CHEMISTRY LETTERS, pp. 335-338, 1988.

Unusual Coordination Mode of Carnosine (β-Alanyl-L-histidine) in a Cobalt(III) Complex

Ken-ichi OKAMOTO,* Takaji YASUI,*† Hiroshi KAWAGUCHI,† Tomoharu AMA,† and Jinsai HIDAKA

Department of Chemistry, University of Tsukuba, Sakura, Ibaraki 305

†Department of Chemistry, Faculty of Science, Kochi University, Akebono-cho, Kochi 780

The peptide complex, $[Co(Hcar)(en)(OH_2)]Cl_2 \cdot H_2O$ (H_2car: β-alanyl-L-histidine) was newly prepared in acidic aqueous solution and its crystal structure was determined by the X-ray diffraction study. In the complex cation, the carnosine ligand coordinates to cobalt(III) as a terdentate through peptide N, carboxyl O, and imidazole N. The amino group is not coordinated to cobalt(III).

It is widely accepted that carnosine (β-alanyl-L-histidine) plays an important physiological role in skeletal muscle by coordination of metal ions. Carnosine is not only a biological active substrate but also a unique ligand, which has four different coordinatable groups. However, there is no report for a cobalt(III)-carnosine complex, though metal complexes with peptides have been extensively investigated.[1 - 6] We have succeeded in obtaining a new cobalt(III)-carnosine complex by reaction of carnosine with $[Co(CO_3)_2(en)]^-$ in acidic aqueous solution. The X-ray diffraction study of the present complex have shown that the carnosine ligand coordinates to cobalt(III) in an unusual coordination mode; that is, it functions as a terdentate with the free amino group. This letter is concerned with the preparation and the X-ray diffraction study of the complex, $[Co(Hcar)(en)(OH_2)]Cl_2 \cdot H_2O$, and with its electronic absorption and CD spectra.

The complex was prepared by allowing to react carnosine with $K[Co(CO_3)_2(en)]$ in water under the conditions of pH 4 - 5, 40 °C, and reaction time 8 h. The

reaction product was chromatographed with an SP-Sephadex column and an eluent of 0.2 mol dm^{-3} KCl to give five bands. The eluate of the second band was concentrated. The desired complex was obtained from this concentrate by addition of methanol and recrystallized from water by addition of ethanol. Found: C, 29.51; H, 5.55; N, 18.77%. Calcd for $[Co(Hcar)(en)(OH_2)]Cl_2 \cdot H_2O$ = $C_{11}H_{25}N_6O_5Cl_2Co$: C, 29.28; H, 5.59; N, 18.63%.

The dark-brown crystal (ca. 0.50 X 0.25 X 0.20 mm^3), $[Co(Hcar)(en)(OH_2)]Cl_2 \cdot H_2O$, is monoclinic with the space group $P2_1$: $C_{11}H_{25}N_6O_5Cl_2Co$, M.W. = 451.2, a = 7.407(2), b = 17.096(4), c = 7.188(1) Å, β = 98.65(3)°, V = 899.8(3) $Å^3$, d_m = 1.65 g dm^{-3} (by flotation), d_x = 1.67 g dm^{-3}, Z = 2, and μ(Mo K_α) = 1.324 mm^{-1}. The crystal structure determination was based on the independent 2528 reflections with $|F_o| > 3\sigma(|F_o|)$ collected on a Rigaku-denki four circle diffractometer (AFC-5) by the ω-2θ scan technique up to 2θ = 60°, employing graphite-monochromatized Mo K_α radiation. The positions of the cobalt and five donor atoms were obtained by the direct method (program MULTAN[7] was used). The difference Fourier maps, based on these atomic positions, revealed the other all non-hydrogen atoms. The structure was refined by the full-matrix least-squares refinements of the positional and anisotropic thermal parameters of all the non-hydrogen atoms (program RFINE[8] was used). The atomic scattering factors for all the non-hydrogen atoms were taken from the literature.[9] The final residual values were R = 0.046 and R_w = 0.059, respectively.

Figure 1 shows a perspective view of the present complex ion. There is an asymmetric carbon on the histidine moiety in this complex ion. The absolute configuration of this asymmetric carbon is S, and thus the configuration of the skew pair consisting of two five-membered chelate about the cobalt(III) is Λ arrangement.

Six atoms, N3, C9, O3, Co, C4, and C10, which form a peptide bond or connect to the peptide bond, are on a plane, that is, the deviations of these atoms from the plane formed by Co-N3-C9 are less than 0.1 Å. Moreover, the N3-C9 bond length (1.307 Å) are shorter than the usual C-N single bond length, and the C9-O3 length (1.271 Å) is longer than the usual C-O double bond. The six bond angles, C4-N3-Co, Co-N3-C9, N3-C9-O3, O3-C9-C10, C10-C9-N3, and C9-N3-C4, are about 120°. The C3 and C4 atoms deviate from the plane formed by Co, O1, and N3, and the values of deviations are 0.4 and 0.6 Å, respectively, to the

side of the coordinating imidazole. In other words, the histidine ring in the $Hcar^-$ is hanged up to the imidazole side.

Previously, the carnosine complex, $[Co(car)(en)]^+$, in which carnosine coordinated to the cobalt(III) ion as a quadridentate was reported.[10] Such a quadridentate mode of the carnosine is also observable for the chromium(III) complex reported by C. M. Murdoch et al.[11] Both the complexes were prepared under the basic conditions. The structural behaviors of these complexes suggest that the quadridentate mode of carnosine is not strained sterically. However, in the present complex, the carnosine ligand functions as a terdentate with the free amino group. The ^{13}C NMR spectral data indicated that the terdentate mode of the carnosine is kept over the pH range 0 to 9.

The absorption and CD spectra of $[Co(Hcar)(en)(OH_2)]^{2+}$ are illustrated in Fig. 2. The present complex shows an absorption maximum at 21230 cm^{-1} with a shoulder at about 18850 cm^{-1}, suggesting that the energy difference between A_{2g} and E_g components is as large as that of the known trans(O)-$[Co(N)_4(O)_2]$ type complexes.[12] This spectral pattern differs significantly from that of $[Co(car)(en)]^+$.[10]

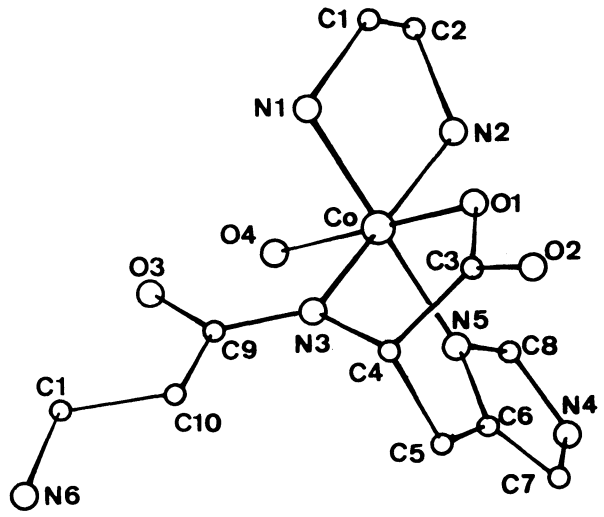

Fig. 1. Perspective view of the $[Co(Hcar)(en)(oH_2)]^{2+}$ ion.

Fig. 2. Absorption and CD spectra of $[Co(Hcar)(en)(OH_2)]^{2+}$ (———) and $[Co(car)(en)]^+$ (- - - -) ions. The ε and Δε values are given in mol^{-1} dm^3 cm^{-1}.

The present work was partially supported by a Grant-in-Aid for Scientific Research No. 58540392 from the Ministry of Education, Science and Culture.

References

1) L. V. Boas, C. A. Evans, R. D. Gillard, P. R. Mitchell, and D. A. Phipps, J. Chem. Soc., Dalton Trans., 1979, 582.

2) T. Yasui, H. Kawaguchi, and T. Ama, Bull. Chem. Soc. Jpn., 54, 2918 (1981).

3) H. Kawaguchi, M. Ishii, T. Ama, and T. Yasui, Bull. Chem. Soc. Jpn., 55, 3750 (1982).

4) C. J. Hawkins and M. T. Kelso, Inorg. Chem., 21, 3681 (1982).

5) E. J. Evans, C. J. Hawkins, J. Rodgers, and M. R. Snow, Inorg. Chem., 22, 34 (1983).

6) C. J. Hawkins and J. Martin, Inorg. Chem., 25, 2146 (1982).

7) G. Germain and M. M. Woolfson, Acta Crystallogr., Sect. A, 27, 368 (1971).

8) L. W. Finger, RFINE-2, Geophysical Lab. Carnegie Institute, Washington, D.C. (1972).

9) "International Tables for X-Ray Crystallography," Kynoch Press, Birmingham (1974), Vol. IV; D. T. Cromer and J. B. Mann, Acta Crystallogr., Sect. A, 24, 321 (1966).

10) M. Uchijima, T. Ama, H. Kawaguchi, and T. Yasui, presented at the Symposium by the Chemical Sciety of Japan, Tokushima, 1986, Abstr., p. 72.

11) C. M. Murdoch, M. K. Cooper, T. W. Hambley, W. N. Hunter, and H. C. Freeman, J. Chem. Soc., Chem. Commun., 1986, 1329.

12) N. Matsuoka, J. Hidaka, and Y. Shimura, Bull. Chem. Soc. Jpn., 40, 1868 (1967).

(Received November 6, 1987)