Refinements of the Crystal Structures of DL-Serine and Anhydrous L-Serine*

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The crystal structure of DL-serine has been refined on the basis of 964 independent reflections measured on an X-ray diffractometer. The refinement has converged to an R index of 0·032, with anisotropic temperature factors for all atoms including hydrogens. The resulting coordinates of the heavy atoms are in good agreement with those reported from an earlier neutron-diffraction study, and there is no indication of systematic differences in the C–C, C–N or C–O bond lengths. The structure of L-serine was refined to an R index of 0·059 for 953 reflections; the absolute configuration was confirmed from the anomalous scattering effects of C, N, and O. The final parameters include isotropic temperature factors for the H atoms. The conformations of the L-serine molecule in three different crystal structures are compared; differences in conformation are directly related to differences in the hydrogen-bond arrangements.

Introduction

We report here the results of accurate X-ray diffraction studies of anhydrous crystal modifications of L-serine and DL-serine. For DL-serine, anisotropic temperature parameters for all atoms were refined, including hydrogens, and we compare our results with the recent neutron-diffraction study of Frey, Lehmann, Koetzle & Hamilton (1973; hereinafter, FLKH). For L-serine, our refinement has included isotropic temperature factors for the hydrogen atoms, and we have made use of the anomalous scattering effects of C, N, and O to confirm the absolute configuration; our results are considerably more accurate than those reported previously by Benedetti, Pedone & Sirigu (1972; hereinafter, BPS).

DL-*Serine*

Crystals were kindly provided by Professor K. N. Trueblood of the University of California, Los Angeles. A rectangular prism, approximately $0·17 \times 0·23 \times 0·17$ mm, was mounted with the c axis slightly tilted with respect to the φ axis of an extensively modified (Samson & Schuelke) Datex-automated General-Electric quarter-circle diffractometer. Cell constants were calculated from a least-squares fit to the $\sin^2 \theta/\lambda^2$ values for 11 reflections; these values (Table 1) are in only moderate agreement with the values of FLKH. Intensity data were collected by a θ–2θ scan at a scan rate of $1°$ min^{-1} and with 20 s background counts at each extremum. A full hemisphere of data was collected to $2\theta = 155°$ (Cu $K\alpha$ radiation); three check reflections were monitored frequently, and showed no significant

changes in intensity. Each intensity was assigned an observational variance based on the following equation:

$$\sigma^2(I) = S + (B_1 + B_2)(T_S/2T_B)^2 + (pS)^2,$$

where S, B_1 and B_2 are the scan and background counts, T_S and T_B are the scan and individual background counting times, and p was taken to be 0·02 (Busing & Levy, 1957). Intensities and weights ($= 1/\sigma^2$) from the two equivalent quadrants were averaged, yielding a total of 964 independent intensities; all of these averaged intensities were positive and only 20 were less than two e.s.d.'s above zero.

Table 1. *Crystal data*

DL-Serine		$C_3H_7NO_3$
Space group, $P2_1/a$		$Z=4$
	KRM*	FLKH†
a	10·739 (2) Å	10·719 (3) Å
b	9·149 (2)	9·136 (4)
c	4·830 (1)	4·833 (2)
β	106·42 (1)°	106·43 (3)°
L-Serine		
Space group, $P2_12_12_1$		$Z=4$
	KRM*	BPS‡
a	8·599 (5) Å	8·571 (2) Å
b	9·348 (3)	9·325 (3)
c	5·618 (2)	5·615 (2)

* This investigation.
† Frey *et al.* (1973).
‡ Benedetti *et al.* (1972).

Refinement, beginning with the parameters of Shoemaker, Barieau, Donohue & Lu (1953), was by full-matrix least-squares minimization of the quantity $\sum w(F_o^2 - F_c^2)^2$, with weights w equal to $1/\sigma^2(F_o^2)$. Atomic form factors for C, N, and O were from *International Tables for X-ray Crystallography* (1962) corrected for

the real components of anomalous dispersion as calculated by Hope (1970): $\Delta f' = 0.019$ e for C, 0.032 e for N, and 0.049 e for O. Eventually, 128 parameters were adjusted: coordinates and anisotropic temperature parameters for all 14 atoms, including hydrogen; a secondary extinction parameter (Larson, 1967); and a scale factor. In the final cycle no shift was as great as $0.2\,\sigma$. The final R index is 0.032 and the goodness-of-fit, $[\sum w(F_o^2 - F_c^2)^2/(n-p)]^{1/2}$, for $n = 964$ observations and $p = 128$ parameters, is 3.9.*

The deviation of the goodness-of-fit from the expectation value of 1.0 is almost certainly due to defects in the model we used. Because of the moderate size of the crystal and its excellent scattering properties, the uncertainties associated with the measured intensities are very small; for example, the assigned standard deviation (see above) for an $|F_o|$ of 5.0 e is approximately 0.08 e. Moreover, the agreement between intensities measured for the two sets of equivalent reflections was well within the variances of these intensities. A difference map calculated at the conclusion of the refinement (Fig. 1) shows significant features in the areas between pairs of bonded atoms, rising to about 0.3 e Å^{-3} between C(1)–C(2) and C(2)–C(3). Our refined model takes no account of these 'bonding electron' features.

Final atomic parameters for DL-serine are given in Table 2. The coordinates of the seven heavy atoms agree moderately well with those reported by FLKH;† the goodness-of-fit between the two sets of values $(=[\sum(\Delta x/\sigma)^2/21]^{1/2}$, where Δx is the difference between two corresponding values and σ is the standard devia-

* Lists of observed and calculated structure factors for L-serine and DL-serine have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 30548 (12 pp., 1 microfiche). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

† Here and throughout this paper we revert to the numbering system originally used by Shoemaker et al. (1953), and also used by BPS as well as by most other authors of crystallographic papers on amino acids, rather than the IUPAC designations used by FLKH.

tion of that difference) is 1.4. There is no marked trend in these differences, suggesting that the somewhat high goodness-of-fit value arises more from over-optimism in one or both sets of standard deviations rather than from a generic difference between neutron-diffraction and X-ray-diffraction results.
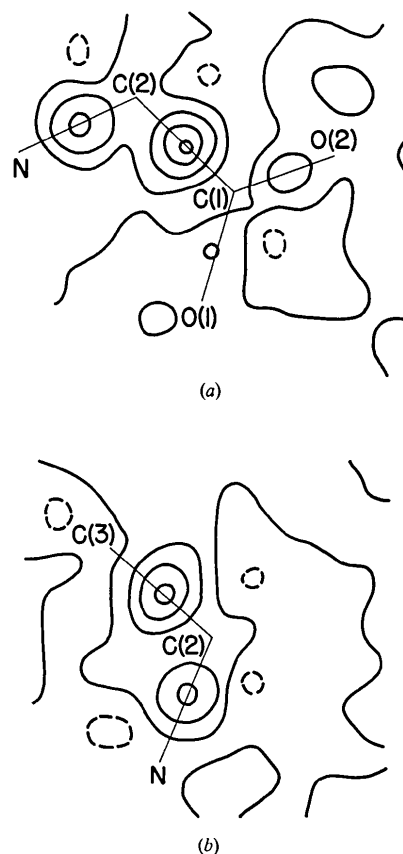

(a)

(b)

Fig. 1. Final difference Fourier maps for DL-serine, evaluated (a) in the plane of the carboxylate group C(1), C(2), O(1), and O(2); (b) in the plane of N, C(2), and C(3). Contours are at intervals of 0.1 e Å^{-3}; the -0.1 e Å^{-3} contour is dashed.

Table 2. *Final parameters for* DL-*serine*

The temperature factor is of the form $\exp(-2\pi^2 U_{11}a^{*2}h^2 \ldots -4\pi^2 U_{23}b^*c^*kl)$. Coordinates have been multiplied by 10^5 for the heavy atoms and by 10^4 for the hydrogen atoms; values of U_{ij} are $\times 10^4$ for the heavy atoms and $\times 10^3$ for H.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	24959 (10)	40569 (10)	16722 (21)	320 (5)	223 (5)	258 (5)	21 (4)	135 (4)	−14 (3)
C(2)	25509 (9)	27897 (11)	37749 (21)	277 (5)	251 (5)	228 (5)	5 (4)	94 (4)	−5 (4)
C(3)	38878 (10)	20927 (13)	47087 (24)	269 (5)	337 (6)	299 (6)	12 (4)	65 (4)	8 (5)
N	15235 (9)	17005 (10)	24408 (22)	241 (5)	241 (5)	284 (5)	17 (3)	93 (4)	40 (4)
O(1)	16393 (8)	40235 (8)	−6837 (17)	405 (5)	285 (4)	283 (4)	−3 (3)	52 (3)	43 (3)
O(2)	33214 (8)	50568 (9)	25288 (17)	449 (5)	276 (5)	341 (5)	−92 (3)	118 (4)	−27 (3)
O(3)	43171 (8)	16902 (11)	22936 (21)	298 (4)	322 (5)	502 (6)	−63 (3)	206 (4)	−118 (4)
H(1)	2338 (13)	3161 (14)	5493 (32)	33 (8)	15 (7)	38 (9)	−9 (6)	12 (7)	−3 (6)
H(2)	3864 (15)	1257 (19)	5921 (35)	38 (8)	52 (10)	41 (10)	4 (8)	19 (8)	27 (9)
H(3)	4505 (14)	2808 (19)	5893 (35)	23 (7)	38 (9)	50 (10)	9 (7)	−1 (7)	−8 (8)
H(4)	1639 (14)	1248 (21)	797 (37)	31 (8)	62 (11)	37 (10)	9 (8)	12 (8)	10 (9)
H(5)	1500 (16)	1023 (19)	3818 (37)	50 (10)	41 (10)	38 (10)	0 (8)	23 (8)	3 (8)
H(6)	710 (16)	2157 (17)	1927 (31)	38 (9)	33 (9)	39 (10)	−1 (8)	−1 (7)	12 (7)
H(7)	4007 (21)	814 (26)	1687 (44)	98 (16)	55 (14)	60 (14)	23 (12)	48 (12)	6 (11)

The agreement between bond lengths and angles involving the heavy atoms (Table 3) is excellent. The largest difference in a heavy-atom bond length, 0·005 Å for C(3)–O(3), is about 2σ (X-ray) and 3σ (neutron); the largest angular deviation, 0·3° for C(1)–C(2)–C(3), is also about 2σ (X-ray) and 3σ (neutron). On the other hand, there are the usual large, systematic differences in the coordinates of the hydrogen atoms, such that our C–H and N–H bond distances are shorter than those of FLKH by amounts ranging from 0·10 to 0·13 Å and the O–H distance is shorter by 0·09 Å. Our values of the bond angles involving hydrogen atoms are in excellent agreement with those of FLKH, none differing by more than 2° (this is about 1·5 of our e.s.d.'s; the corresponding e.s.d.'s reported by FLKH are much smaller, about 0·1°).

As is typical, our values of the anisotropic temperature factors of the heavy atoms correspond to significantly larger atomic displacements than do the neutron-diffraction values of FLKH; the differences average to about 0·004 Å² in mean-square displacement $\bar{U}$. The general tendency of thermal parameters derived by X-ray diffraction to be larger than those derived by neutron diffraction has been documented by Hamilton (1969) and discussed by Coppens (1969); it is presumably due to the inadequacies of free-atom form factors normally used in X-ray work. It has also

been attributed to the use of larger, and hence more perfect, crystals in neutron-diffraction work [see Bugayong, Sequiera & Chidambaram (1972)]; in the present case, however, it appears as though crystals of comparable perfection were used by both groups, as our value of the (isotropic) extinction coefficient, $29(6) \times 10^{-6}$, leads to approximately the same change of 15% in the F value of the strong 011 reflection as reported by FLKH.

We are pleased that our refined anisotropic temperature factors for the hydrogen atoms have resulted in reasonable ellipsoids of vibration (Fig. 2); indeed, the goodness-of-fit between our values and those of FLKH is a moderate 1·5. However, the uncertainties in our values are so high as to make a detailed comparison meaningless.

L-Serine

Our work on L-serine was done prior to, and in ignorance of, the report by Benedetti et al. (1972). Our results are appreciably more accurate.

A sample of 'L-serine' purchased from Sigma Chemical Co., when recrystallized from aqueous solution, yielded principally crystals of DL-serine, and it was only with considerable difficulty that we were able to pick out rather poor crystals of the optically pure compound. For data collection, an irregular-shaped

Table 3. *A comparison between X-ray (X) and neutron diffraction (N) results for the heavy-atom bond lengths and angles in* DL-serine

(a) Bond lengths

	X*	N†		X	N
C(1)–C(2)	1·531 Å	1·531 Å	C(1)–O(1)	1·245 Å	1·248 Å
C(2)–C(3)	1·518	1·518	C(1)–O(2)	1·260	1·257
C(2)–N	1·491	1·487	C(3)–O(3)	1·419	1·414

(b) Bond angles

	X	N		X	N
O(1)–C(1)–O(2)	126·0°	125·8°	C(3)–C(2)–N	111·7°	111·7°
O(1)–C(1)–C(2)	117·9	117·9	C(1)–C(2)–C(3)	111·8	111·5
O(2)–C(1)–C(2)	116·1	116·3	C(2)–C(3)–O(3)	111·4	111·4
C(1)–C(2)–N	109·5	109·6			

* This investigation. Estimated standard deviations: 0·002–3 Å; 0·1–2°.
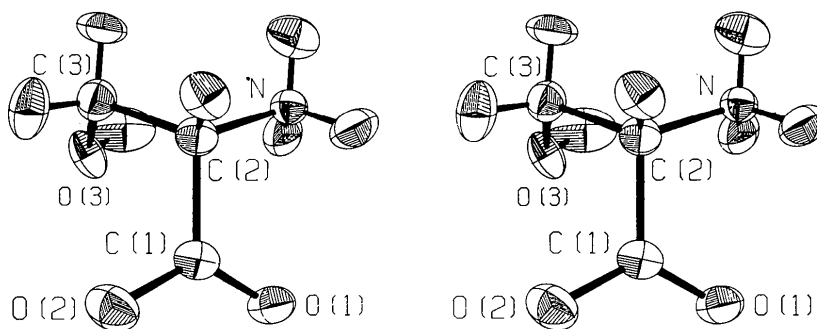† Frey et al. (1973). Estimated standard deviations: 0·001–2 Å; 0·1°.

Fig. 2. A stereo view (Johnson, 1965) of the L-serine molecule in the crystal structure of DL-serine. The thermal ellipsoids are drawn at the 50% probability level.

crystal with maximum and minimum dimensions about 0·25 mm and 0·18 mm was mounted with its c axis slightly skew with respect to the φ axis. The experimental details were the same as for DL-serine. Unit-cell dimensions are given in Table 1; agreement with the values of BPS is no better than fair. One hemisphere of data, comprising two pairs of Friedel-equivalent octants (hkl and $\bar{h}\bar{k}l$; $hk\bar{l}$ and $\bar{h}\bar{k}l$), was collected to $2\theta =$ 155° (Cu $K\alpha$ radiation); initially, data from the four octants were averaged together to give 582 independent observations.

The structure was derived by direct methods, including symbolic addition and tangent refinement. The hydrogen atoms were located on difference maps. Full-matrix least-squares refinement included 93 parameters: coordinates for 14 atoms, anisotropic temperature factors for seven heavy atoms, isotropic temperature factors for seven hydrogen atoms, a scale factor and a secondary-extinction parameter. (Since the intensity data were of considerably lower quality than those for DL-serine, we did not attempt to adjust the anisotropic temperature factors of the hydrogen atoms.)

When convergence was reached ($R = 0·054$), the data were re-averaged, hkl with $\bar{h}\bar{k}l$ and $hk\bar{l}$ with $\bar{h}\bar{k}l$, and the atomic form factors of C, N, and O were corrected for the real and imaginary parts of anomalous dispersion [0·049 and 0·032 e for O, 0·032 and 0·019 for N, 0·019 and 0·010 for C; Hope (1970)]. Least-squares refinement, to convergence, for both isomers gave R indexes for 953 reflections of 0·059 for L-serine and 0·060 for D-serine, and goodness-of-fit values (for 953 observations and 93 parameters) of 0·960 and 0·968; the L-isomer is indicated at the 95% confidence level. A final difference map had features reaching $\pm0·30$ e Å^{-3}, at rather random locations.

As noted above, the experimental data for L-serine are of considerably lower quality than those for DL-serine. Averaged intensities for 57 reflections were less than zero, compared with none for DL-serine, and the standard deviation for an F value of magnitude 5·0 e is about 0·25 e, compared with 0·08 e for DL-serine. Accordingly errors in the data predominate over the errors in the final model; the R index is higher but the goodness-of-fit is lower than for DL-serine. That the goodness-of-fit is slightly less than 1·0 can be attributed to our averaging the weights of the two measurements (hkl and $\bar{h}\bar{k}l$) that constituted a single observation, rather than adding them. One might argue that, under these circumstances, the ideal value for the goodness-of-fit is approximately 0·71 ($= 1/\sqrt{2}$), rather than 1·0. However, the term $(pS)^2$ in the expression for the variance of an individual observation represents the contribution of unknown and perhaps systematic errors, and presumably the weight assigned to an averaged intensity should be something less than the sum of the individual weights.

Final parameters are given in Table 4. The coordinates of the heavy atoms agree only moderately well with those of BPS, who report e.s.d.'s about twice as large as ours; the goodness-of-fit between the two sets is 2·1. BPS did not refine the coordinates of the hydrogen atoms, and report no thermal parameters.
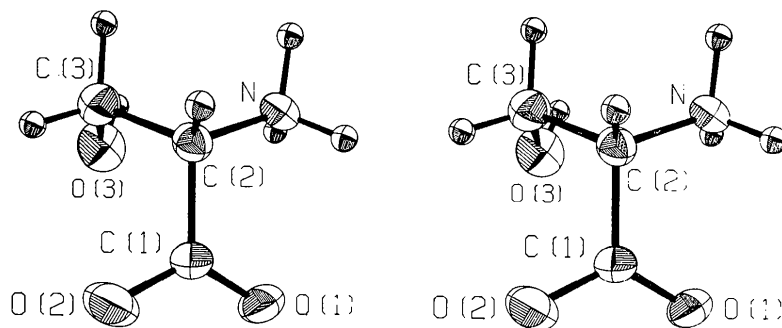

Fig. 3. A stereo view (Johnson, 1965) of the L-serine molecule in crystals of L-serine. The thermal ellipsoids are drawn at the 50% probability level; the hydrogen atoms are represented as spheres of arbitrary radius.

Table 4. *Final parameters of* L-*serine*

Coordinates are multiplied by 10^4 for the heavy atoms and $\times 10^3$ for the hydrogen atoms; values of U_{ij} are $\times 10^3$.

	x	y	z	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C(1)	1148 (3)	1943 (2)	−1406 (4)	34 (1)	32 (1)	26 (1)	2 (1)	5 (1)	−1 (1)
C(2)	835 (3)	2426 (3)	1146 (4)	26 (1)	31 (1)	26 (1)	1 (1)	2 (1)	2 (1)
C(3)	804 (3)	4034 (3)	1394 (5)	42 (1)	32 (1)	35 (1)	2 (1)	3 (1)	−1 (1)
N	2006 (3)	1815 (3)	2801 (4)	34 (1)	33 (1)	23 (1)	−2 (1)	0 (1)	4 (1)
O(1)	2267 (2)	1138 (2)	−1780 (3)	51 (1)	46 (1)	35 (1)	19 (1)	−1 (1)	−10 (1)
O(2)	258 (2)	2425 (2)	−2964 (3)	55 (1)	85 (2)	26 (1)	28 (1)	−2 (1)	1 (1)
O(3)	2288 (3)	4624 (2)	778 (4)	54 (1)	41 (1)	56 (1)	−14 (1)	−1 (1)	3 (1)

Table 4 (*cont.*)

	x	y	z	B
H(1)	−17 (2)	203 (2)	163 (4)	1·8 (4)
H(2)	54 (2)	428 (2)	324 (4)	2·6 (5)
H(3)	2 (3)	445 (2)	28 (5)	3·3 (6)
H(4)	303 (3)	216 (2)	267 (5)	3·3 (6)
H(5)	162 (3)	192 (3)	449 (6)	5·0 (8)
H(6)	214 (3)	80 (3)	262 (5)	3·9 (7)
H(7)	274 (4)	488 (4)	212 (8)	9·2 (13)

A stereo view of the molecule is shown in Fig. 3, and bond distances and angles are given in Table 5. Details of the hydrogen bonds, which differ somewhat from the values calculated by FLKH from the coordinates reported by BPS, are given in Table 6. The most pronounced difference between the bond distances and those reported for L-serine monohydrate and for DL-serine (FLKH and this study, Table 3) is in the C(3)–O(3) bond, which we find to be 0·02 Å longer. We suspect that this lengthening is, at least in part, real. In the anhydrous material, the terminal O–H groups partake in an infinite series of weak hydrogen bonds (O$\cdots$O, 2·918 Å) about the 2_1 axis parallel to c (Fig. 4), whereas in L-serine monohydrate and in DL-serine the O–H groups form stronger hydrogen bonds (2·785 and 2·671 Å) to the more electronegative carboxylate oxygen atoms; as a result of the weaker O–H$\cdots$O interaction, the O–H bond itself would be expected to be stronger and, hence, the C–O bond weaker.

A more easily identifiable consequence of the difference in hydrogen-bonding patterns in DL-serine, L-serine monohydrate, and L-serine crystals can be seen in Fig. 5, which shows views down the C(2)–C(1), C(3)–C(2), and O(3)–C(3) bonds. The conformation about the C(2)–C(1) bond is essentially identical in all
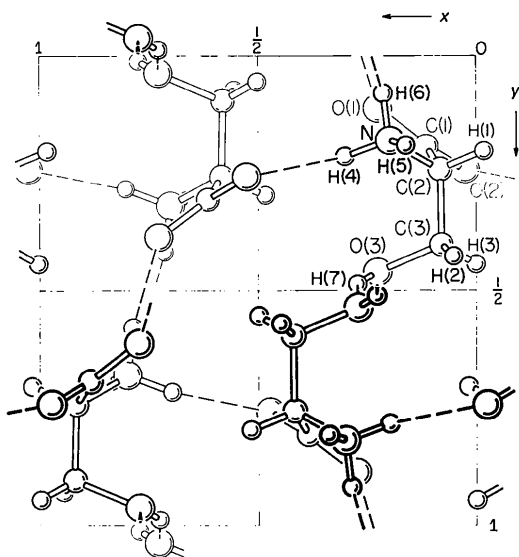

Fig. 4. The structure of L-serine, viewed down c.

Table 5. *Bond distances and angles for* L-*serine*

Standard deviations are about 0·003 Å and 0·2° for bonds involving only the heavy atoms, and 0·03–0·04 Å and 2° for bonds involving hydrogen atoms.

C(1)–O(1)	1·240 Å	C(2)–C(1)–O(1)	118·4°
C(1)–O(2)	1·247	C(2)–C(1)–O(2)	116·3
C(1)–C(2)	1·527	O(1)–C(1)–O(2)	125·2
C(2)–N	1·485	C(1)–C(2)–N	110·8
C(2)–C(3)	1·510	C(3)–C(2)–N	109·7
C(3)–O(3)	1·433	C(1)–C(2)–C(3)	112·6
		C(2)–C(3)–O(3)	110·2
C(2)–H(1)	0·98	C(2)–C(3)–H(2)	108
C(3)–H(2)	1·09	O(3)–C(3)–H(2)	110
C(3)–H(3)	1·00	C(2)–C(3)–H(3)	110
N——H(4)	0·94	O(3)–C(3)–H(3)	108
N——H(5)	1·01	H(2)–C(3)–H(3)	112
N——H(6)	0·96	C(2)–N——H(4)	117
O(3)–H(7)	0·88	C(2)–N——H(5)	109
		C(2)–N——H(6)	113
C(1)–C(2)–H(1)	108°	H(4)–N——H(5)	110
N——C(2)–H(1)	106	H(4)–N——H(6)	103
C(3)–C(2)–H(1)	110	H(5)–N——H(6)	104
		C(3)–O(3)–H(7)	107

Table 6. *Details of the hydrogen bonds,* D–H$\cdots A$, *in* L-*serine*

D	H	A	$D\cdots A$	H$\cdots A$	D–H$\cdots A$
N	H(4)	O(2)(*a*)	2·887 Å	1·96 Å	167°
N	H(5)	O(2)(*b*)	2·871	1·90	159
N	H(6)	O(1)(*c*)	2·840	1·91	161
O(3)	H(7)	O(3)(*d*)	2·918	2·10	153

(*a*) $\frac{1}{2}+x,\frac{1}{2}-y,-z$. (*b*) $x,y,1+z$. (*c*) $\frac{1}{2}-x,-y,\frac{1}{2}+z$. (*d*) $\frac{1}{2}-x,1-y,\frac{1}{2}+z$.

three species, with the NH$_3$ group eclipsed with respect to the carboxylate ion. However, there are significant differences in the conformational angles about the C(3)–C(2) and O(3)–C(3) bonds, and these differences obviously result from the different geometries of the O(3)–H(7)$\cdots$O hydrogen bond.

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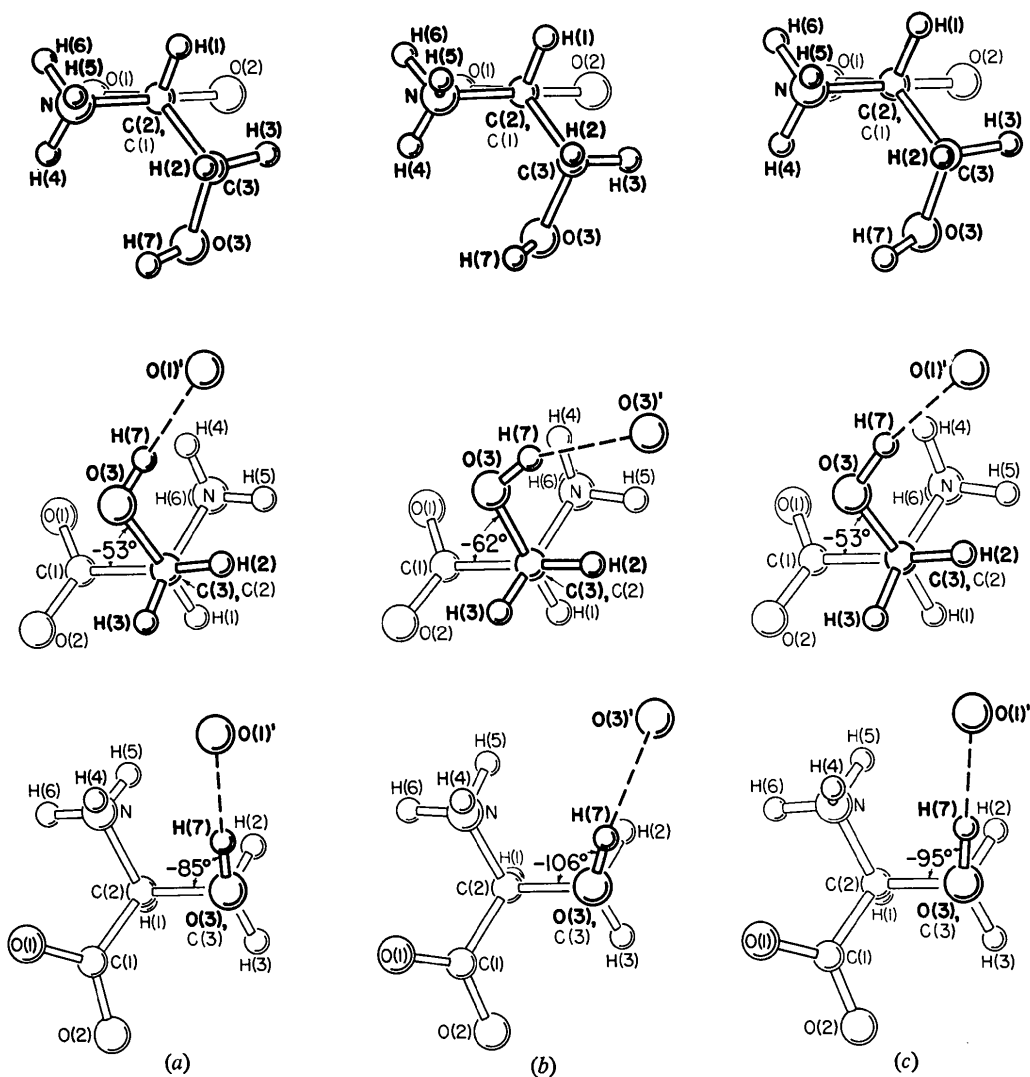
Fig. 5. Views of the L-serine molecule in crystals of (a) DL-serine; (b) L-serine; (c) L-serine monohydrate (FLKH). Top: views down the C(2)–C(1) bonds; center: views down the C(3)–C(2) bonds, with torsion angles; bottom: views down the O(3)–C(3) bonds, with torsion angles.

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