Synthesis and structures of complexes of *N*-2-nitroxyethylpicolinamide and 2-(2-pyridyl)-2-oxazoline with $PdCl_2$

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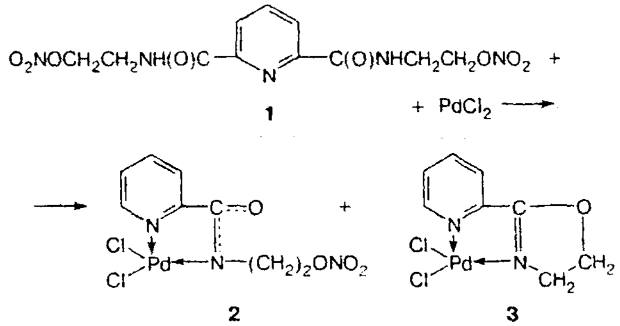
The reaction of *N,N'*-bis(2-nitroxyethyl)pyridine-2,6-dicarboxamide with $PdCl_2$ afforded previously unknown *cis*-(*N*-2-nitroxyethylpicolinamide-*N,N'*)dichloropalladium(II) and *cis*-[2-(2-pyridyl)-2-oxazoline-*N,N'*]dichloropalladium(II), which were isolated as a cocrystallizate of the molecular compounds. Its structure was established by X-ray diffraction analysis.

Key words: *N,N'*-bis(2-nitroxyethyl)pyridine-2,6-dicarboxamide, reaction with palladium(II) chloride, *cis*-(*N*-2-nitroxyethylpicolinamide-*N,N'*)dichloropalladium(II), *cis*-[2-(2-pyridyl)-2-oxazoline-*N,N'*]dichloropalladium(II), crystal structure, X-ray diffraction analysis.

It is known that derivatives of nicotinic acid, such as 2-nitroxyethyl nicotinate and *N*-(2-nitroxyethyl)nicotinamide, readily form palladium and platinum complexes.[1,2] It should be noted that these complexes have a *trans* structure. Data on the synthesis of *cis*-complexes of this type, which possess higher anticancer activity,[3,4] are lacking in the literature. However, one can try to affect physiological activity of metal complexes by varying the number of nitrate groups in the organic ligand. In this connection, we attempted to synthesize a complex of *N,N'*-bis(2-nitroxyethyl)pyridine-2,6-dicarboxamide (**1**) with $PdCl_2$. The introduction of two (2-nitroxyethyl)amide groups at the α,α'-positions of the pyridine ring substantially reduces the donor properties of the N atom of the pyridine ring. Actually, when a solution of compound **1** in aqueous ethanol was mixed with an aqueous solution of $PdCl_2$ and the reaction mixture was acidified with concentrated HCl to pH 2—2.5, complexation was not observed over several hours. On further storage of the solution, a precipitate was slowly formed, which was filtered off after 30 days.



The precipitate appeared to be a crystalline molecular compound of *cis*-(*N*-2-nitroxyethylpicolinamide-*N,N'*)dichloropalladium(II) (**2**) with *cis*-[2-(2-pyridyl)-2-oxazoline-*N,N'*]dichloropalladium(II) (**3**), whose structure was established by X-ray diffraction analysis. Evidently, the ligands were formed as a result of hydrolytic elimination of one nitroxyethylamide group from the initial diamide **1**, which led to an increase in the basicity of the N atom in the pyridine ring to form a chelate complex with $PdCl_2$ (**2**). Apparently, complex **3** was formed upon further elimination of the ONO_2 group accompanied by closure of the oxazoline ring.

Complexes **2** and **3** cocrystallized as a molecular compound containing one molecule of **2**, one molecule of **3**, and three water molecules per asymmetric unit of the triclinic crystal.

In complex **2** (Fig. 1), the Pd^{II} ion has a planar coordination. The Pd(2)Cl(3)Cl(4)N(3)N(4) atoms deviate from the coordination plane by no more than ±0.012 Å. The coordination plane forms angles of 0.6 and 1.9° with the planes of the Pd(2)N(3)N(4)C(9)C(14) chelate unit and the pyridine ring, respectively. The angle between the chelate and pyridine rings is 2.2°. Therefore, all atoms involved in the environment about the Pd^{II} ion are nearly coplanar. On the one hand, the distribution of the C(14)—O(2) and C(14)—N(4) bond lengths (1.22(3) and 1.36(3) Å, respectively) is typical of amide fragments. On the other hand, the H atom cannot be localized at the N(4) atom due to the planar environment about this atom. The C(14)N(4)C(15), C(14)N(4)Pd(2), and C(15)N(4)Pd(2) angles are 118.3, 113.9, and 127.8°, respectively. Apparently, the H atom migrates between the O(2) atom of the carbonyl group and the N(4) atom of the amide group rather than occupying a fixed position. In complex **2**, conformation-dependent orbital interactions between the metal ion and the ligands can occur.

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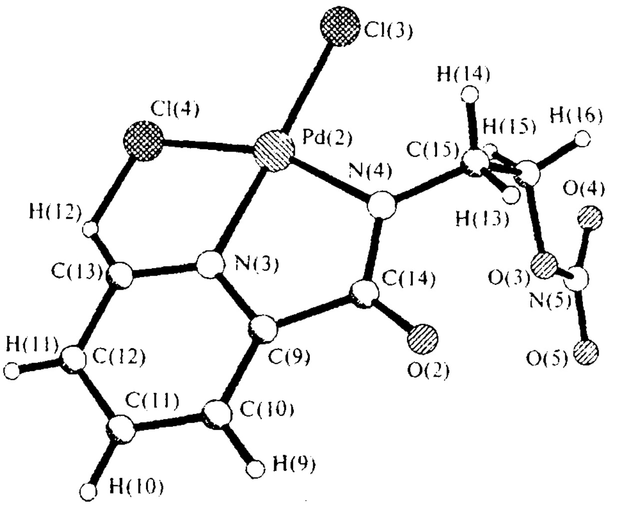

Fig. 1. Molecular structure of *cis*-(*N*-2-nitroxyethylpicolinamide-*N*,*N'*)dichloropalladium(II) (**2**).

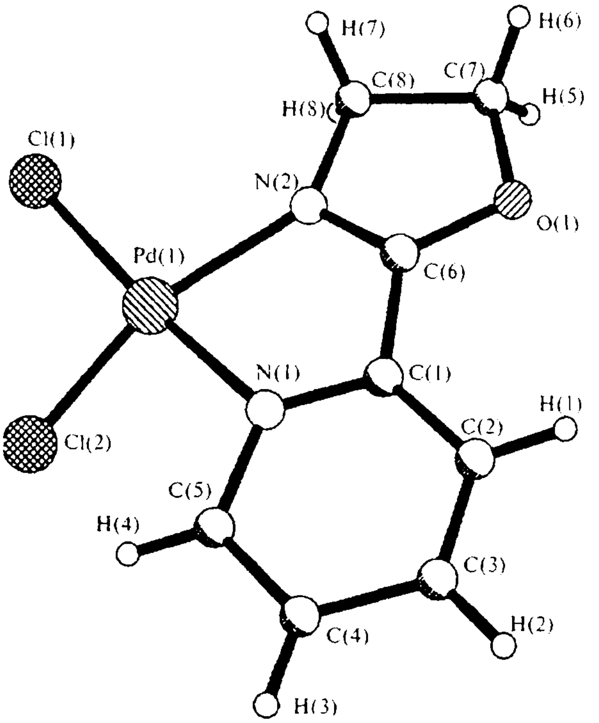

Fig. 2. Molecular structure of *cis*-[2-(2-pyridyl)-2-oxazoline-*N*,*N'*]dichloropalladium(II) (**3**).

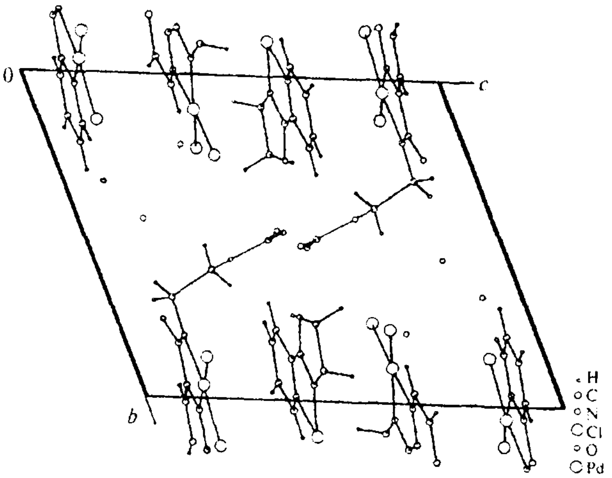

Fig. 3. Projection of the structure of the cocrystallizate onto the *bc* plane.

Complex **3** (Fig. 2) is also a chelate compound with a planar coordination about the Pd^{II} ion. The three fused rings, *viz.*, the pyridine, chelate, and oxazoline rings, form the environment about the Pd^{II} ion. The Pd(1)Cl(1)Cl(2)N(1)N(2) atoms deviate from the coordination plane by no more than ±0.054 Å. The *cis*-coordinated N atoms are involved in the chelate ring. The Pd(1)N(1)N(2)C(1)C(6) plane passing through the chelate unit forms an angle of 2.7° with the coordination plane. The pyridine, chelate, and oxazoline rings are virtually coplanar. The angles between the ring planes are 2.3, 6.9, and 4.6°, respectively. The arrangement of the *cis*-ligands in complex **3** is conformationally responsible for orbital interactions between the d_{xz} and d_{yz} orbitals of the Pd^{II} atom and the π^* orbitals of the pyridine and oxazoline rings. However, these interactions have only an insignificant effect on the bond lengths. Thus, the Pd(1)—N(1) (1.96(2) Å) and Pd(1)—N(2) (2.02(2) Å) bond lengths are actually somewhat smaller than the sum of the covalent radii (2.070 Å). The bond lengths in the pyridine and oxazoline rings have standard values. It should be noted that the C(6)—N(2) bond (1.27(2) Å) is substantially shorter than the adjacent N(2)—C(8) bond (1.48(2) Å) and its length corresponds to that of the double bond. The chelate rings in complexes **2** and **3** have different structures, namely, the C—N and C—C bond lengths are substantially different, the Pd—N bond lengths in both complexes being identical. In complex **3**, the N(1)—C(1), N(2)—C(6), and C(1)—C(6) bond lengths are 1.27(3), 1.27(2), and 1.47 Å, respectively, while in complex **2**, the corresponding N(3)—C(9), N(4)—C(14), and C(9)—C(14) bond lengths are 1.33(3), 1.36(3), and 1.53(4) Å, respectively. Apparently, this fact is attributable to the presence of the oxazoline fragment in complex **3**, which, evidently, leads to a change in the electronic structure of the chelate ring. The projection of the crystal structure onto the *bc* plane is shown in Fig. 3.

Experimental

N,*N'*-Bis(2-nitroxyethyl)pyridine-2,6-dicarboxamide was prepared according to a known procedure,[5] m.p. 145—146 °C. The IR spectrum was recorded on a Specord M-80 spectrometer in KBr pellets. The ^1H NMR spectrum was obtained on a Bruker-200 spectrometer.

Table 1. Atomic coordinates ($\times 10^4$) in the structure of the cocrystallizate of complexes **2** and **3**

Atom	*x*	*y*	*z*
Pd(1)	3146(1)	8907(1)	6226(1)
Pd(2)	214(2)	398(1)	8541(1)
Cl(1)	1645(6)	7525(5)	6159(5)
Cl(2)	4674(22)	7749(18)	6551(14)
Cl(3)	−1850(7)	1262(6)	8170(6)
Cl(4)	35(29)	−1483(25)	8690(20)
C(1)	3931(20)	11283(17)	6132(17)
C(2)	4804(24)	12157(16)	6235(20)
C(3)	6012(22)	11778(19)	6443(18)
C(4)	6419(24)	10525(17)	6653(21)
C(5)	5581(22)	9632(21)	6535(16)
C(6)	2562(23)	11437(18)	5882(19)
C(7)	744(29)	12401(21)	5251(26)
C(8)	715(28)	10960(21)	5477(26)
C(9)	2927(26)	359(21)	8919(19)
C(10)	4107(38)	−133(32)	9123(24)
C(11)	4362(29)	−1398(28)	9301(23)
C(12)	3436(28)	−2177(26)	9251(23)
C(13)	2134(29)	−1626(21)	9043(18)
C(14)	2371(30)	1705(22)	8750(18)
C(15)	465(35)	3113(23)	8455(28)
C(16)	570(27)	3978(20)	7285(22)
N(1)	4303(19)	10128(15)	6351(15)
N(2)	2004(16)	10500(13)	5845(12)
N(3)	1974(20)	−369(15)	8871(14)
N(4)	1076(24)	1915(17)	8561(20)
N(5)	2259(21)	4977(15)	5595(18)
O(1)	1979(16)	12600(13)	5567(15)
O(2)	3002(28)	2446(20)	8919(19)
O(3)	2015(17)	4313(13)	6700(13)
O(4)	1221(20)	5252(15)	5304(16)
O(5)	3514(18)	5192(15)	5134(16)
O(6)	6952(16)	−2179(16)	6855(14)
O(7)	9150(20)	3371(15)	919(13)
O(8)	4967(28)	5509(21)	8443(17)
H(1)	5280(279)	13394(263)	5934(202)
H(2)	6015(286)	12201(259)	5902(203)
H(3)	7359(294)	10370(256)	7162(204)
H(4)	6088(287)	6517(279)	6897(208)
H(5)	1036(282)	13018(267)	4803(221)
H(6)	−170(302)	12170(258)	5572(203)
H(7)	−163(308)	10438(262)	6035(214)
H(8)	958(282)	10811(255)	4769(217)

***cis*-(*N*-2-Nitroxyethylpicolenamide-*N*,*N*′)dichloropalladium(II) (2) and *cis*-[2-(2-pyridyl)-2-oxazoline-*N*,*N*′]dichloropalladium(II) (3).** An aqueous solution of $PdCl_2$ (4 mL, 40 mg mL^{-1}, 0.902 mmol) was added with stirring to a solution of *N*,*N*′-bis(2-nitroxyethyl)pyridine-2,6-dicarboxamide **1** (0.553 g, 1.61 mmol) in a mixture of water (20 mL) and EtOH (40 mL) at 20—30 °C. Then concentrated HCl was added to pH 2—2.5. The reaction mixture was stirred for 2 h and kept at ~20 °C for 30 days. The precipitate that formed was filtered off, washed with water and EtOH, and dried in air. Trihydrate of the molecular compound was obtained in a yield of 0.14 g (22.6%). Recrystallization from MeCN gave yellow crystals, T_{decomp} > 215 °C. Found (%): C, 24.56; H, 2.37; Cl, 18.27; N, 8.96. $C_{16}H_{17}Cl_4N_5O_5Pd_2 \cdot 3H_2O$. Calculated (%): C, 25.02; H, 3.02; Cl, 18.46; N, 9.12. IR (KBr), ν/cm^{-1}: 761 (NO_2); 866 (O—NO_2); 1011 (C—O); 1267 (C—N, amide); 1285 and 1612 (ONO_2); 1091 and 1625 (2-oxazoline ring); 705, 741, 1396, 1490, 1579, and 1557 (2-pyridyl); 2924 (CH_2); 3092 (CH); 3430 (H_2O). ^{1}H NMR (DMSO-d_6), δ: 8.98 (m, 1 H, H(6), $J_{6,5}$ = 5.3 Hz, $J_{6,4}$ = 1.3 Hz, $J_{6,3}$ = 0.4 Hz); 8.36 (m, 1 H, H(4), $J_{4,6}$ = 1.3 Hz, $J_{4,5}$ = 8.0 Hz, $J_{4,3}$ = 7.0 Hz); 7.98 (br.m, 1 H, H(3), $J_{3,4}$ = 7.0 Hz, $J_{3,5}$ = 0.7 Hz, $J_{3,6}$ = 0.4 Hz); 7.94 (m, 1 H, H(5), $J_{5,6}$ = 5.3 Hz, $J_{5,4}$ = 8.0 Hz, $J_{5,3}$ = 0.7 Hz); 5.03 (t, 2 H, CH_2—O (**3**), *J* = 9.8 Hz); 4.62 (t, 2 H, CH_2ONO_2 (**2**), *J* = 5.1 Hz); 3.98 (t, 2 H, CH_2—N (**3**), *J* = 9.8 Hz); 3.50 (t, 2 H, CH_2—N (**2**), *J* = 5.1 Hz).

X-ray diffraction data were collected from a platelet-like single crystal of dimensions 0.05×0.2×0.4 mm on a four-circle KM-4 diffractometer (KUMA-Diffraction, Poland).

Crystals are triclinic, molecular weight is 767.62, a = 9.781(6) Å, b = 11.394(7) Å, c = 14.288(9) Å, α = 66.78(8)°, β = 72.53(8)°, γ = 85.2(7)°, V = 1394.9(5) Å^3, d = 1.827 g cm^{-3}, λ = 1.5418 Å, space group $P1^{-}$, $Z = 2$, μ = 14.35 mm^{-1}.

A total of 4675 reflections were measured using the $\omega/2\theta$ scanning technique in the angle range of $3.5° < \theta < 80.5°$ of which 4394 reflections had $I > 2\sigma(I)$. The structure was solved by the direct method with the use of the SHELX-86 program package. The structure of the complex was refined taking into account the correction for absorption from the crystal habitus. The atomic coordinates of all the components of the unit cell were refined by the full-matrix least-squares method using the SHELX-93 program package. Thermal parameters of the non-hydrogen and H atoms were refined anisotropically and isotropically, respectively, based on 4394 reflections with $F_0 > 4\sigma(F_0)$ to an R factor of 0.090. The atomic coordinates in the structure of the complex are given in Table 1.

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