

The Structure of a 1 : 1 Mixed Crystal of L-Glutamic Acid and L-Pyroglutamic Acid, $C_5H_9NO_4 \cdot C_5H_7NO_3 \cdot H_2O$, and a Refinement of the Structure of Pyroglutamic Acid, $C_5H_7NO_3$ *

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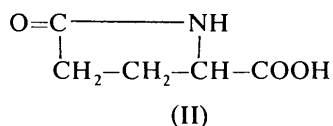
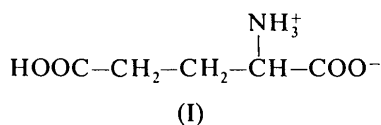
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L-Glutamic acid and L-pyroglutamic acid co-crystallize with one molecule of water to form a structure with an extensive network of hydrogen bonds. The mixed crystal of $C_5H_9NO_4 \cdot C_5H_7NO_3 \cdot H_2O$ belongs to the monoclinic space group $P2_1$ with $a = 18.473$ (5), $b = 7.190$ (1), $c = 5.113$ (1) Å, $\beta = 96.77$ (2)°, $U = 674.3$ (5) Å³ and $Z = 2$. Data were collected by counter techniques and the model was refined to an R factor of 0.0685 utilizing 1178 reflections. L-Glutamic acid exists as the zwitterion in the mixed crystal and exhibits the same conformation as L-glutamic acid in the pure crystal. The C(7) and C(4) atoms are *gauche* with respect to C(5)–C(6). All bond lengths and angles are within 3σ of the neutron diffraction values reported for pure L-glutamic acid. Counter data were collected for pyroglutamic acid, $C_5H_7NO_3$, which crystallizes in the monoclinic space group $P2_1/a$ with $a = 9.194$ (2), $b = 8.744$ (1), $c = 7.976$ (2) Å, $\beta = 116.29$ (2)°, $U = 574.9$ (2) Å³ and $Z = 4$. The model was refined to an R factor of 0.042 using 1015 reflections. In the mixed crystal the five-membered ring of pyroglutamic acid is nearly planar with a maximum internal torsion angle of 4.3°; however, in the pure crystal it is intermediate between the envelope and half-chair conformations with a maximum torsion angle of -24.7° . The conformation of pyroglutamic acid in the mixed crystal is modified to accommodate the formation of a more extensive network of hydrogen bonds.

Introduction

As part of a program to investigate the conformations and interactions of amino acids and small polypeptides, we have prepared mixed crystals of various amino acids. The structure of a 1 : 1 molecular complex containing L-glutamic acid (I) and L-pyroglutamic acid (II) has been determined. The molecular conformations of the two amino acids are compared with the conformation of pure L-glutamic acid reported by Lehmann, Koetzle & Hamilton (1972) and with the refined structure of pyroglutamic acid reported in this paper. The conformation of pyroglutamic acid is modified considerably by changes in hydrogen bonding.



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Experimental

L-Glutamic acid–L-pyroglutamic acid–water

An aqueous solution containing equal molar ratios of L-glutamic acid and L-pyroglutamic acid yields crystals of a 1 : 1 molecular complex containing one molecule of water per asymmetric unit. A crystal of dimensions ca $0.5 \times 0.5 \times 0.2$ mm was selected for intensity and unit-cell measurements. The crystal was found to be monoclinic and room-temperature cell dimensions were obtained by a least-squares fit to 15 reflections. The angles 2θ , ω and χ were refined iteratively for each reflection.

Crystal data: $C_5H_7NO_3 \cdot C_5H_9NO_4 \cdot H_2O$, FW 294.27, $a = 18.473$ (5), $b = 7.190$ (1), $c = 5.113$ (1) Å, $\beta = 96.77$ (2)°, $U = 674.3$ (5) Å³, $Z = 2$, $F(000) = 312$, $\mu = 11.0$ cm⁻¹, $D_c = 1.449$ g cm⁻³. Space group $P2_1$ from systematic absences: $0k0$ when $k \neq 2n$.

The intensity data with $2\theta \leq 120^\circ$ were collected on a Syntex $P2_1$ diffractometer by the $\theta/2\theta$ scanning technique using graphite-monochromated Cu $K\alpha$ radiation ($\lambda = 1.54178$ Å) and a variable scan speed. A periodically monitored reflection showed no significant crystal deterioration. Of the 1241 independent reflections measured, 1178 had intensities greater than $3\sigma(I)$, where $\sigma(I)$ was determined from counting statistics. Lorentz and polarization corrections were applied, but no absorption corrections were made.

Pyroglutamic acid

Crystal data: $C_5H_7NO_3$, $M_r = 129.12$, $a = 9.194$ (2), $b = 8.744$ (1), $c = 7.976$ (2) Å, $\beta = 116.29$ (2)°, $U = 574.9$ (2) Å³, $Z = 4$, $F(000) = 272$, $\mu = 10.8$ cm⁻¹, $D_c = 1.492$ g cm⁻³. Space group $P2_1/a$ from systematic absences: $h0l$ when $h \neq 2n$, $0k0$ when $k \neq 2n$.

Unit-cell measurements and data-collection procedures were similar to those used for the mixed crystal. Of the 1157 independent reflections measured, 1015 had intensities greater than $3\sigma(I)$. The unit-cell dimensions differ significantly from those reported by Pattabhi & Venkatesan (1972).

Structure determination and refinement*L-Glutamic acid–L-pyroglutamic acid–water*

The unit-cell dimensions of L-glutamic acid (Hirokawa, 1955; Lehmann, Koetzle & Hamilton, 1972) are similar to those of the mixed crystal. The molecular orientation and packing in the mixed crystal was assumed to be similar to that in L-glutamic acid and the coordinates for ten atomic positions from the L-glutamic acid structure were selected. A structure factor calculation yielded an R factor of 0.46 and a Fourier map revealed the positions of three additional atoms. Subsequent least-squares refinements followed by difference Fourier maps revealed the positions of all non-hydrogen atoms. After refinement with anisotropic thermal parameters all H atoms were located in a difference map. The H atom contributions to the structure factors were calculated, but the positional and thermal parameters were not refined. A final least-squares refinement reduced R to 0.0685 using the 1178 reflections with $I > 3\sigma(I)$, where $R = (\sum \Delta F_{\text{meas}} / \sum |F_{\text{meas}}|)$. The function minimized was $\sum w(\Delta F_{\text{meas}})^2$, where $w = 1/\sigma^2(F)$; however, w was set equal to unity during the final stages of the refinement. The scattering factors of all atoms were taken from *International Tables for X-ray Crystallography* (1974). All parameter shifts during the final cycle were less than 0.2 of the associated standard deviation, and a final difference Fourier map showed no peak as large as that expected for a H atom. Atomic parameters are listed in Table 1.*

Pyroglutamic acid

The structure was solved by direct methods using *MULTAN* (Germain, Main & Woolfson, 1971) and the

* Lists of structure factors and thermal parameters have been deposited with the British Library Lending Division as Supplementary Publication No. SUP 32834 (16 pp.). Copies may be obtained through The Executive Secretary, International Union of Crystallography, 13 White Friars, Chester CH1 1NZ, England.

Table 1. Atomic positional parameters ($\times 10^4$, for H $\times 10^3$) for the crystal of L-glutamic acid–L-pyroglutamic acid–water

	x	y	z
O(1)	51 (2)	3200 (0)	-1748 (8)
C(2)	51 (3)	3510 (10)	676 (11)
O(3)	-479 (2)	3442 (9)	1944 (8)
C(4)	796 (3)	3918 (9)	2223 (11)
C(5)	1117 (3)	2045 (10)	3280 (13)
C(6)	1827 (3)	2103 (11)	5072 (13)
C(7)	2466 (3)	2783 (11)	3785 (14)
O(8)	3087 (2)	2614 (9)	5377 (10)
O(9)	2441 (2)	3341 (9)	1576 (10)
N(10)	695 (3)	5232 (8)	4435 (10)
O(11)	1767 (3)	8067 (9)	10492 (9)
C(12)	2217 (3)	7263 (10)	9108 (14)
O(13)	2066 (2)	6607 (9)	6943 (10)
C(14)	2990 (4)	7291 (11)	10504 (14)
C(15)	3343 (4)	9232 (12)	10678 (18)
C(16)	4052 (6)	8984 (14)	9350 (27)
C(17)	4051 (4)	7079 (12)	8337 (18)
N(18)	3472 (3)	6205 (9)	8977 (15)
O(19)	4518 (3)	6434 (10)	7093 (15)
O(20)	4286 (3)	3512 (13)	3624 (15)
H(4)	111	452	81
H(5a)	103	108	172
H(5b)	69	131	392
H(6a)	191	62	562
H(6b)	180	263	677
H(8)	352	317	482
H(10a)	53	622	363
H(10b)	113	518	520
H(10c)	55	485	601
H(11)	115	840	993
H(14)	307	722	1285
H(15a)	335	961	1248
H(15b)	300	981	952
H(16a)	440	893	1130
H(16b)	400	1040	963
H(18)	335	510	838
H(20a)	472	328	288
H(20b)	442	465	443

Table 2. Atomic positional parameters ($\times 10^4$, for H $\times 10^3$) for pyroglutamic acid

The numbering system was chosen to correspond to that of the pyroglutamic acid molecule in Table 1.

	x	y	z
O(11)	2828 (2)	3883 (2)	3783 (2)
C(12)	3687 (2)	2646 (2)	4483 (3)
O(13)	4263 (2)	1875 (2)	3692 (2)
C(14)	3805 (2)	2282 (2)	6393 (3)
C(15)	4309 (3)	3633 (2)	7756 (3)
C(16)	5313 (3)	2887 (2)	9661 (3)
C(17)	5868 (2)	1405 (2)	9203 (3)
N(18)	5060 (2)	1147 (2)	7373 (2)
O(19)	6901 (2)	523 (2)	10324 (2)
H(11)	267	401	266
H(14)	265	183	598
H(15a)	322	415	757
H(15b)	493	434	735
H(16a)	450	299	1031
H(16b)	622	355	1045
H(18)	511	25	685

coordinates correspond to those reported by Pattabhi & Venkatesan (1972). H atom coordinates were obtained from a difference map and H atom contributions to the structure factors were calculated but the parameters were not refined. Least-squares refinement with anisotropic thermal parameters yielded a final R value of 0.042 using the 1015 reflections with $I > 3\sigma(I)$. All parameter shifts during the final cycle were less than 0.1 of the associated standard deviation, and a final difference map showed no peak as great as that expected for a H atom. Atomic parameters are listed in Table 2.*

Discussion

Table 3 contains the interatomic distances and bond angles for L-glutamic acid and L-pyroglutamic acid in the mixed crystal and for the refined model of pyro-

* See previous footnote.

Table 3. Bond distances (Å) and angles (°) for L-glutamic acid–L-pyroglutamic acid–water and DL-pyroglutamic acid

L-Glutamic acid			
O(1)–C(2)	1.260 (7)	C(5)–C(6)	1.509 (8)
C(2)–C(4)	1.533 (7)	C(7)–O(8)	1.332 (7)
O(3)–C(2)	1.237 (6)	C(6)–C(7)	1.499 (8)
C(4)–C(5)	1.543 (9)	C(7)–O(9)	1.195 (9)
C(4)–N(10)	1.502 (8)	O(1)C(2)C(4)	115.9 (4)
O(1)C(2)O(3)	126.9 (5)	C(4)C(5)C(6)	117.3 (6)
O(3)C(2)C(4)	117.1 (5)	C(5)C(6)C(7)	114.5 (6)
C(2)C(4)C(5)	107.3 (5)	C(6)C(7)O(8)	111.6 (6)
C(2)C(4)N(10)	108.9 (4)	C(6)C(7)O(9)	125.4 (5)
C(5)C(4)N(10)	111.2 (5)	O(8)C(7)O(9)	122.9 (5)
Pyroglutamic acid			
	Mixed crystal	Pure sample	
O(11)–C(12)	1.291 (7)	1.309 (2)	
O(13)–C(12)	1.206 (9)	1.196 (2)	
C(12)–C(14)	1.519 (9)	1.513 (3)	
C(14)–C(15)	1.539 (11)	1.532 (3)	
C(14)–N(18)	1.475 (9)	1.459 (2)	
C(15)–C(16)	1.556 (13)	1.531 (3)	
C(16)–C(17)	1.465 (13)	1.496 (2)	
C(17)–N(18)	1.315 (9)	1.332 (3)	
C(17)–O(19)	1.222 (10)	1.247 (2)	
O(11)C(12)O(13)	125.7 (5)	124.4 (2)	
O(11)C(12)C(14)	111.5 (6)	111.4 (1)	
O(13)C(12)C(14)	122.7 (5)	124.2 (2)	
C(12)C(14)C(15)	114.0 (6)	114.6 (1)	
C(12)C(14)N(18)	109.6 (6)	111.7 (1)	
C(15)C(14)N(18)	103.5 (5)	103.0 (2)	
C(14)C(15)C(16)	104.1 (7)	103.6 (1)	
C(15)C(16)C(17)	107.2 (7)	104.3 (2)	
C(16)C(17)N(18)	109.0 (7)	109.2 (2)	
C(17)N(18)C(14)	116.0 (7)	113.4 (2)	
C(16)C(17)O(19)	124.6 (8)	126.6 (2)	
N(18)C(17)O(19)	126.4 (8)	124.2 (2)	

glutamic acid. Table 4 gives the torsion angles while Table 5 summarizes the hydrogen bonds. Fig. 1 is an *ORTEP* (Johnson, 1965) drawing of the two molecules in the mixed crystal and Fig. 2 is an *ORTEP* plot of pyroglutamic acid. The numbering system for pyroglutamic acid is the same as that used in describing the structure of the mixed crystal.

The non-hydrogen bond lengths for L-glutamic acid in the mixed crystal differ by less than 2σ from those reported for the neutron diffraction study of pure L-glutamic acid (Lehmann, Koetzle & Hamilton, 1972), except for C(7)–O(8) and C(7)–O(9) which differ by almost 3σ . The bond angles show equally good agreement. In the mixed crystal C–H bond distances range from 0.91 to 1.19 Å with an average of 1.04 Å while N–H distances range from 0.85 to 0.92 Å with an average of 0.87 Å. Although L-glutamic acid exists as the zwitterion, the C(2)–O(1) and C(2)–O(3) distances of 1.260 (7) and 1.237 (6) Å differ by more than 3σ . The non-equivalence may be associated with the difference in hydrogen bonding. The amino and carboxyl groups are not coplanar, as indicated by the O(3)C(2)C(4)N(10) torsion angle of -34.5° . The conformation of the glutamic acid chain is similar to that reported for pure glutamic acid with C(7) *gauche*

Table 4. Torsion angles (°) for L-glutamic acid–L-pyroglutamic acid–water and DL-pyroglutamic acid

Standard deviations average 0.8° for the mixed crystal and 0.3° for DL-pyroglutamic acid.

L-Glutamic acid	Mixed crystal	Neutron data*
O(1)C(2)C(4)C(5)	-91.0	
O(1)C(2)C(4)N(10)	148.5	141.2
O(3)C(2)C(4)C(5)	86.1	
O(3)C(2)C(4)N(10)	-34.5	-42.5
C(2)C(4)C(5)C(6)	-175.0	
N(10)C(4)C(5)C(6)	-55.9	-51.8
C(4)C(5)C(6)C(7)	-65.2	-73.1
C(5)C(6)C(7)O(8)	-173.3	-160.7
C(5)C(6)C(7)O(9)	3.8	18.8
Pyroglutamic acid	Mixed crystal	Pure crystal
O(11)C(12)C(14)C(15)	-69.9	-49.5
O(13)C(12)C(14)C(15)	108.2	132.7
O(11)C(12)C(14)N(18)	174.6	-166.2
O(13)C(12)C(14)N(18)	-7.3	16.1
C(12)C(14)C(15)C(16)	-123.4	-146.2
C(12)C(14)N(18)C(17)	125.3	142.7
N(18)C(14)C(15)C(16)	-4.3	-24.7
C(14)C(15)C(16)C(17)	4.3	22.4
C(15)C(16)C(17)N(18)	-2.5	-11.7
C(16)C(17)N(18)C(14)	-0.5	-4.9
C(17)N(18)C(14)C(15)	3.3	19.1
C(15)C(16)C(17)O(19)	177.3	169.2

* Lehmann, Koetzle & Hamilton (1972).

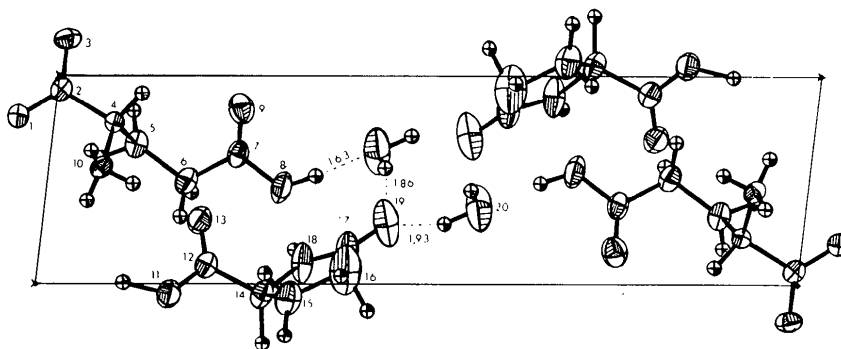


Fig. 1. Unit-cell contents of the mixed crystal L-glutamic acid-L-pyroglutamic acid-water viewed along the b axis. The a axis is horizontal.

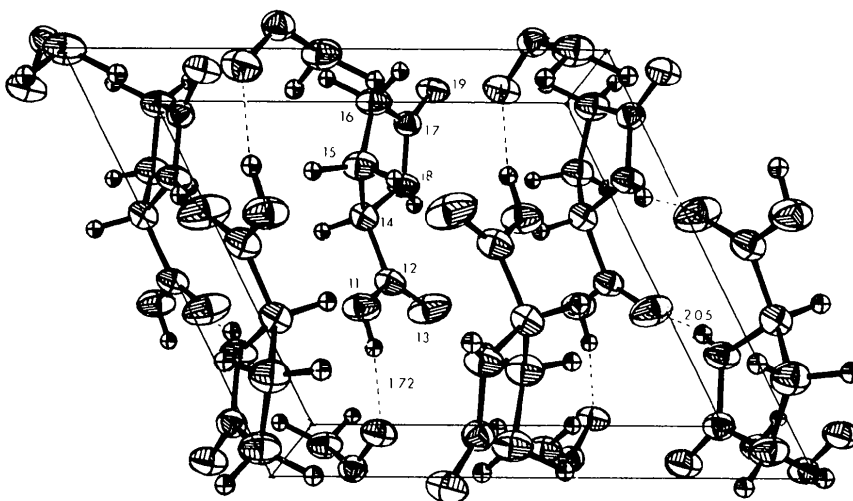


Fig. 2. Crystal-packing diagram for DL-pyroglutamic acid. The a axis is horizontal and the b axis goes into the plane of the drawing.

Table 5. Hydrogen-bond distances (\AA) and angles ($^\circ$) for the mixed crystal L-glutamic acid-L-pyroglutamic acid-water

A	H	B	$A-H$	$H \cdots B$	$A \cdots B$	$\angle A-H-B$
O(8)	H(8)	O(20)	0.97	1.63	2.568	164
N(10)	H(10a)	O(1')	0.85	1.97	2.809	167
N(10)	H(10b)	O(13)	0.85	2.11	2.875	148
N(10)	H(10c)	O(1'')	0.92	1.93	2.811	154
O(11)	H(11)	O(3')	1.17	1.48	2.566	152
O(20)	H(20a)	O(19)	0.94	1.93	2.727	141
O(20')	H(20b')	O(19)	0.94	1.86	2.750	157

(synclinal) to C(4) with respect to the C(5)-C(6) bond, $C(4)C(5)C(6)C(7) = -65.2^\circ$.

The network of hydrogen bonds in the mixed crystal is similar to that reported for the structure of pure L-glutamic acid (Lehmann, Koetzle & Hamilton, 1972). The terminal carboxyl H(8) is hydrogen bonded

strongly to a water molecule, $O(20) \cdots H(8) = 1.63 \text{ \AA}$. Carboxyl O(9) does not participate in hydrogen-bond formation although it experiences a short van der Waals contact with an aliphatic H atom. All three amino H atoms form hydrogen bonds with $H(10a) \cdots O(1') = 1.97$, $H(10b) \cdots O(13) = 2.11$ and

$H(10c) \cdots O(1'') = 1.93 \text{ \AA}$. The carboxyl $O(11)$ of an L-pyroglutamic acid molecule is hydrogen bonded to $O(3')$ of an L-glutamic acid, $H(11) \cdots O(3') = 1.48 \text{ \AA}$. The carbonyl $O(19)$ is bound to the H atoms of two different water molecules with $O(19) \cdots H(20a) = 1.93$ and $O(19) \cdots H(20b') = 1.86 \text{ \AA}$. Although the amine H atom of pyroglutamic acid is directed toward $O(8)$ of a glutamic acid molecule, the $N(16) \cdots O(8)$ distance is 3.207 \AA , indicating a very weak interaction. The network of hydrogen bonds stabilizes the structure and must be similar in stability to that in pure L-glutamic acid because of the ease of co-crystallization.

The conformation of L-glutamic acid in the mixed crystal is the same as that in pure L-glutamic acid; however, the conformation of L-pyroglutamic acid differs significantly from that of DL-pyroglutamic acid in the pure crystal. The five-membered ring in the mixed crystal is nearly planar with a maximum internal torsion angle of 4.3° , with $\Delta = 4.3^\circ$ and $\varphi_m = 4.7^\circ$ (Altona, Geise & Romers, 1968), and $O(19)$ is coplanar with the ring. The five-membered ring in the pure crystal is intermediate between the half-chair and envelope conformations with $\Delta = 15.1^\circ$ and $\varphi_m = 24.9^\circ$. The torsion angles range from -24.7° to $+19.1^\circ$. Two hydrogen bonds, $H(11) \cdots O(19') = 1.72$ and $H(18') \cdots O(13) = 2.05 \text{ \AA}$, are found in the

structure of DL-pyroglutamic acid. The conformation of pyroglutamic acid in the mixed crystal is modified to accommodate the formation of a more extensive network of hydrogen bonds.

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Structure Cristalline du Complexe 4,4',5,5'-Tétraéthyltétrathiofulvalène-Bis(tétracyanoquinodiméthane), (TETTF)(TCNQ)₂

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The crystal structure of the complex (TETTF)(TCNQ)₂ has been determined by single-crystal X-ray techniques. This compound is monoclinic, space group *C2/c*, with $a = 23.64 (1)$, $b = 13.838 (6)$, $c = 22.61 (1) \text{ \AA}$, $\beta = 150.6 (1)^\circ$, $Z = 4$, $\rho_m = 1.32 \text{ g cm}^{-3}$. Intensities of 2894 reflexions were collected on an automatic diffractometer and 1678 of these were used for the structure determination. The structure was solved by Patterson and Fourier methods and refined by least-squares calculations to a final R of 0.055. The packing comprises columns of molecules parallel to the c axis. In each column the sequence is \cdots TETTF–TCNQ–TCNQ–TETTF \cdots and this explains the non-conductivity of the material.

Dans le cadre de la recherche de nouveaux conducteurs organiques, la synthèse des complexes formés en associant le tétracyanoquinodiméthane (TCNQ) avec

des dérivés du tétrathiofulvalène (TTF) a été entreprise dans le laboratoire du Professeur Giral (Chimie Organique, Université des Sciences et Techniques du