Novel 2-aminopyridine liganded Pd(II) N-heterocyclic carbene complexes: Synthesis, characterization, crystal structure and bioactivity properties

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ABSTRACT

In this work, the synthesis, crystal structure, characterization, and enzyme inhibition effects of the novel a series of 2-aminopyridine liganded Pd(II) N-heterocyclic carbene (NHC) complexes were examined. These complexes of the Pd-based were synthesized from PEPPSI complexes and 2-aminopyridine. The novel complexes were characterized by using 13C NMR, 1H NMR, elemental analysis, and FTIR spectroscopy techniques. Also, crystal structures of the two compounds were recorded by using single-crystal X-ray diffraction assay. Also, these complexes were tested toward some metabolic enzymes like α-glycosidase, aldose reductase, butyrylcholinesterase, acetylcholinesterase enzymes, and carbonic anhydrase I, and II isoforms. The novel 2-aminopyridine liganded (NHC)PdI 2(2-aminopyridine) complexes (1a-i) showed Ki values of in range of 5.78 ± 0.33–22.51 ± 8.59 nM against hCA I, 13.77 ± 2.21–30.81 ± 4.87 nM against hCA II, 0.44 ± 0.08–1.87 ± 0.11 nM against AChE and 3.25 ± 0.34–12.89 ± 4.77 nM against BChE. Additionally, we studied the inhibition effect of these derivatives on aldose reductase and α-glycosidase enzymes. For these compounds, compound 1d showed maximum inhibition effect against AR with a Ki value of 360.37 ± 55.82 nM. Finally, all compounds were tested for the inhibition of α-glycosidase enzyme, which recorded efficient inhibition profiles with Ki values in the range of 4.44 ± 0.65–12.67 ± 2.50 nM against α-glycosidase.

1. Introduction

Pd-based NHC complexes are the most remarkable molecules among the heterocyclic liganded metal complexes. One of the most important properties of these complexes is the thermal and oxidative stability of the metal-carbene bond [1]. In addition to this property, the unique properties of the NHC ligand increase the popularity of Pd-based NHC complexes. These ligands which can form stable compounds with most of the transition metals; have unique properties like strong σ-donor, weak π-acceptor, electronic and sterical adjustability [2–5]. For a long time, organometallic chemists have been very interested in Pd-based complexes containing NHC ligands. Recent studies on PEPPSI (Pyridine-Enhanced Precatalyst Preparation Stabilization and Initiation) complexes from these molecules are noteworthy [6,7]. In particular, by binding of ligands of different properties in place of the pyridine ligand in the PEPPSI complexes with ligand exchange in mild conditions, the synthesis of new complexes with different electronic properties increases the interest in these complexes [8–11]. The weaker binding of the pyridine ligand to the metal center than the NHC ligand is the most important factor in this method [8]. A lot of Pd-based complexes containing NHC/triphenylphosphine ligand mixtures were synthesized by this method [8–10].

Pyridine and its derivatives aminopyridines are commonly used in particular starting materials and key intermediates in the production of pharmaceuticals, dyes, rubber, and pesticides [12]. Metal complexes containing 2-aminopyridine ligand are used in different fields. In several previous studies, the 2-aminopyridine ligand was bound to different metal centers and different complexes were synthesized [13–15].

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However, Pd-based complexes containing the mixture of NHC/2-aminopyridine ligand by using the PEPPSI complexes have not been synthesized. The amine (-NH₂) group found in the Pd-based complexes containing the NHC/2-aminopyridine ligand mixture increases the hydrophilic property of the complexes [16]. The use of eco-friendly solvents such as water and ethyl alcohol is very important in terms of Green Chemistry. Therefore, it is very important to the complexes to be synthesized dissolve in polar solvents like water and ethyl alcohol. Recent studies on the enzyme inhibition effects of NHC precursors synthesized by our study group have been remarkable [17–21]. Also, we examined the effects of enzyme inhibition of the Pd-NHC complexes for the first time [11].

Acetylcholine (ACh) molecule is a necessary neurotransmitter for cognitive activities like memory, learning, attention, and motivation [22–24]. There are two key enzymes known as butyrylcholinesterase (BChE) and acetylcholinesterase (AChE), which catalyze the hydrolysis of ACh molecule leading to the decrease of synaptic availability of that substance in the brain cells [25–28]. Indeed, BChE enzyme plays a significant role in controlling brain ACh level as two main enzymes differ in kinetics, rate specificity, and activities in the diverse parts of the brain. Inhibition acts of BChE and AChE have been the main mechanism for the management of AD and also AChE inhibitors have been defined as the major treatment plan [29–31].

Carbonic anhydrase isoenzymes (CAs) are zinc-containing metalloenzymes that catalyze the reversible hydration of carbon dioxide to a proton and bicarbonate [32,33]. This important reaction is necessary for many physiological strategies like pH regulation, respiration, electrolyte secretion, calcification, tumorigenesis, bone resorption, and biosynthetic reactions [34,35].

One of the main efficient procedures to prevent hyperglycemia and diabetes is to regulate the glucose amount in blood. Sugar molecules in blood originate from the hydrolysis of carbohydrate molecules and are catalyzed by some digestive enzymes, like α-glycosidase [36]. This enzyme is an intestinal membrane enzyme that its function is to hydrolyze polysaccharide molecules. Aldose reductase (AR) enzyme is an important enzyme in the polyol pathway. AR enzyme catalyzes the decrease glucose molecule to sorbitol molecule and provides a current link in the onset of diabetic complications in diverse parts of the human body [37,38].

In this work, we have studied the facile synthesis of novel 2-aminopyridine liganded Pd(II) N-heterocyclic carbene complexes (1a-i) and also, the inhibition effects of these compounds against some metabolic enzymes were investigated. On the other hand, the molecular and crystal structures of two molecules were confirmed by the single-crystal X-ray diffraction method.

2. Results and discussion

2.1. Synthesis the (NHC)PdI₂(2-aminopyridine) complexes (1a–i)

The (NHC)PdI₂(2-aminopyridine) complexes (1a–i) recognized in this work illustrated in Scheme 1. Their structures were obtained by using FTIR spectroscopy, ¹H NMR, ¹³C NMR, and elemental analysis techniques. These complexes (1a–i) have been synthesized from the 2-aminopyridine and the (NHC)PdI₂(pyridine) complexes at room temperature for 3 h. The (NHC)PdI₂(2-aminopyridine) complexes (1a–i) were obtained as a yellow solid in between 75% and 87% yield. All complexes (1a–i) were soluble in non-polar solvents such as dichloromethane, chloroform, and toluene. Also, these complexes 1a–i were soluble in polar solvents such as water, ethanol dimethylformamide. The formation of the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) was confirmed by ¹³C NMR spectroscopic methods, ¹H NMR, FT-IR, and elemental analysis techniques. In the ¹H NMR spectra, the characteristic proton peak for (–NH₂) group in the structure of the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) that downfield shifted signals were observed at δ 6.66, 6.68, 6.62, 6.55, 6.58, 6.56, 6.53, 6.50 and 6.58 ppm for (1a–i), respectively. In the ¹³C NMR spectra, the Pd–Ccarbon resonances of these (NHC)PdI₂(2-aminopyridine) complexes in the ¹³C NMR spectra appeared highly downfield shifted at δ 161.5, 165.1, 162.4, 164.8, 164.6, 163.3, 162.8, 162.5 and 162.1 ppm for (1a–i), respectively. The FT-IR data clearly defined the presence of ν(C=N) for 2-Cl, 1447, 1444, 1443, 1445, 1447, 1445, 1441 and 1443 cm⁻¹ for the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) proved, respectively. The FT-IR data clearly defined the presence of ν(C=O) for amino, 1621, 1621, 1621, 1623, 1627, 1625, 1621 and 1625 cm⁻¹ for the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) proved, respectively. The FT-IR data clearly defined the presence of ν(C=O) 3408, 3445, 3438, 3446, 3438, 3446, 3350 and 3438 cm⁻¹ for the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) proved, respectively. The FT-IR data clearly defined the presence of ν(C=O) 3408, 3445, 3438, 3446, 3438, 3446, 3350 and 3438 cm⁻¹ for the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) proved, respectively. The effect on enzyme inhibition studies of the (NHC)PdI₂(2-aminopyridine) complexes (1a–i) have been researched. Also, we obtained single crystal for the (NHC)PdI₂(2-aminopyridine) complexes 1c and 1e with X-ray diffraction method.

2.2. Structural description of the (NHC)PdI₂(2-aminopyridine) complexes 1c and 1e

X-ray structural images of the complexes are depicted in Figs. 1 and 2. The molecular structures revealed that the complexes adopt a slightly distorted square-planar environment with the iodide ligands perpendicular to the plane of the NHC and pyridine trans to it. Differently, the complex 1e crystallizes with a disordered dichloromethane solvent molecule in its unit cell. For both complexes, the iodide ligands are bent towards the NHC ligand for steric reasons. The Pd–I bond lengths are similar to the equivalent values found in the related complexes [39,40]. Pd–Npyridine bond lengths [2.092(4) and 2.114(6) Å, respectively] are longer than the sum of the individual covalent radii of Pd and N (Pd–N = 1.983 Å) [41]. The longer Pd–N(pyridine) distance is attributed to the greater trans effect of the NHC ligand residing diagonally opposite to the pyridine [42–46]. The benzimidazolium ring is twisted from the coordination plane NCPdI₂ with the dihedral angle of 85.692(4)°. As is usual in NHC-bearing complexes, the Pd–Ccarbon distances are 1.965(5) Å and 1.954(7) Å, respectively.

The crystal packing of the complex 1c, intermolecular N–H⋯I and N–H–O type hydrogen bonds lead to the formation of the one-dimensional infinite chain along the [0 1 0] direction. These hydrogen bonds also form R²(12) and R²(20) ring motif structure (Fig. 3). In the crystal structure of 1e, O–H⋯I hydrogen bonds are responsible for the one-dimensional infinite chain along the [1 0 0] direction and give rise to R²(16) and R²(20) ring motifs, together with the N–H⋯O type hydrogen bonds (Fig. 4) (see Table 2).

2.3. Enzyme inhibition studies

In this study, synthesis, design, and biochemical evaluation of novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) have been the center of interest and attention to develop powerful and new anti-AD drugs. AD has been recognized as a multifactorial disease, cholinesterase inhibitors (ChEIs) are still the key purpose for the therapy of moderate and early stages of the disease since FDA approved drugs like galantamine, tacrine, rivastigmine, and donepezil which are important ChEIs [49]. In the continuation of this study, malfunction of CA isoenzymes is often related to diverse diseases, and CA isozymes are interesting therapeutic aims whose inhibition could be utilized to treatment of the range of disturbances such as oxidative stress, anemia, cancer, glaucoma, edema, epilepsy, osteoporosis, sterility, obesity, etc [50].

For hCA I enzyme, the Kᵢ values were obtained in range of 5.78 ± 0.33–22.51 ± 8.59 nM. In comparison, the Kᵢ for the control
hCA inhibitor AZA was 11.87 ± 0.62 nmol/L against hCA I (Table 3). Between novel (NHC)PdI$_2$(2-aminopyridine) complexes (1a-i), novel 1i and 1f compounds were the best hCA I inhibitors (Ki: 5.78 ± 0.33 and 8.33 ± 2.48 nM). As shown in Table 3, IC$_{50}$ values are in the range of 6.54–25.11 nM towards hCA I isoenzyme. In another study, three series of imidazolidinium ligands (NHC precursors) substituted with 4-vinylbenzyl, 2-methyl-1,4-benzodioxane, and N-propylphthalimide demonstrated hCA I isoenzyme inhibition profiles with Ki values in ranging of 166.65–635.38 nM [16]. In a recent study, 2-hydroxyethyl substituted NHC precursors showed Ki values of 13.90–41.46 nM against hCA I isoenzyme [18]. In addition to these results, recent studies showed that novel benzenesulfonamides (Kis: 24.2–49.8 nM), N-substituted rhodanines (Kis: 43.55–89.44 nM), some new mono Mannich bases with piperazines (Kis: 342.7–526.3 nM), new phenolic Mannich bases with piperazines (Kis: 209.6–484.0 nM), and bromophenol derivatives with cyclopropyl moiety (Kis: 7.8–58.3 nM) had effective human carbonic anhydrase I isoenzyme inhibition [50].

Novel (NHC)PdI$_2$(2-aminopyridine) complexes (1a-i) synthesized in this study inhibited hCA II with Ki in the low nanomolar range. For this enzyme, Ki values were found between 13.77 ± 2.21 and 30.81 ± 4.87 nM (Table 3). On the other hand, novel 1b and 1d compounds are in fact the best inhibitors in these compounds (K$_i$: 13.77 ± 2.21 and 20.37 ± 5.08 nM). IC$_{50}$ values are in the range of 10.41–35.54 nM towards hCA II. Recently, imidazolidinium ligands as NHC precursors appeared to strongly inhibit hCA II isoenzyme with Ki values ranging from 43.55–89.44 nM, some new mono Mannich bases with piperazines (K$_i$: 342.7–526.3 nM), new phenolic Mannich bases with piperazines (K$_i$: 209.6–484.0 nM), and bromophenol derivatives with cyclopropyl moiety (K$_i$: 7.8–58.3 nM) had effective human carbonic anhydrase I isoenzyme inhibition [50].

![Scheme 1. Synthesis of the (NHC)PdI$_2$(2-aminopyridine) complexes 1a-i.](image1)

![Fig. 1. X-ray crystal structure of 1c. Anisotropic displacement parameters depicting 50% probability. Selected bond parameters (Å,°): Pd1–I1 2.5926(6), Pd1–I2 2.5952(6), Pd1–Cl1 1.965(5), Pd1–N3 2.092(4), C1–N1 1.336(7), C1–N2 1.362(6), N3–Cl1 1.327(7), N4–Cl1 1.342(8); I1–Pd1–I2 175.59(2), C1–Pd1–N1 92.54(13), N3–Pd1–I2 91.68(13), N1–C8–C9 111.8(7), N2–C10–C11 114.3(5).](image2)

![Fig. 2. X-ray crystal structure of 1e. Anisotropic displacement parameters depicting 30% probability. Selected bond parameters (Å,°): Pd1–I1 2.5924(10), Pd1–I2 2.6027(9), Pd1–Cl1 1.954(7), Pd1–N3 2.114(6), C1–N1 1.336(8), C1–N2 1.348(8), N3–C25 1.310(10), N4–C25 1.363(11); I1–Pd1–I2 175.45(3), C1–Pd1–N3 176.3(3), C1–Pd1–I1 88.4(2), C1–Pd1–I2 87.2(2), N3–Pd1–I1 93.17(18), N3–Pd1–I2 91.14(18), N1–C8–C9 110.6(7), N2–C10–C11 115.1(6).](image3)
Hydroxyethyl substituted NHC precursors had Ki values in the range of 12.82–49.95 nM for hCA II isoenzyme [18]. Also, it was reported that 2-hydroxyethyl substituted NHC precursors had Ki values ranging from 78.79 to 13.06 to 62.04–14.64 nM [16]. It was reported that 2-hydroxyethyl substituted NHC precursors had Ki values ranging from 17.62 to 1.10 to 62.04–14.64 nM [16].

The Ki values of novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) for BChE enzyme and AChE were performed from Lineweaver-Burk factor. Also, tacrine as control had Ki value of 2.38 ± 0.99 nM against cholinergic BChE. As seen in Table 3, IC₅₀ values are in the range of 1.68–5.29 nM towards AChE, for BChE are in the range of 10.19–19.41 nM. In this work, AChE was also extremely inhibited by novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) at the low nanomolar inhibition with Ki values in range of 0.44 ± 0.08–1.87 ± 0.11 nM (Table 3). Indeed, novel compounds of 1f and 1l with Ki values of 0.44 ± 0.08 and 0.46 ± 0.03 nM recorded the most powerful AChE inhibition, respectively. Additionally, tacrine as positive ChEI recorded for the therapy of AD obtained with Ki value of 1.45 ± 0.63 nM against cholinergic AChE. Finally, novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) inhibited BChE with Ki values in range of 3.25 ± 0.34–12.89 ± 4.77 nM (Table 3). However, novel compounds of 1f and 1l with Ki values of 3.25 ± 0.34 and 5.18 ± 0.73 nM demonstrated the most powerful BChE inhibition (Fig. 5).

Aktas et al. reported that newly synthesized some NHC precursors including imidazolidinium ligands substituted with 4-vinylbenzyl, 2-methyl-1,4-benzodioxane, and N-propylphthalimide had excellent inhibitory effects against AChE with Ki values ranging from 17.62 to 1.10 to 62.04–14.64 nM [16]. It was reported that 2-hydroxyethyl substituted NHC precursors had Ki values ranging from 280.92 ± 52.13 to 1370.01 ± 209.94 nM for AChE and 145.82 ± 31.68 to 882.01 ± 218.88 nM for BChE [18]. Also, imidazolidinium from enantiomerically enriched allylic alcohols (Kis: 4.55–32.64 nM), and novel thymol bearing oxypropanolamine namides (Kis: 37.7–89.2 nM), novel tacrine derivatives (Kis: 16.1–55.2 nM), some azolidine ligands as NHC precursors appeared to strongly inhibit cholinergic BChE. As seen in Table 3, IC₅₀ values are in the range of 10.19–19.41 nM. In this work, AChE was also extremely inhibited by novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) at the low nanomolar inhibition with Ki values in range of 0.44 ± 0.08–1.87 ± 0.11 nM (Table 3). Indeed, novel compounds of 1f and 1l with Ki values of 0.44 ± 0.08 and 0.46 ± 0.03 nM recorded the most powerful AChE inhibition, respectively. Additionally, tacrine as positive ChEI recorded for the therapy of AD obtained with Ki value of 1.45 ± 0.63 nM against cholinergic AChE. Finally, novel (NHC)PdI₂(2-aminopyridine) complexes (1a–i) inhibited BChE with Ki values in range of 3.25 ± 0.34–12.89 ± 4.77 nM (Table 3). However, novel compounds of 1f and 1l with Ki values of 3.25 ± 0.34 and 5.18 ± 0.73 nM demonstrated the most powerful BChE inhibition (Fig. 5).

Fig. 3. Crystal packing in the complex 1e showing the part of the infinite chain along the [0 1 0] direction. The bond path, which generates the graph-set ring motifs are drawn as balls, the other atoms are shown as stick drawing style. For the clarity, hydrogen atoms not to play role in bonding are omitted.

Fig. 4. Crystal packing in the complex 1e showing the part of the infinite chain along the [1 0 0] direction. The bond path, which generates the graph-set ring motifs are drawn as balls, the other atoms are shown as stick drawing style. For the clarity, hydrogen atoms not to play role in bonding are omitted.

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<td>2.16</td>
<td>2.966(12)</td>
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Symmetry codes: (i) 1 − x, −y, 1 − z; (ii) 1 − x, 1 − y, 1 − z; (2i) −1 + x, y, z; (2ii) 1 − x, 2 − y, 2 − z.

Table 2 Hydrogen-bonding interactions [Å, °] for the complexes 1c and 1e.

![Image of molecular structure](image-url)
The enzyme inhibition results of novel (NHC)PdI₂(2-aminopyridine) complexes (1a-i) against hCA I, hCA II, α-glycosidase (α-Gly) and α-acetylcholinesterase (AChE) enzymes. Also, inhibition of AR enzyme (Table 3) [54]. For AR enzyme, novel (NHCPdI₂(2-aminopyridine) complexes (1a-i) had IC₅₀ values in the range of 850.70–1330.82 nM (Table 3). IC₅₀ values of these derivatives the following order: 1i (850.70 nM, r²: 0.9555) < 1e (880.36 nM, r²: 0.9776) < 1f (1000.57 nM, r²: 0.9789) < 1a (1030.03 nM, r²: 0.9800) < 1g (1040.11 nM, r²: 0.9895) < 1c (1160.88 nM, r²: 0.9964) < 1d (1220.15 nM, r²: 0.9576) < 1b (1330.43.25 nM, r²: 0.9947) < 1h (1330.82 μM, r²: 0.9940). Indeed, for this enzyme the most effective Kᵢ values were obtained by novel 1d and 1c compounds with Kᵢ values of 360.37 ± 55.82 and 540.43 ± 30.8 nM, respectively (Fig. 5).

In this paper, our group evaluated the α-glycosidase inhibitory potential of the novel (NHCPdI₂(2-aminopyridine) complexes (1a-i). For this enzyme, the complexes had IC₅₀ values in the range of 8.65–18.19 and Kᵢ values in the range of 4.44 ± 0.65–12.67 ± 2.50 nM (Table 3). The results obviously showed that all novel (NHCPdI₂(2-aminopyridine) complexes (1a-i) demonstrated efficient α-glycosidase inhibitory effects than that of acarbose (IC₅₀: 22800 nM) [55,56] as standard α-glycosidase inhibitor. However, the most effective Kᵢ values were obtained by novel 1f and 1h compounds with Kᵢ values of 4.44 ± 0.65 and 5.51 ± 1.95 nM, respectively (Fig. 5).

3. Conclusions

Consequently, in this study, the novel (NHCPdI₂(2-aminopyridine) complexes have been synthesized. Also, all of these complexes have been characterized by using FTIR spectroscopy, ¹³C NMR, ¹H NMR, and elemental analysis techniques. The crystal-chemical structure determination of the (NHCPdI₂(2-aminopyridine) complexes 1c and 1e were performed by single-crystal x-ray diffraction assay. Analyses of crystal structures revealed the slightly distorted square-planar geometry of both complexes. Iodide ligands play a role in the presence of one-dimensional infinite chain in the crystal structures of complexes. All the synthesized the (NHCPdX₂(morpholine) complexes effectively inhibited metabolic enzymes. The novel (NHCPdX₂(2-aminopyridine) complexes (1a-i) used in the present paper recorded efficient inhibition profiles against CA II isoenzymes, BChE, AChE, α-glycosidase and AR enzymes. In this work, nanomolar levels of Kᵢ and IC₅₀ values which obtained for all novel complexes on AR and α-glycosidase enzymes. Thus, these complexes can be selective inhibitors of AR, α-glycosidase and cholesterazyme enzymes.

4. Experiments

4.1. Chemistry

All synthesis containing the novel 2-aminopyridine liganded Pd(II) NH complexes (1a-i) were prepared under an inert atmosphere in flame-dried glassware using standard Schlenk techniques. The solvent samples economically purchased were utilized without display to any drying process and purification. All a reagents were economically accessible by Alfa Aesar, Sigma-Aldrich Chemical Co., Merck, which utilized without subsequent purification. Also, melting points were recognized in glass capillaries under air with an Electrothermal-9200
melting point apparatus. On the other hand, FT-IR spectra assay were kept in the range 400–4000 cm\(^{-1}\) on Perkin Elmer Spectrum 100 FT-IR spectrometer. Carbon (13C) and Proton (1H) NMR spectra were recorded using either a Bruker 400 Merkur spectrometer operating at 100 MHz (13C), 400 MHz (1H) in DMSO-\(d_6\) and CDCl\(_3\) with tetramethylsilane as an internal reference by Inonu University Catalysis Research and Application Center. Elemental methods and analyses were performed by Technology Centre (Malatya, TURKEY) and İnönü University.

The crystal X-ray diffraction studies of the complexes 1c and 1e were performed by \(\omega\)-scan technique, using a Rigaku-Oxford Xcalibur diffractometer with an EOS-CCD area detector operated at 40 mA and 50 kV using graphite-monochromated MoK\(\alpha\) radiation (\(\lambda = 0.71073\) Å) from an enhance X-ray source with CrysAlis\textsuperscript{Pro} software \cite{57}. Analytical absorption corrections and Data reduction were carried out by CrysAlis\textsuperscript{Pro} program \cite{58}. The structures were solved by the Intrinsic Phasing method with SHELXT and refined by means of the SHELXL program \cite{59,60}. Both programs are incorporated into the OLEX2 program package \cite{61}. Some parameters of refinement and the crystallographic data are placed in Table 1. Anisotropic thermal parameters were applied to all non-hydrogen atoms. For both molecules, all the hydrogen atoms were placed using control geometric factors and with their thermal parameters riding on those of their parent atoms. During the structural analysis of 1c, several disordered solvent molecules, which may be dichloromethane (total volume of 579 Å\(^3\)), were observed in the unit cell. These disordered solvent molecules were removed using the solvent mask in Olex2. The hydroxyethyl group of the 1c exhibits a disorder, which was refined with occupancy factors of 0.43(2):0.57(2) for O1A and O1B. Also, to ensure satisfactory refinement of this disordered hydroxyethyl group and some other disordered moieties in the structure, a combination of constraint (EADP) and restraints (RIGU, DFIX) were applied. Similarly, in 1e, a rigid-bond restraint RIGU was employed for the disordered groups. The crystal of 1e was a three-component non-merohedral twin, the refined ratio of the twin components being 0.648(7): 0.146(5):0.206(5).

4.1.1. Synthesis of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene][2-aminopyridine]palladium(II), 1a

The compound 1a was synthesized from the reaction of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II) (138 mg, 0.2 mmol) and 2-aminopyridine (24 mg, 0.25 mmol) in chloroform (15 mL) in room temperature at 3 h. Yield: 106 mg. (75%). m.p.: 199–201 °C; \(\nu\)\textsubscript{(CN for 2-C)}: 1447 cm\(^{-1}\); \(\nu\)\textsubscript{(CN for amino)}: 1621 cm\(^{-1}\); \(\nu\)\textsubscript{(NH)}: 3321 cm\(^{-1}\); \(\nu\)\textsubscript{(OH)}: 3408 cm\(^{-1}\). Anal. Calc. for C\textsubscript{21}H\textsubscript{21}I\textsubscript{2}N\textsubscript{3}OPd: C: 36.47, H: 3.06, N: 6.08. Found: C: 36.45, H: 3.03, N: 6.11. \(^1\)H NMR (400 MHz, CDCl\(_3\)), \(\delta\) 4.47 (s, 2H, -NCH\textsubscript{2}CH\textsubscript{2}OH); 4.97 (s, 2H,
F. Erdemir, et al.

1.2. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(2-methylbenzyl)benzimidazol-2-ylidene](2-aminopyridine)palladium(II), 1b

The synthesis of 1b was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(2-methylbenzyl)benzimidazol-2-ylidene]pyridinepalladium(II) (121 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 154 mg (80%).

1.3. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(3-methylbenzyl)benzimidazol-2-ylidene](2-aminopyridine)palladium(II), 1c

The synthesis of 1c was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(3-methylbenzyl)benzimidazol-2-ylidene]pyridinepalladium(II) (141 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 123 mg (85%).

1.4. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(4-methylbenzyl)benzimidazol-2-ylidene](2-aminopyridine)palladium(II), 1d

The synthesis of 1d was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(4-methylbenzyl)benzimidazol-2-ylidene]pyridinepalladium(II) (141 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 125 mg (87%).

1.5. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(2,3,5,6-tetramethylbenzyl)benzimidazol-2-ylidene](2-aminopyridine)palladium(II), 1e

The synthesis of 1e was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(2,3,5,6-tetramethylbenzyl)benzimidazol-2-ylidene]pyridinepalladium(II) (146 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 130 mg (85%).

1.6. Synthesis of diiodo[1-(bis-(2-hydroxyethyl)benzimidazol-2-ylidene)(2-aminopyridine)palladium(II), 1f

The synthesis of 1f was carried out in the same way as that described for 1a, but diiodo[1-(bis-(2-hydroxyethyl)benzimidazol-2-ylidene)pyridinepalladium(II) (129 mg, 2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 99 mg (75%).

1.7. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(2-methylbenzimidazol-2-ylidene)](2-aminopyridine)palladium(II), 1g

The synthesis of 1g was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(2-methylbenzimidazol-2-ylidene)]pyridinepalladium(II) (123 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 105 mg (83%).

1.8. Synthesis of diiodo[1-(2-hydroxyethyl)-3-(3-methylbenzimidazol-2-ylidene)](2-aminopyridine)palladium(II), 1h

The synthesis of 1h was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-(3-methylbenzimidazol-2-ylidene)]pyridinepalladium(II) (126 mg, 0.2 mmol) was used instead of diiodo[1-benzyl-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridinepalladium(II). Yield: 103 mg (80%).

Bioorganic Chemistry 91 (2019) 103134
Found: C: 30.53, H: 3.03, N: 6.70. 1H NMR (400 MHz, DMSO-δ6), δ 1.59 (s, 3H, -NCH3CH2), 3.10 (s, 2H, -NCH2CH2); 4.14 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 5.27 (s, 1H, -NCH2CH2OH); 6.46 (s, 2H, C6H4NH2); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2). 13C NMR (100 MHz, DMSO-δ6), δ 14.0 (s, 1H, -NC5H4NH2); 55.3 (s, 2H, -NCH2CH2OH); 4.79 (s, 2H, -NCH2CH2OH); 6.68 (d, 2H, J = 23.3 Hz -NCH2NH2); 7.32–7.76 (m, 5H, Ar-H); 8.21 (s, 1H, -NCH2); 14.0 (s, 1H, -NC5H4NH2); 161.8 (2H, C6H4CH2); 162.3 (2H, C6H4NH2).


The synthesis of 1l was carried out in the same way as that described for 1a, but diiodo[1-(2-hydroxyethyl)-3-isopropylbenzimidazol-2-ylidene]pyridinepalladium(II) (129 mg, 0.2 mmol) was used instead of diiodo[1-benzy1-3-(2-hydroxyethyl)benzimidazol-2-ylidene]pyridine palladium(II). Yield: 99 mg. (75%). m.p.: 119–121 °C, t (CH2Cl2) = 1443 min⁻¹; t (CH2Cl2 for amino) = 1625 min⁻¹; t (CH3) = 3438 min⁻¹. Anal. Calc. for C17H21I2N3OPd: C: 31.73, H: 3.29, N: 6.53.

References


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Biorganic Chemistry 91 (2019) 103134