

Fig. 1. The molecular structure of octa(phenylsilasesquioxane) showing the numbering scheme.

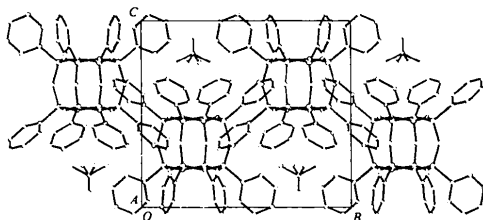


Fig. 2. The molecular packing viewed down [100].

1.833 Å) are shorter than those in the methyl derivative (ave. 1.895 Å), as expected. The angles at the Si atoms are close to tetrahedral. The average angle at the O atom ( $148.5^\circ$ ) is similar to those found in most other eight-membered siloxane ring systems (Shklover, Kalinin, Gusev, Bokii, Struchkov, Andrianov & Petrova, 1973; Carlström & Falkenberg, 1973; Söderholm & Carlström, 1977; Söderholm, 1978). An interesting feature of this crystal structure is that the acetone molecule, which is not lost by the crystals even

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## Structure of L- $\gamma$ -Carboxyglutamic Acid

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**Abstract.**  $C_6H_9NO_6$ ,  $M_r = 191.13$ , monoclinic,  $P2_1$ ,  $a = 5.050$  (3),  $b = 9.600$  (5),  $c = 7.793$  (2) Å,  $\beta = 99.98$  (3) $^\circ$ ,  $V = 371.4$  Å<sup>3</sup>,  $Z = 2$ ,  $D_m = 1.70$ ,  $D_x = 1.71$  Mg m<sup>-3</sup>; refined to a conventional  $R$  value of 0.052 for 749 observed reflections. The molecule is a zwitterion: the amino group is protonated and the C $_{\alpha}$  [C(2)] and a C $_{\gamma}$  [C(4)] carboxyl groups are partially ionized, sharing a proton in the formation of a short

on prolonged exposure to air, is not involved in any specific intermolecular interaction but is trapped in a cavity formed by six silasesquioxane molecules. The packing of the silasesquioxane molecules involves a number of centrosymmetric phenyl–phenyl arrangements but these are not close, the shortest C $\cdots$ C distance being 3.752 Å. The packing of the molecules is shown in Fig. 2.

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hydrogen bond [O...O = 2.455 (8) Å]. The N atom is *trans* to C <sub>$\gamma$</sub>  [ $\chi^1 = -169.8$  (3)°] and C <sub>$\alpha$</sub>  is *trans* to C <sub>$\delta$</sub> 1 [C(6)] [ $\chi^{2,1} = 153.0$  (4)°], placing the molecule in an extended conformation. There is a C—H...O interaction between C <sub>$\gamma$</sub>  and O<sub>c</sub>2,2 [O(4)] of a neighboring molecule [C...O = 3.08 (1) Å].

**Introduction.** The amino acid  $\gamma$ -carboxyglutamic acid was first discovered as the highly anionic residues in the N-terminal portion of the thrombin proenzyme prothrombin (Stenflo, Fernlund, Egan & Roepstorff, 1974; Suttie & Jackson, 1977). These residues are the vitamin-K dependent factors responsible for calcium and phospholipid binding to prothrombin and are necessary for the activation of the proenzyme. This study was undertaken to determine the dimensions and the preferred conformation of this modified amino acid.

Crystals of  $\gamma$ -carboxyglutamic acid were grown at room temperature from an aqueous solution of the ammonium salt of DL- $\gamma$ -carboxyglutamic acid. A crystal of dimensions 0.6 × 0.4 × 0.2 mm was used in the analysis. Preliminary photographs indicated that the crystals belong to the monoclinic system, space group *P*2<sub>1</sub>, with one molecule in the asymmetric unit. Apparently the process of crystallization has selected one enantiomorph from the solution. The successful analysis of the structure confirmed the assignment of the space group. The cell constants were determined from a least-squares analysis of 23 medium-angle reflections measured on an Enraf-Nonius CAD-4 diffractometer. The density was measured by flotation in a mixture of bromoform and carbon tetrachloride.

1029 reflections were collected on the diffractometer to a 2 $\theta$  limit of 154° using Ni-filtered Cu *K* $\alpha$  radiation ( $\lambda = 1.5418$  Å). After correction for Lorentz and polarization effects, the equivalent reflections were averaged into a set of 812 independent reflections. The agreement between the equivalent reflections [ $\sum (F_i - \bar{F})/\sum \bar{F}$ ] was 0.03. No absorption correction was applied. 758 reflections were considered observed based on the criterion  $I > 1.5\sigma(I)$  and were used in the analysis.

The structure was solved by direct methods using the program *MULTAN* (Main, Germain & Woolfson, 1970). An *E* map calculated for the best solution revealed the structure. Two cycles of isotropic full-matrix least-squares refinement on the 13 heavy atoms minimizing  $\sum w(|F_o| - k|F_c|)^2$  followed by two cycles of anisotropic refinement reduced the *R* value to 0.083. All the H atoms, except that involved in the O(1)...O(6) interaction, were located from a difference electron density map. The H atoms were assigned the isotropic thermal parameters of the heavy atoms to which they were bonded and were not varied in the refinement. Another difference electron density map revealed two peaks in the vicinity of O(1) and O(6) with densities of 0.36 and 0.43 e Å<sup>-3</sup> respectively. The

next largest peak was below 0.15 e Å<sup>-3</sup>. Since the geometry of the hydrogen bonds formed by a H atom at either position was reasonable, each peak was treated as a half-H atom. A weighting scheme suggested from an analysis of  $|AF|$  vs  $|F_o|$  [ $w = 1/\sigma^2$  where  $\sigma(F) = 0.12 + 0.064(F_o)$  for  $0 \leq F_o < 2.59$ ,  $\sigma(F) = 0.32 - 0.01333(F_o)$  for  $2.59 \leq F_o < 4.70$  and  $\sigma(F) = -0.071 + 0.069(F_o)$  for  $F_o \geq 4.70$ ] was applied. Nine reflections suffering from secondary extinction were given zero weight.

Further refinement was performed to convergence. The average shift to  $\sigma$  ratio was 0.03 and the maximum value was 0.12. The final *R* value for the 749 observed reflections was 0.052 and for the entire data set of 812 reflections was 0.058. The scattering-factor tables were from Cromer & Waber (1965) for the non-hydrogen atoms, and from Stewart, Davidson & Simpson (1965) for the H atoms.

The atomic parameters are given in Table 1, where the atom designation of the IUPAC-IUB Commission on Biochemical Nomenclature (1970) is given. The thermal ellipsoids for the non-hydrogen atoms are illustrated in the *ORTEP* plot (Johnson, 1965) (Fig. 1). The atom-numbering scheme, the bond lengths and the bond angles are shown in Fig. 1. The average standard deviation in the bond lengths is 0.005 Å and in the bond angles 0.3°.\*

\* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 34509 (6 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 5 Abbey Square, Chester CH1 2HU, England.

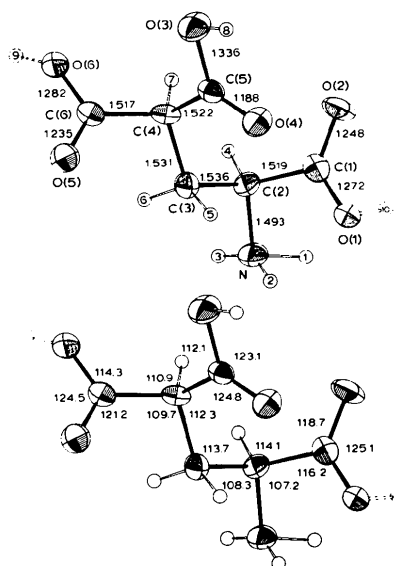


Fig. 1. An *ORTEP* plot of the molecule showing the atom-numbering scheme, the bond lengths (Å), and the bond angles (°). The thermal ellipsoids are drawn at the 50% probability level.

Table 1. *Positional parameters* ( $\times 10^4$ , for H  $\times 10^3$ ) for L- $\gamma$ -carboxyglutamic acid

Atom designation is in accordance with the IUPAC-IUB Commission on Biochemical Nomenclature (1970). Standard deviations are given in parentheses and refer to the least significant digit.

|   | x         | y        | z        |
|---|-----------|----------|----------|
| O(1)                                    | -965 (5)  | 4386 (3) | -869 (3) |
| O(2)                                    | 1510 (5)  | 2448     | -396 (3) |
| O(3)-O <sub>i</sub> 2,1                 | 1223 (5)  | 1511 (3) | 4659 (3) |
| O(4)-O <sub>i</sub> 2,2                 | -1187 (5) | 2918 (3) | 2730 (3) |
| O(5)-O <sub>i</sub> 1,2                 | 3148 (5)  | 4918 (3) | 6422 (3) |
| O(6)-O <sub>i</sub> 1,1                 | 6345 (5)  | 3304 (3) | 6549 (3) |
| N                                       | 3468 (5)  | 5949 (3) | -61 (4)  |
| C(1)                                    | 1162 (6)  | 3725 (4) | -233 (4) |
| C(2)-C <sub><math>\alpha</math></sub>   | 3396 (7)  | 4577 (3) | 832 (4)  |
| C(3)-C <sub><math>\beta</math></sub>    | 3009 (7)  | 4847 (4) | 2716 (4) |
| C(4)-C <sub><math>\gamma</math></sub>   | 3392 (6)  | 3549 (3) | 3875 (4) |
| C(5)-C <sub><math>\delta</math></sub> 2 | 862 (6)   | 2659 (3) | 3677 (4) |
| C(6)-C <sub><math>\delta</math></sub> 1 | 4298 (6)  | 3977 (3) | 5759 (4) |
| H(1)                                    | 316       | 570      | -149     |
| H(2)                                    | 507       | 626      | 40       |
| H(3)                                    | 182       | 627      | -24      |
| H(4)                                    | 533       | 412      | 105      |
| H(5)                                    | 92        | 517      | 244      |
| H(6)                                    | 456       | 545      | 327      |
| H(7)                                    | 481       | 293      | 358      |
| H(8)                                    | -90       | 125      | 443      |
| H(9)                                    | 757       | 341      | 736      |
| H(10)                                   | -308      | 417      | -186     |

**Discussion.** The molecule exists in the crystal as a zwitterion. The amino group is protonated while the C(2) carboxyl group and the O(6)-C(6)-O(5) carboxyl group share a proton, *i.e.* these two carboxyl groups are partially ionized. The carboxyl group O(3)-C(5)-O(4) is neutral. The difference in the C-O bond lengths of the partially ionized carboxyl group of C(4) (0.047 Å) is greater than the difference in the C-O bond distances of the partially ionized carboxyl group of C(2) (0.024 Å) and indicates that the H atom is perhaps attached more often to O(6) than to O(1). The O-C-O angle is 125.1 (3)° for the C(2) carboxyl group and 124.5 (3)° for the C(4) carboxyl group.

The three Csp<sup>3</sup>-Csp<sup>2</sup> bond lengths in this structure are all longer than the usual value of 1.50 Å. The lengthening of the C(1)-C(2) bond, commonly found in amino acids, has been attributed to the non-bonded interaction of the amino N atom and the carboxyl O atom (Sundaralingam & Putkey, 1970). It is likely that similar non-bonded interactions between C(3), and O(4) and O(5) influence the lengths of the Csp<sup>3</sup>-Csp<sup>2</sup> bonds on C(4).

The angles around C(4) and involving the group O(4)-C(5)-O(3) are different from the angles involving the O(5)-C(6)-O(6) carboxyl group (Fig. 1). This is perhaps due to the unusual conformation of the un-ionized carboxyl group, which places C(3) and O(4)

in an eclipsed position across the bond C(3)-C(4), and the resulting steric repulsion of H(5) and C(3) with O(4).

The angle between the least-squares planes *A*, *B*, *C* of the three carboxyl groups [C(1), C(2), O(1), O(2); C(4), C(5), O(3), O(4); and C(4), C(6), O(5), O(6)] are  $A-B = 142^\circ$ ,  $B-C = 105^\circ$ ,  $A-C = 40^\circ$ .

Some relevant torsion angles are listed in Table 2. The carbonyl O(4) is essentially eclipsed with C(3) ( $\chi^{3,2,2} = 0.5^\circ$ ). The molecule assumes an extended conformation: C(4) *trans* to N and C(6) *trans* to C(2). The torsion about the C(1)-C(2) bond is large ( $\psi = -39.1^\circ$ ). The N atom deviates from the four-atom plane formed by the C(2) carboxyl group and C(4) by 0.828 Å. Presumably, rotation about C(1)-C(2) from the usual value of  $\psi = 0^\circ$  positions the O atoms of the C(2) carboxyl group to relieve the close contacts with O(4). A similar feature is found in the structure of the ammonium salt of  $\gamma$ -carboxyglutamic acid (Satyshur, Rao, Stenflo & Suttie, 1979).

The protonated amino group and the hydroxyl group of the neutral carboxyl group O(4)-C(5)-O(3) are donors in hydrogen bonds to O atoms of four neighboring molecules. Translation-related molecules form the fifth interaction through the O(1)···O(6) hydrogen bond. The hydrogen-bonding scheme is illustrated in Fig. 2 and the distances and angles are given in Table 3.

H(1) on the protonated amino group is involved in an apparent bifurcated hydrogen bond to two acceptor atoms, O(4) and O(5), of two neighboring molecules. The distance involving O(4) is longer than the normal H···O distance while that involving O(5) is shorter. H(1) lies in the plane formed by O(4), O(5) and N (deviation = 0.22 Å). This geometry is typical of bifurcated hydrogen bonds (Parthasarathy, 1969; Koetzle, Hamilton & Parthasarathy, 1972).

In the O(6)···O(1) hydrogen bond, the O···O distance is 2.455 Å, 0.25 Å shorter than the usual

Table 2. *Torsional angles in the structure of L- $\gamma$ -carboxyglutamic acid*

Standard deviations are given in parentheses and refer to the least significant digit.

|                     | Conventional* designation |            |
|---------------------|---------------------------|------------|
| N-C(2)-C(1)-O(1)    | $\psi$                    | -39.1 (3)° |
| N-C(2)-C(3)-C(4)    | $\chi^1$                  | -169.8 (3) |
| C(1)-C(2)-C(3)-C(4) |                           | 70.9 (3)   |
| C(2)-C(3)-C(4)-C(6) | $\chi^{2,1}$              | 153.0 (4)  |
| C(2)-C(3)-C(4)-C(5) | $\chi^{2,2}$              | -83.2 (4)  |
| C(3)-C(4)-C(6)-O(6) | $\chi^{3,1,1}$            | -131.0 (4) |
| C(3)-C(4)-C(5)-O(3) | $\chi^{3,2,1}$            | 178.5 (3)  |
| C(3)-C(4)-C(6)-O(5) | $\chi^{3,1,2}$            | 47.6 (5)   |
| C(3)-C(4)-C(5)-O(4) | $\chi^{3,2,2}$            | 0.5 (2)    |

\* Convention adopted by the IUPAC-IUB Commission on Biochemical Nomenclature (1970).

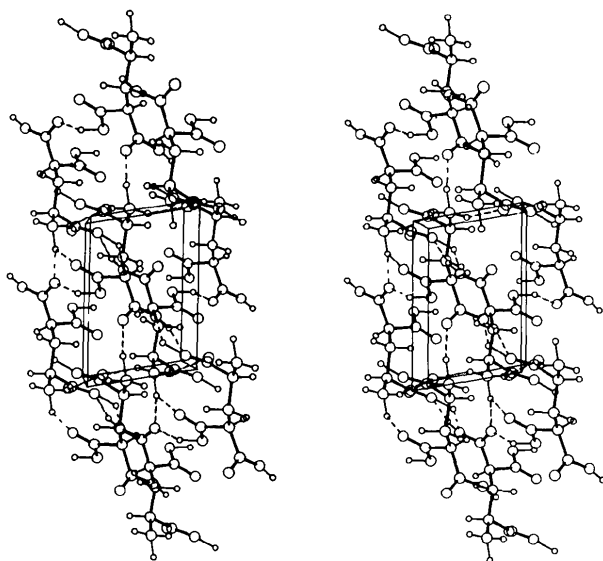


Fig. 2. A stereo packing diagram viewed down the  $b$  axis ( $a$  axis horizontal,  $c$  axis vertical). Dashed lines indicate hydrogen bonds.

distance (Hamilton & Ibers, 1968), and indicates a strong interaction between the O atoms of the two carboxyl groups. The H atom involved in this O—H $\cdots$ O bond is shared by both O atoms and occupies two sites. This sharing of a proton by the partially ionized carboxyl groups is perhaps an effect of crystal-packing constraints and in solution the C(2) carboxyl group would be expected to be fully ionized.

O(4) is also involved in an intermolecular C(4)—H(7) $\cdots$ O(4) interaction. The C $\cdots$ O distance is 3.08 Å, H(7) $\cdots$ O(4) is 2.23 Å, and the H(7)—C(4) $\cdots$ O(4) angle is 25°. The typical C $\cdots$ O and H $\cdots$ O distances in such an interaction are 3.2 and 2.3 Å respectively (Hamilton & Ibers, 1968). The electron-withdrawing power of the carboxyl groups on C $_{\gamma}$  probably results in stabilization of carbanion formation at C $_{\gamma}$  upon loss of the proton at the carboxyl group and promotes such a (C—H $^{\delta+}$  $\cdots$ O $^{\delta-}$ ) stabilizing interaction.

The network of hydrogen bonds forms a tightly packed crystal lattice, as is to be expected from the relatively high value for the density (1.70 Mg m $^{-3}$ ) of the crystal. There are no intermolecular short contacts in the structure.

Table 3. Hydrogen-bond distances and angles

| $A-B-H\cdots C-D$                  | Symmetry operation | H $\cdots$ C | B $\cdots$ C | $\angle H-B-C$ |
|------------------------------------|--------------------|--------------|--------------|----------------|
| C(2)—N—H(1) $\cdots$ O(5)—C(6)     | (a)                | 1.79 Å       | 2.892 Å      | 9°             |
| C(2)—N—H(1) $\cdots$ O(4)—C(4)     | (b)                | 2.47         | 2.898        | 57             |
| C(2)—N—H(2) $\cdots$ O(2)—C(1)     | (c)                | 2.07         | 2.884        | 19             |
| C(2)—N—H(3) $\cdots$ O(2)—C(1)     | (b)                | 2.15         | 2.971        | 18             |
| C(5)—O(3)—H(8) $\cdots$ O(5)—C(6)  | (d)                | 1.76         | 2.697        | 24             |
| C(6)—O(6)—H(9) $\cdots$ O(1)—C(1)  | (e)                | 1.73         | 2.455        | 21             |
| C(1)—O(1)—H(10) $\cdots$ O(6)—C(6) | (f)                | 1.48         | 2.455        | 27             |
| Average standard deviation         |                    |              | 0.008        |                |

#### Symmetry code

|     |        |          |        |     |         |           |        |
|-----|--------|----------|--------|-----|---------|-----------|--------|
| (a) | $x,$   | $y,$     | $-1+z$ | (d) | $-x,$   | $-0.5+y,$ | $1-z$  |
| (b) | $-x,$  | $0.5+y,$ | $-z$   | (e) | $1+x,$  | $y,$      | $1+z$  |
| (c) | $1-x,$ | $0.5+y,$ | $-z$   | (f) | $-1+x,$ | $y,$      | $-1+z$ |

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