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Deamination of the Amino Acid Fragment in Imine Metallacycles: Unexpected Synthesis of an NH-Aldimine Organometallic Compound

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Abstract: We report that the action of Lewis bases, such as triphenylphosphine, pyridine, or trimethylamine, on imine metallacycles derived from amino acids leads to the formation of the first organometallic compound of an NH aldimine, a highly reactive organic species, and the corresponding α-ketoester, in a deamination reaction that mimics the metabolism of α-amino acids. The synthesis of different cyclopalladated compounds by a reaction between palladium acetate and the Schiff bases 2,4,6-$Me_3C_6H_2CH{=}NCH(R^1)COOR^2$ ($R^1 = CH_2Ph$, $R^2 = Et$ and $R^1 = Ph$, $R^2 = Me$) is also reported.

Keywords: aldimines · amino acids · deamination · metallacycles · palladium

Introduction

There is growing interest in the synthesis, reactivity, and applications of organometallic complexes with biologically important ligands, and the term bioorganometallic chemistry has been proposed to describe this new research field on the borderline between biochemistry and organometallic chemistry.[1–3]

α-Amino acids are highly versatile ligands in this field and can afford two different classes of compounds: complexes in which the amino acid is coordinated to an organometallic fragment through the donor atoms (amino, carboxylato, or other basic groups) and complexes in which the amino acid is coordinated to the metal through a carbon–metal bond. The latter is comparatively rare,[1] but some C–N chelates have been synthesized by metallation of amino acid derivatives with palladium.[4–11]

We have investigated the action of palladium acetate on the Schiff bases 2,4,6-$Me_3C_6H_2CH{=}NCH(R^1)COOR^2$ ($R^1 = CH_2Ph$, $R^2 = Et$ and $R^1 = Ph$, $R^2 = Me$), obtained by condensation of mesitaldehyde with the corresponding α-amino acid ester. These reactions lead to new metallacycles, in which the amino acids are coordinated to the metal through a carbon–metal bond, and the first organometallic compound of an NH aldimine, normally a highly reactive organic species.[12]

NH aldimines have been proposed as intermediates in many reactions, and their highly unstable nature is well documented.[13–15] The first evidence for the existence of NH aldimines containing a saturated alkyl group was reported in 1982,[14] and PhCH=NH was identified in 1985 by using NMR studies in $C_6D_5CD_3$ at −70 °C and by the reaction with methylamine to yield *N*-benzylidenemethylamine through transimination.[13] Only two NH aldimines have been isolated, in both cases at low temperatures.[16,17] Recently, Brown and co-workers reported the synthesis of stable adducts of these imines with boranes, as new intermediates for organic synthesis,[18] and Milstein and co-workers described the synthesis of a coordination compound of PhCH=NH by nonsymmetrical rhodium-mediated N–N bond cleavage of aromatic azines.[19]

With few exceptions, amino acid biodegradation involves the removal of the α-amino group to give the corresponding α-keto acid, and imines act as intermediates in this process. This reaction, catalyzed by aminotransferases, begins with the formation of a Schiff base between the pyridoxal 5′-phosphate and the corresponding amino acid, in tautomeric equilibrium between the aldimine and the ketimine forms. The hydrolysis of the ketimine form liberates an α-ketoacid,

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thereby leaving the amino group as part of the pyridoxane structure.[20] Here we describe how the action of Lewis bases, such as triphenylphosphine, pyridine, or trimethylamine, on imine metallacycles leads to the formation of the NH-aldimine organometallic compound and the corresponding α-ketoester, in a deamination process that mimics the metabolism of α-amino acids.

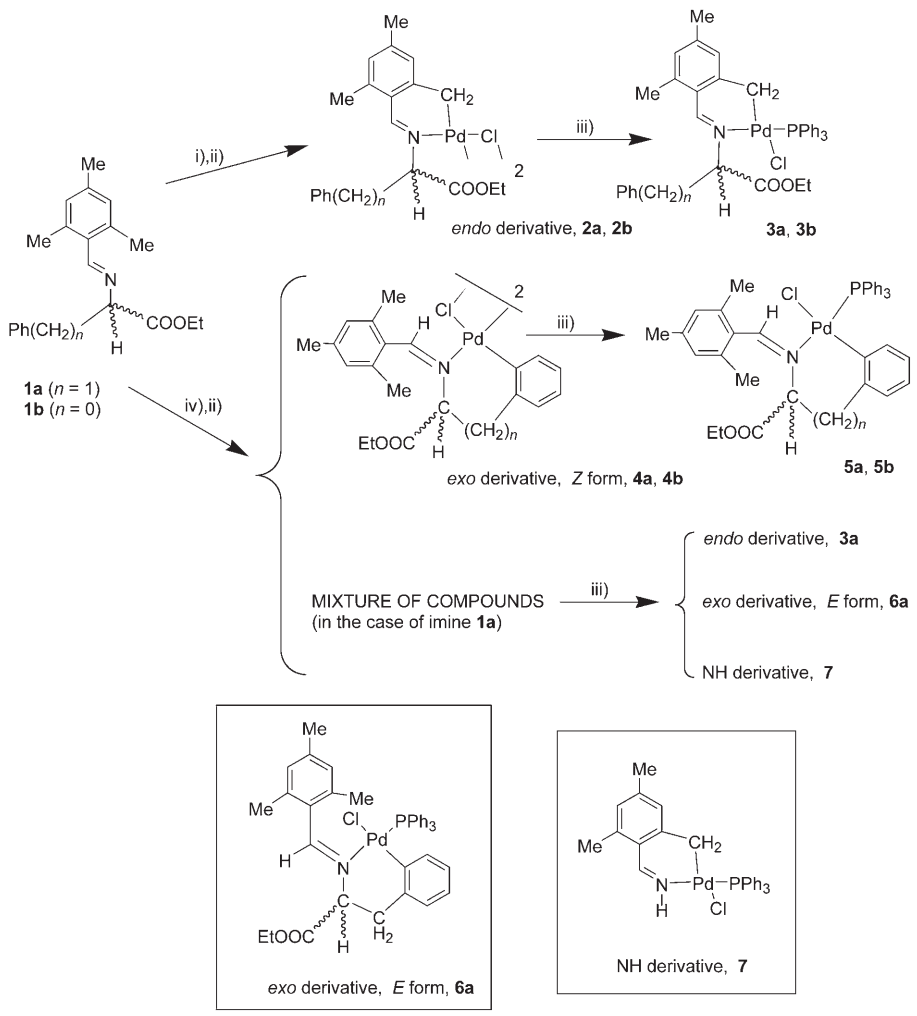
Results and Discussion

Metallation of the phenylalanine imine: The Schiff base 2,4,6-$Me_3C_6H_2CH{=}NCH(CH_2Ph)COOEt$ was treated with palladium acetate in acetic acid for 3 h at 70 °C. Subsequent treatment of the reaction residues with LiCl in acetone afforded a mixture of compounds, and after purification by silica gel column chromatography, the corresponding chloro-bridged cyclopalladated dimer **2a** was obtained (Scheme 1).

Aromatic imines can undergo metallation on different carbon atoms to give organometallic complexes of different structures: *endo* metallacycles, if the C=N bond is included in the metallacycle, or *exo* derivatives. In addition, imines can exist as *E* or *Z* isomers, but in general, N-substituted aldimines adopt the more stable *E* form.[21] *Endo* or *exo* metallacycles can be obtained from imines in the *E* form, but the *Z* isomer can only afford *exo* metallacycles.[22] Proton NMR data showed that **2a** was the six-membered *endo* metallacycle with a CH_2–Pd bond. Reaction of dimer **2a** with PPh_3 led to the formation of the mononuclear complex **3a**. The other fractions collected from the column were made up of a complex mixture of compounds; attempts made to separate this mixture were unsuccessful.

When the imine **1a** was treated with palladium acetate in toluene for one hour at room temperature and the reaction residues were treated with LiCl in acetone, a mixture of compounds was also obtained; after purification by using silica gel column chromatography, the corresponding chloro-bridged cyclopalladated dimer **4a** was isolated (Scheme 1). NMR data showed that this complex is the *exo* derivative, with a $C_{aromatic}$–Pd bond, containing the imine in the *Z* form. Reaction of dimer **4a** with PPh_3 afforded the mononuclear $[PdCl(\widehat{CN})(PPh_3)]$ ($\widehat{CN} = C_6H_4CH_2CH(COOEt)N{=}CH(2,4,6\text{-}Me_3C_6H_2)$) complex **5a**. The aromatic protons of the palladated ring appear to be shifted upfield in the proton NMR spectrum, a result showing the *cis* disposition between the phosphine and the metallated carbon atom,[23] and the HC=N proton is shifted downfield, which shows that the imine is in the *Z* form.[22]

Remarkably, when the crude material obtained by metallation of the imine in toluene was treated first with LiCl in acetone and then with PPh_3, a new mixture of compounds was obtained that could, in this case, be separated by using silica gel column chromatography, to afford the *endo* derivative **3a** (35% yield), the *exo* derivative **6a** (30%), and the unexpected compound **7** (10%) which, to the best of our knowledge, is the first NH-aldimine organometallic compound described (Scheme 1). Proton NMR spectra of these compounds were in good agreement with the proposed structures and showed that the *exo* derivative **6a**, containing the imine in the *E* form, is a mixture of rotamers. A 2D NOESY experiment showed



Scheme 1. i) $Pd(AcO)_2$, acetic acid, 70 °C, 3 h; ii) LiCl, acetone, RT, 30 min; iii) PPh_3, acetone, 30 min; iv) $Pd(AcO)_2$, toluene, RT, 1 h.

that these rotamers were in equilibrium in solution. X-ray crystallographic studies of **6a** (Figure 1) confirmed the structure suggested from the NMR data, with the *E* form adopted by the imine and the *cis* arrangement of the PPh_3 in related bond lengths and angles are given in Table 1. It should be noted that the molecules in the unit cell in this compound are linked in pairs by two N−H···Cl−Pd intermolecular bonds. The coordination plane shows some tetrahedral distortion, with the deviation from the mean plane being 0.079 for P, 0.1063 for N, −0.1019 for Cl and −0.1286 Å for C1. The angles between adjacent atoms are approximately 82.39(17) (C10-Pd-N) and 95.17(4)° (P-Pd-Cl), and the six-membered metallacycle has a screw-boat conformation.

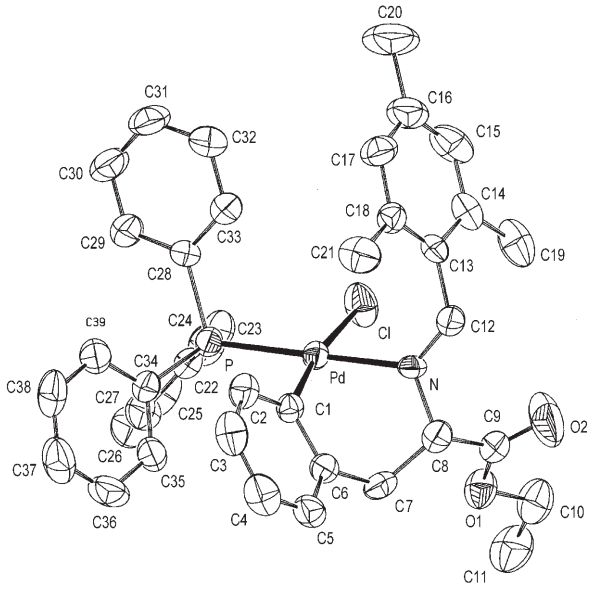


Figure 1. Molecular structure of compound **6a**.

tion to the palladated carbon atom. The crystal structure consists of discrete molecules separated by van der Waals distances. The palladium atom is in a square-planar environment, coordinated to carbon, nitrogen, chlorine, and phosphorus atoms. The distances between the palladium center and the coordinated atoms are similar to those reported for other cyclopalladated compounds.[22–24] The angles between adjacent atoms are approximately 83.14(11) (C1-Pd-N) and 94.21(9)° (C1-Pd-P). The six-membered metallacycle has a chair conformation.

The structure of the NH-aldimine derivative **7** was also determined by X-ray diffraction analyses (Figure 2), which confirmed the structure suggested from the NMR data. Se-

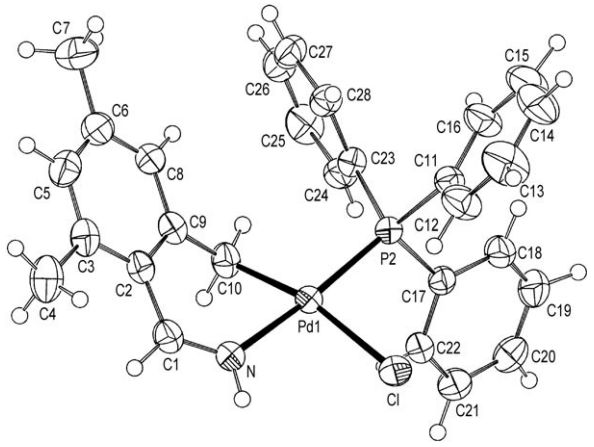


Figure 2. Molecular structure of compound **7**.

Table 1. Selected bond lengths [Å] and angles [°] for **6a** and **7**.

Compound **6a**			
Pd−C1	1.998(3)	C1-Pd-N	83.14(11)
Pd−N	2.093(3)	C1-Pd-P	94.21(9)
Pd−P	2.2686(10)	N-Pd-Cl	89.88(7)
Pd−Cl	2.3770(12)	P-Pd-Cl	92.99(4)
O1−C9	1.299(4)	C9-O1-C10	115.3(3)
O1−C10	1.479(4)	C12-N-C8	117.0(3)
O2−C9	1.173(4)	C12-N-Pd	126.5(2)
N−C12	1.258(4)	C8-N-Pd	116.5(2)
N−C8	1.483(4)		
Compound **7**			
Pd1−C10	2.041(5)	C10-Pd1-N	82.39(17)
Pd1−N	2.067(3)	C10-Pd1-P2	94.15(12)
Pd1−P2	2.2597(10)	N-Pd1-Cl	88.67(12)
Pd1−Cl	2.4354(12)	P2-Pd1-Cl	95.17(4)

Metallation of the 2-phenylglycine imine: The imine **1b** was treated with palladium acetate in acetic acid (for **2**) or toluene (for **4**) for one hour at room temperature, and the reaction residues were treated with LiCl in acetone. The chloro-bridged cyclopalladated dimers **2b** and **4b** were isolated after purification by using silica gel column chromatography (Scheme 1). NMR data showed that **2b** is the six-membered *endo* metallacycle with a CH_2−Pd bond and that **4b** is the *exo* derivative with a $C_{aromatic}$−Pd bond and containing the imine in the *Z* form. Reaction of these dimers with PPh_3 afforded the corresponding mononuclear $[PdCl(\widehat{CN})(PPh_3)]$ complexes **3b** and **5b**, respectively.

The structure of both compounds was determined by X-ray diffraction analyses (Figure 3), which confirmed the structures suggested from the NMR data. Selected bond lengths and angles are given in Table 2. These crystal structures consist of discrete molecules separated by van der Waals distances. The palladium atom is in a square-planar environment, coordinated to carbon, nitrogen, chlorine, and phosphorus atoms. The distances between the palladium center and the coordinated atoms are similar to those reported for other cyclopalladated compounds.[22–24] The angles between adjacent atoms are approximately 83.03(13) (C1-Pd-N) and 97.50(4)° (P-Pd-Cl) for **3b** and 81.20(14) (C1-Pd-N) and 94.62(4)° (P-Pd-Cl) for **5b**. The six-membered metallacycle has a twist-boat conformation in compound **3b**, and the five-membered metallacycle has an envelope conformation in **5b**.

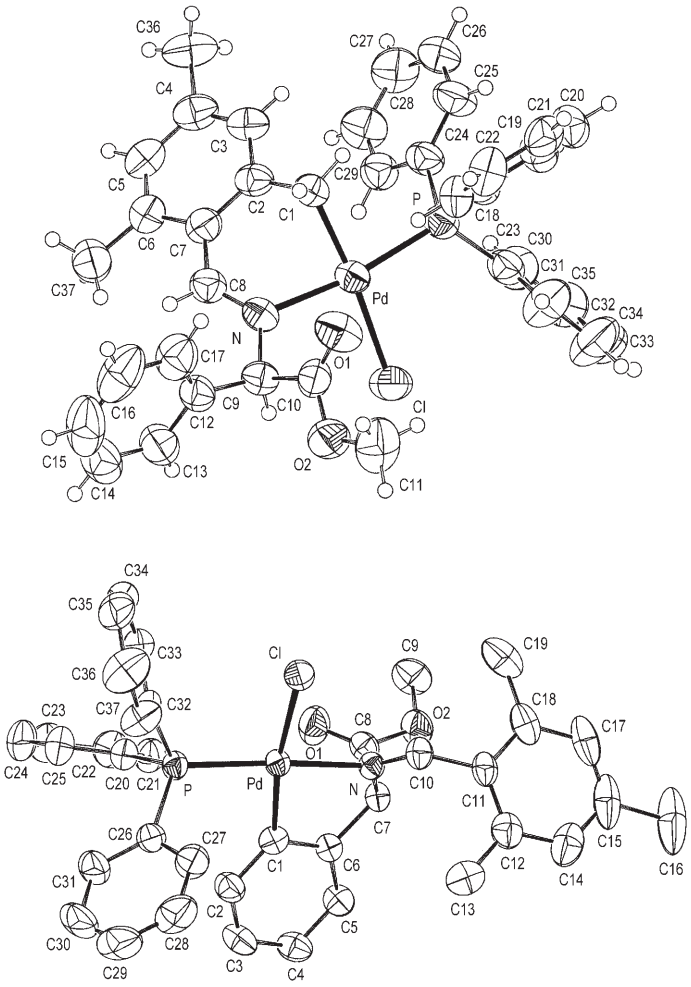


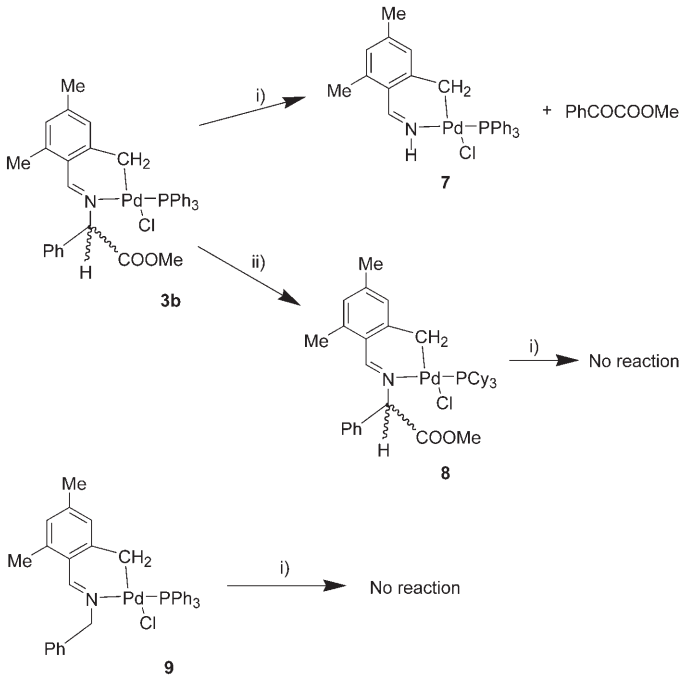
Figure 3. Molecular structures of compound **3b** (top) and **5b** (bottom).

Table 2. Selected bond lengths [Å] and angles [°] for **3b** and **5b**.

Compound **3b**			
Pd–C1	2.035(3)	C1-Pd-N	83.03(13)
Pd–N	2.135(3)	C1-Pd-P	87.78(10)
Pd–P	2.2141(9)	N-Pd-Cl	91.69(8)
Pd–Cl	2.4005(9)	P-Pd-Cl	97.50(4)
O1–C10	1.186(5)	C10-O2-C11	114.5(3)
O2–C10	1.320(5)	C8-N-C9	120.0(3)
O2–C11	1.433(5)	N-C8-C7	123.5(4)
N–C8	1.257(4)	N-C9-C12	114.2(3)
N–C9	1.493(4)	N-C9-C10	108.9(3)
Compound **5b**			
Pd–C1	2.017(4)	C1-Pd-P	93.85(11)
Pd–N	2.090(3)	N-Pd-Cl	90.42(9)
Pd–P	2.2446(10)	P-Pd-Cl	94.62(4)
Pd–Cl	2.3765(12)	C1-Pd-N	81.20(14)
O1–C8	1.182(5)	N-C7-C6	106.8(3)
O2–C8	1.322(5)	O1-C8-O2	124.2(4)
O2–C9	1.452(5)		
N–C10	1.279(5)		
N–C7	1.464(5)		

All the new organometallic compounds described here were characterized by elemental analysis, IR spectroscopy, and ^{1}H and ^{31}P NMR spectroscopy. The ^{1}H NMR spectra of the dinuclear cyclometallated compounds were recorded in $CDCl_3$ in the presence of a few drops of [D_5]pyridine (py) in order to obtain the mononuclear complexes: [PdCl(CN)py]. In some cases, 2D NMR experiments and positive-FAB mass spectra were carried out to complete the characterization. It should be noted that complete racemization of both Schiff bases takes place during the cyclopalladation reaction, but by contrast, racemization does not occur during the cyclopalladation of the 2-phenylglycine methyl ester.[6] This fact can be related to the increased acidity of the H_α atom in these metallacycles (see below).

Synthesis of the NH derivative: All the attempts to obtain the NH-aldimine derivative **7** by reaction between ammonia, mesitylaldehide, triphenylphosphine, and palladium acetate were unsuccessful.[12] Nevertheless, **7** can be obtained in 84% yield by the reaction between **3b** and PPh_3 in a 1:2 ratio in acetone for 24 h at room temperature in the presence of oxygen (Scheme 2). The solid obtained was filtered,



Scheme 2. i) Acetone, L = py, NMe_3, or PPh_3, in the presence of oxygen; ii) acetone, PCy_3, in the presence of oxygen. py = pyridine, Cy = cyclohexyl.

washed with ethyl ether, and characterized as **7**. The resulting solution was concentrated in vacuo, and the solid obtained was purified by using silica gel column chromatography with $CHCl_3$ to obtain the α-ketoester PhCOCOOMe.[25–27] Compound **7** can also be prepared from the metallacycle **3a**, in 54% yield, under the same reaction conditions.

This reaction can also be performed by using other bases such as pyridine or trimethylamine, instead of triphenylphosphine, under the same reaction conditions. By contrast,

when the experiment was performed with the metallacycle **9**, which does not contain the COOR fragment, no reaction was observed (Scheme 2), a result suggesting that the acidity of the H_α atom is essential to the oxidative cleavage of the nitrogen–carbon bond of the amino acid fragment.

It has recently been reported that the acidity of the α-amino carbon atom of the glycine moiety is dramatically increased by the formation of the iminium ion adduct to acetone,[28] and our results suggest that the coordination of the imine to a palladium atom can also result in an increase of the acidity of the H_α atom. These reasons prompted us to investigate the exchange for deuterium of the α-proton of the amino acid moiety in the metallacycle **3a**. A few drops of D_2O were added to a $CDCl_3$ solution of **3a**, and the exchange for deuterium of the α-protons was followed by monitoring the disappearance of the triplet due to the α-proton in the proton NMR spectra. The results are shown in Figure 4. It should be noted that almost 50% of hydrogen

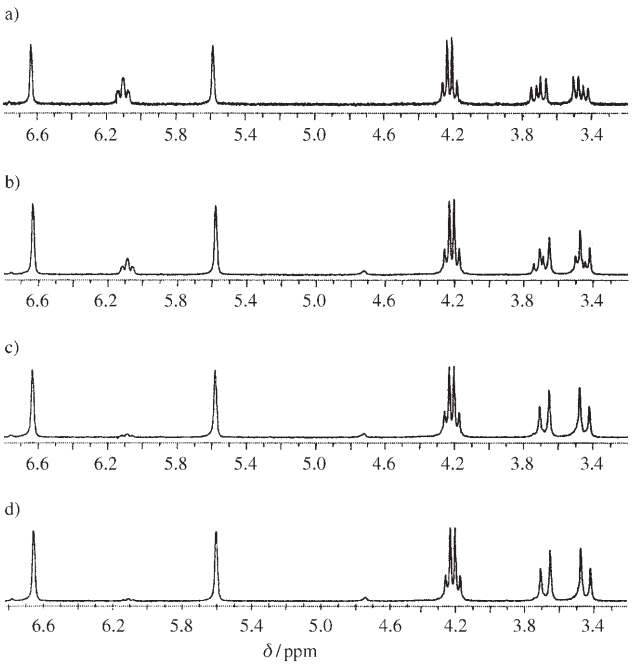


Figure 4. a) Proton NMR spectrum of **3a** in $CDCl_3$. Proton NMR spectra of **3a** in $CDCl_3$ b) 90 min, c) 125 min, and d) 140 min after the addition of D_2O.

had been exchanged at $t=90$ min, and when $t=140$ min, 93% of hydrogen had been exchanged. These results contrast with those obtained when the same experiment was performed with the corresponding imine or the amino acid. No exchange for deuterium of the α-protons was detected in these cases and only some decomposition of the imine was observed. In conclusion, the formation of the metallacycle dramatically increases the acidity of the α-proton of the amino acid moiety.

When compound **3b** was treated with tricyclohexylphosphine, the metallacycle **8** was obtained by a phosphine exchange reaction, but the formation of the NH-aldimine derivative was not observed, even if an excess of phosphine was used. Different attempts to prepare **7** from the tricyclohexyl derivative **8** by using different bases were also unsuccessful. These last results show that the ligands coordinated to palladium also play a role in the oxidative cleavage of the nitrogen–carbon bond of the amino acid fragment in imine metallacycles.

Conclusion

We have shown that the action of Lewis bases, such as triphenylphosphine, pyridine, or trimethylamine, on some imine metallacycles leads to the formation of an NH-aldimine organometallic compound and the corresponding α-ketoester, in a reaction that mimics the metabolism of α-amino acids. We have also shown that these NH aldimines, usually highly reactive intermediates, when coordinated to palladium are stable enough to be characterized, and their crystal structure can even be determined by X-ray diffraction analyses. The acidity of the α-proton of the amino acid fragment seems to be a key factor in the deamination reaction, and it has been shown that the formation of the metallacycle dramatically increases the acidity of this proton.

The formation of NH aldimines during monoamine oxidase catalyzed transformation of amines has been established by biosynthetic investigations.[29,30] Furthermore, it has been shown that the reduction of iron(III) porphyrins by amines also produces these NH imines.[31] The results described here suggest that the NH aldimines could also be formed in the biodegradation of α-amino acids. The synthesis of organometallic compounds containing new NH aldimines from the reaction between metal complexes and different biologically important ligands is currently in progress.

Experimental Section

^1H NMR spectra at 200 MHz were recorded on a Varian Gemini 200 spectrometer; ^1H NMR spectra at 500 MHz and $^{31}P\{^1H\}$ NMR spectra at 101.26 MHz were recorded, respectively, on Varian VXR 500 or Bruker DRX 250 spectrometers. Chemical shifts (δ in ppm) were measured relative to $SiMe_4$ for ^1H NMR spectra and to 85% H_3PO_4 for ^{31}P NMR spectra. Microanalyses were performed at the Institut de Química Bio-Orgànica de Barcelona and the Serveis Científico-Tècnics de la Universitat de Barcelona. Infrared spectra were recorded as KBr disks on a Nicolet 520 FT-IR spectrometer. Mass spectra were recorded on a Fisons VG-Quattro spectrometer. The samples were introduced in a matrix of 2-nitrobenzylalcohol for FAB analysis and then bombarded with cesium atoms.

Materials and synthesis: All solvents were dried and degassed by standard methods. All chemicals were of commercial grade and were used as received. The dinuclear cyclopalladated compounds were not characterized, as is not unusual for this kind of complex,[23c,32] but were used to obtain the corresponding phosphine-containing compounds which were fully characterized. Their proton NMR spectra were performed in $CDCl_3$ in the presence of few drops of [D_5]pyridine (py) in order to obtain the corresponding mononuclear complexes [PdCl(CN)py]. The imines were obtained by the reaction between mesitylaldehyde and the corresponding amino acid (phenylalanine ethyl ester or phenylglycine methyl ester) in

dichloromethane at room temperature for 20 h. The resulting solution was filtered and concentrated in vacuo; the oil obtained was characterized by ^{1}H NMR and IR spectroscopy and was used without further purification.

Cyclometallation reactions

*Metallation of imine **1a** in acetic acid*: A mixture of 2,4,6-$Me_3C_6H_2CH$=NCH(CH_2Ph)COOEt (719 mg, 2.22 mmol) and palladium acetate (500 mg, 2.22 mmol) in acetic acid (30 mL) was stirred at 70 °C for 3 h, and the resulting solution was concentrated in vacuo. The solid obtained was treated with an excess of LiCl (3.5 mmol, 150 mg) in acetone (30 mL) for 30 min at room temperature. The resulting solution was concentrated in vacuo, and the solid obtained was eluted through silica gel column chromatography with chloroform/acetone (100:2) as the eluent to obtain **2a** (15%, 155 mg). **2a**+[D_5]pyridine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.21 (t, J(H,H) = 7.0 Hz, 3H; CH_3CH$_2$O), 2.14 (s, 3H; Me), 2.27 (s, 3H; Me), 2.60 (d, J(H,H) = 8.3 Hz, 1H; CH_2Pd), 2.90 (d, J(H,H) = 8.3 Hz, 1H; CH_2Pd), 3.48 (br, 1H; CH_2Ph), 3.85 (dd, J(H,H) = 14.1, 6.9 Hz, 1H; CH_2Ph), 4.19 (q, J(H,H) = 6.8 Hz, 2H; CH$_3$CH_2O), 6.07 (br, 1H; *H*CCOOEt), 6.74 (s, 1H; aromatic), 6.86 (s, 1H; aromatic), 7.17–7.50 (m, 5H; aromatic), 7.98 ppm (s, 1H; *H*C=N).

*Metallation of imine **1a** in toluene*: A suspension formed of 2,4,6-$Me_3C_6H_2CH$=NCH(CH_2Ph)COOEt (719 mg, 2.22 mmol) and palladium acetate (500 mg, 2.22 mmol) in toluene (30 mL) was stirred at room temperature for 1 h, and the resulting solution was concentrated in vacuo. The solid obtained was treated with an excess of LiCl (3.5 mmol, 150 mg) in acetone (30 mL) for 30 min at room temperature. The resulting solution was concentrated in vacuo, and the solid obtained was eluted through silica gel column chromatography with chloroform/methanol (100:1) as the eluent to obtain **4a** in 15% yield (156 mg) in the first colored band. A mixture of compounds was obtained in the second colored band. **4a**+[D_5]pyridine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.05 (br, 3H; CH_3CH$_2$O), 1.86 (s, 3H; Me), 2.28 (brs, 6H; Me), 3.50–4.20 (brm, 5H; CH_2Ph, *H*CCOOEt, CH$_3$CH_2O), 6.55 (brs, 1H; aromatic), 6.86 (br, 5H; aromatic), 9.80 ppm (brs, 1H; *H*C=N).

*Metallation of imine **1b***: A suspension formed of 2,4,6-$Me_3C_6H_2CH$=NCH(Ph)COOMe (710 mg, 2.4 mmol) and palladium acetate (540 mg, 2.4 mmol) in toluene (30 mL) was stirred at room temperature for 1 h, and the resulting solution was concentrated in vacuo. The solid obtained was treated with an excess of LiCl (130 mg, 3 mmol) in acetone (30 mL) for 30 min at room temperature. The resulting solution was concentrated in vacuo, and the solid obtained was eluted through silica gel column chromatography with chloroform/methanol (100:1) as the eluent to obtain **2b** (15%, 150 mg) and **4b** (10%, 110 mg). **2b**+[D_5]pyridine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 1.94 (s, 3H; Me), 2.25 (s, 3H; Me), 2.42 (d, J(H,H) = 8.2 Hz, 1H; CH_2Pd), 3.64 (d, J(H,H) = 8.2 Hz, 1H; CH_2Pd), 3.86 (s, 3H; MeO), 6.70 (s, 1H; aromatic), 6.90 (s, 1H; aromatic), 7.35–7.50 (m, 6H; aromatic), 7.79 ppm (s, 1H; *H*C=N). **4b**+[D_5]pyridine: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.06 (s, 3H; Me), 2.26 (s, 3H; Me), 2.29 (s, 3H; Me), 3.61 (s, 3H; MeO), 5.39 (s, 1H; *H*CCOOMe), 6.18 (d, J-(H,H) = 7.0 Hz, 1H; aromatic), 6.88 (m, 3H; aromatic), 7.03 (m, 2H; aromatic), 9.78 ppm (brs, 1H; *H*C=N).

Synthesis of monomers with PPh_3

*[PdCl{1-CH_2-3,5-$Me_2C_6H_2CH$=NCH(CH_2Ph)COOEt}(PPh_3)] (**3a**)*: A stirred suspension of **2a** (0.21 mmol, 200 mg) in acetone (30 mL) was treated with PPh_3 (0.43 mmol, 113 mg) for 30 min at room temperature. The solution was concentrated in vacuo, and the solid obtained was washed with diethyl ether to afford **3a** as a yellow solid (85%). ^{31}P{^{1}H} NMR: δ = 35.42 ppm (s); ^{1}H NMR (200 MHz, $CDCl_3$) δ = 1.23 (t, J-(H,H) = 7.2 Hz, 3H; CH_3CH$_2$O), 2.04 (s, 3H; Me), 2.19 (s, 3H; Me), 2.40 (m, 2H; CH_2Pd), 3.52 (m, 2H; CH_2Ph), 4.21 (q, J(H,H) = 7.2 Hz, 2H; CH$_3$CH_2O), 5.58 (s, 1H; aromatic), 6.09 (brt, 1H; *H*CCOOEt), 6.63 (s, 1H; aromatic), 7.40–7.80 (m, 20H; aromatic), 8.28 ppm (d, J(H,P) = 13.2 Hz, 1H; *H*C=N); elemental analysis calcd (%) for $C_{39}H_{39}ClNO_2PPd$: C 64.47, H 5.41, N 1.93; found: C 64.1, H 5.6, N 1.8; MS (positive FAB): 725 $[M]^+$, 690 $[M-Cl]^+$.

*[PdCl{$C_6H_4CH_2CH$(COOEt)N=CH(2,4,6-$Me_3C_6H_2$)}(PPh_3)] (**5a**)*: Compound **5a** was obtained as a yellow solid in 85% yield by an analogous procedure to that used for the preparation of **3a** with **4a** (100 mg, 0.1 mmol) and PPh_3 (60 mg, 0.2 mmol). ^{31}P{^{1}H} NMR: δ = 33.60 ppm (s); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.21 (brt, J(H,H) = 6.8 Hz, 3H; CH_3CH$_2$O), 2.22 (s, 6H; Me), 2.24 (s, 3H; Me), 3.28 (br, 1H; CH_2Ph), 3.89 (br, 2H; CH_2Ph, C*H*COOEt), 4.08 (br, 2H; CH$_3$CH_2O), 6.32 (t, J-(H,H) = 7.2 Hz, 1H; aromatic), 6.56 (dd, J(H,H) = 5.2 Hz, J(H,P) = 7.6 Hz, 1H; aromatic), 6.68 (m, 2H; aromatic), 6.78 (m, 2H; aromatic), 7.26–7.63 (m, 15H; aromatic), 9.35 ppm (brs, 1H; *H*C=N); elemental analysis calcd (%) for $C_{39}H_{39}ClNO_2PPd$: C 64.47, H 5.41, N 1.93; found: C 64.3, H 5.4, N 1.9; MS (positive FAB): 725 $[M]^+$, 690 $[M-Cl]^+$.

*Synthesis and separation of **3a**, **6a**, and **7***: A stirred suspension of the mixture of products obtained from the metallation (250 mg) in acetone (30 mL) was treated with PPh_3 (0.53 mmol, 142 mg) for 30 min at room temperature. The solution was concentrated in vacuo, and the solid obtained was washed with diethyl ether to afford a yellow solid. This solid was carefully eluted through a silica gel column (30×400 mm) at room temperature with chloroform/acetone (100:2) as the eluent. The eluted solutions were collected in fractions of 15 mL, concentrated in vacuo, and checked by ^{31}P{^{1}H} NMR spectroscopy to obtain **3a** (35%), **6a** (30%), and **7** (10%). **6a**: ^{31}P{^{1}H} NMR: δ = 33.60 (s), 33.7 ppm (s); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.19 (br, 3H; CH_3CH$_2$O), 1.42 (br, 3H; CH_3CH$_2$O), 2.10 (s, 6H; Me), 2.38 (s, 12H; Me), 3.40 (brd, 1H; CH_2Ph), 3.48 (br, 1H; CH_2Ph), 4.05 (br, 2H; CH$_3$CH_2O), 4.15 (br, 1H; *H*CCOOEt), 4.45 (br, 3H; CH_2Ph, CH$_3$CH_2O), 4.65 (br, 1H; CH_2Ph), 4.92 (br, 1H; *H*CCOOEt), 6.25 (m, 4H; aromatic), 6.70 (m, 2H; aromatic), 6.90 (s, 4H; aromatic), 7.40–7.80 (m, 32H; aromatic), 8.74 ppm (m, 2H; *H*C=N); elemental analysis calcd (%) for $C_{39}H_{39}ClNO_2PPd$: C 64.47, H 5.41, N 1.93; found: C 64.2, H 5.5, N 1.9; MS (positive FAB): 725 $[M]^+$, 690 $[M-Cl]^+$. **7**: ^{31}P {^{1}H} NMR: δ = 34.19 ppm; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.15 (s, 3H; Me), 2.36 (s, 3H; Me), 2.81 (d, J(H,P) = 5.6 Hz, 2H; CH_2Pd), 6.08 (s, 1H; aromatic), 6.74 (s, 1H; aromatic), 7.20–7.40 (m, 9H; *meta*- and *para*-PPh_3), 7.40–7.80 (m, 6H; *ortho*-PPh_3), 8.49 (t, J-(H,P) = 13.2 Hz, J(H,H) = 13.2 Hz, 1H; *H*C=N), 9.22 ppm (brd, J(H,H) = 13.2 Hz, 1H; *H*N); elemental analysis calcd (%) for $C_{28}H_{27}ClNPPd$: C 61.11, H 4.94, N 2.55; found: C 61.1, H 4.9, N 2.6; MS (positive FAB): 550.9 $[M]^+$, 513.9 $[M-Cl]^+$.

*[PdCl{1-CH_2-3,5-$Me_2C_6H_2CH$=NCH(Ph)COOMe}(PPh_3)] (**3b**)*: Compound **3b** was obtained as a yellow solid in 80% yield by an analogous procedure to that used for the preparation of **3a** with **2b** (100 mg, 0.11 mmol) and PPh_3 (60 mg, 0.22 mmol). ^{31}P{^{1}H} NMR: δ = 35.53 ppm (s); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.97 (s, 3H; Me), 2.03 (s, 3H; Me), 2.10 (br, 1H; CH_2Pd), 3.37 (br, 1H; CH_2Pd), 3.87 (s, 3H; MeO), 5.62 (s, 1H; aromatic), 6.58 (s, 1H; aromatic), 7.30–7.80 (m, 21H; aromatic, *H*CCOOMe), 8.0 ppm (d, J(H,P) = 12.8 Hz, 1H; *H*C=N); elemental analysis calcd (%) for $C_{37}H_{35}ClNO_2PPd$: C 63.62, H 5.05, N 2.01; found: C 62.3, H 5.0, N 1.9; MS (positive FAB): 698 $[M]^+$, 663 $[M-Cl]^+$.

*[PdCl{C_6H_4CH(COOMe)N=CH(2,4,6-$Me_3C_6H_2$)}(PPh_3)] (**5b**)*: Compound **5b** was obtained as a yellow solid in 88% yield by an analogous procedure to that used for the preparation of **3a** with **4b** (100 mg, 0.11 mmol) and PPh_3 (60 mg, 0.22 mmol). ^{31}P{^{1}H} NMR: δ = 40.26 ppm (s); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.02 (s, 3H; Me), 2.25 (s, 3H; Me), 2.31 (s, 3H; Me), 3.74 (s, 3H; MeO), 5.40 (br, 1H; C*H*COOMe), 6.42 (m, 2H; aromatic), 6.81 (m, 3H; aromatic), 7.08 (d, J(H,H) = 7.8 Hz, 1H; aromatic), 7.40–7.80 (m, 15H; aromatic), 9.64 ppm (d, J(H,P) = 5.2 Hz, 1H; *H*C=N); elemental analysis calcd (%) for $C_{37}H_{35}ClNO_2PPd$: C 63.62, H 5.05, N 2.01; found: C 63.0, H 5.0, N 2.0; MS (positive FAB): 698 $[M]^+$, 663 $[M-Cl]^+$.

*Synthesis of [PdCl{1-CH_2-3,5-$Me_2C_6H_2CH$=NH}(PPh_3)] (**7**) and PhCOCOOMe (**9**)*: A stirred suspension of **3a** or **3b** (0.04 mmol) in acetone (30 mL) was treated with PPh_3 (0.08 mmol, 22 mg) for 24 h at room temperature. The solid obtained was filtered, washed with ethyl ether, and characterized as **7** (see above). The resulting solution was concentrated in vacuo, and the solid obtained was eluted through silica gel column chromatography with chloroform as the eluent to obtain compound **9**. The spectroscopic data confirm that **9** is the α-ketoester PhCOCOOMe.[25–27] The yields for the process were 53% and 84% with the starting materials **3a** or **3b**, respectively. **9**: ^{1}H NMR (200 MHz, $CDCl_3$): δ = 3.98 (s, 3H; MeO), 7.52 (t, J(H,H) = 7.8 Hz, 1H; aromatic), 7.68 (t, J-(H,H) = 7.8 Hz, 1H; aromatic), 8.05 ppm (d, J(H,H) = 7.8 Hz, aromatic);

Table 3. Crystal data and structure refinement for **6a**, **7**, **3b**, and **5b**.

compound	**6a**	**7**	**3b**	**5b**
formula	$C_{39}H_{39}ClNO_2PPd$	$C_{28}H_{27}ClNPPd$	$C_{37}H_{35}ClNO_2PPd$	$C_{38}H_{37}Cl_3NO_2PPd$
T [K]	293(2)	293(2)	293(2)	293(2)
λ [Å]	0.71069	0.71069	0.71069	0.71069
crystal system	triclinic	monoclinic	monoclinic	triclinic
space group	P	$P2_1/c$	$P2_1/n$	P
a [Å]	10.314(2)	10.1670(10)	9.6070(10)	9.2580(10)
b [Å]	10.907(4)	24.9410(10)	17.5560(10)	10.5500(10)
c [Å]	15.292(5)	10.6240(10)	19.1000(10)	18.7280(10)
α [°]	88.17(3)	90.0000(10)	90.0000(10)	92.2600(10)
β [°]	80.54(2)	114.2640(10)	91.5760(10)	94.6150(10)
γ [°]	86.88(2)	90.0000(10)	90.0000(10)	100.3000(10)
V [Å^3]	1693.9(9)	2456.0(3)	3220.2(4)	1791.2(3)
Z	2	4	4	2
ρ_{calcd} [mg m^{-3}]	1.424	1.488	1.441	1.453
μ [mm^{-1}]	0.709	0.946	0.743	0.821
$F(000)$	748	1120	1432	800
crystal size [mm]	0.1×0.1×0.2	0.1×0.1×0.2	0.1×0.1×0.2	0.1×0.1×0.2
reflections collected	9852	10751	12326	10284
goodness-of-fit on F^2	0.705	1.072	0.975	10284
final R indices [$I>2\sigma(I)$]	$R1=0.0350$	$R1=0.0454$	$R1=0.0420$	$R1=0.0473$
	$wR2=0.0328$	$wR2=0.1365$	$wR2=0.1128$	$wR2=0.1185$
R indices (all data)	$R1=0.1846$	$R1=0.0556$	$R1=0.0739$	$R1=0.0643$
	$wR2=0.0530$	$wR2=0.1480$	$wR2=0.1277$	$wR2=0.1277$

$^{13}C\{^1H\}$ NMR (75.4 MHz, $CDCl_3$): $\delta=186.0$, 164.0, 134.9, 132.4, 130.1, 128.9, 52.7 ppm; IR: $\tilde{\nu}=1740$, 1690 cm^{-1}; MS (ES$^+$): 165 $[M+H]^+$, 165 $[M]^+$.

X-ray crystallography: The crystal data, data collection, and refinement parameters for the X-ray crystal structures are listed in Table 3. Data were collected by using a MAR345 diffractometer with an image-plate detector. Unit-cell parameters were determined from automatic centering of 25 reflections ($3<\theta<31°$) and refined by the least-squares method. Intensities were collected with graphite monochromatized $Mo_{K\alpha}$ radiation. For **6a**, 9852 reflections were measured in the range $2.00\leq\theta\leq29.96$. 4124 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. For **7**, 10751 reflections were measured in the range $2.26\leq\theta\leq31.49$, of which 4209 were non-equivalent by symmetry (R_{int} (on I)=0.033), and 3524 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. For **3b**, 12326 reflections were measured in the range $1.58\leq\theta\leq31.70$, of which 5550 were non-equivalent by symmetry (R_{int} (on I)=0.036), and 3777 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. For **5b**, 10284 reflections were measured in the range $2.86\leq\theta\leq31.52$, of which 6506 were non-equivalent by symmetry (R_{int} (on I)=0.027), and 5231 reflections were assumed as observed by applying the condition $I>2\sigma(I)$. Lorentz polarization but not absorption corrections were made.

The structures were solved by direct methods, by using the SHELXS computer program,[33] and were refined by the full-matrix least-squares method. The function minimized was $\Sigma w[|F_o|^2-|F_c|^2]^2$, in which $w=[\sigma^2(I)]^{-1}$ for **6a**, $w=[\sigma^2(I)+(0.1030P)^2+2.2441P]^{-1}$ for **7**, $w=[\sigma^2(I)+(0.0914P)^2]^{-1}$ for **3b**, and $w=[\sigma^2(I)+(0.0581P)^2+2.8501P]^{-1}$ for **5b**, with $P=(|F_o|^2+2|F_c|^2)/3$. f, f', and f'' were taken from the International Tables of X-Ray Crystallography.[34]

CCDC-258562 (**6a**), CCDC-258563 (**3b**), CCDC-258564 (**5b**), and CCDC-148187 (**7**) contain 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.

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