Electronic Supplementary Information for "Enhancing the Resolution of ^{1}H and ^{13}C Solid-State NMR Spectra by Reduction of Anisotropic Bulk Magnetic Susceptibility Broadening"

Michael P. Hanrahan,[1,2] Amrit Venkatesh,[1,2] Scott L. Carnahan,[1,2] Julie L. Calahan,[3] Joseph W. Lubach,[4] Eric J. Munson,[3] Aaron J. Rossini,[1,2]**

[1]*Iowa State University, Department of Chemistry, Ames, IA, USA 50011*
[2]*US DOE Ames Laboratory, Ames, Iowa, USA, 50011*
[3]*University of Kentucky, College of Pharmacy, Lexington, Kentucky, USA, 40536*
[4]*Genentech, Inc., Department of Small Molecules Pharmaceutical Sciences, 1 DNA Way, South San Francisco, CA, USA 94080*

Corresponding Authors
*e-mail: arossini@iastate.edu
*e-mail: eric.munson@uky.edu

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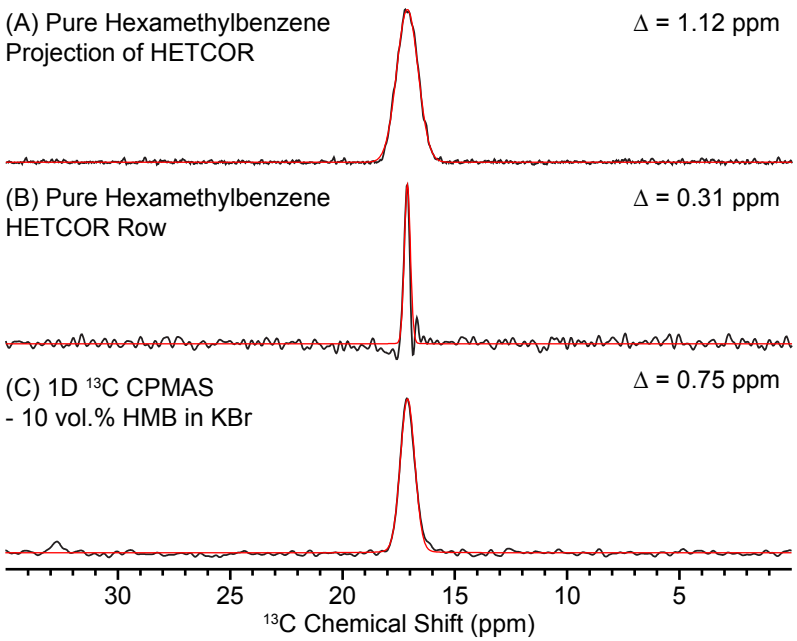

Figure S1. Comparison of the methyl peak widths in the 9.4 T ^{13}C solid-state NMR spectra of hexamethylbenzene (HMB) obtained from a pure sample and HMB diluted in KBr. (A) ^{13}C solid-state NMR spectrum of pure HMB obtained from the positive projection of the 2D ^{1}H-^{13}C CP-HETCOR spectrum, (B) ^{13}C solid-state NMR spectrum of HMB obtained from a row of the 2D ^{1}H-^{13}C CP-HETCOR spectrum, (C) 1D ^{13}C CPMAS spectrum of 10 vol. % HMB in KBr. Fits of ^{13}C methyl peak are overlaid as red traces and the measured FWHM (Δ) is indicated.

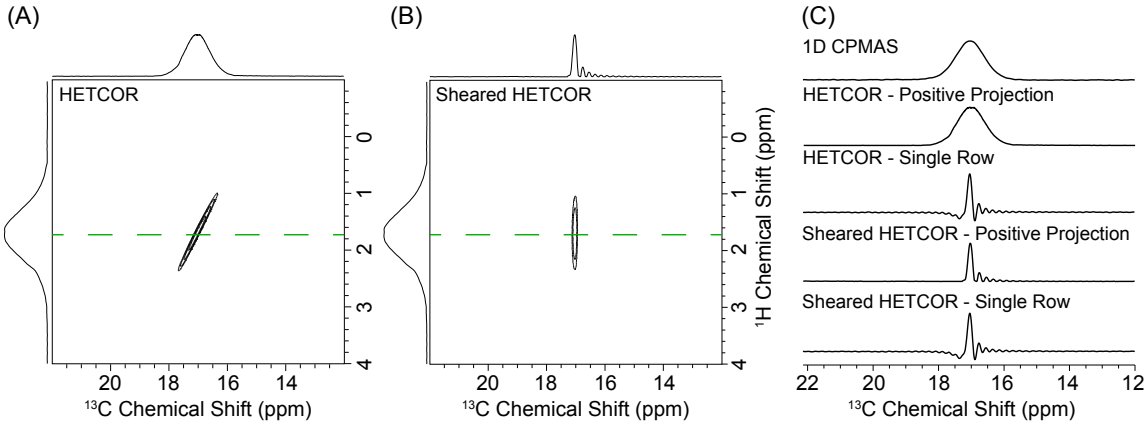

Figure S2. 18.8 T 2D ^{1}H-^{13}C CP-HETCOR spectrum of hexamethylbenzene and comparison of the 1D CPMAS NMR spectrum to spectra obtained from the HETCOR spectrum. (A) Standard 2D HETCOR spectrum and (B) 2D HETCOR spectrum obtained after a shearing transformation to obtain high ^{13}C resolution. (C) Comparison of ^{13}C solid-state NMR spectra obtained from a 1D ^{13}C CPMAS experiment, the positive projection of the 2D HETCOR spectrum, a single row of the 2D HETCOR spectrum, the positive projection of the sheared 2D HETCOR spectrum and a single row of the sheared HETCOR spectrum.

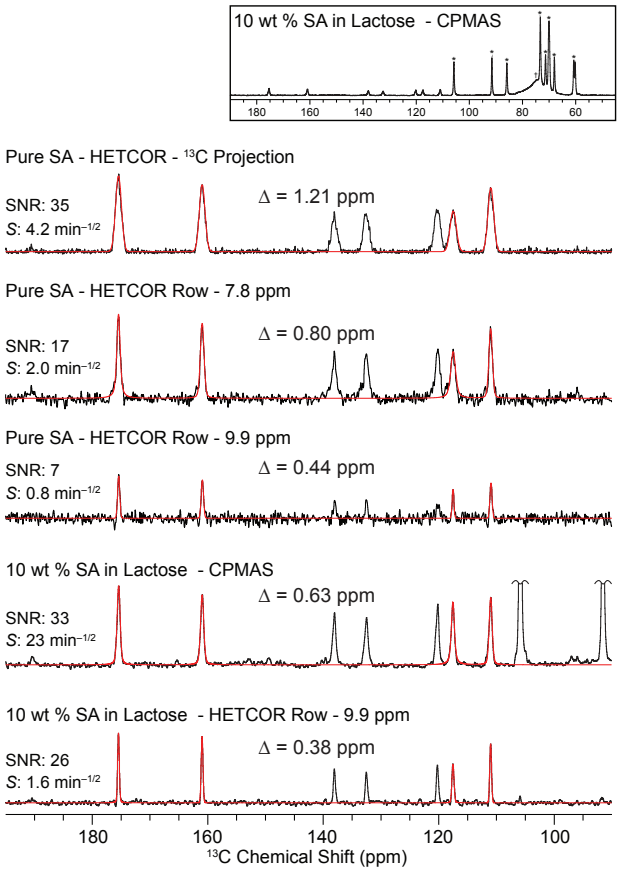

Figure S3. Comparison of DNP enhanced ^{13}C solid-state NMR spectra of pure and diluted salicylic acid (SA). For pure SA, the ^{13}C NMR spectrum of the positive projection of the 2D HETCOR spectrum (top trace) is compared to ^{13}C NMR spectra obtained from rows of the HETCOR spectrum at ^{1}H chemical shifts of 7.8 ppm and 9.9 ppm. For 10 wt.% SA diluted in lactose the 1D ^{13}C CPMAS spectrum is compared to the ^{13}C NMR NMR spectrum obtained from row of the HETCOR spectrum at a ^{1}H chemical shift of 9.9 ppm (lower two traces). Fits of the peaks to Lorentzian/Gaussian functions to measure FWHM (Δ) are shown in red and results are summarized in Table S1. The average FWHM for the fitted peaks is indicated. The complete ^{13}C CPMAS NMR spectrum of dilute SA in lactose is shown in the inset. Asterisks denote lactose signals.

Table S1. Summary of the FWHM of the ^{13}C Peaks Measured in the DNP Enhanced ^{13}C Solid-State NMR Spectra of Pure and Diluted Salicylic Acid.

Isotropic ^{13}C Chemical Shift (ppm)	Δ (Hz/ppm) **Single Row – 9.9 ppm ^{1}H**	Δ (Hz/ppm) **Single Row – 7.8 ppm ^{1}H**	Δ (Hz/ppm) **Projection**	Δ (Hz/ppm) **10 wt. % SA[a] Single Row – 9.7 ppm ^{1}H**	Δ (Hz/ppm) **10 wt. % SA[a] CPMAS**
175.4	46/0.46	70.2/0.70	121/1.20	34/0.34	62/0.62
160.9	49/0.49	76.7/0.77	118/1.17	37/0.37	63/0.63
117.5	37/0.37	101.2/1.01	128/1.27	43/0.43	62/0.62
110.9	45/0.45	73.7/0.74	119/1.18	37/0.37	65/0.65
Average	44/0.44	80.4/0.80	122/1.21	38/0.38	63/0.63

[a]The sample was 10 wt. % salicylic acid and 90% lactose.

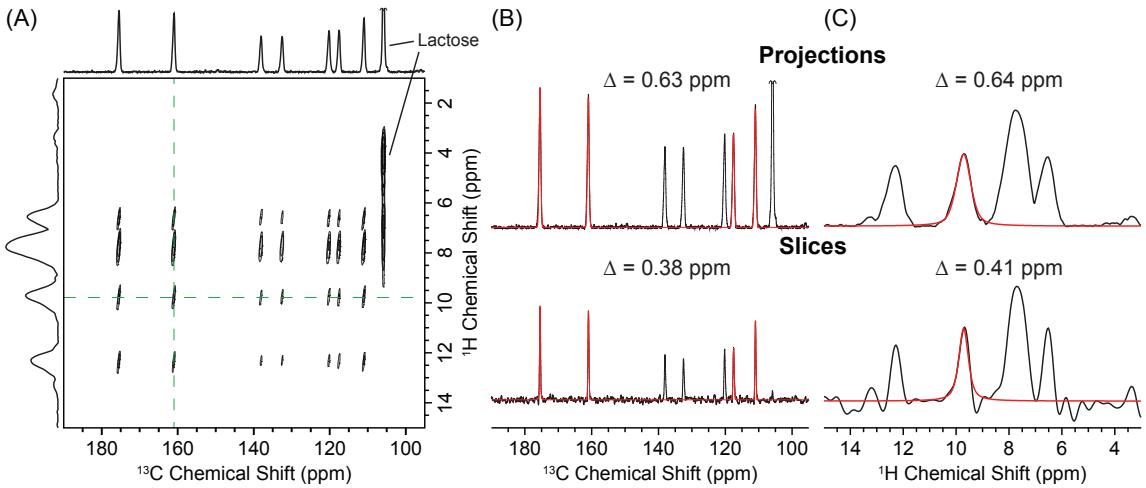

Figure S4. (A) DNP Enhanced 2D ^{1}H-^{13}C CP-HETCOR spectrum of 10 wt.% salicylic acid diluted in lactose. The powdered mixture was impregnated with a solution of 16 mM TEKPol dissolved in tetrachloroethane. (B) Comparison of ^{13}C NMR spectra obtained from the projection of the HETCOR spectrum and the row with a 9.8 ppm ^{1}H chemical shift. (C) Comparison of ^{1}H NMR spectra obtained from the projection of the HETCOR spectrum and the column with a 160.9 ppm ^{13}C chemical shift. Fits of the peaks to Lorentzian/Gaussian functions to measure FWHM (Δ) are shown in red and results are summarized in Table S1. The average FWHM for the fitted peaks is indicated.

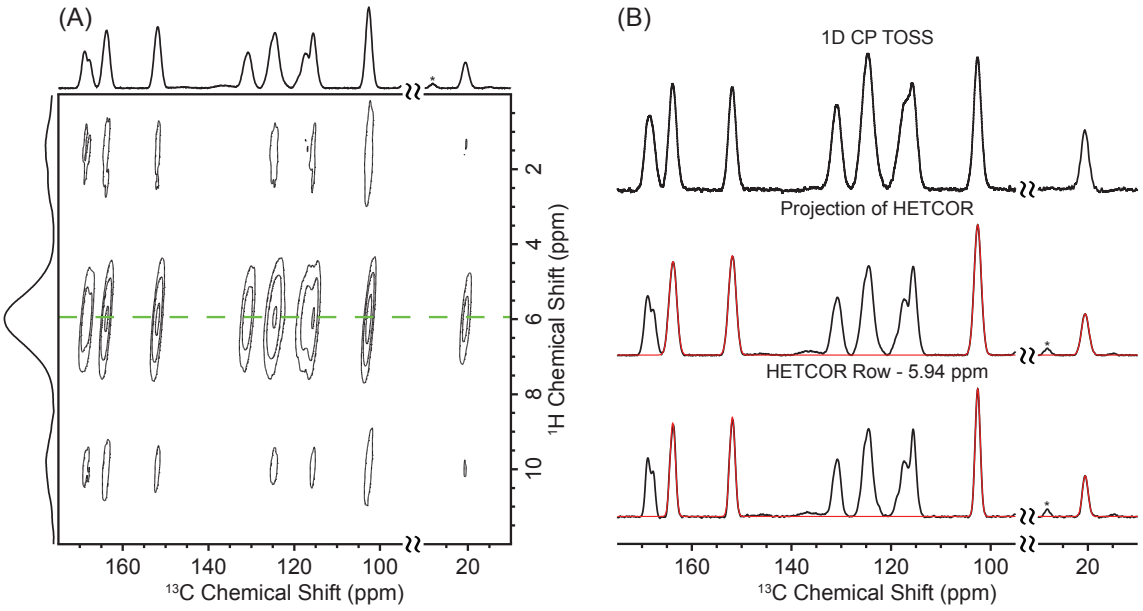

Figure S5. (A) 9.4 T DNP enhanced 2D ^{1}H-^{13}C CP-HETCOR solid-state NMR spectrum of ground dicoumarol impregnated with an 11 mM AMUPol glycerol-d_8/D_2O/H_2O 60/30/10 solution. The MAS frequency was 7500 Hz. (B) Comparison of DNP enhanced ^{13}C solid-state NMR spectra of dicoumarol obtained with a CP-TOSS experiment (top trace), the positive projection of the 2D HETCOR spectrum (middle), and a spectrum extracted from a single row of the HETCOR spectrum at a ^{1}H chemical shift of 5.94 ppm (lower trace). The red traces overlaid on the spectra are fits of the resolved peaks to a mixed Lorentzian/Gaussian function. The FWHM (Δ) determined from the fits are summarized in Table S2.

Table S2. Summary of the FWHM of the ^{13}C Peaks for Dicoumarol.

Isotropic ^{13}C Chemical Shift (ppm)	Δ (Hz/ppm) **Single Row** – 5.9 ppm	Δ (Hz/ppm) **Projection**
163.8	129/1.28	180/1.79
151.9	131/1.30	178/1.77
102.6	121/1.20	170/1.69
20.6	137/1.36	177/1.76
Average	130/1.29	176/1.75

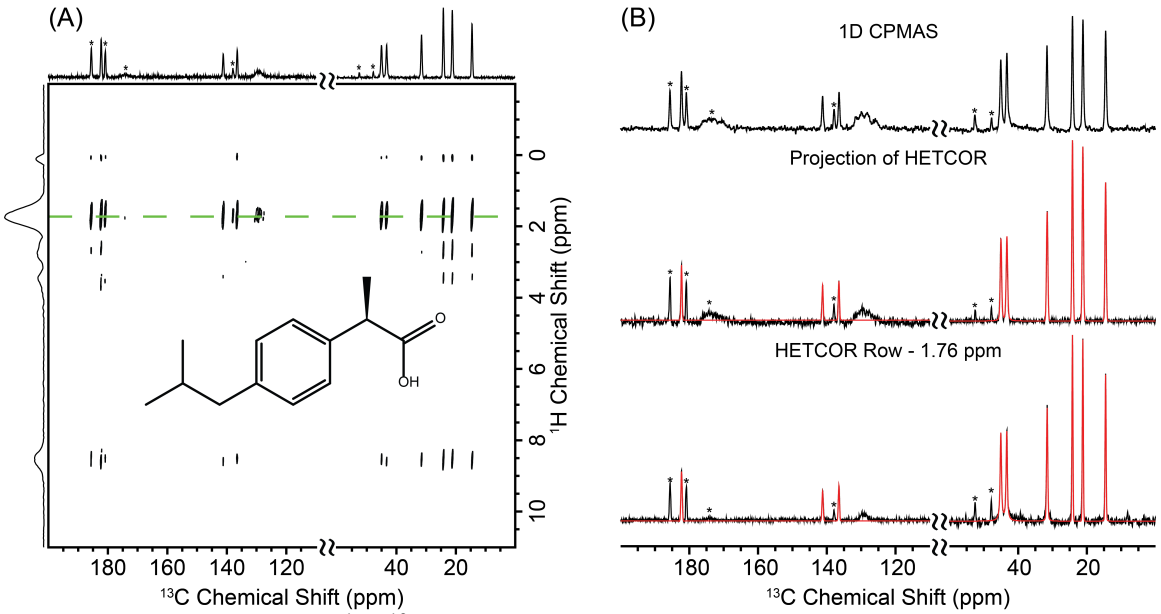

Figure S6. (A) 18.8 T 2D ^{1}H-^{13}C CP-HETCOR solid-state NMR spectrum of ibuprofen. The spectrum was acquired with a 2.5 ms CP contact time and a 8928 Hz MAS frequency. (B) Comparison of ^{13}C solid-state NMR spectra of ibuprofen obtained with a 1D ^{1}H-^{13}C CPMAS experiment (upper spectrum), the projection of the 2D HETCOR spectrum (middle), and a spectrum extracted from a row of the HETCOR spectrum at a ^{1}H chemical shift of 1.76 ppm (lower). The red lines overlaid on the spectra are fits of the resolved peaks to a mixed Lorentzian/Gaussian function. The FWHM (Δ) determined from the fits are summarized in Table S3. Asterisks denote spinning sidebands.

Table S3. Summary of the FWHM of the ^{13}C Peaks for Ibuprofen.

Isotropic ^{13}C Chemical Shift (ppm)	Δ (Hz/ppm) **Single Row 1.8 ppm ^{1}H**	Δ (Hz/ppm) **Projection**
182.3	81/0.40	89/0.44
141.2	81/0.40	86/0.43
136.5	82/0.41	83/0.41
45.0	91/0.45	99/0.49
43.3	85/0.42	102/0.51
31.6	82/0.41	96/0.48
24.2	65/0.32	84/0.42
21.2	67/0.33	88/0.44
14.5	69/0.34	91/0.45
Average	78/0.39	91/0.45

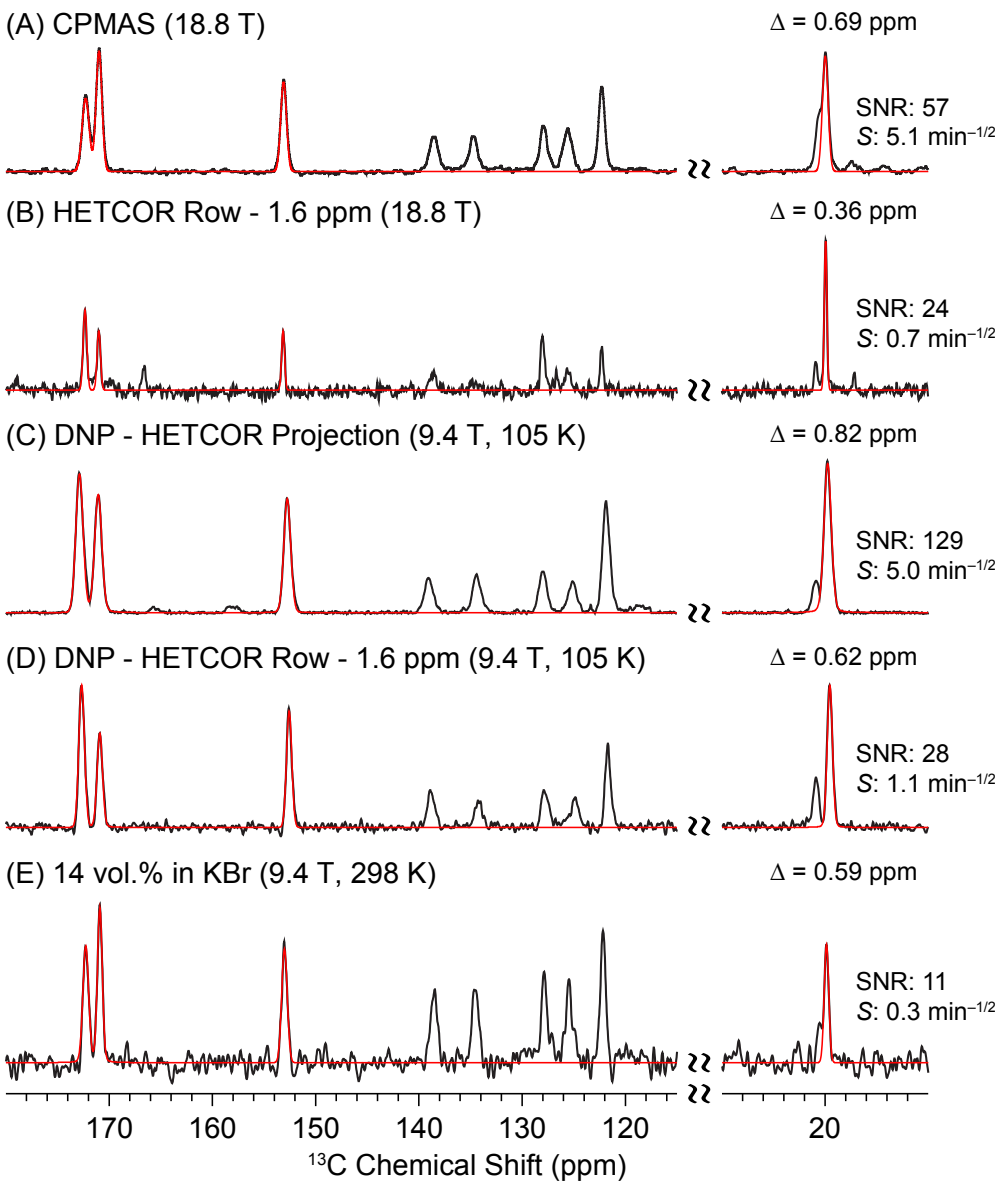

Figure S7. Comparison of ^{13}C solid-state NMR spectra of lyophilized aspirin obtained from (A) ^{13}C CPMAS spectrum at 18.8 T, (B) ^{13}C NMR spectrum extracted from a row of the 2D ^{1}H-^{13}C CP-HETCOR spectrum at 18.8 T, (C) Positive projection of the ^{13}C dimension of the 9.4 T DNP enhanced 2D ^{1}H-^{13}C CP-HETCOR spectrum, (D) ^{13}C NMR spectrum extracted from a row of the DNP enhanced 2D ^{1}H-^{13}C CP-HETCOR spectrum, (E) Conventional ^{13}C CPMAS spectrum at 9.4 T and 298 K of lyophilized aspirin diluted in KBr. The SNR and sensitivity are indicated for each spectrum. Fits of ^{13}C methyl peak are overlaid as red traces and the average FWHM (Δ) measured for the fitted ^{13}C peaks is indicated

Table S4. Summary of the FWHM of the ^{13}C Peaks for Lyophilized Aspirin.

Isotropic ^{13}C Chemical Shift (ppm)	Δ (Hz/ppm) **Single Row 1.6 ppm ^{1}H**[a]	Δ (Hz/ppm) **Projection**[a]	Δ (Hz/ppm) **DNP – Single Row 1.6 ppm ^{1}H**[b]	Δ (Hz/ppm) **DNP – Projection**[b]	Δ (Hz/ppm) **14 vol. % in KBr**[c]
172.3	85/0.42	164/0.81	65/0.65	84/0.83	66/0.66
171.0	79/0.39	135/0.67	62/0.62	82/0.81	56/0.55
153.2	69/0.34	128/0.66	60/0.60	79/0.78	63/0.63
20.0	60/0.30	131/0.65	60/0.60	84/0.83	52/0.52
Average	73/0.36	140/0.69	62/0.62	83/0.82	59/0.59

[a]Conventional solid-state NMR experiments performed on an 18.8 T magnet. [b]DNP Enhanced solid-state NMR experiments were performed on an 9.4 T magnet with a sample temperature of ca. 100 K. [c]The experiment was performed at room temperature with a 9.4 T magnet. 7.9 mg of lyophilized aspirin was diluted into 91.9 mg of finely ground KBr to give a mixture that was ca. 14% by volume aspirin.

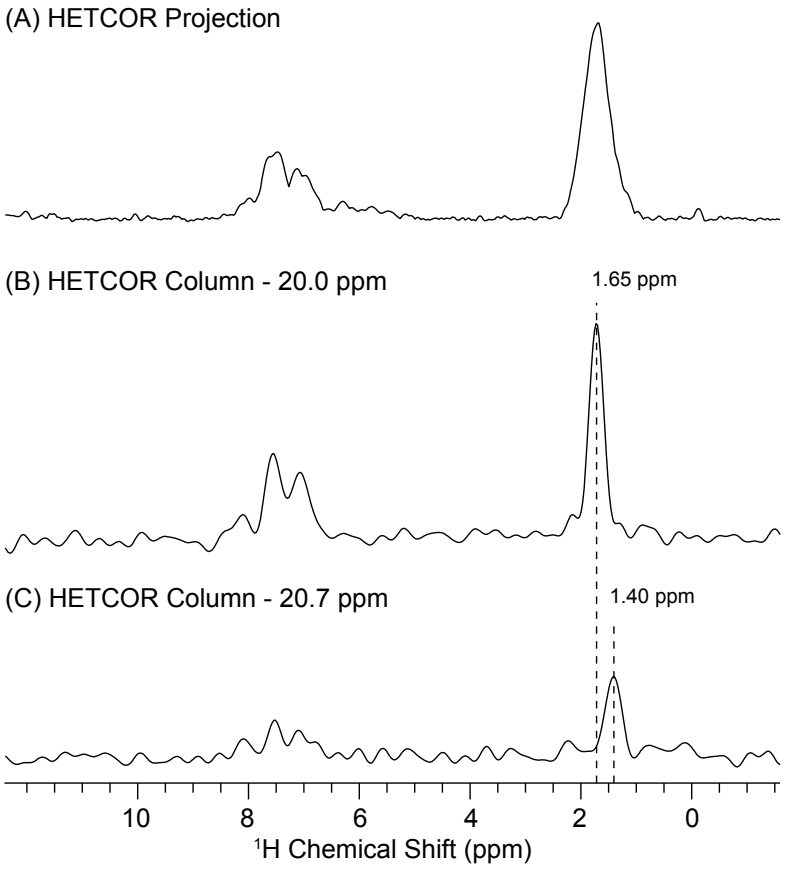

Figure S8. Homonuclear decoupled ^{1}H solid-state NMR spectra of lyophilized aspirin obtained from the 18.8 T 2D ^{1}H-^{13}C CP-HETCOR solid-state NMR spectrum. The 2D HETCOR spectrum was obtained with a 3.0 ms CP contact time and a 8928 Hz MAS frequency. (A) ^{1}H NMR spectrum obtained from the positive projection of the indirect ^{1}H dimension of the HETCOR spectrum. ^{1}H NMR spectra obtained from single columns of the 2D HETCOR spectrum at ^{13}C chemical shifts of (B) 20.0 ppm (form I) and (C) 20.7 ppm (form II). The ^{1}H nuclei of the methyl groups of the two forms clearly show different isotropic chemical shifts.

Table S5. Summary of Calculated ^{13}C Isotropic Chemical Shifts for Aspirin Form I and Form II.

	Form I			Form II			
Atom[a]	σ_{iso} (ppm)	δ_{iso} (ppm) cal.[b]	δ_{iso} (ppm) exp.	σ_{iso} (ppm)	δ_{iso} (ppm) cal.[b]	δ_{iso} (ppm) exp.	δ_{cal}(Form I) – δ_{cal}(Form II) (ppm)
C1	47.99	121.4	122.3	48.07	121.4	122.3	0.07
C2	12.48	155.4	153.1	12.70	155.2	153.1	0.07
C3	44.89	124.4	125.6/ 125.1[c]	43.90	125.4	NA/ 125.4[c]	**-0.96**
C4	30.81	137.9	138.6	31.07	137.6	138.6	0.18
C5	41.78	127.4	127.9	41.74	127.4	127.9	-0.07
C6	34.52	134.3	134.7	34.76	134.1	134.7	0.17
C7	-2.78	170.0	171.0	-2.83	170.0	171.0	-0.24
C8	-6.45	173.5	172.3	-5.99	173.1	172.3	0.24
C9	154.29	19.8	20.0	153.14	20.9	20.9	**-0.72**

[a]The atom numbering is shown in Figure S5. [b]Isotropic shielding values were converted to isotropic shift values by plotting the experimental isotropic chemical shifts for aspirin form I and form II as a function of the corresponding calculated shielding constants. A linear regression analysis of this plot yielded the equation δ_{iso} cal. = $-0.9526\times\sigma_{iso} + 167.33$ ppm. This equation was then used to convert the calculated shielding values to calculated shift values. [c]Measured from the 105 K DNP enhanced 2D ^{1}H-^{13}C HETCOR spectrum. The chemical shifts at low temperature slightly differ from those at room temperature.

Table S6. Summary of Calculated ^{1}H Isotropic Shieldings for Aspirin Form I and Form II.

	Form I			Form II			
Atom[a]	σ_{iso} (ppm)	δ_{iso} cal.[b] (ppm)	δ_{iso} exp.[c] (ppm)	σ_{iso} (ppm)	δ_{iso} calc.[b] (ppm)	δ_{iso} exp.[c] (ppm)	δ_{cal}(Form I) – δ_{cal}(Form II) (ppm)
H1	23.88	7.21	7.0	23.85	7.24	7.1	-0.03
H2	23.26	7.83	7.5	23.24	7.85	7.5	-0.02
H3	23.12	7.97	7.5	23.12	7.97	7.5	0.00
H4	22.46	8.63	8.1	22.46	8.63	8.1	0.00
H5	28.75	2.34	–	30.15	0.94	–	–
H6	30.43	0.66	–	30.47	0.62	–	–
H7	29.14	1.95	–	28.99	2.10	–	–
⟨H5-H7⟩	29.44	1.65	1.6	29.87	1.22	1.4	**0.43**
H8	16.15	14.94	12.7[c]	16.06	15.03	N/A[c]	-0.09

[a]The atom numbering is shown in Figure S5. [b]Isotropic shielding values were converted to isotropic shift values by using the average calculated shielding and experimental chemical shift for the ^{1}H nuclei in the methyl group of form I: $\delta_{iso}(x) = 1.65$ ppm $+ \sigma_{iso,\,avg.}(CH_3\text{-form I}) - \sigma_{iso}(x)$. In this case the experimental chemical shifts were not known with enough certainty to construct a calibration curve. The chemical shifts calculated in this way are likely inaccurate and only their relative differences should be considered. [c]Experimental ^{1}H chemical shifts were measured from columns for the respective methyl group signals of form I and form II within the 2D HETCOR spectrum. See Figure S4. The acid proton ^{1}H chemical shift for form I was determined from a ^{1}H spin echo spectrum obtained with a 12.5 kHz MAS frequency. It was not possible to experimentally determine the acid proton ^{1}H chemical shift for form II.

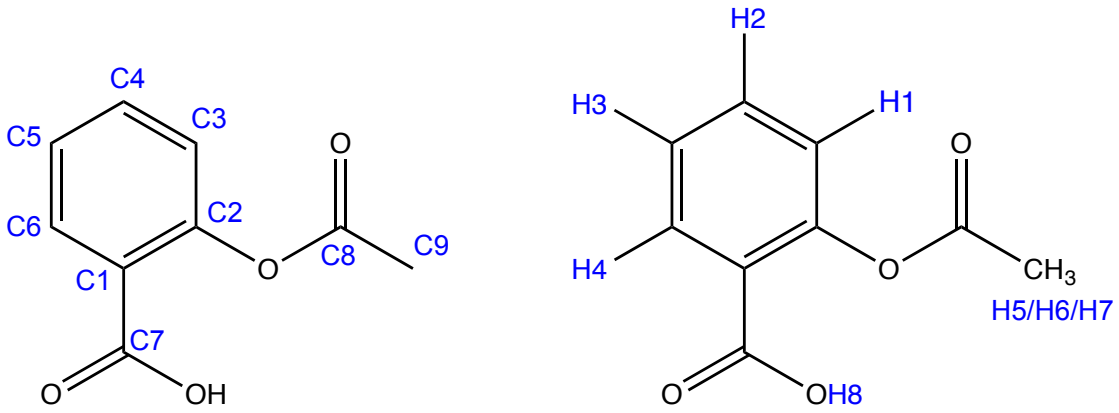

Figure S9. Atom numbering for calculation of ^{1}H and ^{13}C chemical shifts of aspirin.

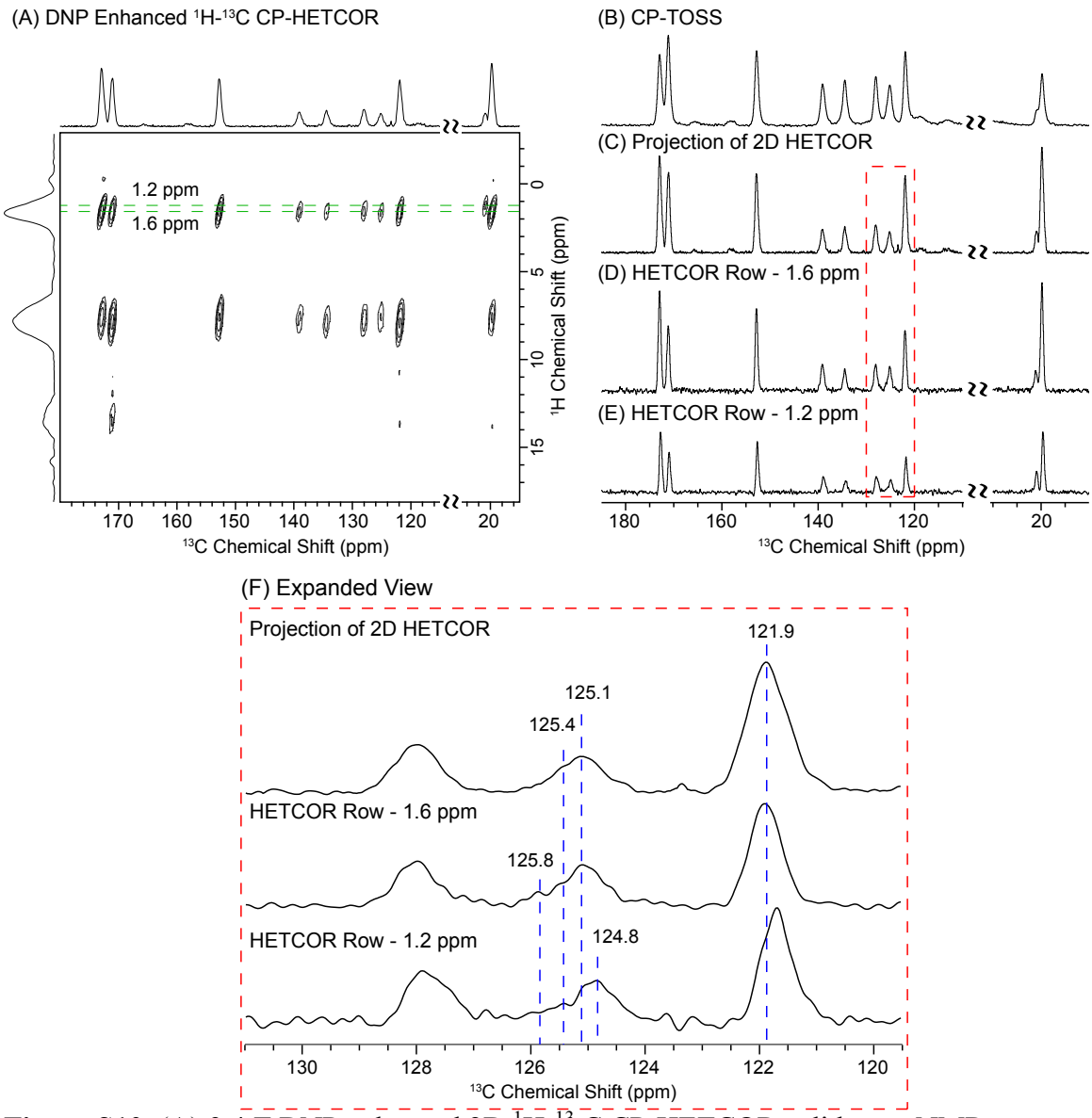

Figure S10. (A) 9.4 T DNP enhanced 2D ^{1}H-^{13} C CP-HETCOR solid-state NMR spectrum of lyophilized aspirin impregnated with a 16 mM TEKPol 1,3-dibromobutane solution. The spectrum was acquired with eDUMBO-1_{22} ^{1}H homonuclear decoupling applied during the t_1 evolution period and a 2.5 ms CP contact time. The MAS frequency was 8000 Hz. (Right) Comparison of 1D ^{13}C solid-state NMR spectra obtained (B) with a CP-TOSS experiment (C) from the projection of the 2D HETCOR spectrum and from rows of the HETCOR spectrum with ^{1}H chemical shifts of (D) 1.6 ppm and (E) 1.2 ppm. (F) Expanded view of the 1D ^{13}C solid-state NMR spectra centered on the C3 resonance. The ^{13}C chemical shift of C3 in form II is assigned to 125.1 ppm. In the 1.2 ppm ^{1}H chemical shift row, there is a second low intensity shoulder observed at a higher carbon chemical shift of 125.4 ppm which is assigned assigned to C3 in form II. As expected, this peak shifts to 125.8 ppm in the 1.6 ppm ^{1}H chemical shift row and has reduced intensity.

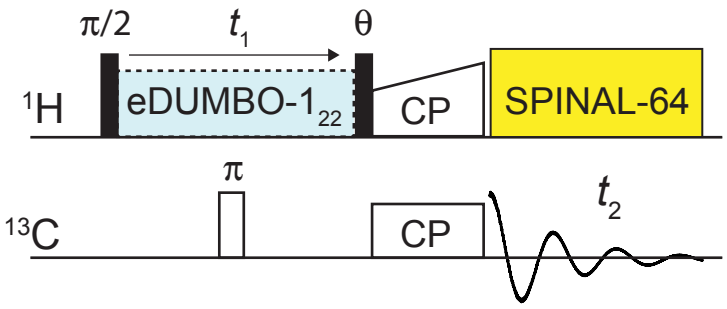

Figure S11. Pulse sequence used for the acquisition of 2D ^{1}H-^{13}C CP-HETCOR spectra.

Table S7. Summary of Shifted Gaussian Apodization Parameters Used for Data Processing.

	^{1}H		^{13}C	
Spectrum	Gaussian Position	Line Broadening (Hz)	Gaussian Position	Line Broadening (Hz)
Hexamethylbenzene				
HETCOR – 9.4 T	0.4	–0.01	0.3	–2.0
HETCOR – 18.8 T	0.3	–10.0	0.3	–2.0
10 vol. % in KBr – 9.4 T	–	–	0.02	–1.0
Salicylic acid				
HETCOR	0.1	–5.0	0.1	–2.0
10 wt. % Salicylic Acid in Lactose				
CPMAS	–	–	0.08	–5.0
HETCOR	0.1	–2.0	0.08	–2.0
Lyophilized aspirin – 18.8 T				
CPMAS	–	–	0.15	–5.0
HETCOR	0.15	–10.0	0.1	–5.0
Lyophilized aspirin – 9.4 T, DNP Enhanced				
HETCOR	0.4	–4.0	0.2	–5.0
14 vol. % lyophilized aspirin in KBr – 9.4 T				
CPMAS	–	–	0.1	–5.0
Dicoumarol				
CP TOSS	–	–	0.15	–10.0
HETCOR	0.15	–5.0	0.15	–10.0
Ibuprofen				
CPMAS	–	–	0.1	–10.0
HETCOR	0.3	–10.0	0.1	–10.0