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Off-Resonance Cross-Polarization: A Technique to Reduce rf Power Requirements for Magnetization Transfer Experiments in Solids

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Cross-polarization of nuclei (*1*) with a low magnetogyric ratio is one of the pillars of many modern solid state NMR experiments, enhancing the sensitivity often by an order of magnitude. Cross-polarization is based upon cross-relaxation in the rotating frame between different nuclides, and occurs when the Hartmann–Hahn condition (*2*) is met. For magnetization transfer from spin I to spin S, this condition requires radiofrequency fields, H_I and H_S, applied simultaneously close to resonance for spin I and spin S, respectively. H_I and H_S must have the relation

$$\gamma_I H_I = \gamma_S H_S \qquad [1]$$

where γ_I and γ_S are the respective magnetogyric ratios. If spin I is abundant, the minimum rf field strength, H_I, required for cross-polarization is dictated by the fact that H_I must be strong enough to generate a spin-lock of spins, I, and is thus determined by the strength of the homonuclear I–I spin interaction (*3, 4*). In practice, a H_I value on the order of 10 G is often needed for protons. This means that if one wants to cross polarize, for example, ^{15}N nuclei, a ^{15}N rf field strength on the order of 100 G is needed. For lower-γ nuclei, even higher rf field strengths are necessary. Due to the very high rf power needed for a spin with low magnetogyric ratio, this type of cross-polarization becomes experimentally very difficult.

We propose a new method that utilizes off-resonance effects (*5*) of the S spin, to lower those difficult power requirements. The principle of off-resonance rf fields in CP experiments has been discussed previously (*6, 7*). The new cross-polarization scheme used in the present work is shown in Fig. 1. This scheme looks very similar to the original cross-polarization experiment (*1*); a $90°_x$ I pulse, followed by fast switching of the phase of the rf field by 90° causes a spin-lock of the I spins (protons) along the y axis of the rotating frame. The difference with conventional cross-polarization is that in the present case the S spin rf field is off-resonance during the actual cross-polarization, hence the term off-resonance cross-polarization (ORCP). The offset, Δ, is chosen such that the effective S spin field strength in the

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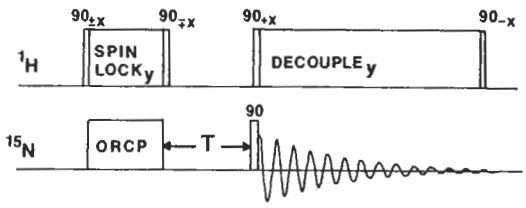

FIG. 1. Pulse scheme of the off-resonance cross-polarization. During the actual cross-polarization period, the ^{15}N rf field is off resonance by such an amount that the ^{15}N effective field matches the on-resonance ^{1}H rf field. During the delay, τ (=200 μs), transverse ^{15}N magnetization defocuses and the ^{15}N transmitter is switched to resonance. The longitudinal component of the cross-polarized magnetization is then observed by the application of a 90° observe pulse. Spin temperature alternation is employed by changing the phase of the initial 90° proton pulse along the $\pm x$ axis in alternate scans. The other three 90° ^{1}H pulses are needed for the flip-back of "unused" ^{1}H polarization.

rotating frame matches the on-resonance I spin rf field. The S spin effective field then makes an angle, α_S, with the static magnetic field (Fig. 2) and its magnitude, H_{eff}, equals $H_{1S}/\sin\alpha_S$. Hence the precession frequency about $H_{\text{eff}S}$ is

$$\omega_{\text{eff}S} = \gamma_S H_{\text{eff}S} = \gamma_S H_{1S}/\sin\alpha_S \qquad [2a]$$

and the new condition for cross-polarization is

$$\gamma_I H_I = \gamma_S H_S/\sin\alpha_S. \qquad [2b]$$

When the off-resonance rf field is switched off (Fig. 1), the transverse component of the S spin magnetization dephases rapidly (no I-spin decoupling) during the

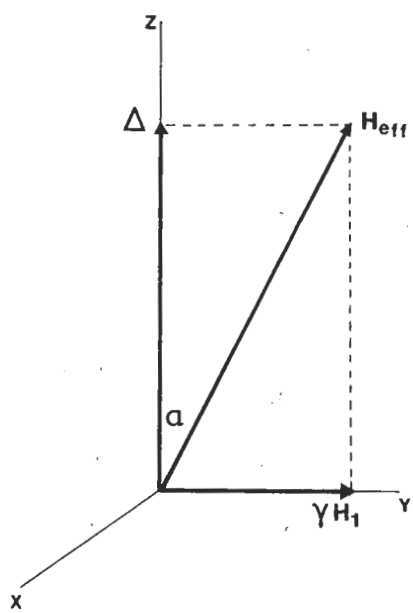

FIG. 2. Orientation of the effective rf field in the rotating frame for S spins.

period, τ, and a fraction $\cos \alpha_S$ remains as longitudinal magnetization. During this delay, τ, the S spin rf frequency is switched to resonance, and a 90° pulse rotates the z component of the cross-polarized magnetization into the transverse plane. Conventional spin temperature alternation (*8*) and flip-back (*9*) are used to suppress artifacts and increase the repetition rate of the experiment, respectively.

The dipolar Hamiltonian for the I–S system is given by

$$H_D = H_{II} + H_{IS} + H_{SS}. \quad [3]$$

The term, H_{IS}, is responsible for the cross-relaxation, and its secular part is given by

$$H_{IS} = \sum_i \sum_k C_{ik} I_{zi} S_{zk} \quad [4a]$$

with

$$C_{ik} = (\gamma_I \gamma_S \hbar / r_{ik}^3)[3 \cos^2(\theta_{ik}) - 1]. \quad [4b]$$

θ_{ik} is the angle between the vector connecting spins labeled i and k, and the direction of the magnetic field. The effect of the scalar coupling, J_{ik}, is usually very small and will be neglected. The operator $R_x(\alpha_I, \alpha_S)$, that transforms the two parallel z axes of the rotating frames to positions parallel to the two effective fields that make angles α_I and α_S with the static magnetic field, is given by

$$R_x(\alpha_I, \alpha_S) = \exp[-i(\alpha_I I_x + \alpha_S S_x)]. \quad [5]$$

In Eq. [5] it is assumed that the cross-polarization rf fields are applied along the y axes of the doubly rotating frame. For on-resonance I-spin irradiation, α_I equals $\pi/2$. The cross-relaxation interaction in the frame of the effective fields is now described by the following Hamiltonian:

$$\begin{aligned} H'_{IS} &= R_x^{-1}(\pi/2, \alpha_S) H_{IS} R_x(\pi/2, \alpha_S) \\ &= -1/4 \sum_i \sum_k C_{ik}(I_{+i}S_{-k} + I_{-i}S_{+k}) \sin(\alpha_S) \end{aligned} \quad [6]$$

where all "nonactive" terms, such as $I_{+i}S_{+k}$, $I_{+i}S_{zk}$, etc., have been omitted, and $I_{+i} = I_{xi} + iI_{yi}$, etc. Equation [6] demonstrates a mechanism for I–S spin–spin flip-flops in terms of I and S quantizations along the H_{1I} and $H_{\mathrm{eff}S}$ directions, respectively. If Eq. [2] is satisfied, these flip-flops are energy conserving. However, the flip-flop transition rate is proportional to $\sin^2 \alpha_S$ and decreases for very large offsets of the S-spin irradiation.

A number of interesting problems are connected with this ORCP method. Exact matching of the effective rf fields only occurs for one particular S spin resonance. For conventional cross-polarization ($\alpha_S \approx \pi/2$), a small change of the angle α_S causes only a very small change in the magnitude of the effective S spin field, so a Hartmann–Hahn match for any of the S spins will be close to a match for essentially any other S spin in the sample. Hence, the manifestation of the I–I modulation of H'_{IS} in effectively broadening the match condition is often not so critical. However, in the ORCP method, this is no longer the case. This means that ORCP can cover only a S spin frequency distribution that is of the order of the I–I dipolar interaction under spin-locked conditions (which equals half the static I–I interaction). At very

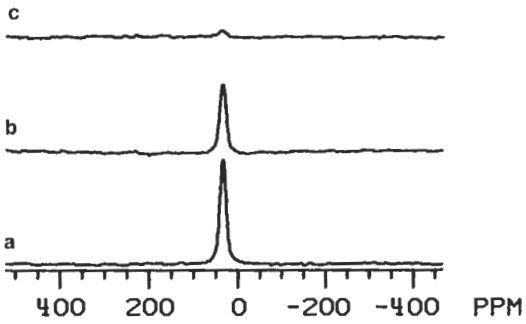

FIG. 3. (a) Regular cross-polarization spectrum of a sample of ^{15}N enriched glycine, recorded at 20 MHz under optimum match conditions (^{1}H and ^{15}N rf fields both 39 kHz), and a contact time of 5 ms. (b) ORCP spectrum, recorded with an offset, Δ, equal to 37 kHz, using the same ^{1}H rf power as in (a), but only 11.4 kHz ^{15}N rf field strength. The contact time was 10 ms. (c) A regular cross-polarization spectrum under mismatched conditions (39 and 11.4 kHz rf field strength), recorded with a 5 ms contact time. Each of the three spectra is the result of 40 accumulations.

high magnetic field strengths or for dilute I spins this may become a serious problem.

In conventional cross-polarization experiments, usually a single, doubly tuned solenoidal coil is used. Any inhomogeneity of the rf field will then approximately

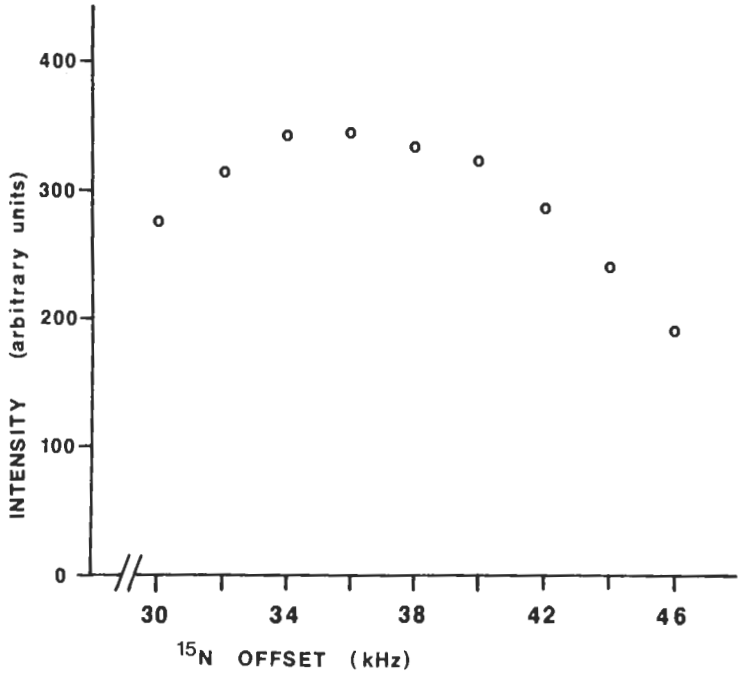

FIG. 4. The intensity of the glycine ^{15}N resonance obtained with the ORCP experiment as a function of the ^{15}N offset during cross-polarization. The ^{1}H and ^{15}N rf field strengths were adjusted to 39 and 11.4 kHz, respectively.

be the same for both spin species, and will not affect the Hartmann–Hahn condition. However, in the ORCP method, one can assume the static field to be perfectly homogeneous compared with the rf field; and hence, the S spin effective field is a factor sin α_S less sensitive to rf inhomogeneity than is the I spin effective field. Therefore, the rf inhomogeneity causes a mismatch of the Hartmann–Hahn condition, which again has to be compensated by the I–I dipolar interaction.

Experiments were performed on a static sample of ^{15}N-enriched glycine on a modified Nicolet NT-200 spectrometer. Figure 3a shows the regular CP spectrum of glycine, under optimized conditions: a contact time of 5 ms, and 39 kHz rf field strengths for both ^{1}H and ^{15}N. The ^{1}H and ^{15}N rf powers are equal to 120 and 450 W, respectively. Figure 3b shows the effectiveness of the ORCP method, using the same proton rf power, but only 34 W (11.4 kHz) for the ^{15}N channel, using a contact time of 10 ms and an offset, Δ, equal to 37 kHz. Figure 3c shows the spectrum obtained in a regular CP experiment using the same ^{1}H and ^{15}N rf powers as used in obtaining the spectrum of Fig. 3b, optimized for a contact time of 5 ms. Each of the three spectra is the result of 40 accumulations.

Figure 4 shows the effect of the offset, Δ, on the effectiveness of the ORCP

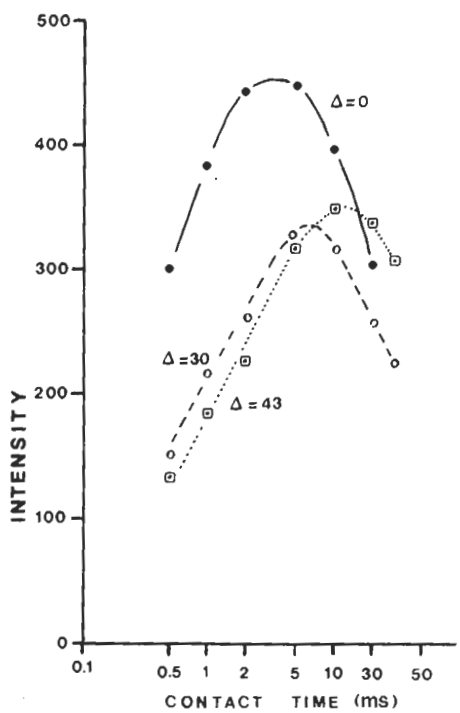

FIG. 5. The intensity of the ^{15}N resonance of glycine as a function of contact time for a regular optimized cross-polarization with both ^{1}H and ^{15}N rf field strengths equal to 45 kHz (filled circles). Open circles show the intensity of the resonance using the ORCP experiment, with ^{1}H and ^{15}N rf field strengths equal to 45 and 27 kHz, respectively, and a ^{15}N offset of 30 kHz. Note that the observed intensity is only ~80% of the total amount of cross-polarized magnetization (see text). Open squares show the intensity obtained with rf field strengths of 45 and 11.4 kHz, and a ^{15}N offset of 43 kHz.

method for proton and ^{15}N rf field strengths of 39 kHz and 11.4 kHz, respectively, and a 10 ms contact time. As expected, optimum polarization occurs when the effective fields are matched, i.e., near a 36 kHz off-resonance frequency.

Figure 5 gives a graphical representation of the observed ^{15}N signal intensity as a function of contact time for three different conditions, using a 45 kHz proton rf field strength. For on-resonance, cross-polarization occurs rapidly and is optimized for a contact time of 5 ms. In the case where the ORCP method was used with an offset of 30 kHz (^{15}N rf field strength optimized at 27 kHz), optimum cross-polarization occurs for a contact time of 8 ms. In this case it is important to note that the effective field makes a significant angle ($\alpha_S = 40°$) with the static magnetic field, and only a fraction ($\cos \alpha_S \approx 0.8$) of the cross-polarized magnitization is observed (and displayed in the graph); this is because the transverse component which is proportional to $\sin \alpha_S$, dephases during the time, τ. For an offset of 43 kHz and a ^{15}N rf field strength of 11.4 kHz ($\sin \alpha_S \approx 0.25$), the optimum contact time is near 12 ms (Fig. 5).

From the above discussion it is clear that the ORCP method does provide a dramatic reduction in power requirements for cross-polarization experiments. It should be of particular importance for very low-γ nuclei. We expect that the ORCP method will enable the cross-polarization of important nuclei such as ^{107}Ag, ^{109}Ag, ^{103}Rh, ^{183}W, and ^{57}Fe. Those applications are under extensive investigation.

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