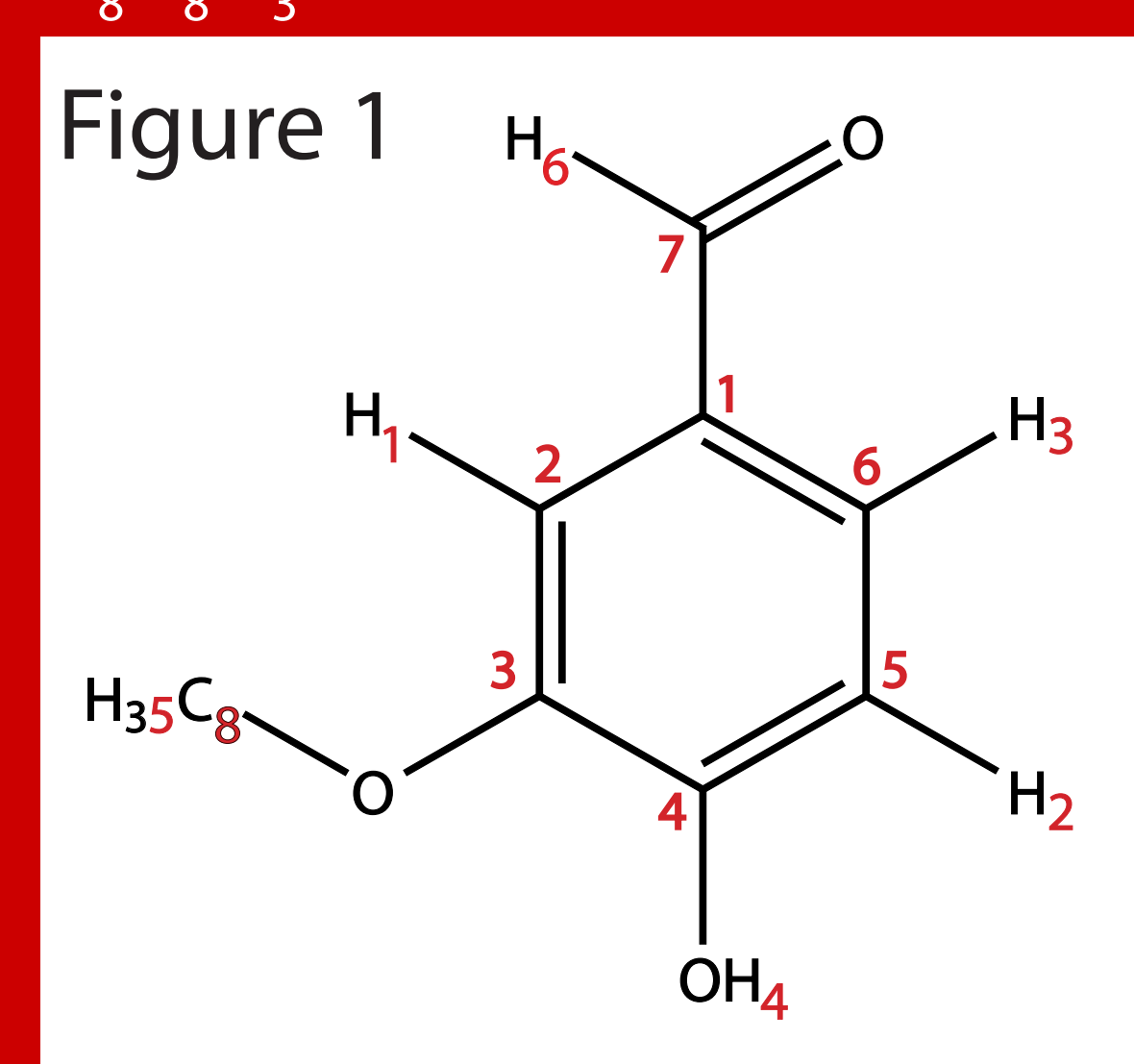


Introduction

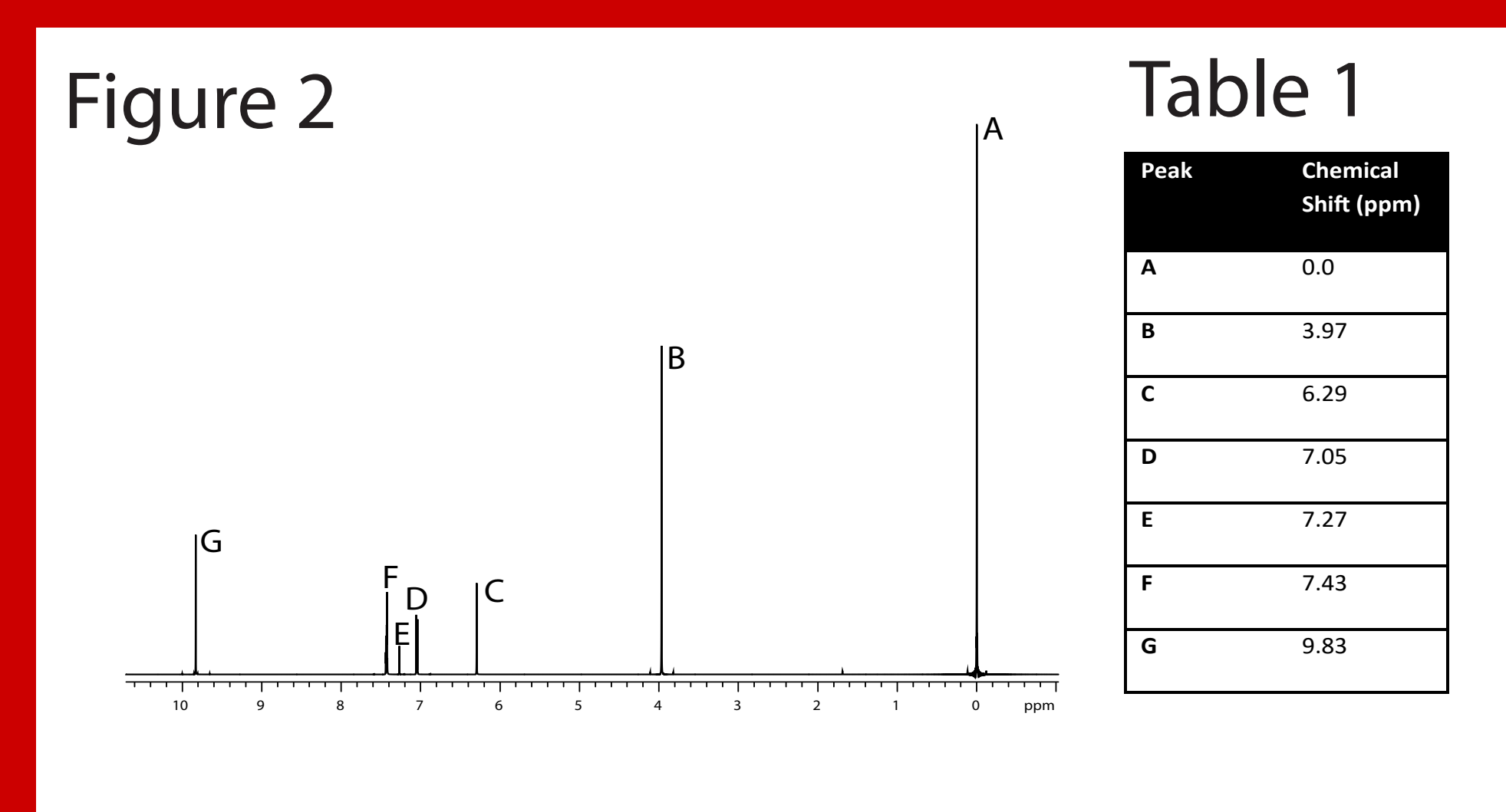
4-Hydroxy-3-methoxybenzaldehyde, commonly known as vanillin, is the principle molecule in culinary vanilla. Vanillin is an 8 carbon molecule consisting of four major functional groups- an aldehyde, an alcohol, and a methoxy group - all bound to an aromatic ring. This gives it the chemical formula of $\text{C}_8\text{H}_8\text{O}_3$. The structure of vanillin is shown in Figure 1.



All spectra for this experiment were recorded on a 500 MHz NMR spectrometer equipped with a cold probe accessory. The sample concentration was 100mM, dissolved in deuterio-chloroform with tetramethylsilane as an internal reference. The spectral width used to record ^1H spectra was 5868.54 Hz (11.737 ppm) while the width for ^{13}C spectra was 31250 Hz (248.31 ppm).

^1H 1D NMR Spectrum

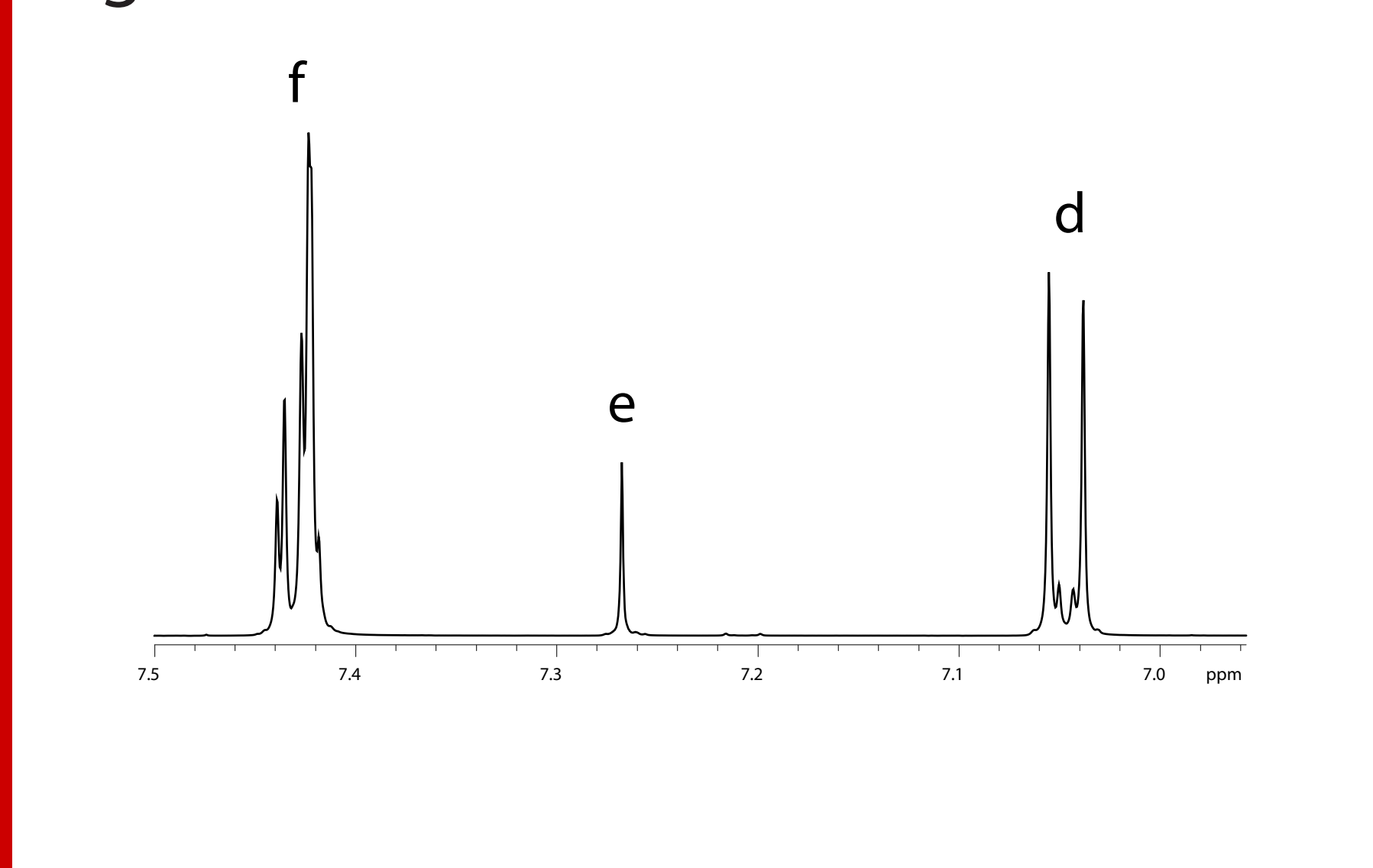
The one dimensional proton spectrum is shown in Figure 2. Each resonance is associated with its chemical shift in Table 1.



Based on the structure of the molecule (see Figure 1), there are six unique proton resonances. The large resonance A at 0.0 ppm is the reference compound tetramethylsilane. Resonance B at 3.97 ppm is assigned to the methoxy H5 hydrogens due to the relatively high electron density present at the nucleus compared to the other hydrogens. Integration data supports this assignment, e.g., the resonance is nearly three times more intense than the other vanillin resonances. Additionally, resonance G at 9.83 ppm is assigned as the aldehydic H6 since the aldehyde moiety results in a large deshielding at the nucleus.

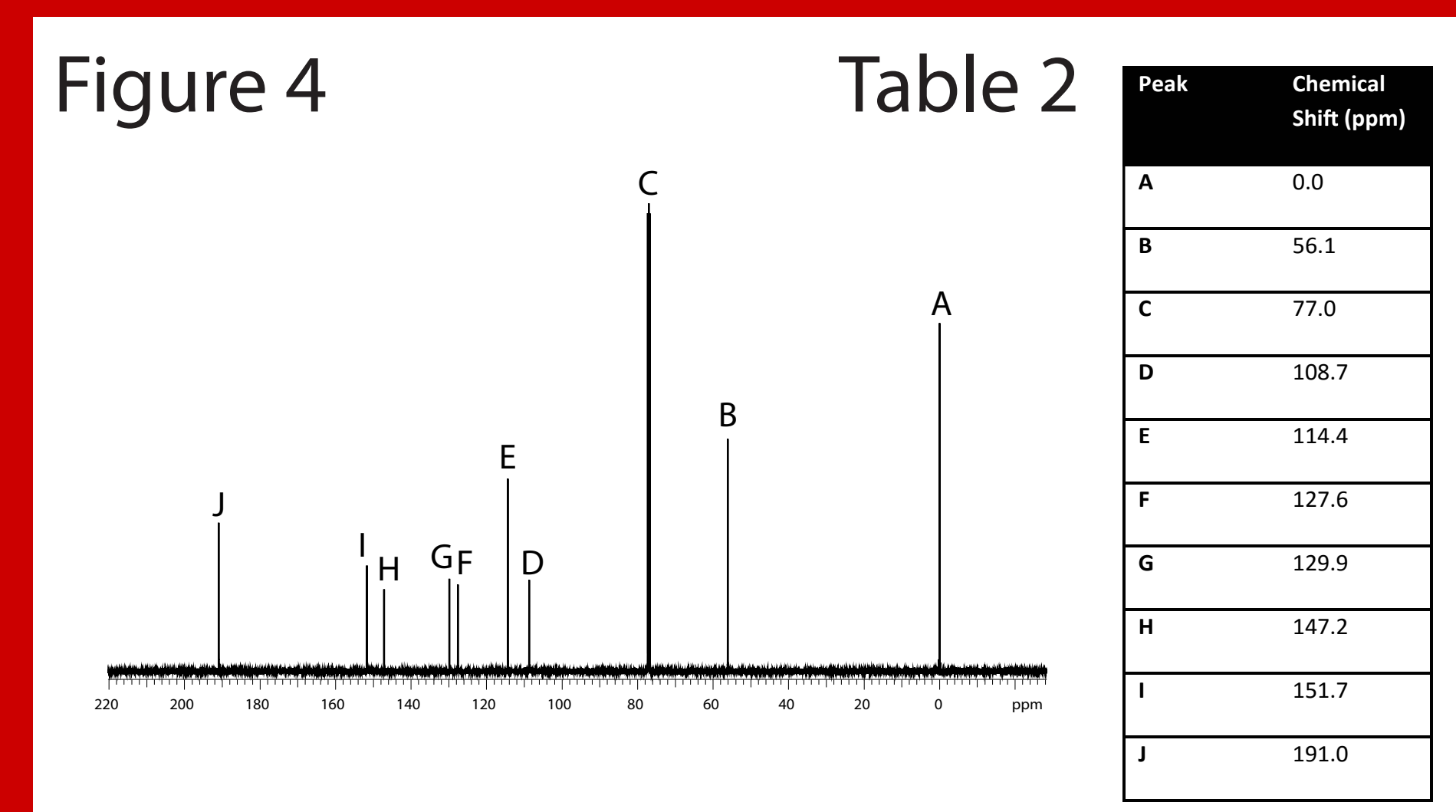
Figure 3 shows an expanded view of the spectral region from 7.0 ppm to 7.5 ppm. Resonance E can immediately be assigned to the solvent, which arises from the approximately 1% residual CHCl_3 in CDCl_3 . This leaves just one more singlet, resonance C, which is tentatively assigned to the hydroxyl proton H4, but will be further explored later. The remaining resonances appear to be multiplets. Close examination of the fine structure suggests there are three distinct resonances here. Resonance D at 7.05 ppm is a doublet while resonance F at 7.4 ppm is suspected to be two separate resonances with nearly the same chemical shift value. This will require further confirmation, however.

Figure 3



^{13}C 1D NMR Spectrum

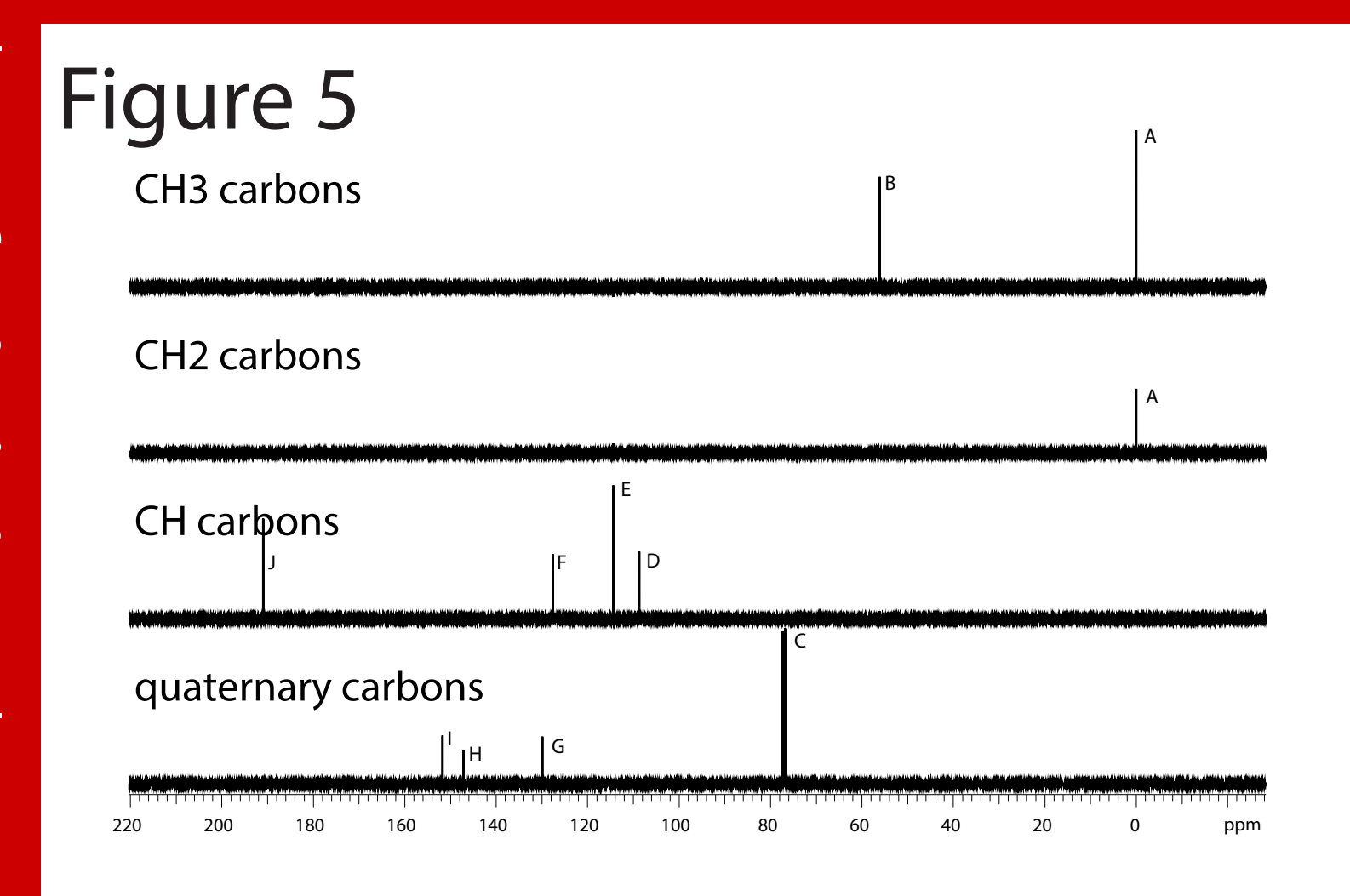
The one dimensional carbon spectrum is shown in Figure 4. Table 2 lists each resonance along with its assigned chemical shift. Based on the structure of the molecule (see Figure 1), there should be 8 unique carbon resonances in the spectrum.



Immediately, resonances A and C at 0.0 ppm and 77.0 ppm can be assigned to TMS and CHCl_3 respectively. Based on the chemical shift, resonance B can be tentatively assigned to the methoxy C8 while resonance J can be tentatively assigned to the aldehyde C7.

^{13}C DEPT NMR Spectrum

The DEPT series of sub-spectra for vanillin shown in Figure 5 displays the primary, secondary, tertiary, and quaternary carbon resonances. The top sub-spectrum contains the CH_3 carbon resonances. Resonance A is TMS while resonance B

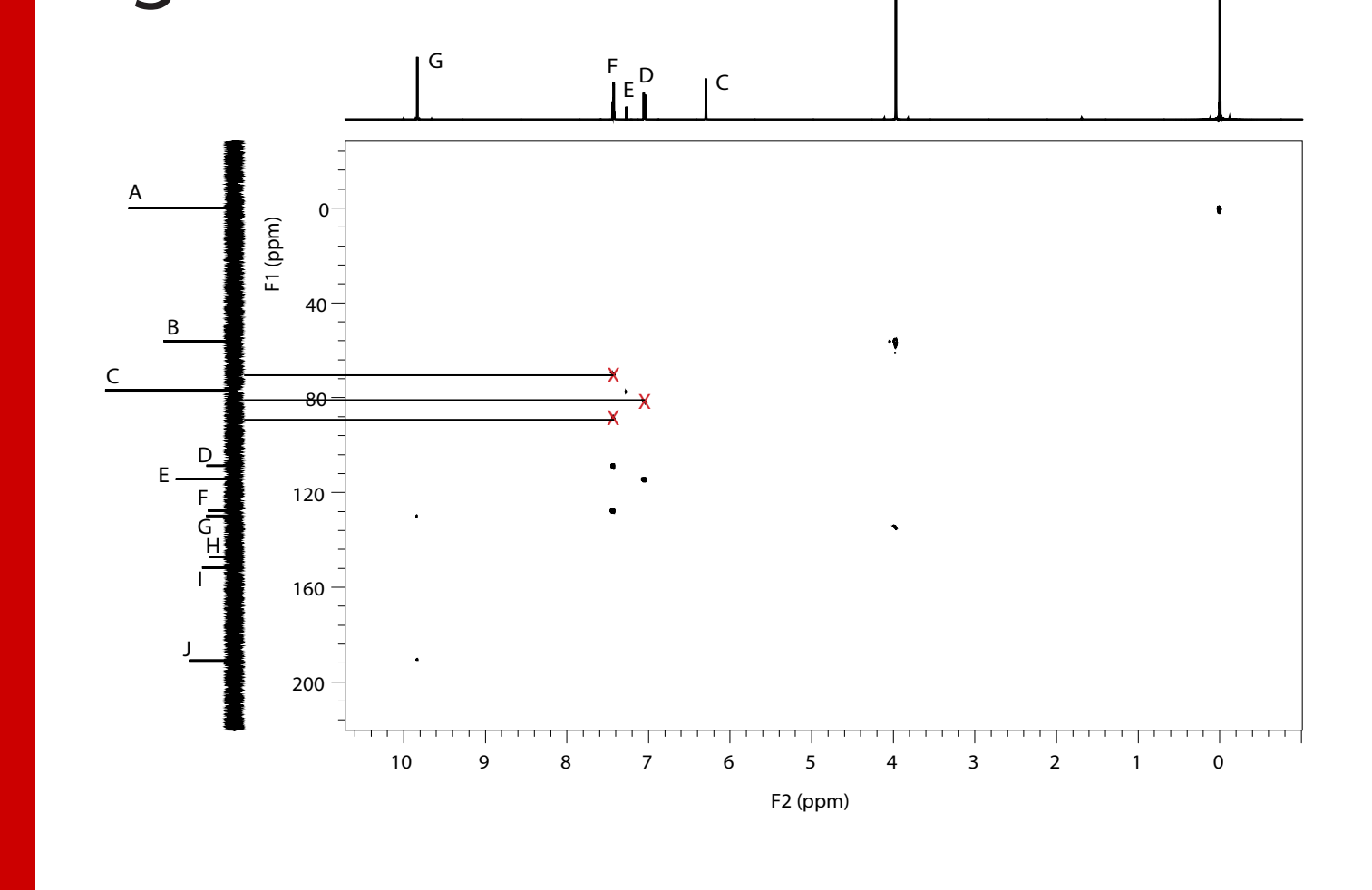


can be confidently assigned to methoxy C8. The second sub-spectrum would typically display methylene resonances, but in this case contains only an artefactual TMS resonance. The third sub-spectrum confirms the aldehyde C7 to be resonance J as it is the most deshielded CH resonance. It also gives key information on the benzylic carbons. The resonances between 108.7 ppm and 127.6 ppm (resonances D, E and F) have the three remaining benzylic protons bound to them- H1, H2, and H3. The fourth sub-spectrum contains the three benzylic quaternary carbons (C1, C3, and C4) that appear between 129.9 ppm and 151.7 ppm (resonances G, H, and I).

gHMQC 2D NMR Spectrum

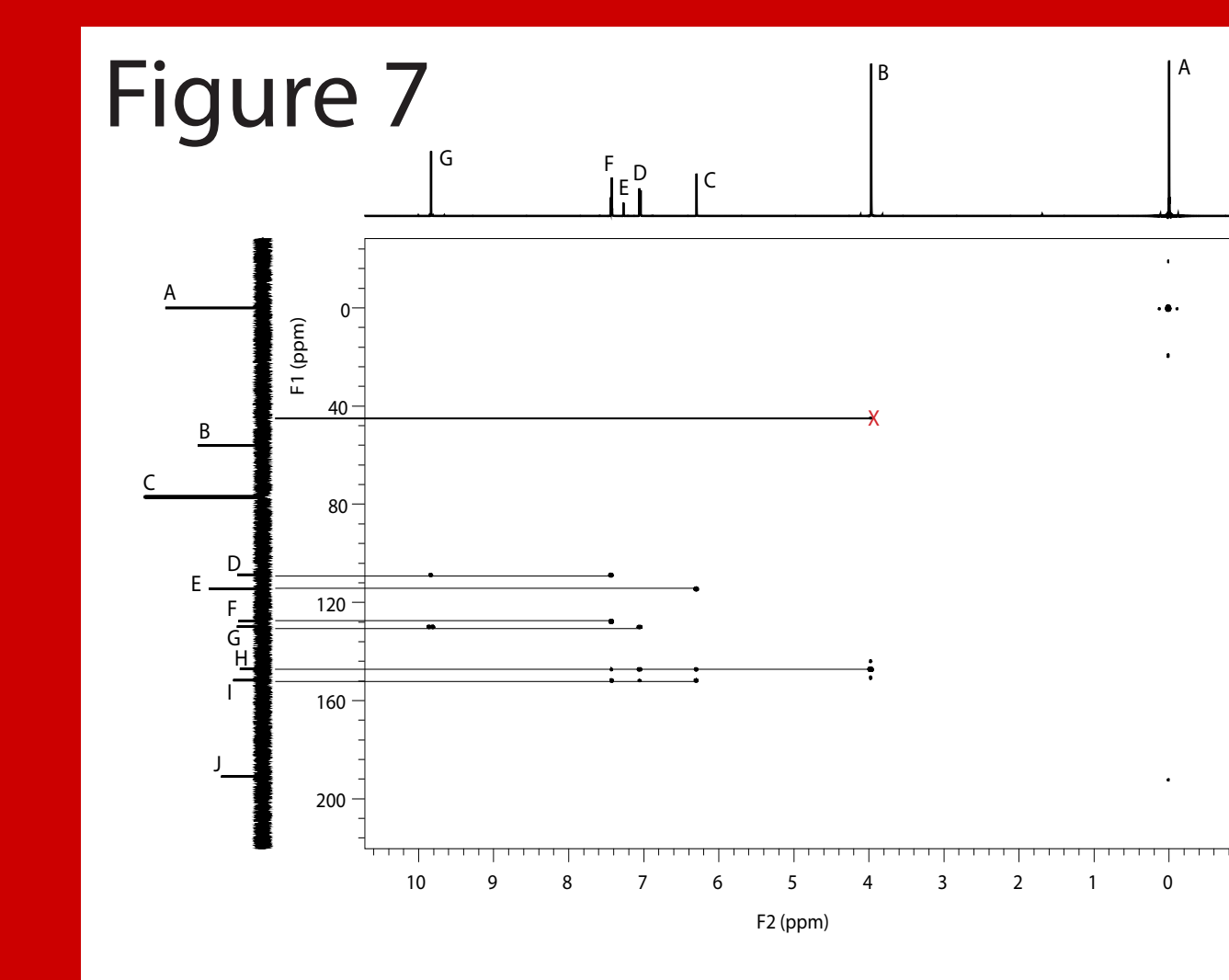
The gHMQC experiment is a two-dimensional heteronuclear correlated experiment that provides a map of one-bond H-C interactions. This experiment is useful for establishing carbon assignments based on known proton assignments and vice-versa. Two-dimensional NMR spectra can contain artefactual peaks, however careful analysis is usually sufficient to clarify real and false correlations. Figure 7 displays the gHMQC for vanillin. Note that three artifacts are apparent and are shown with a red X through them. The most useful area of the gHMQC

Figure 6



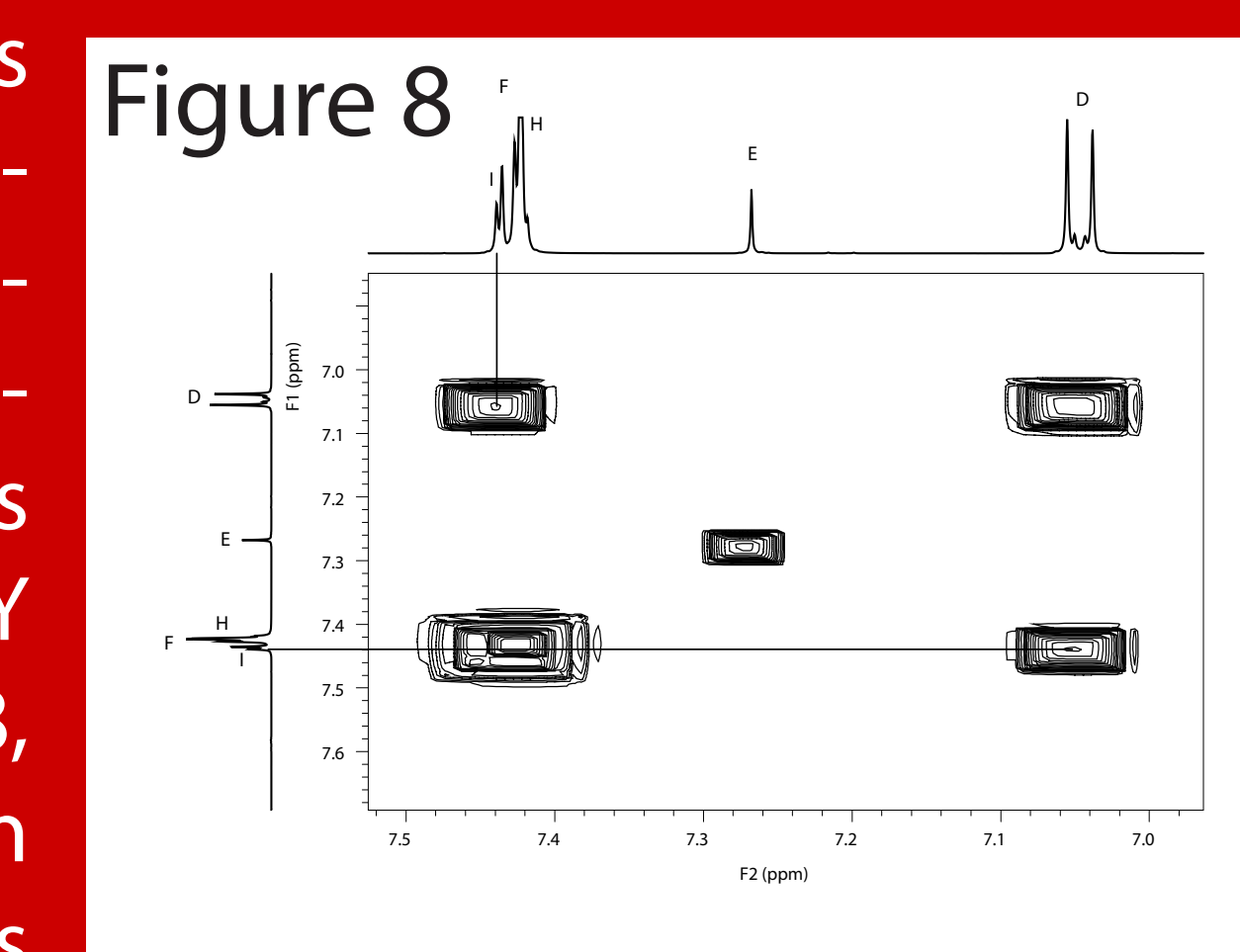
gHMQC, gHMBC, and gCOSY NMR Spectra

The gHMBC spectrum of vanillin is shown in Figure 7. The gHMBC experiment reveals two and three bond hydrogen-carbon interactions. Artefactual resonances are a common feature of gHMBC spectra and have been shown with a red X through them. Lines have been shown horizontally to make it easier to establish the connection between a carbon resonance in the 1D projection with a peak in the HMBC spectrum.



The ^1H resonance B has an exclusive interaction with the ^{13}C resonance H. This confirms that ^{13}C resonance H is associated with C3 since it is the only carbon within three bonds of H5. The hydroxyl ^1H resonance C shows an interaction with ^{13}C resonances E, H, and I. Since ^{13}C resonance H was just assigned, and ^{13}C resonance E is a primary carbon, ^{13}C resonance I is confirmed as C4. Additionally, since ^{13}C resonance E has an exclusive association with H4 through ^1H resonance C, it can be confirmed as C5. ^1H resonance G has an association with ^{13}C resonances D and G. Knowing that ^{13}C resonance G corresponds to a quaternary carbon, it can be confirmed as C1. Consulting the gHMQC, ^{13}C resonance E has an association with ^1H resonance D so the two redundant resonances at the position labeled F are the two protons *meta* to the aldehyde group, by elimination.

In order to confirm C2 and C6 as well as H1 and H3, the gCOSY must be consulted. The gCOSY is a homonuclear correlated experiment wherein off-diagonal resonance reveal J-coupling interactions between proximate protons. The gCOSY spectrum of vanillin is shown in Figure 8, with emphasis on the region between 7.0 ppm and 7.5 ppm. The gCOSY shows that resonance I has a J-coupling interaction with resonance D which was confirmed earlier as H2. Thus, resonance I corresponds to H3 and resonance H corresponds to H1. The carbons bound to H1 and H3 can be determined by examining the gHMQC and locating the proton-carbon correlations. Doing so confirms that ^{13}C resonance F corresponds with C6 and ^{13}C resonance D corresponds with C2.



Concluding Table and References

The concluding table below correlates each carbon to its associated hydrogen, if applicable, and to their ^1H and ^{13}C NMR spectra peaks.

	C	1	2	3	4	5	6	7	8	-	TMS	CHCl_3
^1H Peak	-	1	-	-	2	3	6	5	4	-	A	C
^{13}C Peak	G	D	H	I	E	F	J	B	-	A	0.0 ppm	77.0 ppm
^1H Peak	-	F/H	-	-	D	F/I	G	B	C	A	0.0 ppm	E
		7.43 ppm			7.05 ppm	7.43 ppm	9.83 ppm	3.97 ppm	6.29 ppm	0.0 ppm		7.27 ppm

Claridge, Timothy D. W. *High-Resolution NMR Techniques in Organic Chemistry*. Amsterdam: Elsevier, 2009.