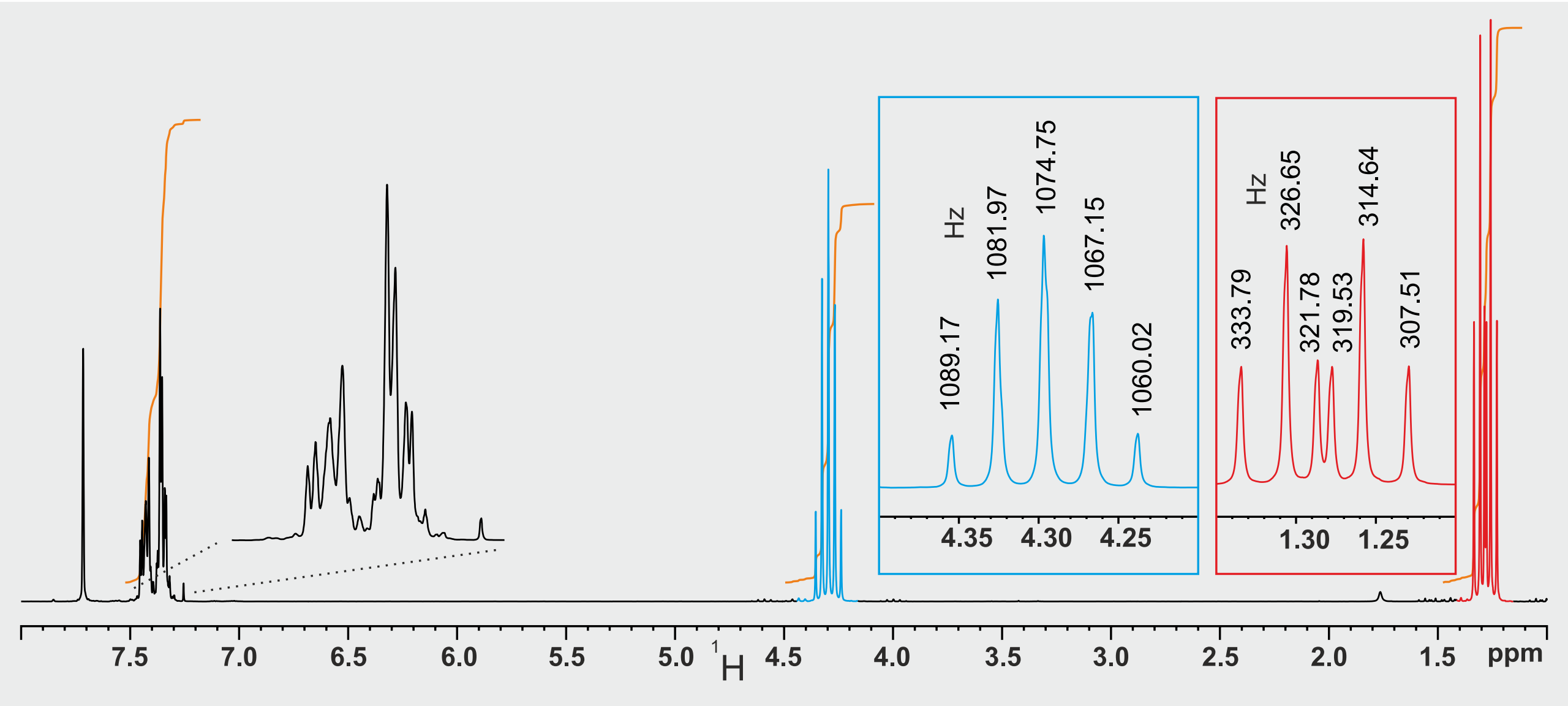
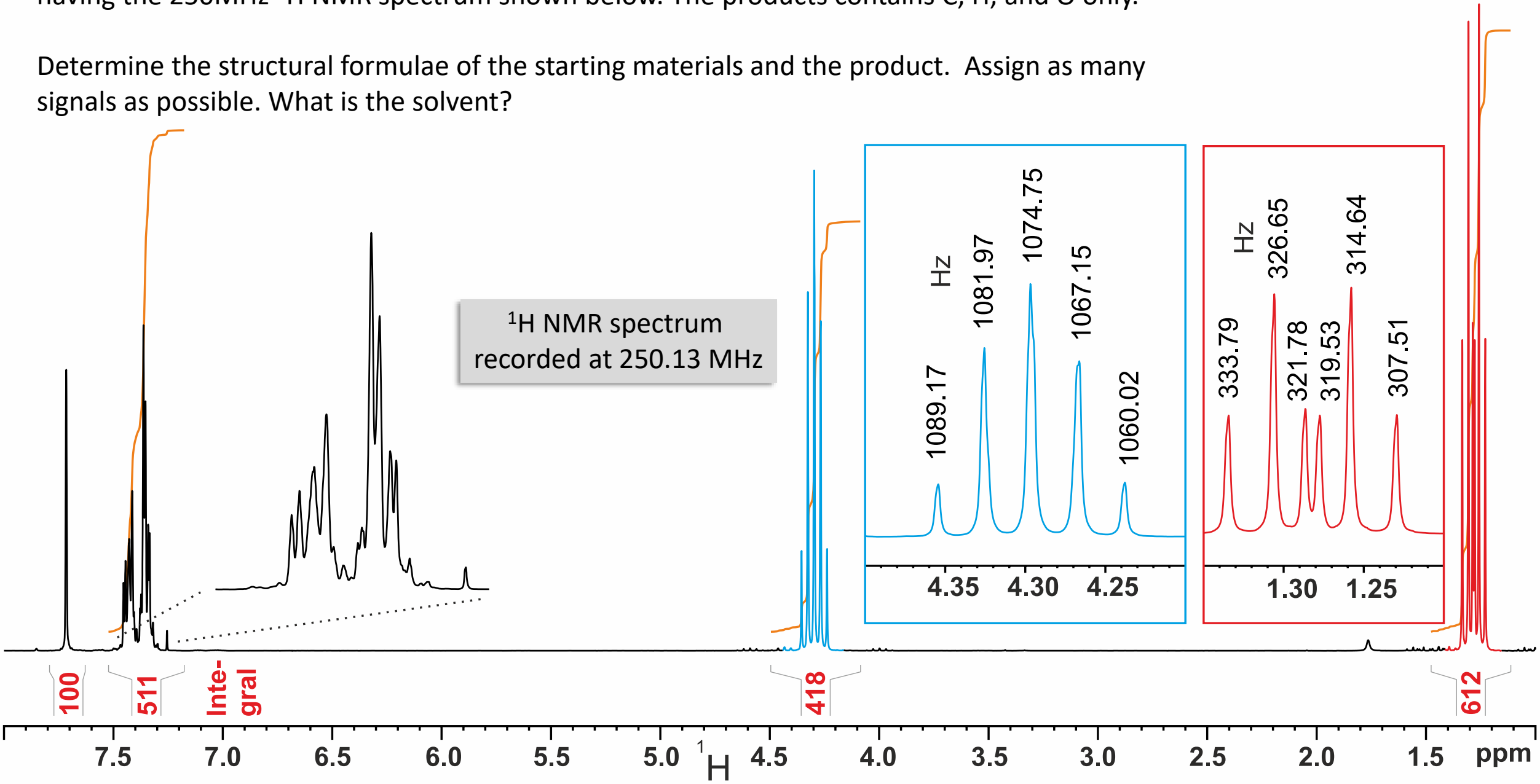
Exercise plus Solution – Quick overview

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.



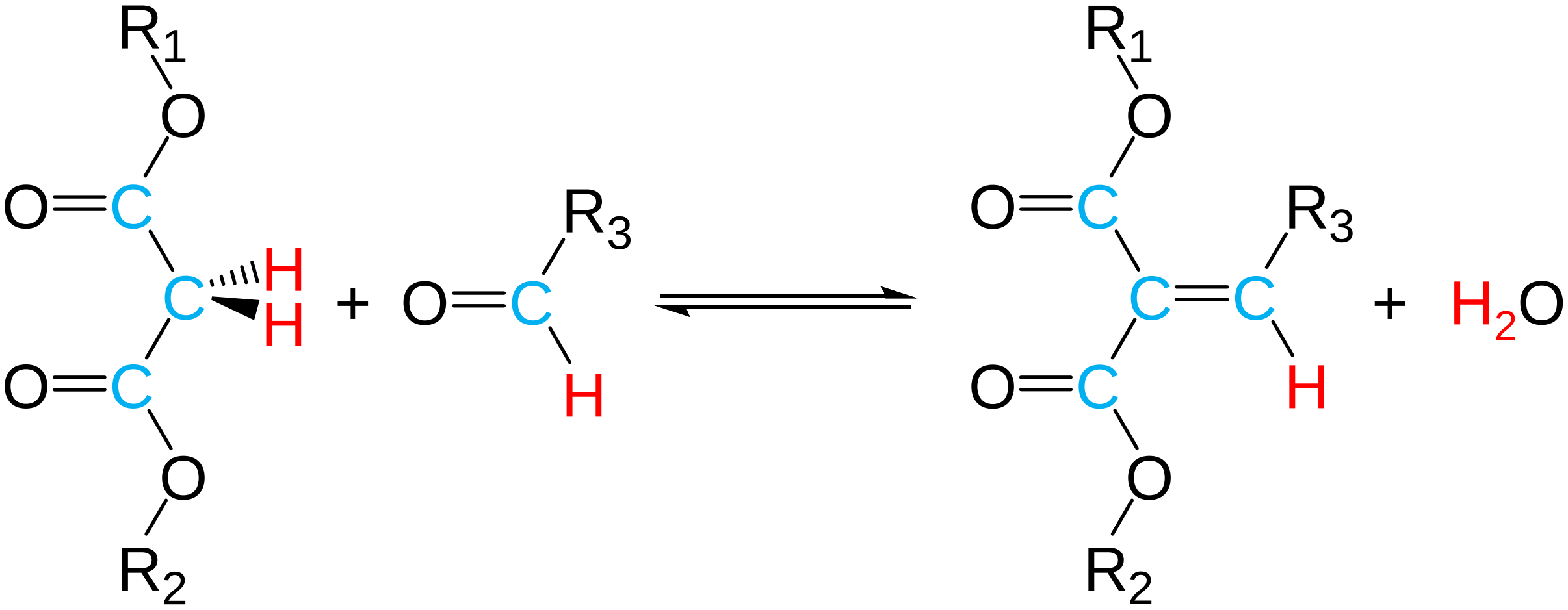
The Knoevenagel reaction between a malonic acid diester and an aldehyde yields a product having the 250MHz ^{1}H NMR spectrum shown below. The products contains C, H, and O only.

Determine the structural formulae of the starting materials and the product. Assign as many signals as possible. What is the solvent?



The question is about this chemical reaction.

Solution



The question is about this chemical reaction.

We are looking for the reaction product.

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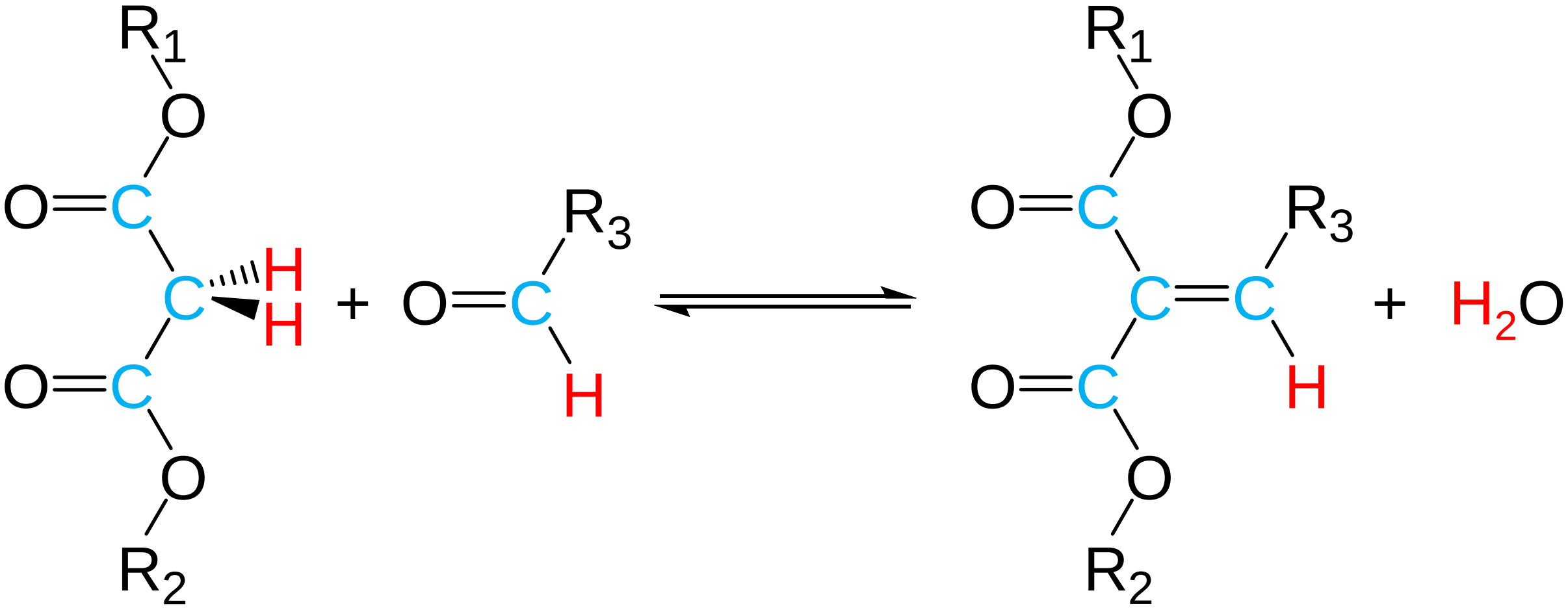
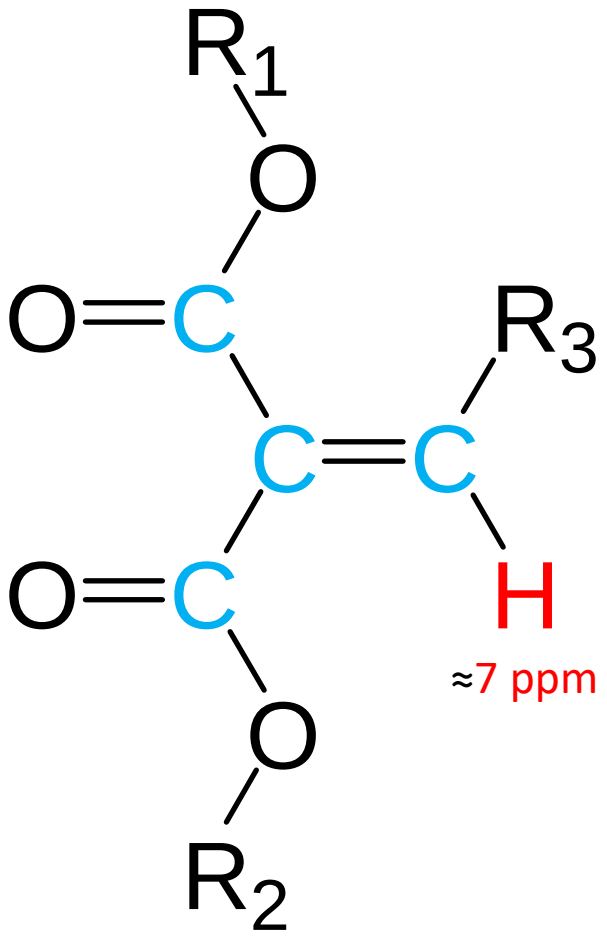


The question is about this chemical reaction.

We are looking for the reaction product.

The proton signal should appear at about 7 ppm, we don't know about the R_1, R_2 and R_3 residues at the moment.



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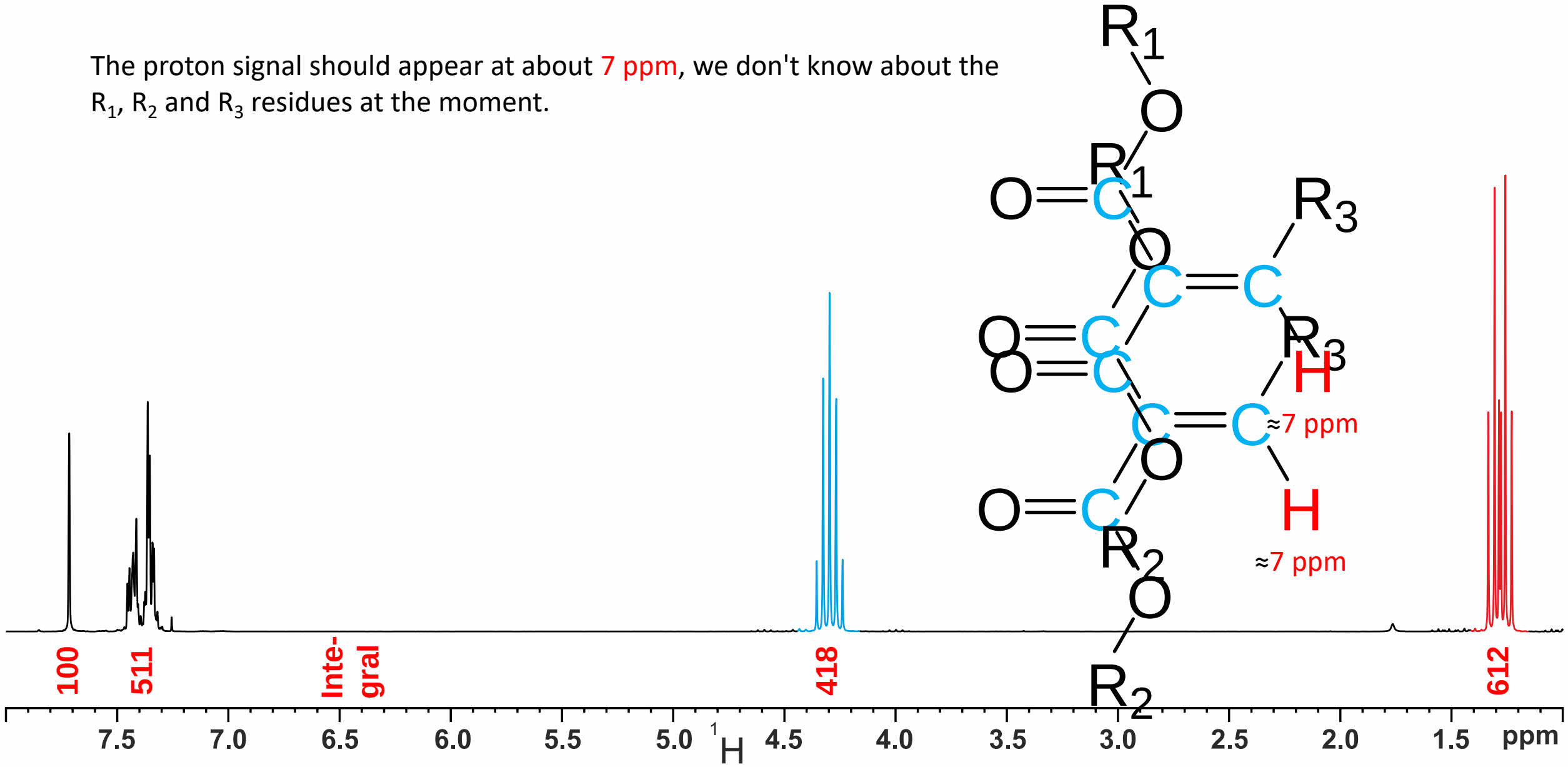
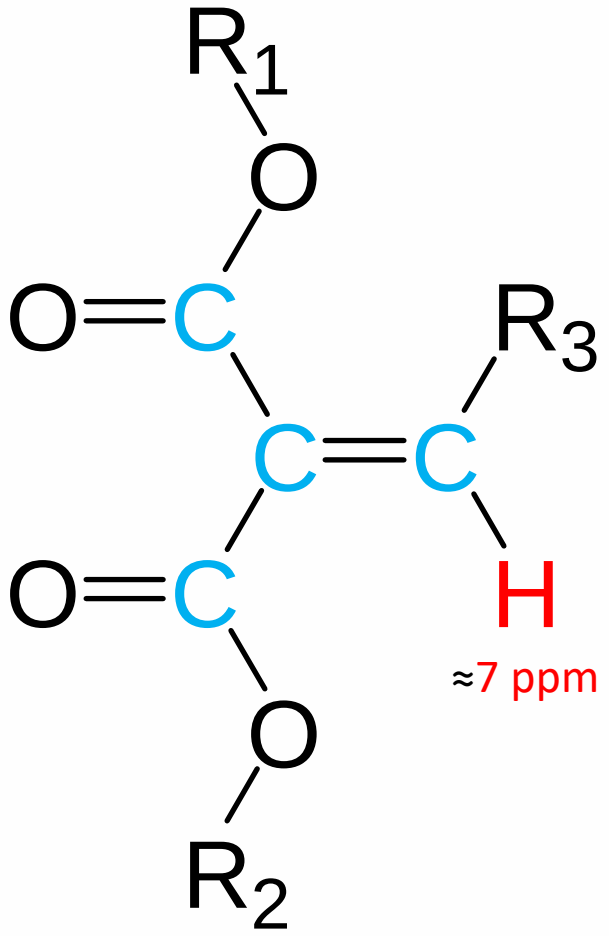


Let's start with the easiest part: the solvent.

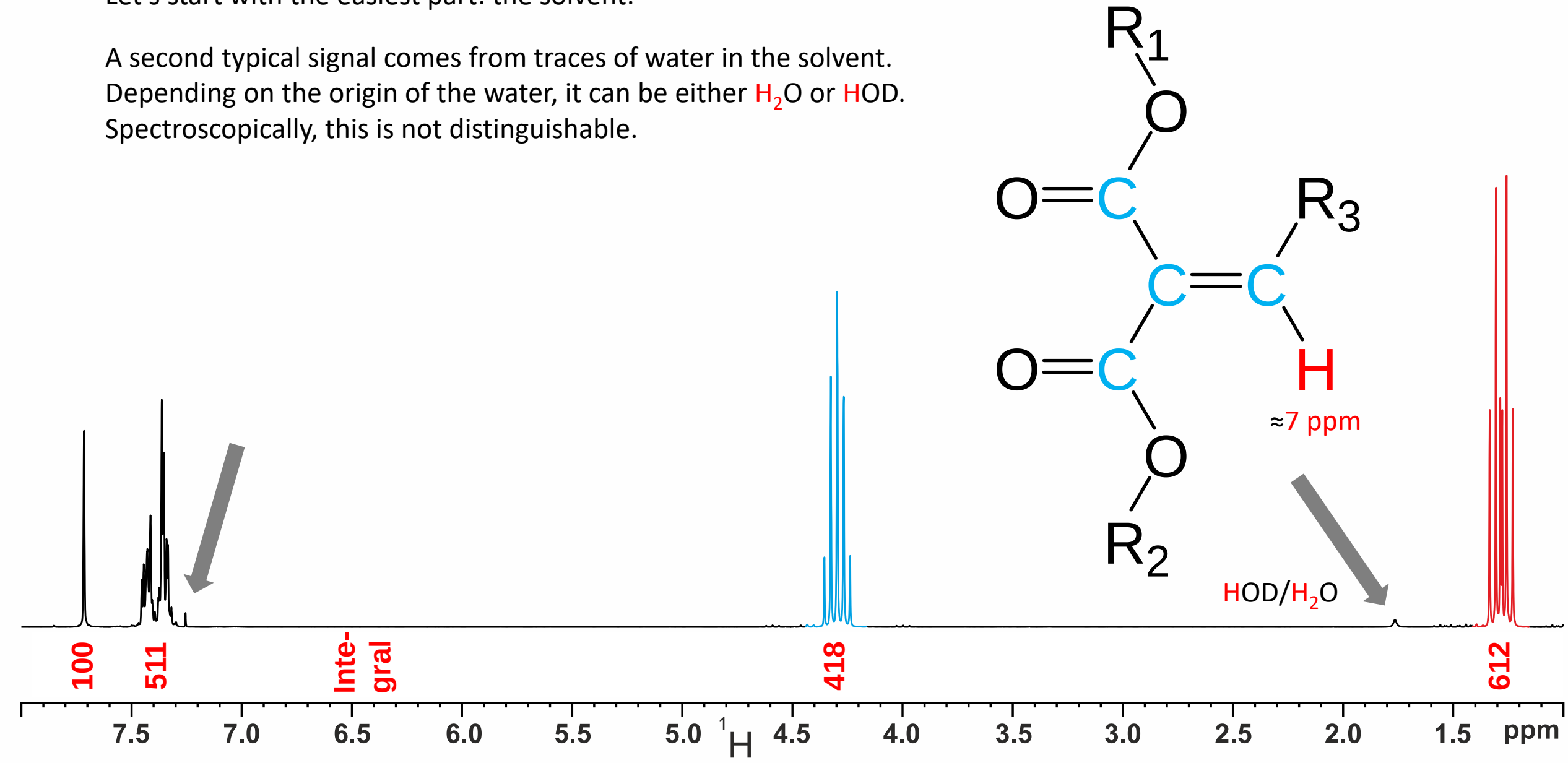
The residual proton signal (the non-deuterated portion) of chloroform appears at about 7.25 ppm.

Here, this signal is hardly visible, but at low sample concentration and/or poor quality of the solvent, the signal might dominate the spectrum.



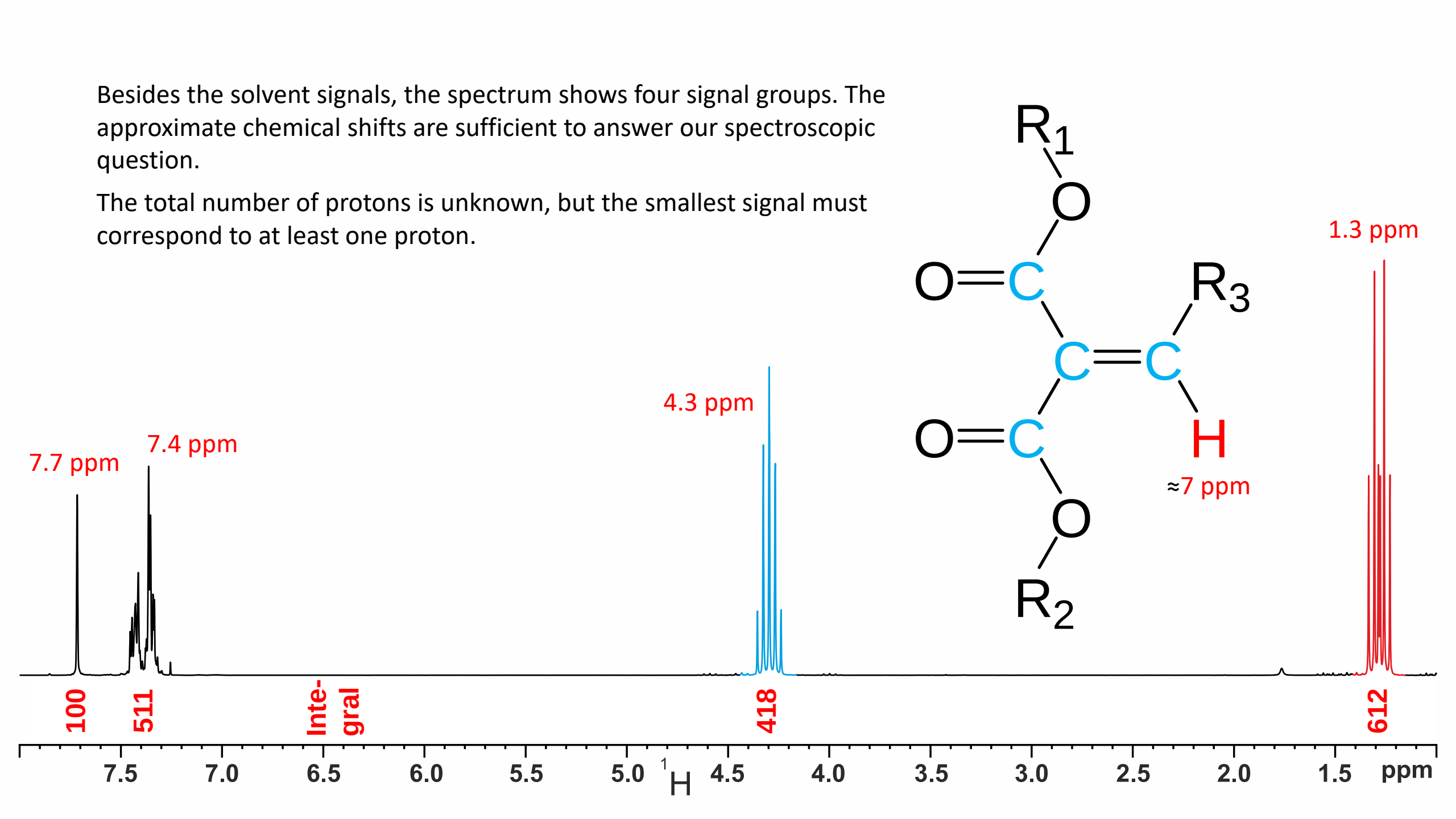
Let's start with the easiest part: the solvent.

A second typical signal comes from traces of water in the solvent.
Depending on the origin of the water, it can be either H_2O or HOD.
Spectroscopically, this is not distinguishable.



Besides the solvent signals, the spectrum shows four signal groups. The approximate chemical shifts are sufficient to answer our spectroscopic question.

The total number of protons is unknown, but the smallest signal must correspond to at least one proton.



The total number of protons is unknown, but the smallest signal must correspond to at least one proton.

This would give us a proportionality factor of

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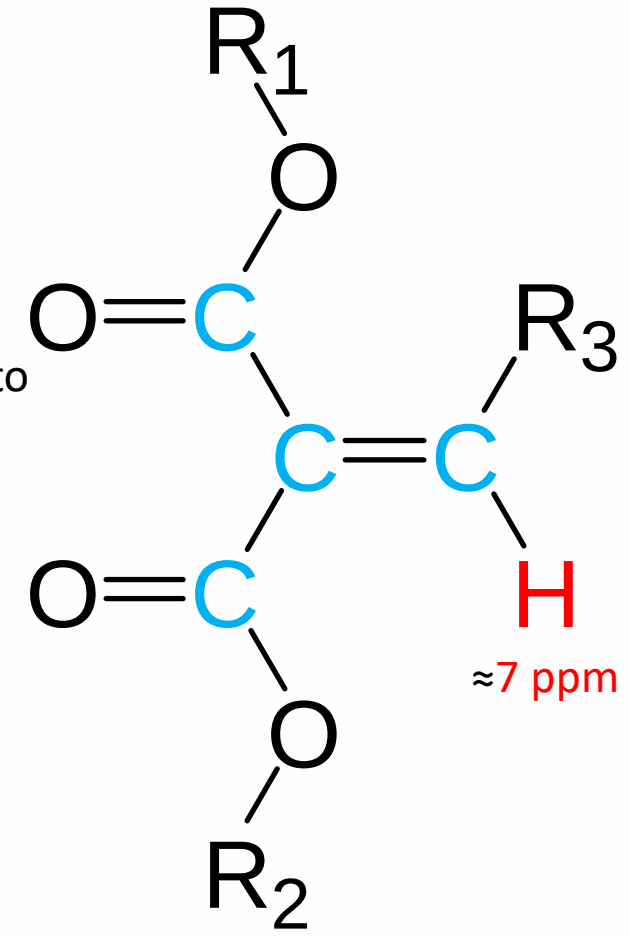
100 a.u. (*arbitrary unit*) = **1H**

and we can convert the integrals of the remaining three signal groups into integer proton values with only minimal rounding.



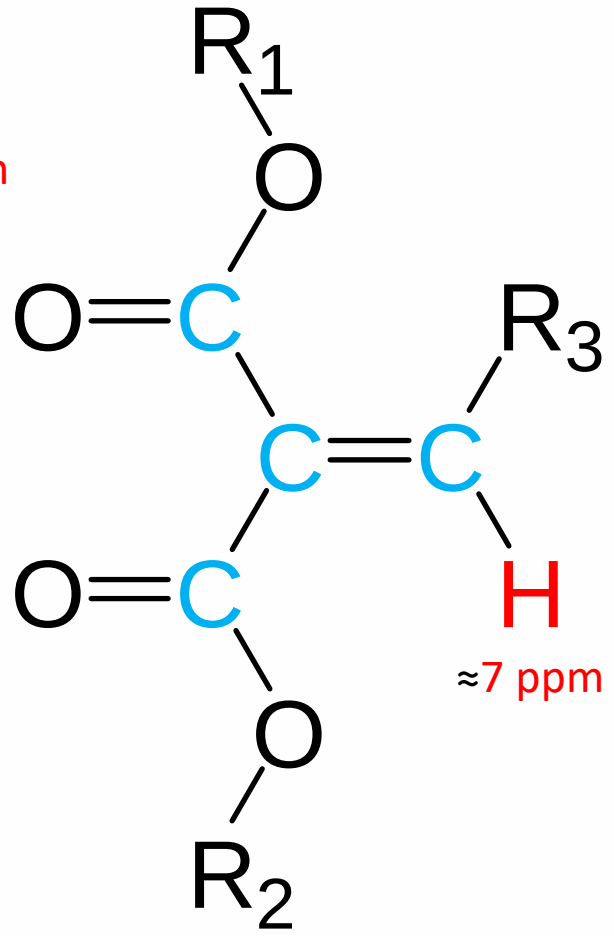
7.7 ppm / 1H

7.4 ppm / 5H

4.3 ppm / 4H (*m*)

1.3 ppm / 6H (*m*)

The essential information consists of four chemical shifts and the corresponding number of protons.
Let's record these 8 pieces of information on four small sticky notes and additionally note that the clean multiplets of the signal groups at 4.3 ppm and 1.3 ppm probably deserve a closer look.



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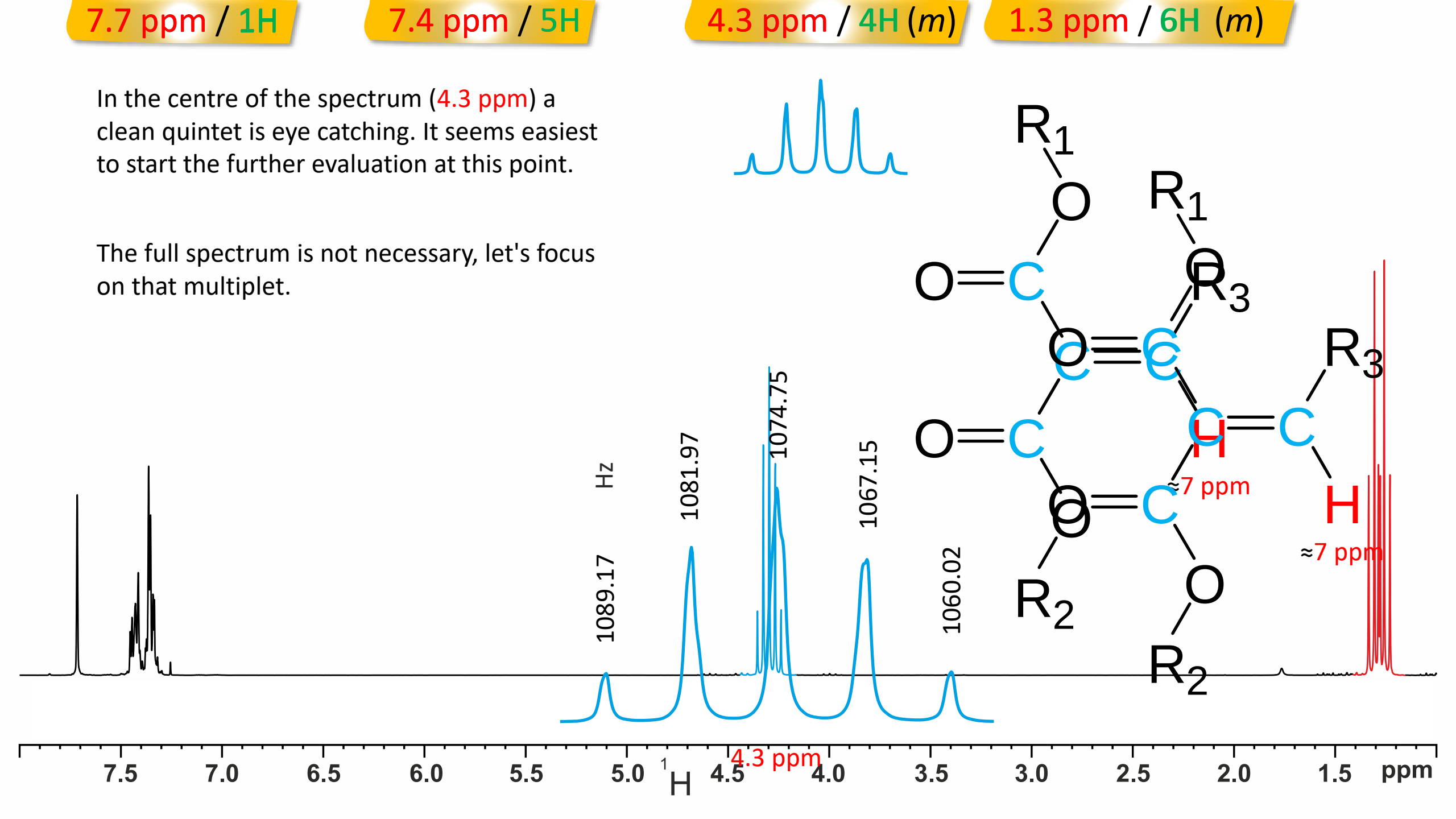
7.4 ppm / 5H

4.3 ppm / 4H (*m*)

1.3 ppm / 6H (*m*)

In the centre of the spectrum (4.3 ppm) a clean quintet is eye catching. It seems easiest to start the further evaluation at this point.

The full spectrum is not necessary, let's focus on that multiplet.



7.7 ppm / 1H ? 7.4 ppm / 5H ? 4.3 ppm / 4H (*m*) 1.3 ppm / 6H (*m*) ?

The full spectrum is not necessary, let's focus on that multiplet.

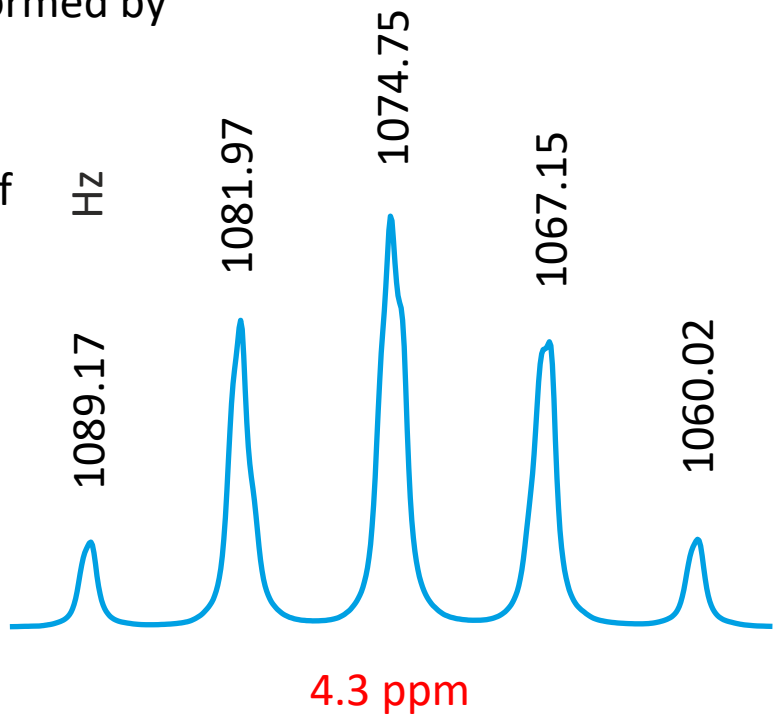
A coupling constant of **7.28 Hz** (*1089.17 Hz – 1060.02 Hz) / 4*) occurs very frequently between neighbouring protons bound to sp^3-hybridised carbon atoms.

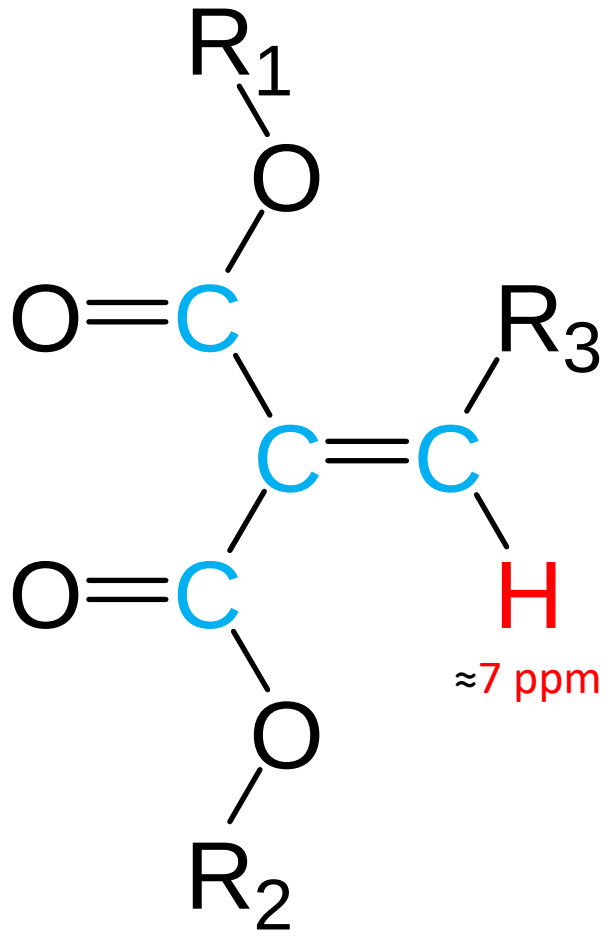
The full spectrum is not necessary, let's focus on that multiplet.

According to the **n+1** rule, a quintet is formed by **four** equivalent neighbouring protons.

On our sticky notes, we see an integral of **4**. But … these are the protons of the quintet itself, not neighbouring protons.

Something is not right. Let's put this quintet on hold for now and try an analysis of the multiplet at 1.3 ppm.





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The multiplet might look a little bit confusing at a first glance. Hopefully this changes if we colour three of the six lines differently.

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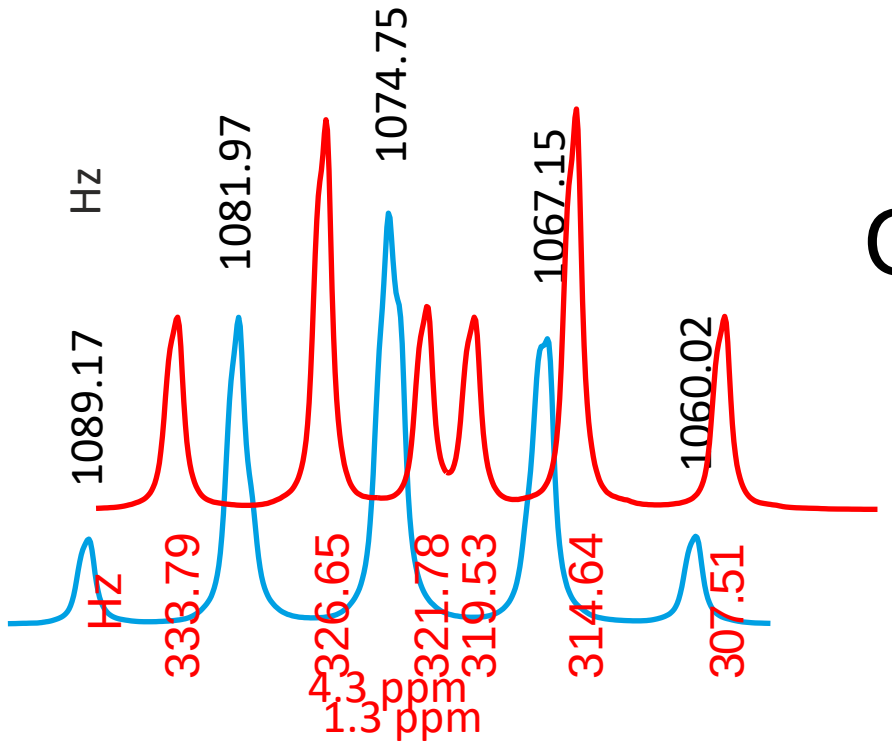
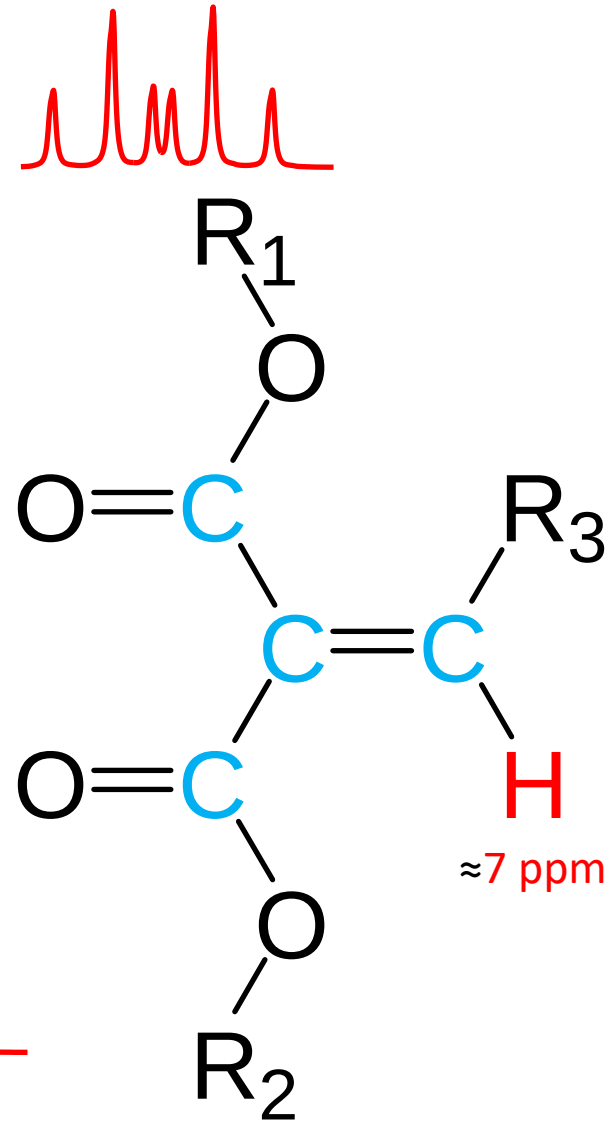




7.7 ppm / 1H

7.4 ppm / 5H

4.3 ppm / 4H (*m*)

1.3 ppm / 6H (*m*)

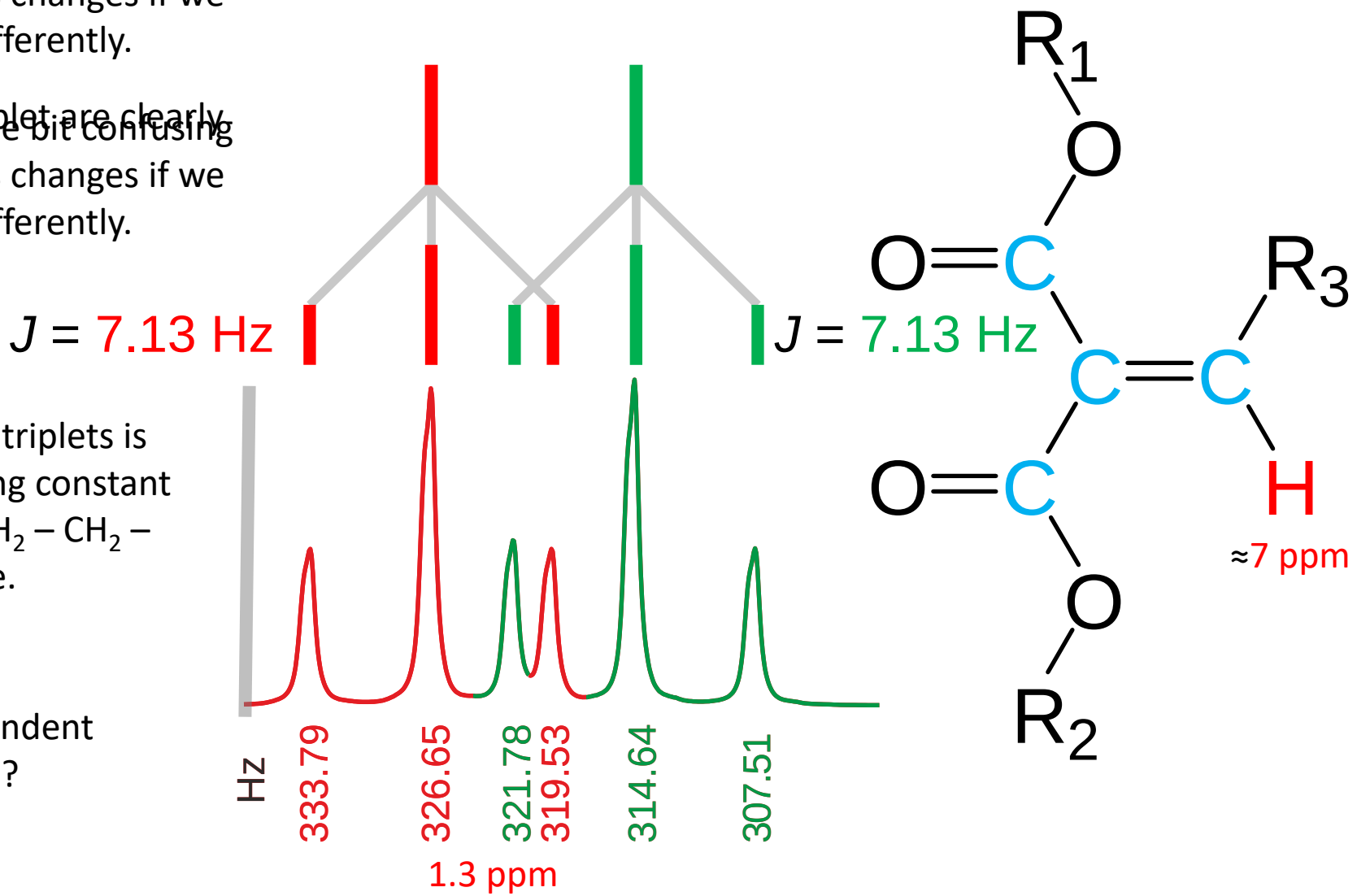
The multiplet might look a little bit confusing at a first glance. Hopefully this changes if we colour three of the six lines differently.

Now a "red" and a "green" triplet are clearly visible.

The multiplet might look a little bit confusing at a first glance. Hopefully this changes if we colour three of the six lines differently.

The coupling constant in both triplets is **7.13 Hz**. For the vicinal coupling constant in the structural fragment – CH_2 – CH_2 – this is a perfect textbook value.

But are these now two independent triplets or a doublet of triplets?



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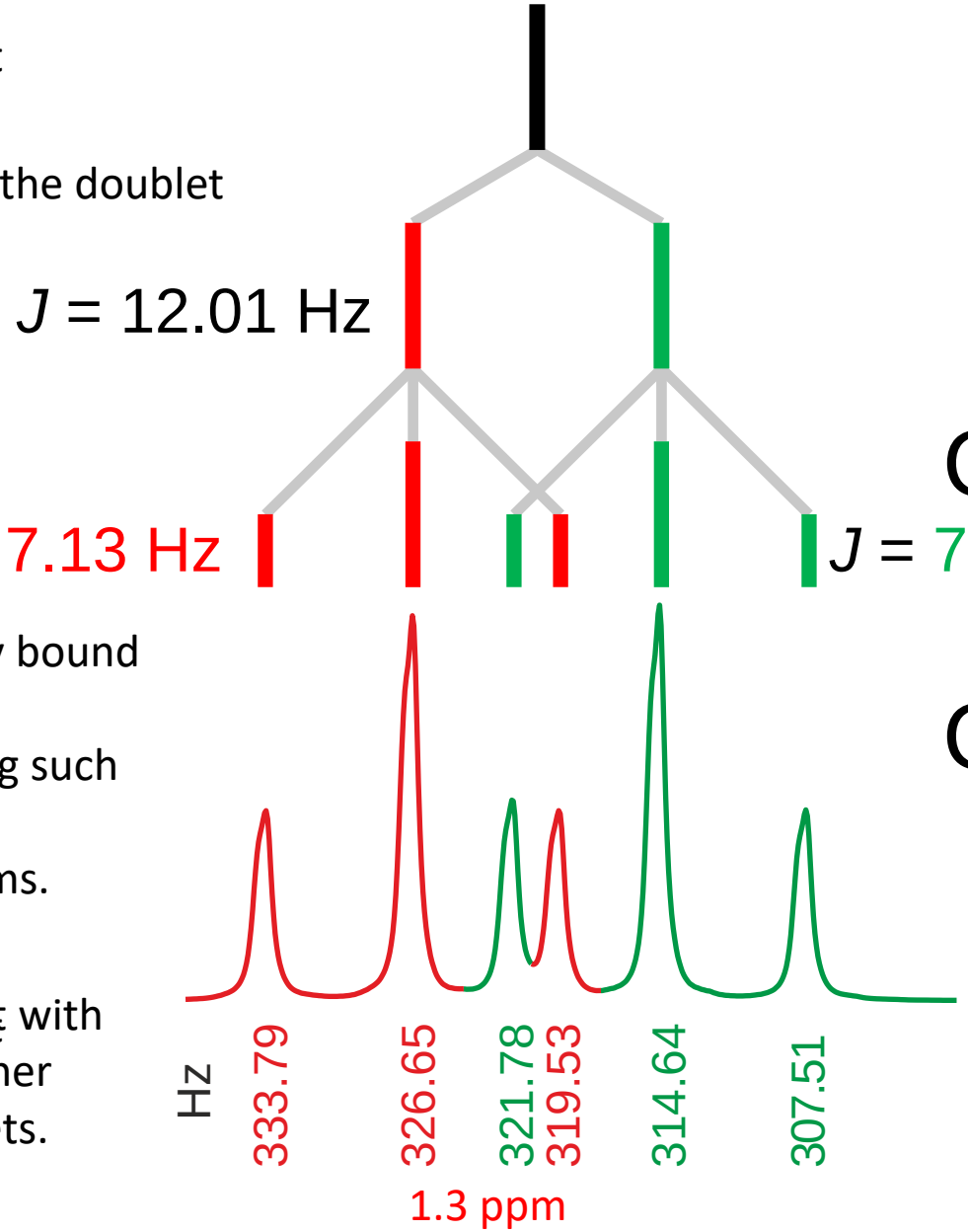
7.4 ppm / 5H

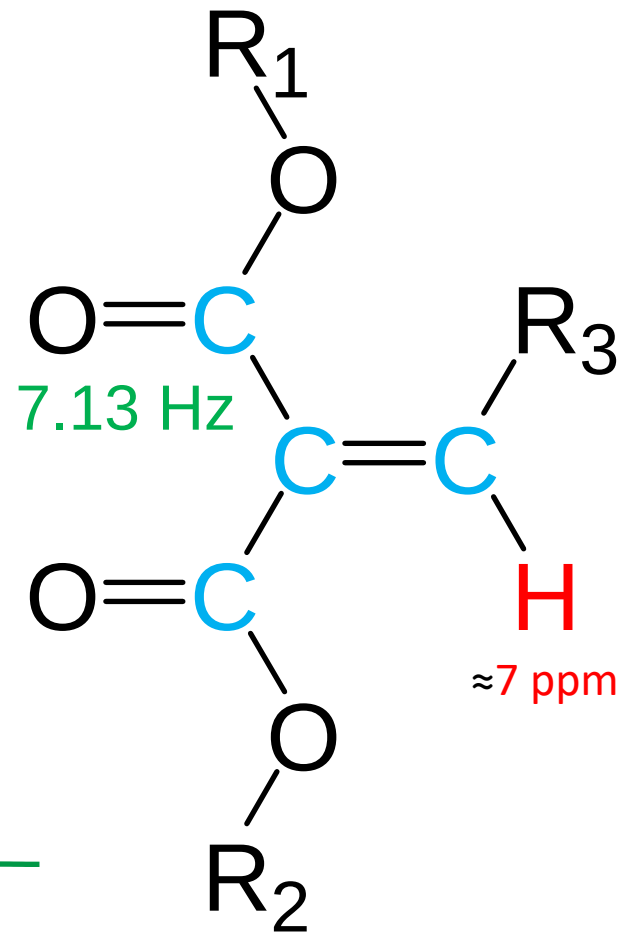
4.3 ppm / 4H (*m*)

1.3 ppm / 6H (*m*)

But are these now two independent triplets or a doublet of triplets?

Let's just complete this multiplet to the doublet of triplets on a trial basis.





The **6** protons at 1.3 ppm are clearly bound to an sp^3-hybridised C atom. Vicinal coupling constants of **12 Hz** involving such protons are only possible with fixed geometry, for example in ring systems.

A ring system could not be ruled out with certainty. But perhaps there is another argument against a doublet of triplets.

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7.7 ppm / 1H

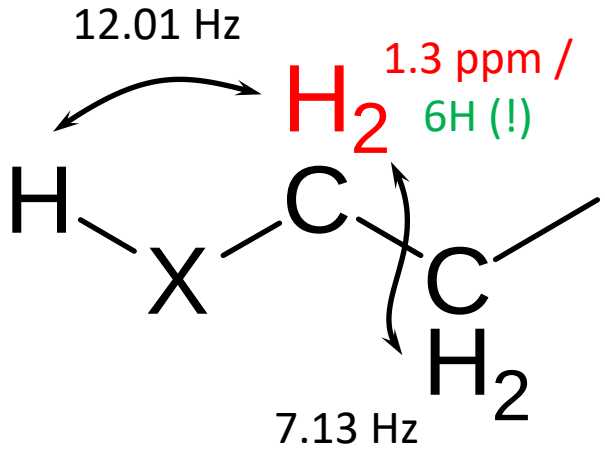
7.4 ppm / 5H

4.3 ppm / 4H (*m*)

1.3 ppm / 6H (*m*)

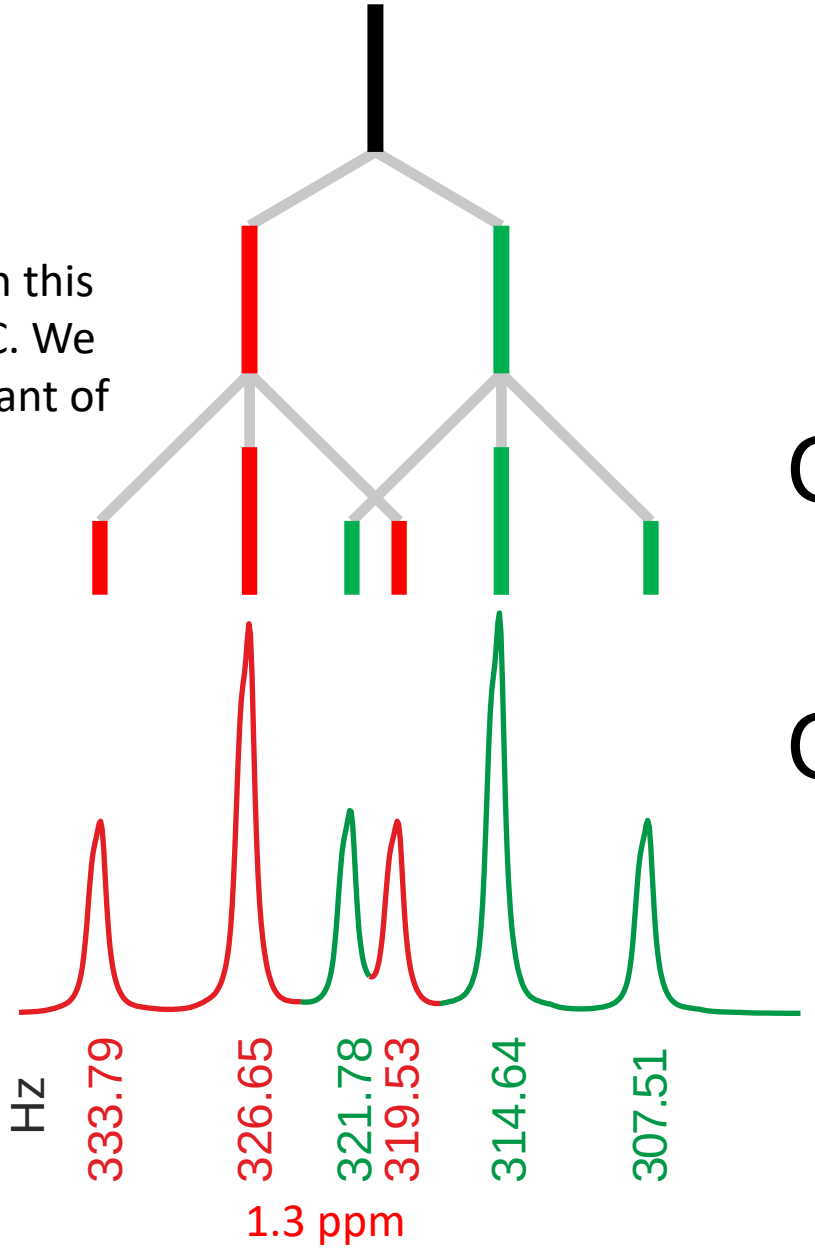
A ring system could not be ruled out with certainty. But perhaps there is another argument against a doublet of triplets.

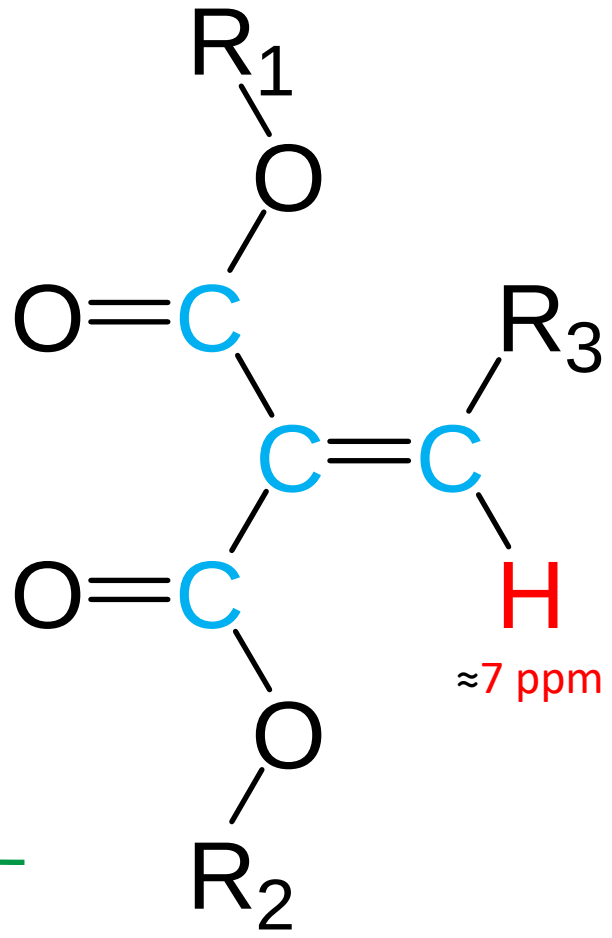
A doublet of triplets would be explained with this kind of a structural fragment. X can be O or C. We ignore the somewhat strange coupling constant of 12.01 Hz.



A ring system could not be ruled out with certainty. But perhaps there is another argument against a doublet of triplets.

But we need not **2**, but **6** protons. For that, this fragment would have to be present three times.





7.7 ppm / 1H

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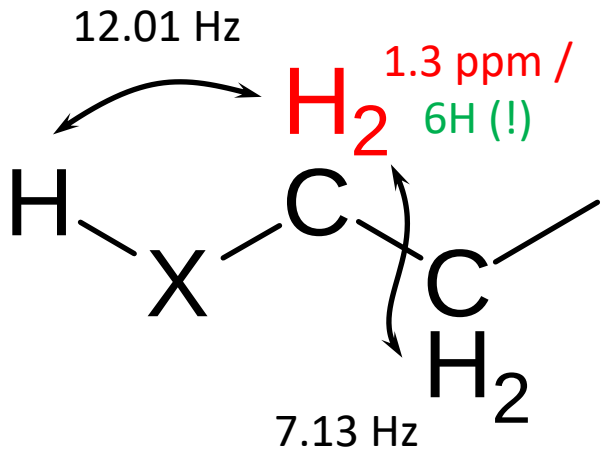
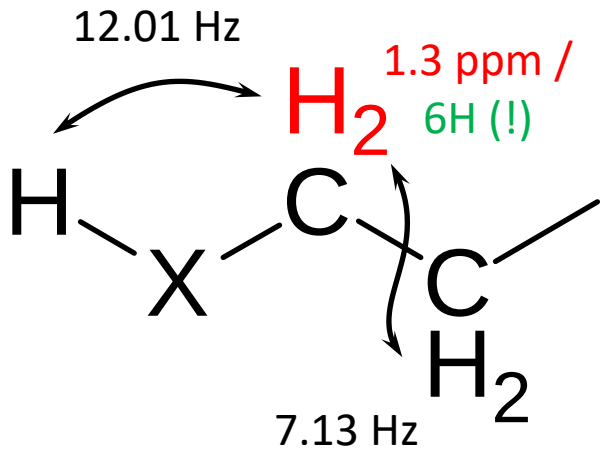
1.3 ppm / 6H (*m*)

3x





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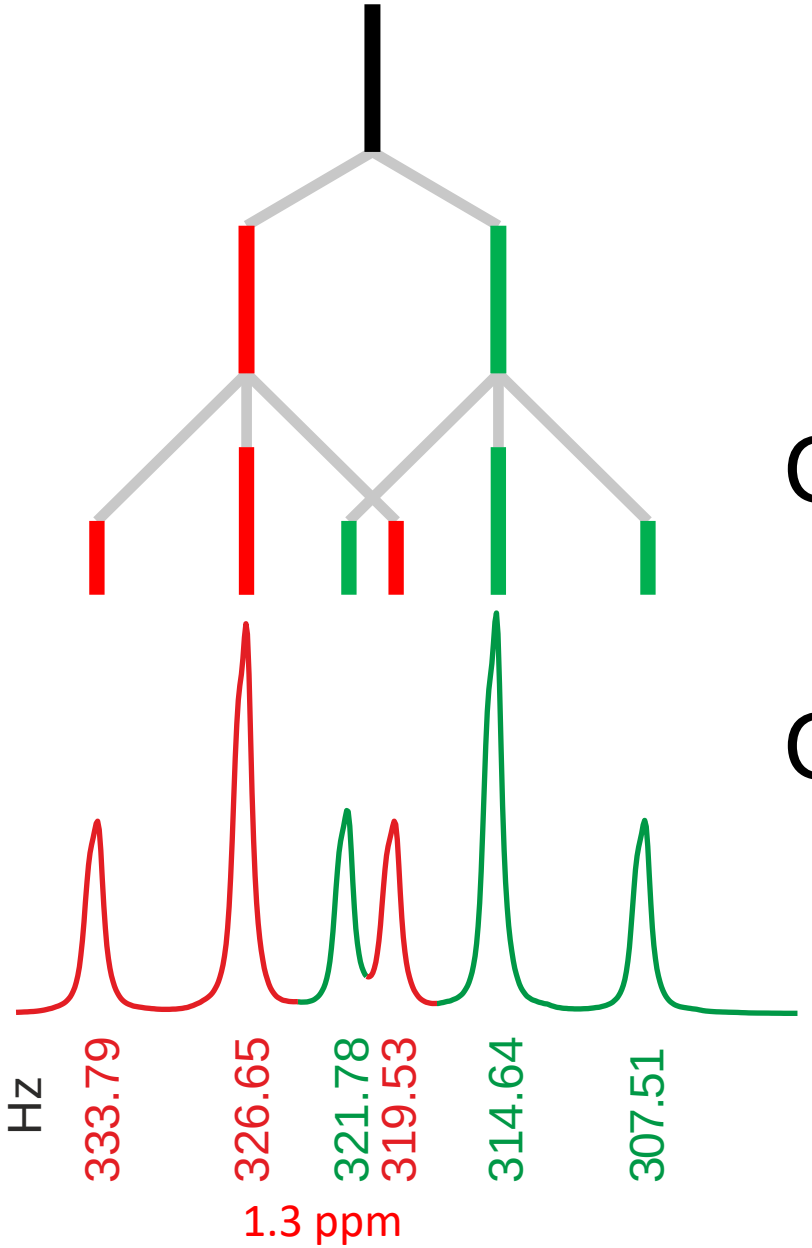

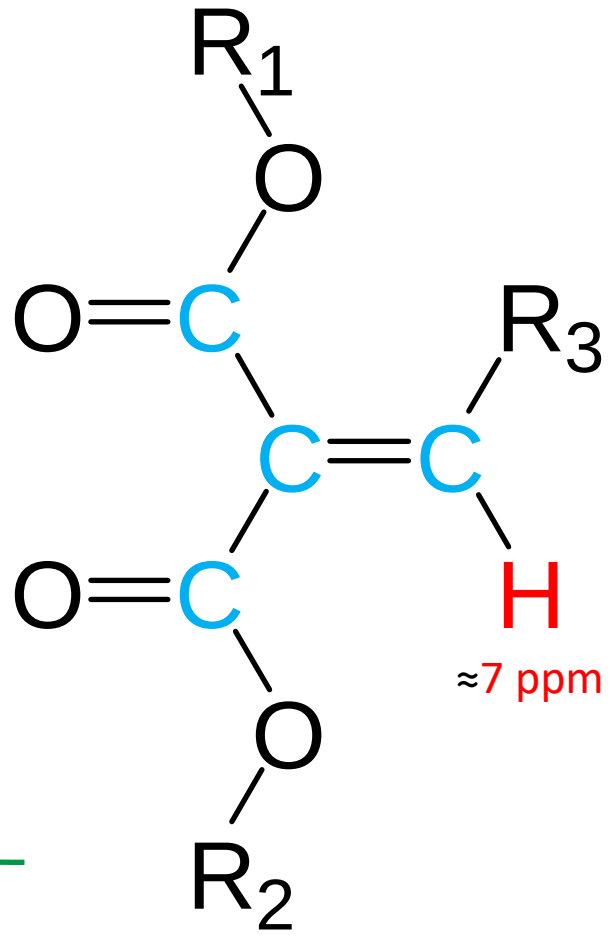

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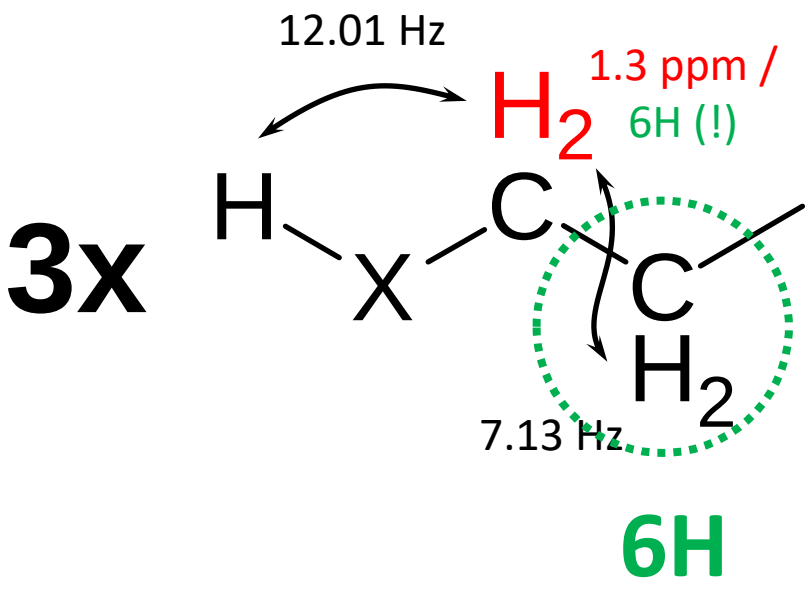
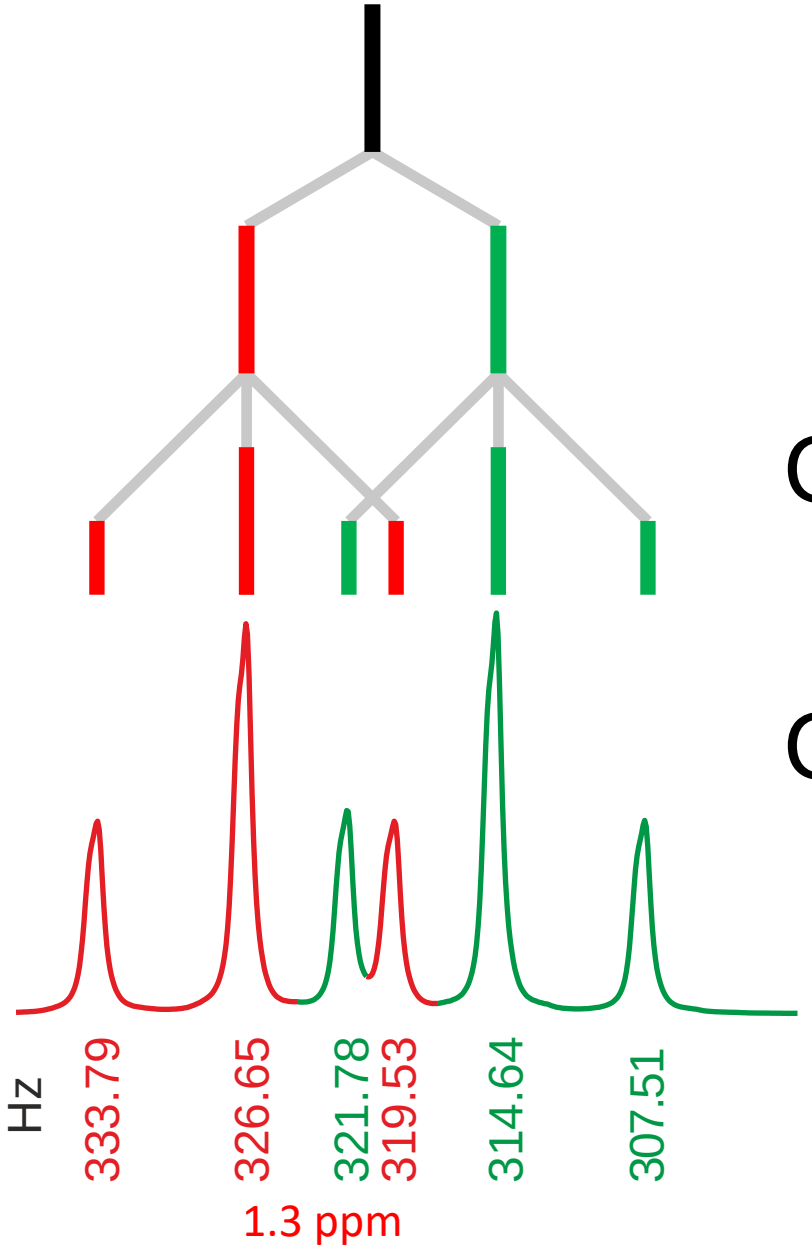
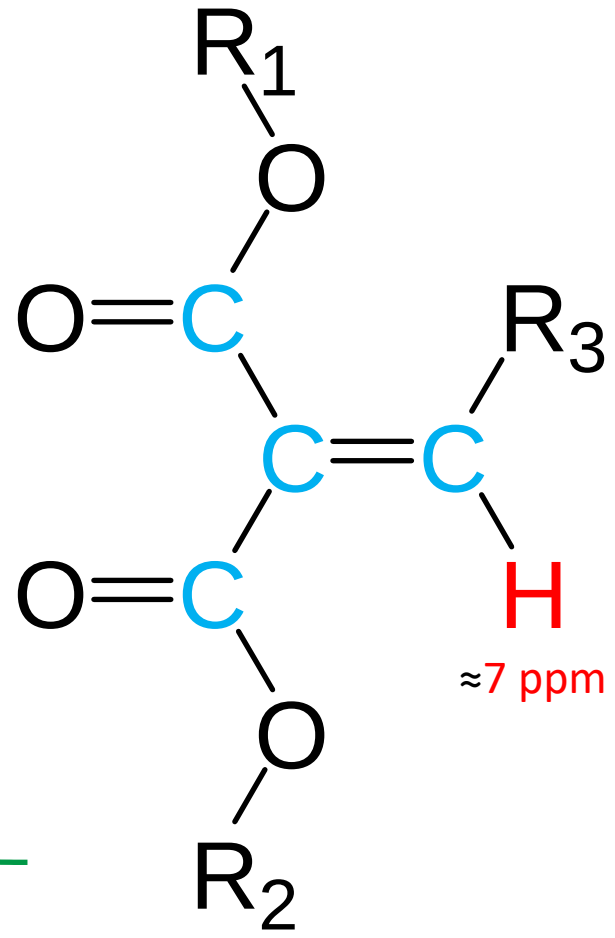


For this fragment, another **3 • 2** protons for the neighbouring CH_2 group would have to appear somewhere in the spectrum. But another multiplet with the integral **6** does not exist.





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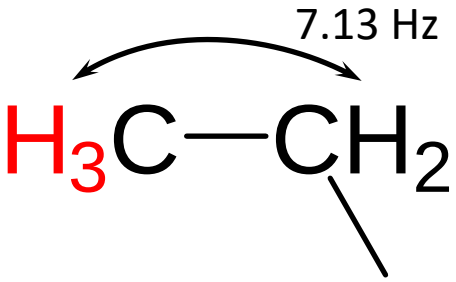
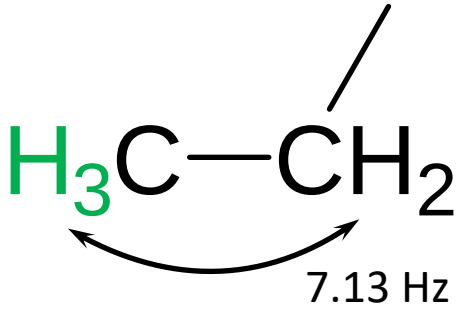
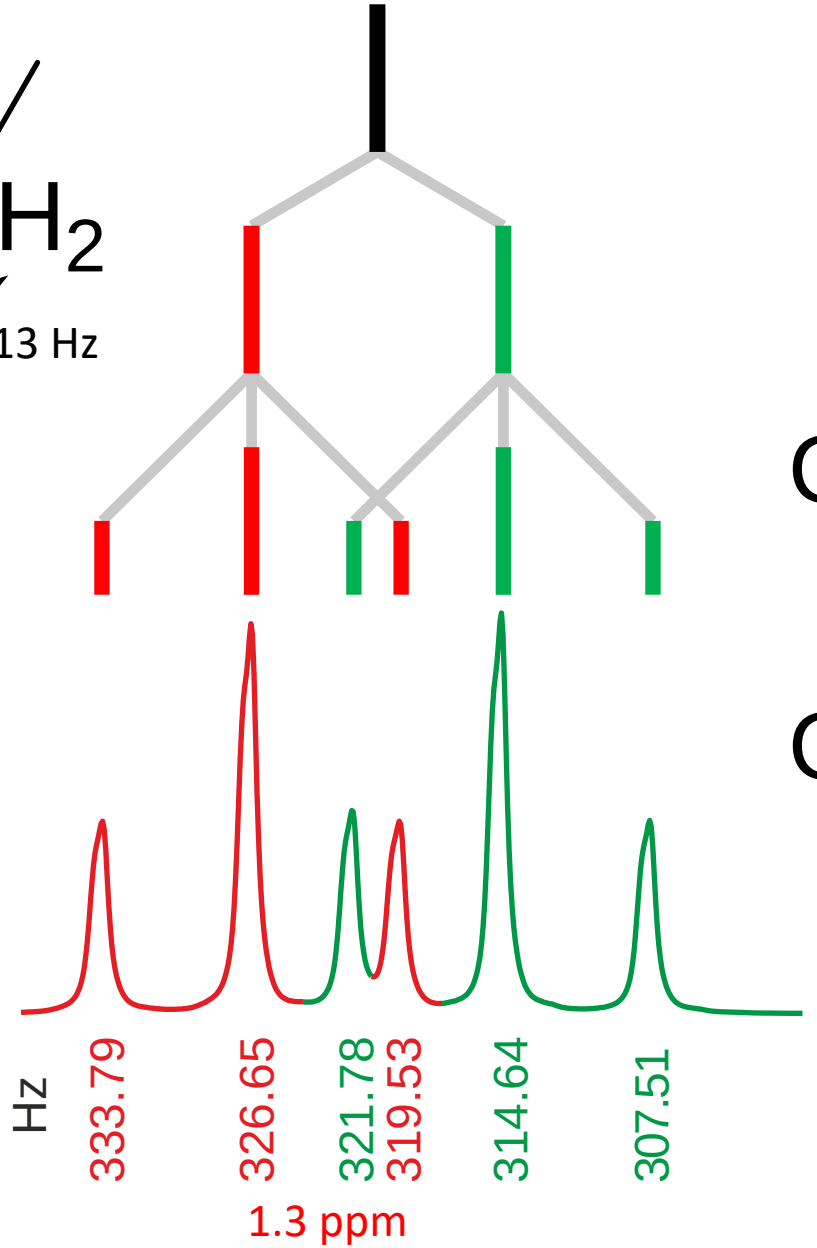
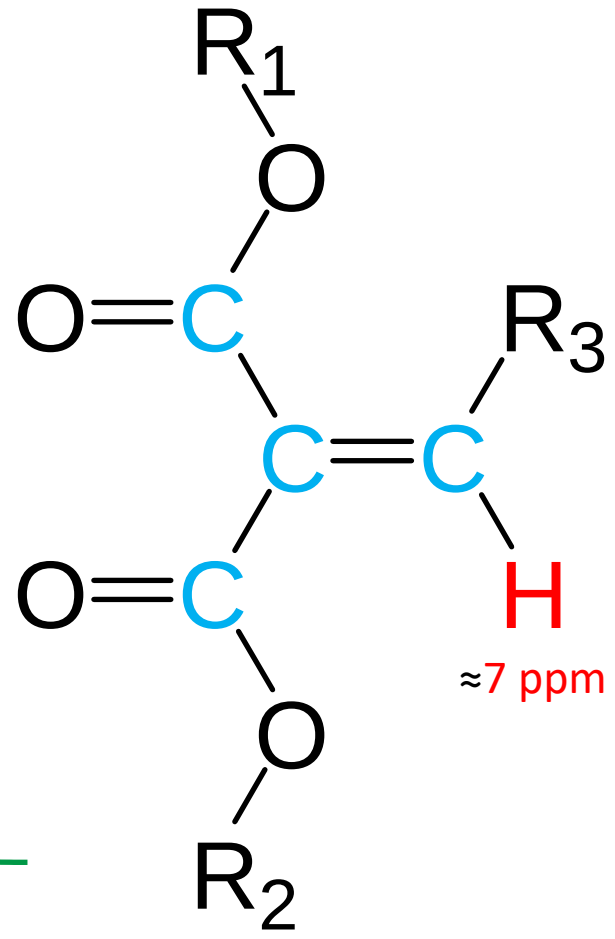




Completely without a strange coupling constant of **12.01 Hz**, two independent triplets with integral **6** can be explained as two chemically distinguishable methyl groups, which are part of ethyl fragments.

A coupling constant of **7.13 Hz** is absolutely typical for this fragment, and the triplet structure results from the two equivalent protons of the adjacent methylene groups.





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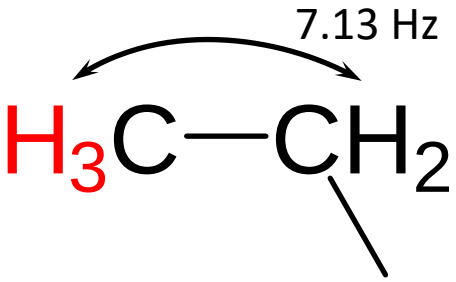
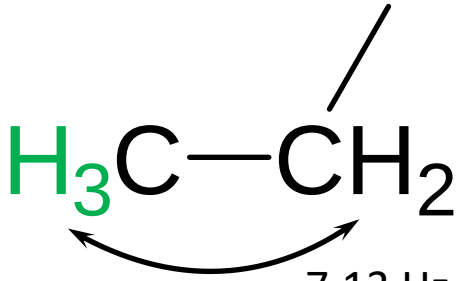
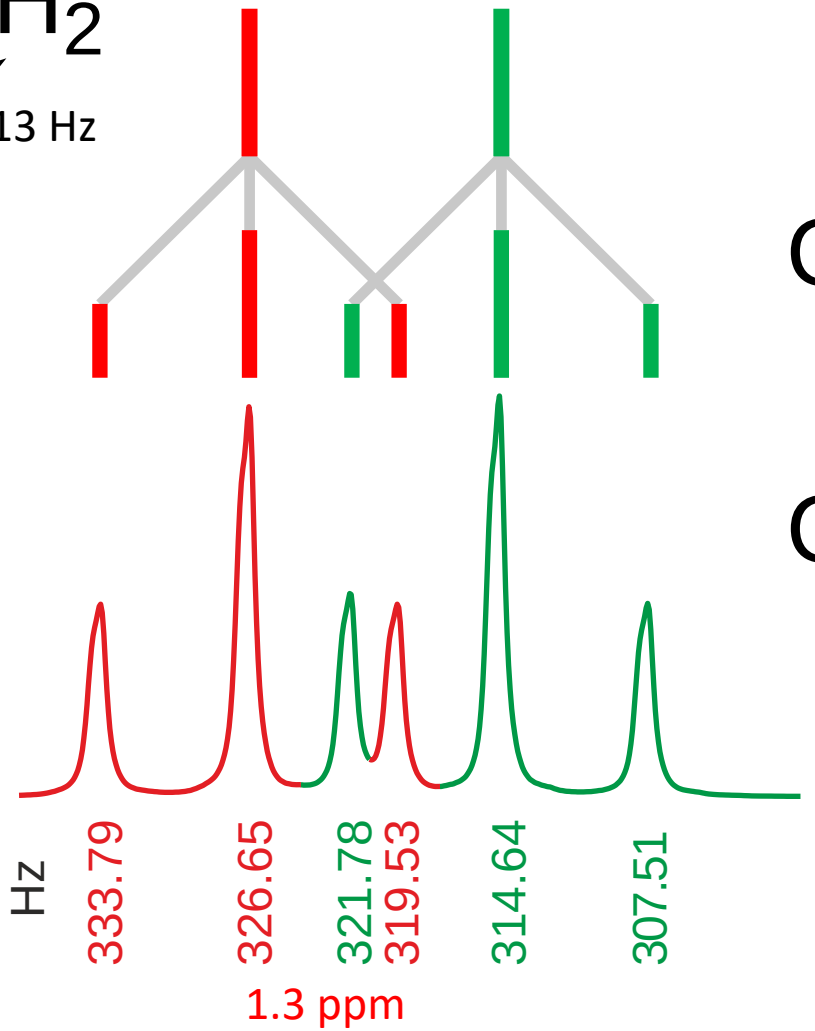


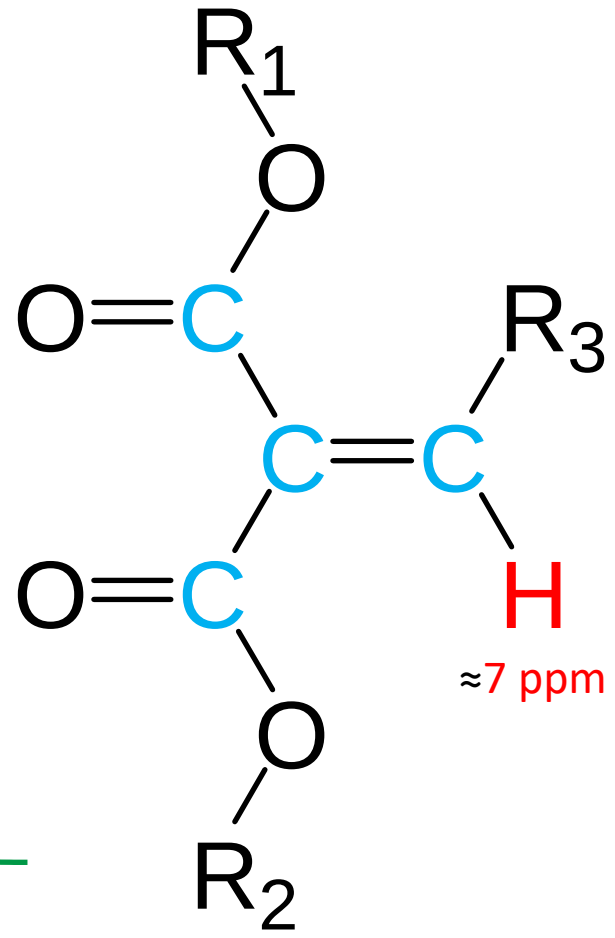


Could the two ethyl groups be the fragments R_1 und R_2?

The molecule is asymmetric, but the chemical environment of R_1 and R_2 is nevertheless very similar. This would explain the small differences in the chemical shifts of the two methyl groups.

Let's just try it.





7.7 ppm / 1H

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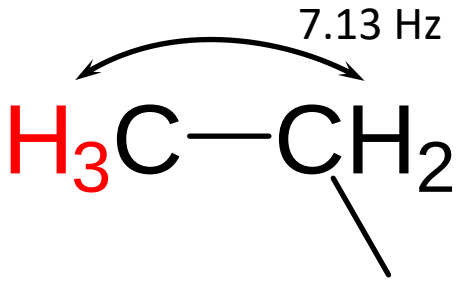
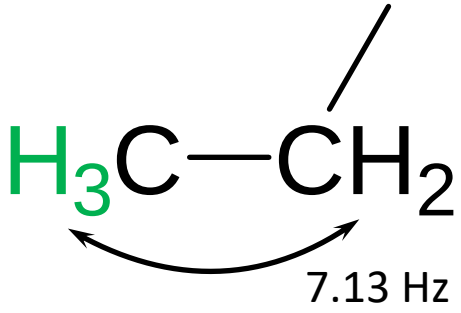


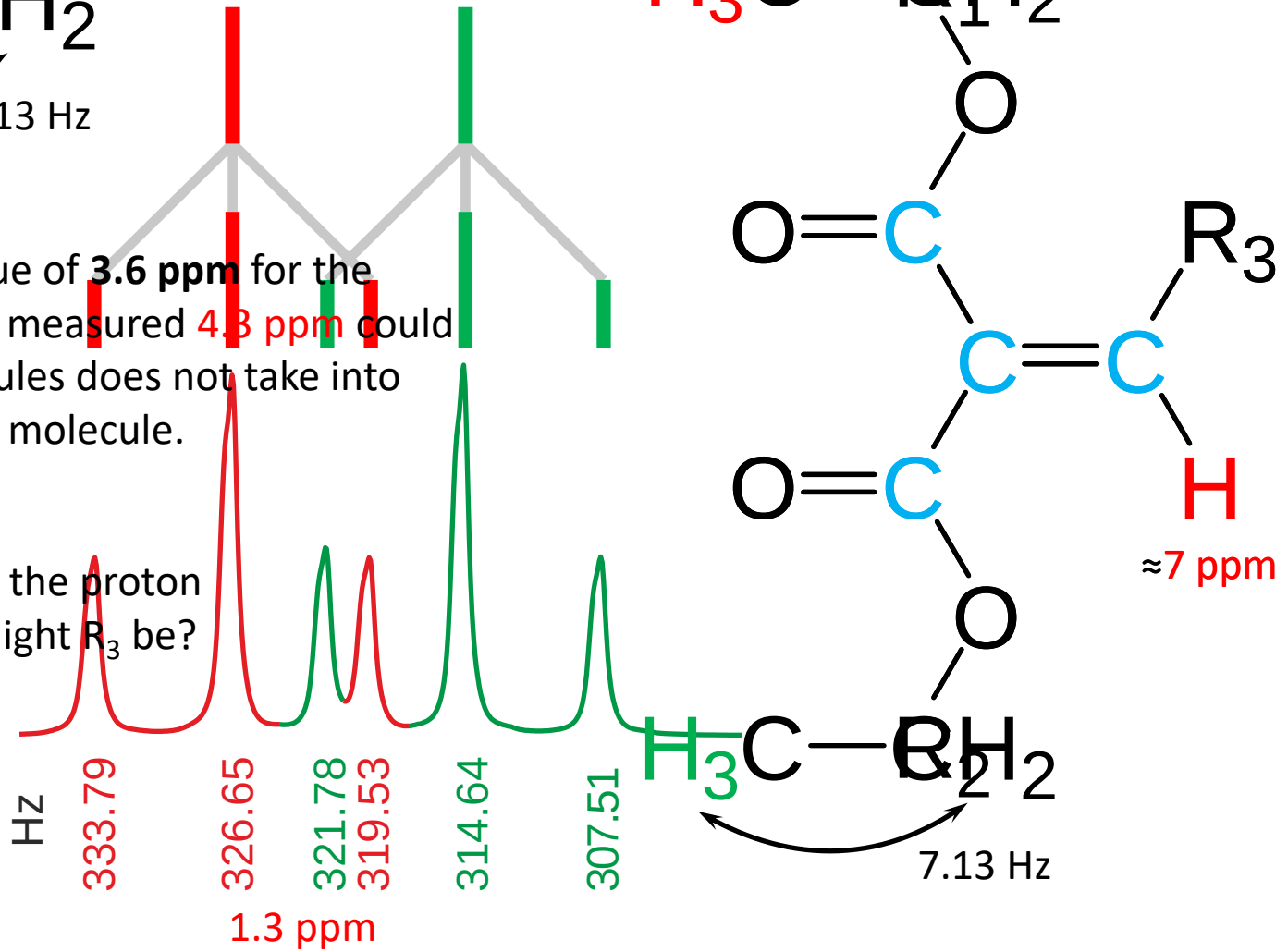


Let's just try it.

The Schoolery rules give an approximate value of **3.6 ppm** for the methylene protons. The agreement with the measured 4.3 ppm could be slightly better, but the simple Schoolery rules does not take into account the conjugated double bonds in this molecule.

The singlet at 7.7 ppm should be assigned to the proton bound to the same carbon as R_3. But what might R_3 be?

Let's just try it.

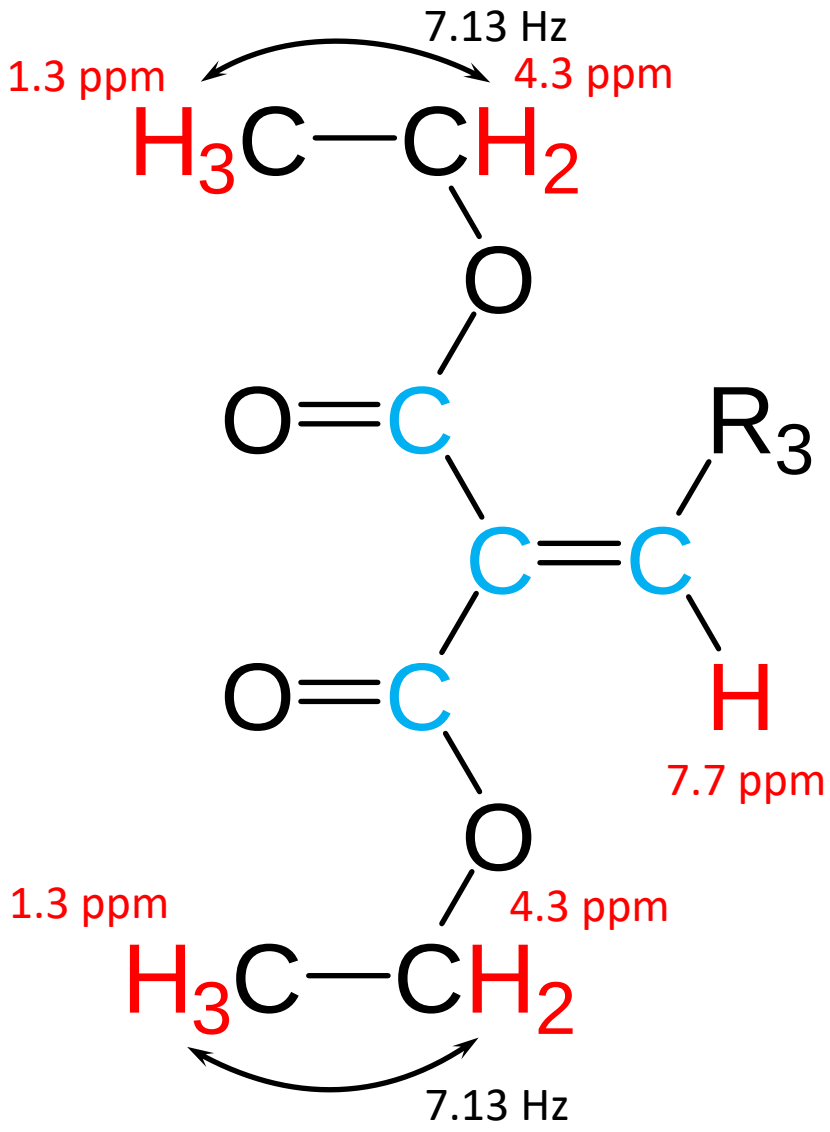


7.4 ppm / 5H

The two ethyl groups are chemically distinguishable, but the exact assignment of the slightly different chemical shifts is impossible with the available data.

5 protons with a chemical shift of about 7 ppm? Since we have no carbon spectrum, some speculations would be possible. From the proton spectrum alone, only one very probable fragment can be deduced: a phenyl group.
The common abbreviation Ø for the phenyl group is used here.

There is one last question.

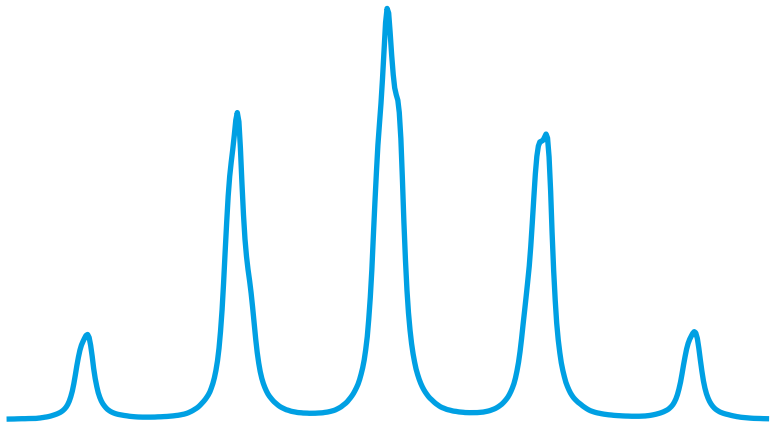


But what might be the last question?

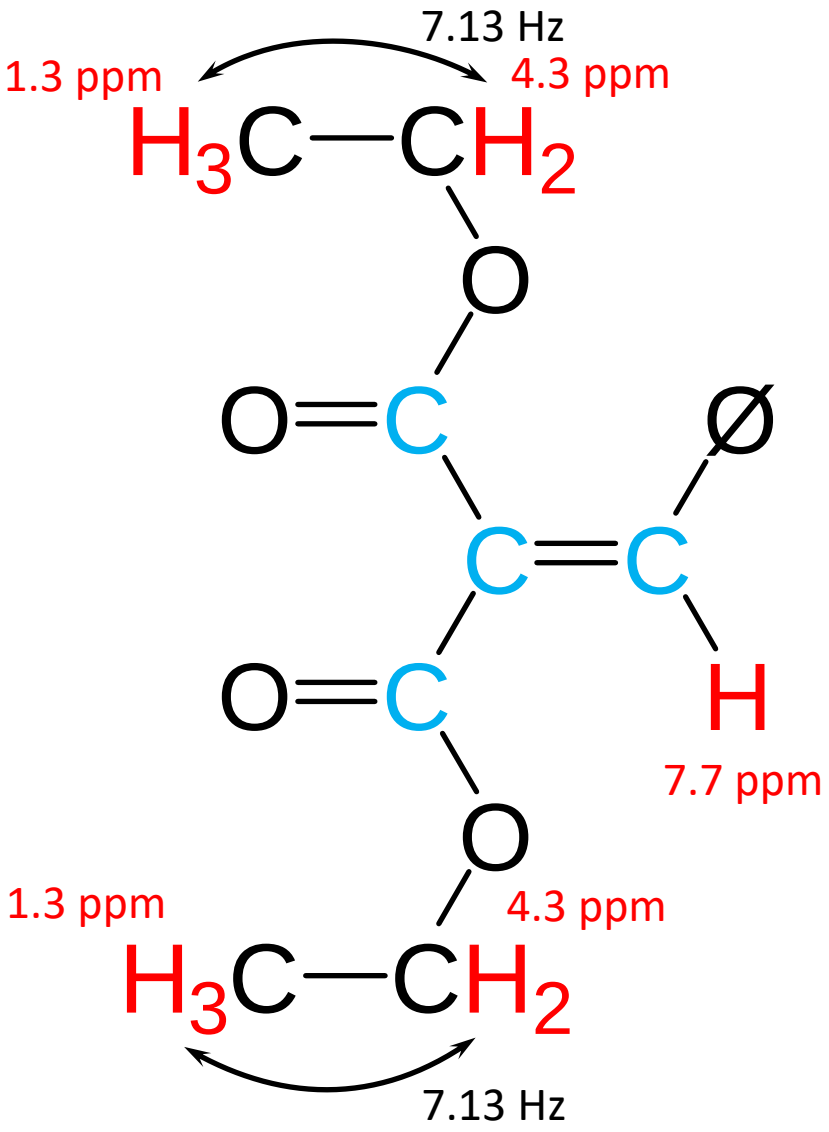
At 4.3 ppm we expect the signals of the methylene protons. Because of the neighbouring methyl group, a quartet and not a quintet should appear there?

Because of the asymmetry of the molecule, the two methylene groups, as well as the two methyl groups, are chemically distinguishable. As a result, we obtain the expected quartet for each of the two methylene groups. Coincidentally, in this compound, the chemical shifts of the two quartets differ almost exactly by the vicinal coupling constant.

Let's change the colours a little for better illustration.



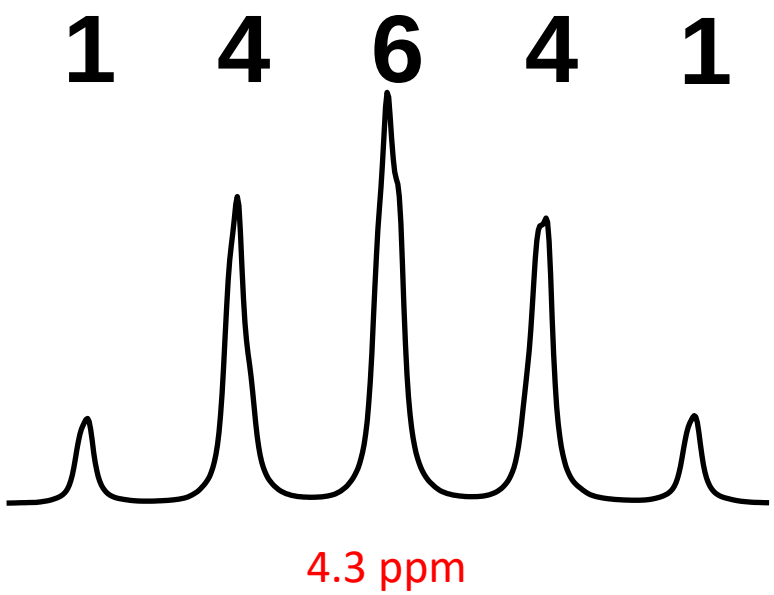
4.3 ppm

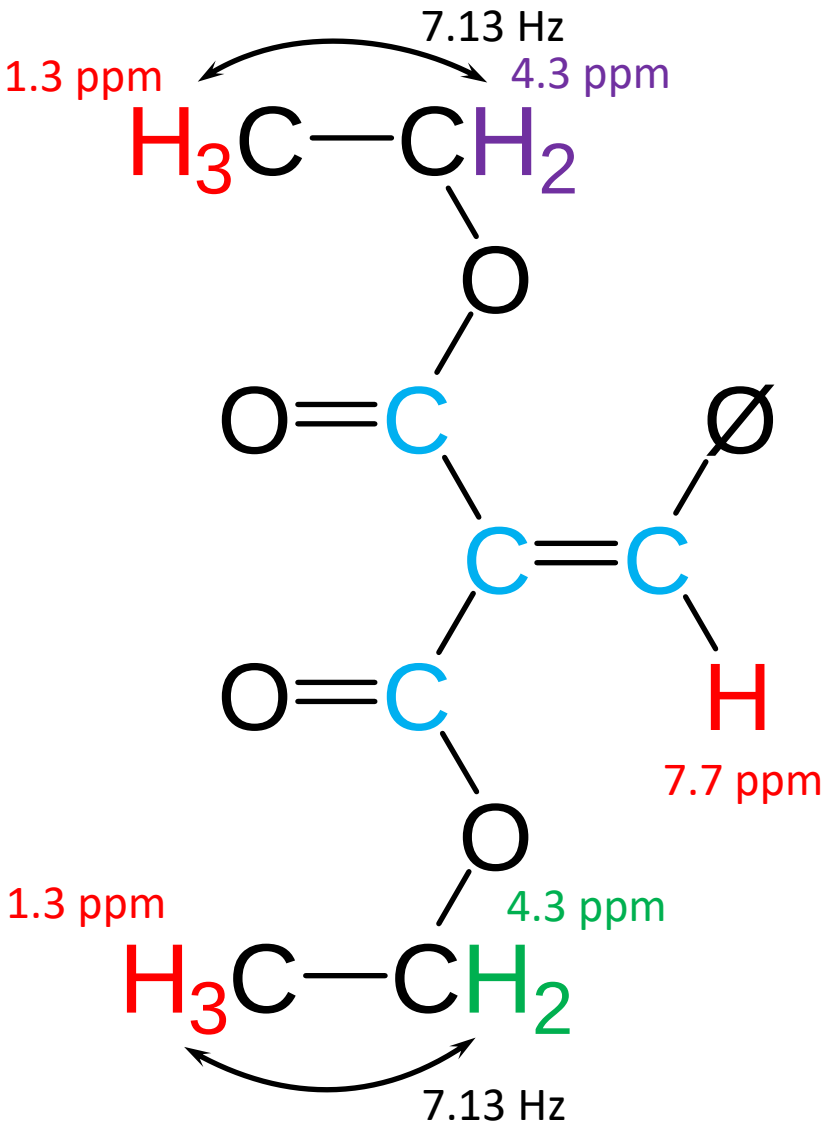


And now the methylene protons marked in green ...

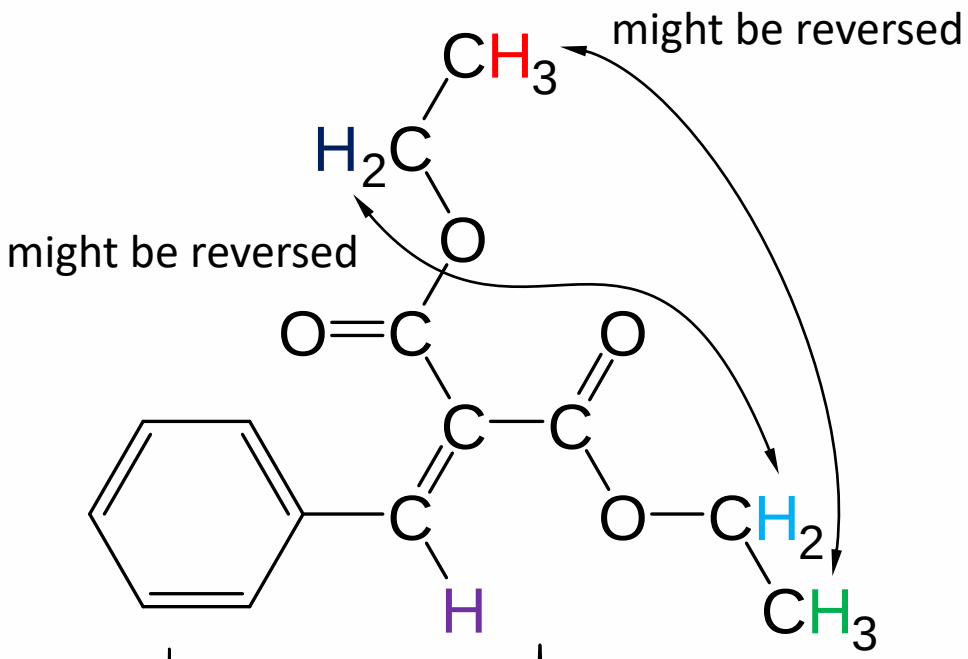
... and add both quartets.

Let's start with the quartet of protons marked in purple.





Summary



protons of the phenyl ring

1 3 3 1

1 3 3 1

Hz

1089.17

1081.97

1074.75

1067.15

1060.02

4.35 4.30 4.25

Hz

333.79

326.65

321.78

319.53

314.64

307.51

1.30 1.25

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 ppm

^{1}H

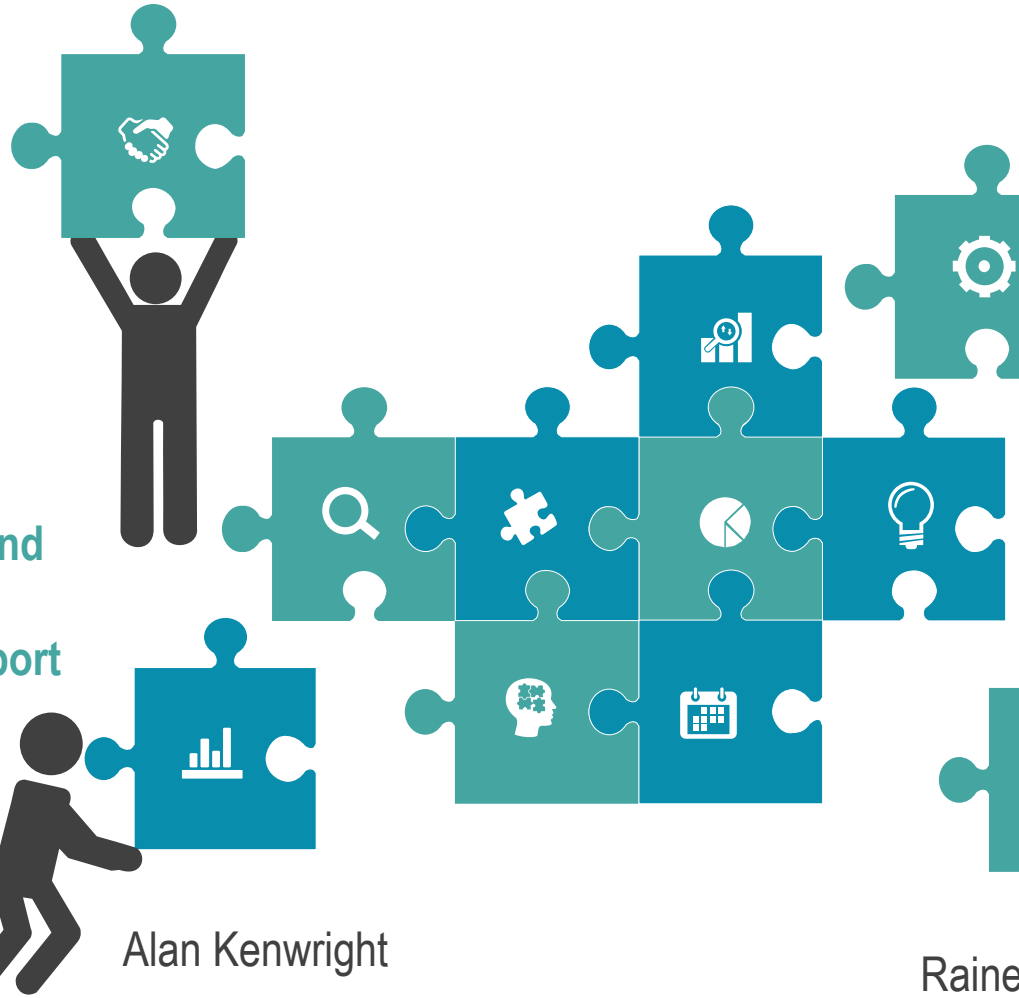
Contributions

Spectrometer time

TU Munich

Measurements

Rainer Haeßner



Discussions and native English language support

Alan Kenwright

Compilation

Rainer Haeßner

More exercises …