

SimEsp NMR: Simulating Intricate Second-Order Subspectra

I. P. de Arruda Campos*

PPGEP, Instituto de Ciências Exatas e Tecnologia, Universidade Paulista, Rua Dr. Bacelar, 1212, 04026-002 São Paulo – SP- Brazil

M. G. Constantino, G. V. J. da Silva, V. C. G. Heleno, I. A. Borin

Departamento de Química, Faculdade de Filosofia, Ciências e Letras de Ribeirão Preto, Universidade de São Paulo, Av. Bandeirantes, 3900, 14040-901 Ribeirão Preto – SP-Brazil

Keywords: computer program; ^1H NMR; spectrum simulation

Abstract: The computer program SimEsp NMR can produce simulated ^1H NMR subspectra (maximum 10 hydrogens) through quantum mechanical calculations, starting from arbitrary or experimentally determined values. In this paper we describe a detailed example of how to use the program to confirm and refine chemical-shift and coupling-constant values obtained as approximate values from experimental spectra.

Resumo: O programa de computador SimEsp NMR pode fazer espectros simulados de RMN de ^1H (máximo de 10 hidrogênios) através de cálculos de mecânica quântica, partindo de valores arbitrários ou determinados experimentalmente. Neste trabalho é descrito detalhadamente um exemplo de como utilizar o programa para confirmar e refinar valores de deslocamentos químicos e de constantes de acoplamento obtidos como valores aproximados por exame de um espectro experimental.

Introduction

The calculation of NMR spectra only from chemical-shift and coupling-constant values, producing graphs virtually identical to the experimental spectra, is one of the most significant triumphs of quantum mechanics. The computer program SimEsp NMR¹ can perform calculations based on the variational method, starting from the usual NMR Hamiltonian operator

$$E(Hz) = -\sum_{i=1}^p m_i \nu_i + \sum_{i=1}^{p-1} \sum_{j=i+1}^p m_i m_j J_{ij},$$

as described elsewhere.² After finding all frequencies and intensities, the program also calculates the resulting curve according to

distribution laws: either Gaussian or Lorentzian distribution, or even a variable combination of these two, can be selected by the user. The peaks maxima are found and printed by the program through examination, point by point, of the Gaussian/Lorentzian curve.

In this paper, we describe a detailed example showing how the program can be used to confirm and refine experimental values of chemical shifts and coupling constants for an ABCD system experimentally found for diketone **1**.³

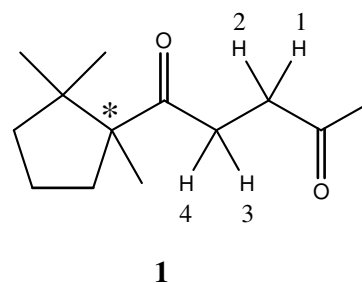


Figure 1. Structural Formula for diketone **1**

* ipdacamp@uol.com.br

Results and discussion

The signals of the ABCD system occur in the region 2.55 – 2.85 δ , clearly suggesting that they refer to hydrogens H1, H2, H3 and H4 as shown in the formula. The reason for the two hydrogens of a same methylene being different from each other is clearly the occurrence of a stereogenic

center in the point where the side chain is attached to the ring. As a consequence, we should expect that the difference in chemical shifts for H3 and H4 should be higher than those for H1 and H2 (if this last difference exists at all). Anyway, the spectrum shown in Figure 2 rules out any simple system such as A_2X_2 (which would appear as two triplets).

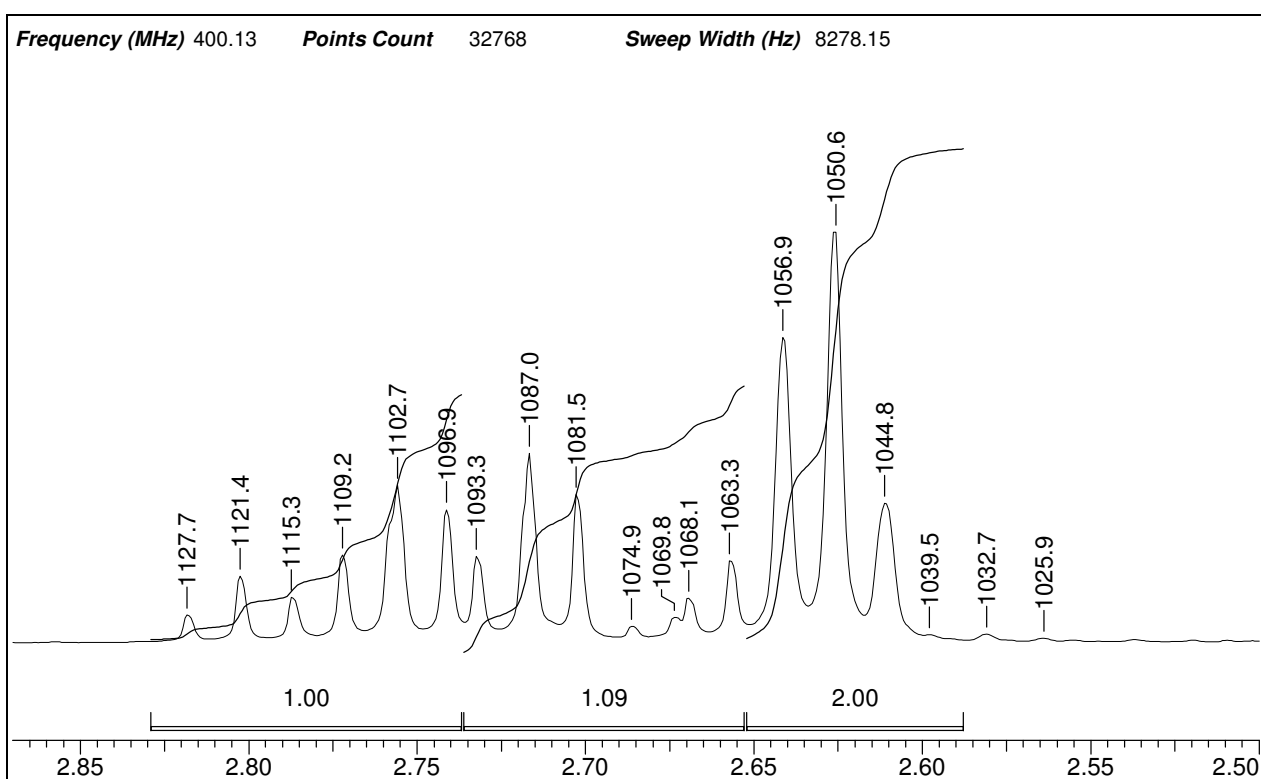


Figure 2. Region of the experimental NMR spectrum containing the ABCD system

The integral values suggest that there are two hydrogens well isolated from each other (and from the other two) and two hydrogens close to each other (or even together). The combination of this information with the distances from the methylenes to the stereogenic center, indicates

that the isolated hydrogens are H3 and H4, while the hydrogens that are close to each other are H1 and H2.

The maximum number of coupling constants (J) values that should be expected for structure **1** is 6: 2 geminal (J_{gem}) values (-12 to -22 Hz,

according to usual tables) and 4 vicinal (J_{vic}) values ($\approx +7$ Hz) (all J values are for acyclic compounds). Moreover, there are no structural features that could suggest any restricted rotation. We can thus expect that the J_{vic} values should be identical or very similar to each other. If the two isolated hydrogens are H3 and H4, the signal to be expected should be 4 lines corresponding to an AB system (the two central lines higher than the two external lines). Each one of these lines would be further split by the two J_{vic} values between each hydrogen and the two hydrogens that are "together" on the right extreme of this group of signals.

The signals located on the left extreme of the multiplet are reasonably far from the right extreme; it is thus possible that these signals on the left side could keep some of the first-order signals characteristic properties, particularly the property of showing J values in the distance between peaks. As the AB system (even being a second-order system) also maintains this property, it is obvious that measuring distances between peaks, especially on the left side of the multiplet, can furnish J values for a simulation. Some of the measures made for this purpose are shown in Figure 3.

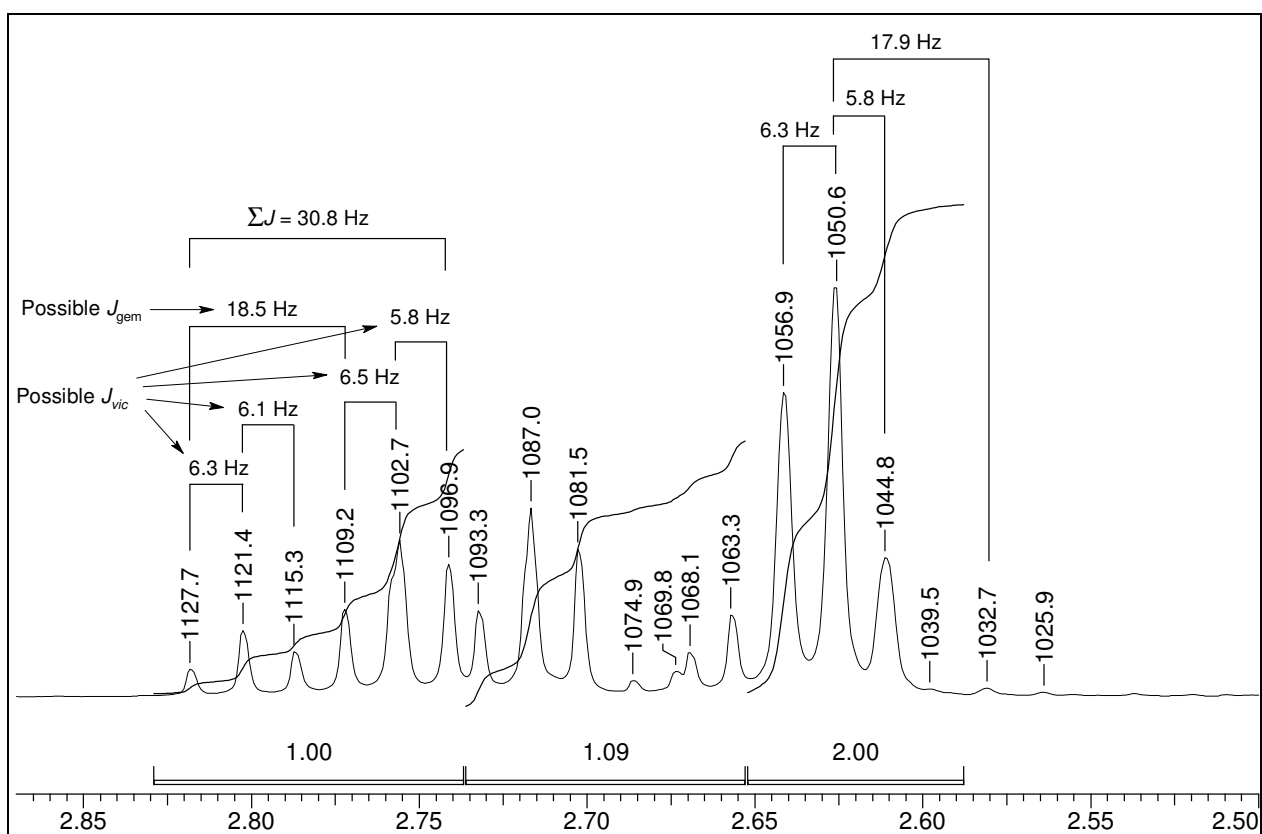


Figure 3. Measuring distances between peaks

As can be seen in Figure 3, there are several values around 6 Hz (that could be J_{vic} values);

we can also see the value 18.5 Hz (that could be the absolute value of J_{gem}). Although it is not

shown in Figure 3, the value $^{***}18.4$ Hz also appears in H3 signals (for instance, in the difference $1093.3-1074.9=18.4$; or in the difference $1081.5-1063.3=18.2$).

On close examination, we can see that H4 signals can be interpreted as two triplets showing the characteristic roof effect for AB systems. The signals of H3 can be also seen as

two triplets with the reciprocal roof effect, except that the rightmost triplet is further split as a double doublet. This would be possibly attributed to a consequence of a second order effect introduced due to the proximity to H1 and H2.

The splitting diagram corresponding to all these considerations is shown in Figure 4.

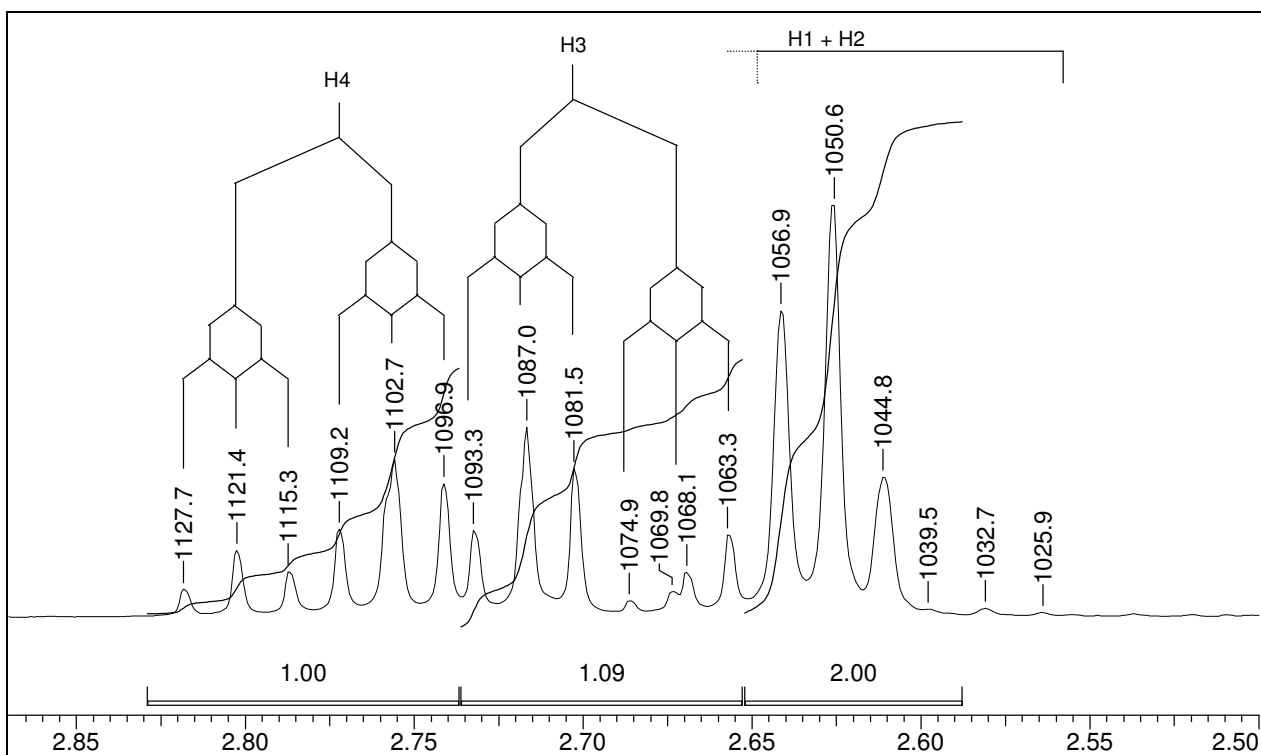


Figure 4. Splitting diagram for H3 and H4

The signals for H1 and H2 could be interpreted as a unique triplet, because the distances between consecutive peaks (6.3 and 5.8 Hz) shown in figure 3) are consistent with the J_{vic} values found in other signals. However, the rather large width of the peaks, combined with the existence of a signal in a position that could correspond to a J_{gem} value between H1 and H2 (see the value 17.9 Hz in Figure 3), suggest that H1 and H2 are close together, but they do not

have exactly the same chemical shift. However, because they are very close, both chemical shifts should be inside the central large peak, around 1050.6 Hz.

Figure 5 shows an illustration of the roof effect for the coupling between H3 and H4. This effect is due to J_{gem} , and it should thus be observed comparing the size of the triplets, with each triplet considered as a block.

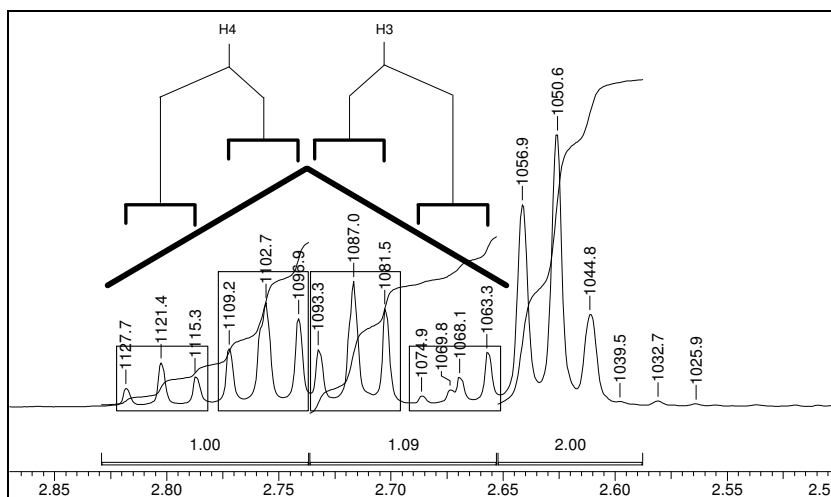


Figure 5. Roof effect for the geminal coupling between H3 and H4

Figure 6 shows the roof effect for the vicinal coupling. It should be noted that J_{vic} exists only between the rightmost signal (corresponding to H1 and H2) and each one of the triplets. As can be observed in this figure, the leftmost triplet (which is more distant from the group H1/H2)

has a small effect (9° inclination); the effect increases for each triplet according to the proximity to the group H1/H2, reaching 33.1° . The triplet of the group H1/H2 shows a very strong reciprocal effect, which could be interpreted as a cumulative effect.

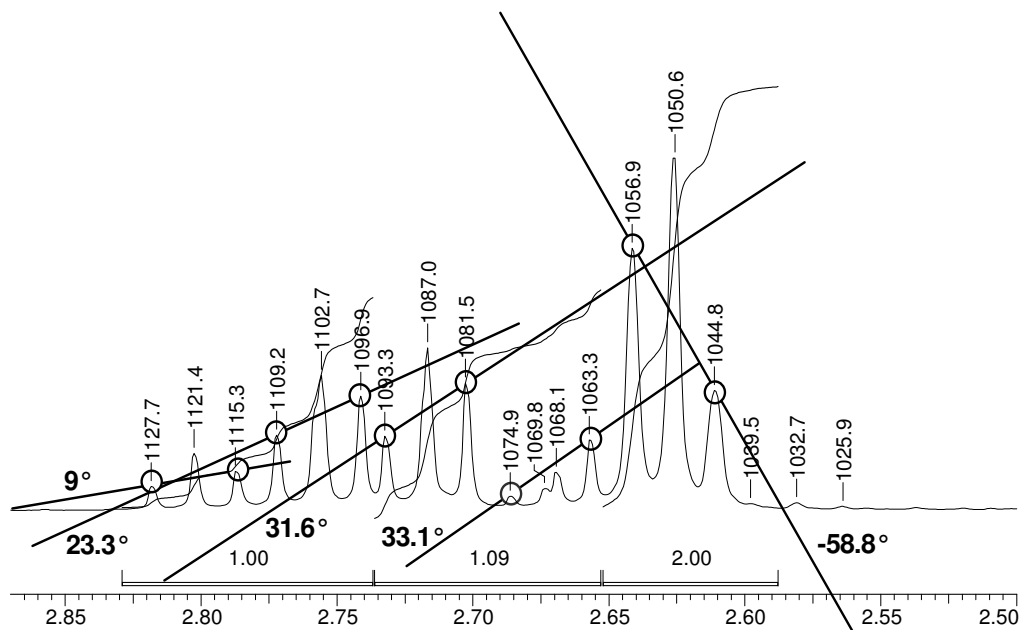


Figure 6. Roof effect for the vicinal couplings

At this point, we have more than enough to start a simulation. The initial data could be the following:

Chemical shifts:

- H1 and H2: around 1050.6 Hz, very close to each other. It can be one on each side of 1050.6 Hz, but not necessarily.
- H3: towards the left of the center of the group of signals between 1093.3 and 1063.3 Hz. A reasonable starting value could be 1081.5 Hz.
- H4: towards the right of the center of the group of signals between 1127.7 and 1096.9 Hz. A reasonable starting value could be 1109.2 Hz.

Coupling constants:

- Around +6 Hz or more for the four J_{vic} values ($J_{1,3}$; $J_{1,4}$; $J_{2,3}$; $J_{2,4}$).
- Around -18.5 Hz for $J_{3,4}$ (J_{gem}).
- Around -17.9 Hz for $J_{1,2}$ (J_{gem}).

Figure 7 shows the simulation obtained with the SimEsp NMR program, using these values.

As split peaks are found in the simulation while they are fused together in the experimental spectrum, we can increase the “width at half height” value from 1.0 to 1.5 Hz. We can also reduce the “minimum intensity” to see if any relevant signals appear, and, if so, we can modify the ratio “Lorentzian/Gaussian”. By carrying out only these modifications, the appearance of the simulated spectrum can show significant changes, as can be observed comparing Figure 7 to Figure 8.

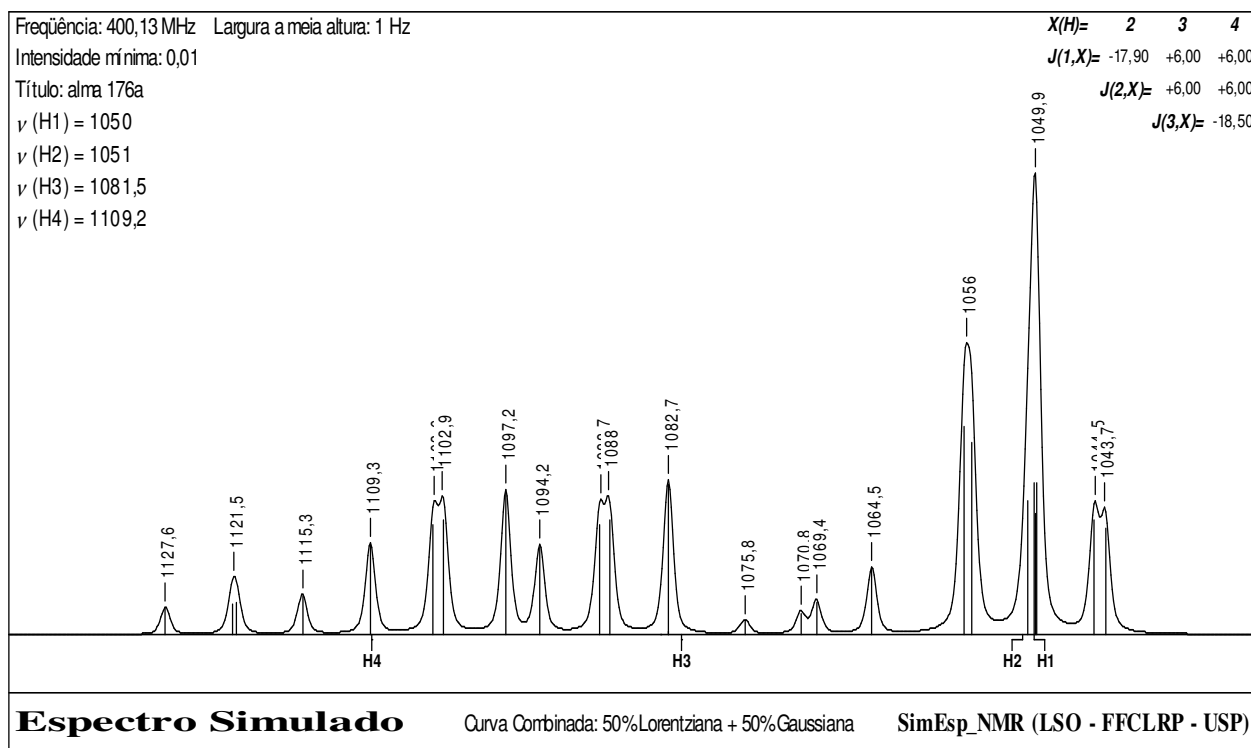


Figure 7. Initial simulation

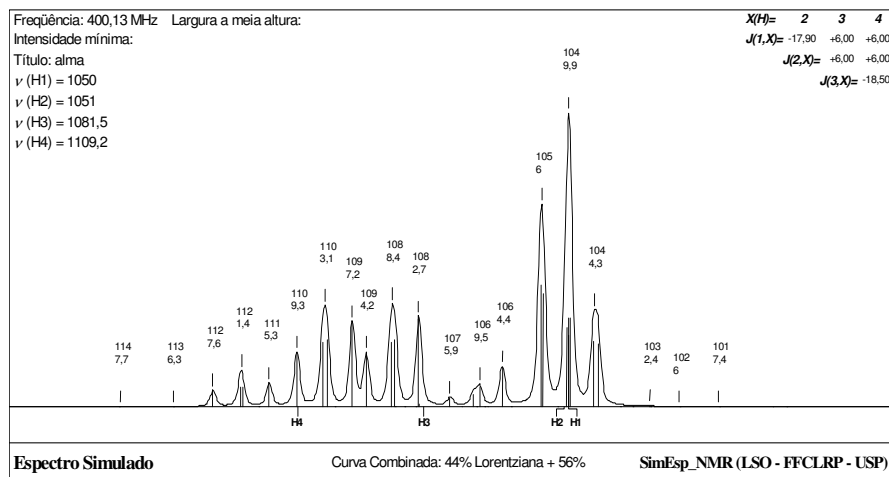


Figure 8. Results of the modification of some parameters

Comparing the chemical shifts of this simulation to the experimental values (Figure 2), we see that the values for H4 are reasonably correct, but the values for H3 are higher in the simulation. We should then try to gradually reduce the chemical shift of H3. The values corresponding to H1/H2 are rather low in the simulation, suggesting that we should slightly increase the chemical shift of H2 and/or of H1.

Although the results of these modifications are what would be expected, they might as well be surprising. For this reason, it is advisable to make only small changes, carefully observing the effect of each small modification. After several modifications carried out as previously suggested, we have obtained the simulation shown in Figure 9.

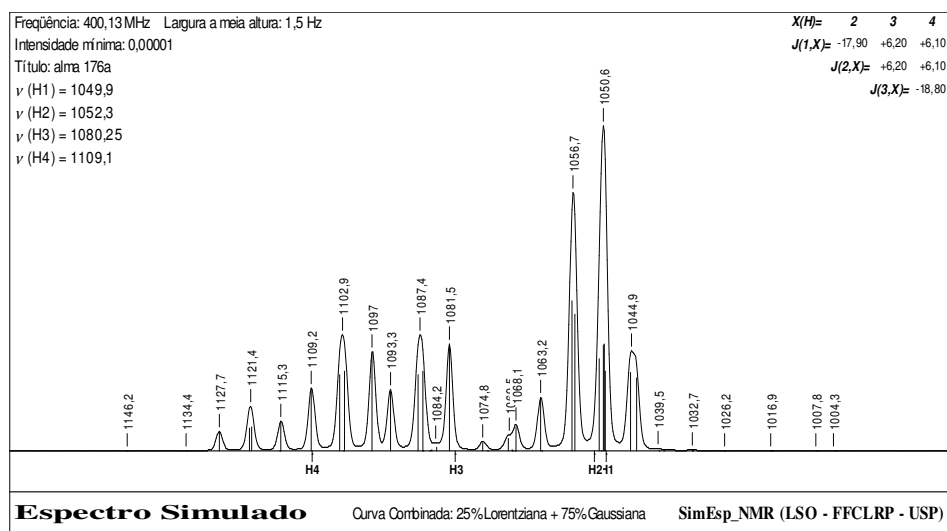


Figure 9. Simulation after several small adjustments

We can now observe a much better correlation with the experimental spectrum, but not a perfect correlation. There are still some numbers subtly different, and also some peaks with a slightly different shape – some of them are somewhat larger; others do not have shoulders as their experimental counterparts, etc. However, the overall correlation is excellent. Also, additional experimentation can indicate that the chemical-shift and coupling-constant values are extremely close to the experimental ones, because if any significant modification is introduced, a worse result is obtained.

Conclusion

The excellent correlation between the simulated (figure 9) and the experimental (figure 2) spectra shows the value of simulation as a tool for confirming and refining experimentally determined values of chemical shifts and coupling constants. The whole process has also the virtue, particularly for students, of convincingly confirming several theoretical aspects of the NMR phenomenon.

Acknowledgments

The authors thank FAPESP, CAPES, CNPq and UNIP for financial support.

References

1. This program can be downloaded from <http://artemis.ffclrp.usp.br/NMR.htm>, and is freeware. At the moment, only a Portuguese version is available, but an English version, revised and improved, is currently being prepared.
2. M.G. Constantino, G.V.J.Silva, V.C. G.Helena, I.A. Borin, I.P.A. Campos, *Quim. Nova* (2005) submetido.
3. A.L.S.M. Araujo, “Estudos Sobre a Síntese de Cuparanos”, PhD Thesis, FFCLRP/USP, Ribeirão Preto, 2004. A digital copy of this thesis is available for download at <http://artemis.ffclrp.usp.br/TesesPDF/AnaDo utCorr.pdf> ; in the thesis, this compound is identified by number 47.