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A note on *cyclo*-(hexaglycyl).

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In the preparation of polyglycine from glycine N-carbonic anhydride Ballard, Bamford & Weymouth (1955) found that a considerable amount of low molecular weight material was produced. The bulk of this material was found to be *cyclo*-(hexaglycyl), and various crystalline forms were obtained. An X-ray investigation has confirmed the molecular weight of this substance and provided more precise information on the degree of hydration of the crystals. The monohydrate and hemihydrate have been isolated and though the crystal material, particularly in the case of the monohydrate, is poor, some preliminary crystal measurements have been made. A comparison of infra-red spectra suggests that the anhydrous material has also been isolated (Holliday, unpublished). This latter material forms very small, fine crystals, identifiable only under the microscope, and so far only powder data have been obtained. Both hydrates show subsidiary or 'ghost' X-ray reflexions indicative of a periodic error in the structure, possibly due to the inclusion of water.

cyclo-(Hexaglycyl) monohydrate crystallizes from aqueous solution cooled to 25° C. in the form of acicular and prismatic crystals or as pseudo-hexagonal plates showing marked clumping. The crystal system is monoclinic and there is a pronounced pseudo unit cell of dimensions

$$a = 9{\cdot}5,\ b = 14{\cdot}5,\ c = 5{\cdot}7\ \text{Å},\ \beta = 93^\circ\ 12'$$

(c is the needle axis).

Molecular formula: $(CH_2CONH)_6.H_2O$; molecular weight = 360; volume of unit cell = 783·9 Å^3; calculated density = 1·525 g.cm.$^{-3}$, observed density = 1·517 g.cm.$^{-3}$; number of molecules in unit cell = 2. The space group of the cell is $P2_1/a$. Subsidiary reflexions indicate a larger unit cell of dimensions a, $2b$, $2c$, space group $A2/a$. The volume is four times that of the sub-cell and contains 8 molecules of *cyclo*-(hexaglycyl) monohydrate. The two space groups can be easily correlated, indicating possibilities for the structural dislocation.

cyclo-(Hexaglycyl) hemihydrate is crystallized from boiling aqueous solution by cooling to 60° C., and forms needles which may be twinned or aggregated. The crystal habit is prismatic, system triclinic. The crystals show oblique optical extinction in polarized light. The space group is probably $P\bar{1}$. There is a pseudo unit cell of dimensions

$$a = 10{\cdot}66,\ b = 15{\cdot}50,\ c = 4{\cdot}76\ \text{Å},$$
$$\alpha = 94^\circ\ 58',\ \beta = 98^\circ\ 40',\ \gamma = 90^\circ\ 1'.$$

The c axis is the needle axis of the crystal. Molecular formula: $(CH_2CONH)_6.\frac{1}{2}H_2O)$; molecular weight=351; volume of unit cell = 799·2 Å^3; calculated density = 1·496 g.cm.$^{-3}$, observed density = 1·501 g.cm.$^{-3}$; number of molecules in unit cell = 2. Subsidiary reflexions indicate a larger unit cell of dimensions $4a$, b, $4c$, containing 32 molecules of *cyclo*-(hexaglycyl) hemihydrate. The distribution of intensity in the subsidiary layer lines suggests that for both hydrates the larger unit cells arise from the occurrence of periodic faults in the packing of the molecules in the small unit cells. These faults appear to be associated with the water of crystallization.

Anhydrous *cyclo*-(hexaglycyl) is produced by crystallization of *cyclo*-(hexaglycyl) from monomethyl formamide. Powder photographs have been taken and measured. It is of interest that there is a very strong spacing at 4·12 Å. The observed reflexions show no hexagonal symmetry.

During the course of this work Sheehan & Richardson (1954) claimed the isolation of *cyclo*-(triglycyl) in two crystalline forms. Single crystals formed from material produced according to the method of Sheehan & Richardson give photographs corresponding to *cyclo*-(hexaglycyl) monohydrate and *cyclo*-(hexaglycyl) hemihydrate, and it is considered that they have in fact isolated *cyclo*-(hexaglycyl) not *cyclo*-(triglycyl) (Bamford & Weymouth, 1955).

Pauling & Corey (1952) have published a possible structure for a cyclic hexapeptide involving a *cis cis* configuration of the amide group and unfavourable orientation about the bonds to the α carbon atom. The structure is hexagonal and the rings are connected to each other in hexagonal array by intermolecular hydrogen bonding to form sheets. Only one such *cyclo*-(hexaglycyl) model can be constructed using *cis* amide groups; it indicates no position for enclosed water and shows marked hexagonal symmetry. This symmetry would be obvious on a single crystal or powder photograph and it is quite clear that such a structure does not occur among the cyclic glycine peptides investigated so far. In the hydrated forms the rings must be puckered or elongated, for a regular hexagon cannot be accommodated in either of the unit cells.

In addition to the crystalline forms discussed here *cyclo*-(hexaglycyl) can be prepared in at least two other forms. Further work on all forms is in progress.

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