CHEMISTRY LETTERS, pp. 979-982, 1976. Published by the Chemical Society of Japan

CONFORMATION OF COORDINATED AMINO ACIDS. II. LONG-RANGE SPIN-SPIN COUPLING IN HISTIDINE AND HINDERED INTERNAL ROTATION OF IMIDAZOLE GROUP IN PENTAMMINE(L-HISTIDINE)COBALT(III) ION

Ushio SAKAGUCHI, Toshiaki TAURA, and Hayami YONEDA

Department of Chemistry, Faculty of Science
Hiroshima University, Hiroshima 730

It is found that in the pentammine(L-histidine)cobalt(III) ion, the imidazole C(5) proton is coupled to only one of the methylene protons with $^4J_{HH}$=0.9 Hz and the internal rotation of the imidazole ring around the C_β-C_γ bond is hindered presumably due to an intramolecular hydrogen bonding.

The histidine C(2) and C(5) protons have been used as "window signals" of NMR spectra in studying biochemically important molecules, because their signals appear at very low fields and are well separated from absorption lines originating from other types of protons.[1] We have found that in the titled complex ion, $[Co(NH_3)_5(hisH)]^{3+}$, the C(5) proton is spin-spin coupled to only one of the methylene protons, which is first evidence for the hindered internal rotation of the imidazole ring.

The perchlorate salt was prepared after Hawkins and Lawson[2] and dissolved in D_2O. The spectrum was obtained at 35°C after complete deuteration of ammine, amino, and imino hydrogens on a Hitachi R-22 spectrometer operating at 90 MHz. The $CH-CH_2$ moiety gives rise to the typical ABX spectrum as shown in Fig. 1, where the calculated

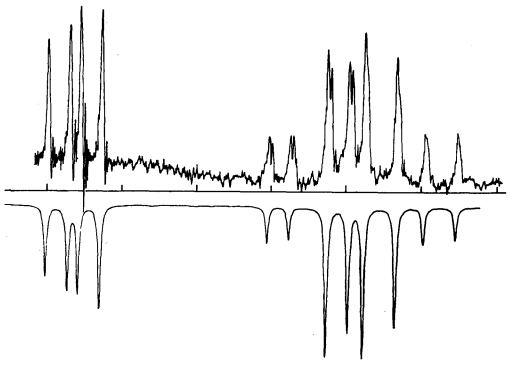

Fig. 1. The ABX part of the observed (upper) and the calculated (below) spectra of $[Co(NH_3)_5(hisH)]^{3+}$ in D_2O after complete deuteration of all N-H hydrogens. The calculated spectrum does not take the spin-spin coupling between the C(5) and methylene protons into account. One division of the abscissa is 20 Hz and the magnetic field increases from left to right.

charge	complex	free amino acid[5,6] +	0	-
J_{AC}	5.75	6.11	6.98	7.85
J_{AB}	8.59	7.09	6.00	5.28
p_I	29	32	40	50
p_{II}	55	41	31	25
p_{III}	16	27	29	25

Table 1. The fractional population of L-histidine. Spin-spin coupling constants are given in Hz. Complex means the $[Co(NH_3)_5(hisH)]^{3+}$ ion.

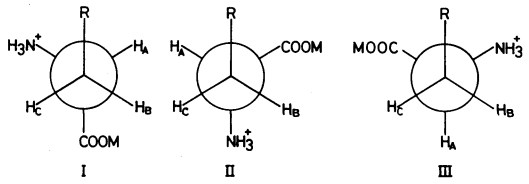

Fig. 2. Three rotational isomers of L-histidine in $[Co(NH_3)_5(hisH)]^{3+}$. R and M stand for the imidazole ring and the pentamminecobalt(III) group, respectively.

spectrum is also given for comparison. The spectral parameters obtained here are summarized in Table 1. Note that the four low-field lines of the AB part of the spectrum are each split into doublets, all the doublet spacings being equal to 0.9 Hz. The imidazole ring protons appear as a slightly broadened singlet at δ=7.42 ppm and a sharp doublet at δ=8.66 ppm with a splitting of 1.4 Hz. It is well established[3] that the histidine C(2) proton resonates at a field 0.7 to 1.1 ppm lower than the C(5) proton and that they are coupled with J=1.4 Hz. We can therefore safely assign the doublet resonating at lower field to the C(2) proton and the singlet at higher field to the C(5) proton.

The decoupling experiment was performed to confirm which proton is coupled to the methylene proton, the C(2) or the C(5) proton. Irradiation of the singlet at δ=7.42 ppm (the C(5) proton) reduced the four low-field doublets of the AB part to four singlets and at the same time the C(2) doublet changed to a singlet. Thus it is evident that the C(5) proton and one of the methylene protons are coupled with J=0.9 Hz and that the C(2) and the C(5) protons are coupled with J=1.4 Hz.

The C(5) proton is coupled to only one of the methylene protons. This can be taken as a clear indication that the imidazole ring assumes some preferred conformation with respect to the methylene group. Otherwise the C(5) proton should equally couple to both protons of the methylene group. The most probable overall structure of the complex ion may be inferred as follows. Firstly, the rotation about the C_α-C_β bond gives rise to three rotational isomers. They are illustrated in Fig. 2. Their fractional populations can be obtained by $p_I=(J_{AC}-J_g)/(J_t-J_g)$, p_{II}

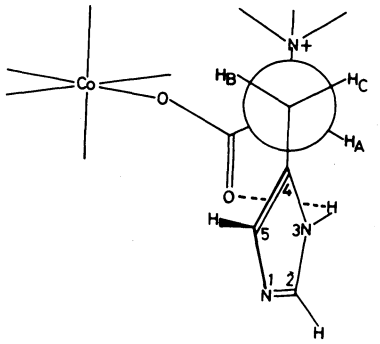

Fig. 3. Schematic presentation of the most probable structure of the complex ion $[Co(NH_3)_5(hisH)]^{3+}$ in aqueous solution. The dotted line is drawn to emphasize the proposed hydrogen bonding. The imidazole N(1) may also be protonated, see Ref. 8.

$=(J_{AB}-J_g)/(J_t-J_g)$, and $p_{III}=1-p_I-p_{II}$.[4] The J_t and J_g values are taken after Espersen and Martin[5] as 13.20 Hz and 2.60 Hz, respectively. The populations of the rotamers I to III are given in Table 1, together with those for the free amino acid.[5,6] The most stable rotamer is thus II, in which the imidazole ring and the NH_3^+ group are trans to each other. This implies that we assigned the four low-field doublets of the AB part to the C proton in Fig. 2. Kainosho[6] has established by stereoselective deuteration that in the cationic form of free histidine the most abundant rotamer is II, which is in line with our result. Secondly, the hindered rotation of the imidazole ring about the C_β-C_γ bond strongly suggests an intramolecular hydrogen bonding, because the spectrum does not change to any appreciable extent upon dilution of the solution. From a molecular model, it is seen that hydrogen bonding is favored between the N(3) proton and the carbonyl oxygen if the imidazole ring is so oriented as depicted in Fig. 3. Figure 3 is drawn for the most stable rotational isomer II. The variation of allylic coupling constants with stereochemistry has been studied both experimentally and theoretically. The results may be summarized as:[7] The parallel and the perpendicular arrangement of the C_β-H(C) bond with respect to the π electron of the C=C bond maximize and minimize, respectively, the coupling between H(C) and C(5)-H. The imidazole ring plane in Fig. 3 is, therefore, inclined toward the C_β-H(B) bond so that the allylic coupling between H(C) and C(5)-H becomes larger than that between H(B) and C(5)-H.

Further study on this system is in progress.

This work was supported in part by The Matsunaga Research Grant. The authors wish to thank Dr. S. Imai for measurements and Dr. M. Kainosho, Ajinomoto Co., Ltd., for informing them of the assignment of the methylene protons of histidine prior to publication. The authors are indebted to Dr. Y. Arata, Tokyo University, for helpful discussions.

References and Notes

1. (a) C. C. McDonald, W. D. Phillips, and J. D. Glickson, J. Amer. Chem. Soc., 93, 235(1971); (b) J. L. Markley, Biochemistry, 14, 3546(1975); (c) D. H. Meadows and O. Jardetzky, Proc. Natl. Acad. Sci., 61, 406(1968); (d) R. I. Schrager, J. S. Cohen, S. R. Heller, D. H. Sachs, and A. N. Schechter, Biochemistry, 11, 541(1972).
2. C. J. Hawkins and P. J. Lawson, Inorg. Chem., 9, 6(1970).
3. (a) F. Taddei and L. Pratt, J. Chem. Soc., 1964, 1553; (b) D. H. Sachs, A. N. Schechter, and J. S. Cohen, J. Biol. Chem., 246, 6576(1971); (c) B. Bak, C. Dambmann, F. Nicolaisen, and E. J. Pedersen, J. Mol. Spectrosc., 26, 78(1968).
4. See, for example, (a) M. Kainosho and K. Ajisaka, J. Amer. Chem. Soc., 97, 5630 (1975); (b) S. Fujiwara, H. Ishizuka, and S. Fudano, Chem. Lett., 1974, 1281.
5. W. G. Espersen and R. B. Martin, J. Phys. Chem., 80, 741(1976).
6. M. Kainosho, private communication(1976).
7. (a) S. Sternhell, Quart. Rev., 23, 236(1969); (b) L. M. Jackman and S. Sternhell, "Applications of NMR Spectroscopy in Organic Chemistry", Pergamon Press, Oxford (1968), Chap. 4.
8. K. Kawano and Y. Kyogoku, Chem. Lett., 1975, 1305.

(Received June 23, 1976)