

SELECTIVE LONG-RANGE POLARIZATION TRANSFER *via* DEPT.

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Introduction

The structural assignment of organic compounds containing quaternary carbons and/or heteroatoms is often greatly helped by measurements of long-range proton-carbon coupling constants, ${}^nJ_{\text{CH}}$, with particular emphasis on two-bond and three-bond couplings which usually show values in the range 3-10 Hz [1,2], depending on carbon hybridization, torsion angles, substituent electronegativity and orientation, etc.

Selective 1D NMR methods, such as the selective INEPT method proposed by Bax [3], have long been used to reveal connectivities with a given proton. Thus, application of a selective INEPT (or, more frequently, refocussed INEPT) pulse sequence on a well resolved proton, with delays optimized for a long-range heteronuclear coupling (usually around 5-7 Hz), results in a 1D carbon spectrum displaying large intensity enhancements at the carbons coupled (at long range) with the perturbed proton. Furthermore, the intensity of these carbons shows a maximum when the true ${}^nJ_{\text{CH}}$ value is used for the delay optimization of the selective INEPT sequence. We have recently shown the use of this dependence to obtain a quick estimate of ${}^nJ_{\text{CH}}$ in several polycyclic derivatives [4].

Selective 2D methods, however, are to be preferred because they can easily yield accurate values for the desired long-range coupling constants, provided the perturbed proton appears as a well resolved multiplet in the proton spectrum. Thus, the selective spin flip method first proposed by Bax and Freeman [5] has been widely used for the determination of ${}^nJ_{\text{CH}}$ values from a given proton.

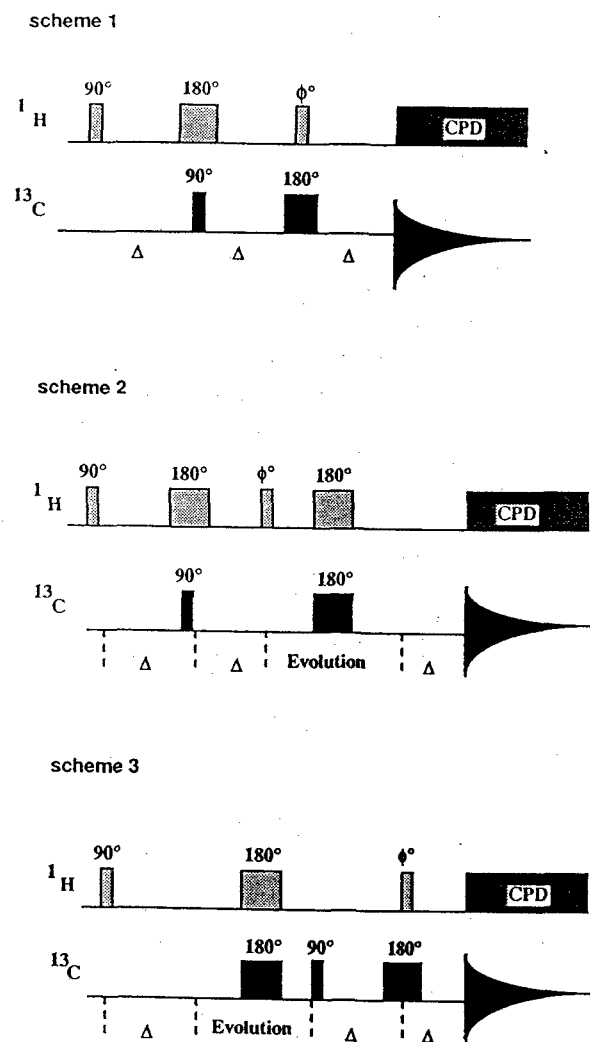
In recent years a number of methods have been suggested which combine the intensity enhancements obtained from selective polarization transfer with the easy measurement of ${}^nJ_{\text{CH}}$ characteristic of the selective spin flip method. Thus, Jippo et al. proposed a 2D selective INEPT method [6] which consists in a conventional 2D INEPT pulse train containing a selective spin echo sequence. We have modified this method by delivering all decoupler pulses in the selective mode [4], and in this way we have suppressed the artefact peaks otherwise observed with this method.

Another combination of polarization transfer and selective spin flip was proposed by Uhrin et al. [7]. In this method, a standard non-selective DEPT preparation period (optimized for ${}^1J_{\text{CH}}$) is followed by a conventional selective (or semiselective) spin flip sequence, yielding a J-resolved 2D spectrum displaying the desired long range couplings. More recently, Poppe and van Halbeek [8] have introduced inverse detection, either in 1D or 2D methods, by combining selective polarization transfer with long range heteronuclear coupling measurements in 1H-detected sequences.

We now report two new ${}^{13}\text{C}$ -detected, 2D J-resolved sequences, based on a DEPT pulse train, which allow fast and accurate measurements of long-range heteronuclear coupling constants from well resolved protons. Both sequences are particularly useful for the determination of couplings to quaternary carbons, and their main feature is that all proton pulses are delivered as soft, selective pulses (20-30 ms).

Parametrization

Starting from the 1D-SDEPT sequence (Scheme 1), we have derived the new sequences 2D-SDEPT1 (Scheme 2) and 2D-SDEPT2 (Scheme 3), in which SDEPT stands for Selective DEPT. Since all proton pulses are selective ($\gamma B_1/2\pi = 20\text{-}30\text{ Hz}$), both sequences achieve a selective polarization transfer from the pulsed proton to long-range coupled carbons, provided that the fixed interpulse delay Δ is optimized for long-range couplings. Both sequences yield comparable results in similar experiment times.



In both sequences the incrementable evolution period t_1 , which brackets a selective spin echo moiety, allows only the evolution of heteronuclear long range couplings which will therefore be detected in F1 dimension in the final 2D J-resolved spectrum.

We have studied the dependence of carbon signal intensities on several experimental parameters, such as the delay Δ or the pulse angle ϕ of the last selective proton pulse in the DEPT part of the sequence, using camphor (Fig. 1) as a readily available, rigid model compound. These determinations have been most conveniently carried out using the 1D selective DEPT sequence 1D-SDEPT.

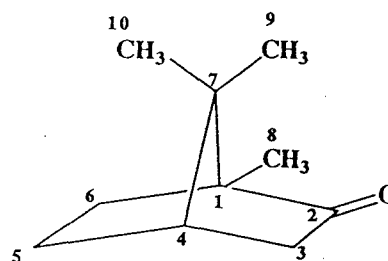


Fig. 1

The extent of polarization transfer is a function of both, the interpulse delay Δ and the pulse angle ϕ . Fig. 2 shows the intensity of the quaternary C-1 carbon signal of camphor when pulsing the H-4 methine proton, for $\phi=45^\circ$ and for $\phi=90^\circ$, as a function of interpulse delay Δ , using sequence 1D-SDEPT. In this case, the heteronuclear coupling constant involved is $^3J_{\text{H4-Cl}} = 4.4\text{ Hz}$. As expected, the quaternary carbon C-1 intensity follows a typical sinus function, and maximum signal is obtained for $\phi=90^\circ$ and $\Delta=50\text{-}90\text{ ms}$, a range which does not contain the theoretical value, $(2 \cdot ^3J_{\text{H4-Cl}})^{-1} = 115\text{ ms}$. Instead, this range of maximum signal is centered around the practical value $(3 \cdot ^3J_{\text{H4-Cl}})^{-1} = 75\text{ ms}$.

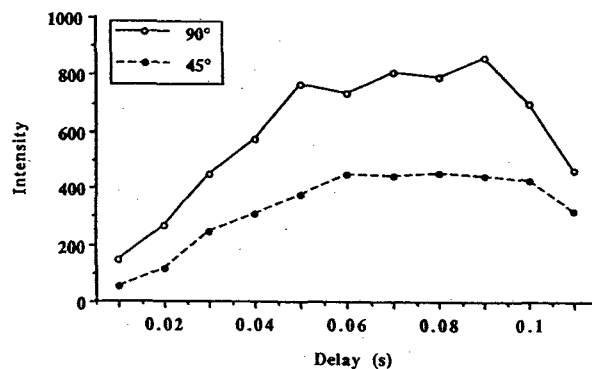


Fig. 2

However, when pulsing on a methyl proton the optimum delay has to be modified. Fig. 3 shows the variation of the quaternary C-7 carbon signal of camphor when pulsing the methyl H-10 protons as a function of the ϕ pulse angle, for three Δ values, using also sequence 1D-SDEPT. In this case, the heteronuclear coupling constant involved is ${}^2J_{\text{H}10\text{-C}7}=4.1$ Hz (sign not determined). If the optimization is carried out as in a conventional DEPT, using $\Delta=(2J)^{-1}$, the intensities follow the typical $\sin\phi*\cos^2\phi$ function, with minimum values at 0° , 90° and 180° and maximum values at 45° and 135° . Therefore, even when observing a quaternary carbon such as C-7, a delay $\Delta=(6*J_{\text{CH}})^{-1}$ is required, which in this case ($J=4.1$ Hz) is $\Delta=40$ ms, as observed in Fig 3. This delay would not give the maximum signal in the case of methine protons (see Fig. 2), but nevertheless would still yield reasonably intense quaternary carbons even in this case.

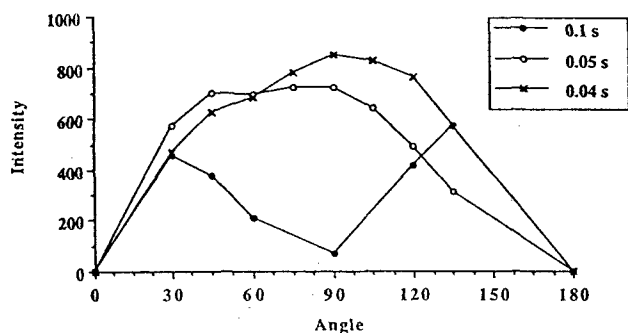


Fig. 3

The observation of long range couplings to protonated carbons can also yield some unexpected results. For instance, Fig. 4 shows the intensity of the methine carbon C-4 as a function of pulse angle ϕ using sequence 1D-SDEPT and pulsing on the methyl protons H-10, for three delay Δ values. Clearly, in the region between $\phi=60^\circ$ and $\phi=120^\circ$ there are large oscillations of the intensity, but always with a maximum for $\phi=90^\circ$, provided the delay Δ is not set around 100 ms. In this case ${}^3J_{\text{H}10\text{-C}4}=3.9$ Hz, and therefore the recommended delay would be $(6*{}^3J_{\text{H}10\text{-C}4})^{-1}=40$ ms.

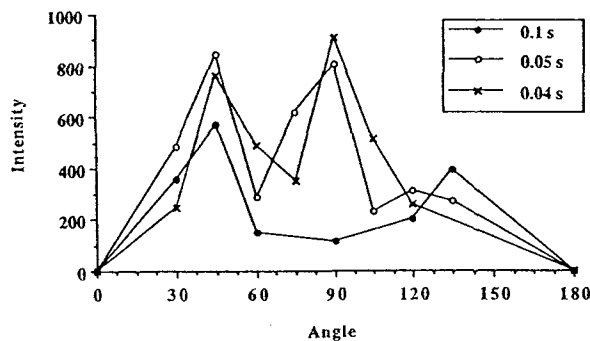


Fig. 4

An additional problem appears when observing methylene carbons. Irrespective of the delay used, these carbons always show a null intensity for pulse angles $\phi=60^\circ$ and $\phi=105^\circ$. An example is shown in Fig. 5, which also displays the perfect sinusoidal behaviour of a quaternary carbon for comparison. We have no explanation for these nulls.

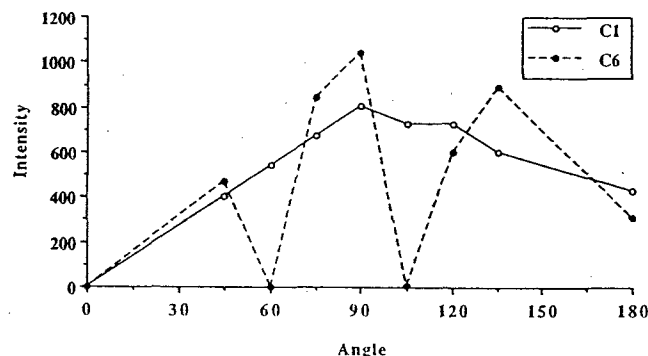


Fig. 5

Applications

Having shown that optimum conditions for efficient long-range polarization transfer require $\Delta=30$ -40 ms for methyl protons (70-80 ms for methine protons) and $\phi=90^\circ$, we tested the two-dimensional sequences 2D-SDEPT1 and 2D-SDEPT2 as a practical method for the measurement of long-range heteronuclear couplings.

Besides obtaining the complete set of long-range heteronuclear coupling constants for camphor, some of which have been mentioned above, we applied the 1D and 2D methods to noscapinium chloride (Fig. 6), pulsing selectively on the H-5 proton ($\delta_{\text{H}}=6.25$ ppm).

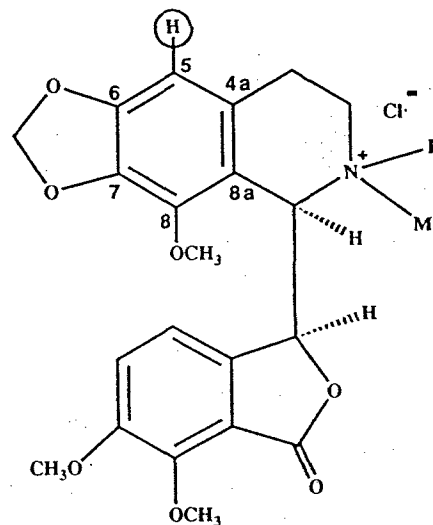


Fig. 6

The results (Fig. 7) easily allow the assignment of the four quaternary carbons coupled to the H-5 proton. The particular example shown was obtained using sequence 2D-SDEPT1, but the alternative sequence 2D-SDEPT2 gave the same results. We also performed a comparison between 2D-SDEPT1 and our previous [4] sequence 2D-SINEPT. Both methods can yield the desired long-range heteronuclear coupling constants in less than one hour of accumulation (using a 400 MHz spectrometer), with excellent sensitivity even for quaternary carbons. However, the SDEPT method is to be preferred, because it is less sensitive to mismatch between the delay Δ and the long range coupling ${}^nJ_{\text{CH}}$.

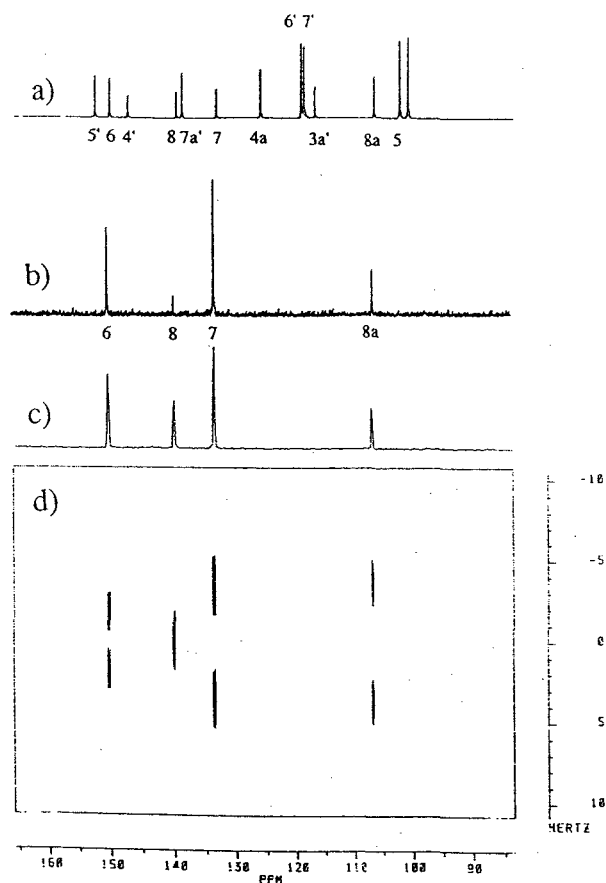


Fig. 7

a) Decoupled ${}^{13}\text{C}$ spectrum; b) 1D-SDEPT spectrum after pulsing on H-5. Only long-range coupled carbons with it are presents. Then, The 2D-J spectra (d) and its internal projection (c) obtained with the pulse sequence of the scheme 2.

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