Electronic Supplementary Information (ESI)

Optimisation of $^1$H PMLG homonuclear decoupling at 60 kHz MAS to enable $^{15}$N-$^1$H through-bond heteronuclear correlation solid-state NMR spectroscopy

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S1. Product operator formalism - INEPT

We review here a product operator analysis of the refocused INEPT pulse sequence element. At the beginning of the refocused INEPT element, the in-phase magnetization $\hat{S}_x$ is along the transverse plane for $^{15}$N. During the first echo period ($\tau_1$), the in-phase magnetization is converted into anti-phase $\hat{S}_y$ $\hat{I}_z$:

$$\hat{S}_x \xrightarrow{\frac{\pi}{2}-\pi} \cos(2\pi J_{IS} \tau_1) \hat{S}_x + \sin(2\pi J_{IS} \tau_1) \hat{S}_y \hat{I}_z, \quad (1)$$

where $\hat{I}$ represents the $^1$H spins. The anti-phase coherence is transferred from $S$ to $I$ with the 90° pulses applied on both channels, which separates the two spin-echo evolution periods:

$$\sin(2\pi J_{IS} \tau_1) \hat{S}_y \hat{I}_z \xrightarrow{\frac{\pi}{2}J_{IS}} \xrightarrow{\frac{\pi}{2}J_{IS}} \sin(2\pi J_{IS} \tau_1) \hat{S}_z \hat{I}_x. \quad (2)$$

Following $\tau_1$, in the second echo period ($\tau_2$), the antiphase $^1$H coherence is converted into in-phase $\hat{I}_x$ that is then detected during acquisition ($t_2$):

$$\sin(2\pi J_{IS} \tau_1) \hat{S}_z \hat{I}_y \xrightarrow{\frac{\pi}{2}-\pi} \sin(2\pi J_{IS} \tau_2) \sin(2\pi J_{IS} \tau_1) \hat{I}_x. \quad (3)$$
S2. Optimisation of PMLG $^1$H homonuclear decoupling on $^{15}$N-glycine

Figure S1. A stacked representation of a two-variable optimization (see Fig. 3a) of both $\tau_{LG,\text{expt}}$ (in steps of 0.25 $\mu$s) and $\nu_1$ in a 1D $^1$H-CRAMPS ($\nu_0 = 500$ MHz) MAS ($\nu_1 = 60$ kHz) NMR experiment of $^{15}$N-glycine, in which windowed PMLG$^{\text{new}}$ was applied with $\tau_{\text{tilt}} = 0.54$ $\mu$s and a $^1$H transmitter offset of $-0.6$ kHz, corresponding to the data shown in Figure 3a of the main text. 8 co-added transients were collected for each optimization point. On the right, slices from the optimization are shown with the associated $\tau_{LG,\text{expt}}$ and $\nu_1$. The relative intensity of the NH$_3^+$ peak with respect to the best $^1$H homonuclear decoupling performance at $2 \tau_{LG,\text{expt}} = 6.25$ $\mu$s and $\nu_1 = 110$ kHz is stated.
Figure S2. Zoom of the region between $\tau_{LG_{\text{expt}}} = 5.5 \, \mu s - 7.5 \, \mu s$ for the two-variable optimization of $\tau_{LG_{\text{expt}}}$ (in steps of 0.25 $\mu s$) and $\tau_l$ in a 1D $^1$H-CRAMPS ($\nu_0 = 500$ MHz) MAS ($\nu_r = 60$ kHz) NMR spectrum of the $^{15}$N-glycine a) CH$_2$ and b) NH$_3^+$ peak intensity, corresponding to the data shown in Figure 3a of the main text. Windowed $PMLG^n_{5\tau_{\text{wm}}}$ was applied with $\tau_w = 7.20 \, \mu s$, $\tau_c = 0.54 \, \mu s$ and a $^1$H transmitter offset of $-0.6$ kHz. 8 co-added transients were collected for each optimization point for a recycle delay of 3 s.

S3. Optimisation of tilt pulses via the NH$_3^+$ signal intensity in a 1D CRAMPS experiment of $^{15}$N-glycine

The duration of the tilt pulses, $\tau_t$, was optimised in a two-variable optimization with $\tau_{LG_{\text{expt}}}$, for the intensity of the NH$_3^+$ resonance in a 1D CRAMPS spectrum of $^{15}$N-glycine at 60 kHz MAS as presented in Fig. S3a with windowed $PMLG^n_{5\tau_{\text{wm}}}$. It is evident from Fig. S3 that the optimum values for the two parameters, $\tau_{LG_{\text{expt}}}$ and $\tau_t$, are linked, i.e., when one becomes longer the other shortens, maintaining the same combined length of $\sim 7.1 \, \mu s$ (considering two sandwich pulses per $PMLG^n_{\phi_R}$ block – see Fig. 2b) to maintain the same cycle time, $\tau_c$ (see eq. 11), and hence ensure a constant optimum $\psi$ (see eq. 12). The couples with best NH$_3^+$ signal intensity were 6.75 & 0.15 $\mu s$, 6.5 & 0.30 $\mu s$ and 6.25 & 0.45 $\mu s$ for 2 $\tau_{LG_{\text{expt}}}$ and $\tau_t$, respectively, with a preference for a longer $\tau_{LG_{\text{expt}}}$ and shorter $\tau_t$ (see Fig. S3b). A fine optimisation with 16 co-added transients was employed to identify the optimum parameters as used in Fig. 3c (and repeated in Fig. S3c, left-hand spectrum).
Figure S3. a) Two-variable optimization of $2 \tau_\text{LG,expt}$ (0.25 $\mu$s step) and $\tau_\text{tilt}$ (0.05 $\mu$s step) for the NH$_3^+$ peak intensity in a 1D $^1$H-CRAMPS ($f_0$ = 500 MHz) MAS ($f_1$ = 60 kHz) spectrum of $^{15}$N-labelled glycine. Windowed PMLG$_{\text{win}}^5$ was applied with $f_1 = 106$ kHz and a $^1$H transmitter offset of $-0.6$ kHz. 4 co-added transients were collected for each optimization point. b) Slices extracted from the contour plot show the best spectrum intensities obtained with the indicated $2 \tau_\text{LG,expt}$ and $\tau_\text{tilt}$. c) 1D $^1$H CRAMPS $^{15}$N-labelled glycine spectra acquired with windowed PMLG$_{\text{win}}^5$ using $2 \tau_\text{LG,expt} = 6.20$ $\mu$s and $\tau_\text{tilt} = 0.54$ $\mu$s (left) and windowed PMLG$_{\text{win}}^5$ without $\tau_\text{tilt}$ (right). 32 co-added transients were added. For all experiments with windowed $^1$H homonuclear decoupling, $\tau_\omega = 7.20$ $\mu$s.

The $^1$H CRAMPS spectrum on the right in Figure S3c was acquired with the same nutation frequency and offset, but with no tilt pulses and $2 \tau_\text{LG,expt}$ was chosen to be 7 $\mu$s such that the cycle time and hence $\psi$ are the same. The intensity of the NH$_3^+$ peak obtained with windowed PMLG$_{\text{win}}^5$, at $\tau_\text{LG,expt} = 6.20$ $\mu$s and $\tau_\text{tilt} = 0.54$ $\mu$s is within 5% of that obtained without tilt pulses. Note, however, that the peak widths for PMLG$_{\text{win}}^5$ without tilt pulses are 235 Hz for the NH$_3^+$ peak, and 224 Hz and 231 Hz for the CH$_2$ peaks. After scaling ($\lambda_\text{CS} = 0.80$), the FWHM become 294 Hz, 280 Hz and 289 Hz, respectively, which is ~15 Hz larger than those stated in Table 3 for windowed PMLG$_{\text{win}}^5$ with $\tau_\text{LG,expt} = 6.20$ $\mu$s and $\tau_\text{tilt} = 0.54$ $\mu$s.
S4. 2D \(^1\)H-\(^1\)H correlation and optimisation of the \(^{15}\)N-glycine NH\(^+\) signal intensity in a 1D-filtered CP-refocused INEPT NMR spectrum for PMLG \(^1\)H decoupling

Each \(^1\)H-detected FID was acquired for 30 ms with a spectral width of 57 ppm. The \(^1\)H indirect dimension was acquired with 96 \(t_1\) FIDs with a dwell time of 29.16 µs (57 ppm spectral width - no \(^1\)H homonuclear decoupling), 12.40 µs (134 ppm spectral width - windowless PMLG\(^{5}_{\text{mm}}\)) and 11.68 µs (143 ppm – windowless PMLG\(^{9}_{\text{mm}}\)). The maximum \(t_1\) were 1.40 ms, 0.59 ms and 0.56 ms using no \(^1\)H homonuclear decoupling, windowless PMLG\(^{5}_{\text{mm}}\) and windowless PMLG\(^{9}_{\text{mm}}\), respectively. The States-TPPI method was employed to achieve sign discrimination in the indirect dimension.

![Diagram showing 2D \(^1\)H-\(^1\)H correlation spectra](image)

**Figure S4.** 2D \(^1\)H-\(^1\)H (\(\nu_b = 600\) MHz) correlation spectra of \(^{15}\)N-Glycine acquired at \(\nu_r = 60\) kHz MAS with a) no \(^1\)H homonuclear decoupling, b) windowless PMLG\(^{5}_{\text{mm}}\) (\(\tau_G = 3.10\) µs, \(\nu_1 = 104\) kHz, \(\Omega = 1\) kHz) and c) windowless PMLG\(^{9}_{\text{mm}}\) (\(\tau_G = 2.92\) µs, \(\nu_1 = 104\) kHz, \(\Omega = -0.8\) kHz). In all the experiments, 4 transients were coadded for 96 \(t_1\) FIDs for a recycle delay of 3 s. The zero-offset is set with the carrier being on resonance with the NH\(^+\) peak in the indirect dimension.
Figure S5. $^1$H RF carrier optimization for a 1D-filtered ($\tau_1 = 0$) $^{15}$N-$^1$H ($\nu_0 = 500$ MHz) CP (contact time = 2 ms)-Refocused INEPT MAS ($\nu = 60$ kHz) NMR experiment for $^{15}$N-labelled glycine, whereby a) windowed $PMLG^{\tau_w}$ $^1$H homonuclear decoupling (See Fig. 5) was applied with $\tau_{LG,expt} = 3.1$ $\mu$s, $\tau_{tilt} = 0.54$ $\mu$s and a $^1$H nutation frequency, $\nu_\text{LT}$, of 106 kHz during $\tau_1$ (1.999 ms, 66 $\tau_c$) and 104 kHz during $\tau_2$ (1.391 ms, 48 $\tau_c$), b) windowless $PMLG^{\tau_w}$ $^1$H homonuclear decoupling was applied with $\tau_{LG,expt} = 3.1$ $\mu$s and a $^1$H nutation frequency, $\nu_\text{LT}$, of 104 kHz during $\tau_1$ (2.096 ms, 169 $\tau_c$) and 102 kHz during $\tau_2$ (0.496 ms, 40 $\tau_c$), c) windowed $PMLG^{\tau_w}$ $^1$H homonuclear decoupling was applied with $\tau_{LG,expt} = 2.92$ $\mu$s, $\tau_R = 0.82$ $\mu$s and a $^1$H nutation frequency, $\nu_\text{LT}$, of 104 kHz during $\tau_1$ (2.085 ms, 71 $\tau_c$) and 106 kHz during $\tau_2$ (1.498 ms, 51 $\tau_c$) and d) windowless $PMLG^{\tau_w}$ $^1$H homonuclear decoupling was applied with $\tau_{LG,expt} = 2.92$ $\mu$s and a $^1$H nutation frequency, $\nu_\text{LT}$, of 104 kHz during $\tau_1$ (2.091 ms, 179 $\tau_c$) and 102 kHz during $\tau_2$ (1.192 ms, 102 $\tau_c$). 16 transients were coadded. For all experiments with windowed decoupling, $\tau_w$ was substituted with a delay of 7.20 $\mu$s. The zero-offset is set with the carrier being on resonance with the NH$_3^+$ peak.
**S5. Cimetidine**

Here, the normalized intensity is related to the respective maximum intensity for each peak, i.e. the maximum intensity is equal to 1 for all the resonances. However, note that the NH15 proton signal intensity is ~30% of that of NH3.

![Cimetidine structure](image)

**Figure S6.** Dephasing of cimetidine NH proton ($\nu_0 = 600$ MHz) resonances as a function of the spin-echo duration, $\tau$, with windowed $PMLG^{5\nu}$ ($\tau_{LG,\text{expt}} = 3.10 \mu$s, $\tau_{\text{tilt}} = 0.54 \mu$s and $\tau_w = 7.20 \mu$s) for a nutation frequency of 106 kHz. Fits to an exponential decay function are shown, with the spin-echo dephasing times, $T'_{2}$, as listed in Table S1. 8 transients were co-added for a recycle delay of 5 s.

*Table S1.* Cimetidine $^1$H dephasing time, $T'_{2}$, for the three NH resonances and $T'_{2}$ scaled by the experimental $\lambda_{CS}$, $\lambda_{CS} T'_{2}$, acquired on a $^1$H spin-echo$^a$ experiment using windowed $PMLG^{5\nu}$.

|          | $\delta$ (ppm) | $\nu_1$ (kHz) | $\lambda_{CS}$ | $T'_{2}$ (ms) | $\lambda_{CS} T'_{2}$ (ms) |
|----------|----------------|---------------|----------------|---------------|---------------------------|
| NH3      | 11.6           | 106           | 0.82           | 1.34          | 1.10                      |
| NH15     | 9.7            |               |                |               |                           |
| NH10     | 8.2            |               |                |               |                           |

$^a$Implemented at $\nu_0 = 600$ MHz and $\nu_1 = 60$ kHz (see Fig. S6). Windowed $PMLG^{5\nu}$ was implemented with $\tau_{LG} = 3.10 \mu$s, $\tau_{\text{tilt}} = 0.54 \mu$s and $\tau_w = 7.20 \mu$s

$^b$ $\Omega_a = -0.8$ kHz, where the zero-offset is set with the carrier being on resonance with the NH$^1$ peak of $^{15}$N-glycine
S6. Simulations of eqs 1 and 2

Figure S7. Simulation of dependence of the $^{15}$N-$^1$H CP-Refocused INEPT intensity on the spin-echo period, $\tau_1$, according to eq. 1 and 2 (from the main text) for a NH (red) or NH$_3$ (blue) group, for a $J_{NH}$ equal to: a) 90 Hz, b) 75 Hz and c) 60 Hz ignoring dephasing, and d) 90 Hz, e) 75 Hz and f) 60 Hz with exponential dephasing with a nominal nitrogen $T_2'$ of 35 ms.