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Preparation and characterization of palladium(II) complexes with *N*-arylalkyliminodiacetic acids. Catalytic activity of complexes in methoxycarbonylation of iodobenzene

Neven Smrečki [a], Boris-Marko Kukovec [a], Jarosław Jaźwiński [b,**], Ye Liu [c,***], Jing Zhang [c], Ana-Matea Mikecin [d], Zora Popović [a,*]

[a] Laboratory of General and Inorganic Chemistry, Department of Chemistry, Faculty of Science, University of Zagreb, Horvatovac 102a, 10000 Zagreb, Croatia
[b] Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44, Warsaw 01-224, Poland
[c] Shanghai Key Laboratory of Green Chemistry and Chemical Processes, Chemistry Department, East China Normal University, 3663 North Zhongshan Road, Shanghai 200062, PR China
[d] Laboratory of Experimental Therapy, Division of Molecular Medicine, Rudjer Bošković Institute, Bijenička 54, 10000 Zagreb, Croatia

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ABSTRACT

The reactions of *N*-arylalkyl derivatives of iminodiacetic acid (H_2Bnida, H_2Peida, H_2Ppida, *o*-H_2Cbida; Bn = benzyl, Pe = 2-phenylethyl; Pp = 3-phenylprop-1-yl; *o*-Cb = *o*-chlorobenzyl) with sodium tetrachloropalladate(II) in aqueous solutions were investigated. Five new palladium(II) complexes [Pd(HBnida)$_2$]·2H_2O (**1a**), [Pd(HBnida)$_2$] (**1b**), [Pd(HPeida)$_2$] (**2**), [Pd(HPpida)$_2$] (**3**) and [Pd(*o*-HCbida)$_2$] (**4**) were prepared and characterized by infrared spectroscopy, ^{1}H, ^{13}C and ^{15}N NMR spectroscopy and thermal analysis (TGA/DTA). The crystal structure of **1a** was determined by single-crystal X-ray structural analysis. The palladium(II) ion in the molecule of **1a** adopts a square planar coordination with two *N*,*O*-bidentate *N*-benzyl-hydrogeniminodiacetate ions. Complex **1a** is a *trans*-isomer. Antitumor properties of the complexes were tested on three human cell lines. The compounds did not significantly inhibit the growth of colon (HCT 116), breast (MCF-7) and lung (H 460) tumor cell lines. All prepared palladium(II) complexes exhibit the acceptable activities towards the methoxycarbonylation of iodobenzene.

1. Introduction

The design of multidentate ligands which have the potential to bind metals in a variety of modes is of great interest to us as we attempt to gain a clear understanding of how the nature of the metal, solvent and also the pH of the reaction mixture combine to give a variety of structures. Using experimental methods for the preparation of various *N*-arylalkyliminodiacetate ligands reported previously [1], we have prepared five palladium(II) complexes due to their possible catalytic and pharmacological properties. Carbonylation represents an important method for transforming bulk and fine chemicals into a diverse set of useful products [2–5], in which CO acts as a most useful C1 building block to introduce carbonyl group into the parent molecules. In the last decades, palladium-catalyzed carbonylation of aryl halides in the presence of nucleophiles has attracted much attention and become a promising tool for the synthesis of aromatic carbonyl compounds such as esters, acids, amides, ketones, alkynones, due to the increasing consciousness of the environmentally benign and efficient methodology in organic synthesis [6–13]. Among the aromatic carbonyl compounds, aromatic esters are conventionally synthesized with the involvement of carboxylic acid precursors. Alternatively, aryl carboxylic acid derivatives can be prepared through palladium-catalyzed carbonylation of the corresponding aryl halides with alcohols, which is defined as alkoxycarbonylation of aryl halides [3,14–17]. The advantages of this method include the broad availability of substrates and the high tolerance of palladium catalysts against a variety of functional groups. Therefore, this route has become a useful tool for the preparation of substituted aromatic esters.

* Corresponding author. Tel.: +385 1 4606354; fax: +385 1 4606341.
** Corresponding author. Tel.: +48 22 3432013; fax: +48 22 6326681.
*** Corresponding author. Tel.: +86 21 62232078; fax: +86 21 62233424.
E-mail addresses: jaroslaw.jazwinski@icho.edu.pl (J. Jaźwiński), yliu@chem.ecnu.edu.cn (Y. Liu), zpopovic@chem.pmf.hr (Z. Popović).

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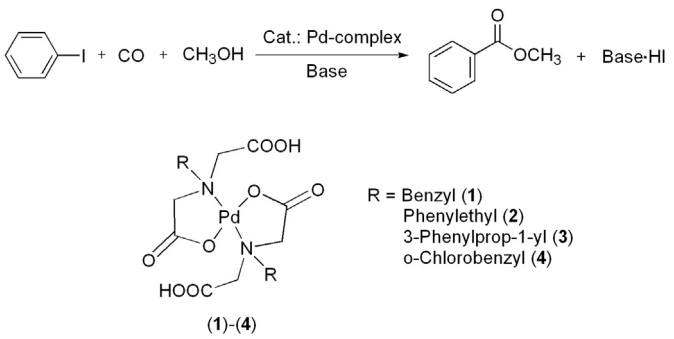
Besides their catalytic aspects, palladium(II) compounds exhibit inherent cytotoxic behavior. On the basis of the structural analogy (d^8 ions in a square-planar geometry) and the thermodynamic difference with platinum(II) complexes, there is much interest in the study of palladium(II) complexes as potential anticancer drugs, especially those bearing the chelating ligands [18–22].

Here we report the preparation, spectroscopic (IR and NMR) and thermal characterization of five new palladium(II) complexes with *N*-arylalkyliminodiacetate ligands as well as their antitumor properties and catalytic activity (Scheme 1). The crystal structure of the complex **1a** is also reported.

2. Experimental

2.1. Materials and physical measurements

Sodium hydroxide and $Na_2PdCl_4 \cdot xH_2O$ ($x \approx 3$), containing 30% Pd by weight, were purchased from Alfa Aesar and used as received without further purification. The ligands were prepared as reported earlier [1]. CHN analyses were performed on Perkin–Elmer 2400 Series II CHNS analyzer in the Analytical Services Laboratories of the Ruđer Bošković Institute, Zagreb, Croatia. The IR spectra were obtained from KBr pellets in the range 4000–450 cm^{-1} with Perkin–Elmer Spectrum RXI FTIR-spectrometer. TGA/DTA measurements were performed at heating rate of 10 °C min^{-1} in the temperature range of 25 – 600 °C, under nitrogen or oxygen flow of 20 mL min^{-1} on instrument Mettler-Toledo TGA/SDTA 851^e. Approximately 10 mg of sample were placed in standard aluminum crucible (40 μL). All NMR measurements were performed on a Bruker DRX AVANCE 500 spectrometer equipped with a 5 mm triple broadband inverse probe (TBI) with a z-gradient coil, and a Varian-NMR-vnmrs 600 spectrometer equipped with a 600 MHz PFG Auto XID ($^1H/^{15}N–^{31}P$ 5 mm) indirect probe. The measurements were carried out in DMSO-d_6 solutions, at the room temperature (303 K), using typical parameter values. Residual solvent signals were used as the secondary references, assuming 2.49 ppm (^1H) and 39.5 ppm (^{13}C) with respect to the TMS signal (0 ppm). Typically, a set of ^1H NMR, ^{13}C NMR, and $^{13}C,^1H$ g-HSQC and HMBC spectra were obtained. The nitrogen-15 chemical shifts were obtained from $^{15}N,^1H$ g-HMBC spectra, optimized for $^nJ(^1H,^{15}N)$ of 3, 6, or 8 Hz, depending on the sample. The nitrogen chemical shifts were given with respect to CH_3NO_2 (0 ppm). The $^1H(^{13}C)$ and ^{15}N NMR chemical shifts of starting ligands (ppm) are given below: H_2Bnida: $^1H(^{13}C)$ [ppm]: 3.41(53.6) $\underline{CH_2}CO_2H$; (172.3) $\underline{C}O_2H$; 3.83(57.1) $\underline{CH_2}Ar$; (138.7) C^i, 7.35(128.7, 128.2) *ortho*, *meta*, 7.26(127.1) *para* Ar; ^{15}N: −349.1 ppm; H_2Peida: $^1H(^{13}C)$ [ppm]: 3.49(54.6) $\underline{CH_2}CO_2H$; (172.4) $\underline{C}O_2H$; 2.88(55.8) $N\underline{CH_2}CH_2Ar$; 2.72(33.7) $NCH_2\underline{CH_2}Ar$; (139.9) C^i, 7.21(128.2) *ortho*, 7.27(128.6) *meta*, 7.18(129.9) *para* Ar; ^{15}N: −350.1 ppm; H_2Ppida: $^1H(^{13}C)$ [ppm]: 3.43(54.8) $\underline{CH_2}CO_2H$; (172.4) $\underline{C}O_2H$; 2.67(53.5) $N\underline{CH_2}CH_2CH_2Ar$; 1.68(29.2) $NCH_2\underline{CH_2}CH_2Ar$; 2.57(32.6) $NCH_2CH_2\underline{CH_2}Ar$; (142.0) C^i, 7.19(128.2) *ortho*, 7.26(128.2) *meta*, 7.16(125.6) *para*, Ar; ^{15}N: −353.1 ppm; *o*-H_2Cbida: $^1H(^{13}C)$ [ppm]: 3.46(53.9) $\underline{CH_2}CO_2H$; (172.3) $\underline{C}O_2H$; 3.96(54.2) $\underline{CH_2}Ar$; (132.9) C^i, 7.63(130.5), (136.4) *ortho*, 7.28(127.1), 7.41(129.1) *meta*, 7.23(128.6) para Ar; ^{15}N: −353.1 ppm. The samples have been measured about one hour after dissolution. In a few days, the samples slowly decomposed in DMSO solutions.



Scheme 1. Methoxycarbonylation of iodobenzene with methanol catalyzed by the palladium(II) complexes **1**–**4**.

2.2. Synthesis of the complexes

An aqueous solution of $Na_2PdCl_4 \cdot xH_2O$ ($x \approx 3$), (0.18 g; 0.5 mmol in 20 mL) was added to a hot solution containing 1 mmol of the appropriate ligands H_2Bnida, H_2Peida, H_2Ppida and *o*-H_2Cbida (Bn = benzyl, Pe = 2-phenylethyl; Pp = 3-phenylprop-1-yl; *o*-Cb = *o*-chlorobenzyl) and 0.04 g (1 mmol) NaOH in 25 mL of water. The resulting yellow solution was left to stand at room temperature for 48 h in case of complex **1a** (the crystallization starts few hours after mixing of the reactants) or overnight in case of the complexes **2**–**4** (**2** crystallizes after few minutes, while **3** and **4** precipitate immediately). The complexes were filtered off by suction, washed with water (5 mL for **1a**, 15 mL for **2**–**4**) and dried. Complex **1a** was dried by standing in air for a few hours, while **2**–**4** were dried first by standing in air for a few days and then in a desiccator over anhydrous $CaCl_2$. Drying the sample of **1a** in a desiccator over solid KOH at room temperature for one week gave $[Pd(HBnida)_2]$ (**1b**). The complexes are soluble in dimethyl sulfoxide and *N*,*N*-dimethylformamide but almost insoluble in water and pyridine.

$[Pd(HBnida)_2] \cdot 2H_2O$ (**1a**). From 0.23 g H_2Bnida. Yellow crystals; yield: 0.19 g (64%). After ~2 weeks, yellow prismatic crystals of **1a** (0.05 g; 17%), suitable for X-ray structural analysis, were obtained by the slow evaporation of the filtrate. Total yield 82%. Anal. Calc. for $C_{22}H_{28}N_2O_{10}Pd$ (586.89): C, 45.02; H, 4.81; N, 4.77%. Found: C, 46.02; H, 4.84; N, 5.08%. The assigned IR data (cm^{-1}): 3586(s) (ν(OH) of H_2O); ~3370(m, broad), 1718(s), 1231(m), 709(w) (ν(OH), ν(C=O), δ(OH) and π(OH) of COOH); 1628(vs) and 1358(m) (ν_{as} and ν_s of COO^-). Other IR data (cm^{-1}): 2932(w), 2711(w), 2602(w), 2515(w), 2365(w), 1942(w, br), 1494(w), 1459(w), 1434(w), 1418(w), 1319(m), 1288(w), 1114(w), 1084(w), 1065(w), 994(w), 964(w), 949(w), 921(m), 898(w), 871(w), 779(w), 751(w), 669(w), 636(w), 598(w), 571(w), 573(w).

$[Pd(HBnida)_2]$ (**1b**). The assigned IR data (cm^{-1}): ~3450 (m, broad), 1736(vs), 1216(s), 698(m) (ν(OH), ν(C=O), δ(OH) and π(OH) of COOH); 1612(vs) and 1380(vs) (ν_{as} and ν_s of COO^-). Other IR data (cm^{-1}): 2928(m), 2744(m), 2674(m), 2598(m), 2534(m), 1494(w), 1456(w), 1416(m), 1326(m), 1260(m), 1112(m), 1084(w), 1050(w), 1026(m), 964(m), 932(m), 892(m), 872(m), 748(m), 636(w), 588(w), 558(w), 524(w), 502(w). $^1H(^{13}C)$ NMR (δ, ppm; *J*, Hz): 3.15, 3.66 (56.1), ^2J 17.6 Hz CH_2 (het. ring); (168.9) (het. ring); 3.37, 4.36 (63.3), ^2J 15.9 $\underline{CH_2}CO_2H$; (176.7) $\underline{C}O_2H$; 3.80, 4.03 (64.0), ^2J 12.5 $N\underline{CH_2}Ar$; (132.3) C^i, 8.21(132.4) *ortho*, 7.49(128.5) *meta*, 7.43(129.1) *para*, Ar. The main to secondary product molar ratio: 1:0.16.

$[Pd(HPeida)_2]$ (**2**). From 0.24 g H_2Peida. Yellow crystals; yield: 0.27 g (93%). Anal. Calc. for $C_{24}H_{28}N_2O_8Pd$ (578.88): C, 49.79; H, 4.88; N, 4.84%. Found: C, 49.87; H, 5.06; N, 4.82%. The assigned IR data (cm^{-1}): ~3450(w, broad), 1731(vs), 1216(s), 701(m) (ν(OH), ν(C=O), δ(OH) and π(OH) of COOH); 1604(vs) and 1370(s) (ν_{as} and ν_s of COO^-). Other IR data (cm^{-1}): 3026(w), 2930(m), 2870(m), 2534(w), 2367(w), 1496(w), 1456(m), 1436(w), 1416(w), 1327(m), 1259(m), 1114(m), 1076(w), 1033(w), 996(w), 884(broad, m), 826(w), 754(m), 625(w), 584(w), 546(w), 522(w), 500(w), 481(w). $^1H(^{13}C)$ NMR (δ, ppm; *J*, Hz): 3.33, 3.72 (58.2), ^2J 17.3 Hz CH_2 (het. ring); (169.3) (het. ring); 3.31, 4.07 (62.7), ^2J 16.5 $\underline{CH_2}CO_2H$; (178.2) $\underline{C}O_2H$; 2.89 (63.5) $N\underline{CH_2}CH_2Ar$; 3.49, 3.92 (32.7) $NCH_2\underline{CH_2}Ar$; (138.1) C^i, 7.48(129.1) *ortho*, 7.33 (128.6) *meta*, 7.28 (126.5) *para*, Ar.

[Pd(HPpida)$_2$] (**3**). From 0.25 g H_2Ppida. Pale yellow powder; yield: 0.28 g (92%). Anal. Calc. for $C_{26}H_{32}N_2O_8Pd$ (606.93): C, 51.44; H, 5.31; N, 4.62%. Found: C, 51.25; H, 5.63; N, 4.54%. The assigned IR data (cm^{-1}): ~3440(w, broad), 1732(s), 1210(w), 699(w) (ν(OH), ν(C=O), δ(OH) and π(OH) of COOH); 1590(vs) and 1383(s) (ν_{as} and ν_s of COO$^-$). Other IR data (cm^{-1}): 3026(w), 2940(w), 2864(w), 2761(w), 2464(w), 2364(w), 1893(w), 1495(w), 1454(w), 1424(w), 1334(m), 1281(m), 1115(w), 1072(w), 1050(w), 1020(w), 1005(w), 976(w), 956(w), 933(w), 896(m), 847(w), 806(w), 750(m), 626(w), 594(w), 562(w), 506(w), 457(w). ^{1}H(^{13}C) NMR (δ, ppm; *J*, Hz; DMSO-d_6): *major component*: 3.22, 3.62 (58.6), ^2J 17.3 CH_2 (het. ring); (169.0) (het. ring); 3.11, 4.05 (63.0), ^2J 16.3 $\underline{CH_2}CO_2H$; (178.0) $\underline{CO_2}H$; 2.70 (61.5) N$\underline{CH_2}CH_2CH_2$Ar; 2.45, 2.77 (27.7) NCH$_2\underline{CH_2}$CH$_2$Ar; 2.72, 2.76 (32.6) NCH$_2$CH$_2\underline{CH_2}$Ar; (140.9) C^i, 7.16–7.38 (126.0, 128.3, 128.4) Ar; *minor component*: 3.35, 3.85 (58.6), ^2J 17.3 CH_2 (het. ring); (168.3) (het. ring); 3.32, 3.99 (63.2), ^2J 16.5 $\underline{CH_2}CO_2H$; (178.1) $\underline{CO_2}H$; 2.77, 2.84 (60.4) N$\underline{CH_2}CH_2CH_2$Ar; 2.38, 2.72 (28.9) NCH$_2\underline{CH_2}$CH$_2$Ar; n.a. NCH$_2$CH$_2\underline{CH_2}$Ar; (140.8) C^i, 7.16–7.38 (126.1, 128.2, 128.4) Ar. Major to minor components molar ratio: 1:0.35. n.a. – not assigned due to superposition with the signals of the major component.

[Pd(*o*-HCbida)$_2$] (**4**). From 0.26 g *o*-H_2Cbida. Pale yellow powder; yield: 0.28 g (90%). Anal. Calc. for $C_{22}H_{22}N_2O_8Cl_2Pd$ (619.74): C, 42.63; H, 3.58; N, 4.52%. Found: C, 42.71; H, 3.65; N, 4.46%. The assigned IR data (cm^{-1}): ~3450(w, broad), 1738(s), 1217(s), 683(w) (ν(OH), ν(C=O), δ(OH) and π(OH) of COOH); 1612(vs) and 1377(m) (ν_{as} and ν_s of COO$^-$). Other IR data (cm^{-1}): 2914(br, w), 2508(w), 2364(w), 1479(w), 1434(m), 1410(m), 1327(m), 1281(w), 1259(w), 1139(w), 1111(w), 1053(w), 1027(w), 965(w), 922(w), 899(w), 879(w), 866(w), 840(w) 757(m), 637(w), 602(w), 562(w), 530(w), 511(w), 477(w). ^{1}H(^{13}C) NMR (δ, ppm; *J*, Hz; DMSO-d_6): *major component*: 3.35, 3.80 (57.2), ^2J 17.4 CH_2 (het. ring); (168.6) (het. ring); 3.61, 4.29 (63.4), ^2J 16.1 $\underline{CH_2}CO_2H$; (176.6) $\underline{CO_2}H$; 4.06, 4.15 (60.0) ^2J 13.5 N$\underline{CH_2}$Ar "*linear*" *component*: 3.68, 4.47 (65.5), ^2J 15.7 $\underline{CH_2}CO_2H$; 4.09 (62.1) N$\underline{CH_2}$Ar. Major to linear components molar ratio: 1:0.79.

2.3. Single crystal X-ray diffraction analysis and structure determination

The suitable single crystal of **1a** was selected and mounted in air onto the thin glass fiber. The data collection for **1a** was carried out by an Oxford Diffraction Xcalibur four-circle kappa geometry diffractometer with Xcalibur Sapphire 3 CCD detector, using a graphite monochromated MoKα (λ = 0.71073 Å) radiation, and by applying the CrysAlis Software system, Version 1.171.32.29 [23] at room temperature (296(2) K). The data reduction was done by the same program [23].

The X-ray diffraction data were corrected for Lorentz-polarization factor and scaled for absorption effects by multi-scan. The structure was solved by direct methods, implemented in SHELXS-97 [24]. A refinement procedure by full-matrix least squares methods, based on F^2 values against all reflections, was performed by SHELXL-97 [24], including anisotropic displacement parameters for all non-H atoms.

The position of hydrogen atoms belonging to the carbon atoms was geometrically optimized applying the riding model (0.97 Å, U_{iso}(H) = 1.2U_{eq}(C) for methylen H atoms and 0.93 Å, U_{iso}(H) = 1.2U_{eq}(C) for aromatic H atoms). The hydrogen atoms belonging to the water molecules were found in the difference Fourier maps. The distance between the water molecule O atoms and the corresponding hydrogen atoms was restrained to the average value of 0.82 Å using SHELXL-97 DFIX instruction. The isotropic U_{iso}(H) values for these hydrogen atoms were fixed at the same time (U_{iso}(H) = 1.2U_{eq}(O)).

The affirmation of chosen space groups and the analysis of the molecular geometry and hydrogen bonds were performed by PLATON [25]. The molecular graphics were done with ORTEP-3 [26] and MERCURY (Version 3.1) [27].

The crystal parameters, data collection and refinement results for **1a** are summarized in Table 1.

3. Results and discussion

3.1. Synthesis and general properties of the complexes

All complexes **1**–**4** were prepared from sodium tetrachloropalladate(II), sodium hydroxide and the appropriate *N*-arylalkyliminodiacetic acid in slightly acidic aqueous solution. The molar ratio which was described in the Experimental section was found to be optimal for these preparations. The formation of these complexes was most probably assisted by their very low solubility, which allowed these reactions to proceed in a high yield (Scheme 2).

All these complexes are air-stable substances which are practically insoluble in common laboratory solvents other than dimethyl sulfoxide and *N*,*N*-dimethylformamide. Their solubility in water is increased by the addition of sodium hydroxide or sodium hydrogencarbonate, but the dissolution is not complete when only two moles of the base per mole of the complex are used.

It is worthwhile to mention that we were unable to obtain analogous complexes of platinum(II) by this method. Metallic platinum was formed when tetrachloroplatinate(II) was used instead of tetrachloropalladate(II).

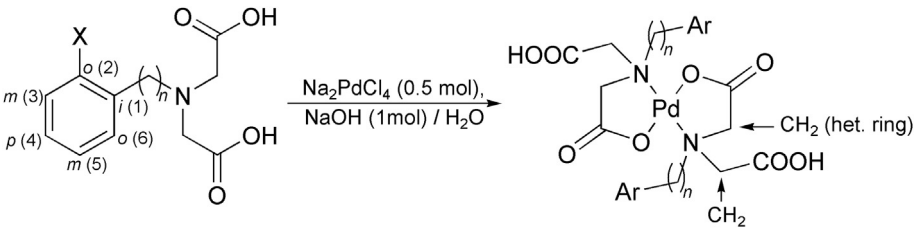
3.2. Crystal structure

The palladium(II) ion is placed at the inversion center and coordinated by two *N*,*O*-bidentate HBnida$^-$ ligands in **1a**, resulting with the square-planar coordination and the formation of *trans* isomer. HBnida$^-$ ligands are coordinated to palladium(II) ion via imino N1 and carboxylate O1 atoms (d(Pd1–N1), 2.057(1) Å; d(Pd1–O1), 1.989(1) Å), forming two five-membered chelate rings (Fig. 1). There are two co-crystallized water molecules in the structure of **1a**.

Table 1
Crystal data and details of the structure determination for **1a**.

Formula	$C_{22}H_{28}PdN_2O_{10}$
M_r	586.86
Color and habit	Yellow, prism
Crystal system, space group	Orthorhombic, *Pbca*
Crystal dimensions (mm^3)	0.70 × 0.33 × 0.14
a (Å)	13.8847(2)
b (Å)	10.0232(2)
c (Å)	16.9479(2)
V (Å)	2358.62(6)
Z	4
D_{calc} (g cm^{-3})	1.653
μ (mm^{-1})	0.847
F(000)	1200
θ Range for data collection (°)	4.31–30.00
h,k,l range	−19:19, −13:14, −23:23
Scan type	ω, φ
No. measured reflections	32768
No. independent reflections (R_{int})	3404 (0.0345)
No. observed reflections, $I \geq 2\sigma(I)$	1680
No. refined parameters	169
R,[a] wR[b] [$I \geq 2\sigma(I)$]	0.0241, 0.0511
R, wR [all data]	0.0765, 0.0579
Goodness of fit on F^2, S[c]	0.841
Max., min. electron density (e Å^{-3})	0.35, −0.25
Maximum Δ/σ	<0.001

[a] $R = \sum||F_o| - |F_c||/\sum|F_o|$.
[b] $wR = [\Sigma(F_o^2 - F_c^2)^2/\Sigma w(F_o^2)^2]^{1/2}$.
[c] $S = \Sigma[w(F_o^2 - F_c^2)^2/(N_{obs} - N_{param})]^{1/2}$.



Scheme 2. Preparation of the complexes **1**–**4** and numbering scheme for ^{1}H and ^{13}C nuclei of the ligands and complexes. X = H, $n = 1$ for H_2Bnida and $[Pd(HBnida)_2]\cdot 2H_2O$ (**1a**); X = H, $n = 2$ for H_2Peida and $[Pd(HPeida)_2]$ (**2**); X = H, $n = 3$ for H_2Ppida and $[Pd(Ppida)_2]$ (**3**); X = Cl, $n = 1$ for *o*-H_2Cbida and $[Pd(o\text{-}HCbida)_2]$ (**4**). Ar = aromatic ring; *i* = *ipso* (1), *o* = *ortho* (2, 6), *m* = *meta* (3,5), *p* = *para* (4).

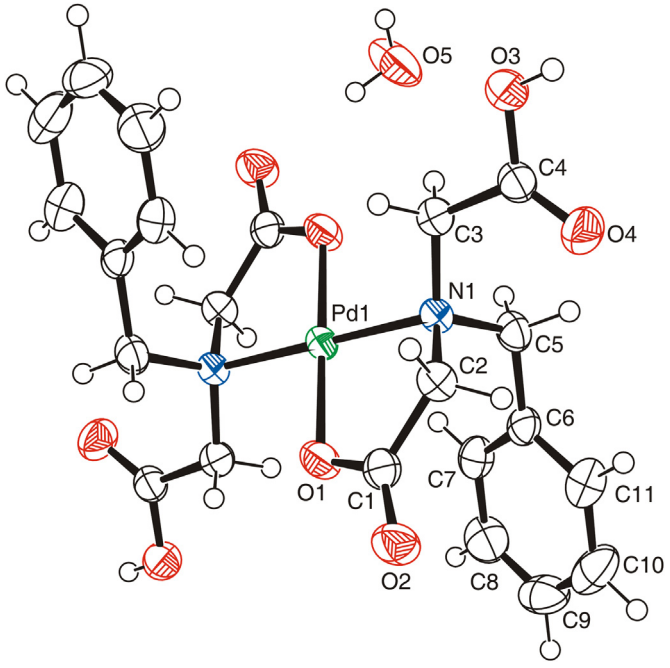


Fig. 1. ORTEP-3 drawing of $[Pd(HBnida)_2]\cdot 2H_2O$ (**1a**) with the atomic numbering scheme of the asymmetric unit. The thermal ellipsoids are drawn at the 50% probability level at 296(2) K. The selected bond distances (Å) and angles (°): Pd1–O1 1.989(1), Pd1–N1 2.057(1), O1–Pd1–$O1^{i}$ 180, N1–Pd1–$N1^{i}$ 180, O1–Pd1–N1 84.68(5), O1–Pd1–$N1^{i}$ 95.32(5) (symmetry code (i): $1 - x, 1 - y, 1 - z$).

The index τ_4, proposed for the geometry of four-coordinated complexes [28,29], is 0 which indicates perfect square-planar geometry. Moreover, the square is only slightly distorted, as it is evident from the values of the *cis* pairs of donor atoms, including the bite angles ($\angle$O1–Pd1–N1, 84.68(5)°), while the values of the *trans* pairs of donor atoms amount exactly 180° due to the symmetry. The dihedral angle between the rings, defined by Pd1/O1/C1/C2/N1 and Pd1/$O1^{i}$/$C1^{i}$/$C2^{i}$/$N1^{i}$ atoms (symmetry code (i): $1 - x$, $1 - y, 1 - z$) amounts 0.02(7)°. The Pd1/O1/C1/C2/N1 chelate ring is not planar, but twisted on C2–N1 line.

The Pd–N and Pd–O bond distances (N and O atoms from $HBnida^{-}$) in **1a** are similar to those of palladium(II) complexes with iminodiacetate [30], hydrogeniminodiacetate [31], 2-hydroxyethyliminodiacetate [32], ethylenediaminetetraacetate [33], 2-hydroxypropane-1,3-diaminetetraacetate [34] and cyclohexanediaminetetraacetate [35].

There are three intermolecular O–H···O hydrogen bonds and one weak intermolecular C–H···O hydrogen bond in the crystal structure of **1a** (Table 2). The molecules of $[Pd(HBnida)_2]$ and co-crystallized water molecules in the crystal structure of **1a** are assembled together into an infinite 3D framework (Fig. 2). Each $[Pd(HBnida)_2]$ molecule is hydrogen-bonded to six neighboring water molecules, while each water molecule is hydrogen-bonded to three neighboring $[Pd(HBnida)_2]$ molecules in this 3D framework.

3.3. Infrared spectroscopy

Complexes **1**–**4** exhibit similar solid-state infrared spectra. The infrared spectrum of **1a** shows ν_a(COO) at 1628 cm^{-1} and ν_s(COO) at 1358 cm^{-1}. Similar peaks of ν_a(COO) and ν_s(COO) are also observed in this region for complexes **1b** (1612 cm^{-1}, 1380 cm^{-1}), **2** (1604 cm^{-1}, 1370 cm^{-1}), **3** (1590 cm^{-1}, 1383 cm^{-1}), **4** (1612 cm^{-1}, 1377 cm^{-1}). The difference between ν_a(COO) and ν_s(COO), Δ value, is greater than 200 cm^{-1} for each of these complexes, indicating the monodentate coordination of the carboxylate group [36,37]. The stretching of the carbonyl group, ν(C=O), which appears in the spectra of the free ligands H_2Bnida (1729 and 1714 cm^{-1}), H_2Peida (1709 cm^{-1}), H_2Ppida (1738 cm^{-1}) and *o*-H_2Cbida (1685 cm^{-1}), is also present in the spectra of **1a** (1718 cm^{-1}), **1b** (1736 cm^{-1}), **2** (1731 cm^{-1}), **3** (1732 cm^{-1}) and **4** (1738 cm^{-1}). The broad bands observed in the range of 2300–3500 cm^{-1} indicate the extensive hydrogen bonding in **1a**, in accordance with its crystal structure.

3.4. NMR spectroscopy

The assignments of ^{1}H and ^{13}C signals of the ligands were straightforward. The $C\underline{H}_2COOH$ signal appeared as a singlet (4H), as well as $ArC\underline{H}_2$ signals in H_2Bnida and *o*-H_2Cbida (2H). Signal order in $N(CH_2)_nAr$ ($n = 2, 3$) chains was confirmed by means of DFT GIAO NMR calculations, which were performed at the 6-311G++(2d,p)/B3PW91//6-311G++(2d,p)/B3PW91 theory level, assuming a single arbitrarily selected rotamer for each compound and neglecting solvent effect. Such an approach appeared to be sufficient for signal assignments. The calculations were performed with the Gaussian 03 package [38].

The ^{1}H and ^{13}C NMR techniques were applied for the samples $[Pd(HBnida)_2]$ (**1**), $[Pd(HPeida)_2]$ (**2**), $[Pd(HPpida)_2]$ (**3**), and [Pd(*o*-

Table 2
Hydrogen bond geometry for **1a**.

D–H···A	*d*(D–H)/Å	*d*(H···A)/Å	*d*(D···A)/Å	∠(D–H···A)/°	Symmetry code on A
O3–H31···O5	0.82(2)	1.75(2)	2.552(2)	166(2)	$x - 1/2, y, 3/2 - z$
O5–H51···O2	0.80(2)	2.01(2)	2.814(2)	174(3)	$1 - x, 1 - y, 1 - z$
O5–H52···O4	0.78(2)	2.18(2)	2.784(2)	135(3)	$1 - x, y + 1/2, 3/2 - z$
C10–H10···O3	0.93	2.45	3.351(3)	164	$x, y - 1, z$

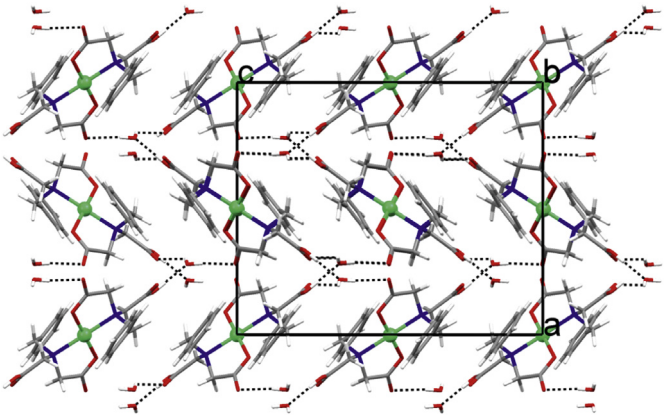


Fig. 2. The packing diagram of $[Pd(HBnida)_2]\cdot 2H_2O$ (**1a**) (a view in the (010) plane). The $[Pd(HBnida)_2]$ and co-crystallized water molecules are assembled into an infinite 3D framework by intermolecular O–H···O hydrogen bonds (shown by the dotted lines).

HCbida)$_2$] (**4**). Each complex contains two five-membered rings and two nitrogen atoms bearing four substituents. Consequently, two nitrogenous stereogenic centers were expected for each compound, and all CH_2 groups in the complex were expected to contain two chemically non-equivalent hydrogen atoms, showing two signals in a ^{1}H spectrum and correlating with the signal of one carbon atom in a 2D ^{1}H, ^{13}C HSQC spectrum. Furthermore, the 2D ^{1}H, ^{13}C HMBC spectra allow the identification of C=O, COOH and C^i(Ar) ^{13}C signals. Careful inspection of ^{1}H, ^{13}C and 2D ^{1}H, ^{13}C spectra allows the identification of all signals. The most diagnostic region in ^{1}H NMR spectra was that from 3 to 5 ppm. As an example, a part of the spectrum of $[Pd(HBnida)_2]$ was shown in Fig. 3.

The ^{1}H NMR spectrum of **1** contains the signals of main complex and unidentified minor signals of the secondary compound. The spectrum of **3** evidently contains the signal of two species exhibiting similar structural features. The presence of two sets of signals may be explained assuming that two diastereomers exist in the mixture, one with two nitrogenous stereogenic centers with the same configuration, N^R/N^R (N^S/N^S) and the second with different configurations, N^S/N^R.

The spectra of **4** were the most complicated. The inspection of all spectra revealed the presence of at least three sets of signals. One set of signals was identified as the signals of the free ligand; the second one as the signals of the complex, [Pd(*o*-HCbida)$_2$]. The assignment of remaining signals was not straightforward. A pair of doublets suggested a molecule bearing stereogenic centers or having ring structure; on the other side chemical shift of CO_2H carbon atom (177.4 ppm) was close to the value observed for the free ligands. Broad signals indicate an exchange process, medium fast at the NMR timescale. Tentatively, we suggest a non-cyclic structure for this compound (Fig. 4).

Our NMR investigations can be summarized as follows: (i) the signals assigned to main components of each sample agreed with the structures of complexes: $[Pd(HBnida)_2]$, $[Pd(HPeida)_2]$, $[Pd(HPpida)_2]$, and [Pd(*o*-HCbida)$_2$]; (ii) most of the samples contained additive of the secondary product, probably diastereomers of main component of the mixture. Three species were detected in one sample: the starting ligand and two complexes; (iii) The presence of diastereomers and various adducts in mixtures suggests the equilibrium between species in DMSO-d_6 solutions.

3.5. Thermal analysis (TGA/DTA)

With the exception of complex **1a**, which decomposes in two clear consecutive steps, all other complexes **1b**–**4** decompose in

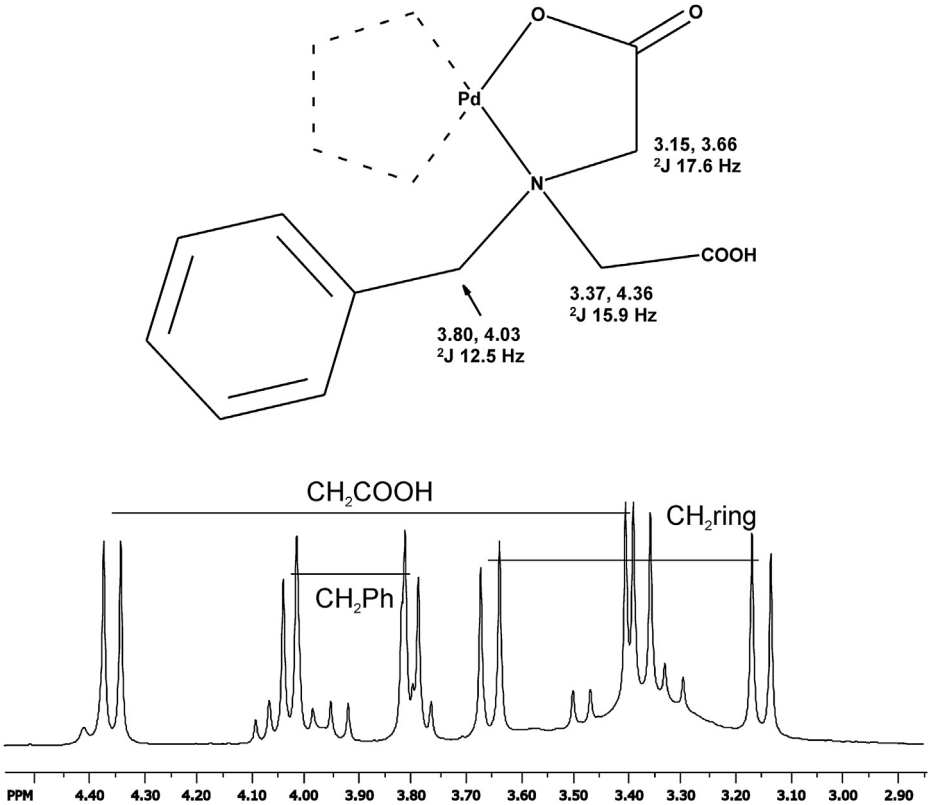


Fig. 3. A part of the ^{1}H NMR spectrum of $[Pd(HBnida)_2]$. For clarity reasons, only one ligand molecule was shown. Two protons of each CH_2 group are chemically non-equivalent and produce two signals (doublets) in the ^{1}H NMR spectrum. However, it is not the case of all complexes; some of CH_2 group produced only one signal in ^{1}H NMR.

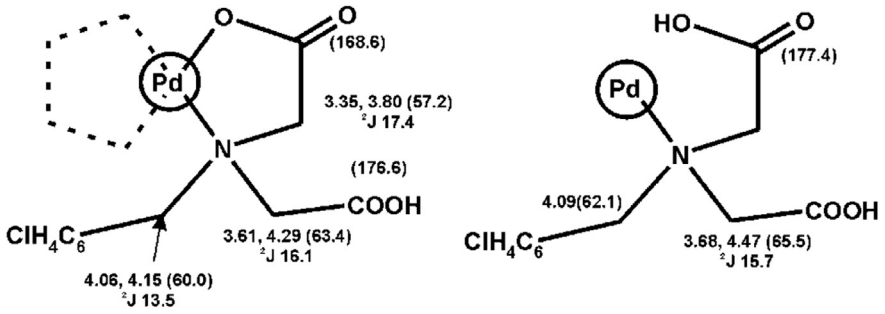


Fig. 4. The structure of [Pd(*o*-HCbida)$_2$] and suggested structure of the second complex in the mixture. For clarity reasons, only one ligand molecule was shown. Numbers in the figure denote ^{1}H (^{13}C) chemical shifts (ppm) and geminal $^2J(H,H)$ coupling constants (Hz).

Table 3
Thermal analysis data for complexes **1**–**4** under nitrogen atmosphere.

Complex	Temperature range (°C)	Mass loss (%); observed/calculated	Assignment	Observed residue at 600 °C (%)
1a	Step 1: 50–155	6.1/6.1	Two water molecules	19.6
	Step 2: 155–600	74.3/75.6	Two HBnida$^-$ ions	
1b	240–600	75.5/80.6	Two HBnida$^-$ ions	24.6
2	240–600	73.3/81.5	Two HPeida$^-$ ions	26.7
3	200–600	80.7/82.4	Two HPpida$^-$ ions	19.5
4	220–600	74.1/82.7	Two *o*-(HCbida)$^-$ ions	26.0

only one step or two overlapped consecutive steps. The first step in case of **1a** corresponds to the release of two water molecules. Thermal analysis data for these complexes are shown in Tables 3 and 4.

3.6. Catalytical performance

Compared with the phosphine-ligated palladium complexes which are environmentally unfriendly and toxic, the phosphine-free palladium complexes have attracted much attention in alkoxycarbonylation of aryl iodides with alcohols, from the point of view of potential application in green catalysis. As shown in Table 5, the developed phosphine-free palladium(II) complexes (**1**–**4**) exhibit the acceptable activities towards the methoxycarbonylation of iodobenzene with the yields up to 68% for methyl benzoate. In the case of **2**, a high activity was observed in comparison with the typical phosphine-ligated palladium(II) complex $PdCl_2(PPh_3)_2$.

Based on the mechanistic studies reported so far [39], it is suggested that methoxycarbonylation of iodobenzene with CO, catalyzed by the complexes **1**–**4** (L = Bnida, Peida, Ppida and *o*-Cbida), proceeds through the following steps: oxidative addition of iodobenzene (PhI) to Pd(0)L$_2$ complex (intermediate **I**) (formed in situ by the reduction of the starting palladium(II) complex (**1**–**4**)) to form organometallic intermediate (**II**) PhPdL$_2$I; coordination of CO to the palladium(II) ion to form the carbonyl complex PhPd(CO)LI

Table 5
Methoxycarbonylation of iodobenzene with methanol catalyzed by the different palladium(II) complexes.[a]

Entry	Pd-complex	Yield (%)[b]
1	**1**	75
2	**2**	85
3	**3**	73
4	**4**	68
5	$PdCl_2(PPh_3)_2$	95

[a] Palladium(II) complex concentration 2 mol%, PhI 1 mmol, Et_3N 1.5 mmol, MeOH 2 mmol, CO 1.5 MPa, Time 2 h, Temp. 100 °C, solvent [BMIM]PF_6 (1-butyl-3-methylimidazolium hexafluorophosphate) 2 mL.
[b] GC yields (with 100% selectivity to methyl benzoate).

(intermediate **III**) and insertion of CO into the Pd–Ph bond to give organometallic acyl palladium(II) complex PhCOPdL$_2$I (intermediate **IV**); reaction of **IV** with triethylamine and methanol to release methyl benzoate (PhCOOMe) and to regenerate the palladium(0) catalyst (**I**) (Scheme 3). Therefore, although our complexes **1**–**4** are not organometallic compounds themselves, the reaction catalyzed by these complexes contains organometallic intermediates according to the described mechanism.

3.7. Evaluation of antiproliferative effect of palladium(II) complexes in vitro

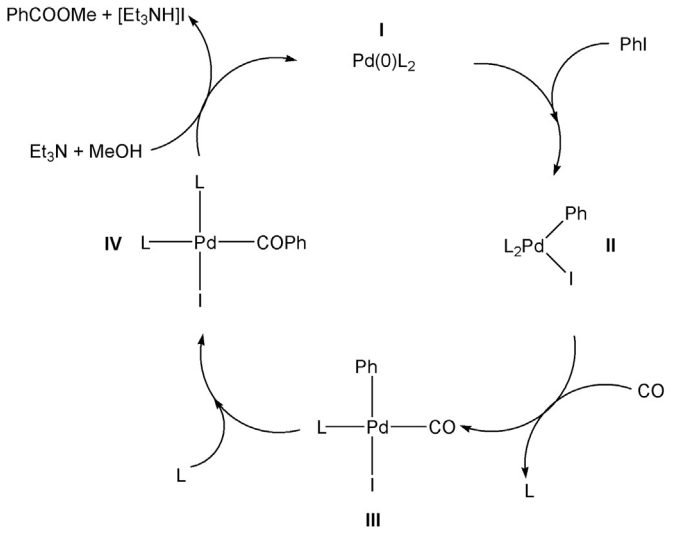
The tested palladium(II) compounds did not show antiproliferative activity towards tested cell lines. Slight activity was observed on HCT 116 cells, after the treatment with compound [Pd(HPeida)$_2$] (**2**), and on all cell lines after the treatment with [Pd(HPpida)$_2$] (**3**), but it did not inhibit the growth of cells for 50% at the maximal tested concentration (100 μM). The GI_{50} values for the complexes **1**, **2** and **3** are equal or greater than 100 μM in case of all three tested cell lines.

4. Conclusions

Several palladium(II) complexes were prepared by the reactions of sodium tetrachloropalladate(II) with various *N*-

Table 4
Thermal analysis data for complexes **1**–**4** under oxygen atmosphere.

Complex	Temperature range (°C)	Mass loss (%); observed/calculated	Assignment	Residue at 600 °C (%)	
				Observed	Calculated for PdO
1a	Step 1: 50–150	6.1/6.1	Two water molecules	19.1	20.8
	Step 2: 150–320	75.2/75.6	Two HBnida$^-$ ions		
1b	240–400	80.6/80.6	Two HBnida$^-$ ions	19.6	22.2
2	240–500	79.8/81.5	Two HPeida$^-$ ions	20.2	20.4
3	240–500	80.3/82.4	Two HPpida$^-$ ions	20.1	20.1
4	220–550	80.9/82.7	Two *o*-(HCbida)$^-$ ions	19.5	19.5



Scheme 3. The proposed mechanism for methoxycarbonylation of iodobenzene (PhI) in the presence of triethylamine (Et_3N), catalyzed by the complexes **1**–**4** (L = Bnida, Peida, Ppida and *o*-Cbida), with the reaction intermediates **I**–**IV**.

arylalkyliminodiacetatic acids in aqueous solutions. Complex **1a** is a *trans*-isomer. According to the great similarity of their infrared spectra, all other complexes **1b**–**4** presumably have molecular structures analogous to **1a**, but without co-crystallized water molecules. The coexistence of several species in dimethyl sulfoxide solutions of these complexes was observed by NMR spectroscopy.

The complexes did not significantly inhibit the growth of colon, breast and lung tumor cell lines. However, all prepared complexes exhibit the acceptable activities towards the methoxycarbonylation of iodobenzene. The choice of the ligand non-coordinating moiety in the prepared complexes affects the efficiency of these complexes as catalysts. The yield of the product was the lowest for the complex containing *o*-chlorobenzyl derivative of the ligand, possibly because of the steric or electronic influence of the chlorine atom attached to the aromatic ring in the *ortho* position. At this stage it is not yet clear why the efficiency of the complex containing 2-phenylethyl group is significantly greater when compared with the analogous complexes containing shorter (benzyl) or longer (3-phenylprop-1-yl) carbon chains.

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Appendix A. Supplementary material

CCDC 949216 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Appendix B. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2013.10.010.

References

[1] N. Smrečki, B.-M. Kukovec, M. Đaković, Z. Popović, Inorg. Chim. Acta 400 (2013) 122.
[2] J. Tsuji, Palladium Reagents and Catalysts, Wiley, Chichester, UK, 2004, p. 265.
[3] R. Skoda-Foldes, L. Kollar, Curr. Org. Chem. 6 (2002) 1097.
[4] M. Mori, in: E. Negishi (Ed.), Handbook of Organopalladium Chemistry for Organic Synthesis, vol. 2, Wiley-Interscience, New York, 2002, p. 2663.
[5] T.Y. Luh, M. Leung, K.T. Wong, Chem. Rev. 100 (2000) 3187.
[6] X. Wu, H. Neumann, M. Beller, Chem. Soc. Rev. 40 (2011) 4986.
[7] D.M. D'Souza, T.J.J. Müller, Nat. Protoc. 3 (2008) 1660.
[8] B. Willy, T.J.J. Müller, Arkivoc 1 (2008) 195.
[9] J. Marco-Contelles, E. de Opazo, J. Org. Chem. 67 (2002) 3705.
[10] C.J. Forsyth, J. Xu, S.T. Nguyen, I.A. Samdal, L.R. Briggs, T. Rundberget, M. Sandvik, C.O. Miles, J. Am. Chem. Soc. 128 (2006) 15114.
[11] L.F. Tietze, R.R. Singidi, K.M. Gericke, H. Bockemeier, H. Laatsch, Eur. J. Org. Chem. (2007) 5875.
[12] A. Arcadi, M. Aschi, F. Marinelli, M. Verdecchia, Tetrahedron 64 (2008) 5354.
[13] P. Bannwarth, A. Valleix, D. Grée, R. Grée, J. Org. Chem. 74 (2009) 4646.
[14] Y.V. Gulevich, N.A. Bumagin, I.P. Beletskaya, Russ. Chem. Rev. 37 (1988) 299.
[15] M. Beller, B. Cornils, C.D. Frohning, C.W. Kohlpaintner, J. Mol. Catal. A 104 (1995) 17.
[16] T.A. Stromnova, I.I. Moiseev, Russ. Chem. Rev. 67 (1998) 485.
[17] A.S. Prasada, B. Satyanarayanaa, J. Mol. Catal. A: Chem. 370 (2013) 205.
[18] H. Daghriri, F. Huq, P. Beale, Chem. Rev. 248 (2004) 119.
[19] A.S. Abu-Surrah, M. Kettunen, Curr. Med. Chem. 13 (2006) 1337.
[20] A.S. Abu-Surrah, H.H. Al-Sa'doni, M.Y. Abdalla, Cancer Ther. 6 (2008) 1.
[21] A. Garoufis, S.K. Hadjikakou, N. Hadjiliadis, Coord. Chem. Rev. 253 (2009) 1384.
[22] E. Gao, L. Lin, L. Liu, M. Zhu, B. Wang, X. Gao, Dalton Trans. 41 (2012) 11187.
[23] Oxford Diffraction CrysAlis CCD and CrysAlis RED, Version 1.171.32.29, Oxford Diffraction Ltd., Abingdon, Oxfordshire, England, 2008.
[24] G.M. Sheldrick, Acta Crystallogr. A64 (2008) 112.
[25] A.L. Spek, J. Appl. Crystallogr. 36 (2003) 7.
[26] L.J. Farrugia, J. Appl. Crystallogr. 30 (1997) 565.
[27] C.F. Macrae, I.J. Bruno, J.A. Chisholm, P.R. Edgington, P. McCabe, E. Pidcock, L. Rodriguez-Monge, R. Taylor, J. van de Streek, P.A. Wood, J. Appl. Crystallogr. 41 (2008) 466.
[28] L. Yang, D.R. Powell, R.H. Houser, Dalton Trans. (2007) 955.
[29] S. Balboa, R. Carballo, A. Castiñeiras, J.M. González-Pérez, J. Niclós-Gutiérrez, Polyhedron 50 (2013) 512.
[30] J. Chakraborty, M.K. Saha, P. Banerjee, Inorg. Chem. Commun. 10 (2007) 671.
[31] J. Chakraborty, H. Mayer-Figge, W.S. Sheldrick, P. Banerjee, Polyhedron 24 (2005) 771.
[32] I.N. Polyakova, T.N. Polynova, M.A. Porai-Koshits, A.M. Grevtsev, J. Struct. Chem. 20 (1979) 555.
[33] A.L. Poznyak, A.B. Ilyukhin, V.S. Sergienko, Russ. J. Inorg. Chem. 42 (1997) 1660.
[34] R.-F. Song, C.-Z. Zhang, F. Li, S.-C. Jin, Z.-S. Jin, Chem. Res. Chin. Univ. 8 (1992) 399.
[35] I.N. Polyakova, A.L. Poznyak, V.S. Sergienko, Crystallogr. Rep. 48 (2003) 278.
[36] G.B. Deacon, R.J. Phillips, Coord. Chem. Rev. 33 (1980) 227.
[37] K. Nakamoto, Infrared and Raman Spectra of Inorganic and Coordination Compounds, Part B, sixth ed., Wiley, Hoboken, 2009.
[38] M.J. Frisch, G.W. Trucks, H.B. Schlegel, G.E. Scuseria, M.A. Robb, J.R. Cheeseman, J.A. Montgomery, T. Vreven Jr., K.N. Kudin, J.C. Burant, J.M. Millam, S.S. Iyengar, J. Tomasi, V. Barone, B. Mennucci, M. Cossi, G. Scalmani, N. Rega, G.A. Petersson, H. Nakatsuji, M. Hada, M. Ehara, K. Toyota, R. Fukuda, J. Hasegawa, M. Ishida, T. Nakajima, Y. Honda, O. Kitao, H. Nakai, M. Klene, X. Li, J.E. Knox, H.P. Hratchian, J.B. Cross, C. Adamo, J. Jaramillo, R. Gomperts, R.E. Stratmann, O. Yazyev, A.J. Austin, R. Cammi, C. Pomelli, J.W. Ochterski, P.Y. Ayala, K. Morokuma, G.A. Voth, P. Salvador, J.J. Dannenberg, V.G. Zakrzewski, S. Dapprich, A.D. Daniels, M.C. Strain, O. Farkas, D.K. Malick, A.D. Rabuck, K. Raghavachari, J.B. Foresman, J.V. Ortiz, Q. Cui, A.G. Baboul, S. Clifford, J. Cioslowski, B.B. Stefanov, G. Liu, A. Liashenko, P. Piskorz, I. Komaromi, R.L. Martin, D.J. Fox, T. Keith, M.A. Al-Laham, C.Y. Peng, A. Nanayakkara, M. Challacombe, P.M.W. Gill, B. Johnson, W. Chen, M.W. Wong, C. Gonzalez, J.A. Pople, Gaussian 03, Revision B.5, Gaussian, Inc., Pittsburgh PA, 2003.
[39] J. Liu, B. Liang, D. Shu, Y. Hu, Z. Yang, A. Lei, Tetrahedron 64 (2008) 9581.