Amino Acids (2009) 37:537–541
DOI 10.1007/s00726-009-0258-3

ORIGINAL ARTICLE

Synthesis and characterization of new Pd(II) complexes of L-ethylphenylalanate

Abdol R. Hajipour · Kazem Karami · Azadeh Pirisedigh · Arnold E. Ruoho

Received: 7 November 2008 / Accepted: 5 February 2009 / Published online: 21 February 2009

Abstract Complex (S,S)-[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)$}($\mu$-Br)]$_2$ (**3**) was prepared following the method by Vicente and Saura-Llamas (Organometallics 26:2768–2776, 2007), by the reaction of L-ethylphenylalanate and $Pd(OAc)_2$ in 1:1 molar ratio under acetonitrile heating conditions and subsequently treating with NaBr. In addition, the cleavage of halogeno-bridge of the complex **3** via nucleophilic attack of some neutral ligands such as triphenylphosphine, pyridine, 2,4,6-trimethylpyridine and piperidine were investigated and the corresponding complexes (S)-[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)(Y)(Br)$}] (**4a–f**) were obtained in moderate yields. The six-member orthopalladated complexes were characterized by ^{1}H-NMR, ^{31}P-NMR, FT-IR and elemental analysis techniques.

Keywords Phenylalanine · Cyclopalladation · Orthometallate

Introduction

The combination of bio and organometallic chemistry is one of the most interesting fields in chemistry (Riordan 2004; Gellett et al. 2008). Synthesis, reaction and application of organometallic complexes using bioligands are important field of bioorganometallic researches (Severin et al. 1998; Barisic et al. 2003; Fish and Jaouen 2003).

Since aromatic α-amino acids (e.g., L-phenylalanine) as very versatile bioligands coordinate with palladium via amino and carboxylic functional groups, prevent the synthesis of orthopalladated complexes. To avoid this problem the ester derivatives of aromatic α-amino acids have been frequently used in literature (Ryabov et al. 1984; Freiesleben et al. 1995; Albert et al. 2002).

Synthesis of cyclometallated complexes of α-amino esters, especially L-phenylalanine esters, is attractive subject due to their interesting properties involving: potential cytotoxicity (Mylonas et al. 1981; Paul et al. 1993; Blaha et al. 1997; Mital et al. 1991; Zamora et al. 1997) and their application in organic synthesis (Ryabov 1985; Pfeffer 1992; Omae 2004; Dupont et al. 2005). These compounds also may be applied as useful reagents for resolution of racemic mixtures and determination of absolute configuration of chiral phosphines (Albert et al. 1997, 2006; Wild 1997; Camus et al. 2005), amino acids (Bohm et al. 1999; Bohm and Seebach 2000) and other ligands (Kurita et al. 2000; Okajima et al. 2002).

The preliminary works by Cope's group indicated that cyclopalladation of amine compounds needs three essential conditions involving: the use of substrates with ability to form five-member rings, exclusively tertiary amines and also using aromatic rings without electron withdrawing substitutions (Cope and Friedrich 1968). Using α-amino esters breaks down two primary conditions of Cope's rules, however by employing the improved methodology the cyclopalladation reactions of α-amino esters can be carried out (Vicente et al. 1995, 2003, 2005, 2007). The cyclopalladation reactions of such compounds using palladium

A. R. Hajipour (✉) · K. Karami · A. Pirisedigh
Pharmaceutical Research Laboratory, Department of Chemistry, Isfahan University of Technology, Isfahan 84156-83111, I.R. Iran
e-mail: haji@cc.iut.ac.ir

A. R. Hajipour · A. E. Ruoho
Department of Pharmacology, University of Wisconsin, Medical Science Building, 1300 University Avenue, Madison, WI 53706-1532, USA

acetate as a modified method have been reported (Ryabov et al. 1984; Fuchita et al. 1995).

In this study new dimeric complex of orthopalladated L-phenylalanine ethyl ester hydrochloride has been synthesized and splitted to a series of monomeric orthopalladated complexes with six-membered ring structures, using several neutral ligands such as triphenylphosphine, pyridine, 2,4,6-trimethylpyridine, 3-methylpyridine, piperidine and 4-methylpiperidine. The products were characterized by ^{1}H-NMR, ^{31}P-NMR, FT-IR and elemental analysis techniques.

Experimental

Materials

L-Phenylalanine ethyl ester hydrochloride, triphenylphosphine, pyridine, 2,4,6-trimethylpyridine, 3-methylpyridine, piperidine, 4-methylpiperidine and palladium acetate were purchased from Merck and Aldrich and used as received.

Instruments

All melting points were taken on a Gallenkamp melting apparatus and are uncorrected. ^{1}H-NMR (500 MHz) and ^{31}P-NMR were recorded on a Bruker Avance 500 instrument (Rheinstetten, Germany) using $CDCl_3$ as solvent (TMS and H_3PO_4 was used as an internal standard in ^{1}H-NMR and ^{31}P-NMR respectively). FT-IR spectra were recorded on a spectrophotometer (Jasco-680, Japan). Spectra of solids were carried out using KBr pellets. Vibrational transition frequencies are reported in wavenumber (cm^{-1} in the range 4,000–400 cm^{-1}).

Synthesis of dimer (S,S)-$[Pd\{C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)\}(\mu\text{-}Br)]_2$(**3**)

L-Phenylalanine methyl ester hydrochloride (1.00 g, 4.64 mmol) was added to a solution of $Pd(OAc)_2$ (1.04 g, 4.64 mmol) in acetonitrile (60 ml) and the resulting solution was heated for 4 h at 70°C (under the temperature of reflux). During the cyclopalladation a small amount of metallic palladium was formed as a side reaction. The mixture was filtered off through a plug of $MgSO_4$. The filtrate was concentrated to dryness and the residue was dissolved in CH_2Cl_2 (5 ml) and *n*-hexane (30 ml) was added to produce an orange solid which was filtered off, washed with Et_2O (2 × 2 ml), and air-dried. To a solution of mixture in acetone (50 ml) was added NaBr (1.50 g, 19.4 mmol) and the reaction mixture was stirred for 8 h, then the acetone was evaporated. The residue was taken up in CH_2Cl_2 (30 ml), the suspension was filtered off through a plug of $MgSO_4$, the filtrate was concentrated to dryness, and *n*-hexane (30 ml) was added and the orange solid was filtered, washed with Et_2O (2 × 2 ml), and air-dried to afford crude complex **3**. The residue was purified by recrystallization from CH_2Cl_2/Et_2O to afford the pure complex **3**. ^{1}H-NMR (500 MHz): δ 1.25 (br t, 3H, CH_3), 3.59 (br m, 1H, CH_2), 3.62 (br m, 1H, CH_2), 3.72 (br s, 1H, NH), 4.05 (br s, 1H, NH), 4.15 (br m, 3H, OCH_2, CH), 6.80 (m, 2H, H4, H6, C_6H_4), 6.90 (m, 2H, H3, H5, C_6H_4). IR (cm^{-1}): ν(NH) 3,229, 3,350; ν(CO) 1,727. Yield: 51.7%, 0.85 g. Mp: 125°C dec. Elemental analysis ($C_{22}H_{28}N_2O_4Br_2Pd_2$); calculated: C, 34.90; H, 3.73; N, 3.70. Found: C, 34.80; H, 3.90; N, 3.70.

Synthesis of monomer (S)-$[Pd\{C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)(Br)(Y)\}]$

To a suspension of the complex **3** (0.11 mmol, 0.083 g) in dichloromethane (12 ml) was added appropriate nucleophiles (0.22 mmol). After the mixture was stirred for 8 h at room temperature, it was filtered through $MgSO_4$ plug and concentrated to around 3 ml, then *n*-hexane (15 ml) was added to precipitate the complexes **4a–f**. These new products were filtered off, washed with diethyl ether and air-dried.

$[Pd\{C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)\}$ Br(pyridine)] (**4a**)

^{1}H-NMR (500 MHz): δ 1.30 (t, 3H, CH_3, $^{3}J_{HH} = 7.1$ Hz), 3.30 (br d, 1H, CH_2), 3.65 (br m, 2H, CH_2, CH), 4.15 (m, 3H, OCH_2, NH), 4.19 (br m, 1H, NH), 6.52 (d, 1H, H3, C_6H_4, $^{3}J_{HH} = 7.6$ Hz), 6.76 (td, 1H, H4, C_6H_4, $^{3}J_{HH} = 7.2$ Hz, $^{4}J_{HH} = 1.9$ Hz), 6.93 (m, 2H, H6, H5, C_6H_4), 7.80 (m, 2H, Py), 8.74 (m, 2H, Py), 8.89 (dd, 1H, Py, $^{3}J_{HH} = 15.2$ Hz, $^{3}J_{HH} = 5.2$ Hz). IR (cm^{-1}): ν(NH) 3,190, 3,215; ν(CO) 1,732, ν(C = N) 1,604. Yield: 44.1%, 0.042 g. Mp: 160°C dec. Anal. calculated for $C_{16}H_{19}N_2O_2BrPd$: C, 44.55; H, 4.48; N, 6.49. Found: C, 44.50; H, 4.60; N, 6.50.

$[Pd\{C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)\}$ Br(3-Me-pyridine)] (**4b**)

^{1}H-NMR (500 MHz): δ 1.26 (br t, 3H, CH_3, $^{3}J_{HH} = 7.2$ Hz), 2.45 (br s, 3H, CH_3) 3.30 (m, 1H, CH_2), 3.58 (br m, 2H, CH_2, CH), 4.14 (m, 3H, OCH_2, NH), 4.31 (br m, 1H, NH), 6.52 (d, 1H, H3, C_6H_4, $^{3}J_{HH} = 7.4$ Hz), 6.76 (br t, 1H, H4, C_6H_4), 6.94 (m, 2H, H6, H5, C_6H_4), 7.60 (m, 1H, Py), 8.50 (m, 1H, Py), 8.64 (br s, 1H, Py), 8.67 (m, 1H, Py). IR (cm^{-1}): ν(NH) 3,187, 3,260; ν(CO) 1,732, ν(C = N) 1,603. Yield: 45.9%, 0.047 g. Mp: 108°C

dec. Anal. calculated for $C_{17}H_{21}N_2O_2BrPd$: C, 43.29; H, 4.49; N, 5.94. Found: C, 43.10; H, 4.60; N, 6.10.

[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)$}Br(2, 4, 6-trimethyl-pyridine)] (**4c**)

^{1}H-NMR (500 MHz): δ 1.24 (t, 3H, CH_3, $^3J_{HH} = 6.4$ Hz), 2.34 (br s, 3H, CH_3), 2.36 (br s, 6H, CH_3), 3.21 (m, 2H, CH_2), 3.53 (m, 1H, CH), 4.17 (m, 4H, OCH_2, NH_2), 6.31 (m, 1H, H3, C_6H_4), 6.69 (m, 1H, H4, C_6H_4), 6.90 (m, 2H, H6, H5, C_6H_4), 7.51 (s, 2H, Py). IR (cm^{-1}): ν(NH) 3,228, 3,350; ν(CO) 1,734, ν(C = N) 1,624. Yield: 46.2%, 0.050 g, Mp: 118°C dec. Anal. calculated for $C_{19}H_{25}N_2O_2BrPd$: C, 45.66; H, 5.04; N, 5.61. Found: C, 45.50; H, 5.20; N, 5.50.

[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)$}Br($PPh_3$)] (**4d**)

^{1}H-NMR (500 MHz): δ 1.23 (br t, 3H, CH_3), 3.32 (dd, 1H, CH_2, $^2J_{HH} = 13.4$ Hz, $^3J_{HH} = 3.1$ Hz), 3.75 (dd, 1H, CH_2, $^2J_{HH} = 13.3$ Hz, $^3J_{HH} = 5.5$ Hz), 3.92 (br s, 1H, NH), 4.02 (br s, 1H, NH), 4.14 (br m, 3H, OCH_2, CH), 6.35 (br t, 1H, H6, C_6H_4), 6.53 (t, 1H, H3, C_6H_4, $^3J_{HH} = 6.8$ Hz), 6.73 (br t, 1H, H5, C_6H_4), 6.78 (d, 1H, H6, C_6H_4, $^3J_{HH} = 6.8$ Hz). 7.32 (m, 5H, PPh_3), 7.41 (m, 5H, PPh_3), 7.57 (m, 5H, PPh_3). IR (cm^{-1}): ν(NH) = 3,219, 3,312; ν(CO) = 1,734. ^{31}P-NMR: 35.20. Yield: 42.2%, 0.062 g. Mp: 105°C dec. Anal. calculated for $C_{28}H_{29}NO_2BrPPd$: C, 44.62; H, 4.31; N, 2.07. Found: C, 44.70; H, 4.30; N, 2.20.

[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)$}Br(piperidine)] (**4e**)

^{1}H-NMR (500 MHz): δ 1.25 (br t, 3H, CH_3), 1.32 [br m, 1H, CH_2 (piper)], 1.58 [br m, 1H, CH_2 (piper)], 2.58 [br m, 1H, NH (piper)], 3.05 [br m, 2H, CH_2 (piper)], 3.17 [br m, 2H, CH_2 (piper)], 3.22 [br m, 2H, CH_2 (piper)], 3.21 [m, 3H, CH_2 (piper)], 3.41 (m, 2H, CH_2), 3.56 (m, 1H, CH), 4.10 (br m, 3H, OCH_2, NH), 4.31 (br m, 1H, NH), 6.80 (br d, 1H, H6, C_6H_4), 6.85 (br d, 1H, H4, C_6H_4), 6.95 (m, 1H, H_5, C_6H_4), 7.03 (m, 1H, H_3, C_6H_4). IR (cm^{-1}): ν(NH) 3,254, 3,360; ν(CO) 1,733. Yield: 46.7%, 0.046 g. Mp: 90°C dec. Anal. calculated for $C_{17}H_{21}N_2O_2BrPd$: C, 41.44; H, 5.43; N, 6.04. Found: C, 41.30; H, 5.50; N, 6.20.

[Pd{$C_6H_4(CH_2CHNH_2CO_2CH_2CH_3)$ }Br (4-Me-piper)] (**4f**)

^{1}H-NMR (500 MHz): δ 1.05 (br d, 3H, CH_3), 1.24 (t, 3H, CH_3, $^3J_{HH} = 7.1$ Hz), 1.66 [br m, 3H, CH (piper), CH_2 (piper)], 1.86 [br m, 2H, CH_2 (piper)], 2.87 [br t, 4H, CH_2 (piper)], 3.24 [m, 1H, NH (piper)], 3.45 (m, 2H, CH_2), 3.57 (m, 1H, CH), 4.13 (br m, 4H, OCH_2, NH_2), 6.84 (br d, 1H, H6, C_6H_4), 6.95 (m, 1H, H4, C_6H_4), 7.03 (m, 2H, H3, H5, C_6H_4). IR (cm^{-1}): ν(NH) 3,200, 3,350; ν(CO) 1,735. Yield: 48.2%, 0.050 g. Mp: 108°C dec. Anal. calculated for $C_{17}H_{27}N_2O_2BrPd$: C, 42.74; H, 5.69; N, 5.86. Found: C, 42.60; H, 5.73; N, 5.70.

Results and discussion

Synthesis and structure of dimeric complex

When (L-ethylphenylalanate hydrochloride) (**1**) was reacted with $Pd(OAc)_2$ in 1:1 molar ratio in acetonitrile for 4 h (Vicente et al. 2007; Scheme 1), the black solution containing compound **2** was obtained. The darkness of solution indicates the partially decomposition of Pd(II) to Pd(0) (Vicente et al. 1997, 2003).

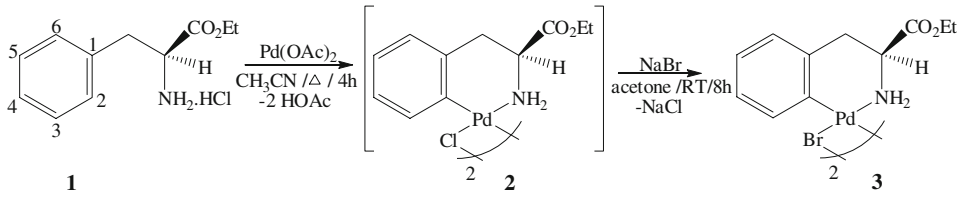
When the isolation of such complexes is impossible, they have been converted to equivalent bromo-bridge derivatives using metathesis reaction with NaBr (Vicente et al. 2003, 2007). We succeeded in isolating the pure bromo-bridged binuclear orthometallated complex [$Pd_2\{\kappa^2$(C,N)-$C_6H_4CH_2CH(CO_2Et)NH_2\}_2(\mu$-$Br)_2$] (**3**) in 51.7% yield.

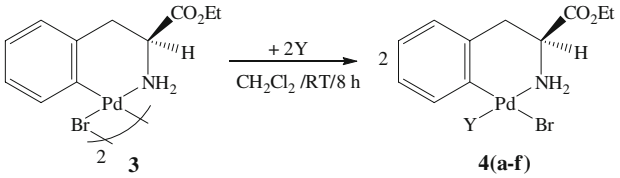
Recently Vicente (Vicente et al. 2007) has investigated the synthesis of bromo-bridge cyclopalladated complex of phenylalanine methyl ester hydrochloride and studied the splitting of the complex to the monomeric complex using 4-picoline. They utilized the cyclopalladated complexes in synthesis of a series of new derivatives by reacting with carbon monoxide and isocyanides as well as halogens (Br_2 and I_2). Similarly we split our dimeric bromo-bridge complex to the monomeric ones. Also for more extension a series of neutral ligands such as pyridine, 2,4,6-trimethyl-pyridine, 3-methylpyridine, triphenylphosphine, piperidine, 4-methylpiperidine have been employed to split the bromo-bridges in complex **3** (Scheme 2) to provide the mononuclear complex [Pd{κ^2(C,N)-$C_6H_4CH_2CH$-$(CO_2Et)NH_2$}Br(Y)].

As previously has been reported there are two possible isomers for complexes **4a–f**, but only the one with the two nitrogen atoms in commonly trans positions is acquired, as confirmed by ^{1}H-NMR. This is the normal manner for cyclopalladated complexes of benzylamine (Ryabov et al. 1995; Calmuschi and Englert 2005; Gong et al. 2007; Vicente et al. 2007).

The ^{1}H-NMR spectra of complexes **3** and **4a–f** confirm the offered structure. The ^{1}H-NMR spectrum of complex **3** demonstrates two multiplet signals at 6.80 and 6.90 ppm, matching to the four remaining protons in the orthometallated ring. In ^{1}H-NMR spectrum of the mononuclear complex **4a–d**, H3 is notably shifted to up field and appear around 6.30–6.50 ppm due to the anisotropic shielding

Scheme 1 Synthesis of dimeric bromo-bridge cyclopalladated complex





Y = a: py; b: 3-Me-Py; c:2,4,6-triMe-Py; d: PPh_3; e: Piper; F: 4-Me-Piper

Scheme 2 Breakage of bromo-bridge using neutral ligands

from the pyridine or the phenyl rings. This observation is in a good agreement with the result of Vicente. This effect supports the mutually trans position of the pyridine or phosphine ligand and the NH_2 group in solution (Ryabov et al. 1995; Calmuschi and Englert 2005; Gong et al. 2007; Vicente et al. 2007). In the ^{1}H-NMR spectra of the mononuclear complexes, four aromatic protons were noticeably distinguished around 6–7 ppm which show no perturbation of orthopalladated systems. Moreover, the observation of a signal at 35.20 ppm in ^{31}P-NMR spectra of complex **4d**, confirms the existence of only one isomer. The FT-IR spectra of new synthesized orthopalladated complexes illustrated the significant vibration modes. N–H bond stretching vibration appeared at 3,187–3,360 cm^{-1} which confirms the coordination of NH_2 groups to Pd(II). Ester carbonyl groups showed stretching vibration at 1,725–1,740 cm^{-1} and C = N bonds of the pyridine rings appeared at 1,600–1,610 cm^{-1}.

Conclusions

In this paper a new dimeric bromo-bridge cyclopalladated complex of L-phenylalanine methyl ester hydrochloride has been synthesized. Breakage of this complex via nucleophilic attack of several neutral ligands has led to the synthesis of a novel series of monomeric orthopalladated complexes. All of the new compounds were characterized by ^{1}H-NMR, FT-IR, ^{31}P-NMR spectroscopy and elemental analysis techniques. Resulting orthopalladated complexes have significant importance because of their cytotoxic activities, use in resolution of racemates, etc.

Acknowledgments We gratefully acknowledge the funding support received for this project from the Isfahan University of Technology (IUT), I.R. Iran. Further financial support from Center of Excellence in Sensor Research (IUT) is gratefully acknowledged.

References

Albert J, Cadena JM, Granell J (1997) Cyclopalladation of the primary amine (R)-(+)-1-(1-naphthyl)ethylamine: a new resolving agent for monodentate phosphines. Tetrahedron Asymmetry 8:991–994. doi:10.1016/S0957-4166(97)00087-6

Albert J, Cadena JM, Gonzalez A, Granell J, Solans X, Font-Bardia M (2002) Cyclopalladation of schiff bases from phenylalanine and 2-phenylglicine. J Organomet Chem 663:277–283. doi:10.1016/S0022-328X(02)01928-9

Albert J, Granell J, Muller G (2006) Synthesis and applications of optically active metallacycles derived from primary amines. J Organomet Chem 691:2101–2106. doi:10.1016/j.jorganchem.2005.10.041

Barisic L, Rapic V, Pritzkow H, Pavlovic G, Nemet I (2003) Ferrocene compounds part XXXIII. Synthesis and characterization of amino acids containing skeletal 1,1′-ferrocenylene unit. J Organomet Chem 682:131–142. doi:10.1016/S0022-328X(03)00774-5

Blaha T, Lukes I, Rohovec J, Hermann P (1997) Complexes of platinum(II) and palladium(II) with aminomethylphosphonic acid and glycylaminomethylphosphonic acid. J Chem Soc Dalton Trans 2621–2628. doi:10.1039/a607736f

Bohm A, Seebach D (2000) Determination of enantiomer purity of β- and γ-amino acids by NMR analysis of diastereoisomeric palladium complexes. Helv Chim Acta 83:3262–3277. doi:10.1002/1522-2675(20001220)83:12<3262::AID-HLCA3262>3.0.CO;2-P

Bohm A, Hauck T, Beck W (1999) Metal complexes of biologically important ligands, CXXIV [1]. NMR-Spectroscopic determination of the enantiomeric ratio of α-amino acids by use of a chiral orthometallated palladium complex. Z Naturforsch 54b:1360–1362

Calmuschi B, Englert E (2005) Crystal engineering based on preferred mirror image recognition in square planar Pd(II) complexes. Cryst Eng Comm 7:171–176

Camus JM, Roy-Garcıa P, Andrieu J, Richard P, Poli R (2005) Resolution of β-aminophosphines with chiral cyclopalladated complexes. J Organomet Chem 690:1659–1668. doi:10.1016/j.jorganchem.2005.01.023

Cope AC, Friedrich EC (1968) Electrophilic aromatic substitution reactions by platinum(II) and palladium(II) chlorides on N, N-dimethylbenzylamines. J Am Chem Soc 90:909–913. doi:10.1021/ja01006a012

Dupont J, Consorti CS, Spencer J (2005) The potential of palladacycles: more than just precatalysts. Chem Rev 105:2527–2572. doi:10.1021/cr030681r

Fish RH, Jaouen G (2003) Bioorganometallic chemistry: structural diversity of organometallic complexes with bioligands and molecular recognition studies of several supramolecular hosts with biomolecules, alkali-metal ions, and organometallic pharmaceuticals. Organometallics 22:2166–2177. doi:10.1021/om0300777

Freiesleben D, Polborn K, Robl C, Sunkel K, Beck W (1995) Metal complexes of biologically important ligands, LXXVIII. Synthesis of palladium complexes of ferrocenyl substituted amino acid derivatives. Can J Chem 73:1164–1174. doi:10.1139/v95-143

Fuchita Y, Tsuchiya H, Miyafuji A (1995) Cyclopalladation of secondary and primary benzylamines. Inorg Chim Acta 233:91–96. doi:10.1016/0020-1693(94)04440-7

Fuchita Y, Yoshinaga K, Ikeda Y, Kinoshita-Kawashima J (1997) Synthesis of optically active cyclopalladated complexes of primary benzylamine derivatives, (R)-(2)-2-phenylglycine methyl ester and (±)-L-phenylethylamine. J Chem Soc Dalton Trans 2495–2500. doi:10.1039/a608622e

Gellett AM, Huber PW, Higgins PJ (2008) Synthesis of the unnatural amino acid Nα-Nε-(ferrocene-1-acetyl)-L-lysine: a novel organometallic nuclease. J Organomet Chem 693:2959–2962. doi:10.1016/j.jorganchem.2008.06.012

Gong JF, Xu C, Zhang YH, Zhu Y, Yang-Jie W (2007) Synthesis, characterization and crystal structures of two cis/trans pyridine-cyclopalladated ferrocenylimine complexes. Transit Met Chem 32:1000–1004

Kurita J, Usuda F, Yasuike S, Tsuchiya T, Tsuda Y, Kiuchi F, Hosoi S (2000) Resolution of racemic Sb-chiral stibindoles using an optically active ortho-palladated benzylamine derivative, via their diastereomeric complexes. Chem Commun (Camb) 191–192. doi:10.1039/a909200e

Mital R, Srivastava TS, Parekh HK, Chitnis MP (1991) Synthesis, characterization, DNA binding, and cytotoxic studies of some mixed-ligand palladium(II) and platinum(II) complexes of α-diimine and amino acids. J Inorg Biochem 41:93–103. doi:10.1016/0162-0134(91)80003-Z

Mylonas S, Valavanidis A, Voukouvalidis V (1981) Platinum(II) and palladium(II) complexes with amino acid derivatives. Synthesis, interpretation of IR and 1H NMR spectra and conformational implications. Inorg Chim Acta 55:125–128. doi:10.1016/S0020-1693(00)90793-X

Okajima S, Yasuike S, Kakusawa N, Osada A, Yamaguchi K, Seki H, Kurita (2002) Synthesis of Sb-chiral organoantimony compounds having intramolecular Sb-N interaction and their separation into optically pure compounds via ortho-palladated benzylamine complexes. J Organomet Chem 656:234–242. doi:10.1016/S0022-328X(02)01622-4

Omae I (2004) Coordination chemistry of 1, 3, 5-triaza-7-phosphaadamantane (PTA): transition metal complexes and related catalytic, medicinal and photoluminescent applications. Coord Chem Rev 248:955–993. doi:10.1016/j.ccr.2004.05.011

Paul AK, Mansuri-Torshizi H, Srivastava TS, Chavan SJ, Chitnis MP (1993) Some potential antitumor 2, 2′-dipyridylamine Pt(II)/Pd(II) complexes with amino acids: their synthesis, spectroscopy, DNA binding, and cytotoxic studies. J Inorg Biochem 50:9–20. doi:10.1016/0162-0134(93)80010-7

Pfeffer M (1992) Selected applications to organic synthesis of intramolecular C–H activation reactions by transition metals. Pure Appl Chem 64:335–342. doi:10.1351/pac199264030335

Ryabov AD (1985) Cyclopalladated complexes in organic synthesis. Synthesis 233–252. doi:10.1055/s-1985-31169

Ryabov AD, Polyakov VA, Yatsimirsky AK (1984) Some complexes of palladium(II) with C-phenylglycine and its derivatives. Cyclopalladation of N, N-dimethyl-C-phenylglycine ethyl ester. Inorg Chim Acta 91:59–65. doi:10.1016/S0020-1693(00)84220-6

Ryabov AD, Kuzmina LG, Polyakov VA, Kazankov GM, Ryabova ES, Pfeffer M, van Eldik R (1995) Kinetics and mechanism of halogen-bridge cleavage in dimethylaminomethylphenyl-C,N pallada- and platina-cycles by pyridines. Pressure effects, and crystal structures of the *N*,*N*-cis reaction product, its *N*,*N*-trans orthometallated analogue and a dimer of similar reactivity. J Chem Soc Dalton Trans 999–1006. doi:10.1039/dt9950000999

Severin K, Bergs R, Beck W (1998) Bioorganometallic chemistry-transition metal complexes with α-amino acids and peptides. Angew Chem Int Ed Engl 37:1634–1654. doi:10.1002/(SICI)1521-3773(19980703)37:12<1634::AID-ANIE1634>3.0.CO;2-C

Vicente J, Saura-Llamas I, Palin MG, Jones PG (1995) The first orthopalladation of a primary nitrobenzylamine. Synthesis of chiral cyclopalladated complexes derived from (S)-±- methyl-4-nitrobenzylamine. J Chem Soc Dalton Trans 2535–2539. doi:10.1039/dt9950002535

Vicente J, Saura-Llamas I, Palin MG, Jones PG, de Ramírez Arellano MC (1997) Orthometallation of primary amines. 4. Orthopalladation of primary benzylamines and (2-phenylethyl)amine. Organometallics 16:826–833. doi:10.1021/om9609574

Vicente J, Saura-Llamas I, Cuadrado J, de Ramírez Arellano MC (2003) Ortho-metalated primary amines. 6. The first synthesis of six-membered palladacycles from primary amines containing electron-withdrawing substituents: end of the limiting rules of Cope and Friedrich on cyclopalladation of benzyl- and phenethylamines. Organometallics 22:5513–5517. doi:10.1021/om030480d

Vicente J, Saura-Llamas I, Bautista D (2005) Regiospecific functionalization of pharmaceuticals and other biologically active molecules through cyclopalladated compounds. 2-Iodination of phentermine and L-tryptophan methyl ester. Organometallics 24:6001–6004. doi:10.1021/om0506522

Vicente J, Saura-Llamas I, Garcia-Lopez JA, Calmuschi-Cula B, Bautista D (2007) Orthopalladation and functionalization of L-phenylalanine methyl ester. Organometallics 26:2768–2776. doi:10.1021/om070127y

Wild SB (1997) Resolutions of tertiary phosphines and arsines with orthometallated palladium(II)-amine complexes. Coord Chem Rev 166:291–311. doi:10.1016/S0010-8545(97)00046-5

Zamora F, Gonzalez VM, Perez JM, Masaguer JR, Navarro Ranninger C (1997) Pd(II) and Pt(II) complexes of 2-phenyl- and 2-benzyl-imidazoline: synthesis, structural characterization, DNA modification and in vitro antileukaemic activity. Appl Organomet Chem 11:659–666. doi:10.1002/(SICI)1099-0739(199708)11:8<659::AID-AOC614>3.0.CO;2-B