Communication

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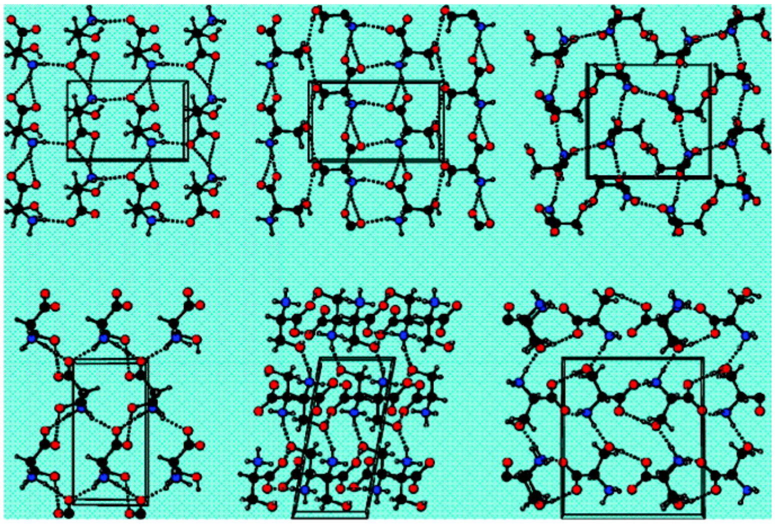

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Different Dynamics of Chiral and Racemic (L- and DL-) Serine Crystals: Evidenced by Incoherent Inelastic Neutron and Raman Scattering

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The chemistry of life is chiral. Therefore, stereochemistry is inherent in nearly all biochemical processes, pharmaceutical and agricultural applications, cosmetics, and nutrition industries. Although the racemic and enantiomerically pure crystal forms contain the same molecule, their physical properties often differ because many solid-state properties are governed by the crystal structure. The pair of L- and DL-serine ($C_3H_7NO_3$) is one of the most striking examples. Serine is prone to form clusters of molecules of the same chirality even in racemic mixtures. In the crystals of DL-serine one can find the chains and the two-dimensional arrays of L-serine molecules alternating with chains and layers formed by D-molecules, but their structures are different from those in the crystals of L-serine.[1] Understanding the structure−properties relation in this system is interesting by itself, and because of the biological applications. Serine−serine interactions account for many biochemical processes, in particular for the functioning of polar clamps and serine zippers in membrane proteins.[2]

L-Serine is denser than DL-serine,[1] which contradicts the so-called "Wallach's rule",[3,4] stating that racemic compounds tend to be denser than their chiral counterparts. The denser structure of L-serine is about four times more compressible on cooling at ambient pressure, than that of the DL-serine.[1] The isothermal bulk compressibility with increasing pressure is the same for L- and DL-serine, up to about 5 GPa, after which, with an increase of the pressure further, the crystal structure of DL-serine remains stable, whereas that of L-serine undergoes two reversible phase transitions at 5.5 and at 7.8 GPa.[5−9] The anisotropy of the structural strain in L-serine and in DL-serine both on cooling and with increasing hydrostatic pressure is remarkably different.[1] Small anomalies in the heat capacity were found for L-serine (a narrow one near 13 K and a broad peak at about 70 K). The difference between the $C_P(T)$ of the chiral and the racemic forms increases rapidly from −0.01 J mol^{-1} K^{-1} at 5K to +6.5 J mol^{-1} K^{-1} near 130 K, which is larger compared to other studied chiral/racemic pairs or polymorphs.[10]

The difference in the properties of the chiral and racemic crystals of serine should be sought in the intramolecular dynamics and in the structure and properties of the hydrogen bond (HB) networks. A recent NMR study of the dynamic properties of the NH_3^+ group in L-serine and DL-serine has shown the activation energy for reorientation of the NH_3^+ to be substantially (1.7 times) lower for L-serine (the denser form!), as compared to the racemic crystal. This difference is greater than any reported previously for an amino acid in different crystal forms. The OH group is not dynamic on the ^{2}H NMR scale.[11] The IR and Raman spectra of the crystalline L- and DL-serine reflect the different characteristics of their HB networks, in particular, of the OH···O bonds in the structure.[12]

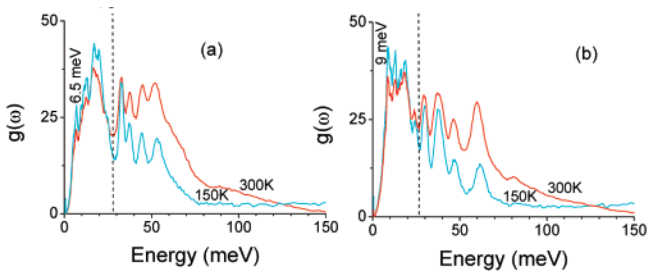

Figure 1. g(ω) at 300 K (red line) and 150 K (cyan line) for L-serine (a) and DL-serine (b). The HB modes are located below the dashed line, that is, <30 meV. For band assignment (see supporting material), we used the IINS data for L-serine at 10 K,[14] and the vibrational spectra of the deuterated and nondeuterated samples of L- and DL-serine,[12,15] as well as our own polarized Raman spectra. In L-serine the lowest vibration is observed at 6.5 meV as indicated in the figure.

To assess the hydrogen dynamics in crystalline L- and DL-serine and to understand better the origin of the radical difference in the properties of the two structures, we carried out variable-temperature incoherent inelastic neutron scattering (IINS) (35−300 K) and a Raman spectroscopy (3−300 K) studies.

IINS measurements were obtained with an incident wavelength $\lambda = 5$ Å ($\Delta E = 100$ μev) at the FOCUS spectrometer at PSI. Slab geometry with samples thickness of 0.6 mm (calculated normal-beam transmission, 0.75) was used to achieve high scattered intensities. After removing the Bragg peaks, the spectra were transformed into the generalized density of vibrational states (g(ω))[13] (Figure 1).

Two intriguing features are worthy of note on the g(ω) of L- and DL-serine: (i) the softer structure of L-serine is reflected by the observation of lower energy vibrations; (ii) the strong vibration at 52 meV in L-serine indicates an enhancement of the HBs between the amino and the adjacent carboxy-groups. Besides, changes caused by disorder in the HB structure induce anharmonicity, as reflected in the variation in the intensity of g(ω) on temperature.

To probe if the onset of anharmonicity is connected to relaxation processes in the instrumental time window (hundreds of ps), we analyzed the elastic incoherent scattering response, $S_{\mathrm{inc}}(Q, \omega = 0)$. Similarly to the X-ray Debye−Waller effect, $[S(Q, \omega = 0)(T)/S(Q, \omega = 0)(35\ \mathrm{K})]$, can be related to the Debye−Waller factor,[16] $S(Q,\omega = 0) = \exp(-{}^1/_3\langle u(T)^2\rangle Q^2)$. The term $\langle u(T)^2\rangle$ is the mean square displacement of the atoms around their equilibrium positions, dominated, in this case, by the incoherent scattering of the H atoms. As shown in Figure 2, $\langle u^2\rangle$ as a function of temperature reveals a

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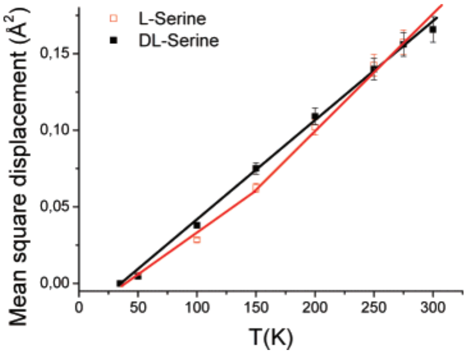

Figure 2. Evolution of $\langle u^2\rangle$ for L-serine (red open squares) and DL-serine (black full squares) deduced from the normalized elastic intensity. No broadening (relative to the resolution function) could be detected.

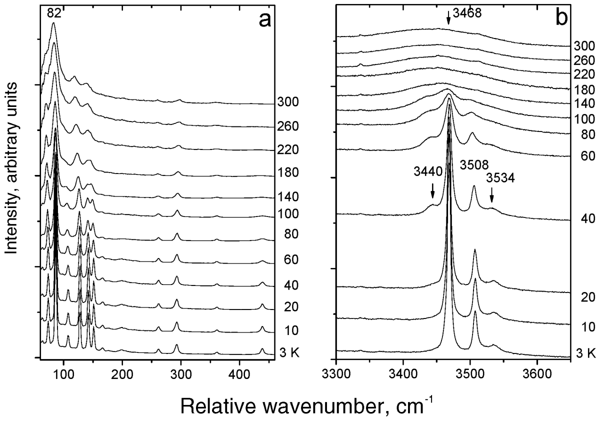

Figure 3. Raman spectra of L-serine crystals versus temperature: (a) the external modes region, sensitive to changes of crystal symmetry; (b) the OH-stretching vibrations, ν(O-H), is observed as a broad band at 300 K.

clear deviation from linearity for L-serine near 150 K that may be indicative of a dynamical transition.

X-ray diffraction data,[1,17] and $C_P(T)$ measurements[10,18] did not display any structural rearrangement in chiral L(D)-serine. NMR studies of the NH_3^+ group dynamics were limited to a higher-temperature range (153−313 K).[11] Therefore, to verify the hypothesis on a dynamic transition inferred by the $S_{inc}(Q, \omega = 0)$ data, we measured Raman spectra of the L- and DL-serine between 3 and 300 K (Triplemate SPEX spectrometer, spectral resolution 2 cm^{-1}, CCD detector LN-1340 PB, Princeton Instruments, Ar laser 488 nm, helium cryostat "MicrostatHe", Oxford Instruments).

The temperature variations of the Raman spectra of DL-serine do not show any striking features. The $\tau(NH_3)$ vibration related to the frozen rotations of the NH_3^+ groups around the C−N bond (510 cm^{-1} at 3 K) looses intensity with increasing temperature and is no longer observable at 300 K (presumably, due to the transition from restricted to free rotations of NH_3^+ group). The stretching C−H and N−H vibrations do not reveal noticeable changes with temperature, while the vibrations of the O−H groups were not observed in the whole temperature range. The Raman- spectra of L-serine and their temperature dependence (Figure 3) differ much from those of DL-serine. Whereas no significant changes occur in the region of the intramolecular C−H and N−H stretching vibrations, some lattice modes (∼200, ∼320, ∼435 cm^{-1}) broaden noticeably on heating, and a new lattice vibration (60−80 cm^{-1}) is clearly observed at ∼140 K. The major changes with temperature involve the OH-stretching vibrations, ν(O−H), (3300−3600 cm^{-1}). While at 3 K three lines are observed (3468, 3508, and 3534 cm^{-1}), on heating, the half-width of the two lower modes rapidly increases and a new mode appears at ∼3440 cm^{-1}. Above 140 K only one broad band (an envelope of several modes) is observed. The intensity gain of the mode at ∼3440 cm^{-1} unambiguously correlates with the intensity loss of the mode at 3468 cm^{-1}. Thus, Raman spectroscopy supports the conclusion from the IINS measurements that the dynamical properties of the crystals of L-serine change above 140 K. These changes involve the reorientation of the OH groups resulting in the positional disorder of the O−H···O intermolecular H-bonds. The additional lattice mode between 60 and 80 cm^{-1} can be related to the translational vibrations of the O−H···O H-bond.

Thus, in measuring with neutron and Raman scattering over a wide temperature range, instead of just comparing the data measured at room temperature to a single selected low temperature point, (10 K) we could asses a subtle dynamical transition in L-serine that was not noticed before.[12,14,15] It is very important for understanding the different temperature sensitivity of the motions of different groups in proteins,[18] that the dynamics of NH_3^+- and OH-groups are active on different time and temperature scales (compare NMR,[11] IINS, and Raman scattering data), and depend also on the spatial arrangement of several molecules and on the intermolecular hydrogen bonds they form.

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Supporting Information Available: Full set of IINS spectra for L- and DL-serine versus temperature. This material is available free of charge via the Internet at http://pubs.acs.org.

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