Stereoselective Chelate and Amino-acid Synthesis with Chelated 2-Iminopropionate; *X*-Ray Crystal and Molecular Structures of α-(N^2-2-Aminoethylamidino)-alaninato-*ONN''N'''*-(ethylenediamine)cobalt(III) and α-(N^2-2-Aminoethylamidino)alanine-*NN''N'''*-(chloro)ethylenediaminecobalt(III) Tetrachlorozincates

By JOHAN SPRINGBORG

(*The Royal Veterinary and Agricultural University, Chemistry Department, Thorvaldsenvej* 40-*DK* 1871 *Copenhagen, Denmark*)

RODNEY J. GEUE, ALAN M. SARGESON, and DONALD TAYLOR

(*The Research School of Chemistry, The Australian National University, Canberra, A.C.T.* 2600, *Australia*)

and MICHAEL R. SNOW

(*Department of Physical and Inorganic Chemistry, University of Adelaide, Adelaide, S. A.* 5001, *Australia*)

Summary An intramolecular reaction follows the rapid addition of CN^- at the imine centre of the bis(ethylenediamine)-2-iminopropionatocobalt(III) ion (**1**) where a deprotonated amine centre attacks the added CN group to give a quadridentate amidine with substantial stereospecificity; the crystal and molecular structures of the

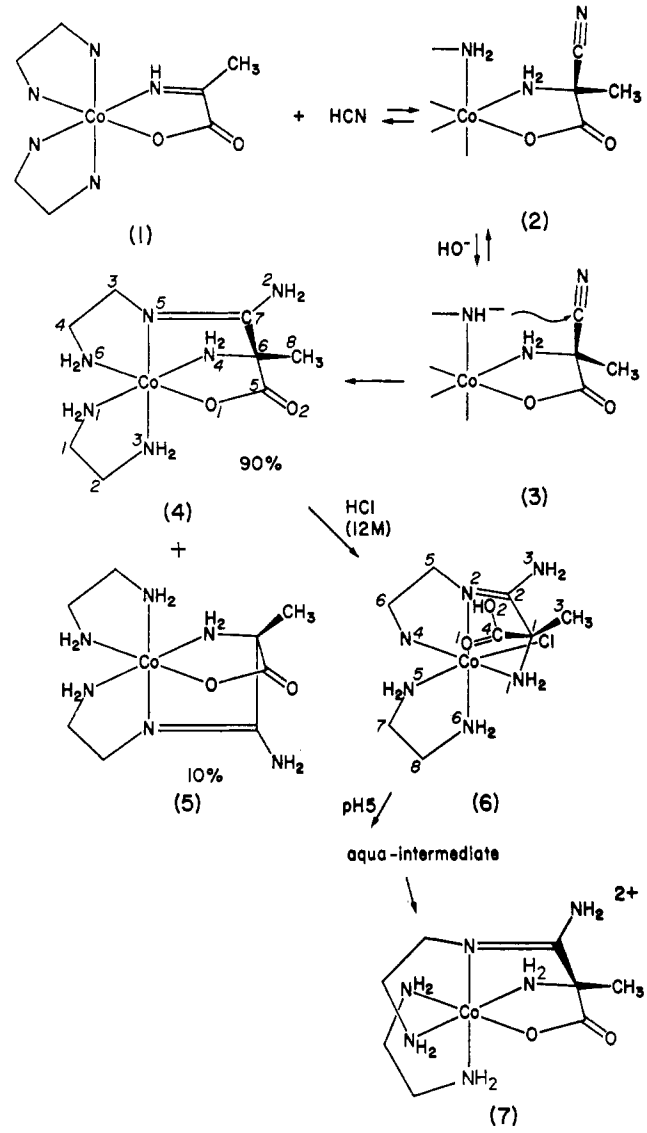
tetrachlorozincates of two inter-related complexes, α-(N^2-2-aminoethylamidino)alaninato-*ONN''N'''*-(ethylenediamine)cobalt (**4**) and α-(N^2-2-aminoethylamidino)alanine-*NN''N'''*-(chloro)ethylenediaminecobalt (**6**), have been determined.

THE chelated 2-iminopropionate in the bis(ethylenediamine)cobalt(III) ion (**1**) rapidly adds HCN at pH 8—10 ($t_{\frac{1}{2}}$ *ca.* 1 min; CN^- 0·1 M; 25 °C) to give the 2-cyano-alanine complex (**2**) which rapidly condenses [structure (**3**)] with a deprotonated ethylenediamine unit to form the quadridentate amidine products (**4**) (90%) and (**5**) (10%). The substantial stereoselectivity in the reaction is striking especially when it is realised that addition of CN^- at the imine centre in (**1**) is very likely to be non-specific in the sense that it can add equally easily to either side of the 2-iminopropionate chelate and that related reactions show little or no specificity and indicate a degree of reversibility.[1] We presume that the selectivity occurs during the irreversible[2] amidine formation.

An *X*-ray crystallographic analysis† shows that the most abundant product has the structure (**4**) which we would expect to be the more strained isomer largely because of the deformation about the bound amidine N atom and therefore less stable than its diastereoisomer (**5**). Subsequent chemistry shows this to be true.

Treatment of (**4**) with HCl (12 M) yields, nearly quantitatively, the chloro-complex (**6**) where a Co–carboxylate-O-bond has been cleaved. The reactant has undergone an edge displacement of the bound amidine chelate nitrogen atom to give the essentially planar tridentate (**6**) thereby relieving the strain in this entity. An *X*-ray crystallographic analysis† of this product establishes the structure (**6**). It is clear that under the conditions of the synthesis no rearrangement at the chiral carbon centre is possible and that structures (**4**) and (**6**) must have the same chirality at this site. It follows that the ethylenediamine chelates are orientated Λ about the cobalt(III) ion. The anation is relatively slow ($t_{\frac{1}{2}}$ *ca.* 4 h; 25 °C) and we presume that the rearrangement of the amidine chelate occurs during either the formation or the anation of an aqua-intermediate. However the ^1H n.m.r. spectra throughout the process are consistent only with the presence of the quadridentate reactant and the single chloro-complex (**6**). The concentration of the presumed aqua-complex must therefore be small, but nevertheless a path involving such a species would be more consistent with the general pattern of substitution in cobalt(III) amine complexes[3] than a path involving direct substitution of Cl^- and concomitant rearrangement.

Finally the chloro-complex (**6**) in aqueous solution at pH 5 releases Cl^- ($t_{\frac{1}{2}}$ *ca.* 5 min; 25 °C) to yield an aqua-intermediate which is observable by ^1H n.m.r. spectroscopy and which finally yields (quantitatively) the least strained diastereoisomeric form (**7**) in which the chiral C centre has



SCHEME. Addition of CN^- to the 2-iminopropionate bis(ethylenediamine)cobalt(III) ion (**1**) and the structures of complexes (**4**) and (**6**).† The numbering in structures (**4**) and (**6**) corresponds to the atomic numbering in the supplementary crystallograpic data.

† *Crystal data:* complex (**4**), $C_8H_{21}CoN_6O_2ZnCl_4 \cdot H_2O$, monoclinic, $a = 12{\cdot}654(6)$, $b = 11{\cdot}073(6)$, $c = 14{\cdot}06(7)$ Å, $\beta = 99{\cdot}72(5)°$, space group $P2_1/c$, $D_m = 1{\cdot}81(2)$, $D_c = 1{\cdot}77$ g cm^{-3} for $Z = 4$. Intensity data were measured on a STOE automatic Weissenberg diffractometer using graphite crystal-monochromated Mo-K_α radiation. The structure was solved by Patterson and difference Fourier techniques and refined by full-matrix least-squares on 2009 unique reflections with $I \geqslant 2\sigma(I)$ (corrected for absorption, $\mu = 26{\cdot}93$ cm^{-1}) to a final R factor of 0·033. Relevant bond lengths: Co–O, 1·93(1); Co–N(5), 1·90(1); Co–N(av.), 1·97(1); N(5)–C(7), 1·31(1); N(2)–C(7), 1·34(1); N–C, 1·47—1·53(1); C–C, 1·48—1·56(1); C(5)–O(1), 1·29(1); C(5)–O(2), 1·23(1) Å.

Crystal data: complex (**6**), $C_8H_{22}ClCoN_6O_2 \cdot ZnCl_4$, monoclinic, $a = 8{\cdot}340(1)$, $b = 11{\cdot}493(1)$, $c = 20{\cdot}789(1)$ Å, $\beta = 102{\cdot}91(1)°$, space group $P2_1/c$, $D_m = 1{\cdot}83(1)$, $D_c = 1{\cdot}83$ g cm^{-3} for $Z = 4$. Intensity data were collected on a Picker FACS-I diffractometer using graphite crystal-monochromated Cu-K_α radiation. The structure was solved by direct methods (MULTAN), and refined by full-matrix least-squares on 1565 reflections with $I \geqslant 3\sigma(I)$ (corrected for absorption, $\mu = 149{\cdot}0$ cm^{-1}) to a residual R of 0·052. Hydrogen atoms were included at calculated positions. Relevant bond lengths: Co–Cl, 2·26(1); Co–N(2), 1·88(1); Co–N(av.), 1·95(1); N(3)–C(2), 1·34(1); N(2)–C(2), 1·29(1); N–C(av.), 1·48(1); C–C, 1·48—1·54; C(4)–O(1), 1·24(1); C(4)–O(2), 1·30(1) Å.

The atomic co-ordinates for this work are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Rd., Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

the same configuration as (**4**) and (**6**) and the ethylenediamine chelates are arranged in the Δ configuration. This configuration resists further change at pH 7.

The origin of the stereoselectivity in the condensation is an interesting question. All indications point to the rate of condensation to the quadridentate amidine as the governing factor. This implies that HCN addition and loss is at least quasi-reversible on this time scale. Addition of NO_2Me has been shown to have this property in essentially analogous chemistry,[1] so it is not a radical proposal. The selectivity for the addition at the two possible sites on the ethylenediamine chelates can be ascribed to the orientation of the deprotonated lone pair of electrons. In the precursor to the favoured isomer the lone pair of electrons is directed towards the carbon atom of the nitrile in a manner ideal for formation of the activated complex. However in the precursor to the less favoured isomer the nitrile lies directly between the two possible sites for a lone pair of electrons and neither prospect leads to ideal geometry for the activated complex. The activation energy difference between the two products need only be 1·3 kcal mol^{-1} so it is not unreasonable that a rather subtle orbital steering of the nature outlined could account for the selectivity.

Finally it will be appreciated that release of the amino-acid by reduction of the cobalt(III) centre in aqueous acid will yield the chiral amino methyl malonic acid-half-amide. The chirality of this species will depend on the chirality of the reactant imine complex and if the diastereoisomer is isolated, the half amide should be optically pure.

Although the structural analyses have been carried out on racemate crystals, the arguments relating the chiralities of the bis(ethylenediamine)cobalt(III) units follow from the immutable carbon centre as described. The chemistry has also been carried out commencing with the Λ imine complex (**1**) and finishing with the Δ amidine quadridentate ion (**7**).[4]

The authors are grateful to Statens Naturvidenskabelige Forskningsraad for support (to J. S.) to allow this work to be undertaken.

(*Received*, 18*th April* 1978; *Com.* 404.)

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[3] A. M. Sargeson, *Pure Appl. Chem.*, 1973, **33**, 527, and references therein.
[4] J. Springborg, unpublished results.