The Crystal Structures of the Glycylglycine *O*-Ethyl Ester and Chloroaquo-complexes of β-(Triethylenetetramine)cobalt(III)

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IT was shown by Buckingham *et al.*[1] that the reaction of selected peptides with the β-hydroxo-aquotriethylenetetraminecobalt(III) ion results in a specific hydrolysis. The NH_2-terminal amino-acid of the peptide is cleaved and remains attached to the Co(trien) residue. Thus the hydrolysis of glycylglycine *O*-ethyl ester leads to the formation of the glycinatotriethylenetraminecobalt(III) complex ion. The complex ion (triethylenetetramine-*O*-ethylglycylglycine)cobalt(III) is an intermediate and can be isolated from the solution as a perchlorate.[2,3] The structure of this complex has now been established by an *X*-ray crystal structure analysis of $[Co(trien)(Gly–Gly–OEt)](ClO_4)_3,H_2O$ (V).

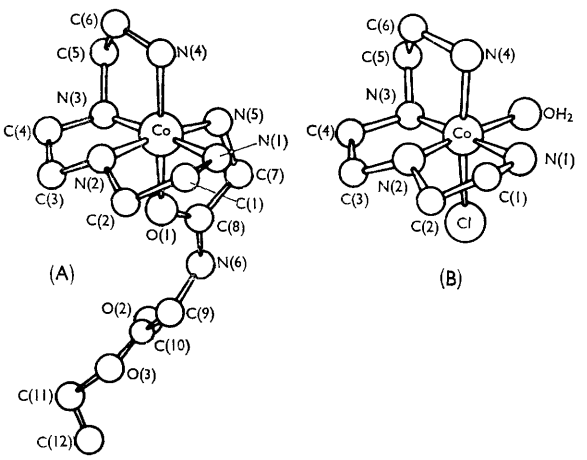


FIGURE (A). *Structure of the* β-$[Co(trien)(Gly–Gly–OEt)]^{3+}$ *ion.*
(B) *Structure of the* β-$[Co(trien)ClOH_2]^{2+}$ *ion.*

The peptide is co-ordinated through the terminal $-NH_2$ group and the carbonyl oxygen atom from the same amino-acid residue. As in other metal–peptide complexes,[4] the carbonyl oxygen atom O(1) is here preferred to the peptide nitrogen N(6) as a metal binding site at pH's where the peptide proton is not dissociated. This mode of co-ordination accounts for the ease of hydrolysis of the second residue of the dipeptide and for the reactivity of other related species:[5] the chelate ring is not required to break for hydrolysis to occur, and the positively charged metal ion renders the carbonyl carbon atom more susceptible to nucleophilic reagents.

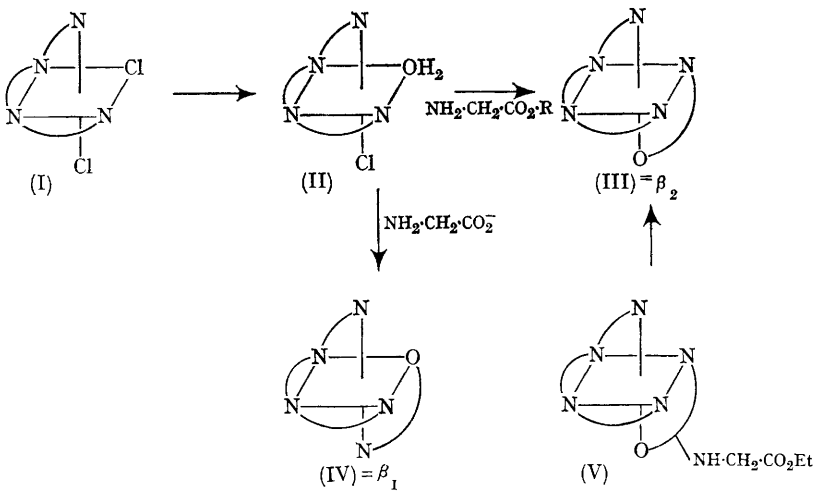
The structure analysis confirms the stereochemistry of the β-configuration of disubstituted triethylenetetraminecobalt(III) ions, as deduced from the kinetic data for the aquation of the β- and *trans*-dichloro-isomers.[6–10] The modes of aquation of (±)-*trans*-$[Co(trien)Cl_2]^+$ [6,10] and of optical isomers[9] have also been used to predict the positions of the OH_2 molecules and chloride ion in the β-chloroaquo-complex. These predictions are verified by the crystal structure analysis† of racemic β-$[Co(trien)ClOH_2](ClO_4)_2$.

Crystals of racemic β-(triethylenetetramine-*O*-ethylglycylglycine)cobalt(III) perchlorate hydrate, β-$[Co(trien)(Gly–Gly–OEt)](ClO_4)_3,H_2O$, are monoclinic with $a = 17{\cdot}94_7$, $b = 15{\cdot}96_9$, $c = 10{\cdot}19_3$ Å, $\beta = 106{\cdot}9°$, $D_m = 1{\cdot}71 \pm 0{\cdot}1$, $Z = 4$, $D_c = 1{\cdot}71$ g. cm.$^{-3}$; space group $P2_1/a$; 1983 *X*-ray reflections (710 unobservably weak).† At present the residual *R* is 0·13. The correctness of the structure is not in doubt, although the precision of the final result may be reduced by what appears to be disorder or free rotation of two perchlorate ions and disorder of the terminal ester group.

Crystals of racemic β-(chloroaquo-triethylenetetramine)cobalt(III) perchlorate, β-$[Co(trien)(Cl)(OH_2)](ClO_4)_2$, are orthorhombic, space group $Pna2_1$, with $a = 12{\cdot}09_0$, $b = 8{\cdot}34_0$, and $c = 15{\cdot}73_8$ Å, $D_m = 1{\cdot}90 \pm 0{\cdot}01$, $Z = 4$, $D_c = 1{\cdot}91$; 1592 *X*-ray reflections (466 unobservably weak).† After three cycles of full matrix least-squares refinement with isotropic and three cycles with anisotropic thermal parameters, the residual *R* is 0·074.

As shown in (B) and formula (II), the co-ordinated OH_2 molecule is *trans* to that secondary amine nitrogen, N(2), which connects the two chelate rings in the same co-ordination plane. The conformations of the chelate rings are the same

† Data for both structure analyses were recorded with Cu-K_α radiation, using a Supper equi-inclination diffractometer.



as those in the glycylglycine *O*-ethyl ester complex. Both structures have the proton on N(2) directed towards the apical chelate ring as required by previous kinetic and stereochemical studies in these and related complexes.[6–10] With this orientation of the proton on N(2), the distortion from tetrahedrality about N(2) is minimised if the co-planar chelate rings are mirror-images.[8–10] The occurrence of the same conformational arrangement in both $[Co(trien)(Gly–Gly–OEt)]^{3+}$ and $[Co(trien)ClOH_2]^{2+}$ is also in agreement with the conclusion[7] that it is the most stable one for the β-configuration.

The reactions of the β-chloroaquo-ion (II) with glycine ethyl ester and glycinato-ion, respectively, give two isomeric β-glycinato-complexes.[11] Formulae (III) and (IV) have been proposed for these, on the grounds that the co-ordinated water molecule is replaced by the basic $-NH_2$ group of the ester in one instance (β_2), and by the basic $-CO_2^-$ group in the other (β_1). This assignment is supported by both the present structure analyses, for the structure now established for the chloroaquo-ion is that on which the above reasoning was based, and the glycylglycine ethyl ester complex (V) is hydrolysed at pH 8–10 to the same β_2-glycinato-complex which is formed from the chloroaquo-ion and glycine ester.[2] The structure analysis of (V) thus confirms that the β_2-isomer has the configuration (III), provided that hydrolysis of the peptide proceeds without rupture of the chelate ring.

It has also been found that the β-dichlorotriethylenetetramine ion aquates to give largely the chloroaquo-isomer depicted in (A).[6,10] The ratio of the two possible chloroaquo-species was assessed as *ca.* 24 : 1,[10] but it was not apparent why the two sites in the parent dichloro-ion differ so much in reactivity for aquation. Conformationally the β-dichloro-ion must be substantially the same as that found for the β-chloroaquo-ion, (B) and (I). The present structure implies that non-bonded interactions between the bound Cl^- ions and the nearest ligand protons are insufficient to account for the large difference in reactivity. Though there is some evidence[10] to suggest that $\Delta H^{\ddagger}$ is significant in determining the rate ratio, this is not certain and the difference may reside substantially in the entropy of solvation for the transition states.

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