Metal Complexes of Biologically Important Ligands, CLXIX [1]. Palladium(II) and Platinum(II) N,O-Chelate Complexes (R3P)(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-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 (R3P)(Cl)M(µ-Cl)2M(PR3)(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 31P NMR and 13C 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 LnM(µ-Cl)2MLn 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 (R3P)(Cl)(µ-Cl)2M(PR3)(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)(Ph3P)Pt(α-amino isobutyrate) from (Cl)(Ph3P)Pt(µ-Cl)2Pt(Cl)(PPPh3), 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 (R3P)(Cl)M(α-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 CuC10H12H2O4 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 (R3P)(Cl)(µ-Cl)2M(PR3)(Cl) with the potassium salts of serine, threonine, 3,4-dehydroproline and 4-hydroxyproline in a CH2Cl2/CH3OH medium.

The reactions of 3,4-dehydroproline with Pd(II) or Pt(II) salts resulted in the precipitation of the metal.
The IR spectra (Table 1) of 1–10 exhibit the characteristic absorptions of the coordinated $\alpha$-amino carboxylate ligand at 3200 (NH) and 1600–1640 cm$^{-1}$ (CO$_2$). The $\nu$(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$_3$P)M(µ-Cl)$_2$M(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$_4$·7H$_2$O in 5 mL of water 1.0 mL of 1N NaOH (1.00 mmol) was added. The formed precipitate of Ni(OH)$_2$ was centrifuged off.
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 (318.96): calcd. C 37.66, H 4.62, 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 · 2H2O (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)palladium(II) (3) and chloro(tri-n-butylphosphine)(L-threoninato)palladium(II) (4)

To a solution of 400 mg (0.50 mmol) of (Et3P)2Pd(μ-Cl)2Pd(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 h at r.t. When the formed KCl 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.

Cloro(triphenylphosphine)(L-serinato)palladium(II) (5) and chloro(triphenylphosphine)(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.

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.

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(Ph3P)(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.

Yield 62 %, m. p. 179 °C (dec.). – C21H23ClNO3PPd (508.23): calcd. C 49.63, H 4.17, N 2.76; found C 49.10, H 4.40, N 2.71.

Yield 68 %, m. p. 196 °C (dec.). – C22H25ClNO3PPd (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\(^a\).

<table>
<thead>
<tr>
<th></th>
<th>(\text{CO}_2) trans/cis</th>
<th>(\alpha)-CH trans/cis</th>
<th>other trans/cis</th>
<th>(\text{P-(C}_2\text{H}_2)_n\text{-CH}_3), (n = 1,3)</th>
<th>(\text{P-(C}_2\text{H}_2)_n\text{-CH}_3), (n = 1,3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>serine (D(_2)O)</td>
<td>173.1</td>
<td>57.4</td>
<td>CH(_2)OH : 61.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>threonine (D(_2)O)</td>
<td>173.8</td>
<td>61.7</td>
<td>CH(_2)CH(_3)OH : 67.1</td>
<td>CH(_2)CH(_3)OH : 20.8</td>
<td></td>
</tr>
<tr>
<td>3 (CDCl(_3))</td>
<td>184.4(^b) (2.1)</td>
<td>57.7(^b)</td>
<td>CH(_2)OH : 63.0(^b)</td>
<td>13.6(^d)/14.0(^s) (38.8)</td>
<td>7.5(^d)/7.7(^d) (3.2)</td>
</tr>
<tr>
<td>4 (CDCl(_3))</td>
<td>183.9(^d)(^b) (4.2)</td>
<td>57.7(^b)</td>
<td>CH(_2)CH(_3)OH : 67.1(^b)</td>
<td>13.6(^d)/14.0(^s) (37.8)</td>
<td>7.5(^d)/7.7(^d) (3.1)</td>
</tr>
<tr>
<td>5 (CDCl(_3))</td>
<td>180.8(^d)/181.7(^s) (2.1)</td>
<td>61.4(^s)/58.6(^d) (2.1)</td>
<td>CH(_2)OH : 63.1(^s)/63.8(^s)</td>
<td>26.0(^d)/25.8(^d) (2.1)</td>
<td>13.7(^s)/13.6(^s)</td>
</tr>
<tr>
<td>6 (CDCl(_3))</td>
<td>182.3(^d)(^b)</td>
<td>65.9(^s)/61.9(^d) (2.5)</td>
<td>CH(_2)CH(_3)OH : 68.6(^s)/67.4(^s)</td>
<td>25.8(^d)/25.7(^d) (2.1)</td>
<td>13.5(^s)/13.6(^s)</td>
</tr>
<tr>
<td>7 (CDCl(_3))</td>
<td>178.9(^d)(^b) (3.1)</td>
<td>61.0(^s)/58.7(^s)</td>
<td>CH(_2)OH : 61.8(^s)/62.4(^s)</td>
<td>22.9(^d)/24.0(^d) (14.7)</td>
<td>21.5(^d) (29.9)</td>
</tr>
<tr>
<td>8 (CDCl(_3))</td>
<td>179.1(^d)(^b) (3.1)</td>
<td>57.7(^d)/61.8(^s)</td>
<td>CH(_2)CH(_3)OH : 66.5(^d)/66.8(^s)</td>
<td>22.9(^d)/21.5(^d) (31.5)</td>
<td>21.5(^d) (29.9)</td>
</tr>
</tbody>
</table>

\(^a\) \(\delta \) 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\(^a\).

<table>
<thead>
<tr>
<th>C–1</th>
<th>C–2</th>
<th>C–3</th>
<th>C–4</th>
<th>C–5</th>
<th>P((\text{CH}_2)_3\text{CH}_3)</th>
<th>P((\text{CH}_2)_3\text{CH}_3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C–1</td>
<td>172.2</td>
<td>68.5</td>
<td>125.7/125.4</td>
<td>52.4</td>
<td>25.7(^d) (3.2)</td>
<td>13.6(^s)</td>
</tr>
<tr>
<td></td>
<td>182.2(^d) (3.2)</td>
<td>70.2(^d) (3.2)</td>
<td>126.7(^d)/128.2(^s) (1.6)</td>
<td>56.8(^d) (2.6)</td>
<td>24.0(^d) (13.6)</td>
<td>21.5(^d) (29.9)</td>
</tr>
<tr>
<td>C–3</td>
<td>175.2</td>
<td>61.1</td>
<td>38.7</td>
<td>71.3</td>
<td>54.2</td>
<td>25.8(^d) (2.4)</td>
</tr>
<tr>
<td></td>
<td>184.9(^d) (2.8)</td>
<td>61.3(^d) (3.1)</td>
<td>39.9(^s)</td>
<td>70.3(^d) (3.1)</td>
<td>57.6(^d) (2.4)</td>
<td>24.1(^d) (14.0)</td>
</tr>
</tbody>
</table>

\(^a\) In D\(_2\)O; \(\delta \) 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 (\(\text{n}-\text{Bu}_3\text{P})(\text{Cl})\text{Pd}(\mu-\text{Cl})_2\text{Pd}(\text{n}-\text{Bu}_3\text{P})(\text{Cl}) in 15 mL of dichloromethane. Immediately, the color changed from red to yellow. After stirring for 1 1/2 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.


10: Yield 75 \%; m. p. 133 °C. – C\(_{17}\)H\(_{35}\)ClNO\(_3\)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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