

Novel complexes of N-substituted-4,5-dimethoxy-phenylethyl-2-arylketoamides with metal ions

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The current work presented the synthesis and characterization of a new Pd(II) complex of N-(2-benzoyl-4,5-dimethoxyphenethyl)-2-phenylacetamide (L1) and Zn(II) complex of ethyl-(4,5-dimethoxy-2-(2-phenylacetyl)phenethyl) carbamate (L2). The complexes were analyzed using IR-, ¹H-NMR-, ¹³C-NMR-spectra and Raman spectroscopy. For Pd(II)L1 and Zn(II)L2 complexes we suppose that L1 was coordinated monodentate with NH group and L2 was coordinated as bidentate ligand with N- and O-atoms involved in complexation. The IR spectral data for Pd(II)L1 and Zn(II)L2 complexes showed presence of OH⁻ groups, most probably coordinated to the metal ion, thus forming square planar or octahedral geometry, respectively.

Keywords: metal complexes, ketoamides, synthesis

INTRODUCTION

The pharmacological activity of tetrahydroisoquinolines has long been established. The tetrahydroisoquinoline motif is present in a variety of natural products, including cactus alkaloids (peyoruvic acid), mammalian alkaloids (salsoline carboxylic acid), Esteinascidine family (ET743) and spiro-benzo-quinoline alkaloids (parfumine).

The biological activity of isoquinoline derivatives, as analogues of various drugs, has provided great deal of interest for the synthesis of new compounds. In our previous reports [1] we described ortho-acylation of 2-phenethylamines in polyphosphoric acid. The products were obtained after ortho-acylation of 2-phenethylamides in polyphosphoric acid (Figure 1).

The obtained ketoamides are interesting from the synthetic point of view as starting compounds for the synthesis of isoquinoline ring system. The construction of isoquinoline ring has been a popular area of research in natural product chemistry. The aim of the present study was the synthesis and structural elucidation of new complexes of palladium(II) and zinc(II) with N-(2-benzoyl-4,5-dimethoxyphenethyl)-2-phenylacetamide (L1) and ethyl-(4,5-dimethoxy-2-(2-phenylacetyl)phenethyl) carbamate (L2) as ligands. The Zn as transition metal was chosen because of its important biological role in enzyme system of animals and plants [2, 3], whereas Pd(II) coordinates differently with interesting site in amide ligands [4]. The structure of the obtained complexes was studied by means of experimental IR, Raman, ¹H- and ¹³C-NMR methods.

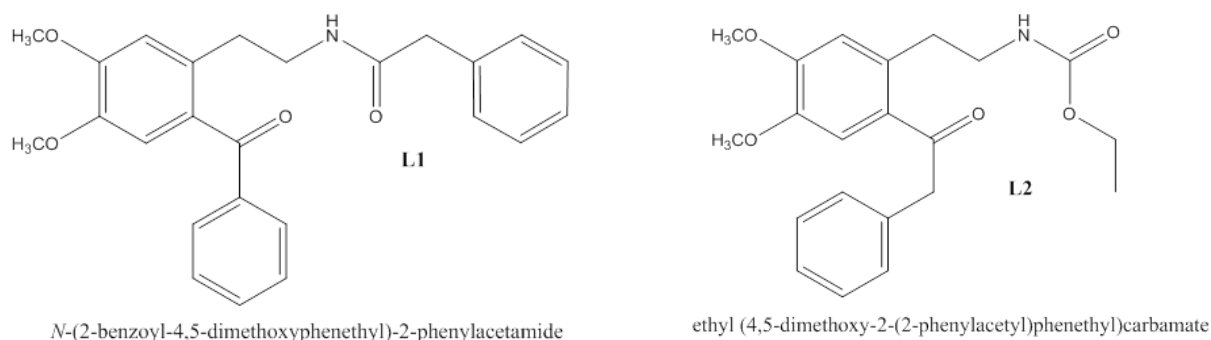


Figure 1. Structural formulas of the ketoamides

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EXPERIMENTAL

The metal salts $(\text{NH}_4)_2[\text{PdCl}_4]$ and $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 3\text{H}_2\text{O}$ - Sigma-Aldrich or Merck) and the solvents used for synthesis of the complexes were with p.a. qualification. The two organic ligands L1 and L2 were synthesized according to methods previously reported [1]. The IR spectra of all compounds were registered in KBr pellets on a Bruker FT-IR VERTEX 70 spectrometer from 4000 cm^{-1} to 400 cm^{-1} at resolution 2 cm^{-1} with 25 scans. The Raman spectra of the free ligands and the Pd(II)L1 and Zn(II)L2 complexes were measured on a spectrometer RAM II (Bruker Optics) with a focused laser beam of 20 mW and 200 mW power of Nd:YAG laser (1064 nm) from 4000 cm^{-1} to 50 cm^{-1} at resolution 2 cm^{-1} with 25 scans. The NMR spectra were taken on a Bruker Avance II+ 600MHz NMR spectrometer operating at 600.130 and 150.903 MHz for ^1H and ^{13}C , respectively, using the standard Bruker software. Chemical shifts were referenced to tetramethylsilane (TMS). Measurements were carried out at ambient temperature.

Synthesis of Pd(II) and Zn(II) complexes of N-(2-benzoyl-4,5-dimethoxyphenethyl)-2-phenylacetamide (L1) and ethyl-(4,5-dimethoxy-2-(2-phenylacetyl)phenethyl)carbamate (L2)-general procedure

5 mL NaOH (0.0004 mol (0.016 g) in 5 mL H_2O) was added slowly to the solution of L1 (0.0004 mol (0.1612 g) in 5 mL DMSO) or L2 (0.0004 mol (0.1484 g) in 5 mL DMSO). The solution of metal salts (0.0002 mol (0.05686 g) $(\text{NH}_4)_2[\text{PdCl}_4]$ in 10 mL H_2O or 0.0002 mol (0.0475 g) $\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 3\text{H}_2\text{O}$ in 10 mL H_2O) was added dropwise from a burette during stirring with an electromagnetic stirrer. Non-charged complexes Pd(II)L1 and Zn(II)L2 were formed as orange-red or yellow amorphous precipitates, respectively. The precipitates were filtered off and washed with $\sim 2\text{ mL}$ H_2O . These were dried over CaCl_2 for 2 weeks. It was found that the all newly-synthesized complexes were soluble in DMSO and insoluble in water.

mp (L1) = $108\text{--}111^\circ\text{C}$, mp (PdL1) = $124\text{--}127^\circ\text{C}$; W(Pd)% = 11.2%;

mp (L2) = $93\text{--}95^\circ\text{C}$, mp (ZnL2) = $206\text{--}208^\circ\text{C}$; W(Zn)% = 7.8%.

RESULTS AND DISCUSSION

Complexation with Pd(II) and Zn(II) using metal salts, namely $(\text{NH}_4)_2[\text{PdCl}_4]$ and

$\text{Zn}(\text{CH}_3\text{COO})_2 \cdot 3\text{H}_2\text{O}$ at a molar ratio $\text{M:L:OH}^- = 1:2:2$ for all complexes were studied. All complexes were isolated as amorphous precipitates and have rather poor solubility in the most common organic solvents, except for strongly coordinating solvents such as DMSO.

The IR band at 3307 cm^{-1} of L1 that was observed may refer to the stretching vibrations of the N-H group of the ketoamide. In the IR spectrum of L1 the bands at 1662 cm^{-1} can be attributed to stretching vibrations of C=O group from the keto group and 1652 cm^{-1} to stretching vibrations of C=O group from the amide group. The first band in the Raman spectra of L1 and Pd(II)L1 complex appeared at 1670 cm^{-1} . The band at 1652 cm^{-1} missed in the Raman spectra of L1 and Pd(II)L1. Several bands in the Raman spectrum of the ligand L1 ($3058, 3004\text{ cm}^{-1}$) and in the IR spectrum ($3078, 3059, 3025, 3002\text{ cm}^{-1}$) were for stretching vibrations of CH in the benzene moiety. In the IR spectrum of the Pd(II)L1 complex a broad band was observed at $3500\text{--}3400\text{ cm}^{-1}$, confirming the presence of OH group. The $^1\text{H-NMR}$ data of the Pd(II)L1 complex showed that NH signal changes from 8.1 ppm (t, 1H, NH, $J=5.4\text{ Hz}$) in the ligand's NMR to 7.0 ppm (t, 1H, NH, $J=5.4\text{ Hz}$) in the $^1\text{H-NMR}$ of the complex. According to the NMR-data we can suggest that NH from the ketoamide is involved in the complex structure. The ^1H - and ^{13}C -NMR spectral data for L1 and its Pd(II) complex are given in Table 1.

The suggested structure of the metal complex of Pd(II) with N-(2-benzoyl-4,5-dimethoxyphenethyl)-2-phenylacetamide (L1) is presented in Figure 2. Shehata *et al.* reported palladium complexes with coordinated water molecules (OH group) [5-12].

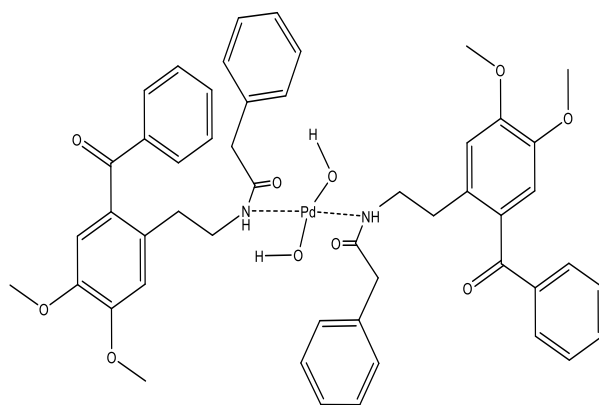


Figure 2. Suggested structure of the Pd(II)L1 complex

Table 1. ¹H and ¹³C NMR spectral data for N-(2-benzoyl-4,5-dimethoxyphenethyl)-2-phenylacetamide (L1) and Pd(II)L1[600.13 MHz (¹H) and 150.903 MHz (¹³C)]^a

Atom	δ (¹³ C) ppm	δ (¹ H) ppm	Multiplicity (J, Hz)	δ (¹³ C) ppm Pd(II)L1	δ (¹ H) ppm Pd(II)L1	Multiplicity (J, Hz) Pd(II)L1
CH ₂	32.7	2.5	(q, 2H, CH ₂ , J ₁ =2.4; J ₂ =3)	32.7	2.3	(t, 2H, J=6.6)
CH ₂ NH	40.4	2.7	(t, 2H, CH ₂ , J=7.2)	40.4	1.0	(t, 2H, J=7.2)
(NH)	-	8.1	(t, 1H, NH, J=5.4)	-	7.0	(t, 1H, NH, J=5.4)
COPh	197.3	-	-	197.3	-	-
COBn	150.8	-	-	150.8	-	-
2×OCH ₃	56.0	3.7; 3.8	(s, 3H, OCH ₃); (s, 3H, OCH ₃)	56.0	3.6; 3.8	(s, 3H, OCH ₃) (s, 3H, OCH ₃)
Ar	150.8	6.8	(s, 1H, o-Ar)	150.8	6.8	(s, 1H, o-Ar)
	138.3	7.0	(s, 1H, o-Ar)	138.3	6.9	(s, 1H, o-Ar)
	133.6	7.2-7.3	(m, 5H, Ar)	133.6	7.4-7.5	(m, 2H, Ar)
	130.3	7.5-7.7	(m, 5H, Ar)	130.3	7.6	(m, 1H, Ar)
	129.4			129.4	7.6-7.7	(m, 2H, Ar)
	129.1			129.1		
	128.6			128.6		
	126.7			126.7		
	114.3			114.3		
	113.2			113.2		

a) In DMSO-*d*₆ solution.

On the other hand the IR-spectra of L2 showed a band at 3339 cm⁻¹ that may refer to the stretching vibrations of the N-H group of the ketoamide. The vibrational stretching modes did not appear in the Raman spectrum of L2 and Zn(II)L2. In the IR spectrum of the Zn(II)L2 complex a broad band was observed at 3500-3400 cm⁻¹, confirming the presence of OH group. The C=O stretching vibration gives rise to strong IR bands and weak Raman bands [13]. The carbonyl C=O stretching band was easily identified in the IR spectrum because of its intensity and its lack of interference from most other group frequencies. In the IR spectrum of L2 the bands at 1691 cm⁻¹ can be attributed to stretching vibrations of C=O group from the keto group and at 1656 cm⁻¹ to C=O from the carbamate group. The first vibrational stretching modes did not appear in the Raman spectrum of the free ligand and the second appeared at 1652 cm⁻¹. The same bands in the Raman spectrum of the Zn(II)L2 complex appeared at 1689 cm⁻¹ and 1652 cm⁻¹. Unfortunately, there is a little difference in the stretching vibration of the CO from the ester COOCH₂CH₃ group. The cleavage of the intramolecular hydrogen bond is probably observed. According to that presuming it would be difficult to handle the characteristic bands and the observed changes in the complex spectra would be insignificant. Several bands in the Raman spectrum of the ligand L2 (3065, 3014 cm⁻¹) and in the IR spectrum (3082, 3065, 3055, 3026, 3011 cm⁻¹) were for stretching vibrations of CH in the benzene moiety.

The Raman data of the free ligands L1 and L2 and their metal complexes with Zn(II) and Pd(II) are presented in Table 2.

Table 2. Raman data of the free ligands L1 and L2 and their metal complexes with Zn(II) and Pd(II)

Raman data of free ligand L1	Pd(II)L1 complex
3058, 3004, 2936, 1670, 1598, 1574, 1449, 1347, 1268, 1240, 1173, 1103, 1061, 1031, 1000, 878, 830, 749, 721, 616, 552, 475, 408, 371, 349, 241.	3059, 2935, 1670, 1598, 1574, 1448, 1341, 1031, 1000, 760, 720.
Raman data of free ligand L2	Zn(II)L2 complex
3065, 3014, 2939, 2606, 1652, 1599, 1571, 1452, 1391, 1362, 1346, 1332, 1298, 1268, 1218, 1176, 1104, 1062, 1031, 1002, 971, 950, 888, 852, 818, 751, 721, 688, 617, 578, 552, 496, 476, 411, 379, 345, 304, 278, 248, 229.	3065, 2935, 1689, 1652, 1599, 1571, 1444, 1362, 1345, 1332, 1268, 1176, 1104, 1062, 1031, 1002, 888, 751, 721, 617, 552, 496, 410, 381, 345, 228.

The ¹H-NMR data of the Zn(II)L2 complex showed that NH signal changes from 7.06 ppm (t, 1H, NH, J=6 Hz) in the ligand's NMR to 8.02 ppm (t, 1H, NH, J=5.4 Hz) in the complex NMR. The ¹³C-NMR spectral data showed that the signal for C-atom from keto group (COOC₂H₅) was observed at 156.5 ppm in the ligand L2, while that in the Zn(II) complex at 170.4 ppm. The observed chemical shifts (14 ppm) clearly indicate

P.E. Marinova *et al.*: Novel complexes of *N*-substituted-4,5-dimethoxy-phenylethyl-2-arylketoamides with metal ions coordination of keto group to the metal center. According to the NMR-data we can suggest that NH and CO group from the carbamate are involved in complexation with the Zn(II) ion. The signal for the carbonyl group (from the ketone) in the ^{13}C -NMR spectrum of the complex and ligand was observed at 197.3 ppm and did not change.

The most probable structure of the Zn(II)L2 complex was suggested with two ligand molecules coordinated in a bidentate fashion and two OH groups coordinated to the metal centre (octahedral geometry for metal ion) (Figure 3). The structure of the obtained Zn(II)L2 complex was similar to those presented by Bhagwan *et al.* for *N*-(pyridyl)-3-carboxypropanamide and *N*-(pyridyl)-3-carboxybenzamide with Zn(II) [13].

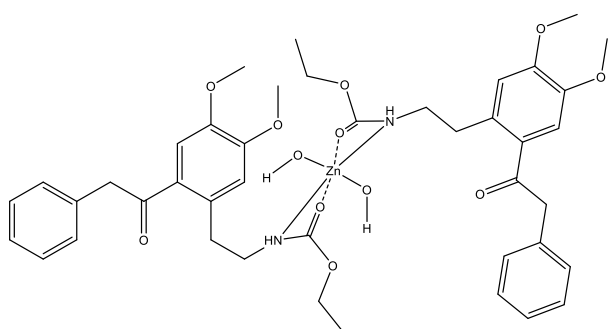


Figure 3. Suggested structure for the Zn(II) complex

CONCLUSIONS

The synthesis of new Pd(II) and Zn(II) complexes with ketoamide and ketoester, respectively have been described. The IR and ^1H - ^{13}C -NMR data showed, that in Pd(II)L1 complex the ligand behaves as a monodentate with N-atom from NH group. For Zn(II)L2 complex we suggested that L2 coordinates as a bidentate ligand

with N- and O-atoms involved in complexation and formed the chelate structure. The IR data for both complexes showed presence of OH group, most probably coordinated to the metal center, thus forming square planar (Pd(II)L1) and octahedral geometry (Zn(II)L2).

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