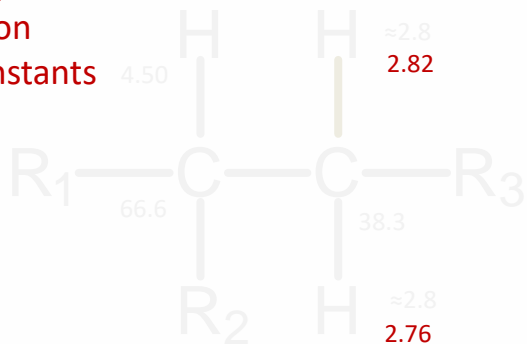


Problem of the Month:

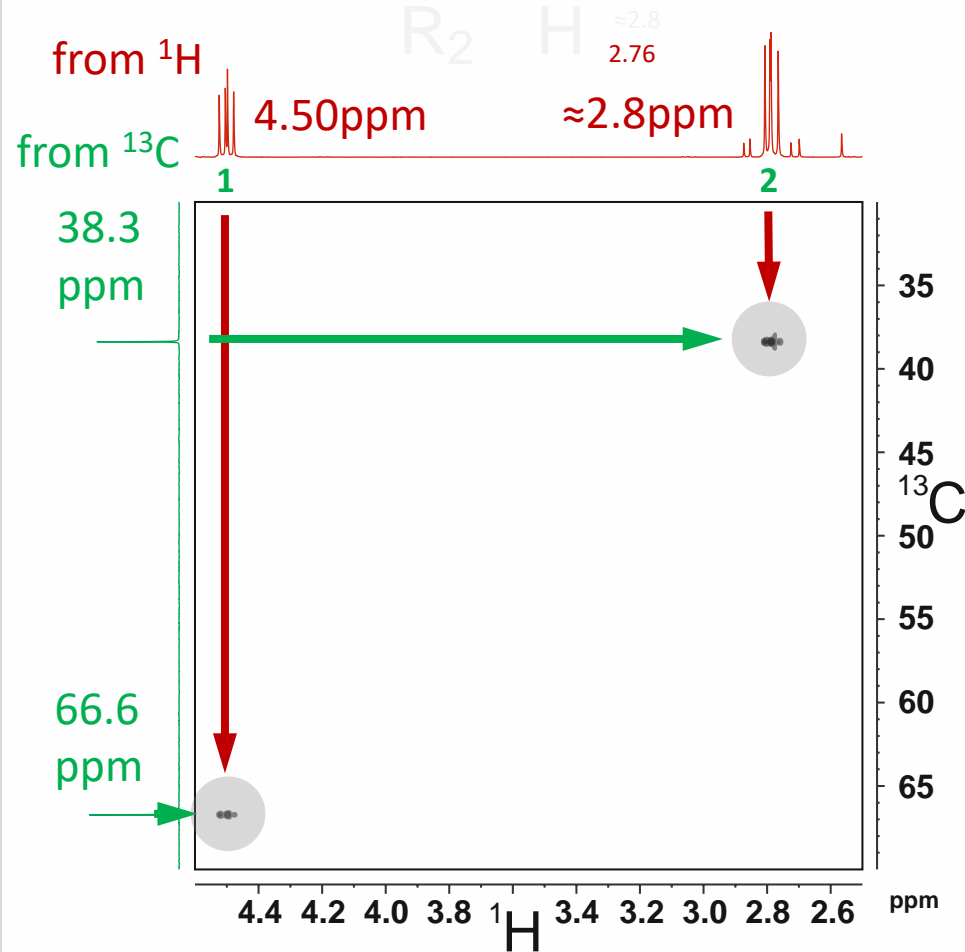
June 2020

Solution

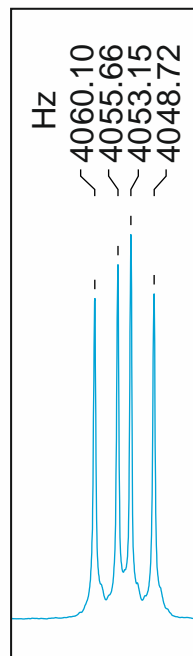
assuming typical
proton-proton
coupling constants



Let us examine the multiplet at approx. 2.8 ppm using a higher magnetic field and as a first approach according to 1st order rules.

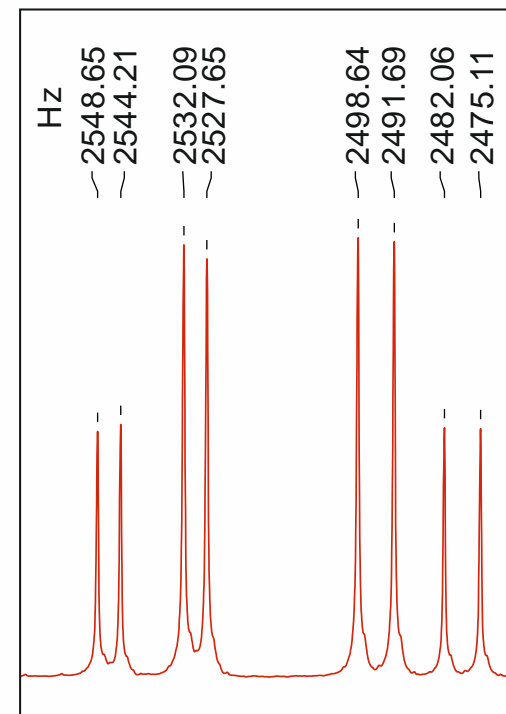


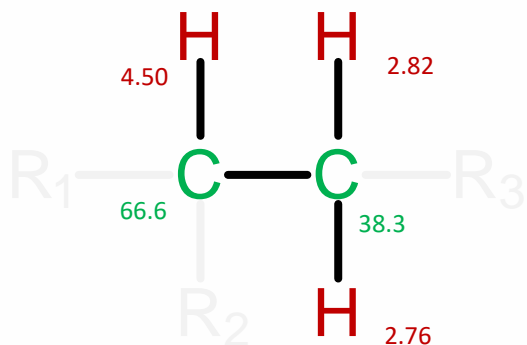
4.50 ppm



2.82 ppm

2.76 ppm





molecular formula



already assigned

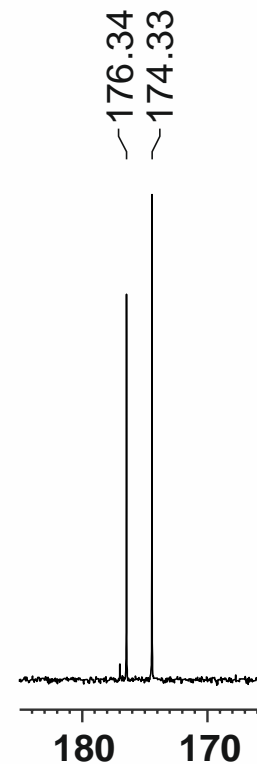


still to assign



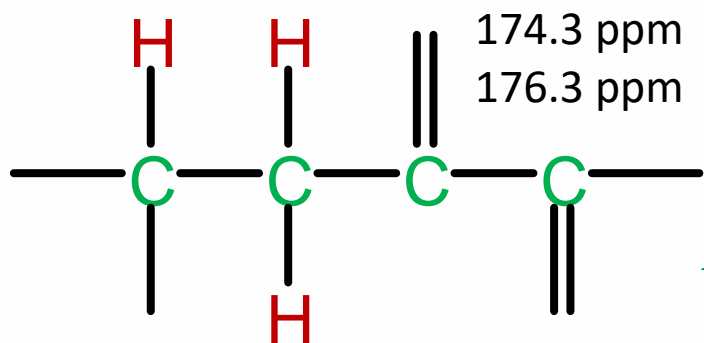
2 double bond equivalents
(degrees of unsaturation)

two carbons and two degrees of
unsaturation are here:



all carbons are assigned now

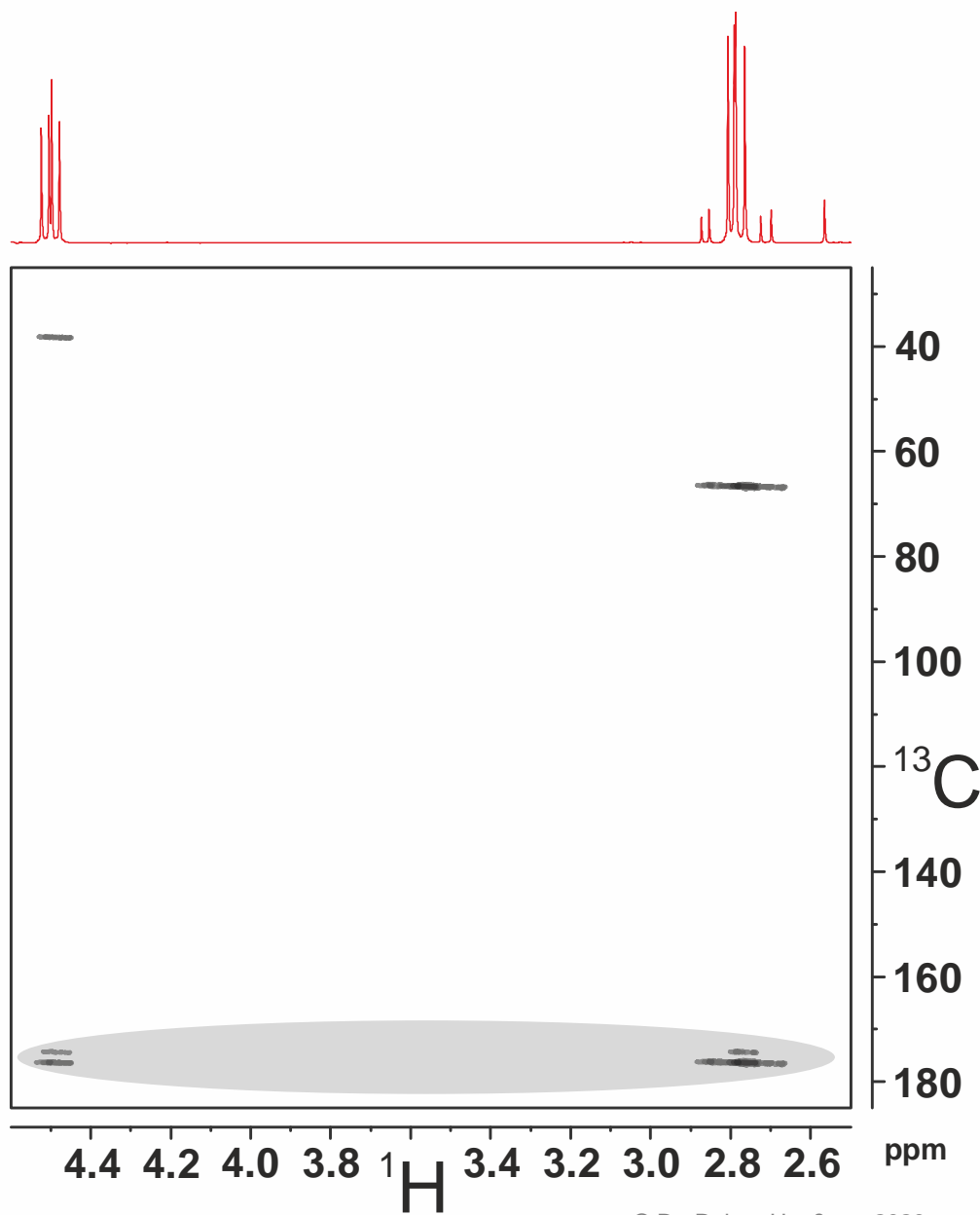
because there are no more HSQC
peaks, the missing three protons
can only be OH-protons

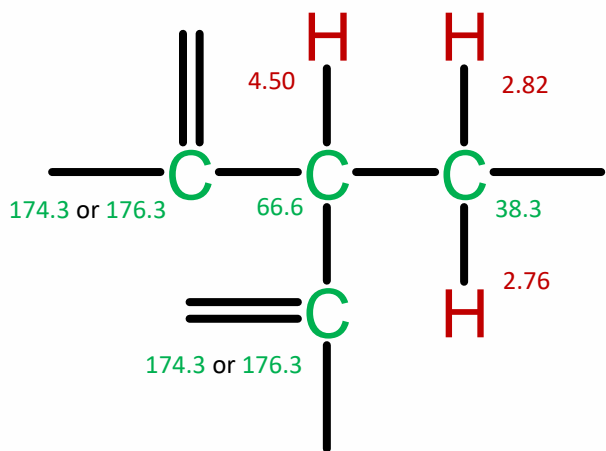


Could the carbon signals with the chemical shifts 174.3 and 176.3 ppm be adjacent like above?

The red labelled coupling path across 4 bonds should not be visible in HMBC. Usually, HMBC cross peaks indicate a proximity of up to three bonds only.

But the HMBC indicates a proximity between each of the sp^2 carbons and all protons.

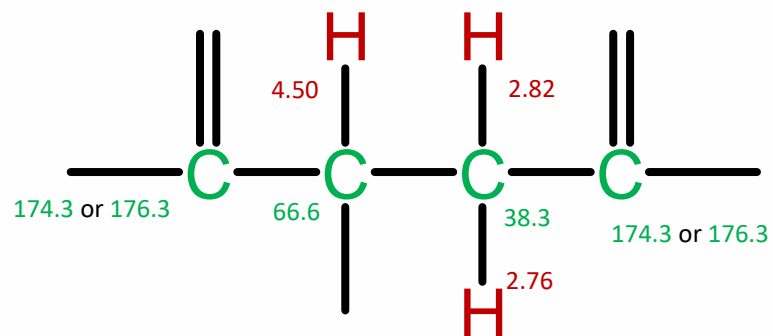




still to assign

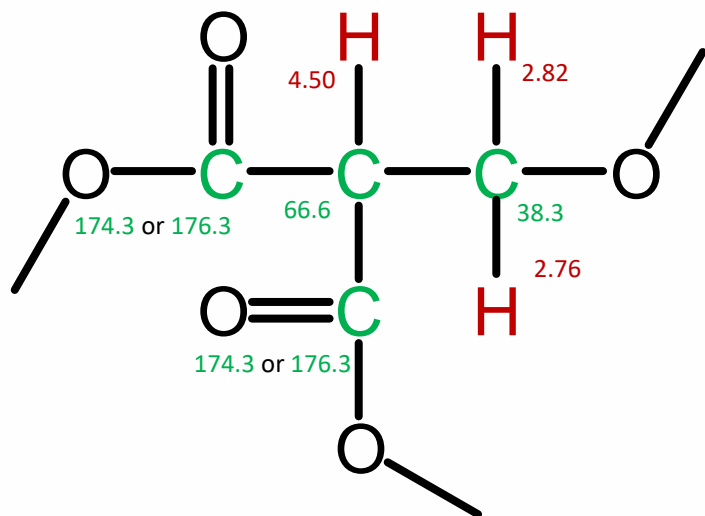


or

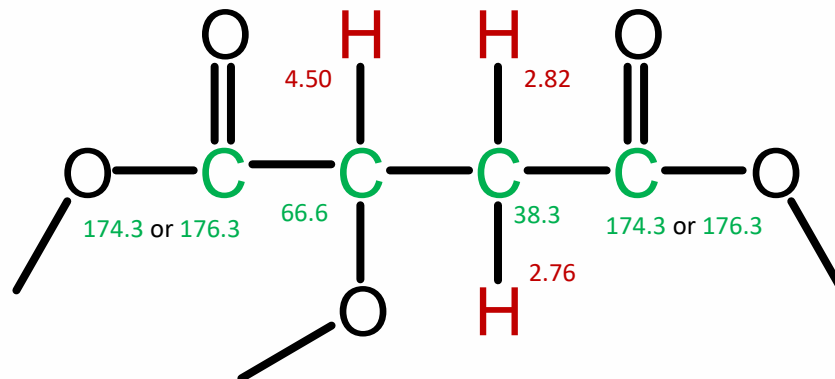


Since there are only two correlations in the HSQC spectrum (already assigned), none of the three remaining protons can be directly bonded to carbon.

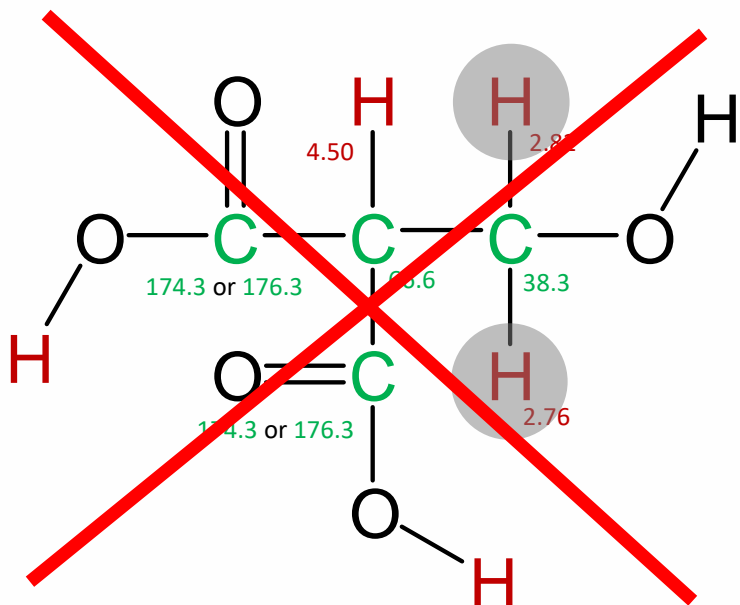
Which results in ...



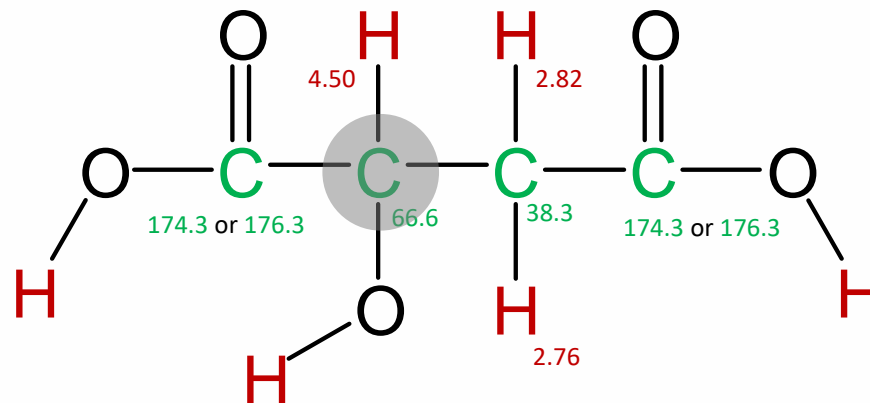
or



...leading to the final two structure recommendations after adding the three missing protons.



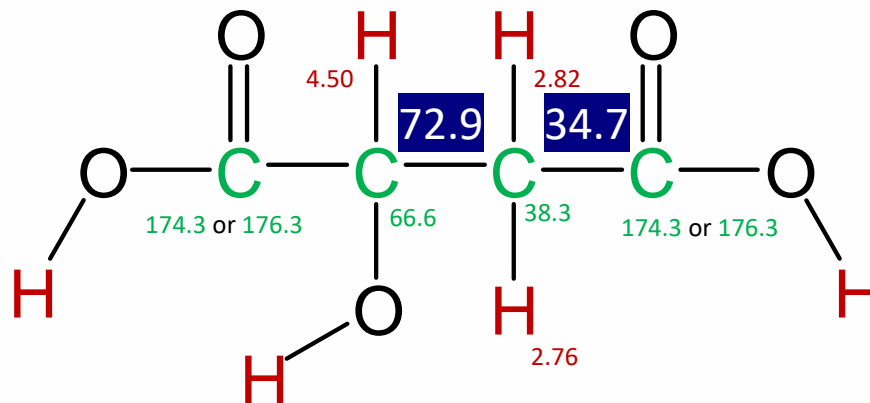
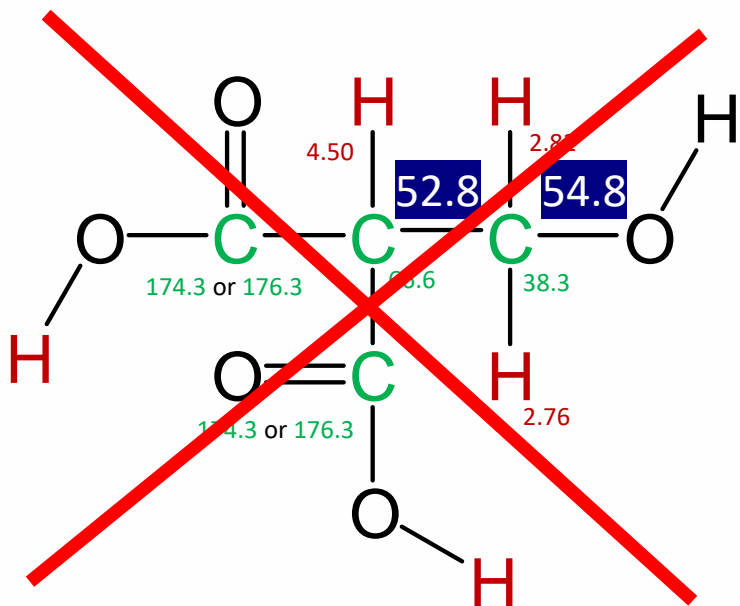
In this structure the labelled protons have to be identical!



Because of the center of chirality, all the chemical and NMR spectroscopical properties of all three CH protons are different.

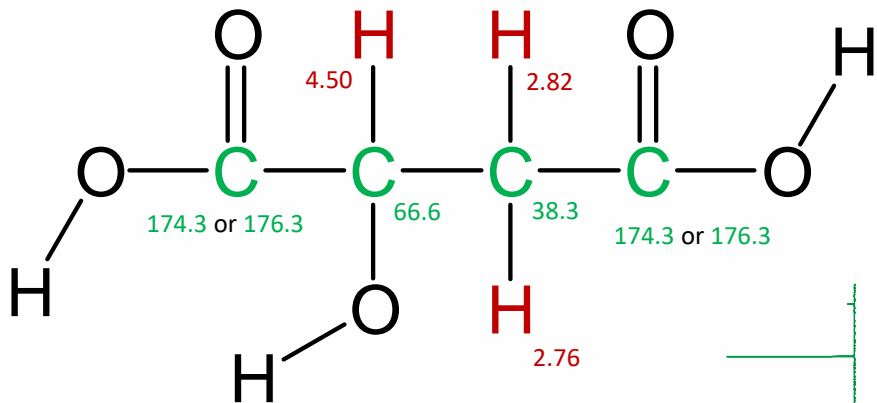
For a more detailed explanation of the non-equivalence, please compare with the solution to the "Problem of the month April 2020"!

The exclusion of the non-chiral compound is unambiguous,
but not necessarily easy to detect.



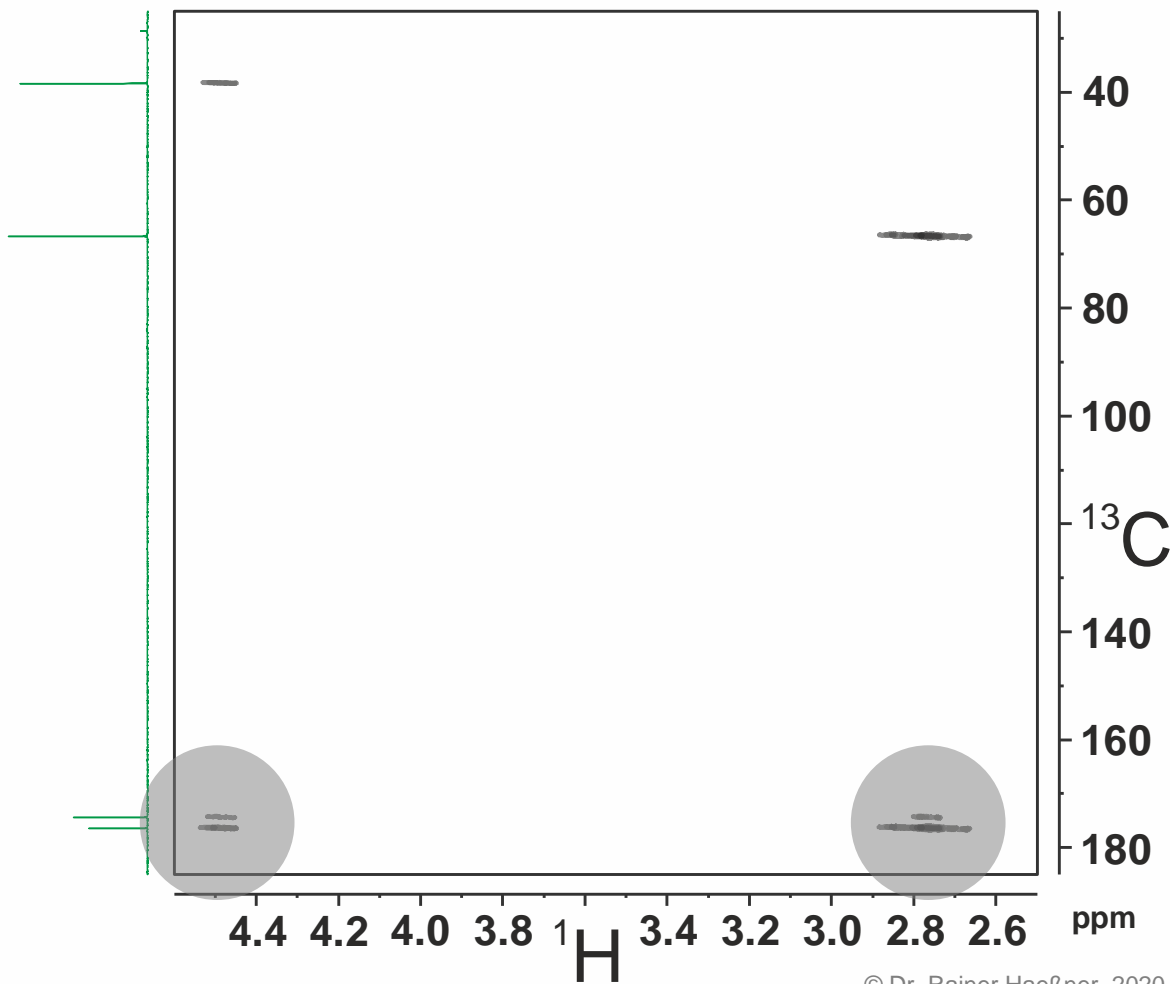
A quick decision might be done by estimating the chemical shifts of the carbon atoms using an increment scheme (e.g. <https://www.chem.wisc.edu/areas/reich/nmr/06-cmr-03-shift-effects.htm>)

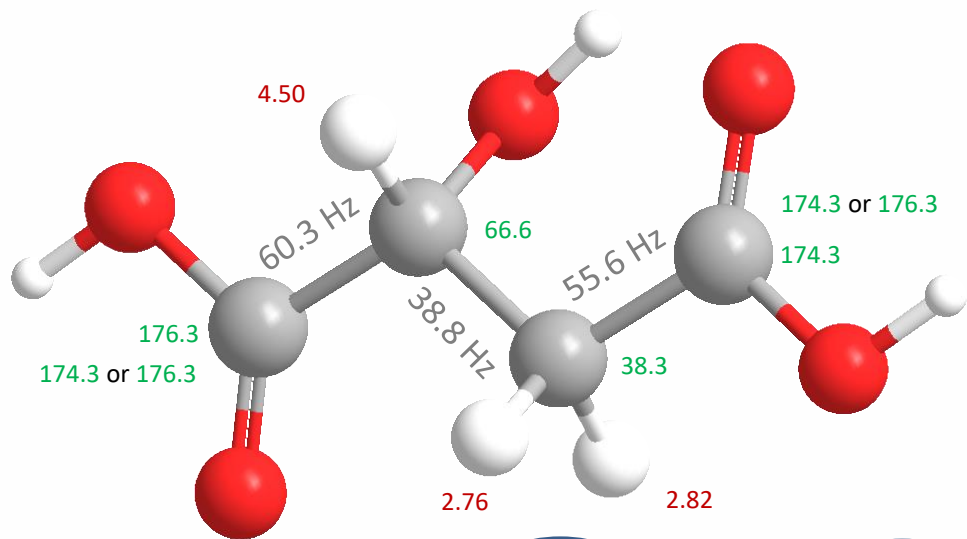
The **calculated values** correlate well with the right and not at all with the left chemical structure.



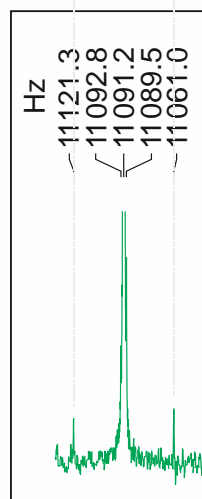
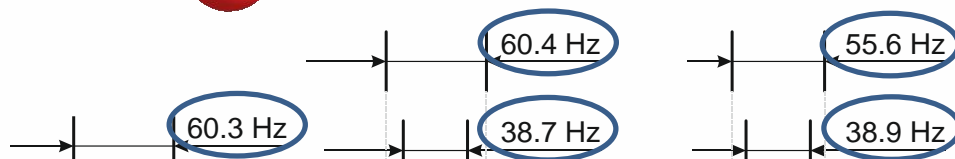
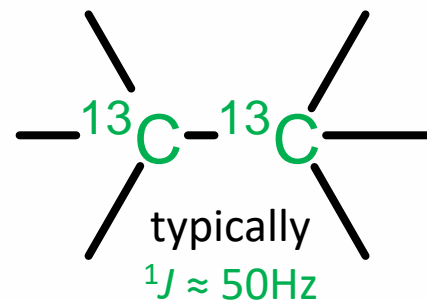
Now the constitution is known. As a challenge we might try to assign the carbonyl signal unambiguously.

The HMBC is useless, because both carbonyl signals show correlation to **all** proton signals.

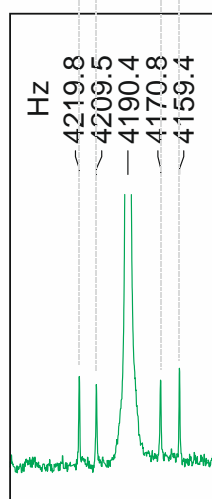




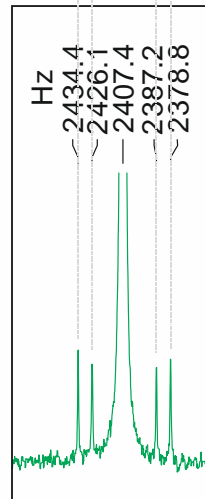
The unambiguous carbonyl assignment is only possible via one bond carbon-carbon couplings.



176.3 ppm



66.6 ppm

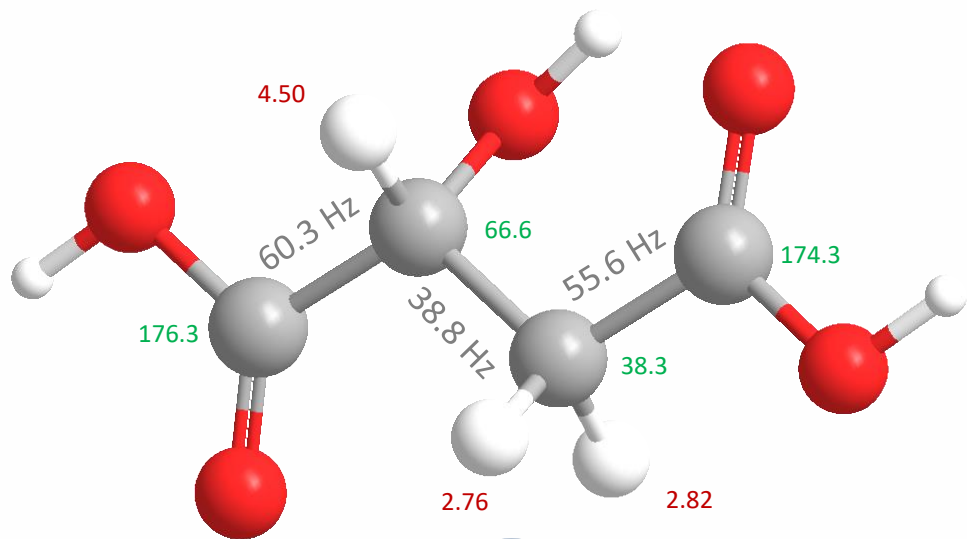


38.3 ppm

Lets start with already assigned carbon signals.

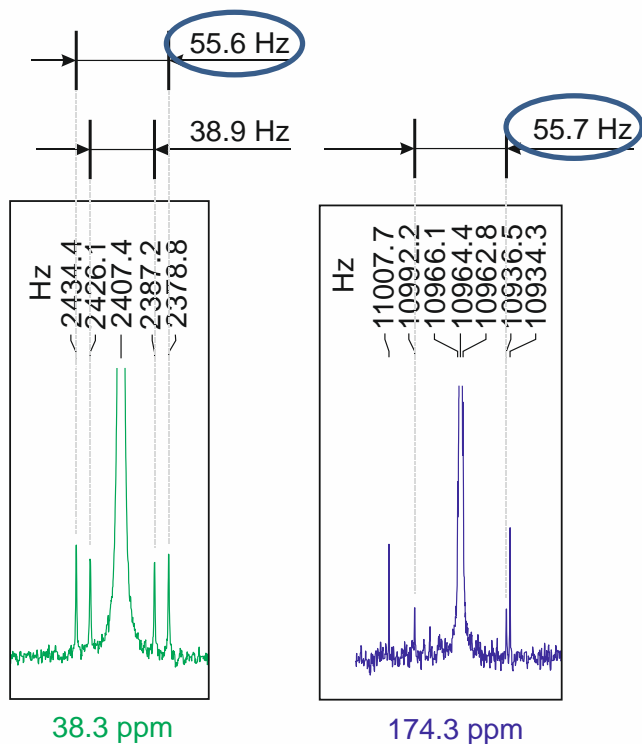
Tentatively lets inspect the carbon signal at 176.3 ppm.

Now it's easy to finalize the assignment.

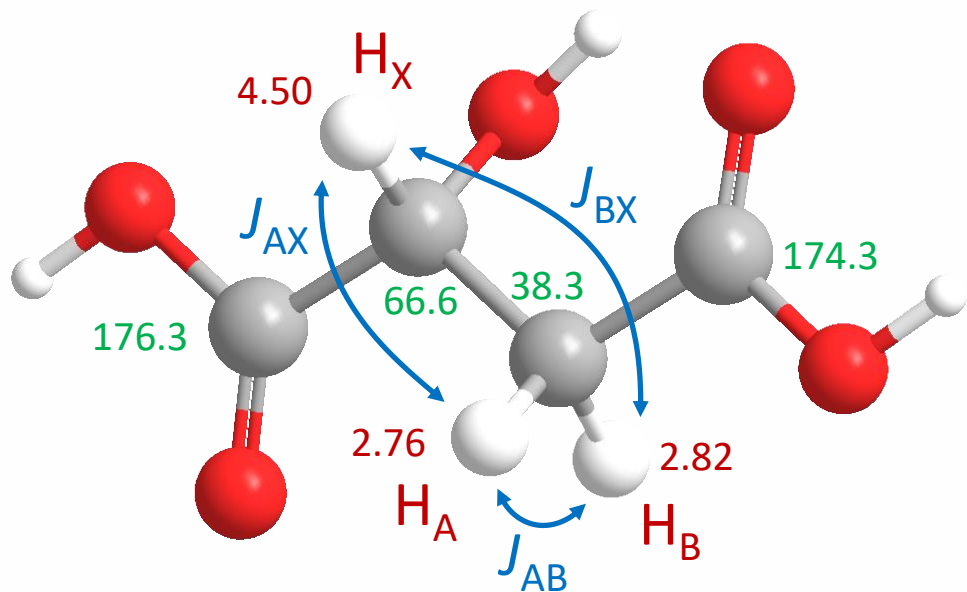


At this point the signal assignment is already finalized.

Nevertheless let's have a look for the ^{13}C - ^{13}C coupling constant of 55.6 Hz in the carbon signal at 174.3 ppm



Due to some impurity signals we have to check four possible solutions. It might be helpful to look for lines symmetrical to both sides of the main line.



Detailed analysis of the proton spin system

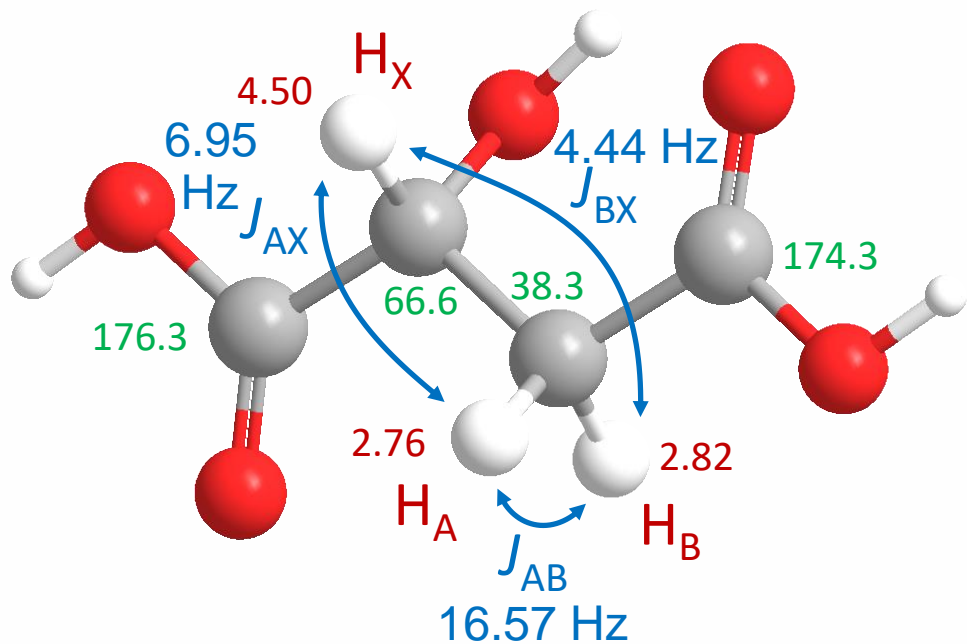
Due to the chemical exchange with the solvent (D_2O) the OH-protons are not visible.

Only the three CH protons (2.76, 2.82 and 4.50 ppm) can be observed.

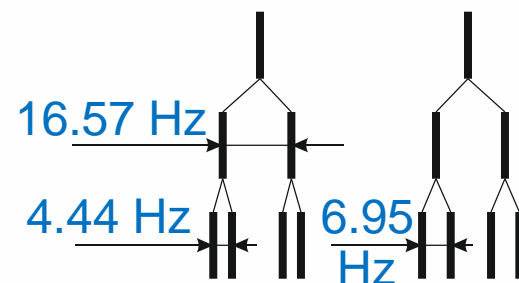
All three protons are different and hence their chemical shifts are different too.

By convention we call them H_A (2.76 ppm), H_B (2.82 ppm) and H_X (4.50).

We expect a doublet of doublets as coupling pattern for each of the three protons .



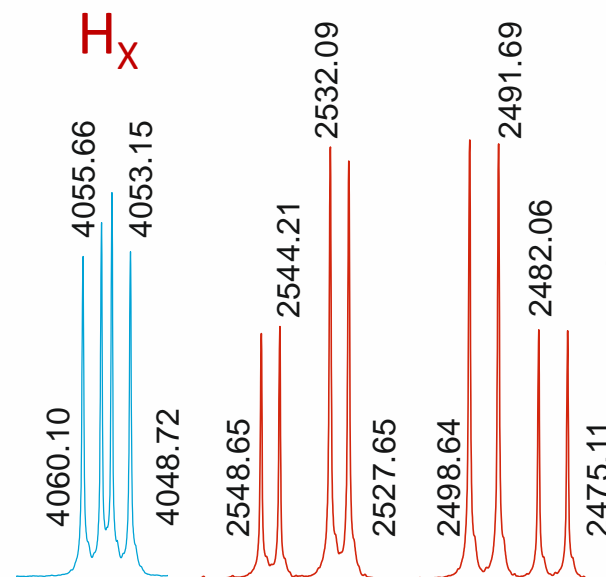
H_B	H_A
$\delta = 2.818$	$\delta = 2.764$

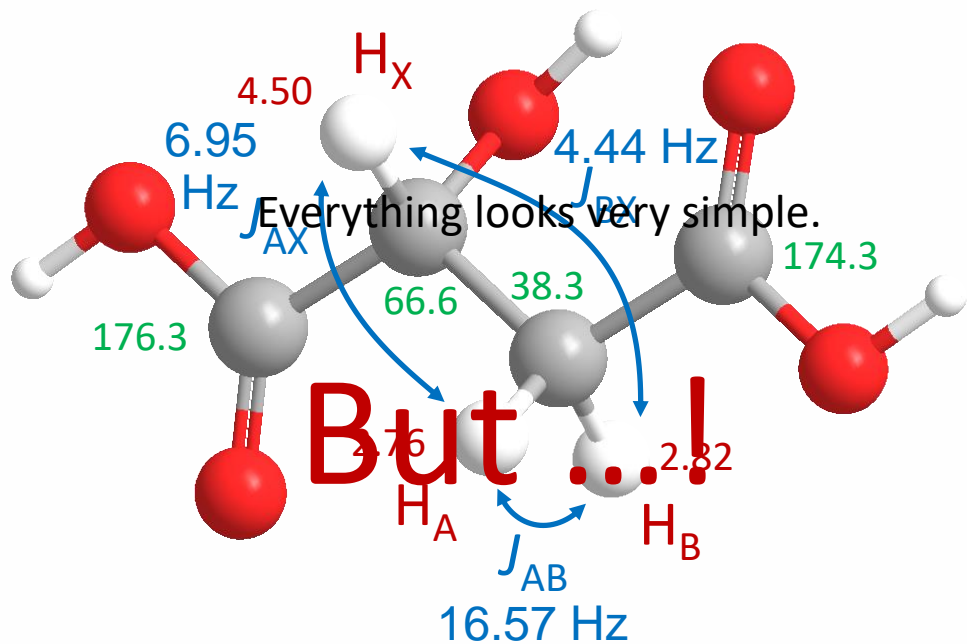


The AB system of the protons H_A and H_B is easily visible at 900 MHz base frequency.

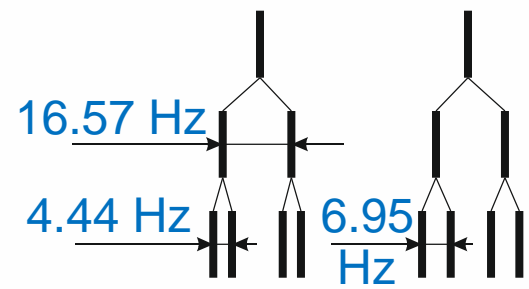
Between H_A and H_X we see a vicinal coupling constant of 6.95 Hz .

Between H_B and H_X we see a vicinal coupling constant of 4.44 Hz .





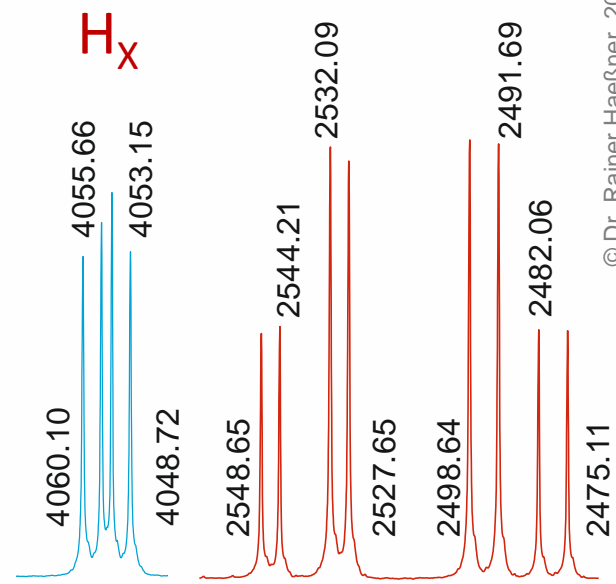
H_B	H_A
$\delta = 2.818$	$\delta = 2.764$



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Everything looks very simple.

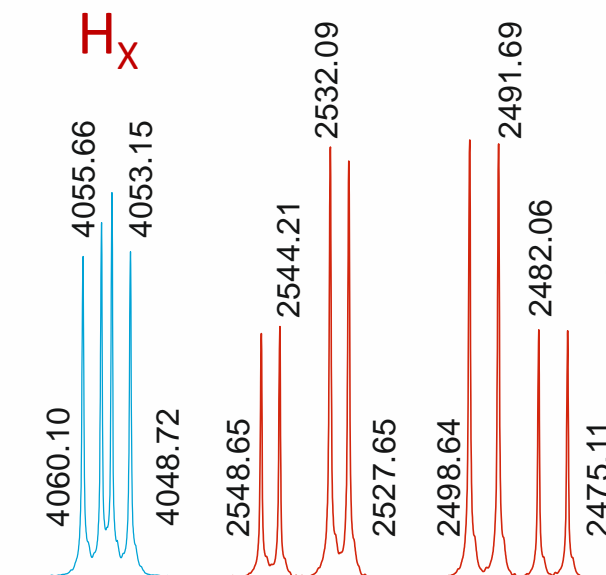
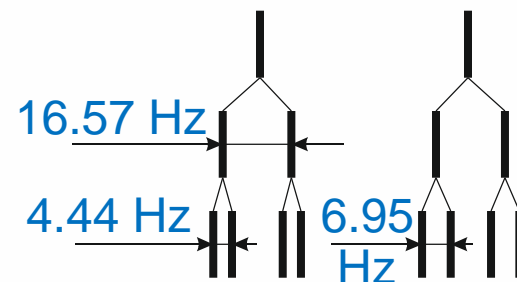
But ...!

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H_B	H_A
$\delta =$	$\delta =$
2.818	2.764



J_{AX} and J_{BX} (but not J_{AB}) seem to depend on the base frequency.

Everything looks very simple.

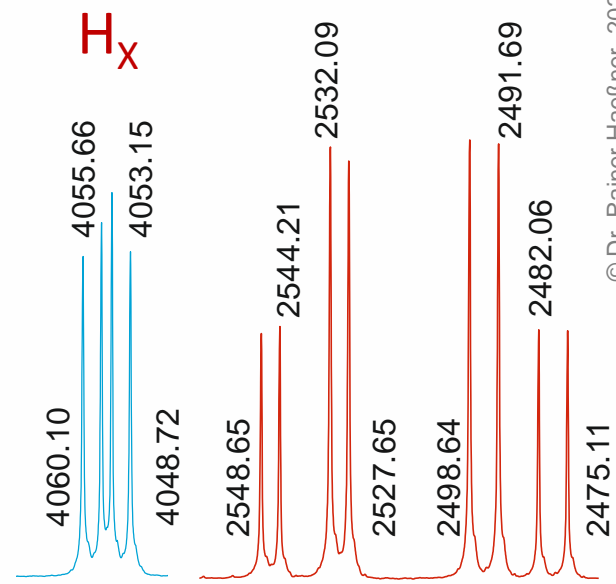
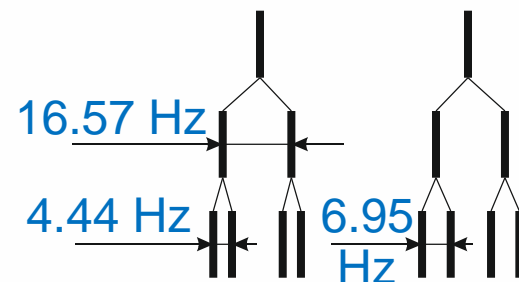
But ...!

The AB system of the protons H_A and H_B is easily visible at 900 MHz base frequency.

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Between H_B and H_X we see a vicinal coupling constant of 4.44 Hz.

H_B H_A
 $\delta =$ $\delta =$
2.818 2.764



J_{AX} and J_{BX} (but not J_{AB}) seem to depend on the base frequency.

J_{AX}

J_{BX}

$\delta = 2.820$ $\delta = 2.764$

$\delta = 2.820$ $\delta = 2.766$

$\delta = 2.818$ $\delta = 2.764$

200 MHz

600 MHz

900 MHz

16.56 Hz

16.58 Hz

16.57 Hz

4.92 Hz

4.51 Hz

4.44 Hz

6.47 Hz

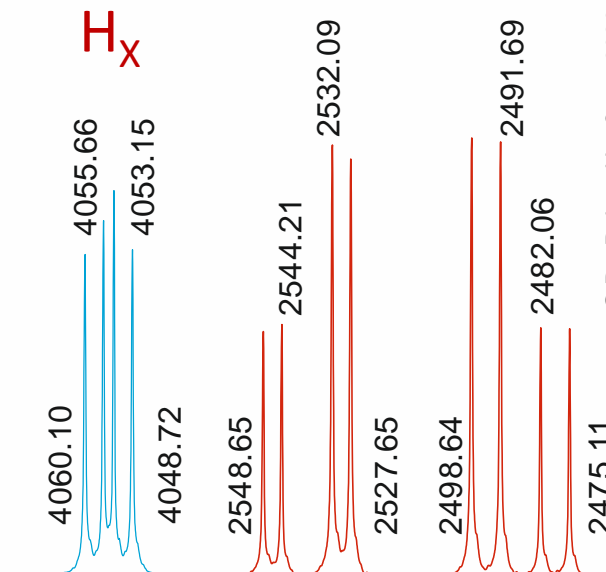
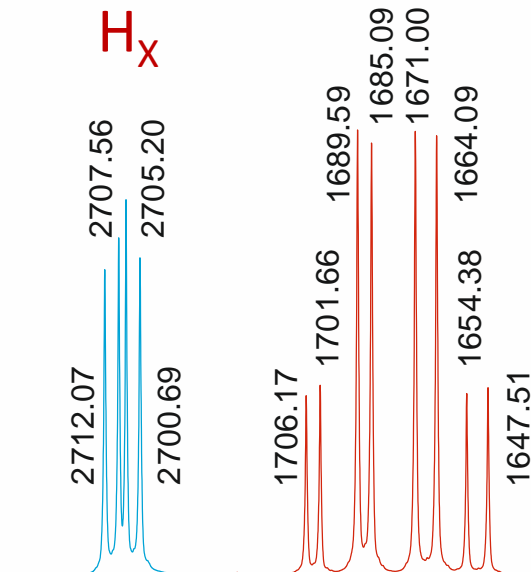
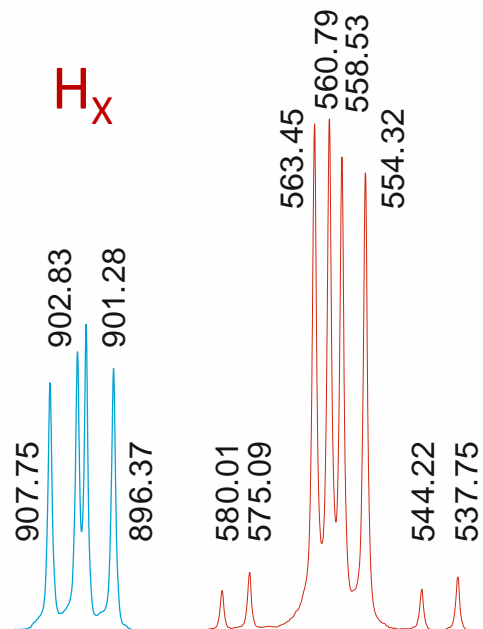
6.89 Hz

6.95 Hz

H_X

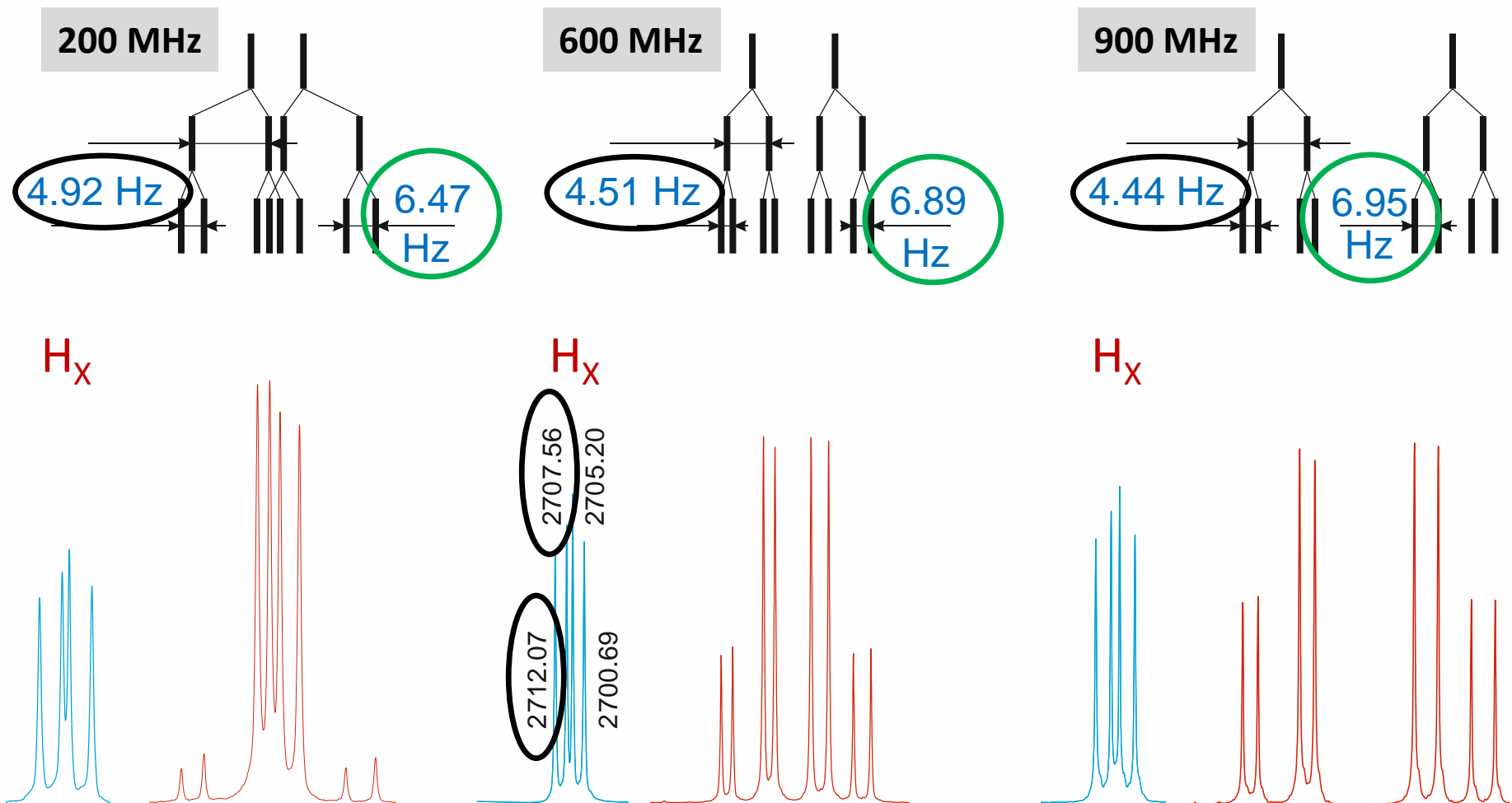
H_X

H_X



Of course J_{AX} and J_{BX} are visible in the multiplet of H_x ($\delta = 4.50$ ppm) as well.

(To keep it simple, only $J_{BX} = 4.51$ Hz at 600 MHz is chosen as an example.)



Caution

The spectrum can no longer be evaluated according to 1st order rules, even if it looks like this.

In the NMR world the term "**deceptively simple**" is used for such spectra.

Using the link below you might simulate the proton spectrum using different base frequencies and different coupling constants. The chemical shifts of the protons cannot be changed.

[https://www.nmr.tips/Spektrensimulation/ABX/ABX als Funktion der Messfrequenz/](https://www.nmr.tips/Spektrensimulation/ABX/ABX%20als%20Funktion%20der%20Messfrequenz/)