¹H–¹³C N.M.R. Chemical Shift Correlation

By Christian Le Cocq, Marc-André Delsuc, and Jean-Yves Lallemand*

(*Laboratoire de Chimie de l'Ecole Normale Supérieure, Associé au C.N.R.S.,*
24 *rue Lhomond,* 75231 *Paris Cedex* 05, *France*)

Summary A ¹H–¹³C n.m.r. correlation map is obtained by low-power heteronuclear decoupling, with carbon signal acquisition under proton broad-band decoupling in order to suppress off-resonance effects.

¹³C N.M.R. studies on large molecules still remain difficult owing to the generally poor reliability of precise peak assignments. As ¹H assignments are more easy to attain by homonuclear decoupling techniques including tickling and INDOR, various methods have already been proposed to correlate ¹H and ¹³C chemical shifts either by means of heteronuclear double irradiation[1] or by 2-dimensional n.m.r. experiments.[2]
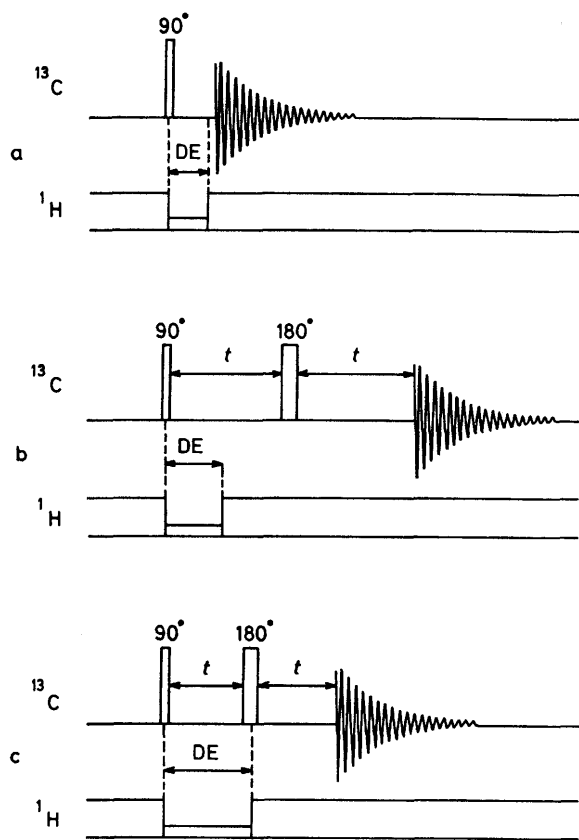

FIGURE 1. Excitation sequences. (a) Fundamental sequence, DE is constant and equal to $1/2J_0$; (b) high resolution sequence. A spin echo is added to avoid phase distortion, DE is incremented from A to B (4 to 84 ms) and t is constant and equal to B (84 ms), the maximum value of DE; (c) same sequence as in (b), except that t is set equal to DE.

We report in this communication a new method allowing correlation, using a selective heteronuclear excitation during a spin preparation period and acquisition performed under broad-band ¹H decoupling.

The basic experiment is depicted on Figure 1a: after a ¹³C 90° pulse, the spin system is submitted to low-power proton continuous wave (C.W.) irradiation during a period DE during which carbon atoms bearing a proton exhibit a residual coupling constant J_r[3] (off-resonance conditions) (equation 1).† Carbon signal acquisition then occurs under proton broad-band decoupling. If DE is given a value of

$$J_r = \sqrt{[(\Delta v - J_0/2)^2 + (\gamma H_2)^2]} - \sqrt{[(\Delta v + J_0/2)^2 + (\gamma H_2)^2]} \quad (1)$$

4 ms, all sp³ carbon atoms bearing proton(s) with resonances far from the decoupling frequency and then exhibiting a $J_0 = 125$ Hz coupling constant give zero signals because of mutual cancellation of lines.[5] After Fourier transformation the spectrum shows only peaks corresponding to quaternary carbon atoms and to carbon atoms bearing proton(s) resonating close to the decoupler frequency.

However, the resolution of this experiment is not sufficient for practical use: the amplitude of a CH_n signal is modulated by $\cos^n \pi J_r DE$.

Figure 1b displays a modified excitation sequence that enhances proton resolution. A ¹³C spin-echo has been introduced to avoid frequency-dependent phase distortion. In this experiment the value of DE is linearly incremented at each scan. The time t between the two pulses and between the second pulse and the acquisition is kept constant and equal to the maximum value of DE. A C–H carbon, with a residual coupling constant J_r during DE, gives a peak with an amplitude given by equation (2), where A and B

$$M(J_r) = \frac{M_0}{B - A} \int_A^B \cos(\pi J_r DE) d(DE)$$

$$= \frac{2M_0}{\pi J_r (B - A)} \cdot \sin[(\pi J_r (B - A)/2] \cdot \cos[\pi J_r (B + A)/2] \quad (2)$$

are the minimum and maximum values of DE, respectively, and provided that the number of scans is sufficient to neglect the influence of the DE increment value. $M(J_r)$ is maximum for $J_r = 0$ and then decreases approximately as $(\sin J_r)/J_r$. A and B values are selected so that $M(125$ Hz$) = 0$ and the appropriate proton–carbon sensitivity and selectivity are achieved: for example A $= 4$ ms and B $= 84$ ms.

The correlation map is then generated by a set of spectra corresponding to different values of the decoupling fre-

---

† The efficiency of all the experiments described in this paper increases as the decoupling power decreases. However, at very low power some complex phenomena occur.[4] Experimentally, we find that γH_2 *ca.* 125—250 Hz gives good results if protons are pre-saturated by noise or C.W. high-power decoupling before the ¹³C pulse.
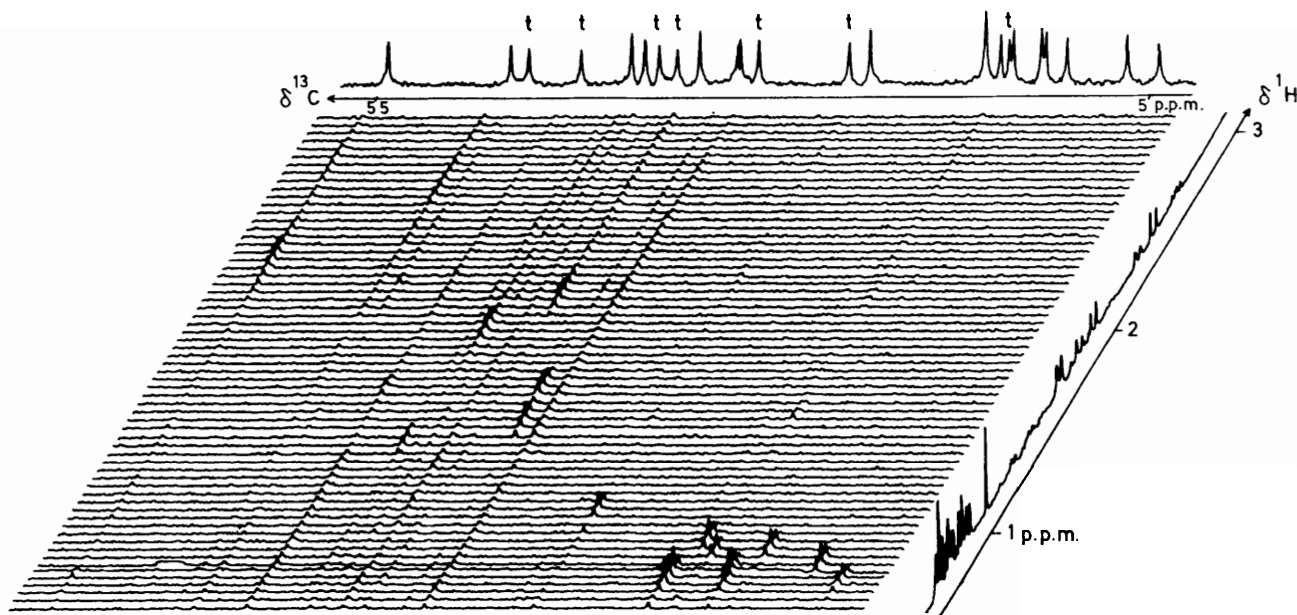
FIGURE 2. Correlation map of lysocellin (1) obtained with sequence 1b (Figure 1) recorded at 5·7 T; t = triplets with non-equivalent protons. ^{1}H and ^{13}C chemical shifts are in p.p.m. from Me$_4$Si. Trace separation = 10 Hz. ^{13}C Noise-decoupled- and ^{1}H-n.m.r. spectra were recorded by standard methods.

quency. The decoupler can be swept through the whole proton spectrum or only through parts of this spectrum, with possibly different frequency increments for each part.

Figure 1c shows a modified sequence where DE is incremented in the same way as in sequence 1b, but where the time t between the 90° and the 180° pulses and between the 180° pulse and the acquisition is kept equal to DE at each scan. Basic features of sequence 1c are the same, but the sensitivity is enhanced, owing to T_2 ^{13}C relaxation effects. However, scans corresponding to a long DE give a smaller signal, so the correlation is less precise.
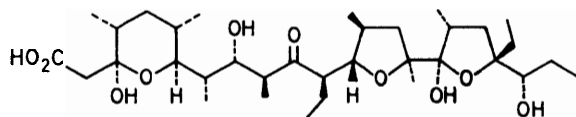
(1)

The efficiency of sequence 1b is shown by the correlation of the spectra (Figure 2) of lysocellin (1), an ionophorous

antibiotic. Examination of the literature shows that the assignments of ^{13}C n.m.r. spectral peaks of such products were tedious, whereas the ^{1}H n.m.r. peaks had been assigned.[6] The usual ^{1}H and ^{13}C spectra are displayed along their frequency axes. The correlation is very selective for CH and CH$_3$ signals, whereas most of CH$_2$ carbons give a broad correlation pattern, or sometimes an almost zero signal. This is because the chemical shifts of the two hydrogens born by the same carbon atom are very different (up to 2 p.p.m.) for almost every CH$_2$ group in this compound. The complex behaviour of the ABX system in low-power off-resonance conditions (during DE delay) produces the observed result.

This method has the same field of application as heteronuclear selective decoupling. It leads to high selectivity, and gives easy-to-read spectra even in the case of large molecules.

[1] R. Freeman and H. D. W. Hill, J. Chem. Phys., 1971, 54, 3367; B. Birdsall, N. J. M. Birdsall, and J. Feeney, J. Chem. Soc., Chem. Commun., 1972, 316.
[2] G. Bodenhausen and R. Freeman, J. Magn. Reson., 1977, 28, 471; A. A. Maudsley, L. Müller, and R. R. Ernst, ibid., p. 463.
[3] W. A. Anderson and R. Freeman, J. Chem. Phys., 1962, 37, 85.
[4] A. D. Bain, R. M. Lynden-Bell, W. M. Litchman, and E. W. Randall, J. Magn. Reson. 1977, 25, 315.
[5] C. Le Cocq and J. Y. Lallemand, J. Chem. Soc., Chem. Commun., 1981, 150.
[6] M. J. O. Anteunis, Bull. Soc. Chim. Belg., 1977, 86, 187; N. Otake, H. Seto, and M. Koenuma, Agric. Biol. Chem., 1978, 42, 1879.