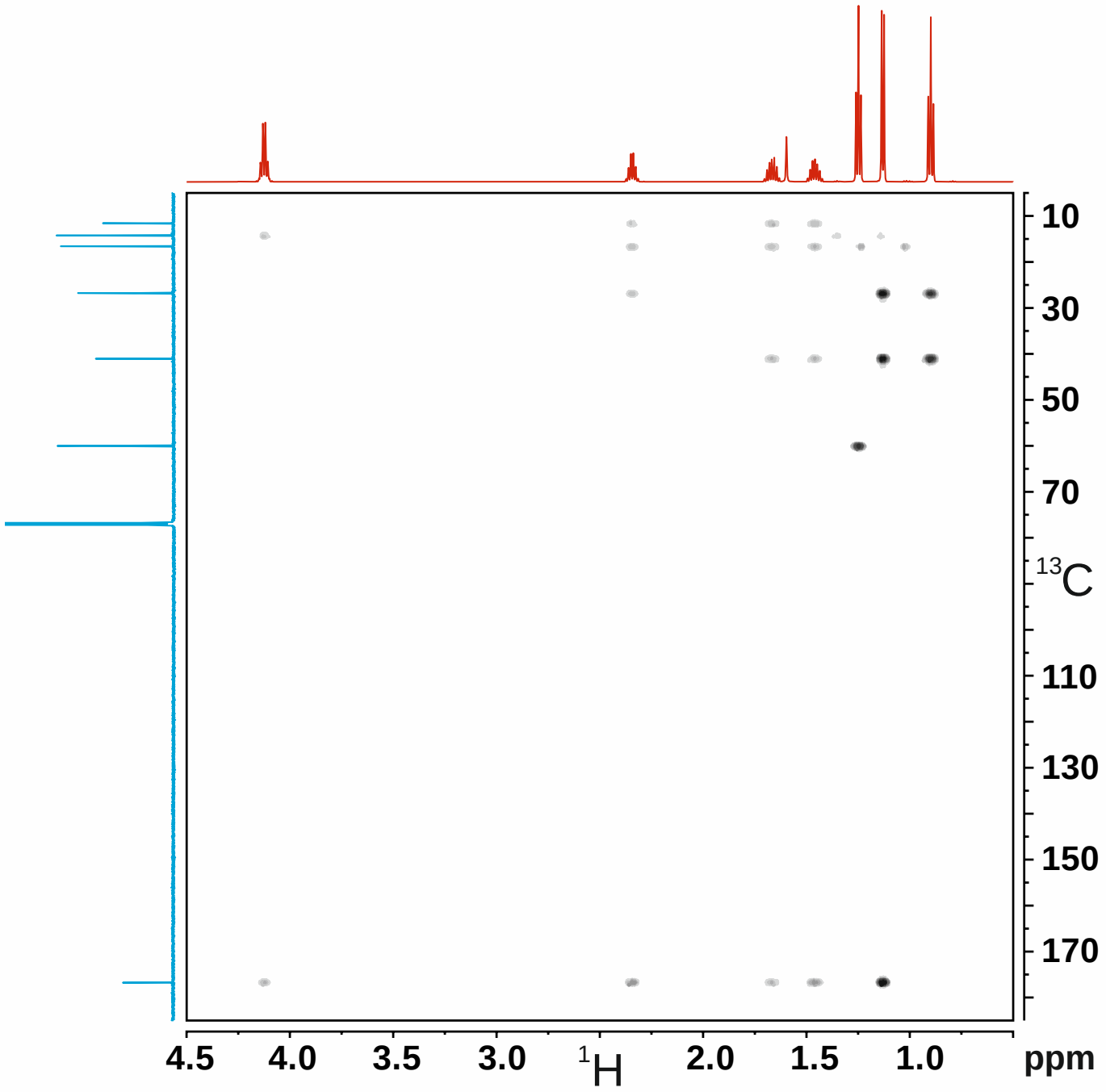
Multiplicity edited $^{1}H/^{13}C$ HSQC
measured at 599.74/150.82 MHz




$^{1}H/^{1}H$ COCY
measured at 599.74 MHz



$^{1}H/^{13}C$ HMBC
measured at 599.74/150.82 MHz

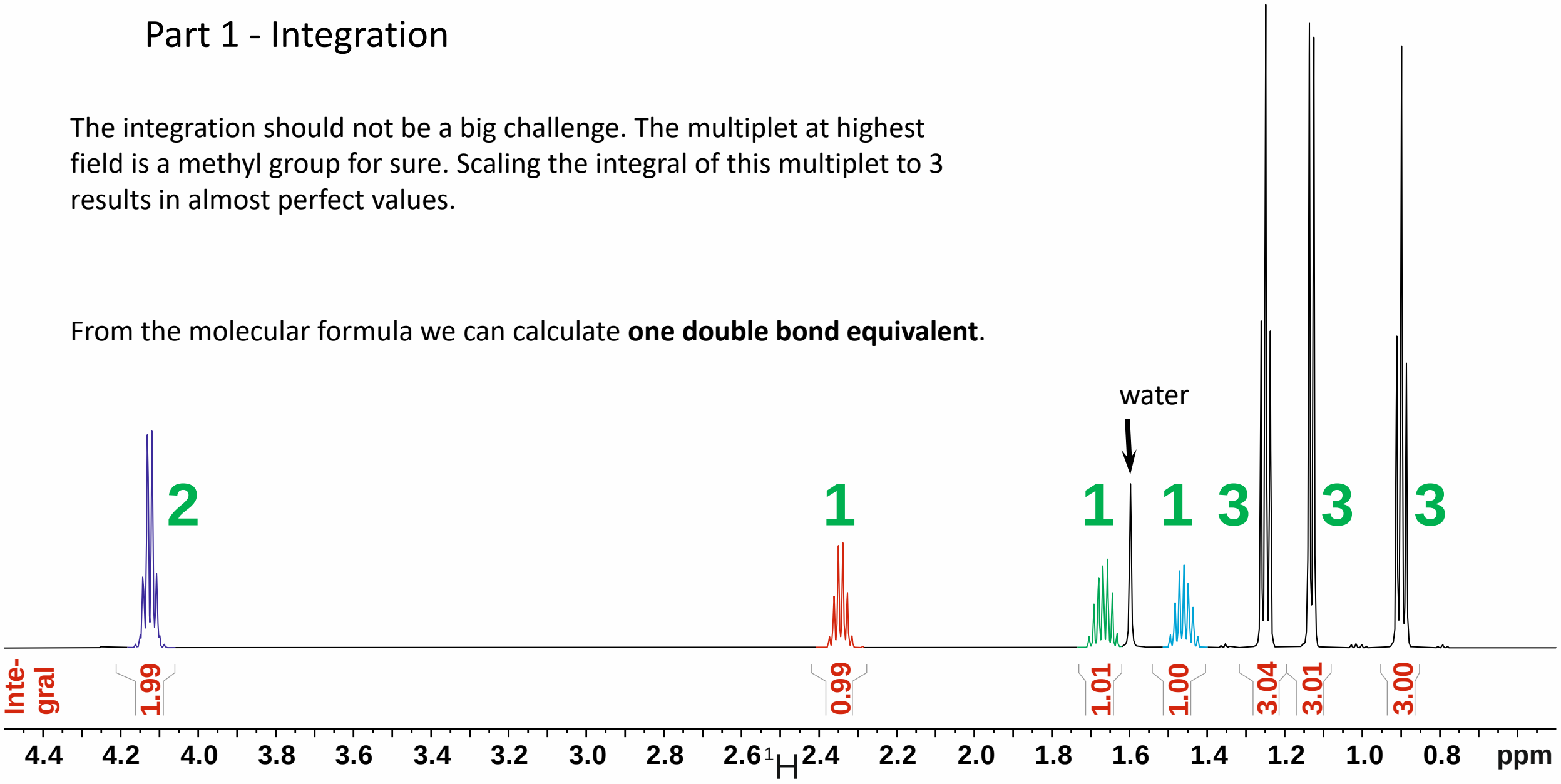


# Solution

## Part 1 - Integration

The integration should not be a big challenge. The multiplet at highest field is a methyl group for sure. Scaling the integral of this multiplet to 3 results in almost perfect values.

From the molecular formula we can calculate **one double bond equivalent**.



# Solution

## Part 2 – Building blocks

If available, the HSQC/HMQC is nearly always the best starting point to collect all or a large number of substructures as an unordered pile of building blocks.

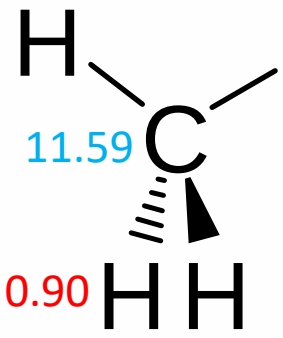
The integrals from the proton spectrum have just been determined, the chemical shifts of the carbon signals can be taken from the one-dimensional carbon spectrum.

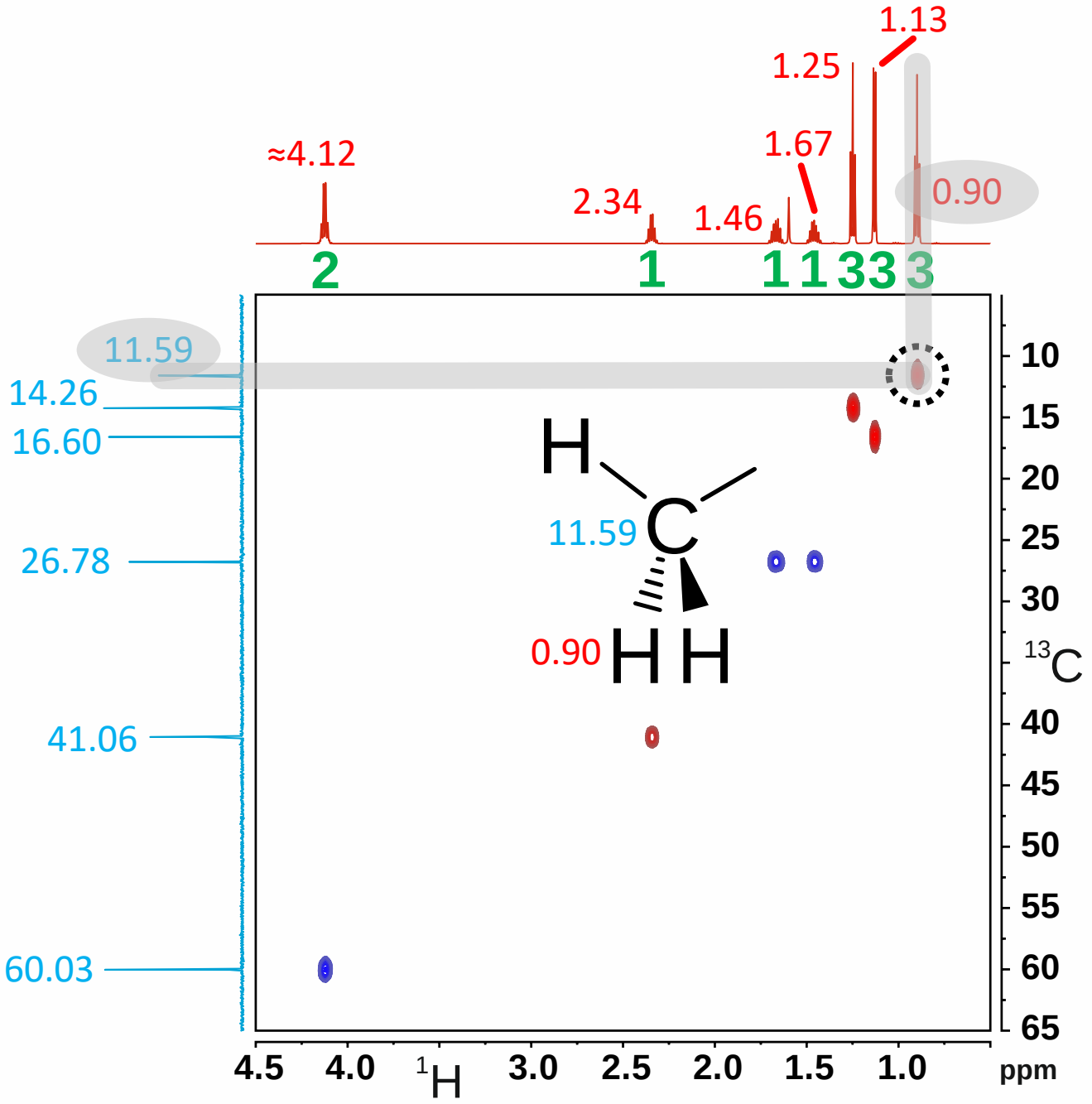
To get the chemical shifts of the proton multiplets, a little bit of first rules of arithmetic are required. An example for the low-field "quartet":
(2484.90 Hz + 2462.11 Hz/ ( 2 * 599.74 MHz)

# Solution

## Part 2 – Building blocks

The first building block is a methyl group.

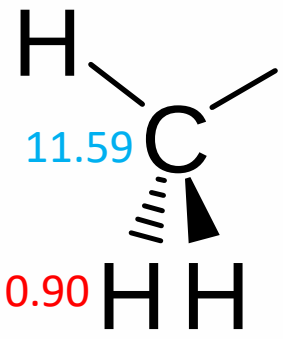


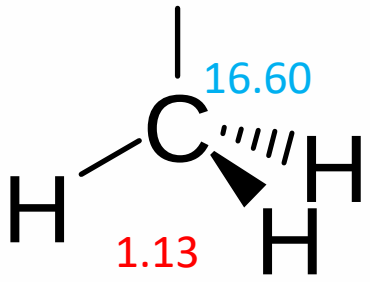



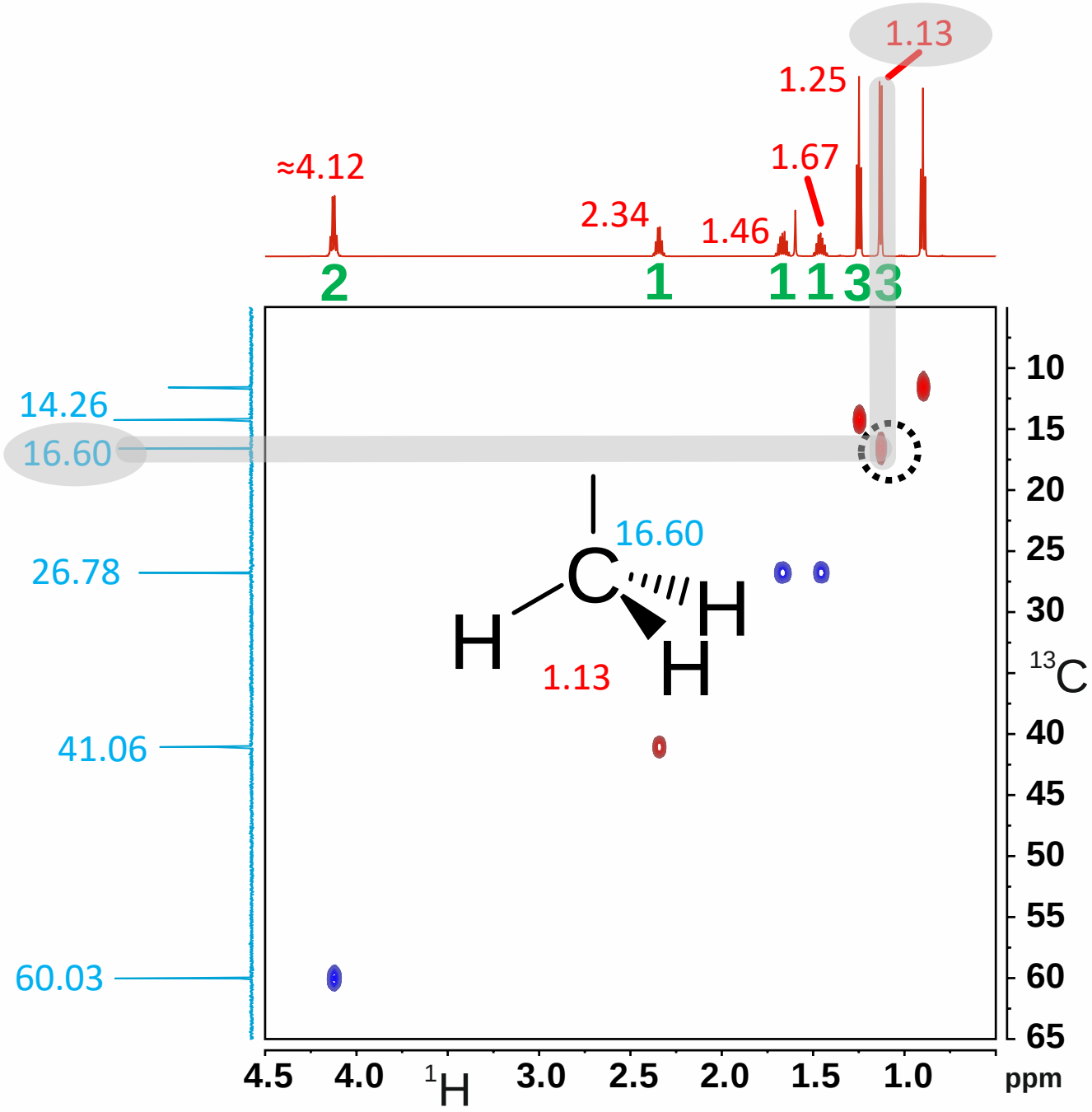
# Solution

## Part 2 – Building blocks

Next cross peak, next methyl group …



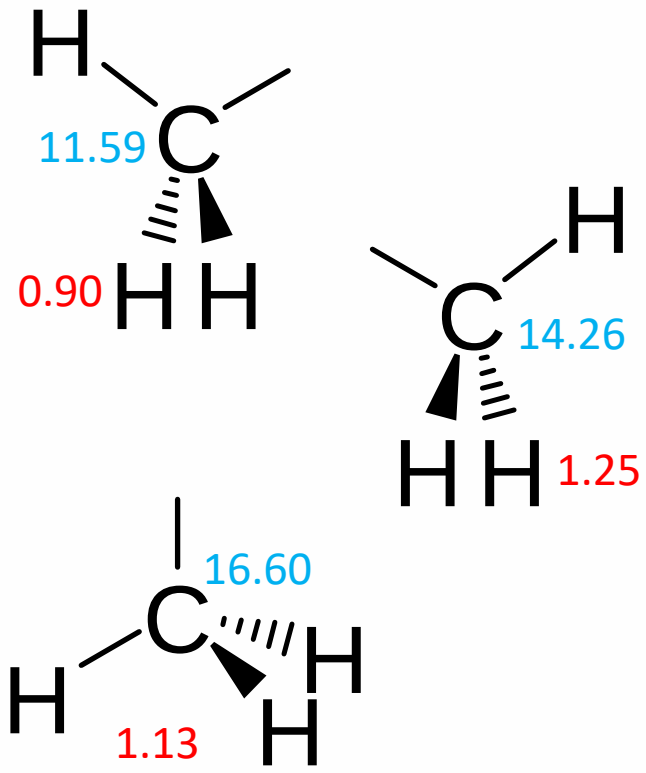



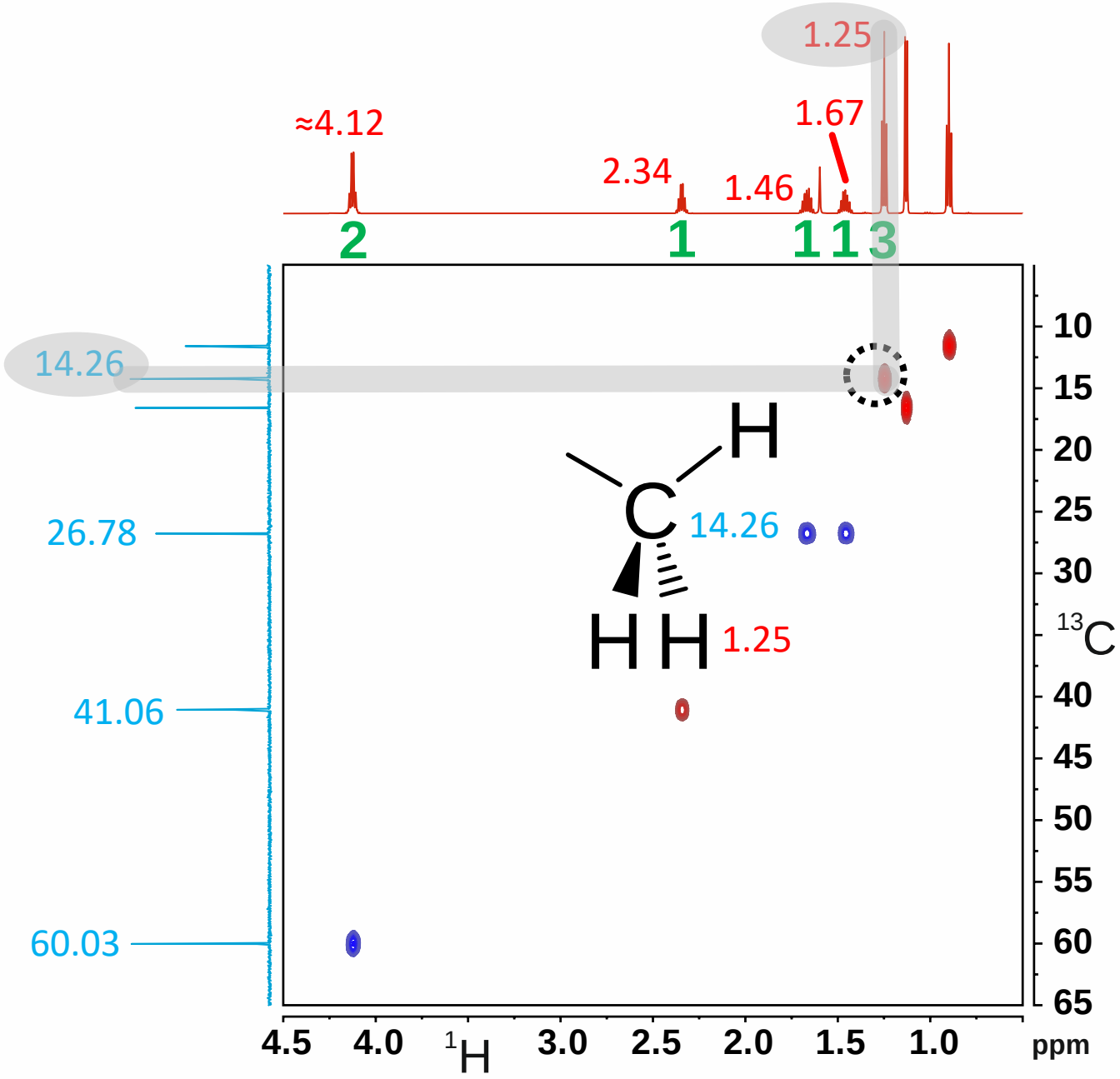



# Solution

## Part 2 – Building blocks

All good things come in threes - the third cross peak is also a methyl group…

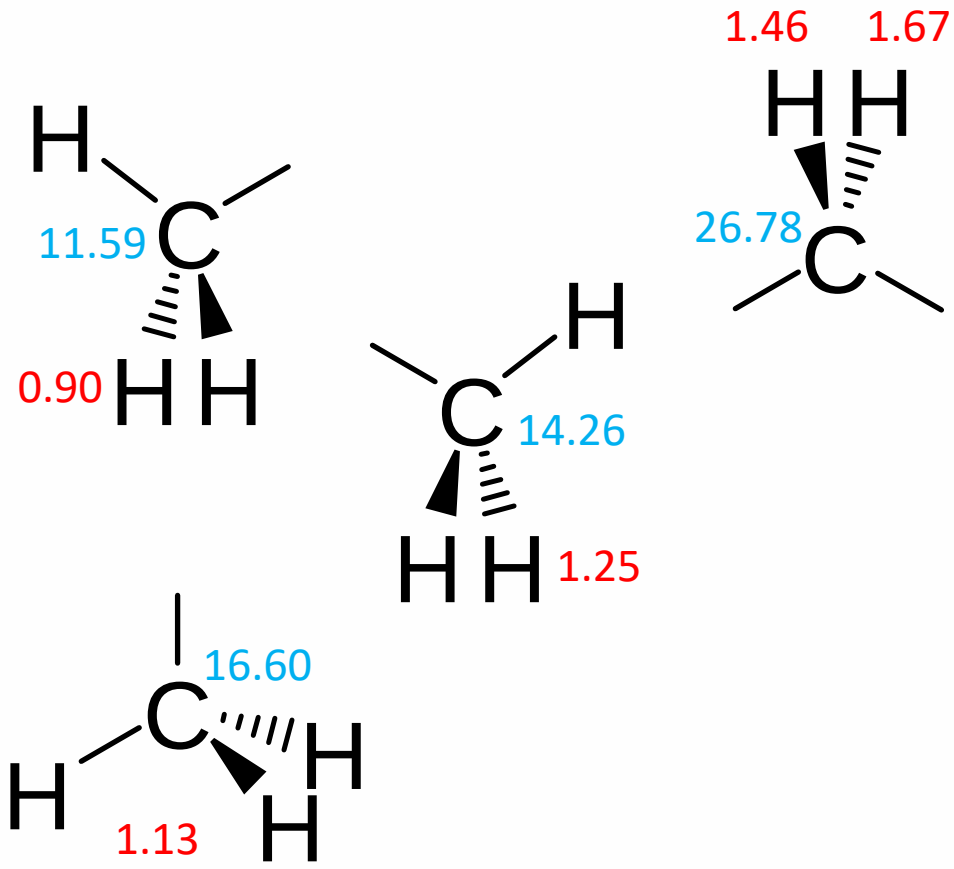


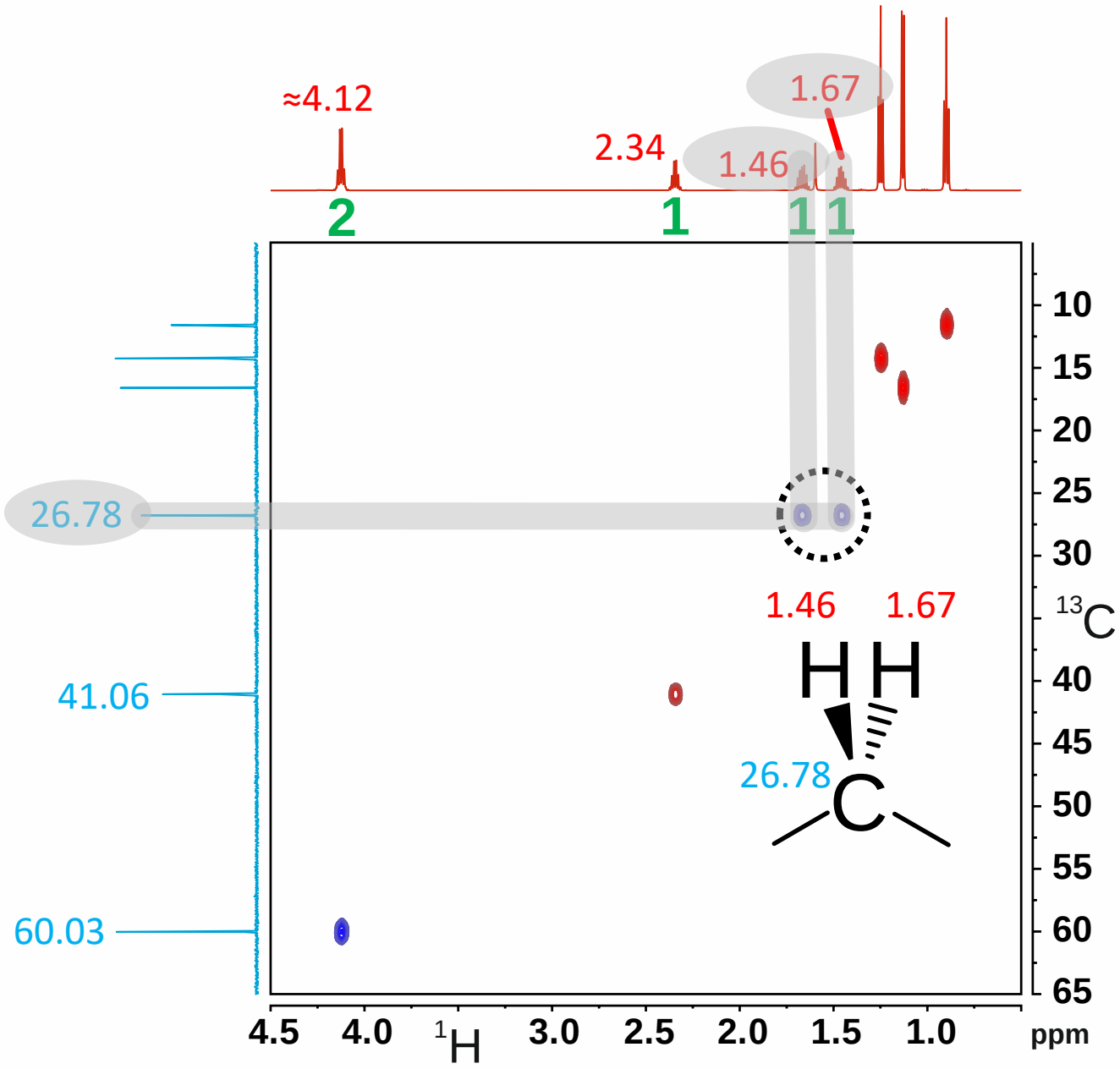



# Solution

## Part 2 – Building blocks

The sign in the HSQC reveals that the next building block must be a methylene group.

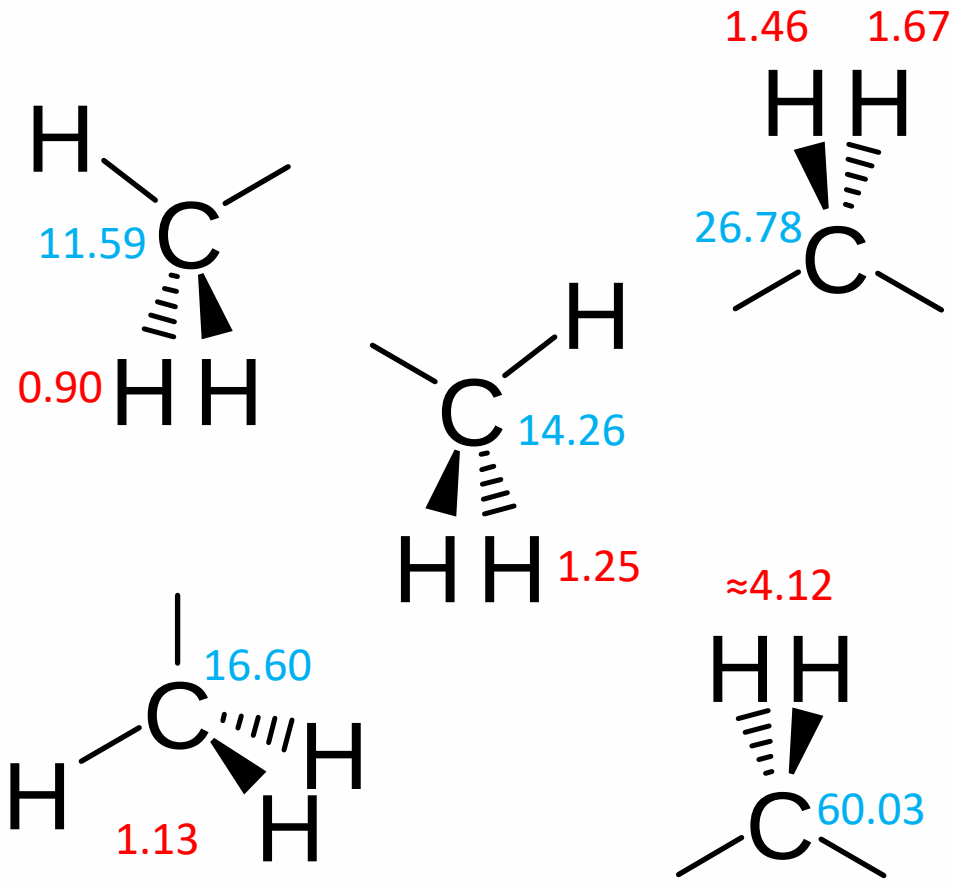


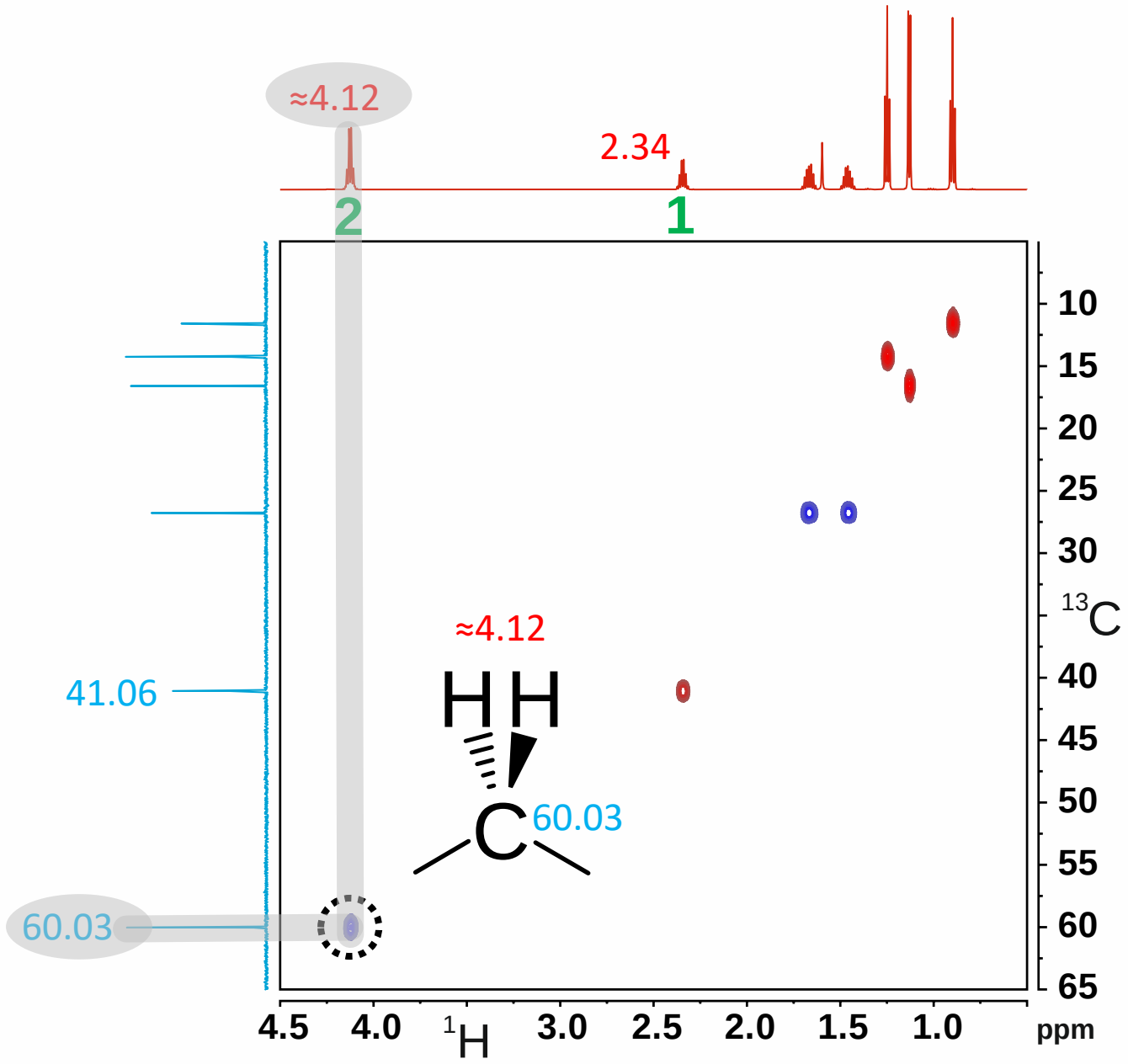



# Solution

## Part 2 – Building blocks

The sign of the lowest field cross peak in the HSQC indicates another methylene group.

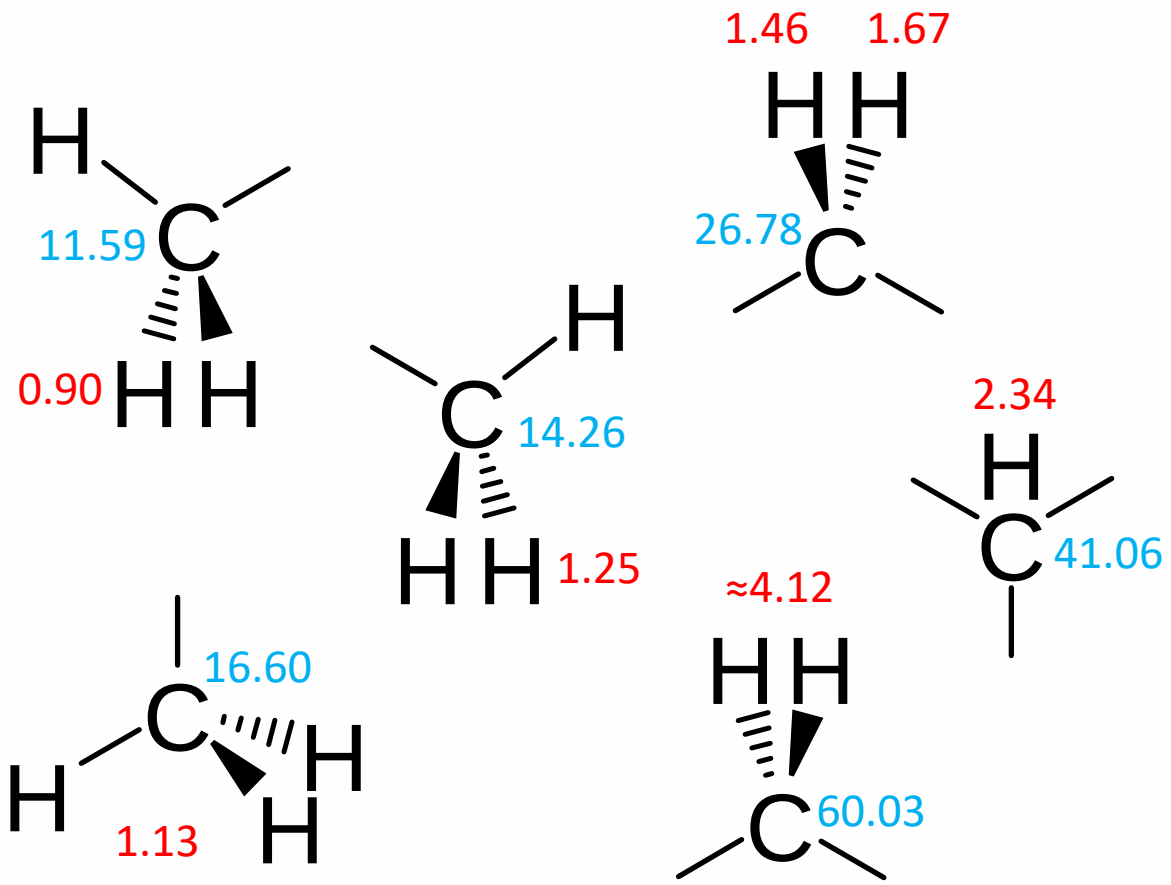


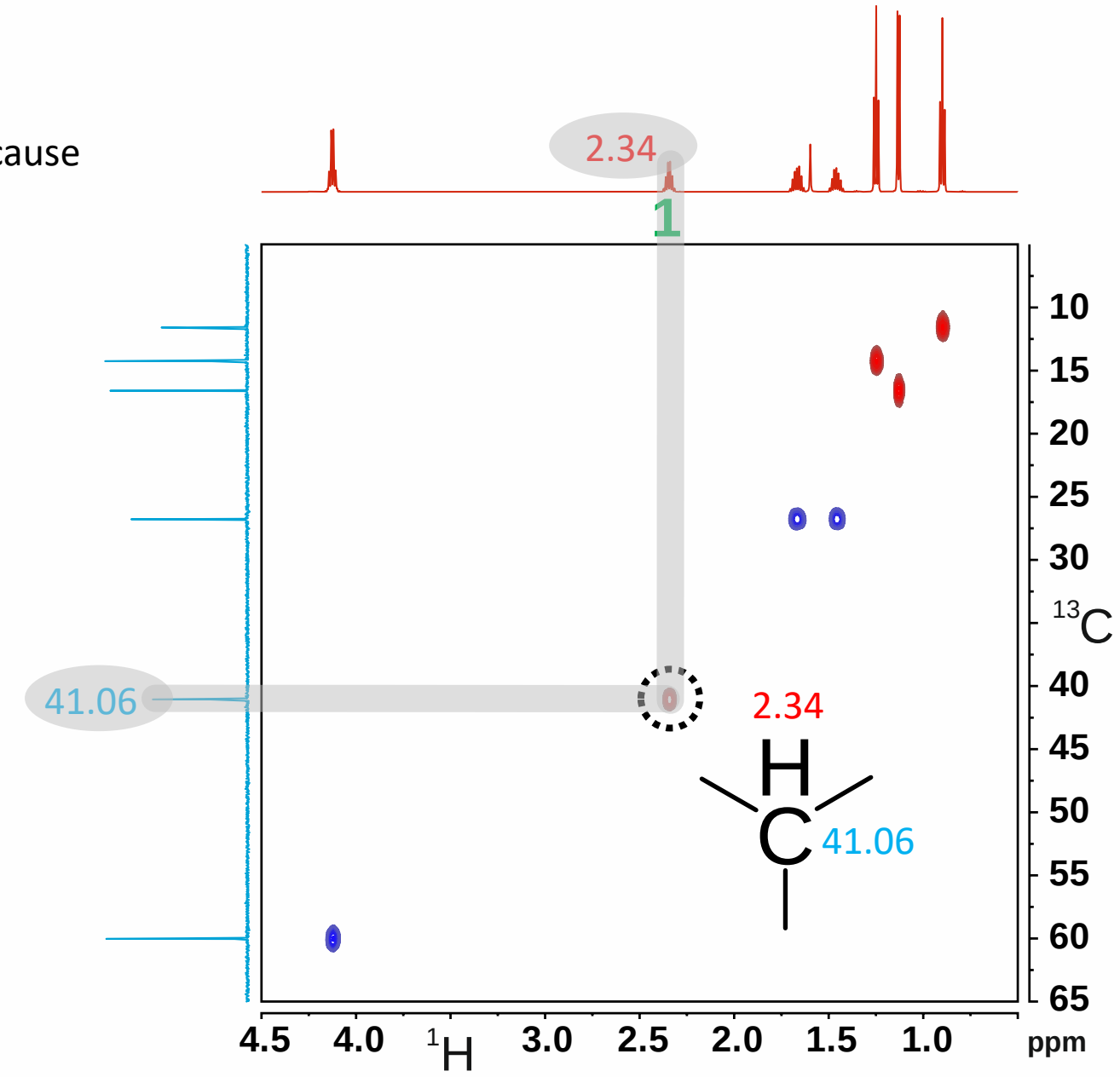



# Solution

## Part 2 – Building blocks

A methine group remains. sp hybridisation is ruled out because only one double bond equivalent is available.



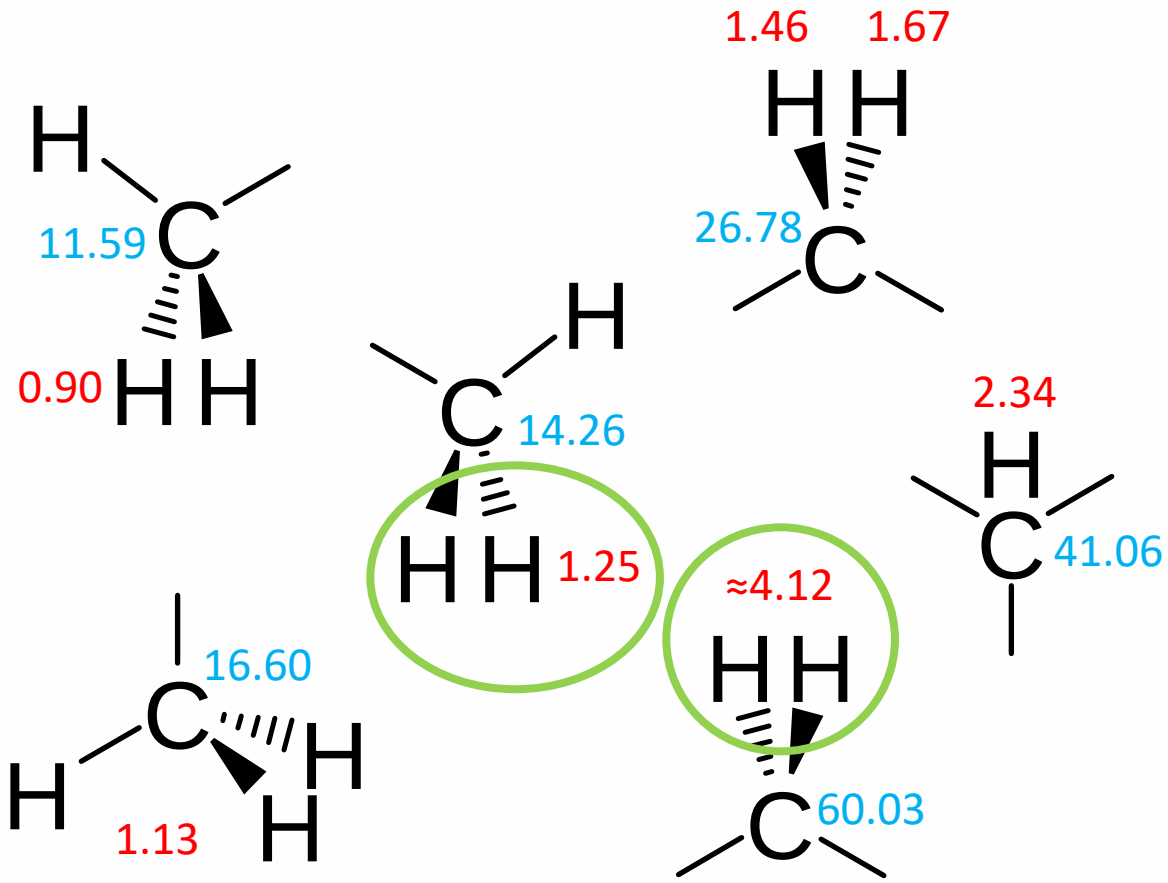



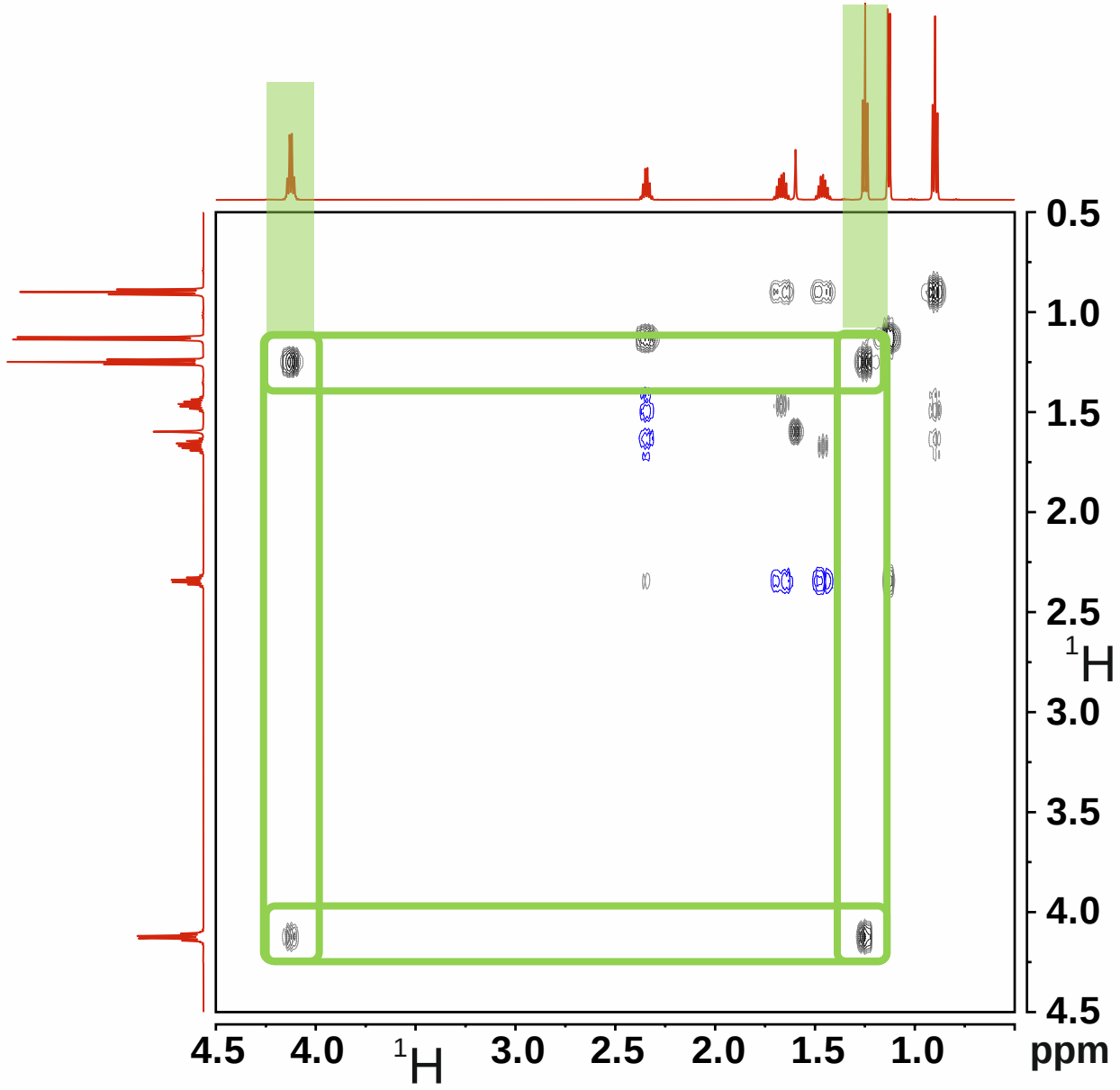
# Solution

## Part 3 - Substructures

There are two spin systems visible in the COSY.

One of them shows the connection of two fragments only.

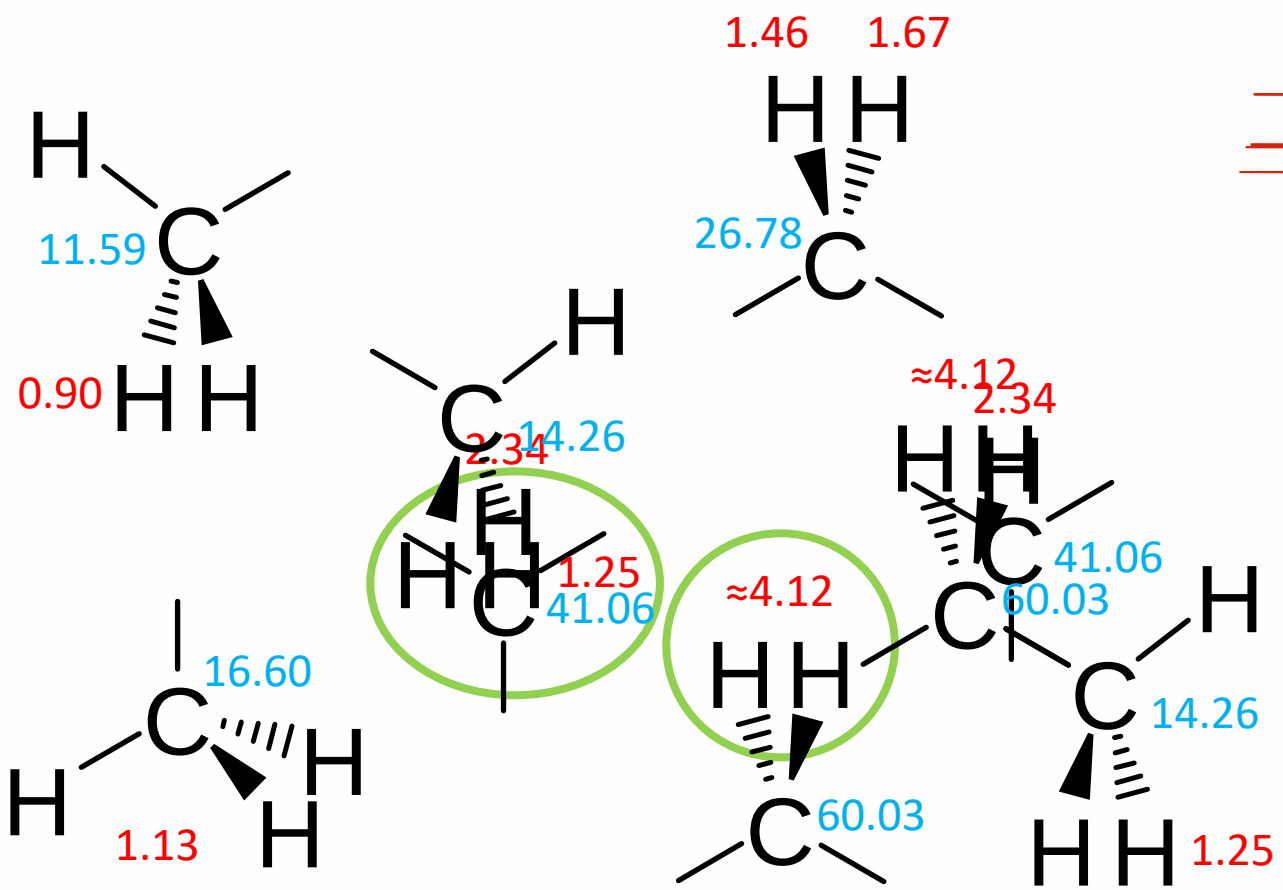


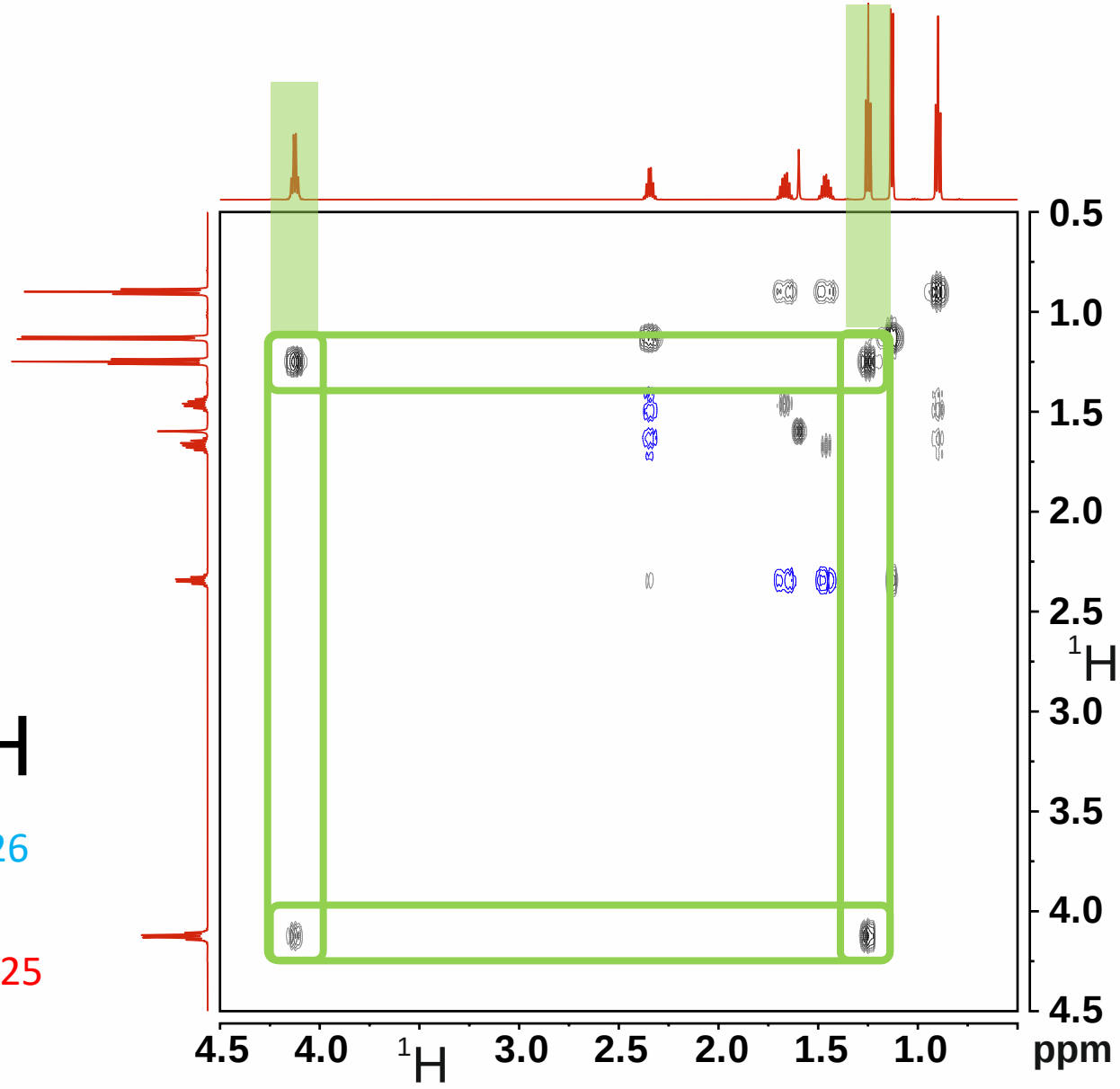



# Solution

## Part 3 - Substructures

These $CH_n$ fragments are neighbours.

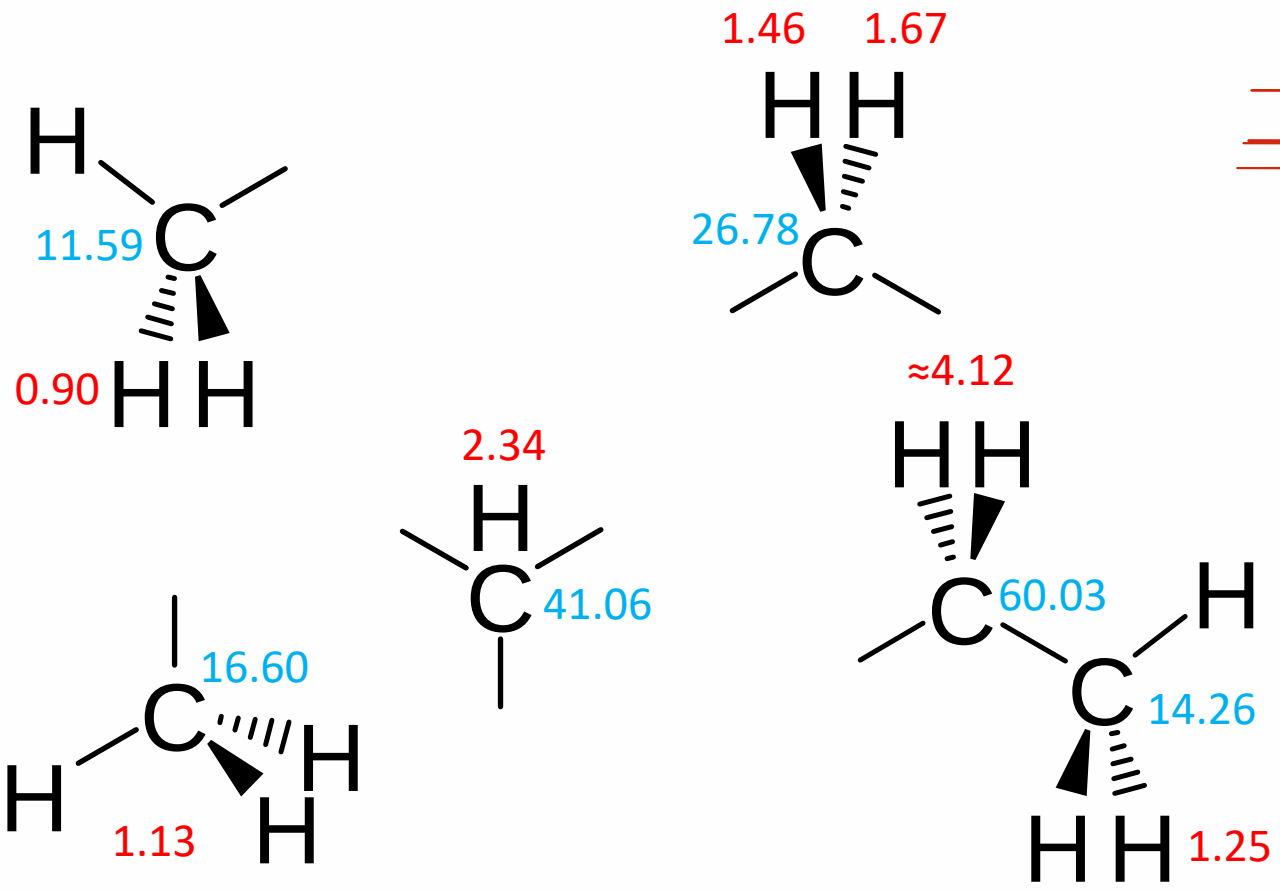


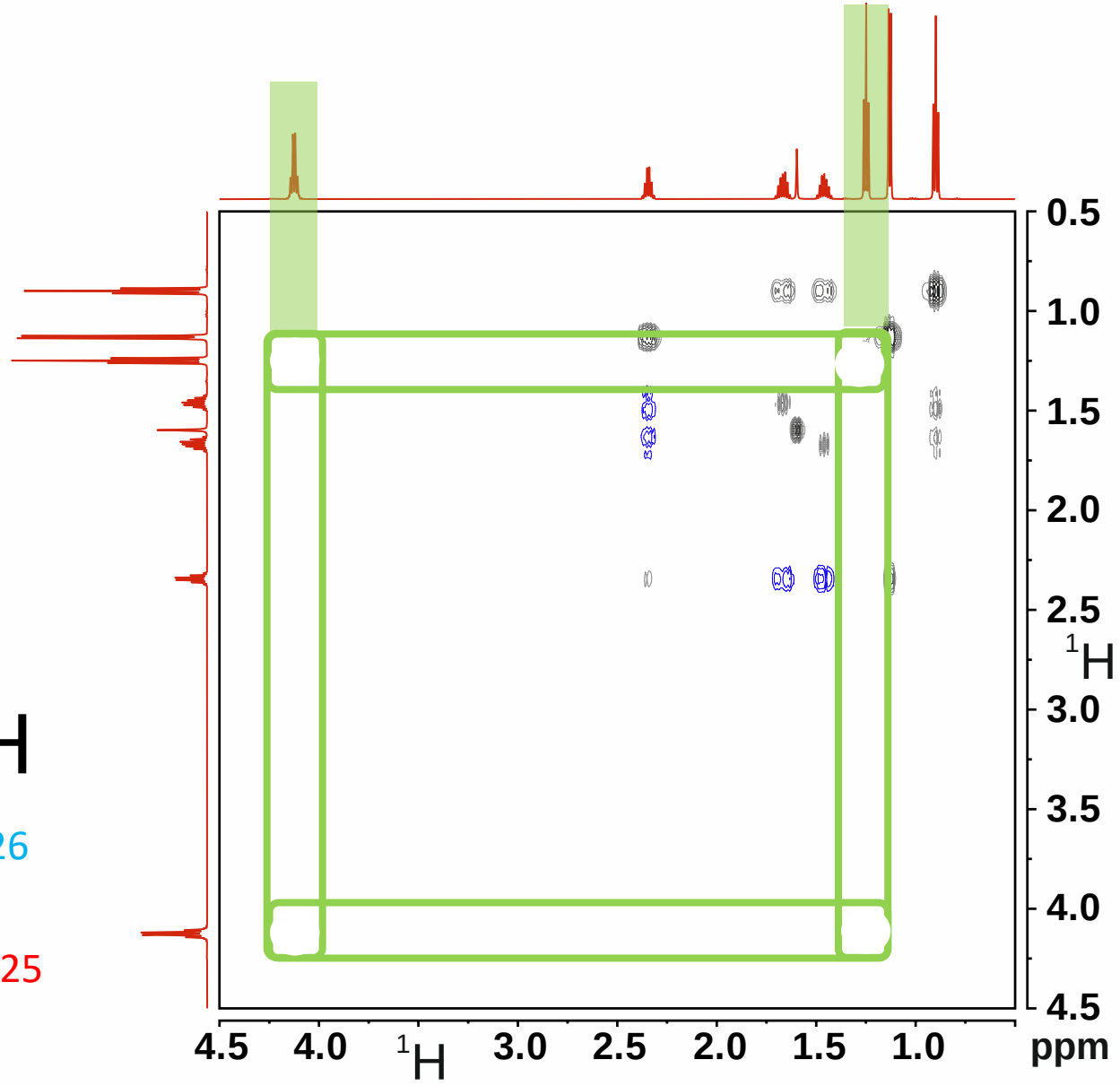



# Solution

## Part 3 - Substructures

For the sake of clarity let us delete all pieces of information from the COSY that are not necessary anymore.

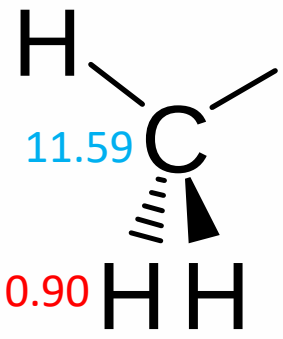


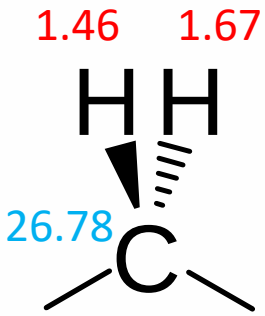



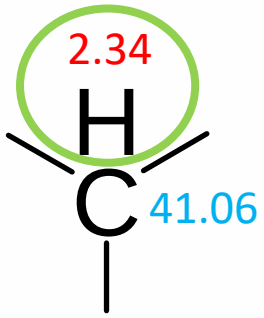
# Solution

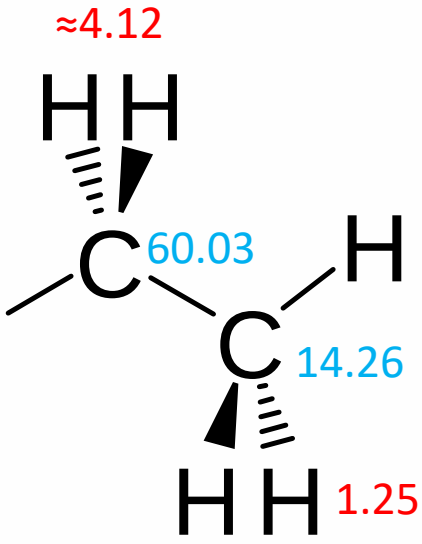
## Part 3 - Substructures

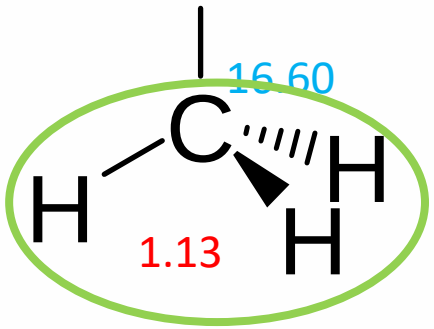
According to another cross peak one methyl and one methine group are neighbours.

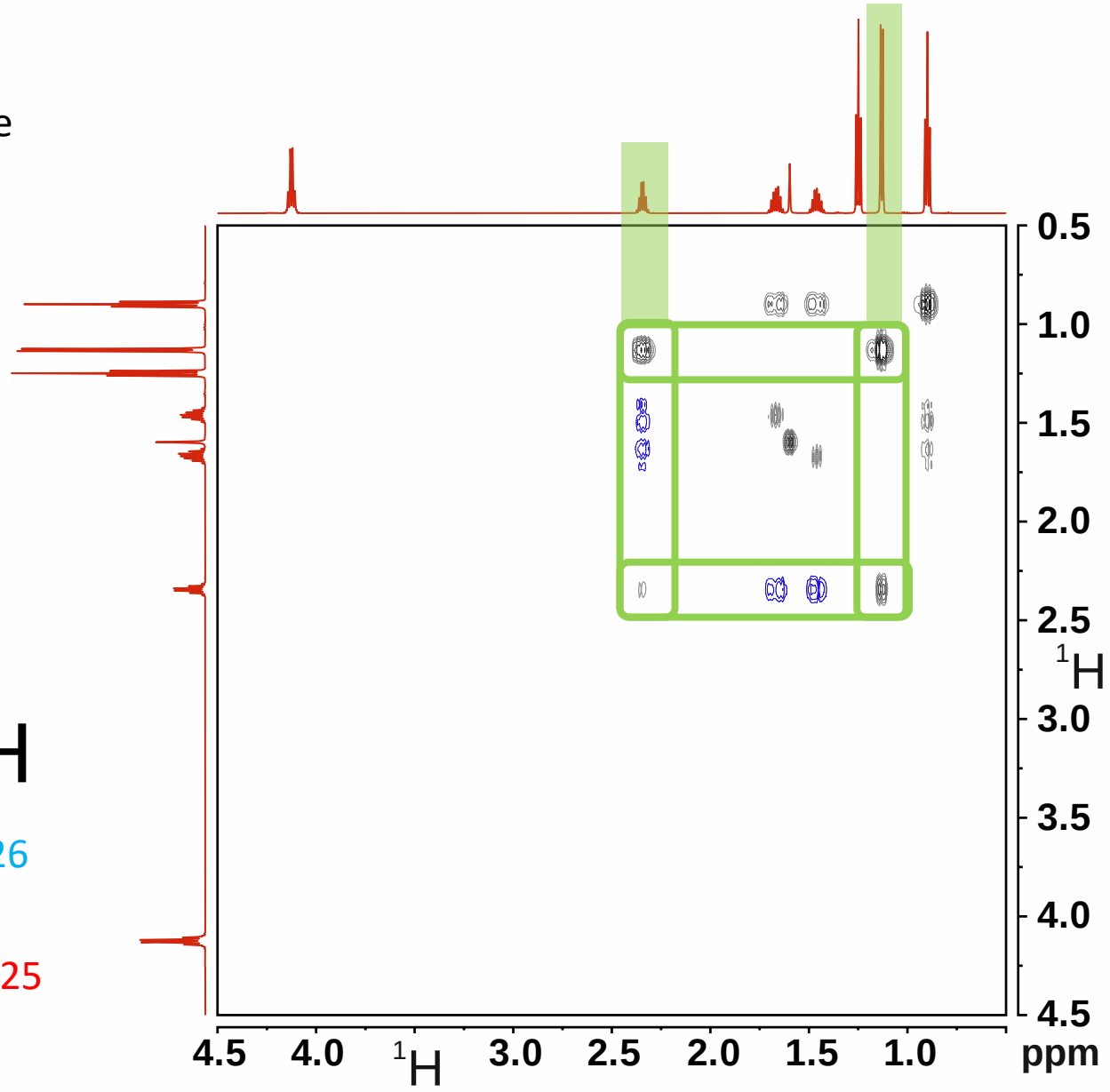


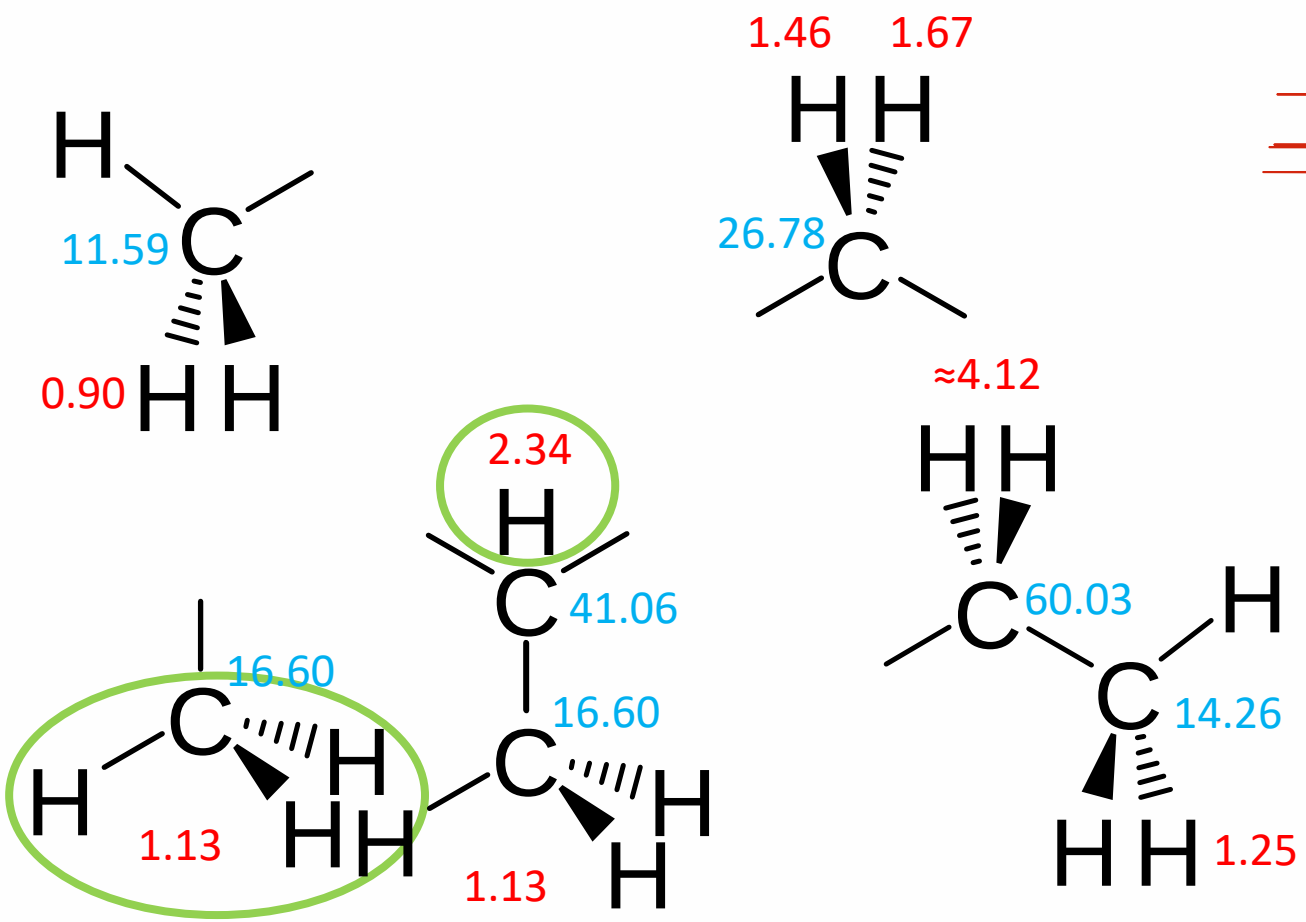



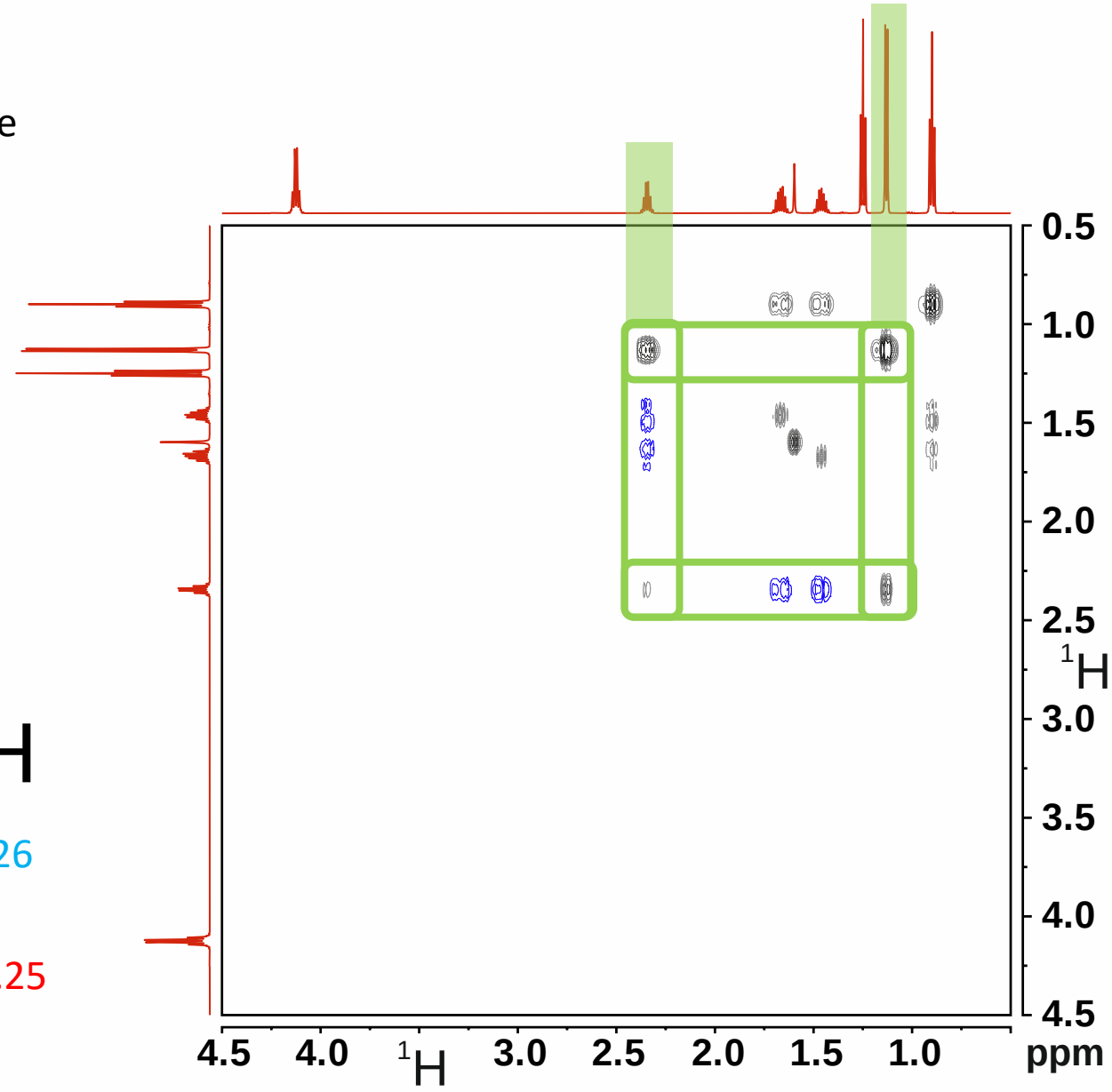



# Solution

## Part 3 - Substructures

According to another cross peak one methyl and one methine group are neighbours.

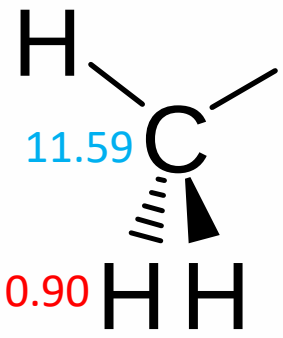


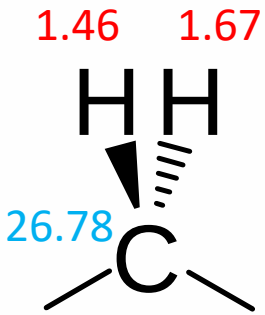



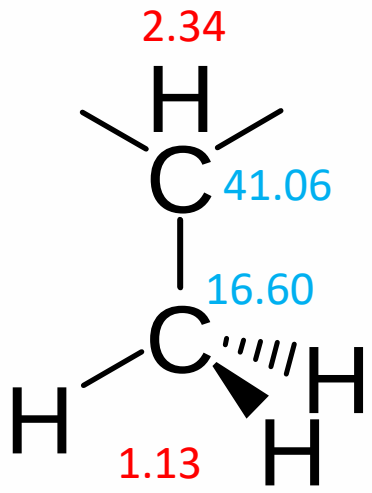
# Solution

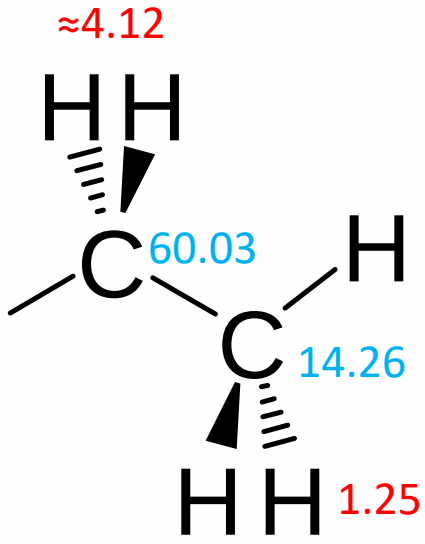
## Part 3 - Substructures

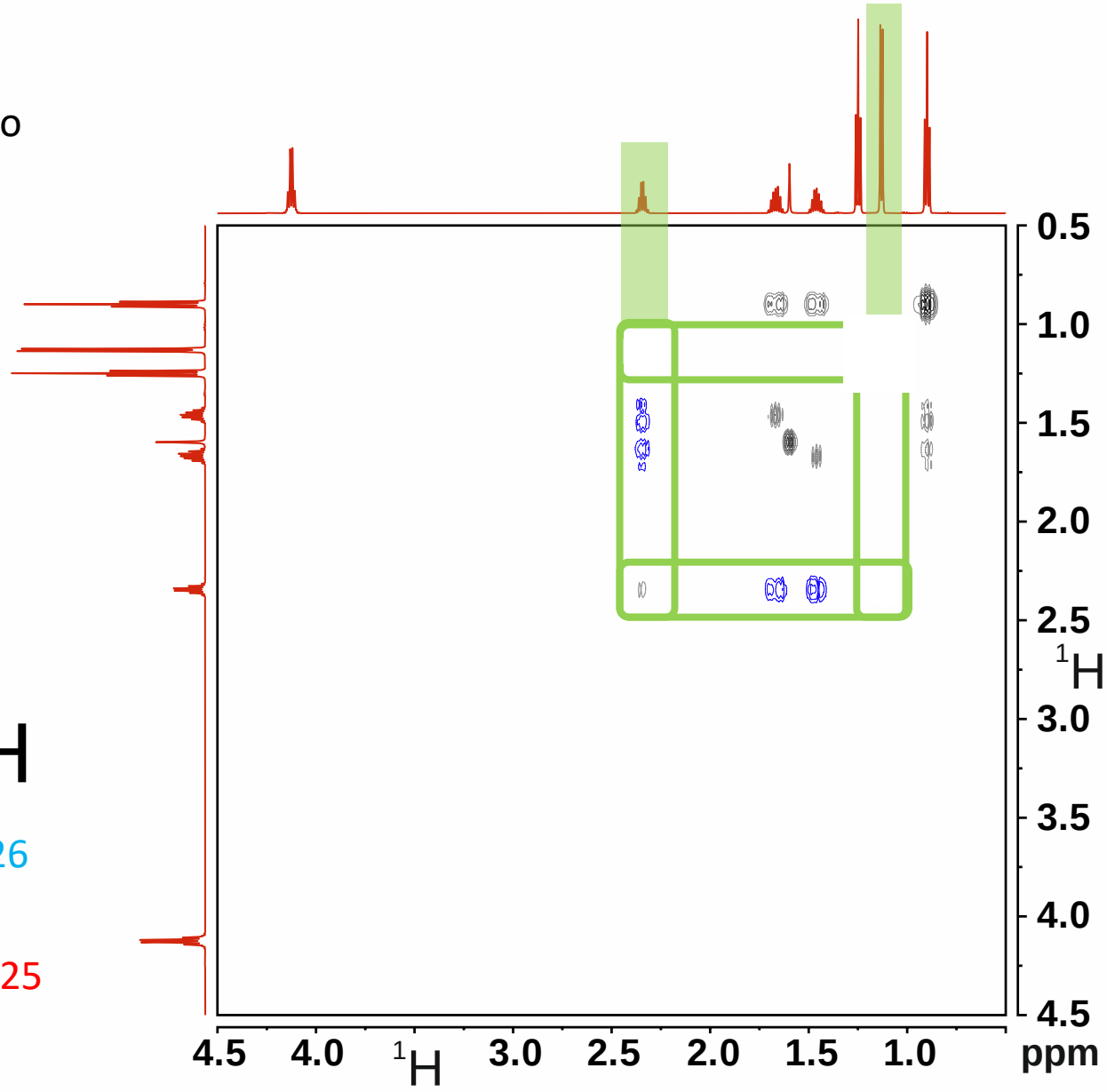
In the interest of clarity, we again remove all peaks that are no longer needed.



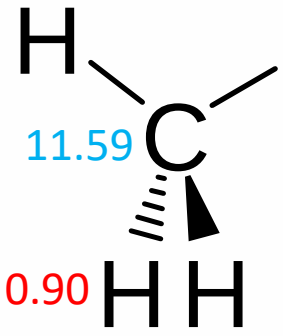



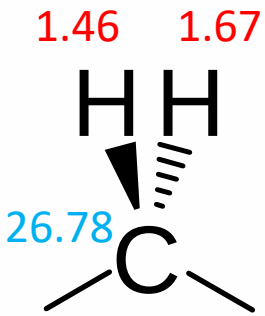



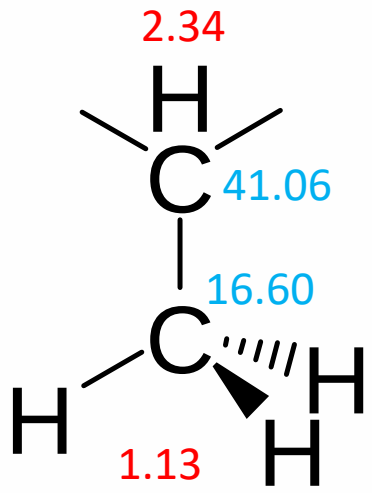
# Solution

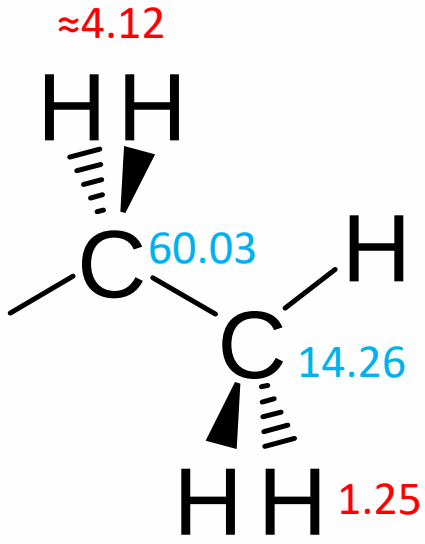
## Part 3 - Substructures

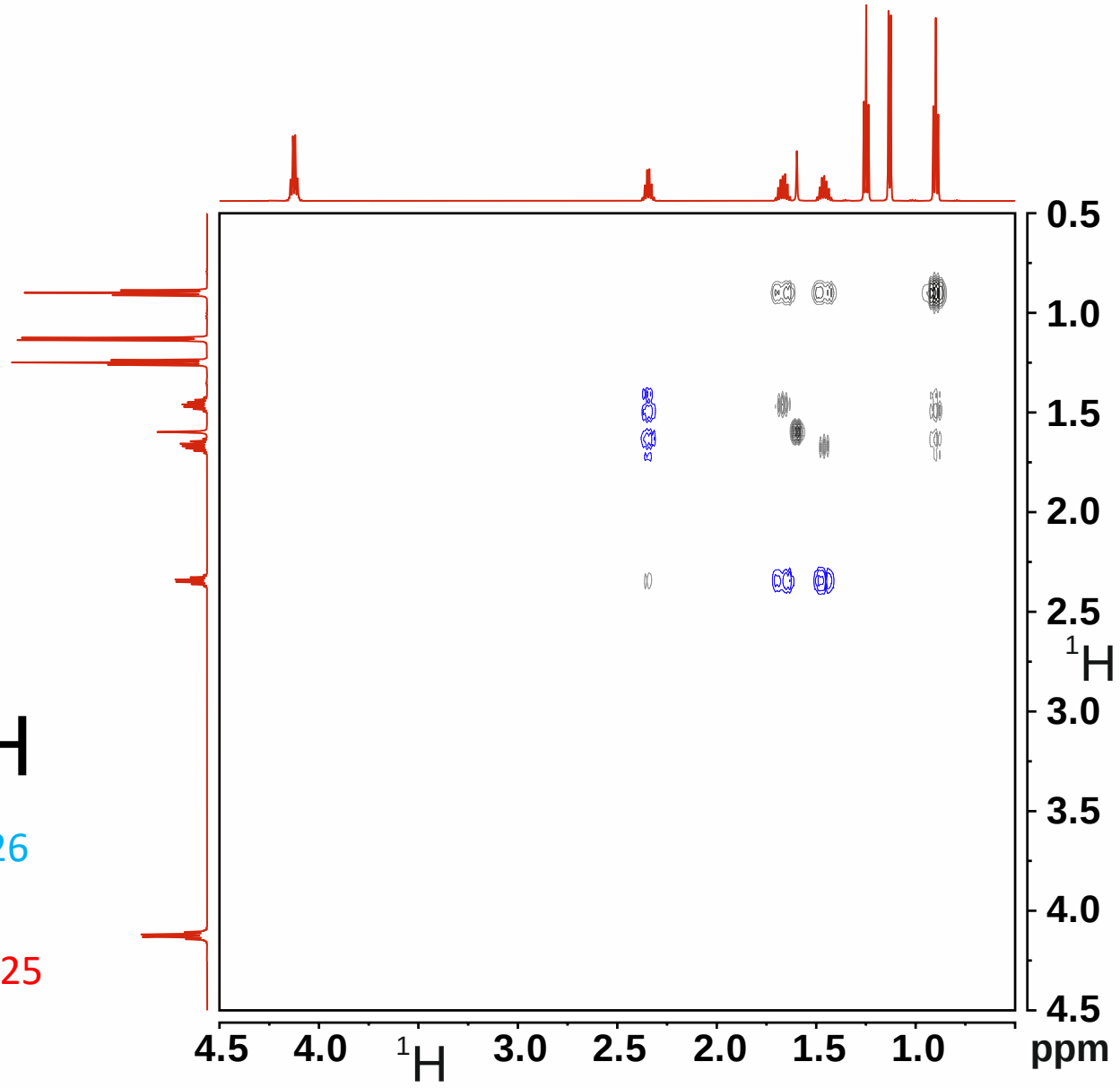
Two protons with the chemicals shifts of 1.46 and 1.67 ppm belong to the same $CH_n$ fragment.



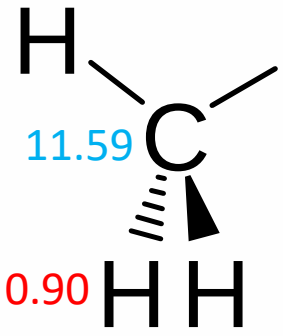



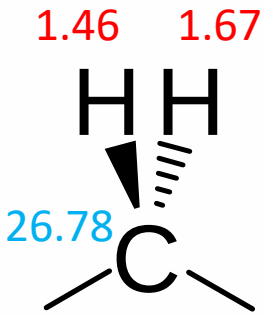



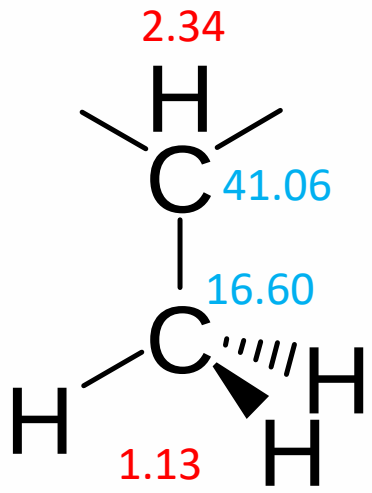
# Solution

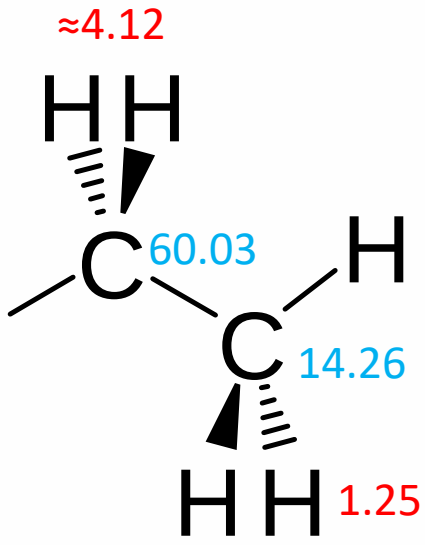
## Part 3 - Substructures

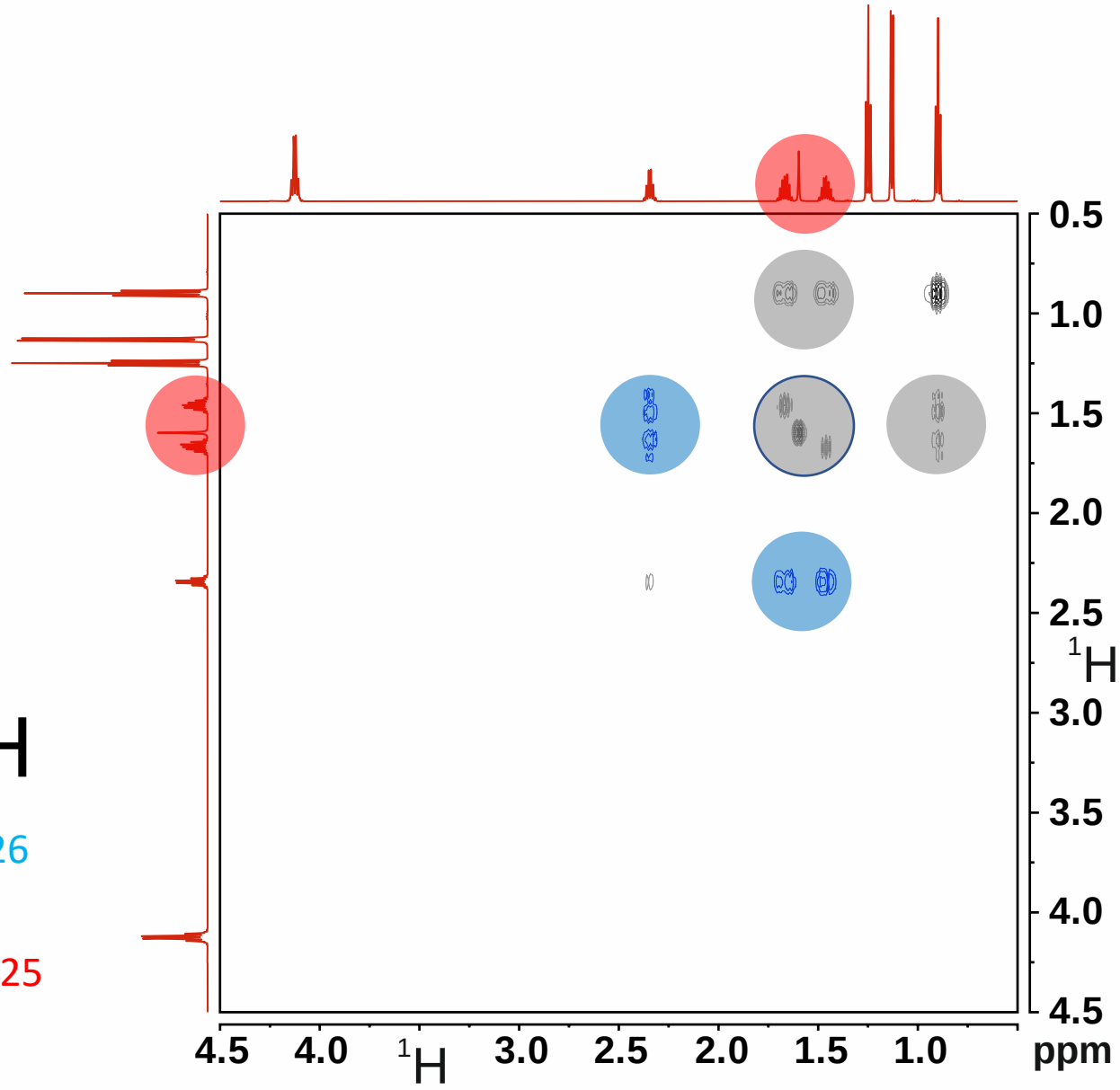
It simplifies our work to handle both their diagonal and cross peaks as a single block.



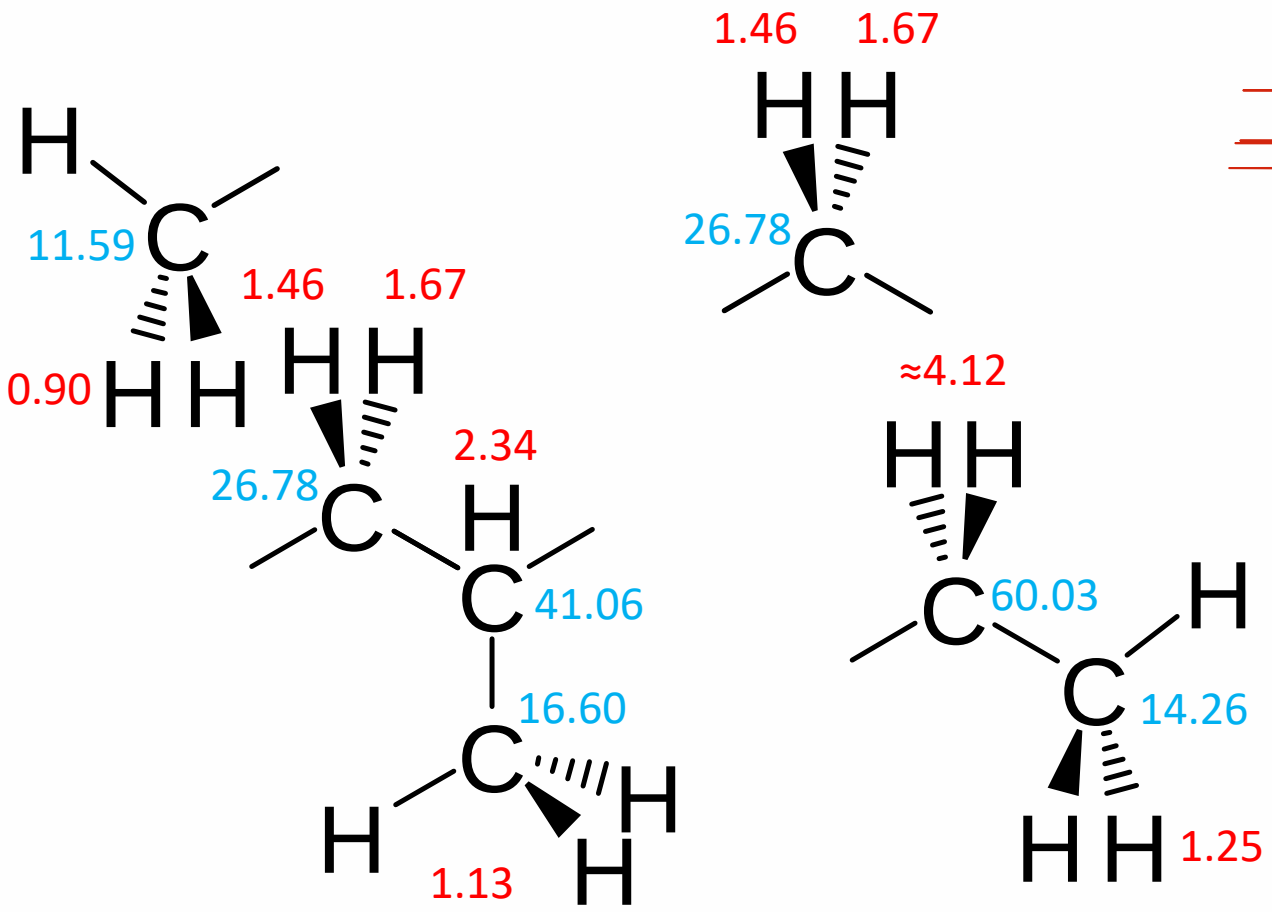



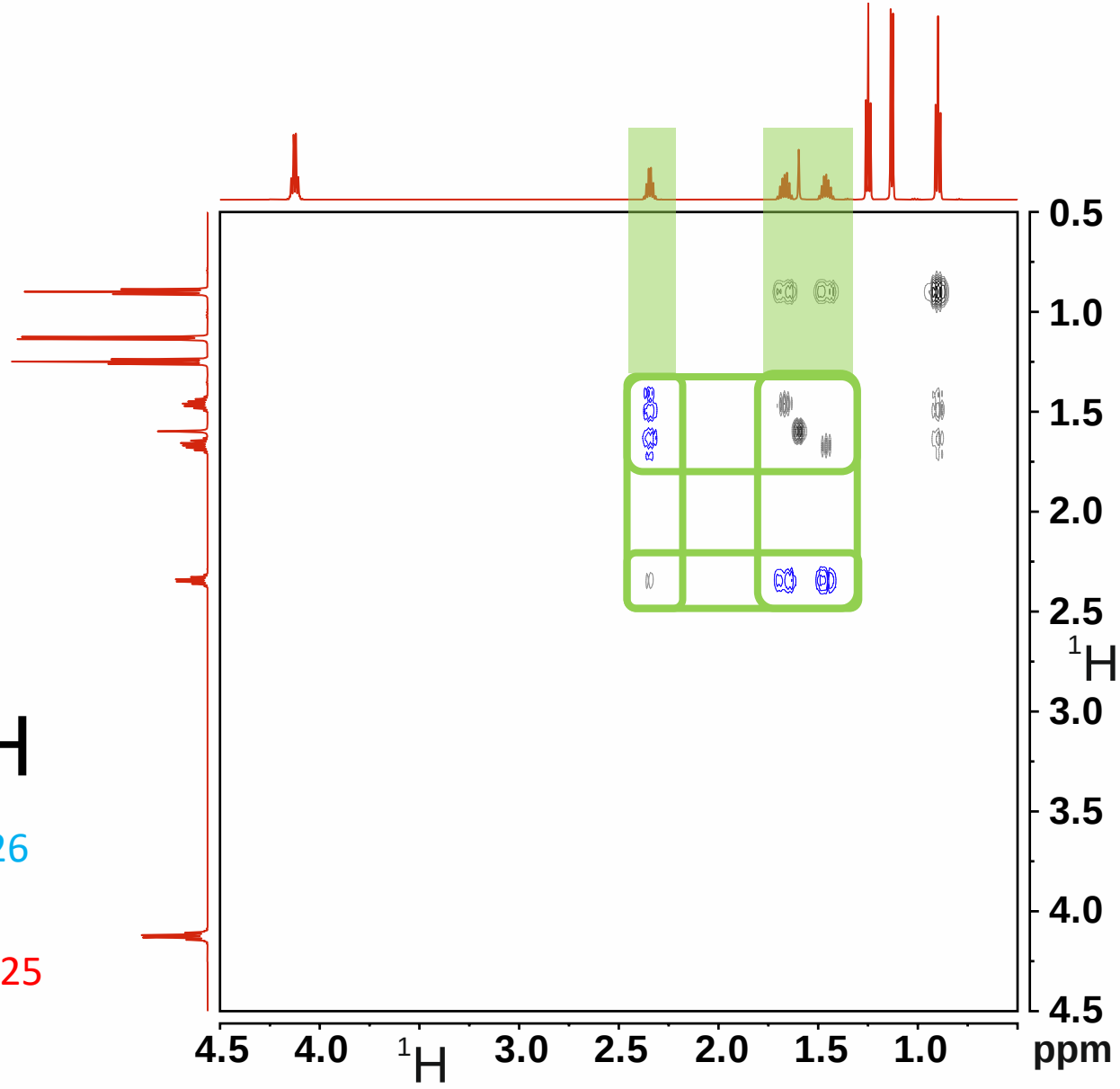



# Solution

## Part 3 - Substructures

The first „combined“ cross peak shows adjacency between a methine and a methylene group.

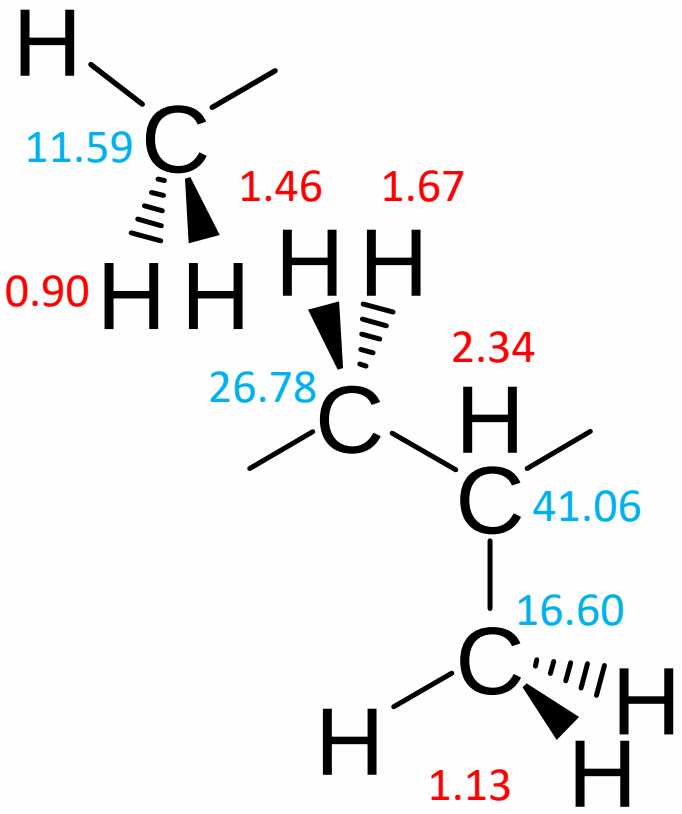


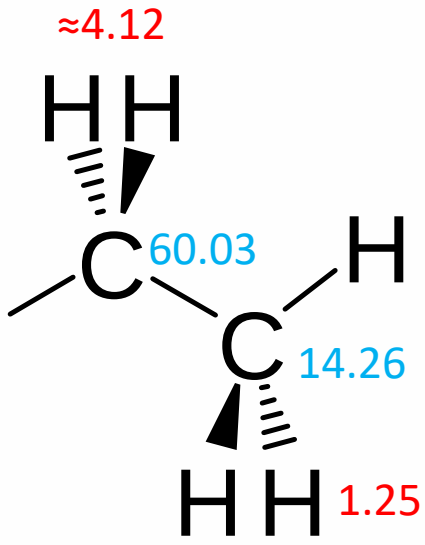



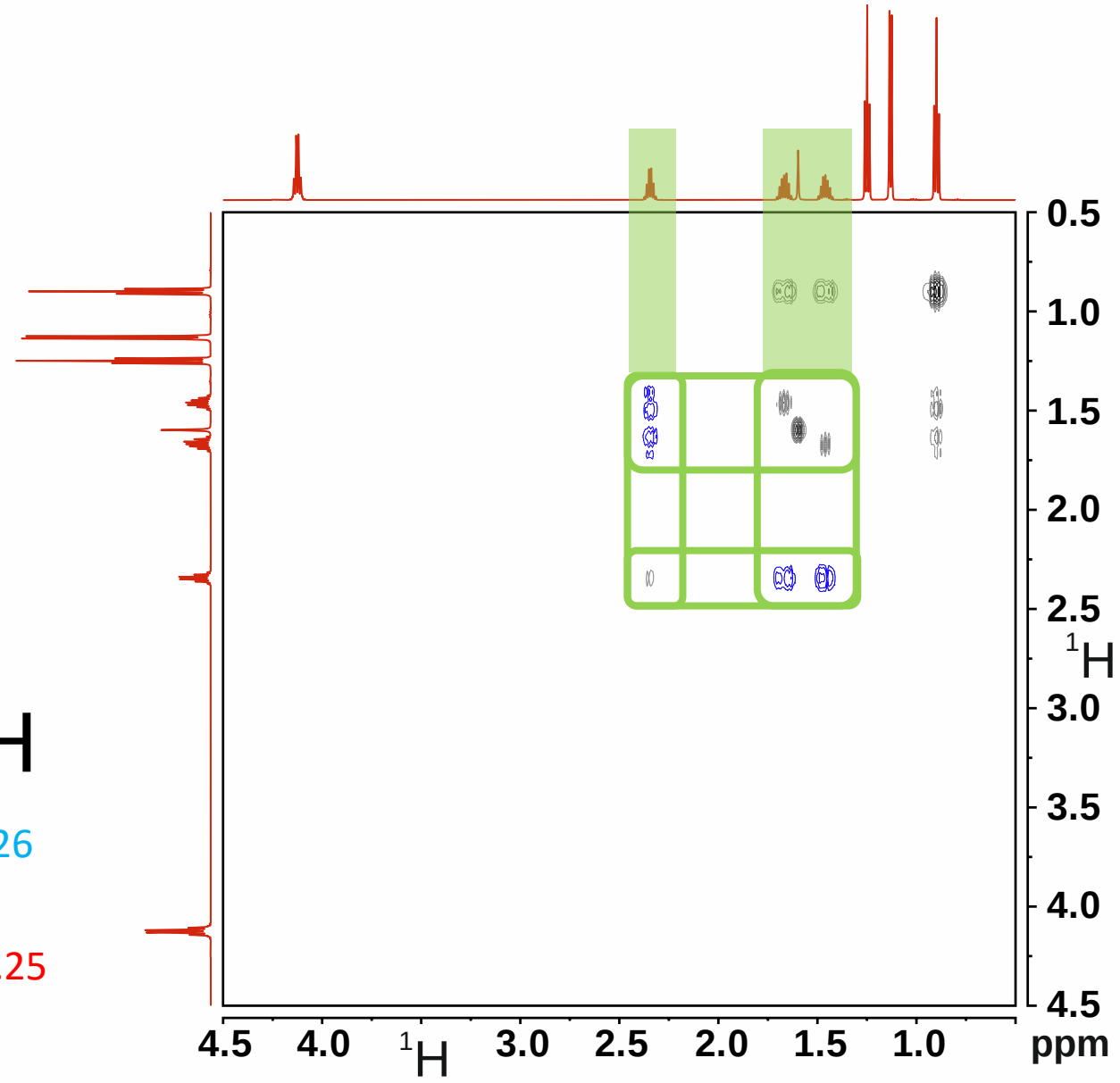
# Solution

## Part 3 - Substructures

There is only one remaining cross peak.



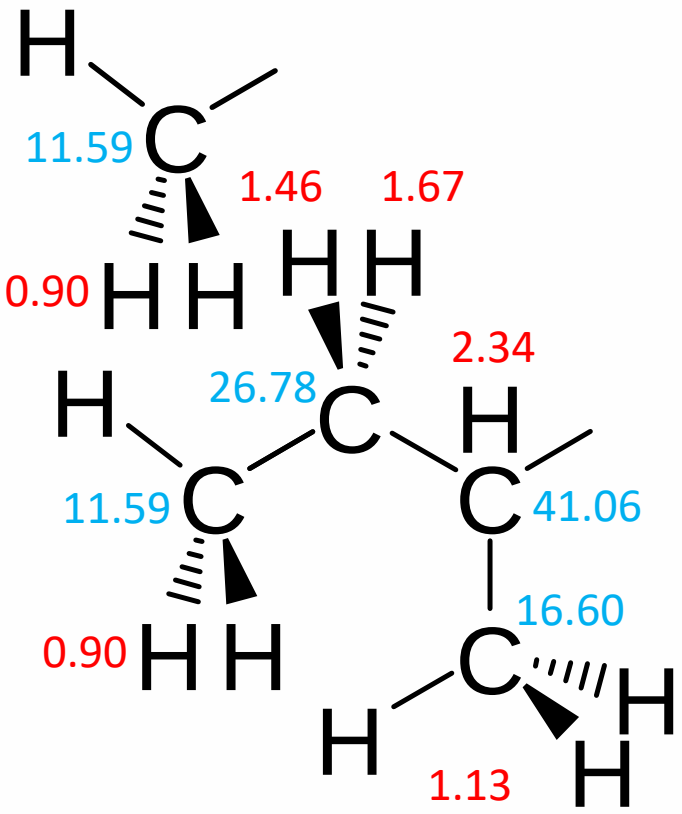



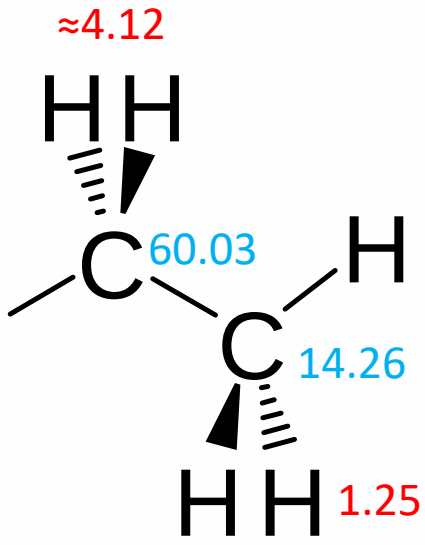



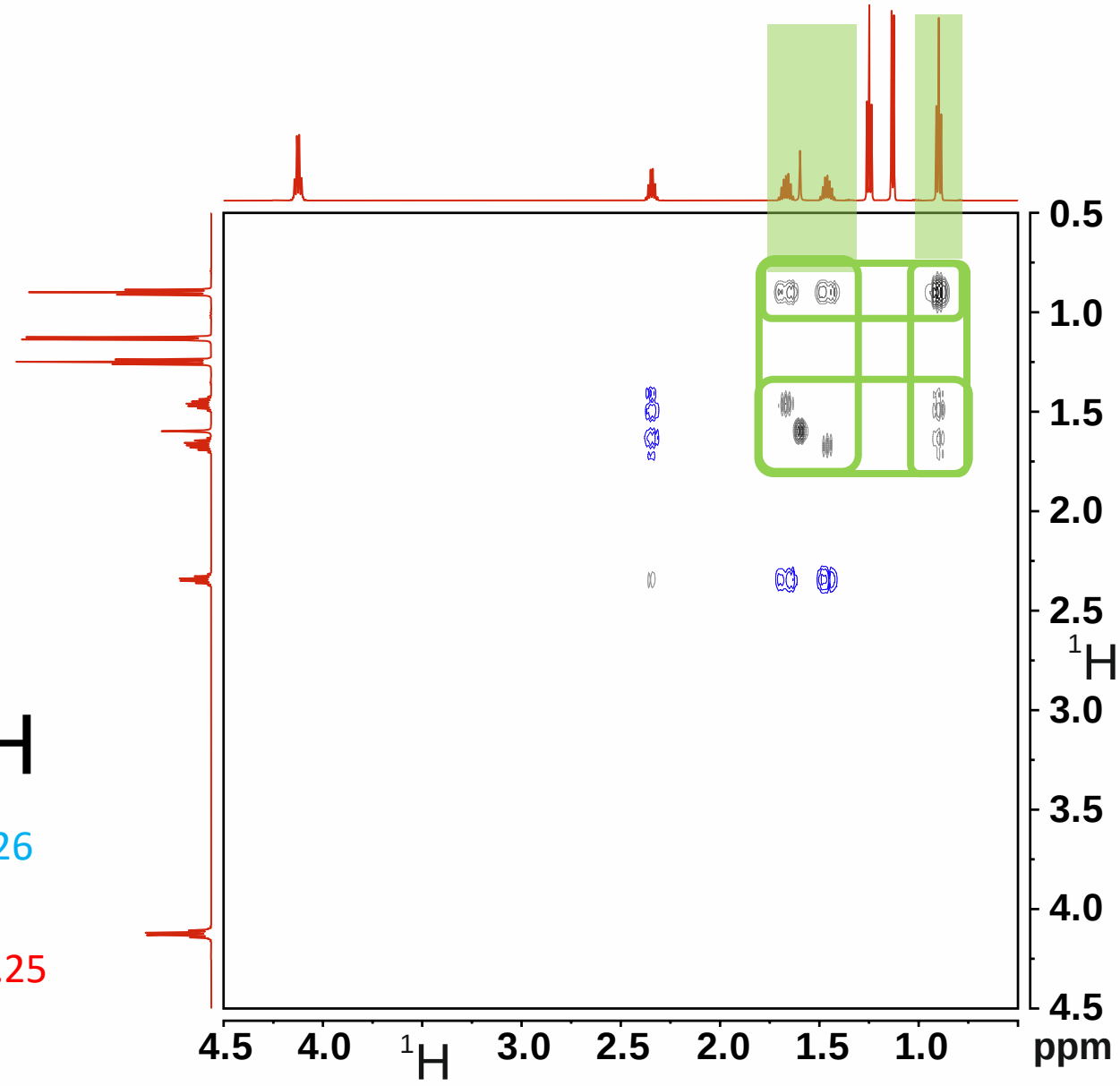
# Solution

## Part 3 - Substructures

There is only one remaining cross peak.



# Solution

Part 4 – Putting all together

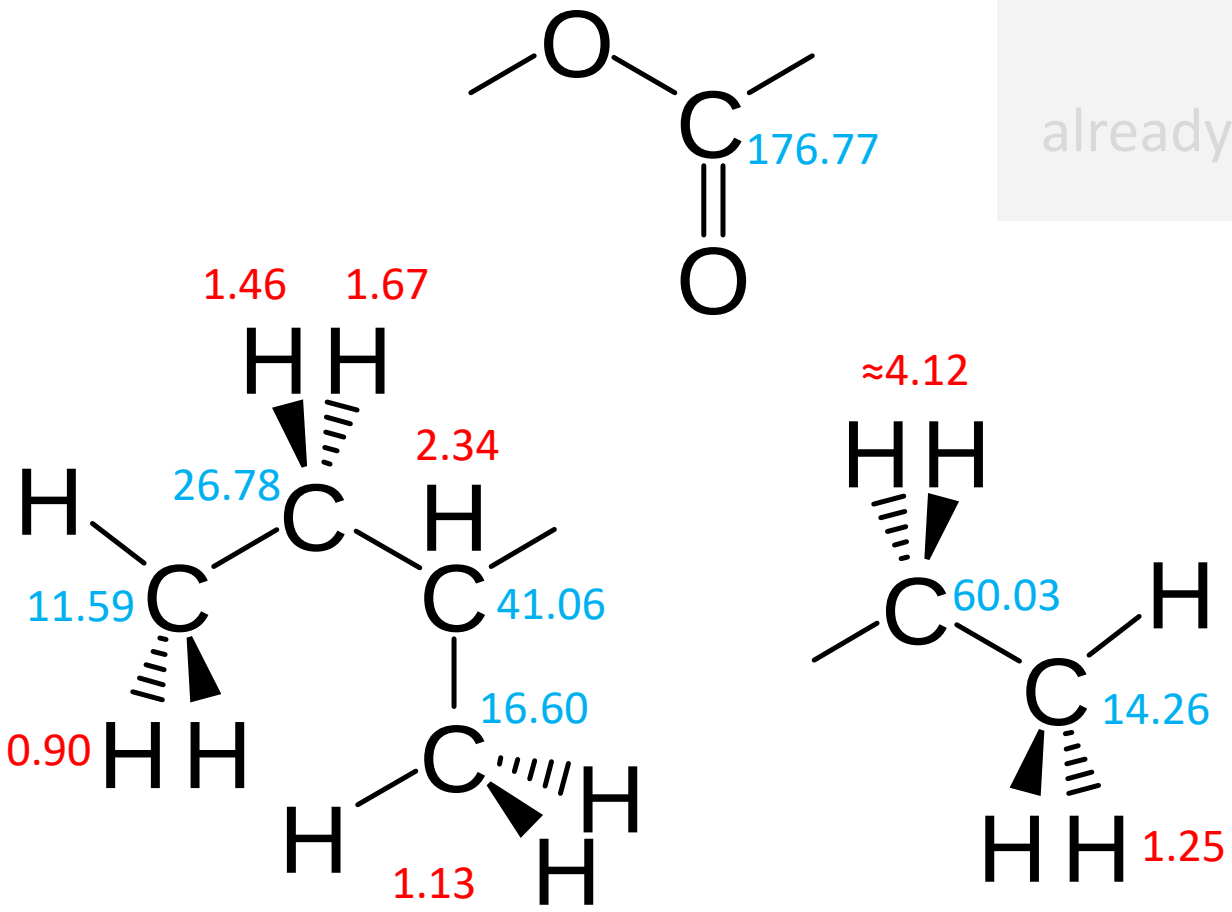
molecular formula - $C_7H_{14}O_2$

number of double bond equivalents - 1

already known fragments - $C_6H_{14}$

missing

- $CO_2$
- 1 double bond equivalent
- quaternary C at 176.77 ppm



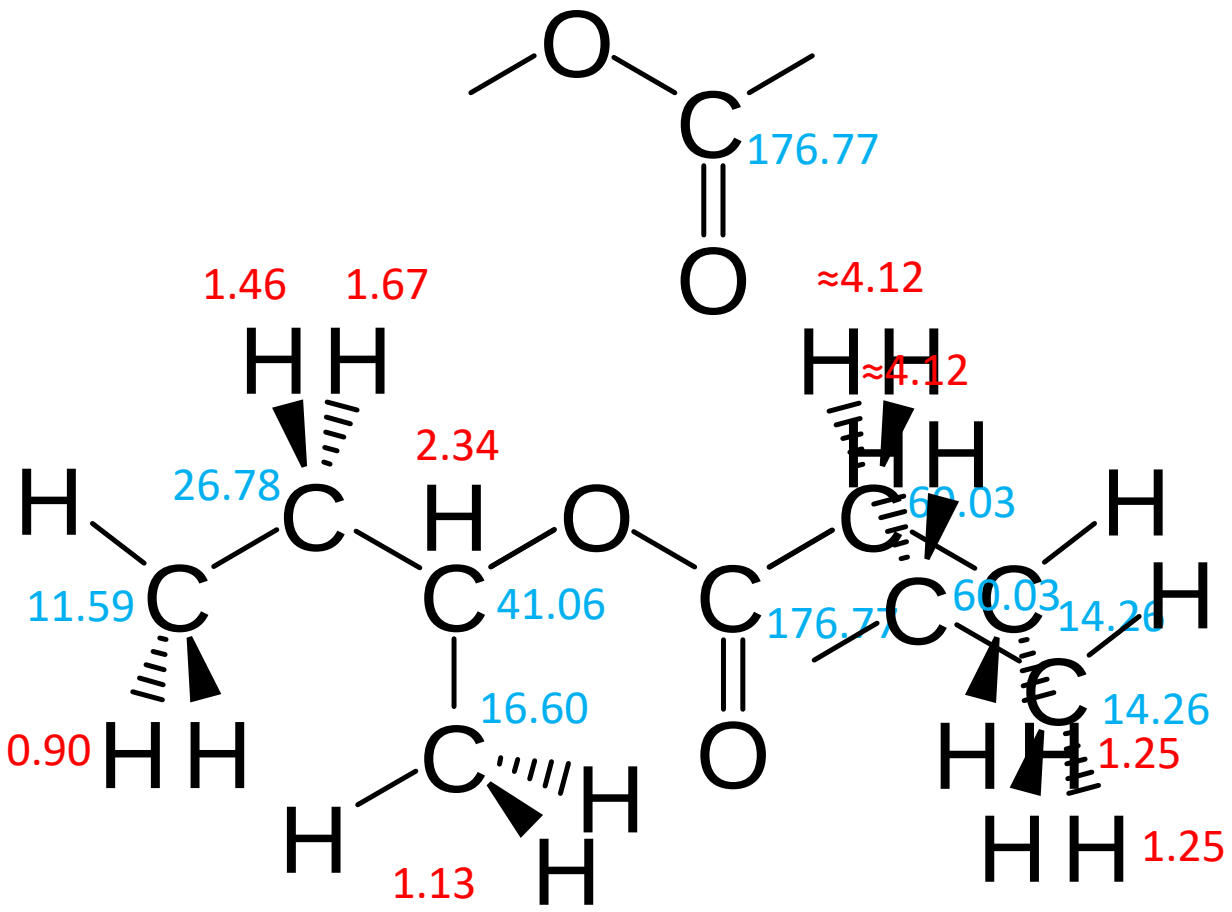




The missing fragment has to have two open bonds.

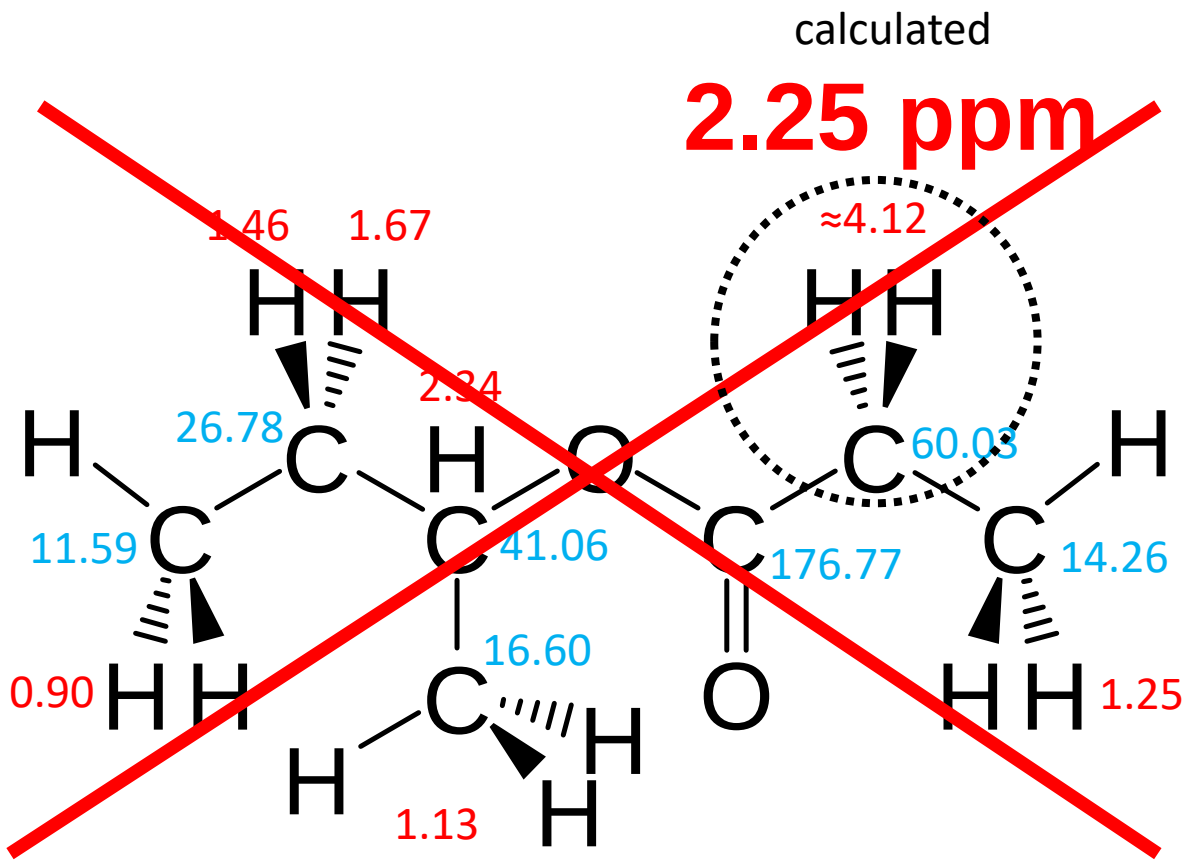
# Solution

Part 4 – Putting all together



# Solution

## Part 4 – Putting all together




There would be two possibilities to place the carboxyl group between the two known fragments.

To test the correctness of this structure, the methylene group with a proton signal at approx. 4.12 ppm is a good target.

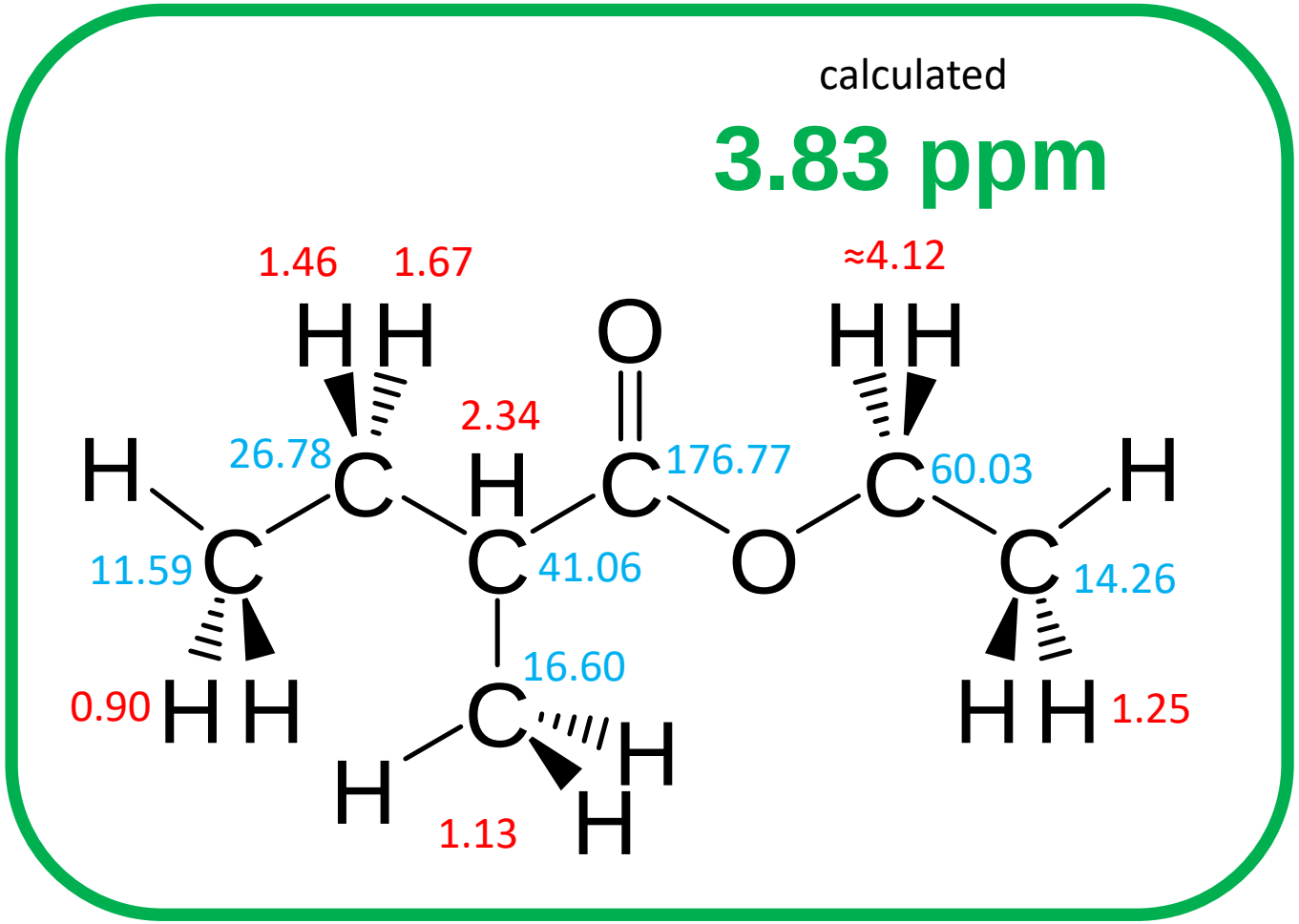
The chemical shift of these methylene protons can be predicted very well using the Schoolery rules.

For the methylene protons, we expect a chemical shift of

**2.25 ppm**

# Solution

Part 4 – Putting all together




For comparison, let us test the prediction of the chemical shift for the same methylene protons in the alternative structure.

We get

**3.83 ppm**

This is not perfect, but significantly better than the prediction done before.

# Solution

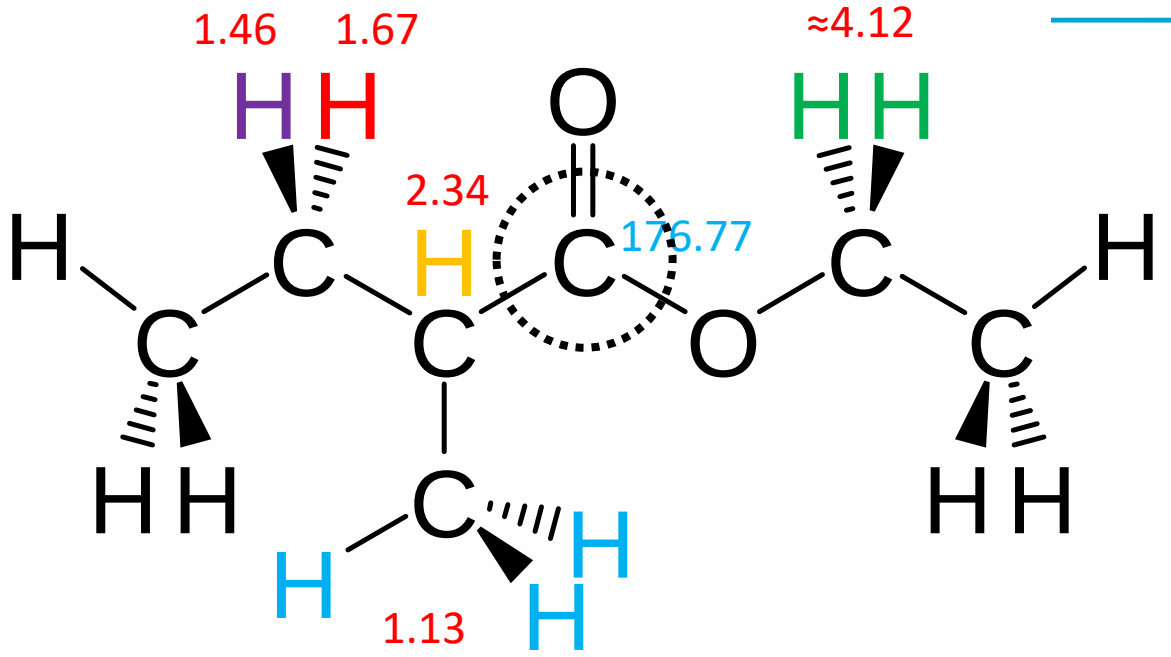
## Part 4 – Putting all together

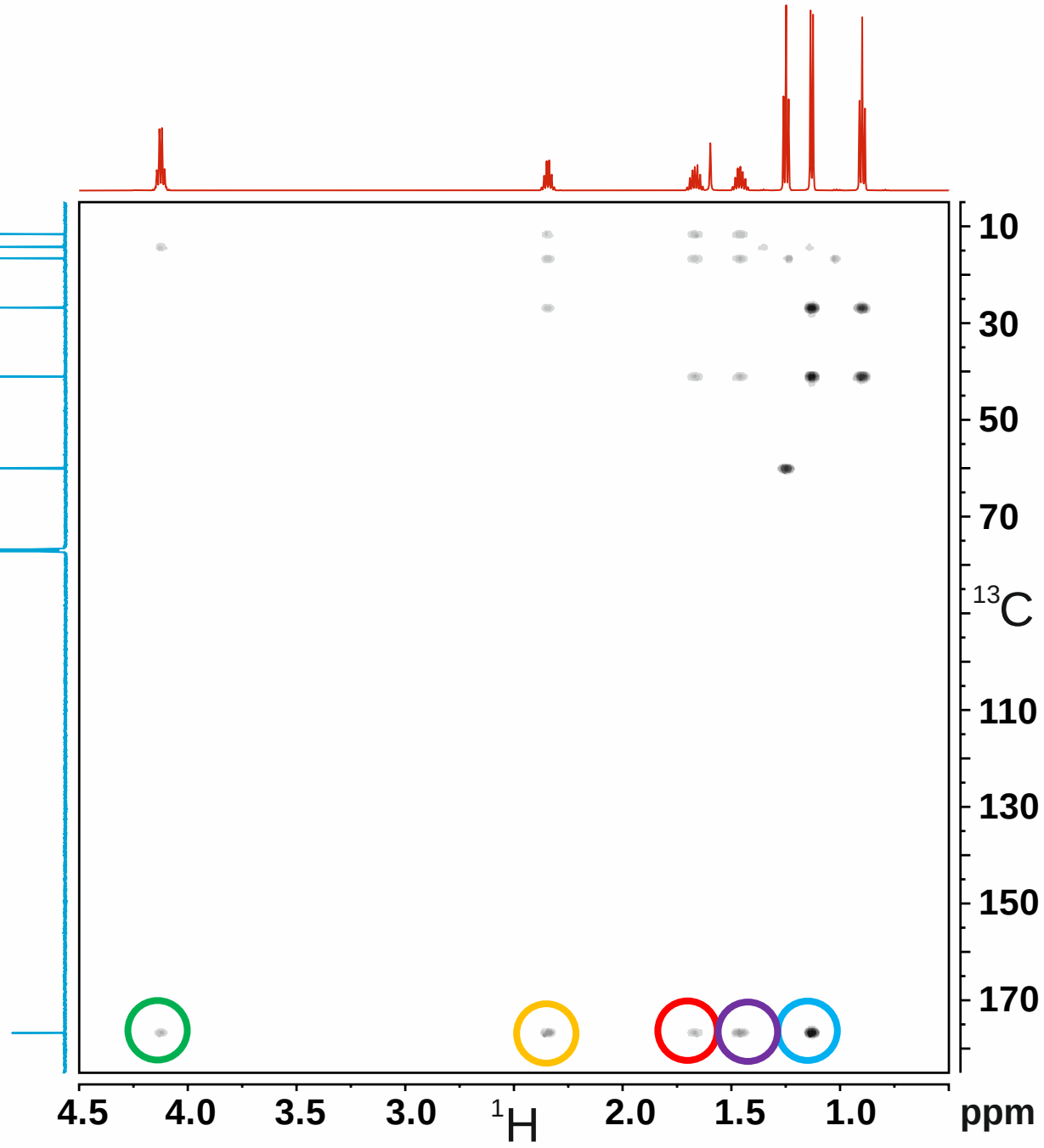
Alternatively, we can use the HMBC to test whether we have chosen correctly between the two alternative structures.

# Solution

## Part 4 – Putting all together

In the HMBC, starting from the carbonyl carbon, five cross peaks can be seen. Each of the associated protons is two or three bonds away.
Two- and three-bond correlations are HMBC standard.

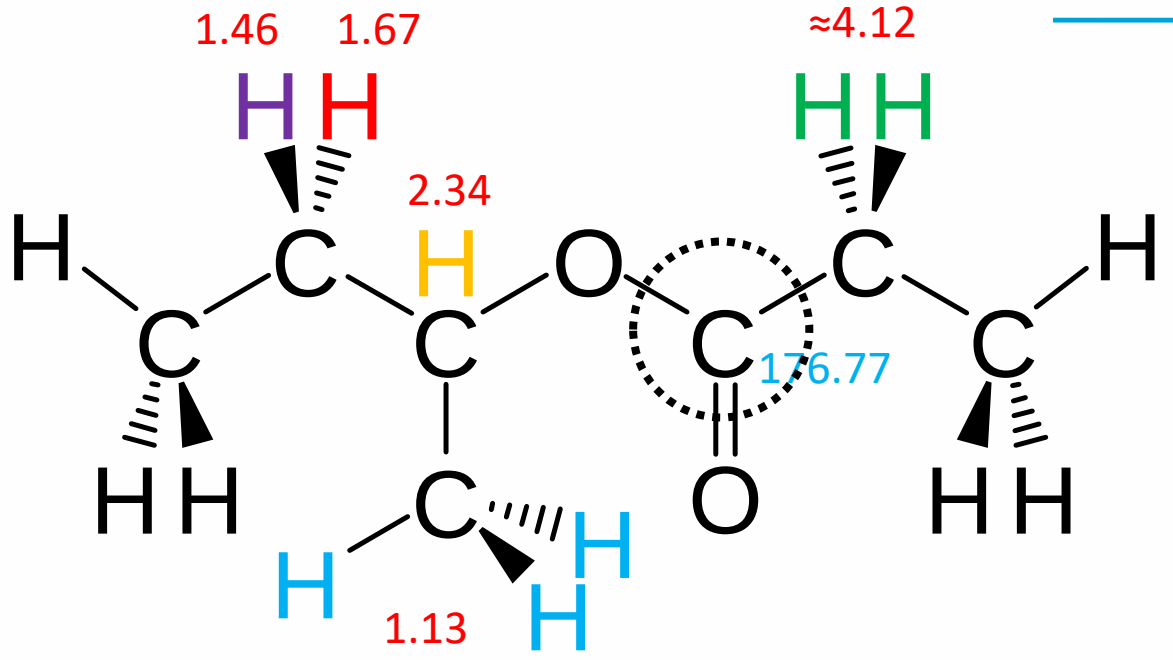


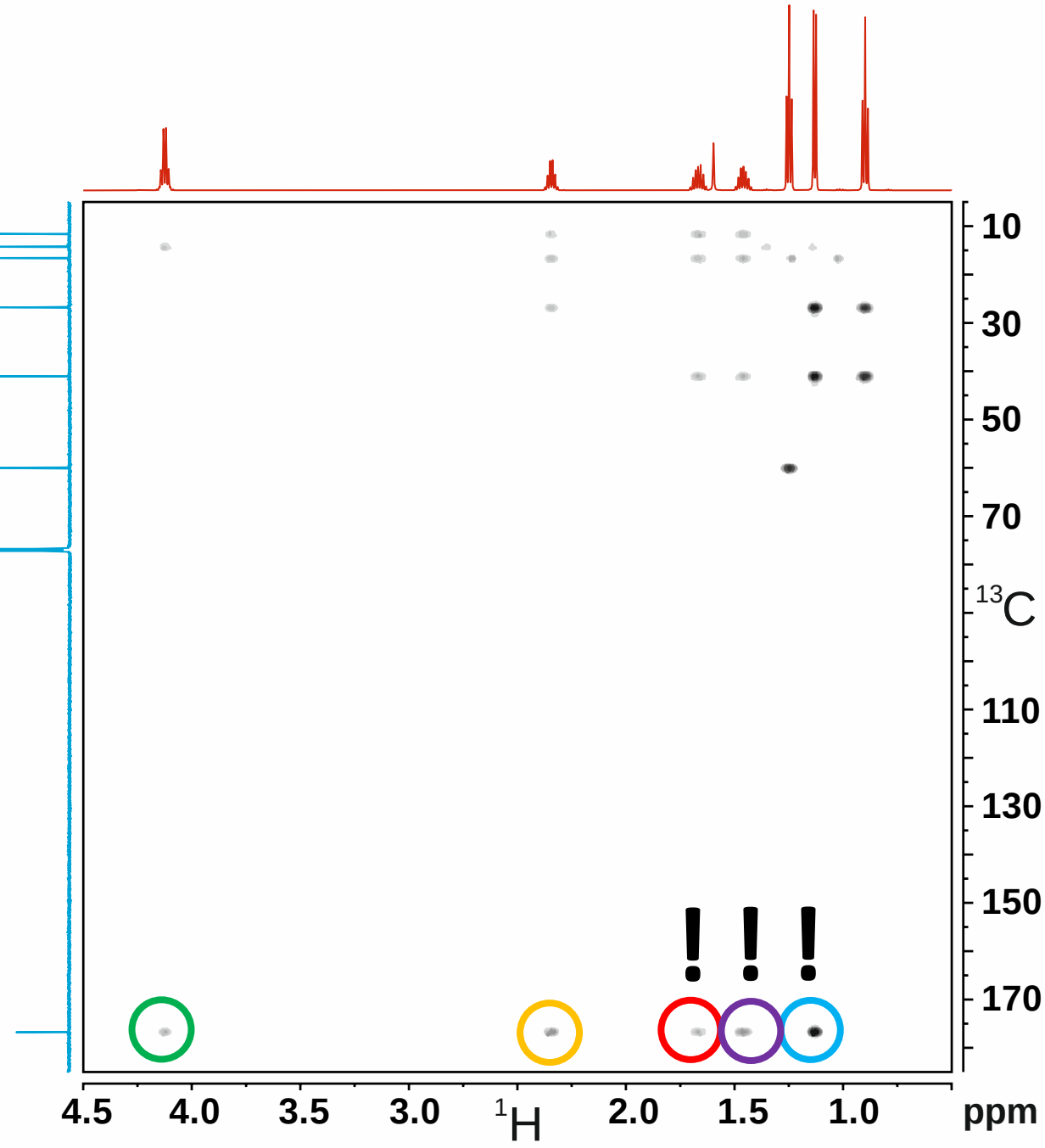



# Solution

## Part 4 – Putting all together

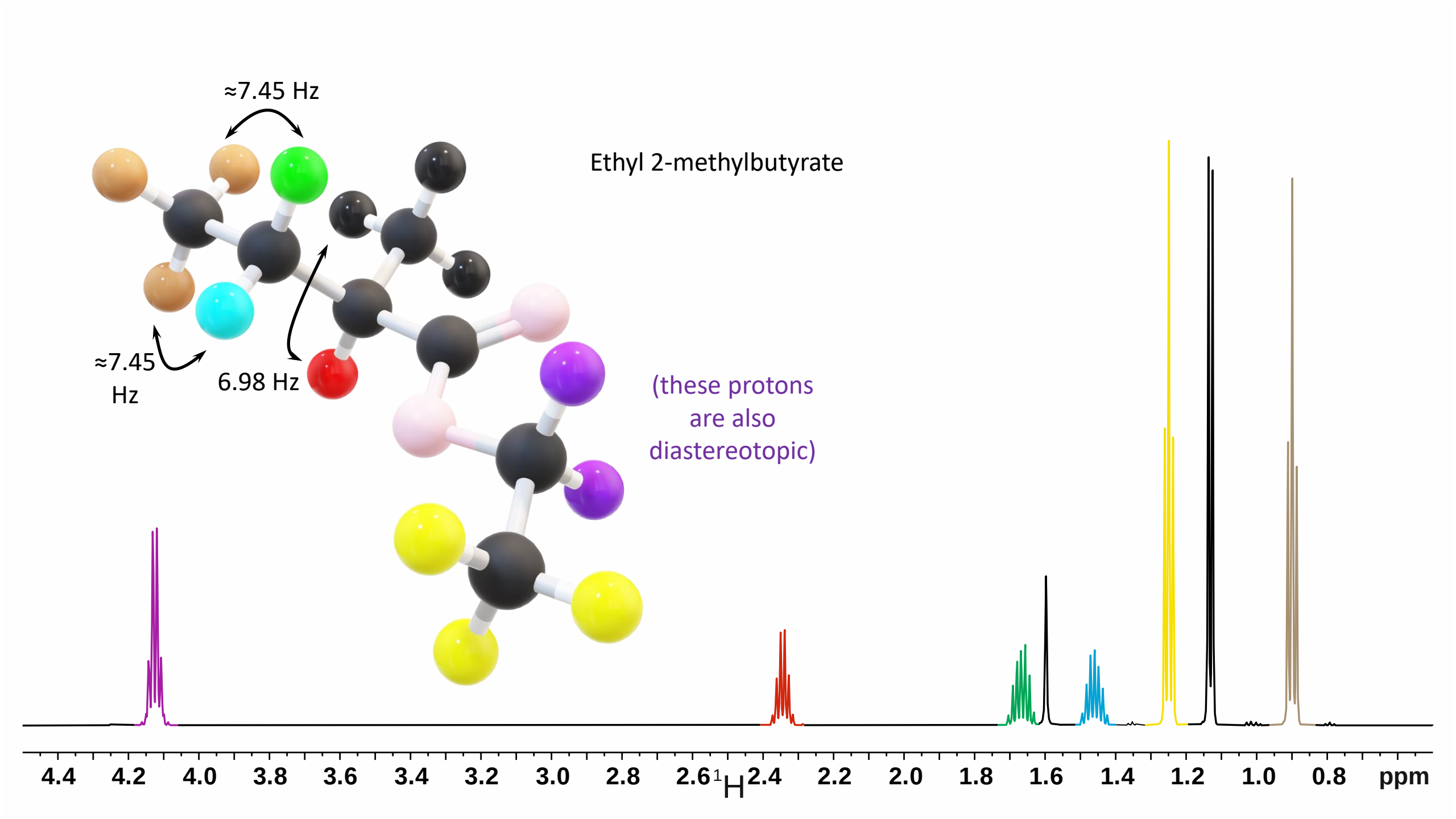
In the second possible structure, the signals labeled with ! in the HMBC would each correspond to a four-bond coupling. Four-bond couplings are not impossible in HMBC, but they are very unlikely if there are no double bonds along the coupling path.

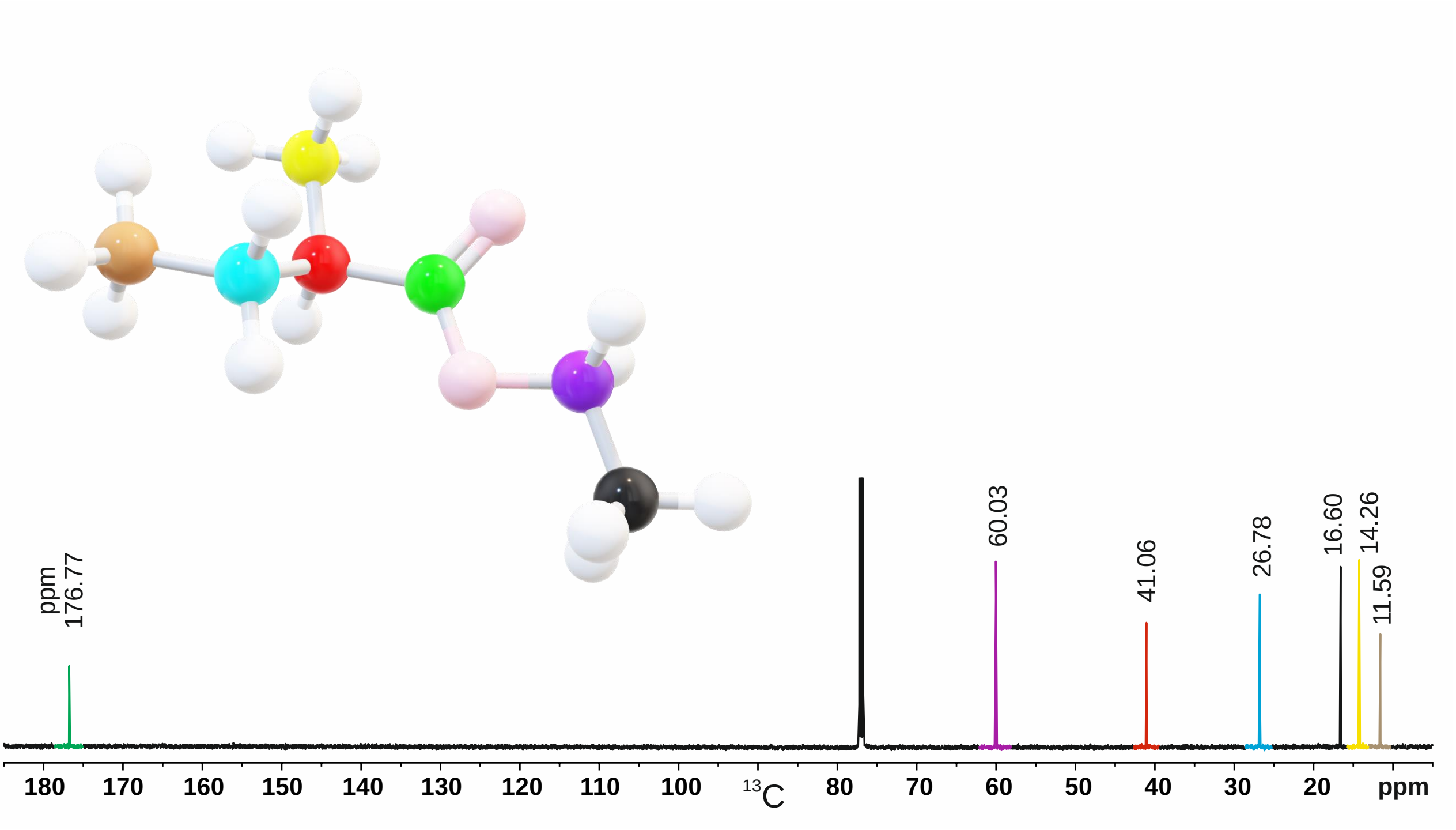


# Graphical summary

The colour of the proton multiplet or the carbon signals correlates with the colour of the protons or the carbon atoms in the 3D structure.


≈7.45 Hz
≈7.45 Hz
6.98 Hz
Ethyl 2-methylbutyrate
(these protons are also diastereotopic)
4.4
4.2
4.0
3.8
3.6
3.4
3.2
3.0
2.8
2.6
2.4
2.2
2.0
1.8
1.6
1.4
1.2
1.0
0.8
ppm
$^1$H


ppm
176.77
60.03
41.06
26.78
16.60
14.26
11.59
180
170
160
150
140
130
120
110
100
$^{13}$C
80
70
60
50
40
30
20
ppm

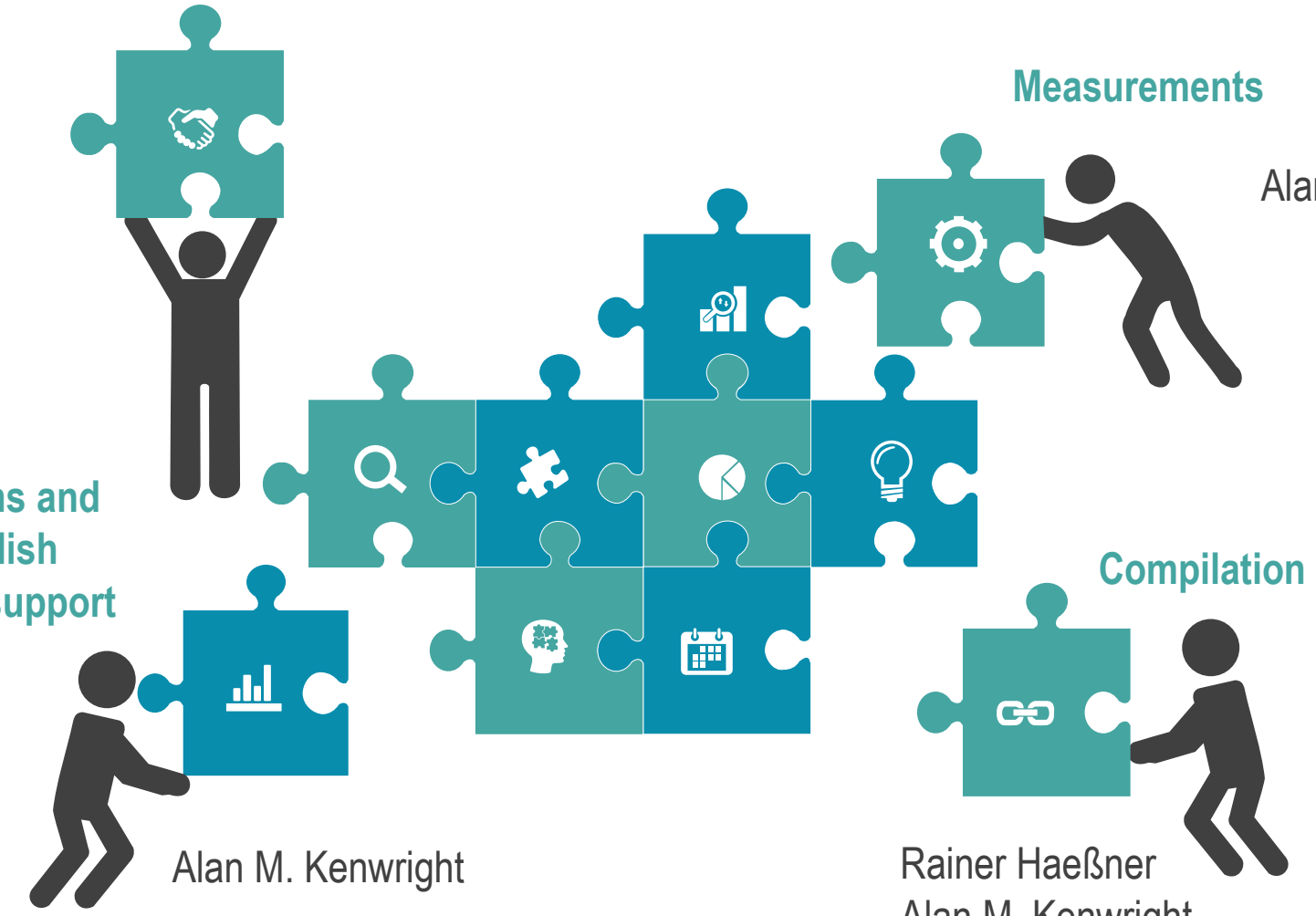
# Contributions

**Spectrometer time**

Durham university

**Measurements**

Alan M. Kenwright



**Discussions and native English language support**

Alan M. Kenwright

**Compilation**

Rainer Haeßner
Alan M. Kenwright

More exercises ...