

Metal Complexes of Biologically Important Ligands, CLXIX [1]. Palladium(II) and Platinum(II) *N,O*-Chelate Complexes (R_3P)(Cl)M(α -aminoacidate) with the Anions of Serine, Threonine, 3,4-Dehydroproline and 4-Hydroxyproline

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Dedicated to the memory of Professor Heinz Peter Fritz

The *N,O*-chelates $M(3,4\text{-dehydro-D,L-proline})_2$ ($M = \text{Ni, Cu}$) have been obtained from $\text{Ni}(\text{OH})_2$ or $\text{Cu}(\text{OH})_2$ and the amino acid. The complexes $(R_3P)(\text{Cl})M(\alpha\text{-aminoacidate})$ ($M = \text{Pd, Pt}$) have been synthesized from the chloro bridged compounds $(R_3P)(\text{Cl})M(\mu\text{-Cl})_2M(\text{PR}_3)\text{Cl}$ ($M = \text{Pd, Pt}$; $R = \text{Et, } n\text{-Bu, Ph}$) and the potassium salts of the α -amino acids D,L-serine, D,L-threonine, 3,4-dehydro-D,L-proline and 4-hydroxy-L-proline. According to the ^{31}P NMR and ^{13}C NMR spectra the complexes with serinate and threoninate are formed as mixtures of *cis/trans* N-M-P isomers, whereas for the palladium complexes with 3,4-dehydroproline and 4-hydroxyproline a single isomer is observed.

Key words: α -Aminoacidate, Palladium, Platinum, Serine, Threonine, 3,4-Dehydroproline, 4-Hydroxyproline

Introduction

Chloro-bridged metal complexes $L_nM(\mu\text{-Cl})_2ML_n$ have been proven to be ideal starting compounds for the synthesis of complexes with amino acids and their derivatives as ligands [2, 3]. The anions of amino acids react with the complexes under cleavage and substitution of the bridging chloro ligands.

Recently, the reactions of various chloro-bridged complexes with amino acids have been reviewed [3]. In our group in Munich the phosphine-containing palladium(II) and platinum(II) complexes $(R_3P)(\text{Cl})M(\mu\text{-Cl})_2M(\text{PR}_3)(\text{Cl})$ have often been used as synthons for the preparation of amino acid complexes [4–18].

Benedetti and coworkers reported the synthesis of *trans* N-Pt-P (Cl)(Ph_3P)Pt(α -amino isobutyrate) from (Cl)(Ph_3P)Pt($\mu\text{-Cl})_2\text{Pt}(\text{Cl})(\text{PPh}_3)$, and the structure of this complex was determined by X-ray diffraction [19].

DFT calculations were carried out for *cis* and *trans* isomers of complexes of the type $(R_3P)(\text{Cl})M(\alpha\text{-aminoacidate})$ [20], and it was shown that the *trans* N-M-P complexes are more stable than the *cis* isomers.

In the following we report palladium(II) and platinum(II) complexes with the anions of serine, threo-

nine, 3,4-dehydroproline and 4-hydroxyproline. These α -amino acids can be found rather scarcely as ligands in metal complexes.

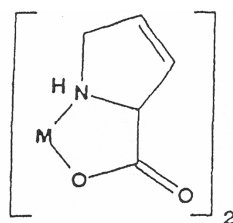
Already in 1912, E. Fischer and F. Gerlach [21] isolated the “copper salt” of 3,4-dehydroproline $\text{CuC}_{10}\text{H}_{12}\text{H}_2\text{O}_4$ by reduction of pyrrole amide and reaction of the product with precipitated copper oxide at 100 °C. With 1,2-dehydroproline (pyrroline-2-carboxylate) several complexes have been reported [22–24].

Results and Discussion

The bis(chelate) complexes **1** and **2** have been obtained from aqueous suspensions of the metal hydroxides and 3,4-dehydroproline at r. t.

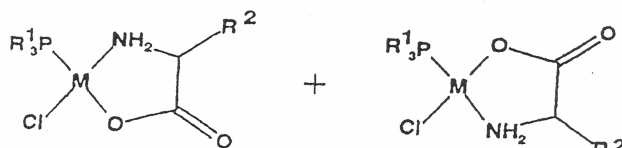
The phosphine-containing chelate complexes **3–10** are formed by reaction of the chloro-bridged palladium(II) and platinum(II) compounds $(R_3P)(\text{Cl})M(\mu\text{-Cl})_2M(\text{PR}_3)(\text{Cl})$ with the potassium salts of serine, threonine, 3,4-dehydroproline and 4-hydroxyproline in a $\text{CH}_2\text{Cl}_2/\text{CH}_3\text{OH}$ medium.

The reactions of 3,4-dehydroproline with Pd(II) or Pt(II) salts resulted in the precipitation of the metal.



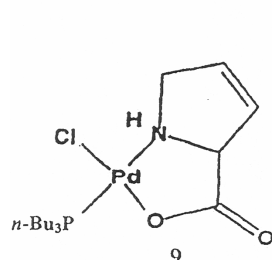
1 M = Ni

2 M = Cu

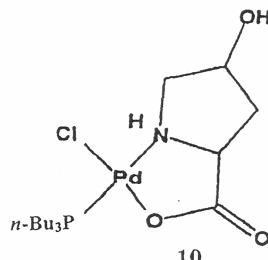


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	R ¹	M	amino acid	R ²
3	C ₂ H ₅	Pt	serine	CH ₂ OH
4	C ₂ H ₅	Pt	threonine	CH(CH ₃)OH
5	C ₄ H ₉	Pd	serine	CH ₂ OH
6	C ₄ H ₉	Pd	threonine	CH(CH ₃)OH
7	C ₆ H ₅	Pd	serine	CH ₂ OH
8	C ₆ H ₅	Pd	threonine	CH(CH ₃)OH



9



10

The IR spectra (Table 1) of **1–10** exhibit the characteristic absorptions of the coordinated α -amino carboxylate ligand at 3200 (NH) and 1600–1640 cm^{-1} (CO_2). The $\nu(\text{M}-\text{Cl})$ bands are observed at 300–340 cm^{-1} .

The ^{31}P NMR data of **3–8** (Table 2) prove the existence of *cis/trans* isomers. According to DFT calculations [20] we assume that the more stable *trans* N-M-P isomers are formed predominantly (Table 2). For **9** and **10** only one ^{31}P NMR signal was observed, and we attribute this signal to the *trans* N-Pd-P isomer.

The ^{13}C NMR spectra (Tables 3 and 4) confirm the existence of *cis/trans* isomers for **3–8**; two signals have been observed for almost every carbon atom. In

accordance with the ^{31}P NMR data for **9** and **10** only one set of ^{13}C NMR signals was found. For the assignment of the signals, the DEPT technique was used.

Experimental Section

The starting chloro-bridged complexes $(\text{Cl})(\text{R}_3\text{P})\text{M}(\mu\text{-Cl})_2\text{M}(\text{Cl})\text{PR}_3$ (M = Pd, Pt; R = Et, *n*-Bu, Ph) were prepared as described by Hartley [25]. The amino acids were purchased.

N,O-Bis(3,4-dehydro-D,L-prolinato)nickel(II) (**1**)

To a solution of 141 mg (0.50 mmol) of $\text{NiSO}_4 \cdot 7\text{H}_2\text{O}$ in 5 mL of water 1.0 mL of 1N NaOH (1.00 mmol) was added. The formed precipitate of $\text{Ni}(\text{OH})_2$ was centrifuged off

Table 1. Characteristic IR absorptions of **1–10**^a.

	ν (OH)	ν (NH)	ν (C=O)	δ (NH)	ν (M–Cl)
1 · H ₂ O	3300	3220	1590		
2 · H ₂ O	3430	3205	1595		
3	3530	3280	1635	1565	345
		3220			320
		3140			
4	3400	3280	1635	b	340
		3210			325
		3130			
5	3500	3260	1630	b	320
		3200			305
		3110			
6	3400	3270	1625	b	310
		3200			
		3110			
7	3450	3260	1630	b	318
		3200			
		3140			
8	3420	3280	1620	b	310
		3200			
		3120			
9		3160	1640	b	320
10	3400	3220	1635	b	320

^a In cm^{−1}; nujol; **6**, **8** in KBr; ^b overlapping with ν (C=O).

and washed with water. The suspension of Ni(OH)₂ and of 113 mg (1.00 mmol) of 3,4-dehydro-D,L-proline were stirred in 5 mL of water for 1 h at 40 °C, and the green color of the solid turned to blue. The blue solid was washed with water, ethanol and diethyl ether. – Yield 76 %, m. p. (dec.) > 310 °C. – C₁₀H₁₂N₂NiO₄ · 2H₂O (318.96): calcd. C 37.66, H 5.06, N 8.78; found C 37.39, H 5.12, N 8.63.

N,O-Bis(3,4-dehydro-D,L-prolinato)copper(II) (**2**)

To a freshly prepared suspension of 49 mg (0.50 mmol) of copper(II) hydroxide 113 mg (1.00 mmol) of 3,4-dehydro-D,L-proline was added. After stirring for 2 h at 40 °C the blue solid was washed with water, ethanol and diethyl ether. – Yield 54 %, m. p. > 225 °C (dec.). – C₁₀H₁₂CuN₂O₄ · H₂O (305.78): calcd. C 39.28, H 4.62, N 9.16; found C 39.31, H 4.81, N 9.02.

Chloro(triethylphosphine)(*L*-serinato)platinum(II) (**3**) and *chloro*(triethylphosphine)(*L*-threoninato)platinum(II) (**4**)

To a solution of 400 mg (0.5 mmol) of (Et₃P)(Cl)Pt(μ-Cl)₂Pt(PEt₃)(Cl) in 10 mL of dichloromethane a solution of 1.04 mmol of the amino acid and of 69 mg (1.23 mmol) of KOH in 5 mL of methanol was added. The mixture was stirred for 2 1/2 h at r. t. Then the formed KCl was centrifuged off and the solvent was removed *in vacuo*. The yellow solid was washed several times with diethyl ether.

3: Yield 52 %, m. p. 53 °C. – C₉H₂₁ClNO₃PPt · H₂O (470.80): calcd. C 22.96, H 4.92, N 2.98; found C 23.00, H 4.70, N 2.79.

Table 2. ³¹P NMR data of **3–10**^a.

	³¹ P (N- <i>trans</i>)	³¹ P (N- <i>cis</i>)	² J (Pt-P _{N-<i>trans</i>})	² J (Pt-P _{N-<i>cis</i>})	<i>trans</i> / <i>cis</i>	Solvent
3	5.75	1.75	3595	^b	90/10	CDCl ₃
4	6.13	2.00	3622	^b	77/23	CDCl ₃
5	29.04	26.54			80/20	CDCl ₃
6	28.72	27.12			80/20	CDCl ₃
7	27.71	24.13			90/10	DMF
8	27.15	23.55			90/10	DMF
9	27.94					CDCl ₃
10	26.66					CDCl ₃

^a δ in ppm; H₃PO₄ as external standard; *J*(Pt-P) in Hz;

^b not observed.

4: Yield 78 %, m. p. 64 °C. – C₁₀H₂₃ClNO₃PPt (466.82): calcd. C 25.73, H 4.97, N 3.00; found C 25.65, H 5.13, N 3.09.

(Tri-n-butylphosphine)(chloro)(L-serinato)palladium(II) (**5**) and *(tri-n-butylphosphine)(chloro)(L-threoninato)-palladium(II)* (**6**)

2.10 mmol of the amino acid and 136 mg (2.42 mmol) of finely powdered KOH were dissolved in 3 mL of methanol, and this solution was slowly added with a pipette to a solution of 1.05 mol of (Et₃P)(Cl)Pd(μ-Cl)₂Pd(PEt₃)(Cl) in 10 mL of dichloromethane. After stirring for 2 h at r. t. the yellow solid was centrifuged off and the solvent was removed *in vacuo*. The yellow residue was stirred several times with diethyl ether or with *n*-pentane. Complex **5** can be recrystallized from methanol solution, **6** from acetone solution.

5: Yield 65 %, m. p. 175 °C (dec.). – C₁₅H₃₃ClNO₃PPd (448.26): calcd. C 40.19, H 7.42, N 3.12; found C 39.54, H 7.64, N 3.15.

6: Yield 71 %, m. p. 163 °C (dec.). – C₁₆H₃₅ClN₃PPd (462.29): calcd. C 41.57, H 7.63, N 3.03; found C 41.36, H 7.64, N 3.14.

Chloro(triphenylphosphine)(*L*-serinato)palladium(II) (**7**) and *chloro*(triphenylphosphine)(*L*-threoninato)palladium(II) (**8**)

To a solution of 800 mg (0.91 mmol) of (Ph₃P)(Cl)Pd(μ-Cl)₂Pd(PPh₃)(Cl) in 15 mL of dichloromethane a solution of 1.82 mmol of the amino acid and of 117 mg (2.08 mmol) of KOH in methanol was added. The mixture was stirred for 2 h at r. t., and the solvent was removed *in vacuo*. The yellow solid was washed with water, ethanol and diethyl ether.

7: Yield 62 %, m. p. 179 °C (dec.). – C₂₁H₂₁ClNO₃PPd (508.23): calcd. C 49.63, H 4.17, N 2.76; found C 49.10, H 4.40, N 2.71.

8: Yield 68 %, m. p. 196 °C (dec.). – C₂₂H₂₃ClNO₃PPd (522.26): calcd. C 50.60, H 4.44, N 2.68; found C 49.48, H 4.61, N 2.79.

Table 3. ^{13}C NMR data of the free amino acids and of complexes **3**–**8**^a.

	$-\text{CO}_2$ <i>trans/cis</i>	α -CH <i>trans/cis</i>	other <i>trans/cis</i>	$\text{P}-(\text{CH}_2)_n-\text{CH}_3$, $n = 1,3$	$\text{P}-(\text{CH}_2)_n-\text{CH}_3$, $n = 1,3$
serine (D_2O)	173.1	57.4	CH_2OH : 61.3		
threonine (D_2O)	173.8	61.7	$\text{CH}(\text{CH}_3)\text{OH}$: 67.1		
			$\text{CH}(\text{CH}_3)\text{OH}$: 20.8		
3 (CDCl_3)	184.4d ^b (2.1)	57.7s ^b	CH_2OH : 63.0s ^b	13.6d/14.5s (38.8)	7.5d/7.7d (3.2) (3.2)
4 (CDCl_3)	183.9d ^b (4.2)	61.2d ^b (2.1)	$\text{CH}(\text{CH}_3)\text{OH}$: 67.1s ^b	13.6d/14.0s (37.8)	7.5d/7.7d (3.1) (3.2)
			$\text{CH}(\text{CH}_3)\text{OH}$: 19.4s/20.2s		
5 (CDCl_3)	180.8d/181.7s (2.1)	61.4s/58.6d (2.1)	CH_2OH : 63.1s/63.8s	26.0d/25.8d (2.1) (3.2)	13.7s/13.6s
				24.1d ^b (13.6)	
				23.0d/21.9d (31.4) (30.4)	
6 (CDCl_3)	182.3s ^b	65.9s/61.9d (2.5)	$\text{CH}(\text{CH}_3)\text{OH}$: 68.6s/67.4s	25.8d/25.7d (2.1) (3.2)	13.5s/13.6s
			$\text{CH}(\text{CH}_3)\text{OH}$: 20.7s/18.8s	24.1d ^b (14.7)	
				22.9d/21.5d (31.5) (30.4)	
7 (DMSO)	178.9d ^b (3.1)	61.0s/58.7s	CH_2OH : 61.8s/62.4s		
8 (DMSO)	179.1d ^b (3.1)	65.1s/61.8s	$\text{CH}(\text{CH}_3)\text{OH}$: 66.5s/66.8s		
			$\text{CH}(\text{CH}_3)\text{OH}$: 20.3s/20.0s		

^a δ in ppm; solvent as internal standard; ^{13}C - ^{31}P NMR coupling constants in Hz in parentheses; ^b not observed.Table 4. ^{13}C NMR data of 3,4-dehydroproline, 4-hydroxyproline and of **9** and **10**^a.

	C-1	C-2	C-3	C-4	C-5	$\text{P}(\text{CH}_2)_3\text{CH}_3$	$\text{P}(\text{CH}_2)_3\text{CH}_3$
3,4-dehydroproline	172.2	68.5	125.7/125.4		52.4		
9	182.2d (3.2)	70.2d (3.2)	126.7d/128.2s (1.6)		56.8d (2.6)	25.7d (3.2)	13.6s
						24.0d (13.6)	
						21.5d (29.9)	
4-hydroxyproline	175.2	61.1	38.7	71.3	54.2		
10	184.9d (2.8)	61.3d (3.1)	39.9s	70.3d (3.1)	57.6d (2.4)	25.8d (2.4)	13.7s
						24.1d (14.0)	
						21.5d (29.9)	

^a In D_2O ; δ in ppm; solvent as internal standard; ^{13}C - ^{31}P NMR coupling constants in Hz in parentheses.

Tri-n-butylphosphine(chloro)(3,4-dehydro-D,L-prolinato)-palladium(II) (9) and tri-n-butylphosphine(chloro)-(trans-4-hydroxy-L-prolinato)palladium(II) (10)

A solution of 2.11 mmol of the amino acid and of 136 mg (2.42 mmol) of finely powdered KOH in 3 mL of methanol was dropped to a solution of 800 mg (1.05 mmol) of $(n\text{-Bu}_3\text{P})(\text{Cl})\text{Pd}(\mu\text{-Cl})_2\text{Pd}(n\text{-Bu}_3\text{P})(\text{Cl})$ in 15 mL of dichloromethane. Immediately, the color changed from red to yellow. After stirring for 1½ h at r. t. the formed KCl was centrifuged off, and the solvent was removed *in vacuo*. The yellow solids were washed with diethyl ether. Complexes **9** and **10** can be recrystallized from methanol solution.

9: Yield 70 %, m. p. 180 °C (dec.). – $\text{C}_{17}\text{H}_{33}\text{ClINO}_2\text{PPd}$ (456.28): calcd. C 44.75, H 7.29, N 3.07; found C 44.23, H 7.38, N 3.26.

10: Yield 75 %, m. p. 133 °C. – $\text{C}_{17}\text{H}_{35}\text{ClINO}_3\text{PPd}$ (474.30): calcd. C 43.05, H 7.44, N 2.95; found C 42.16, H 7.57, N 3.10.

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