Drug nano-domains in spray-dried ibuprofen-silica microspheres

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ELECTRONIC SUPPLEMENTARY INFORMATION (ESI)

Table 1. Characteristic dihedral angles in degrees of the optimized monomer structures, shown in ESI Fig. 1.

Table 2. Characteristic dihedral angles in degrees of the optimized dimer structures, shown in ESI Fig. 2.

Fig. 1. Optimised structures of ibuprofen monomers, for which ^{13}C NMR chemical shifts of carbon C1 have been computed.

Fig. 2. Optimised structures of ibuprofen dimers, for which ^{13}C NMR chemical shifts of carbon C1 have been computed.

Fig. 3. Variations of the sum of all ^{1}H peak intensities as a function of the mixing time τ_m.

Fig. 4. ^{1}H-^{29}Si 2D CP MAS heteronuclear correlation

ESI Table 1. Characteristic dihedral angles in degrees of the optimized monomer structures, shown in **ESI Fig. 1**. The atomic numbers are given in Scheme 1 in the main text.

Dihedral angles	*S* (1)	*S* (2)	*S* (3)	*R*	*R* -1 H_2O	*R*-2 H_2O	*S* (2)-1 H_2O	*S* (2)-2 H_2O
C1-C2-C4-C5	-120	121	111	-120	-95	-141	108	105
C1-C2-C4-C9	58	-60	-68	58	84	43	-72	-76
C3-C2-C4-C5	-10	-116	-120	-10	141	94	-127	-131
C3-C2-C4-C9	168	63		168	-40	-82	53	50

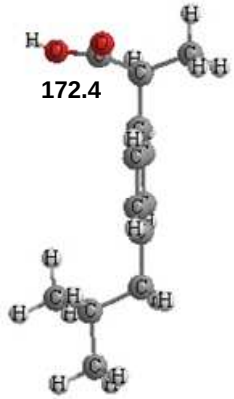
ESI Table 2. Characteristic dihedral angles in degrees of the optimized dimer structures, shown in **ESI Fig. 2**. The atomic numbers are given in Scheme 1 in the main text.

Dihedral angles	N-*RS* [a]	N-*SS*	U-*RS* [a]	U-*SS*	U-*SS*-2 H_2O	U-*SS*-3 H_2O [b]	U-*SS*-4 H_2O	U-*SS*-8 H_2O
C1-C2-C4-C5	78	119	70	120	-67	104	113	-74
C1-C2-C4-C9	-102	-63	-110	-60	113	-74	-67	104
C3-C2-C4-C5	-51	-114	-55	-120	57	-131	-124	51
C3-C2-C4-C9	128	63	123	60	-124	50	57	-131

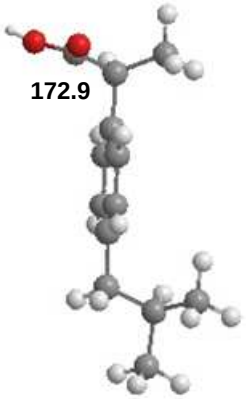
[a] dihedral angles for the *R*-isomer in the RS dimer;

[b] dihedral angles for the left-side *S*-isomer forming two H-bonds

ESI Fig. 1. Optimised structures of ibuprofen monomers, for which ^{13}C NMR chemical shifts of carbon C1 have been computed. The ^{13}C chemical shift values in ppm are reported next to the C1 atom of each ibuprofen molecule. For atomic numbering see Scheme 1 in the main text.



***S* (1)**



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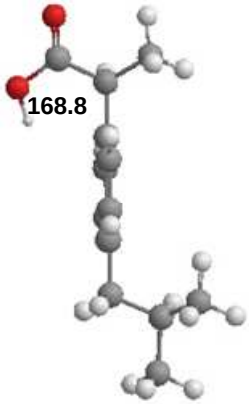

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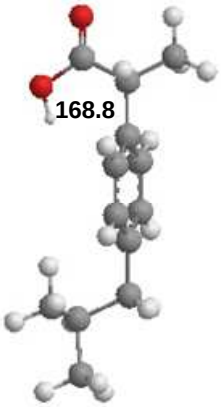
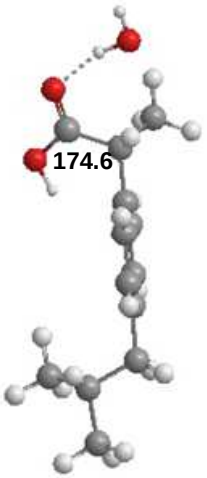
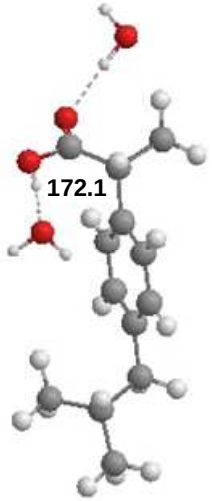


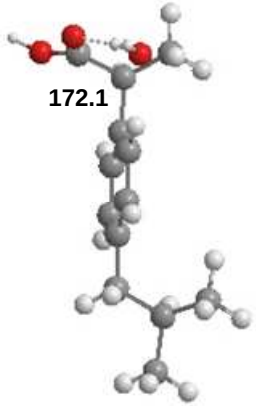
R



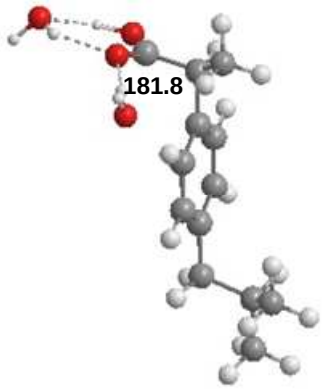
***R*-1 H_2O**



***R*-2 H_2O**

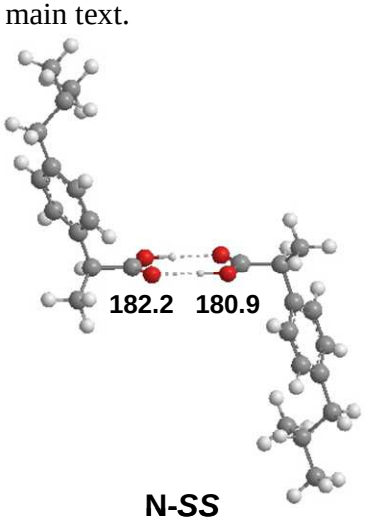


***S* (2)-1 H_2O**

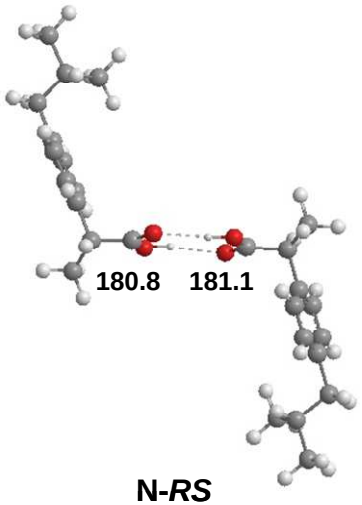


***S* (2)-2 H_2O**

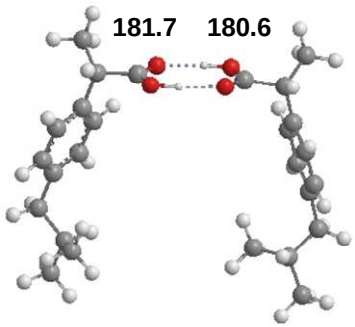
ESI Fig. 2. Optimised structures of ibuprofen dimers, for which ^{13}C NMR chemical shifts of carbon C1 have been computed. The ^{13}C chemical shift values in ppm are reported next to the C1 atom of each ibuprofen molecule. For atomic numbering see Scheme 1 in the main text.



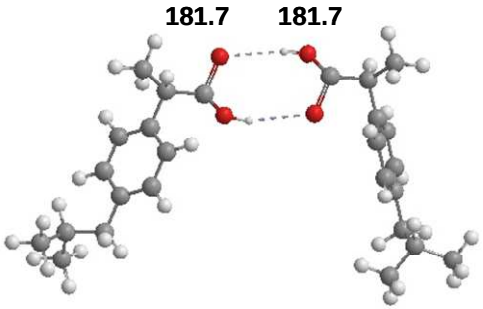
N-*SS*



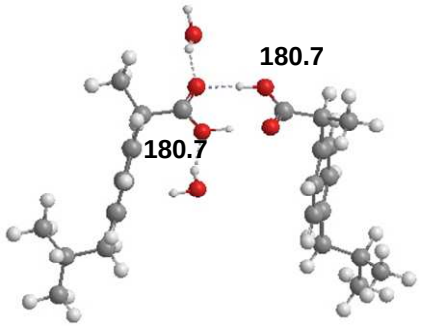
N-*RS*



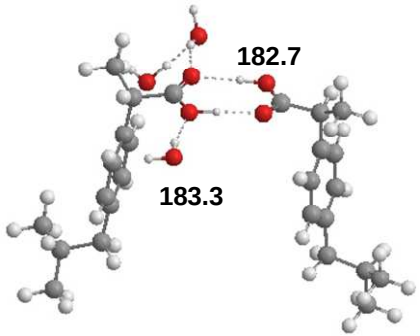
U-*RS*



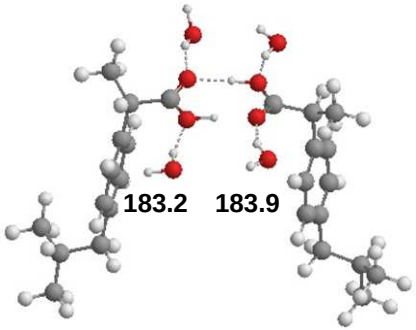
U-*SS*



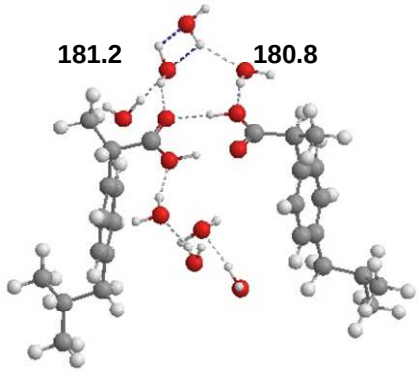
U-*SS*-2 H_2O



U-*SS*-3 H_2O



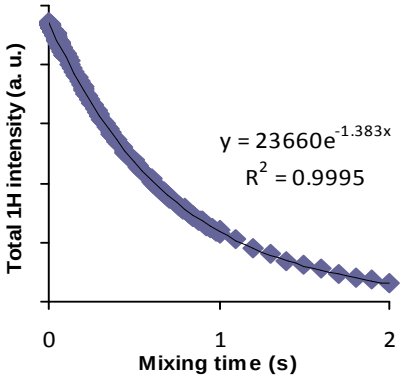
U-*SS*-4 H_2O



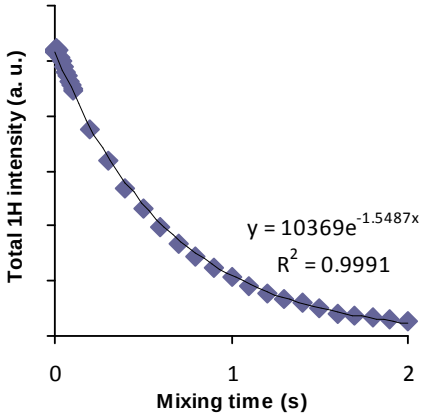
U-*SS*-8 H_2O

ESI Fig. 3. Variations of the sum of all ^{1}H peak intensities as a function of the mixing time τ_m.

1st series (magnetic field of 17.6 T, ν_{MAS} = 30 kHz and T_{stator} = 293 K). From the exponential decay of the total ^{1}H intensity with the mixing time τ_m, we obtain a characteristic time of 723 ms that belongs to the range of longitudinal relaxation times T_1 measured (400-900 ms).



2nd series (magnetic field of 17.6 T, ν_{MAS} = 30 kHz and T_{stator} = 278 K). From the exponential decay of the total ^{1}H intensity with the mixing time τ_m, we obtain a characteristic time of 646 ms that belongs to the range of longitudinal relaxation times T_1 measured (500-900 ms).



3rd series (magnetic field of 9.4 T, ν_{MAS} = 15 kHz and T_{stator} = 295 K). From the exponential decay of the total ^{1}H intensity with the mixing time τ_m, we obtain a characteristic time of 428 ms that belongs to the range of longitudinal relaxation times T_1 measured (400-600 ms).

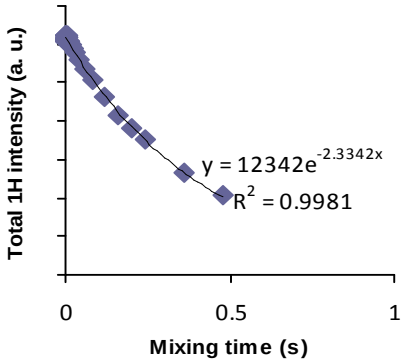


Fig. 4. ^{1}H-^{29}Si 2D CP MAS heteronuclear correlation

^{1}H-^{29}Si 2D HETCOR spectrum of spray-dried silica microspheres containing ibuprofen (ϕ_{drug} = 0.25). The contact time was set to τ_c = 5 ms, and MAS frequency to ν_{MAS} = 12 kHz.