Longer-range distances by spinning-angle-encoding solid-state NMR spectroscopy

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Supporting Information: Further Experimental Details

Angle switching

The spinning angle change was implemented as a movement between two positions, determined by adjustable stoppers. A solenoid actuator, positioned 80 cm below the bottom flange of the magnet, activated motion to the off-angle position via a pulley, with a counter-acting spring returning the stator to the on-angle position after release of the solenoid actuator.

For the rotors of 1.8 mm outer diameter (15 μL volume), angle switching was tested for rotation frequencies up to 20 kHz. The physical flipping of the stator position corresponding to an angle change of up to approximately 5 degrees is achieved in a time of ~5-10 ms, including time for stabilisation. The change in angle is controlled using the TTL output from the spectrometer, as triggered from the pulse program. The TTL needs to be activated slightly before (~5 ms) the desired flip time due to the time which it takes for the current to build up in the solenoid of the actuator. The length of the *z*-filter (see pulse sequence in Fig. 1) during which the rotor angle was flipped from the spin-echo off-angle position to the on-angle position for detection was 15 and 20 ms for histidine and Ac-VL, respectively.

Angle calibration

Determination of the angle offset was performed by recording spectra of 1-^{13}C *L*-alanine in the off-MAS position. As discussed in the SI of Ref,[1] the significant chemical shift anisotropy (CSA) of the alanine carboxyl ^{13}C site results in a good sensitivity of its line shape to the angle between the rotor axis and the B_0 magnetic field direction. The SPINEVOLUTION[2] program was used to simulate the line shape at different rotor axis angles using a ^{13}C Larmor frequency of 150.9 MHz (corresponding to a ^{1}H Larmor frequency of 600.0 MHz), $\delta_{CSA} = -70$ ppm, $\eta_{CSA} =$

0.78 and 2 Hz exponential line broadening. Fig. S1 shows a plot of the horn-to-horn CSA line width in Hz against the offset from the magic angle. A good fit to the following linear function is obtained:

$$\text{angle offset in degrees } (\Delta) \ = \ 0.002119 \text{ line width in Hz} - 0.05891 \qquad \text{(S1)}$$

Using this equation, the experimental line width was used to determine the offset from the magic angle. In this way, the angle offsets were determined to be $\Delta = 2.27 \pm 0.10$ degrees and $\Delta = 4.20 \pm 0.10$ degrees for the histidine and Ac-VL experiments, respectively.
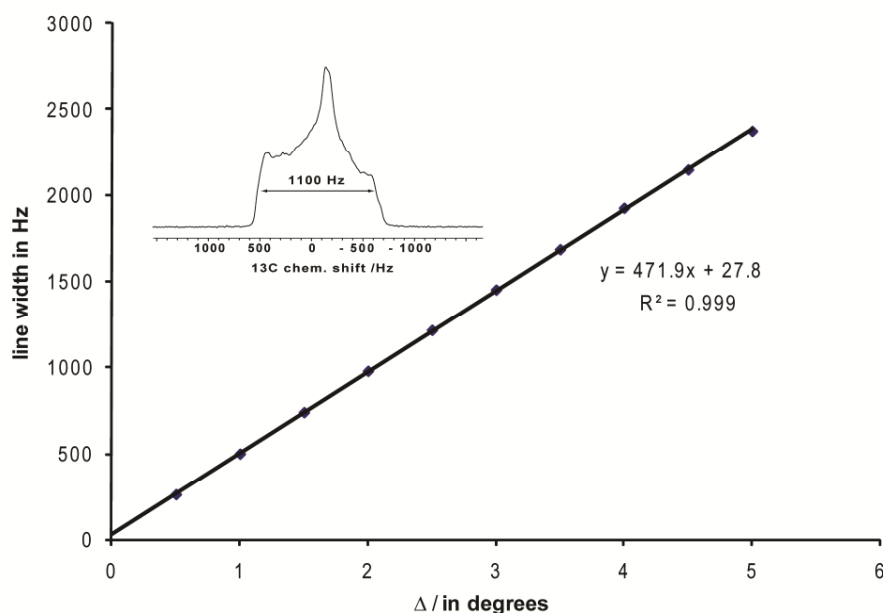
Fig. S1. Plot of the angle offset Δ against the horn-to-horn line width of a simulated spectrum of the carbonyl line in *L*-alanine. The symbols indicate the points for which a simulation was performed and the solid line shows the best linear fit. The best-fit linear equation is stated in the plot. Rearrangement gives eqn (S1). The insert shows the off-MAS spectrum of 1-^{13}C-alanine, that was recorded with the angle offset ($\Delta = 2.27$ degrees) used for the experiments on the histidine sample. The horizontal double-headed arrow indicates the line width measurement.

Double Gaussian selective pulse

A doubly selective 180° pulse at two frequencies ω_1^{iso} and ω_2^{iso} is achieved using a cosine modulated Gaussian pulse as described by Pileio et al (eqn 18):[3]

$$\omega_e(t) = \omega_e(t_b) \cos(\omega_m(t - t_b)) \exp\{-\alpha(t - t_b)^2\} \tag{S2}$$

where t_b is the time corresponding to the centre (and maximum intensity) of the pulse and the cosine modulation frequency, ω_m, is equal to half of the difference between the two isotropic chemical shifts, i.e.,

$$\omega_m = (1/2) (\omega_1^{iso} - \omega_2^{iso}), \tag{S3}$$

with the *rf* carrier frequency set to the mean of ω_1^{iso} and ω_2^{iso}, i.e., halfway between the two frequencies.

The time shift in eqn (1) in the main text is determined (see eqn 22 of Ref.[3]) as the width of the time-domain Gaussian envelope at 76.69 % of its maximum height:

$$\exp\{-\alpha(t_s/2)^2\} = 0.7669 \tag{S4}$$

i.e.,

$$t_s = 2\sqrt{\{-\ln[0.7669]/\alpha\}}. \tag{S5}$$

The parameter α can be determined from the pulse width, t_w (equal to $t_c - t_a$ in the notation of section 2.1 of Ref.[3]) if the Gaussian pulse is truncated at 1% of its maximum intensity:
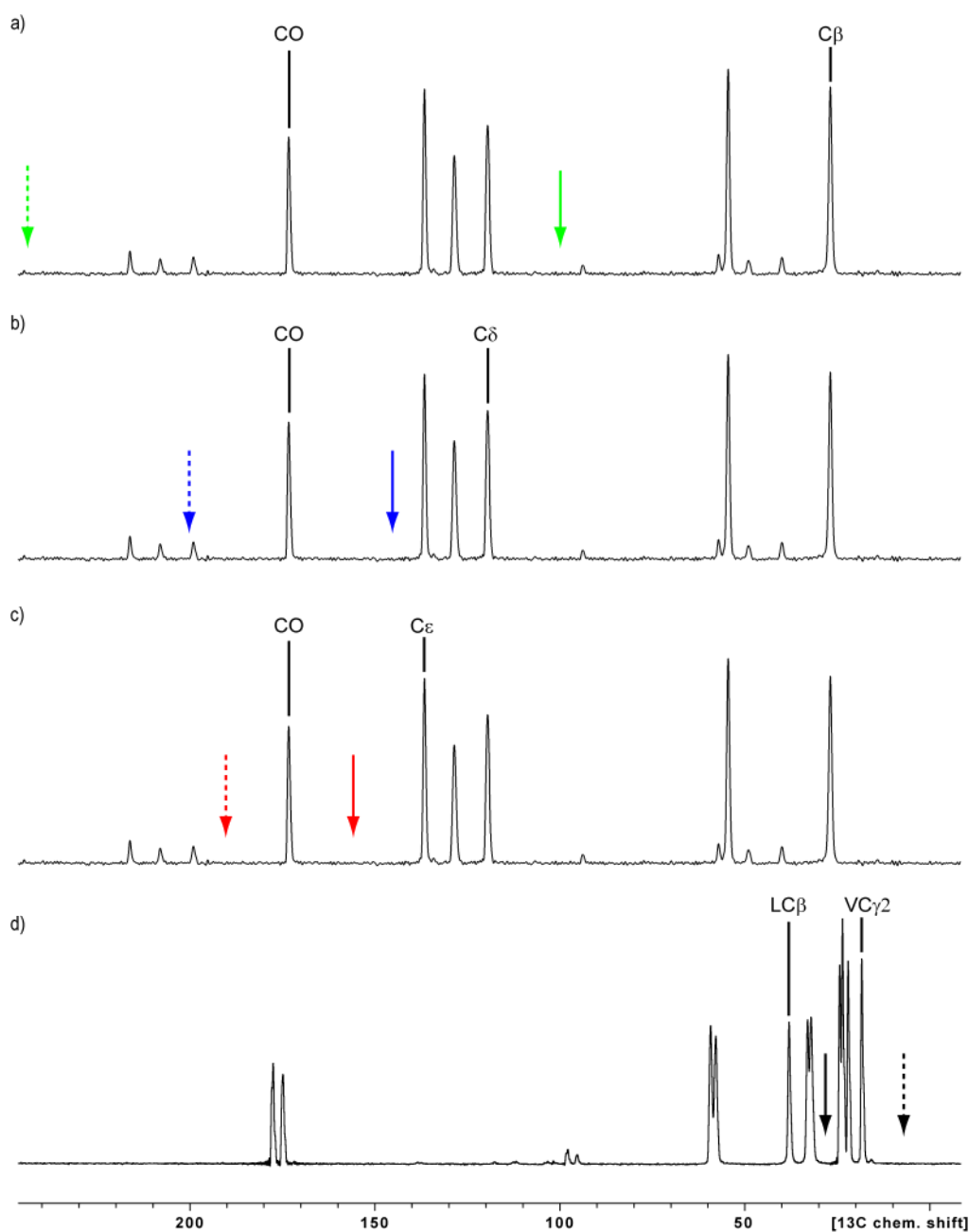
$$\exp\{-\alpha(t_w/2)^2\} = 0.01 \tag{S6}$$

i.e.,

$$\alpha = \sqrt{\{-\ln[0.01]/(t_w/2)^2\}}. \tag{S7}$$

Substituting eq S7 into eq S5,

$$t_s = t_w \sqrt{\{\ln[0.7669]/\ln[0.01]\}} = 0.240 * t_w. \tag{S8}$$

Fig. S2. ^{13}C CP MAS (on angle) spectra of (a-c) U-^{13}C,^{15}N *L*-histidine.HCl.H$_2$O and (d) Ac-U-^{13}C,^{15}N-VL. The arrows indicate the irradiation frequency for the dipolar-modulated (solid lines) and reference experiments (dashed lines). The resonances selected by the double-Gaussian selective pulse in the dipolar-modulated experiments are indicated, i.e., (a) CO-Cβ, (b) CO-Cδ, (c) CO-Cε and (d) Cγ$_2$(V)-Cβ(L).

The double Gaussian pulse was of duration 1.25 and 5 ms for the histidine and AcVL experiments, respectively, corresponding to t_s equal to 0.3 and 1.2 ms, respectively.

The irradiation frequencies of the Gaussian pulse for the dipolar-modulated and reference experiments are shown in Fig. S2.

Anti-phase signals in spin-echo experiments

As stated in the Experimental Details section of the main text, the spin-echo intensity, $s(\tau)$, is obtained by integration over the corresponding lineshape (after Fourier transformation with respect to the acquisition time, t_2). This section explains why this procedure has been employed in previous (on-angle) MAS spin-echo experiments for determining J couplings.[4-7] Specifically, an analysis is presented using product-operator theory[8-9] for a pair of coupled nuclei (the description here is for a J coupling, but can be considered to apply also for a residual dipolar coupling).

Assume that CP creates x magnetisation, noting the initial magnetisation may differ for the two spins (labelled 1 and 2):

$$\sigma(\tau = 0) = a\, I_x^{(1)} + b\, I_x^{(2)} \,. \tag{S9}$$

Considering the evolution under the homonuclear (J) coupling during the spin echo ($\tau/2 - \pi - \tau/2$) as well as transverse relaxation:

$$\sigma(\tau) = a\, \{\, I_x^{(1)} \cos(\pi\, J_{12}\, \tau) + 2\, I_y^{(1)}\, I_z^{(2)} \sin(\pi\, J_{12}\, \tau)\,\} \exp(-\tau / T_2'^{(1)})$$
$$+ b\, \{\, I_x^{(2)} \cos(\pi\, J_{12}\, \tau) + 2\, I_z^{(1)}\, I_y^{(2)} \sin(\pi\, J_{12}\, \tau)\,\} \exp(-\tau / T_2'^{(2)}) \,. \tag{S10}$$

Only single-spin transverse magnetisation induces a current in the NMR coil, i.e., only the I_x terms and not the $2I_yI_z$ terms are directly observable in an NMR experiment. If the homonuclear coupling is still active during the acquisition time (t_2), the $2I_yI_z$ terms evolve under an active coupling into observable I_x magnetisation:

$$2\, I_y^{(1)}\, I_z^{(2)} \;\rightarrow\; -I_x^{(1)} \sin(\pi\, J_{12}\, t_2) \,, \tag{S11}$$

i.e., corresponding to the observation of an anti-phase lineshape (after Fourier transformation with respect to t_2) with respect to the coupling. Likewise,

$$I_x \;\rightarrow\; I_x \cos(\pi\, J_{12}\, t_2) \,, \tag{S12}$$

i.e., corresponding to the observation of an in-phase lineshape (after Fourier transformation with respect to t_2) with respect to the coupling. Hence, if the homonuclear J coupling is resolved, there is a change in the observed NMR lineshape as a function of the echo time due to the different contributions of the I_x (in-phase lineshapes) and $2I_yI_z$ (anti-phase lineshapes) terms. However, if the integrated frequency-domain signal is considered, the anti-phase lineshapes due to the I_yI_z terms do not contribute, i.e.,

$$S^{\text{integrated}}(\tau)_{\text{spin 1}} = a \cos(\pi J_{12} \tau) \exp(-\tau / T_2'^{(1)}) . \tag{S13}$$

$$S^{\text{integrated}}(\tau)_{\text{spin 2}} = b \cos(\pi J_{12} \tau) \exp(-\tau / T_2'^{(2)}) . \tag{S14}$$

Consider now the case where a z filter ($90°_y - \tau_{zf} - 90°_y$) is introduced between the spin-echo ($\tau/2 - \pi - \tau/2$) and the acquisition time. After the first $90°_y$ pulse of the z-filter,

$$\sigma(\tau) = a \{ -I_z^{(1)} \cos(\pi J_{12} \tau) + 2 I_y^{(1)} I_x^{(2)} \sin(\pi J_{12} \tau) \} \exp(-\tau / T_2'^{(1)})$$
$$+ b \{ -I_z^{(2)} \cos(\pi J_{12} \tau) + 2 I_x^{(1)} I_y^{(2)} \sin(\pi J_{12} \tau) \} \exp(-\tau / T_2'^{(2)}) . \tag{S15}$$

Expanding the $2I_xI_y$ product operators as shift operators:

$$2 I_x^{(1)}I_y^{(2)} = \{I_+^{(1)} + I_-^{(1)}\} i/2 \{I_-^{(2)} - I_+^{(2)}\}$$
$$= i/2 \{-I_+^{(1)}I_+^{(2)} + I_-^{(1)}I_-^{(2)} + I_+^{(1)}I_-^{(2)} - I_-^{(1)}I_+^{(2)}\} \tag{S16}$$

and retaining only the terms corresponding to zero-quantum coherence (double-quantum coherence terms are removed by phase cycling),

$$\sigma(\tau) = a \{ -I_z^{(1)} \cos(\pi J_{12} \tau) + i/2 \{ -I_+^{(1)} I_-^{(2)} + I_-^{(1)} I_+^{(2)} \} \sin(\pi J_{12} \tau) \} \exp(-\tau / T_2'^{(1)})$$
$$+ b \{-I_z^{(2)} \cos(\pi J_{12} \tau) + i/2 \{I_+^{(1)} I_-^{(2)} - I_-^{(1)} I_+^{(2)}\} \sin(\pi J_{12} \tau)\} \exp(-\tau / T_2'^{(2)}) . \tag{S17}$$

Removal of the zero-quantum coherence terms (with their undesired $\sin(\pi J_{12} \tau)$ modulation) is only achieved if $a = b = 1$ and $T_2'^{(1)} = T_2'^{(2)}$. Otherwise, the effect of the zero-quantum coherence terms must be considered:

$$I_+^{(1)}I_-^{(2)} = \{I_x^{(1)} + i\,I_y^{(1)}\}\,\{I_x^{(2)} - i\,I_y^{(2)}\}$$

$$= (1/2)\,(2\,I_x^{(1)}I_x^{(2)} + 2\,I_y^{(1)}I_y^{(2)} - i\,2\,I_x^{(1)}I_y^{(2)} + i\,2\,I_y^{(1)}I_x^{(2)})\,. \tag{S18}$$

$$I_-^{(1)}I_+^{(2)} = \{I_x^{(1)} - i\,I_y^{(1)}\}\,\{I_x^{(2)} + i\,I_y^{(2)}\}$$

$$= (1/2)\,(2\,I_x^{(1)}I_x^{(2)} + 2\,I_y^{(1)}I_y^{(2)} + i\,2\,I_x^{(1)}I_y^{(2)} - i\,2\,I_y^{(1)}I_x^{(2)})\,. \tag{S19}$$

Thus, eqn (S17) becomes:

$$\sigma(\tau) = a\,\{\,-I_z^{(1)}\cos(\pi\,J_{12}\,\tau) - (1/2)\,\{2I_x^{(1)}I_y^{(2)} - 2I_y^{(1)}I_x^{(2)}\}\,\sin(\pi\,J_{12}\,\tau)\,\}\,\exp(-\tau/T_2'^{(1)})$$

$$+ b\{-I_z^{(2)}\cos(\pi\,J_{12}\,\tau) + (1/2)\{2I_x^{(1)}I_y^{(2)} - 2I_y^{(1)}I_x^{(2)}\}\,\sin(\pi\,J_{12}\,\tau)\}\,\exp(-\tau/T_2'^{(2)}) \tag{S20}$$

The second 90°$_y$ pulse of the *z*-filter gives:

$$\sigma(\tau) = a\,\{\,-I_x^{(1)}\cos(\pi\,J_{12}\,\tau) + (1/2)\,\{2I_z^{(1)}I_y^{(2)} - 2I_y^{(1)}I_z^{(2)}\}\,\sin(\pi\,J_{12}\,\tau)\,\}\,\exp(-\tau/T_2'^{(1)})$$

$$+ b\{-I_x^{(2)}\cos(\pi\,J_{12}\,\tau) - (1/2)\{2I_z^{(1)}I_y^{(2)} + 2I_y^{(1)}I_z^{(2)}\}\,\sin(\pi\,J_{12}\,\tau)\}\,\exp(-\tau/T_2'^{(2)}) \tag{S21}$$

Thus, as in the case of the spin-echo experiment without a *z* filter discussed above, integration over the frequency-domain lineshapes is required to obtain a clean cosine modulation:

$$S^{integrated}(\tau)_{spin\,1} = -a\,\cos(\pi\,J_{12}\,\tau)\,\exp(-\tau/T_2'^{(1)})\,. \tag{S22}$$

$$S^{integrated}(\tau)_{spin\,2} = -b\,\cos(\pi\,J_{12}\,\tau)\,\exp(-\tau/T_2'^{(2)})\,. \tag{S23}$$

Note that the incomplete suppression of anti-phase zero-quantum coherence terms by a *z* filter in the refocused INADEQUATE experiment (that involves the evolution of double-quantum coherence in t_1) is presented in Ref.[10] Specifically, while anti-phase zero-quantum coherence can be removed by turning off ^{1}H decoupling during the *z* filter, this has the disadvantage of allowing spin diffusion to affect an unwanted transfer of magnetisation between the spins. For this reason, ^{1}H decoupling is kept on during the *z* filter delays in our experiment.

Finally, we note that the above discussion assumes that the coupling is still active during the acquisition time. For the switched-angle spin-echo experiment employed

here, this is actually not the case for the residual dipolar coupling which, while active for the off-magic-angle evolution during the spin-echo period τ, is not active for the on-magic-angle evolution during the acquisition time. Thus, the "standard procedure" of integrating over the lineshape employed in this work is not essential to ensure the observation of the desired modulation (i.e., that described by eqn (1) in the main text).

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