Inorganica Chimica Acta, 46 (1980) L63–L64

^{1}H NMR Spectroscopic Evidence for Ligand–Ligand Interactions in the Ternary Palladium(II)–L-Cysteate–L-Threoninate System in Aqueous Solution

AKIRA ODANI and OSAMU YAMAUCHI*

Faculty of Pharmaceutical Sciences, Osaka University, 133-1 Yamadakami, Suita, Osaka 565, Japan

Received February 14, 1980

Noncovalent ligand–ligand interactions between charged or polar side chains of coordinated ligands have been inferred for various ternary amino acid–copper(II) complexes [1, 2]. For the histidine-containing ternary copper(II) systems we proposed a structure involving a hydrogen bond between the carboxylate oxygen of histidine (His) and the hydroxyl or the carbamyl group of the other amino acid (AA), such as asparagine (Asn), serine, and threonine (Thr), coordinated to the same copper(II) ion [2]. Such ligand–ligand interactions around the central metal ion affect the conformations of coordinated amino acids, which should be reflected on the population of rotational isomers. With a view to obtaining direct evidence for the interactions in analogous systems, we have studied the amino acid–palladium(II) complexes in solution by the ^{1}H NMR spectroscopic method. We now report the results of the conformational study of the title system where hydrogen bonding as inferred for Cu(His)(AA) is expected between the sulfonate group of L-cysteate (L-$CySO_3H$) and the hydroxyl group of L-Thr.

Experimental

^{1}H NMR spectra (90 MHz) were recorded with a Hitachi R-900 spectrometer operating in the Fourier transform mode with a digital resolution of 0.09 Hz/point. The probe temperature was measured with a thermocouple. Samples were prepared by mixing the solutions of Na_2PdCl_4, L-$CySO_3H$, and L-AA in D_2O in the molar ratio of 1:1:1 or 1:2:0 and adjusting the pD value at 6.0, the concentration of palladium(II) being 0.04 *M* (*M* = mol dm^{-3}). ^{13}C NMR spectra were obtained similarly at a palladium(II) concentration of 0.5 *M*. Absorption and circular dichroism (CD) spectra were recorded for 10^{-3} *M* solutions on a Union Giken SM-401 high sensitivity recording spectrophotometer and a JASCO MOE-1 spectropolarimeter, respectively.

*Address all correspondence to this author.

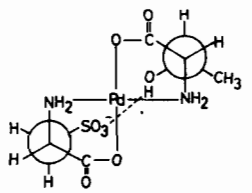
Results and Discussion

The absorption and CD spectral data of the Pd(II)–L-$CySO_3H$–L-Thr and related systems in the d–d region are listed in Table I, which indicates that

TABLE I. Absorption and CD Spectral Data.

System	pH	Absorption spectrum		CD spectrum	
		λ_{max} (nm)	ϵ	λ_{max} (nm)	$\Delta\epsilon$
$Pd(L\text{-}CySO_3H)_2$	6.5	305	330	305	−0.89
				346	0.42
$Pd(L\text{-}CySO_3H)$(L-Ala)	6.6	304	330	303	−0.76
				344	0.32
$Pd(L\text{-}CySO_3H)$(L-Thr)	6.4	319	320	311	−1.45
				353	0.37

the amino acids are coordinated to palladium(II) in the glycine-like mode [3]. Similar results were obtained from the ^{13}C NMR spectra, where all the signals of the carbonyl carbons shifted downfield by 10–11 ppm at pD 6.0 relative to the corresponding signals in the absence of palladium(II), while those of the α- and β-carbons of the coordinated amino acids shifted in the same direction only by 2–4 ppm and 0–3 ppm, respectively. The ligand–ligand interaction expected between the side chains of L-$CySO_3H$ and L-Thr in $Pd(L\text{-}CySO_3H)(L\text{-Thr})^-$ requires that they assume the conformations illustrated by structure 1,



structure 1

which corresponds to the rotamers III shown in Fig. 1. According to Pachler's approximation [4], we estimated the fractional population of the rotamer III (P_{III}) of L-$CySO_3H$ involved in various systems in 50% methanol. Temperature dependence of the P_{III} value (Fig. 2) clearly shows that it increases with temperature decrease significantly except in $Pd(L\text{-}CySO_3H)_2^{2-}$ and $Pd(L\text{-}CySO_3H)(L\text{-Ala})^-$ where it increases slightly [5]. When viewed on the part of L-Thr, the $P_I + P_{III}$ value also increases with temperature decrease in accordance with P_{III} of L-$CySO_3H$, but we could not estimate P_I and P_{III} separately

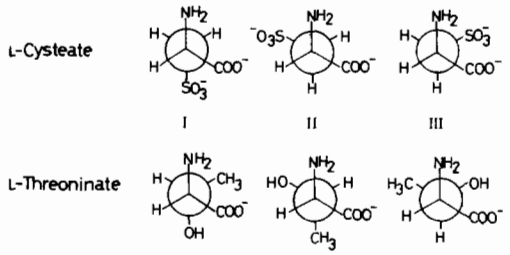


Fig. 1. Staggered rotamers of L-cysteate and L-threoninate.

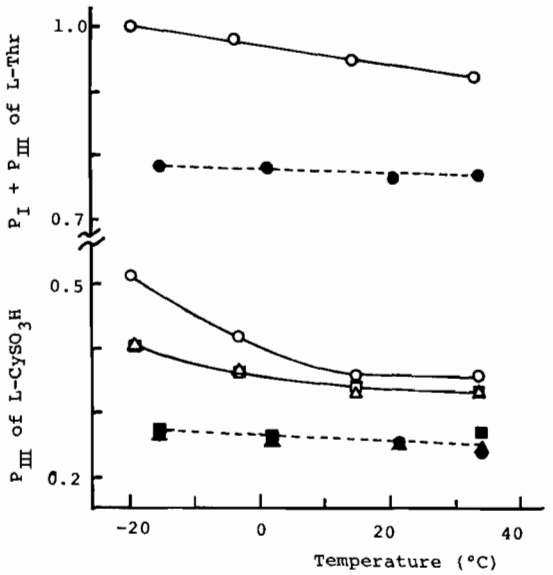


Fig. 2. Temperature dependence of P_{III} of L-cysteate and ($P_I + P_{III}$) of L-threoninate.
○ Pd(L-CySO$_3$H)(L-Thr) ● L-CySO$_3$H + L-Thr
△ Pd(L-CySO$_3$H)(L-Ala) ▲ L-CySO$_3$H + L-Ala
□ Pd(L-CySO$_3$H)$_2$ ■ L-CySO$_3$H

because only one vicinal coupling constant is available between α-H and β-H. Considering that the populations of L-CySO$_3$H and L-Thr are appreciably affected when both are coordinated to the same palladium(II) ion and are almost independent of temperature in the absence of palladium(II), we take the P_{III} increase at lower temperatures as evidence for the ligand–ligand interaction within the complex molecule. The difference between the P_{III} values of free and coordinated L-CySO$_3$H would have been caused by contributions from interactions with the water structure as well as polar or ionic groups present in solution [6].

The existence of the ligand–ligand interaction in the Pd(II)–L-CySO$_3$H–L-Thr system serves as strong evidence for analogous interactions in Pd(L-His)(L-AA), whose molecular models suggest that the steric requirement for the interactions is comparable with that in Pd(L-CySO$_3$H)(L-AA)$^-$. Since the apical coordination present in copper(II) complexes does not seem to interfere with the ligand–ligand interaction, we may further expect that the situation is very similar in Cu(L-His)(L-AA). Although the structures of Cu(L-His)(L-Thr) [7] and Cu(L-Asn)(L-His) [8] in the solid state as revealed by X-ray analysis are devoid of ligand–ligand interactions of the type discussed above, they do not exclude the possibility of such interactions in solution, where rotation around the C–C bonds and chelate ring deformation can bring the two interacting groups into close contact with each other to form a noncovalent bond under favorable conditions. Taken together, the present finding supports the explanation given for preferential formation of Cu(L-His)(L-Thr) and related ternary copper(II) complexes in human blood serum [9].

Acknowledgments

We gratefully acknowledge the valuable discussion by Professor Yoshio Sasaki of Osaka University. This work was supported in part by a grant-in-aid from the Ministry of Education of Japan, to which our thanks are due.

References

1 O. Yamauchi, Y. Nakao and A. Nakahara, *Bull. Chem. Soc. Jpn., 48,* 2572 (1975); T. Sakurai, O. Yamauchi and A. Nakahara, *ibid., 49,* 169 (1976); *ibid., 49,* 1579 (1976); *ibid., 51,* 3203 (1978).
2 O. Yamauchi, T. Sakurai and A. Nakahara, *J. Am. Chem. Soc., 101,* 4164 (1979).
3 E. W. Wilson, Jr. and R. B. Martin, *Inorg. Chem., 9,* 528 (1970).
4 K. G. R. Pachler, *Spectrochim. Acta, 20,* 581 (1964); J. Feeney, *J. Magn. Reson., 21,* 473 (1976); H. Kozłowski and M. Jezowska, *Chem. Phys. Lett., 47,* 452 (1977); H. Kozłowski, G. Formicka-Kozlowska and B. Jezowska-Trzebiatowska, *Org. Magn. Reson., 10,* 146 (1977); H. Kozłowski, M. Jezowska and H. Szyszuk, *J. Mol. Struct., 50,* 73 (1978); H. Kozłowski, *Inorg. Chim. Acta, 31,* 135 (1978).
5 The P values are accurate to within 0.008 depending on the accuracy of coupling constants.
6 M. Kainosho and K. Ajisaka, *J. Am. Chem. Soc., 97,* 5630 (1975).
7 H. C. Freeman, J. M. Guss, M. J. Healy, R.-P. Martin, C. E. Nockolds and B. Sarkar, *Chem. Commun.,* 225 (1969).
8 T. Ono, H. Shimanouchi, Y. Sasada, T. Sakurai, O. Yamauchi and A. Nakahara, *Bull. Chem. Soc. Jpn., 52,* 2229 (1979).
9 P. Z. Neumann and A. Sass-Kortsak, *J. Clin. Invest., 46,* 646 (1967); B. Sarkar and T. P. A. Kruck, in 'The Biochemistry of Copper', J. Peisach, P. Aisen and W. E. Blumberg Eds., Academic Press, New York and London (1966), p. 183.