Oxidation of Amino Acids Co-ordinated to Cobalt(III)

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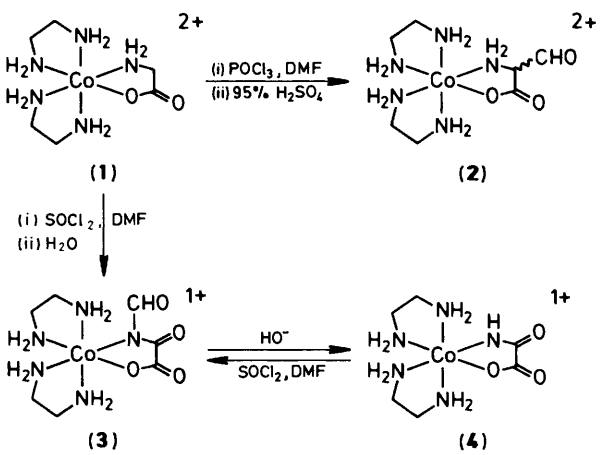
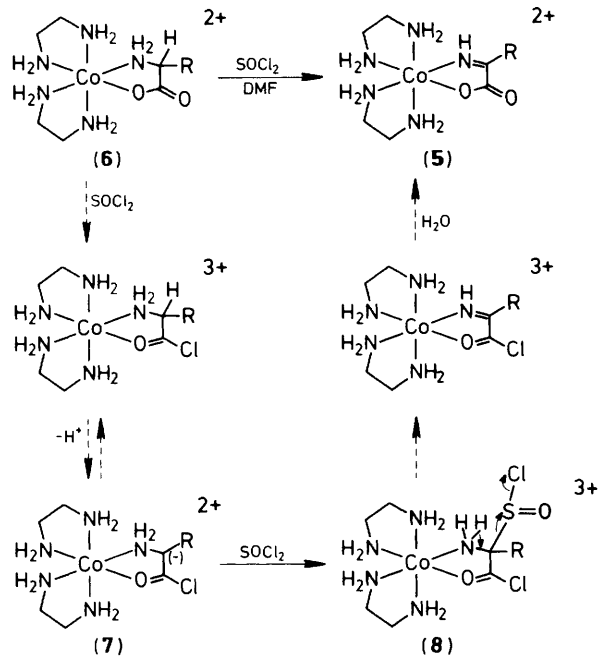
Rapid oxidation of chelated amino acids to imines and amides by thionyl chloride in *N,N*-dimethylformamide is described.

Bidentate *N,O*-attachment of an α-amino acid to a metal centre such as cobalt(III) serves to protect the ligating groups and to activate the C-2 proton(s). It thereby facilitates carbanion formation. Thus, treatment of the glycinato complex $\Lambda(+)_{589}$-$[(en)_2Co(OOCCH_2NH_2)]^{2+}$ (**1**) (en = ethylenediamine) with $POCl_3$ in *N,N*-dimethylformamide (DMF) followed by hydrolysis introduces a formyl group in a Vilsmeier–Haack-type formylation reaction (Scheme 1).[1] The resulting 2-formylglycinate complex (**2**) constitutes a useful starting point for stereospecific synthesis of C-3-modified alanine derivatives.[1]

By contrast, when (**1**) was treated with $SOCl_2$ *in lieu* of $POCl_3$, an altogether different ligand reaction ensued, as evidenced by the product reported here. $\Lambda(+)_{589}$-$[(en)_2Co(OOCCH_2NH_2)](O_3SCF_3)_2 \cdot HO_3SCF_3$,[1] dissolved in DMF, was treated with $SOCl_2$ at ≤5 °C. Dilution with water followed by cation exchange chromatography led to a major orange band containing the *N*-formyloxamato complex $\Lambda(+)_{589}$-$[(en)_2Co(OOCCONCHO)]^+$ (**3**) [62% yield from (**1**)]. The molecular structure and absolute configuration of this ion (ClO_4^- salt) were established by *X*-ray crystallography, details of which will be published elsewhere. In the $SOCl_2$ reaction free sulphur was also produced and the structural result clearly shows oxidation of the glycinate $-CH_2-$ group as well as formylation of the nitrogen atom. Oxidation to form chelated oxamate (**4**) followed by *N*-for-



Scheme 1



Scheme 2

mylation is certainly possible, as the oxamato complex (**4**), obtained on base hydrolysis of (**3**),[2] can be *N*-formylated under these same reaction conditions ($SOCl_2$ in DMF) (Scheme 1).

A likely initial oxidation product of chelated glycine is the imino acid complex (**5**, R = H). In order to test this hypothesis the analogous alaninato complex $[(en)_2Co(OOC\text{-}CHMeNH_2)](O_3SCF_3)_2$ (**6**) was treated in a similar manner with $SOCl_2$ since the related imino acid complex (**5**, R = Me) is known to be stable[3] and obviously cannot be oxidised further to an oxamate species. ^1H and ^{13}C N.m.r. spectra of the product were identical to that for the pyruvate imine complex (**5**, R = Me)[3] and the elemental analysis was consistent with this assignment. This result implies that the *N*-formyloxamato complex (**3**) may be formed *via* a chelated imine intermediate.

Other examples of $SOCl_2$ oxidations of organic substrates exist[4] but only for a limited number of cases. Büchi and Lukas have suggested a mechanism[4] for this type of oxidation which can be readily adapted to this case, as shown in Scheme 2. The C-2 proton(s) are further activated by formation of the acid chloride[5] and nucleophilic attack of the carbanion (**7**) on $SOCl_2$ would result in the chlorosulphite (**8**) which, on extrusion of sulphur monoxide, would give the imine product. Disproportionation of sulphur monoxide accounts for the observed elemental sulphur.[6] The reaction could, conceivably, proceed *via* an *N*-centred chlorosulphite but by analogy to the mechanism of 2-formylglycinate formation[5] the C-centred intermediate (**8**) is preferred.

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