

Experimental Chemical Shift Correlation Maps in Nuclear Magnetic Resonance Spectroscopy

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Summary An experimental technique is described which identifies the chemical shifts of directly bonded protons and carbon-13 nuclei and presents the result in the form of a shift correlation map.

PROTON and carbon-13 chemical shifts, the n.m.r. parameters most generally used in organic chemistry, are readily measured by standard techniques, but correlation of these shifts—the process of identifying proton and carbon-13 resonances of directly bonded atoms—has proved difficult to achieve experimentally. Coherent off-resonance decoupling, repeated over a range of proton irradiation frequencies,¹ often produces spectra that are difficult to interpret. This communication describes an alternative method based on two-dimensional Fourier transformation,^{2,3} which generates a chemical shift correlation map directly.

The method is based on a magnetization transfer experiment originated by Ernst⁴ and later applied to chemical shift correlation.⁵⁻⁷ In a spectrometer tuned to observe carbon-13, radiofrequency pulses are first applied to protons (Figure 1) using the proton decoupler as radiofrequency

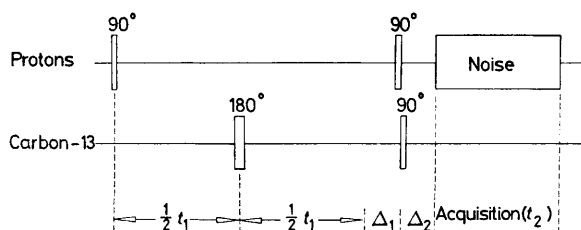


FIGURE 1. Pulse sequence used for obtaining chemical shift correlation maps.

source. Transverse proton magnetization excited by the initial 90° pulse is allowed to precess freely during a short evolution period t_1 , building up a net precession angle in the proton rotating frame $\phi = 2\pi t_1 \Delta F$, where ΔF is the frequency offset with respect to the transmitter. The second 90° pulse converts the Y-component of this magnetization, which is a function of $\cos \phi$, into longitudinal magnetization. The 90°- t_1 -90° sequence therefore behaves in a frequency selective manner. Non-equilibrium proton spin populations necessarily perturb carbon-13 populations when a common energy level is involved, and thus information about the proton resonance frequencies is coded into the t_1 dependence of the carbon-13 longitudinal magnetization. A 90° carbon pulse 'reads' this information by exciting a free induction signal, and the entire sequence is then repeated for a series of different values of t_1 to map out the modulation as a function of t_1 .

Fourier transformation with respect to t_1 displays this information in the form of a proton spectrum: essentially the carbon-13 satellites of a conventional proton spectrum, no signals arising from carbon-12 molecules. This becomes the F_1 dimension. The large single-bond splitting represents an undesirable complication in a shift correlation map, and it is therefore eliminated by means of a 180° refocusing pulse applied to carbon-13 at the mid-point of the evolution period (see Figure 1). Since the low and high-field parts of this doublet are in antiphase,⁴ mutual cancellation is avoided by the introduction of a fixed delay Δ_1 which shifts the relative phase of the two signals by π radians.⁵ This process also eliminates all signals transferred by weak long-range couplings.

Fourier transformation of the carbon-13 free induction signals with respect to t_2 (the running time variable for acquisition) generates a carbon-13 spectrum in the F_2

dimension, with doublet, triplet, or quartet structure due to coupling to protons. In order to simplify the correlation map, these splittings are removed by noise irradiation of the protons during acquisition, signal cancellation again being avoided by a suitable phase shift during the interval Δ_2 .

Spectra have been obtained on a Varian CFT-20 spectrometer with software for two-dimensional Fourier transformation.⁸ The clearest mode of display appears to be the intensity contour plot⁹ and it has the advantage over multiple-trace displays of permitting more direct measurement of the frequencies. Figure 2 shows the shift correlation

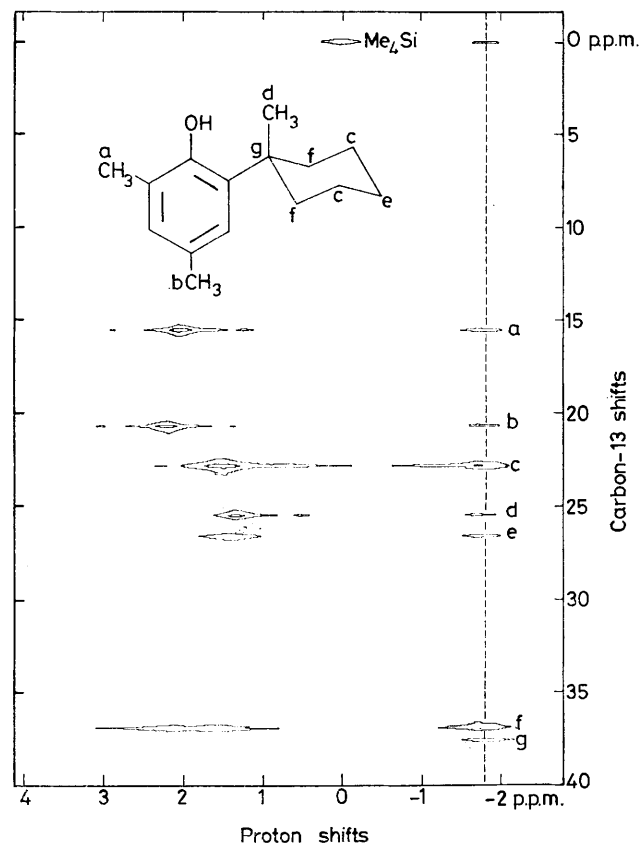


FIGURE 2. Chemical shift correlation map of the aliphatic resonances of 2-(1-methylcyclohexyl)-4,6-dimethylphenol showing contours of equal intensity. Tetramethylsilane acts as the reference point for both frequency dimensions.

map of the aliphatic region of 2-(1-methylcyclohexyl)-4,6-dimethylphenol obtained by this technique, the assignment being based on chemical shifts and the long-range splittings observed on the methyl resonances in the two-dimensional J -spectrum.¹⁰ The peaks which fall on the dashed vertical line represent unmodulated carbon-13 signals which carry no shift correlation information; their position on the proton shift axis is determined by the arbitrary choice of transmitter frequency. Peaks to the left of this line arise from the corresponding modulated signals and fall at frequency coordinates determined by the proton and carbon-13 chemical shifts. All these peaks arise from magnetization transferred through one-bond couplings, and there is therefore no response from the quaternary site g. The response from site

f shows a doubling of approximately 50 Hz ascribed to an increased chemical shift difference between axial and equatorial protons caused by the aryl substituent; in contrast site c has a much smaller shift difference owing to the proximity effect of the axial methyl group.

Shift correlation maps such as this show considerable promise for the investigation of the various different shielding contributions appropriate to protons and carbon-13, for

the assignment of resonances in situations where the shielding effects are well understood, and as a quite characteristic 'fingerprint' of a given organic molecule, far more 'personal' than the proton and carbon-13 spectra taken in isolation.

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