Unprecedented Oxidative Decarboxylation of α-Amino-α-methylmalonate on a "Hindered" Cyclic Tetraaminecobalt(III) Complex

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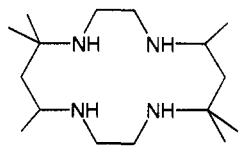
Regulation of the reactivity of transition metal complexes by stereochemical modification is an interesting subject in particular in relation to a model study of metalloenzymes, because a well-designed ligand field with a distorted arrangement of donor atoms has been regarded as one of the important factors for the specific reactivity of the metal ion at the active center of a metalloenzyme. However, there is only limited information concerning the regulation of reactivity of metal complexes containing small ligands by stereochemical modification,[1] although many studies suggest that electronic properties of metal complexes are largely dependent on the ligand.[2] We now wish to report a novel oxidative decarboxylation of α-amino-α-methylmalonate (AMM) on a cobalt(III)–tetraamine complex. The reaction is remarkably regulated by the tetraamine ligand and is specifically observed for a complex containing a *C*-methyl-substituted cyclic tetraamine which constructs a very hindered structure.

In the course of our study on the asymmetric synthesis of α-alanine from prochiral AMM using a chiral tetraamine–cobalt(III) complex,[3] we recently used a cyclic tetraamine, 5,5,7,12,12,14-hexamethyl-1,4,8,11-tetraazacyclotetradecane (Me_6[14]aneN_4, Me_6cyclam). The reaction of AMM with *trans*-[$CoCl_2$(*rac*-Me_6[14]aneN_4)]ClO_4[4] did not yield an AMM complex, contrary to our expectation from the previous study.[3] The main product was a 2-iminopropionato complex, which is produced by an oxidative decarboxylation of AMM.

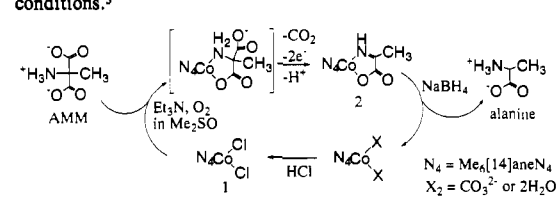


Me_6[14]aneN_4

To a suspension of 0.76 g (4.0 mmol) of ammonium α-amino-α-methylmalonate[3b] and 2.17 g (5.0 mmol) of *trans*-[$CoCl_2$(*rac*-Me_6[14]aneN_4)]ClO_4 (**1**) in 80 mL of Me_2SO was added 3.2 g of distilled triethylamine, and the mixture was stirred at 70 °C for 2 h. The reaction mixture was dissolved in 250 mL of water and poured on a column (o.d. 45 mm, h = 700 mm) of SP-Sephadex C-25 in sodium form. Elution with 0.1 M NaCl produced a violet fraction along with a number of minor fractions. The eluate from the main fraction was concentrated, and addition of $NaClO_4$ yielded violet crystals (**2**).

^{1}H and ^{13}C NMR spectroscopies of **2** suggest the coordination of Me_6[14]aneN_4. However, ^{13}C NMR spectrum showed only three signals at δ 186.4, 173.7 (>C=), and 22.3 (–CH_3)[5] ppm apart from those due to the tetraamine, although four signals are expected for the AMM chelate.[3b] The ^{1}H NMR spectrum showed a singlet (–CH_3) at δ 2.48 ppm, which is in a considerably lower magnetic field than the corresponding signal of known AMM complexes at about δ 1.7 ppm. The color of the solution changes dramatically from reddish violet to dark orange on basification. The color changes reversibly depending upon pH, and titrimetry indicated that the change is related to dissociation of one proton at pK_a = 9.4. These observations suggest the formation of the 2-iminopropionato chelate,[6] and elementary analysis strongly supported the structure.[8] The ^{1}H NMR spectrum observed in Me_2SO-d_6 showed a characteristic signal at δ 12.55 ppm due to an imino proton, which was replaced by a deuterium on addition of D_2O. The treatment of **2** with an equimolar amount of sodium borohydride in water at room temperature gave free alanine and a Co(III)–Me_6[14]aneN_4 complex, which were separated using a column of SP-Sephadex C-25 (Na^+ form) and characterized by ^{1}H NMR spectroscopy.[9]

In order to obtain further information concerning the structure of **2**, the following ^{13}C NMR spectroscopy was conducted. **2** was dissolved in an H_2O/D_2O (1:1) mixture and was left to stand for 1 d. Due to partial deuterium replacement and slow exchange rate on coordinated nitrogens, carbon signals adjacent to coor-



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(5) The intensity of this signal gradually decreases in a basic D_2O solution due to deuterium replacement. **2** is stable in aqueous solutions, and no decomposition was observed during NMR measurements.
(6) 2-Imino carboxylates, which are usually unstable, have been isolated as metal complexes by the reaction of a α-keto acid with ammine,[7a] elimination of chloromethylglycinato,[7b] or oxidation of a coordinated amino acidato ligand.[7c]
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(8) Anal. Calcd for [Co($C_3H_4NO_2$)($C_{16}H_{36}N_4$)](ClO_4)$_2$: C, 36.31; H, 6.42; N, 11.14. Found: C, 36.10; H, 6.55; N, 11.14. Absorption spectral data, $\nu_{max}/10^3$ cm^{-1} (log ε), pH = 7: 18.96 (2.29), 26.72 (2.57), 39.86 (4.28). pH = 13; 22.04 (2.93), 27.78 (3.22), 34.00 (4.02). ^{13}C NMR spectral data, ppm: pH = 6, 186.4, 173.7 (>C=O); 56.8, 56,8 (>C<); 53.5, 53.2 (>CH–); 52.2, 51.9, 48.9, 47.6, 42.6, 42.4 (–CH_2–); 29.6, 29.0, 27.7, 26.0, 22.3, 20.7, 20.3 (–CH_3); pH = 13, 179.5, 173.9 (>C=O); 56.5, 55.8 (>C<); 52.8, 50.3 (>CH–); 50.2, 50.1, 48.8, 47.1, 42.8, 42.8 (–CH_2–); 29.6, 29.0, 27.7, 25.9, 21.5, 21.1, 19.4 (–CH_3).
(9) The amino acidato chelate readily dissociates from the Co(III)–Me_6[14]aneN_4 complex in basic aqueous solutions,[3a,14] and the complex facilely takes up carbonate in the solution.[13] The resulting complex was converted to **1** by treatment with HCl almost quantitatively. Thus, we can propose a novel route to convert prochiral AMM to α-alanine which is very different from the stereospecific decarboxylation under acidic conditions.[3]

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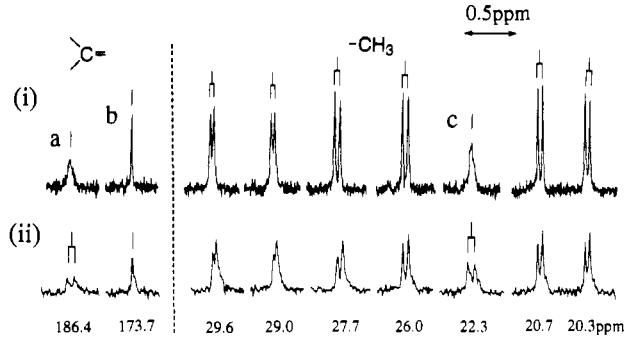

Figure 1. Proton-decoupled ^{13}C NMR spectra (100 MHz) obtained in an H_2O/D_2O (1:1) mixture at pH = 6 (i) and 1 (ii). Signals due to >C= and methyl carbons are shown.

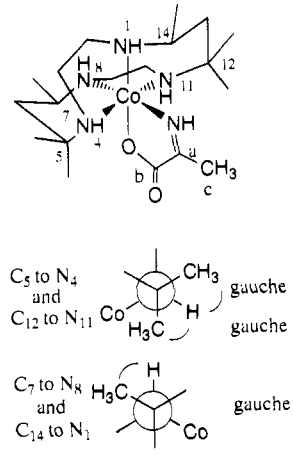

Figure 2. Proposed stereochemistry of **2** (upper) and the chelate conformations of the tetraamine unit (lower).[11] Only an enantiomer of the racemic mixture is shown.

dinated NH_2 or NH groups are observed as "isotopic multiplets".[10] The multiplet patterns of signals due to methyl and sp^2 carbons are shown in Figure 1.

Each of the six separate methyl signals in the tetraamine moiety splits into two due to partial deuterium replacements of Co–NHs. In contrast, the signals of carbons a and c of the imine ligand (at 186.4 and 22.3 ppm, respectively) are observed as broad lines at pH 6 (Figure 1(i)) and split into two only on acidification (Figure 1(ii)). This observation suggests the existence of NH in the vicinity of carbons a and c, whose deuterium replacement is faster than Co–NHs in the tetraamine moiety at pH 6. This is consistent with formation of the 2-iminopropionato chelate. The proposed structure of **2** is shown in Figure 2.[11]

The yield of the 2-iminopropionato complex strongly depended on the tetraamine ligand, and no formation of 2-iminopropionato was observed for an unsubstituted tetraamine–cobalt(III) system (Table 1).[12] Electronic absorption spectra of [Co(alaninato)(tetraamine)]$^{2+}$ [13] indicate that the ligand field strength of the complex containing Me_6[14]aneN$_4$ is unusually weak compared with that of one containing the unsubstituted tetraamine. The very broad ^{59}Co NMR line width for [Co(alaninato)(Me_6[14]aneN$_4$)]$^{2+}$ indicates distortion from the octahedral geometry. The effect of *C*-methyl substitutions on the ligand field strength is surprisingly larger than that observed for linear tetraamines.[14]

Table 1. Yield of 2-Iminopropionato Complexes by the Reaction of AMM with *trans*-[$CoCl_2$(tetraamine)]$^+$ and Electronic Absorption and ^{59}Co NMR Spectroscopic Data[a] for [Co(alaninato)(tetraamine)]$^{2+}$

tetraamine	% yield of a 2-imino-propionato complex	abs max of [Co(*S*-ala)-(tetraamine)]$^{2+}$, λ/nm		^{59}Co NMR chem shift, δ/ppm	^{59}Co NMR line width, Δν/Hz
[14]aneN$_4$[b]	*c*	511	360	8337	2300
rac-Me_6[14]aneN$_4$	27[d]	543	373	9337	4300

[a] Observed at 95 MHz, 22 °C, with concentration 0.2 M in D_2O. A saturated D_2O solution of $K_3[Co(CN)_6]$ was used as an external standard. [b] Bosnich, B.; Poon, C. K.; Tobe, M. L. *Inorg. Chem.* **1965**, *4*, 1102. [c] Not observed. Alaninato (40%) and AMM (trace) complexes were obtained. [d] Large amounts of brown products which strongly retained on the column were formed. No formation of AMM and alaninato complexes was observed.

We previously reported oxidation of α-aminomalonate (AM) on a cobalt–polyamine complexes which in part accompanies decarboxylation.[15] This reaction has been widely observed for cobalt complexes containing a variety of polyamines, and C–H bond cleavage at the α-position of AM is the important step for the oxidation. In contrast, the oxidation of AMM, which has no active C–H at the α-position, has not been achieved by the usual cobalt–polyamine complexes.[3] The characteristic electronic property of the complex by the formation of a hindered structure should be important for the oxidation of AMM. The electron transfer presumably undergoes through coordinated nitrogen of AMM to cobalt(III), which results in the cleavage of the C–COO^- bond. Oxygen plays an important role in this process, because no formation of **2** has been observed by the reaction under nitrogen.

In conclusion, α-amino-α-methylmalonate is oxidatively decarboxylated on a cobalt complex containing a C-substituted cyclic tetraamine. This is a novel example of reactions which could be regulated by the stereochemical modification of the complex.[16]

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(11) The magnitude of the isotope shift for six methyl signals in the tetraamine moiety is in the range 32–52 ppb. From the dihedral angular dependence of the three-bond isotope shifts of methyl carbons,[10a] the conformations of *CH*$_3$–C–N–*H* are suggested to be all gauche rather than anti. Thus, the stereochemistry of the tetraamine is proposed as is depicted in Figure 2. The same configuration has been found in Ni(II) complexes. (Whimp, P. O.; Bailey, M. F.; Curtis, N. F. *J. Chem. Soc. A.* **1970**, 1956. Curtis, N. F.; Swann, D. A.; Waters, T. N. *J. Chem. Soc., Dalton Trans.* **1973**, 1408. Ito, H.; Fujita, J.; Toriumi, K.; Ito, T. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 2988.)

(12) Any oxidation product for an unsubstituted [14]aneN$_4$–cobalt(III) system was not detected by thorough investigation of the products by ^{13}C NMR spectroscopy. For the complex system containing the dimethyl-substituted ligand (Me_2[14]aneN$_4$), a small amount of the 2-iminopropionato complex was obtained (8%).

(13) Alaninato complexes are prepared by the reaction using alanine instead of AMM. Details of their characterizations and properties will be reported in a subsequent paper.

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