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On the Structure of L-DOPA

(2S-3-(3,4-Dihydroxyphenyl)alanine)

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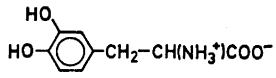
The crystal and molecular structure of L-DOPA, $C_9H_{11}O_4N$, has been determined by X-ray methods using 2149 reflections above background level collected by counter methods. The crystals are monoclinic, space group $P2_1$, with cell dimensions $a = 13.62_9$ Å; $b = 5.30_8$ Å; $c = 6.04_9$ Å; $\beta = 97.5_3°$. Estimated standard deviations in bond lengths are about 0.002 Å and in angles 0.1 – 0.2°. The absolute configuration of the molecule is found to be *S*. The conformation about the Cα – Cβ bond is such as to bring the $(COO)^-$ group *anti* relative to the catechol moiety. The hydrogen bond system is discussed.

L-3,4-Dihydroxyphenylalanine (L-DOPA)



is found to occur in animals and in certain plants.[1,2] From metabolic studies it appears that this amino acid is formed by enzymatic action on tyrosine.[3] Such studies have also shown L-DOPA to be a precursor of dopamine as well as of noradrenaline, both believed to be neuro-transmitters.[4,5] Moreover, L-DOPA seems to be involved in the formation of certain melanines [6] and in abnormal conditions such as malignant melanoma [7] and neuroblastoma.[8] Much of the current interest in L-DOPA, however, originates from its potency as a drug against Parkinsonism which is reported to be characterized by a greatly reduced activity of L-DOPA decarboxylase in the striatum.[9] The activity of L-DOPA is believed to be based on its ability to cross the blood-brain barrier and restore deficiencies in brain dopamine. The increased demand for the compound caused by the terapeutic use has also focused the interest on its synthesis.[10] Hence L-DOPA is an interesting substance from several points of view, and we believe that a structure determination is of importance for the physical characterization of the molecule as well as for the study of the conformation of amino acids in general.

The lack of activity of D-DOPA as an antiparkinsonian drug,[11] even if the decarboxylation of this compound also results in dopamine, may presumably be attributed to enzyme specificity. A study of the absolute configuration is therefore included in the present paper.

Some of the results from this investigation have previously been reported.[12]

EXPERIMENTAL

Commercially obtained L-DOPA was recrystallized by slow diffusion of absolute ethyl alcohol into a solution of the compound in formic acid. Rectangular, colourless plate-formed crystals were formed in the course of one or two weeks. Infra-red spectra showed that no salt formation had occurred and that the crystals were identical with the original compound.

Oscillation and Weissenberg photographs indicated monoclinic symmetry; ($0k0$) reflections were systematically absent for k odd. For an optically active isomer this uniquely determines the space group to be $P2_1$.

Unit cell parameters were determined from diffractometer measurements of 7 general reflections and their Laue-symmetric equivalents. A Picker manual diffractometer was applied using Cu$K\beta$ radiation ($\lambda = 1.3922$ Å) and a take-off angle of 1.0°. The computer program used in the least-squares calculations of cell parameters, as well as the programs employed during all subsequent calculations are parts of an assembly of programs for a CD-3300 computer and described in Ref. 13.

Three-dimensional intensity data were recorded with the use of an automatic Picker four-angle diffractometer using graphite crystal monochromated Mo$K\alpha$ radiation. The take-off angle was 4°, and the temperature was kept constant to within 1° at 18°C.

Two crystals were used for the data collection; one of dimensions $0.2 \times 0.5 \times 0.4$ mm^3 for reflections with 2θ less than 60°, and one of dimensions $0.1 \times 0.5 \times 0.25$ mm^3 for reflections with 2θ from 60° to 80°. They were mounted with the crystallographic b axis along the diffractometer ϕ-axis. The ω-2θ scanning mode with a 2θ scan speed of 1°min^{-1} was applied. Background counts were taken for 40 sec at each of the scan range limits for the low angle data and for 20 sec for the high angle set. Reflections for which the count rate exceeded 10^4 cps were remeasured with reduced primary beam intensity. Intensities of three standard reflections were measured for every 50 reflections of the data set and the data were adjusted according to the variations in the test reflection intensity. The estimated standard deviations were taken as the square root of the total counts with a 2 % addition for the uncertainty in adjustments.

Out of the 2764 unique reflections measured, 2149 had intensities larger than twice the standard deviation. These were regarded as "observed" reflections whereas the remaining reflections were excluded from further calculations.

The intensity data were corrected for Lorentz, polarization, and absorption effects.

Atomic form factors used were those of Hanson *et al.*[14] for oxygen, nitrogen, and carbon and of Stewart *et al.*[15] for hydrogen. Anomalous scattering factors were obtained from Cromer and Liberman ($\Delta f_C' = 0.021$, $\Delta f_C'' = 0.010$, $\Delta f_N' = 0.036$, $\Delta f_N'' = 0.019$, $\Delta f_O' = 0.055$, $\Delta f_O'' = 0.034$).[16]

In order to determine the absolute configuration of the molecule, measurements were made of Friedel equivalent reflections. The ratio $D = (|F_c(hkl)| - |F_c(\bar{h}\bar{k}\bar{l})|)^2/\sigma^2(F_o(hkl))$ were calculated [17] for Cu$K\alpha$ radiation for reflections with $\sin\theta/\lambda > 0.3$. Atomic parameters from the refined structure were used and anomalous atomic scattering factors were employed for carbon, oxygen, and nitrogen atoms; the structure factor variances were as found for the Mo$K\alpha$ data.

13 reflections with the highest D-value were selected for the measurements. The Bijvoet pairs $F(hkl)$, $F(\bar{h}\bar{k}\bar{l})$ and $F(\bar{h}k\bar{l})$, $F(h\bar{k}l)$ were all measured, constituting 26 pairs of reflections as the basis for absolute configuration determination. For these measurements a manual Picker diffractometer with Ni-filtered Cu$K\alpha$ radiation was used.

CRYSTAL DATA

L-3,4-Dihydroxyphenylalanine (L-DOPA), $C_9H_{11}O_4N$, decomposes above 265°C, monoclinic.

$a = 13.629$ (0.004) Å; $b = 5.308$ (0.002) Å, $c = 6.049$ (0.002) Å; $\beta = 97.53°$ (0.01).

Figures in parentheses are estimated standard deviations.

$V = 433.8$ Å^3; $M = 197.2$; $F(000) = 208$, $\mu = 0.28$ cm^{-1}, $Z = 2$.

σ_{obs} (flotation) $= 1.50$ g cm^{-3}, $\sigma_{calc} = 1.509$ g cm^{-3}.

Absent reflections: $(0k0)$ for k odd; space group $P2_1$.

STRUCTURE DETERMINATION

The structure was solved using the low angle data (1285 reflections). The observed structure factors were brought on an approximately absolute scale by Wilson's statistical methods, the preliminary value of 1.9 Å^2 being found for the B-value in the isotropic temperature factor. The Patterson function was calculated and the orientation of the (planar) catechol part of the molecule was established by inspection of the peaks near the origin. The position as projected along the b axis was found from the Harker section, and after a couple of Fourier refinements x and z parameters of all non-hydrogen atoms were obtained. From the projection two sets of trial y parameters were estimated, one of which turned out to be correct; this model was refined isotropically to an R-factor of 0.12. Introduction of anisotropic thermal parameters and three cycles of least-squares refinement of all parameters brought the R-factor down to 0.053. Positions of the hydrogen atoms bonded to carbon were calculated, the other hydrogen atoms were localized from a difference Fourier map. Least-squares refinements of all positional parameters, anisotropic thermal parameters for non-hydrogen atoms and isotropic thermal parameters for hydrogen atoms yielded a conventional R-factor of 0.035 and a weighted R-factor of 0.044.

At this stage the high-angle data were introduced. The refinement of the same parameters as before resulted, however, only in insignificant shifts. The estimated standard deviations of the parameter values decreased by 20 % even if the R-factor for the total data set increased to 0.067 and the weighted R-factor increased to 0.059. The overdetermination ratio was 12.7, 171 parameters being refined on the basis of 2169 observed reflections with $\sin\theta/\lambda < 1.13$.

A total difference Fourier map showed electron densities less than 0.3 e Å^{-3} only. The largest densities were found at the position of the carboxyl group and a negative electron density was localized at the ammonium group.

A comparison of observed and calculated structure factors is given in Table 1; the final parameters for non-hydrogen atoms are listed in Table 2 and for hydrogen atoms in Table 3.

Magnitudes and directions of the principal axes of the ellipsoids of vibration are given in Table 4. The r.m.s. discrepancy between the atomic vibration tensor components obtained in the structure analysis and those calculated from the rigid-body parameters found by analysis of the librational, translational and screw motion of the molecule, is 0.0031 Å^2. This indicates that the

molecule may be regarded as a rigid body, and the atomic positions were accordingly corrected for the librational motion. As the discrepancies are larger for atoms C7 and C8 than for the others, the corrections involving these two atoms may be less significant. The eigenvalues of **T** are 0.15, 0.14, and

Table 1. Observed and calculated structure factors. The columns are h, k, l, $10\,|F_o|$, $10\,|F_c|$.

h	k	l	$10\,\|F_o\|$	$10\,\|F_c\|$
2	0	0	54	50
4	0	0	72	65
5	0	0	119	114
6	0	0	103	98
7	0	0	148	141
8	0	0	10	9
9	0	0	63	63
10	0	0	20	19
11	0	0	33	34
12	0	0	96	100
13	0	0	57	59
14	0	0	74	76
15	0	0	27	29
16	0	0	83	86
17	0	0	11	13
14	0	1	102	102
13	0	1	212	219
11	0	1	49	51
10	0	1	180	182
9	0	1	111	104
8	0	1	47	43
7	0	1	65	62
6	0	1	17	15
5	0	1	132	128
4	0	1	50	49
3	0	1	13	15
2	0	1	36	41
-1	0	1	68	66
-8	0	1	37	38
-9	0	1	95	94
-10	0	1	139	133
-12	0	1	28	30
-13	0	1	17	14
-15	0	1	27	25
-16	0	1	41	43
-18	0	1	19	17
-18	0	2	17	17
-17	0	2	13	13
-16	0	2	11	11
-14	0	2	39	40
-13	0	2	64	66
-12	0	2	160	161
-11	0	2	61	64
-10	0	2	43	43
-9	0	2	43	42
-8	0	2	143	142
-7	0	2	40	40
-6	0	2	24	25
-5	0	2	68	66
-4	0	2	132	126
-2	0	2	123	112
3	0	2	122	113
5	0	2	44	43
6	0	2	118	118
7	0	2	16	18
8	0	2	39	39
9	0	2	21	22
10	0	2	141	146
11	0	2	167	169
12	0	2	24	23
13	0	2	8	6
15	0	2	32	32
16	0	2	10	12
17	0	2	19	21
16	0	3	18	18
15	0	3	33	33
14	0	3	15	14
13	0	3	22	23
11	0	3	8	12
10	0	3	112	113
9	0	3	141	146
8	0	3	158	162
6	0	3	84	78
5	0	3	147	142
4	0	3	20	19
3	0	3	18	17
2	0	3	10	9
0	0	3	50	55
-2	0	3	42	40
-6	0	3	62	62
-7	0	3	42	44
-8	0	3	87	85
-10	0	3	25	25
-11	0	3	39	39
-12	0	3	74	75
-13	0	3	47	51
-14	0	3	20	19
-15	0	3	20	20
-16	0	3	20	19
-17	0	3	14	13
-18	0	3	26	26
-16	0	4	12	12
-15	0	4	81	79
-14	0	4	21	19
-13	0	4	16	14
-12	0	4	46	46
-10	0	4	13	14
-9	0	4	183	181
-8	0	4	52	47
-6	0	4	73	71
-5	0	4	8	6
-4	0	4	78	82
-3	0	4	71	67
-2	0	4	66	64
-1	0	4	23	21
0	0	4	78	81
1	0	4	7	10
2	0	4	26	22
3	0	4	15	15
4	0	4	87	81
5	0	4	54	55
6	0	4	92	89
7	0	4	37	41
8	0	4	57	62
10	0	4	61	61
11	0	4	8	4
13	0	4	16	18
14	0	4	64	62
15	0	4	44	40
13	0	5	75	74
12	0	5	59	54
11	0	5	51	47
10	0	5	12	10
9	0	5	79	77
8	0	5	54	52
6	0	5	32	31
5	0	5	80	95
4	0	5	119	121
3	0	5	73	71
2	0	5	44	44
1	0	5	61	67
0	0	5	106	113
-1	0	5	62	62
-2	0	5	141	145
-3	0	5	120	125
-4	0	5	168	169
-5	0	5	41	40
-6	0	5	16	15
-7	0	5	11	14
-8	0	5	57	61
-10	0	5	46	48
-11	0	5	9	5
-12	0	5	15	17
-13	0	5	10	11
-14	0	5	21	21
-15	0	5	48	48
-16	0	5	101	99
-14	0	6	28	29
-13	0	6	10	11
-11	0	6	21	20
-10	0	6	46	45
-9	0	6	35	36
-8	0	6	20	20
-7	0	6	26	26
-6	0	6	52	51
-5	0	6	154	154
-4	0	6	138	136
-3	0	6	142	139
-2	0	6	71	71
-1	0	6	36	35
1	0	6	15	14
2	0	6	56	60
3	0	6	90	91
4	0	6	23	28
5	0	6	31	32
6	0	6	58	59
7	0	6	44	42
9	0	6	40	39
10	0	6	26	24
11	0	6	40	40
8	0	7	79	73
7	0	7	37	36
6	0	7	31	28
5	0	7	35	32
4	0	7	41	40
3	0	7	11	11
2	0	7	37	35
1	0	7	96	95
0	0	7	62	62
-2	0	7	13	13
-4	0	7	99	97
-5	0	7	57	58
-6	0	7	27	26
-7	0	7	75	73
-8	0	7	59	61
-9	0	7	8	4
-10	0	7	8	8
-12	0	7	71	68
-8	0	8	44	44
-7	0	8	32	30
-6	0	8	18	16
-5	0	8	21	21
-3	0	8	13	12
-2	0	8	25	24
-1	0	8	50	48
0	0	8	38	33
1	0	8	99	95
3	0	8	24	22
2	1	8	12	8
1	1	8	40	38
0	1	8	23	22
-1	1	8	61	58
-2	1	8	24	23
-3	1	8	9	8
-4	1	8	20	22
-5	1	8	15	15
-6	1	8	21	21
-7	1	8	59	58
-12	1	7	22	22
-11	1	7	31	31
-10	1	7	32	31
-9	1	7	35	34
-8	1	7	41	40
-7	1	7	76	75
-6	1	7	67	67
-5	1	7	51	49
-3	1	7	37	36
-2	1	7	54	54
-1	1	7	89	88
0	1	7	39	39
1	1	7	54	54
2	1	7	40	39
3	1	7	50	49
4	1	7	34	33
6	1	7	37	37
7	1	7	49	46
11	1	6	95	90
10	1	6	27	24
9	1	6	10	7
8	1	6	45	43
6	1	6	19	20
5	1	6	15	16
4	1	6	32	33
3	1	6	31	34
2	1	6	41	41
1	1	6	73	73
0	1	6	55	55
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-5	1	5	77	80
-4	1	5	17	17
-3	1	5	76	79
-1	1	5	129	131
0	1	5	122	125
1	1	5	84	86
2	1	5	29	34
3	1	5	44	49
4	1	5	65	64
5	1	5	41	43
6	1	5	20	20
7	1	5	20	19
8	1	5	53	54
9	1	5	31	28
10	1	5	73	71
11	1	5	67	70
12	1	5	88	84
13	1	5	30	30
15	1	4	44	44
14	1	4	18	18
13	1	4	46	43
12	1	4	9	9
11	1	4	23	21
10	1	4	24	24
9	1	4	56	59
8	1	4	28	33
7	1	4	75	83
6	1	4	50	54
5	1	4	43	42
4	1	4	106	106
3	1	4	41	43
2	1	4	148	146
1	1	4	74	73
0	1	4	121	117
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-3	1	4	76	76
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-5	1	4	46	46
-6	1	4	25	25
-7	1	4	62	60
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-1	1	3	119	116
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1	1	3	105	103
4	1	3	60	62
5	1	3	71	70
6	1	3	174	178
7	1	3	31	30
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9	1	3	56	57
10	1	3	119	123
11	1	3	45	47
12	1	3	66	68
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16	1	3	23	22
17	1	2	31	30
16	1	2	55	55
15	1	2	42	42
14	1	2	18	19
13	1	2	20	19
12	1	2	43	44
11	1	2	137	142
10	1	2	13	16
9	1	2	190	196
8	1	2	146	150
7	1	2	105	110
6	1	2	136	134
5	1	2	134	126
4	1	2	67	63
0	1	2	16	17
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-4	1	2	36	39
-5	1	2	129	126
-6	1	2	62	60
-7	1	2	145	143
-8	1	2	68	67
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-14	1	2	41	42
-15	1	2	33	34
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-18	1	2	37	38
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-10	1	1	43	43
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6	1	1	104	94
8	1	1	103	100
9	1	1	72	69
10	1	1	52	55
11	1	1	48	48
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18	1	1	41	40
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17	1	0	42	45
16	1	0	43	42
15	1	0	99	103
14	1	0	122	125
13	1	0	35	34
12	1	0	28	29
11	1	0	59	61
10	1	0	51	51
9	1	0	21	19
8	1	0	64	63
7	1	0	124	116
6	1	0	64	63
2	2	0	146	133
5	2	0	83	75
6	2	0	92	86
7	2	0	62	59
8	2	0	90	86
9	2	0	91	90
10	2	0	44	47
11	2	0	97	99
12	2	0	106	110
13	2	0	30	29
14	2	0	39	42
15	2	0	48	51
16	2	0	58	57
17	2	0	54	54
17	2	1	29	27
16	2	1	8	10
15	2	1	16	15
14	2	1	22	23
13	2	1	20	23
12	2	1	78	82
11	2	1	61	64
10	2	1	105	107
9	2	1	67	64
8	2	1	25	21
7	2	1	156	155
6	2	1	38	36
5	2	1	11	13
4	2	1	119	113
3	2	1	140	130
0	2	1	114	117
-2	2	1	92	89
-4	2	1	97	96
-5	2	1	91	86
-6	2	1	60	59
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-17	2	1	50	49
-18	2	1	38	40
-18	2	2	12	12
-16	2	2	28	29
-15	2	2	10	8
-14	2	2	19	29
-13	2	2	63	62
-12	2	2	85	85
-11	2	2	91	94
-10	2	2	30	28
-9	2	2	62	61
-8	2	2	94	98
-7	2	2	199	204
-3	2	2	23	22
-1	2	2	96	93
0	2	2	57	61
2	2	2	65	63
3	2	2	106	105
4	2	2	23	20
5	2	2	129	133
6	2	2	73	73
7	2	2	83	85
8	2	2	80	82
9	2	2	76	76
10	2	2	26	27
11	2	2	66	64
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- 6	8	5	19	16
- 8	8	5	20	11
- 4	9	3	20	15
- 1	9	3	24	28

Table 2. Fractional atomic coordinates and thermal parameters with estimated standard deviations (× 10^5) for non-hydrogen atoms. The temperature factor is given by $\exp-(B_{11}h^2+B_{22}k^2+B_{33}l^2+B_{12}hk+B_{13}hl+B_{23}kl)$.

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
C1	21346	45408	66000	249	1764	998	353	15	157
	10	40	22	7	53	32	34	23	77
C2	22891	64723	51249	265	1529	1226	−43	−66	−95
	11	40	24	7	57	34	31	25	70
C3	16687	67491	31145	275	1412	1128	178	118	159
	10	39	22	7	51	31	33	24	73
C4	8992	50487	25664	240	1792	1108	147	−37	−308
	10	40	23	7	55	33	35	24	78
C5	7469	31129	40136	243	1919	1502	−180	43	−91
	11	42	25	7	60	40	34	26	83
C6	13600	28604	60378	286	1941	1405	2	174	616
	11	42	26	7	60	38	36	26	80
C7	27791	43034	88201	308	1835	1030	394	−6	−178
	11	44	24	8	56	32	36	25	76
C8	34685	20185	89927	227	1435	842	28	−49	1
	9	41	20	6	45	28	32	21	69
C9	40227	18312	113728	302	1370	940	30	−179	44
	11	40	21	7	49	30	33	23	72
O1	17751	86177	16159	407	1775	1267	−243	−113	711
	9	19	19	6	43	28	30	22	59
O2	3148	54270	5702	361	2296	1317	−230	−480	−16
	9	40	20	7	55	29	30	22	64
O3	49185	23725	116787	265	2634	1467	−160	−335	138
	7	37	18	5	52	28	30	19	70
O4	35108	11698	128445	424	3741	909	−841	−57	839
	9	40	17	7	66	26	39	21	72
N	41908	22159	73470	271	2526	927	224	42	−11
	9	44	20	6	54	26	35	19	72

Table 3. Fractional atomic coordinates ($\times 10^4$) and isotropic thermal parameters with estimated standard deviations for hydrogen atoms.

H2	2820	7644	5423	1.50
	13	47	29	40
H5	178	2007	3584	2.70
	16	60	35	46
H6	1270	1599	7137	2.46
	14	51	33	49
H71	3227	5856	9101	2.86
	16	59	36	53
H72	2353	4148	−42	2.75
	15	54	35	52
H8	3063	558	8616	0.97
	12	41	28	38
NH1	3883	2125	5850	2.08
	13	58	33	40
NH2	4706	1071	7637	2.71
	17	57	37	54
NH3	4587	3864	7528	3.18
	18	55	41	61
O1H	2267	9493	2126	2.23
	17	67	34	59
O2H	62	4230	265	3.87
	22	70	50	74

0.12 Å while the r.m.s. librational amplitudes are 4.5, 2.0, and 1.2°, the major axis of libration being nearly parallel to a line through O2 and C8.

Standard deviations were calculated from the correlation matrix ignoring standard deviations in cell parameters.

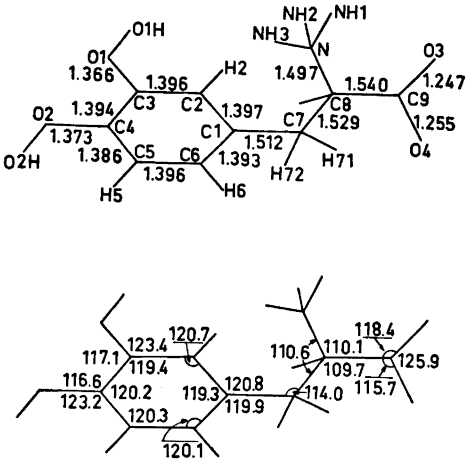

Fig. 1. Bond lengths (Å) (corrected for thermal vibration effects) and angles (°) in L-DOPA.

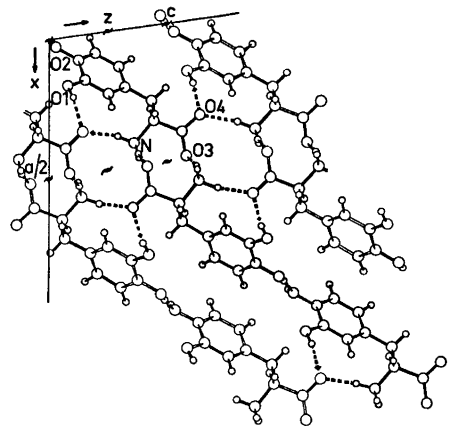

Fig. 2. The crystal structure as seen along the *b* axis.

Table 4. R.m.s. amplitudes of vibration $(\overline{u^2})^{\frac{1}{2}}$(Å) and B-values (Å^2) along the principal axes of vibration given by the components of a unit vector **e** in fractional coordinates ($\times 10^3$).

Atom	$(\overline{u^2})^{\frac{1}{2}}$	B	e_x	e_y	e_z
C1	.175	2.42	49	140	−5
	.143	1.62	−30	92	119
	.126	1.25	49	−86	117
C2	.169	2.27	−55	1	96
	.149	1.75	17	−177	48
	.138	1.50	47	66	128
C3	.164	2.13	67	79	11
	.146	1.68	−10	76	147
	.134	1.43	30	−153	79
C4	.172	2.33	38	135	−68
	.147	1.71	−44	131	55
	.134	1.41	46	14	142
C5	.172	2.33	−36	135	77
	.167	2.21	2	−107	137
	.143	1.60	65	77	61
C6	.178	2.50	1	147	104
	.167	2.09	74	−5	22
	.147	1.70	1	118	−129
C7	.190	2.84	55	116	−28
	.142	1.60	−39	147	46
	.135	1.44	31	−21	158
C8	.152	1.83	64	32	−59
	.143	1.61	−9	186	18
	.119	1.11	36	−9	155
C9	.179	2.53	65	106	−62
	.140	1.54	1	188	16
	.121	1.16	36	−17	154
O1	.209	3.44	−61	66	55
	.161	2.04	40	134	86
	.135	1.44	12	−115	132
O2	.215	3.65	−57	45	82
	.179	2.52	8	181	−40
	.125	1.24	47	25	140
O3	.201	3.20	−34	137	75
	.186	2.73	30	129	−91
	.128	1.29	69	112	118
O4	.256	5.18	−39	154	25
	.172	2.32	62	104	12
	.124	1.20	11	131	164
N	.193	2.95	24	178	5
	.156	1.93	−66	63	28
	.129	1.32	22	−05	164

DISCUSSION

Bond lengths and angles are listed in Table 5 and may also be found in Fig. 1, in which the numbering of the atoms is indicated.

Bond lengths and angles in the alanine moiety are in good agreement with those found in other α-amino acid derivatives measured with corresponding

Table 5. Bond length (Å) and bond angles (°). Estimated standard deviations in parentheses.

Bond length		e.s.d ($\times 10^4$)	Corrected bond length	Bond angle		e.s.d.
C1 – C2	1.393	(22)	1.397	C1 – C2 – C3	120.7	(.14)
C2 – C3	1.395	(19)	1.396	C2 – C3 – C4	119.4	(.13)
C3 – C4	1.390	(21)	1.394	C3 – C4 – C5	120.2	(.12)
C4 – C5	1.383	(23)	1.386	C4 – C5 – C6	120.3	(.14)
C5 – C6	1.395	(21)	1.396	C5 – C6 – C1	120.1	(.14)
C6 – C1	1.390	(23)	1.393	C6 – C1 – C2	119.3	(.12)
C1 – C7	1.511	(20)	1.512	C2 – C1 – C7	120.8	(.14)
C7 – C8	1.529	(22)	1.538	C6 – C1 – C7	119.9	(.14)
C8 – C9	1.539	(18)	1.540	C1 – C7 – C8	114.0	(.12)
C3 – O1	1.364	(19)	1.366	C7 – C8 – C9	109.7	(.12)
C4 – O2	1.371	(18)	1.373	C2 – C3 – O1	123.4	(.14)
C9 – O3	1.244	(19)	1.247	O1 – C3 – C4	117.1	(.12)
C9 – O4	1.251	(19)	1.255	C3 – C4 – O2	116.6	(.14)
C8 – N	1.493	(18)	1.497	O2 – C4 – C5	123.2	(.14)
C2 – H2	.95			C8 – C9 – O3	118.4	(.12)
C5 – H5	.98			C8 – C9 – O4	115.7	(.12)
C6 – H6	.96			O3 – C9 – O4	125.9	(.12)
C8 – H8	.96			C7 – C8 – N	110.6	(.13)
C7 – H71	1.02			N – C8 – C9	110.1	(.11)
C7 – H72	.96					
O1 – O1H	.84			Hydrogen bond lengths		
O2 – O2H	.74					
N – NH1	.95			O2 – O2($-x, y-1/2, -z$)		2.846
N – NH2	.93			O1 – O4($x, 1+y, z-1$)		2.743
N – NH3	1.03			N – O3($1-x, y+1/2, 2-z$)		3.021
				N – O3($1-x, y-1/2, 2-z$)		2.871
				N – O4($x,y,z-1$)		2.815

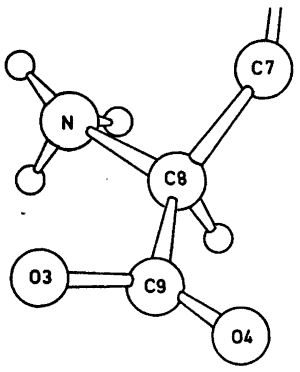

Fig. 3. The absolute configuration of the asymmetric carbon atom.

accuracy. The zwitterionic nature is revealed not only by the equal carbon-oxygen bond lengths in the carboxyl group, but also by the location of the three hydrogen atoms on the nitrogen atom. The nitrogen atom is situated near the plane of the carboxylic group, the dihedral angle N – C8 – C9 – O3

being 14.4°. The conformation about the C8 – N bond is staggered even if all the hydrogen atoms bonded to the nitrogen atom are engaged in hydrogen bond formation. The dihedral angle C1 – C7 – C8 – C9 is 175.2°. The dihedral angle between the plane of the benzene ring and the one defined by C1, C7, and C8 is about 70°, and the plane of C8 – CO_2 forms an angle of approximately 40° with the benzene plane.

The asymmetric centre of the molecule is the α-carbon atom (C8). Structure factor calculations of the 52 reflections (26 pairs) selected for differentiation between the two enantiomeric forms yielded conventional R values of 0.042 neglecting anomalous scattering, 0.037 if this effect was applied for the S-enantiomer and 0.044 for the R-enantiomer. We conclude that the L-DOPA has indeed the S configuration. A schematical drawing of the configuration about C8 is shown in Fig. 3. The result is in agreement with the absolute configuration determination of L-tyrosine [18] and with that assigned to the L-amino acids according to the Fischer convention. Greater biological activity for this kind of molecules seems to be associated with an α-S-configuration.[19]

The bond between the catechol and the alanine parts, C1 – C7, of 1.512 Å is as expected for a single bond formed between sp^2 and sp^3 hybridized carbon atoms.

The catechol moiety is nearly planar, the atoms being displaced from a least-squares plane through the non-hydrogen atoms by less than 0.03 Å. The C7, O1, and O2 atoms are situated on the same side of the benzene ring plane, the atoms of which deviate less than 0.006 Å from planarity. The mean C – C bond length is 1.394 Å as in benzene, and the internal angles are less than one degree from 120°. The C – O bond lengths are nearly the same as in catechol.[20] The distortions of the external angles from 120° at the C3 and C5 atoms are analogous to what has often been found in phenols and are possibly connected with the hydrogen bond formation at the oxygen atoms bonded to these carbon atoms.

The structure of the L-DOPA molecule in the crystals is in the "extended" form, the carboxyl group being in the *anti* position to the aromatic part with respect to the Cα – Cβ-bond. The conformation about this bond is thus different from that in L-tyrosine hydrochloride [21] in which the amino group occupies the *anti* position and from that in L-phenylalanine [22] where the amino and the carboxyl groups both are *gauche* relative to the phenyl group.

The molecular arrangement in the crystals is visualized in Fig. 2. The structure seems to be dominated by hydrogen bonds with few van der Waals contacts. All hetero-atoms are involved in hydrogen bonding resulting in a close molecular packing as indicated by the high density and melting point and by the relatively low values obtained for the amplitudes of vibration. The hydroxyl and ammonium hydrogen atoms are all engaged in hydrogen bonds.

The crystal structure may be described as layers of hydrogen bonded molecules parallel to the (201) plane. In the layer every molecule is bonded to four neighbouring molecules. The O2 atom acts as hydrogen donor and acceptor for O2 atoms related by the screw axis through the origin; the hydrogen bond length is 2.846 Å. At the other end of the molecule the zwitter ions are connected along the screw axis in $(\frac{1}{2},y,1)$. The O3 atom of the COO^- group is

acceptor in two hydrogen bonds to NH_3^+ groups displaced by one translation along *b*; two hydrogen atoms of the ammonium group are thus engaged in such bonds. The two N–H · · · O3 hydrogen bond lengths are 2.871 Å and 3.021 Å, respectively.

The layers are connected through hydrogen bonds in which O4, the other oxygen atom of the COO^- group, is hydrogen acceptor in bonds to two adjacent molecules in another layer. Hydrogen donors are O1 and N atoms and the hydrogen bond lengths are 2.743 Å and 2.815 Å, respectively. Hence, each molecule is linked to eight neighbouring molecules by ten hydrogen bonds.

The O1 atom is engaged in only one hydrogen bond. This atom is involved in *inter*-molecular contacts with C7 $(x,y,z-1)$ of 3.25 Å, C5 $(x,y+1,z)$ of 3.21 Å and O2 $(-x,y+\frac{1}{2},-z)$ of 3.13 Å.

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