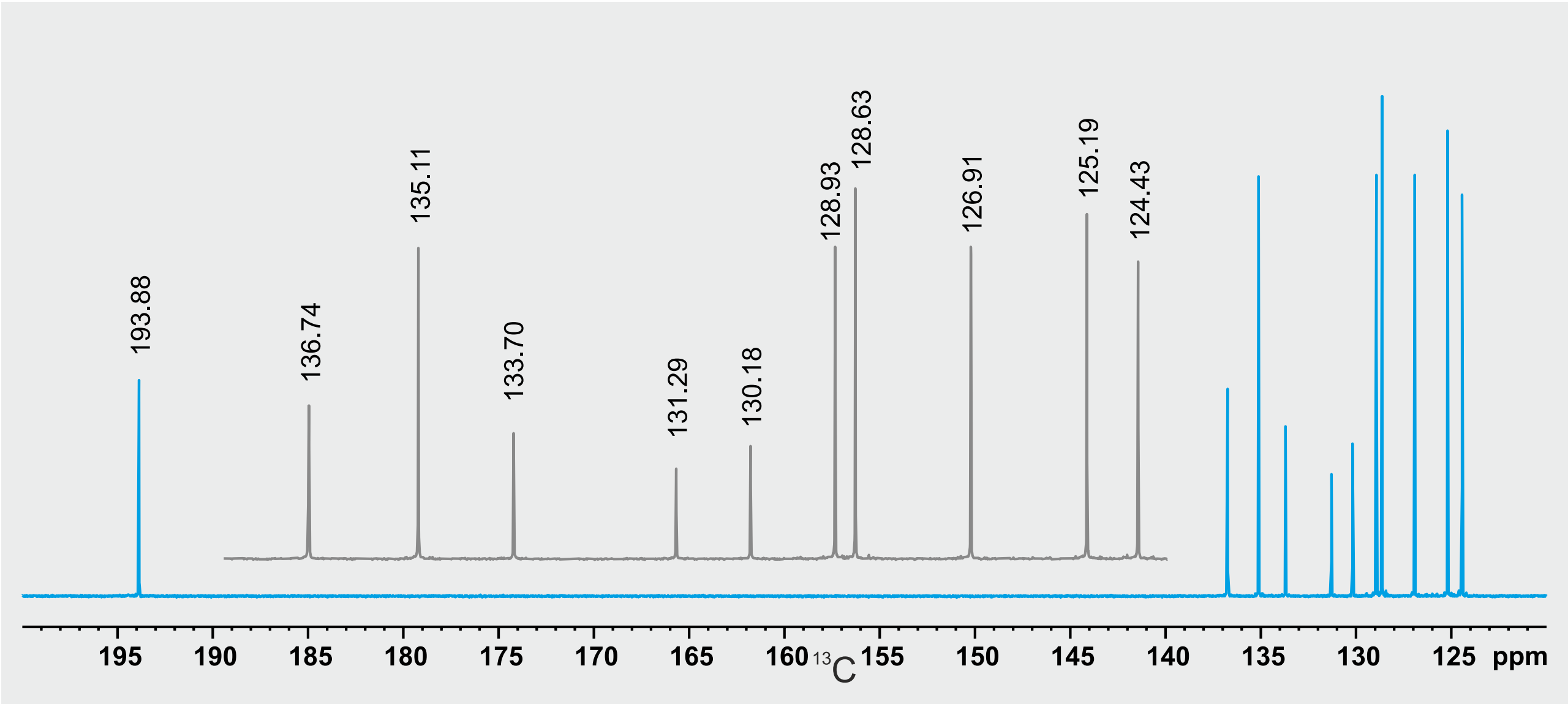
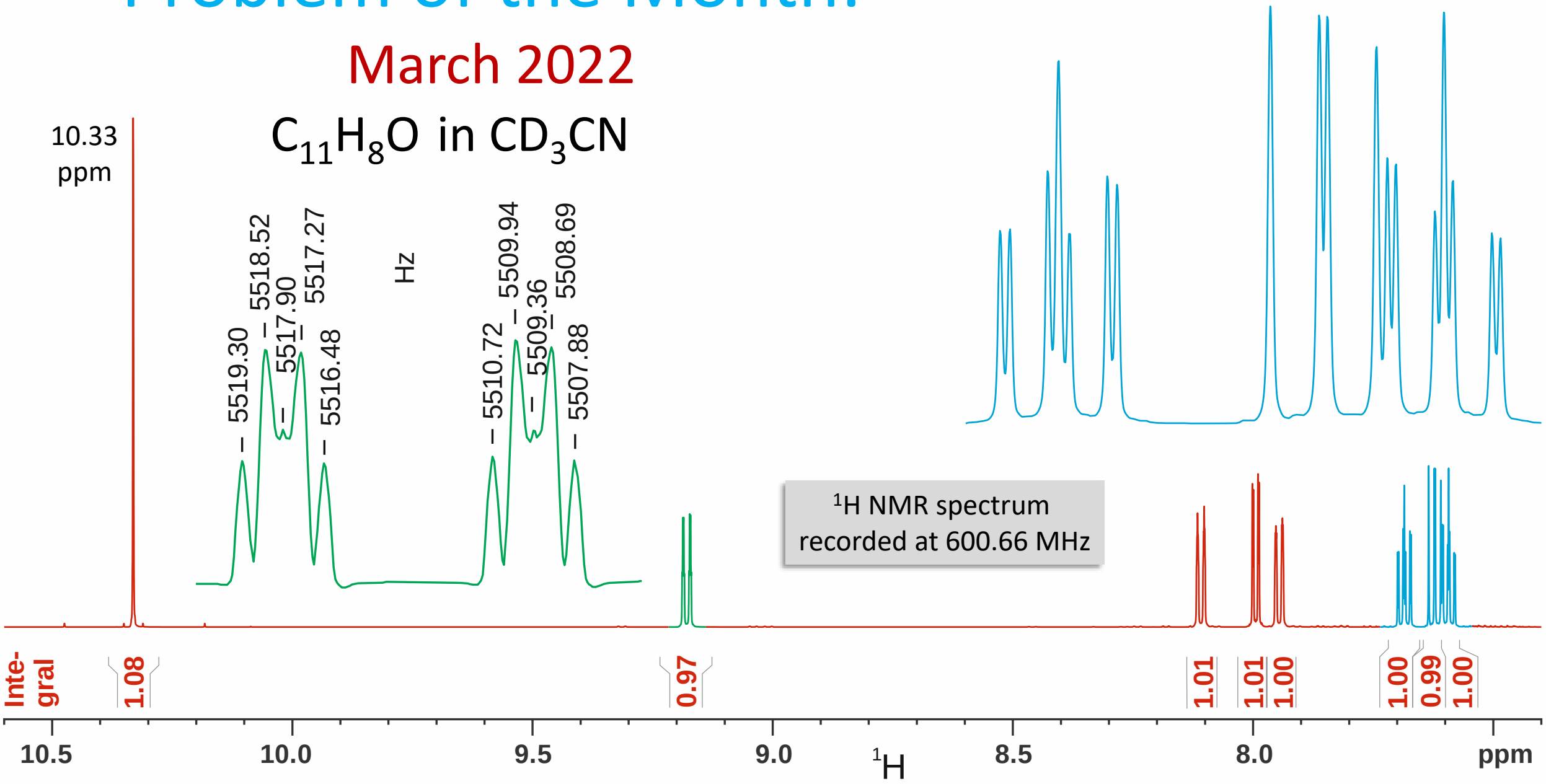
Exercise plus Solution – Quick PDF overview

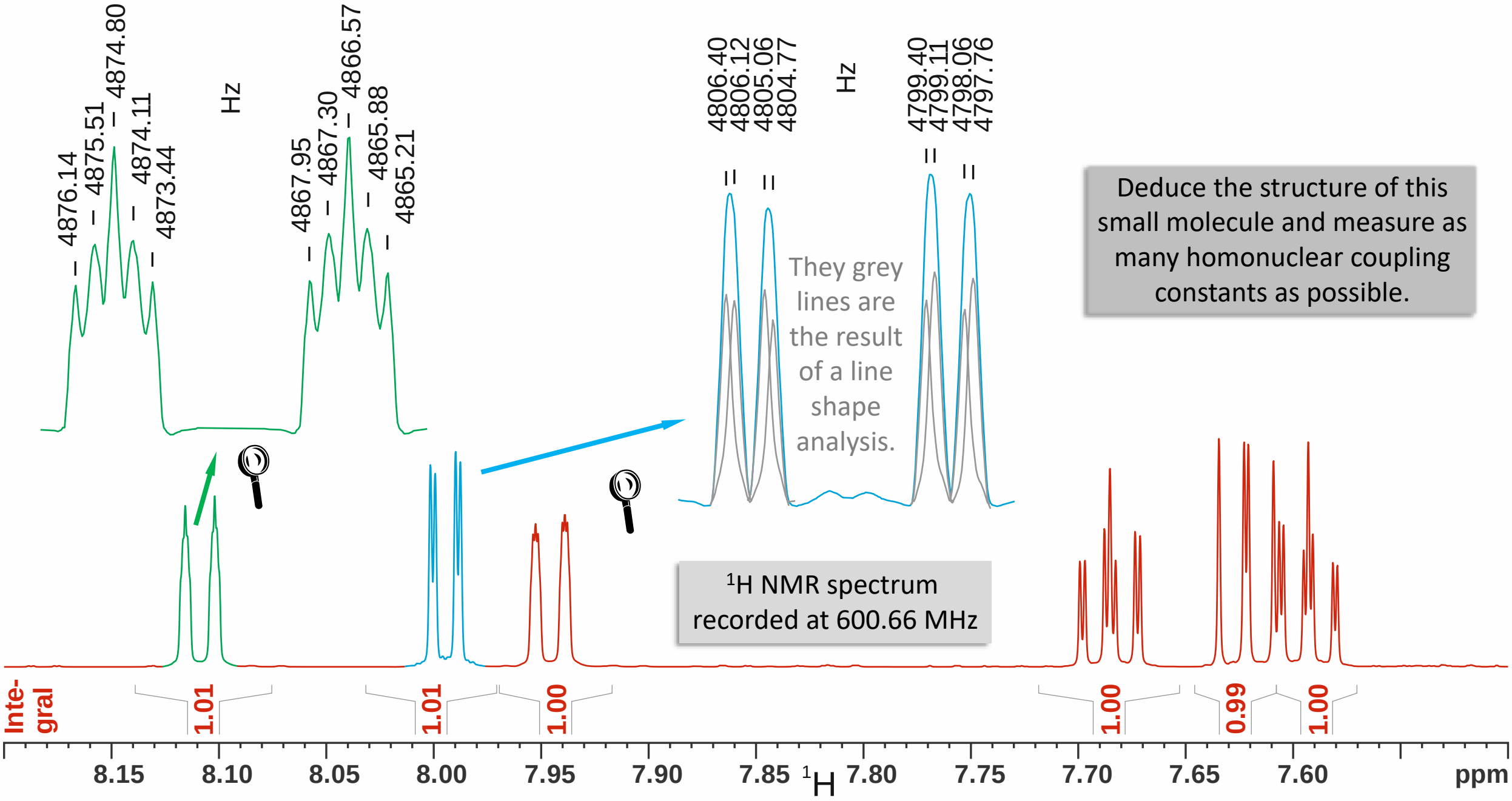
It is recommended to use this PDF version only for a quick overview of the NMR challenge. All animations of the PowerPoint version are missing, under certain circumstances quality deficiencies may also occur.
The higher quality PowerPoint files are freely available for download at any time.

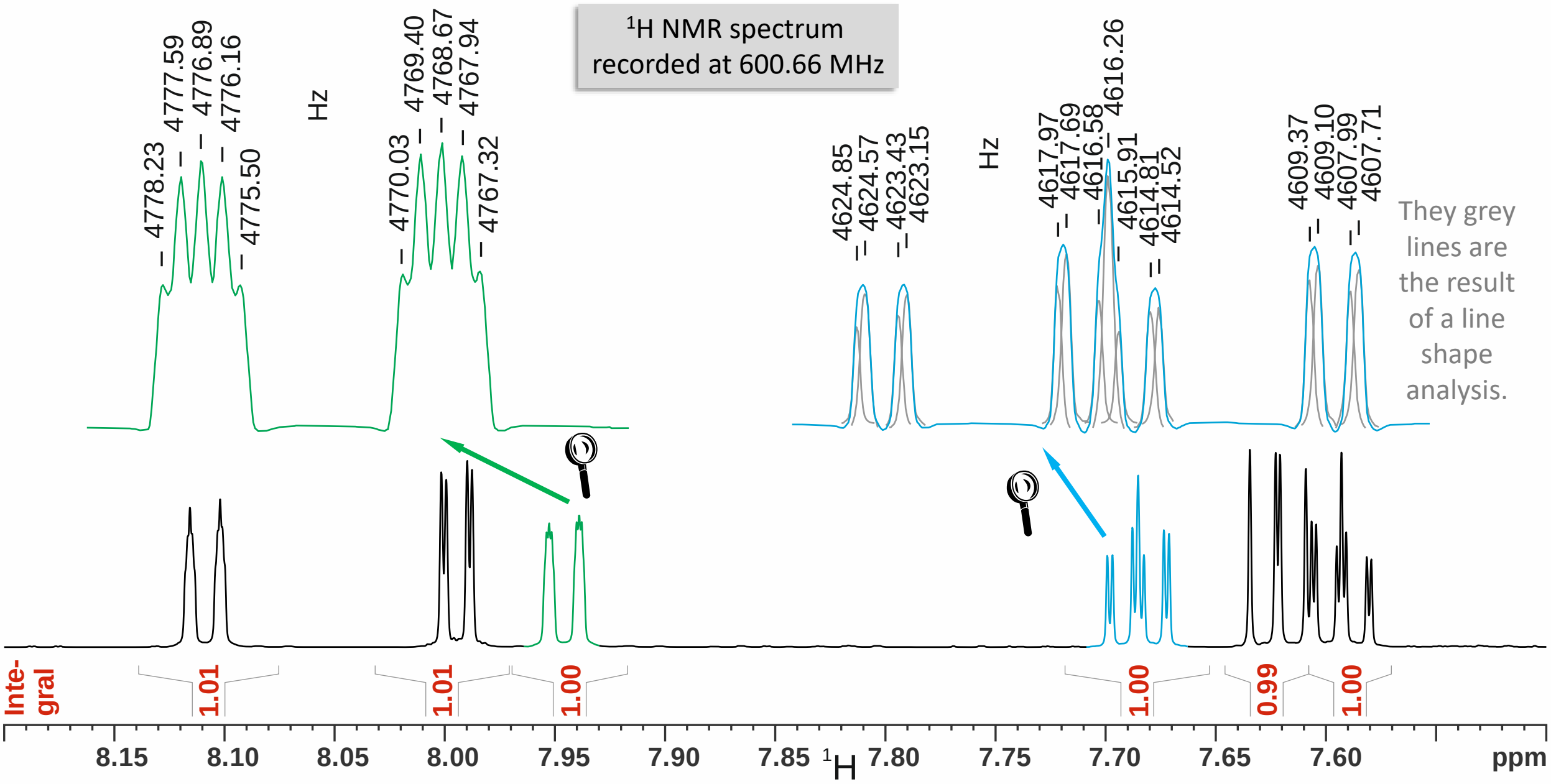


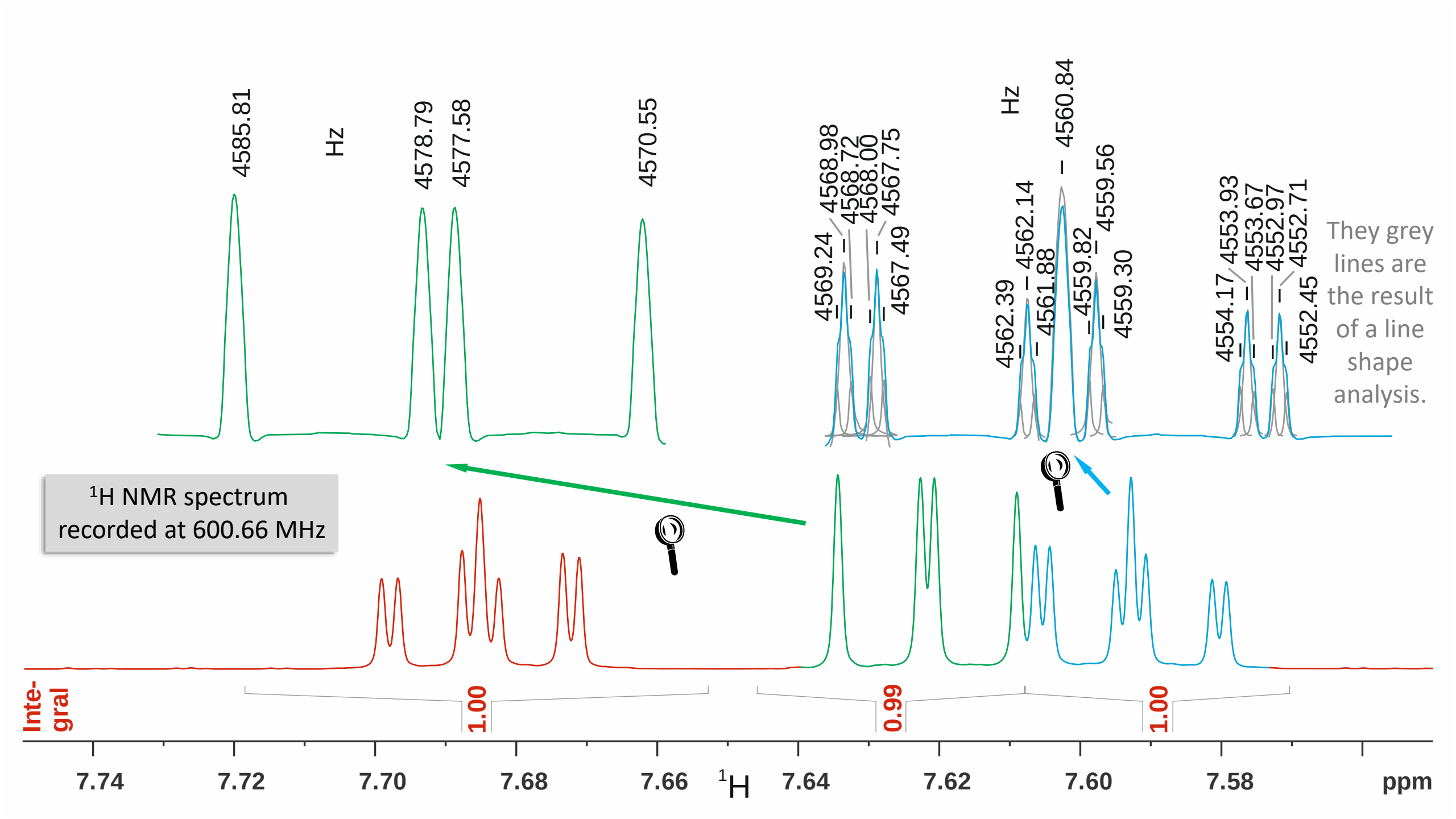
Problem of the Month:

March 2022

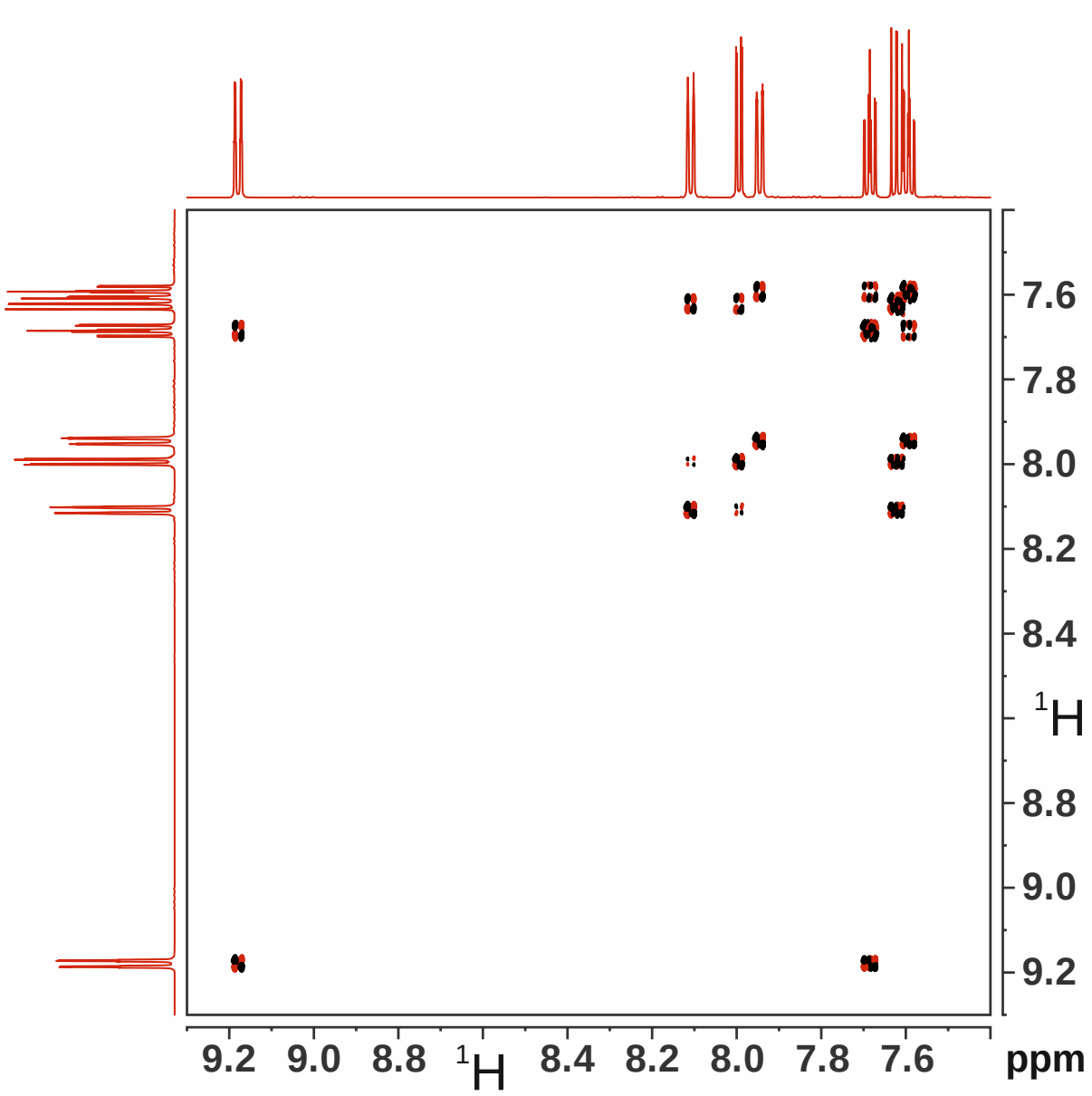


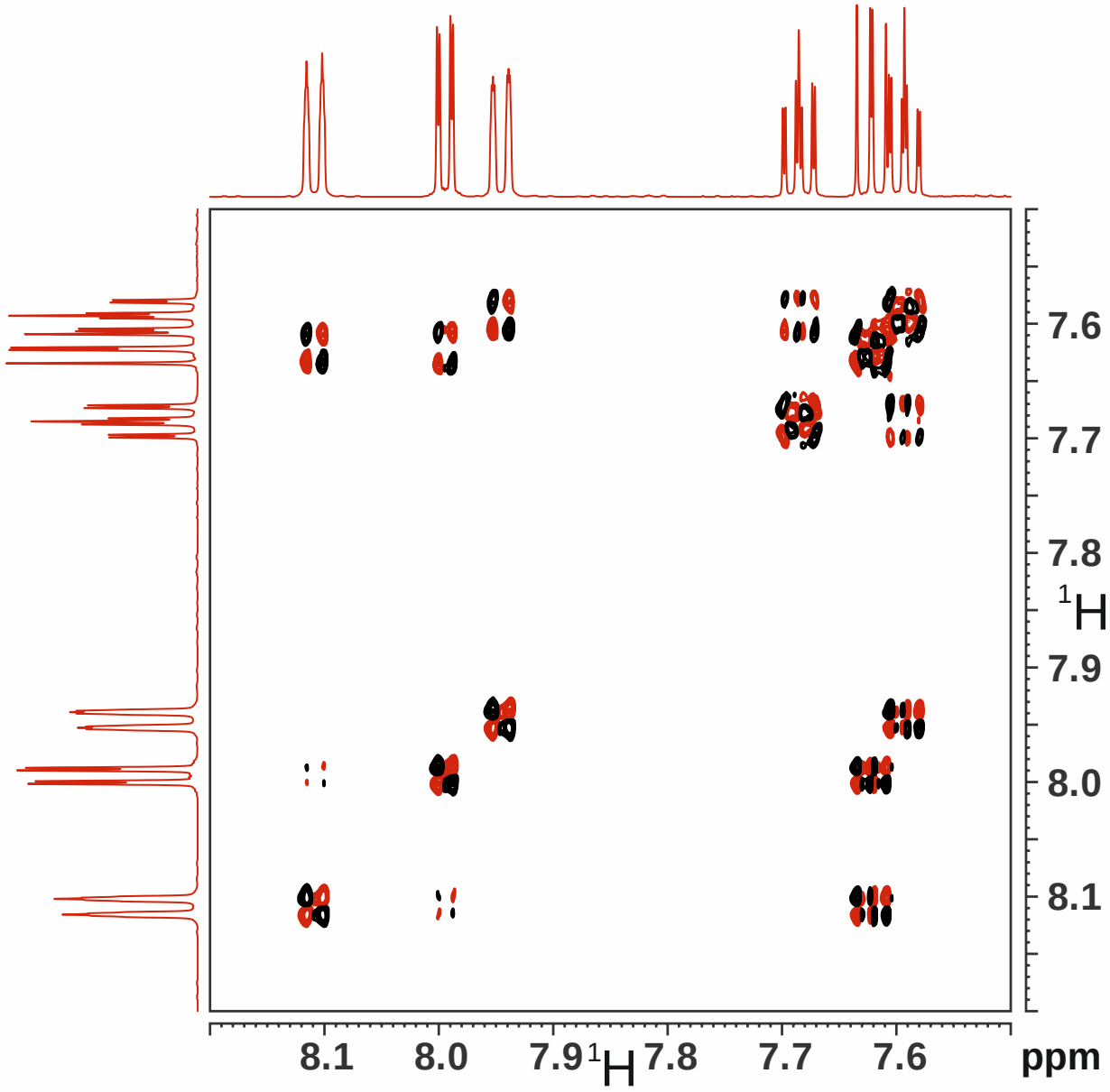

4876.14
4875.51
4874.80
4874.11
4873.44
Hz
4867.95
4867.30
4866.57
4865.88
4865.21
4806.40
4806.12
4805.06
4804.77
Hz
4799.40
4799.11
4798.06
4797.76
They grey lines are the result of a line shape analysis.
Deduce the structure of this small molecule and measure as many homonuclear coupling constants as possible.
^{1}H NMR spectrum recorded at 600.66 MHz
Inte-gral
1.01
1.01
1.00
1.00
0.99
1.00
8.15
8.10
8.05
8.00
7.95
7.90
7.85
7.80
7.75
7.70
7.65
7.60
^{1}H
ppm

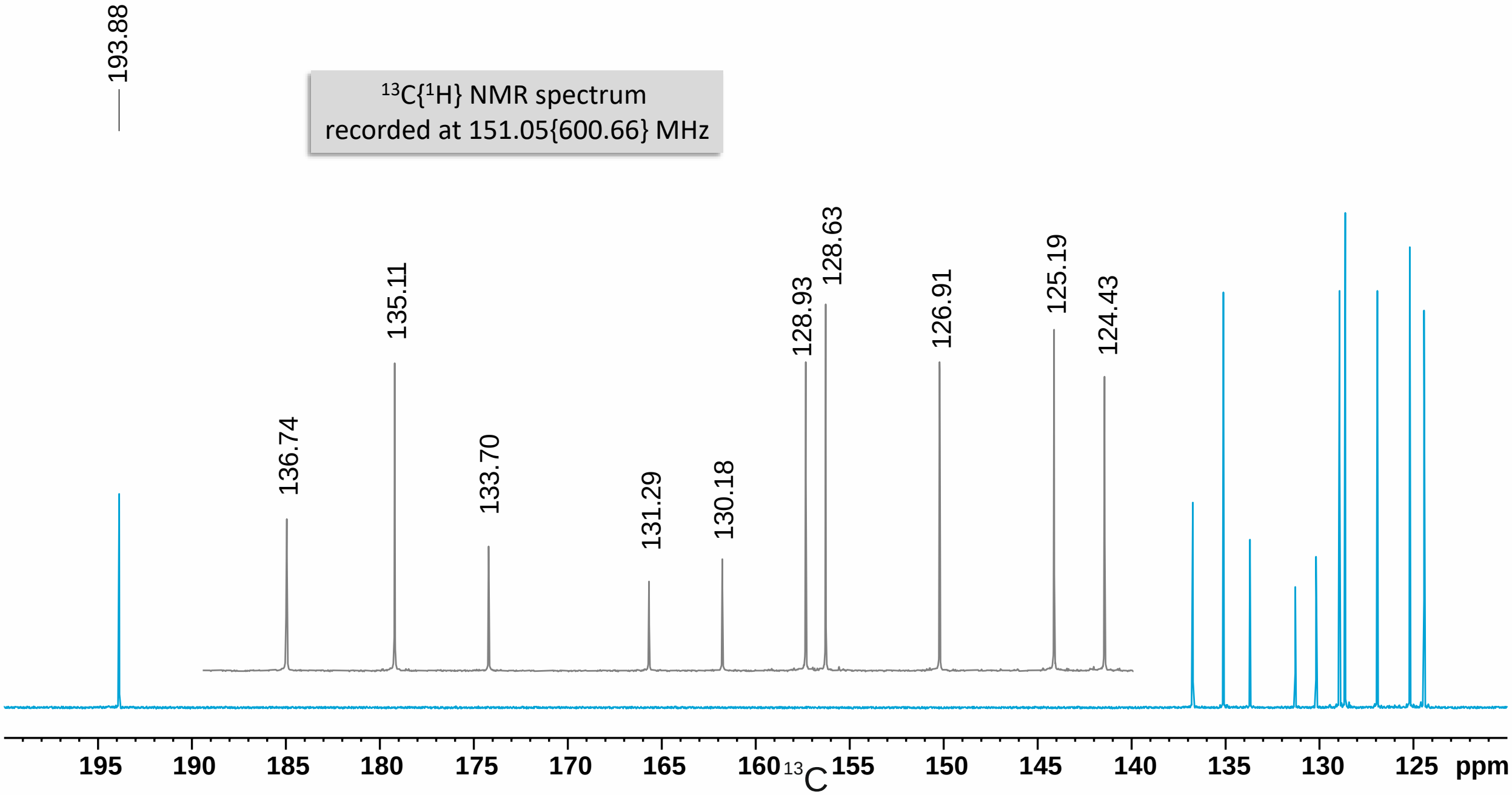

^{1}H NMR spectrum recorded at 600.66 MHz
Hz
4778.23
4777.59
4776.89
4776.16
4775.50
4770.03
4769.40
4768.67
4767.94
4767.32
Hz
4624.85
4624.57
4623.43
4623.15
4617.97
4617.69
4616.58
4616.26
4615.91
4614.81
4614.52
4609.37
4609.10
4607.99
4607.71
They grey lines are the result of a line shape analysis.
Inte-gral
1.01
1.01
1.00
1.00
0.99
1.00
8.15
8.10
8.05
8.00
7.95
7.90
7.85
7.80
7.75
7.70
7.65
7.60
ppm
^{1}H


4585.81
Hz
4578.79
4577.58
4570.55
4569.24
4568.98
4568.72
4568.00
4567.75
4567.49
Hz
4562.39
4562.14
4561.88
4560.84
4559.82
4559.56
4559.30
4554.17
4553.93
4553.67
4552.97
4552.71
4552.45
They grey lines are the result of a line shape analysis.
^{1}H NMR spectrum recorded at 600.66 MHz
Inte-gral
1.00
0.99
1.00
7.74
7.72
7.70
7.68
7.66
^{1}H
7.64
7.62
7.60
7.58
ppm

$^{1}H/^{1}H$ COSY
recorded at 600.66 MHz

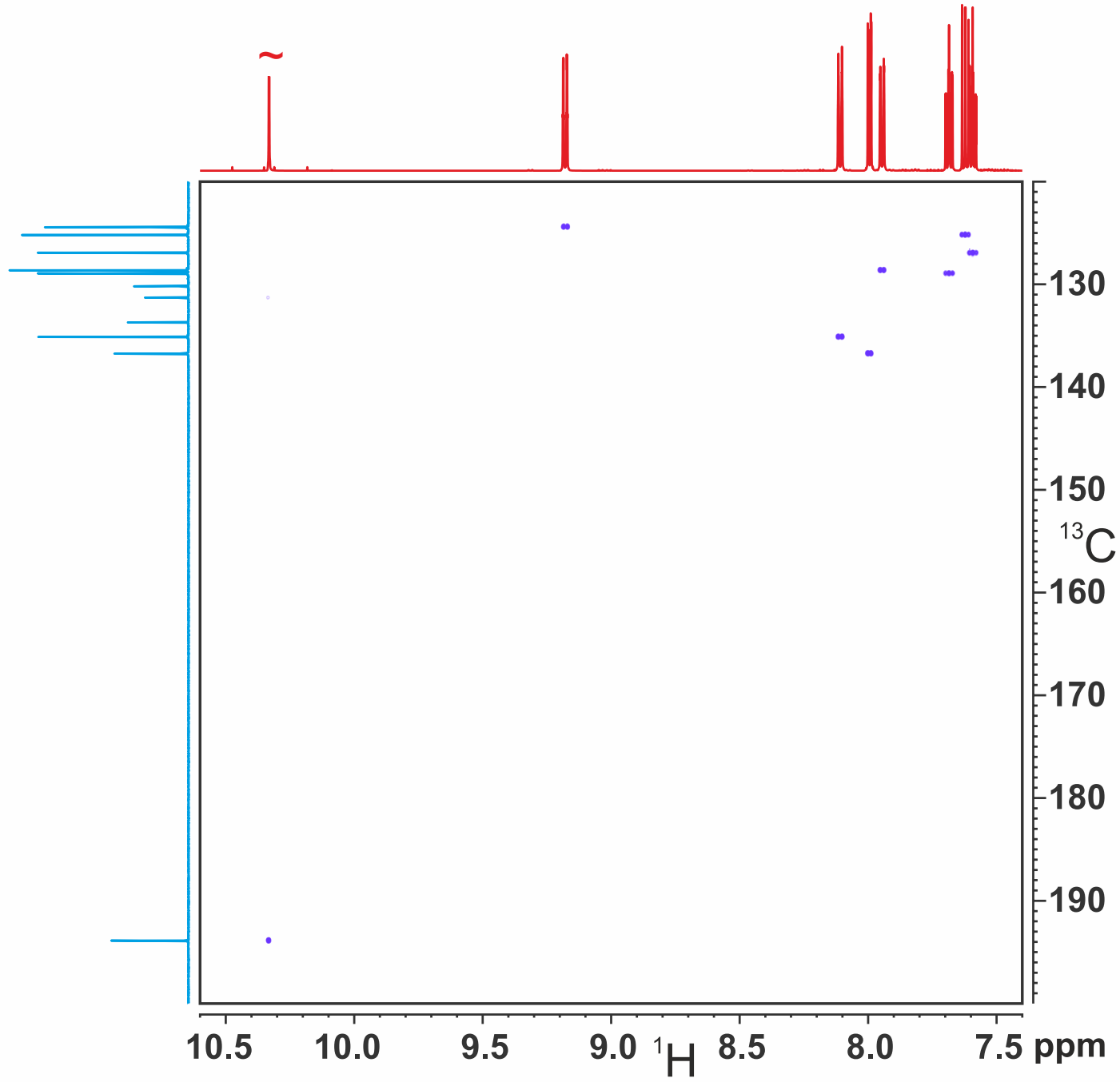




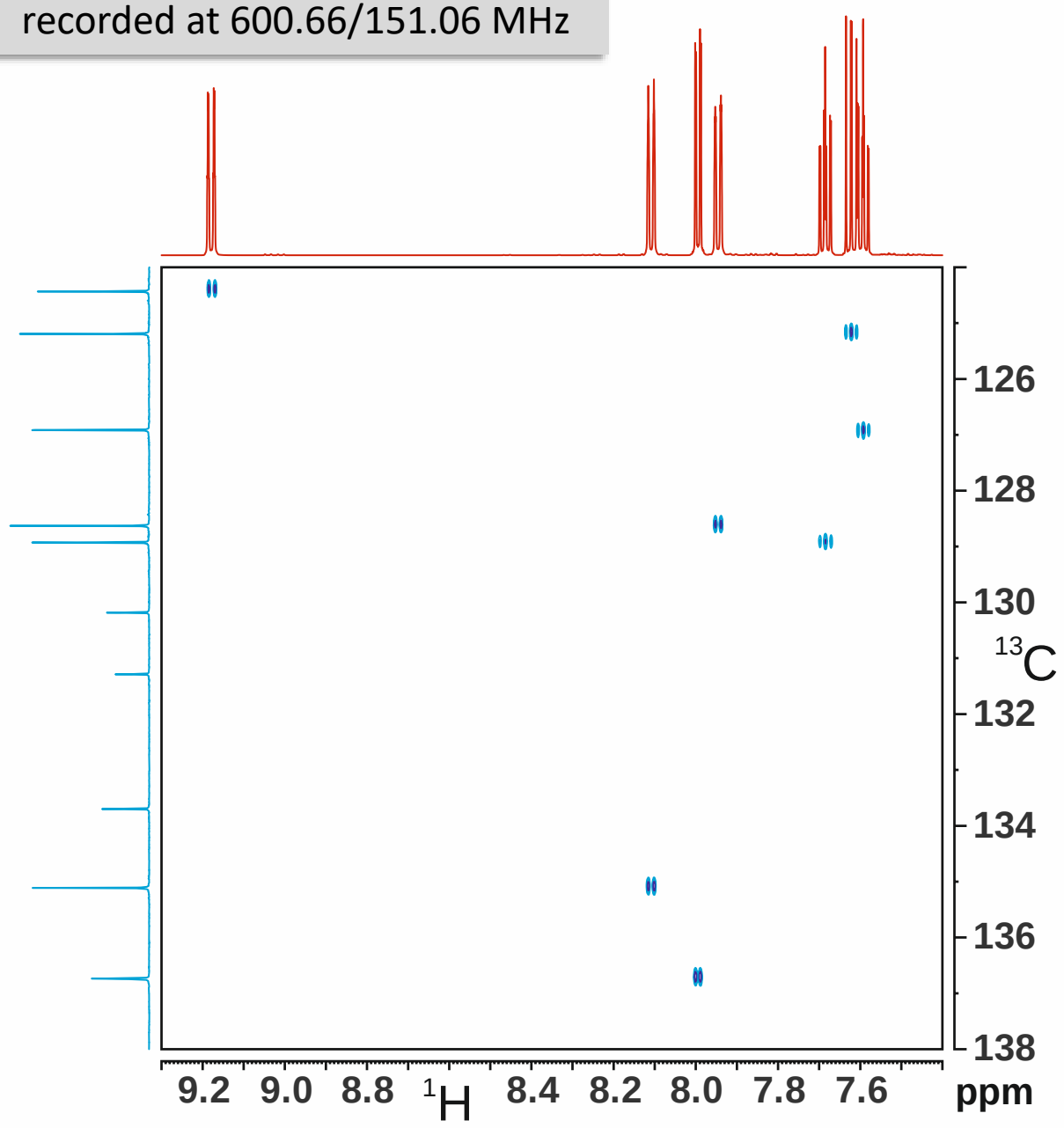

193.88
$^{13}C\{^{1}H\}$ NMR spectrum
recorded at 151.05{600.66} MHz
136.74
135.11
133.70
131.29
130.18
128.93
128.63
126.91
125.19
124.43
195
190
185
180
175
170
165
160
155
150
145
140
135
130
125
ppm
^{13}C

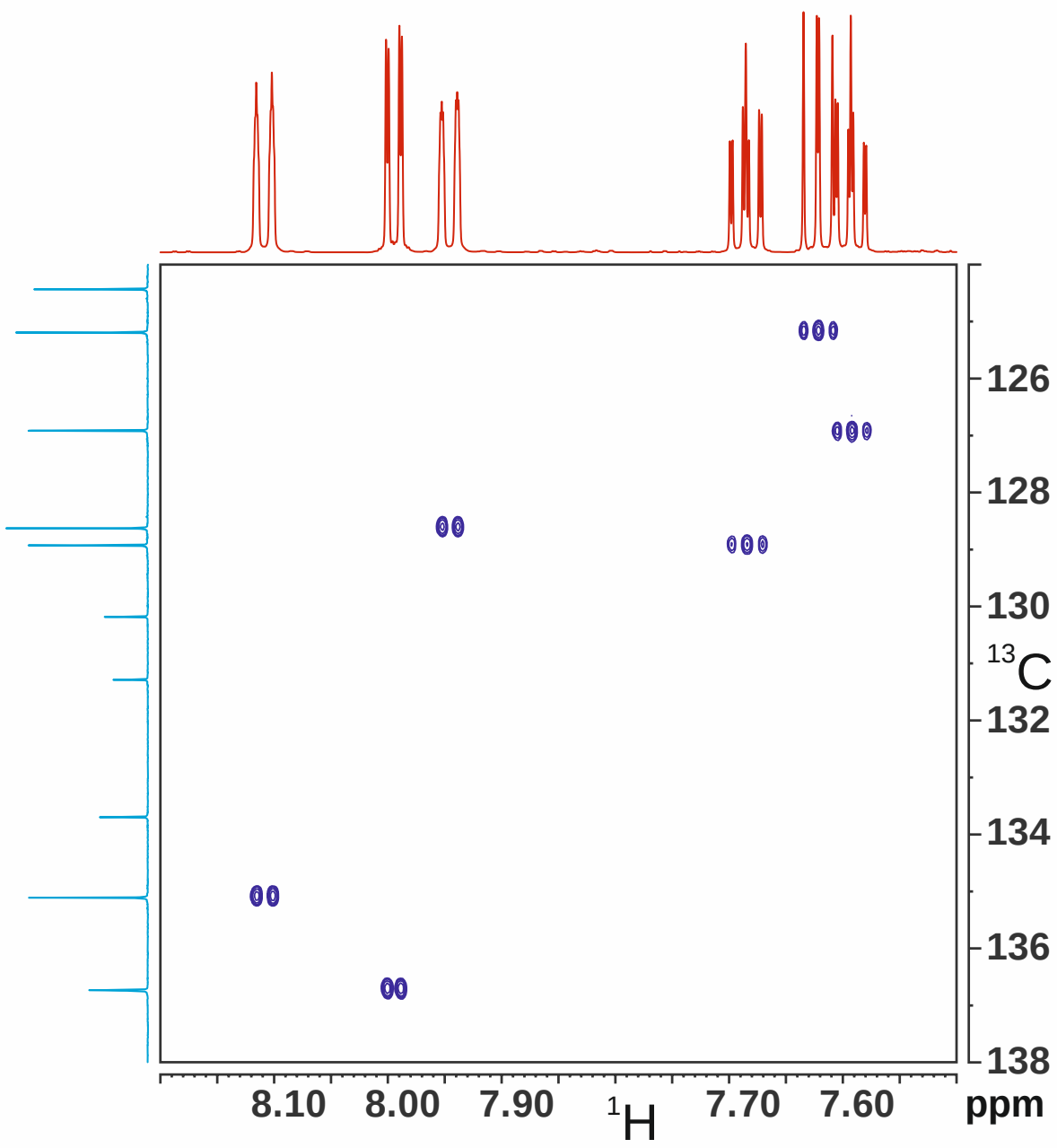
$^{1}H/^{13}C$ HSQC
recorded at 600.66/151.06 MHz

Some details in the HSQC, can be better analyzed in the enlargements on the next slide.



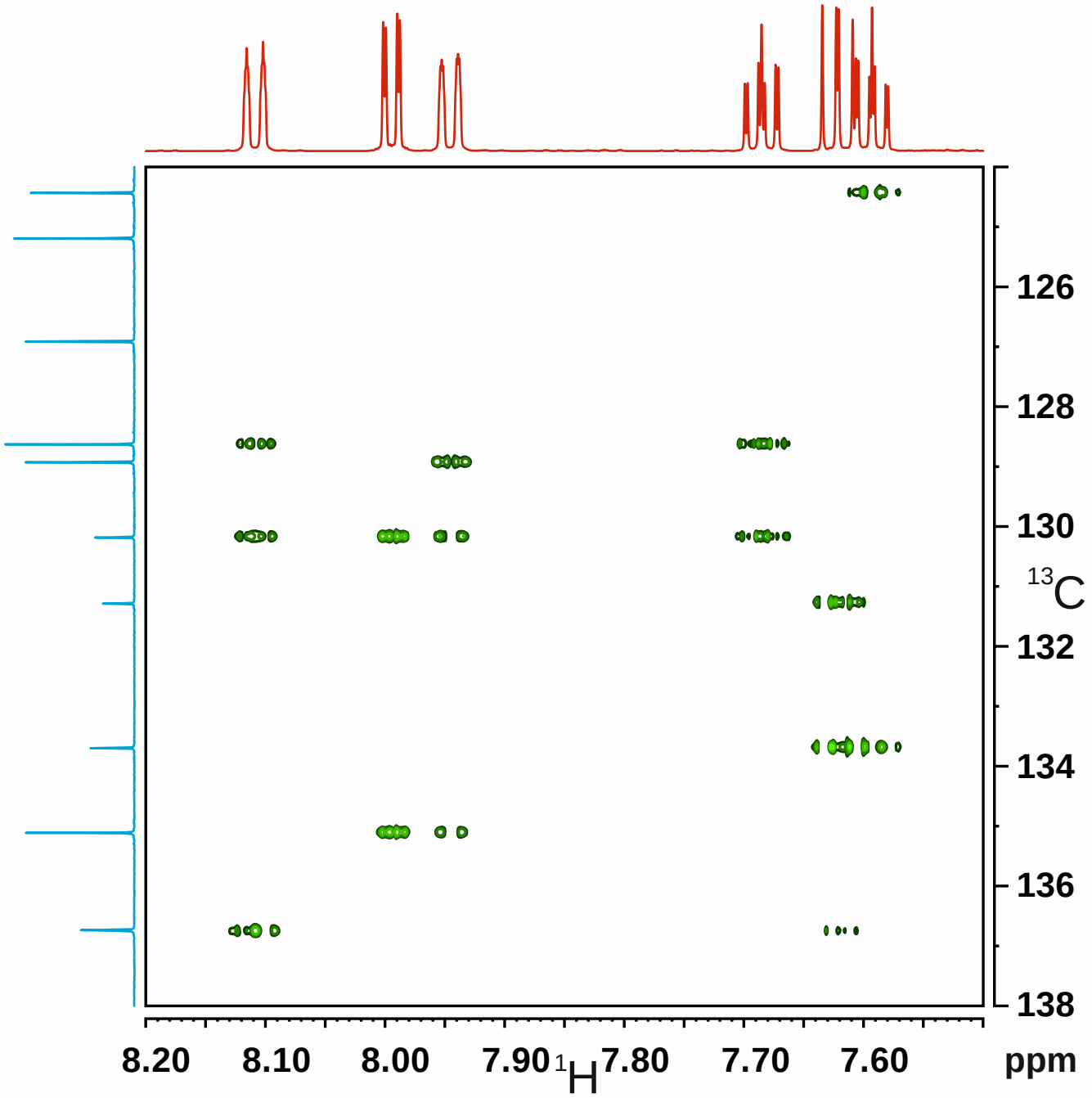
$^{1}H/^{13}C$ HSQC
recorded at 600.66/151.06 MHz



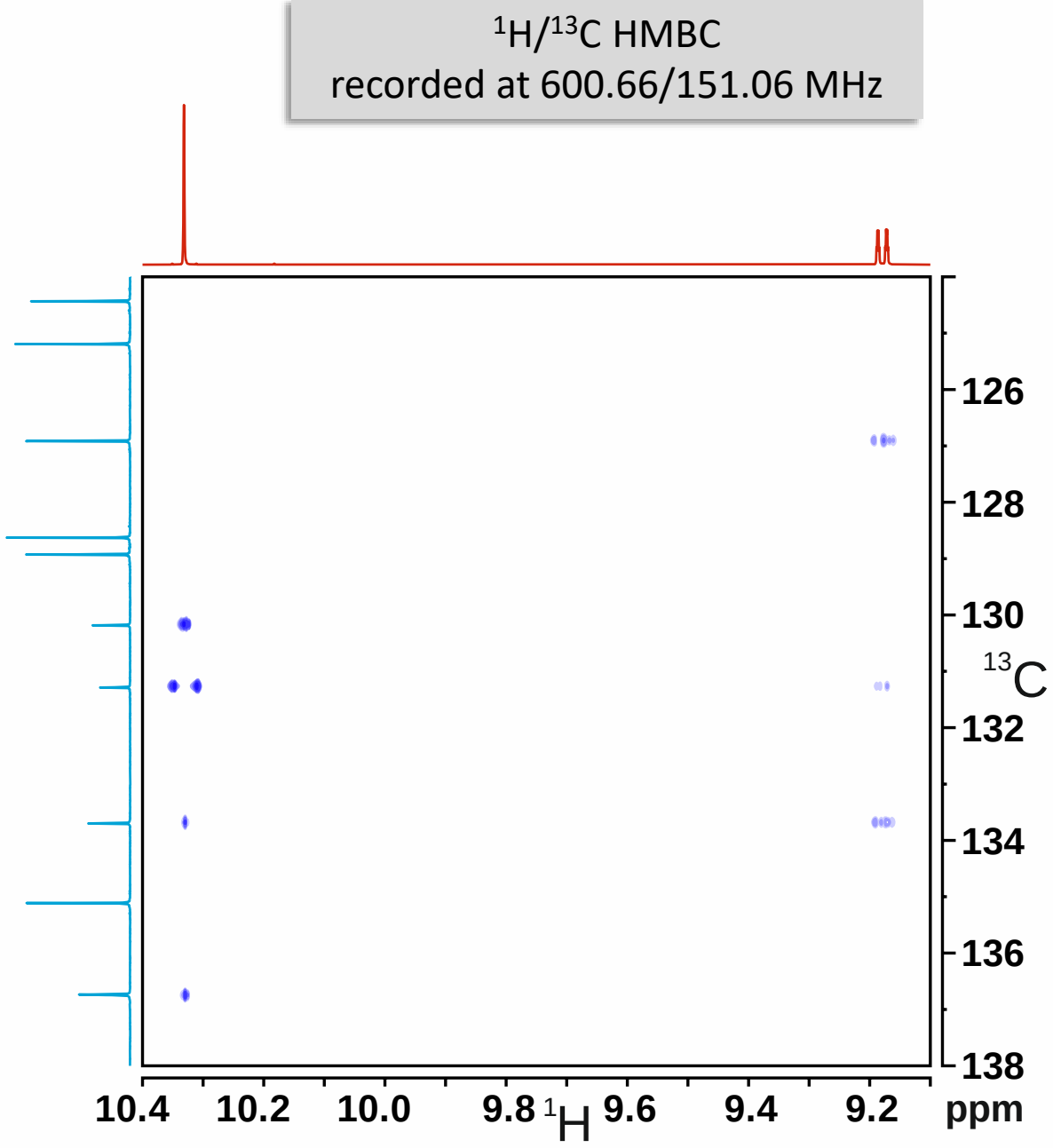


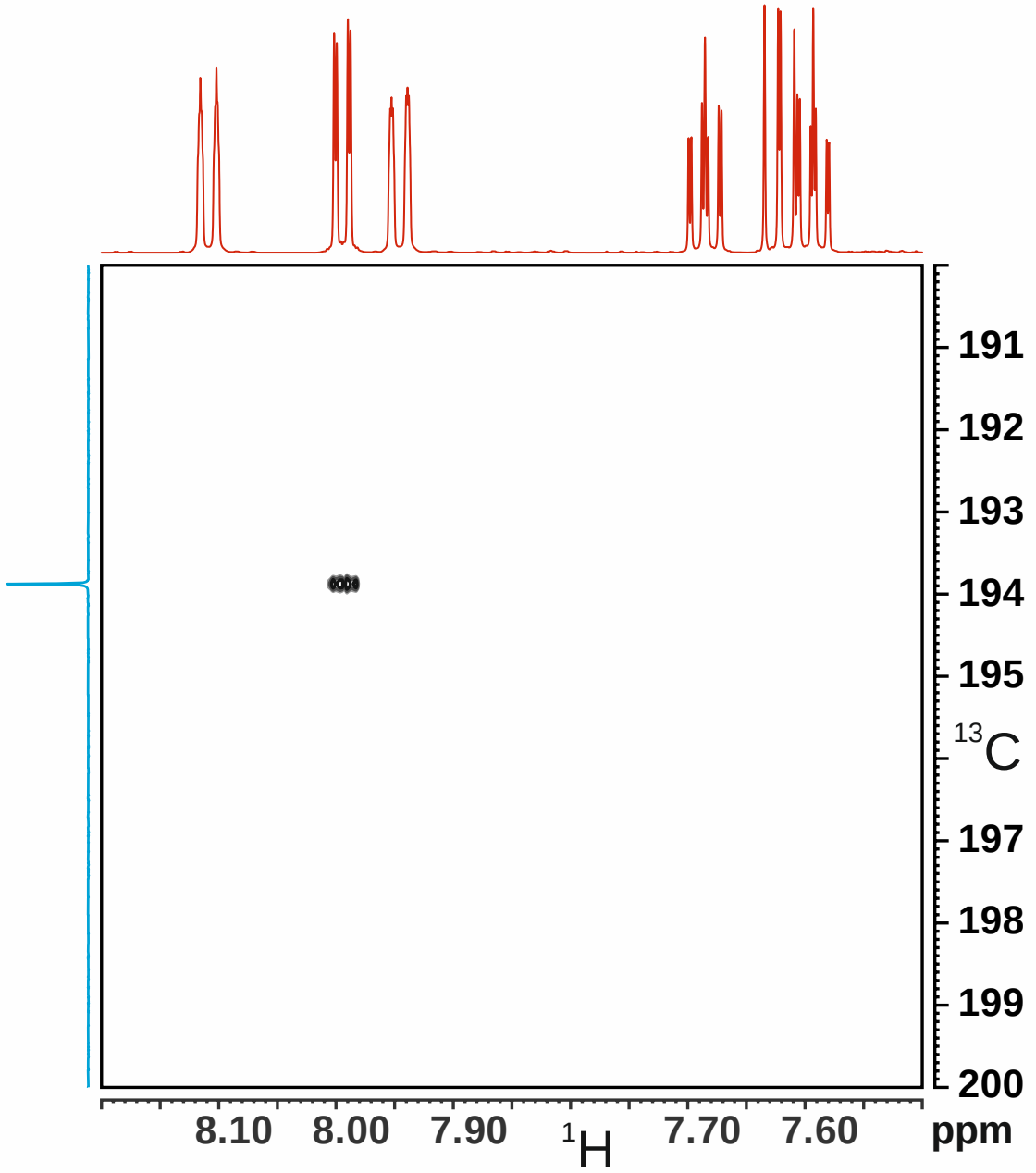
$^{1}H/^{13}C$ HMBC
recorded at 600.66/151.06 MHz

On this slide and the next, only the significant parts of the HMBC are shown.



$^{1}H/^{13}C$ HMBC
recorded at 600.66/151.06 MHz





Problem of the Month:

March 2022

Solution

Basic considerations

Double bond equivalents, integration

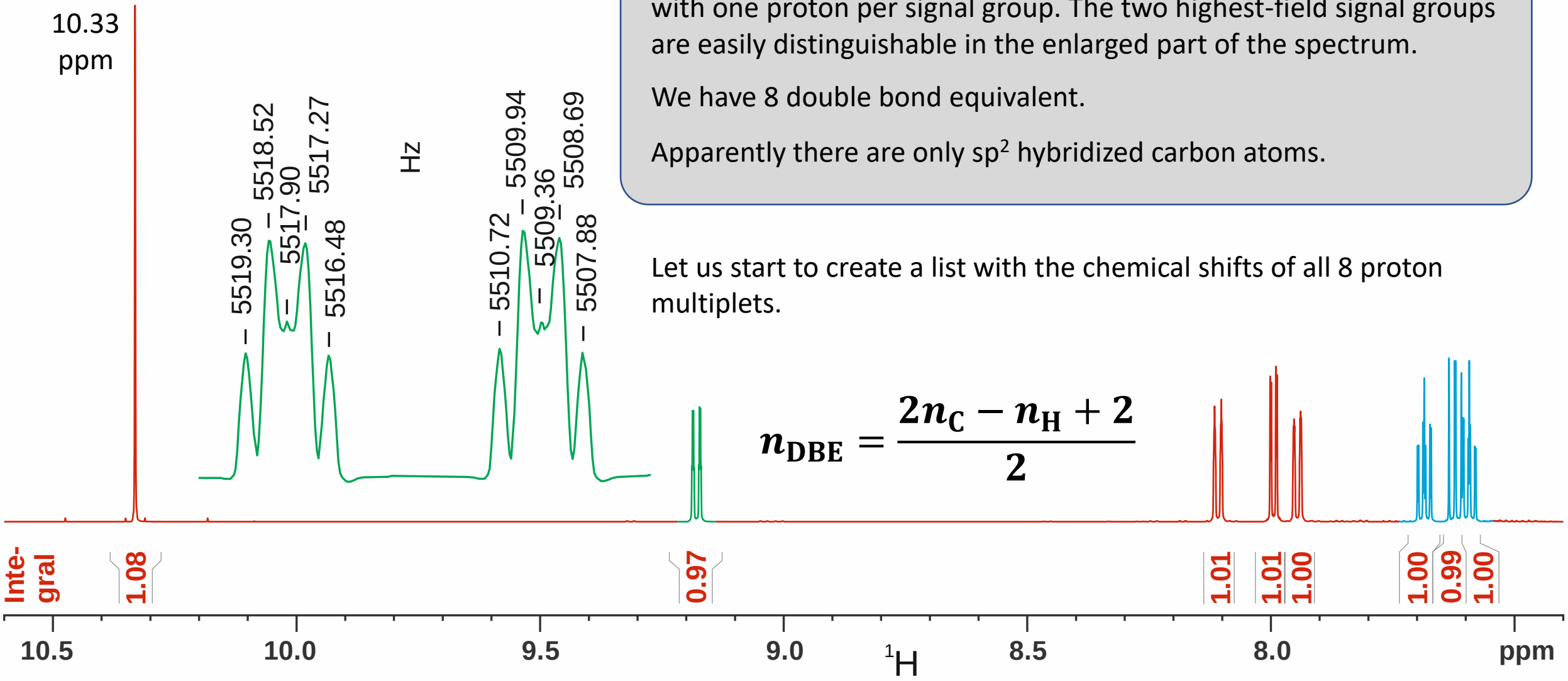
$C_{11}H_8O$ in CD_3CN

There are 8 distinguishable signal groups in the proton spectrum with one proton per signal group. The two highest-field signal groups are easily distinguishable in the enlarged part of the spectrum.

We have 8 double bond equivalent.

Apparently there are only sp^2 hybridized carbon atoms.

Let us start to create a list with the chemical shifts of all 8 proton multiplets.



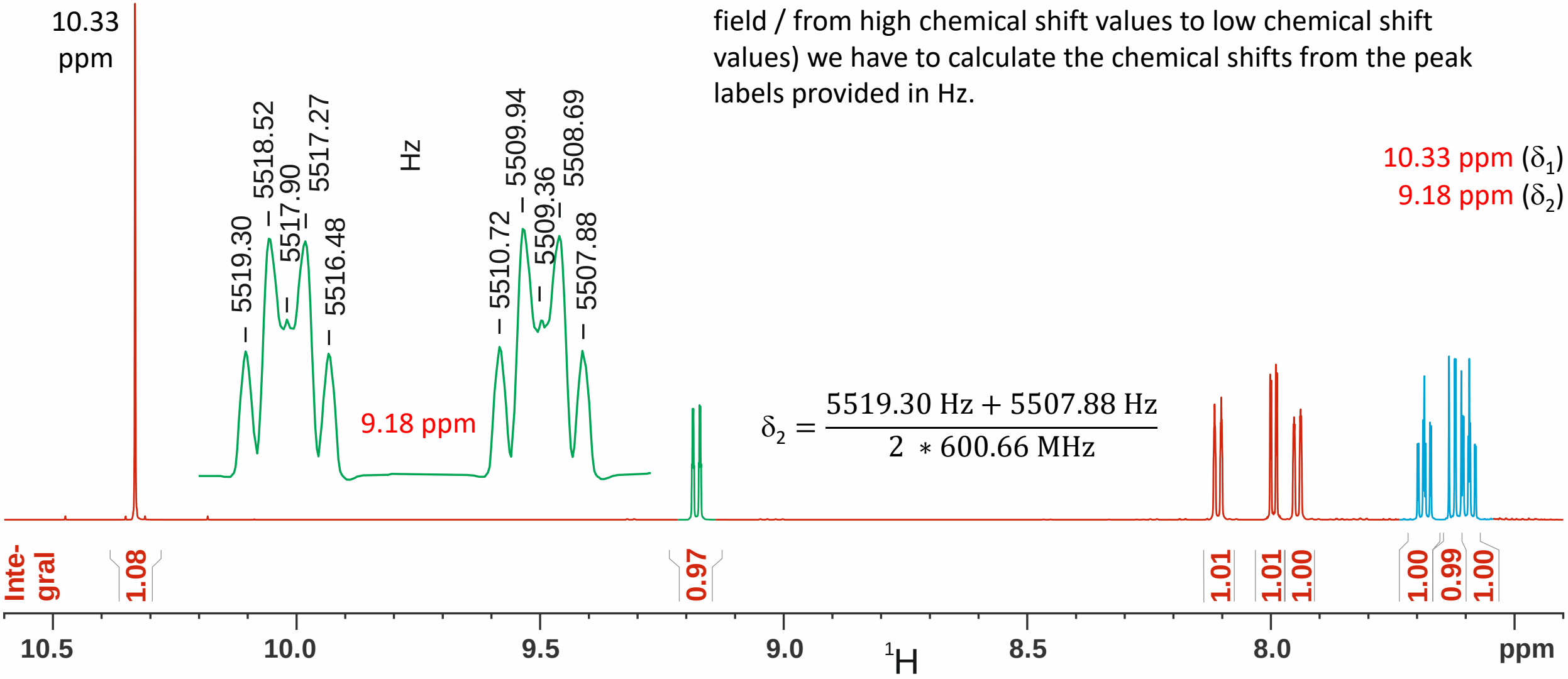
$$n_{DBE} = \frac{2n_C - n_H + 2}{2}$$

Basic considerations

Proton chemical shifts

The first chemical shift is obvious.

In the case of the second multiplet (moving from low to high field / from high chemical shift values to low chemical shift values) we have to calculate the chemical shifts from the peak labels provided in Hz.



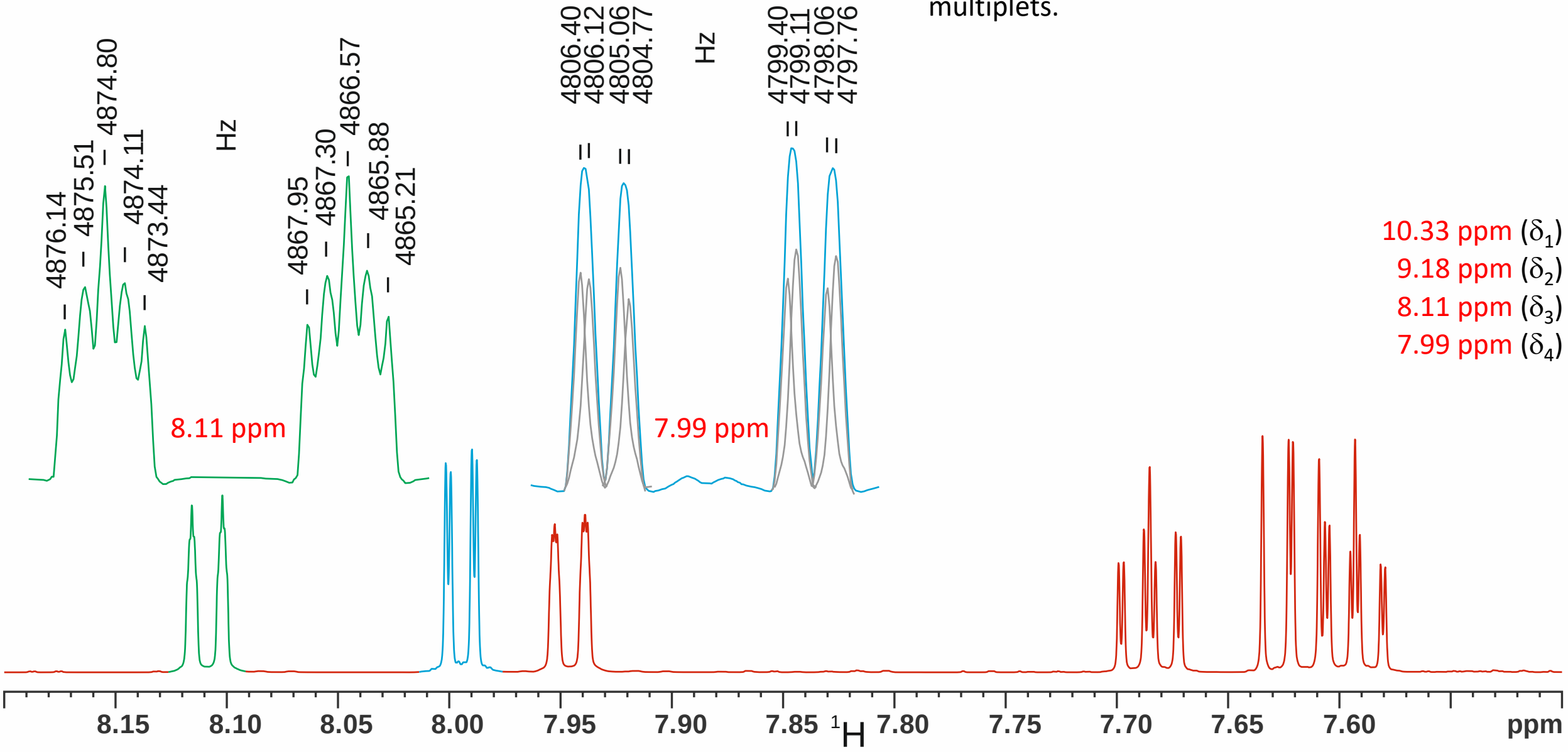
10.33 ppm (δ_1)
9.18 ppm (δ_2)

$$\delta_2 = \frac{5519.30\ \text{Hz} + 5507.88\ \text{Hz}}{2\ * 600.66\ \text{MHz}}$$

Basic considerations

Proton chemical shifts

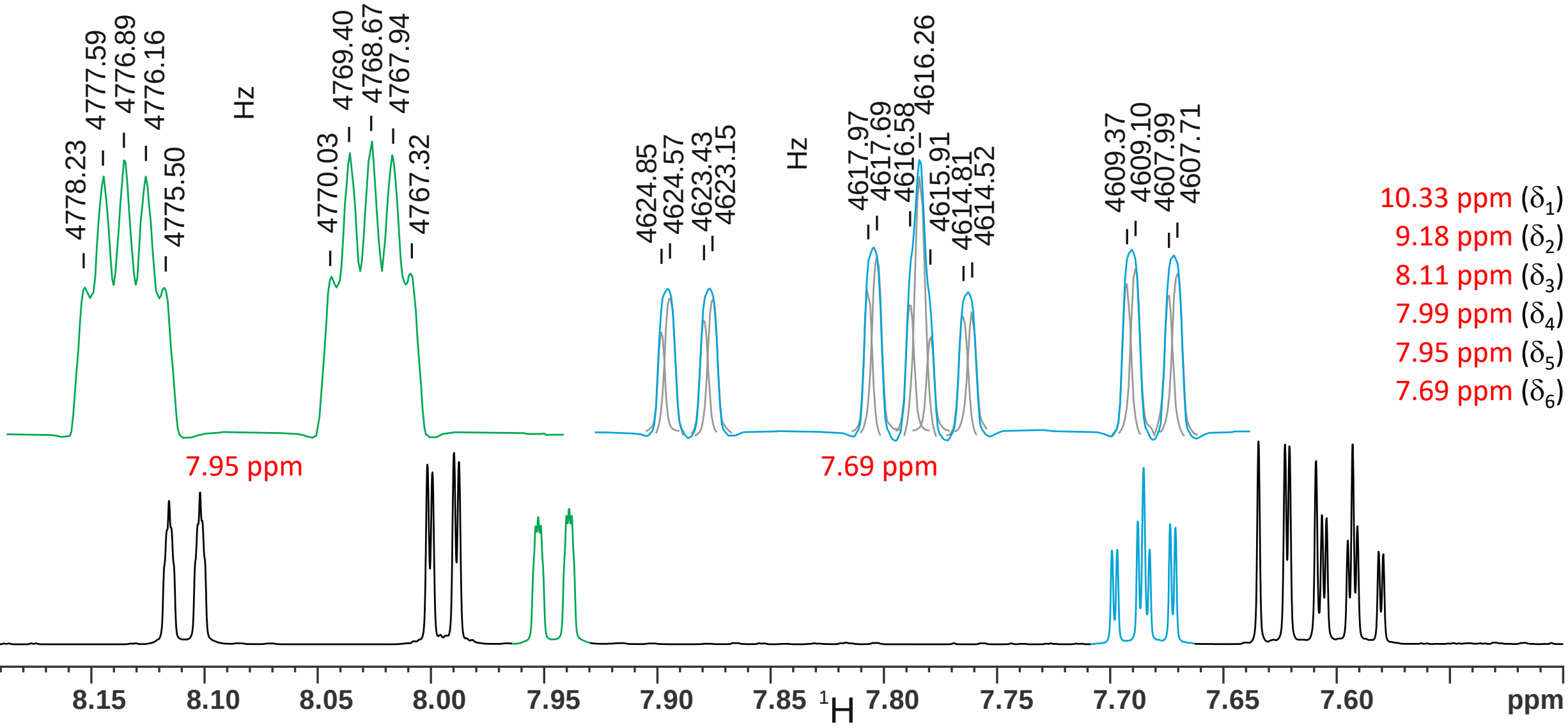
The procedure is the same for the next two multiplets.



Basic considerations

Proton chemical shifts

Two more multiplets.

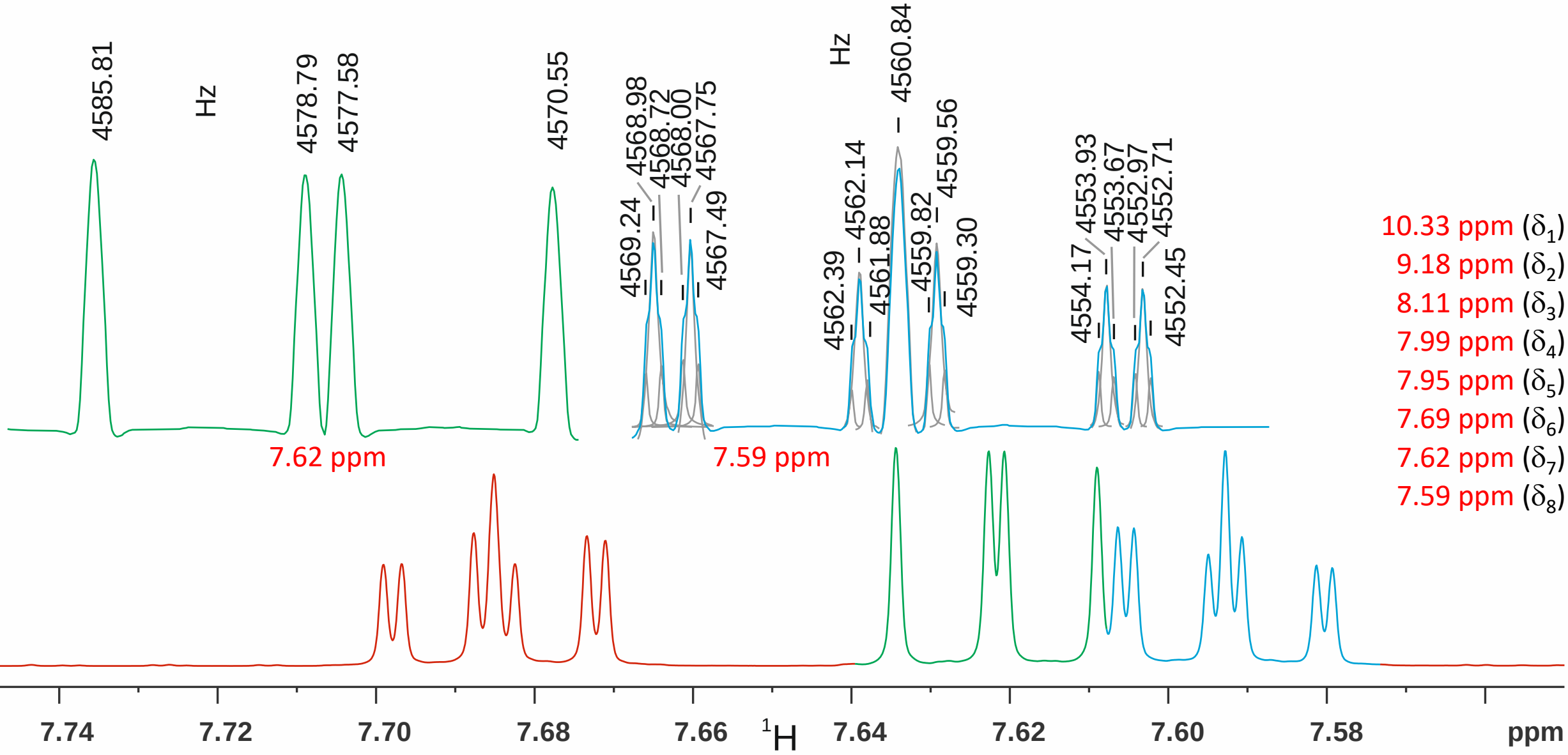


10.33 ppm (δ_1)
9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)

Basic considerations

Proton chemical shifts

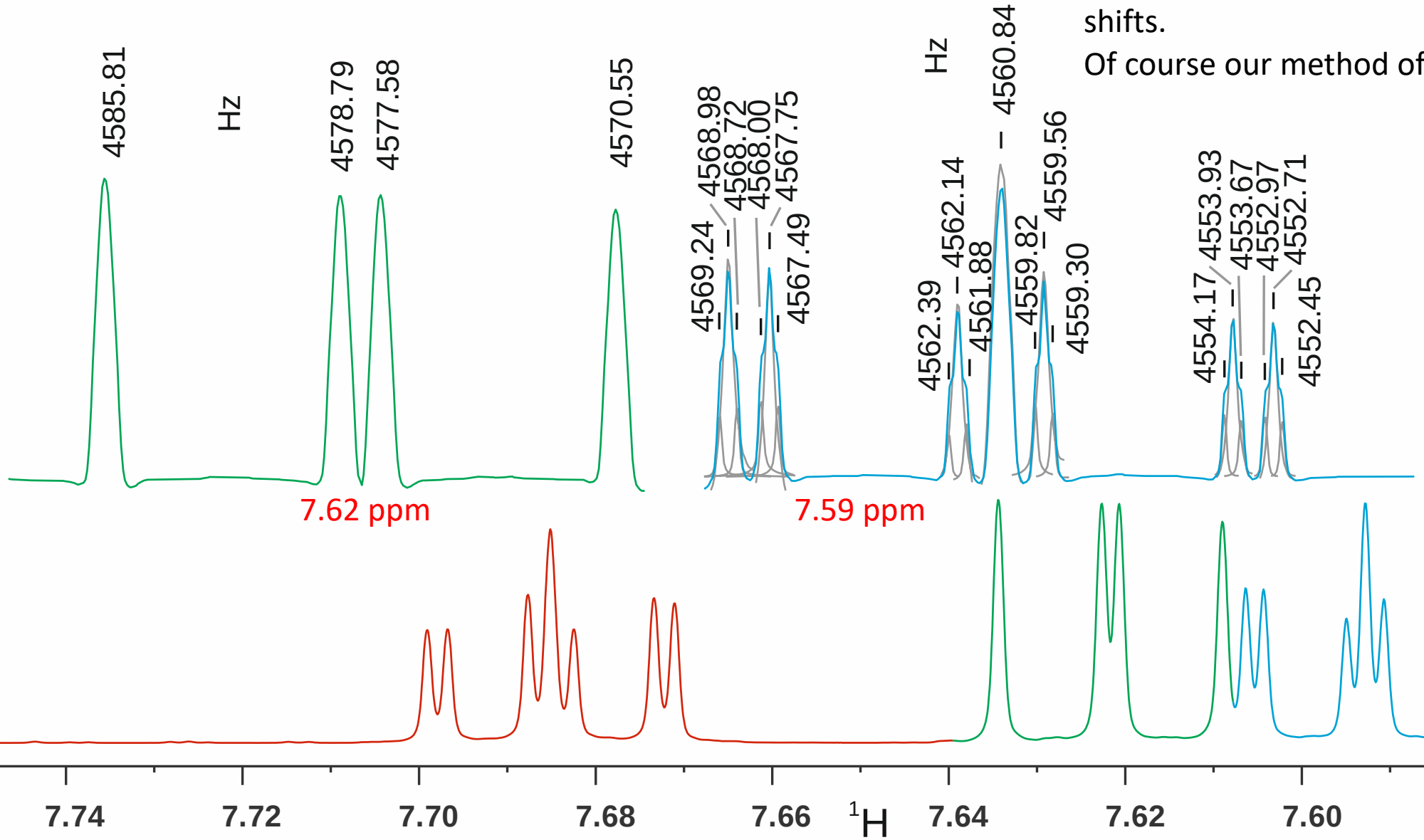
And finally, the two highest-field multiplets mentioned in the basic considerations..



Basic considerations

Proton chemical shifts

Now we have to search for the connectivity between the protons with these chemical shifts.
Of course our method of choice is the COSY.



10.33 ppm (δ_1)
9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)

Proton spin systems

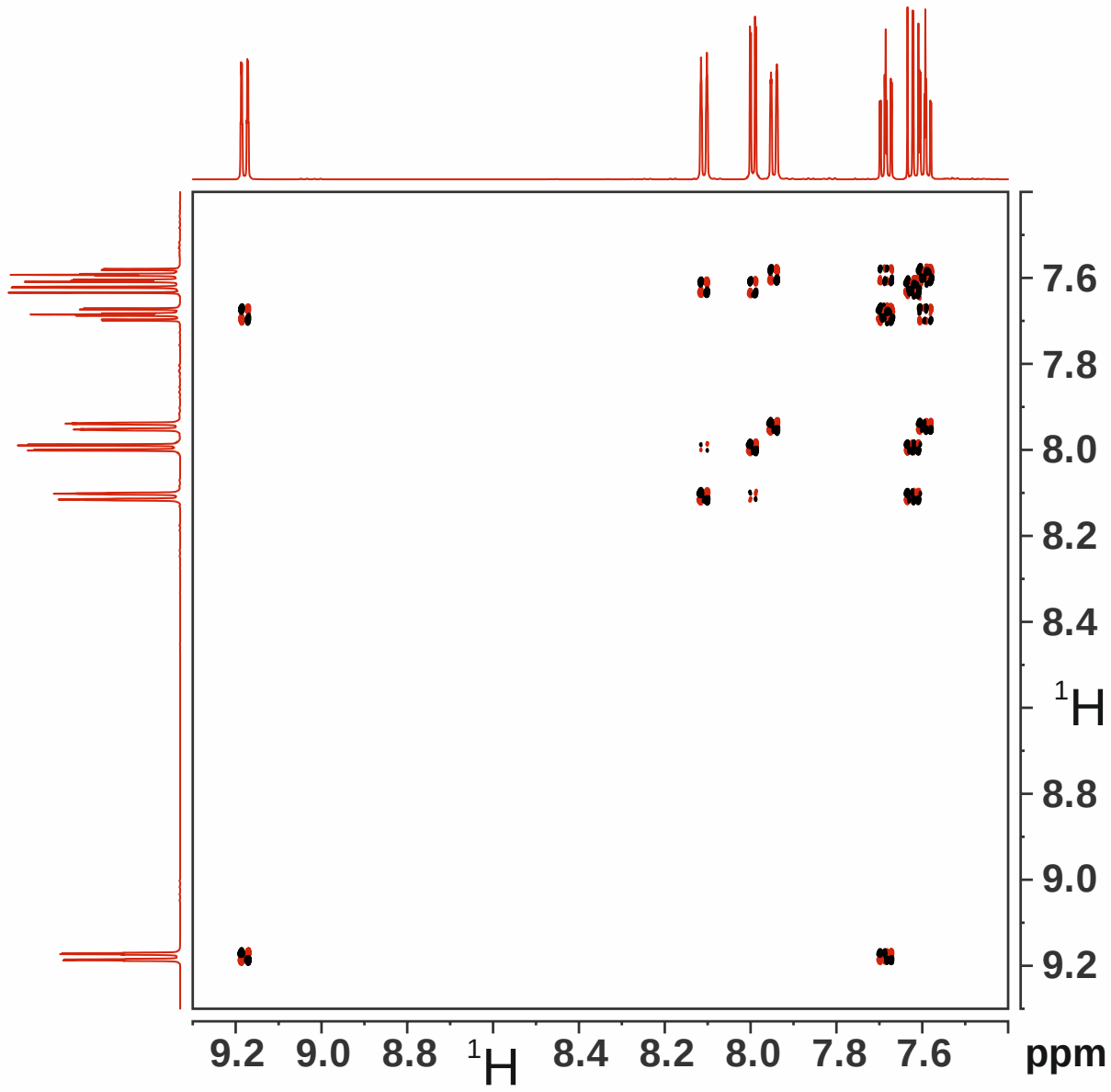
Two chains and a singlet

As is often done, one could also start in this case with the HSQC for the evaluation.

Here, however, it is much easier to first extract three independent spin systems from the COSY.

Having these spin systems, adding the carbon atoms using the HSQC would result in three structural fragments.

10.33 ppm (δ_1)
9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)



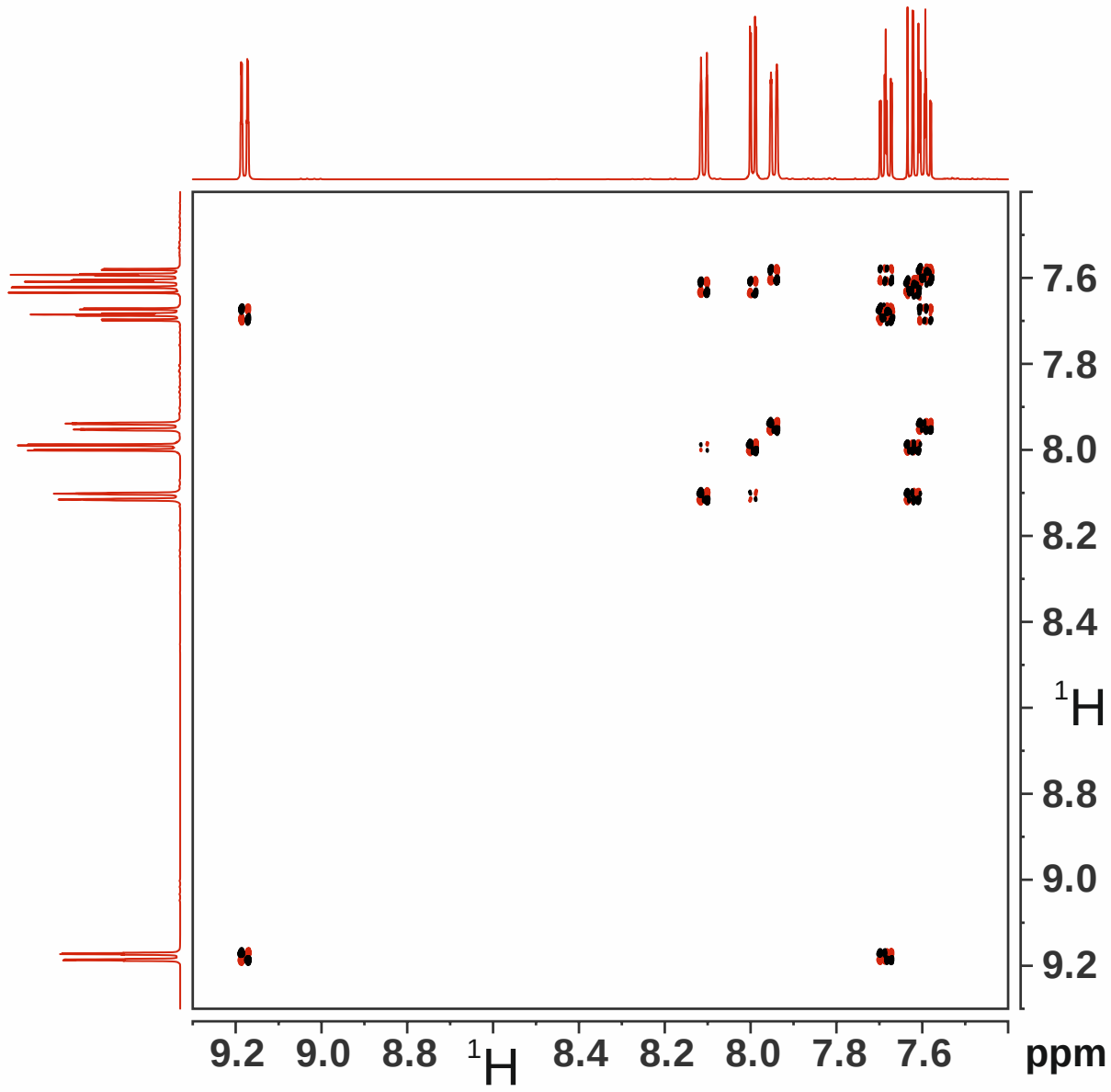
Proton spin systems

Two chains and a singlet

The proton signal at 10.33 ppm is a singlet. There is no correlation at all visible in the COSY.

At the moment, we can't do anything with this signal. Let's take a sticky note and keep the value for later use.

10.33 ppm (δ_1)
9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)



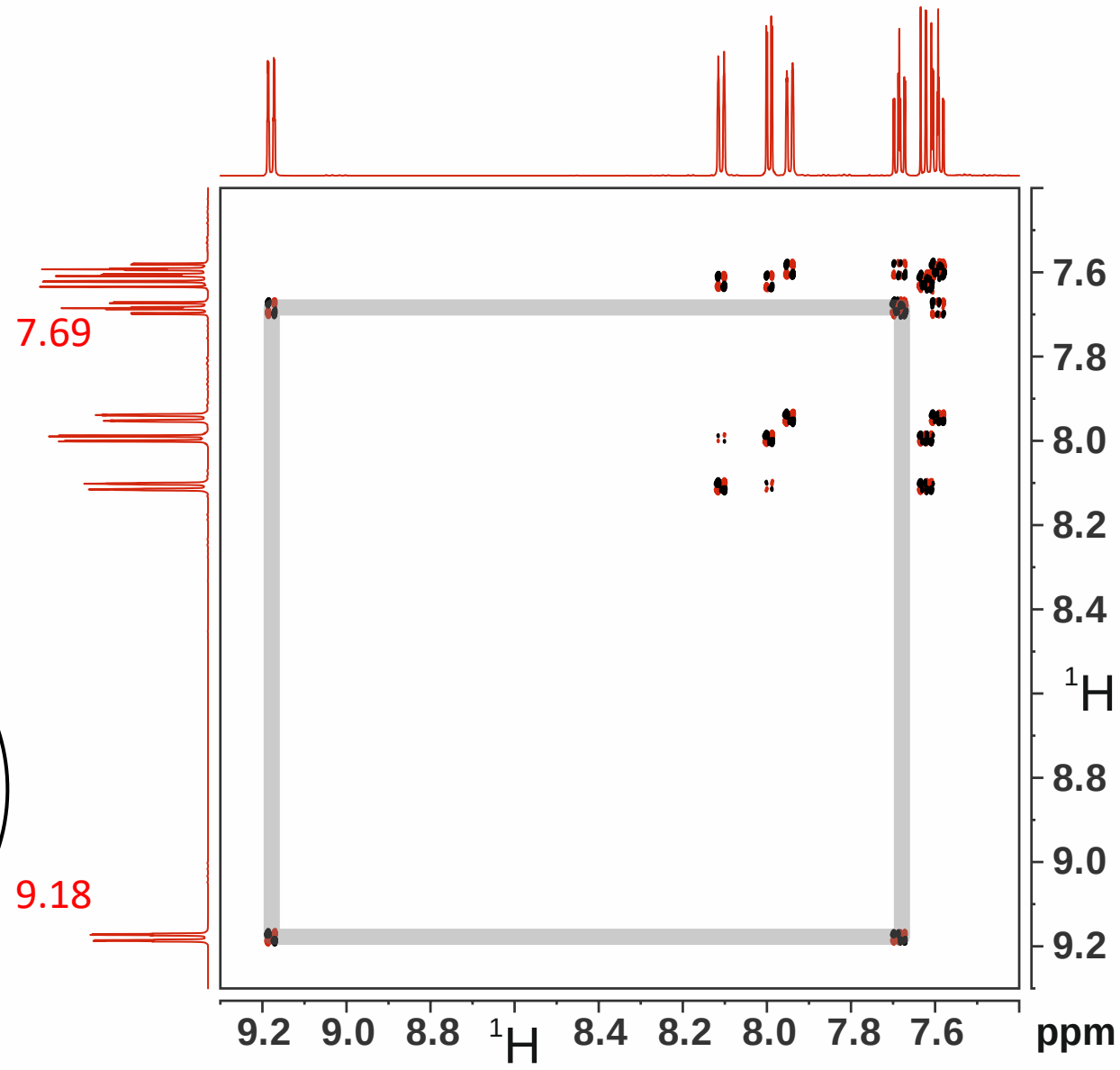
Proton spin systems

Two chains and a singlet

A first correlation is easy visible between the protons with the chemical shifts of 9.18 ppm and 7.69 ppm.

We note this connectivity using a simple line.

9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)



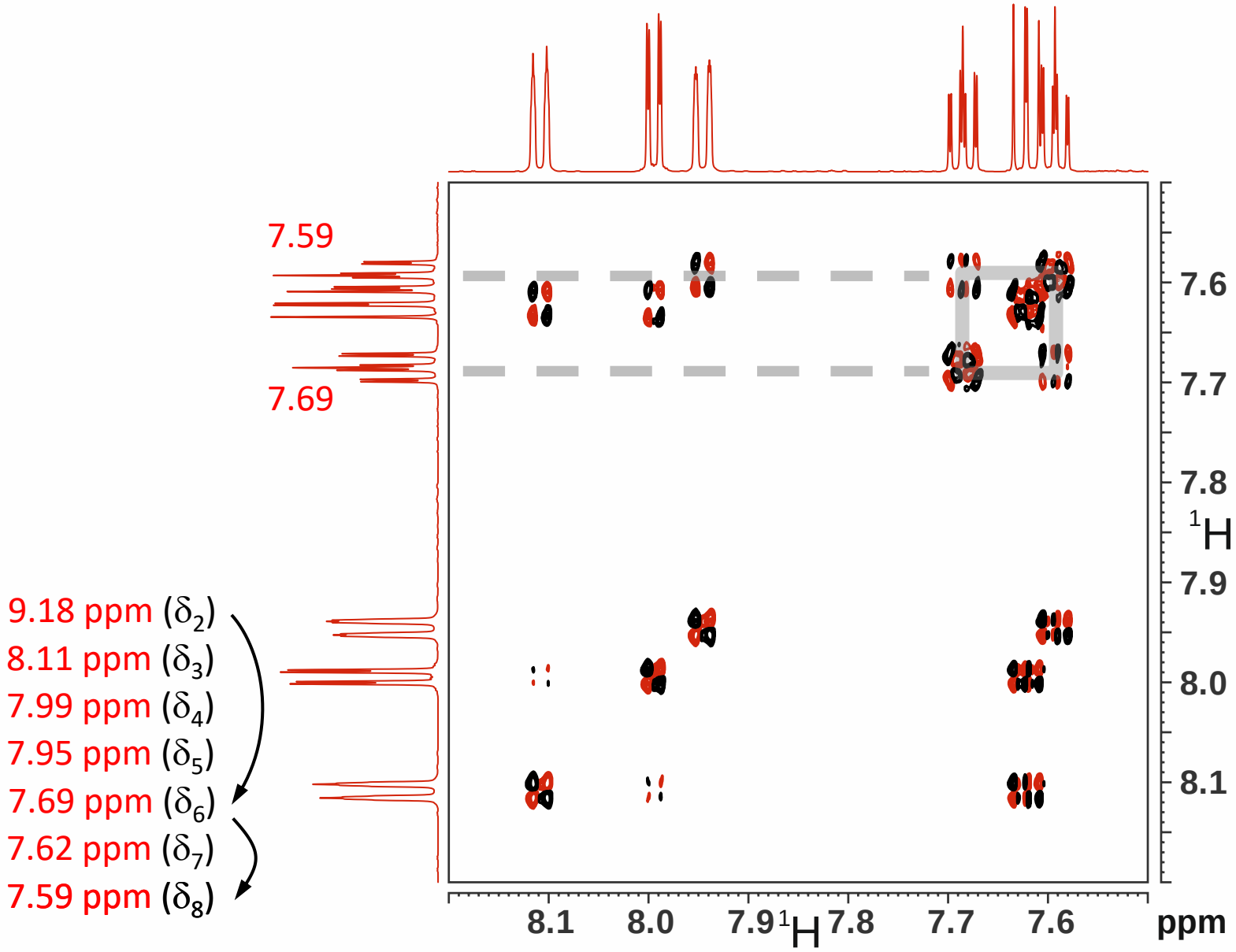
Proton spin systems

Two chains and a singlet

For all other correlations it is better to use a smaller part of the COSY. This makes the separation of some multiplets, especially those at highest field, easier.

Coming from the proton with the chemical shift of 7.69 ppm, we see a clear connectivity to the proton with the chemical shift of 7.59 ppm.

Once again we note this connectivity using a simple line.

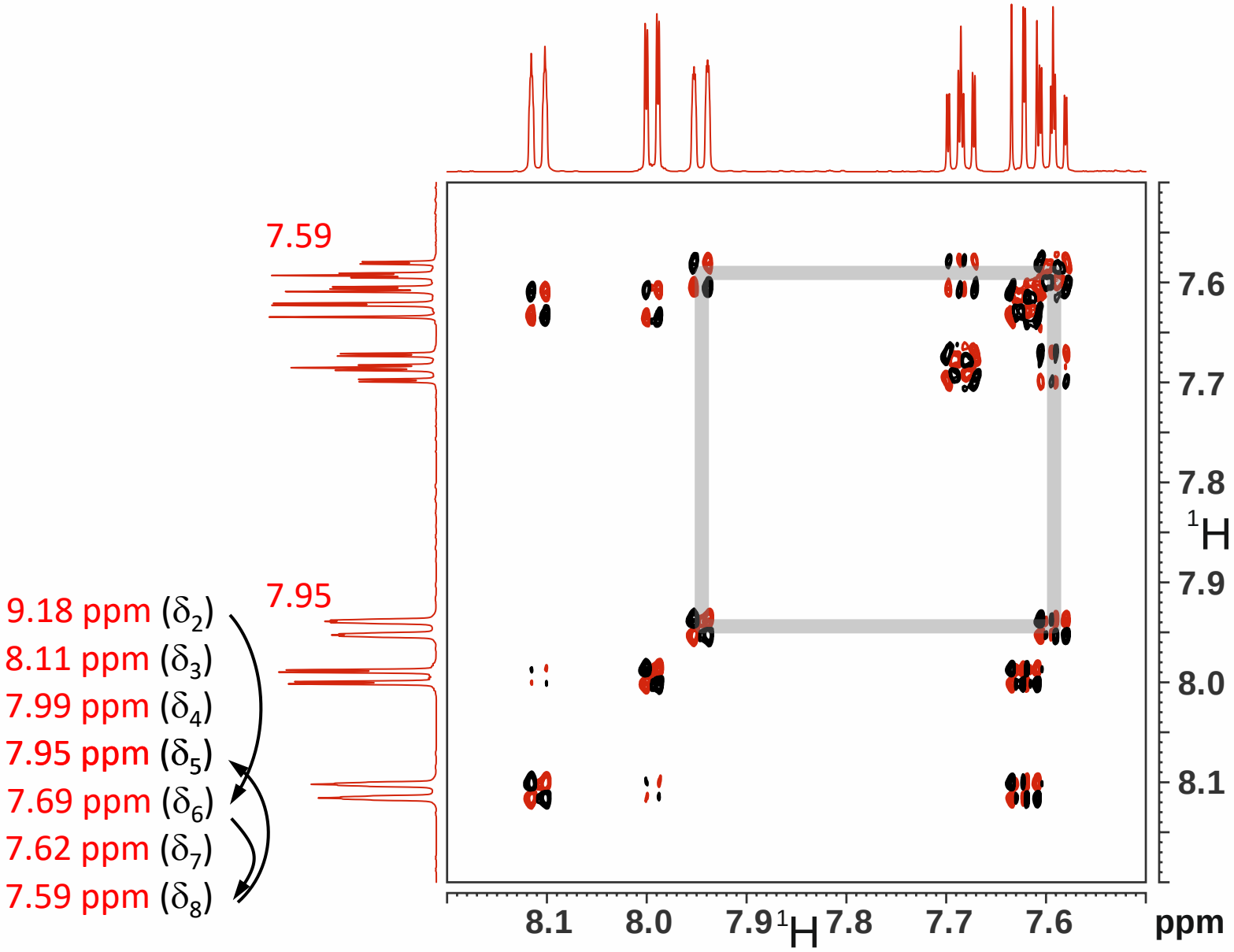


Proton spin systems

Two chains and a singlet

There is one more correlation.

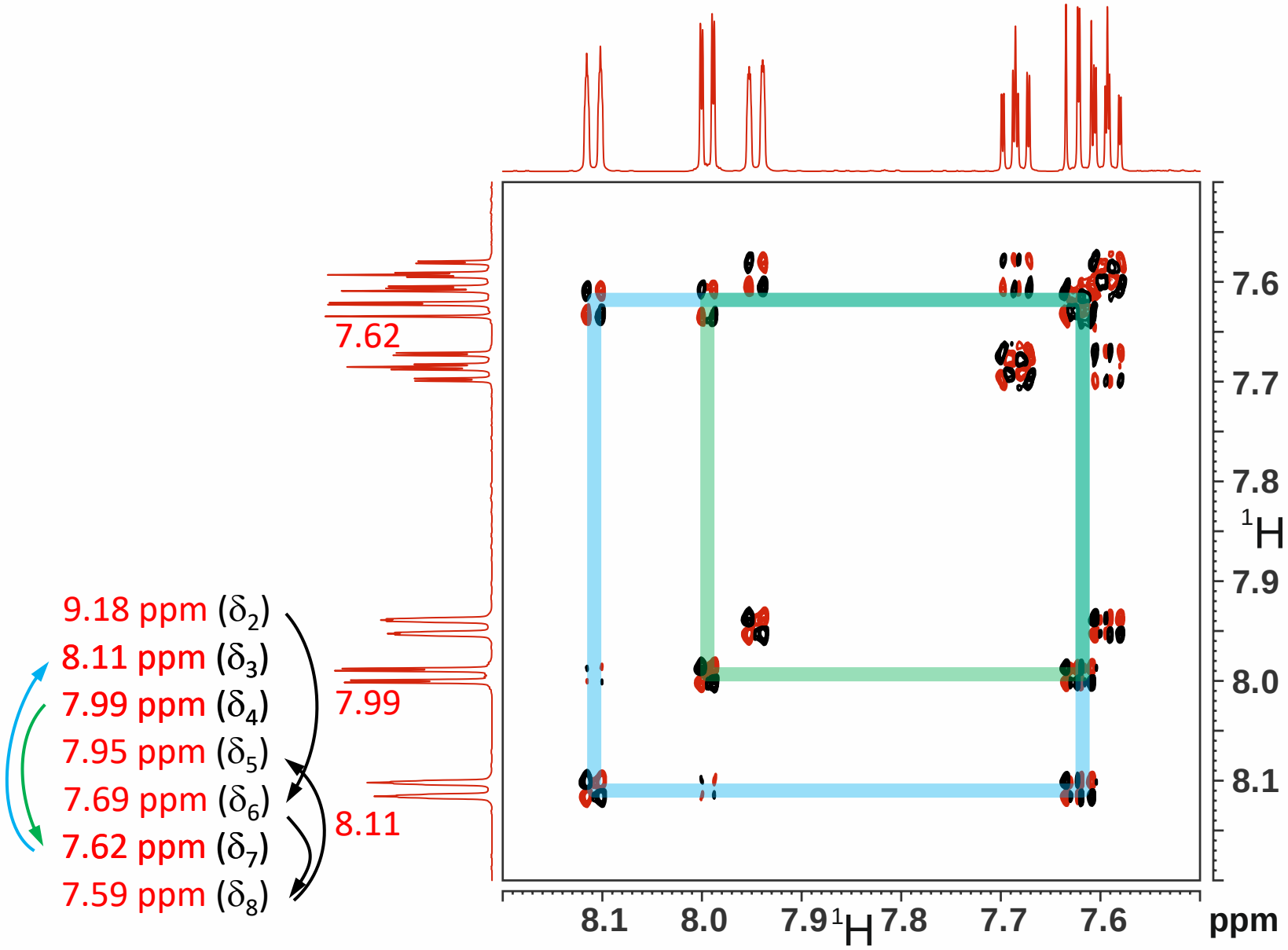
Once again we note this connectivity using a simple line.



Proton spin systems

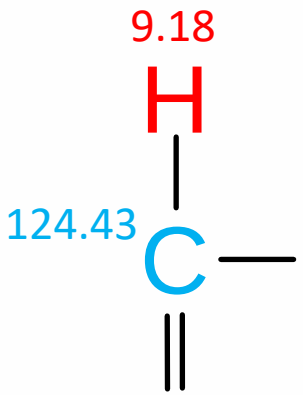
Two chains and a singlet

Now we repeat the procedure with the three remaining multiplets.



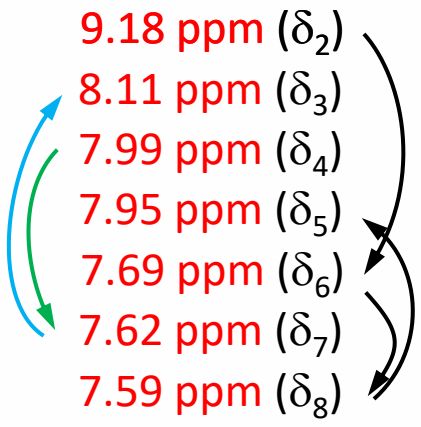
Adding carbon atoms

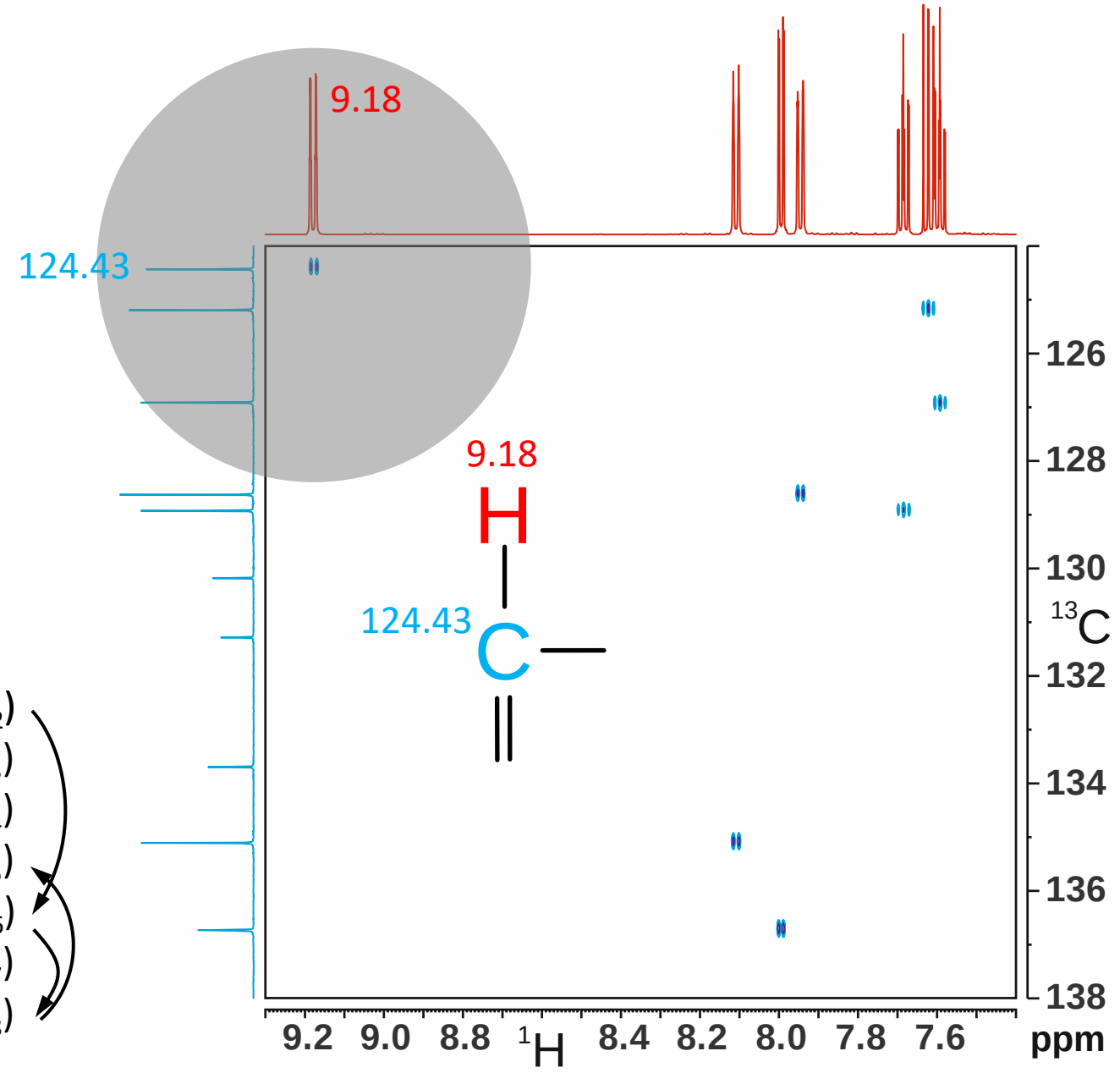
Two chains



From this point it's rather simple.

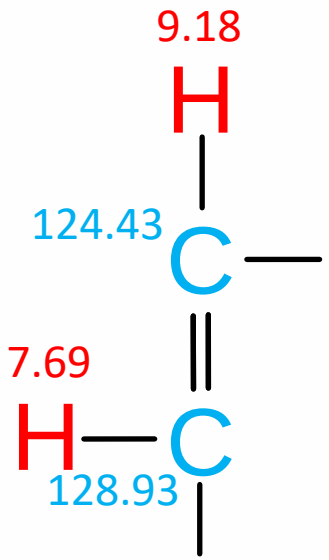
From the HSQC we take the chemical shifts of the carbon atoms attached to the protons. We still neglect one proton signal (see the sticky note at the upper right corner) and get two chains of CH fragments.





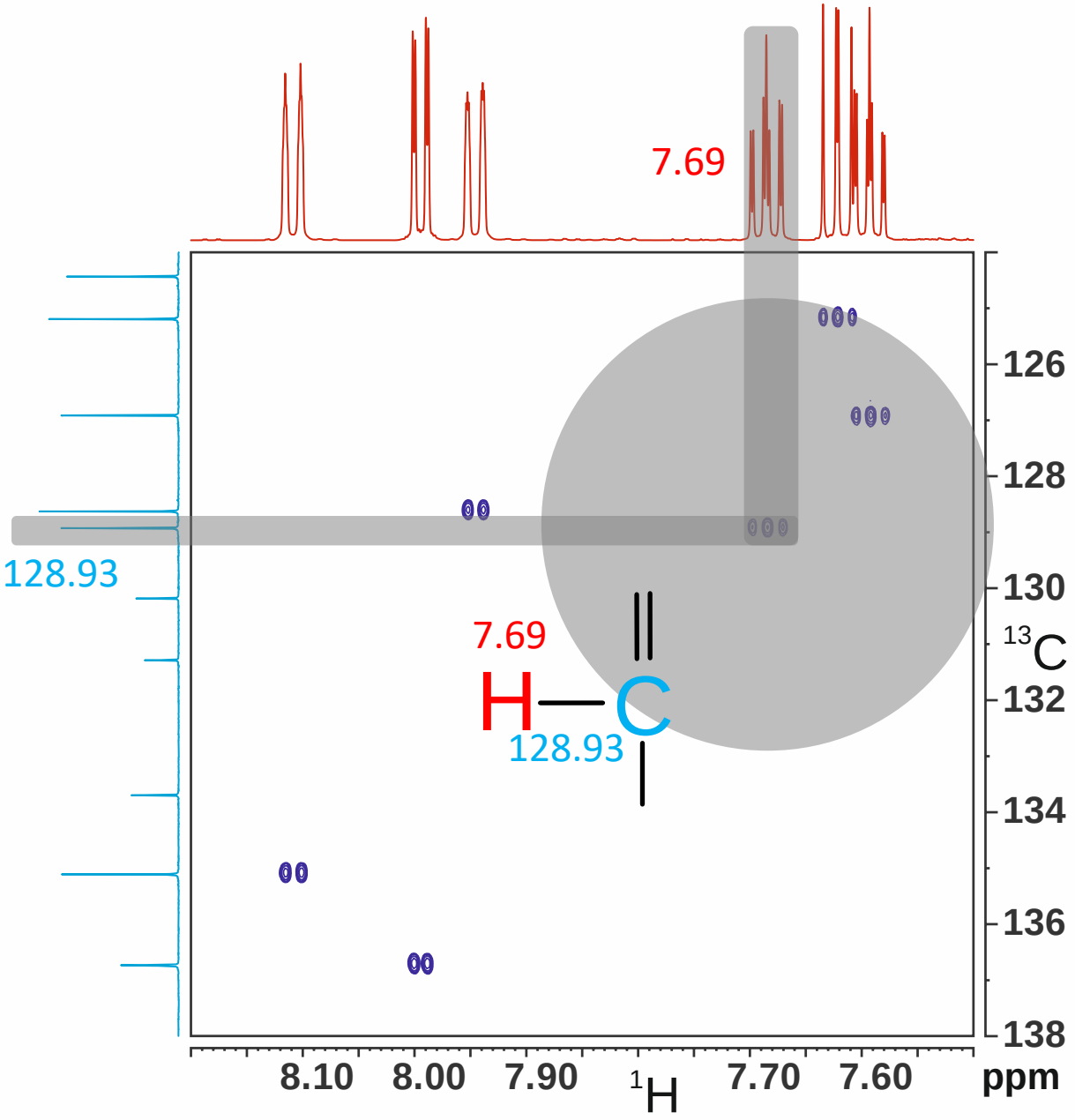
Adding carbon atoms

Two chains



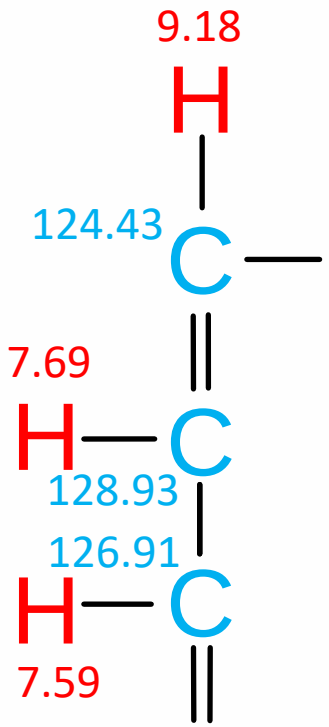
The next CH please.

9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)



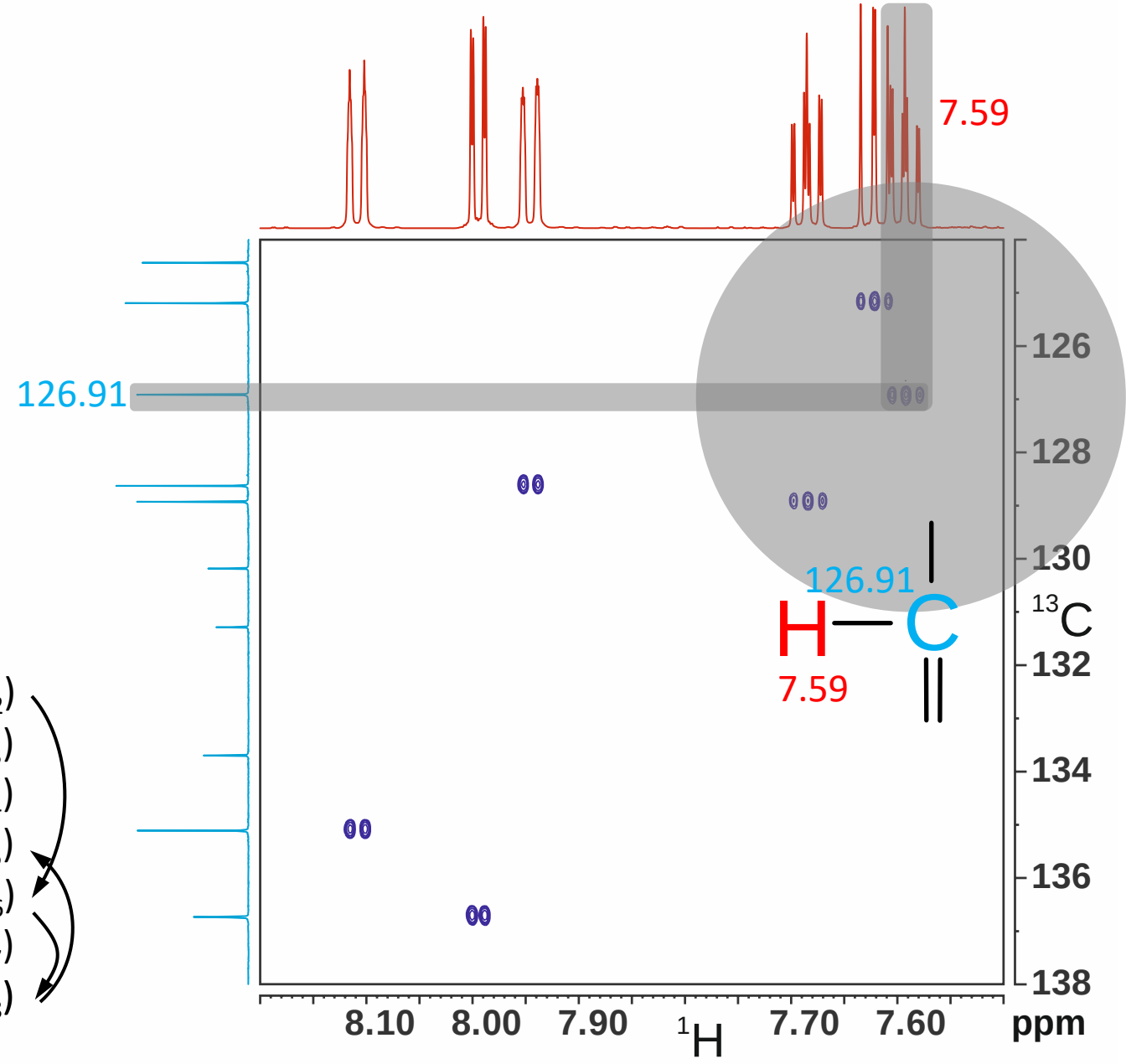
Adding carbon atoms

Two chains



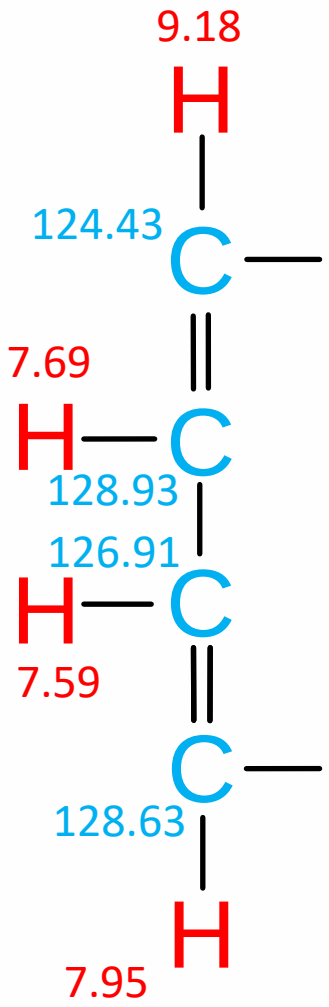
One CH more.

9.18 ppm (δ_2)
8.11 ppm (δ_3)
7.99 ppm (δ_4)
7.95 ppm (δ_5)
7.69 ppm (δ_6)
7.62 ppm (δ_7)
7.59 ppm (δ_8)

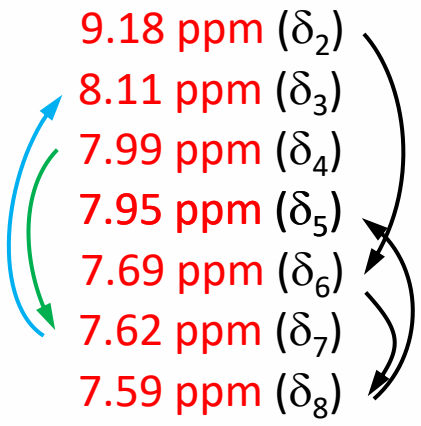


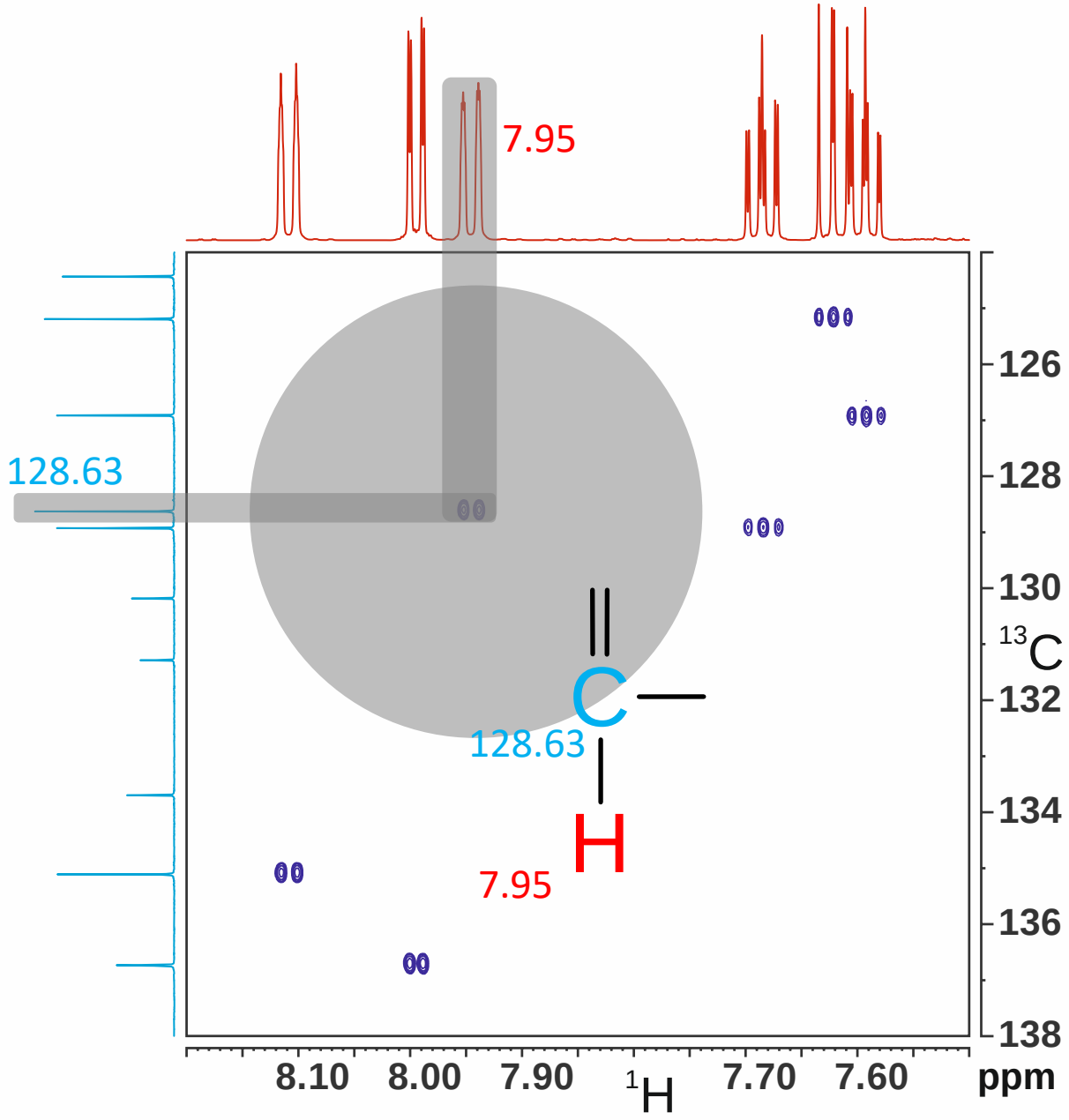
Adding carbon atoms

Two chains



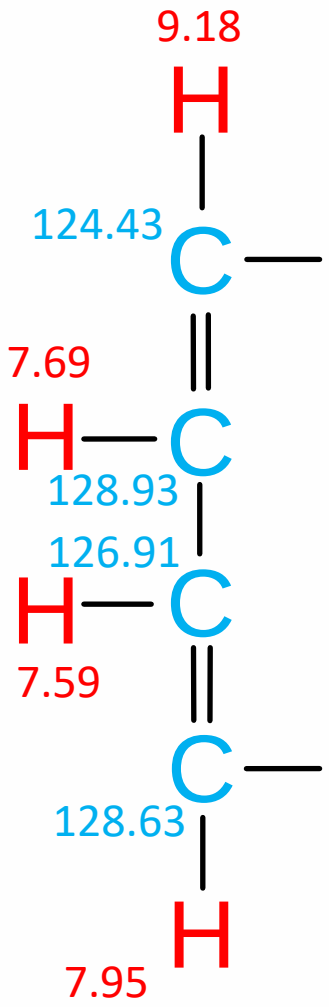
And finally the last CH of this spin system.



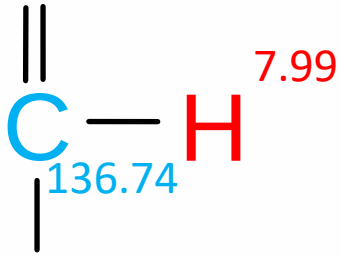


Adding carbon atoms

Two chains



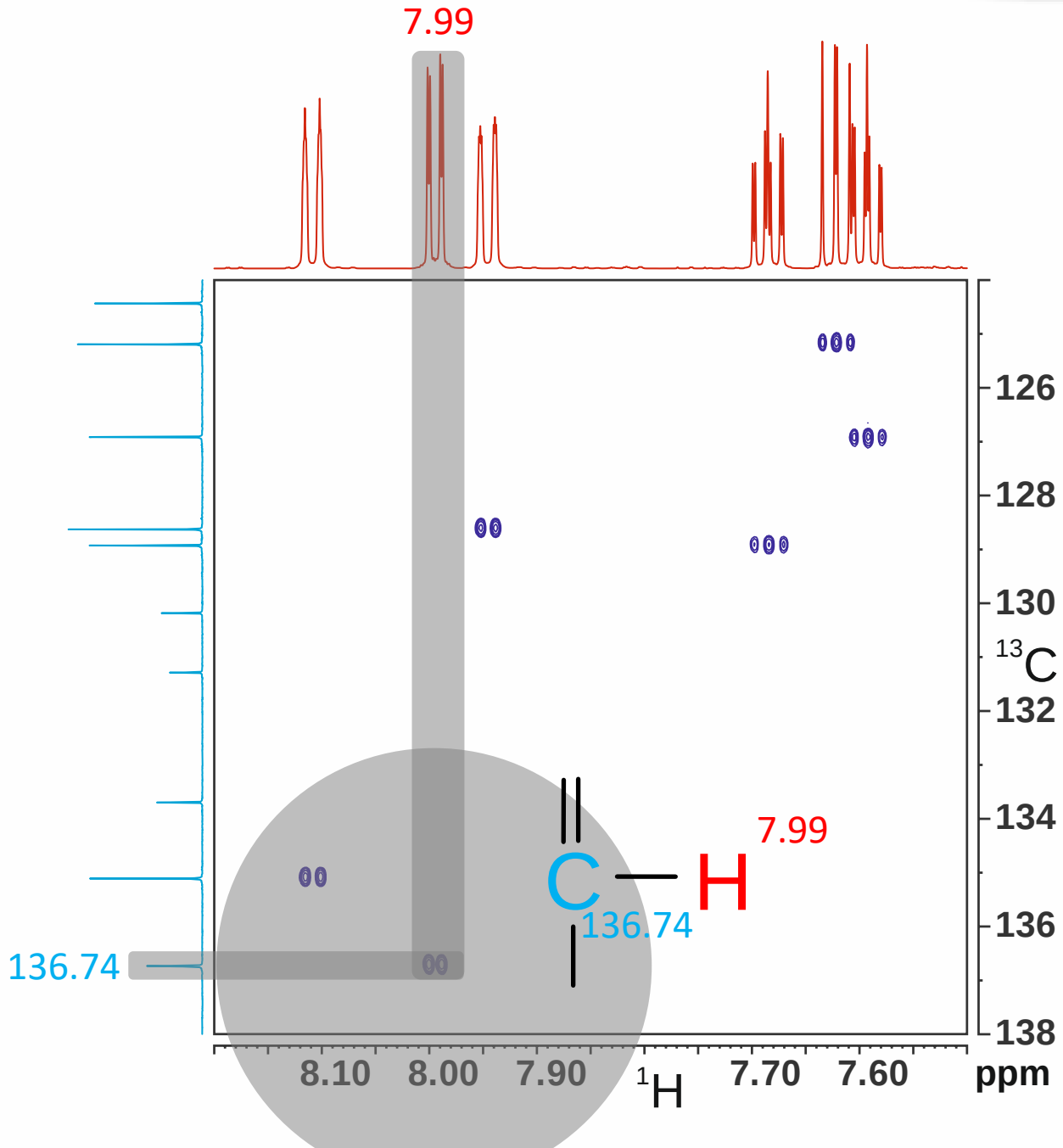
Let's repeat the same procedure with the three remaining proton signals.



8.11 ppm (δ_3)

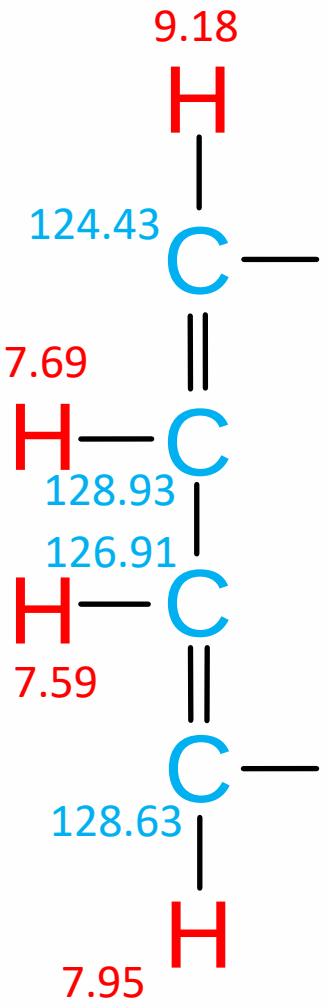
7.99 ppm (δ_4)

7.62 ppm (δ_7)

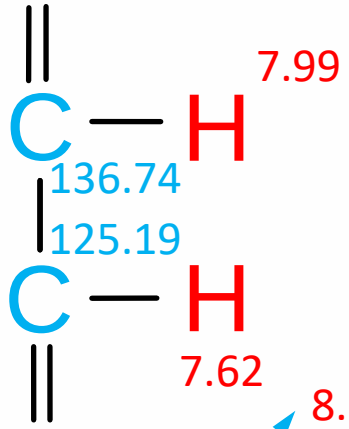


Adding carbon atoms

Two chains



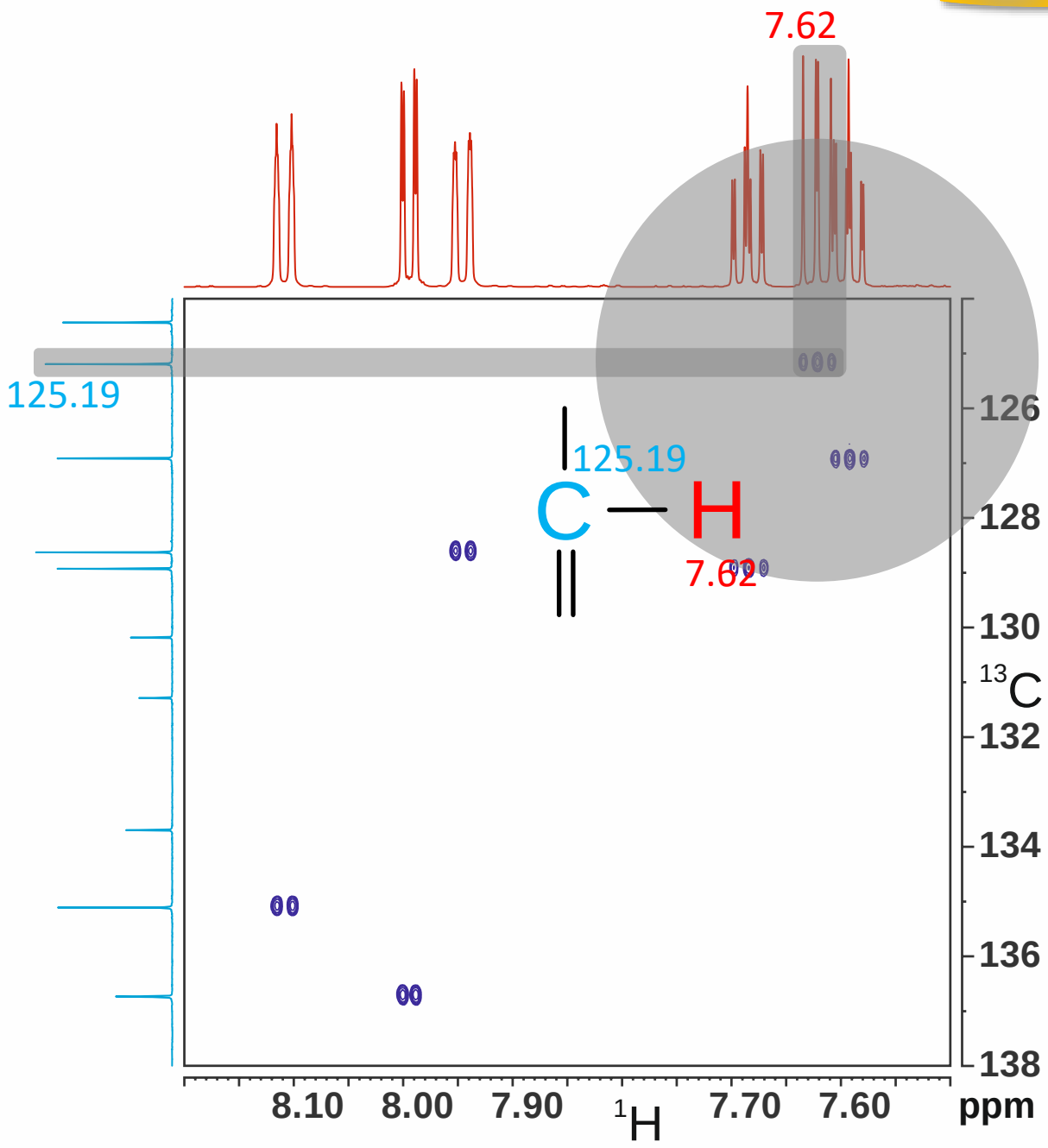
Let's repeat the same procedure with the three remaining proton signals.



8.11 ppm (δ_3)

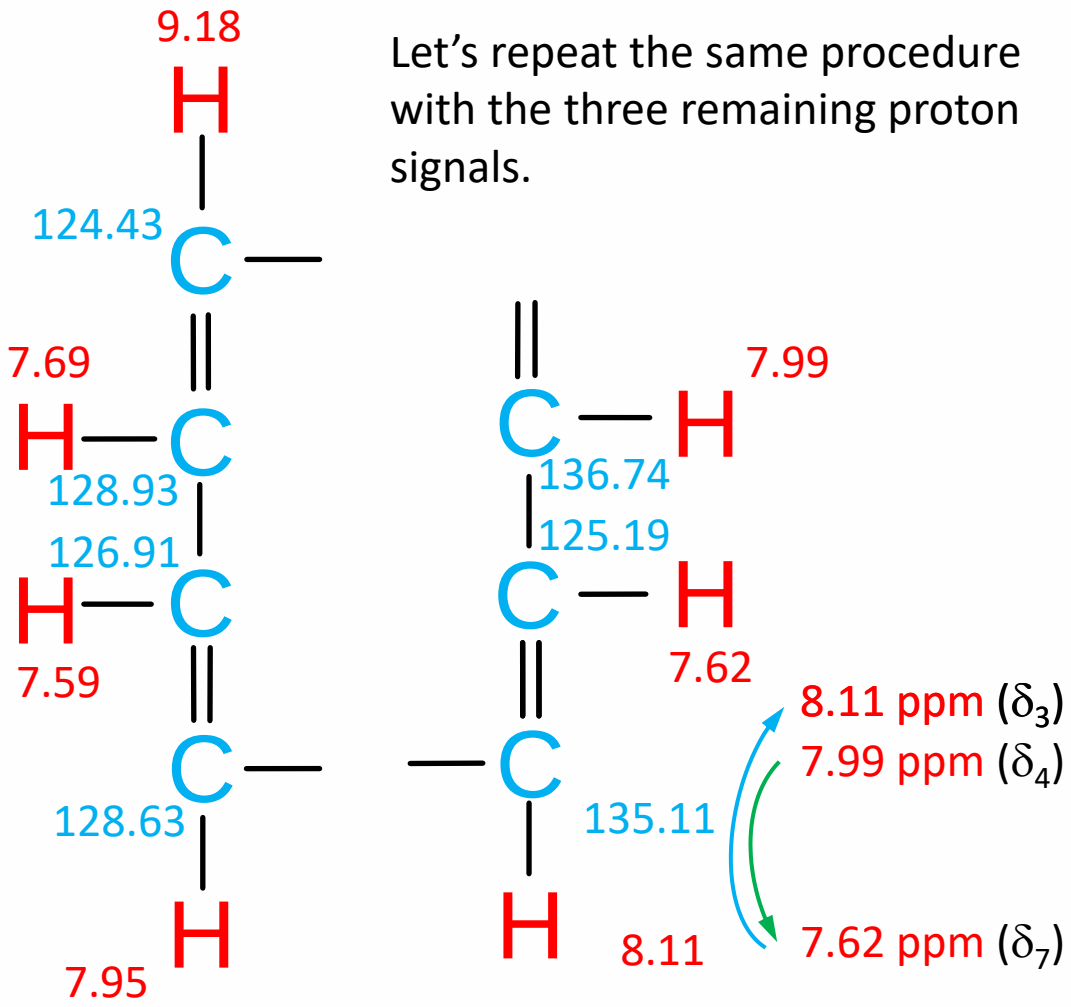
7.99 ppm (δ_4)

7.62 ppm (δ_7)

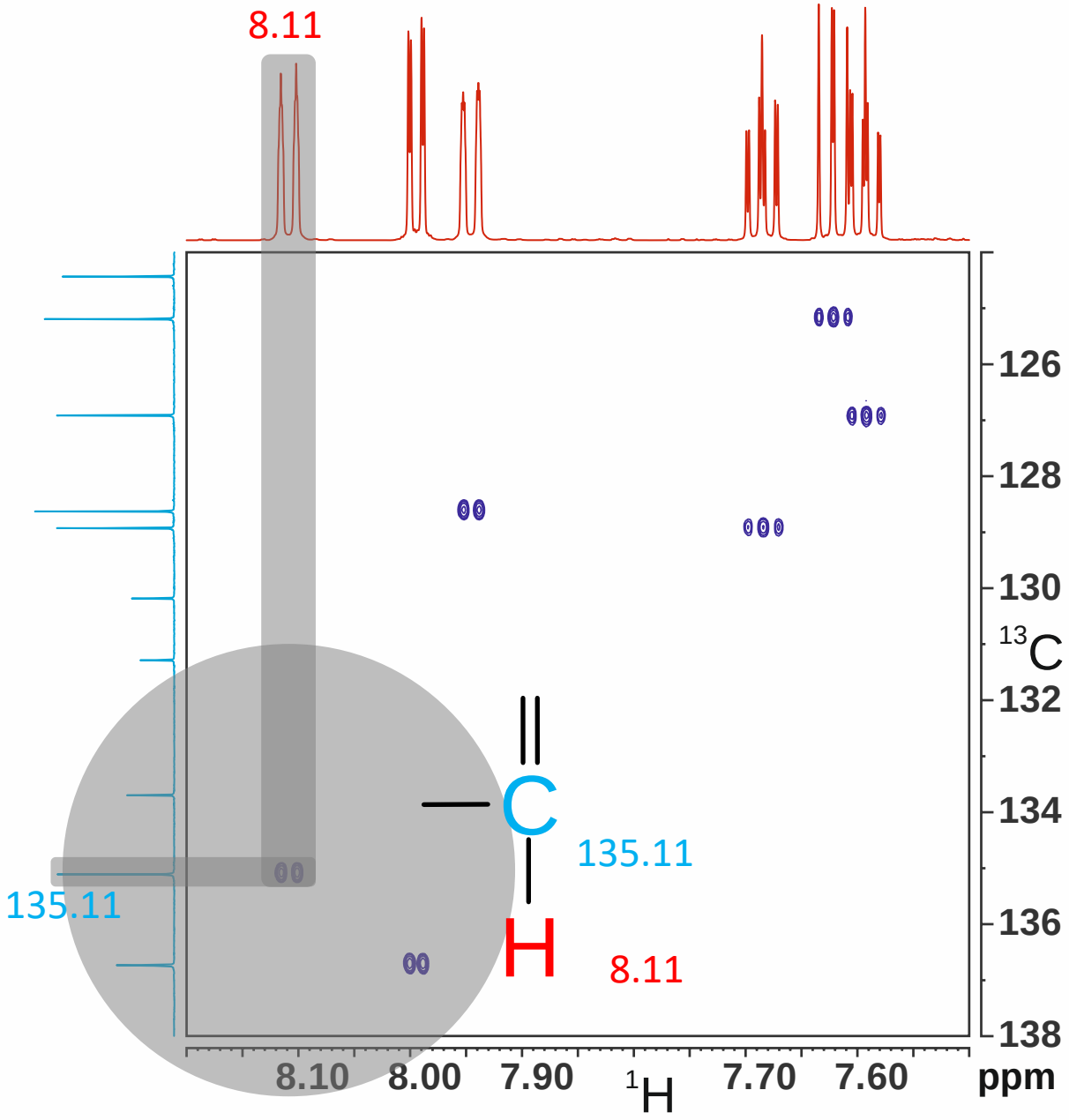


Adding carbon atoms

Two chains

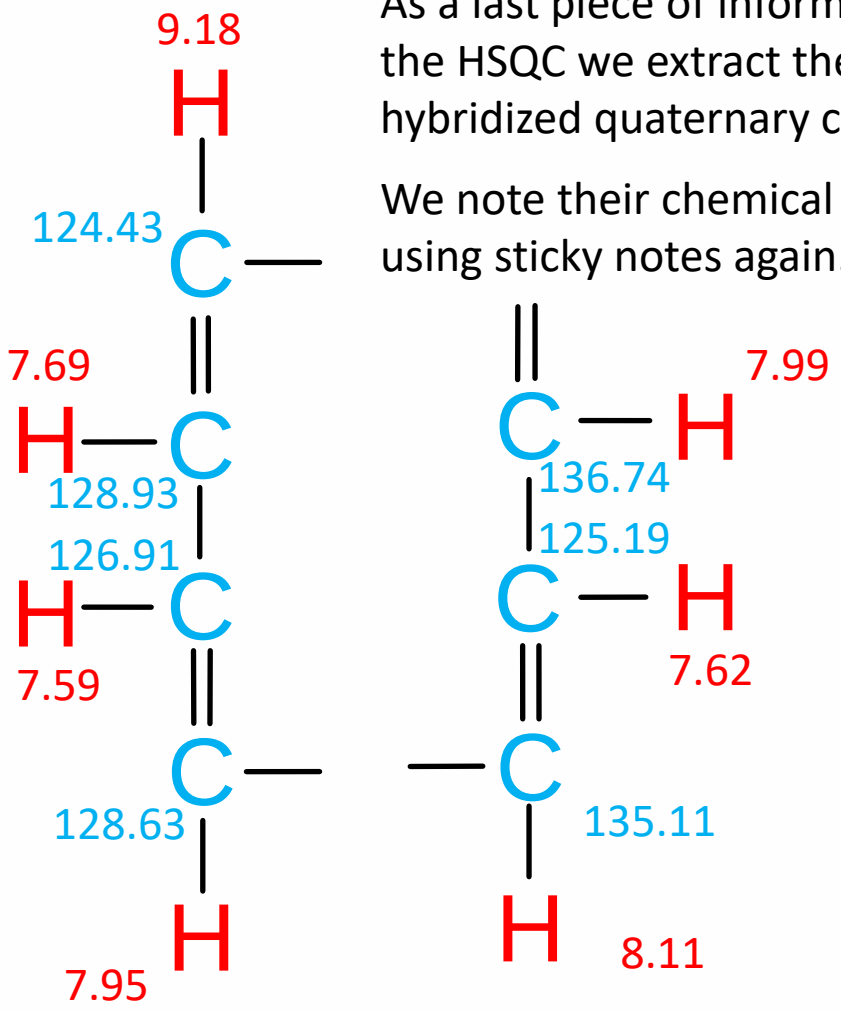


Let's repeat the same procedure with the three remaining proton signals.



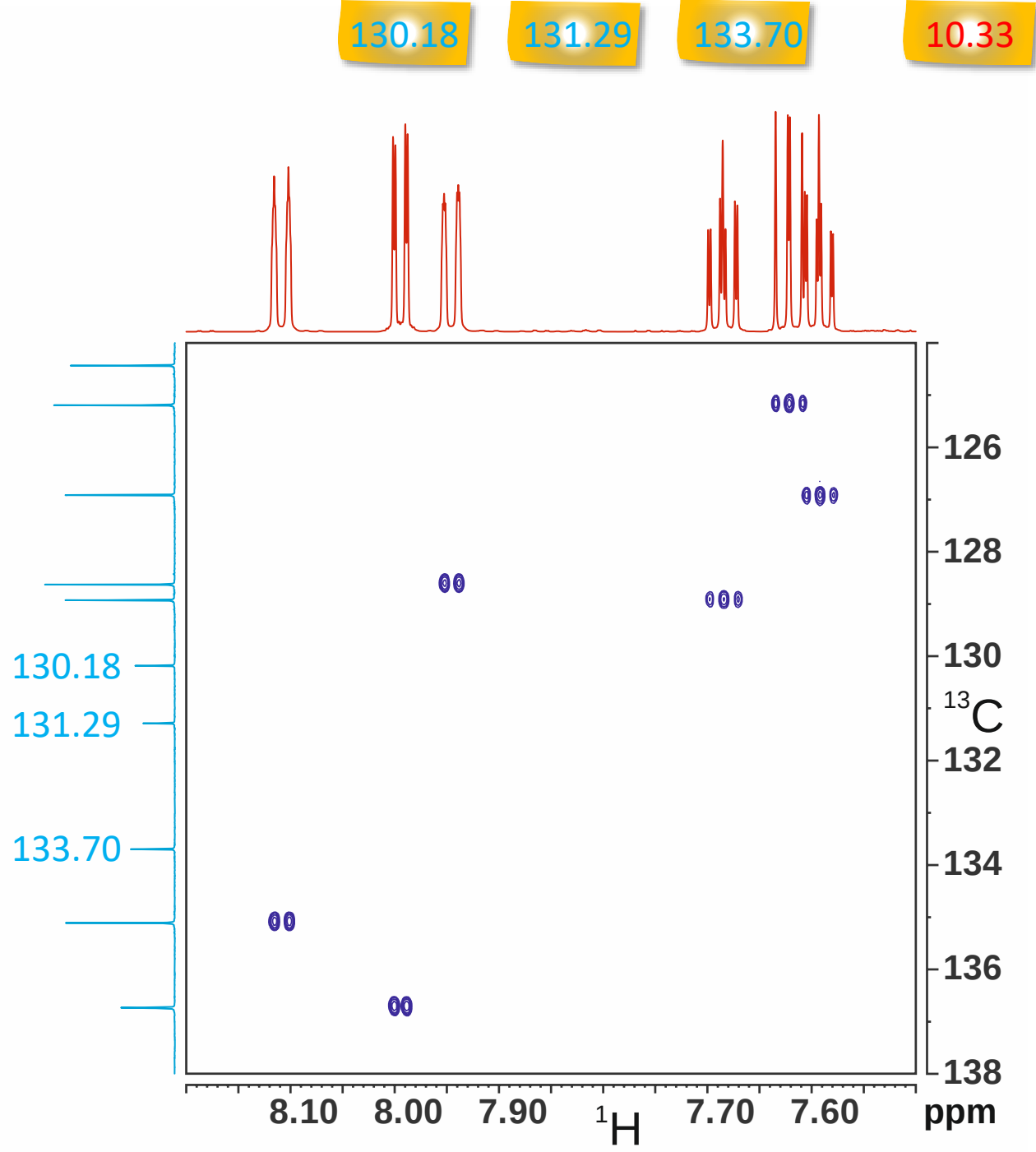
Adding carbon atoms

Two chains



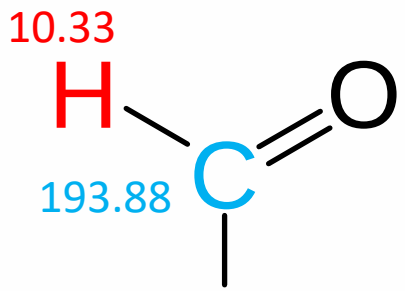
As a last piece of information from the HSQC we extract the three sp^2 hybridized quaternary carbon atoms.

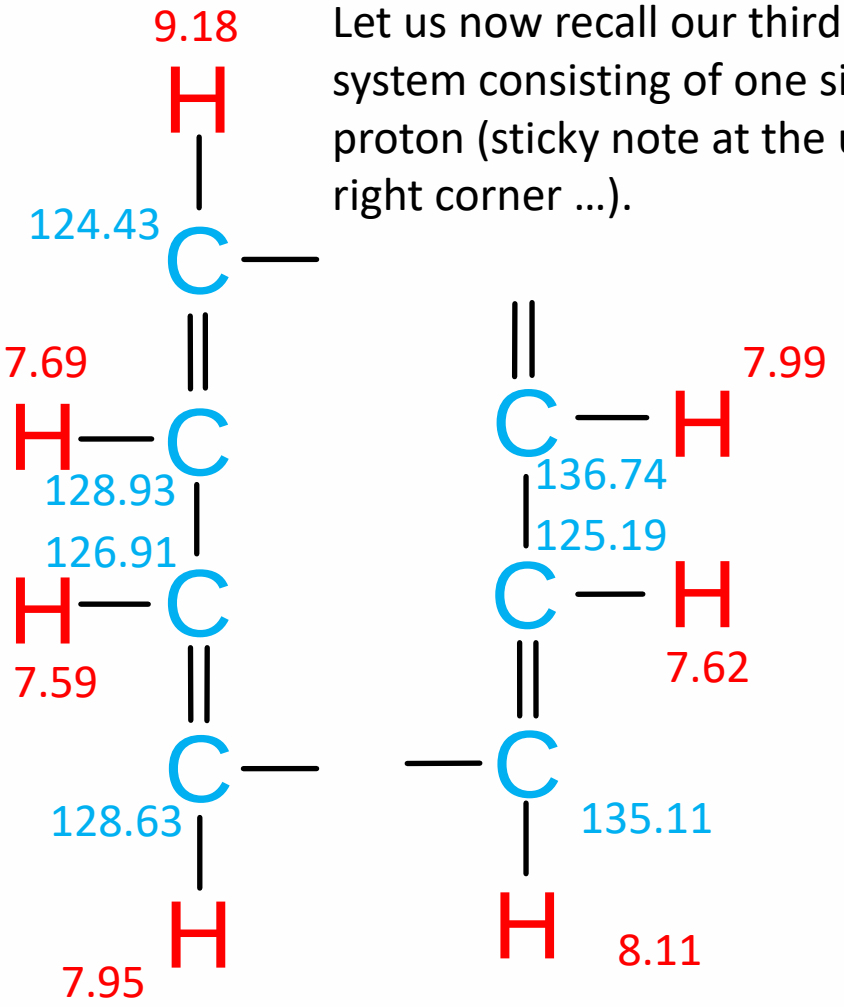
We note their chemical shifts using sticky notes again.



Linking the chains

Exclude oxygen link

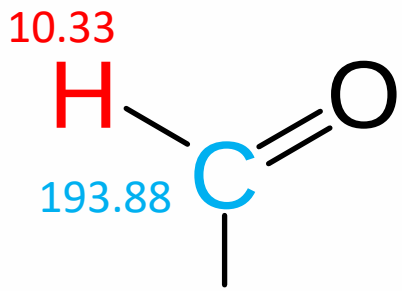


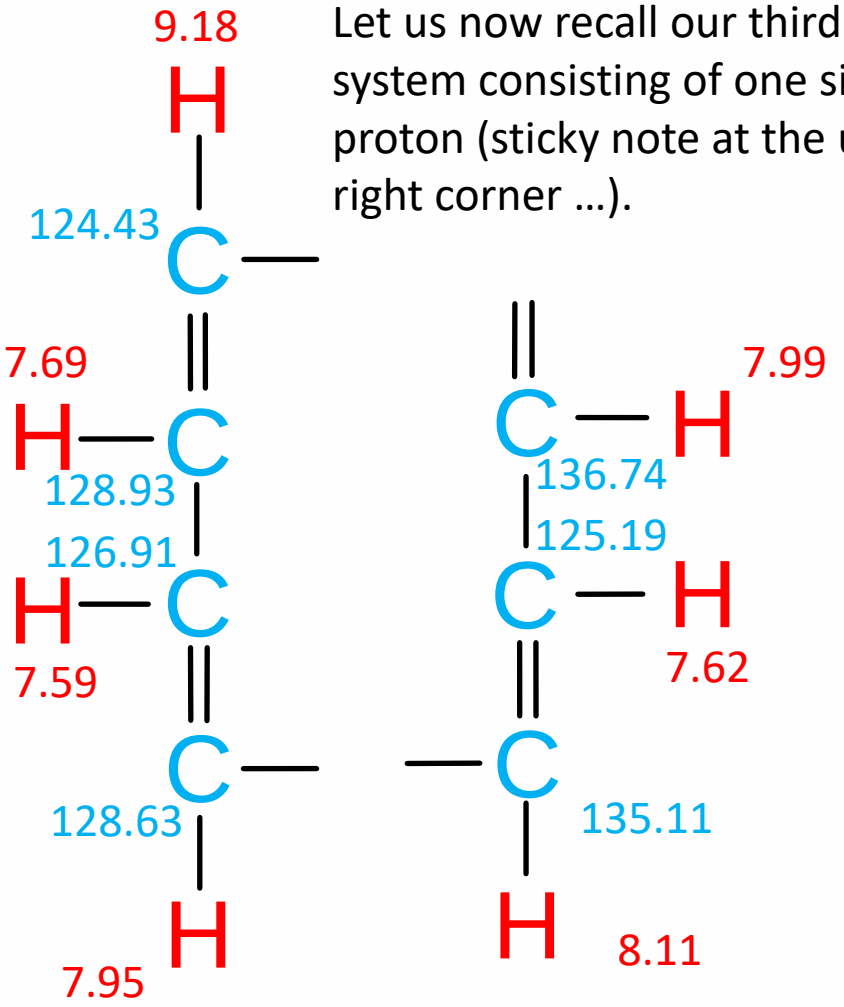


Let us now recall our third spin system consisting of one single proton (sticky note at the upper right corner …).

Linking the chains

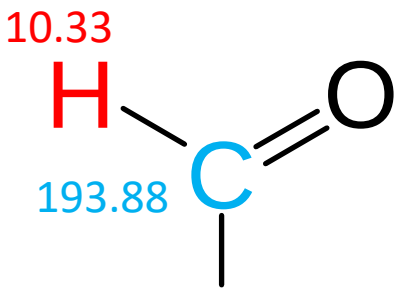
Exclude oxygen link



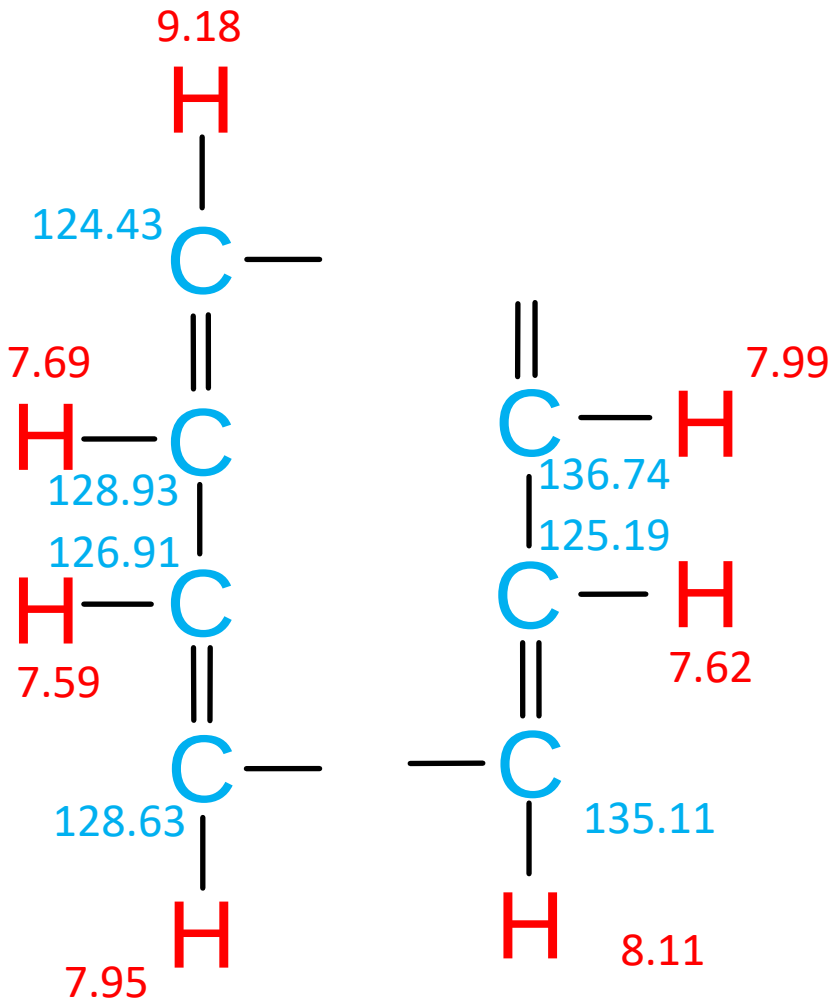


Let us now recall our third spin system consisting of one single proton (sticky note at the upper right corner …).

Intermediate summary



130.18 131.29 133.70



Let us count.

We have:

C_4H_4 (left chain)
C_3H_3 (right chain)
CHO (aldehyde)
3 x quaternary C atoms (see sticky notes)

$C_{11}H_8O$ (alltogether)

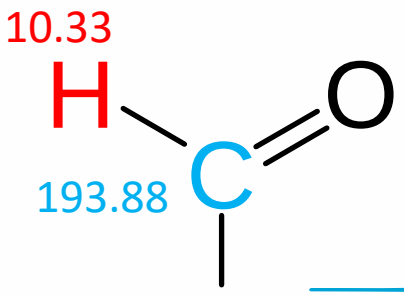
Molecular formula:

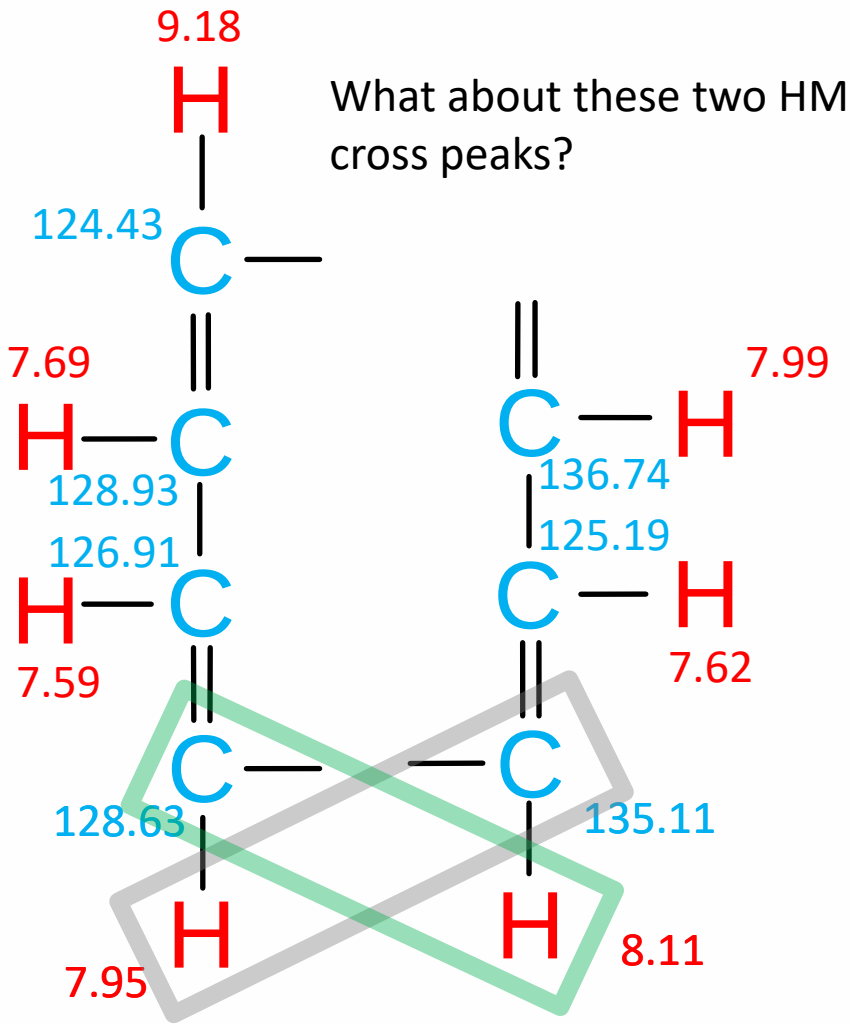
$C_{11}H_8O_8$

No atom is missing. We have to connect everything in the right order.

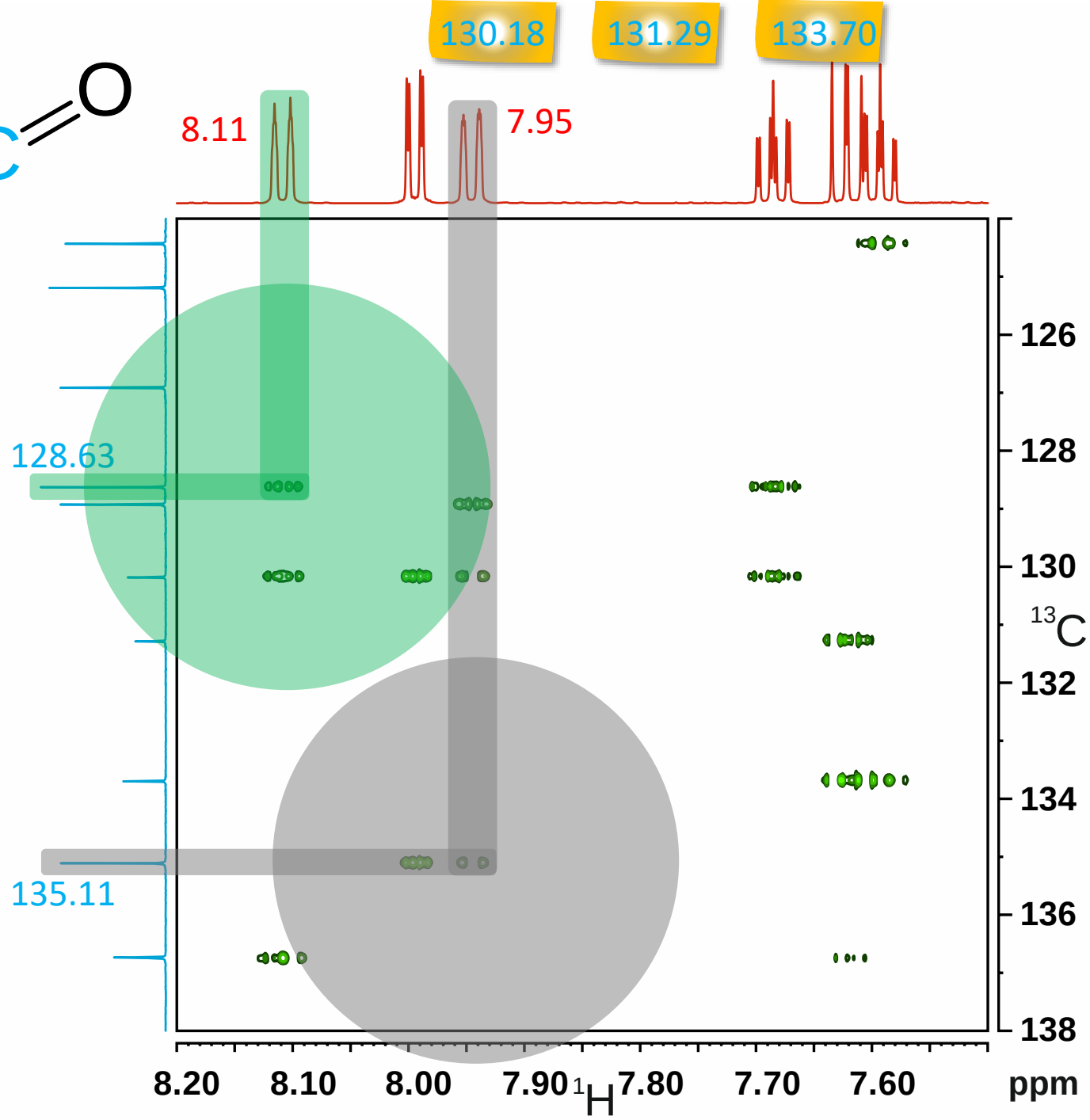
Linking the chains

Three quaternary C atoms



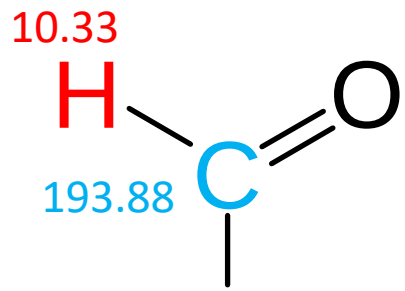


What about these two HMBC cross peaks?

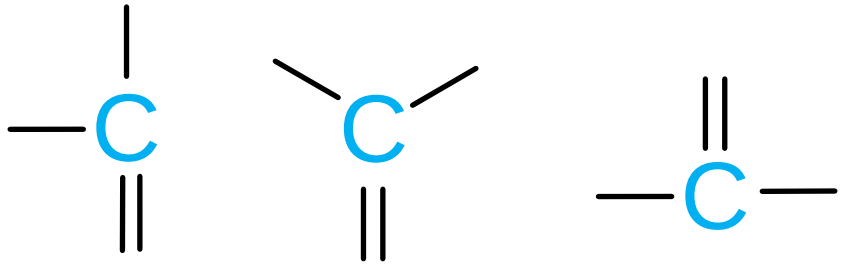


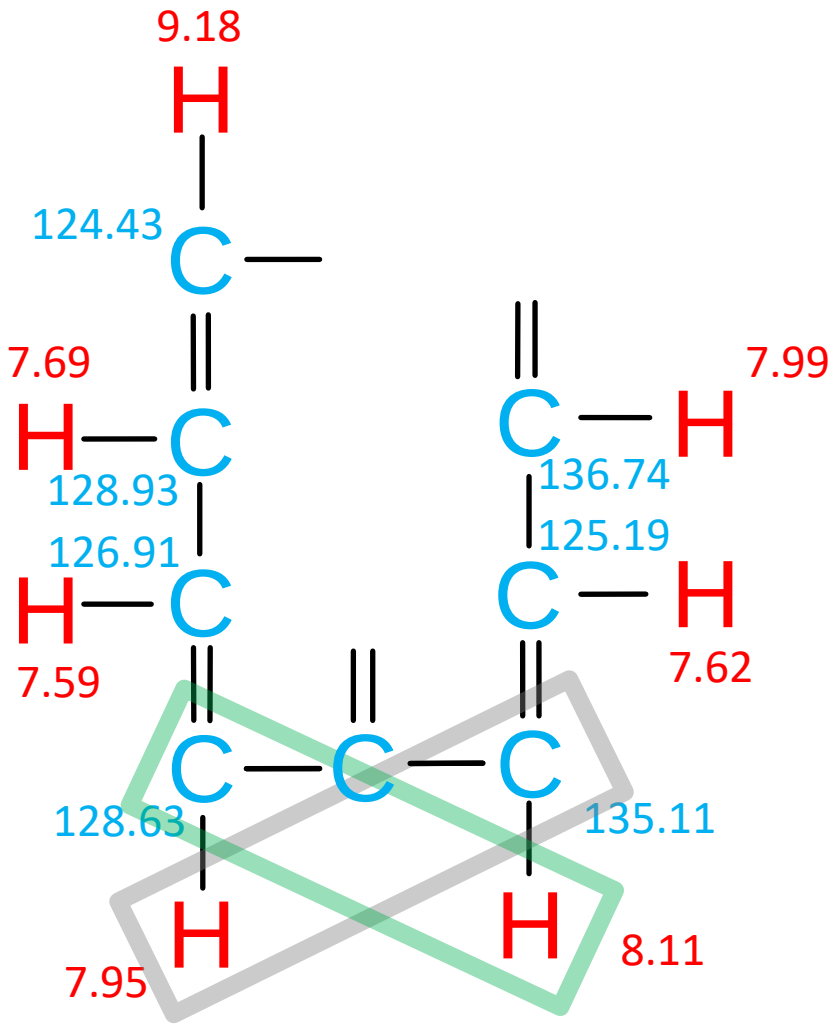
Linking the chains

Three quaternary C atoms



130.18 131.29 133.70





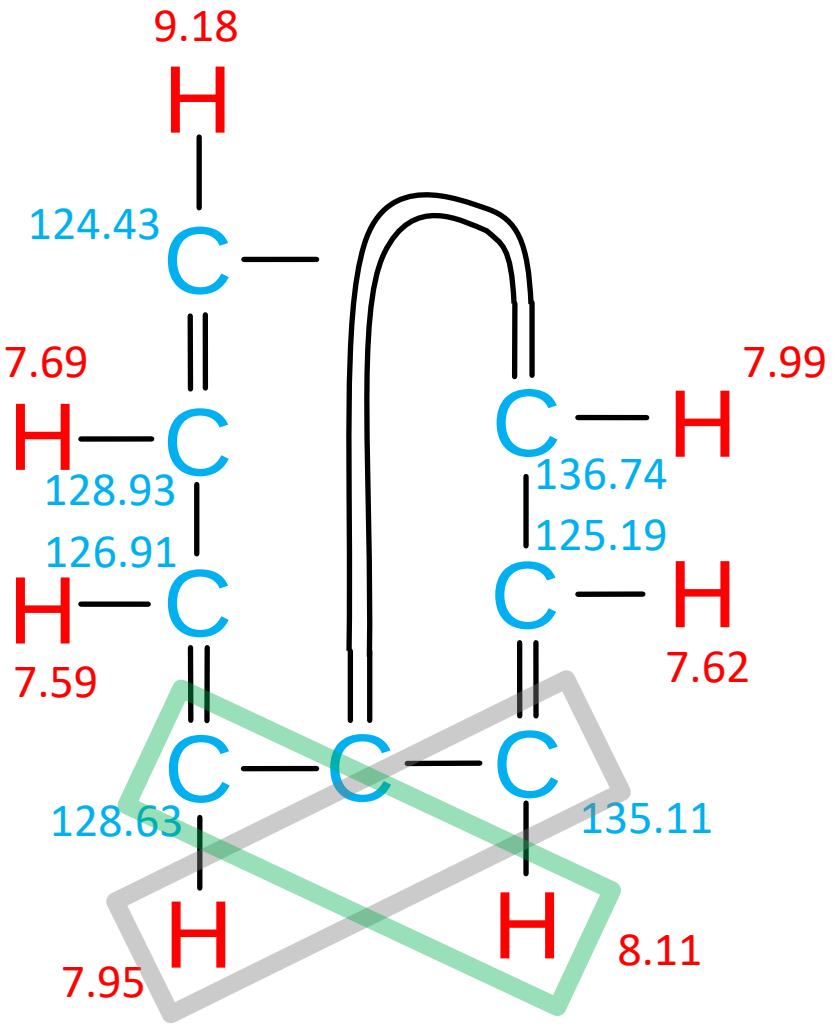
Let us display our three quaternary sp^2 hybridized carbon atoms, although we don‘t know their assignment just now.

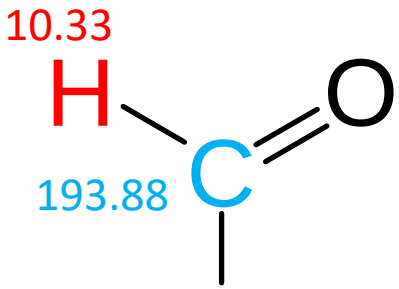
Of course, the carbon atoms with the chemical shifts of 128.63 ppm and 135.11 ppm cannot be linked directly. That would require a cross peak in the COSY between the protons with the chemical shifts of 7.95 ppm and 8.11 ppm, and there was no such cross peak.

There has to be something between the two carbon atoms and the only possibility is one of the quaternary carbon atoms.

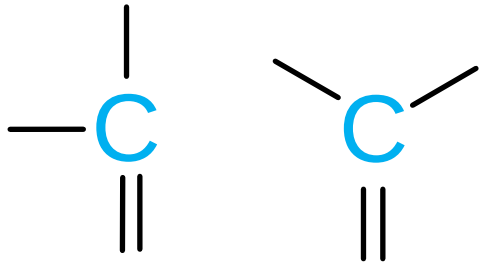
Linking the chains

Three quaternary C atoms





130.18 131.29 133.70

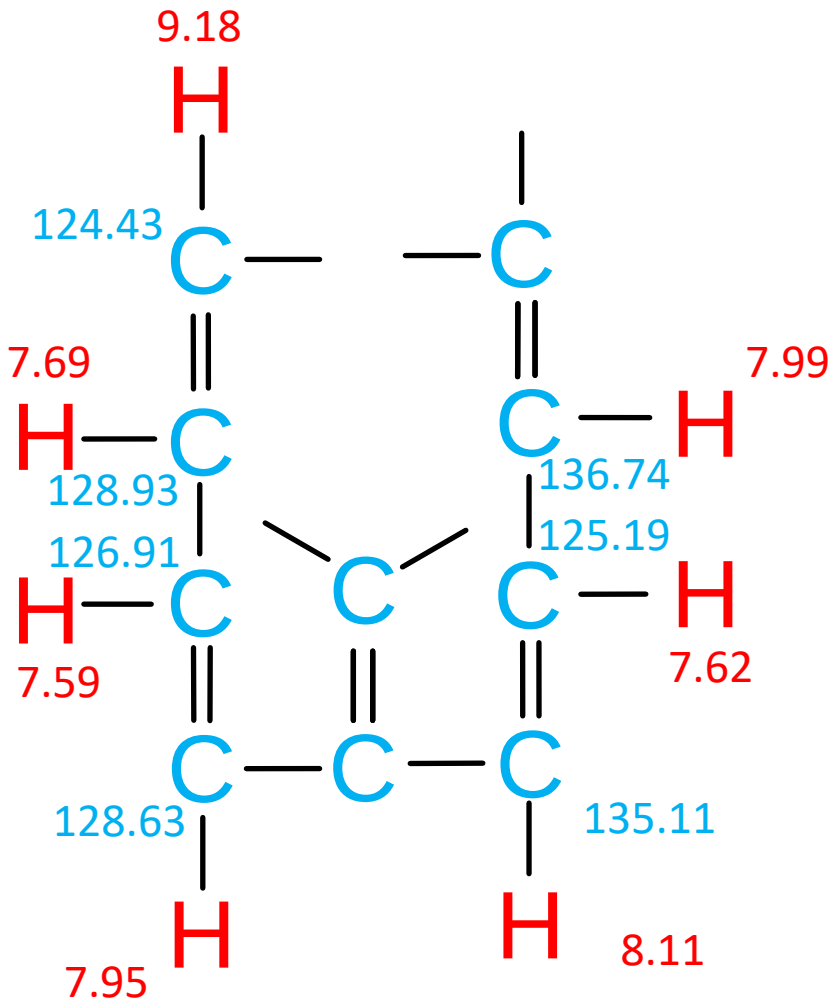


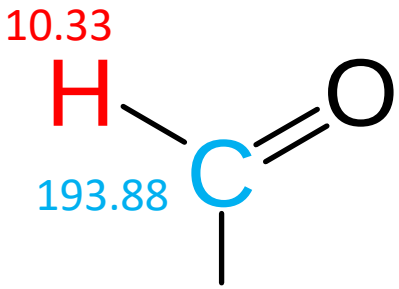
Now our molecula fragment shows two open double bonds. We might think about closing a ring.

The result is not totally impossible, but very, very strange. We should look for simpler solutions before we continue with this strange partial structure.

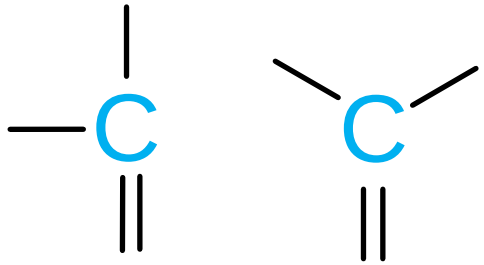
Linking the chains

Three quaternary C atoms





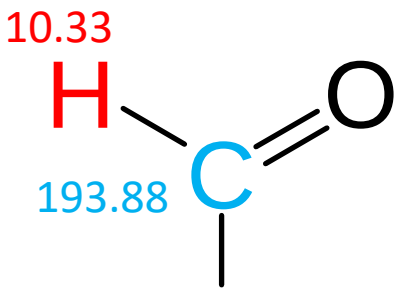
130.18 131.29 133.70



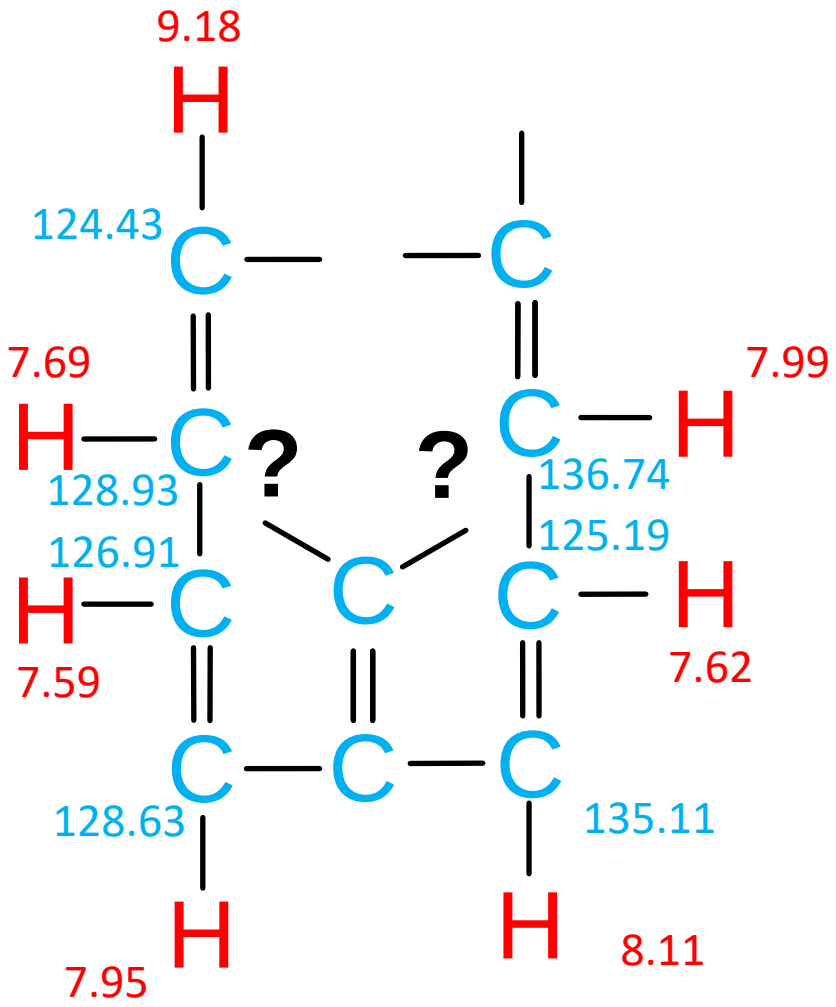
Instead we might try to attach the remaining two quaternary carbon atoms to the open double bonds.

Linking the chains

Three quaternary C atoms



130.18 131.29 133.70



Finally we have to attach the aldehyde group.

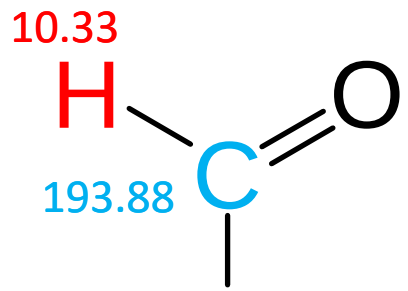
The aldehyde group cannot be attached to the carbon with the chemical shift of 124.43 ppm, because that would require a cross peak in the COSY between the protons at 9.18 ppm and 10.33 ppm. There is no such cross peak.

But what about connecting the aldehyde group to one of these bonds?

Let us try.
After attaching the aldehyde group to one of these bonds, there remains only one – slightly strange - possibility to finalyze the whole molecule.

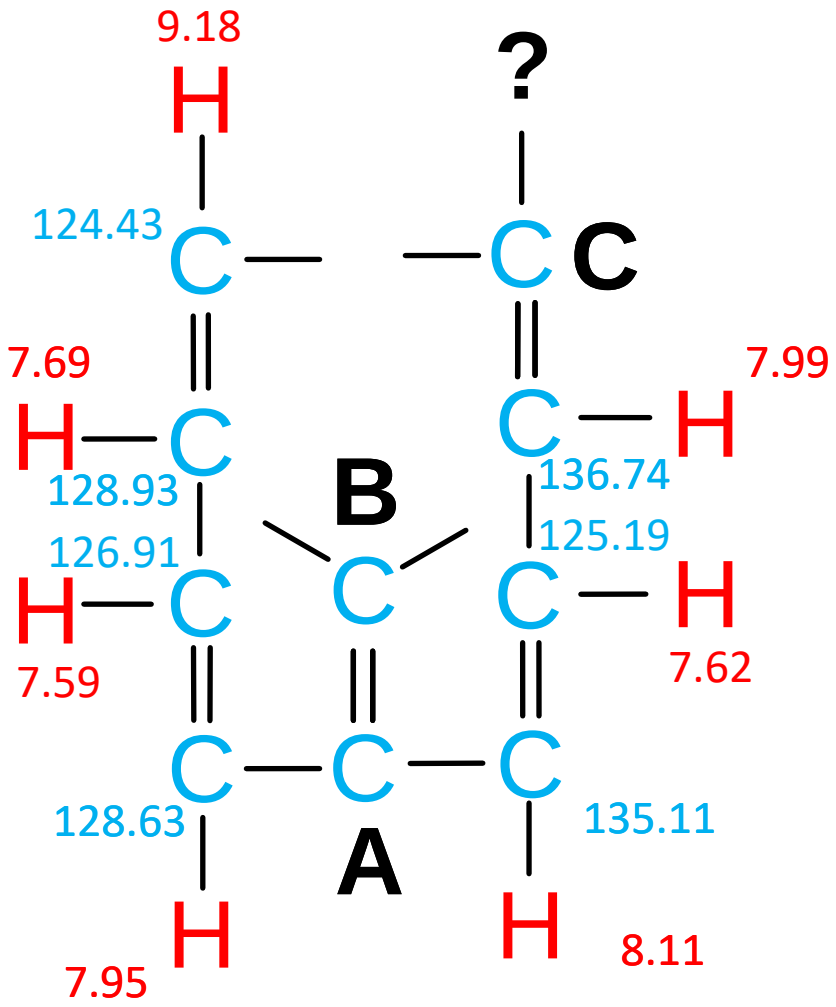
Linking the chains

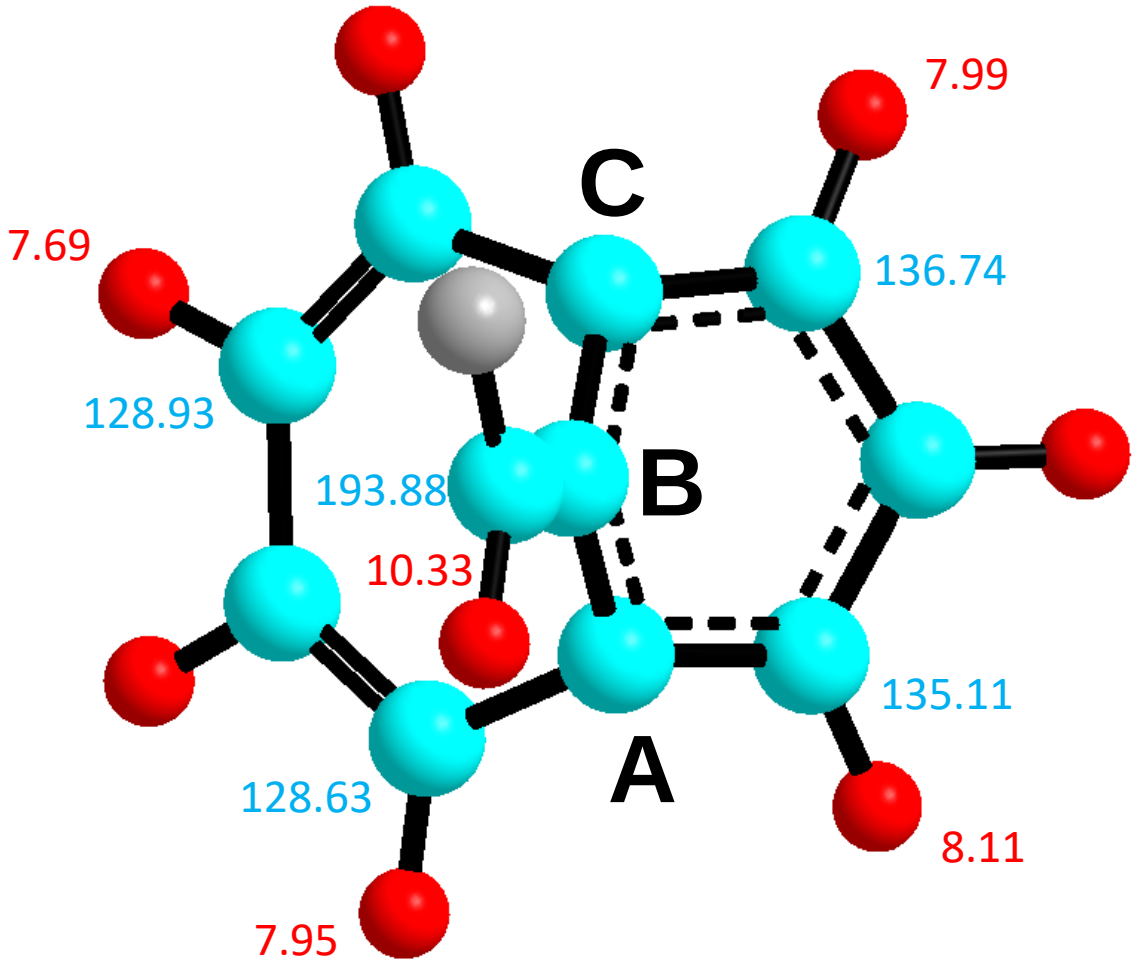
Three quaternary C atoms



130.18 131.29 133.70

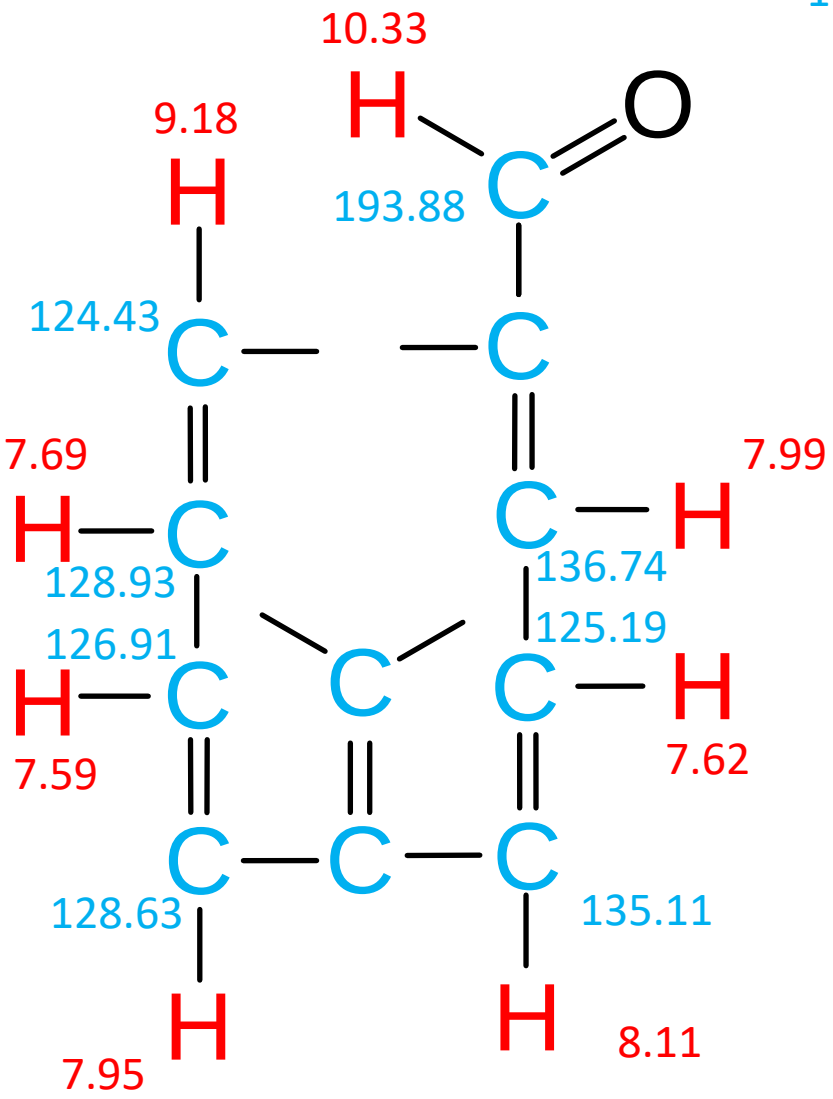
Of course, coming to this 3D structure looks a little bit confusing. Let us add some of the chemical shifts already assigned to identify parts of the structure. Not impossible, but what about attaching the aldehyde group here?

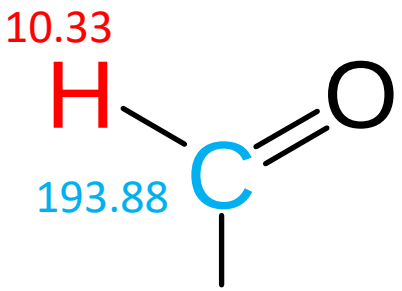




Linking the chains

Three quaternary C atoms





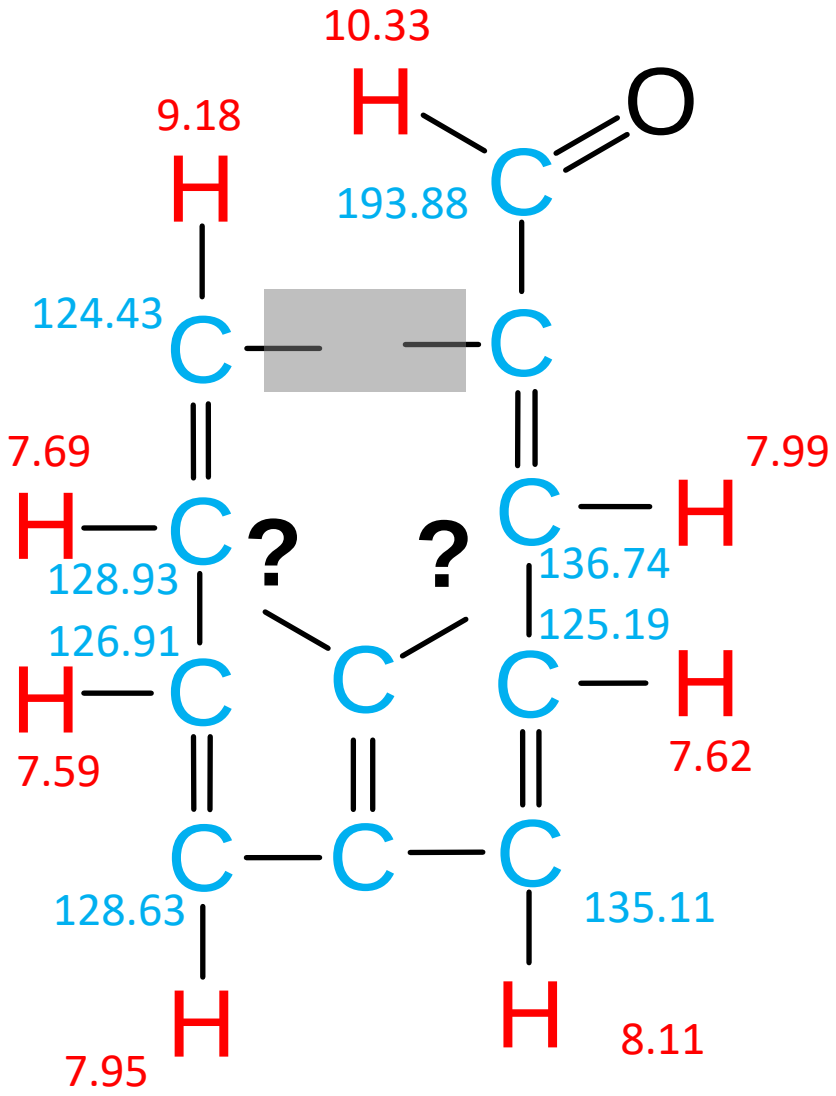
130.18 131.29 133.70

Not impossible, but what about attaching the aldehyde group here?

130.18 131.29 133.70

Linking the chains

Three quaternary C atoms



Not impossible, but what about attaching the aldehyde group here?

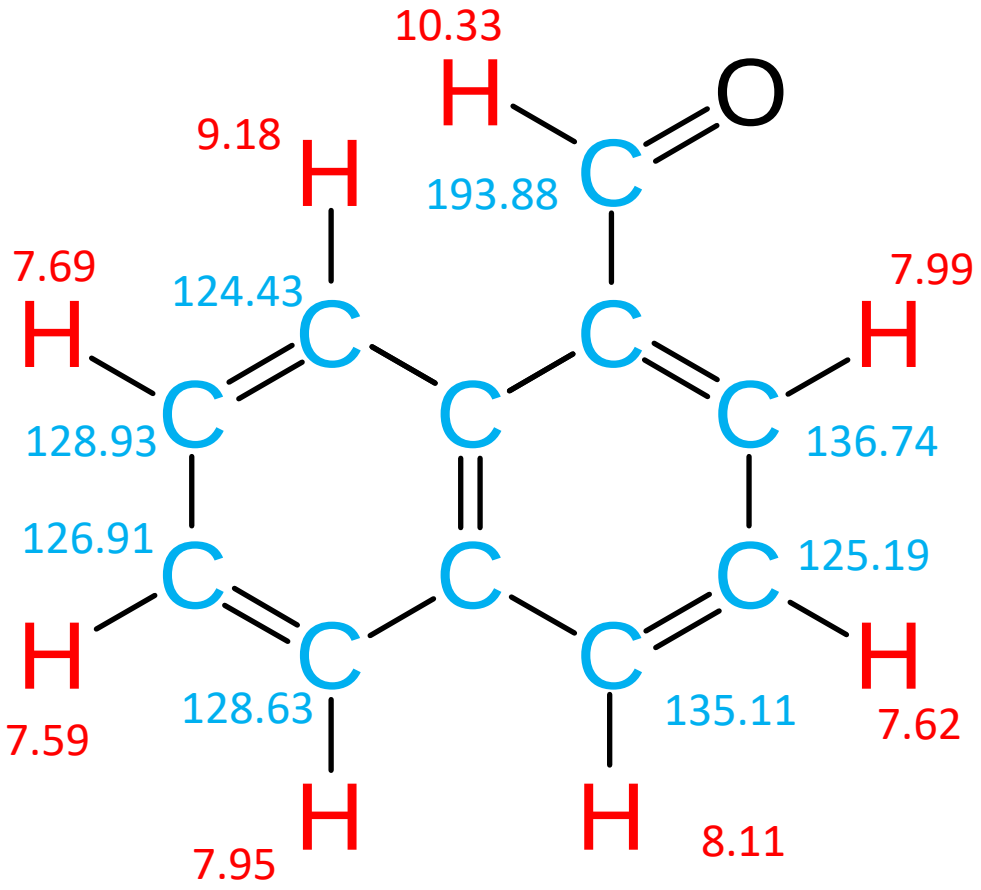
We cannot introduce a bond here, because we would finish up with two remaining open bonds?

Our alternative to connect the open bonds is …

130.18 131.29 133.70

Linking the chains

Three quaternary C atoms



Our alternative to connect the open bonds is …

… which looks like the best alternative so far.
1-Naphthaldehyde is a very common substance.

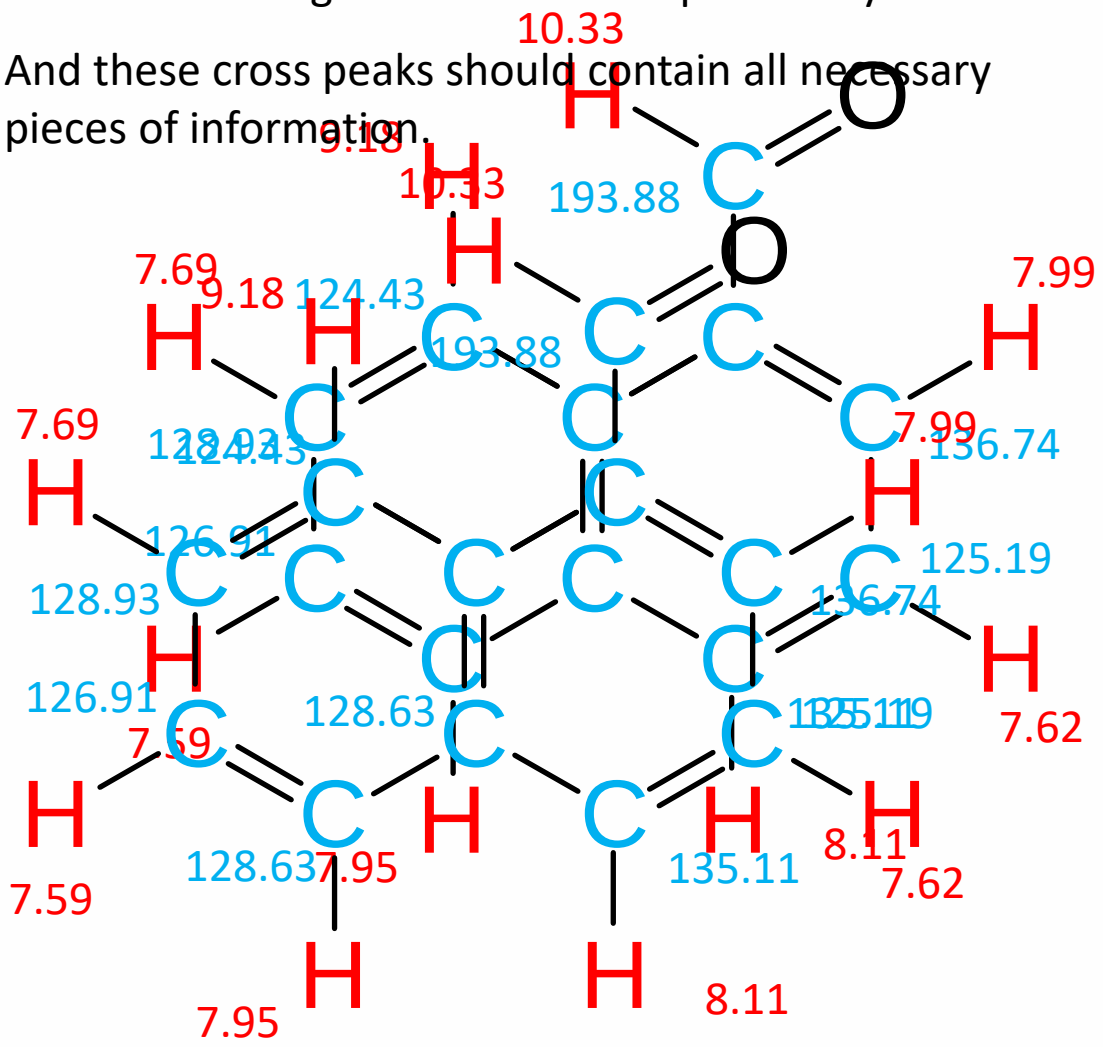
If this structure is correct, the assignment of the quaternary carbon atoms using the HMBC should also be very simple.

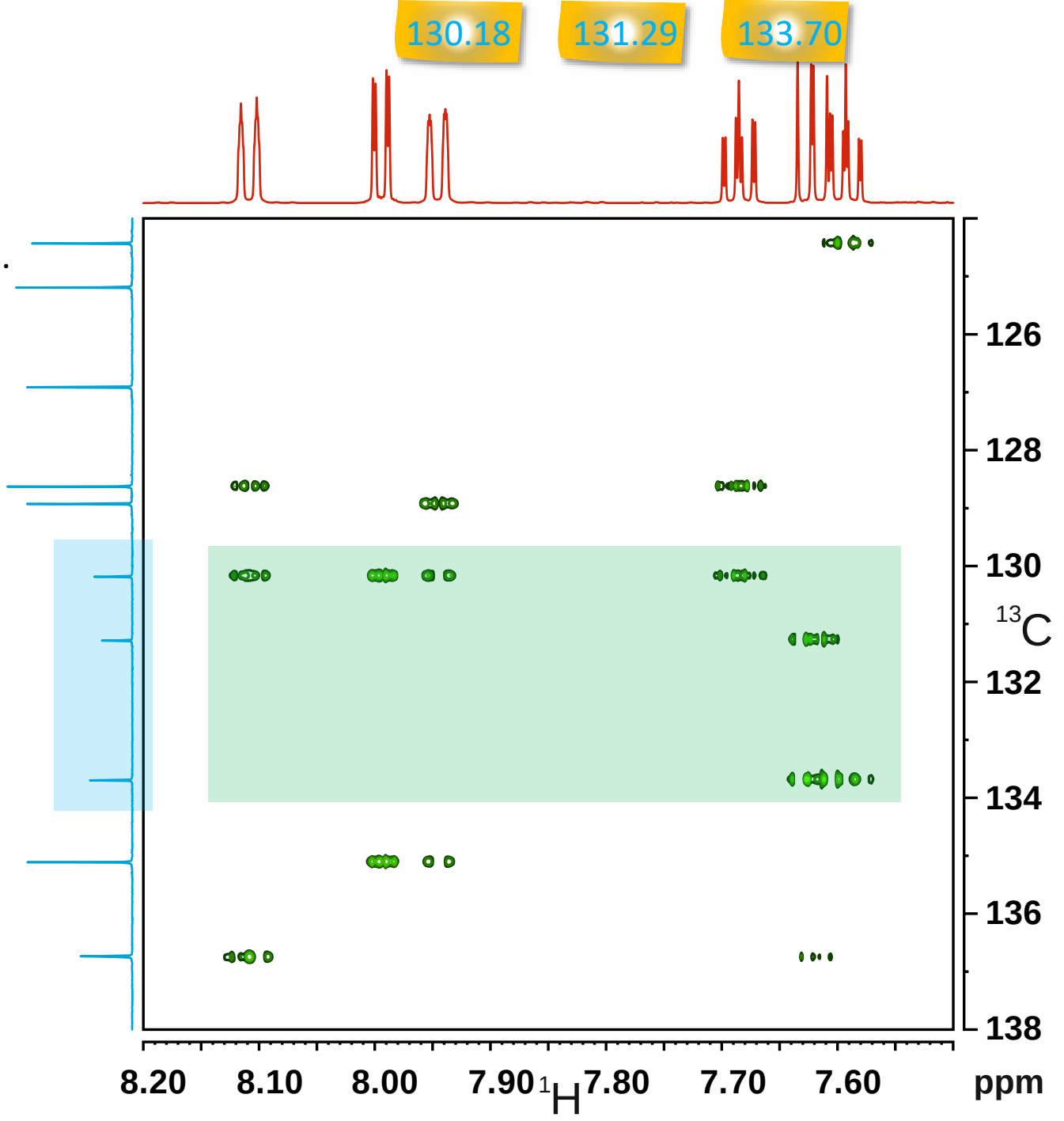
Linking the chains

Assign the quaternary C atoms

These are the signals of the three quaternary carbon atoms.

And these cross peaks should contain all necessary pieces of information.



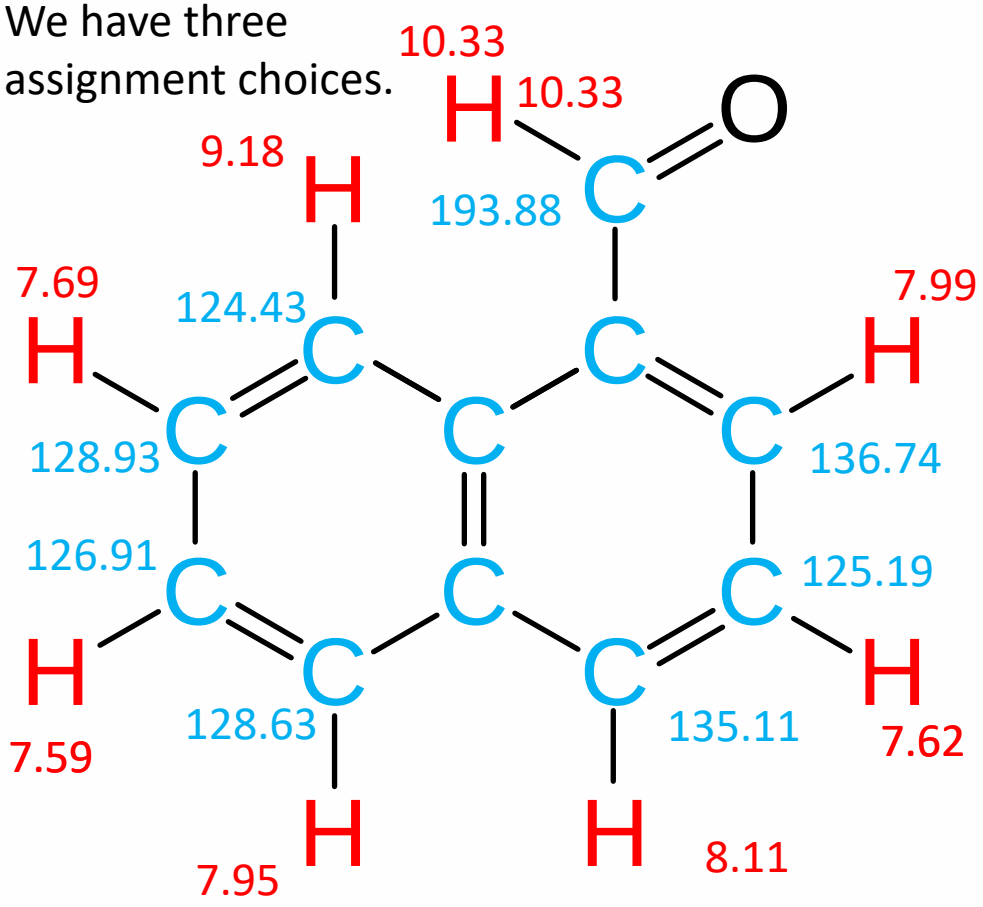


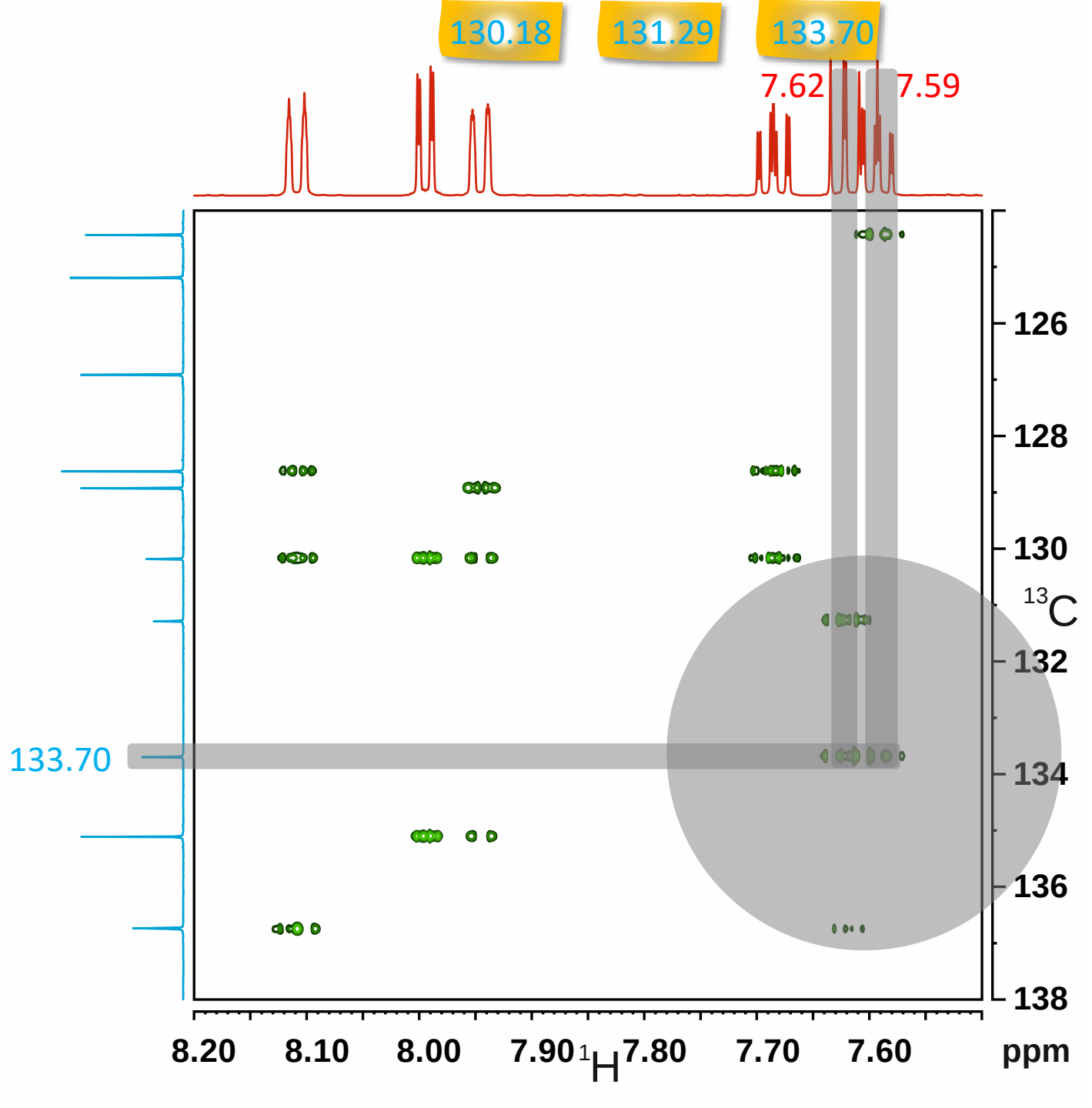
Linking the chains

Assign the quaternary C atoms

There are two cross peaks between the carbon with the chemical shift of 133.70 ppm and two different proton signals.

We have three assignment choices.

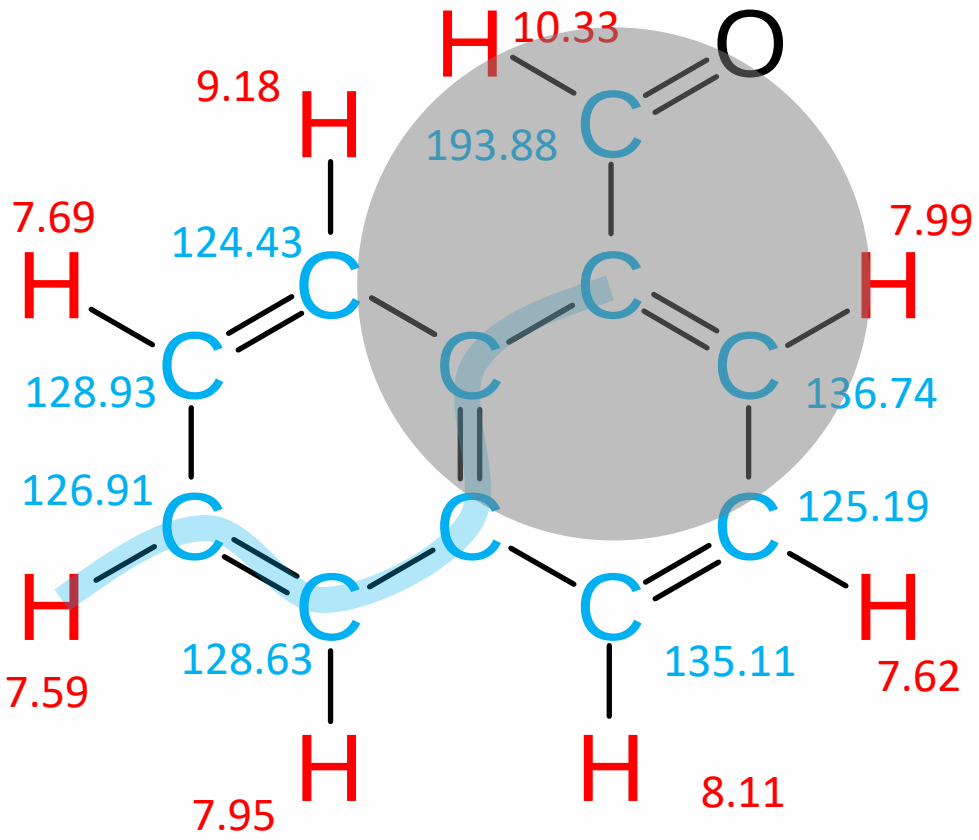


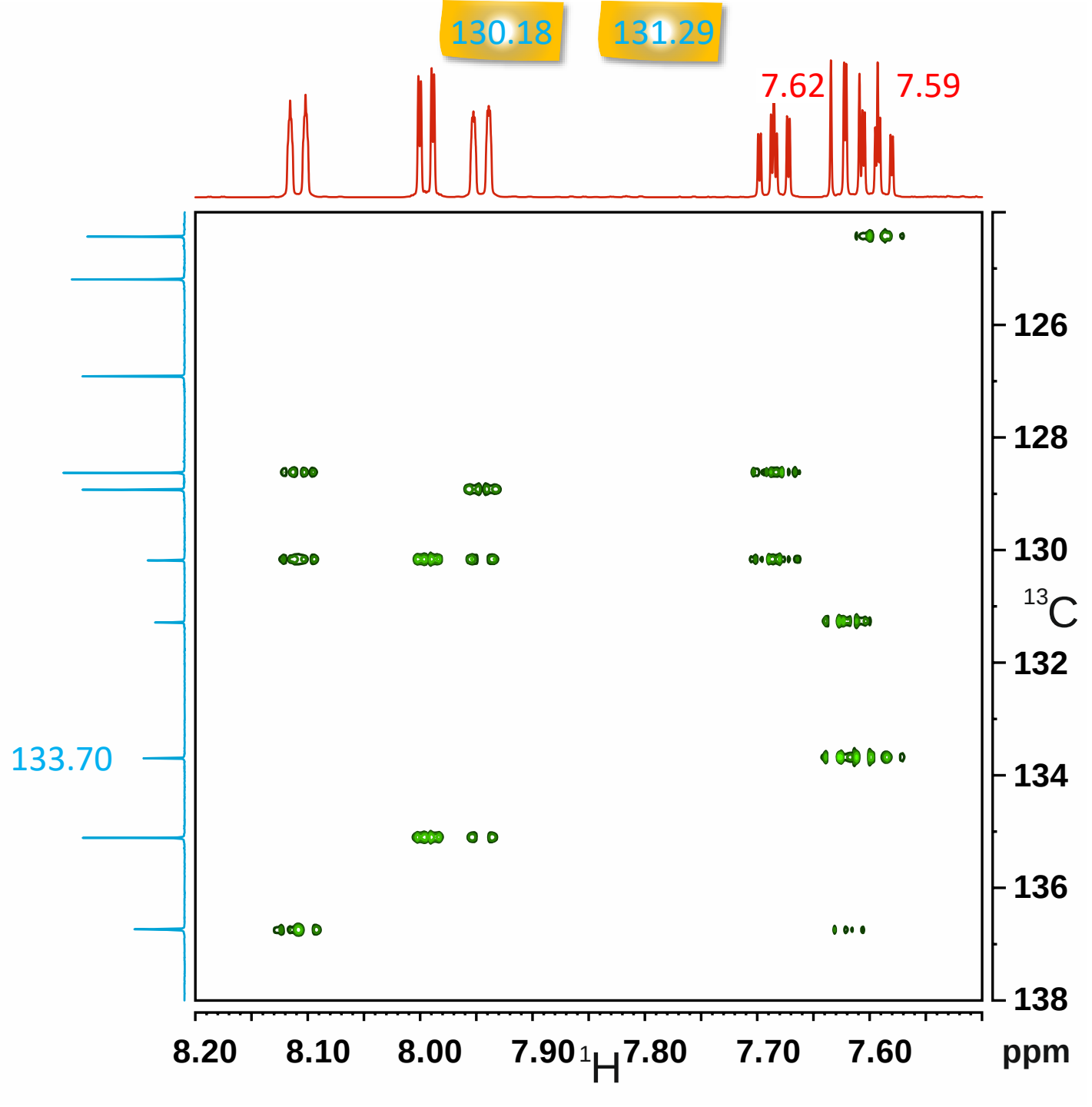


Linking the chains

Assign the quaternary C atoms

If we assume the chemical shift of 133.70 ppm at this carbon atom, one of the cross peaks would correspond to a five bond correlation.

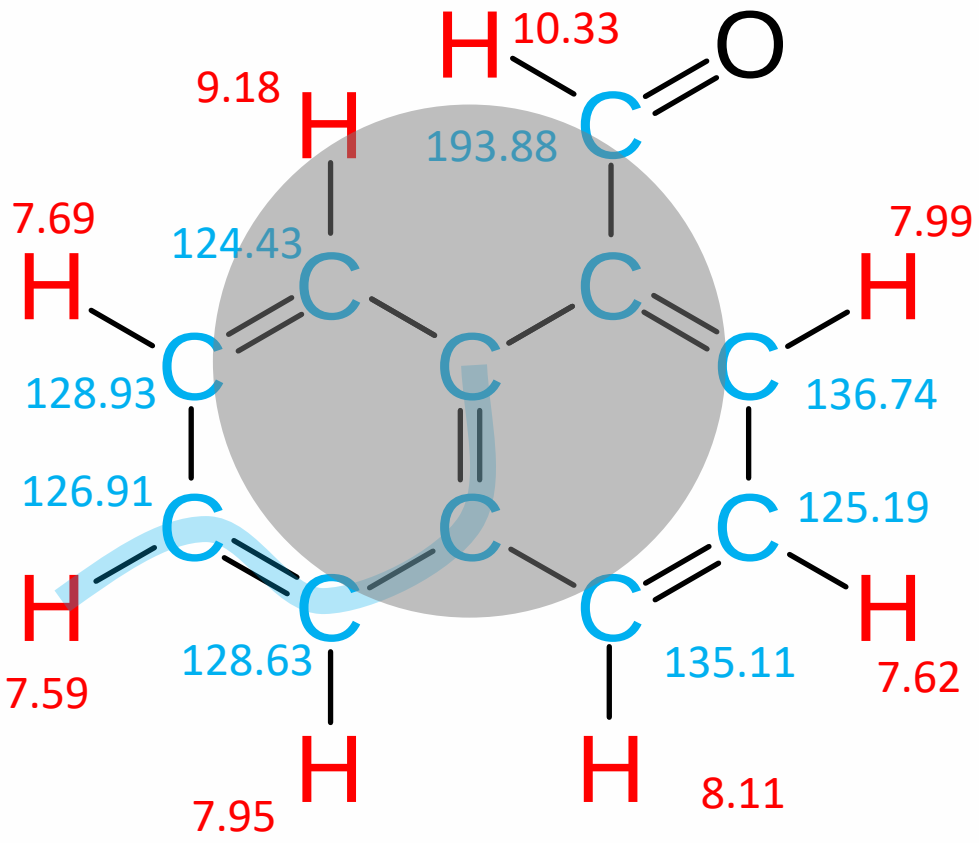


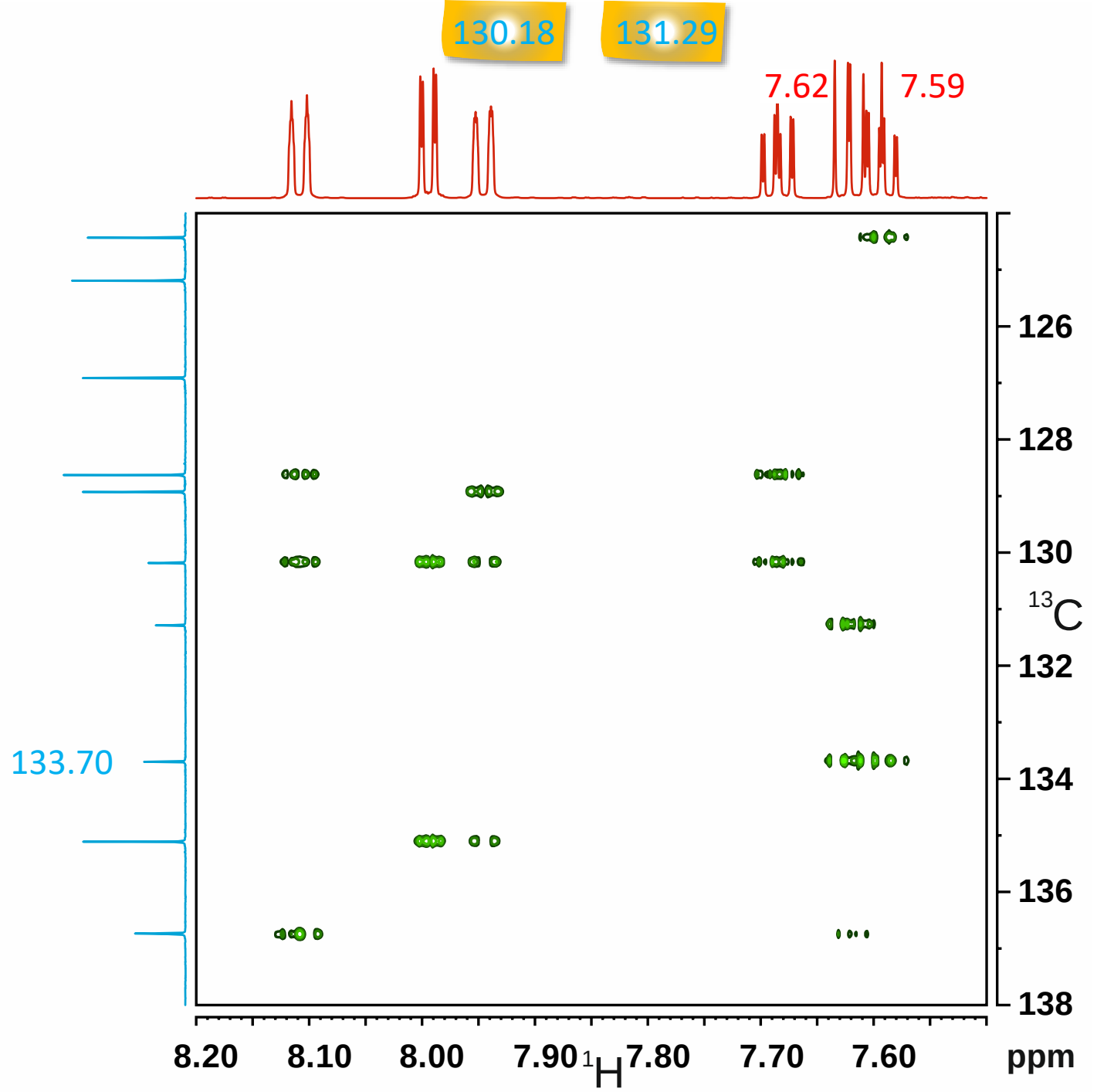


Linking the chains

Assign the quaternary C atoms

If we assume the chemical shift of 133.70 ppm at this carbon atom, both cross peak would correspond to a four bond correlation (one of them is shown).

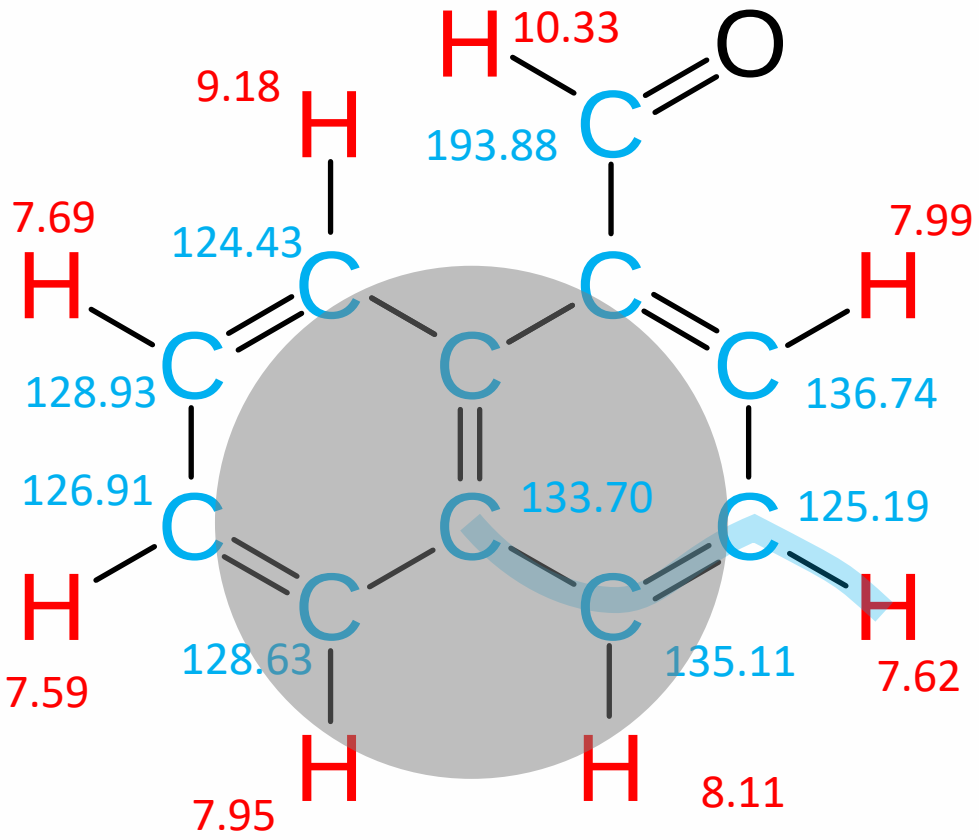


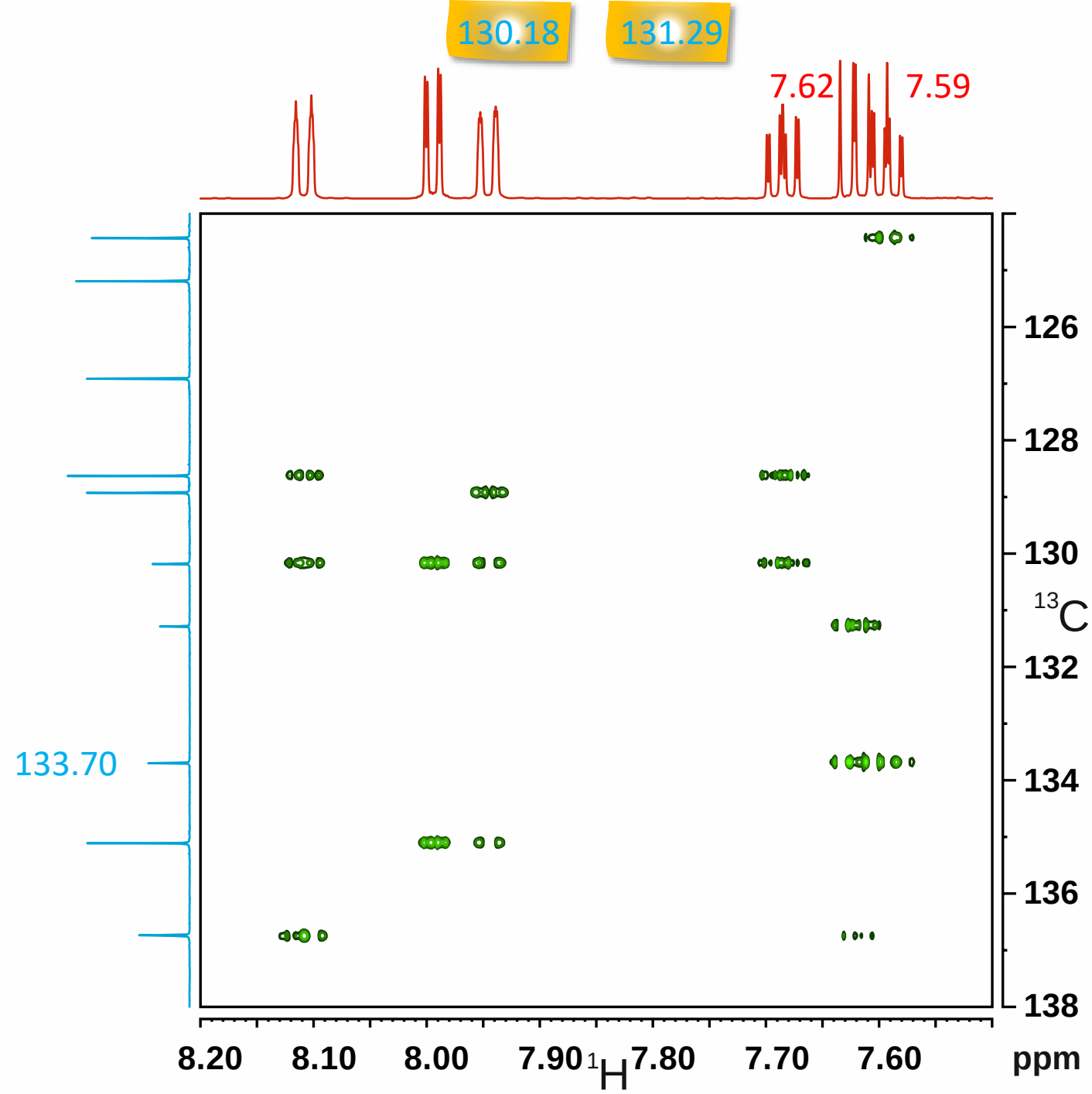


Linking the chains

Assign the quaternary C atoms

If we finally assume the chemical shift of 133.70 ppm at this carbon atom, both cross peaks would correspond to a three bond correlation (one is shown), which is by far the most likely possibility.

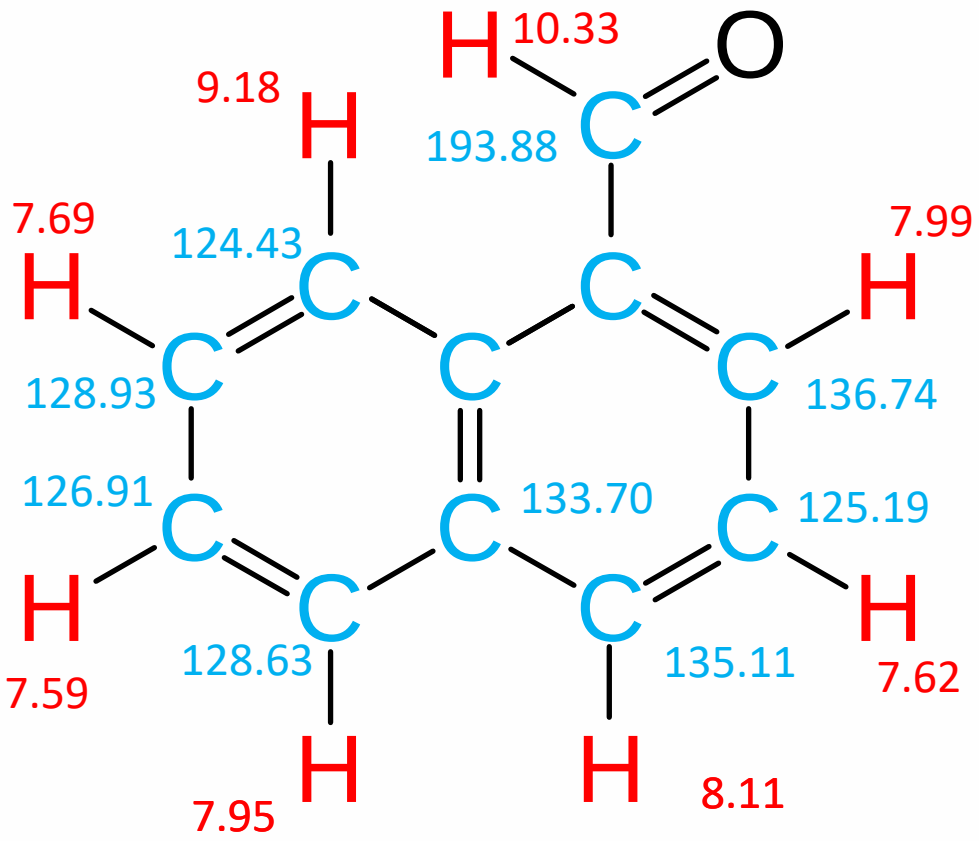


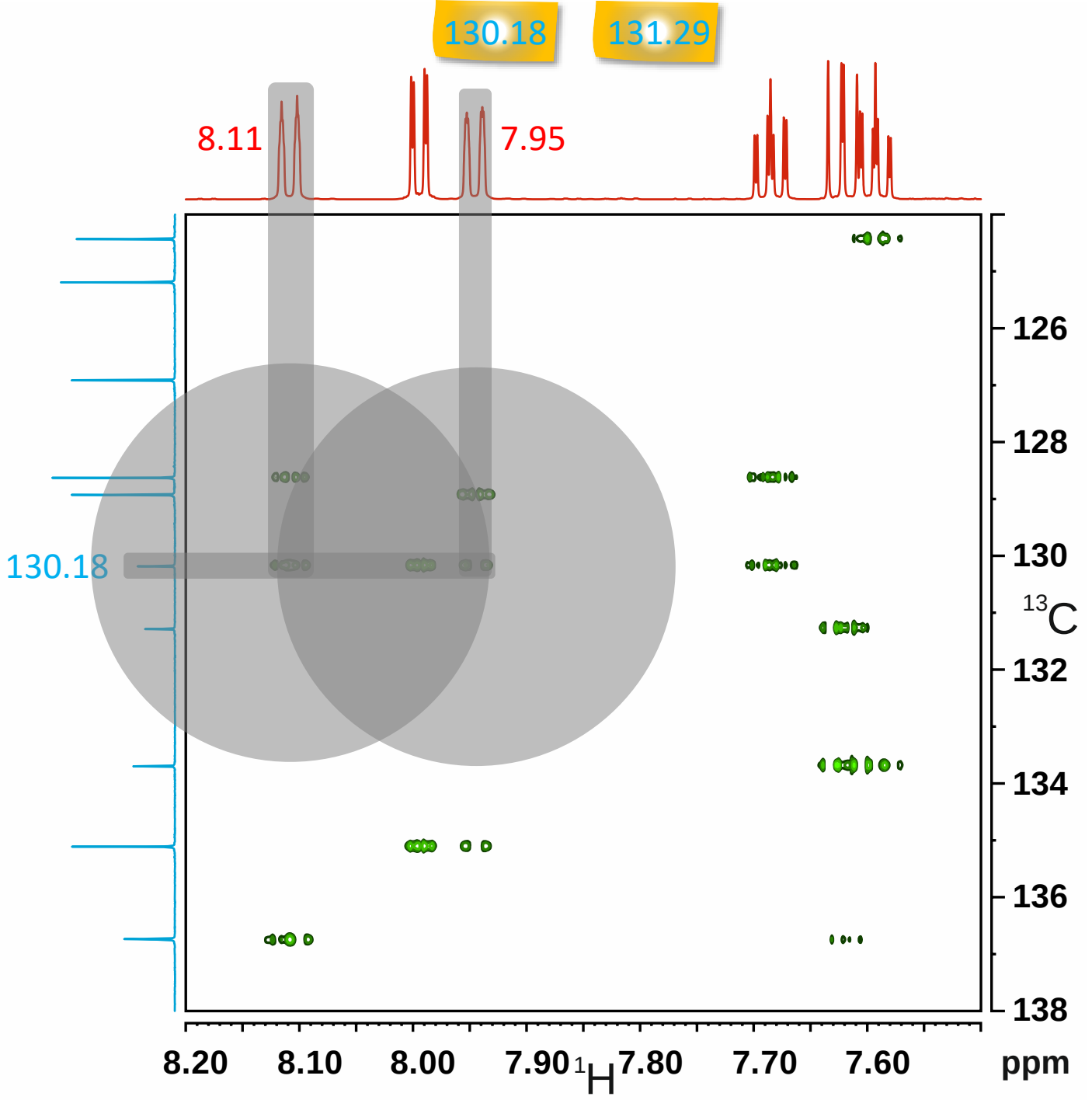


Linking the chains

Assign the quaternary C atoms

The HMBC shows two cross peaks between the protons with the chemical shifts of 7.95 ppm and 8.11 ppm and the quaternary carbon atom at 130.18 ppm.



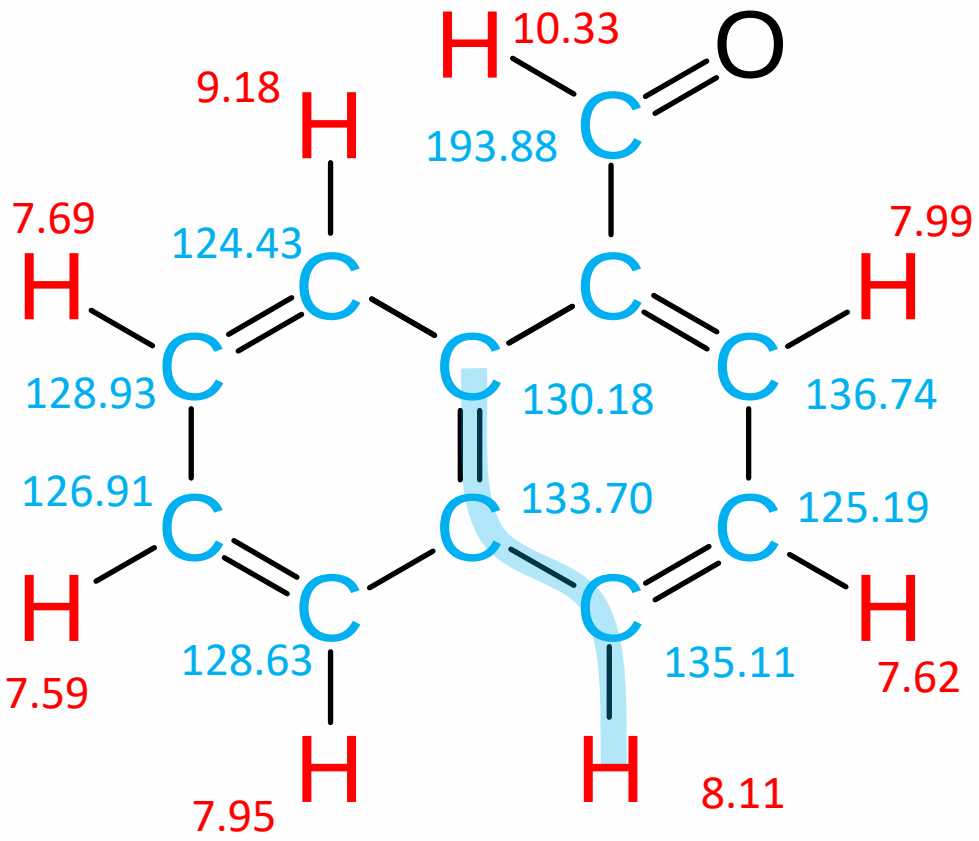


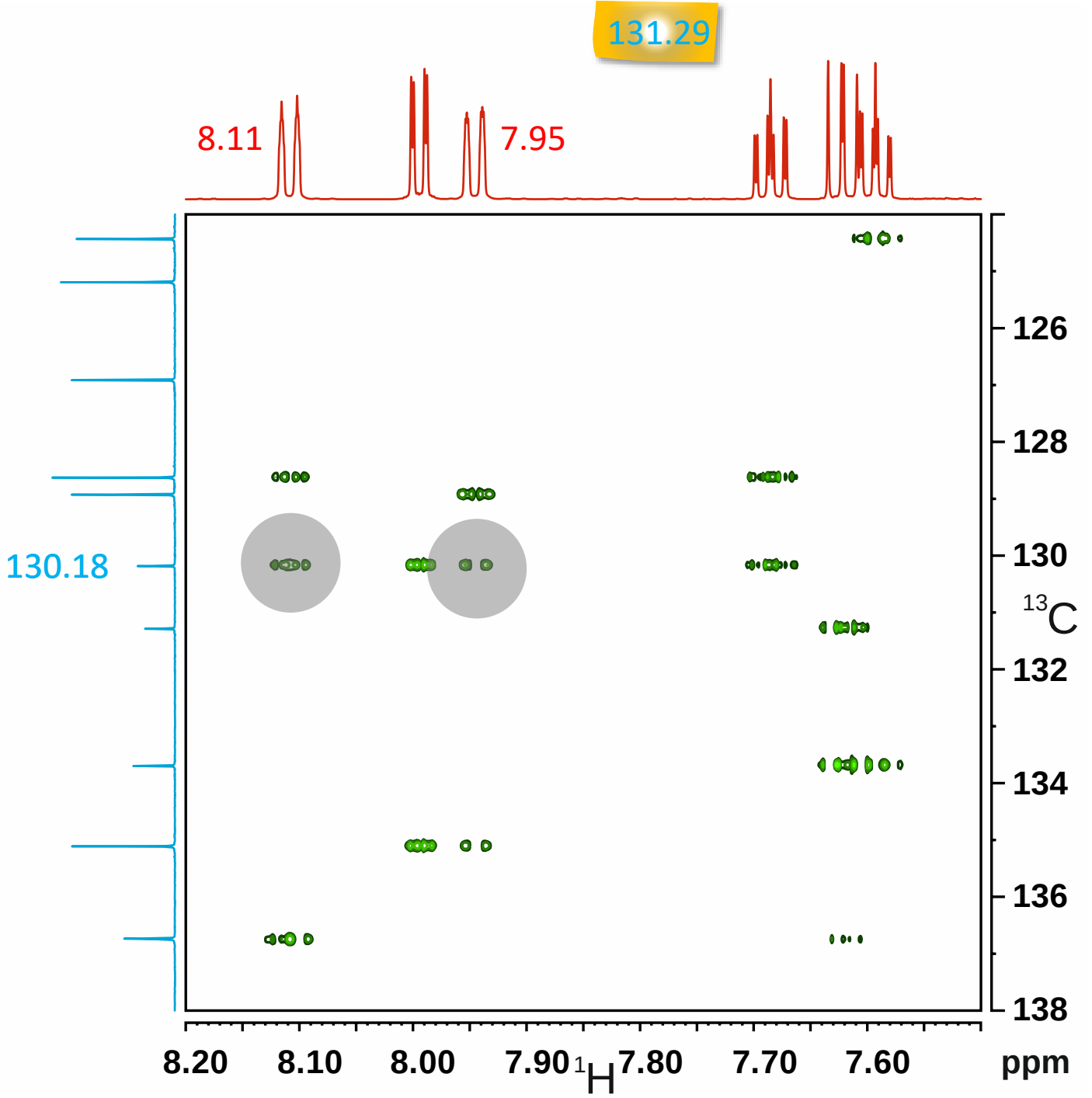
Linking the chains

Assign the quaternary C atoms

Using this assignment both cross peaks are the result of heteronuclear coupling across three bonds, which is very common.

One pathway is shown here.



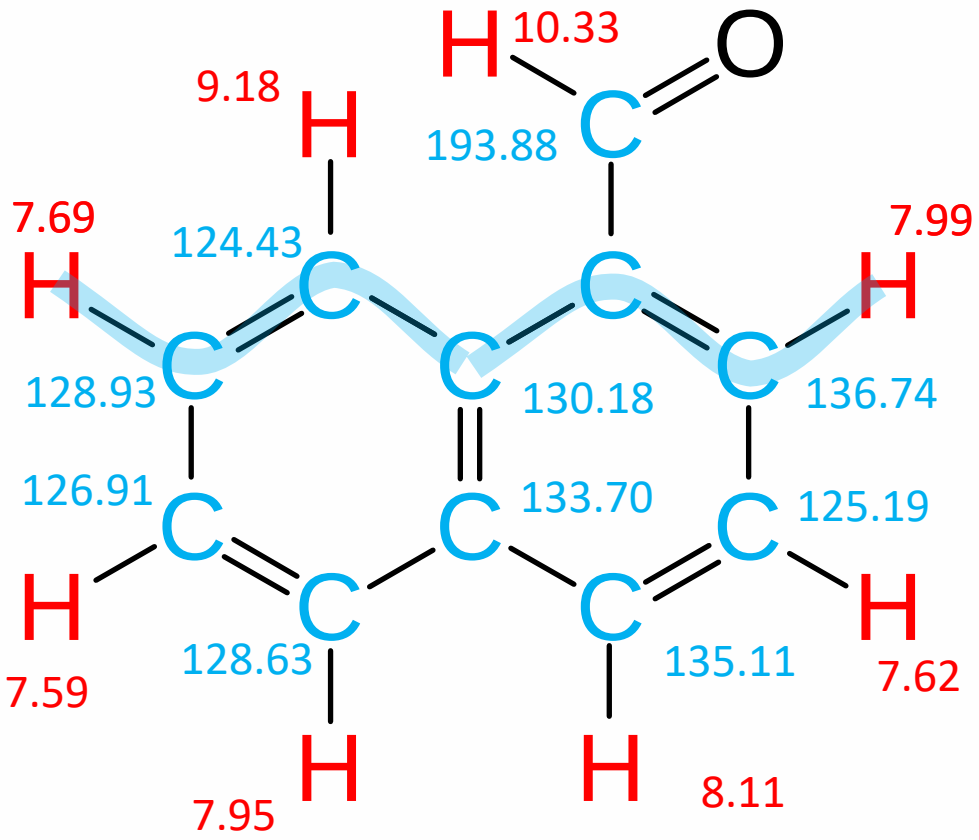


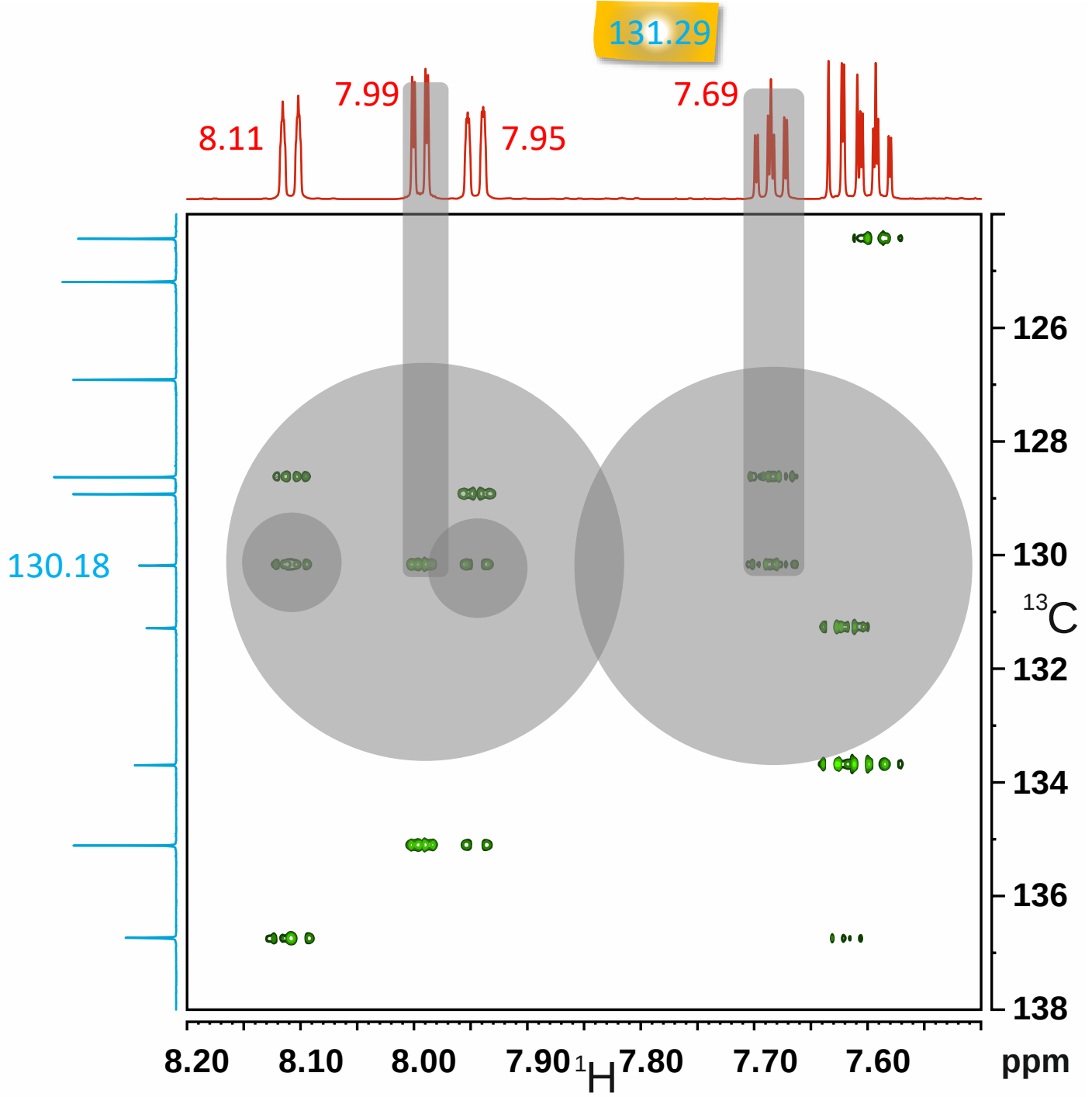
Linking the chains

Assign the quaternary C atoms

But what about the pathway shown here or that to the proton with the chemical shift of 7.69 ppm?

In theory there should be at least two more cross peaks. Let us try.



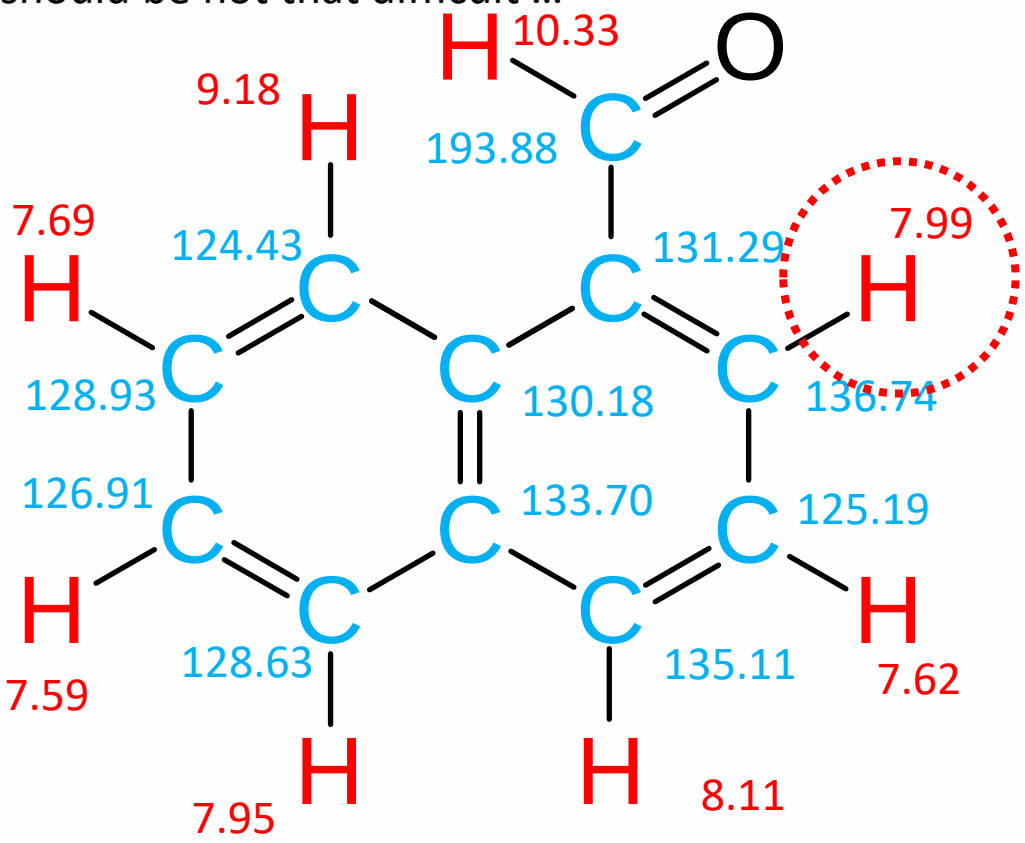


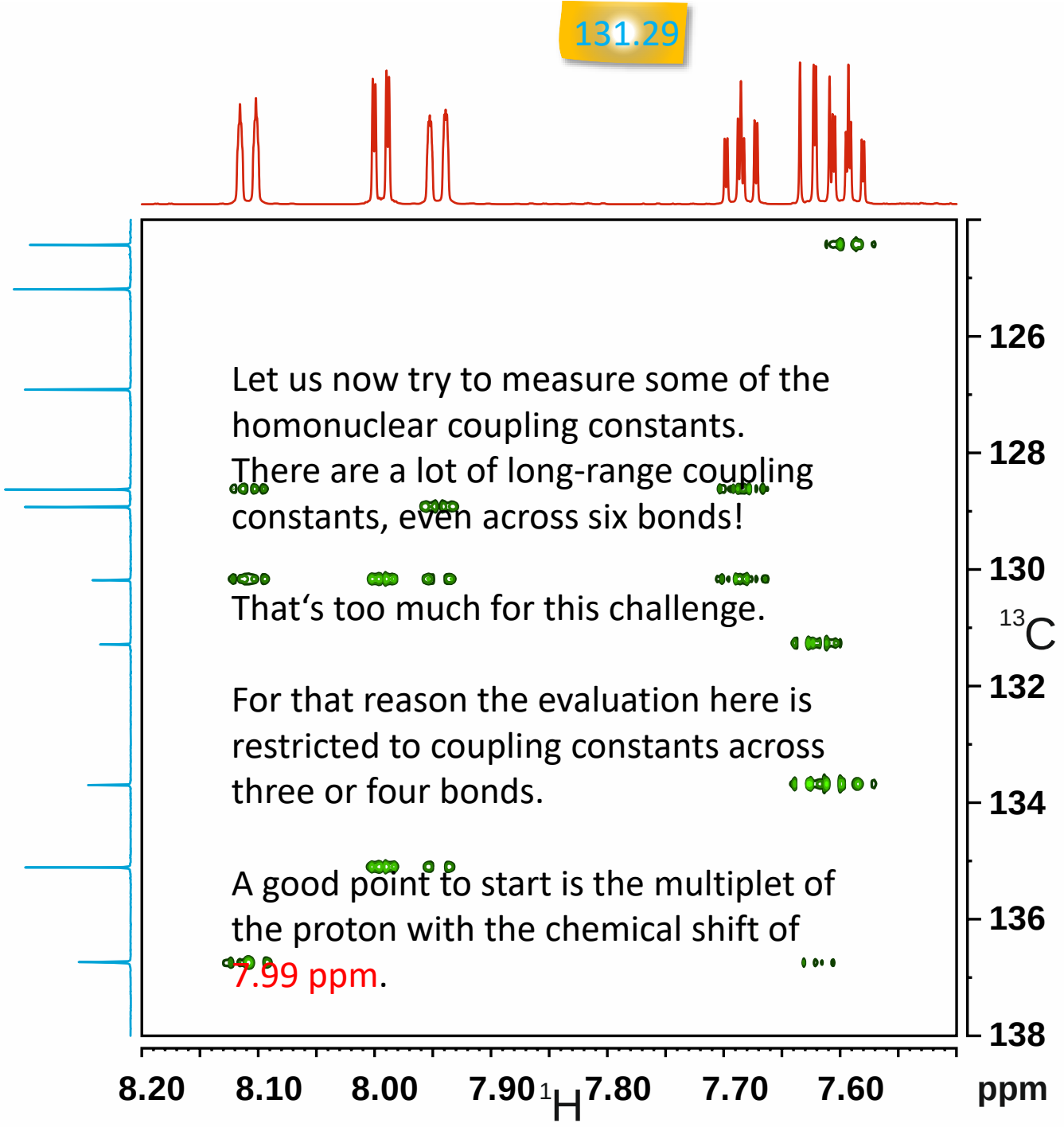
Linking the chains

Assign the quaternary C atoms

There is one more cross peak between the carbon at 130.18 ppm and the proton at 10.33 ppm, which is not visible in this enlarged part of the HMBC.

The assignment of the last quaternary carbon atom should be not that difficult …

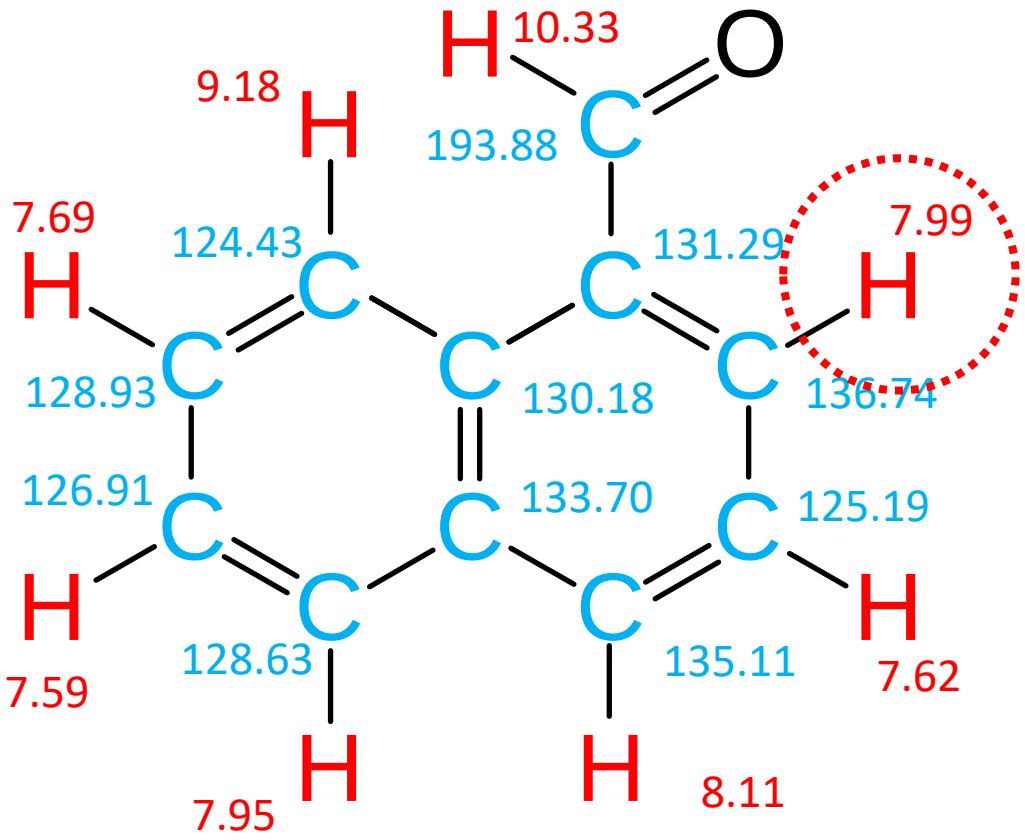


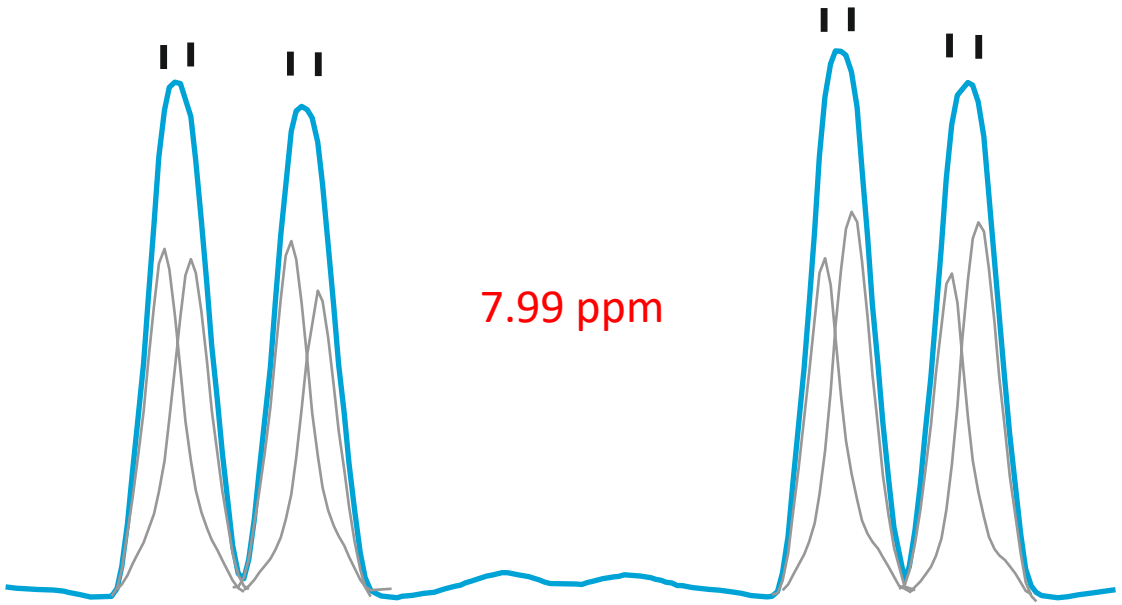


Coupling constants

Right six-membered ring

For the sake of clarity let us remove all carbon chemical shifts and, for the moment, even the proton chemical shifts of the left side six-membered ring.



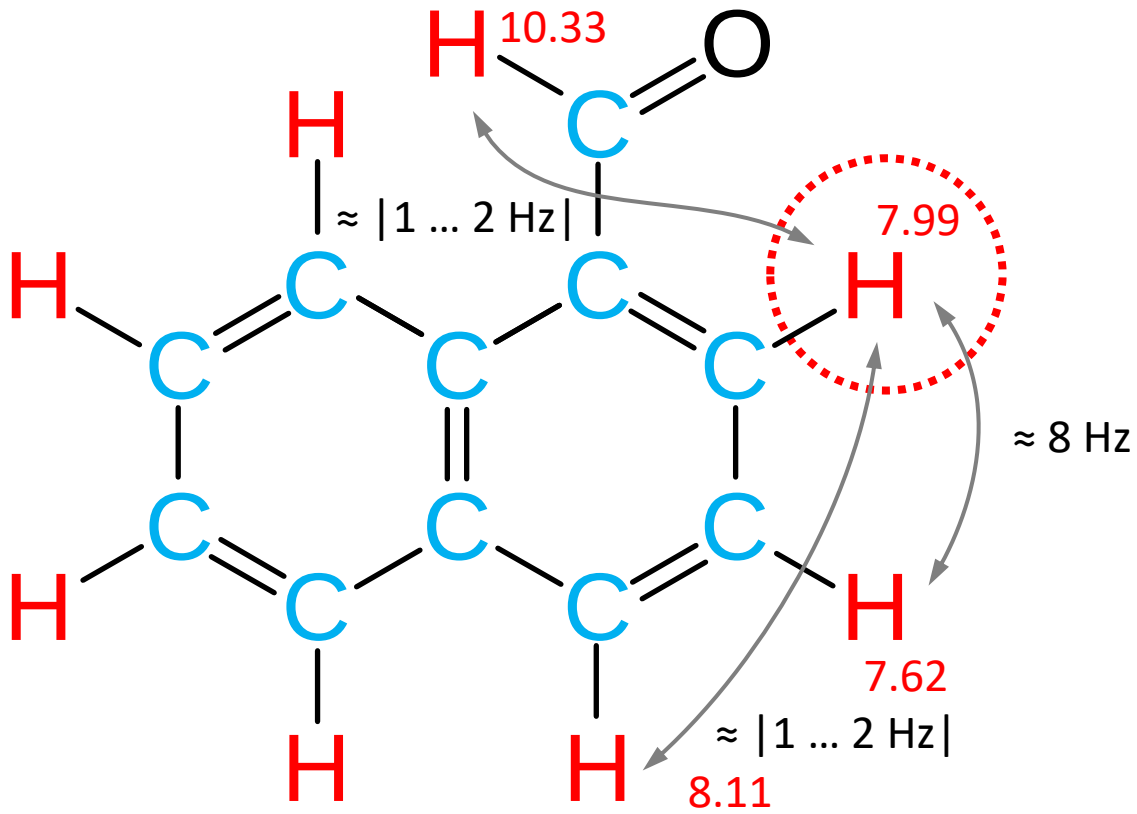


Coupling constants

Right six-membered ring

We expect three different coupling constants, one vicinal and two four bond coupling constants.

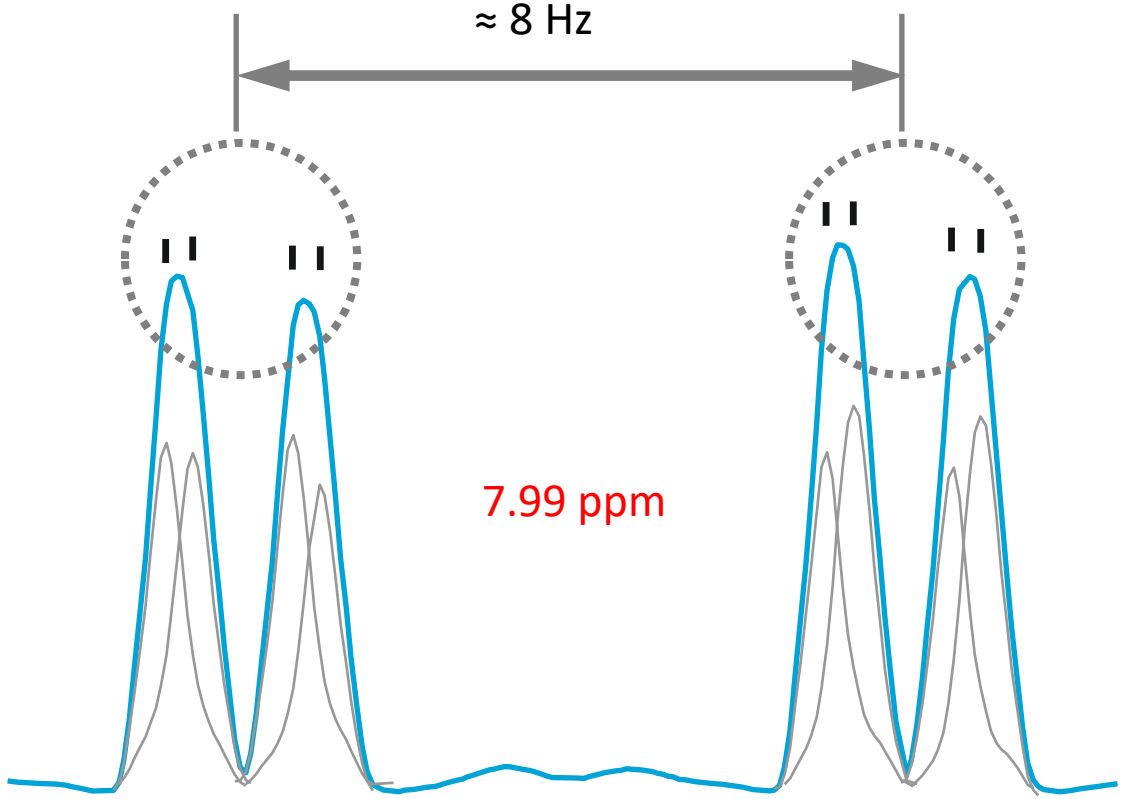
The sign of the four bond coupling constants is unknown, but we are able to estimate the magnitude.



The aldehyde as coupling partner is an assumption. The fine structure of the aldehyde group proton signal is not known here. Later we don't take care about this coupling pathway.

Apparently the small long-range coupling constants are hidden in the circled areas.

The larger vicinal coupling constant is the difference between the two circled areas.



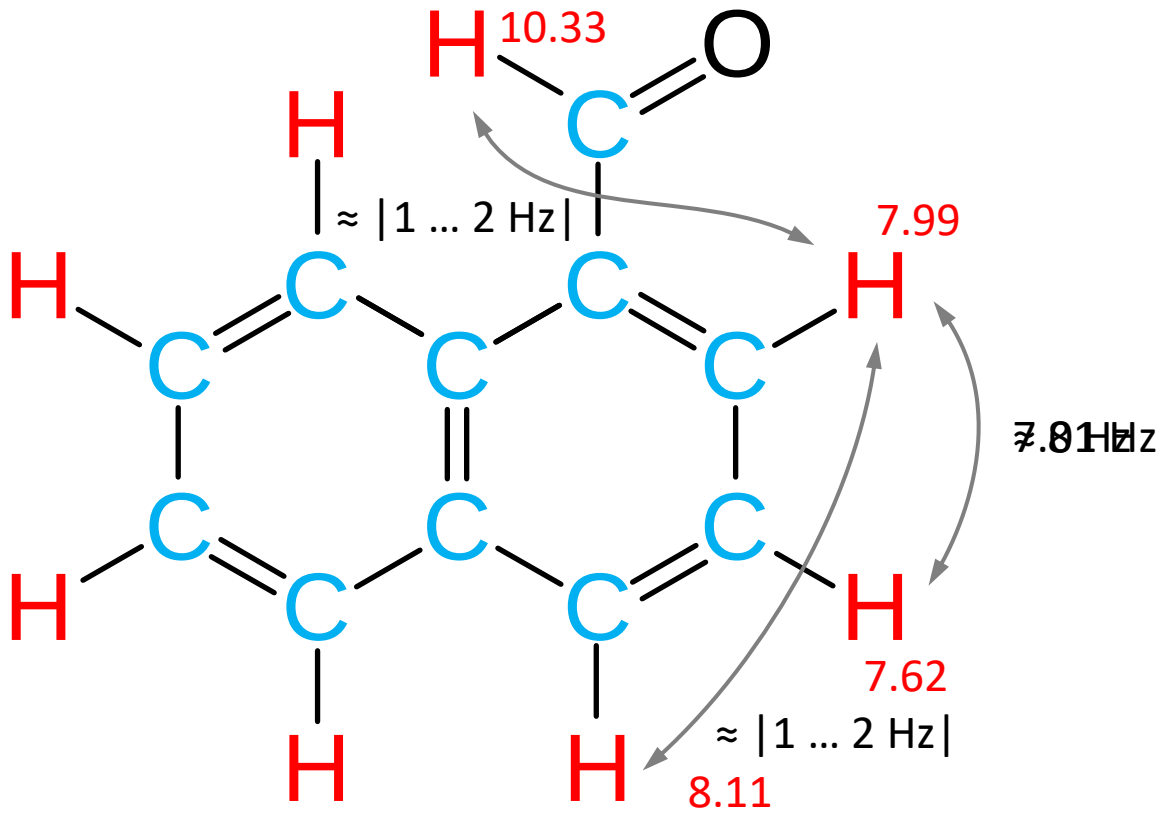
Coupling constants

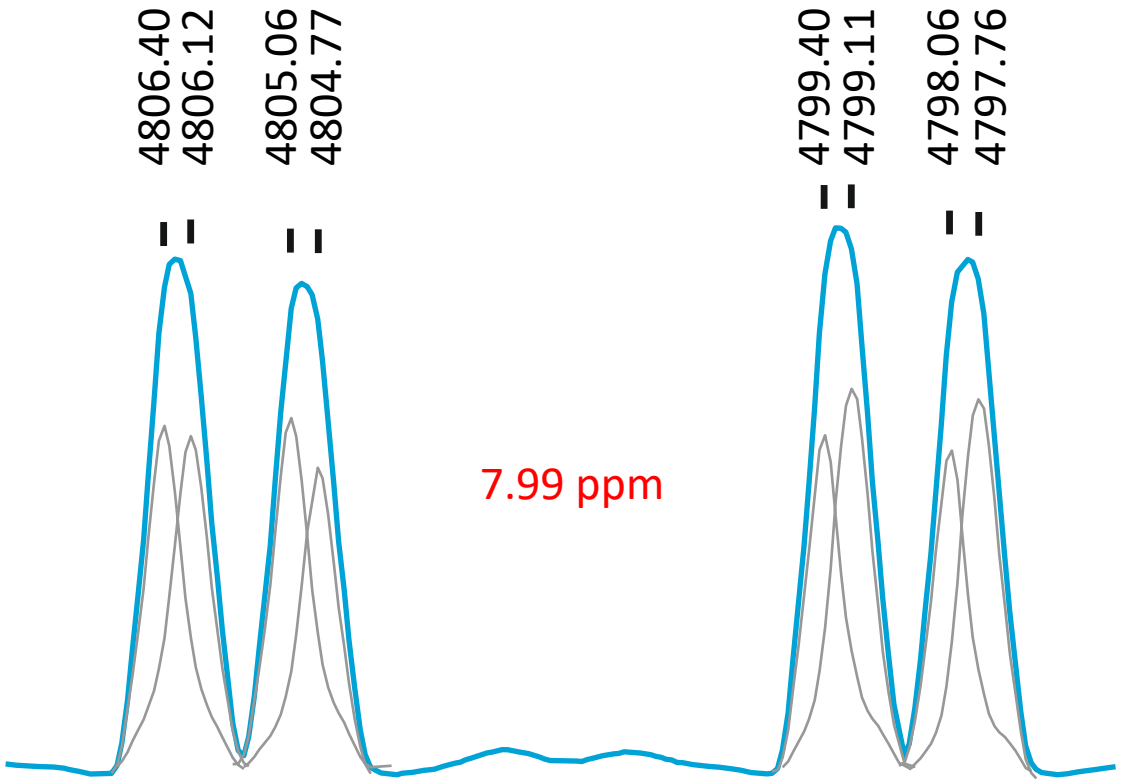
Right six-membered ring

Doing the calculation in detail we get …

$$J = \frac{(4806.40\text{Hz} + 4804.77\text{Hz})}{2} - \frac{(4799.40\text{Hz} + 4797.76\text{Hz})}{2}$$

$$J = 7.01\text{Hz}$$

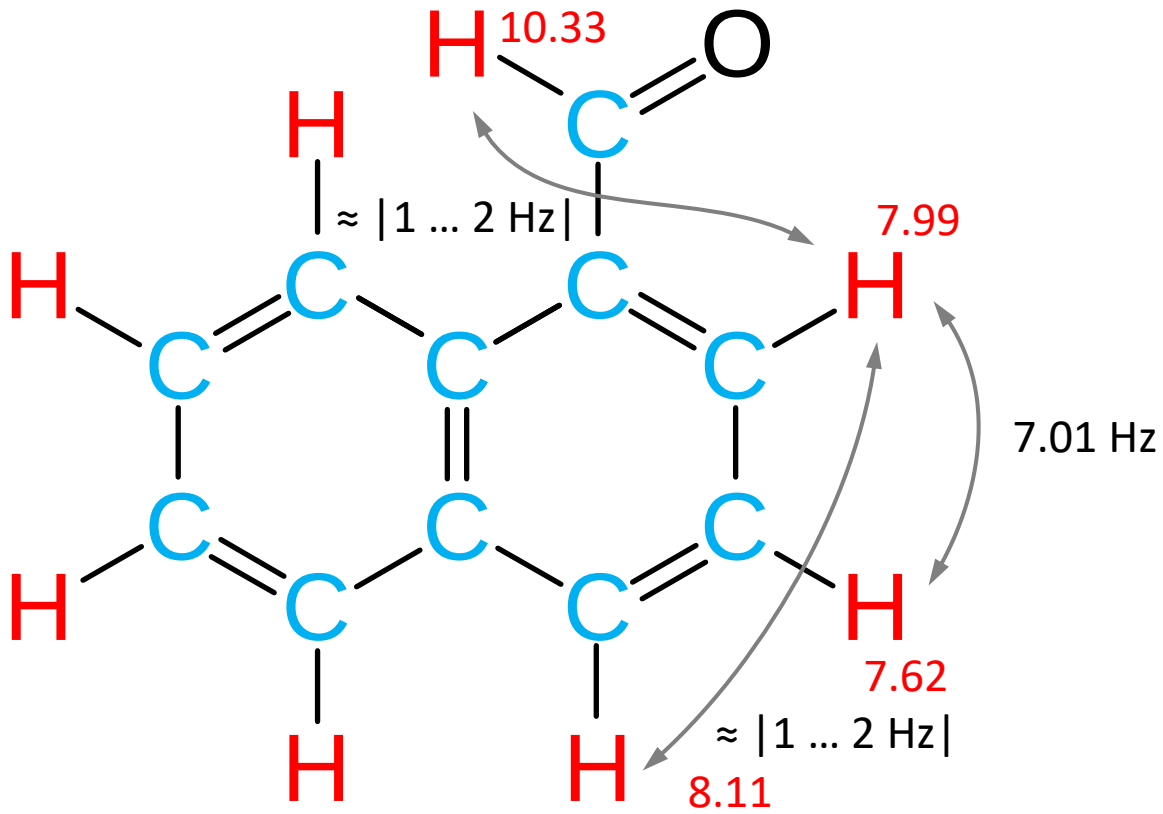


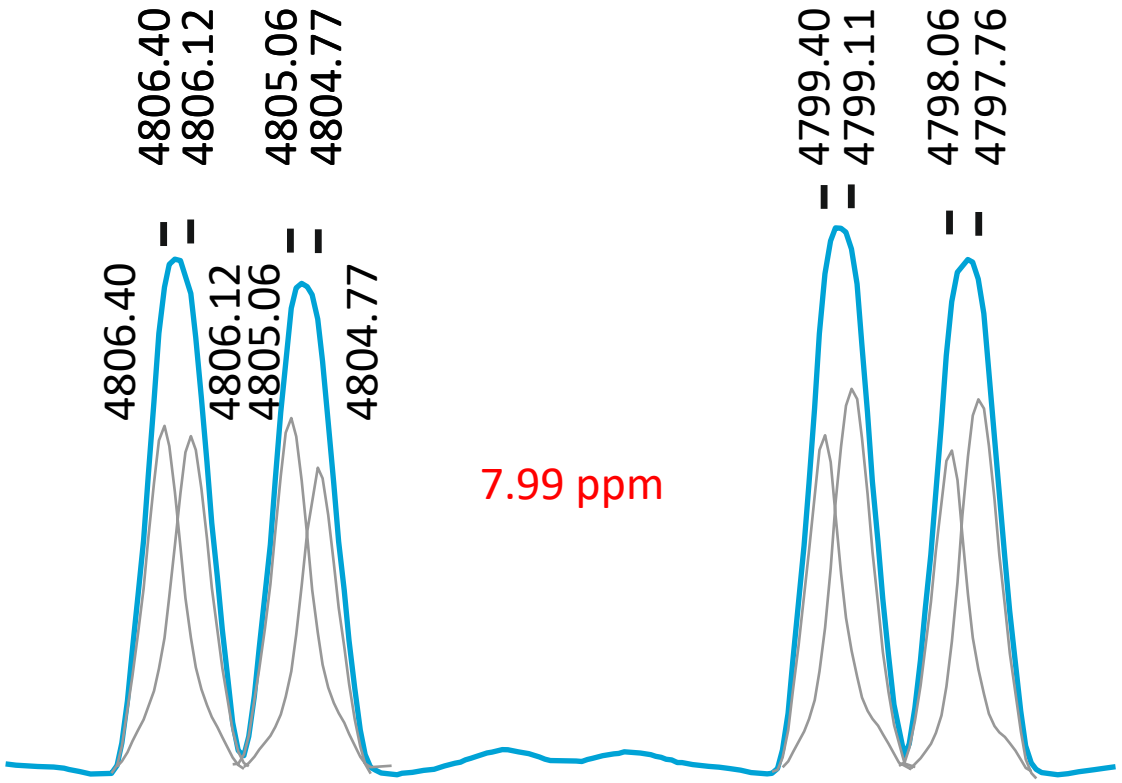


Coupling constants

Right six-membered ring

To measure the smaller coupling constants, one half of the multiplet is sufficient.

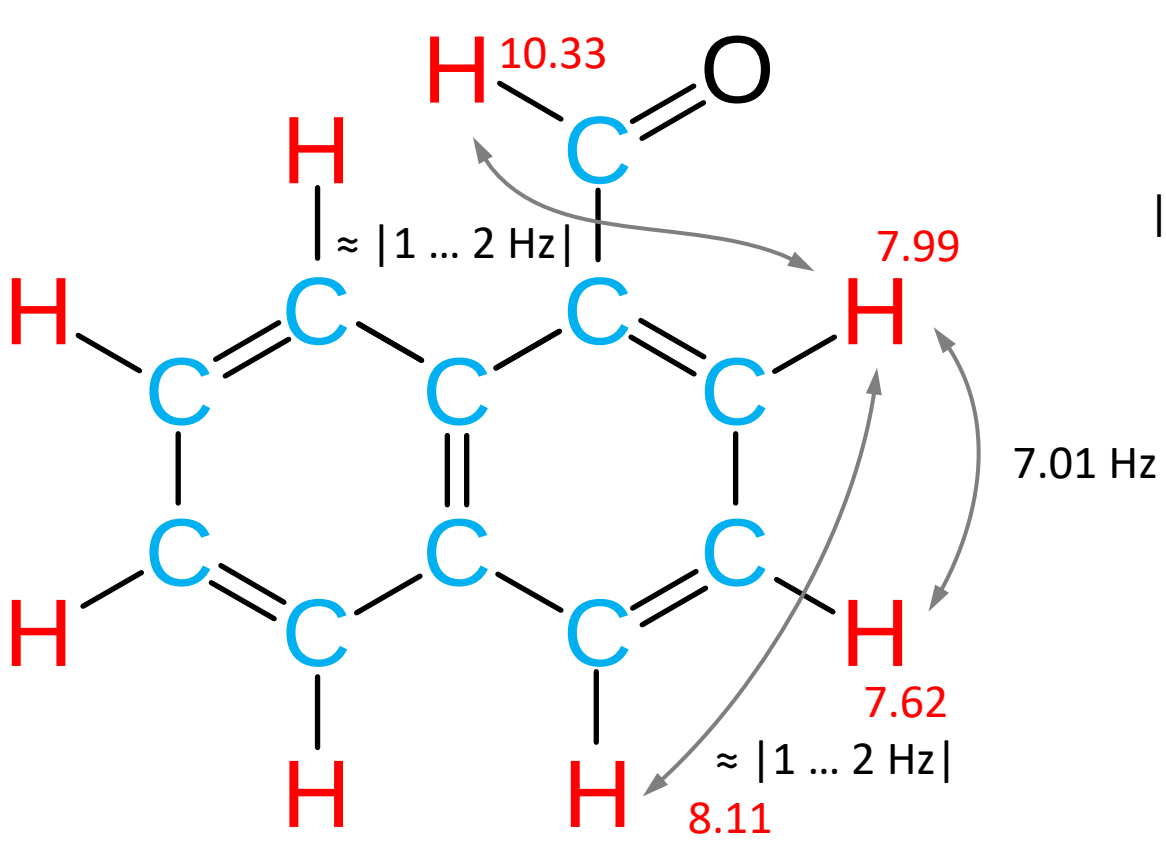


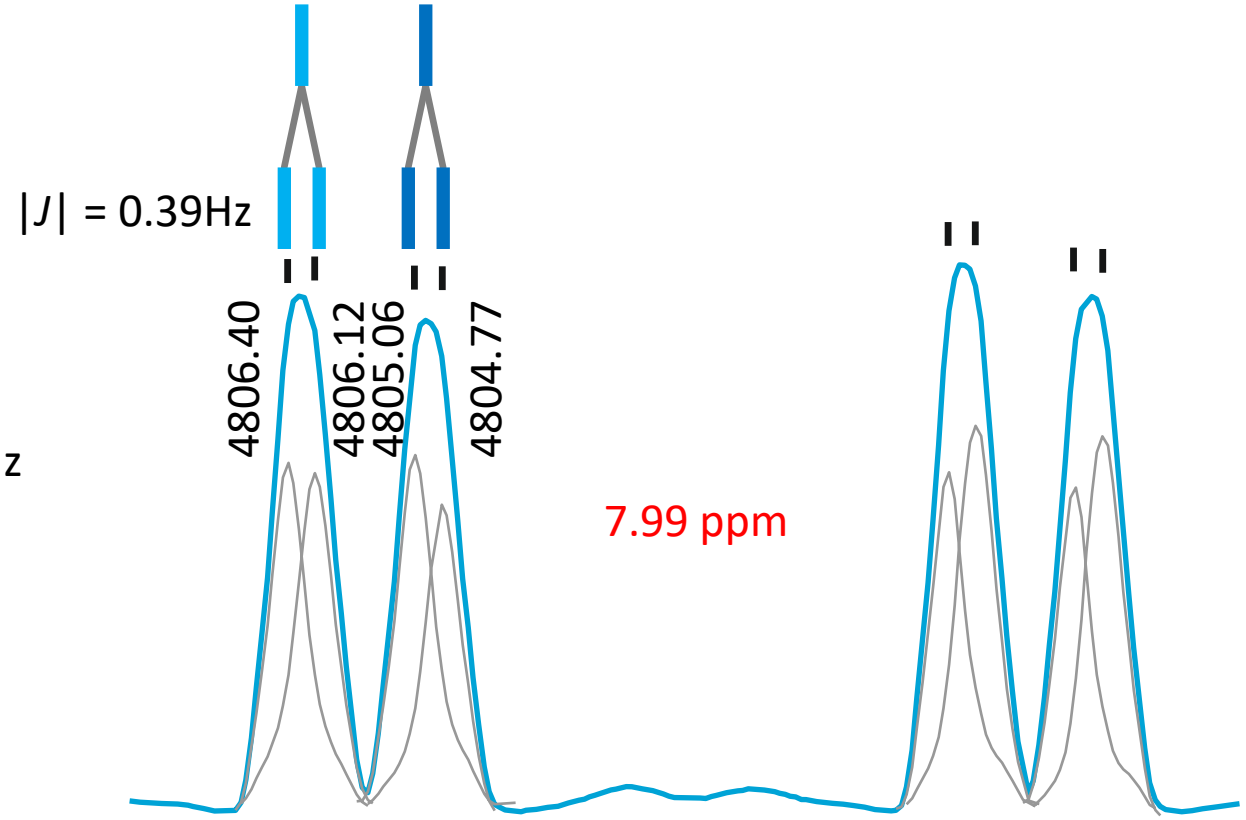


Coupling constants

Right six-membered ring

There are clearly two doublets with the same coupling constant.



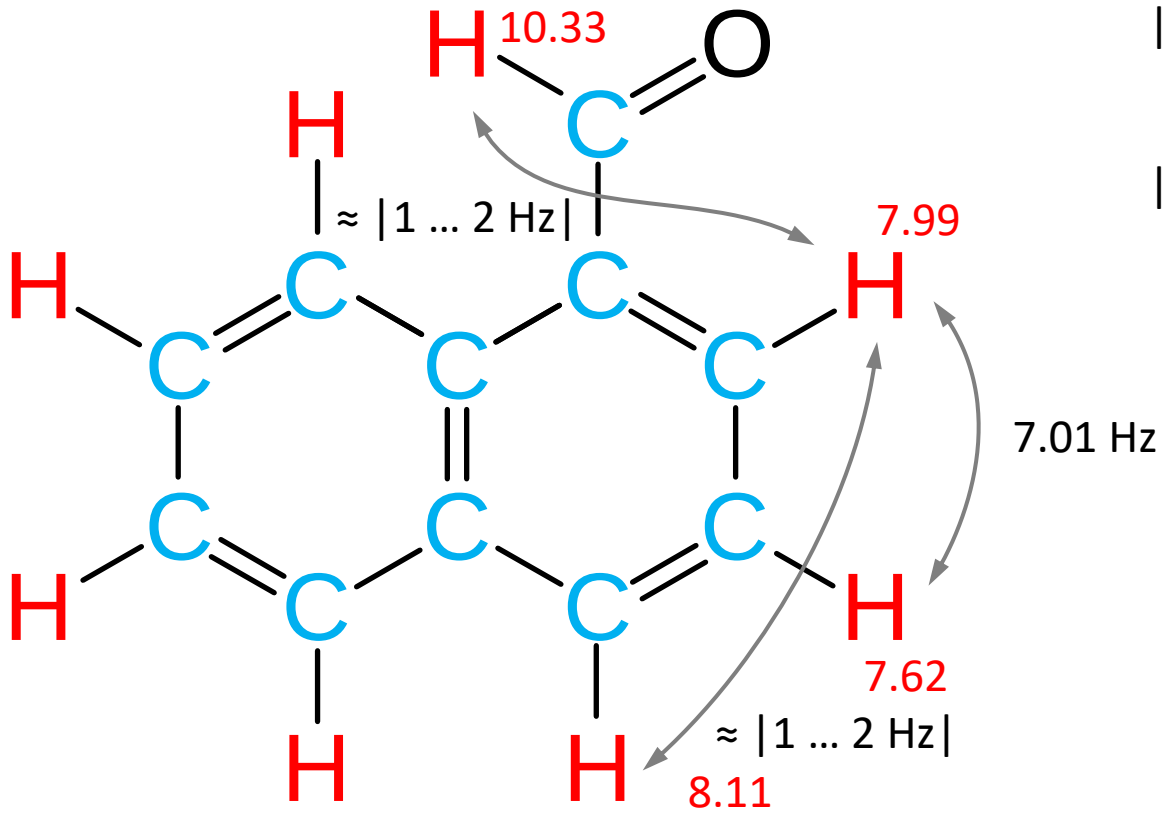


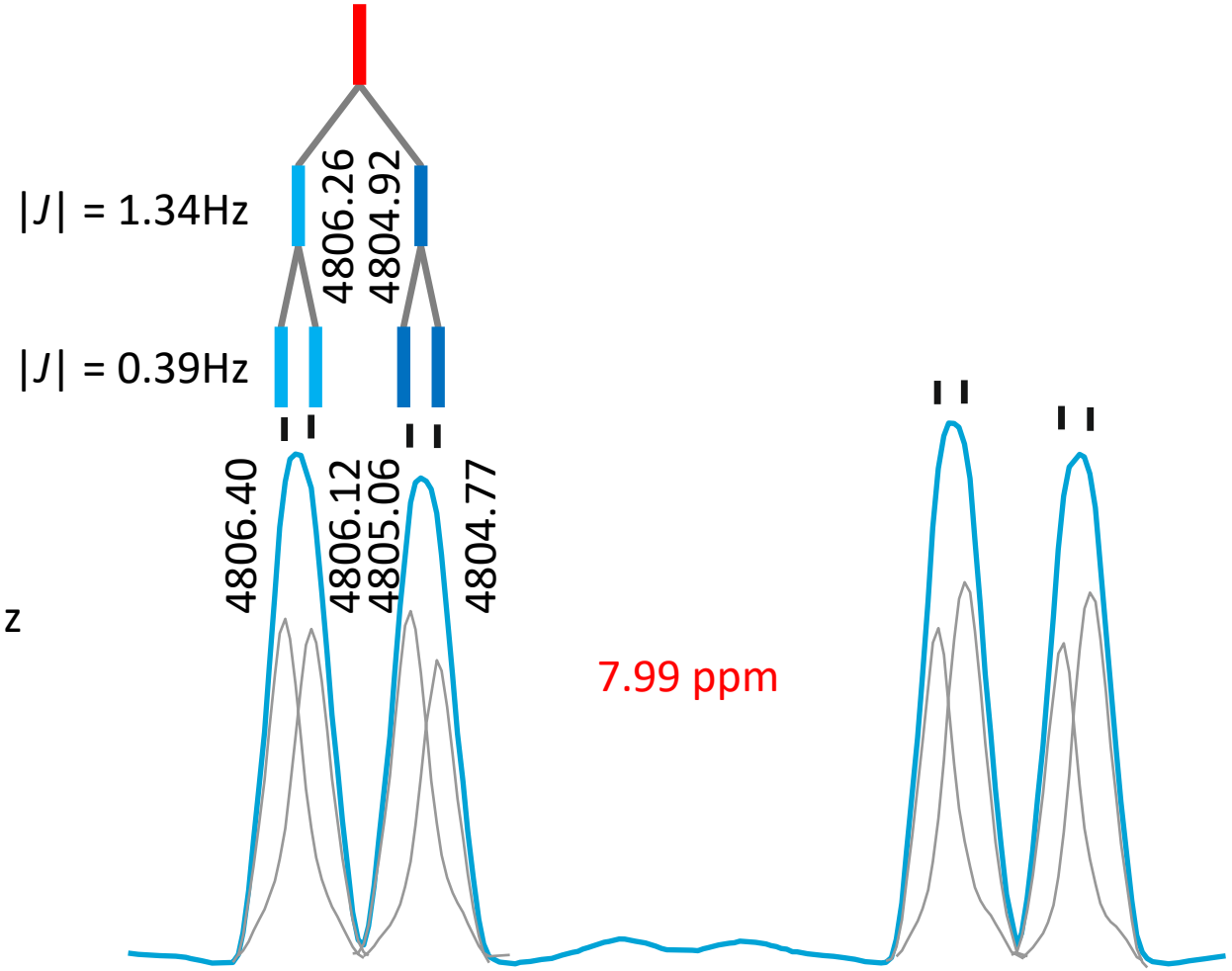
Coupling constants

Right six-membered ring

We got a new doublet. To get the chemical shifts of both lines of this multiplet we average the chemical shifts of each of the blue doublets.

Now it is easy to calculate the coupling constant.

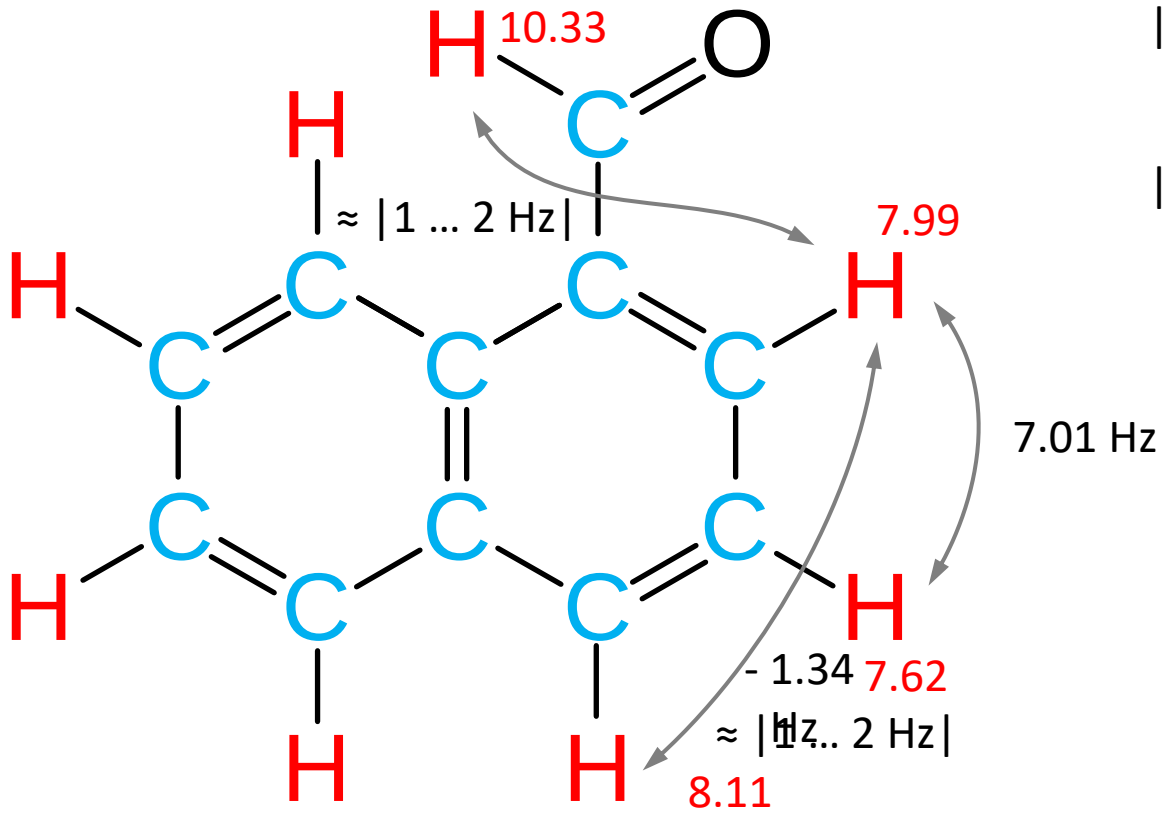


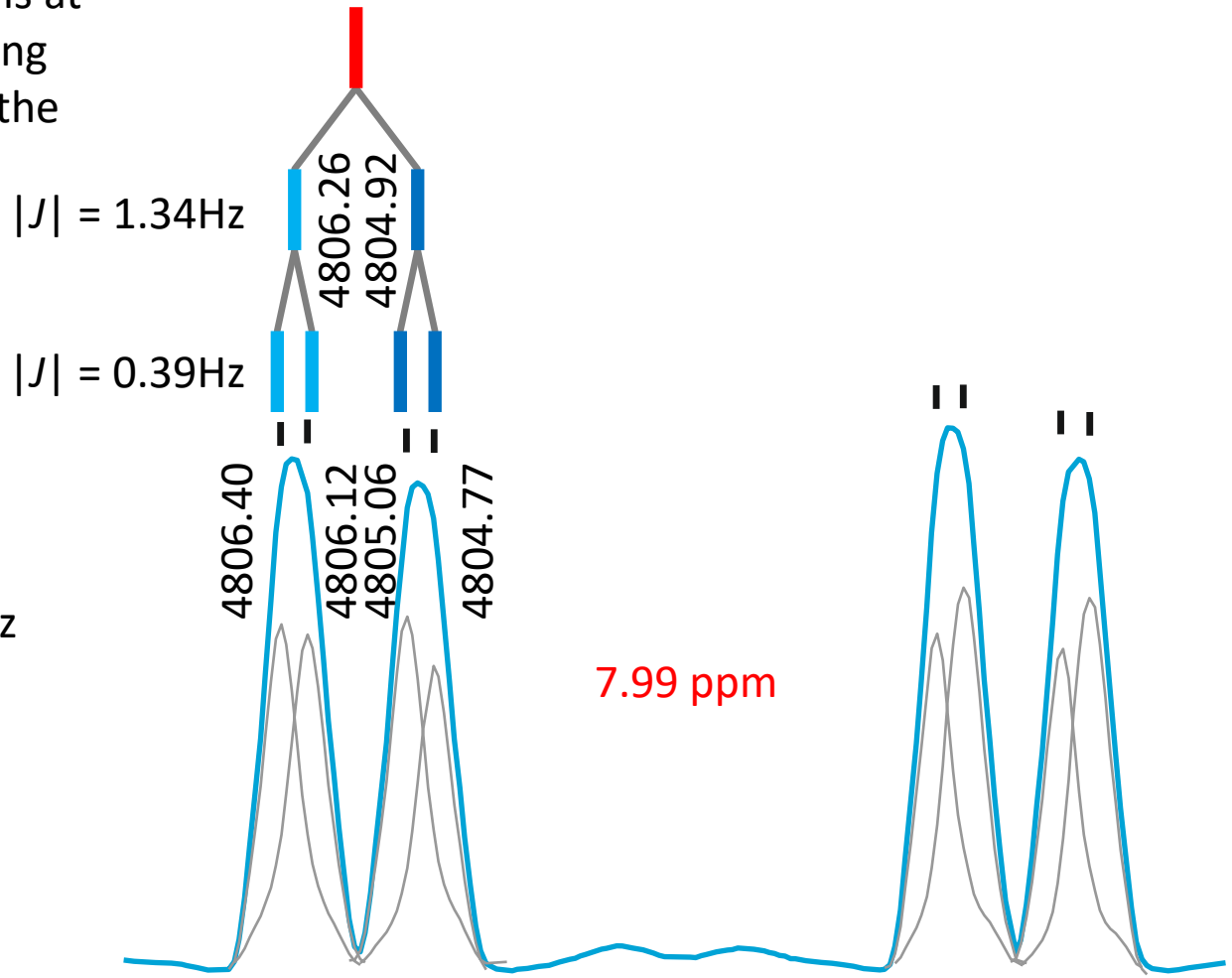


Coupling constants

Right six-membered ring

From these two values an absolute value of **|1.34 Hz|** means clearly the four bond coupling constant between the protons at 7.99 ppm and 8.11 ppm. Even more, the sign of such coupling constants is always negative, although we cannot measure the sign here.

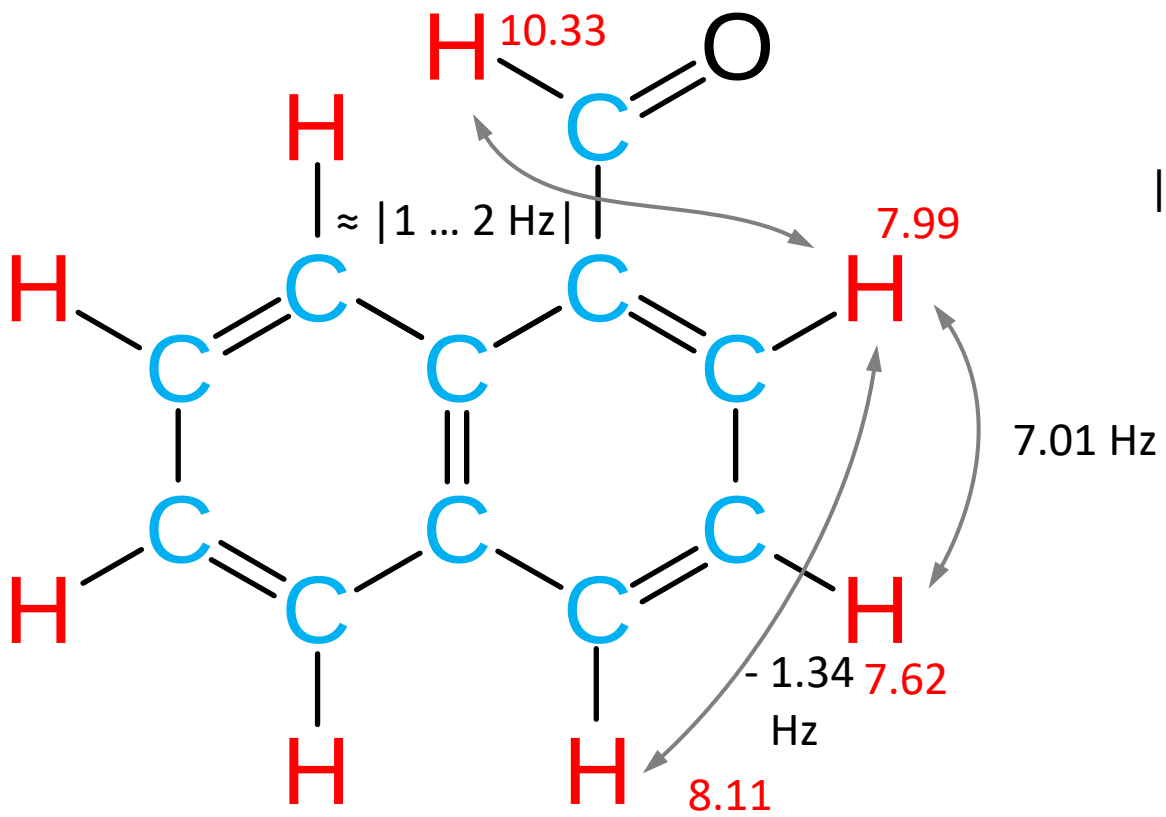


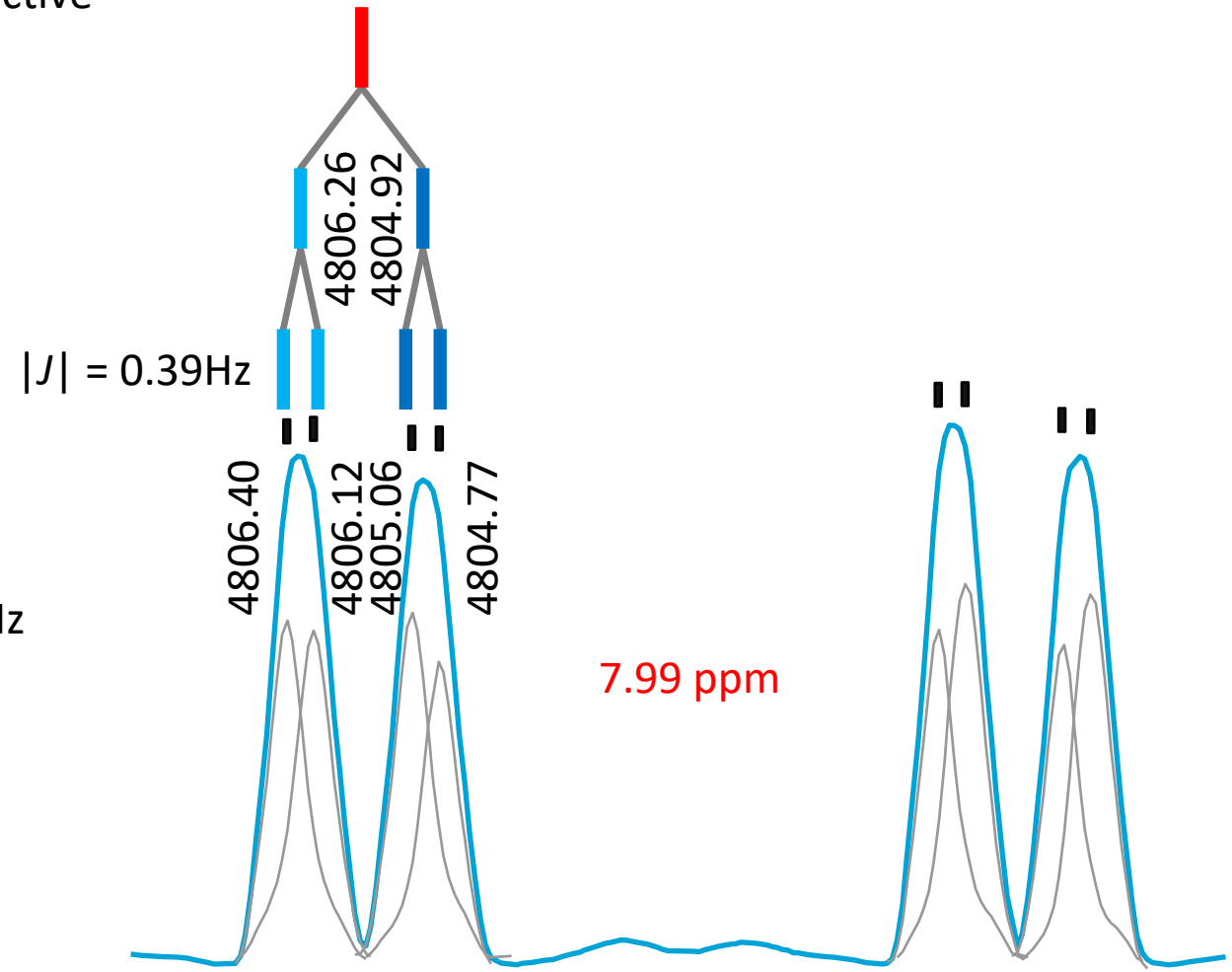


Coupling constants

Right six-membered ring

We cannot verify, whether the second value is really the four bond coupling shown here. Without more specific (i.e. selective decoupling) measurements we have to neglect this value.

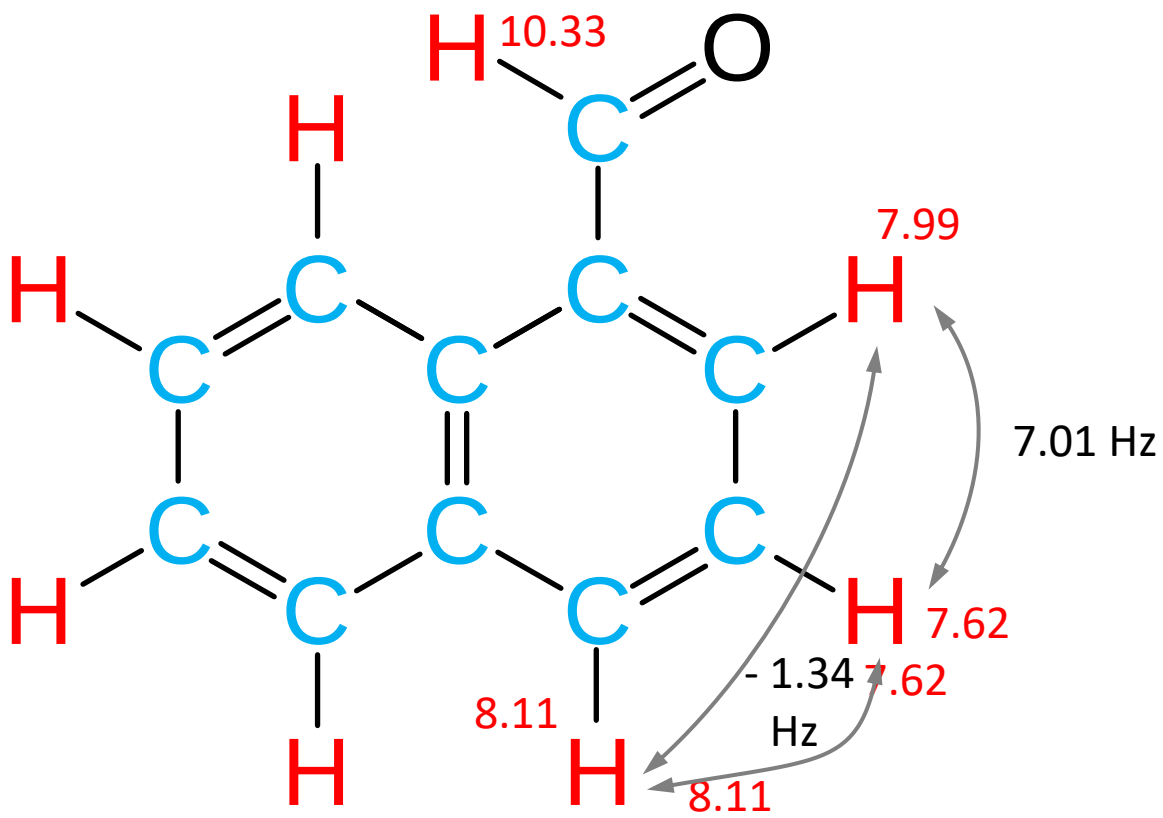


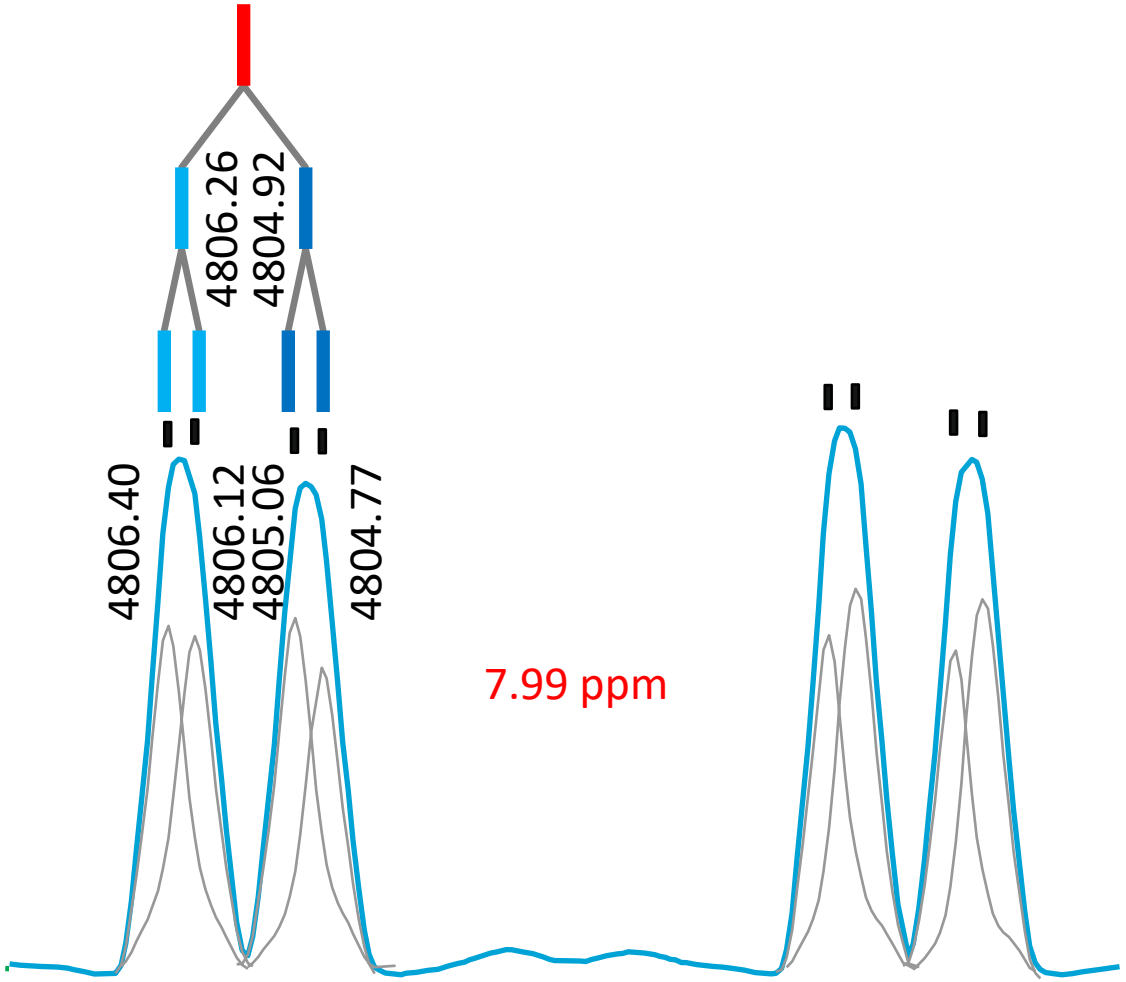


Coupling constants

Right six-membered ring

To get the second vicinal coupling constant we have to analyze the multiplet of the proton signal with the chemical shift of 8.11 ppm.





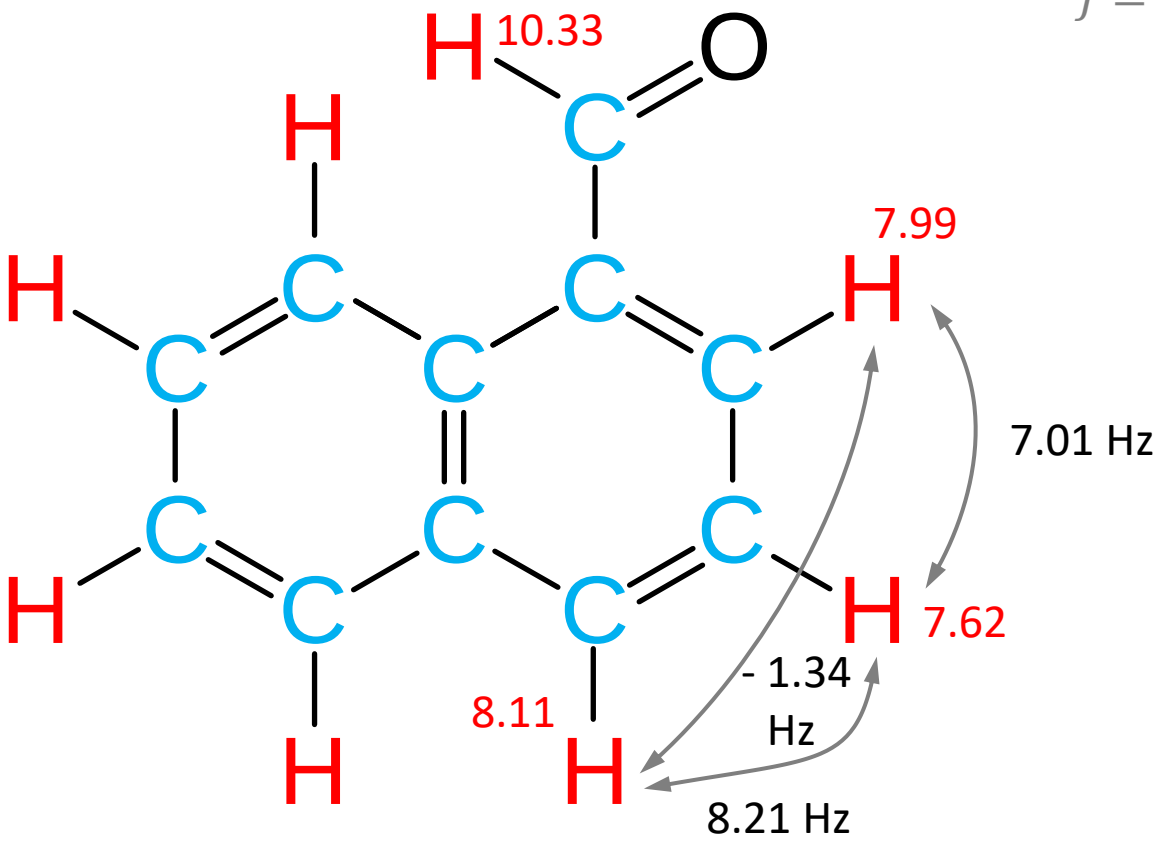
Coupling constants

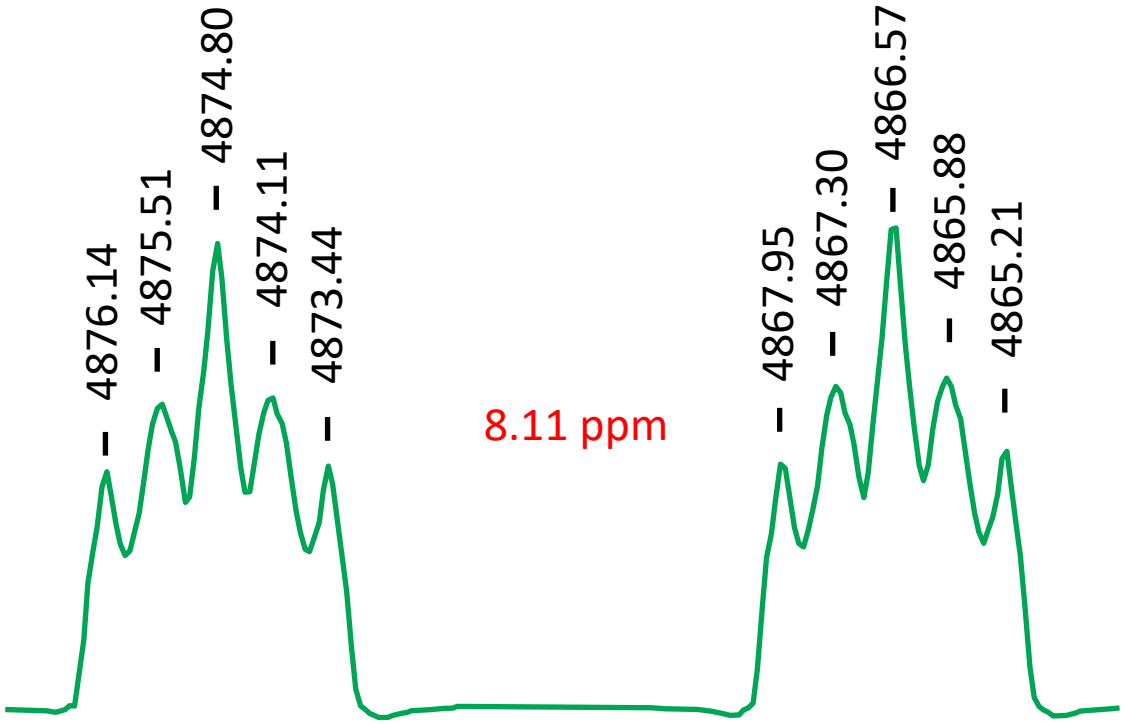
Right six-membered ring

We cannot deal with the fine structure (which has to be twice a doublet of doublet of doublets with a total of 8 lines each), but we are able to measure the vicinal coupling constant as done before.

$$J = \frac{(4876.14\text{Hz} + 4873.44\text{Hz})}{2} - \frac{(4867.95\text{Hz} + 4865.21\text{Hz})}{2}$$

$$J = 8.21\text{Hz}$$

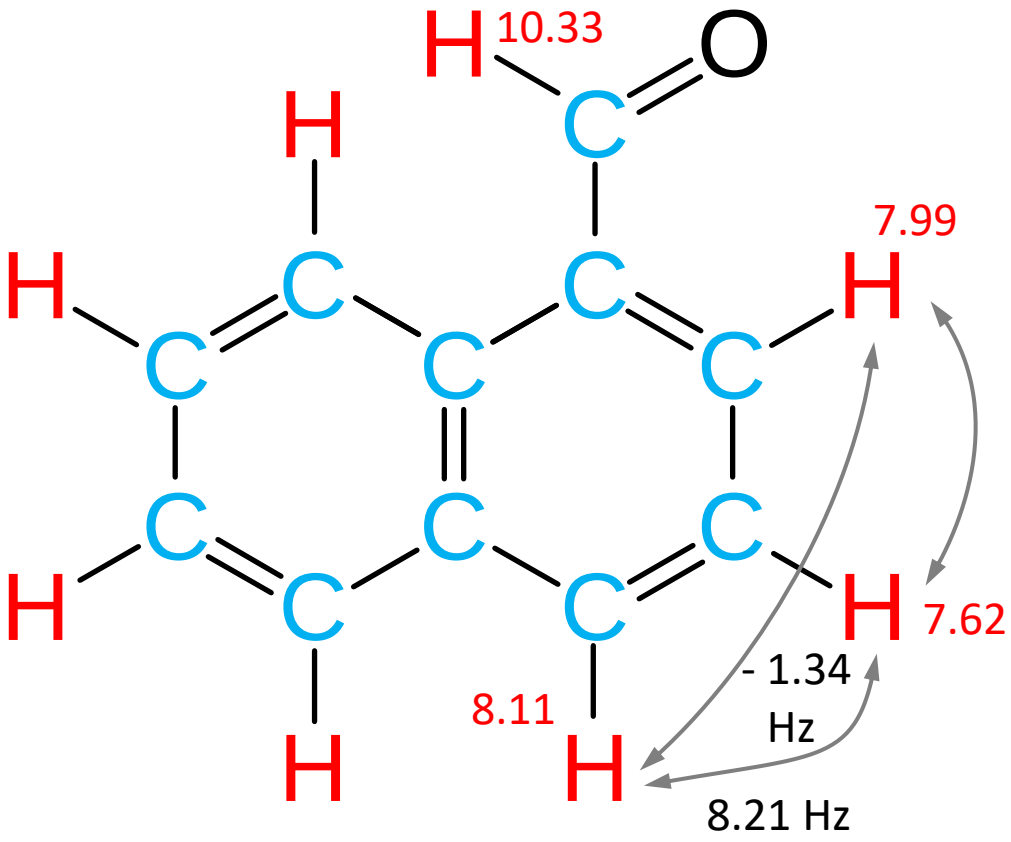




Coupling constants

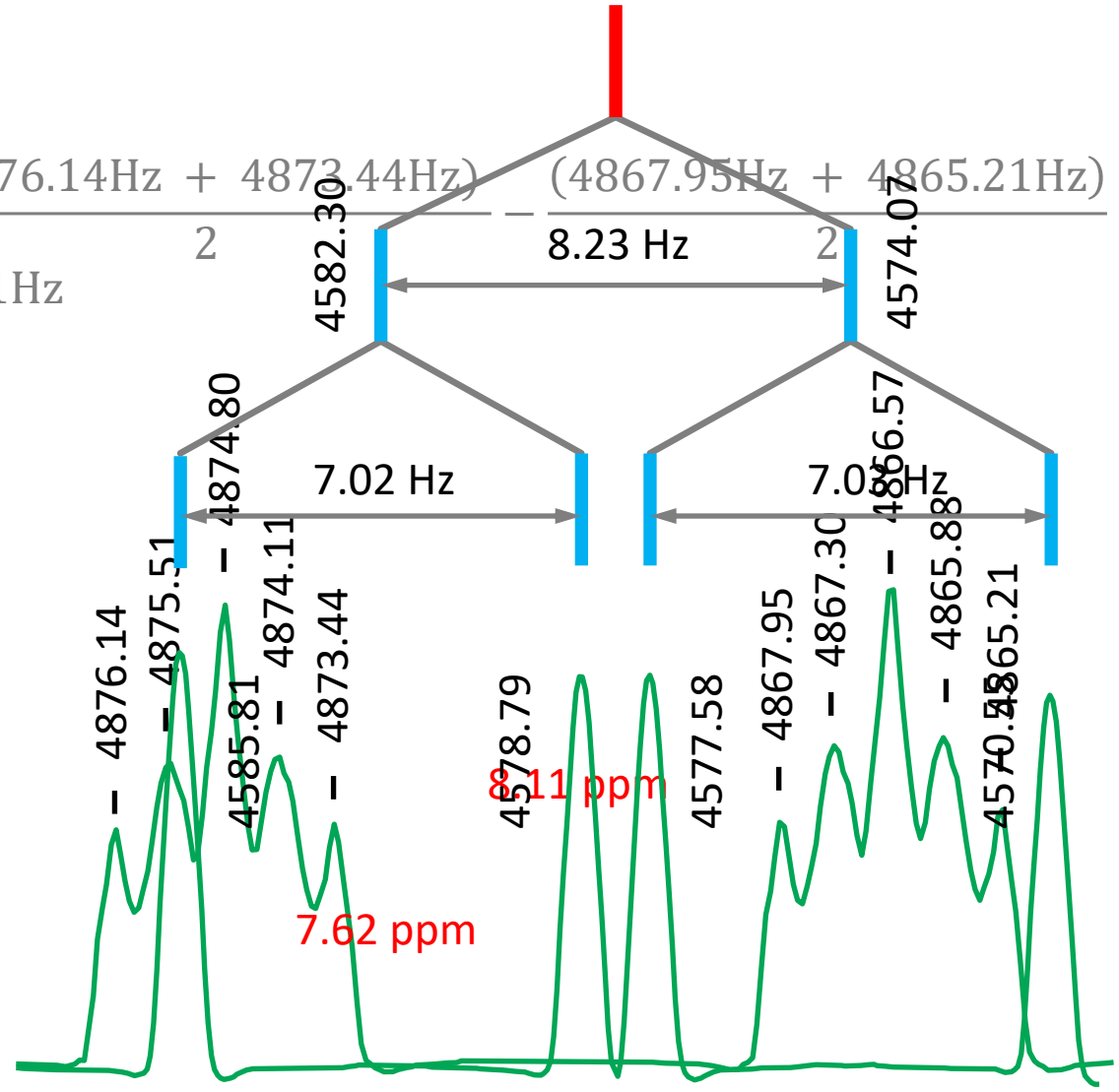
Right six-membered ring

We should see the coupling constants of **7.01 Hz** and **8.21 Hz** in the multiplet of the proton with the chemical shift of 7.62 ppm.
Let us check (without additional explanation).



$$J = \frac{(4876.14\text{Hz} + 4873.44\text{Hz})}{2} - \frac{(4867.95\text{Hz} + 4865.21\text{Hz})}{2}$$

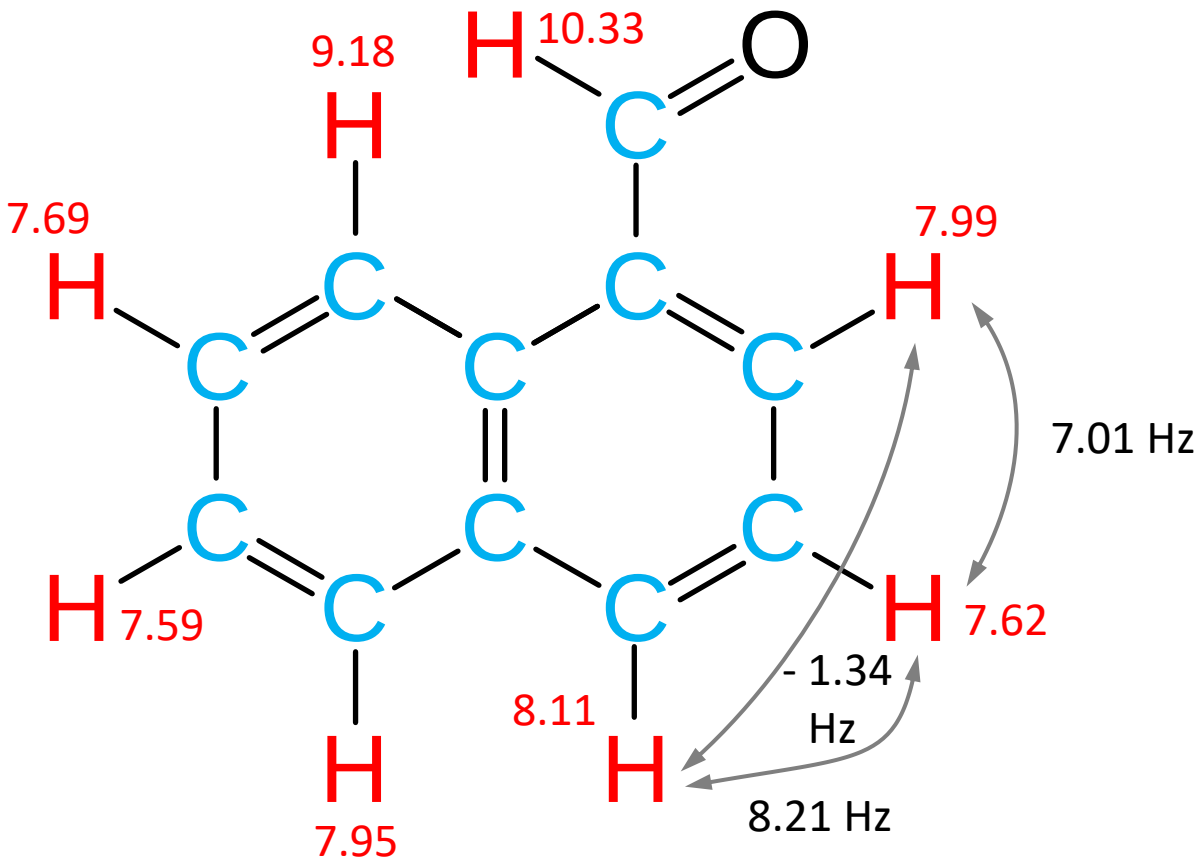
$$J = 8.21\text{Hz}$$



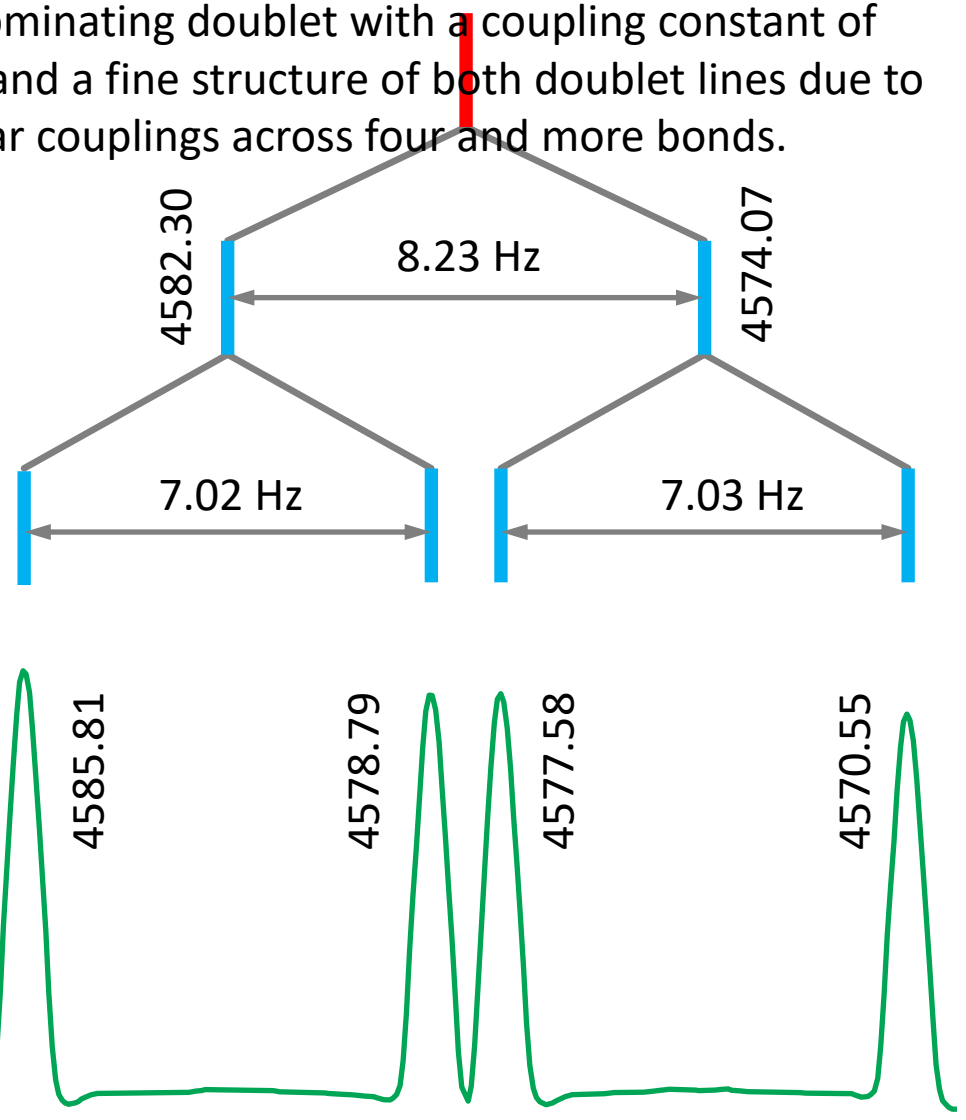
Coupling constants

Left six-membered ring

Let us now extract the coupling constants from the left six-membered ring.
First we need to restore all the proton chemical shifts we previously removed for the sake of clarity.



The structure of the multiplets at 9.18 ppm and 7.95 ppm is essentially the same as for the multiplets at 7.99 and 8.11 ppm.
We see a dominating doublet with a coupling constant of about **8 Hz** and a fine structure of both doublet lines due to homonuclear couplings across four and more bonds.



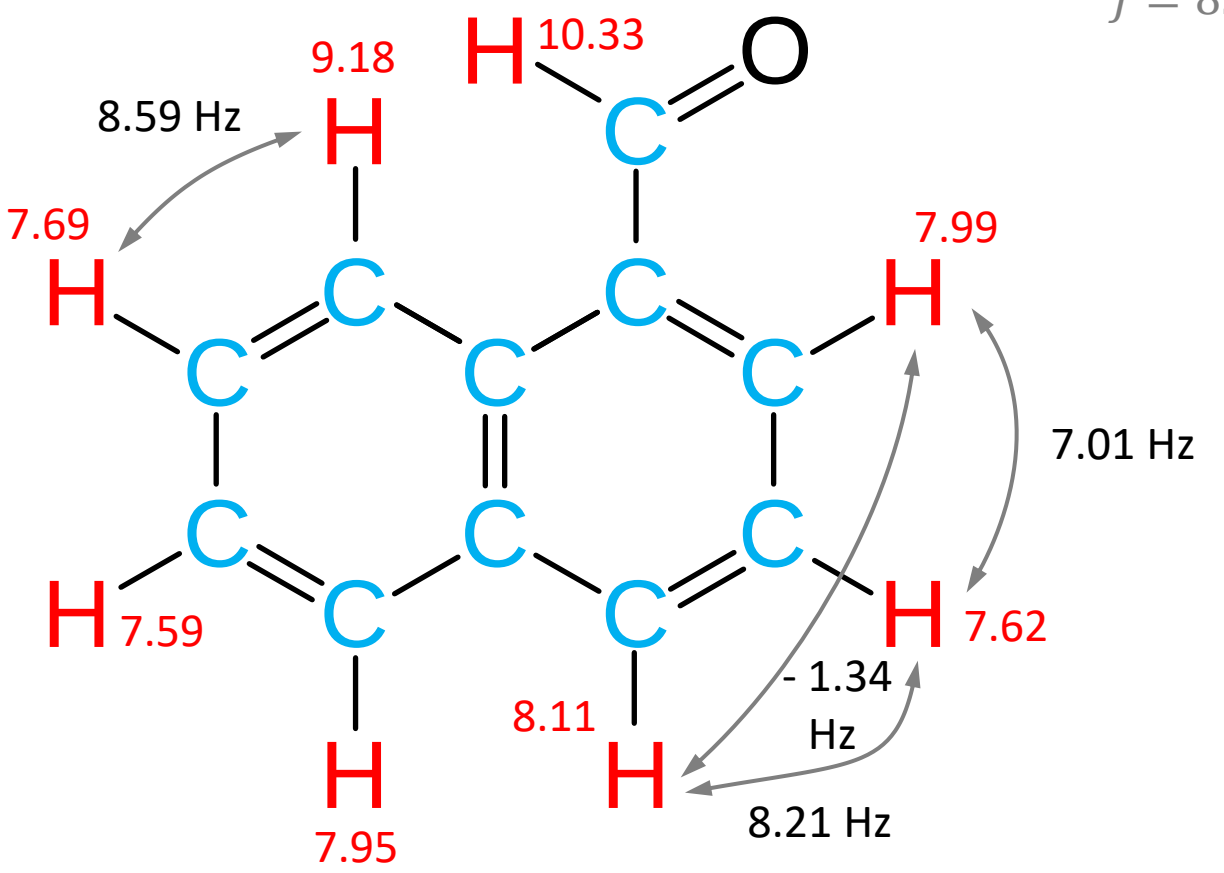
Coupling constants

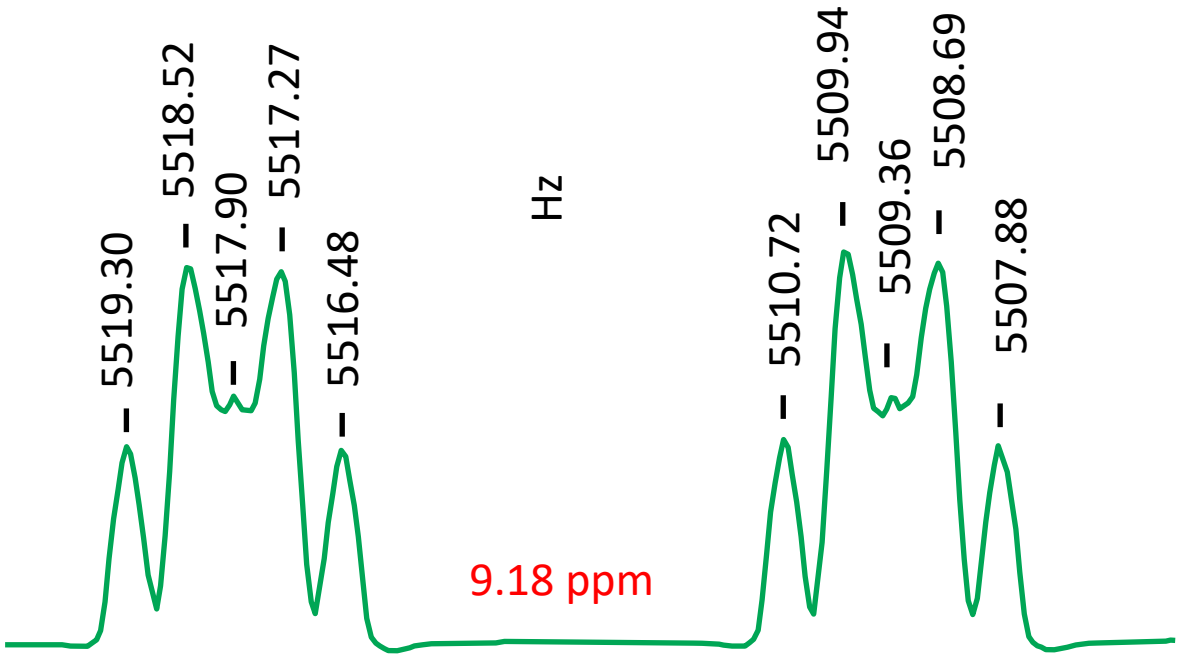
Left six-membered ring

We start with the multiplet with the chemical shift of 9.18 ppm. We already used the calculation method to get the vicinal coupling constant twice.

$$J = \frac{(5519.30\text{Hz} + 5516.48\text{Hz})}{2} - \frac{(5510.72\text{Hz} + 5507.88\text{Hz})}{2}$$

$$J = 8.59\text{Hz}$$





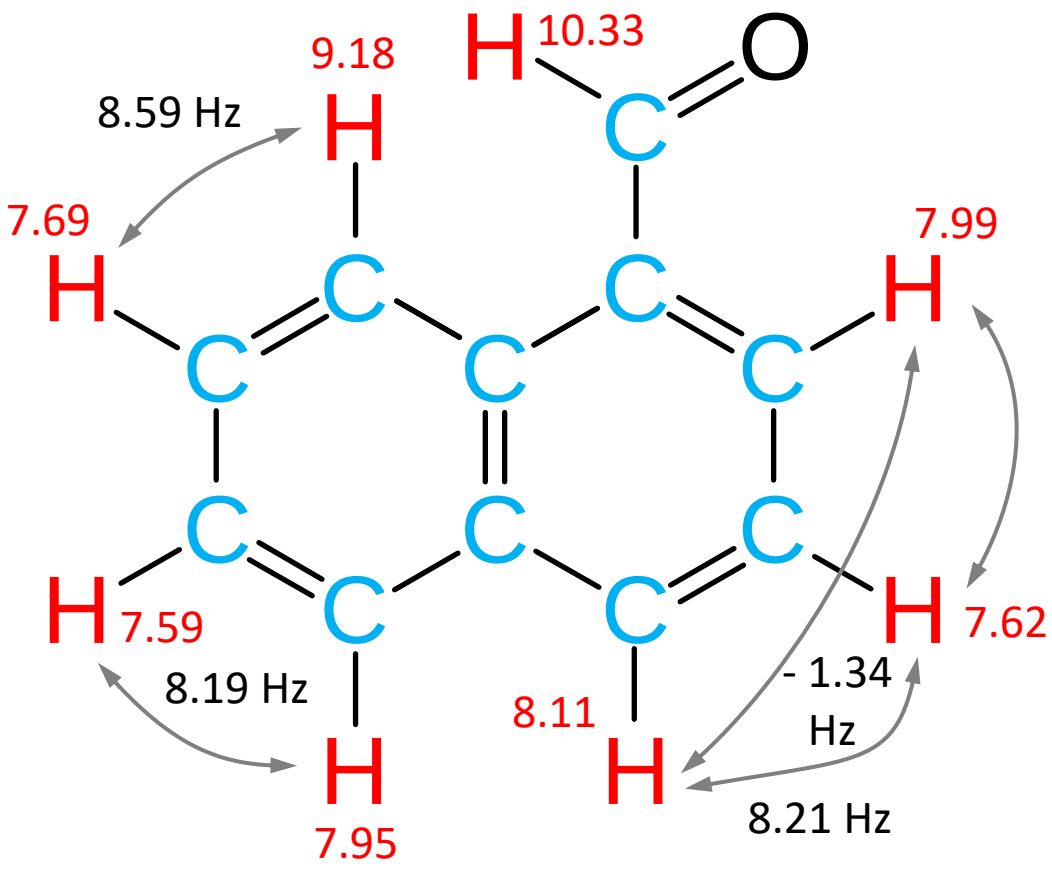
Coupling constants

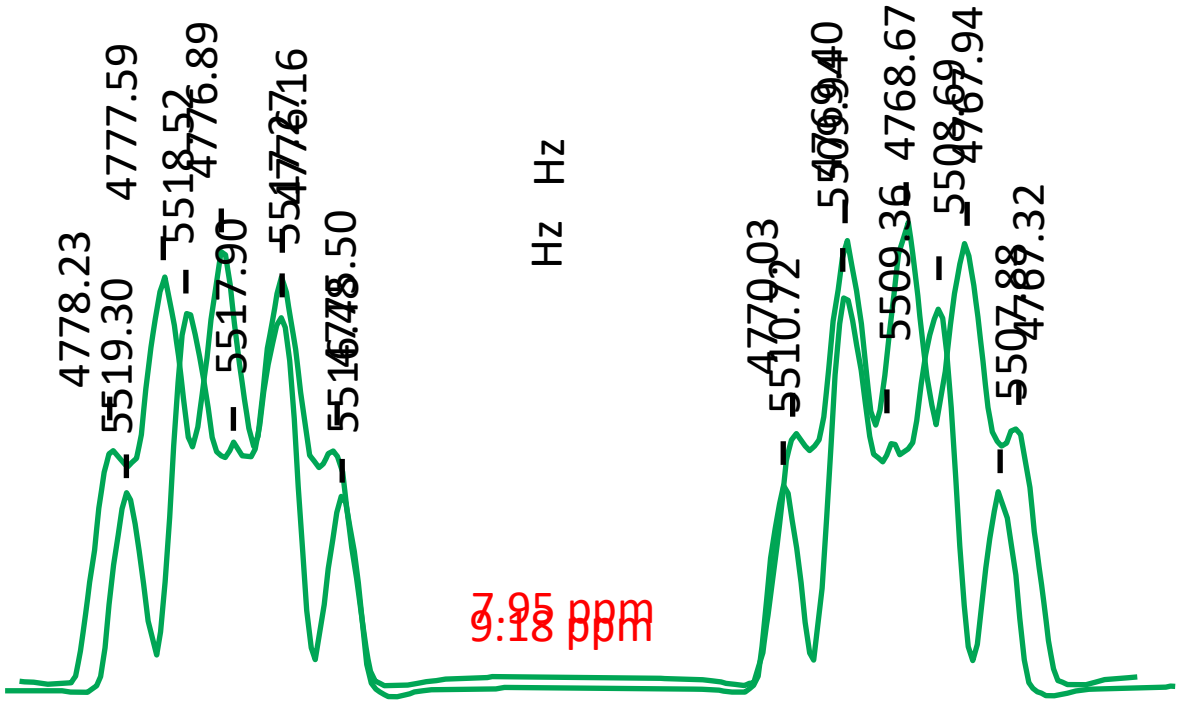
Left six-membered ring

Using the same procedure again, we get the vicinal coupling constant between the protons with the chemical shifts of 7.95 ppm and 7.59 ppm.

$$J = \frac{(4779.20\text{Hz} + 4775.50\text{Hz})}{2} - \frac{(4770.02\text{Hz} + 4767.32\text{Hz})}{2}$$

$$J = 8.59\text{Hz}$$

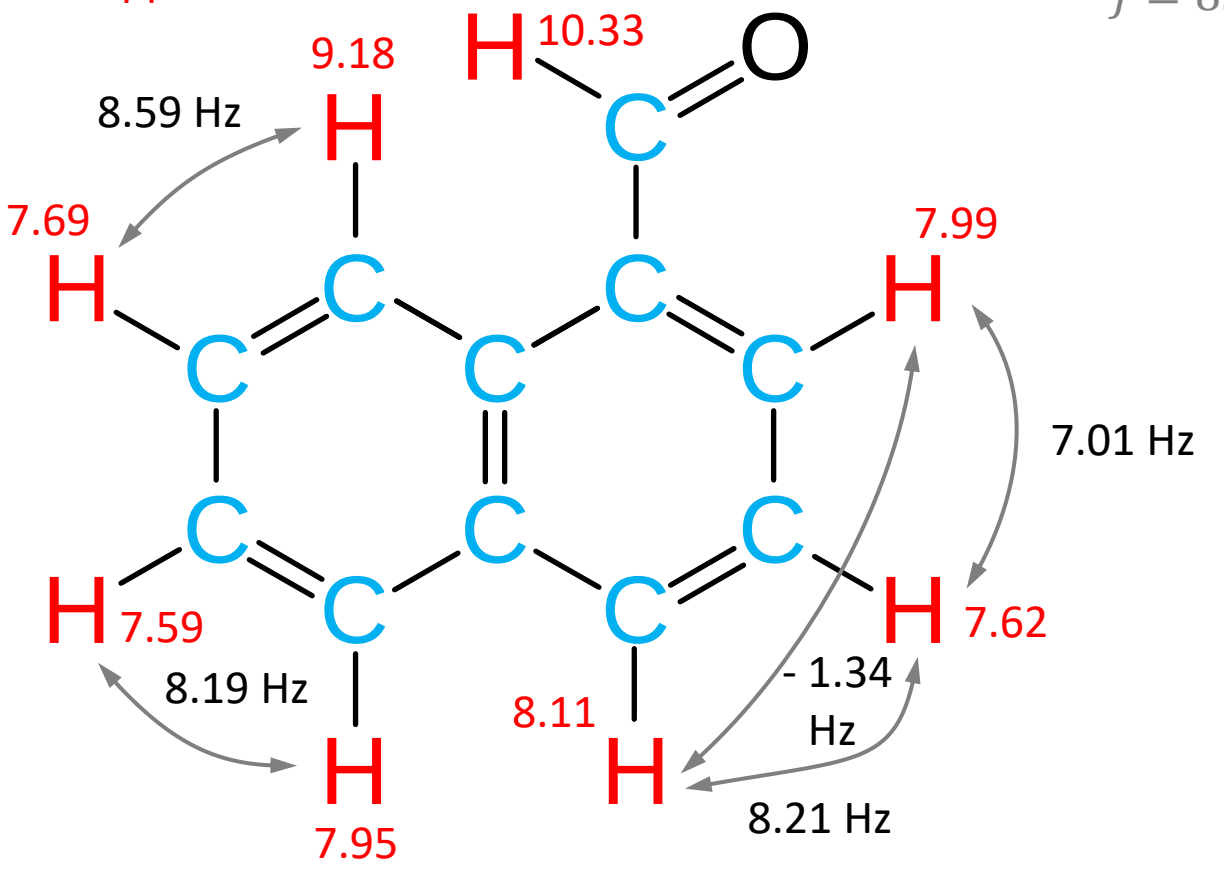




Coupling constants

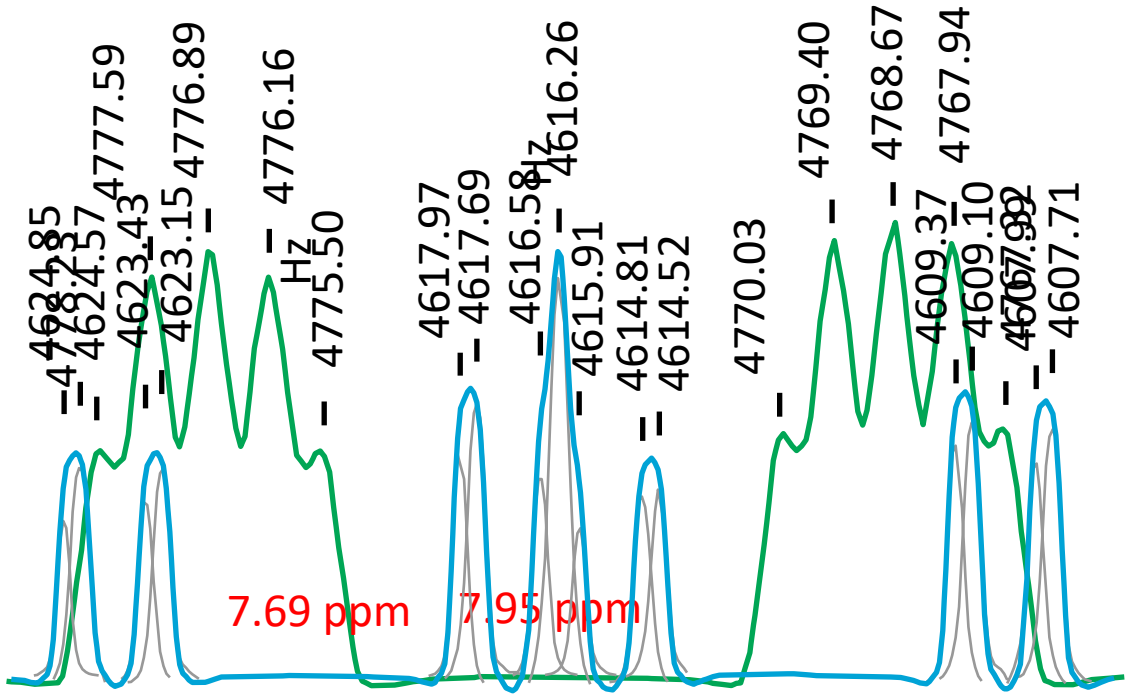
Left six-membered ring

In the multiplet of the proton at 7.69 ppm we should see the already known vicinal coupling constant of **8.59 Hz** and the still missing vicinal coupling constant between this and the proton at 7.59 ppm.



$$J = \frac{(4778.23\text{Hz} + 4775.50\text{Hz})}{2} - \frac{(4770.03\text{Hz} + 4767.32\text{Hz})}{2}$$

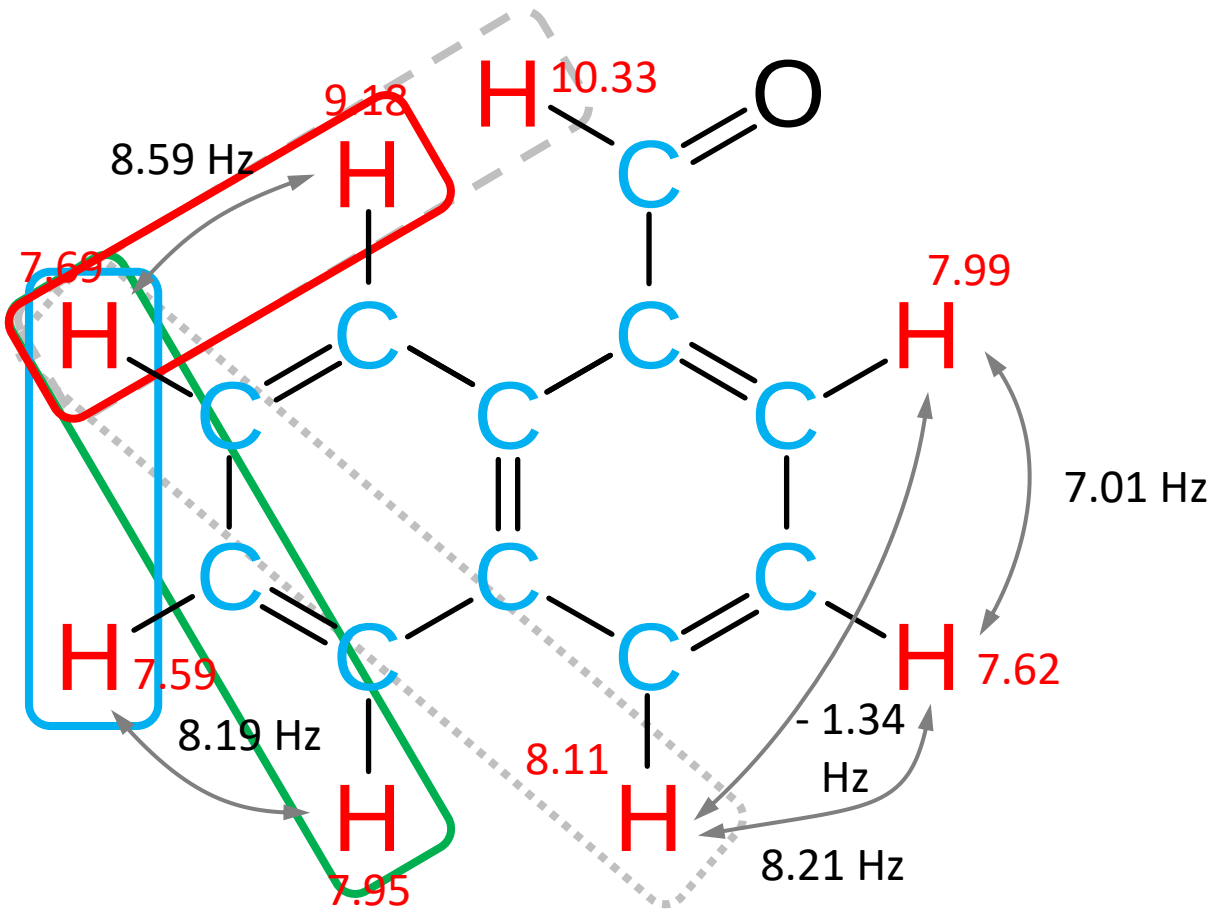
$$J = 8.19\text{Hz}$$



Coupling constants

Left six-membered ring

Which homonuclear coupling constants could we expect in the multiplet of the proton with the chemical shift of 7.69 ppm?

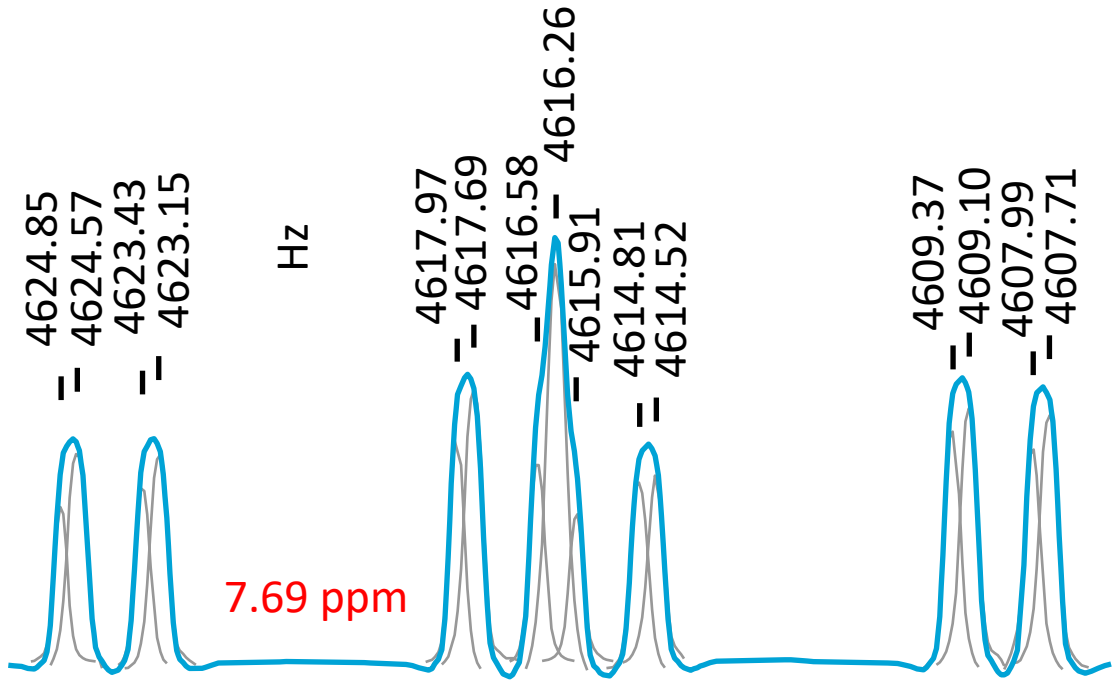


A doublet of **8.59 Hz**.

Another doublet of **about 7 Hz**.

A doublet of about **-1 … -2 Hz**.

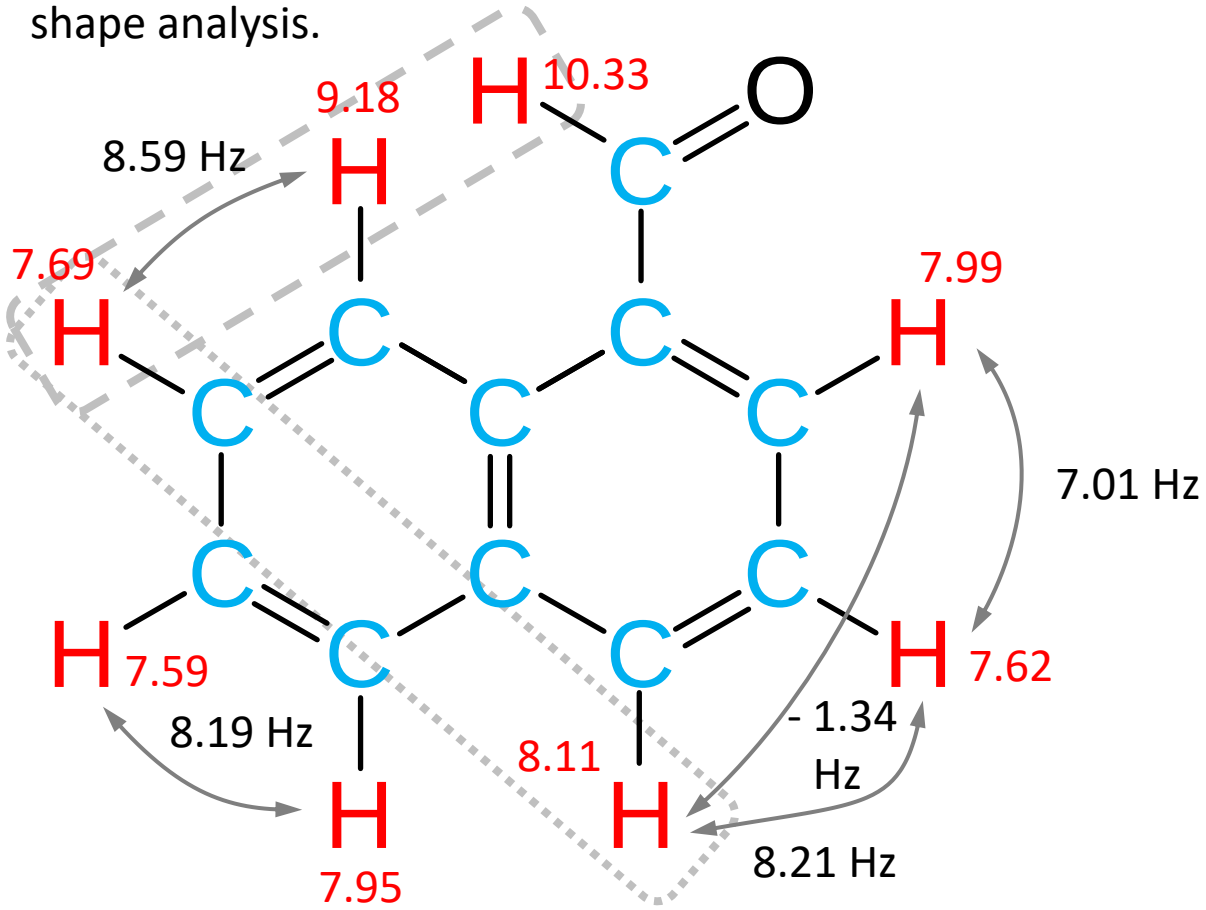
And there remains a tiny coupling constant of about **0.28 Hz** (4624.85 Hz – 4624.57 Hz). This has to be a long-range coupling constant via six bonds!
There are two possible coupling pathways, but no detailed analysis will be done here.

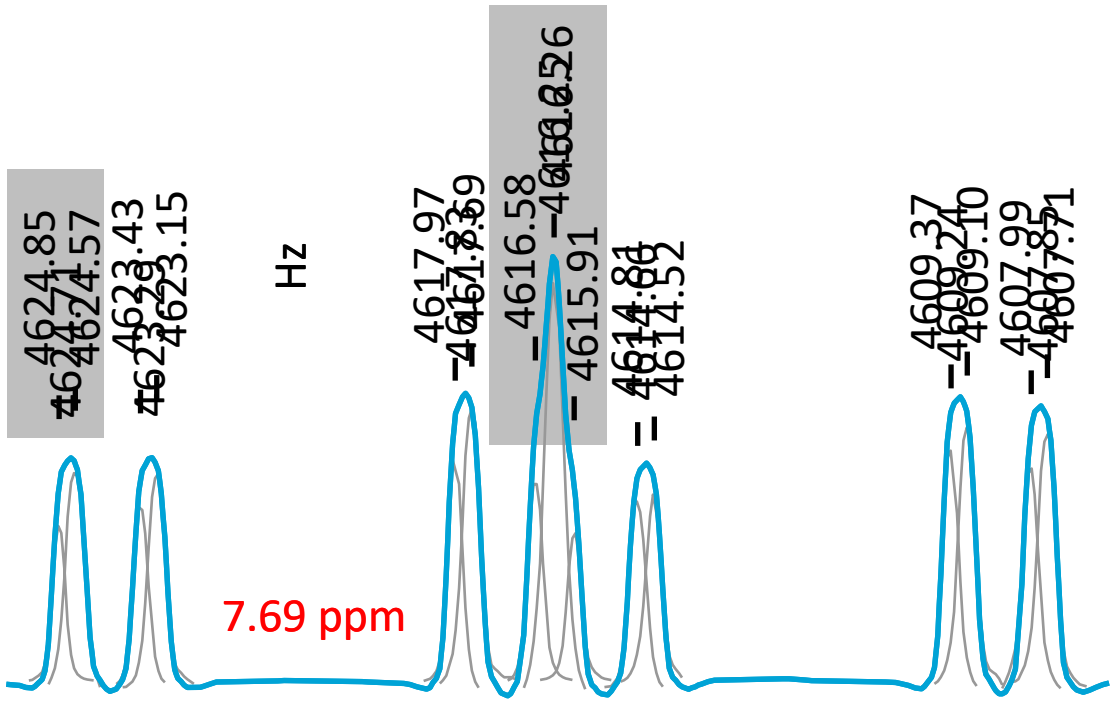


Coupling constants

Left six-membered ring

Since we do not evaluate the coupling across six bonds, we can virtually decouple by averaging (see examples). One gets about the same result if one simply searches for the peak maxima - without line shape analysis.

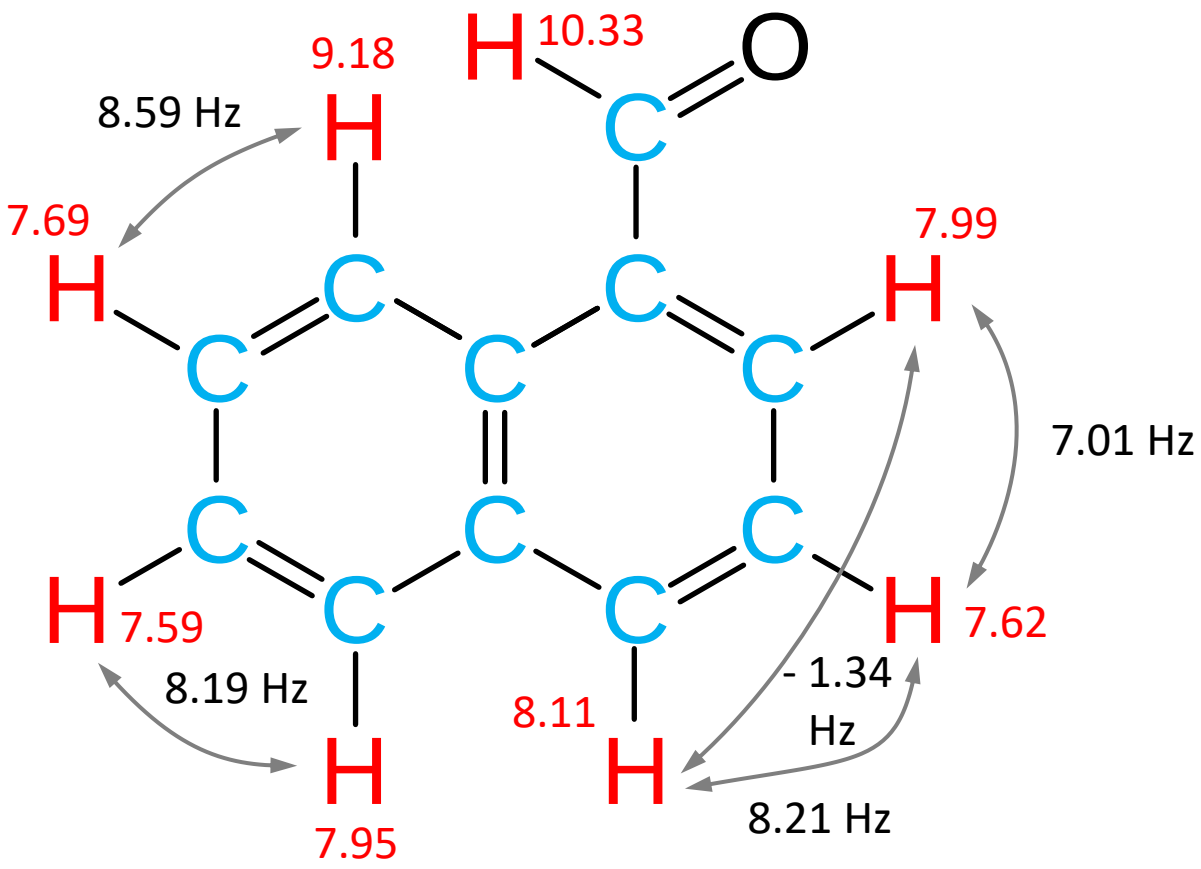


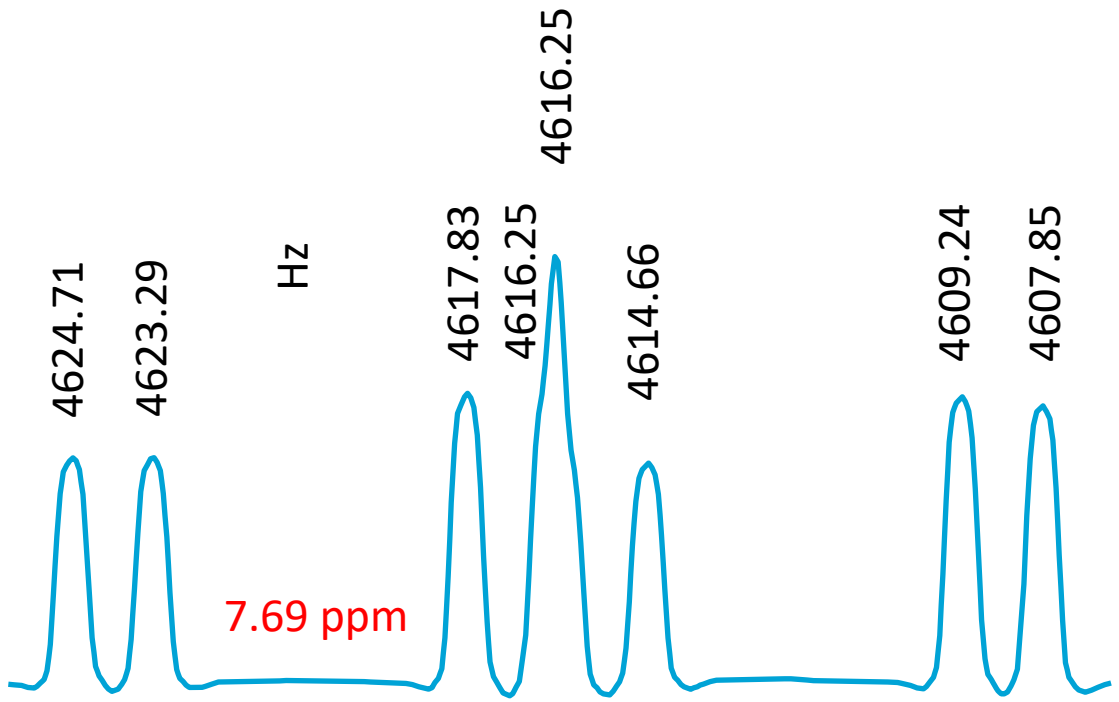


Coupling constants

Left six-membered ring

The “reduced” multiplet now is a doublet of doublet of doublets with altogether 8 lines. Apparently the center line is an overlay of two lines.

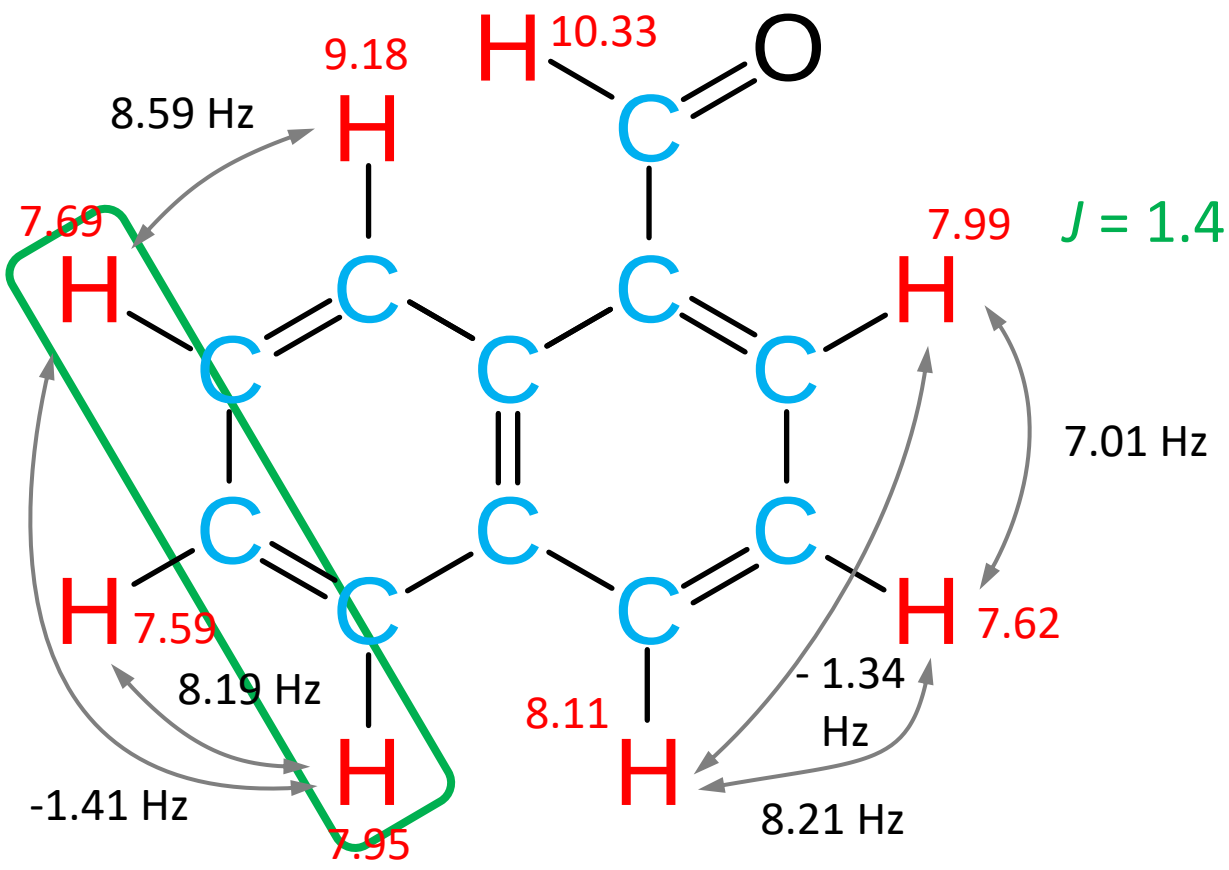




Coupling constants

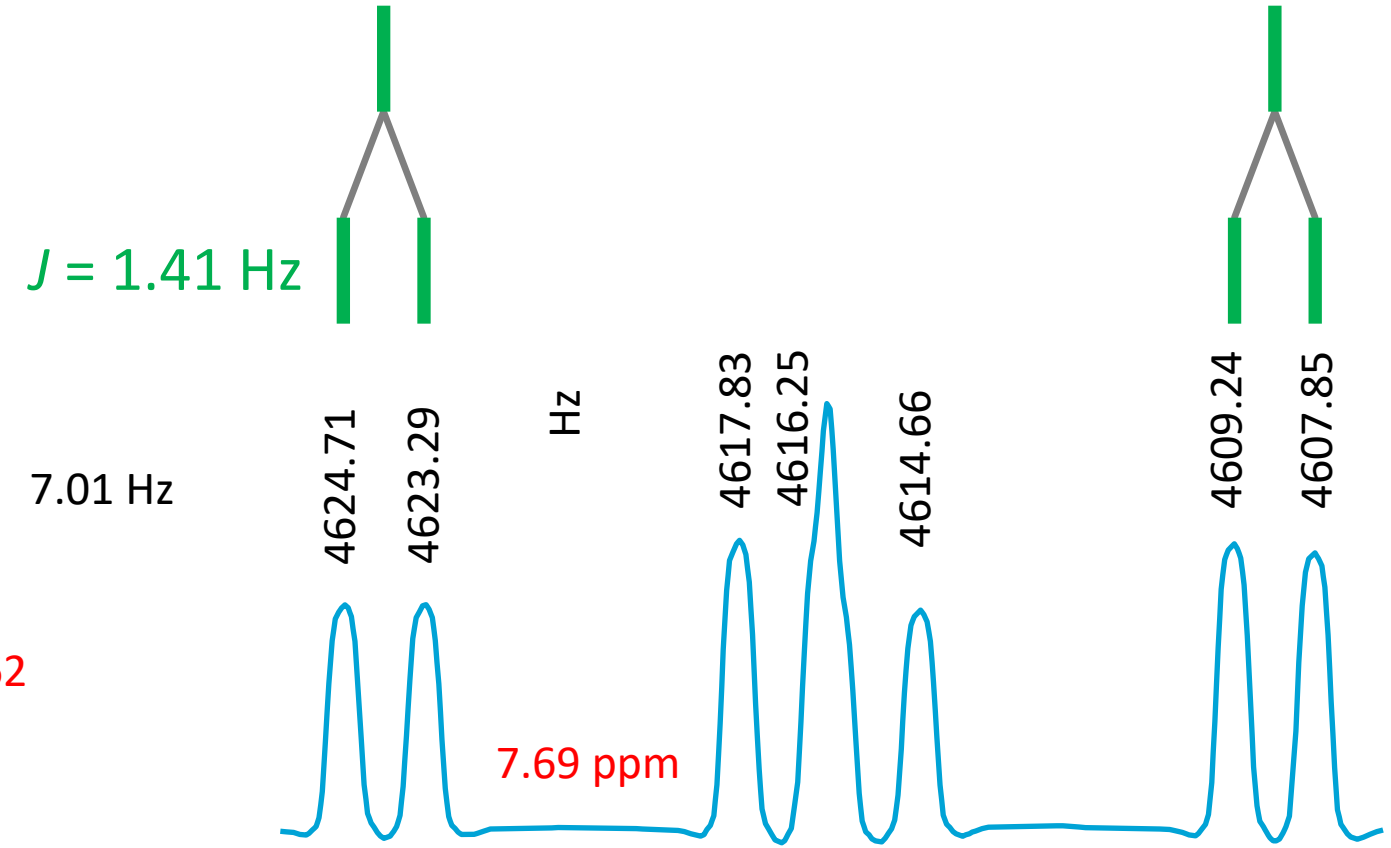
Left six-membered ring

The coupling constant of the doublet with the small coupling constant is easy to measure. There is no overlay at the left and at the right side of the multiplet.



This is clearly the already mentioned coupling constant between the protons with the chemical shifts of 7.69 ppm and 7.95 ppm.

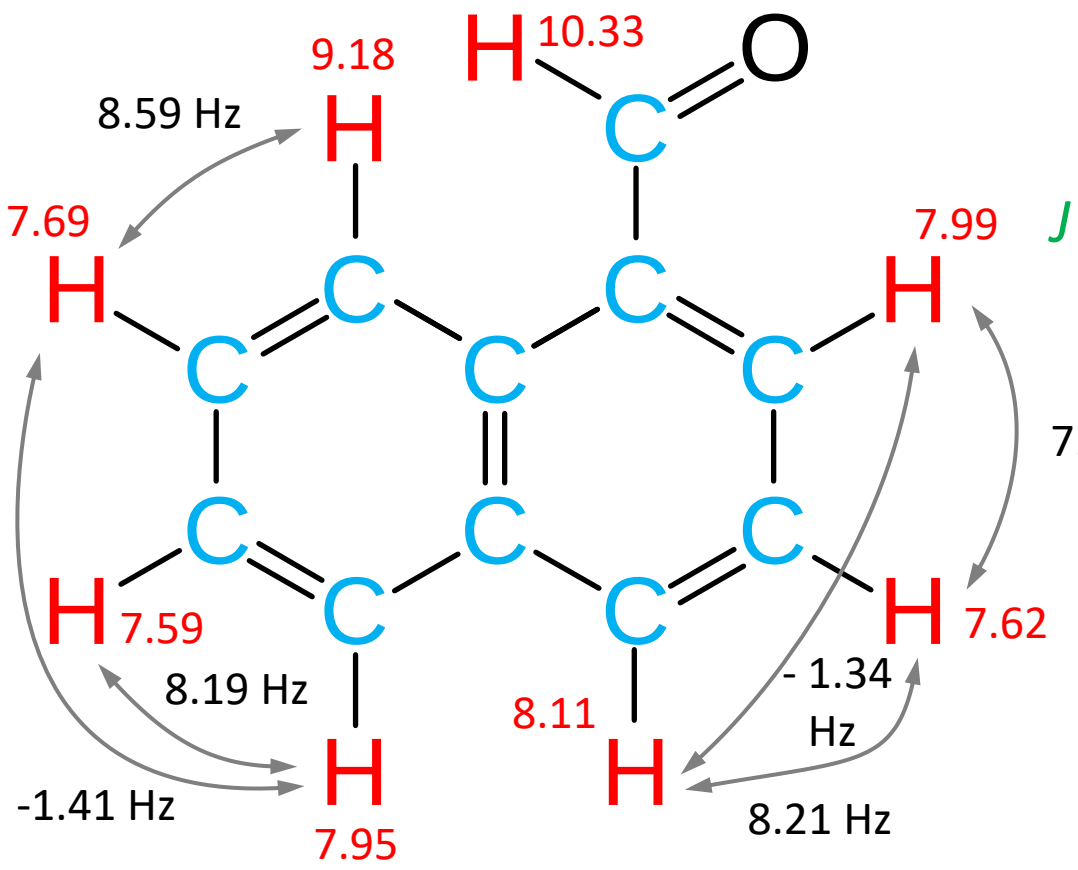
Of course there is no possibility here to get the sign, but such coupling constants in six membered aromatic rings are always negative.

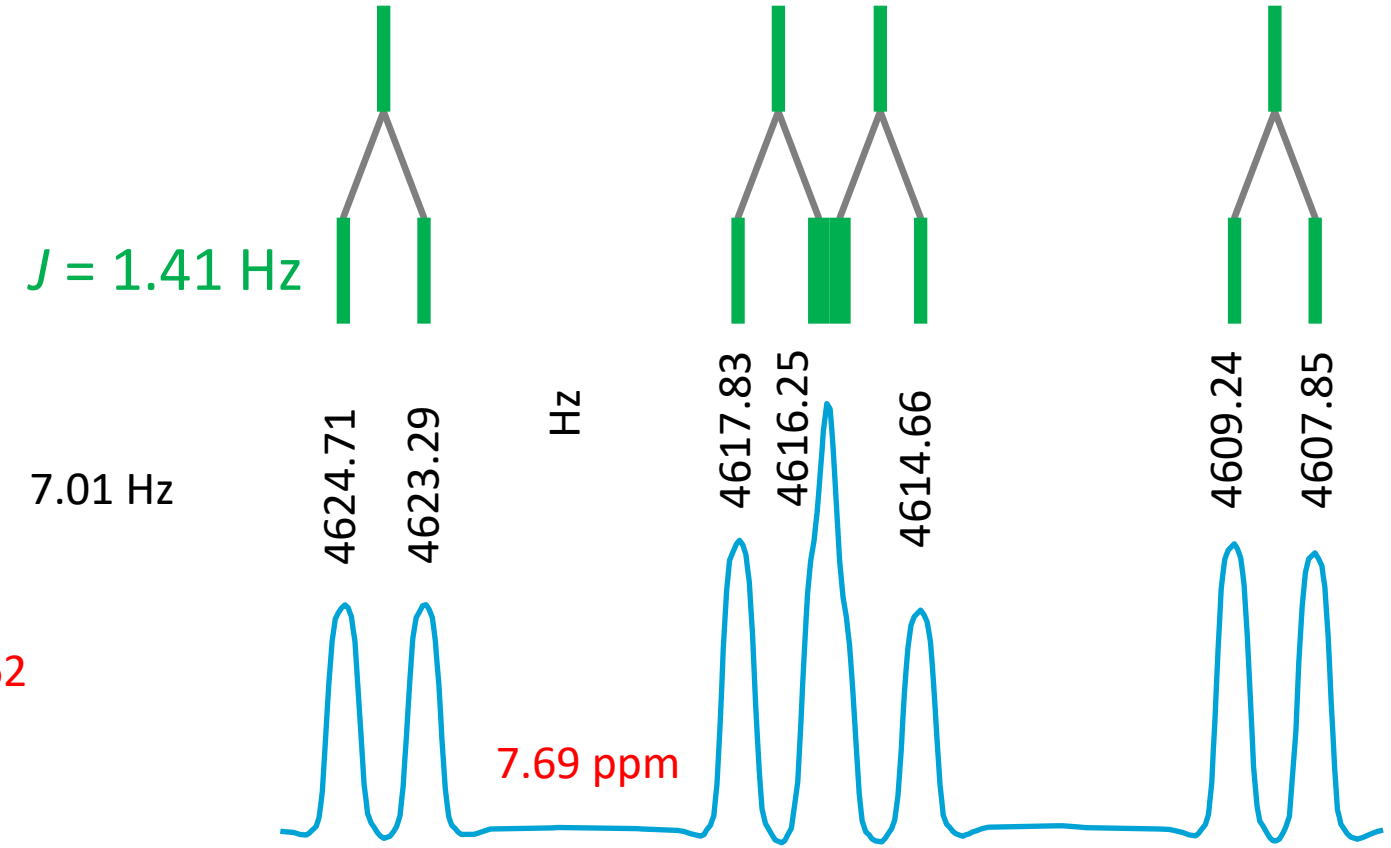


Coupling constants

Left six-membered ring

The same doublet appears two more times within the multiplet but we cannot measure the coupling constant there, because we cannot see the degree of overlap.

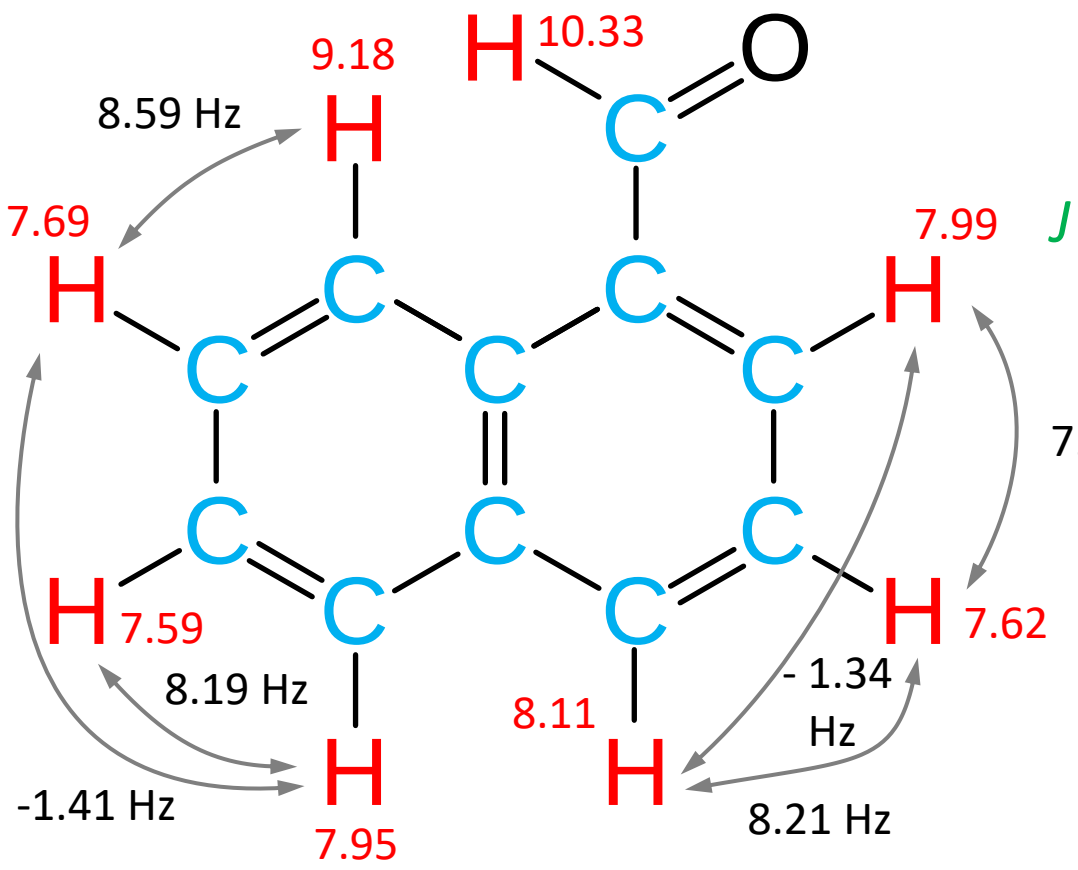


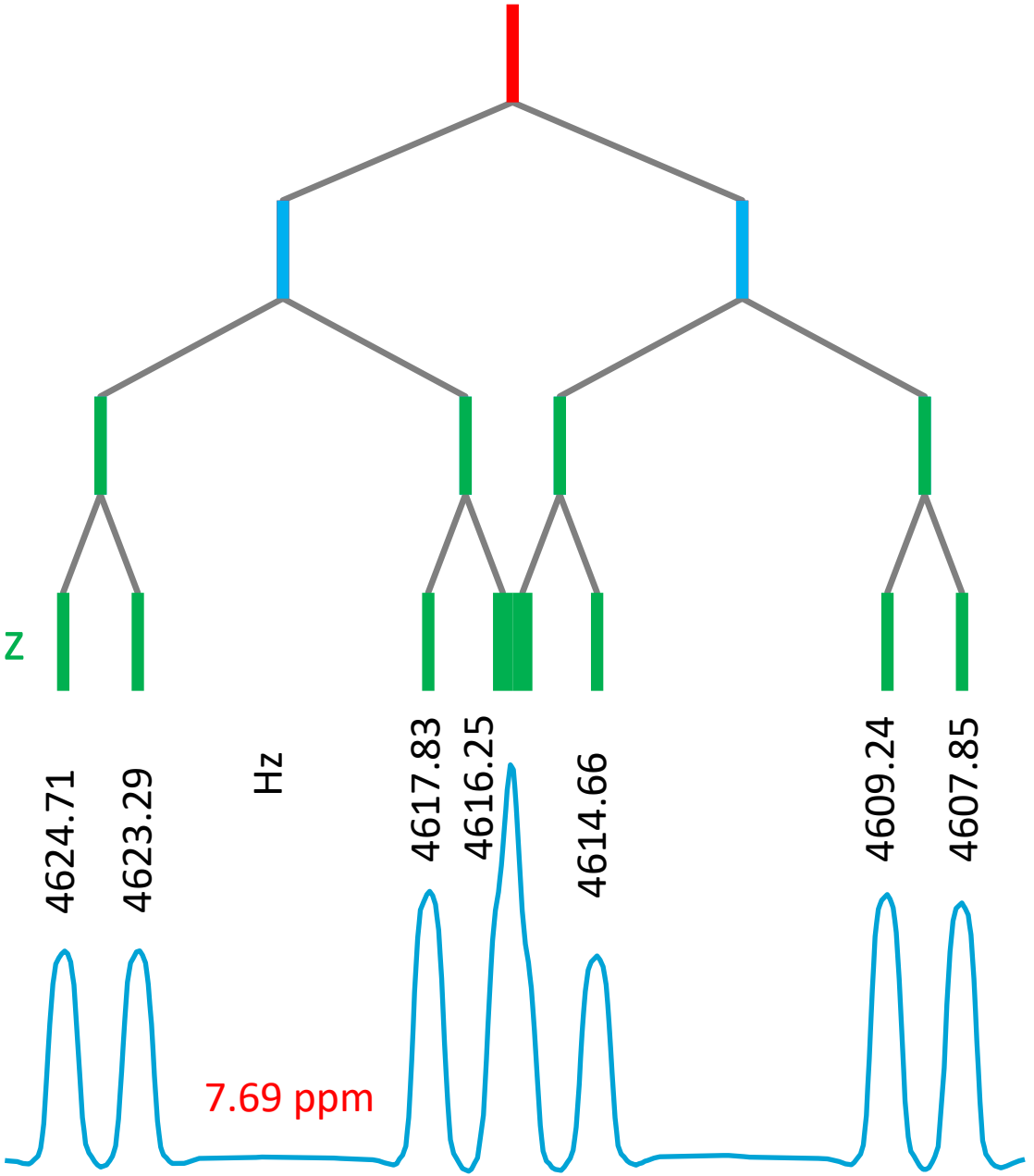


Coupling constants

Left six-membered ring

Now we have four lines which makes it easy to finalize the coupling tree.

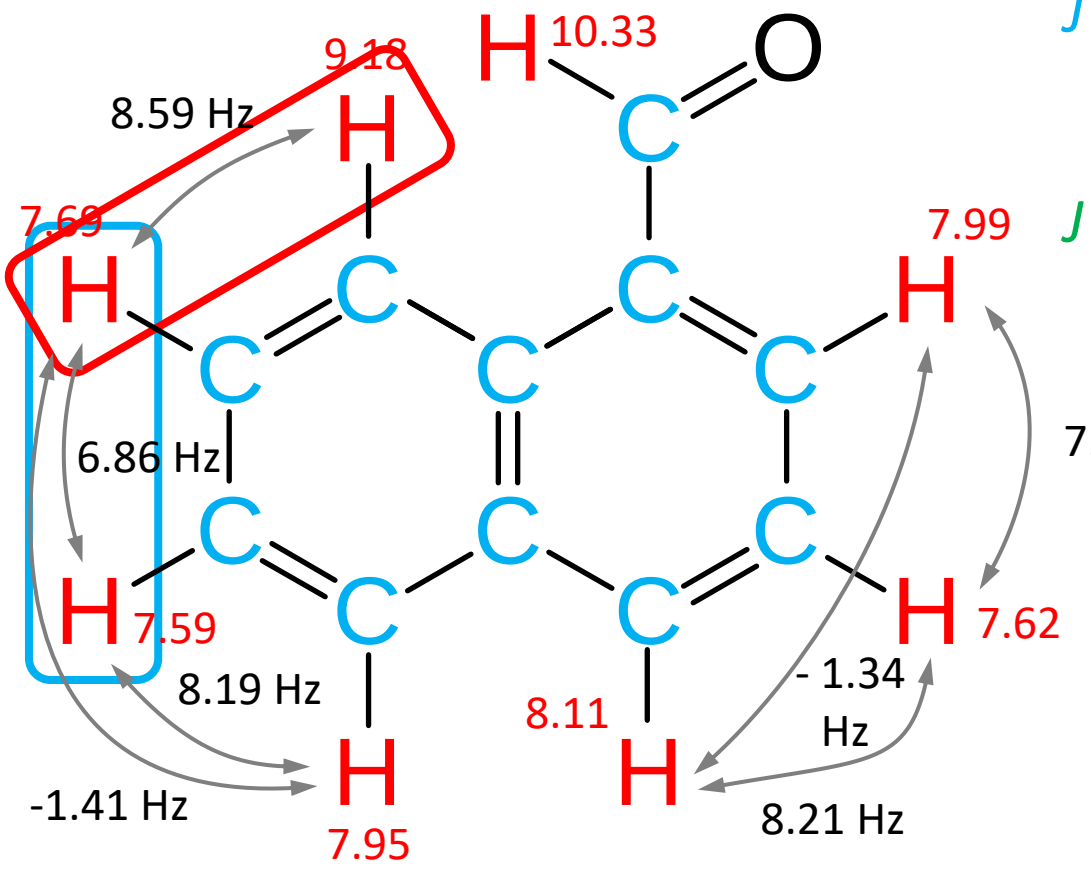


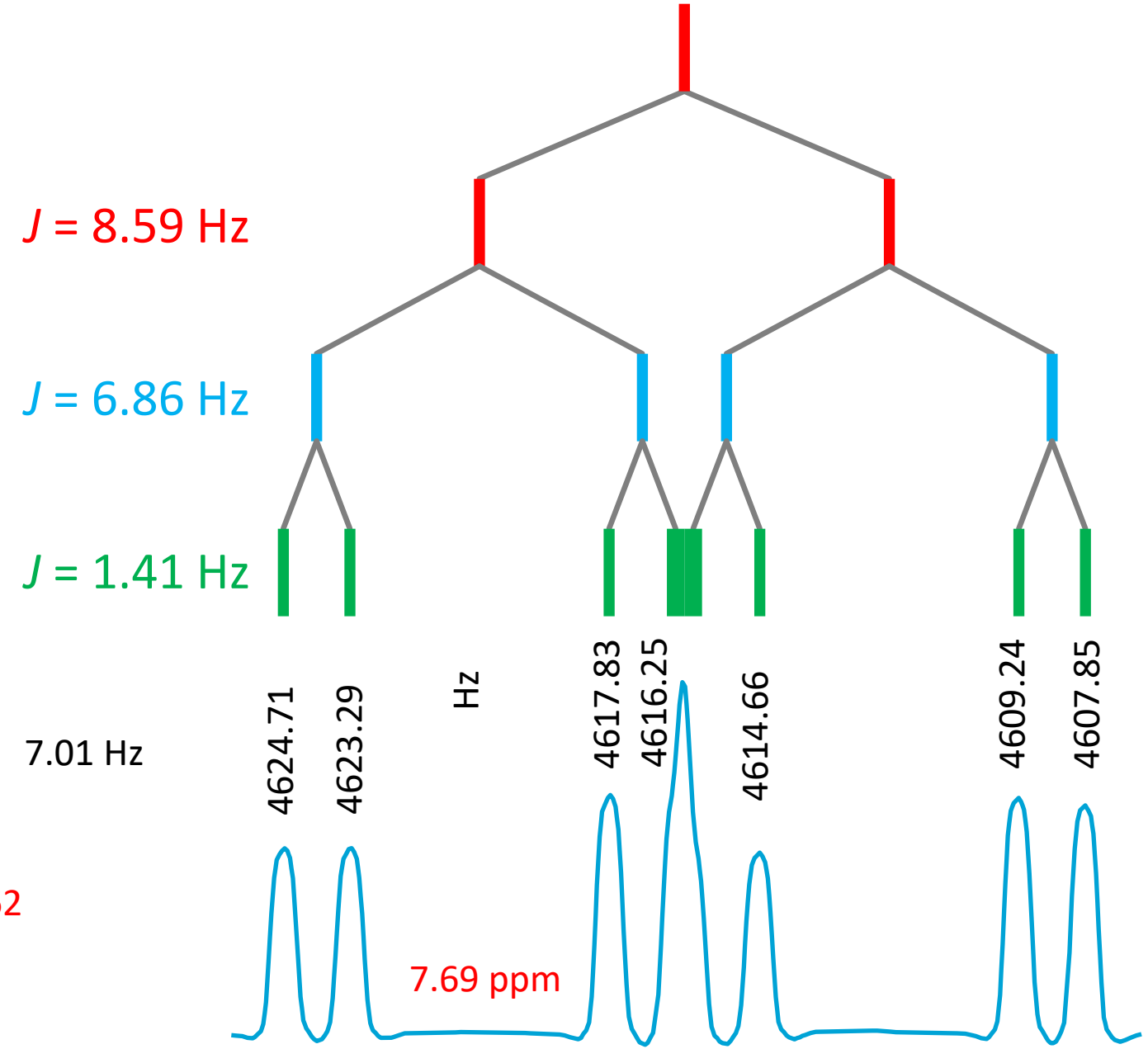


Coupling constants

Left six-membered ring

The value of one of the two unlabeled coupling constants is **8.59 Hz**, the sum of all three coupling constants is **16.86 Hz** (4624.71 Hz – 4507.85 Hz), which means the value of the remaining coupling constant is **6.86 Hz**.

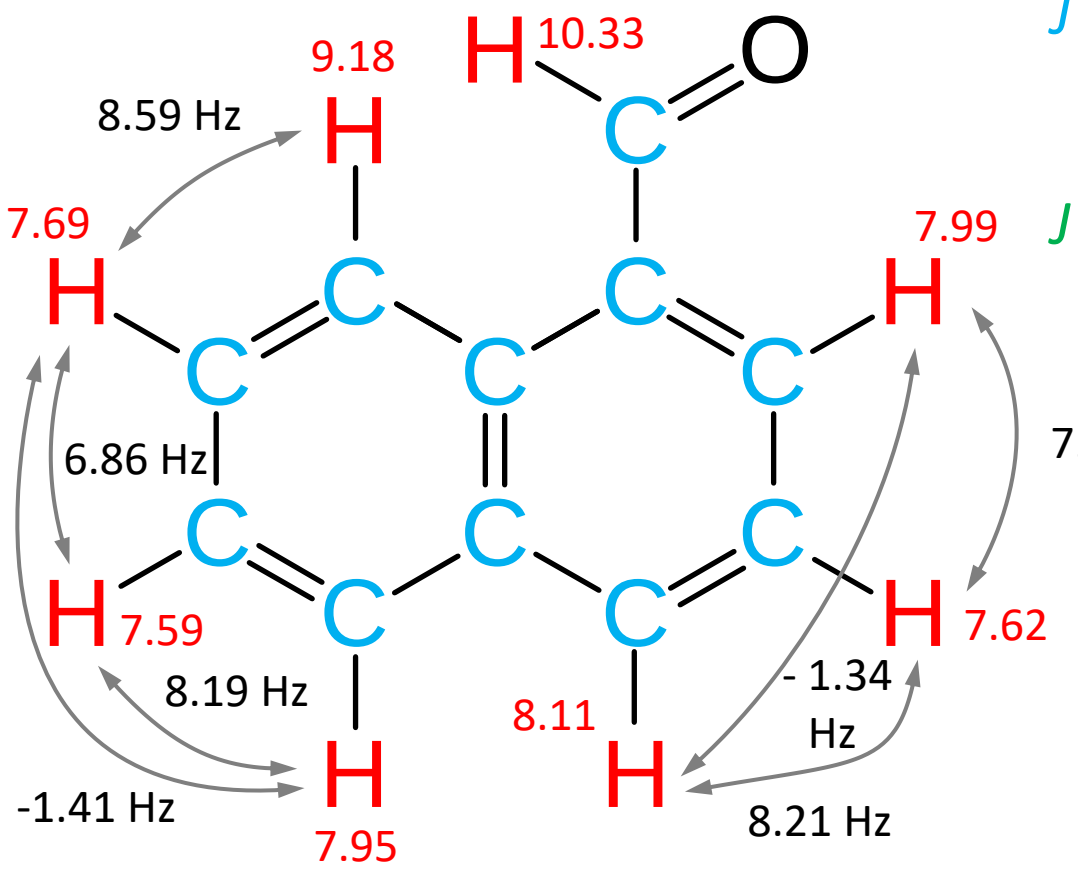


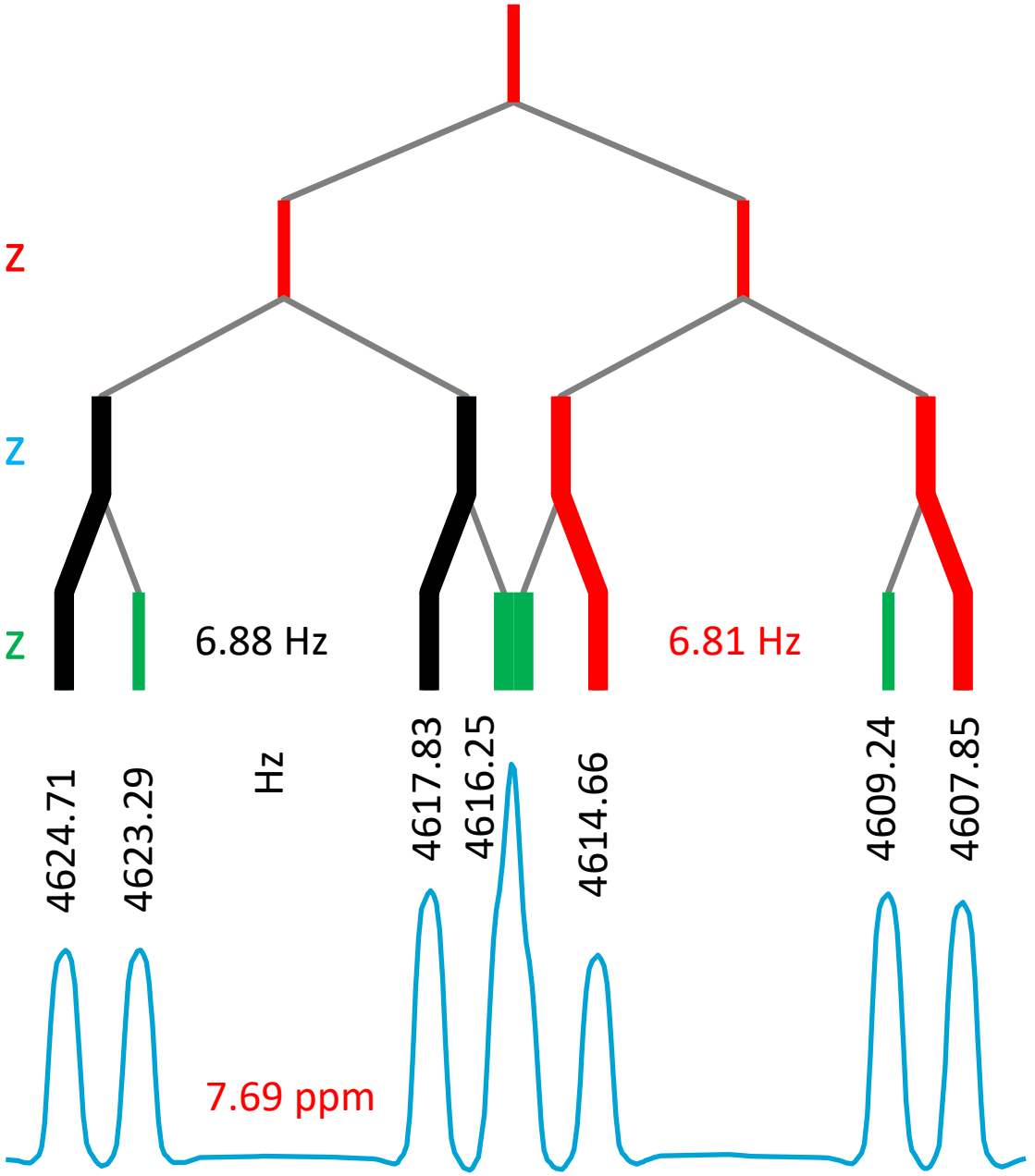


Coupling constants

Left six-membered ring

There is another way to get the missing coupling constant. Simply follow the way along the coupling path as shown here. You have two possibilities, resulting in slightly different values of the coupling constant.

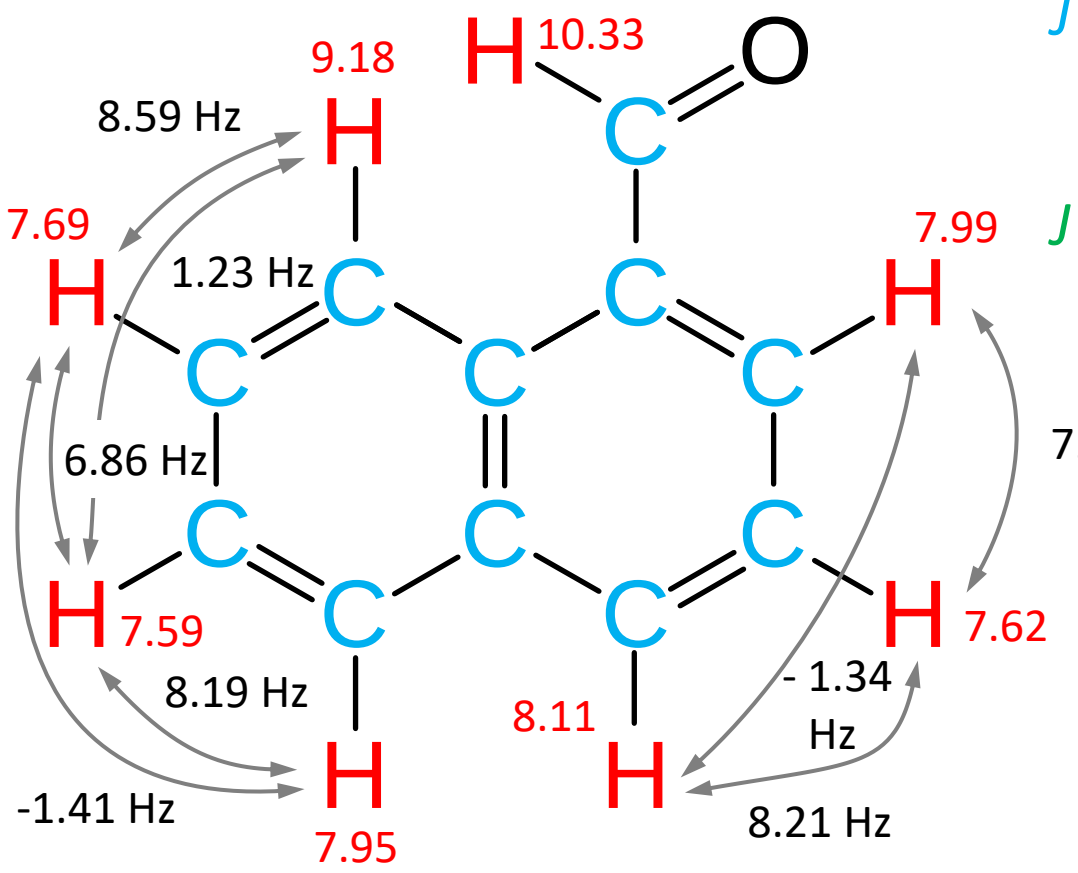


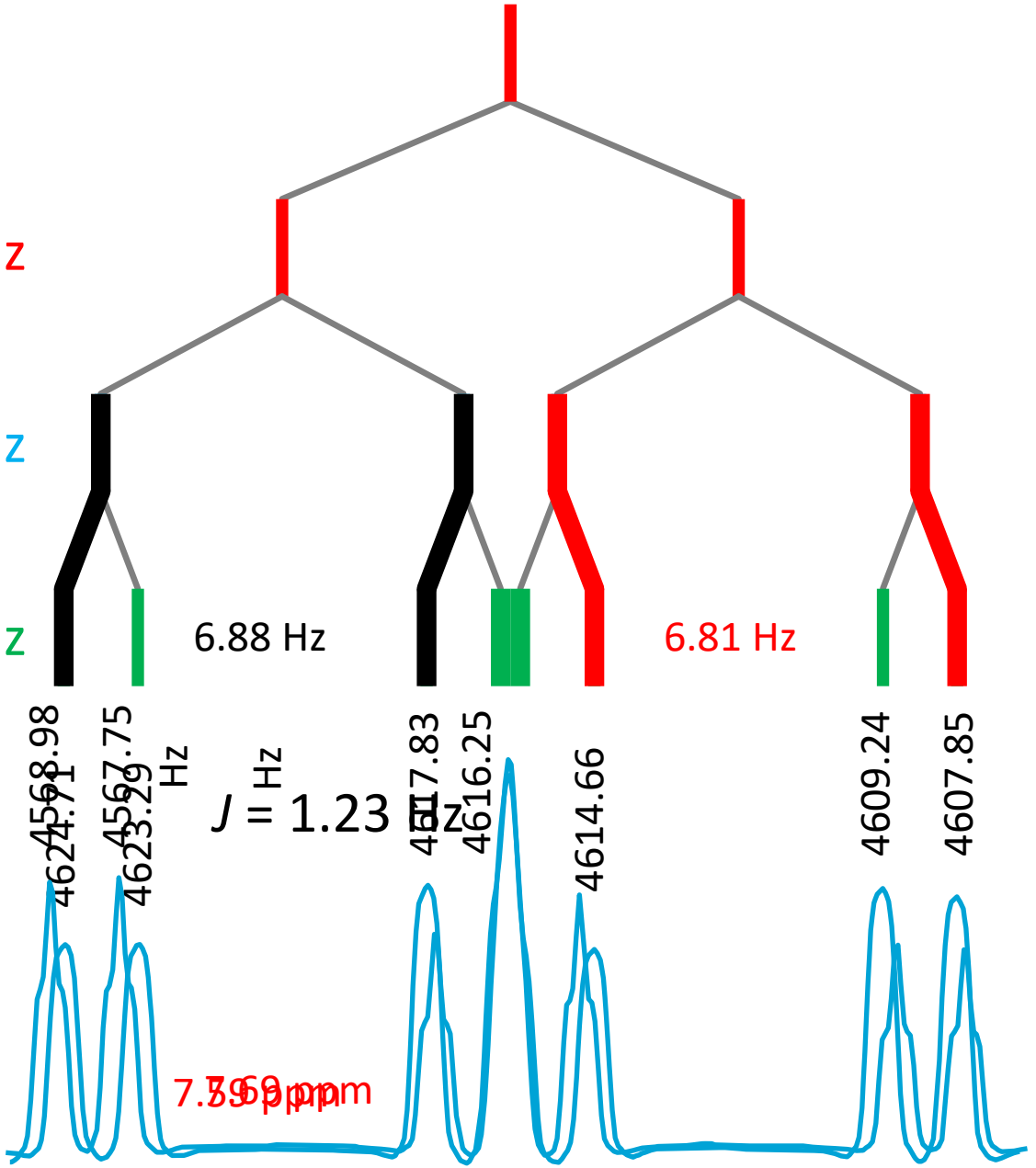


Coupling constants

Left six-membered ring

We get our last four-bond coupling constant from the multiplet at 7.59 ppm. Its nearly the same multiplet as just described, that's why the explanation is reduced to a few numbers.





Contributions

Spectrometer time

TU Munich

Measurements

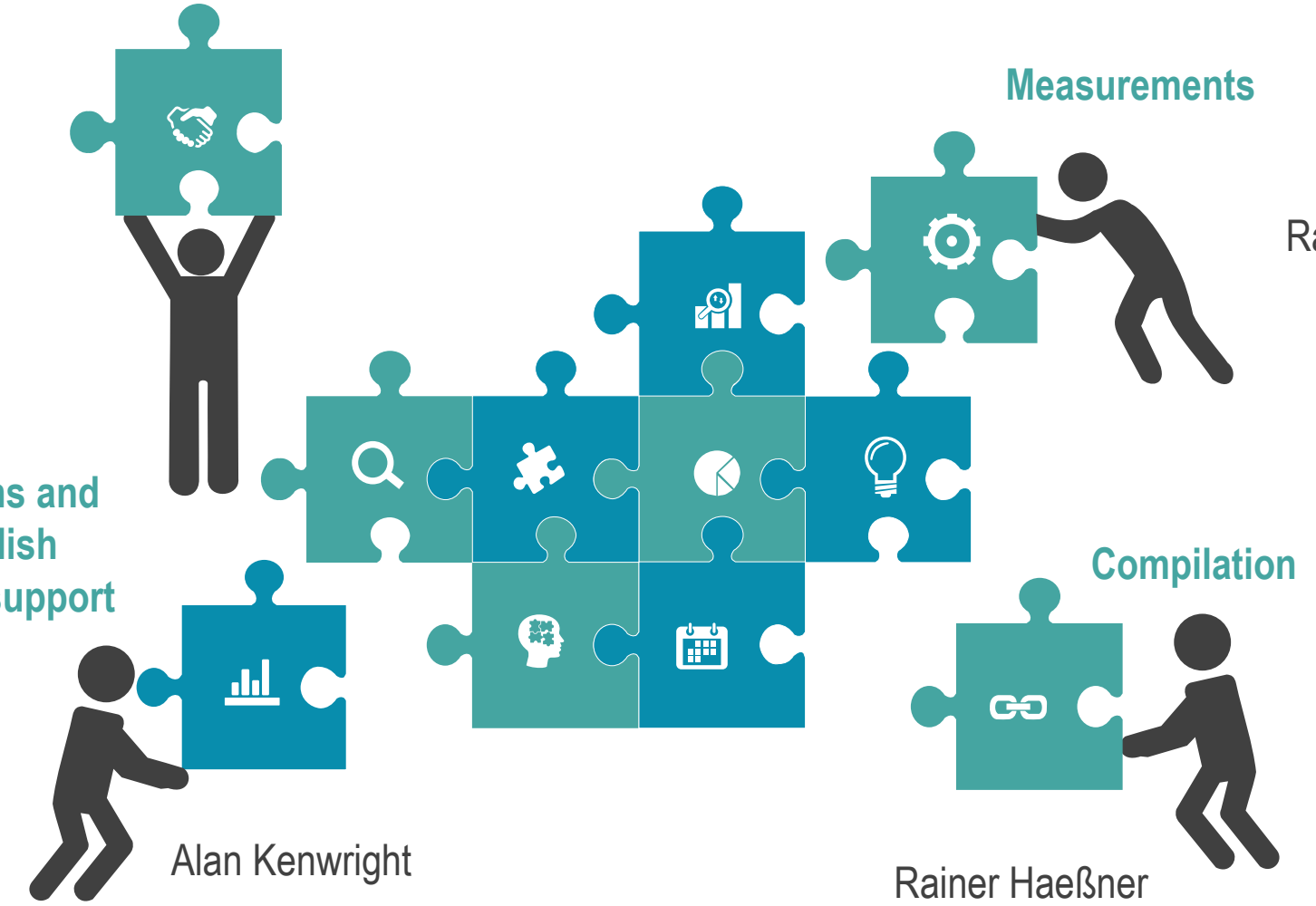
Rainer Haeßner

Discussions and native English language support

Alan Kenwright

Compilation

Rainer Haeßner



More exercises …