Solution to doubling spectroscopy challenge

Reinhard Meusinger¹

© Springer-Verlag Berlin Heidelberg 2016

The winner of the doubling spectroscopy challenge (published in volume 407, issue 27) is:

Sami T. Tuomivaara, Complex Carbohydrate Research Center, University of Georgia, Athens, GA, USA

The award entitles the winner to select a Springer book of his choice up to a value of €100,-.

Our Congratulations!

Solution

The reason for the signal doubling of the H-6 hydrogen signal in the ¹H-NMR spectrum of dexelvucitabine (DFC) is the presence of the fluorine at position 5 (Fig. 1).

Fluorine has only one isotope, ¹⁹F, with a spin ½ nucleus. Since both ¹H-6 and ¹⁹F-5 are connected in DFC by a vicinal coupling ³J_{H6,F5}, the NMR signal of each ¹H-6 nucleus is split by the interaction with the ¹⁹F-5 nucleus and vice versa. Therefore, no cross-peak will be observed for the H-6 doublet in the H,H-COSY spectrum. As expected, noticeable cross-peaks were observed in the NOESY spectrum for interactions between H-6, H-2', H-5', and –OH protons, indicating correct signal assignment (Fig. 2).

Considerable cross-peaks were also observed between the pair of twin amino proton signals in the NOESY spectrum.

This article is the solution to the Analytical Challenge to be found at <http://dx.doi.org/10.1007/s00216-015-9002-x>

✉ Reinhard Meusinger
meusi@oc.chemie.tu-darmstadt.de

¹ Institute of Organic Chemistry and Biochemistry, University of Technology Darmstadt, Alarich-Weiss-Str. 4, 64287 Darmstadt, Germany

However, the phase of these cross-peaks (red color) is opposite to that of the other NOESY cross-peaks (blue color). This indicates that there is a slow exchange process between both amino protons during the 700-ms continuous mixing time at room temperature.

The energy barrier for this exchange process can be calculated using the experimentally determined coalescence temperature T_c and the frequency difference $\Delta\nu$ between the separate signals of the amino-group protons. Both of these parameters were determined twice at different magnetic field strengths:

$$\begin{aligned} T_{c,300\text{ MHz}} &= 314\text{ K} & T_{c,500\text{ MHz}} &= 322\text{ K} \\ \Delta\nu_{300\text{ MHz}} &= 73.5\text{ Hz} & \Delta\nu_{500\text{ MHz}} &= 123\text{ Hz} \end{aligned}$$

By using the Boltzmann constant k_B , the Planck constant h , and the universal gas constant R , the

Fig. 1 Three-dimensional structure of DFC with observed NOEs for proton H-6 (black arrows)

Fig. 2 Two-dimensional ^1H -correlated double quantum filtered COSY spectrum (*left*) and NOESY spectrum (*right*) of DFC. The phase of the NOE cross-peaks (*blue*) is opposite to that of the diagonal peaks (*red*). The *red-colored cross-peaks* between both amino protons relate to the intramolecular exchange process

energy of activation can be calculated as the Gibbs energy

$$G^{\#} = RT_c \ln \frac{\sqrt{2} k_B T_c}{\pi h \nu}$$

$$G^{\#} = 8.314 \text{ J K}^{-1} \text{ mol}^{-1} \cdot T_c \ln(22.96 \text{ K}^{-1} \text{ s}^{-1} \cdot T_c / \nu).$$

This yields $\Delta G_{300 \text{ MHz}}^{\#} = 63.7 \text{ kJ mol}^{-1}$ and $\Delta G_{500 \text{ MHz}}^{\#} = 64.0 \text{ kJ mol}^{-1}$.

Accounting for small experimental deviations, a very similar result of 64 kJ mol^{-1} was obtained in both experiments.