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

Elfriede Schuhmann and Wolfgang Beck

Department Chemie und Biochemie der Ludwig-Maximilians-Universität, Butenandtstr. 5 – 13, 81377 München, Germany

Reprint requests to Prof. W. Beck. E-mail: wbe@cup.uni-muenchen.de

Z. Naturforsch. **2008**, *63b,* 124 – 128; received October 9, 2007

Dedicated to the memory of Professor Heinz Peter Fritz

The *N,O*-chelates M(3,4-dehydro-D,L-prolinate)$_2$ (M = Ni, Cu) have been obtained from $Ni(OH)_2$ or $Cu(OH)_2$ and the amino acid. The complexes $(R_3P)(Cl)M(\alpha$-aminoacidate) (M = Pd, Pt) have been synthesized from the chloro bridged compounds $(R_3P)(Cl)M(\mu\text{-}Cl)_2M(PR_3)Cl$ (M = Pd, Pt; R = Et, *n*-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-dehydroprolinate and 4-hydroxyprolinate 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 $(R_3P)(Cl)M(\mu\text{-}Cl)_2M(PR_3)(Cl)$ 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 $(Cl)(Ph_3P)Pt(\alpha$-amino isobutyrate) from $(Cl)(Ph_3P)Pt(\mu\text{-}Cl)_2Pt(Cl)(PPh_3)$, 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 $(R_3P)(Cl)M(\alpha$-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, threonine, 3,4-dehydroproline and 4-hydroxyproline. These α-amino acids can be found rather scarcely as ligands in metal complexes.

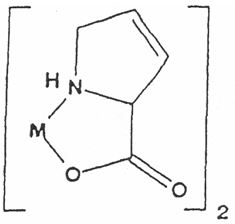
Already in 1912, E. Fischer and F. Gerlach [21] isolated the "copper salt" of 3,4-dehydroprolinate $CuC_{10}H_{12}H_2O_4$ by reduction of pyrrole amide and reaction of the product with precipitated copper oxide at 100 °C. With 1,2-dehydroprolinate (pyrroline-2-carboxylate) several complexes have been 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.

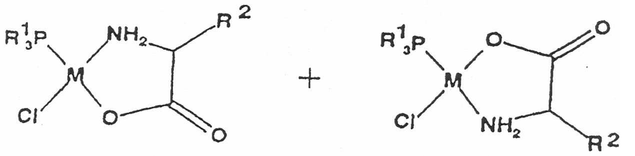
The phosphine-containing chelate complexes **3 – 10** are formed by reaction of the chloro-bridged palladium(II) and platinum(II) compounds $(R_3P)(Cl)(\mu\text{-}Cl)_2M(PR_3)(Cl)$ with the potassium salts of serine, threonine, 3,4-dehydroproline and 4-hydroxyproline in a CH_2Cl_2/CH_3OH medium.

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



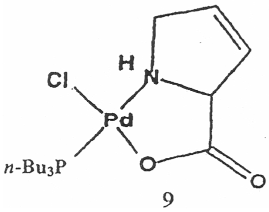
1 M = Ni

2 M = Cu

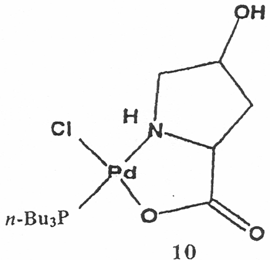


3 - 8

	R^1	M	amino acid	R^2
3	C_2H_5	Pt	serine	CH_2OH
4	C_2H_5	Pt	threonine	$CH(CH_3)OH$
5	C_4H_9	Pd	serine	CH_2OH
6	C_4H_9	Pd	threonine	$CH(CH_3)OH$
7	C_6H_5	Pd	serine	CH_2OH
8	C_6H_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 ν(M–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 $(Cl)(R_3P)M(\mu\text{-}Cl)_2M(Cl)PR_3$ (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 $NiSO_4 \cdot 7H_2O$ in 5 mL of water 1.0 mL of 1N NaOH (1.00 mmol) was added. The formed precipate of $Ni(OH)_2$ 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_2O	3300	3220	1590		
2 · H_2O	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. – $C_{10}H_{12}N_2NiO_4 \cdot 2H_2O$ (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.). – $C_{10}H_{12}CuN_2O_4 \cdot H_2O$ (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 $(Et_3P)(Cl)Pt(\mu\text{-}Cl)_2Pt(PEt_3)(Cl)$ 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 2½ 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. – $C_9H_{21}ClNO_3PPt \cdot H_2O$ (470.80): calcd. C 22.96, H 4.92, N 2.98; found C 23.00, H 4.70, N 2.79.

Table 2. ^{31}P NMR data of **3** – **10**[a].

	^{31}P (N-*trans*)	^{31}P (N-*cis*)	^2J (Pt-$P_{N-trans}$)	^2J (Pt-P_{N-cis})	*trans* /*cis*	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; H_3PO_4 as external standard; J(Pt-P) in Hz;
[b] not observed.

4: Yield 78 %, m. p. 64 °C. – $C_{10}H_{23}ClNO_3PPt$ (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 $(Et_3P)(Cl)Pd(\mu\text{-}Cl)_2Pd(PEt_3)(Cl)$ 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.). – $C_{15}H_{33}ClNO_3PPd$ (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.). – $C_{16}H_{35}ClN_3PPd$ (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 $(Ph_3P)(Cl)Pd(\mu\text{-}Cl)_2Pd(PPh_3)(Cl)$ 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.). – $C_{21}H_{21}ClNO_3PPd$ (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.). – $C_{22}H_{23}ClNO_3PPd$ (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].

	$–CO_2$ *trans/cis*	α-CH *trans/cis*	other *trans/cis*	P-$(\mathit{C}H_2)_n$-CH_3, *n* = 1,3	P-$(CH_2)_n$-$\mathit{C}H_3$, *n* = 1,3
serine (D_2O)	173.1	57.4	$\mathit{C}H_2OH$: 61.3		
threonine (D_2O)	173.8	61.7	$\mathit{C}H(CH_3)OH$: 67.1 $CH(\mathit{C}H_3)OH$: 20.8		
3 ($CDCl_3$)	184.4d/[b] (2.1)	57.7s/[b]	$\mathit{C}H_2OH$: 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)	$\mathit{C}H(CH_3)OH$: 67.1s/[b] $CH(\mathit{C}H_3)OH$: 19.4s/20.2s	13.6d/14.0s (37.8)	7.5d/7.7d (3.1) (3.2)
5 ($CDCl_3$)	180.8d/181.7s (2.1)	61.4s/58.6d (2.1)	$\mathit{C}H_2OH$: 63.1s/63.8s	26.0d/25.8d (2.1) (3.2) 24-1d/[b] (13.6) 23.0d/21.9d (31.4) (30.4)	13.7s/13.6s
6 ($CDCl_3$)	182.3s/[b]	65.9s/61.9d (2.5)	$\mathit{C}H(CH_3)OH$: 68.6s/67.4s $CH(\mathit{C}H_3)OH$: 20.7s/18.8s	25.8d/25.7d (2.1) (3.2) 24.1d/[b] (14.7) 22.9d/21.5d (31.5) (30.4)	13.5s/13.6s
7 (DMSO)	178.9d/[b] (3.1)	61.0s/58.7s	$\mathit{C}H_2OH$: 61.8s/62.4s		
8 (DMSO)	179.1d/[b] (3.1)	65.1s/61.8s	$\mathit{C}H(CH_3)OH$: 66.5s/66.8s $CH(\mathit{C}H_3)OH$: 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	$P(\mathit{C}H_2)_3CH_3$	$P(CH_2)_3\mathit{C}H_3$
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) 24.0d (13.6) 21.5d (29.9)	13.6s
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) 24.1d (14.0) 21.5d (29.9)	13.7s

[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 $(n\text{-}Bu_3P)(Cl)Pd(\mu\text{-}Cl)_2Pd(n\text{-}Bu_3P)(Cl)$ 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.). – $C_{17}H_{33}ClNO_2PPd$ (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. – $C_{17}H_{35}ClNO_3PPd$ (474.30): calcd. C 43.05, H 7.44, N 2.95; found C 42.16, H 7.57, N 3.10.

Acknowledgement

We thank Fonds der Chemischen Industrie, Wacker-Chemie AG, München, and Ludwig-Maximilians-Universität, München, for generous support.

---

[1] Contribution No. 168: A. Böhm, H. Brunner, W. Beck, *Z. Anorg. Allg. Chem.* **2008**, in press.

[2] K. Severin, R. Bergs, W. Beck, *Angew. Chem.* **1998**, *110*, 1722; *Angew. Chem. Int. Ed.* **1998**, *37*, 1634.

[3] Th. Hauck, K. Sünkel, W. Beck, *Z. Anorg. Allg. Chem.* **2006**, *632*, 2305 and refs. therein.

[4] W. Beck, M. Girnth, *Chem. Ber.* **1976**, *109*, 965. The reactions of the complex $(n\text{-}Bu_3P)(Cl)Pt(glyO)$ at the coordinated glycinate ligand could not be reproduced in our group.

[5] L. Olgemöller, W. Beck, *Chem. Ber.* **1984**, *117*, 1241.

[6] I. Zahn, K. Polborn, W. Beck, *Chem. Ber.* **1989**, *122*, 253; I. Zahn, K. Polborn, B. Wagner, W. Beck, *Chem. Ber.* **1991**, *124*, 1065.

[7] E. Schuhmann, C. Robl, W. Beck, *Z. Naturforsch.* **1994**, *49b*, 1569.

[8] T. Hauck, K. Sünkel, W. Beck, *Inorg. Chim. Acta* **1995**, *235*, 391.

[9] A. Fehn, O. Briel, W. Beck, *Chem. Ber./Recueil* **1997**, *130*, 1467.

[10] B. Schreiner, M. Prem, W. Bauer, K. Polborn, W. Beck, *Z. Naturforsch.* **1997**, *52b*, 1199.

[11] W. Bauer, W. Ponikwar, W. Beck, *Z. Naturforsch.* **2000**, *55b*, 946.

[12] St. Krawielitzki, W. Beck, *Z. Naturforsch.* **2001**, *56b*, 69.

[13] A. Fehn, Th. Ederer, S. Mihan, W. Beck, *J. Organomet. Chem.* **2001**, *621*, 109.

[14] D. Koch, W. Beck, *Z. Naturforsch.* **2001**, *56b*, 1271; D. Koch, K. Sünkel, W. Beck, *Z. Anorg. Allg. Chem.* **2003**, *629*, 1322.

[15] W. Hoffmüller, K. Polborn, J. Knizek, H. Nöth, W. Beck, *Z. Anorg. Allg. Chem.* **1997**, *623*, 1903.

[16] B. Kayser, W. Beck, *Z. Naturforsch.* **2004**, *59b*, 1423; H. Dialer, P. Mayer, K. Polborn, W. Beck, *Eur. J. Inorg. Chem.* **2001**, 1051.

[17] W. Hoffmüller, R. Krämer, M. Maurus, K. Polborn, W. Beck, *Z. Naturforsch.* **2000**, *55b*, 855.

[18] W. Ponikwar, W. Beck, *Z. Naturforsch.* **2003**, *58b*, 318.

[19] A. Lombardi, O. Maglio, V. Pavone, B. DiBlasio, M. Saviano, F. Nastri, C. Pedone, E. Benedetti, *Inorg. Chim. Acta* **1993**, *204*, 87.

[20] W. Beck, Th. Klapötke, W. Ponikwar, *Z. Naturforsch.* **2002**, *57b*, 1120.

[21] E. Fischer, F. Gerlach, *Ber. Dtsch. Chem. Ges.* **1912**, *45*, 2453.

[22] A. Hammershoi, R. M. Hartshorn, A. M. Sargeson, *J. Chem. Soc., Chem. Commun.* **1988**, 1267; P. J. Lawson, M. G. McCarthy, A. M. Sargeson, *J. Am. Chem. Soc.* **1982**, *104*, 6710.

[23] E. F. Birse, P. A. Williams, R. S. Vagg, *Inorg. Chim. Acta* **1988**, *148*, 57; E. F. Birse, P. A. Williams, S. Stephens, R. S. Vagg, *Inorg. Chim. Acta* **1988**, *148*, 63.

[24] B. Wagner, U. Taubald, W. Beck, *Chem. Ber.* **1989**, *122*, 1031.

[25] F. R. Hartley, *Organomet. Chem. Rev. A* **1970**, *6*, 119.