positioned to overlap directly in a $\sigma$ fashion with the bridging moiety. There can be an antiferromagnetic coupling via $\sigma$ orbitals of the bridge for complexes with structure I; however, it would not involve the main lobe of the copper(II) $d_{z^2}$ orbitals. The structure of the binuclear cation in $[(bpy)_2Cu-OH-Cu(bpy)_2](ClO_4)_3$ approaches the limiting structure I, and this explains why the interaction for this complex is weaker than that observed for the tren single hydroxo-bridged complex.

The Cu-O-Cu bridge angle in $[(bpy)_2Cu-OH-Cu(bpy)_2](ClO_4)_3$ is 141.6 (3)°, which is considerably out of the range of bridge angles (95-104°) known for dihydroxo-bridged copper(II) complexes. In the case of the dihydroxo-bridged complexes,[50] the slope of the plot of $J$ vs. bridge angle is $-37.3$ cm$^{-1}$ deg$^{-1}$ with $J = 0$ for a bridge angle of 97.6°. Bridge angles greater than 97.6° lead to antiferromagnetic interactions. If the data for $[(bpy)_2Cu-OH-Cu(bpy)_2](ClO_4)_3$ fit onto the same correlation line, the exchange parameter $J$ would have been predicted to be $-1641$ cm$^{-1}$ for the Cu-O-Cu angle found. Instead, a value of $-161$ cm$^{-1}$ is found. The obvious explanation for this apparent discrepancy lies in the fact that the single hydroxo-bridged complexes have different electronic ground states (trigonal-bipyramidal $d_{z^2}$) than are present in the dihydroxo-bridged complexes (square-pyramidal $d_{x^2-y^2}$). It would be interesting to prepare and characterize a series of binuclear copper(II) complexes bridged only by a single hydroxide ion where the nonbridging ligands are, for example, various substituted 2,2'-bipyridines, and such a study is being undertaken. With a single hydroxide ion as the only bridge it should be possible to encompass a larger range of bridgehead Cu-O-Cu angles than the 9° range observed for the dihydroxo-bridged complexes; indeed, in the analogous Cr(III) complexes a range of over 30° has already been reported.[44-49] While a linear correlation of $J$ with bridge angle $\phi$ might not be expected, we anticipate that there will again be a strong correlation between $\phi$ and $J$.

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**Supplementary Material Available:** Tables of observed and calculated magnetic susceptibility data and thermal parameters and a listing of observed and calculated amplitudes (31 pages). Ordering information is given on any current masthead page.

# Electrostatic Ligand-Ligand Interactions in Ternary Amino Acid-Palladium(II) Complexes. Synthetic Studies and Spectroscopic Evidence

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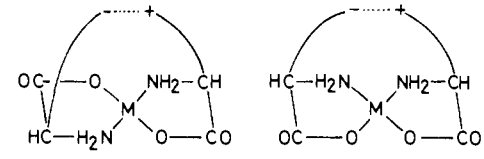
**Abstract:** Synthetic and spectroscopic studies have been carried out on electrostatic ligand-ligand interactions in ternary amino acid-palladium(II) complexes containing an acidic amino acid (A) and a basic amino acid (B). Thus, the ternary complexes Pd(A)(L-B)(H), where A refers to L- or D-aspartate, L- or D-glutamate, or L-cysteate and B to argininate with a proton (H) attached to the basic side group, have been isolated as crystals. The circular dichroism spectral magnitudes in the d-d region observed for neutral solutions of Pd(L-A)(L-B)(H) involving argininate or lysinate as B are smaller than the magnitudes estimated from those exhibited by $Pd(L-A)_2$ and $Pd(L-B)_2(H)_2$ by assuming the magnitude additivity, whereas the ternary systems without the possibility of ligand-ligand interactions such as Pd(L-A)(L-Ala) (Ala = alaninate) exhibit the spectra with magnitudes close to the estimated ones. $^1$H NMR signal patterns and chemical shifts of A in the systems Pd(L- or D-A)(L-B)(H) in neutral solution are significantly different from those of $Pd(L- \text{ or } D-A)_2$ and Pd(L- or D-A)(L-Ala). Calculation of the fractional populations of three staggered rotational isomers of free and coordinated aspartate and cysteate from the $\alpha$-CH-$\beta$-$CH_2$ coupling constants shows that the population of the isomer with the conformation enabling an electrostatic ligand-ligand interaction increases with addition of methanol and a decrease in temperature, directly reflecting the interactions within the complex molecule. In the absence of palladium(II), the populations remain unaffected. Preferential incorporation of an enantiomer of DL-aspartic acid and DL-arginine are observed in the ternary complex formation with optically pure arginine and aspartic acid, respectively. This supports the NMR study and substantiates the stereoselectivity in the palladium(II) coordination plane due to the ligand-ligand interaction.

A number of transition-metal ions play vital roles in biological processes, often forming active centers of metalloenzymes. In enzyme-metal-substrate (EMS) complexes formed in enzymatic reactions involving metal ions,[1] noncovalent interactions between enzyme and substrate molecules around the central metal ion are essential for the efficiency and specificity of the reactions.[2,3] Structural evidence for EMS complex formation has been provided by the X-ray analysis of the carboxypeptidase A-glycyl-L-tyrosine complex,[3] which demonstrates the molecular arrangement and various enzyme-substrate interactions such as the electrostatic interaction between the carboxylate group of glycyl-L-tyrosine and

Chart I




M(L-A)(L-B)(H) M(D-A)(L-B)(H)

M = Cu(II); Pd(II)

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the guanidinium group of arginine 145 of the enzyme.

In view of the importance of such noncovalent interactions in biological systems, we have been studying ligand–ligand interactions within ternary amino acid–copper(II) complexes as models for EMS intermediates.[4-8] On the basis of a substantial body of experiments, electrostatic interactions have been inferred to exist between the oppositely charged side chains of the amino acids in Cu(A)(B)(H), where A and B refer to acidic and basic amino acids, respectively, and H to proton attached to the basic side group of B. Steric requirements for the interactions suggested that the ternary complexes exist as cis and trans isomers illustrated in chart I.[4,5] Partial optical resolution of racemic amino acids DL-A and DL-B via the ternary copper(II) complex formation with L-B and L-A, respectively, has shown that the D-enantiomers of the racemic amino acids are preferentially incorporated into the complexes with the L-enantiomers, supporting the stereoselectivity due to ligand–ligand interactions.[6] However, the stability constants for the diastereomers, Cu(L-A)(L-B)(H) and Cu(D-A)(L-B)(H), where A denotes aspartate (Asp) or glutamate (Glu) and B denotes argininate (Arg), lysinate (Lys), or ornithinate (Orn), coincide with each other to within experimental errors with no appreciable stereoselectivity, and only the constants for the acid dissociation of Cu(A)(B)(H) to give Cu(A)(B) seem to reflect the effect of electrostatic interactions.[8]

While the abnormal circular dichroism (CD) spectral magnitudes sensitive to the state of asymmetric centers in the ligands and partial optical resolution of amino acids support the existence of electrostatic interactions in aqueous media, they are inconclusive and the interaction itself is too weak to be studied thermodynamically. Such interactions, however, most probably give rise to the conformational changes of the interacting amino acids A and B, which can be investigated by the NMR spectroscopic methods. With these points in mind, we have carried out synthetic and spectroscopic studies on the ternary palladium(II) complexes containing A and B as substitutes for the copper(II) complexes. The present paper describes the results obtained therefrom and the discussion of the side chain conformations mainly based on the NMR spectra and aims at providing conclusive evidence for the existence of electrostatic ligand–ligand interactions in the ternary palladium(II) complexes in solution.

## Experimental Section

**Materials.** Reagent grade monosodium salts of L-aspartic acid and L-glutamic acid, DL-aspartic acid, L-cysteic acid (L-$CySO_3H$), L-ornithine hydrochloride, L-lysine hydrochloride, L-, DL-, and D-arginine hydrochloride, and L-alanine (L-Ala) were purchased from Nakarai. D-Aspartic acid and D-glutamic acid were obtained from Wako, L-2,4-diaminobutyric acid dihydrochloride was obtained from Fluka, disodium tetrachloropalladate(II) was obtained from Mitsuwa, and palladium (II) chloride was obtained from Kishida. The deuterated solvents, $D_2O$ (99.75% pure), $CD_3OD$, and DCl in $D_2O$, were from Merck. Deuterium *tert*-butoxide was prepared from potassium *tert*-butoxide and $D_2O$. All other chemicals used were of highest grade available.

**Syntheses. [Pd(L-Arg)$_2$]Cl$_2$·3H$_2$O.**[9] To a solution of palladium(II) chloride (0.36 g, 2.0 mmol) in 2 M HCl (2 mL; M = mol dm$^{-3}$) was added an aqueous solution of L-arginine hydrochloride (0.84 g, 4.0 mmol), and the pH of the mixture was adjusted at 5–6 with aqueous NaOH. The resulting solution was concentrated in vacuo to a small volume at room temperature. When the solution was diluted with ethanol and kept for 1 week in a refrigerator, it gave light yellow crystals, which were recrystallized from aqueous ethanol. Anal. Calcd for $C_{12}Cl_2H_{28}N_8O_4Pd·3H_2O$: C, 24.86; H, 5.91; N, 19.35. Found: C, 24.72; H, 5.88; N, 19.01.

**[Pd(L-Asp)(L-Arg)]·0.5H$_2$O.** To a solution of palladium(II) chloride (0.36 g, 2.0 mmol) in 2 M HCl (2 mL) were added aqueous solutions of monosodium L-aspartate (0.35 g, 2.0 mmol), NaOH (0.08 g, 2.0 mmol), and L-arginine hydrochloride (0.42 g, 2.0 mmol) sucessively. The pH of the resulting solution was adjusted at 6–7 with aqueous NaOH. When being left standing at room temperature, the solution gave light yellow crystals, which were recrystallized from water. Anal. Calcd for $C_{10}H_{19}N_5O_6Pd·0.5H_2O$: C, 28.55; H, 4.79; N, 16.65. Found: C, 28.43; H, 4.92; N, 16.47.

The following ternary complexes were prepared in similar manners except Pd(L-Glu)(L-Arg) and Pd(D-Glu)(L-Arg), which were crystallized from aqueous ethanol under cooling.

**[Pd(D-Asp)(L-Arg)]·0.5H$_2$O.** Anal. Calcd for $C_{10}H_{19}N_5O_6Pd·0.5H_2O$: C, 28.55; H, 4.79; N, 16.65. Found: C, 28.63; H, 4.79; N, 16.77.

**[Pd(L-Glu)(L-Arg)]·2.5H$_2$O.** Anal. Calcd for $C_{11}H_{21}N_5O_6Pd·2.5H_2O$: C, 28.07; H, 5.57; N, 14.88. Found: C, 27.80; H, 5.55; N, 14.82.

**[Pd(D-Glu)(L-Arg)]·3H$_2$O.** Anal. Calcd for $C_{11}H_{21}N_5O_6Pd·3H_2O$: C, 27.54; H, 5.67; N, 14.60. Found: C, 27.34; H, 5.69; N, 14.75.

**[Pd(L-$CySO_3H$)(L-Arg)]·2.5H$_2$O.** Anal. Calcd for $C_9H_{19}N_5O_7PdS·2.5H_2O$: C, 22.77; H, 4.67; N, 14.75. Found: C, 22.63; H, 4.54; N, 14.72.

**Instruments.** Absorption spectra were recorded in the range 200–400 nm on a Union Giken SM-401 high sensitivity recording spectrophotometer. CD spectra were measured in a 1-cm path length quartz cell in the range 270–400 nm with a JASCO MOE-1 spectropolarimeter. Infrared spectra in the range 4000–650 cm$^{-1}$ were obtained with Hitachi 215 and 260-10 grating infrared spectrophotometers with the KBr disk method and those in the range 700–200 cm$^{-1}$ with a Hitachi EPI-L grating infrared spectrophotometer in the dry air with the Nujol mull method. $^1$H NMR spectra at 90 MHz were recorded at 35 °C on a Hitachi R-22 NMR spectrometer equipped with a Hitachi A 1600A signal averaging analyzer internally locked, and $^1$H chemical shifts were read with a Takeda Riken TR 3965 frequency counter, the probe temperature being measured with a thermocouple. $^{13}$C NMR spectra at 22.63 MHz were recorded at 35 °C on a Hitachi R-900 Fourier transform NMR spectrometer with D lock with a digital resolution of 0.02 ppm. All pH measurements were made with a TOA HM-18A pH meter with a TOKO CE 103 combination microelectrode.

**Spectral Measurements. (1) Absorption and CD Spectra.** Absorption and CD spectra were measured at room temperature for the systems involving Pd(II) and amino acids A and B in the ratio of 1:2:0, 1:0:2, and 1:1:1 at pH 6.0–6.5 at a Pd(II) concentration of 1 mM. The samples were prepared from a freshly prepared aqueous solution of sodium tetrachloropalladate(II) and 0.01 M stock solutions of amino acids in water. The pH values were adjusted with aqueous NaOH (0.05 M) and hydrochloric acid (0.01 M).

**(2) NMR Spectra.** The samples were prepared at pD 6.0 by using deuterated solvents in the manner described above, the Pd(II) concentrations being ca. 0.05 or 0.1 M for $^1$H and ca. 0.3 M for $^{13}$C NMR spectral measurements. Deuterium *tert*-butoxide and DSS were used as internal references for $^1$H NMR spectra, and the chemical shift difference between them was constant (111.1 Hz) in all the systems studied. All carbon chemical shifts were measured relative to the internal reference of dioxane ($\delta_{dioxane}$) and converted to the $Me_4Si$ scale ($\delta_{Me_4Si}$) according to the relationship:[10]

$$\delta_{Me_4Si} = \delta_{dioxane} + 67.11 \text{ ppm}$$

**Calculations.** Spin analyses of the NMR spectra and the CD curve resolutions were made with the use of the programs LAOCN-4A and LGNCD, respectively, on a NEAC 2200 Model S900 computer at the Osaka University Computer Center.

**Complex Formation with DL-Amino Acids.** Aqueous solutions of monosodium L-aspartate hydrate (0.35 g, 2.0 mmol) and DL-arginine hydrochloride (0.84 g, 4.0 mmol) were added successively to a solution of palladium(II) chloride (0.35 g, 2.0 mmol) in 1 M HCl (2 mL), and the pH of the mixture was adjusted at ~6 with aqueous NaOH. The resulting solution gave at room temperature light yellow crystals of the composition [Pd(L-Asp)(Arg)]·0.5H$_2$O in 77% yield based on the amount of palladium(II) used. Anal. Calcd for $C_{10}H_{19}N_5O_6Pd·0.5H_2O$: C, 28.55; H, 4.79; N, 16.65. Found: C, 28.66; H, 4.65; N, 16.66. This complex was also crystallized from 50% aqueous methanol. Found: C, 28.45; H, 4.63; N, 16.87.

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Table I. Absorption and CD Spectral Data

| system | sample[a] | solvent | pH | absorption spectrum $\lambda_{max}$, nm | absorption spectrum $\epsilon$ | CD spectrum $\lambda_{max}$, nm | CD spectrum $\Delta\epsilon$ | rel magnitude,[b] $\Delta\epsilon/\Delta\epsilon_{calcd}$ |
|---|---|---|---|---|---|---|---|---|
| Pd(L-Asp)(L-Ala) | A | $H_2O$ | 6.4 | 326 | 410 | 345 | 0.57 | 1.00 |
| | | | | | | 306 | −0.84 | 1.00 |
| Pd(L-Asp)(L-Lys) | A | $H_2O$ | 6.2 | 328 | 390 | 351 | 0.41 | 0.70 |
| | | | | | | 308 | −0.94 | 0.80 |
| Pd(L-Asp)(L-Arg) | A | $H_2O$ | 6.4 | 327 | 420 | 351 | 0.41 | 0.86 |
| | | | | | | 309 | −1.08 | 0.92 |
| | B | $H_2O$ | 6.2 | 328 | 420 | 351 | 0.48 | |
| | | | | | | 309 | −1.08 | |
| Pd(L-Glu)(L-Ala) | A | $H_2O$ | 6.2 | 325 | 330 | 353 | 0.26 | 1.00 |
| | | | | | | 310 | −1.20 | 1.00 |
| Pd(L-Glu)(L-Lys) | A | $H_2O$ | 6.2 | 325 | 310 | 362 | 0.15 | 0.92 |
| | | | | | | 313 | −1.41 | 0.97 |
| Pd(L-Glu)(L-Arg) | A | $H_2O$ | 6.2 | 325 | 330 | 360 | 0.20 | 0.93 |
| | | | | | | 312 | −1.53 | 0.98 |
| | B | $H_2O$ | 6.0 | 325 | 330 | 360 | 0.20 | |
| | | | | | | 312 | −1.43 | |
| Pd(L-CySO$_3$H)(L-Ala) | A | $H_2O$ | 6.6 | 304 | 330 | 344 | 0.32 | 1.00 |
| | | | | | | 303 | −0.76 | 0.99 |
| Pd(L-CySO$_3$H)(L-Lys) | A | $H_2O$ | 6.4 | 304 | 330 | 349 | 0.20 | 0.87 |
| | | | | | | 306 | −0.89 | 0.90 |
| Pd(L-CySO$_3$H)(L-Arg) | A | $H_2O$ | 6.5 | 304 | 330 | 349 | 0.26 | 0.92 |
| | | | | | | 306 | −0.97 | 0.94 |
| Pd(L-Lys)(L-Ala) | A | $H_2O$ | 6.1 | 325 | 320 | 356 | 0.15 | 1.00 |
| | | | | | | 311 | −1.08 | 0.99 |
| Pd(L-Arg)(L-Ala) | A | $H_2O$ | 6.1 | 325 | 320 | 356 | 0.20 | 1.00 |
| | | | | | | 311 | −1.20 | 1.00 |
| Pd(L-CySO$_3$H)(L-Ala) | A | 50% MeOH | 6.8 | 321 | 320 | 344 | 0.39 | 0.98 |
| | | | | | | 306 | −0.89 | 0.98 |
| Pd(L-CySO$_3$H)(L-Lys) | A | 50% MeOH | 6.9 | 320 | 320 | 348 | 0.20 | 0.74 |
| | | | | | | 306 | −0.99 | 0.95 |
| Pd(L-CySO$_3$H)(L-Arg) | A | 50% MeOH | 7.3 | 321 | 330 | 348 | 0.30 | 0.76 |
| | | | | | | 305 | −1.16 | 0.99 |

[a] The samples were prepared by mixing the aqueous solutions of the components in the ratio of 1:1:1 (A) or dissolving the isolated complexes in water (B). [b] $\Delta\epsilon_{calcd}$ is the average of the $\Delta\epsilon$ values for the parent systems at the maximum wavelength of the corresponding ternary system.

The following complexes were isolated as crystals in the same manner.

**[Pd(D-Asp)(Arg)]·0.5H$_2$O.** Anal. Calcd for $C_{10}H_{19}N_5O_6Pd\cdot0.5H_2O$: C, 28.55; H, 4.79; N, 16.65. Found: C, 28.50; H, 4.58; N, 16.68.

**[Pd(Asp)(L-Arg)]·0.5H$_2$O.** Found: C, 28.66; H, 4.64; N, 16.80. This complex was also crystallized from 50% aqueous methanol. Found: C, 28.59; H, 4.69; N, 16.71.

**[Pd(Asp)(D-Arg)]·0.5H$_2$O.** Found: C, 28.69; H, 4.66; N, 16.83.

The optical purities of the amino acids incorporated into the complexes were determined by CD calibration curves set up in the manner described previously.[6,7]

## Results

**Synthesis of Ternary Complexes.** That the ternary palladium(II) complexes, Pd(A)(B)(H), containing argininate as B and aspartate, glutamate, or cysteate as A have been successfully isolated as crystals corresponds well with the results obtained for the copper(II) complexes of the same type.[5] Although ornithine has a positively charged δ-amino group at neutral pH and may be favorably paired with A in ternary complexes Pd(A)(Orn), these were not isolated probably because the δ-amino group is readily bound to palladium(II) at this pH (vide infra).[11] Lysine, on the other hand, gave analytically impure ternary complexes with A, which could not be purified under the conditions employed.

The infrared spectra in the region below 700 cm$^{-1}$, where Pd(II)–N and Pd(II)–O stretching bands are to be expected,[12-15] show that the spectral patterns of the active complexes Pd(L-Asp)(L-Arg) and Pd(L-Glu)(L-Arg) are similar to each other but are different from those of the meso complexes Pd(D-Asp)(L-Arg) and Pd(D-Glu)(L-Arg). Such a classification of the patterns may imply that there exists geometrical isomerism between the active and meso complexes owing to the ligand–ligand interaction as shown in Chart I.[5]

**Absorption and CD Spectra.** At neutral pH the ternary systems Pd(L-A)(L-Ala) and Pd(L-A)(L-B)(H), where A refers to aspartate, glutamate, or cysteate and B to argininate or lysinate, exhibit absorption maxima at 304–328 nm with ε 310–420 (Table I), which indicates that the amino acids in the ternary complexes assume a glycine-like mode of coordination and hence points out that the ε-amino group and the guanidinium group of lysine and arginine, respectively, are not involved in coordination to palladium(II).[11] When dissolved in water, the isolated complexes Pd(L- or D-Asp)(L-Arg) and Pd(L- or D-Glu)(L-Arg) exhibit essentially the same spectral properties as those of the samples prepared by mixing the stock solutions of Pd(II) and the amino acids, substantiating the ternary complex formation and ready equilibrium in aqueous solution.[16] The CD spectra of the ternary systems invariably have a positive peak at 344–360 nm and a negative peak at 303–310 nm. Since CD magnitude additivity holds in the copper(II) and palladium(II) systems with two or three amino acid residues coordinated in the same mode,[5,11,17] we estimated the CD magnitudes for the ternary systems Pd(A)(B)(H) by summing up half the magnitudes for the binary systems Pd(A)$_2$ and Pd(B)$_2$(H)$_2$. Table I clearly shows that for the L-Ala-containing ternary systems where no intramolecular ligand–ligand interaction is expected, the observed CD magnitudes agree well with the estimated values ($\Delta\epsilon_{calcd}$). For the ternary systems involving aspartate or cysteate as A and lysinate or argininate as B, the relative CD magnitudes defined as $\Delta\epsilon/\Delta\epsilon_{calcd}$ deviate

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Table II. $^{13}C$ Chemical Shifts of Binary Amino Acid-Palladium(II) Complexes[a]

| system | $^{13}C$ chem shifts α-C=O | α-C | β-C | γ-C | δ-C | others |
|---|---|---|---|---|---|---|
| $Pd(L\text{-}Asp)_2$ | 185.11 | 56.52 | 40.31 | | | β-C=O 178.63 |
| $Pd(L\text{-}CySO_3H)_2$ | 183.10 | 55.87 | 53.25 | | | |
| $Pd(L\text{-}Glu)_2$ | 185.76 | 59.14 | 29.90 | 33.72 | | γ-C=O 181.71 |
| $Pd(L\text{-}DABA)_2$ | 178.02 | 55.38 | 31.79 | 40.59 | | |
| $Pd(L\text{-}Orn)_2$[b] | 185.17 | 58.66 | 30.37 | 23.43 | 39.64 | |
| | 177.89 | 58.66 | 30.37 | 27.94 | 44.09 | |
| $Pd(L\text{-}Lys)_2$ | 185.80 | 58.95 | 32.75 | 26.93 | 22.12 | ε-C 39.84 |
| $Pd(L\text{-}Arg)_2$ | 185.53 | 58.87 | 30.44 | 24.62 | 41.27 | $C_g$[c] 157.22 |

[a] In ppm downfield relative to $Me_4Si$ at pD 6.0. [b] The peaks ascribable to two species are observed. [c] The carbon atom of the guanidinium group.

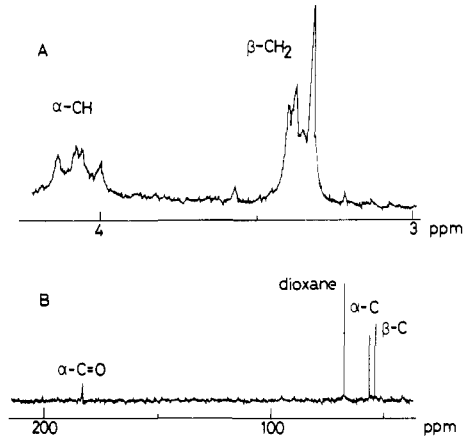


Figure 1. $^1H$ (A) and $^{13}C$ (B) NMR spectra of $Pd(L\text{-}CySO_3H)_2$ at pD 6.0. $^1H$ and $^{13}C$ chemical shifts are expressed relative to DSS and $Me_4Si$, respectively.

considerably from unity to smaller values and thus reflect the stereochemical effects of the electrostatic interaction between the oppositely charged side groups. In this connection, analogous copper(II) complexes exhibit magnitude enhancement ascribed to the ligand-ligand interaction.[4,5]

**NMR Spectra.** The $^{13}C$ and $^1H$ NMR spectra of the 1:2 palladium(II)-amino acid systems, as illustrated for $Pd(L\text{-}CySO_3H)_2$ in Figure 1, are suggestive of the existence of a single 1:2 species, which implies either that the 1:2 binary species assume a *cis* or a *trans* configuration only or that interconversion between the geometrical isomers is fast as compared with the NMR time scale. The $^{13}C$ chemical shifts of the coordinated amino acids at pD 6.0 are summarized in Table II together with the signal assignment based on the substituent effects and the chemical shifts observed for amino acids in the absence of palladium(II).[18-21] The system $Pd(L\text{-}Orn)_2$ gives two kinds of closely related signals, which are assigned to two complexes with different modes of coordination. The broadening of the α-carbon signal in the spectrum for $Pd(L\text{-}Asp)_2$ is probably attributed to moderately fast interconversion between the geometrical isomers, since the chemical shift difference between them is expected to be largest at the α-carbon[22] and the interconversion tends to cause line broadening by averaging the signals.[23] When being viewed from the $^{13}C$ complex shifts, which are defined as the chemical shift differences

Table III. Complex Shifts of Binary Amino Acid-Palladium(II) Complexes[a]

| system | $^{13}C$ complex shifts α-C=O | α-C | β-C | γ-C | δ-C | others |
|---|---|---|---|---|---|---|
| $Pd(L\text{-}Asp)_2$ | 10.33 | 3.81 | 3.16 | | | β-C=O 0.61 |
| $Pd(L\text{-}CySO_3H)_2$ | 11.01 | 3.97 | 2.35 | | | |
| $Pd(L\text{-}Glu)_2$ | 10.78 | 3.98 | 2.43 | 0.26 | | γ-C=O 0.08 |
| $Pd(L\text{-}Lys)_2$ | 10.82 | 3.89 | 2.27 | −0.04 | 0.04 | ε-C 0.11 |
| $Pd(L\text{-}Arg)_2$ | 10.82 | 3.96 | 2.31 | 0.07 | 0.16 | $C_g$[b] 0.00 |
| $Pd(L\text{-}Orn)_2$ | 10.70 | 3.95 | 2.36 | 0.04 | 0.14 | |
| | 3.42 | 3.95 | 2.36 | 4.55 | 4.59 | |
| $Pd(L\text{-}DABA)_2$ | 4.31 | 2.36 | 3.17 | 3.41 | | |

[a] In ppm downfield at pD 6.0. Complex shifts are defined as the chemical shift differences between the complexed and free amino acids. [b] The carbon of the guanidinium group.

Table IV. $^1H$ Chemical Shift[a] Differences between the $\delta_{CH_2}$ Values in Binary and Ternary Systems at 90 MHz

| system | ω-$CH_2X$[b] chem shift difference, Hz β-$CH_2$ (Asp) | γ-$CH_2$ (Glu) | δ-$CH_2$ (Arg) | ε-$CH_2$ (Lys) | $CH_3$ (Ala) |
|---|---|---|---|---|---|
| Pd(L-Asp)(L-Arg) | −0.5 | | +0.5 | | |
| Pd(D-Asp)(L-Arg) | −0.4 | | +0.5 | | |
| Pd(L-Asp)(L-Ala) | +0.1 | | | | +0.1 |
| Pd(L-Arg)(L-Ala) | | | −0.1 | | −0.1 |
| Pd(L-Glu)(L-Alg) | | +0.5 | +0.1 | | |
| Pd(L-Glu)(L-Ala) | | 0.0 | | | −0.2 |
| Pd(L-Asp)(L-Lys) | +0.4 | | | +1.3 | |
| Pd(D-Asp)(L-Lys) | +0.3 | | | +1.0 | |
| Pd(L-Lys)(L-Ala) | | | | +0.1 | +0.1 |
| Pd(L-Glu)(L-Lys) | | +0.6 | | +0.3 | |

[a] The chemical shifts (in ppm relative to DSS at pD 6.0) at the peaks of the ω-$CH_2$ groups are as follows: β-$CH_2$ (Asp), 2.64; γ-$CH_2$ (Glu), 2.4; δ-$CH_2$ (Arg), 3.25; ε-$CH_2$ (Lys), 3.04; $CH_3$ (Ala), 1.42. [b] X = $COO^-$; $-NH_3^+$; $-NHC(NH_2)_2^+$.

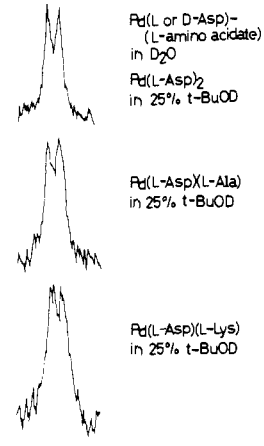


Figure 2. $^1H$ NMR signal patterns of aspartate in binary and ternary systems (*t*-BuOD = deuterium *tert*-butoxide).

(18) Keim, P.; Vigna, R. A.; Morrow, J. S.; Marshall, R. C.; Gurd, F. R. N. *J. Biol. Chem.* **1973**, *248*, 7811-7818.
(19) Freedman, M. H.; Lyerla, J. R.; Chaiken, I. M.; Cohen, J. S. *Eur. J. Biochem.* **1973**, *32*, 215-226.
(20) Voelter, W.; Jung, G.; Breitmaier, E.; Bayer, E. *Z. Naturforsch., B: Anorg. Chem., Org. Chem., Biochem., Biophys., Biol.* **1971**, *26B*, 213-222.
(21) Voelter, W.; Fuchs, St.; Seuffer, R. H.; Zech, K. *Monatsh. Chem.* **1974**, *105*, 1110-1135.
(22) The palladium(II) complex of L-proline (L-Pro), $Pd(L\text{-}Pro)_2$, gave two kinds of signals ascribable to the cis and trans isomers, and the chemical shift difference between them was found to be largest at the α-carbon.
(23) Lynden-Bell, R. M. "Nuclear Magnetic Resonance Spectroscopy"; Thomas Nelson & Sons: Middlesex, 1969.

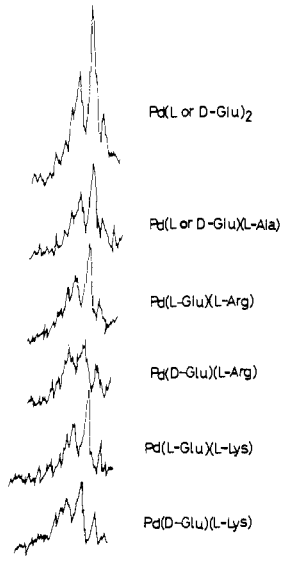


**Figure 3.** $^1$H NMR signal patterns of glutamate in binary and ternary systems.

between the free and complexed amino acids at pD 6.0, the $\alpha$-carbonyl carbons normally suffer downfield shifts of 10–11 ppm upon coordination, while L-2,4-diaminobutyrate (DABA) and ornithine show smaller shifts (3–4 ppm) of the $\alpha$-carbonyl carbons and larger shifts (3–5 ppm) of the carbons to which the $\omega$-amino groups are bound, demonstrating the involvement of the $\omega$-amino groups in coordination (Table III).

The $^1$H NMR signals of the methylene groups adjacent to the charged groups in the side chains of coordinated A and B are individually detected in the binary and ternary systems. The chemical shifts observed for the ternary systems (Table IV) are nearly identical with those of the binary systems. Except for L-cysteate the $\alpha$-CH proton signals overlap the rest of the peaks in the ternary systems. The signal patterns of the $\beta$-$CH_2$ group of coordinated L- and D-aspartate in $D_2O$ are not affected by the other amino acid B coordinated to the same palladium(II) ion. In aqueous *tert*-butyl alcohol, however, the Pd(L-Asp)(L-Lys) system undergoes signal splittings in contrast to Pd(L-Asp)(L-Ala) (Figure 2), thus pointing to conformational changes produced by the solvent polarity decrease. The spectral patterns exhibited by the $\gamma$-$CH_2$ group of L-glutamate in Pd(L-Glu)(L-Arg or L-Lys) differ appreciably from those in Pd(L-Glu)$_2$ and Pd(L-Glu)(L-Ala) and remain unchanged upon lowering the concentration down to 0.02 M (Figure 3). Analogous but larger differences in patterns are observed for the systems Pd(D-Glu)(L-B)(H) than for Pd(L-Glu)(L-B)(H). In both of these systems L-arginine affects the patterns more than L-lysine.

**Curve Resolution.** All the CD spectra of the ternary systems have two extrema at ~350 and ~310 nm, which are assigned to the electronic transitions $d_{xy} \rightarrow d_{x^2-y^2}$ and $d_{xz,yz} \rightarrow d_{x^2-y^2}$, respectively, because the transition $d_{z^2} \rightarrow d_{x^2-y^2}$ is magnetic dipole forbidden and CD inactive in $D_{4h}$ symmetry.[16,24] With use of the CD spectral data, the broad absorption curves were resolved into three bands by assuming the Gaussian distribution.[25] Table V shows that the resolved peaks correspond satisfactorily with the CD curves, the three components being reasonably assigned to the transitions $d_{xy} \rightarrow d_{x^2-y^2}$, $d_{z^2} \rightarrow d_{x^2-y^2}$, and $d_{xz,yz} \rightarrow d_{x^2-y^2}$ in the order of increasing energy.[26] Curve resolution assuming the $d_{z^2} \rightarrow d_{x^2-y^2}$ band to be the highest energy component gave an unreasonably broad band with low intensity.

Table V. Gaussian Analysis of Absorption and CD Spectra of Ternary Systems

| | resolved spectra | | | |
|---|---|---|---|---|
| | absorption | | CD | |
| system | $\lambda_{max}$, nm | $\epsilon$ | $\lambda_{max}$, nm | $\Delta\epsilon$ |
| Pd(L-Asp)(L-Ala) | 340 | 140 | 339 | 1.59 |
| | 323 | 140 | | |
| | 310 | 130 | 310 | −1.98 |
| Pd(L-Asp)(L-Lys) | 337 | 160 | 340 | 0.61 |
| | 328 | 160 | | |
| | 313 | 150 | 313 | −1.05 |
| Pd(L-Asp)(L-Arg) | 332 | 170 | 342 | 1.31 |
| | 326 | 160 | | |
| | 313 | 150 | 311 | −2.36 |
| Pd(L-Glu)(L-Ala) | 340 | 140 | 344 | 0.92 |
| | 325 | 140 | | |
| | 311 | 140 | 310 | −2.38 |
| Pd(L-Glu)(L-Lys) | 341 | 130 | 345 | 0.43 |
| | 326 | 140 | | |
| | 311 | 140 | 313 | −1.44 |
| Pd(L-Glu)(L-Arg) | 340 | 130 | 346 | 0.85 |
| | 325 | 140 | | |
| | 311 | 140 | 313 | −3.06 |
| Pd(L-CySO$_3$H)(L-Ala) | 340 | 140 | 337 | 0.51 |
| | 326 | 150 | | |
| | 310 | 150 | 306 | −0.82 |
| Pd(L-CySO$_3$H)(L-Lys) | 344 | 140 | 338 | 0.40 |
| | 325 | 150 | | |
| | 309 | 150 | 309 | −0.95 |
| Pd(L-CySO$_3$H)(L-Arg) | 340 | 130 | 338 | 0.45 |
| | 326 | 140 | | |
| | 311 | 140 | 309 | −1.03 |
| Pd(L-Ala)(L-Lys) | 341 | 130 | 344 | 0.36 |
| | 326 | 140 | | |
| | 308 | 140 | 313 | −1.10 |
| Pd(L-Ala)(L-Arg) | 340 | 120 | 344 | 0.92 |
| | 322 | 140 | | |
| | 310 | 140 | 312 | −2.44 |

## Discussion

**Modes of Coordination.** The glycine-like mode of coordination in the binary palladium(II) complexes as inferred from the absorption and CD spectra is substantiated by the $^{13}$C complex shifts, which are largest at the $\alpha$-carbon and the carbonyl carbon attached to it (Table III).[27] Of the two modes of coordination for Pd(L-Orn)$_2$, i.e., the one through the $\alpha$-amino and $\alpha$-carboxyl groups and the other through the $\alpha$- and $\delta$-amino groups, the latter is concluded from the complex shifts and is in accord with the conclusion from the CD spectra by Wilson and Martin.[11] In the acid–weak alkaline region, the side groups of lysine and arginine are protonated and not involved in bonding with palladium(II), allowing a glycine-chelate structure.[28] Accordingly, the ternary systems containing A and lysine or arginine have the same $N_2O_2$ donor set in the coordination plane as that for the corresponding binary systems.

As regards the geometrical isomers, the assumed electrostatic ligand–ligand interaction requires that the configuration of the active complexes Pd(L-A)(L-B)(H) should be trans and that of the meso complexes Pd(D-A)(L-B)(H) cis (Chart I). In fact, the active complexes exhibit similar infrared spectral patterns that appear to differ from those of the meso complexes, suggesting that there exists cis–trans isomerism[12-15,29] and that the configurations

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(26) Livingstone, S. E. In "Comprehensive Inorganic Chemistry"; Emeléus, H. J., Nyholm, R., Trotman-Dickenson, A. F., Eds.; Pergamon: Oxford, 1973; Vol. III, p 1285.
(27) The sums of the individual complex shifts of the carbon atoms constituting the amino acids are approximately the same irrespective of their structures and thus indicate that the shifts can be regarded as substituent effects caused by the electron-withdrawing ability of palladium(II).
(28) Coordination of the two amino groups in Pd(L-Lys)$_2$ at pD 6.0 was inferred to occur to a small extent from the $^1$H NMR spectrum, while no such coordination was detected for the Pd(L-Arg)$_2$ system. The difference in the side group involvement may have affected the crystallization of the complexes.
(29) (a) Condrate, R. A.; Nakamoto, K. *J. Chem. Phys.* **1965**, *42*, 2590–2598. (b) Herling, A. W.; Wenhold, S. L.; Long, T. V. *J. Am. Chem. Soc.* **1970**, *92*, 6474–6481.

Table VI. $^{13}C$ Chemical Shift Differences in Ternary Systems[a]

| system | amino acid | $^{13}C$ chem shift differences α-C=O | α-C | β-C | γ-C | δ-C | others |
|---|---|---|---|---|---|---|---|
| Pd(L-Asp)(L-Lys) | Asp | 0.70[b] | 0.04 | −0.06 | | | β-C=O −0.24 |
| | Lys | 0.01 | 0.01 | −0.05 | 0.00 | −0.01 | ε-C 0.00 |
| Pd(L-Glu)(L-Ala) | Glu | −0.06 | −0.05 | −0.06 | −0.07 | | γ-C=O −0.02 |
| Pd(L-Glu)(L-Lys) | Glu | 0.01 | −0.03 | −0.03 | −0.02 | | γ-C=O 0.02 |
| | Lys | −0.03 | 0.01 | −0.04 | 0.00 | −0.01 | ε-C −0.06 |
| Pd(L-Glu)(L-Arg) | Glu | −0.27[b] | −0.05 | −0.03 | −0.01 | | γ-C=O −0.02 |
| | Arg | −0.04 | −0.08 | −0.03 | −0.02 | −0.04 | $C_g$[c] −0.10 |
| Pd(L-Arg)(L-Ala) | Arg | 0.02 | −0.02 | −0.03 | −0.02 | −0.01 | $C_g$[c] −0.04 |

[a] In ppm downfield relative to the corresponding binary systems at pD 6.0. [b] The value may not be accurate because of the overlapping peaks. [c] The carbon atom of the guanidinium group.

are determined by the steric requirements as illustrated in Chart I. Analogous observations have been made for the corresponding copper(II) complexes.[5]

**CD Spectral Magnitudes.** The relative CD magnitudes for the L-Ala-containing ternary systems clearly establish CD magnitude additivity in the systems without ligand–ligand interactions (Table I), and this coincides well with our previous observations on the copper(II) complexes[4a,5] as well as the hexadecant rule[17,30] and the theoretical approach.[31] In the systems Pd(L-A)(L-B)(H), on the other hand, the additivity no longer holds, and more remarkable deviations of the relative magnitudes from unity are observed for the lower energy component of the CD spectra assigned to the $d_{xy} \rightarrow d_{x^2-y^2}$ transition. We may infer that the complexes suffer structural changes in the *xy* plane owing to the interaction depicted in Chart I. According to the hexadecant rule, abnormal CD magnitudes are ascribed to the deviation of coordinated atoms and chromophores from the boundary line of neighboring sectors. Interestingly, the deviations of the relative magnitudes from unity are greater for the L-Asp- and L-$CySO_3H$-containing systems than the L-Glu-containing ones. This may be interpreted in terms of greater strains in the former because of the shorter side-chain lengths.

**NMR Spectroscopic Evidence for Electrostatic Ligand–Ligand Interactions. (1) Chemical Shifts and Spectral Patterns.** The $^{13}C$ chemical shift differences summarized in Table VI indicate that ternary complex formation does not affect appreciably the chemical shifts of the carbon atoms including the ω-carboxyl carbon of A, despite the expectation that the differences should be much larger under the influence of electrostatic interactions possible at neutral pH. Since such interactions are by nature considerably weakened in polar solvents,[32] the rather small chemical shift differences have probably resulted from ineffective interactions in aqueous media with high salt concentrations.[33]

On the other hand, careful comparison of the $^1H$ chemical shifts of the methylene protons adjacent to the interacting groups discloses small but reproducible chemical shift differences between the binary systems containing A or B and the ternary systems containing both (Table IV), whereas no such difference can be detected for the ternary systems with L-alanine. The spectral patterns exhibited by the γ-$CH_2$ group of L-glutamate in Pd(L-Glu)(L-B)(H) differ significantly from the corresponding patterns in Pd(L-Glu)$_2$ and Pd(L-Glu)(L-Ala) and suggest the conformational changes due to the electrostatic ligand–ligand interaction. Because the observed spectral changes are independent of the concentrations of the complexes, the interaction is inferred to be intramolecular.

As stated previously for copper(II) complexes,[5] the ligand–ligand interaction in Pd(D-Glu)(L-B)(H) requires on stereochemical grounds a cis configuration with respect to the amino groups. The fact that greater changes of the signals ascribable

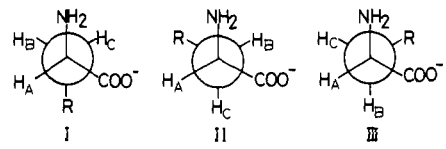
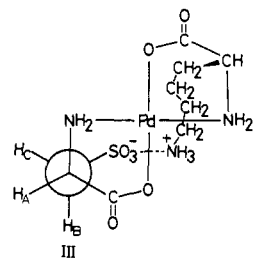



Figure 4. Three staggered rotational isomers of α-amino acids.




Pd(L-$CySO_3H$)(L-Lys)

Figure 5. Conformations of α-amino acids in a palladium(II) complex with a ligand–ligand interaction.

to glutamate are observed for Pd(D-Glu)(L-B)(H) than for Pd(L-Glu)(L-B)(H) suggests that the binary complexes Pd(L- or D-Glu)$_2$ are predominantly in the trans form, which is further supported by their spectral similarity to trans-Pt(L-Glu)$_2$.[34] The ionic bonds between the carboxylate group and the guanidinium group have been established for the salt, arginine glutamate,[35] and appear to be particularly favored in biological systems. Since more remarkable spectral changes of glutamate are observed for the ternary systems with arginine rather than with lysine, arginine probably interacts with glutamate more effectively.

Lack of spectral changes in the Asp-containing systems does not necessarily mean that the β-carboxyl group of aspartate can not interact with a positively charged group, because simple patterns such as ABX exhibited by aspartate and other three-spin systems may not be affected by small conformational changes.[36] Substantial spectral changes observed for Pd(L-Asp)(L-B)(H) in aqueous *tert*-butyl alcohol reasonably point to the ligand–ligand interaction that is made more effective in less polar solvents.

**(2) Rotational Isomers of Aspartate and Cysteate.** Free and palladium(II)-coordinated L-aspartate and L-cysteate are represented by three staggered rotational isomers, I, II, and III (Figure 4), which are in equilibrium with each other, and the observed NMR spectral data are regarded as the weighted averages of the spectra exhibited by them. Space-filling molecular models show that only the isomer III fulfills the requirements for effective intramolecular interactions with the positive side groups of lysine and arginine (Figure 5). Therefore, the fractional population of III ($P_{III}$) in ternary systems with and without the possibility

(30) Martin, R. B.; Tsangaris, J. M.; Chang, J. W. *J. Am. Chem. Soc.* **1968**, *90*, 821–823.
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(32) Vinogradov, S. N.; Linnell, R. H. "Hydrogen Bonding"; Van Nostrand-Reinhold: New York, 1971.
(33) Jencks, W. P. "Catalysis in Chemistry and Enzymology"; McGraw-Hill: New York, 1969.
(34) Erickson, L. E.; McDonald, J. W.; Howie, J. K.; Clow, R. P. *J. Am. Chem. Soc.* **1968**, *90*, 6371–6392.
(35) Batt, T. N.; Vijaya, M. *Acta Crystallogr., Sect. B* **1977**, *B33*, 1754–1759.
(36) Bovey, F. R. "Nuclear Magnetic Resonance Spectroscopy"; Academic Press: New York, 1969.

Table VII. Fractional Populations of Rotational Isomers of Cysteate and Aspartate in Binary and Ternary Systems at 35 °C

| system | solvent | $\lvert J_{AB} + J_{AC}\rvert$, Hz | fractional pop. $P_I + P_{II}$ | fractional pop. $P_{III}$ |
|---|---|---|---|---|
| Pd(L-$CySO_3H$)$_2$ | $D_2O$ | 11.7 | 0.59 | 0.41 |
| Pd(L-$CySO_3H$)(L-Ala) | $D_2O$ | 11.7 | 0.59 | 0.41 |
| Pd(L-$CySO_3H$)(L-Lys) | $D_2O$ | 11.3 | 0.55 | 0.45 |
| Pd(L-$CySO_3H$)(L-Arg) | $D_2O$ | 11.5 | 0.57 | 0.43 |
| Pd(L or D-Asp)$_2$ | $D_2O$ | 10.4[a] | 0.47 | 0.53 |
| Pd(L or D-Asp)(L-Ala) | $D_2O$ | 10.4[a] | 0.47 | 0.53 |
| Pd(L or D-Asp)(L-Lys) | $D_2O$ | 10.2[a] | 0.46 | 0.54 |
| Pd(L or D-Asp)(L-Arg) | $D_2O$ | 10.2[a] | 0.46 | 0.54 |
| Pd(L or D-Asp)$_2$ | 25% *t*-BuOD[b] | 10.2[a] | 0.46 | 0.54 |
| Pd(L or D-Asp)(L-Ala) | 25% *t*-BuOD[b] | 10.2[a] | 0.46 | 0.54 |
| Pd(L or D-Asp)(L-Lys) | 25% *t*-BuOD[b] | 10.0[a] | 0.44 | 0.56 |

[a] Estimated by $^1/_2\lvert J_{AB} + J_{AC}\rvert$. [b] *t*-BuOD = deuterium *tert*-butoxide.

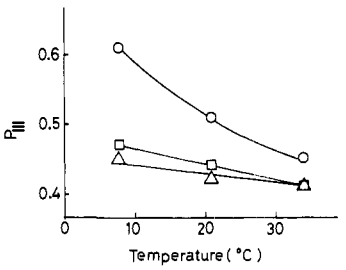


**Figure 6.** Temperature dependence of $P_{III}$ of cysteate in binary and ternary systems: ○, Pd(L-$CySO_3H$)(L-Lys); △, Pd(L-$CySO_3H$)(L-Ala); □, Pd(L-$CySO_3H$)$_2$.

of ligand–ligand interactions should serve as a measure of their effect. The $P_I$, $P_{II}$, and $P_{III}$ values of isomers I, II, and III, respectively, can be calculated from the coupling constants $J_t$, $J_g$, $J_{AB}$, and $J_{AC}$ according to eq 1,[37,38] where $J_t$ (=13.56 Hz) and

$$P_I = (J_{AC} - J_g)/(J_t - J_g)$$

$$P_{II} = (J_{AB} - J_g)/(J_t - J_g) \quad (1)$$

$$P_{III} = [(J_t + J_g) - (J_{AB} + J_{AC})]/(J_t - J_g)$$

$J_g$ (=2.60 Hz) have been shown to be constant for various α-amino acids.[37] Because the vicinal coupling depends on the dihedral angle[39] and the couplings between the protons of the α- and β-carbons in free and palladium(II)-coordinated alanine have the same value of 7.2 Hz at pD 6.0,[40] we may assume that the $J_t$ and $J_g$ values for the palladium(II) complexes are the same as those for the free amino acids.[41-45] Such an assumption has also been shown to hold in zinc(II) complexes.[46] The spectra of Pd(L-$CySO_3H$)$_2$ (Figure 1) and Pd(L-Asp)$_2$ have ABX patterns with some degeneracy, suggesting small chemical shift differences between the methylene protons, and we could obtain only the sum of the vicinal coupling constants, $\lvert J_{AB} + J_{AC}\rvert$, from the spectra.[47] As $J_{AB}$ and $J_{AC}$ for α-amino acids are positive,[48] eq 1 gives $P_{III}$,

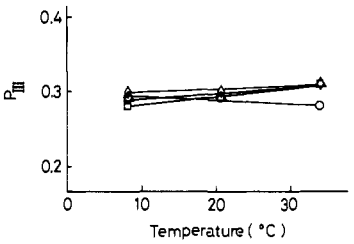


**Figure 7.** Temperature dependence of $P_{III}$ of cysteate in the absence of palladium(II): ○, 2(L-$CySO_3H$); △, L-$CySO_3H$ + L-Ala; □, L-$CySO_3H$ + L-Lys; ◇, L-$CySO_3H$ + L-Arg.

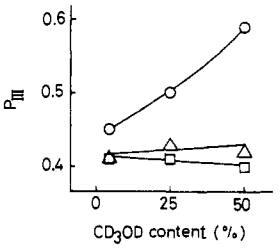


**Figure 8.** Effect of polarity of solvent on $P_{III}$ of cysteate in binary and ternary systems: ○, Pd(L-$CySO_3H$)(L-Lys); △, Pd(L-$CySO_3H$)(L-Ala); □, Pd(L-$CySO_3H$)$_2$.

Table VIII. Preferential Incorporation of Enantiomers of Amino Acids into Ternary Complexes

| system | solvent | % yield[a] | incorpd L enantiomer,[b] % |
|---|---|---|---|
| $Pd^{II}$-L-Asp-DL-Arg | $H_2O$ | 77 | 35 |
| | 50% MeOH | 95 | 44 |
| $Pd^{II}$-DL-Asp-L-Arg | $H_2O$ | 66 | 49 |
| | 50% MeOH | 71 | 42 |
| $Pd^{II}$-D-Asp-DL-Arg | $H_2O$ | 76 | 63 |
| $Pd^{II}$-DL-Asp-D-Arg | $H_2O$ | 58 | 55 |

[a] Yield of the isolated complex based on the amount of palladium(II) used. [b] Estimated by the CD calibration curves.

from which $P_I + P_{II}$ can be calucalted. Table VII shows that at 35 °C the $P_{III}$ values for Pd(L- or D-A)(L-B)(H) are slightly higher than those for Pd(L- or D-A)$_2$ and Pd(L- or D-A)(L-Ala) where no ligand–ligand interaction is expected. A drastic increase of $P_{III}$ in Pd(L-A)(L-B)(H) as compared with Pd(L-A)(L-Ala) is observed at lower temperatures that favor the electrostatic interaction by reducing molecular motions,[49] the value for Pd(L-$CySO_3H$)(L-Lys) increasing to about 0.65 at 8 °C (Figure 6). In the absence of palladium(II), the $P_{III}$ values remain virtually constant irrespective of the presence of sodium chloride and L-lysine, L-arginine, or L-alanine (Figure 7).

**(3) Effect of Solvent Polarity.** A similar trend in $P_{III}$ was observed with the decrease of polarity of the medium, in which the complexes were dissolved, by addition of methanol (Figure 8). This is due to stronger electrostatic interactions resulting from weaker hydration of the interacting groups in a less polar medium. The increase of $P_{III}$ coincides with the CD magnitude anomaly for the Pd(L-$CySO_3H$)(L-Lys) system in 50% methanol, where the relative magnitude of the positive CD peak assigned to the $d_{xy} \rightarrow d_{x^2-y^2}$ transition deviates from unity more than in water (Table I).

All these observations of the $P_{III}$ increase provide convincing evidence for the existence of the ligand–ligand interaction between the oppositely charged groups of A and protonated B. Further, they suggest that under favorable conditions the stabilization by the interaction compensates the disadvantage incurred from

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puckered structures necessary for the ineraction but is not so large as to fix the complex geometry in solution.[50]

**Ligand Selectivity around Palladium(II).** In accordance with the successful optical resolution of DL-A and DL-B via stereoselective incorporation of an enantiomer into the copper(II) complexes of L-B and L-A, respectively, the present experiment has confirmed the preferential incorporation of D enantiomers of A and B into the palladium(II) complexes Pd(A)(L-B)(H) and Pd(L-A)(B)(H), respectively (Table VIII). Use of D-A for resolution of DL-B affords Pd(D-A)(B)(H) abounding with the L enantiomer of B, which is consistent with the expectation based on the results for Pd(A)(L-B)(H).

**Biological Significance of Ligand-Ligand Interactions.** Reactions of metalloenzymes with the substrates certainly involve various enzyme-substrate interactions, which are regarded as ligand-ligand interactions around the central metal ion. As typically shown by the X-ray structure analysis of the carboxypeptidase A-substrate complex, hydrogen bonding and electrostatic and hydrophobic interactions are of utmost importance for enzymatic reactions.[3,51-54] The ligand-ligand interaction in the corresponding copper(II) complexes, which have hitherto received broad experimental support,[4-8] is reasonably substantiated by the evidence presented in this study for palladium(II) complexes, because both palladium(II) and copper(II) exhibit similar complexing properties preferring square-planar structures and nitrogen donors. Also, the apical bonding in copper(II) complexes does not seem to propound a problem regarding the interaction.

The effect of addition of methanol on the rotamer populations strongly suggests that hydrophobic environments in biological systems favor electrostatic interactions around copper(II) and other metal ions and make them an important driving force for placing a molecule in a proper orientation enabling biological reactions.

Based on this view, we may further expect to work out model systems which provide specific reaction pathways mimicking biological processes, if ligands are coordinated in a preferred configuration with favorable side-chain conformations by virtue of ligand-ligand interactions.

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# Chemical and X-ray Structural Studies on the (Acetato)- and (Trifluoroacetato)pentacarbonylmetalates of Chromium and Molybdenum

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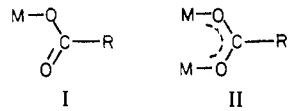
**Abstract:** The reaction of $[PNP][Mo(CO)_5Cl]$, $PNP = [Ph_3PNPPh_3]^+$, with $AgO_2CCH_3$ and $AgO_2CCF_3$ in dichloromethane readily affords the complexes $[PNP][Mo(CO)_5(O_2CCH_3)]$ (**1**) and $[PNP][Mo(CO)_5(O_2CCF_3)]$ (**2a**) in good yield. The trifluoroacetate derivative of chromium (**2b**) is conveniently prepared in a similar manner. All three compounds crystallize in the triclinic space group $P\bar{1}$ with cell dimensions $a = 10.563$ (1) Å, $b = 12.154$ (2) Å, $c = 17.047$ (2) Å, $\alpha = 104.01$ (1)°, $\beta = 106.86$ (1)°, and $\gamma = 91.79$ (1)° for **1**, $a = 10.766$ (2) Å, $b = 12.210$ (1) Å, $c = 17.115$ (2) Å, $\alpha = 104.10$ (1)°, $\beta = 106.59$ (1)°, and $\gamma = 92.77$ (1)° for **2a**, and $a = 10.715$ (2) Å, $b = 12.141$ (2) Å, $c = 17.070$ (2) Å, $\alpha = 104.21$ (1)°, $\beta = 106.57$ (1)°, and $\gamma = 92.56$ (2)° for **2b**. The structure of **1** was refined to values of $R_1 = 0.069$ and $R_2 = 0.083$ for 54 atoms (18 anisotropic) and 2860 reflections with $I > 3\sigma(I)$, while **2b** was refined to values of $R_1 = 0.073$ and $R_2 = 0.089$ for 57 atoms (21 anisotropic) and 3470 reflections with $I > 3\sigma(I)$. The structure of **2a** converged with $R_1 = 0.050$ and $R_2 = 0.070$ for 5338 reflections with $I > 3\sigma(I)$ and 57 anisotropic atoms. The most significant structural aspects are essentially equivalent (M)O—C and C=O bond lengths and short trans M—C(O) bond distances. Ligand substitutional processes involving displacement of either the acetate or carbonyl ligands in $[PNP][Mo(CO)_5(O_2CCH_3)]$ are very facile, thus making them interesting and useful for preparing other compounds.

## Introduction

The acetate and trifluoroacetate ions are known to bind to a variety of metals in one of three modes: monodentate (I), bidentate, or bridging (II).[1,2] Although the latter mode of carboxylate ion coordination is widely seen in metal dimers (e.g., $Mo_2(O_2CR)_4$),[3] monodentate binding of the trifluoroacetate ion has been noted recently in these species as well.[4] Other characterized molybdenum(II) complexes containing monodentate and bidentate carboxylates include the $(C_5H_5)Mo(CO)_3O_2CCF_3$[5] and $(C_6H_6)Mo(C_3H_5)O_2CCH_3$[6] derivatives. On the other hand little

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