

MASSACHUSETTS INSTITUTE OF TECHNOLOGY

ORGANIC CHEMISTRY 5.46

The following is an approximate algorithm for assigning the resonances of a known structure.

Predict the multiplicities and shifts of the individual proton resonances. Compare with the proton 1D spectrum.

Tabulate the shifts you have and characterize the multiplets. In the absence of double bonds and/or strained ring systems, you generally only need to consider 2J 's and 3J 's. Remember that couplings can be zero if the dihedral angle is around 90° .

Examine the ^1H - ^{13}C HMQC or HSQC spectrum to identify diastereotopic protons on methylene groups (two protons on same carbon), methyl groups (strong peaks, often a little distorted, at low proton and carbon shift values), and methine protons (by process of elimination). Remember that the HMQC and HSQC pulse sequences are 'tuned' to the average $^1J_{\text{CH}}$ (140 Hz) so some CH species may not produce signals. In considering the HMQC/HSQC data, also keep in mind that a resonance that is J-coupled to many other spins will produce a weaker-looking signal because it is spread out (volume integrals of the cross peaks compensate for this effect, but are not generally given for 'simple' organic molecules).

Examine the ^1H - ^1H COSY spectrum to piece together strongly coupled proton resonances. Try to 'work' your way around the molecule, using the COSY cross peaks, so that you can establish what is adjacent to what. Every time a tentative assignment is made, examine the proton 1D spectrum to verify that the shifts, couplings, and integrals are consistent with your assignment.

In crowded regions of the spectrum, the ^1H - ^1H TOCSY spectrum may also assist you in assigning one spin to a spin more than 3 bonds distant via an intermediate in a very crowded region of the spectrum. TOCSY spectra acquired with short mixing times ($\sim 25\text{ms}$) will produce results similar to COSY spectra, while TOCSY spectra acquired with longer mixing times (80-120ms) will produce relayed cross peaks.

Recall that areas of the molecule with aromatic or double-bond systems may perturb the chemical shifts of nearby spins.

Building a model of the molecule may help, especially when it comes to assessing the magnitude of a given through-bond (J) interaction.

^1H - ^1H ROESY and/or NOESY data provide information on proximity via the through-space dipolar interaction. Keep in mind that ROESY spectra can sometimes produce TOCSY cross peaks, and that NOESY spectra sometimes fail to show cross peaks if the rate of molecular tumbling is on an 'intermediate' time scale (MW ~ 1000 for typical organic solvents).

Finally, remember that the 1D proton spectrum is the single most important piece of data. All your conclusions should agree with this spectrum.