^{1}H and ^{13}C NMR Assignments for Acetylsalicylic Acid (Aspirin)

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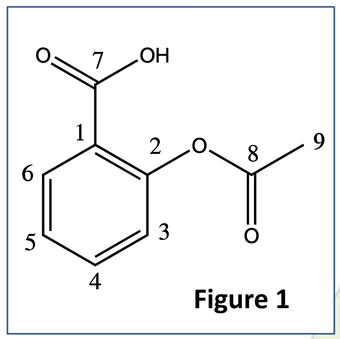


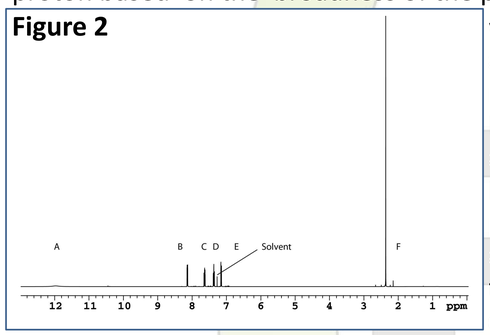
Figure 1

Acetylsalicylic Acid (Aspirin) formally 2-acetoxybenzoic acid has a M_w of 180.157 g/mol. Aspirin is used in the treatment of a number of conditions, including fever, pain, rheumatic fever, and inflammatory diseases. The Concentrated sample (<300 mMol) was prepared in deuterated chloroform.

^{1}H 1D NMR Analysis:

The ^{1}H NMR spectrum was recorded at 500MHz (^{1}H) using a spectral width of 6510.42 Hz and 16384 complex points. We can identify the ^{1}H resonance at 11.95 ppm as the carboxylic proton based on the broadness of the peak and the canonical values for carboxylic acid protons. The resonances designated B - E correspond to aromatic protons. Resonance B at 8.14 ppm can be identified as the proton attached to C6 because of its downfield shift due to the proximity to the carboxyl group and its doublet fine structure caused by correlation to resonance C or D. Resonances C and D will be assigned using the gCOSY experiment. Resonance E at 7.14 ppm can be assigned to H3 based on the fact that it is a doublet. These assignments will be confirmed using the gHMBC analysis. Resonance F at 2.36 ppm is assigned to the proton attached to C9 based the canonical values of methyl groups.

Figure 2



gCOSY Analysis:

The gCOSY spectrum was recorded on a 500 MHz (^{1}H) spectrometer with a spectral width of 6510.42 Hz and 1024 complex points in the direct (^{1}H/F2) dimension, 512 points in the indirect (^{1}H/F1) dimension. Review of Figures 3 and 4 reveal correlations between resonances H6 and D, C and D, and C and H3. Using these correlations we can assign resonance C at 7.63 ppm to the proton attached to C4 because of the correlation to H3. We then assign resonance D at 7.36 ppm to the proton attached to C5 due to the correlation to H6. We see no correlations from H9, confirming its identity as the methyl group. We also see no correlations from the carboxylic acid proton to any other proton.

Figure 3

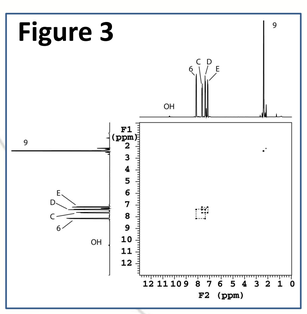
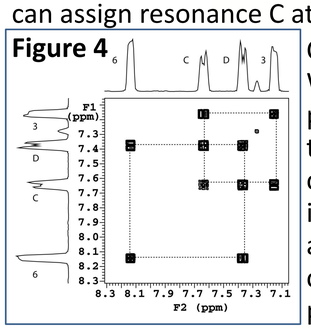
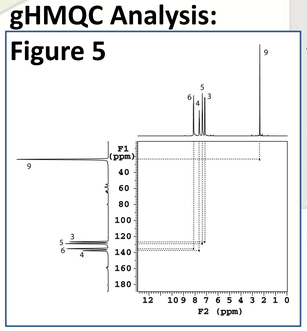


Figure 4



gHMQC Analysis:

Figure 5

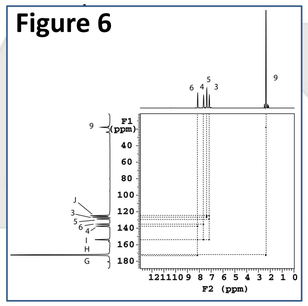


The gHMQC spectrum was recorded on a 500 MHz (^{1}H) spectrometer with a spectral width of 6510.45 Hz and 1024 complex points in the direct (^{1}H/F2) dimension and a spectral width of 23584.9 Hz and 512 complex points in the indirect (^{13}C/F1) dimension. We use this spectrum to assign carbon resonances using correlations from the directly bound proton resonances. By inspection of Figure 5, we can assign carbons 3, 4, 5, 6 and 9. We also see no correlation between the carboxylic acid proton and any carbon. This further confirms our previous assignments. Exact chemical shifts will be given in the ^{13}C 1D NMR spectrum.

gHMBC Analysis:

The gHMBC spectrum was recorded on a 500 MHz (^{1}H) spectrometer with a spectral width of 6510.45 Hz and 1024 complex points in the direct (^{1}H/F2) dimension, and a spectral width of 23584.9 Hz and 512 points in the indirect (^{13}C/F1) dimension. Using the gHMBC we will be able to assign quaternary carbons 1, 2, 7 and 8. We will designate the unknown resonances as G, H, I, and J respectively. While we see a single peak in our spectrum around 170 ppm, we can see that it is the combined peak of both G and H by inspecting the correlations to resonances 6 and 9. We see that the correlation peak with H6 is slightly farther downfield in the F1 dimension than the correlation with H9. There are no other correlations, so we can assign resonance G to C7 and resonance H to C8 respectively. Resonance I has a correlations to H3, H4, and H6, and these correlations would only occur if the resonance corresponded to C2, so we make that assignment. Similarly resonance J would correspond to C1 due to correlations to H3, H5 and H6. This is confirmed by correlation to H3, H5 and H6. Specific chemical shifts will be given in the ^{13}C analysis.

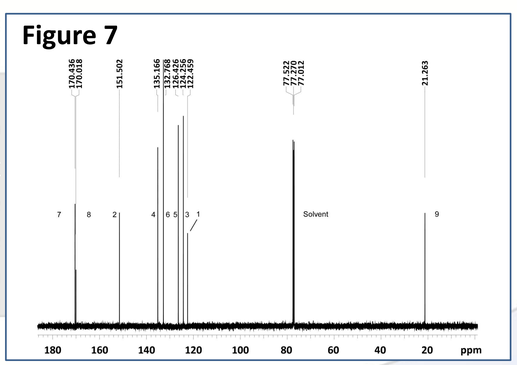
Figure 6



^{13}C 1D NMR Analysis:

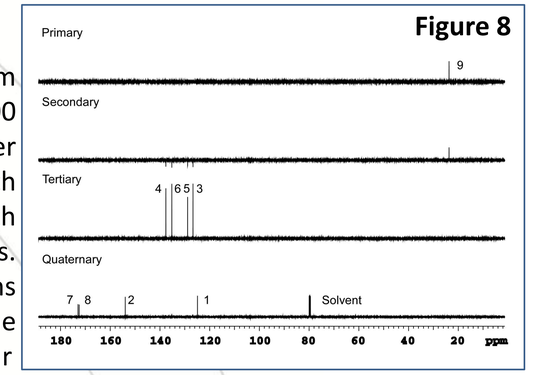
The ^{13}C spectrum was recorded on a 500 MHz (^{1}H) spectrometer with a spectral width of 23584.9 Hz and 32768 complex points. Using the assignments made using the gHMQC and gHMBC we can give the precise chemical shift values as follows: C1 at 122.46 ppm, C2 at 151.50 ppm, C3 at 124.25 ppm, C4 at 135.16, ppm C5 at 126.43 ppm, C6 at 132.77 ppm, C7 at 170.44 ppm and C8 at 170.02 ppm and C9 at 21.26 ppm respectively. Although the ^{13}C assignments can only be made based on the 2D data, chemical shifts values are best made using the higher resolutions 1D spectrum.

Figure 7



DEPT Analysis:

Figure 8



The DEPT spectrum was recorded on a 500 MHz (^{1}H) spectrometer with a spectral width of 23584.9 Hz with 32768 complex points. The spectrum confirms the analysis of the substitution of our carbons: The resonance corresponding to C9 is a methyl group (primary); the resonances corresponding to C3, C4, C5, and C6 are all methine groups (tertiary); and the resonances corresponding to C1, C2, C7, and C8 are all quaternary moieties.

Results and Conclusions:

Using the experiments shown we were able to assign all of the resonances of 2-acetoxybenzoic acid. We were able to make the proton resonance assignments using the ^{1}H 1D NMR and gCOSY experiments. The gHMBC provided critical proton assignment confirmation. The carbon resonances were assigned based on the assigned ^{1}H resonances using the gHMQC and gHMBC experiments, while using the ^{13}C 1D NMR spectrum to assign exact chemical shifts. The DEPT experiment provided critical carbon assignment confirmation.

Proton Assignments (ppm):

COOH	3	4	5	6	9
11.95	7.14	7.63	7.36	8.14	2.36

Carbon Assignments (ppm):

1	2	3	4	5	6	7	8	9
122.46	151.50	124.25	135.17	126.43	132.77	170.44	170.02	21.26

References and Acknowledgments:

Claridge, Timothy D W. *High-Resolution NMR Techniques in Organic Chemistry*. 2nd ed. Oxford: Elsevier, 2009. Print

Mayne, Charles L. "NMRanalyst Sample Application: Verbenol." *NMRanalyst Sample Application: Verbenol*. Science Soft LLC, n.d. Web. 12 Feb. 2013.

Crews, Phillip, Jaime Rodríguez, and Marcel Jaspars. *Organic Structure Analysis*. New York: Oxford UP, 1998. Print.