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# Reaction of Nickel(II)–Glycylglycyl-L-histidine Complex with Molecular Oxygen and Formation of Decarboxylated Species

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Glycylglycyl-L-histidine (GGH) has attracted wide attention as a model for the specific copper-transport site of serum albumin, hence the complexation of copper(II) with GGH has been extensively investigated [1–3]. The copper(II) complex of GGH has a square planar structure, in which GGH is coordinated to Cu(II) through the amino, two deprotonated amides and imidazole nitrogens. Since the Ni(II) complex of GGH has a similar structure, it was expected that investigation of the Ni(II)–GGH system would contribute to the understanding of the process of copper-transport in blood.

It was found unexpectedly that the Ni(II)–GGH system is extraordinarily sensitive to $O_2$, especially

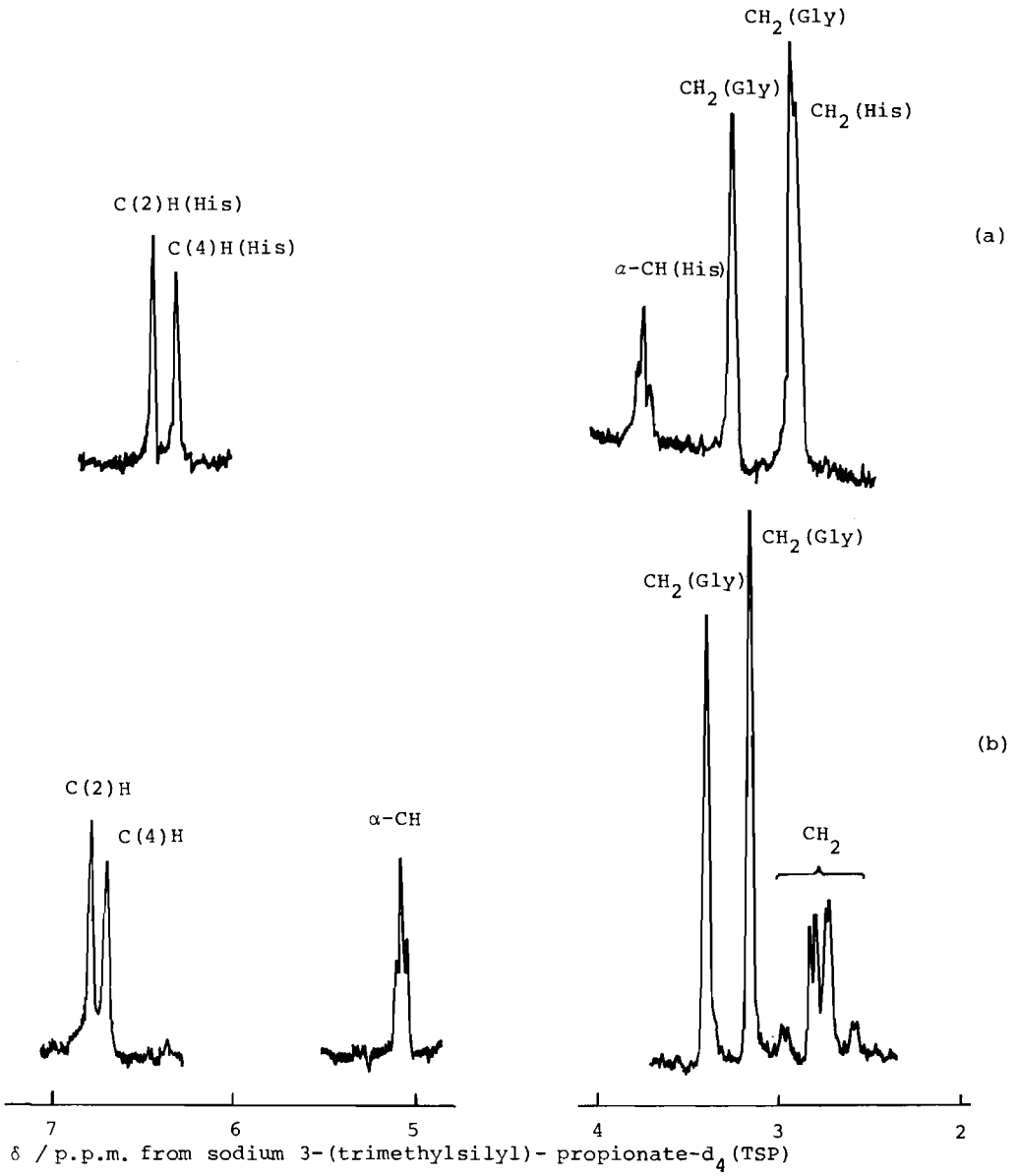
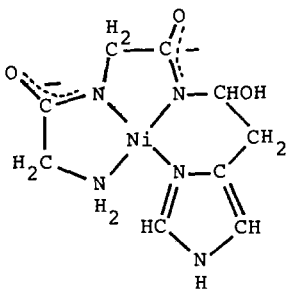



Fig. 1. PMR spectra of (a) Ni–GGH system recorded on a JEOL-JNM-MH-100 instrument at 100 MHz in $D_2O$ (pD ≈ 12) and (b) the isolated complex (*I*) recorded on a JEOL-JNM-FX-100 instrument at 100 MHz in $D_2O$ (pD = 13) with 1000 times accumulations.

at neutral pH. In the absence of $O_2$, the Ni(II)–GGH system exhibits an absorption band at 426 nm ($\epsilon$ = 144, I = 0.1 $KNO_3$), whereas when $O_2$ is incompletely removed from solvent water or when $O_2$-free solution is exposed to air, the original yellow solution turns brown rather rapidly and new absorption bands appear at *ca.* 310 and 370 nm, making the band at 426 nm only a shoulder. Concomitant with the above spectral change, a decrease of intensities of the CD bands at 410 nm ($\Delta\epsilon$ = 1.56) and 478 nm ($\Delta\epsilon$ = −0.88) is observed.

From the resulting brown solution an optically inactive yellow Ni(II) complex was isolated as crystals, whose analytical values indicated that a decarboxylation reacton from GGH occurred (*Anal.* Found: C, 36.22; H, 4.35; N, 23.44%. Calcd for $C_9H_{13}N_5O_3Ni$: C, 36.28; H, 4.40; N, 23.51%). The complex is only slightly soluble in basic solution. The RMR spectrum (Fig. 1) revealed that the complex bears methine and methylene groups which quite differ from those of the parent histidine residue. The prominent shift of the signal for the methine group to the lower field suggested the binding of an electron withdrawing group there. On the other hand, methylene groups of glycine residues were unchanged. From the above information, the structure of the isolated complex was assigned as (*1*), in which an OH group is introduced into the methine group in place of the original carboxylate group.



The present reaction is supposed to occur *via* the oxidation of Ni(II) to Ni(III) under the effect of $O_2$ dissolved in water, since an $O_2$-free Ni(II)–GGH system undergoes no change for many days. Addition of an oxidizing agent such as $Ir(IV)Cl_6^{2-}$, $H_2O_2$ or $S_2O_8^{2-}$, to the Ni(II)–GGH system immediately gave the intense bands at *ca.* 310 and 370 nm. Recently, Margerum *et al.* [4, 5] found that Ni(II) or Cu(II)–tetraglycine systems undergo autoxidation which begins with the formation of trivalent metal ion under the effect of molecular oxygen. A number of compounds were obtained and identified in the course of reaction. The decarboxylated complex (*1*) isolated in the present study may afford a clue to clarify the reaction mechanism, which is now under investigation. Of interest is the fact that Meester and Hodgson [6, 7] isolated $\alpha\beta$-didehydroglycylglycylhistaminatocopper(II), in which GGH had undergone an oxidative decarboxylation at an elevated temperature. Although the Cu(II)–GGH system may consume $O_2$ as well as the present Ni(II)–GGH system, the reaction mechanism for both systems might appreciably differ from each other as was reported for the case of tetraglycine-containing systems [4, 5].

It is now increasingly recognized that metal ions in high oxidation states are not so unusual as considered earlier [8, 9], and their participation in living systems is not improbable [10].

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