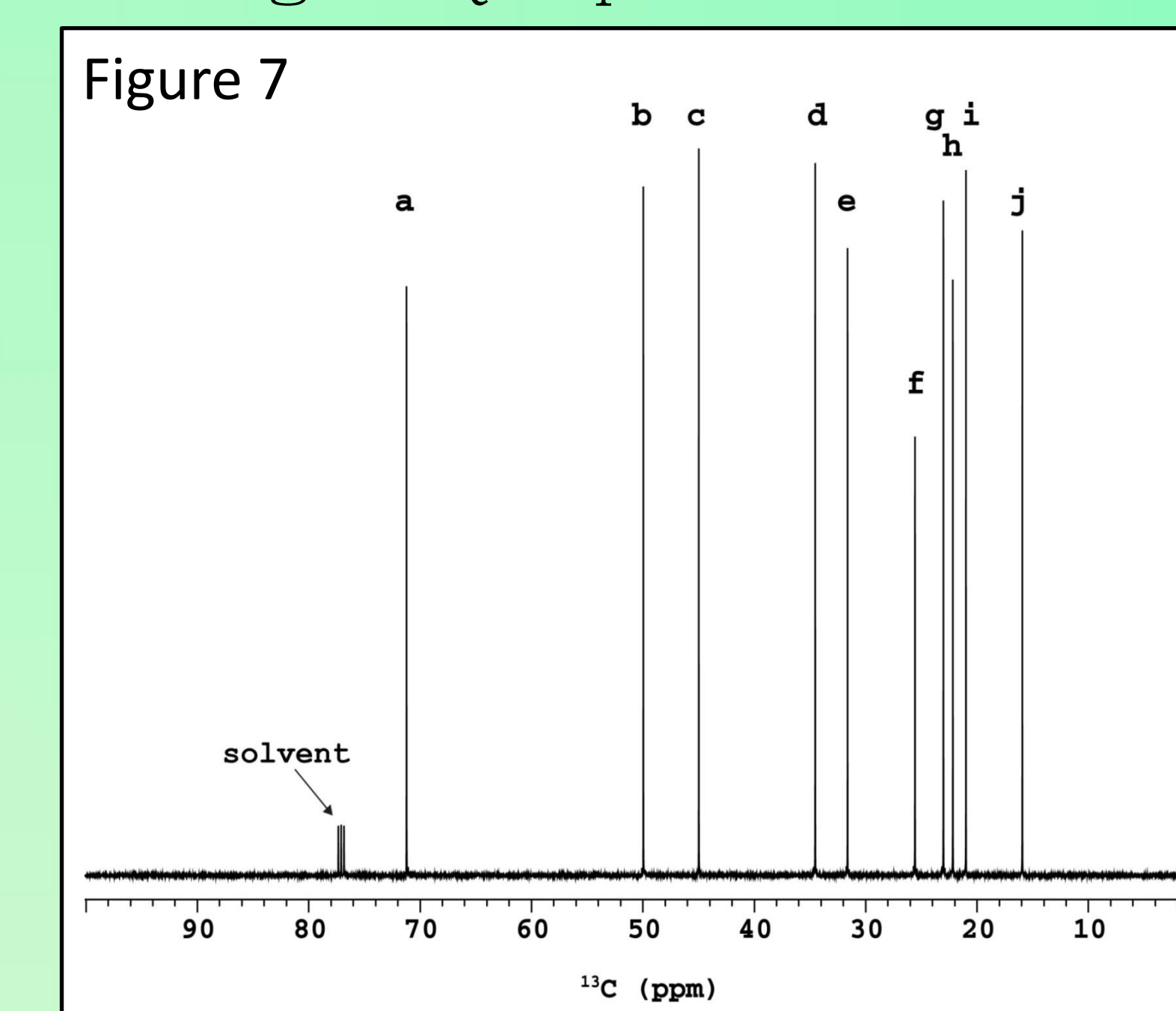


Assignments of $^1\text{H}/^{13}\text{C}$ NMR Resonances of Menthol

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^{13}C NMR 1-D Spectrum

The ^{13}C spectrum of menthol is shown in Figure 7. The spectrum was recorded at 500 MHz (^1H) using a spectral width of 12626.3 Hz and 16399 complex points. The assignments to this spectrum can be made using the analysis of the gHMQC spectrum.

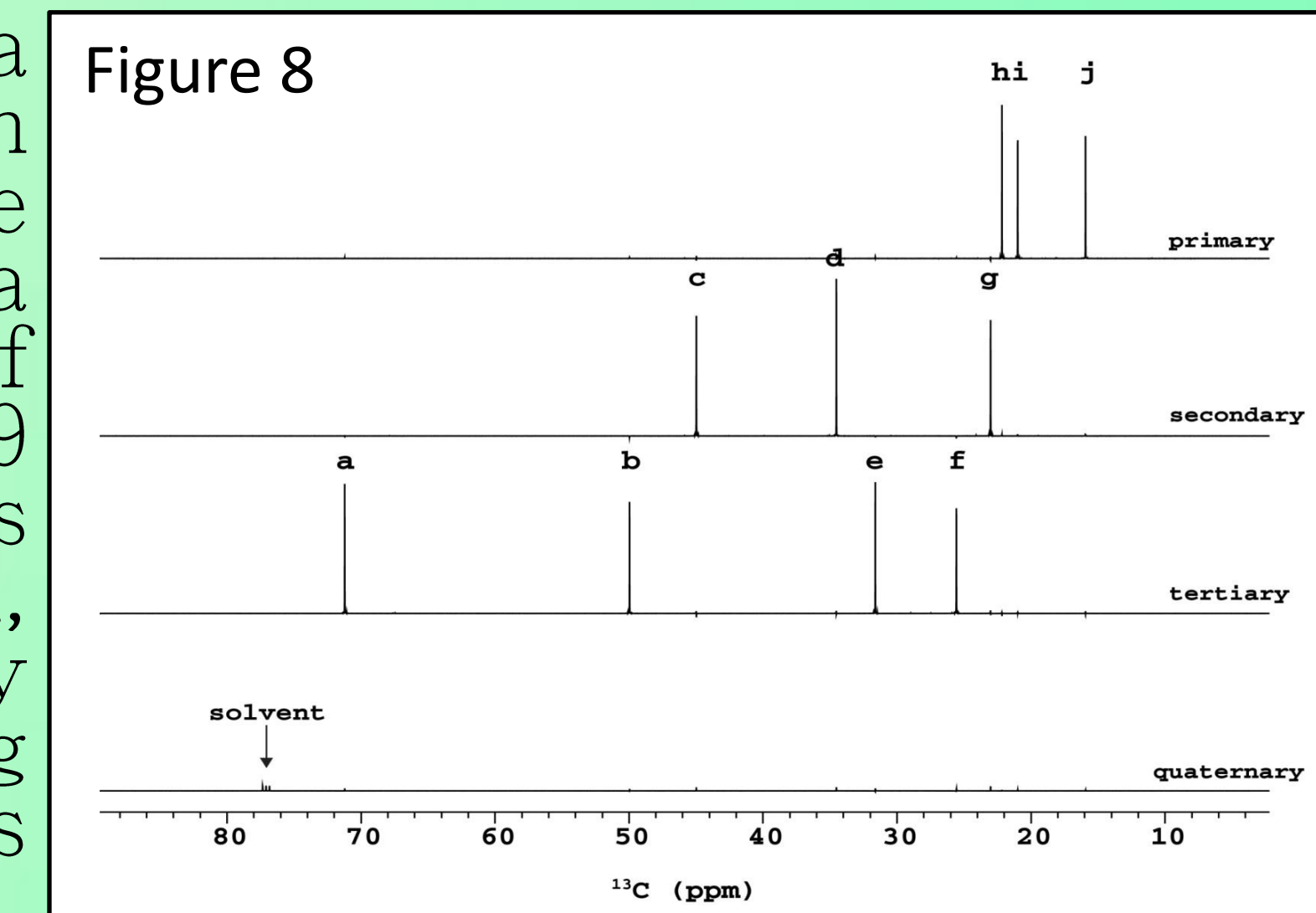


Peak	Chemical Shift (ppm)
a	71.7
b	50.01
c	42.53
d	34.36
e	31.98
f	25.92
g	23.32
h	22.17
i	21.03
j	16.23

Resonance **a** corresponds to position 1, which makes intuitive sense because of the proximity to the hydroxyl group. Peak **b** corresponds to position 2, which likewise makes sense since this resonance is expected to be more downfield than the other two methine carbons due to the proximity to the hydroxyl group. Peaks **c** and **d** correspond to the methylene carbons in positions 6 and 4 respectively, and peaks **e** and **f** correspond to the two other methine carbons in positions 8 and 5. Peak **g** corresponds to position 3 and peaks **h**, **i**, and **j** are confirmed as the methyl carbons in positions 7, 10, and 9 respectively.

^{13}C DEPT NMR 1-D Spectrum

The ^{13}C DEPT spectra shown are shown in Figure 8. The data were recorded using a spectral width of 12626.3 Hz and 16399 complex points. Peaks previously labeled **h**, **i**, and **j** appear as primary carbons, confirming their identity as methyl groups in the sample of menthol. Peaks identified as **c**, **d**, and **g** appear as secondary carbons confirming their previous assignments, and peaks **a**, **b**, **e**, and **f** are tertiary carbons which confirms their prior assignments as well.



Results

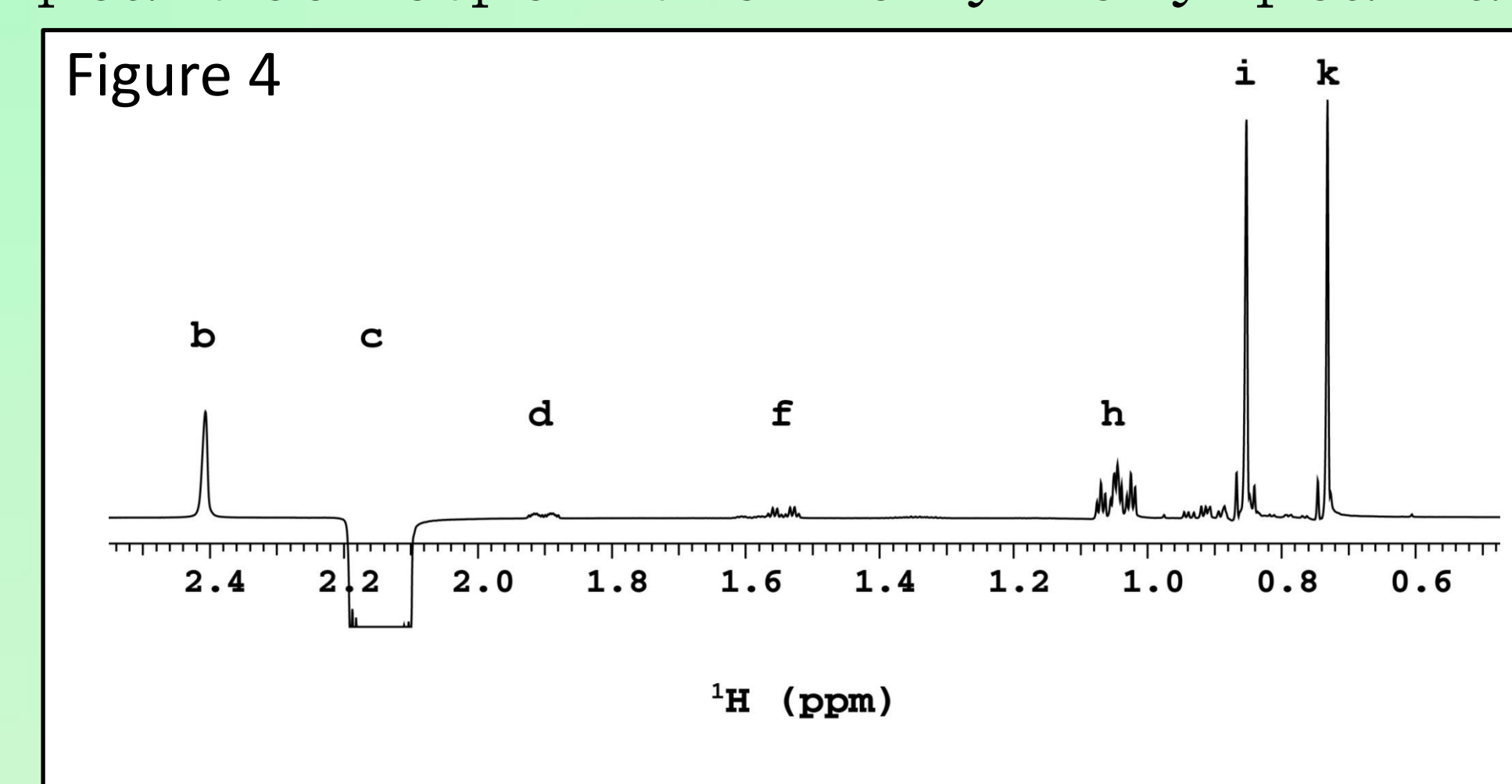
Most of the ^1H resonances present in the spectra of menthol could be assigned based on a careful analysis of the chemical shifts and fine structure present in the 1D spectrum. These ^1H assignments were then used to assign the ^{13}C index in the 2D HMQC spectrum. The ambiguities that arose in the ^1H spectrum could be definitively assigned by irradiating specific peaks in the NOESY experiment. This allowed for the unique assignment of the three methyl $^1\text{H}/^{13}\text{C}$ resonances.

References

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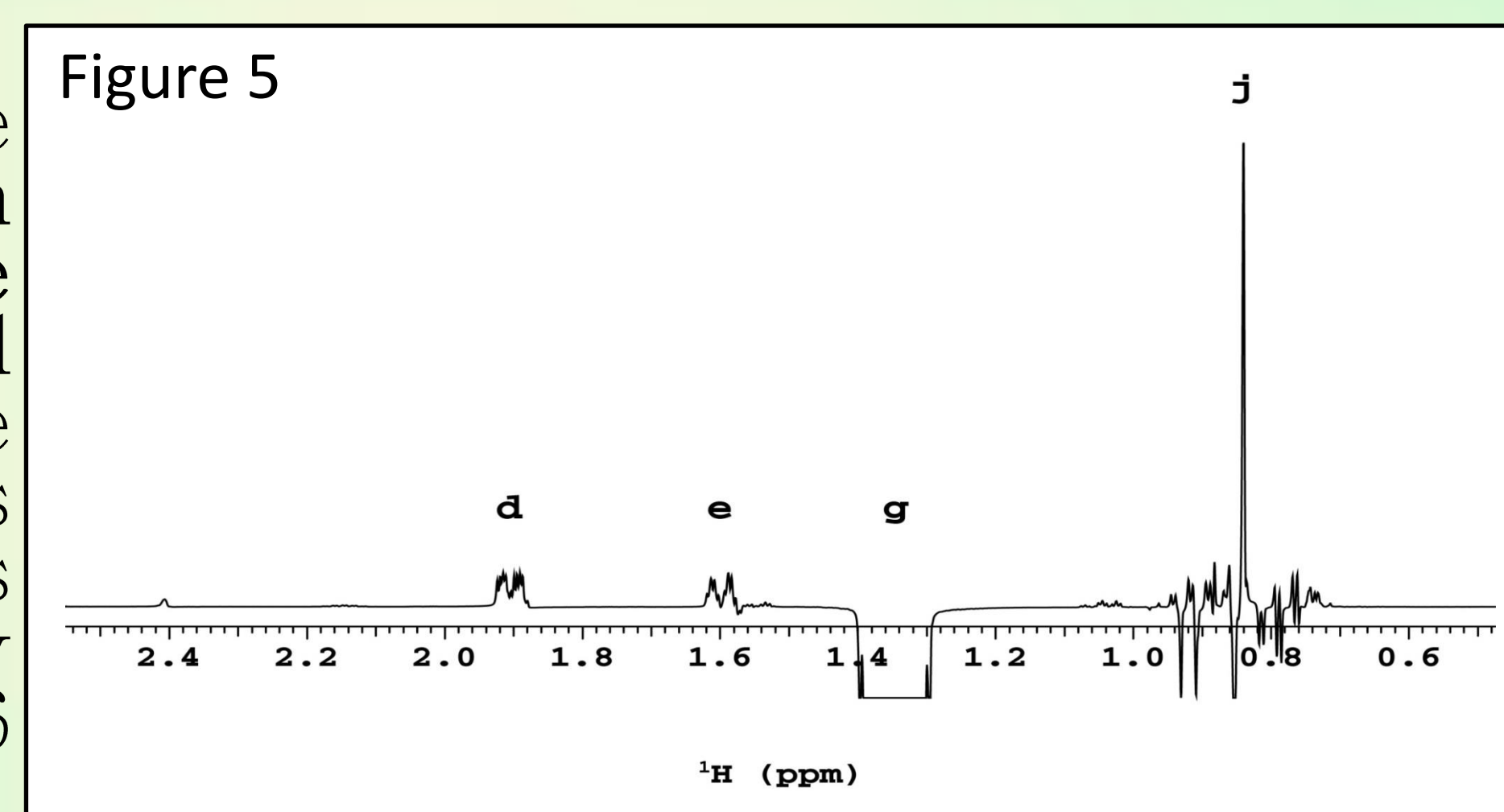
NOESY NMR 1-D Spectrum

In order to resolve the aforementioned ambiguities in the spectrum of menthol, it was necessary to analyze data collected from the spectrum of Nuclear Overhauser Effect spectroscopy. The data were recorded using a mixing time of 500 ms and a spectral width of 5230.13 Hz. The spectrum shown in Figure 4 is the result of irradiating the resonance at 2.15 ppm. The irradiated resonance corresponds to the methine at position 8, and is labeled **c**. The resulting NOE peaks corresponds to the hydroxyl peak labeled **b** and the



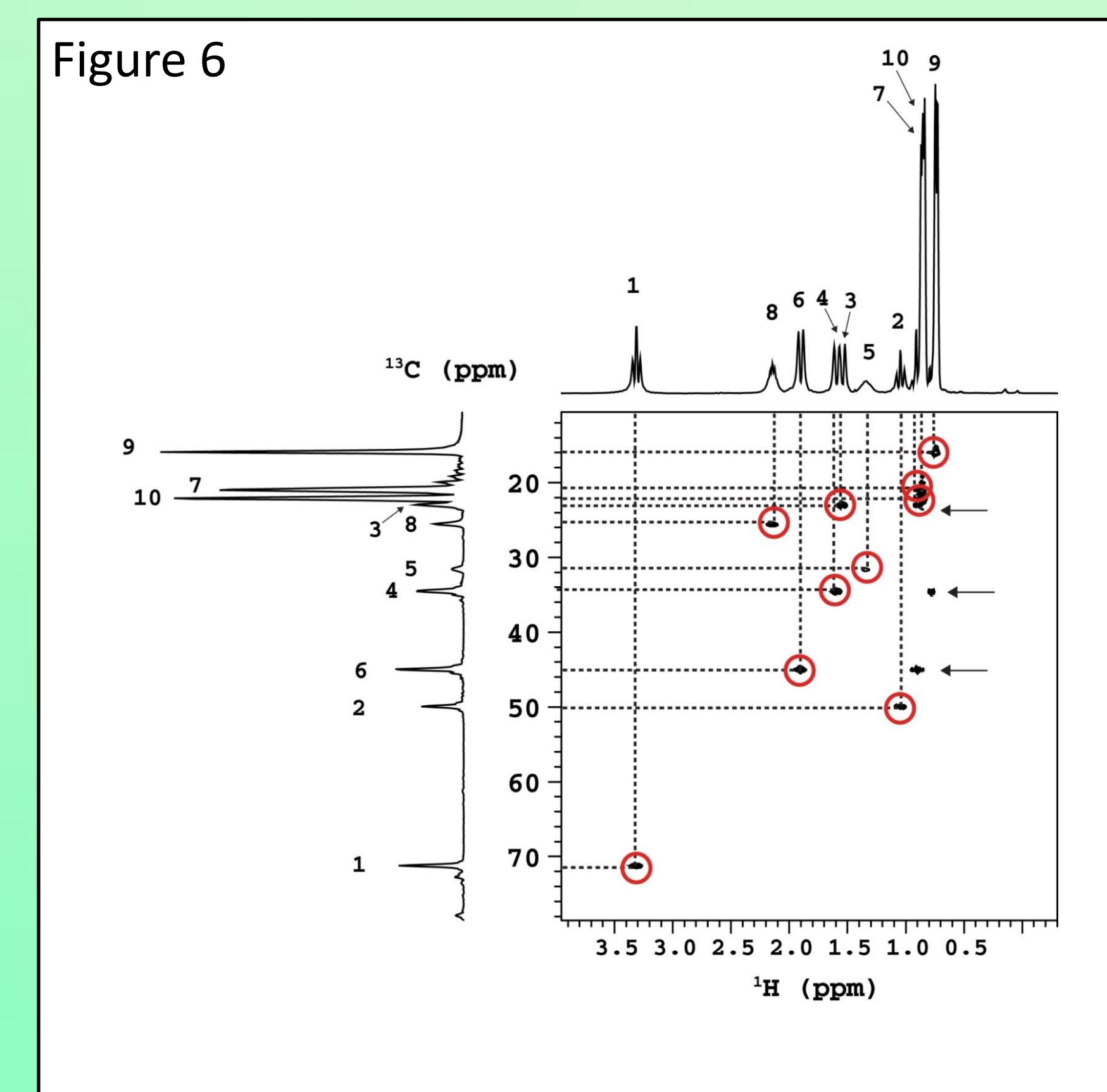
peak labeled **h**, which confirms the previously made assignment to position 2. NOEs are also observed to peaks **i** and **k**, which provides enough information based on the structure

of the molecule to assign peaks **i** and **k** to the methyl groups in positions 9 and 7 accordingly. Similarly, in Figure 5 the peak we previously assigned to the methine in position 5 is irradiated. There is a NOE between **g** and peaks **d** and **e**, which are assigned as two of the methylene protons. We also observe a NOE to peak **j** which further confirms our methyl group assignments, making this the methyl in position 10. Peaks **d** and **e** have been assigned as methylene groups and this correlation allows us to confirm they are in positions 6 and 4 respectively.



gHMQC 2-D NMR Spectrum

The Gradient-Enhanced Heteronuclear Multiple Quantum Correlation spectrum reveals ^{13}C - ^1H chemical shift correlations between directly bonded hydrogen and carbon nuclei. The gHMQC spectrum is shown in Figure 6. The data were recorded at 500MHz (^1H) using spectral widths of 5230.13 Hz in the direct (^1H) dimension (F2, horizontal axis) and 12626.3 Hz in the indirect (^{13}C) dimension (F1, vertical axis) with 1024 complex points in the direct dimension (F2) and 512 complex points in the indirect dimension (F1). We can

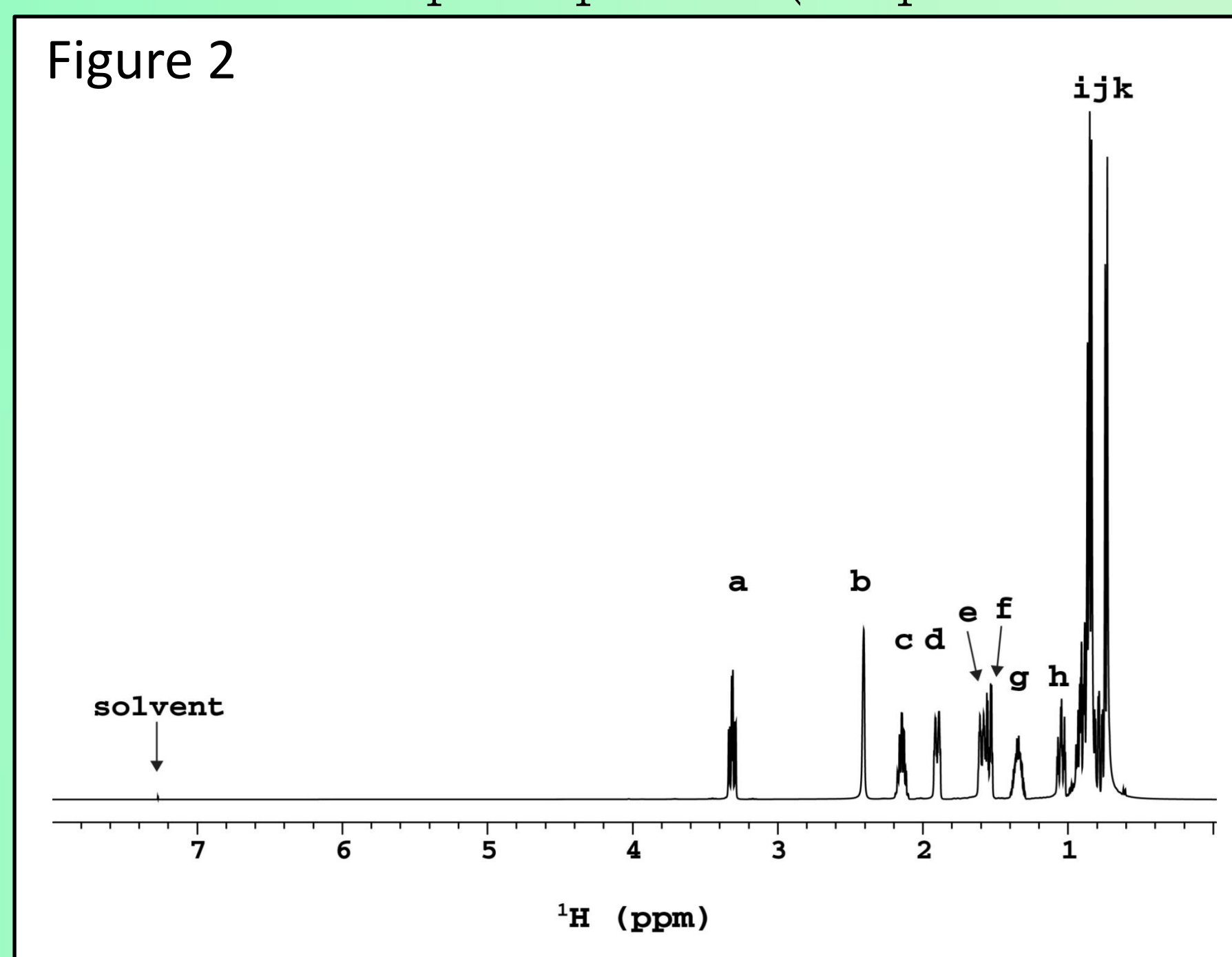


map the ^1H assignments to the projections on the gHMQC spectrum. Following the projections to the 2D resonances allows us to assign ^{13}C based on the previously assigned ^1H resonances. Correlations indicated by arrows represent artifactual correlations arising from the presence of the intense methyl resonances.

Figure 1 (1R,2S,5R)-2-isopropyl-5-methylcyclohexanol, commonly known as menthol, is a 9 carbon structure containing a 6 membered ring, an isopropyl group branching from the second carbon, a hydroxyl group bonded to the first carbon and a methyl group bonded to the fifth carbon. The molecular formula of menthol is $\text{C}_{10}\text{H}_{20}\text{O}$ and the molecular weight is 156.27 g/mol. Menthol can be made synthetically or extracted from coriander, peppermint, or other mint oils. The structure of menthol is shown in Figure 1.

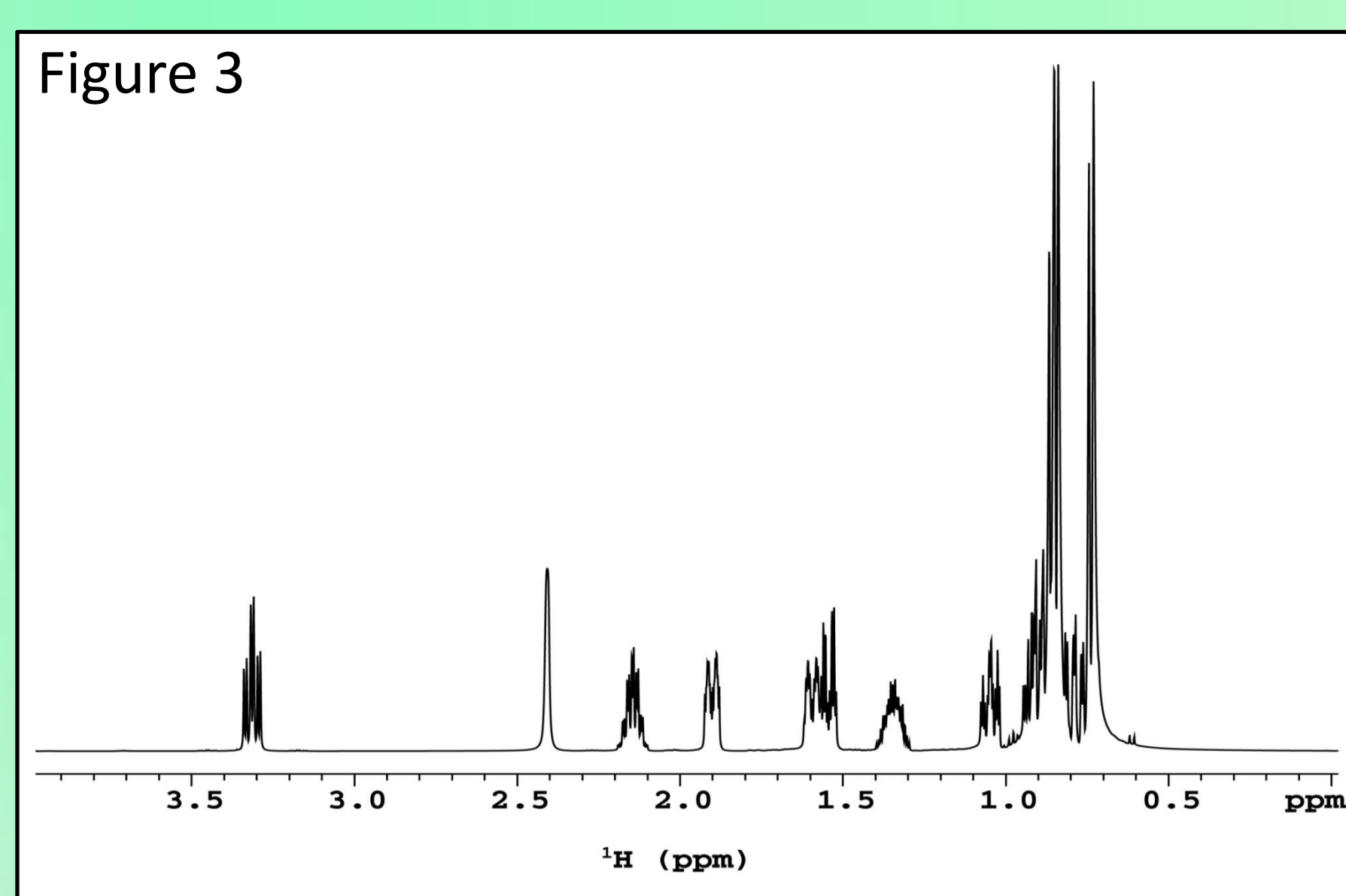
^1H 1D NMR Spectrum

The ^1H spectrum of menthol is shown in Figure 2. The spectrum was recorded at 500 MHz (^1H) using a spectral width of 5230.13 Hz and 8192 complex points (acquisition time of 1.5s).



The region between 0 ppm and 4 ppm has been expanded in Figure 3, which allows us to examine the fine structure in detail. The solvent resonance (residual CHCl_3) appears at 7.27 ppm. The most downfield resonance in menthol, **a**, is at 3.31 ppm,

which we can assign to the proton in position 1 because of the proximity to the electronegative oxygen. The resonance at 2.41 ppm, **b**, is a singlet that we can confidently assign to the hydroxyl proton bonded to the carbon in position 1.



By carefully examining the fine structure of the resonance labeled **c**, which appears at 2.15 ppm, we can distinguish a septet of doublets. We can assign this to the single hydrogen at position 8 because the resonance is split by the methine

at position 2 and the 6 equivalent protons in positions 7 and 9, giving rise to the observed complex splitting pattern. The resonances at 1.89 ppm and 1.53 ppm labeled **d**, **e** and **f** are likely the three methylene groups in positions 3, 4 and 6 but we cannot definitively assign them without further experimentation. Resonance **g** at 1.34 ppm is a complex multiplet (proton is coupled to four nonequivalent protons) which allows us to tentatively assign it to position 5. We can also infer that the most upfield peaks **i**, **j**, and **k** correspond to the methyl groups in positions 7, 9 and 10 but we cannot definitively assign them yet. The remaining peak at 1.04 ppm, labeled **h**, would correspond to position 2 through the process of elimination but further experimentation is needed to confirm this assignment.