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Crystal and Molecular Structure of DL-Serine Hydrochloride Studied by X-Ray Diffraction, Low-Temperature Fourier Transform Infrared Spectroscopy and DFT(B3LYP) Calculations

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The structure of DL-serine·HCl was studied by three complementary techniques. Experimental Fourier transform infrared (FT-IR) spectra of pure NH/OH polycrystalline DL-serine·HCl [$HO-CH_2-CH(NH_3^+)-COOH\cdot Cl^-$] and the respective deuterated derivatives [$ND/OD_{Alcohol/Acid}$ (<10% and ca. 60% D)] were recorded in the region 4000−400 cm^{-1} in the temperature range 300−10 K and interpreted. The assignments were confirmed by comparison with the vibrational spectra of crystalline DL- and L-serine zwitterions [$HO-CH_2-CH(NH_3^+)-COO^-$]. Further insight into the structure of the title compound was provided by theoretical DFT(B3LYP)/6-311++G(d,p) calculations of the infrared spectra and energies of 13 different conformers. Potential energy distributions resulting from normal coordinate analysis were calculated for the most stable conformer (**I**) in its hydrogenated and deuterated modification. Frequencies of several vibrational modes were used in the estimation of enthalpies of individual H-bonds present in the crystal, using empirical correlations between enthalpy and the frequency shift that occurs as a result of the establishment of the H-bonds. X-ray crystallography data for DL-serine·HCl were recorded for the first time and, together with the experimental vibrational spectra and the theoretical calculations, allowed a detailed characterization of its molecular structure.

Introduction

It is well-known that amino acids in the gaseous phase and isolated in gas noble matrices adopt the nonionic form ($H_2N-CHR-COOH$),[1,2] while in the neat solid state they exist in the zwitterionic form ($H_3N^+-CHR-COO^-$).[3–5] In solutions, amino acids appear as ionic species whose nature is determined by the pH and by the specific structure of the particular amino acid that determines its isoelectric point. At high pH, amino acids appear predominantly as anionic species ($H_2N-CHR-COO^-$), while at low pH they are prone to adopt a cationic form ($H_3N^+-CHR-COOH$).[6] The latter situation can occur, for example, for amino acid hydrochlorides. As the subject of the present study, we have selected serine hydrochloride since we have previously studied this amino acid under other experimental conditions, such as monomers isolated in cryogenic inert matrices[2] and in its neat crystalline states.[4,5]

In our previous studies on serine in the solid crystalline state, the crystals were constituted by different enantiomeric forms: racemic mixture DL-serine (DL-Ser)[4] and enantiomerically pure L-serine (L-Ser) crystals.[5] In those studies, we used low-temperature Fourier transform infrared (FT-IR) spectroscopy and isotopic dilution techniques to investigate the crystalline H-bonding networks. The general approach used was formulated recently by Rozenberg et al.[7–11] These previous results unequivocally demonstrated the existence of non-negligible H-bonding disorder in some crystalline amino acids,[8] which cannot be determined using standard structural methods (e.g., X-ray and neutron diffraction). Indeed, very often, the number of hydrogen bond contacts found by IR spectroscopy is larger than that obtained by structural methods, because of the higher sensitivity of the former method to short-range interactions as compared with the long-range periodic order seen by the latter techniques.[12–14] This fact further reinforces the relevance of spectroscopic methods to investigate hydrogen bonding characteristics in the solid phases. The present study takes advantage of the complementary nature of the FT-IR spectroscopy/isotopic dilution method and X-ray diffraction in the investigation of the structural properties of serine in its acid form: DL-serine·HCl [DL-Ser·HCl; $HO-CH_2-CH(NH_3^+)-COOH\cdot Cl^-$].

Besides the studies undertaken in the solid state, theoretical [DFT(B3LYP)/6-311++G(d,p)] structural and vibrational studies on the isolated cationic form of serine followed by normal coordinate analysis calculations were also performed in order to help interpret the experimental data. To the best of our knowledge, only two studies have been performed previously on this species.[15,16] Chakraborty and Manogaran[15] studied the transferability of scale factors from glycine hydrochloride and ethanol to serine hydrochloride in an attempt to interpret the infrared spectra of serine in acidic solution. Noguera et al.[16] studied theoretically, among other aminoacids, the structures of neutral and protonated serine. For the latter species they reported only a limited number of conformers (six).

Materials and Methods

Computational Details. DL-Ser in the cationic form has four conformationally relevant dihedral angles [they correspond to the single bonds in the following simplified formula: $HO-CH_2-CH(NH_3^+)-C(=O)-OH$], which can result in 36 different conformations. Exploration of all possible forms, using high-level theoretical methods, will be computationally very expensive. Hence, a preliminary conformational search on the potential energy surface (PES) was carried out at the semiem-

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pirical PM3 level, using a stochastic approach based on modification of the four selected torsion angles.[17] The structures resulting from the preliminary conformational search were used as starting geometries and optimized at a higher level, using the density functional theory (DFT) approach. These calculations revealed the existence of 13 conformers. The theoretical calculations were performed with the Gaussian 98 program package.[18]

The DFT calculations were performed with the 6-311++G(d,p) basis set[19] and the three-parameter density functional, abbreviated as B3LYP, which includes the Becke's gradient exchange correction[20] and the Lee−Yang−Parr correlation functional.[21] All the structures were subjected to full geometry optimization, having both the molecular charge and multiplicity set to 1. Optimizations were followed by frequency calculations, performed at the same level of theory. The nature of the obtained stationary points was characterized by inspection of the corresponding Hessian matrices. The DFT(B3LYP)/6-311++G(d,p) harmonic frequencies were scaled using a single scaling factor of 0.978.[2]

The most stable conformer of DL-Ser in a cationic form, found by DFT calculations, was reoptimized at the *ab initio* MP2[22] level of theory, and the respective IR spectrum was calculated using the same basis set.

In this paper, the structural parameters "bond distance" and "bond angle" are designated by the letter *d* and the symbol ∠, respectively.

Experimental Details. The acid salt of DL-Ser with natural isotopic content was prepared from commercial DL-Ser (Sigma) by adding an excess of concentrated HCl to the solid amino acid, the remaining solvent being evaporated later. The deuterated samples were obtained from DL-Ser·HCl by exchange with D_2O (Aldrich) in recirculating cyclohexane at 81 °C as described elsewhere.[23] Three types of isotopic mixtures were studied: pure NH/OH, 10% ND/OD, and ca. 60% ND/OD.

The studied compound was suspended in a KBr (1:200) pellet, attached to the coldfinger of an APD Cryogenics closed-cycle helium refrigeration system with a DE-202A expander. The temperature (300−10 K) was measured directly at the sample holder by a silicon diode temperature sensor connected to a Scientific Instruments temperature controller (model 9650) and was stabilized to ca. ± 0.2 K during registration of the spectra. Infrared spectra of the pellets were recorded with a Mattson Infinity 60AR series FT-IR spectrometer, with spectral resolution of 1 cm^{-1}. The temperature-induced spectral changes observed for all substances were found to be reversible and highly reproducible.

X-ray data were collected on a Bruker APEX II-CCD diffractometer, using a transparent plate-shaped crystal with dimensions 0.57 × 0.24 × 0.12 mm^3 inserted in a sealed glass capillary. The crystallographic structure was solved by direct methods using SHELXS-97. Refinements were carried out with the SHELXL-97 package. All refinements were made by full-matrix least-squares on F^2 with anisotropic displacement parameters for all non-hydrogen atoms.

Results and Discussion

In our previous studies on DL- and L-Ser,[4,5] the interpretation of the experimental vibrational spectra was aided by the already existing structural data on the crystals of these molecules.[24,25] In the case of DL-Ser hydrochloride, such structural information, according to the best of our knowledge, is not available. Therefore, this essential information was obtained in the present study.

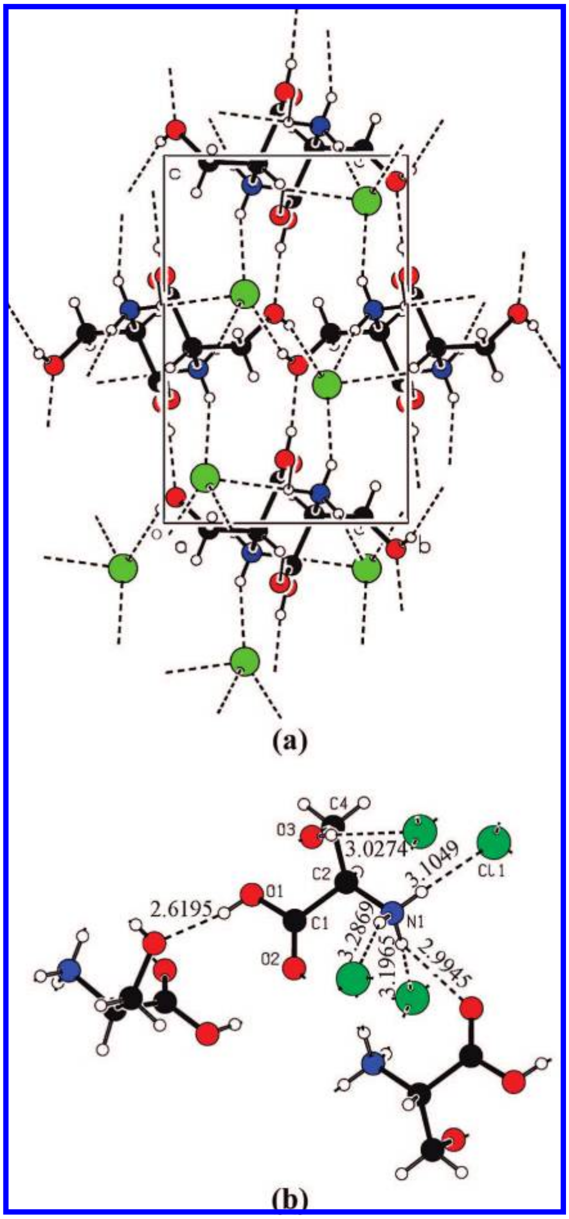

Figure 1. Crystalline structure of DL-Ser·HCl determined by X-ray diffraction: (a) Packing diagram viewed along the *a* axis. Hydrogen bonds are depicted as dashed lines. (b) Detail of the hydrogen bond network showing one of the D enantiomers and its nearest neighbours. Numbers correspond to donor−acceptor distances in angstroms.

The DL-Ser·HCl crystal was found to be monoclinic (space group: $P2_1/c$), with one independent molecule in the unit cell, whose volume is 624.89(3) Å^3 and lattice constants are a = 9.3040(2), b = 6.6665(2), and c = 11.7804(3) Å, and β = 121.216(2)°, at ambient conditions. The D- and L-components assume the same conformation in the crystal, being mirror images of each other. In the L-component, the $N-C_\alpha-C_\beta-O$ torsional angle is −64.37°, and the $C-C_\alpha-C_\beta-O$ angle is 56.67°. As expected, the carboxylic group is protonated, as shown by the CO distances: 1.31 Å for $C-O_{Acid}$ and 1.20 Å for C═O. There is a complex three-dimensional hydrogen bonding network. The cations exhaust their capacity as hydrogen donors, and the chloride anions accept four hydrogen atoms from distinct cations (Figure 1 and Table 1).

The hydrophilic side chain of serine endows an additional −OH group, which, like the ammonium group ($-NH_3^+$) forms hydrogen bonds in crystals. However, unlike the ammonium

TABLE 1: X-ray Data on the Hydrogen-Bonding Related Geometric Parameters in the Crystal of DL-Ser·HCl

donor−H···acceptor	donor−H (Å)	H···acceptor (Å)	donor···acceptor (Å)	donor−H···acceptor (°)
$O-H_C\cdots O_A$	0.8004[a]	1.8284	2.6195	169.52
$O-H_A\cdots Cl^-$	0.6525[a]	2.3958	3.0274	163.60
$N-H(1)\cdots Cl^-$	0.8544	2.3195	3.1049	152.96
$N-H(2)\cdots Cl^-$	0.8768	2.4433	3.2869	161.59
$N-H(3)\cdots Cl^-$	0.9332	2.3045	3.1965	159.77
$N-H(3)\cdots O=$	0.9332	2.5384	2.9945	110.41
$C_\alpha-H\cdots O_C$	0.9981	2.5811	3.4163	141.15

[a] Distances shorter than usual. The positions of hydrogen atoms were determined by difference Fourier synthesis ($R = 0.035$) and refined free of constraints. As it is well-known, the weak dispersion of X-rays by a single electron makes it difficult to accurately determine the hydrogen positions.

TABLE 2: Calculated DFT(B3LYP)/6-311++G(d,p) Structural and Energetic Parameters of the L-Form of Cationic Serine [$HO-CH_2-CH(NH_3^+)-COOH$] and Experimental X-ray Structural Parameters of the L-Form in the Crystal of DL-Ser·HCl

conformer	O=COH (°)	$O=CC_\alpha N$ (°)	$O=CC_\alpha C_\beta$ (°)	$CC_\alpha C_\beta O$ (°)	$C_\alpha C_\beta OH$ (°)	ΔE_{ZPE}[a] (kJ mol^{-1})
			Calculated			
I	0.09	11.16	130.56	−72.68	175.83	0
II	−0.10	−10.42	108.09	−161.75	−176.71	1.57
III	−0.13	−163.79	−43.76	−77.04	168.48	12.95
IV	−0.50	−179.92	−58.27	−170.20	−173.64	14.98
V	1.75	8.62	131.92	80.66	−81.43	36.95
VI	−3.17	−23.35	94.20	65.34	−179.80	37.97
VII	0.87	5.83	129.19	86.51	−160.60	37.97
VIII	175.44	−16.01	101.21	−161.68	−179.27	39.11
IX	178.67	8.75	127.81	−70.39	179.11	40.68
X	−174.06	9.90	133.38	61.95	178.29	41.14
XI	−1.81	−155.79	−30.93	74.44	−77.03	49.32
XII	2.48	137.91	−101.97	57.58	179.97	56.07
XIII	2.84	143.72	−96.53	44.49	86.59	57.93
			Experimental			
X-ray	−11.8	1.6	124.2	−56.7	−97.2	

[a] The DFT(B3LYP)/6-311++G(d,p) calculated energy for conformer I is −1048438.743 kJ mol^{-1} (nonscaled zero-point energy is included) and it was chosen as the relative zero level.

group, the side-chain −OH group has great flexibility and may lead to different patterns of the hydrogen-bonded networks. For example, in crystals of glycine hydrochloride,[26] the molecules are organized in cyclic dimers typical of carboxylic acids. On the contrary, the present X-ray data reveal that this type of dimer is not characteristic of DL-Ser·HCl crystals, most likely on account of an increased number of H-bonds to the chlorine atom and the flexibility of the side-chain −OH group.

Along with strong intermolecular hydrogen bonds present in the crystal (Figure 1 and Table 1), the experimental X-ray geometry suggests that weak intramolecular H-bonds may also be formed in protonated serine. Indeed, two hydrogen atoms of the protonated amino group are located in close vicinity of the carbonyl oxygen. The experimental =O···H distances are equal to 2.60 and 2.54 Å.

Since the experimental X-ray structure of DL-Ser·HCl revealed that the main building unit of the crystals is not the typical dimer, but rather resembles monomeric molecules, it would be interesting to theoretically characterize the monomeric structure of the serine cation. The cation represents a conformationally flexible entity due to different possible orientations of the −COOH and $-CH_2OH$ groups with respect to the $-NH_3^+$ group. On the monomeric level, the D- and L-Ser will produce the same set of conformers; therefore all calculations were carried out on the L-form. Thirteen conformers were localized on its PES (Figures S1 and S2; suffix "S" in the names of figures and tables stands for Supporting Information). The conformationally relevant parameters of these structures along with their relative energies are collected in Table 2 and compared with the structural parameters obtained by X-ray. A more extended version of Table 2, with all the structural parameters (i.e., bond lengths, bond angles and dihedrals) of the thirteen conformers and the respective dipole moments and relative energies, is presented in Table S1. It is interesting to note that the four lowest energy conformers of the protonated serine found in the present work match well with the four lowest energy forms of this species found previously.[16] The conformational search performed by Noguera et al. started from the well-studied conformations of glycine. Using this approach, these authors found six minima for protonated serine; however, they pointed out that such an approach may fail in finding some conformational minima. Indeed, in the present study, exploration of the entire conformational space by allowing all possible combinations of single-bond rotamers revealed the existence of seven additional minima, but no new low-energy minima could be found in the 0−30 kJ mol^{-1} range.

The structural results obtained for the calculated conformer **I** are in the best agreement with the X-ray results for the crystal. Consequently, the calculated geometric and, in particular, vibrational parameters of conformer **I** will be used, when required, in the interpretation of the experimental spectroscopic results. The definition of the internal symmetry coordinates used in the normal coordinates analysis is given in Table S2. The theoretical frequencies, infrared intensities, and the potential energy distribution (PED) of the corresponding normal modes for the non-deuterated [$HO-CH_2-CH(NH_3^+)-COOH$] and deuterated [$DO-CH_2-CH(ND_3^+)-COOD$] species are collected in Tables S3 and S4, respectively.

In order to check the agreement between the calculated and experimental spectra of the cationic form of serine, MP2/6-311++G(d,p) calculations on the most stable conformer (**I**) of this species were also performed (see Tables S1 and S5 for the structural and vibrational data, respectively). It was concluded that the calculated vibrational spectra at both levels of theory (DFT and MP2) are essentially equal. Thus, the calculated DFT results will be used in the interpretation of the experimental data.

The analysis of the FT-IR spectra will be divided into two regions: 4000−2000 cm^{-1} (XH stretching region, X = N, O, C) and 2000−400 cm^{-1} (fingerprint region). Each of them includes the vibrational results of crystals of DL-Ser•HCl with natural isotopic abundance and isotopically doped samples (NH/$OH_{A/C}$ in a D-bulk and ND/$OD_{A/C}$ in an H-bulk; where the subscript A stands for alcohol, while the subscript C stands for carboxylic group). The observed frequencies and qualitative intensities are given in Table 3 together with the proposed assignments.

Of particular interest in this study are the temperature and isotopic shift effects on the NH and OH proton modes, which provide useful information both on the structure of DL-Ser•HCl crystal and on its associated H-bond energetics. Table 4 shows the observed frequencies and assignments for the bands corresponding to uncoupled NH/$OH_{A/C}$ and ND/$OD_{A/C}$ modes in isotopically diluted DL-Ser•HCl crystals, which are associated with vibrations of individual bonds.

The frequencies of the proton vibrational modes of crystalline DL-Ser•HCl have never been correlated with H-bond energies. In nonisotopically doped crystalline DL-Ser•HCl, the proton stretching modes of ammonium group give rise to a very broad and extensively structured band, not allowing any direct identification of the features due to the individual N−H stretching vibrations. On the other hand, in the partially isotopically labeled DL-Ser•HCl crystals, such features could be easily identified. At deuterium doping concentrations less than 10%, a minority of D-containing molecules is surrounded by an H-bulk. Under these circumstances, the vibrational modes with dominant contribution from the deuterated fragments are free from both internal dynamic coupling, because of mass and/or symmetry restrictions, and coupling with neighboring hydrogen bonds. Furthermore, application of low temperature considerably enhances the power of the isotopic doping method in the study of hydrogen-bonding interactions in crystals, since, under these experimental conditions, thermal broadening is also minimized,[27] and the intrinsic resolution of the IR bands considerably improves. Note that both the stretching and out-of-plane (wagging and torsional) vibrations of the groups taking part in H-bonding as donors have been found to be very sensitive to the properties of the specific hydrogen bonds in which they are involved,[13,14] and may be used as suitable probes of the hydrogen bonding interactions. This analysis will be described in detail in another section of the paper.

The Range 4000−2000 cm^{-1}. The spectra of natural (100% H) and isotopically doped (NH/$OH_{A/C}$ in a D-bulk and ND/$OD_{A/C}$ in an H-bulk) samples of DL-Ser•HCl are shown in Figures 2–4. Additionally, the spectra of natural and isotopically doped samples of DL-Ser•HCl at four different temperatures (300, 200, 100, and 10 K) are shown in Figures S3−S5. The peak positions are denoted for the spectra at 10 K.

Both neutral serine [HO−CH_2−CH(NH_2)−COOH] and its acid salt [HO−CH_2−CH(NH_3^+)−COOH•Cl^-] contain the OH alcohol and acid groups in their constitution. Thus, two features due to the stretching vibrations of these two OH groups should contribute to their IR spectra. On the other hand, in the IR spectra of both DL- and L-Ser crystals, where serine appears in a zwitterionic form [HO−CH_2−CH(NH_3^+)−COO^-], just the spectral feature due to the OH alcohol stretching should appear.

For conformer **I** of the cationic form of serine, investigated at the DFT(B3LYP)/6-311++G(d,p) level of theory, νOH_A is predicted to appear at higher wavenumbers than νOH_C (3751 versus 3639 cm^{-1}; Table S3). In the crystal of DL-Ser•HCl, X-ray results show that both hydroxyl groups are involved in intermolecular H-bonds acting as proton donor groups [$O-H_C\cdots O_A$: $d(O_C\cdots O_A)$ = 2.6195 Å, $\angle(O-H_C\cdots O_A)$ = 169.52°; $O-H_A\cdots Cl^-$: $d(O_A\cdots Cl^-)$ = 3.0274 Å; $\angle(O-H_A\cdots Cl^-)$ = 163.60°]. Thus, in the crystal, the corresponding frequencies should undergo a pronounced red shift relative to the frequencies calculated for the monomer. And, indeed, the observed OH_A stretching mode gives rise to the features in the 3550−3250 cm^{-1} range, whereas the OH_C stretching mode contributes to the very broad and structured absorption located between 3150 and ca. 2850 cm^{-1}.

At room temperature, the band due to the OH_A stretching mode appears as a broad feature centered at about 3350 cm^{-1} (Figure 2a, dashed line). As expected, this band becomes progressively narrower and more intense upon cooling as a result of the depopulation of thermal phonons. At the lowest temperature attainable in our experiments (10 K), the OH_A stretching vibration corresponds to the band with the main maximum at 3341/3339 cm^{-1} (Figure 2a, solid line; Table 3).

It is very interesting to compare the relative position of the band ascribed to νOH_A in the crystals of DL-, L-Ser and DL-Ser•HCl. In the crystal of L-Ser, the $O-H_A\cdots O_A$ intermolecular H-bonds were found to be relatively weak, the H-bond distance being 2.9181 Å.[25] On the other hand, in the crystal of DL-Ser, the alcohol group is H-bonded to the carboxylic group of a neighbor molecule.[24,28] This $O-H_A\cdots O_C$ intermolecular H-bond is considerably stronger than the $O-H_A\cdots O_A$ H-bond in L-Ser crystal, as reflected by the corresponding H-bond distance: 2.671 Å.[28] Finally, the present X-ray data revealed that, for the crystal of DL-Ser•HCl, the $O-H_A$ group establishes an intermolecular H-bond with a chlorine ion, $O-H_A\cdots Cl^-$. This interaction is characterized by a distance of 3.0274 Å and an angle of 163.60°, which is close to the linearity. For such a voluminous acceptor as the chlorine atom, the observed H-bond distance corresponds to a moderately strong interaction, situated between those of the DL- and L-Ser, where an oxygen atom is acting as a proton acceptor. Accordingly, the position of the νOH_A infrared absorption band in the three crystals clearly reflects the different packing appearing in the inverse order relative to the strength of the H-bond. The highest frequencies are observed in the spectrum of L-Ser (3529, 3501, and 3465 cm^{-1}),[5] followed by DL-Ser•HCl [3341/3339 cm^{-1} (Figure 2a and Table 3)], and, finally, in the spectrum of DL-Ser (ca. 2900 cm^{-1}).[4]

The bands in the IR spectrum of the crystal of DL-Ser•HCl in the range 3255−2735 cm^{-1} are assigned to the νNH_3^+ and νCH vibrations (Table 3). The νCH frequencies were calculated for the monomer in the range 3050−2950 cm^{-1} (Table S3). As expected, the νCH vibrations do not shift much in the IR spectrum of the crystal, since they are not involved in the H-bonding (Table 3).

The DFT(B3LYP)/6-311++G(d,p) calculations for the monomer predict the stretching modes of $-NH_3^+$ group in the range 3400−3200 cm^{-1} (Table S3). In the crystal of DL-Ser•HCl, the ammonium group, like the $-OH_A$ group, is also involved in different intermolecular H-bonds, acting as a proton-donor [$N-H(1)\cdots Cl^-$, $N-H(2)\cdots Cl^-$, and $N-H(3)\cdots Cl^-$/$N-H(3)\cdots O=$] (Table 1). Thus, in the IR spectrum of the

TABLE 3: Peak Frequencies (cm^{-1}), Qualitative Intensities,[a] and Assignment of Bands in the Infrared Spectra of Pristine and Isotopically Diluted DL-Ser·HCl Polycrystals at 10 K, in the Range 4000−400 cm^{-1}[b]

	DL-Ser·HCl	isotopically diluted DL-Ser·HCl	
assignment[c]	100% H	> 90% H	ca. 40% H
νOH_A	3394 (sh)	3365 (sh)	
	3341 (vs)	3338 (vs)	
	3339 (vs)	3304 (sh)	
νOH_C	3250−2500	3250−2500	
νNH_3^+ as.″			
νNH_3^+ as.′			
νNH_3^+ s.			
$\nu C_\beta H_2$ as.	2974 (s)	2974 (s)	2974 (s)
$\nu C_\beta H_2$ s.	2951 (vs)	2951 (vs)	2951 (vs)
$\nu C_\alpha H$			2943 (sh)
νOD_A			2480 (vs)
			2473 (sh)
			2457 (sh)
νOD_C			2400−2100
νND_3^+ as.″			
νND_3^+ as.′			
νND_3^+ s.			
$\nu C{=}O$	1776 (sh)	1749 (vs)	1746 (vs)
	1753 (vs)	1745 (vs)	1742 (vs)
	1743 (vs)		1737 (vs)
δNH_3^+ as.′	1594 (sh)	1594 (sh)	
	1587 (s)	1588 (m)	
δNH_3^+ as.″	1554 (s)	1568 (sh)	
	1532 (vs)	1552 (m)	
		1532 (s)	
δNH_3^+ s.	1499 (vs)	1499 (vs)	
	1494 (vs)	1495 (vs)	
		1493 (vs)	
$\delta C_\beta H_2$	1454 (m)	1454 (m)	1460 (sh)
	1447 (m)	1448 (m)	1458 (m)
			1454 (m)
			1448 (m)
νCO_C	1429 (s)	1429 (s)	1435 (sh)
	1405 (sh)	1407 (sh)	1428 (s)
	1400 (m)	1399 (m)	1409 (s)
			1396 (sh)
$\omega C_\beta H_2$	1373 (m)	1385 (m)	1385 (sh)
	1370 (sh)	1380 (sh)	1382 (m)
		1373 (m)	1376 (sh)
		1368 (sh)	1367 (s)
$\delta C_\alpha H$	1350 (sh)	1353 (w)	1352 (sh)
	1349 (w)	1336 (w)	1348 (sh)
			1345 (sh)
			1338 (m)
$\gamma C_\alpha H$	1315 (vw)	1313 (w)	1301 (s)
	1299 (sh)	1298 (m)	
	1297 (m)		
δCOH_C	1259 (vs)	1254 (vs)	
	1247 (m)		
δCOH_A	1228 (s)	1228 (m)	
δND_3^+ as.′			1180 (s)
			1175 (m)
δND_3^+ as.″			1165 (m)
			1160 (w)
			1155 (sh)
$twC_\beta H_2$	1140 (s)	1146 (sh)	1146 (sh)
		1139 (s)	1143 (m)
			1138 (sh)
$\gamma NH_3^{+\prime}$			
$\gamma NH_3^{+\prime\prime}$	1120 (sh)	1114 (m)	
	1115 (m)		
	1109 (sh)		
δND_3^+ s.			1124 (sh)
			1116 (s)
$\gamma C_\beta H_2$	1083 (sh)	1077 (m)	1083 (s)
	1076 (m)	1067 (s)	
	1060 (vw)		
	1048 (vw)		
δCOD_C			1066 (sh)
			1061 (m)
			1053 (sh)
			1033 (w)
			1026 (m)
			1019 (s)
νCO_A	1008 (vs)	1007 (vs)	1009 (m)
	1003 (s)	1004 (sh)	1003 (m)
	991 (sh)	990 (sh)	990 (m)
νCN; $\nu C_\alpha{-}C_\beta$	973 (sh)	966 (w)	971 (w)
	968 (w)	962 (w)	966 (w)
		959 (w)	962 (w)
			959 (w)
			956 (w)
δCOD_A			946 (sh)
			942 (w)
			930 (m)
			925 (m)
			920 (m)
			918 (m)
τOH_C	915 (vs)	932 (sh)	
νCN; $\nu C_\alpha{-}C_\beta$	893 (s)	921 (sh)	
		913 (s)	
		892 (s)	
$\nu C_\alpha{-}C$	812 (m)	810 (m)	817 (sh)
	805 (sh)	804 (w)	812 (m)
$\gamma ND_3^{+\prime}$			804 (sh)
			794 (w)
			788 (w)
γCOO	770 (m)	769 (m)	775 (w)
			767 (m)
			756 (w)
$\gamma ND_3^{+\prime\prime}$			744 (sh)
			740 (m)
			738 (sh)
τOD_C			668 (s)
			663 (sh)
$\delta C{=}O$	620 (vw)	607 (m)	621 (vw)
	609 (vw)	598 (m)	611 (vw)
	598 (m)	589 (sh)	604 (vw)
	589 (sh)		597 (vw)
			592 (vw)
			589 (vw)
τNH_3^+	576 (sh)	560 (s)	
	561 (s)	557 (s)	
	557 (s)		
	554 (s)		
τOH_A	502 (m)	502 (m)	
		492 (w)	
τOD_A			439 (w)
			434 (w)
			412 (m)

[a] (vs) - very strong; (s) - strong; (m) - medium; (w) - weak; (vw) - very weak; (sh) - shoulder. [b] In reference to the OH groups, the subscript A stands for alcohol, while the subscript C stands for carboxylic group. [c] ν - bond stretching; δ - bending; ω - wagging; γ - rocking (out-of-plane); tw - twisting; τ - torsion; as. - asymmetric; s. - symmetric.

TABLE 4: Peak Frequencies (cm^{-1}) and Assignment of the Bands of Uncoupled NH/$OH_{A/C}$ and ND/$OD_{A/C}$ Modes in Isotopically Diluted DL-Ser·HCl Polycrystals at 10 K, in the Range 4000−400 cm^{-1}[a]

	isotopically diluted DL-Ser·HCl	
assignment[b]	>90% H ($-NDH_2^+$; $OD_{A/C}$)	ca. 40% H ($-NHD_2^+$; $OH_{A/C}$)
νOH_A		3371
		3332
		3288
νOH_C		*overlapped*
$\nu N-H(1)$		3100
$\nu N-H(2)$		3036
$\nu N-H(3)$		3010
νOD_A	2472	
	2456	
	2442	
νOD_C	*overlapped*	
$\nu N-D(1)$	2274	
$\nu N-D(2)$	2240	
$\nu N-D(3)$	2233	
$\delta N-H(3)$		1597
		1588
$\delta N-H(2)$		1575
		1571
$\delta N-H(1)$		1560
		1555
δCOH_C		1277
		1274
		1261
		1256
		1253
δCOH_A		1239
		1233
$\delta N-D(3)$	1169	
$\delta N-D(2)$	1098	
$\delta N-D(1)$	1089	
$\gamma N-H(3)$		1108
$\gamma N-H(2)$		1101
$\gamma N-H(1)$		1095
δCOD_C	1045	
	1025	
δCOD_A	*overlapped*	
τOH_C		905−825
$\gamma N-D(3)$	866	
$\gamma N-D(2)$	853	
$\gamma N-D(1)$	801	
	795	
	792	
τOD_C	668	
	664	
τOH_A		540
		536
		531
		527
		500
		492
		484

[a] In reference to the OH groups, the subscript A stands for alcohol, while the subscript C stands for carboxylic group. See Table 1 for numbering of hydrogen atoms involved in H-bonding. [b] v - bond stretching; δ - bending; γ - rocking (out-of-plane); τ - torsion.

crystal, the bands due to the νNH_3^+ vibrations are expected to appear at much lower wavenumbers than those calculated for the monomer, namely, in the same range as the CH stretching vibrations. Moreover, as mentioned above, the OH_C stretching mode also contributes to absorption in this spectral range. As a result, it is difficult to do a detailed assignment in this region of spectrum for the nondeuterated compound. However, as shown below, the isotopic doping technique allows one to distinguish between these proton-related modes in the IR spectra of D-doped DL-Ser·HCl crystal.

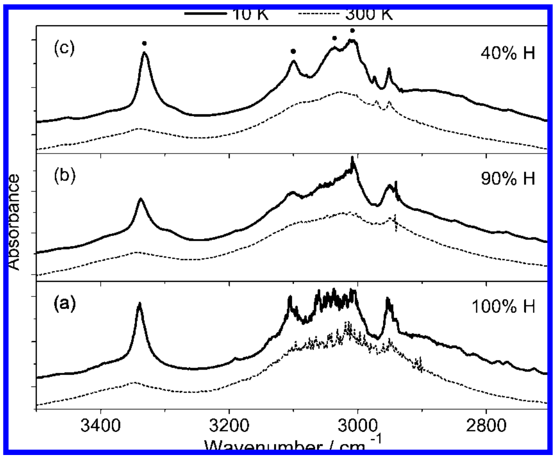

Figure 2. 3500−2700 cm^{-1} spectral range (X−H stretching vibrations; X = C, N, O) of the IR spectra of DL-Ser·HCl containing: (a) natural isotopic composition (∼100% H), (b) >90% H, and (c) ca. 40% H. In all frames, the dashed lines correspond to samples at room temperature (300 K), and the solid lines correspond to maximum cooling (10 K). The bands marked with a circle are due to the uncoupled modes and are discussed in the text.

Crystal Doped with Minority H Molecules (Figure 2c). In the spectrum recorded at room temperature, the quite intense and broad band at ca. 3341 cm^{-1} is assigned to the OH stretching mode of the alcoholic group. This band becomes narrower and more intense upon cooling. At 10 K, this vibration gives rise to a band with a main maximum at 3332 cm^{-1}. The spectral position of this band is in agreement with the frequency of the OH stretching vibration in the nondeuterated sample (Figure 2a).

When the percentage of deuteration of DL-Ser·HCl is above 60% D, the vibrations of the NH bond become uncoupled from the remaining two ND bonds in the partially deuterated ammonium group ($-NHD_2^+$). In the spectral region characteristic of the νNH vibrations, several bands were observed, whose maxima, at 10 K, are located at 3100, 3036, and 3010 cm^{-1} (Table 4). They correspond to the vibrations related with the hydrogen bonds of increasing strength present in the crystal, $N-H(1)\cdots Cl^-$, $N-H(2)\cdots Cl^-$, and $N-H(3)\cdots Cl^-$/$N-H(3)\cdots O=$, respectively (with associated N−H bond lengths of 0.8544, 0.8768 and 0.9332 Å, respectively; see Table 1). The ND stretching vibrations of $-NHD_2^+$ and $-ND_3^+$ groups are assigned to bands in the 2400−2100 cm^{-1} range (Figure 3c).

In the crystal of DL-Ser·HCl, the OH_C group is involved in an $O-H_C\cdots O_A$ H-bond, which is much stronger than the H-bond of the OH_A group, $O-H_A\cdots Cl^-$, (see Table 1 for geometric parameters). The more elongated $O-H_C$ bond should give rise to the absorption band (originated in the $O-H_C$ stretching vibration) that appears at a much lower wavenumber and should be much more broadened. Since there are no obvious candidates for this absorption in the experimental spectra, we suggest that the spectral position of the broad OH_C stretching band has a frequency similar to that of the ammonium stretching vibrations. The broad spectral envelope in the 3250−2700 cm^{-1} region cannot be attributed exclusively to the NH stretching vibrations and, with all probability, also includes the contribution due to the band of the OH_C stretching mode.[29]

The narrow bands observed at 2974 and 2951 cm^{-1} with a shoulder at 2943 cm^{-1} at 10 K are undoubtedly assigned to

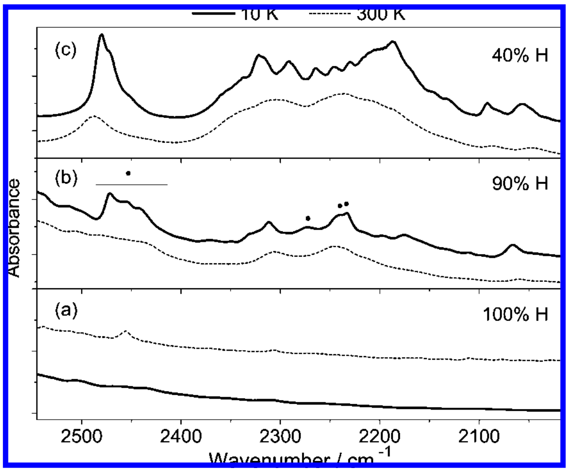

Figure 3. 2550−2000 cm^{-1} spectral range (X−D stretching vibrations; X = N, O) of the IR spectra of DL-Ser·HCl containing (a) natural isotopic composition (∼100% H), (b) >90% H, and (c) ca. 40% H. In all frames, the dashed lines correspond to samples at room temperature (300 K), and the solid lines correspond to maximum cooling (10 K). The bands marked with a circle are due to the uncoupled modes and are discussed in the text.

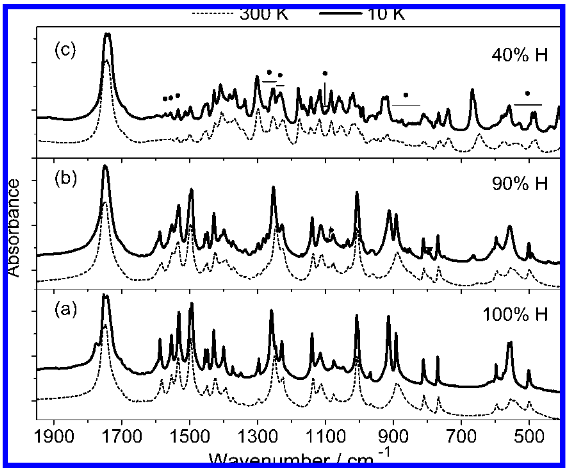

Figure 4. 1900−400 cm^{-1} spectral range (fingerprint region) of the IR spectra of DL-Ser·HCl containing (a) natural isotopic composition (∼100% H), (b) >90% H, and (c) ca. 40% H. In all frames, the dashed lines correspond to samples at room temperature (300 K), and the solid lines correspond to maximum cooling (10 K). The bands marked with a circle are due to the uncoupled modes and are discussed in the text.

$\nu C_\beta H_2$ as. and $\nu C_\beta H_2$ s./$\nu C_\alpha H$, respectively (Table 3). As expected, these vibrations do not differ much from the corresponding vibrations in crystals of DL-Ser $\nu C_\beta H_2$ as. − 2971 cm^{-1}; $\nu C_\beta H_2$ s./$\nu C_\alpha H$ − 2943 cm^{-1})[4] and L-Ser ($\nu C_\beta H_2$ as. − 3004 cm^{-1}; $\nu C_\beta H_2$ s. − 2943 cm^{-1}; $\nu C_\alpha H$ − 2905 cm^{-1}).[5]

Crystal Doped with Minority D Molecules (Figure 3b). In the low-temperature IR spectrum of the DL-Ser·HCl crystal with a low concentration of deuterium, a band with three main maxima at 2472, 2456, and 2442 cm^{-1} is well resolved and assigned to the νOD vibrations of the alcohol group (Table 4).

The broad band with maximum at room temperature at 2246 cm^{-1} shows a substantial change in its profile and a red shift upon cooling. At 10 K, the band is split into several components, with maxima at 2274, 2240, and 2233 cm^{-1}, which correspond to the three uncoupled νND vibrations of the $-NDH_2^+$ deuterons involved in the three different H-bonds involving the ammonium group existing in the crystal (Tables 1 and 4).

The isotopic ratios of the three isotopically decoupled pairs of NH/ND stretching bands (at 10 K), N−H(1)···Cl$^-$, N−H(2)···Cl$^-$ and N−H(3)···Cl$^-$/N−H(3)···O=, are 1.363, 1.355, and 1.348, respectively. These isotopic ratios are consistent with the values found previously for other amino acids[4] and support the assignment of these bands to the stretching mode originated in each one of the three individual N−H or N−D bonds in $-NH_3^+$ or $-ND_3^+$ groups.

Spectral Range below 2000 cm^{-1} (Fingerprint Region). Unlike the carboxylate stretching bands observed in the IR spectra of zwitterionic amino acids [νCOO$^-$ asymmetric (ca. 1600 cm^{-1}) and νCOO$^-$ symmetric (ca. 1400 cm^{-1})],[4,5,26] a single band at a frequency typical of the carbonyl bond stretching of the carboxylic group (O=C−O−H) in protonated amino acids[26] is observed in the IR spectrum of DL-Ser·HCl (about 1747 cm^{-1}). In the IR spectrum of matrix-isolated serine, the νC=O vibrations appear at higher wavenumbers; six main bands due to monomeric serine were observed between 1850 and 1740 cm^{-1}.[2] The lower frequency of the C=O stretching vibrations observed in the crystals indicates that the carbonyl group is, in this case, involved in a stronger hydrogen bond interaction than in the matrix isolated monomers.

The bands due to the δCOH of alcohol and acid groups, and those ascribable to the deformation modes of the $-NH_3^+$ group (three bending and two rocking modes) can be easily identified by comparing the spectrum of deuterium-free DL-Ser·HCl (Figure 4a) with that of DL-Ser·HCl with high deuterium content (Figure 4c), where the bands due to these vibrations have vanishing intensity. The δNH_3^+ as.′, δNH_3^+ as.″ and δNH_3^+ s. modes are then assigned to the pairs of bands at 1594/1587, 1554/1532, and 1499/1494 cm^{-1}, respectively, which exhibit strong temperature dependence and noticeably reduce their intensity in the spectra of $-NHD_2^+$ doped crystals. In turn, the δCOH_C and δCOH_A modes are assigned to the bands at 1259/1247 and 1228 cm^{-1}, respectively (Table 3). As it could be anticipated, the δCOH bands show a pronounced dependence on temperature (Figure 4a). The δCOH_A vibration was assigned to the bands at 1224, 1218, and 1209 cm^{-1} in the IR spectrum of the L-Ser crystal and at 1249 cm^{-1} in the spectrum of DL-Ser crystal.[4,5] It is worth mentioning that δCOH_A appears at considerably lower wavenumbers in the vibrational spectra of DL-Ser·HCl and L-Ser when compared with DL-Ser crystal, in agreement with the much weaker H-bond formed by the $-CH_2OH$ side chain in DL-Ser·HCl and L-Ser crystals compared to that of DL-Ser.[4,5]

The rocking modes of the ammonium group ($\gamma NH_3^{+\prime}$ and $\gamma NH_3^{+\prime\prime}$) were assigned to the bands at 1140 and 1115 cm^{-1}. The tw$C_\beta H_2$ mode also contributes to the band at 1140 cm^{-1} (Table 3). These assignments were based on the comparison with the frequencies of the same modes in the crystals of DL- and L-Ser.[4,5]

On the basis of the DFT(B3LYP)/6-311++G(d,p) frequency calculations, νCO_C = 1377 cm^{-1} and νCO_A = 1015 cm^{-1} (Table S3), and also on the relative bond lengths obtained by X-ray diffraction, dCO_C = 1.31 Å and dCO_A = 1.42 Å, the νCO_C and νCO_A vibrations were assigned to the groups of bands at 1429/1405/1400 cm^{-1} and 1008/1003/991 cm^{-1}, respectively (Table 3).

The assignments of deformational vibrations of methylene ($\delta C_\beta H_2$, $\omega C_\beta H_2$, tw$C_\beta H_2$, and $\gamma C_\beta H_2$) and methyne ($\delta C_\alpha H$ and $\gamma C_\alpha H$) groups are collected in Table 3. These assignments were carried out on the basis of comparison of these modes in DL-Ser·HCl crystal with the corresponding modes in the DL- and L-Ser crystals,[4,5] which were found to give rise to bands

TABLE 5: H-Bond Enthalpies Estimated for the Different H-Bonds Present in the Crystals of DL-Ser•HCl, DL-Ser, and L-Ser

DL-Ser•HCl	$-\Delta H$/kJ mol^{-1}	DL-Ser	$-\Delta H$/kJ mol^{-1}	L-Ser	$-\Delta H$/kJ mol^{-}
$O-H_A\cdots Cl^-$	17	$O-H_A\cdots O_C$	33	$O-H_A\cdots O_A$	10
$N-H(1)\cdots Cl^-$	20	$N-H(1)\cdots O_C$	21	$N-H(1)\cdots O_C$	20
$N-H(2)\cdots Cl^-$	23	$N-H(2)\cdots O_C$	23	$N-H(2)\cdots O_C$	23
$N-H(3)\cdots Cl^-$	24	$N-H(3)\cdots O_A$	24	$N-H(3)\cdots O_C$	25

at nearly the same positions. In particular, the proposed assignments are $\delta C_\beta H_2$ to the doublet at 1454/1447 cm^{-1} (1451 cm^{-1} in DL-Ser[4] and 1470/1459 cm^{-1} in L-Ser[5]); $\omega C_\beta H_2$ to the band at 1373 cm^{-1} with a shoulder at 1370 cm^{-1} (1375/1372 cm^{-1} in DL-Ser[4] and four bands in the 1390−1350 cm^{-1} region in L-Ser[5]); tw$C_\beta H_2$ to the band at 1140 cm^{-1} (1189 cm^{-1} in DL-Ser[4] and 1140 cm^{-1} in L-Ser[5]); $\gamma C_\beta H_2$ to the group of bands in the 1085−1045 cm^{-1} region (1065−1025 cm^{-1} in DL-Ser[4] and the doublet at 1022/1015 cm^{-1} in L-Ser[5]); $\delta C_\alpha H$ to the weak band at 1349 cm^{-1} with a shoulder at 1350 cm^{-1} (1363/1355 cm^{-1} in DL-Ser[4] and 1339/1330 cm^{-1} in L-Ser[5]); and $\gamma C_\alpha H$ to a set of bands at 1315/1299/1297 cm^{-1} (1321/1315/1303 cm^{-1} in DL-Ser[4] and a group of bands in the 1315−1300 cm^{-1} region in L-Ser[5]). It is worth noting that the bands ascribed to the bending vibrations of both the $-CH_2$ and $-CH$ groups show a substantial dependence on temperature, clearly indicating that these modes are considerably coupled with vibrations originating in the $-NH_3^+$ or/and $-OH$ groups.

The τOH_C, τOH_A, and τNH_3^+ modes appear below 1000 cm^{-1}. The bands corresponding to τOH_C and τNH_3^+ vibrations were observed at 915/893 cm^{-1} and 580−550 cm^{-1}, respectively. Among all bands in the spectra of the different crystals, these features exhibit the most pronounced temperature dependence, strongly increasing in peak intensity and shifting to higher frequencies upon cooling (Figure 4a). This behavior could have been anticipated considering the nature of the modes and the direct involvement of the acid and ammonium protons in the H-bond network of the crystals. Contrarily to the bands ascribed to the τOH_C and τNH_3^+ modes, the band assigned to the τOH_A vibration (502 cm^{-1}) does not exhibit pronounced temperature dependence. In the IR spectrum of DL-Ser crystal,[4] the τOH_A mode appears at 744 cm^{-1} and in the IR spectrum of L-Ser crystal in the 500−420 cm^{-1} range.[5] As it was mentioned above, the H-bond formed by the $O-H_A$ group in the crystal of DL-Ser•HCl is weaker than in DL-Ser and stronger than in L-Ser crystals. That is then in agreement with the observation of the band due to τOH_A mode in the DL-Ser•HCl crystal between those found in the IR spectra of DL- and L-Ser crystals.[4,5]

Finally, the γCOO and $\delta C{=}O$ modes do also absorb in this spectral range. These modes were assigned to the band at 770 cm^{-1} and the multiplet at 620/609/598/589 cm^{-1}, respectively (Figure 4a and Table 3), based on the DFT(B3LYP)/6-311++G(d,p) calculations, which predict the γCOO and $\delta C{=}O$ modes to appear at about 800 and 600 cm^{-1}, respectively (Table S3).

Crystal Doped with Minority H Molecules (Figure 4c). In the spectrum of the crystal doped with minority H molecules, new low intensity bands are observed, which belong to the uncoupled NH and ND_2 deformational modes of the $-NHD_2^+$ group, as well as to the OH_A and OH_C modes. These weak bands can be clearly seen only in the spectra collected at lower temperatures, and they exhibit a blue shift on cooling. The bands observed in the spectral range 1610−1480 cm^{-1}, whose maxima, at 10 K, are at 1597, 1571, and 1555 cm^{-1}, are assigned to the three δNH uncoupled vibrations, $\delta N-H(3)$, $\delta N-H(2)$, and $\delta N-H(1)$, respectively (Table 4). On the other hand, the bands observed in the spectrum recorded at room temperature at 1274 and 1254 cm^{-1} are assigned to the δCOH_C vibration, and that at 1225 cm^{-1} is assigned to the δCOH_A vibration. These three bands show a blue shift and become much more structured upon cooling (Table 4).

The bending vibrations related with the $-ND_3^+$ group of the (bulk) deuterated molecules appear at much lower wavenumbers: 1180/1175 cm^{-1}, 1165/1160 cm^{-1}, and 1116 cm^{-1}, assigned respectively to the δND_3^+ as.′, δND_3^+ as.″ and δND_3^+ s. modes (Table 3). In turn, the δCOD_C vibration is assigned to the medium-intensity bands whose maxima at room temperature are observed at 1055 and 1016 cm^{-1}, and the δCOD_A mode gives rise to bands in the 950−900 cm^{-1} region (Table 3). All these bands show a blue shift upon cooling.

To estimate the position of the uncoupled γNH bands, we used the empirical correlation[30] between the red shift of the uncoupled νNH bands in the crystal (relative to the frequency of a similar mode in a non-hydrogen-bonded molecule) and the blue shift of the band due to the corresponding out-of-plane mode. Following conventional Herzberg's notation, the proton-related stretching modes will here be designated as ν_1, while ν_4 will stand for the out-of-plane rocking modes of the same group. The red shift of ν_1 and the blue shift of ν_4 modes associated with a given proton correlate as

$$\Delta\nu_4^{\,2} = 2.5(\Delta\nu_1)^{1/2} - 18 \tag{1}$$

where $\Delta\nu_4^2 \equiv 10^{-4}\,[(\nu_4)^2 - (\nu_4^0)^2]$ and $\Delta\nu_1 = \nu_1^0 - \nu_1$ (both ν_1 and ν_4 are expressed in cm^{-1}).[30] The ν_1^0 and ν_4^0 reference values will be taken as 3450 and 1000 cm^{-1}, respectively, which correspond to rounded average values for free NH amine stretching and rocking vibrations in amines, amino acids, and other compounds bearing amino groups.[1,8,31] Then, according to the correlation above, the three out-of-plane uncoupled vibrations originating in individual NH protons are predicted at 1148, 1141, and 1124 cm^{-1}. These frequencies can be associated with the three progressively weaker $N-H\cdots Cl^-$ bonds formed in the crystalline phase. In the experimental spectrum of DL-Ser•HCl with ca. 60% D, two bands with the required characteristics (low intensity, substantial dependence on temperature, absence in the spectra of the remaining crystals here studied) are observed at 1101 and 1095 cm^{-1}, fairly close to the predicted frequencies, and were then assigned to the uncoupled γNH modes associated with the two weakest $N-H\cdots Cl^-$ bonds (Table 4). The band originated in the rocking vibration of the remaining proton is much probably buried underneath the intense band due to the δND_3^+ s. bulk mode at 1116 cm^{-1} (see Table 3). Indeed, there is a shoulder at 1108 cm^{-1}, which can be tentatively assigned to the γNH mode associated with the strongest hydrogen bond [$N-H(3)\cdots Cl^-$/$N-H(3)\cdots O{=}$] (Table 4). The deuterated counterparts of these bands in the spectrum of DL-Ser•HCl with ≤10% D (uncoupled γND modes) are observed at 866, 853, and 801/795/792 cm^{-1} (Figure 4b), exhibiting frequency isotopic ratios of 1.279, 1.291, and 1.376, respectively.

It is interesting to report on the large number of new weak bands that appear in the 905−825 cm^{-1} range, ascribable to the torsion of the OH_C group (Table 4) and to the νCN and

$\nu C_\alpha - C_\beta$ skeletal vibrations (Table 3). Finally, the bands at 540, 536, 531, and 527 cm^{-1} are assigned to the torsion of the OH_A group (Table 4).

Crystal Doped with Minority D Molecules (Figure 4b). As in the spectra of the crystal doped with minority H molecules (Figure 4c), in the crystal doped with minority D molecules, new and low intensity bands, due to the uncoupled ND and NH_2 deformational modes of the $-NDH_2^+$ group, as well as the OD_A and OD_C modes, are observed. These bands show a blue shift upon cooling and can be clearly observed in the spectra collected at lower temperatures.

The bands at 1570 and 1463 cm^{-1} are assigned to δNH_2 as. and δNH_2 s. modes, respectively. Because of their low intensity, both bands become discernible only at low temperatures.

The three bands located at 1169, 1098, and 1089 cm^{-1} are associated with the uncoupled δND vibrations of the D-doped molecules in DL-Ser•HCl crystals, which were assigned to δN−D(3) [N−D(3)•••Cl$^-$/N−D(3)•••O=; strongest H-bond], δN−D(2) [N−D(2)•••Cl$^-$] and δN−D(1) [N−D(1)•••Cl$^-$; weakest H-bond], respectively (Tables 1 and 4).

The very weak bands with maxima at 1045 and 1025 cm^{-1} were assigned to the δCOD_C vibration (Table 4). On the other hand, the δCOD_A vibration in DL-Ser•HCl could be expected to give rise to absorb between 934 and ca. 880 cm^{-1}, which are the frequencies at which the analogous mode absorbs in DL- and L-Ser crystals.[4,5] However, this spectral region also contains the stronger intensity bands due to the τOH_C, νCN, and $\nu C_\alpha - C_\beta$ vibrations, which precludes a clear observation of the absorption due to the δCOD_A mode.

Finally, the band at ca. 665 cm^{-1}, which shows a pronounced blue shift upon cooling (15 to 20 cm^{-1}), was assigned to the torsion of the OD_C group in the spectra of two deuterated DL-Ser•HCl crystals (Tables 3 and 4). As expected, this feature does not appear in the spectrum of the sample with natural isotopic abundance.

Characterization of H-bonds: Spectra/Energy Correlations. The observed frequency red shifts of the ν_1 stretching modes and blue shifts of the ν_4 out-of-plane bending modes upon H-bond formation and the corresponding H-bond enthalpies (in kJ mol^{-1}) were shown[13,32] to obey the empirical correlations:

$$(\Delta H)^2 = 1.92(\Delta\nu_1 - 40) \qquad (2)$$

and

$$-\Delta H = 0.67\Delta\nu_4^{\,2} \qquad (3)$$

These correlations satisfactorily describe a considerable number of H-bonded systems, including crystalline carbohydrates,[13,14] nucleobases (cytosine,[9] uracil, and thymine[10]), nucleosides (cytidine,[10] adenosine, and uridine[11]) and several amino acids (e.g., glycine, alanine, glutamine, hystidine, tyrosine, and threonine).[8] They were also successfully validated for crystalline DL- and L-Ser.[4,5]

In order to estimate the H-bond enthalpies using these empirical correlations, a suitable reference frequency value for the non-hydrogen-bonded NH (or OH) ν_1 and ν_4 vibrations in DL-Ser•HCl shall be defined. The choice of these values for the N−H vibrations was presented above (see eq 1). Concerning the O−H alcohol vibrations, the ν_1^0 and ν_4^0 reference values were taken as 3640 and 300 cm^{-1}, respectively, which correspond to the calculated scaled frequencies for νOH_A and τOH_A of isolated serine conformers that do not have the −OH group involved in any intramolecular H-bond.[2] These values also closely match the observed frequencies for these two modes in the spectrum of *t*-butanol in CCl_4 diluted solutions.[32]

The average H-bond energies resulting from the two empirical correlations presented above for crystalline DL-Ser•HCl are 17, 20, 23, and 24 kJ mol^{-1}, for the O−H$_A$•••Cl$^-$ and the three N−H•••Cl$^-$ hydrogen bonds, respectively. These values are compared with those obtained using the same empirical correlations for crystalline DL- and L-Ser in Table 5. In all these crystals, the estimated enthalpies for the three N−H•••X (X = O or Cl) hydrogen bonds are similar. In contrast, the energies of the O−H$_A$•••X hydrogen bonds differ very much in the three crystals. These results clearly confirm that the hydroxyl side-chain of serine amino acid plays a major role in defining the very different H-bonding networks in the three crystals. This idea corroborates conclusions of our previous studies on the structures of crystalline DL- and L-Ser.[4,5]

Conclusion

Crystals of DL-Ser•HCl were obtained, and their structure was solved by X-ray technique. This structural information was then used in the interpretation of the vibrational spectra of the substance measured in a wide range of temperatures (300−10 K). Spectra of isotopically doped DL-Ser•HCl, obtained in the same range of temperatures, were also investigated and allowed for the identification of bands associated with individual (uncoupled) proton-related vibrational modes in the studied crystals, which exhibit a complex H-bonding network. From these data, the enthalpies of different H-bonds were estimated using well-known empirical correlations between the observed frequency red shifts of the stretching modes (ν_1) and blue shifts of the out-of-plane bending modes (ν_4) upon H-bond formation and the corresponding H-bond enthalpies. A systematic comparison between the results obtained in the present study with those of our previous studies[4,5] on DL- and L-Ser crystals revealed that the vibrational spectra of the three crystals reflect well the different characteristics of their H-bond networks and, in particular, doubtlessly confirm that the hydroxyl side-chain of serine amino acid plays a major role in defining the very different H-bonding networks in these three crystals.

As a complement to the experimental studies undertaken for crystalline DL-Ser•HCl, DFT(B3LYP)/6-311++G(d,p) theoretical calculations of the vibrational spectra of the isolated cation of DL-Ser were also carried out, providing further support to the interpretation of the experimental data.

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Supporting Information Available: Additional details regarding the structural parameters of the title compound and 13 of its conformers. This material is available free of charge via the Internet at http://pubs.acs.org.

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