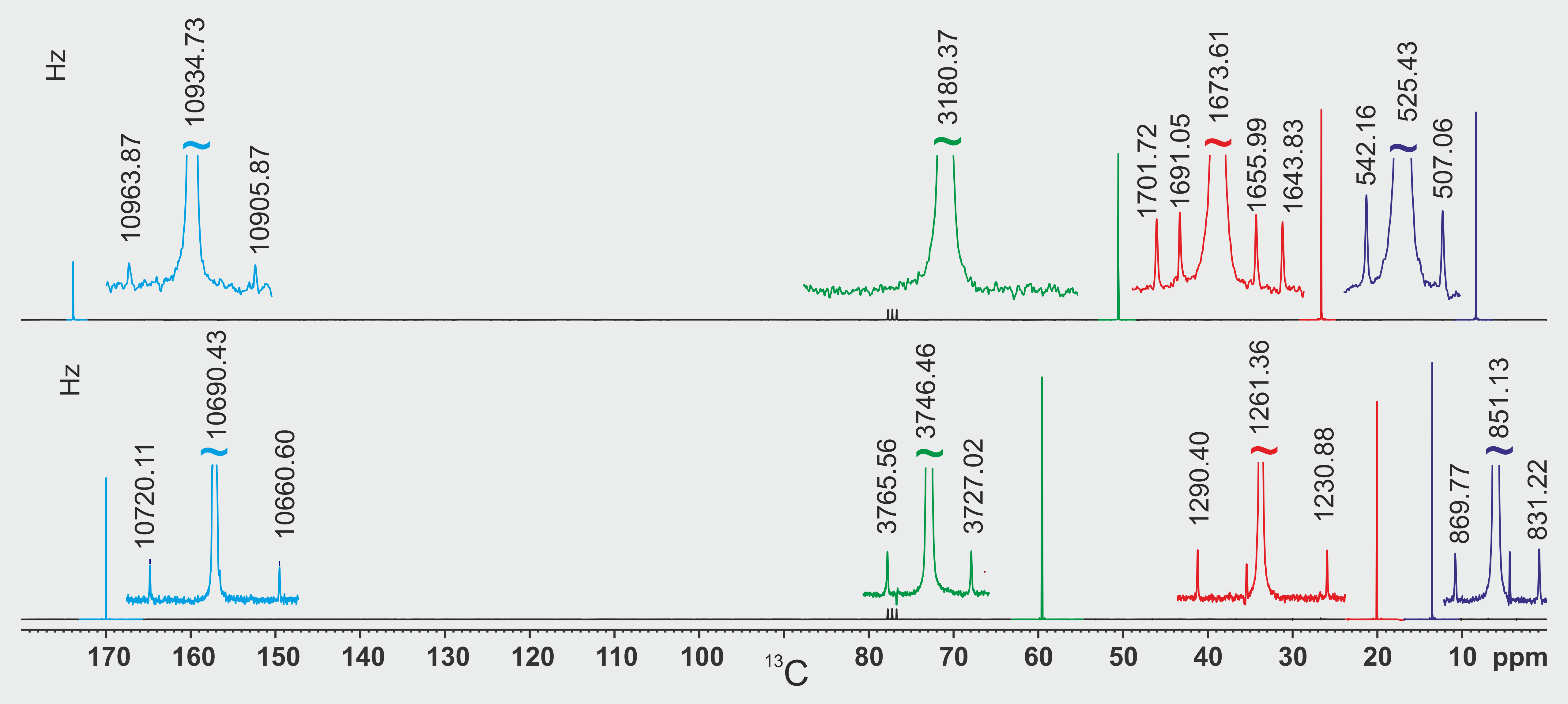
Exercise plus Solution – Quick overview

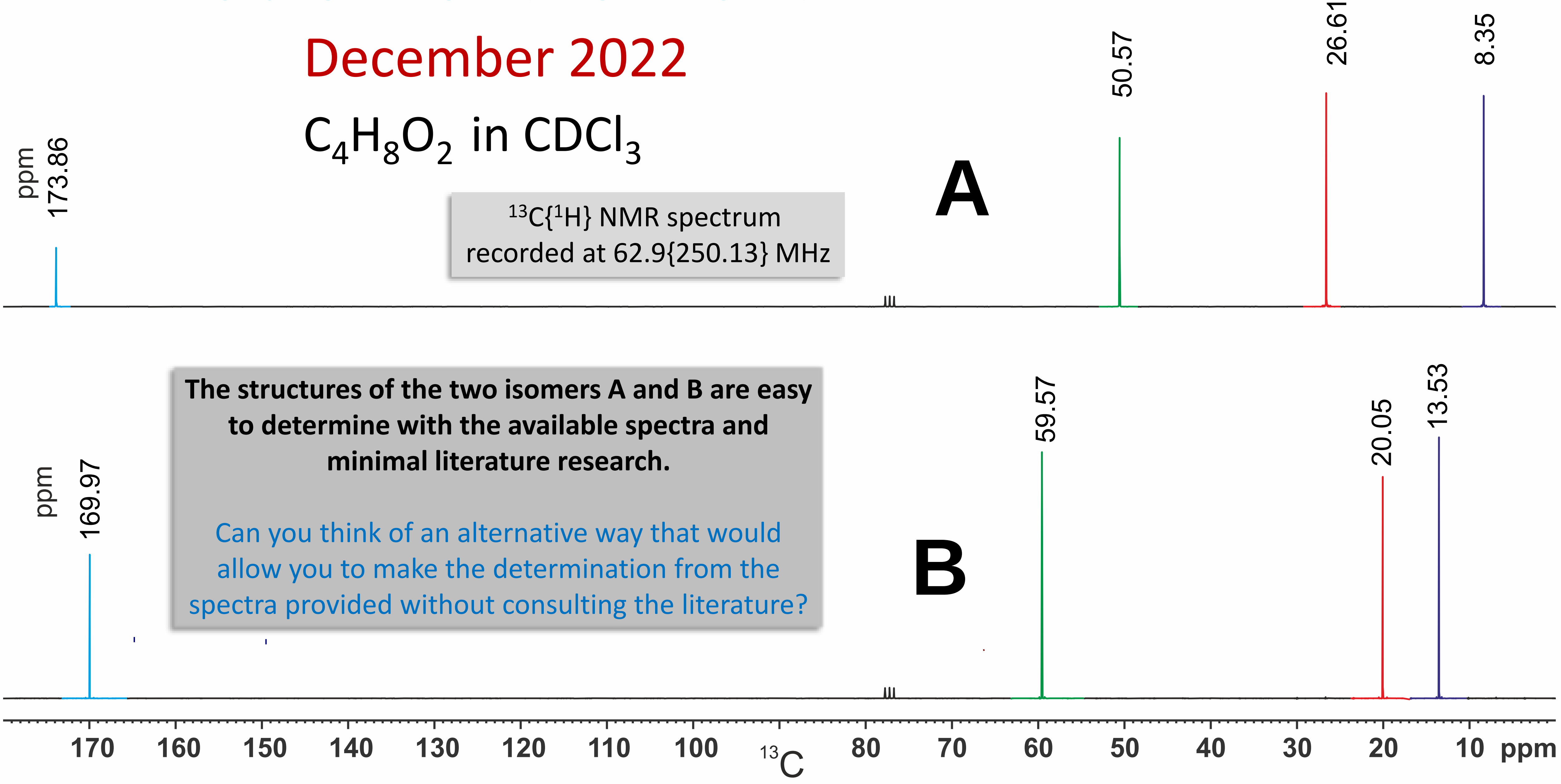
It is recommended to use this version only for a quick overview of the NMR challenge. All animations of the PowerPoint version are missing, under certain circumstances quality deficiencies may also occur.
The higher quality PowerPoint files are freely available for download at any time.



Problem of the month

December 2022

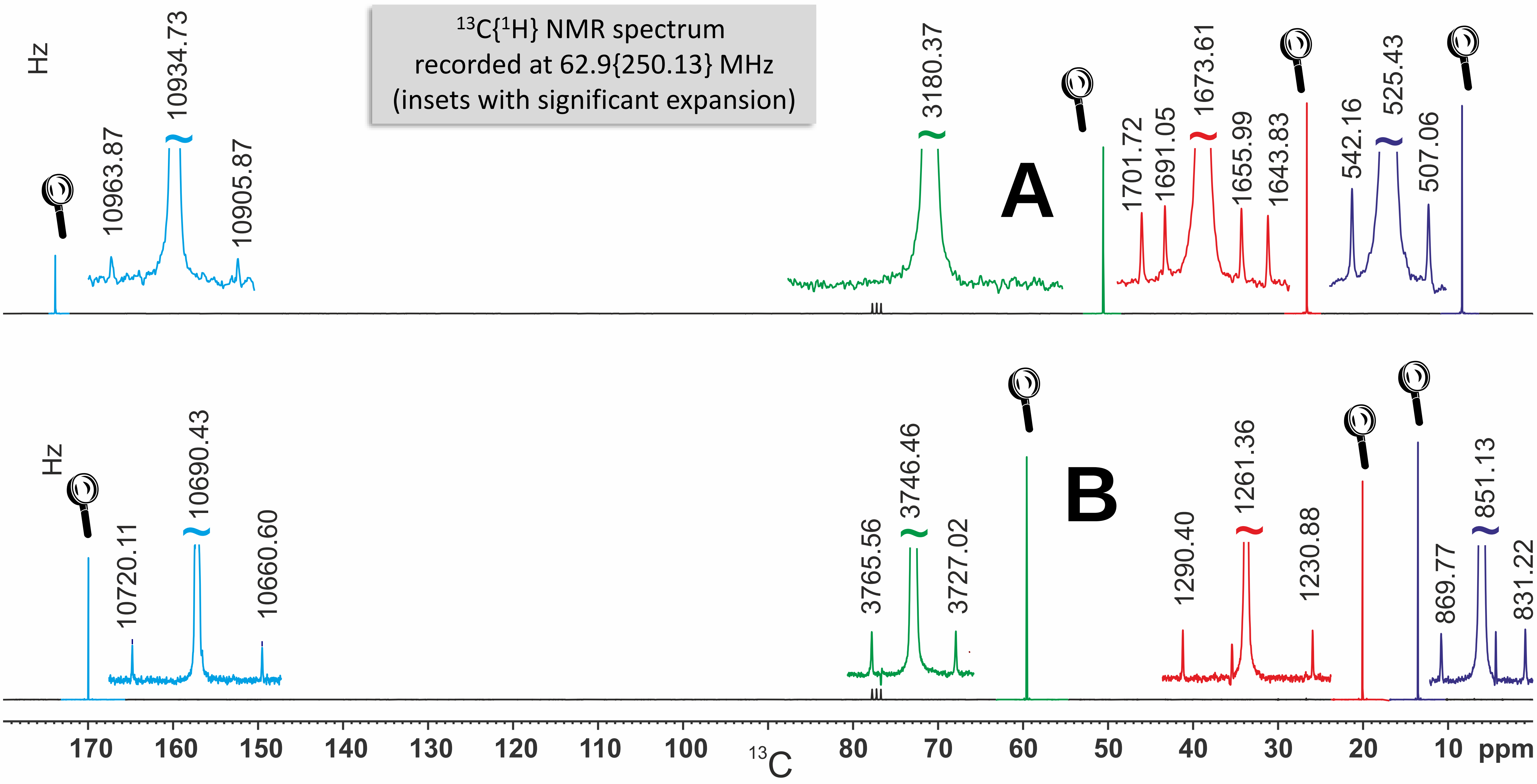
$C_4H_8O_2$ in $CDCl_3$

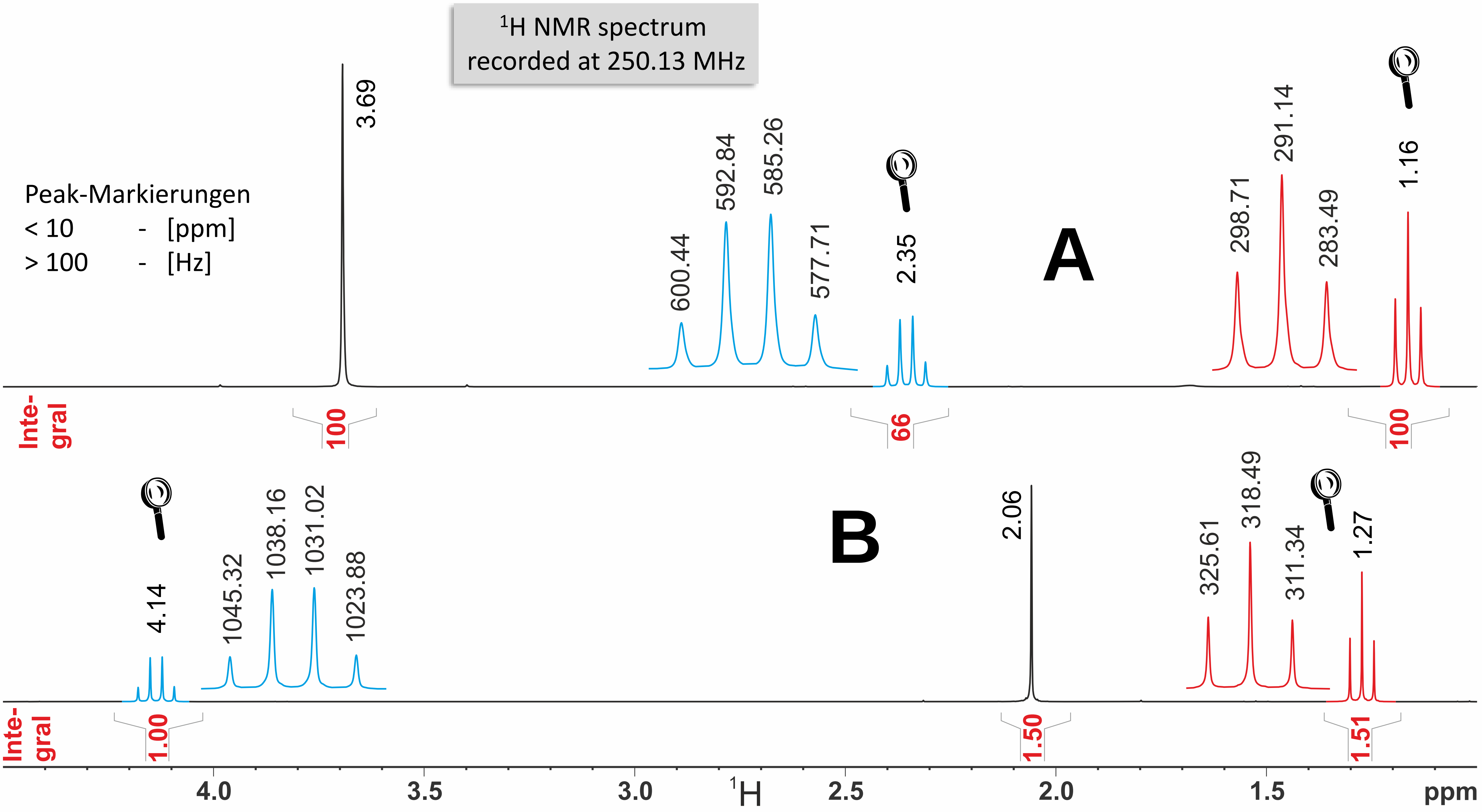


$^{13}C\{^1H\}$ NMR spectrum recorded at 62.9{250.13} MHz

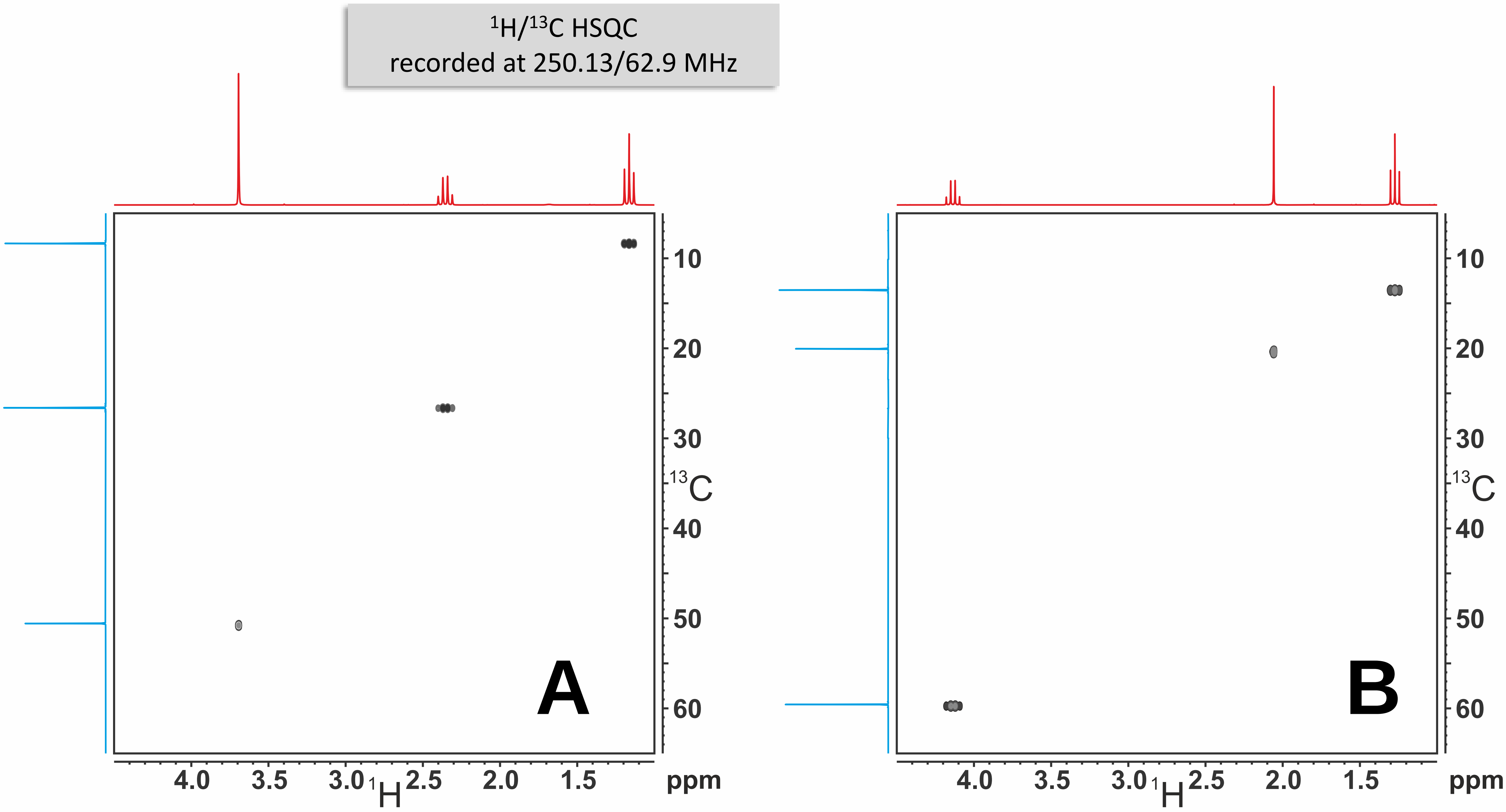
The structures of the two isomers A and B are easy to determine with the available spectra and minimal literature research.

Can you think of an alternative way that would allow you to make the determination from the spectra provided without consulting the literature?


$^{13}C\{^1H\}$ NMR spectrum
recorded at 62.9{250.13} MHz
(insets with significant expansion)
Hz
10963.87
10934.73
10905.87
3180.37
A
1701.72
1691.05
1673.61
1655.99
1643.83
542.16
525.43
507.06
Hz
10720.11
10690.43
10660.60
3765.56
3746.46
3727.02
B
1290.40
1261.36
1230.88
869.77
851.13
831.22
170
160
150
140
130
120
110
100
^{13}C
80
70
60
50
40
30
20
10
ppm



^{1}H NMR spectrum
recorded at 250.13 MHz
Peak-Markierungen
< 10 - [ppm]
> 100 - [Hz]
A
3.69
600.44
592.84
585.26
577.71
2.35
298.71
291.14
283.49
1.16
Inte-
gral
100
66
100
B
4.14
1045.32
1038.16
1031.02
1023.88
2.06
325.61
318.49
311.34
1.27
Inte-
gral
1.00
1.50
1.51
4.0
3.5
3.0
^{1}H
2.5
2.0
1.5
ppm



$^1H/^{13}C$ HSQC
recorded at 250.13/62.9 MHz

Problem of the Month

December 2022

Solution

Basics

Integration,double bond equivalents, symmetry

$C_4H_8O_2$ in $CDCl_3$

Let us take isomer **B** to get the constitution. The procedure would be exactly the same for isomer **A**.

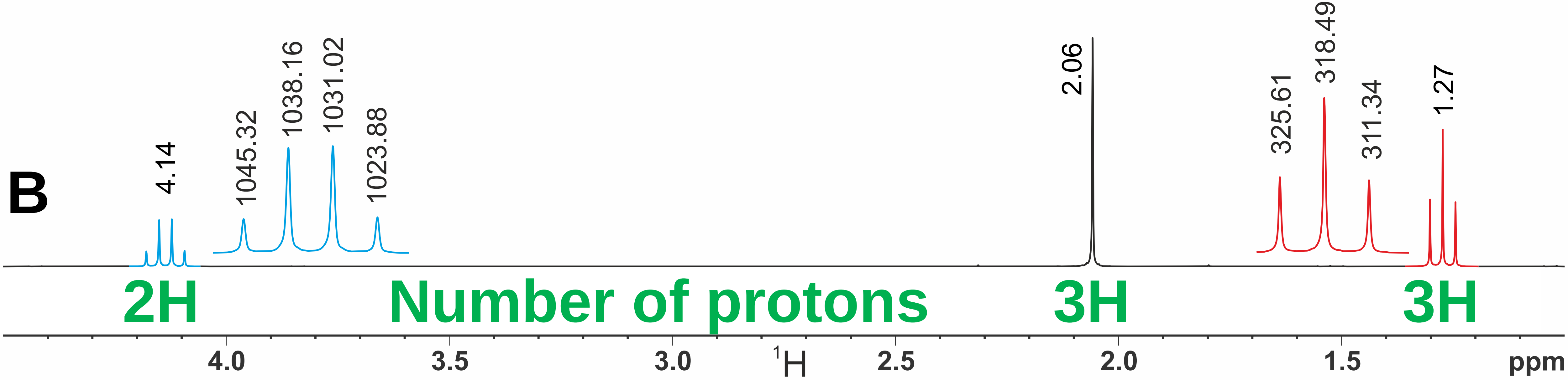
In both isomers, as well as the same molecular formula, we have:

- the same number of carbon signals and
- the same proton multiplets with the same corresponding integrals.

The main difference is

- the chemical shift of the quartet.

The integration of the proton spectrum of isomer **B** is easy. We only have to multiply each integral by a factor of 2.

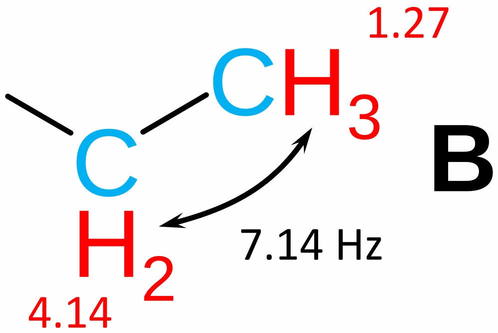


Basics

Integration,double bond equivalents, symmetry

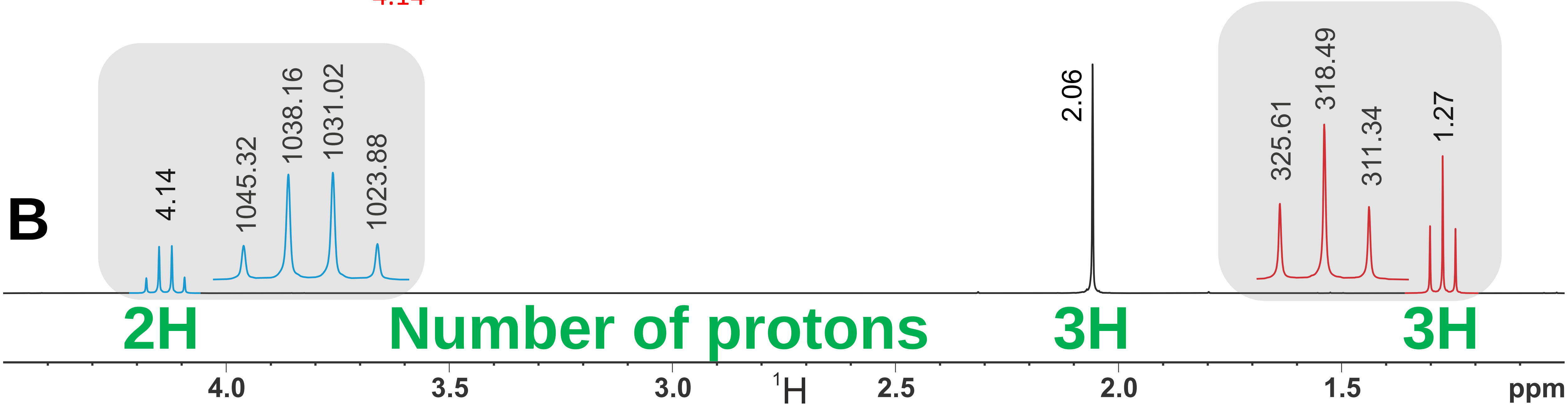
$C_4H_8O_2$ in $CDCl_3$

We have only two multiplets with a typical vicinal coupling constant of **7.14 Hz**. An ethyl group easily explains a quartet with two protons and a triplet with 3 protons.



B

B

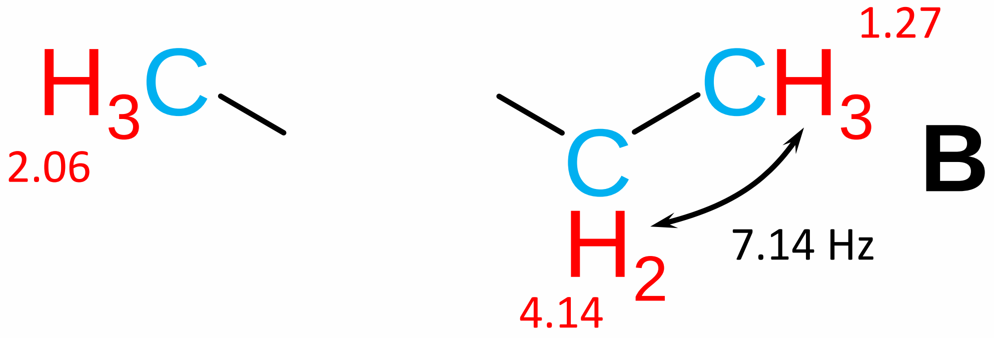


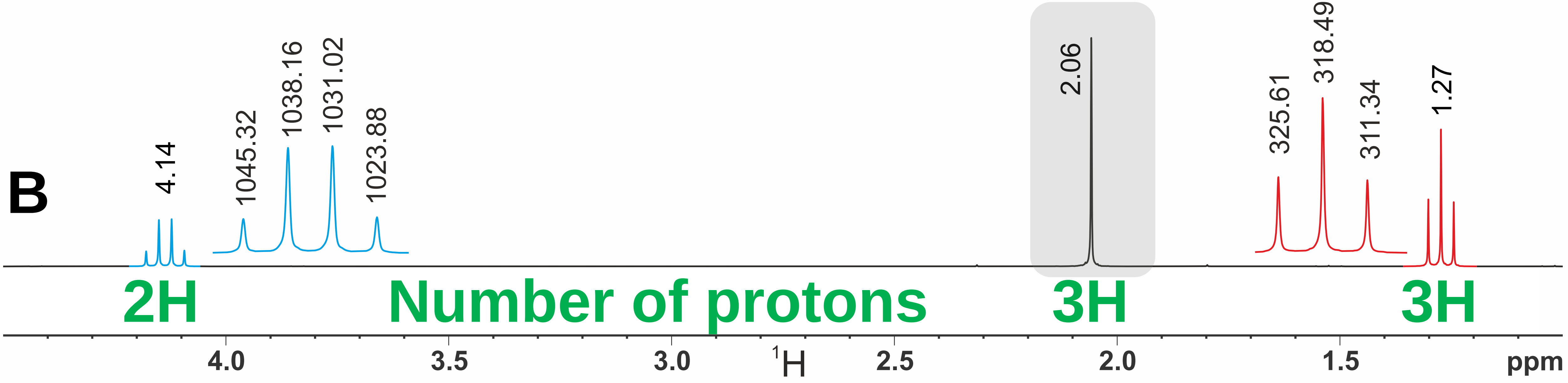
Basics

Integration,double bond equivalents, symmetry

$C_4H_8O_2$ in $CDCl_3$

A singlet with three protons has to be a methyl group.





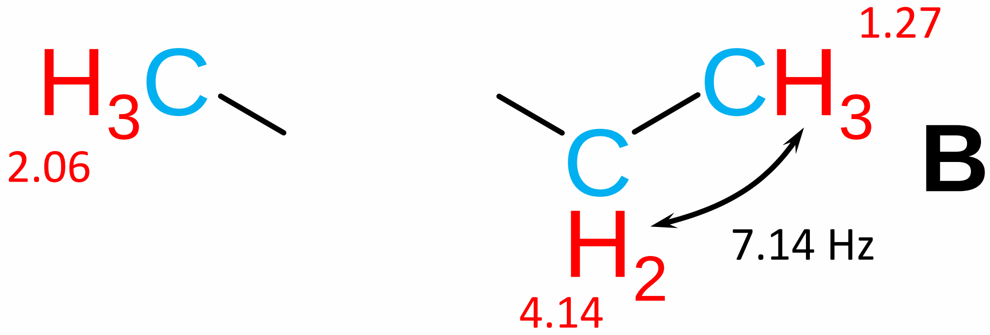
Basics

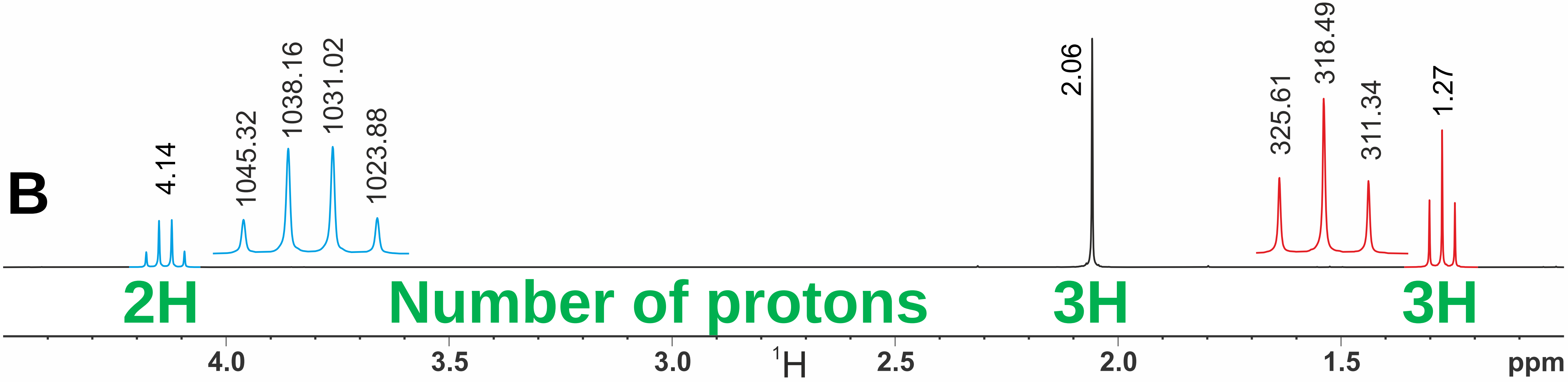
Integration,double bond equivalents, symmetry

$C_4H_8O_2$ in $CDCl_3$

The sum of both fragments is C_3H_8, which means we still have to assign

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





Basics

Integration,double bond equivalents, symmetry

$C_4H_8O_2$ in $CDCl_3$

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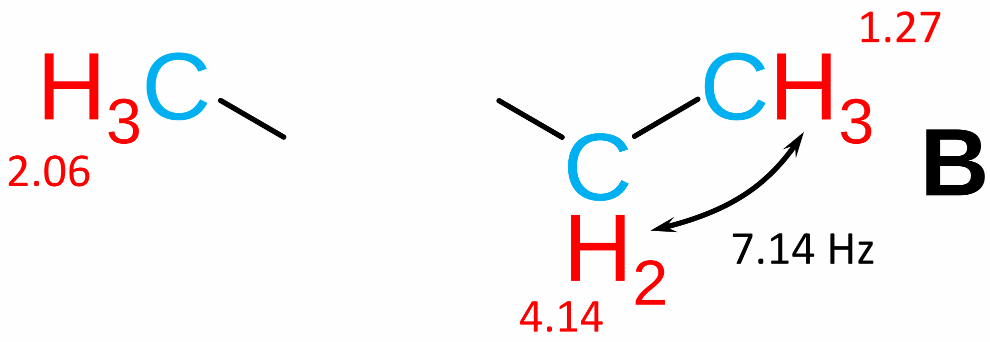
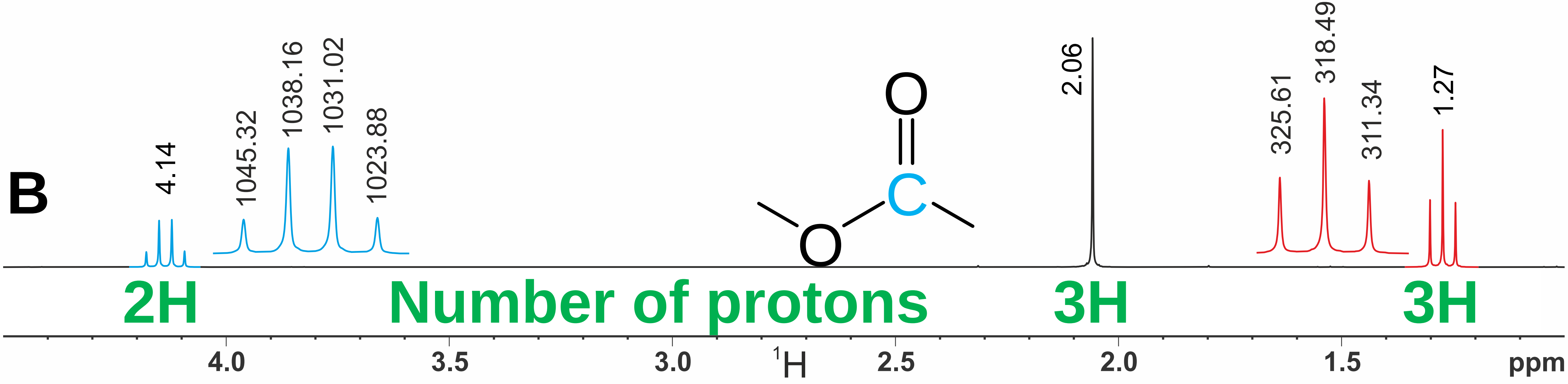


B

The result is this fragment with two possibilities to insert it between our already existing parts of the molecule.

Simply let us try both possibilities.



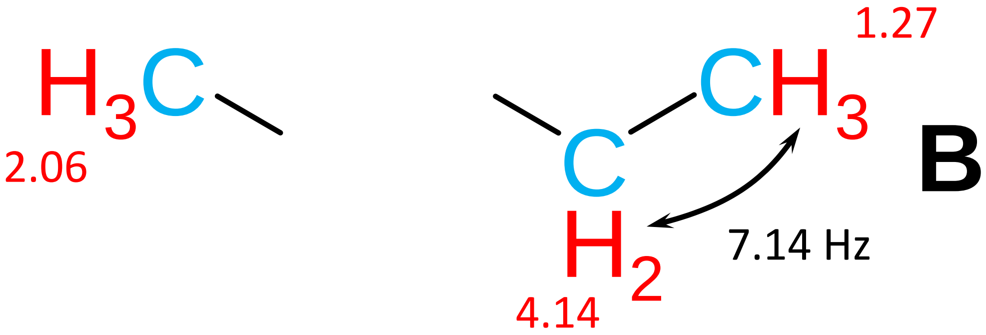
Basics

Integration,double bond equivalents, symmetry

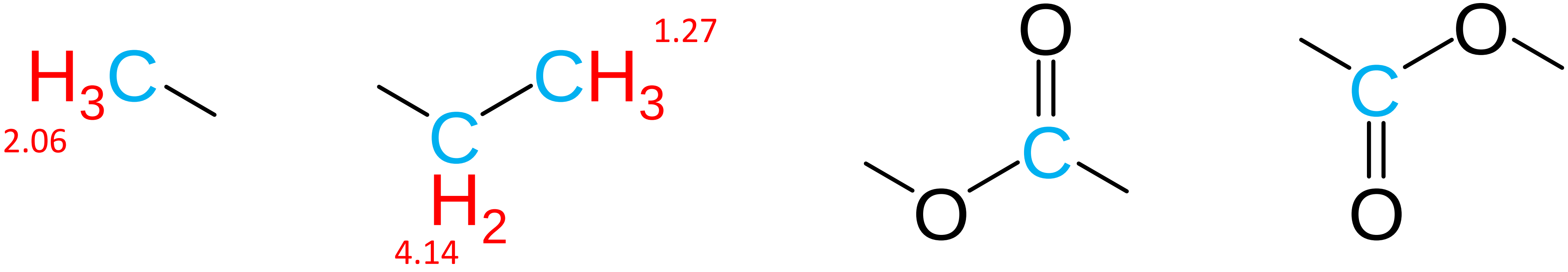
$C_4H_8O_2$ in $CDCl_3$

What we have to do is to create a copy of all already known pieces of information with a minor different geometric orientation of the –CO–O– group.

Now there are two possible final structures.



B



Basics

Integration,double bond equivalents, symmetry

$C_4H_8O_2$ in $CDCl_3$

Now there are two possible final structures.

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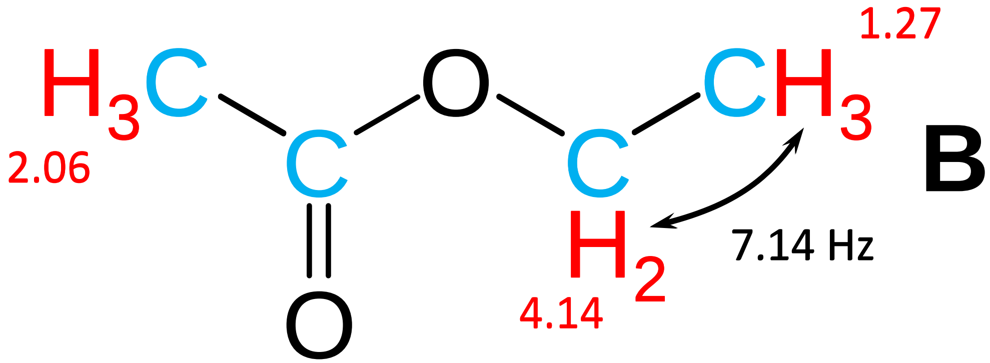
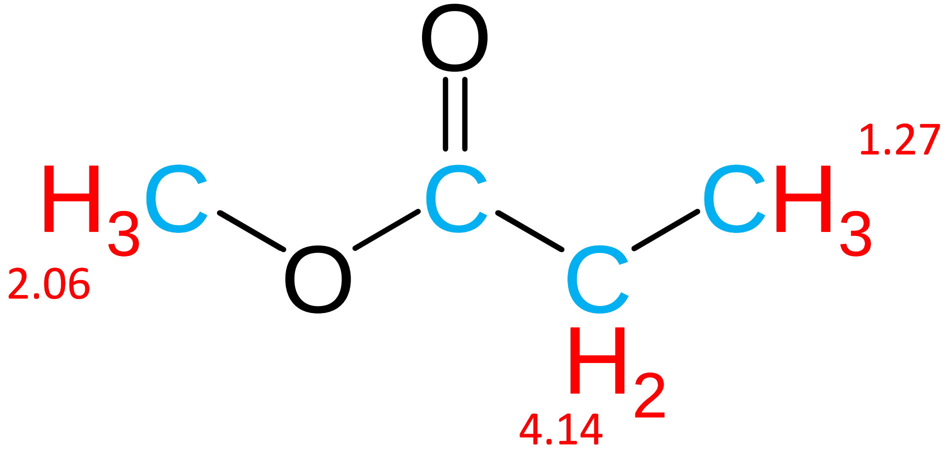
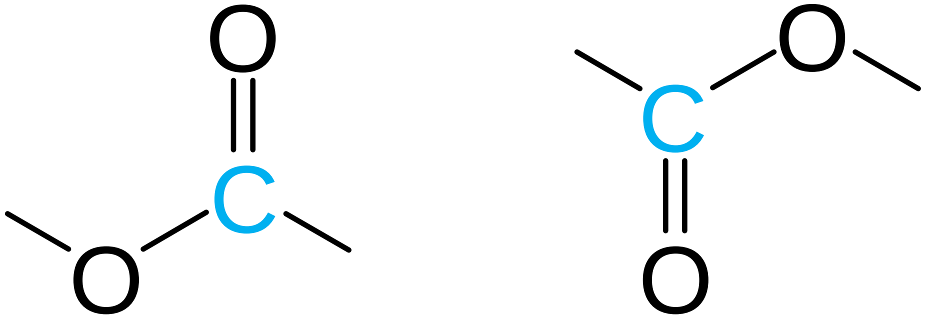


B

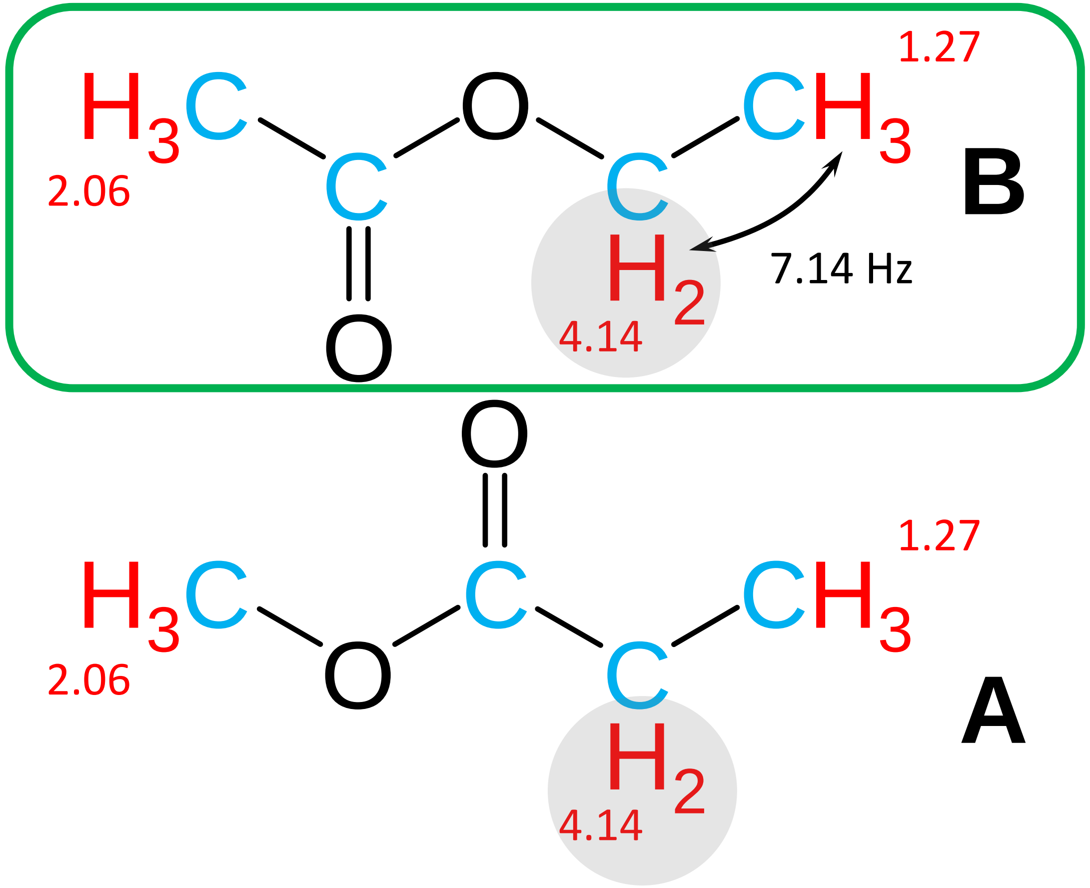




Easy solution

Now there are two possible final structures.

The easiest way to select the correct one is the estimation of the chemical shifts of the methylene protons. That‘s possible using the good old Schoolery rules.



$\delta(CH_2) = (0.23 + 0.47 + 3.13)$ ppm = **3.83 ppm**

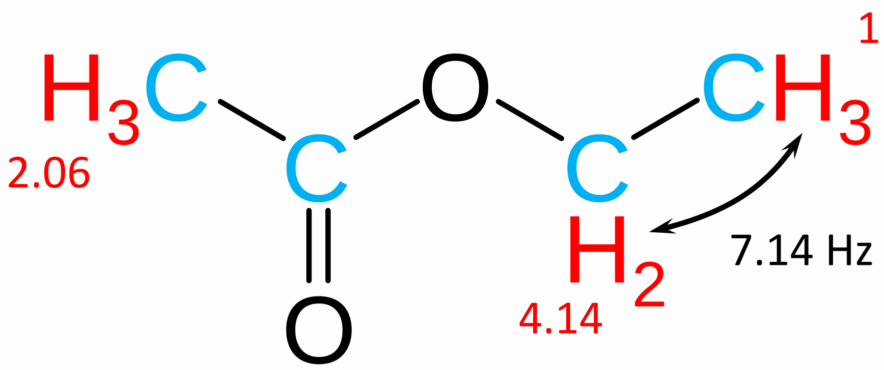
$\delta(CH_2) = (0.23 + 0.47 + 1.55)$ ppm = **2.25 ppm**

Apparently this estimation best fits to the upper structure. The lower structure appently belongs to isomer **A**, but of course all chemical shifts derived for isomer **B** are wrong. Let‘s remove all of them.

Full assignment

Carbon signals

We didn‘t assign the carbon chemical shifts so far. For this task, of course, our spectrum of choice is the HSQC.



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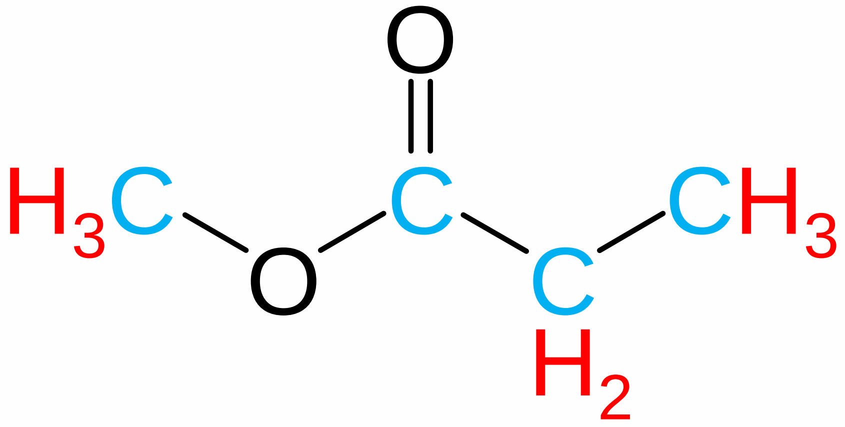
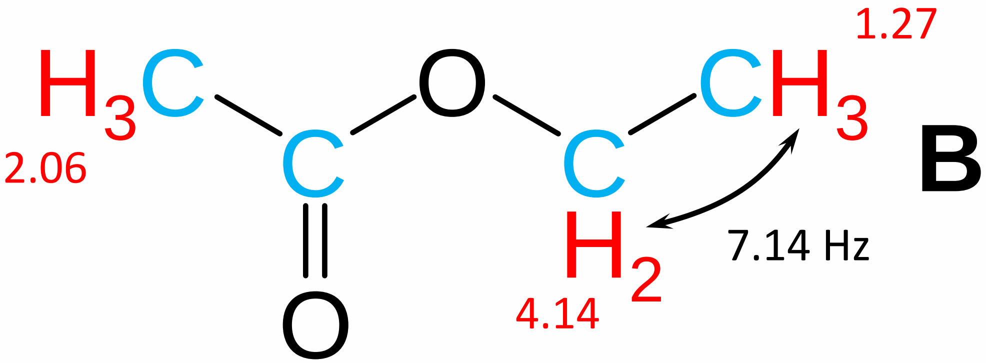


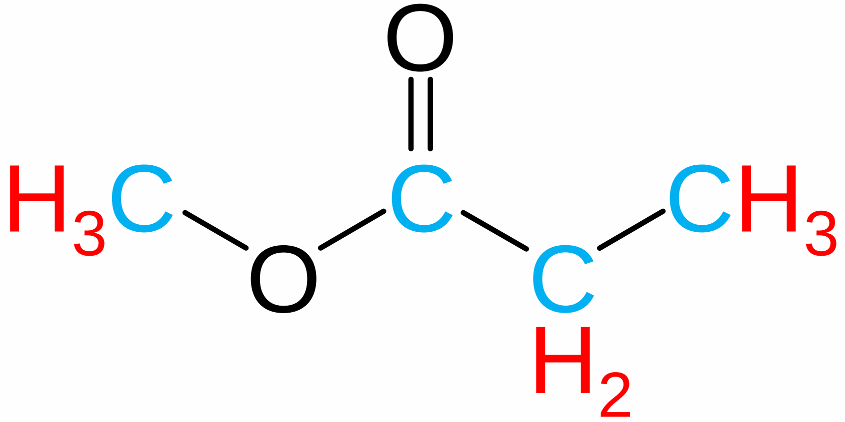
A

We didn‘t assign the carbon chemical shifts so far. For this task, of course, our spectrum of choice is the HSQC.

The chemical shifts for the pseudo projections come from the one dimensional proton and carbon spectra.



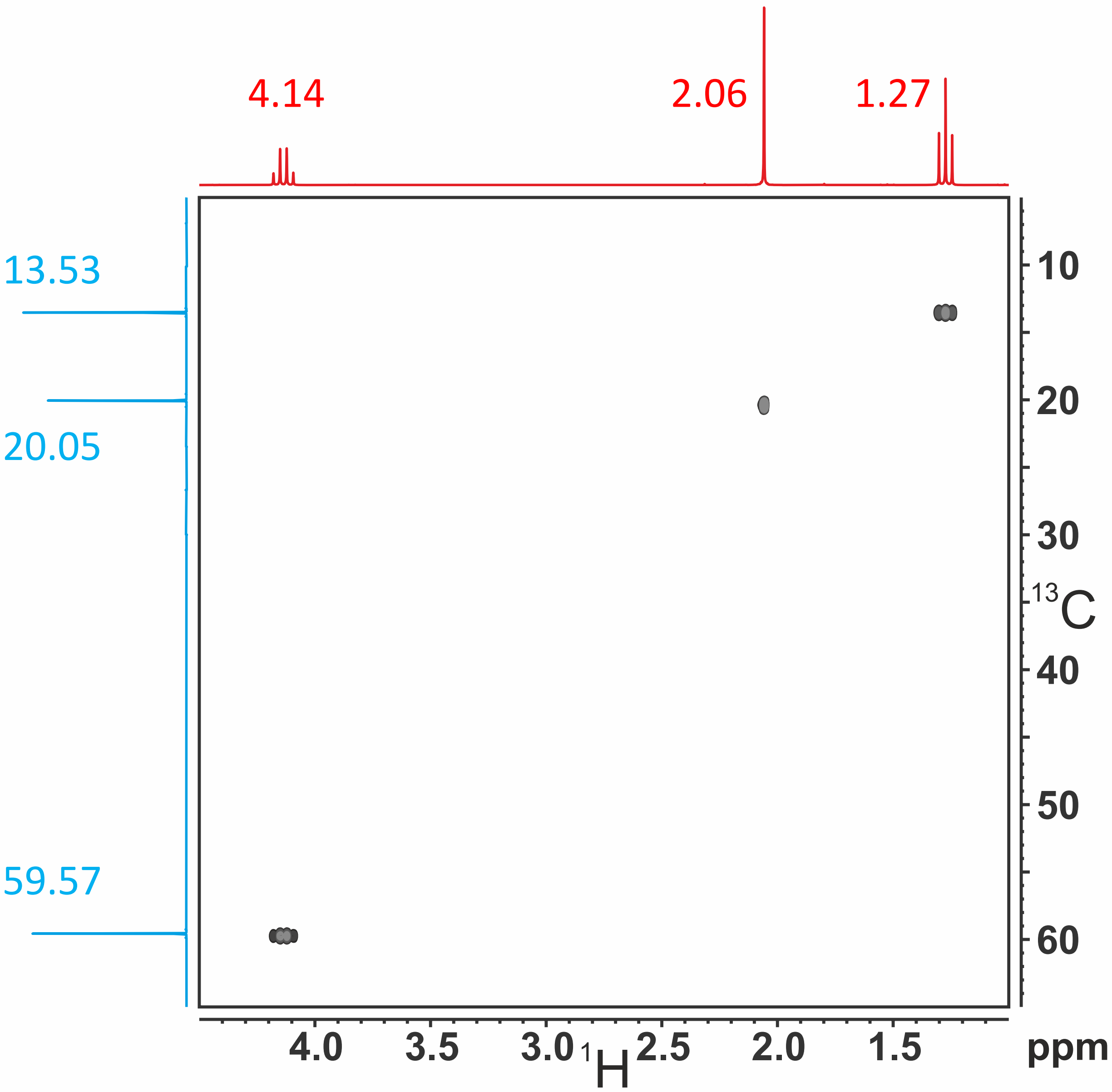
B



A

Full assignment

Carbon signals

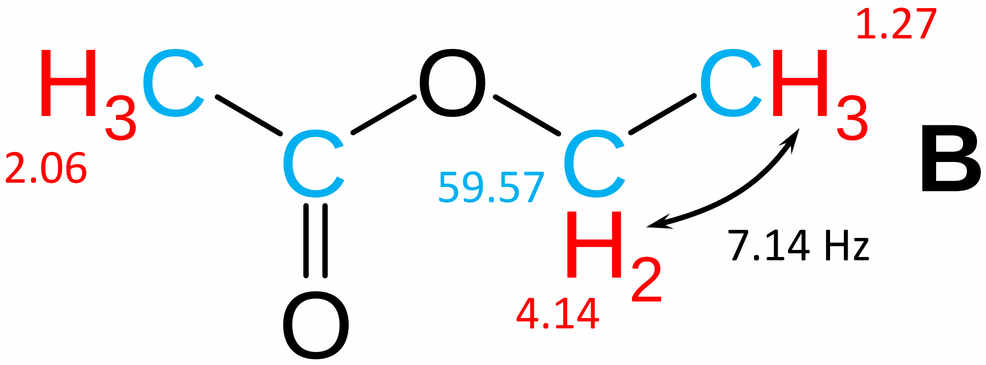


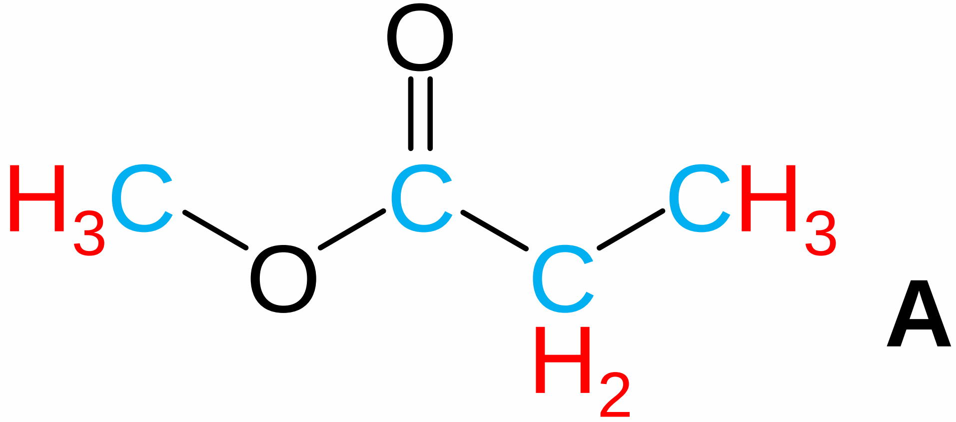
Full assignment

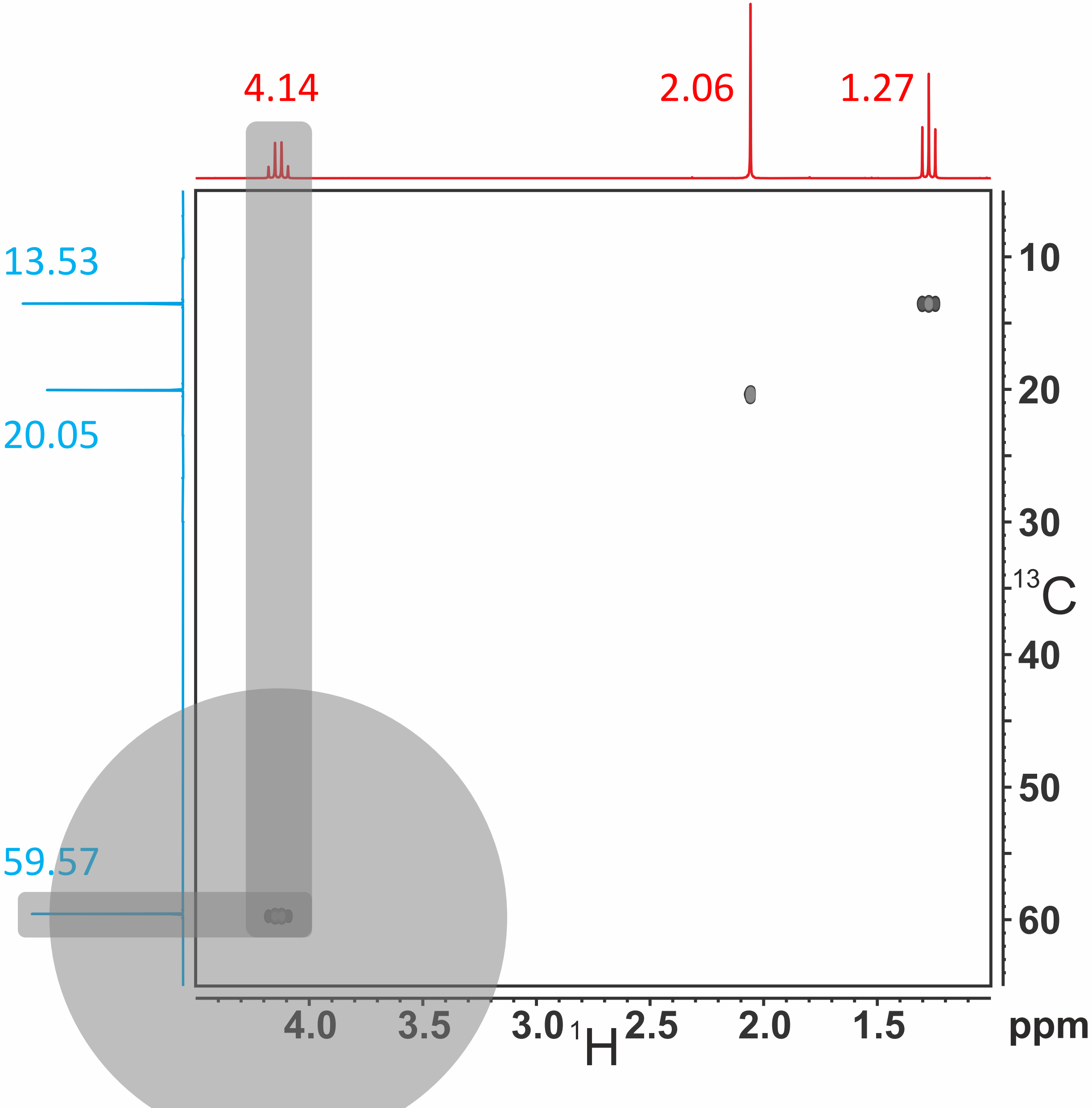
Carbon signals

Let‘s select one cross peak to demonstrate the carbon signal assignment in detail.

The assignment procedure for both methyl groups is the same.



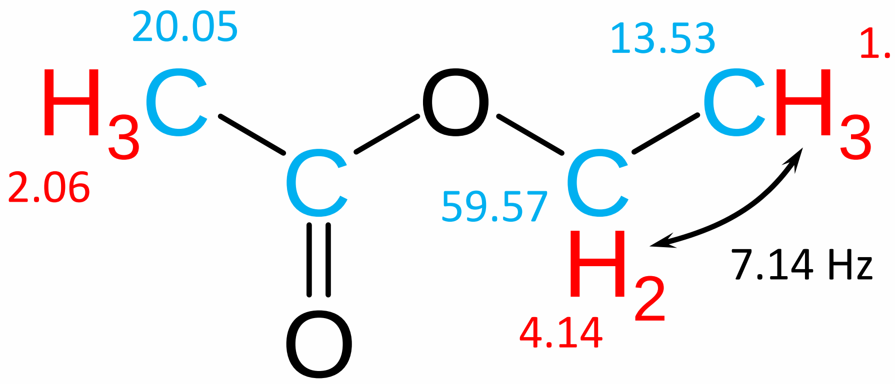




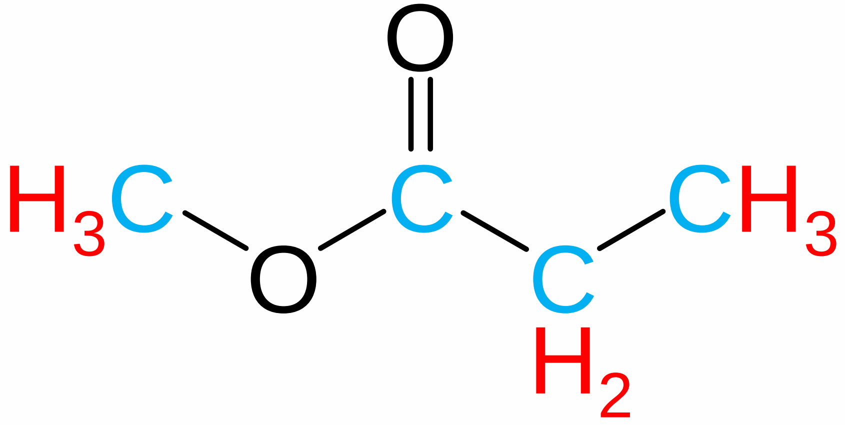
Full assignment

Carbon signals

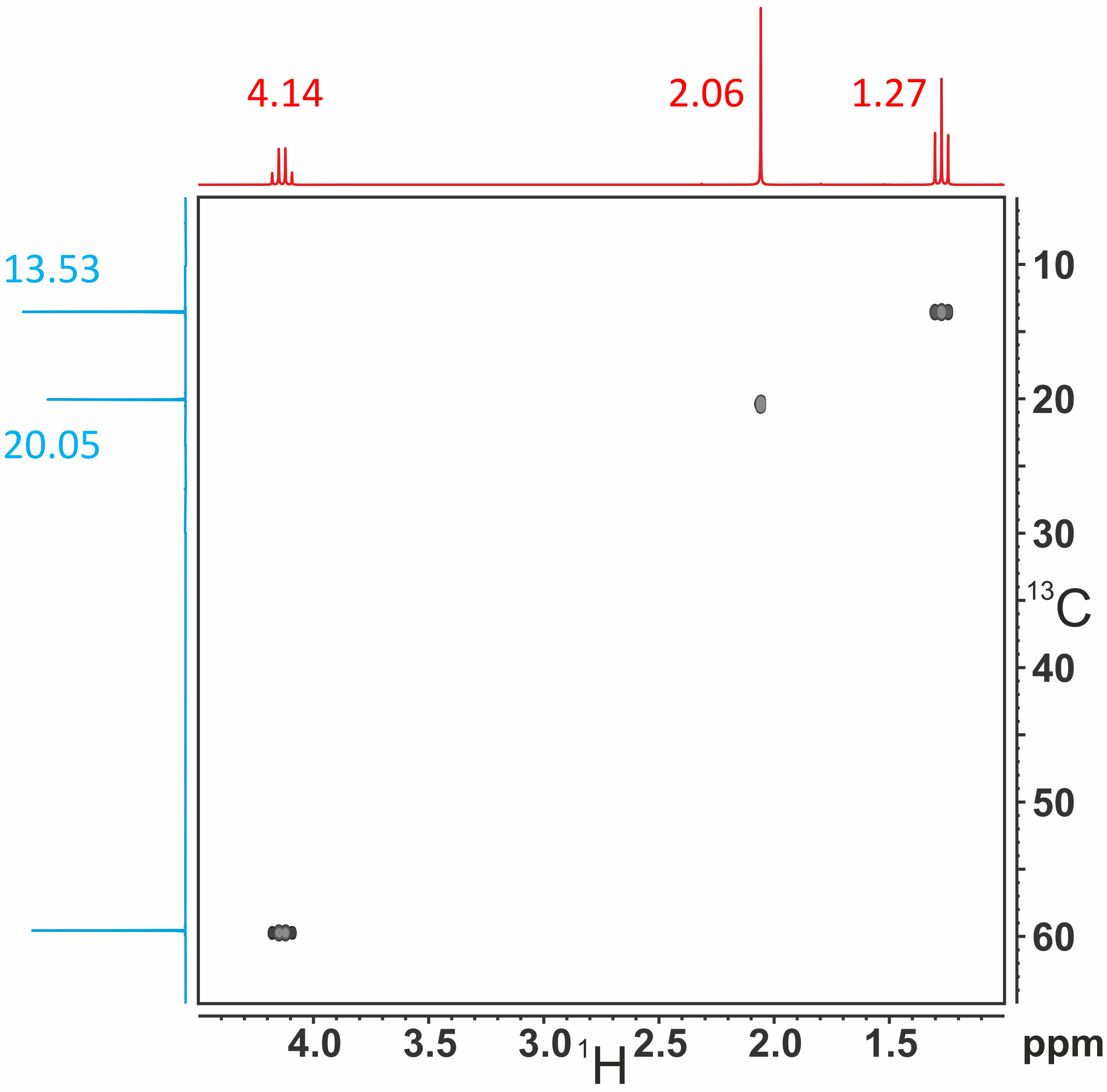
The assignment procedure for both methyl groups is the same.



B



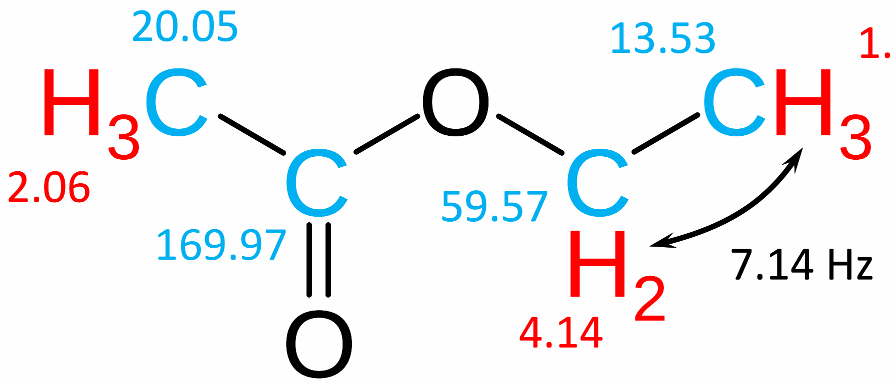
A



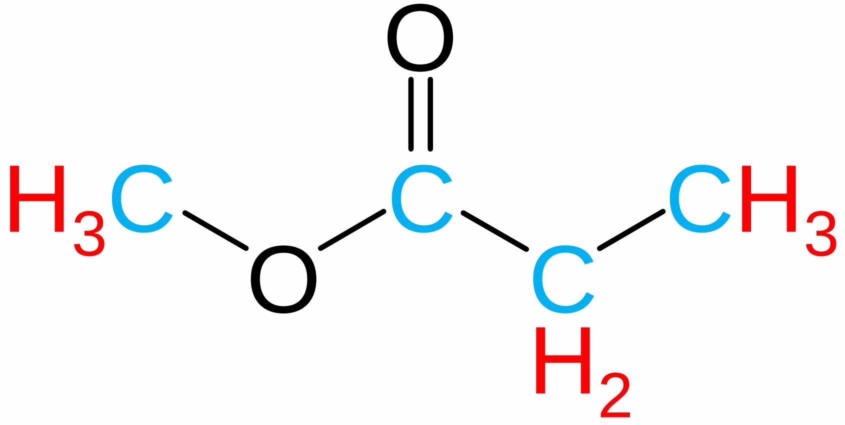
Full assignment

Carbon signals

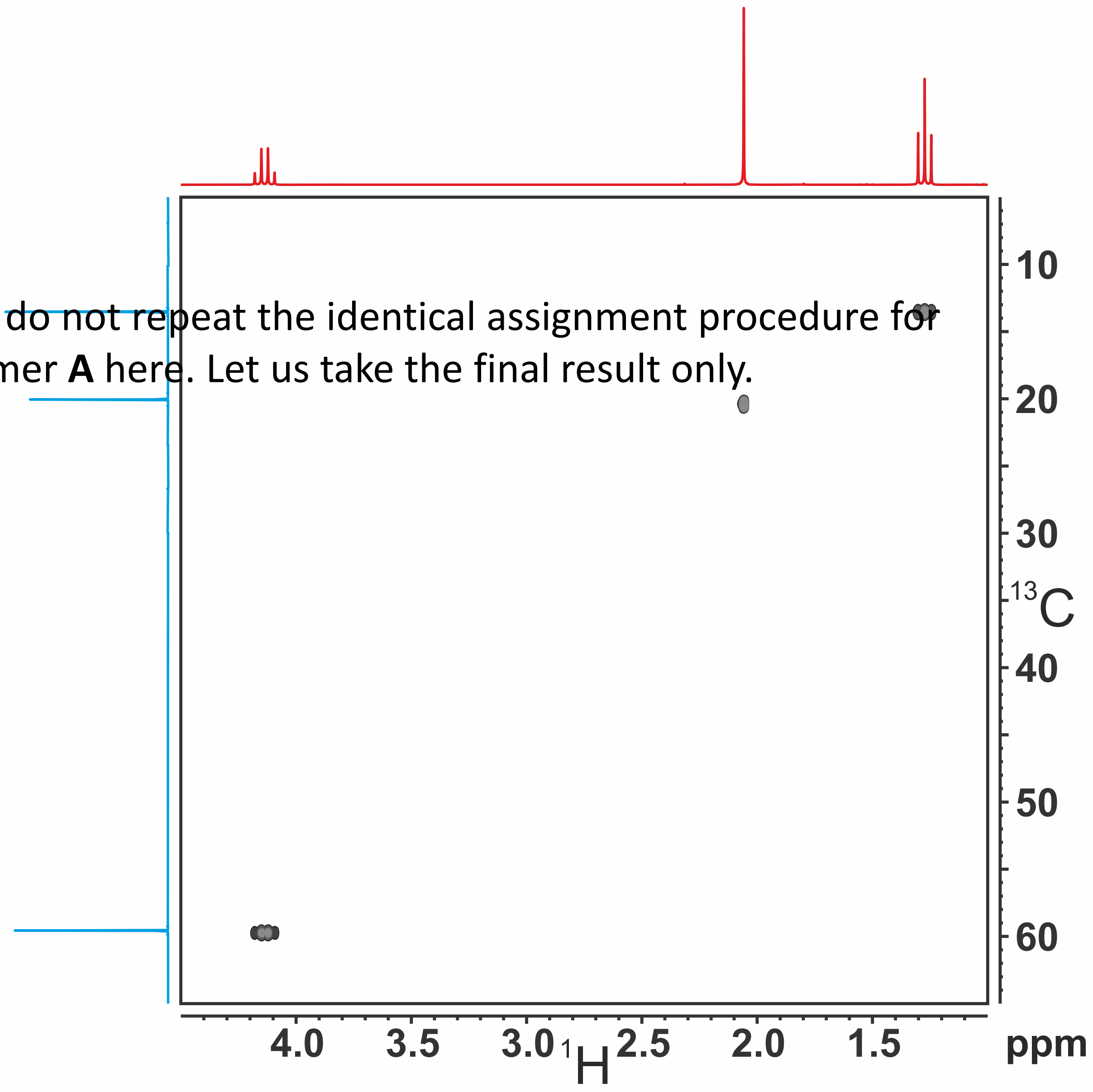
The chemical shift for the carbonyl group carbon atom comes from the one dimensional carbon spectrum.



B



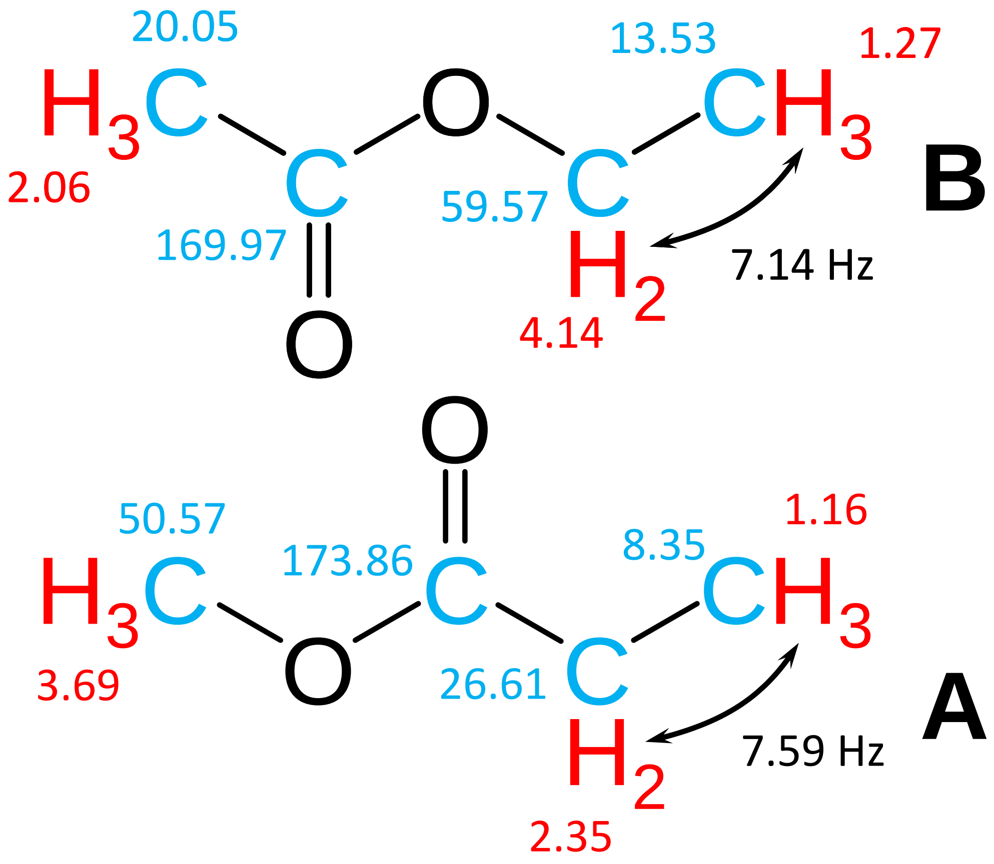
A



We do not repeat the identical assignment procedure for isomer **A** here. Let us take the final result only.

The alternative way

Don‘t use a textbook

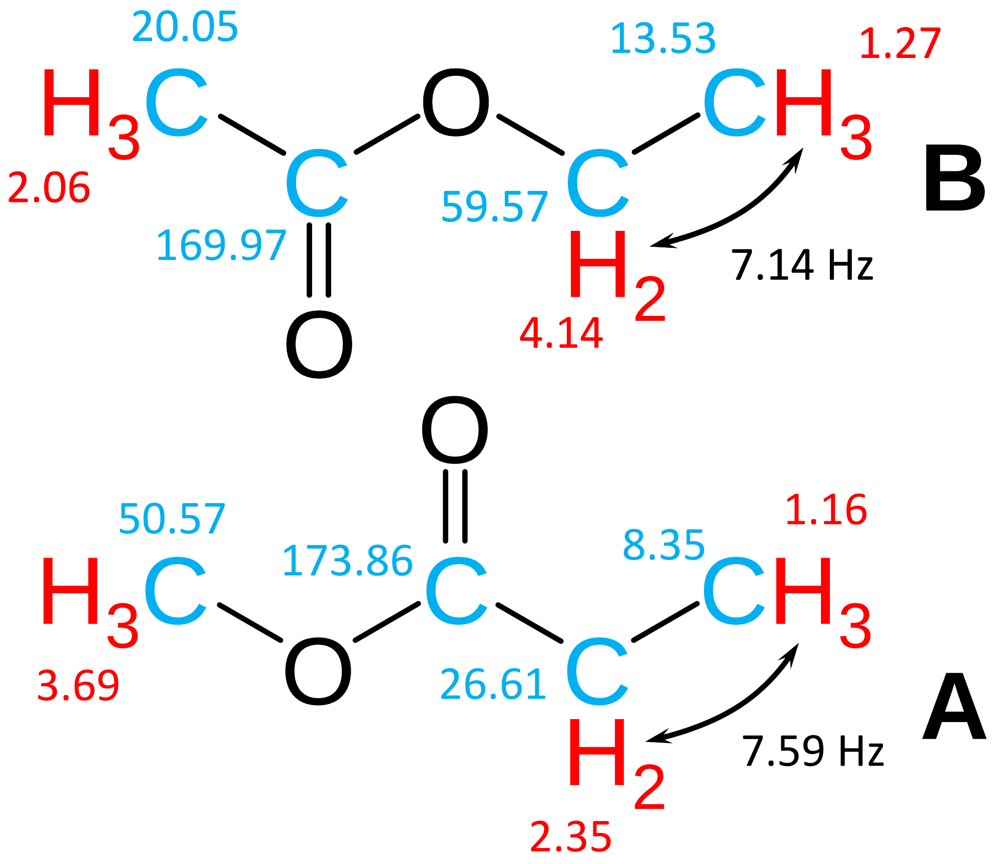


But how can we distinguish between isomer **A** and isomer **B** without using Schoolery‘s rule?

There has to be a way to differentiate between the two isomers using the carbon-carbon coupling pattern. The signal-to-noise ratio of the carbon spectrum is good enough to show these couplings.
But how to use these couplings without refering to a textbook about the typical size of such coupling constants?

The alternative way

Don‘t use a textbook

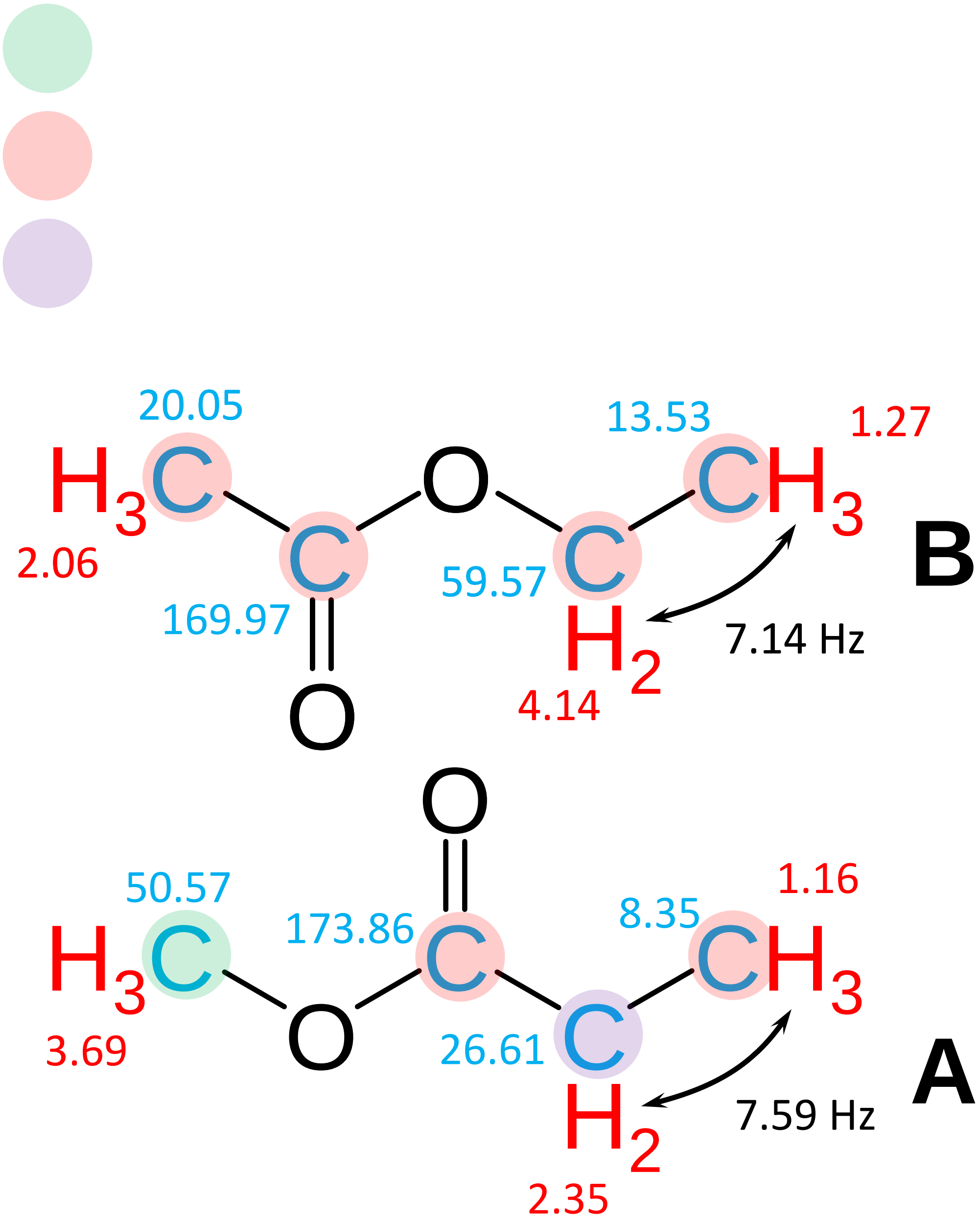


Do you see any difference between the isomers, which might be helpful in using the carbon-carbon satellites without any prior knowledge?

It is a question of pattern recognition. But, what on earth might be the pattern?

The alternative way

Don‘t use a textbook



Do you see any difference between the isomers, which might be helpful in using the carbon-carbon satellites without any prior knowledge?

It is a question of pattern recognition. But, what on earth might be the pattern?

Let us label the eight carbon atoms using three different colours. What could distinguish carbon atoms that have been marked with the same colour?

And now?

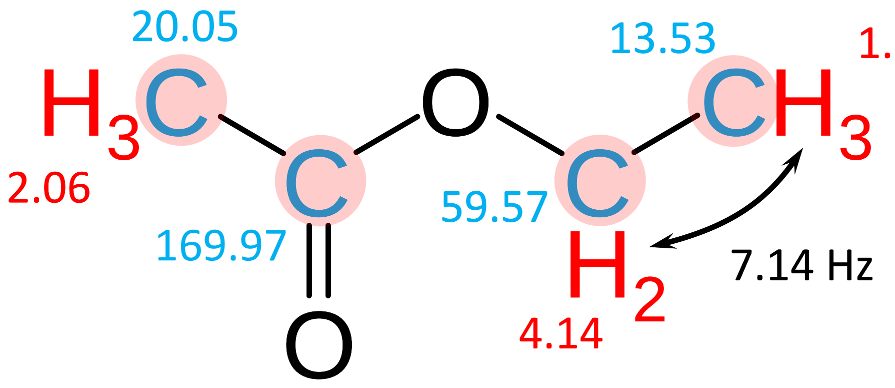
The alternative way

Don‘t use a textbook

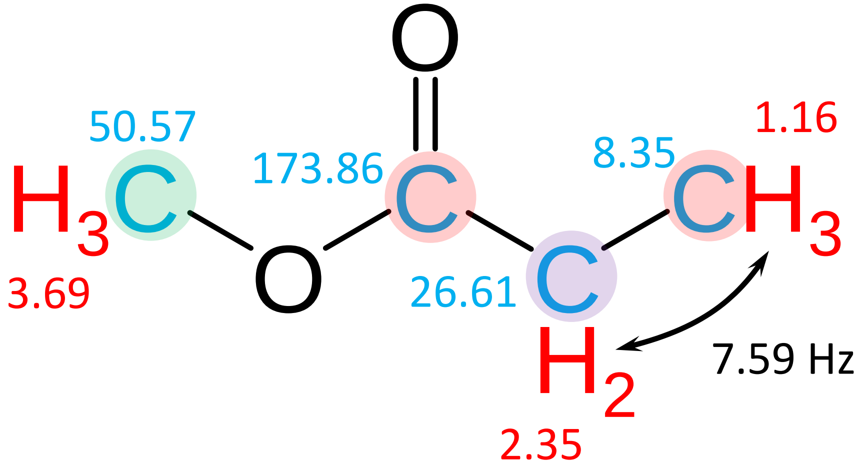
🟢 **no** neighbouring carbon atom with a distance of one bond

🔴 **one** neighbouring carbon atom with a distance of one bond

🟣 **two** neighbouring carbon atom with a distance of one bond



B



A

It is a reasonable assumption, that all one bond carbon-carbon coupling constants are of comparable size.

Each of the three cases results in a different pattern for the satellite signals due to carbon-carbon coupling.
Let us assume a model compund and think about what the pattern might look like.

Carbon-carbon couplings

Probability and spectra

We should remember, that **every** NMR spectrum is **not** the result of **one molecule**, but of a huge ensemble of molecules.

Let‘s simulate the carbon spectrum of the single (asymmetric) model compound (equivalent to the right part of isomer **A**)

— C — C — C —

(no signal at all)

≈ 97% — ^{12}C — ^{12}C — ^{12}C —

≈ 1% — ^{13}C — ^{12}C — ^{12}C —

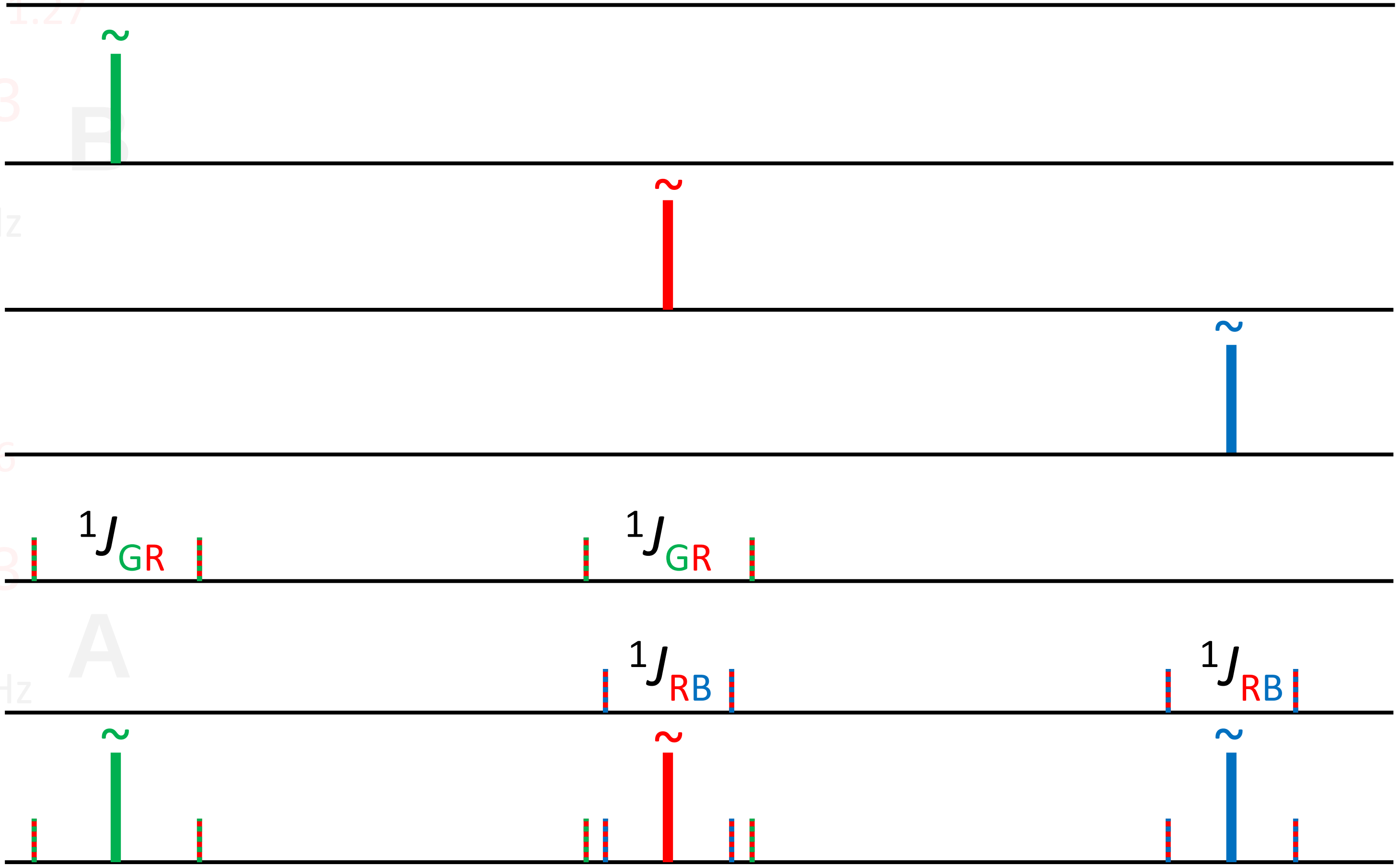
≈ 1% — ^{12}C — ^{13}C — ^{12}C —

≈ 1% — ^{12}C — ^{12}C — ^{13}C —

≈ 0.01% — ^{13}C $\overset{^1J_{GR}}{—}$ ^{13}C — ^{12}C —

≈ 0.01% — ^{12}C — ^{13}C $\overset{^1J_{RB}}{—}$ ^{13}C —

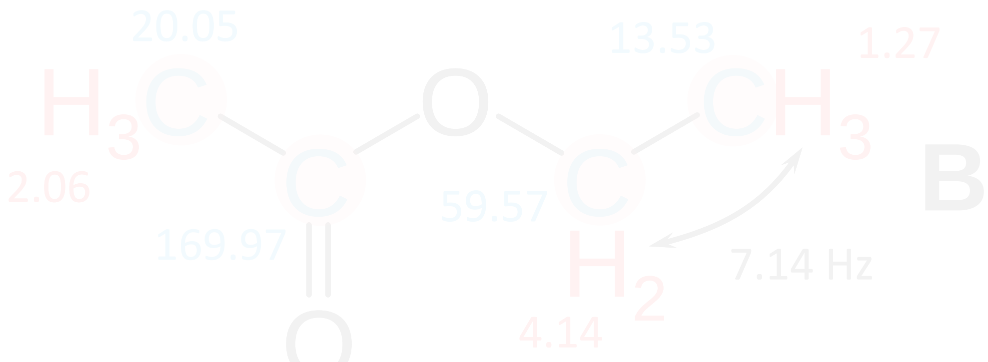
Sum of all components



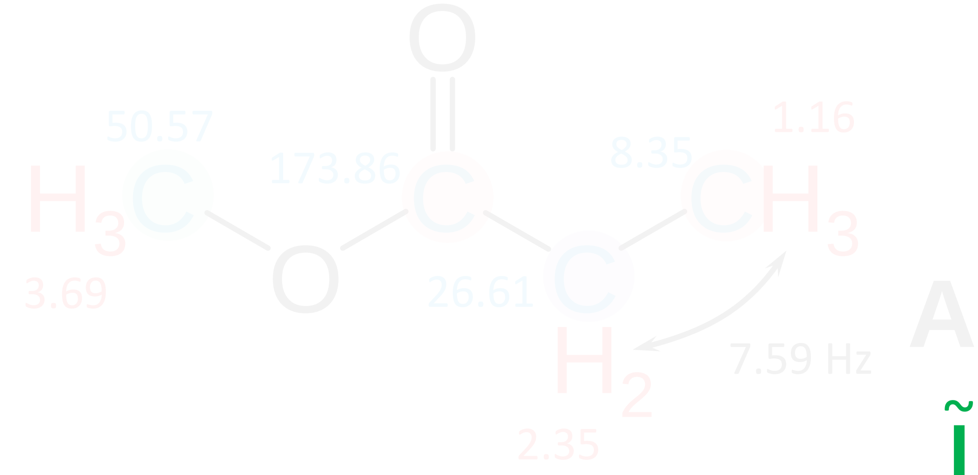
Carbon-carbon couplings

Probability and spectra

— C — C — C —



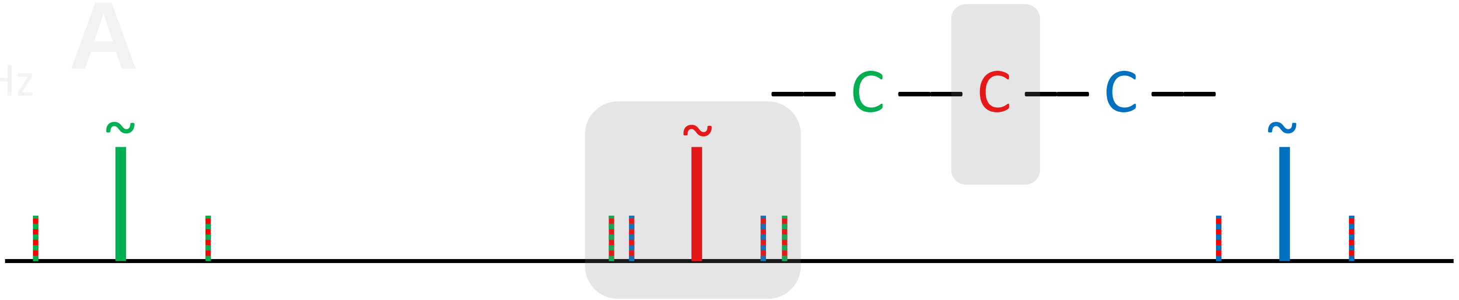
B



A

Please note, that the carbon-carbon multiplet pattern for the red carbon atom is neither a triplet nor a doublet of doublets. Rather, it is two nested independent doublets.

For a triplet or a doublet of doublets we would need three ^{13}C atoms within the same molecule. The probability is very, very low: about 0,0001%



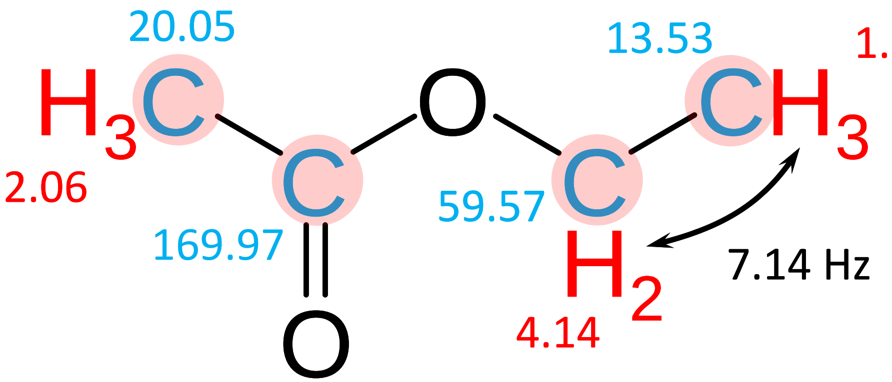
Carbon-carbon couplings

Practical use

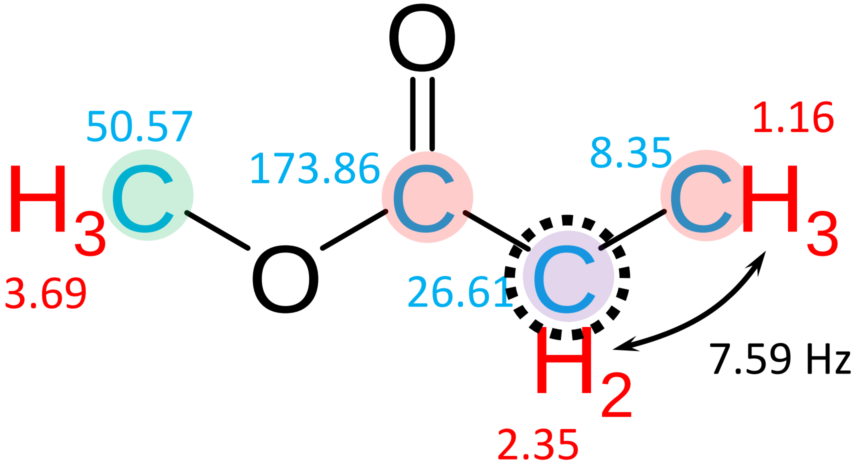
🟢 **no** satellites due to carbon-carbon coupling

🔴 **one** doublet due to carbon-carbon coupling

🟣 **two** nested doublets due to carbon-carbon coupling



B

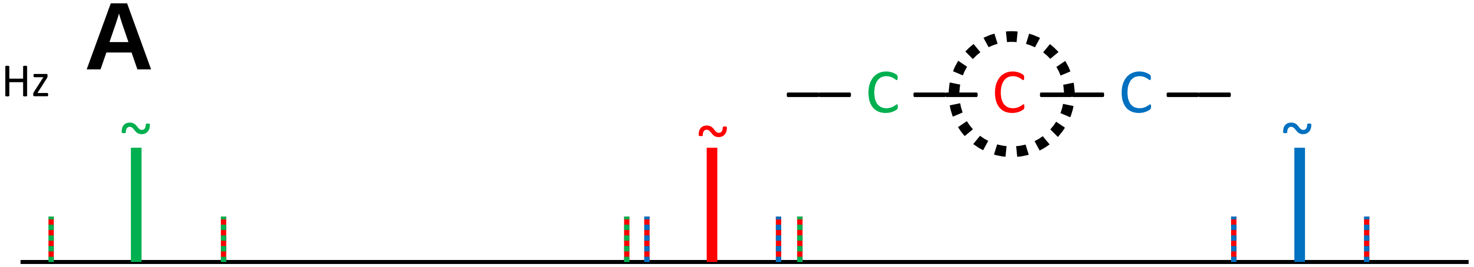


A

Which satellite pattern due to carbon-carbon coupling do we expect for the three types of carbon atoms shown before?

Apparently the coupling pattern for the carbon atom marked in mauve is unique and we have to look wether this pattern is visible in the carbon spectra of isomer **A** or isomer **B**.

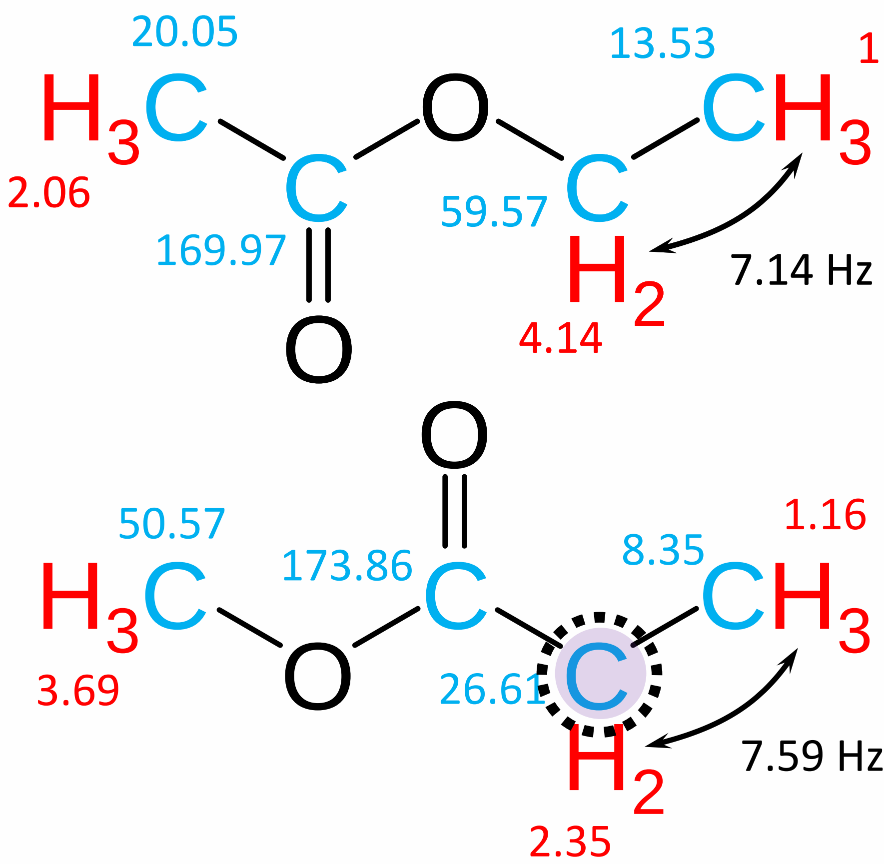
Due to the use of Schoolery‘s rule we already know the solution. Let us forget this solution to demonstrate the use of the carbon-carbon coupling pattern.

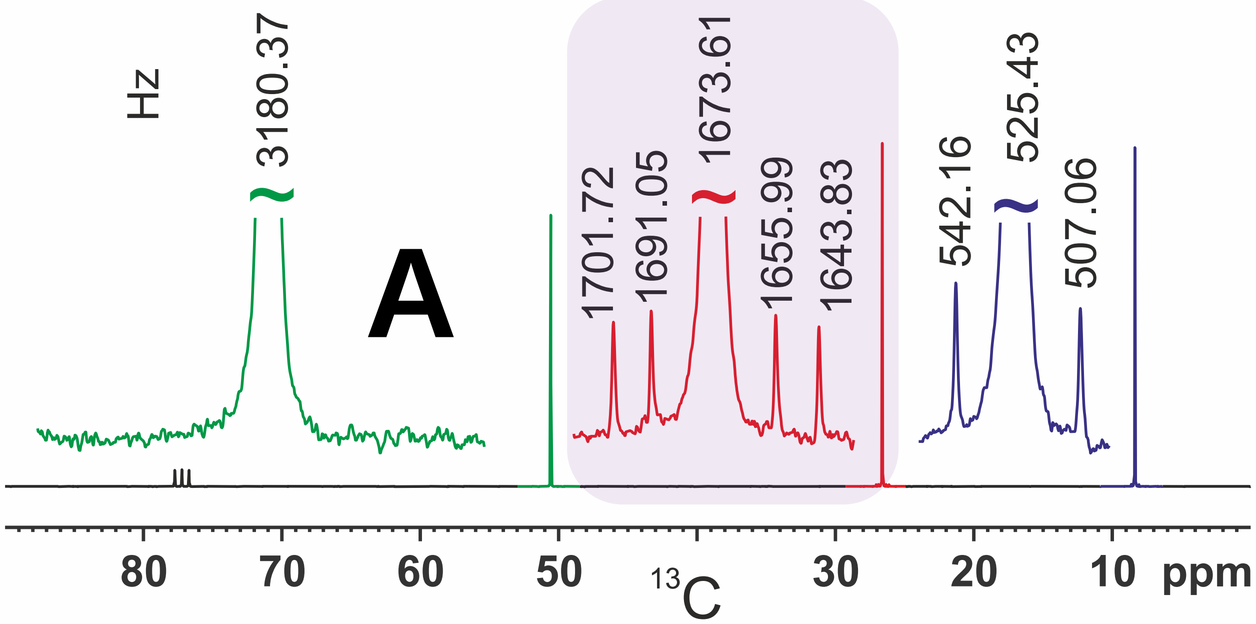


Carbon-carbon couplings

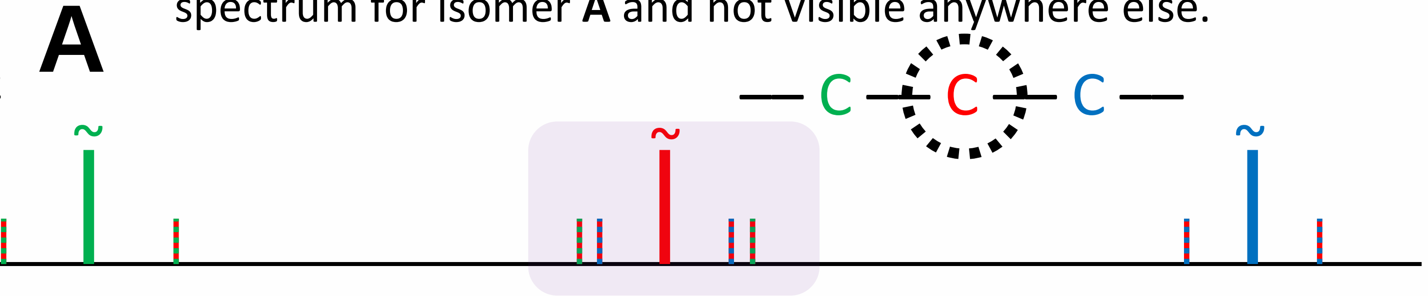
Practical use

● **two** nested doublets due to carbon-carbon coupling





The pattern we are looking for is part of the carbon spectrum for isomer **A** and not visible anywhere else.

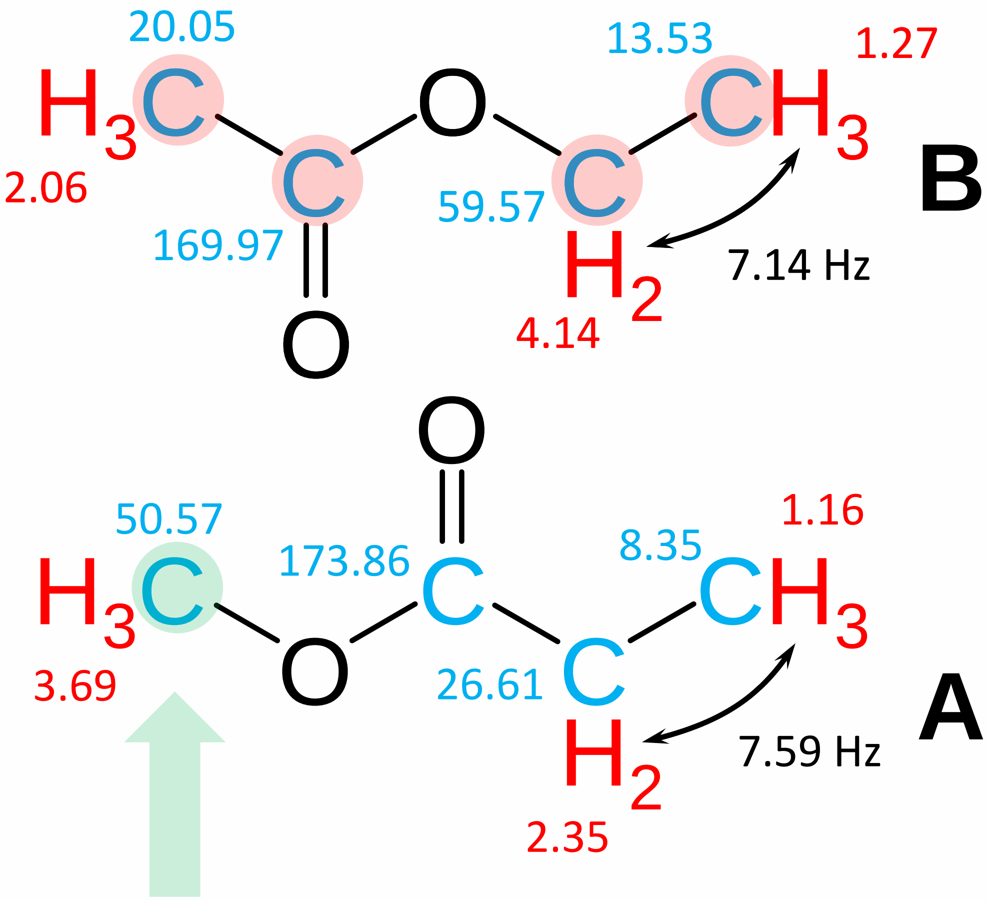


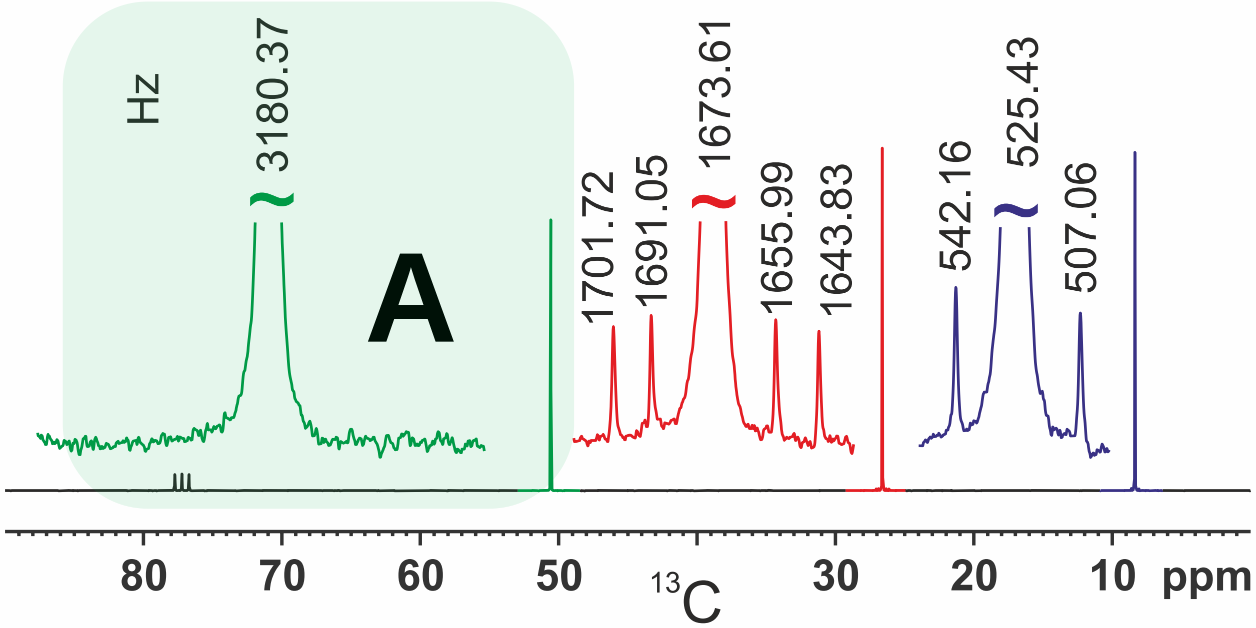
Carbon-carbon couplings

Practical use

🟢 **no** satellites due to carbon-carbon coupling

🔴 **one** doublet due to carbon-carbon coupling





The pattern we are looking for is part of the carbon spectrum for isomer **A** and not visible anywhere else.

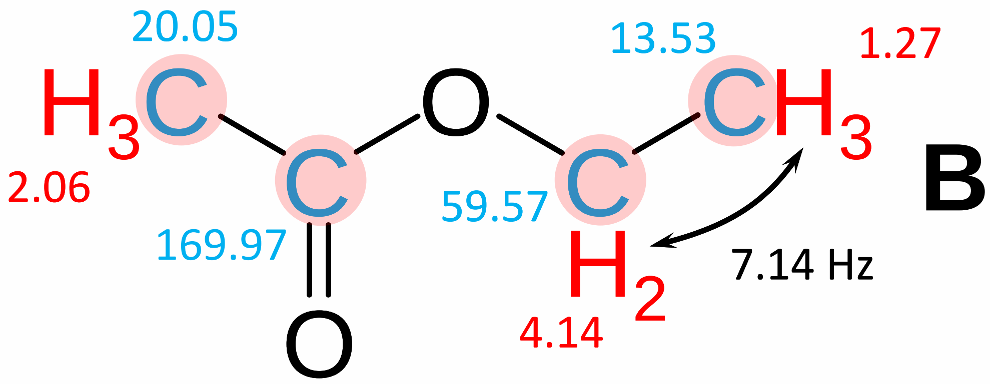
And there is no carbon-carbon splitting here.

In the case of isomer **B** we should see only doublets as satellites due to carbon-carbon coupling.
Let‘s check.

Carbon-carbon couplings

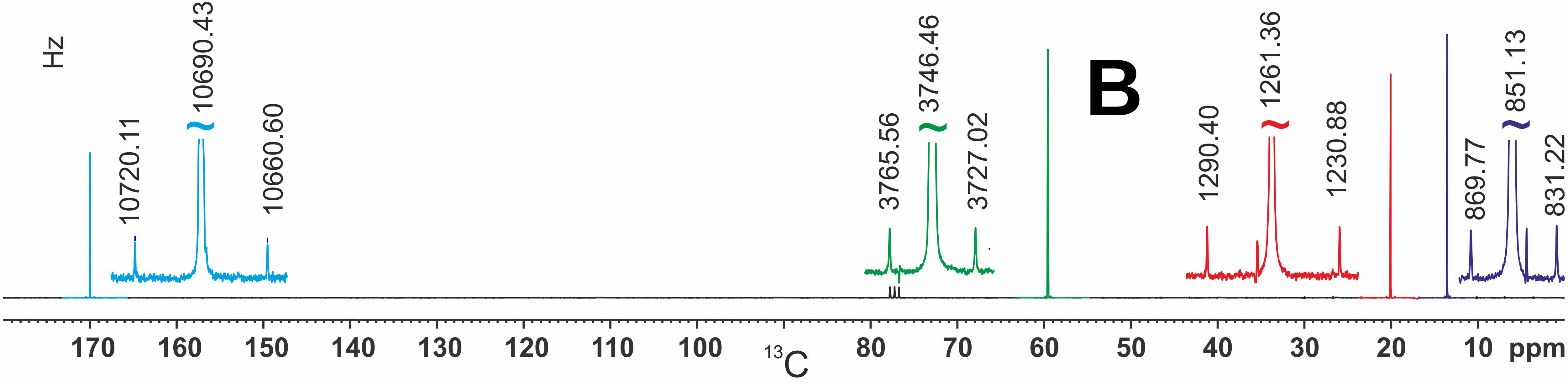
Practical use

● **one** doublet due to carbon-carbon coupling

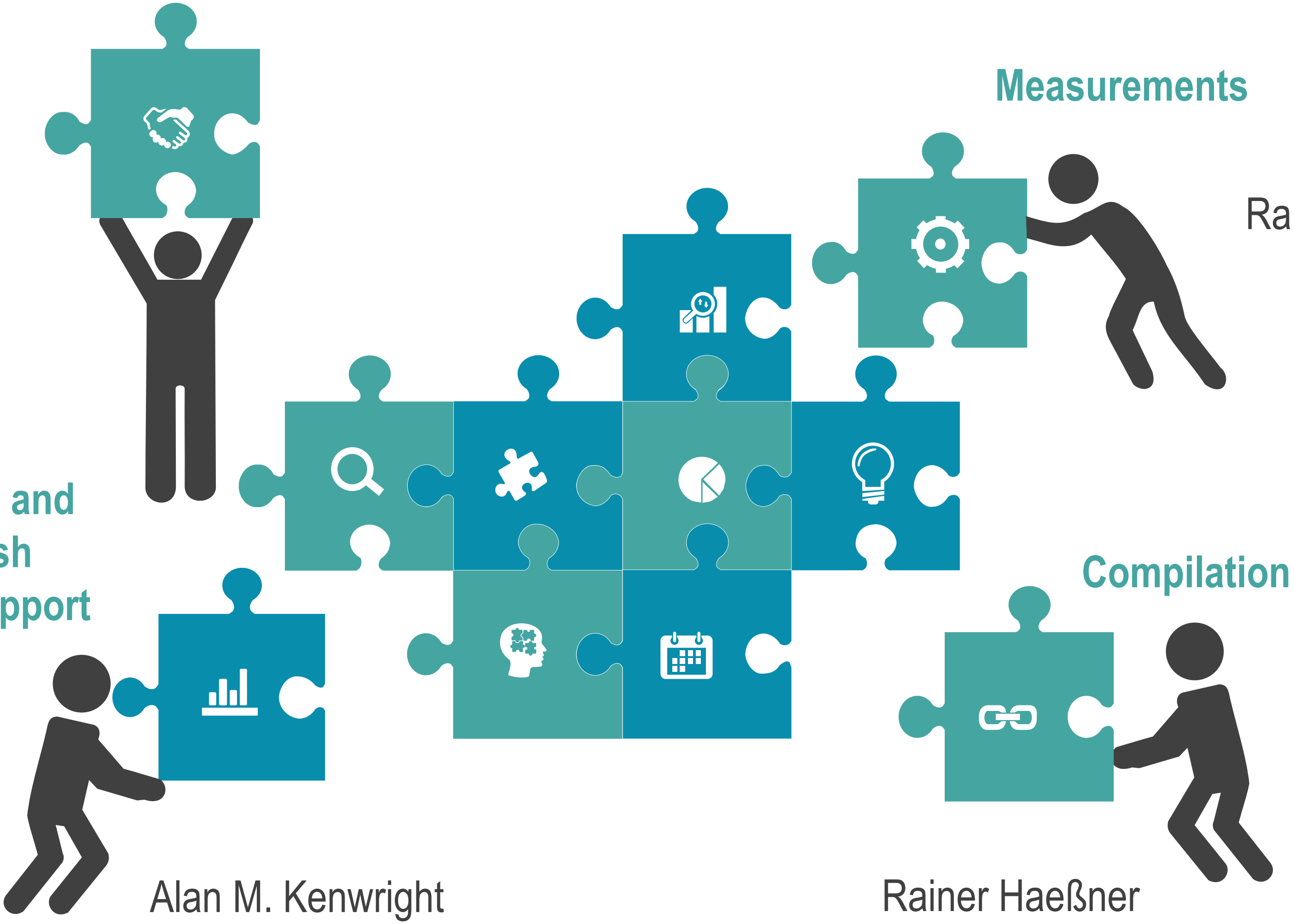


Apart from three spikes of unknown source, we see exactly the four expected doublets.

Of course, in practice, one would not solve this simple question with this enormous measurement effort. The objective here was to motivate the search for solutions off the beaten track.



Contributions



Spectrometer time

TU Munich

Measurements

Rainer Haeßner

Discussions and native English language support

Alan M. Kenwright

Compilation

Rainer Haeßner