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Ortho-Palladation of the Phenethylamines of Biological Relevance, L-Tyrosine Methyl Ester and Homoveratrylamine. Reactivity of the Palladacycles towards CO and Isocyanides. Synthesis of the Natural Alkaloid Corydaldine

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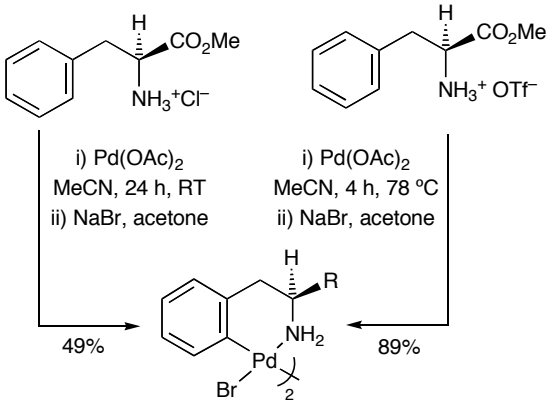
ABSTRACT: The palladacycle derived from L-tyrosine methyl ester, (*S*)-[Pd_2{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}$_2(\mu$-Br)$_2$] (**1a-Br**), or homoveratrylamine, [Pd_2{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}$_2(\mu$-Br)$_2$] (**1b-Br**) can be easily prepared in good yield by reacting $Pd(OAc)_2$, the corresponding ammonium triflate and NaBr. Under the same reaction conditions, the reaction of $Pd(OAc)_2$ with the free amine affords low yield of the corresponding acetato complex, **1a-OAc** or **1b-OAc** (the latter only detected in solution). In our hands, the previously reported palladation at the C2 position of homoveratrylamine with $Pd(OAc)_2$ is not observed. Instead, a complex mixture is obtained, mainly containing [$Pd(OAc)_2${$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$_2$] and minor amounts of **1b-OAc**, which reacts with NaBr to afford a new mixture from which [$PdBr_2${$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$_2$] can be isolated and characterized. These and other adducts can be isolated from $Pd(OAc)_2$, homoveratrylamine and various ligands (PPh_3 or Br^-). 6-Bromohomoveratrylamine reacts with $Pd(dba)_2$ in the presence of tmeda to give the complex [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(tmeda)]Br. Reactions of complexes **1** with acetylacetonato or neutral (PR_3) ligands give products resulting from substitution or bridge-splitting reactions. While complex **1a-Br** reacts with XyNC (1:2 molar ratio) to give (*S*)-[Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}Br(CNXy)], **1b-Br** gives [Pd{*C*,*N*-C(=NXy)-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}Br(CNXy)]. (*S*)-7-Hydroxy-3-(methoxycarbonyl)-3,4-dihydroisoquinolin-1(2*H*)-one and 6,7-dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one (corydaldine) are synthesized through the stoichiometric carbonylation of palladacycles **1a-Br** and **1b-Br**. The crystal structures of a solvento-intermediate in the ortho-metalation reaction of the triflate derivative of L-tyrosine methyl ester, and four other complexes have been determined by X-ray diffraction studies.

INTRODUCTION

Ortho-palladated complexes have been widely used as precatalysts in organic synthesis[1,2] or as reagents toward unsaturated compounds to afford organic derivatives of the corresponding arenes.[2-4] We have contributed to this last topic,[5] preparing organic derivatives of benzyl-[6] and phenethyl-amines[7-10] by reaction of the corresponding cyclopalladated complexes with CO, RNC, RNCS, halogens, or olefins. A parallel study is being carried out with orthopalladated benzylamines.[11] We are particularly interested in using this method to prepare derivatives of phenethylamines because some pharmaceuticals (i.e., amphetamines) and biologically active amino acids belong to this family of compounds.[12]

For a long time, primary arylalkylamines were believed to be inert toward direct activation of C–H bonds by Pd(II),[13] but their cyclometalation was proved to be possible when the adequate reaction conditions were used.[14,15] Nevertheless, most derived halogen-bridged ortho-metalated complexes were obtained in low to moderate yields (17–63%).[8,16-18] Very recently, we have found that those yields can be significantly improved if the ortho-palladation reactions are carried out using the corresponding ammonium triflates as starting materials, instead of the free amines or their hydrochlorides.[19] For instance, the dimeric bromo-bridged palladacycle derived from L-phenylalanine methyl ester can be obtained from $Pd(OAc)_2$, NaBr and: (1) L-phenylalanine methyl ester hydrochloride, in 49% yield,[8] or (2) the triflate derived of L-phenylalanine methyl ester, in 89% yield (Scheme 1).[19]

Scheme 1. Reported Syntheses of the Bromo-bridged Ortho-palladated Derivative of (L)-Phenylalanine Methyl Ester.



We report in this work the application of this improved method to (1) the synthesis of the new palladacycle derived from L-tyrosine methyl ester, a derivative of a natural amino acid and (2) improve the yield of the previously reported product of the ortho-palladation of homoveratrylamine,[20] a hallucinogenic compound closely related to the amphetamines family.[12] This second objective was not achieved because, in our hands, the ortho-palladation of homoveratrylamine takes place in a position of the aryl ring different from that reported.[20] We also (1) analyze the differences and advantages of using the triflate salts instead of the free amines as starting materials in these ortho-metalation reactions, (2) prepare some derivatives of the cyclopalladated complexes by reacting them with anionic and neutral ligands, and (3) prepare the lactams derived of both phenethylamines via carbonylation of their corresponding palladacycles.

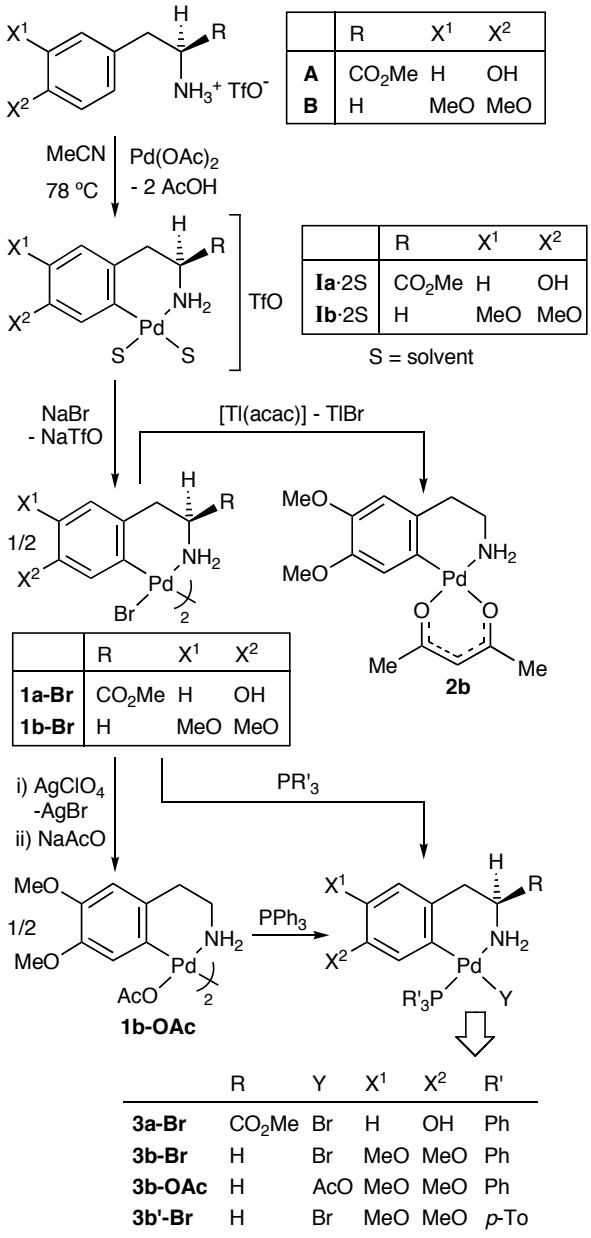
RESULTS AND DISCUSSION

Synthesis of Ortho-Palladated Complexes. Consistent with our recently described method of ortho-palladation of primary arylalkylamines,[19] the ammonium triflate derived from L-tyrosine methyl ester, (*S*)-[4-OH-$C_6H_4CH_2CH(CO_2Me)NH_3$]OTf (**A**), or homoveratrylamine, [3,4-$(MeO)_2C_6H_3CH_2CH_2NH_3$]OTf (**B**), reacted with $Pd(OAc)_2$ in a 1:1 molar ratio, in acetonitrile at 78 ºC, to give HOAc and, likely, an ortho-metalated solvento-intermediate (**Ia**·2S, **Ib**·2S; Scheme 2), which in turn reacted with NaBr to afford the bromo-bridged cyclopalladated complex **1a-Br** or **1b-Br**. The addition of NaOAc to solutions of the intermediate **Ib** in acetone afforded the acetato-bridged complex **1b-OAc**, which could not be isolated pure from the reaction mixture. The metathesis reaction between **1b-Br** and NaOAc afforded complex **1b-OAc** contaminated with unreacted **1b-Br**, even when long reaction times and a large excess of NaOAc were used. However, the reaction of complex **1b-Br** with $AgClO_4$ in a 1:2 molar ratio, and the subsequent addition of NaOAc, allowed the synthesis of pure **1b-OAc** (Scheme 2).

When **1b-Br** was treated with [Tl(acac)] (Hacac = acetylacetone), precipitation of TlBr took place and the complex [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(*O*,*O*'-acac)] (**2b**) was obtained (Scheme 2). Complex **1a-Br**, **1b-Br** or **1b-OAc** reacted with two equiv of PR_3 (R = Ph, *p*-To) to give the

mononuclear phosphino adduct [Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}Br(PPh_3)] (**3a-Br**) or [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}X(PR_3)] (X = Br, R = Ph (**3b-Br**), To (**3b'-Br**); X = OAc, R = Ph (**3b-OAc**); Scheme 2).

Scheme 2. Synthesis of Palladacycles Containing L-Tyrosine Methyl Ester and Homoveratrylamine



	R	X¹	X²
A	CO_2Me	H	OH
B	H	MeO	MeO

	R	X¹	X²
Ia·2S	CO_2Me	H	OH
Ib·2S	H	MeO	MeO

	R	X¹	X²
1a-Br	CO_2Me	H	OH
1b-Br	H	MeO	MeO

	R	Y	X¹	X²	R'
3a-Br	CO_2Me	Br	H	OH	Ph
3b-Br	H	Br	MeO	MeO	Ph
3b-OAc	H	AcO	MeO	MeO	Ph
3b'-Br	H	Br	MeO	MeO	*p*-To

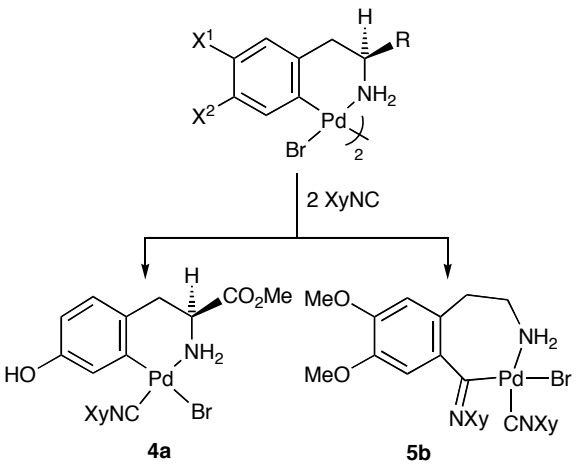
Complex **1a-Br** reacted with two equiv of XyNC to give [Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-6,(OH)-4}Br(CNXy)] (**4a**) (Scheme 3). When an analogous reaction was tried using **1b-Br** as starting material, a mixture of the unreacted bromo-bridged cyclometalated compound and the complex [Pd{*C*,*N*-C(=NXy)-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}Br(CNXy)] (**5b**) was isolated. Complex **5b** could be

prepared in good yield by reaction of complex **1b-Br** with four equiv of XyNC. The same reaction with **1a-Br** gave a solid insoluble in all common organic solvents.

The mechanism of the insertion of isocyanides into the Pd–C bond, that has been thoroughly studied, involves (1) coordination of the ligand to the metal center and (2) migratory insertion of the aryl group to the coordinated isocyanide.[6,21-24] According to this mechanism, the different behavior between palladacycles **1a-Br** and **1b-Br** towards isocyanide insertion can be attributed to the increased nucleophilicity of the carbon atom bonded to palladium(II) in the homoveratrylamine derivative, which favors the insertion of the isocyanide into the Pd–C bond.[24,25] The easy insertion of the isocyanide into the Pd–C bond of **1b-Br** resembles the behavior of the palladacycle derived from benzyl methyl sulfide, which undergo rapid isocyanide insertion at room temperature,[22] and contrasts with that exhibited by complexes derived from classical *N*,*N*-bencylamines, for which high temperatures or an excess of isocyanide are required to obtain the iminoacyl complexes.[6,21]

Scheme 3. Reactions of Ortho-Palladated Complexes with XyNC

	R	X^1	X^2
1a-Br	CO_2Me	H	OH
1b-Br	H	MeO	MeO



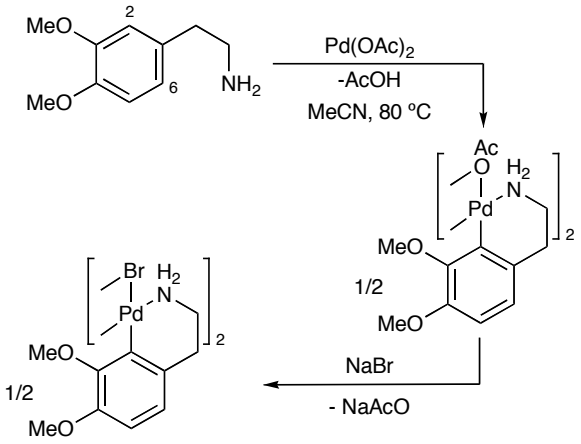
The NMR data support the structures of compounds **1**–**5** shown in Schemes 2 and 3. The ^{1}H NMR spectra of homoveratrylamine derivatives show that only the isomer palladated at C6 was obtained. Thus, for non-phosphino complexes (**1b-Br**, **1b-OAc**, **2b** and **5b**) H2 and H5 protons give singlets (δ:

6.43–6.68 (H2), 6.69–7.60 (H5)). Coordination of PR_3 to the metal produces, with respect to its precursor, a large shielding of the aromatic proton next to the metalated carbon (e.g., δ(H5): 6.69 (**1b-OAc**), 6.01 (**3b-OAc**)) and of the adjacent methoxy protons of the homoveratrylamine derivatives (e.g., δ(MeO): 3.80, 3.81 (**1b-OAc**), 3.02 (**3b-OAc**)), as observed in other cases.[26] Additionally, coupling of H5 with ^{31}P nucleus was observed in all complexes ($^4J_{HP}$ = 4.8–5.2 Hz). These features are consistent with coordination of the PPh_3 in trans position to the amino group,[27] which is the expected geometry taking into account the great *transphobia*[28] between PPh_3 and aryl ligands.[29,30] ^1H and ^{13}C NMR spectra of complex **5b** show the restricted rotation of the Xy group of the inserted isocyanide, probably caused by steric hindrance. We propose that, in both complexes, the coordinated isocyanide is located in trans position to the amino group, because this is the normal behavior for palladacycles containing arylalkylamines,[6,9,10,21,23,31,32] and it is in agreement with the well-established *transphobia* between C-donor ligands.[29,33]

On the Ortho-Palladation of Homoveratrylamine. Our results on the ortho-metalation of homoveratrylamine agree with those obtained by other authors for similar N-ligands. For instance, Vila et al. have studied the influence on the metalation position of different substituents at the aromatic ring in some Schiff bases,[34] and conclude that a methoxy group at the C3 hinders palladation at C2. Pfeffer et al. have observed similar steric hindrance in the synthesis of cyclometalated ruthenium(II) complexes containing substituted *N*,*N*-dimethylbenzylamines.[35] Direct palladation of *N*,*N*-diethyl-3-methoxy-4-benzyloxy-benzylamine,[26] *N*,*N*-dimethyl-3,4-dimethoxybenzylamine,[36] *N*-methyl-*N*-buthyl-3,4-dimethoxybenzylamine,[37] *N*-buthyl-3,4-dimethoxybenzylamine,[38] *N*-(3,4-dimethoxybenzylidene)benzenamine,[39] *N*-(3,4-dimethoxybenzylidene)-2,4,6-trimethylbenzenamine,[40] *N*-(2-hydroxoethyl)-3,4-dimethoxybenzylideneamine,[41] *N*-(2,6-dichlorobenzylidene)-2-(3,4-dimethoxyphenyl)ethylamine,[42] and 4-(3,4-dimethoxybenzylidene)-2-(3,4-dimethoxyphenyl)oxazol-5(4*H*)-one[43] (among others) have also been reported to occur regiospecifically at the C6 position. Surprisingly, Hajipour et al.[20] described the reaction between homoveratrylamine and $Pd(OAc)_2$ in

acetonitrile at 80 ºC to give the ortho-palladated complex at C2 position. The acetato-bridged complex could not be isolated pure, but metathesis reaction with NaBr afforded the corresponding bromo-bridged derivative (Scheme 4) in a 39% overall yield (based on $Pd(OAc)_2$).

Scheme 4. Reported Synthesis of Palladacycles Containing Homoveratrylamine[20]



With the aim of elucidating if the use of the triflate salt instead of the free amine as starting material could modify the result of the metalation reaction, we repeated it under the same conditions used by Hajipour et al.[20] However, in our hands, when a 1:1 mixture of homoveratrylamine and $Pd(OAc)_2$ was refluxed in acetonitrile for 4 h, a dark orange solid **X** could be isolated, along with metallic palladium. The ^{1}H NMR spectrum of **X** (Figure 1, spectrum b) corresponds to a mixture in which $[Pd(OAc)_2\{NH_2CH_2CH_2C_6H_3(OMe)_2\text{-}3,4\}_2]$ (**6b-OAc**; signals marked with red circles in Figure 1) is the major component, and the ortho-palladated complex **1b-OAc** (signals marked with green stars in Figure 1) is also present. Using other reaction times (4–48 h) and temperatures (25–80 ºC), mixtures very similar to **X** were obtained. We could not discard that a small amount of the ortho-metalated complex at C2 position was present in this mixture, since their ^{1}H NMR signals could be obscured by those corresponding to other components (Figure 1, spectra b–e). When **X** was treated with an excess of NaBr, a new mixture was obtained from which complex $[PdBr_2\{NH_2CH_2CH_2C_6H_3(OMe)_2\text{-}3,4\}_2]$ (**6b-Br**) could be isolated in a 48% yield. Complexes **6b-OAc** and **6b-Br** were independently prepared by reaction of $Pd(OAc)_2$ and the free amine at room temperature in a 1:2 molar ratio (Scheme 5). To characterize the components of **X**, the reaction of **6b-OAc** or **6b-Br** with one equiv of PPh_3 was carried

out and [PdX_2{$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$(PPh_3)$] (X = OAc (**7b-OAc**), Br (**7b-Br**); Scheme 5) was isolated. Surprisingly, the phosphino ligand only displaced one of the two amines coordinated to palladium(II), even when an excess of PPh_3 was used.

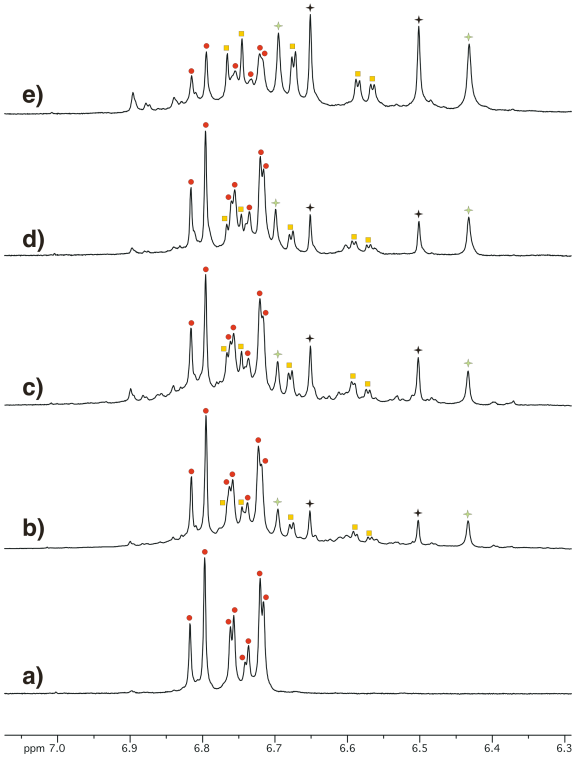
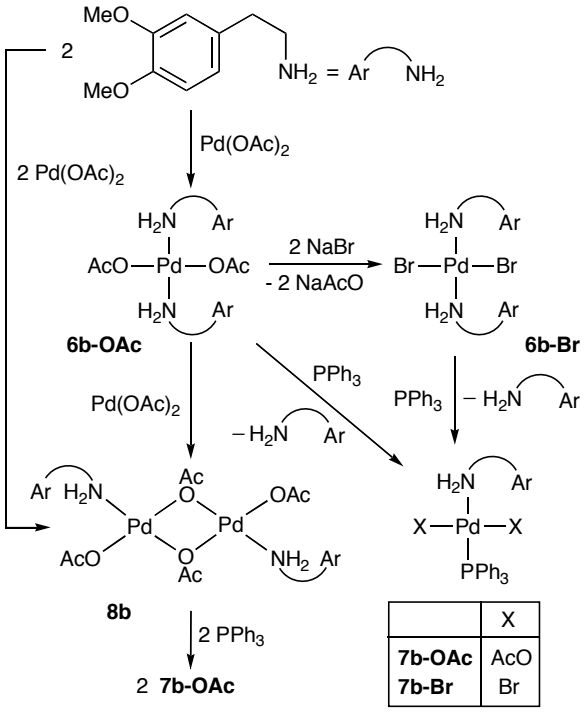


Figure 1. ^{1}H NMR (6.4–7.0 ppm) spectra of complex **6b-OAc** (a), and mixture **X** obtained from the reaction of $Pd(OAc)_2$ and free homoveratrylamine in acetonitrile at different reaction times and temperatures: 4 h at 80 ºC (b), 7 h at 78 ºC (c), 7 days at room temperature (d), 2 h at 70 ºC and then 48 h at room temperature (e). Signals corresponding to complex **6b-OAc** are marked with red circles; signals of complex **1b-OAc**, with green stars. At least, other two species are present in mixture **X**: an ortho-metalated complex at C6 position (signals marked with black stars) and a non ortho-metalated compound (signals marked with yellow squares).

We have proved[15,17,18] that the reaction of $Pd(OAc)_2$ with one equiv of arylalkylamines in acetonitrile, gives initially the complex [$Pd(OAc)_2(amine)_2$], which further reacts with the remaining $Pd(OAc)_2$ to give the dinuclear complex [$Pd_2(\mu\text{-}OAc)_2(OAc)_2(amine)_2$] (Scheme 5), which, in turn, can undergo the ortho-palladation reaction upon heating in acetonitrile. By reacting at room temperature $Pd(OAc)_2$ and one equiv of homoveratrylamine in CH_2Cl_2, a mixture was obtained after one hour from which

complexes **6b-OAc** (40%) and $[Pd_2(\mu\text{-}OAc)_2(OAc)_2\{NH_2CH_2CH_2C_6H_3(OMe)_2\text{-}3,4\}_2]$ (**8b**; 35%) were isolated. When longer reaction times were used, complex **8b** evolved to a mixture **Y**, which contained some of the species present in the mixture **X**. Moreover, when heated in the solid state, complex **8b** also evolved to the mixture **Y** (Figure 2). The complex **7b-OAc** (Scheme 5) could also be prepared by reaction of **8b** with two equiv of PPh_3.

Scheme 5. Synthesis of non Ortho-Palladated Complexes Containing Homoveratrylamine



In addition of complexes **6b-OAc** (present in mixture **X**), **8b** (present in mixture **Y**), and **1b-OAc** (present in **X** and **Y**), two other sets of signals were observed in the ^1H NMR spectra (in $CDCl_3$) of both mixtures: one pair of singlets at 6.50 and 6.65 ppm (relative intensities = 1:1), probably corresponding to an ortho-palladated compound at C6 position (**C**), and a doublet of doublets (δ: 6.57, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 2.0 Hz) plus two doublets (δ: 6.67, $^4J_{HH}$ = 2.0 Hz; 6.75, $^3J_{HH}$ = 8.0 Hz) with relative intensities 1:1:1, that could be assigned to a non ortho-palladated complex (**D**). In order to characterize **C** and **D**, we reacted mixtures **X** and **Y** with 1–2 equiv PPh_3/Pd, which afforded a mixture of two complexes in both cases, as observed by ^{31}P NMR: **3b-OAc** (Scheme 2), formed from **1b-OAc** (Scheme 2) and **C**, and **7b-OAc**, formed from **6b-OAc**, **8b** (Scheme 5) and **D**. Consistent with these data, **C** could be an isomer of

1b-OAc (Scheme 2) and **D** an isomer of **8b** or **6b-OAc**, because they would give the same complexes with PPh_3 that **1b-OAc** and **8b** or **6b-OAc**, respectively.

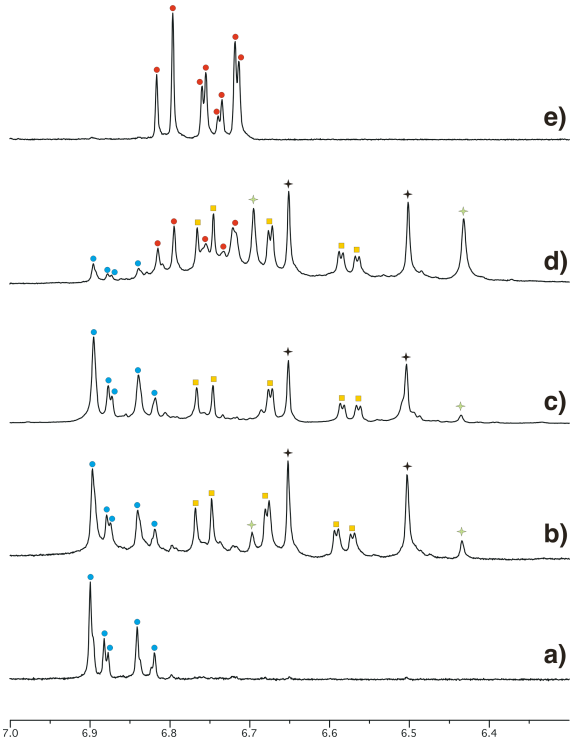


Figure 2. ^{1}H NMR (6.4–7.0 ppm) spectra of: (a) complex **8b**, (b) mixture **Y**, obtained when a solution of complex **8b** in CH_2Cl_2 is maintained at room temperature for 40 h, (c) mixture **Y**, obtained by heating solid **8b** at 65 ºC for 5 h, (d) mixture **X**, and (e) complex **6b-OAc**. Signals corresponding to complex **6b-OAc** are marked with red circles; signals of complex **8b**, blue circles; signals of complex **1b-OAc**, green stars. Two other species are present in both mixtures: an ortho-palladated complex at C6 position (signals marked with black stars) and a non ortho-palladated compound (signals marked with yellow squares).

The crystal structures of complexes **6b-Br** (Figure 3), **6b-OAc**·H_2O (Figure 4) and **7b-OAc** (Figure 5) have been determined by X-ray diffraction. The molecules of complexes **6b-Br** and **6b-OAc**·H_2O are centrosymmetric, with the palladium atoms coordinated to two bromo (**6b-Br**) or two terminal acetato (**6b-OAc**·H_2O) ligands and the nitrogen atoms of two amines, in an almost perfect square-planar geometry. For complex **6b-Br** there are two independent molecules in the asymmetric unit. The amino ligands adopt a mutually trans disposition, which is the normal geometry for this type of complexes.[7,44]

In complex **7b-OAc**, the palladium(II) center is bound to the NH_2 group of the homoveratrylamine, one triphenylphosphine and two trans acetato ligands. To our knowledge this is the first structurally characterized bis-acetato-complex of Pd(II) containing a primary arylalkylamine and a phosphino ligand, although the crystal structures of complexes of the type *trans*-[$PdCl_2$(arylalkylamine)(PR_3)] have been reported.[45]

The molecules of complex **6b-Br** and **6b-OAc**·H_2O are associated through N–H···Br and N–H···O_{OAc} hydrogen bonds to give chains and double chains, respectively. In complex **6b-Br**, the chains are connected through a weak interaction C_{OMe}–H···O_{OMe} to generate layers, while in complex **6b-OAc**·H_2O the chains are connected through O–H···O_{OAc} hydrogen bonds involving the crystallization water, to form a tridimensional net. In complex **7b-OAc**, two adjacent molecules are connected through four N–H···O_{OAc} hydrogen bonds to give dimers which, in turn, are connected through non classical C–H···O_{OAc} hydrogen bonds to give double chains along the *a* axis (see Supporting Information).

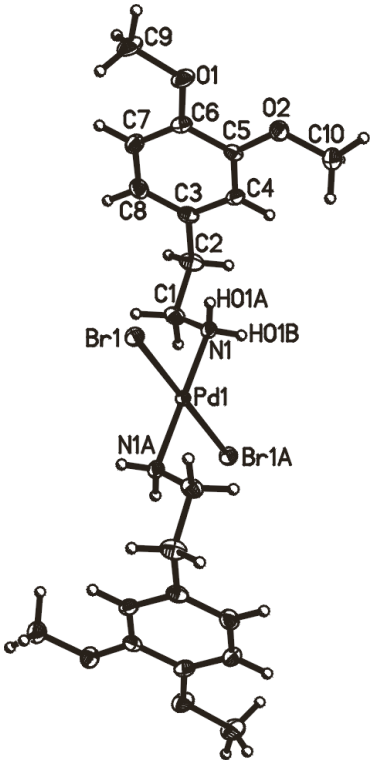


Figure 3. X-ray thermal ellipsoid plot of one (A) of the two independent molecules of complex **6b-Br** (50% probability) showing the labeling scheme. Selected bond lengths (Å) and angles (deg) are given for both independent molecules. For A: Pd(1)–N(1) = 2.029(2), Pd(1)–Br(1) = 2.4213(3); N(1)–Pd(1)–

Br(1) = 89.33(7), N(1)–Pd(1)–Br(1A) = 90.67(7). For B: Pd(2)–N(2) = 2.030(2), Pd(2)–Br(2) = 2.4276(3); N(2)–Pd(2)–Br(2) = 88.73(7), N(2)–Pd(2)–Br(2A) = 91.27(7).

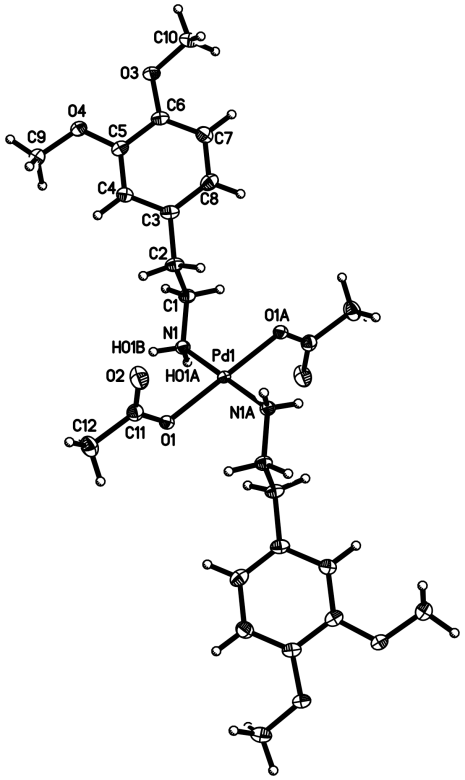


Figure 4. X-ray thermal ellipsoid plot of complex **6b-OAc**·H_2O (50% probability) showing the labeling scheme (the solvent molecule has been omitted for clarity). Selected bond lengths (Å) and angles (deg): Pd(1)–N(1) = 2.0451(17), Pd(1)–O(1) = 2.0161(14); N(1)–Pd(1)–O(1) = 86.83(7), N(1)–Pd(1)–O(1A) = 93.17(7).

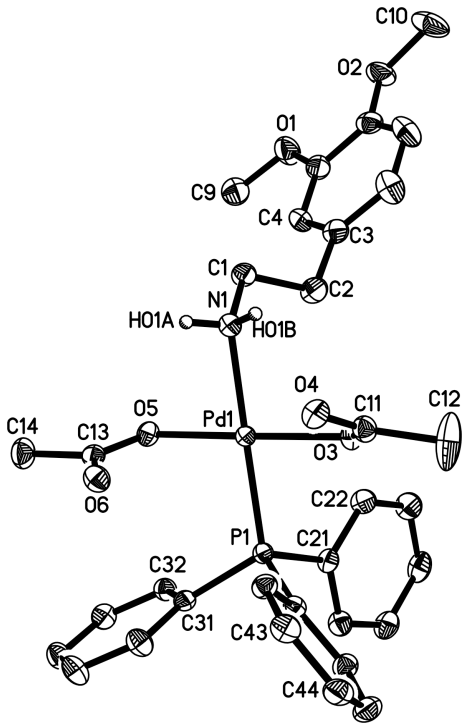


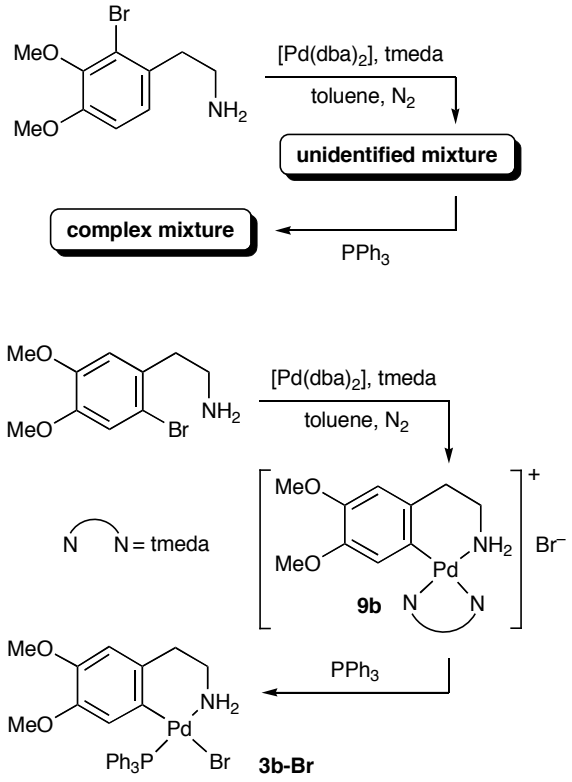
Figure 5. X-ray thermal ellipsoid plot of complex **7b-OAc** (50% probability) showing the labeling scheme (hydrogen atoms bonded to carbon have been omitted for clarity). Selected bond lengths (Å) and angles (deg): Pd(1)–N(1) = 2.1000(14), Pd(1)–O(3) = 2.0234(11), Pd(1)–P(1) = 2.2539(4), Pd(1)–O(5) = 2.0042(11); N(1)–Pd(1)–O(3) = 92.77(5), O(3)–Pd(1)–P(1) = 86.20(3), P(1)–Pd(1)–O(5) = 93.24(3), O(5)–Pd(1)–N(1) = 87.89(5).

On the Synthesis of Ortho-Palladated Derivatives of Homoveratrylamine by Oxidative Addition. As we were not able to obtain the ortho-palladated derivative of homoveratrylamine at C2 position by C–H activation, we tried to prepare it by oxidative addition of 2-bromo-3,4-dimethoxyphenethylamine (see Experimental Section and Supporting Information) to "$Pd(dba)_2$" ($[Pd_2(dba)_3]$·dba; dba = dibenzylideneacetone) in the presence of tmeda (tmeda = *N*,*N*,*N*',*N*'-tetramethylethylenediamine). When these three reagents (molar ratio = 1:1:1) were stirred in dry toluene, at room temperature, for 24 h, a mixture was obtained from which no pure complex could be isolated. Addition of PPh_3 to this mixture afforded a new mixture of at least five P-containing compounds, as observed by ^{31}P NMR, that could not be separated (Scheme 6). When an analogous reaction was carried out from 6-bromo-3,4-dimethoxyphenethylamine, the complex [Pd{*C*,*N*-

$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(tmeda)]Br (**9b**) precipitated in the reaction medium and could be isolated in a 72% yield (Scheme 6). Reaction of **9b** with PPh_3 (molar ratio = 1:1) gave complex **3b-Br**.

The oxidative addition of 2-bromo-3,4-dimethoxyphenethylamine to "$Pd(dba)_2$" was tried under nitrogen atmosphere using other solvents, temperatures and in the presence or absence of auxiliary ligands, but no satisfactory results were obtained. For instance, when the reaction was carried out (1) in the absence of any auxiliary ligand, in toluene, at 25–60 ºC, unreacted starting material was obtained, along with other unidentified compounds, and (2) in presence of ethylenediamine and NaBr, in THF, at room temperature, abundant decomposition to metallic palladium was observed.

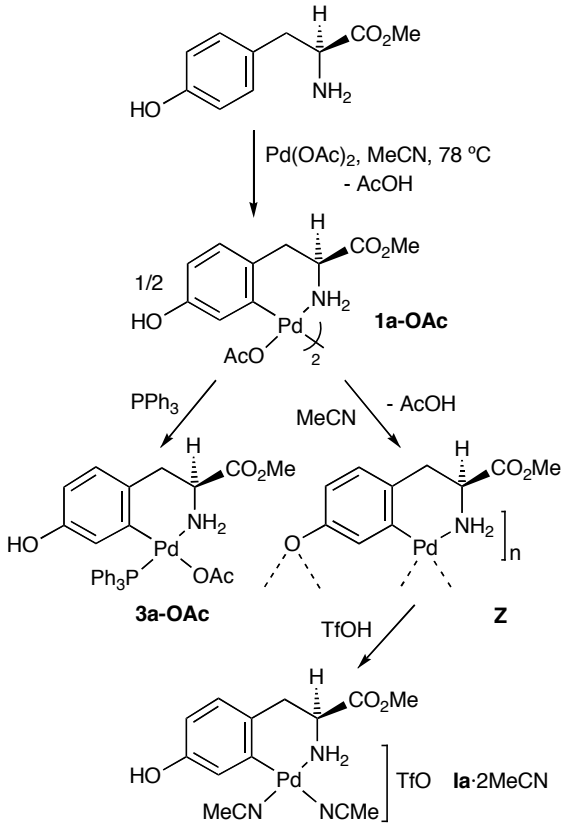
Scheme 6. Oxidative Addition of 2- and 6-Bromo-3,4-dimethoxyphenethylamine to $Pd(dba)_2$



On the Ortho-Palladation of L-Tyrosine Methyl Ester. To check the advantages of using the triflate salt instead of the free amino acid derivative, we tried the reaction of L-tyrosine methyl ester with one equiv of $Pd(OAc)_2$ in acetonitrile at 78 ºC for 8 h. In these conditions, a dark brown solid (**Z**) precipitated in the reaction medium. From the filtrate, complex [Pd_2\{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4\}$_2$(μ-$OAc)_2$] (**1a-OAc**) was isolated in a 15% yield (Scheme 7).

Z is very insoluble in all common organic solvents, including acetonitrile and DMSO, which prevented the removal of the metallic palladium that contaminated it. Its elemental analysis detected C, H and N and its IR spectrum showed a strong peak corresponding to the $\nu_{sym}(CO_2)$ at 1724 cm^{-1}. **Z** did not react with PPh_3 or pyridine, even when heated at 80 ºC in acetonitrile. When treated with XyNC or ^{t}BuNC very complex mixtures were obtained, which showed in their ^{1}H NMR signals attributable to several types of isocyanide molecules. When **Z** was reacted with triflic acid, a deep-red solution formed, from which an oily residue was obtained, the ^{1}H NMR of which showed, in the aromatic region, the signals corresponding to an ortho-palladated ring, along with other unidentified product. All our efforts to obtain a solid from this residue were fruitless. In one of these attempts the residue was repeatedly washed with Et_2O. An X-ray diffraction study of a single crystal obtained from the combined extracts, showed it to be **Ia**·2MeCN (Figure 6), the solvento-complex proposed as an intermediate in the ortho-palladation reaction when the triflate salt is used as starting material (Scheme 2; S = MeCN). Finally, when complex **1a-OAc** was stirred in acetonitrile for 18–36 h, the solid **Z** formed and acetic acid could be detected in the reaction mixture. Based on all these data, we conclude that **Z** is mainly a polymeric complex (Scheme 7), derived from **1a-OAc**.

Scheme 7. Ortho-Palladation of L-Tyrosine Methyl Ester



The formation of polymer **Z** can be partially eluded by changing the reaction conditions. The lowest yield (29%) of **Z** was reached when a 1:1 mixture of L-tyrosine methyl ester and $Pd(OAc)_2$ was stirred in CH_2Cl_2 at room temperature for 4 h, the solvent was removed, acetonitrile was added, and the solution heated at 70 ºC for 2.5 h. In these conditions, complex **1a-OAc** was obtained in 63% yield. When longer heating times or higher temperatures were used, the yield of **Z** increased. Contrarily, if the ortho-palladation reaction was carried out in the presence of 2 equiv of HOAc, the amount of polymer **Z** decreased to 10%, and when 3 equiv of HOAc were used, formation of **Z** was not observed. In a similar way, when the triflate **A** was used as starting material, two equivalents of HOAc were generated during the ortho-palladation reaction (Scheme 2) preventing the deprotonation of the OH group and the formation of **Z**. Complex **1a-OAc** reacted with PPh_3 in a 1:2 molar ratio to give the mononuclear phosphino adduct [Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}(OAc)PPh_3] (**3a-OAc**; Scheme 7).

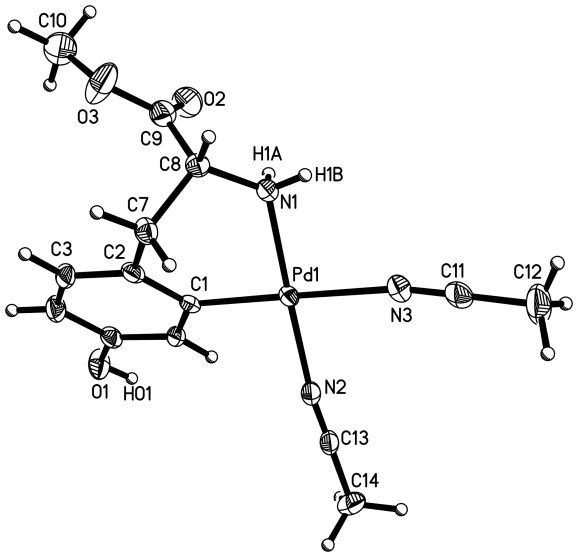


Figure 6. X-ray thermal ellipsoid plot of the cation of intermediate **Ia**·2MeCN (50% probability) showing the labeling scheme. Selected bond lengths (Å) and angles (deg): Pd(1)–C(1) = 1.979(4), Pd(1)–N(1) = 2.044(4), Pd(1)–N(2) = 2.008(4), Pd(1)–N(3) = 2.143(4); C(1)–Pd(1)–N(1) = 87.77(16), N(1)–Pd(1)–N(3) = 92.39(15), N(3)–Pd(1)–N(2) = 88.35(15), N(2)–Pd(1)–C(1) = 91.64(16), Pd(1)–N(2)–C(13) = 171.6(4), Pd(1)–N(3)–C(11) = 170.3(4).

The crystal structures of intermediate **Ia**·2MeCN (Figure 6) and complex **3a-OAc** (Figure 7) have been determined by X-ray diffraction studies and they show the palladium atom in a slightly-distorted square-planar environment (mean deviation: 0.0552 Å, **Ia**·2MeCN; 0.0332 Å, **3a-OAc**) with dihedral angles of 5.7º (**Ia**·2MeCN) and 4.2º (**3a-OAc**) between the N(1)–Pd(1)–C(1) and N(2)–Pd(1)–N(3) planes (**Ia**·2MeCN) and the N(1)–Pd(1)–C(1) and P(1)–Pd(1)–O(4) planes (**3a-OAc**). In both complexes, the chelating amino ligand forms a six-membered metallacycle with a boat conformation. These structural features are similar to those of analogous complexes containing primary ortho-palladated phenethylamines.[8,17-19,46] In complex **3a-OAc**, the phosphine and the amino group are mutually trans, according to the previously mentioned transphobia between the P/Ar pair of ligands.

Surprisingly, the X-ray crystallographic studies do not reveal the (*S*) absolute configuration of the α-carbon stereocenter in complexes **Ia**·2MeCN and **3a-OAc**. As we consider discardable the racemization of the amine during the ortho-palladation reaction, the single crystal used in the diffraction study must

correspond to a racemic mixture of our products plus those formed from the small amount of the (*R*) enantiomer present in the starting material (L-tyrosine methyl ester of 98%). In fact, the crystals suitable for X-ray diffraction studies were obtained in very low yield.

Otra alternativa:

Surprisingly, the X-ray crystallographic studies of complexes **Ia**·2MeCN and **3a-OAc** correspond to a racemic mixture, which must arise from the co-crystallization of the (*S*)-products with those formed from the small amount of the (*R*) enantiomer present in the starting material (L-tyrosine methyl ester of 98%). In fact, the crystals suitable for X-ray diffraction studies were obtained in very low yield.

For complex **Ia**·2MeCN, the cationic units are connected to the triflate groups through classical and non-classical hydrogen bonds, generating double chains along the *a* axis. For complex **3a-OAc**, two adjacent molecules are associated through two hydrogen bonds, both of them involving the OH group, giving rise to dimers, which in turn are associated through non-classical hydrogen interactions (involving also the OH group), generating double chains along the *b* axis (see Supporting Information).

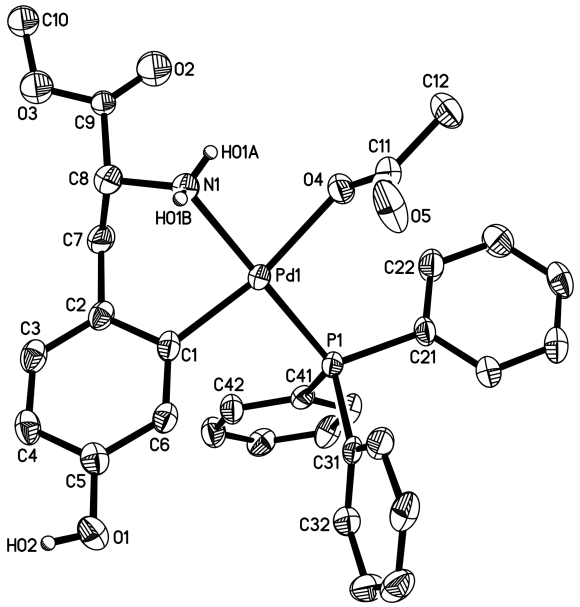


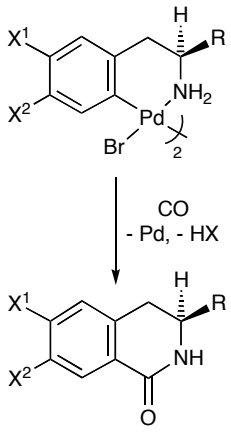
Figure 7. X-ray thermal ellipsoid plot of complex **3a-OAc** (50% probability) showing the labeling scheme. Selected bond lengths (Å) and angles (deg): Pd(1)–C(1) = 2.001(3), Pd(1)–N(1) = 2.120(2), Pd(1)–O(4) = 2.119(2), Pd(1)–P(1) = 2.2500(10); C(1)–Pd(1)–N(1) = 86.83(10), N(1)–Pd(1)–O(4) = 82.66(9), O(4)–Pd(1)–P(1) = 96.72(6), P(1)–Pd(1)–C(1) = 93.73(8).

Synthesis of Lactams by Insertion of Carbon Monoxide into the Pd–C Bond of Cyclopalladated Complexes. The insertion of CO into the Pd–C bond of ortho-palladated benzyl or phenethylamines is a well-known process,[2,3,31,47] which constitutes the key step in the Pd(II)-catalyzed carbonylation of *N*-protected arylalkylamines via C–H aryl activation, to give lactams or esters.[48,49]

However, with the notably exception of a few α-alkyl-substituted phenethylamines,[50] the catalytic cycle seems to fail for primary arylalkylamines.[49] This result is not surprising since ortho-palladation of primary benzyl or phenethylamines does not occur (or it is extremely slow) when an excess of the amine is present.[14,15,17] Although catalytic conversion is not generally achieved, primary arylalkylamines could be converted to benzolactams through an stoichiometric process.[8,9,11,51]

The reaction of complexes **1a-Br** or **1b-Br** with CO in CH_2Cl_2 at room temperature gave palladium(0) and the lactam **10a** or **10b** (Scheme 8). Previous reports on the synthesis of compound **10b**, a natural alkaloid known as corydaldine,[52,53] involved drastic reaction conditions or moisture sensitive reagents.[54]

Scheme 8. Synthesis of Lactams **10a** and **10b**



	R	X^1	X^2
1a-Br	CO_2Me	H	OH
1b-Br	H	OMe	OMe

	R	X^1	X^2
10a	CO_2Me	H	OH
10b	H	OMe	OMe

EXPERIMENTAL SECTION

Caution! Special precautions should be taken in handling thallium(I) compounds, which are toxic. Also, perchlorate salts of organic cations may be explosive. Preparations on a larger scale than that reported herein should be avoided.

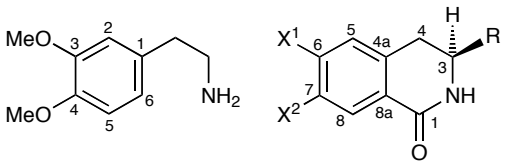
General procedures. Infrared spectra were recorded in the range 4000–200 cm^{-1} on a Perkin Elmer 16F-PC-FT spectrometer, using Nujol mulls between polyethylene sheets. Conductivities in acetone

were measured with a Crison Micro CM2200 conductimeter. Melting points were determined on a Reichert apparatus and are uncorrected. C, H, N and S analyses were carried out with a Carlo Erba 1106 microanalyzer. Specific optical rotations were measured in a 1 dm thermostated quartz cell on a Jasco-P1020 polarimeter. Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in Bruker Avance 200, 300 or 400 spectrometers. Chemical shifts are referenced to TMS (^1H and $^{13}C\{^1H\}$) or H_3PO_4 ($^{31}P\{^1H\}$). Signals in the ^1H and ^{13}C NMR spectra of all complexes were assigned with the help of APT, HMQC and HMBC techniques. Reactions were carried out at room temperature without special precautions against moisture, unless otherwise indicated.

L-Tyrosine methyl ester, 3,4-dimethoxyphenethylamine (homoveratrylamine), trifluoromethanesulfonic acid (triflic acid), $AgClO_4$ (Aldrich), XyNC, PPh_3, P(*p*-To)$_3$, *N*,*N*,*N*',*N*'-tetramethylethylenediamine (tmeda; Fluka), CO (Air Products), NaBr (Scharlau), NaOAc (Sigma), and $Pd(OAc)_2$ (Johnson Matthey) were used as received. [Tl(acac)][55] (Hacac = acetylacetone) and $[Pd_2(dba)_3]\cdot dba$[56] were prepared according to published procedures. 2-(2-Bromo-3,4-dimethoxyphenyl)ethanamine has been prepared according to the method reported by Weinstock. *et al*.,[57] but using a solution 1 M of BH_3 in THF instead of B_2H_6 in the last step. Chart 1 gives the numbering scheme for the free ligands, the palladacycles and the tetrahydroisoquinolones.

Most complexes containing ortho-palladated homoveratrylamine are obtained as hydrates. Only for complex **6b-OAc**$\cdot H_2O$, the crystallization water can be removed by heating the sample at 60 ºC for 2 h in a vacuum oven. Likely, the water molecules are connected through hydrogen interactions with the OMe or the OAc groups of the complexes, in a stronger way than that observed in the crystal structure of complex **6b-OAc**$\cdot H_2O$ (see Supporting Information).

Chart 1. Numbering Schemes for the Free Ligands, the Ortho-Palladated Palladacycles and the Tetrahydroisoquinolones.[a]



[a]For the convenience of the reader, the notation of the free homoveratrylamine ligand is maintained in the ortho-palladated complexes.

Synthesis of (*S*)-[4-(OH)-$C_6H_4CH_2CH(CO_2Me)NH_3$]OTf (A). Triflic acid (0.8 mL of a solution containing 11.3 mmol/mL, 9.04 mmol) was slowly added to a solution of L-tyrosine methyl ester (500 mg, 2.56 mmol) in Et_2O (50 mL), and the resulting white suspension was vigorously stirred for 20 min. The mixture was filtered, and the solid was washed with Et_2O (3 x 5 mL) and air-dried to give compound **A** as a white solid. Yield: 731 mg, 2.12 mmol, 83%. Mp: 85 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 70 (4.98 x 10^{-4} M). Anal. Calcd for $C_{11}H_{14}F_3NO_6S$ (345.292): C, 38.26; H, 4.09; N, 4.06; S, 9.29. Found: C, 38.50; H, 4.60; N, 4.13; S, 8.98. IR (cm^{-1}): ν(OH) 3592 s; ν(NH) 3353 s; ν(CO) 1737 s. ^{1}H NMR (300.1 MHz, DMSO-d_6): δ 2.91 (d, 2 H, CH_2, $^3J_{HH}$ = 5.7 Hz), 3.66 (s, 3 H, OMe), 4.08 ("t", 1 H, CH, $^3J_{HH}$ = 6.0 Hz), 6.70 (d, 2 H, *m*-H, C_6H_4, $^3J_{HH}$ = 7.8 Hz), 6.98 (d, 2 H, *o*-H, C_6H_4, $^3J_{HH}$ = 7.8 Hz). The OH and NH_3 resonances were not observed. ^{13}C NMR (75.45 MHz, DMSO-d_6): δ 36.4 (s, CH_2), 52.4 (s, OMe), 54.0 (s, CH), 115.4 (s, *m*-CH, C_6H_4), 120.7 (q, CF_3, $^1J_{CF}$ = 324.4 Hz), 125.1 (s, *i*-C), 130.4 (s, *o*-CH, C_6H_4), 156.6 (s, C–OH), 170.9 (s, CO). (+)ESI-MS *m/z* 91.1, 136.1, 179.1 [(M – OH – CF_3SO_3)$^+$], 196.1 [(M – CF_3SO_3)$^+$], 218.1 [(M – H – CF_3SO_3 + Na)$^+$]. (–)ESI-MS *m/z* 149.0 ($CF_3SO_3^-$). (+)ESI-HRMS: exact mass calcd for $C_{10}H_{14}NO_3$ 196.0974 [(M – CF_3SO_3)$^+$]; found 196.0971. $[\alpha]_D^{20}$ = +13.69 (c = 0.20, MeOH).

Synthesis of [3,4-$(MeO)_2C_6H_3CH_2CH_2NH_3$]OTf (B). Triflic acid (0.8 mL of a solution containing 11.3 mmol/mL, 9.04 mmol) was slowly added to a solution of homoveratrylamine (1 mL, 6.02 mmol) in Et_2O (50 mL), and the resulting white suspension was vigorously stirred for 20 min. The mixture was filtered, and the solid was washed with Et_2O (3 x 5 mL) and air-dried to give compound **B** as a white solid. Yield: 1.61 g, 4.87 mmol, 81%. Mp: 99 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 95 (5.22 x 10^{-4} M). Anal. Calcd for $C_{11}H_{16}F_3NO_5S$ (331.309): C, 39.88; H, 4.87; N, 4.23; S, 9.68. Found: C, 40.02; H, 4.50; N, 4.27; S,

9.50. IR (cm^{-1}): ν(NH) 3243 br m, 3158 br m, 3078 br m. ^{1}H NMR (400.91 MHz, DMSO-d_6): δ 2.77 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 8.0 Hz), 3.02 ("t", 2 H, CH_2N, $^3J_{HH}$ = 8.0 Hz), 3.71 (s, 3 H, OMe), 3.74 (s, 3 H, OMe), 6.75 (dd, 1 H, H6, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 2.0 Hz), 6.84 (d, 1 H, H2, $^4J_{HH}$ = 2.0 Hz), 6.89 (d, 1 H, H5, $^3J_{HH}$ = 8.4 Hz), 7.61 (br s, 3 H, NH_3). ^{13}C NMR (100.81 MHz, DMSO-d_6): δ 32.7 (s, CH_2Ar), 40.2 (s, CH_2N), 55.4 (s, OMe), 55.5 (s, OMe), 112.1 (s, CH, C5), 112.6 (s, CH, C2), 120.6 (s, CH, C6), 129.5 (s, C1), 147.7 (s, C4, *C*OMe), 148.8 (s, C3, *C*OMe). The ^{13}C signal corresponding to the OTf group was not observed. (+)ESI-MS *m/z* 165.1, 182.1 [$(M - CF_3SO_3)^+$], 204.1 [$(M - H - CF_3SO_3 + Na)^+$]. (–)ESI-MS *m/z* 149.0 ($CF_3SO_3^-$), 480.0 [$(M + CF_3SO_3)^-$]. (+)ESI-HRMS: exact mass calcd for $C_{10}H_{16}NO_2$ 182.1181 [$(M - CF_3SO_3)^+$]; found 182.1183.

Synthesis of (*S*,*S*)-[Pd_2{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}$_2$(μ-Br)$_2$] (1a-Br). The ammonium triflate **A** (800 mg, 2.32 mmol) was added to a suspension of $Pd(OAc)_2$ (520 mg, 2.32 mmol) in acetonitrile (50 mL), and the resulting solution was heated at 60 ºC for 1 h and then at 78 ºC for 4 h. The mixture was filtered through a plug of Celite, the solution was concentrated to dryness, acetone (40 mL) and NaBr (1 g, 9.72 mmol) were added, and the suspension was stirred for 12 h. The solvent was removed, and CH_2Cl_2 (40 mL) was added. The suspension was filtered, and the solid was washed with H_2O (2 x 5 mL) and Et_2O (2 x 5 mL), and air-dried to give a first crop of complex **1a-Br** (570 mg). The Et_2O washing was concentrated to ca. 2 mL, and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) to give a second crop of complex **1a-Br** as an orange solid (71 mg). Yield: 641 mg, 0.84 mmol, 73%. Mp: 202 °C. Anal. Calcd for $C_{20}H_{24}Br_2N_2O_6Pd_2$ (761.062): C, 31.56; H, 3.18; N, 3.68. Found: C, 31.14; H, 3.38; N, 4.22. IR (cm^{-1}): ν(OH) 3423 br s; ν(NH) 3295 s, 3233 s; ν(CO) 1727 m. ^{1}H NMR (400.91 MHz, DMSO-d_6): δ 3.00 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 9.2 Hz), 3.12 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 3.6 Hz), 3.28 (m, 1 H, CH), 3.69 (s, 3 H, OMe), 4.46 (br s, 1 H, NH_2), 5.40 (br s, 1 H, NH_2), 6.37 (br d, 1 H, H3, $^3J_{HH}$ = 6.8 Hz), 6.74 (br d, 1 H, H2, $^3J_{HH}$ = 6.8 Hz), 6.91 (d, 1 H, H5, $^4J_{HH}$ = 2.4 Hz), 9.03 (br s, 1 H, OH). ^{13}C NMR (100.81 MHz, DMSO-d_6): δ 44.6 (s, CH_2), 50.7 (s, CH), 52.8 (s, OMe), 111.7 (s, CH, C3), 119.8 (s, CH,

C5), 126.7 (s, CH, C2), 127.3 (s, C1), 150.2 (s, C6, C–Pd), 154.1 (s, C4, C–OH), 172.3 (s, CO). The insolubility of complex **1a-Br** in all common solvents prevented us from recrystallizating it to obtain completely satisfactory elemental analyses (it showed poor value for N), and to measure its specific optical rotation.

Synthesis of (*S*,*S*)-[Pd$_2${*C*,*N*-C$_6$H$_3$CH$_2$CH(CO$_2$Me)NH$_2$-2,(OH)-4}$_2$(μ-OAc)$_2$] (1a-OAc). L-tyrosine methyl ester (500 mg, 2.56 mmol) was added to a suspension of Pd(OAc)$_2$ (575 mg, 2.56 mmol) in CH_2Cl_2 (25 mL), and the resulting mixture was stirred at room temperature for 4 h. The solvent was removed, and acetonitrile (35 mL) was added. The resulting solution was heated at 70 ºC for 2.5 h. A dark brown solid formed. The mixture was filtered, the solution was concentrated to dryness, and CH_2Cl_2 (20 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **1a-OAc** as a dark yellow solid. Yield: 585.2 mg, 0.81 mmol, 63%. Mp: 201 °C. Anal. Calcd for $C_{24}H_{30}N_2O_{10}Pd_2$ (719.342): C, 40.07; H, 4.20; N, 3.89. Found: C, 40.30; H, 3.76; N, 3.92. IR (cm^{-1}): ν(NH) 3240 br vs; ν(CO) 1735 s; $\nu(CO)_{OAc}$ 1567 br vs. ^{1}H NMR (400.91 MHz, DMSO-d_6): δ 1.80 (s, 3 H, Me, OAc), 3.01 (dd, 1 H, CH$_2$, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 7.6 Hz), 3.14 (dd, 1 H, CH$_2$, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 3.6 Hz), 3.24–3.30 (br m, partially obscured by the signal of H_2O of the solvent, 1 H, CH), 3.63 (s, 3 H, OMe), 5.36 (br s, 1 H, NH$_2$), 6.01 (br s, 1 H, NH$_2$), 6.32 (dd, 1 H, H3, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 2.1 Hz), 6.68 (d, 1 H, H2, $^3J_{HH}$ = 8.1 Hz), 6.87 (d, 1 H, H5, $^4J_{HH}$ = 2.1 Hz), 8.93 (br s, 1 H, OH). ^{13}C NMR (100.81 MHz, DMSO-d_6): δ 44.6 (s, CH$_2$), 50.3 (s, CH), 52.5 (s, OMe), 111.3 (s, CH, C3), 120.7 (s, CH, C5), 126.6 (s, CH, C2), 127.6 (s, C1), 144.8 (s, C6, C–Pd), 153.5 (s, C4, C–OH), 172.2 (s, CO). The ^{13}C signals corresponding to the acetate group were not observed. $[\alpha]_D^{20}$ = +3.44 (c = 0.20, MeOH).

Synthesis of [Pd$_2${*C*,*N*-C$_6$H$_2$CH$_2$CH$_2$NH$_2$-6,(OMe)$_2$-3,4}$_2$(μ-Br)$_2$]·H$_2$O (1b-Br·H$_2$O). The ammonium triflate **B** (1 g, 3.02 mmol) was added to a suspension of Pd(OAc)$_2$ (678 mg, 3.02 mmol) in acetonitrile (50 mL), and the resulting solution was heated at 60 ºC for 2 h and then at 78 ºC for 6 h. The mixture was filtered through a plug of Celite, the solvent was removed from the filtrate, acetone (40 ml)

and NaBr (1 g, 9.72 mmol) were added, and the suspension was stirred for 12 h. The solvent was removed, and CH_2Cl_2 (40 mL) was added. The suspension was filtered, and the solid was washed with H_2O (2 x 5 mL) and Et_2O (2 x 5 mL), and air-dried to give complex **1b-Br**·H_2O as a yellow solid. Yield: 1062 mg, 1.41 mmol, 94%. Dec pt: 163 °C. Anal. Calcd for $C_{20}H_{28}Br_2N_2O_4Pd_2$·$H_2O$ (751.117): C, 31.98; H, 4.02; N, 3.73. Found: C, 31.90; H, 3.70; N, 3.79. IR (cm^{-1}): ν(NH) 3340 w, 3218 m, 3265 s. ^{1}H NMR (400.91 MHz, DMSO-d_6): δ 2.31 (br s, 2 H, CH_2N), 2.76 (br s, 2 H, CH_2Ar), 3.31 (s, H_2O), 3.67 (s, 3 H, OMe), 3.68 (s, 3 H, OMe), 4.72 (br s, 2 H, NH_2), 6.63 (s, 1 H, H2), 7.08 (s, 1 H, H5). ^{13}C NMR (100.81 MHz, DMSO-d_6): δ 37.6 (s, CH_2N), 41.7 (s, CH_2Ar), 55.7 (s, OMe), 55.8 (s, OMe), 110.9 (s, CH, C2), 117.3 (br s, CH, C5), 131.2 (s, C1), 138.3 (br s, C6), 144.8 (s, C4), 146.5 (s, C3).

Synthesis of [Pd_2{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}$_2$(μ-OAc)$_2$]·H_2O (1b-OAc·H_2O). $AgClO_4$ (68 mg, 0.33 mmol) was added to a suspension of complex **1b-Br**·H_2O (120 mg, 0.16 mmol) in acetone (30 mL), and the resulting suspensión was stirred for 1 h. The mixture was filtered through a plug of Celite to remove the AgBr formed. NaOAc (1 g, 12.20 mmol) was added, and the suspension was stirred for 12 h. The solvent was removed, and CH_2Cl_2 (30 mL) was added. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give complex **1b-OAc**·H_2O as a yellow solid. Yield: 83 mg, 0.12 mmol, 73%. Mp: 139 °C. Anal. Calcd for $C_{24}H_{34}N_2O_8Pd_2$·H_2O (709.398): C, 40.63; H, 5.11; N, 3.95. Found: C, 40.54; H, 5.36; N, 3.89. IR (cm^{-1}): ν(OH) 3413 br, ν(NH) 3272 m, 3215 m; $\nu(CO)_{OAc}$ 1563 br s. ^{1}H NMR (400.91 MHz): δ 1.80 (s, 2 H, H_2O), 2.02 (s, 3 H, Me, AcO), 2.21–2.32 (br s, 1 H, CH_2Ar), 2.33–2.38 (br s, 1 H, CH_2Ar), 2.48 (m, 1 H, CH_2N), 2.69 (br dd, 1 H, CH_2N, $^2J_{HH}$ = 14.8 Hz, $^3J_{HH}$ = 6.4 Hz), 2.88 (br s, 1 H, NH_2), 3.40 (br s, 1 H, NH_2), 3.80 (s, 3 H, OMe), 3.81 (s, 3 H, OMe), 6.43 (s, 1 H, H2), 6.69 (s, 1 H, H5). ^{13}C NMR (75.45 MHz): δ 24.3 (s, Me), 39.2 (s, CH_2Ar), 40.6 (s, CH_2N), 55.8 (s, OMe), 55.9 (s, OMe), 110.9 (s, CH, C2), 115.4 (s, CH, C5), 124.6 (s, C, C6), 129.6 (s, C1), 144.8 (s, C4), 146.1 (s, C3), 181.2 (s, CO).

Synthesis of [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(*O*,*O*'-acac)] (2b). Tl(acac) (125 mg, 0.41 mmol) was added to a suspension of complex **1b-Br**·H_2O (150 mg, 0.20 mmol) in acetone (25 mL), and the mixture was stirred for 1 h. The solvent was removed under vacuum, and CH_2Cl_2 (30 mL) was added. The resulting suspension was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **2b** as a yellow solid. Yield: 120.4 mg, 0.31 mmol, 78%. Mp: 195 °C. Anal. Calcd for $C_{15}H_{21}NO_4Pd$ (385.736): C, 46.71; H, 5.49; N, 3.63. Found: C, 46.36; H, 5.52; N, 3.83. IR (cm^{-1}): ν(NH) 3273 m, 3220 m, 3148 m; ν(CO) 1588 s, 1508 s. ^{1}H NMR (300.1 MHz): δ 1.91 (s, 3 H, Me), 2.02 (s, 3 H, Me), 2.68 (quint, 2 H, CH_2N, $^3J_{HH}$ = 5.6 Hz), 2.88 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 5.7 Hz), 3.24 (br s, 2 H, NH_2), 3.82 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 5.32 (s, 1 H, CH), 6.49 (s, 1 H, H2), 7.14 (s, 1 H, H5). ^{13}C NMR (75.45 MHz): δ 27.7 (s, *Me*CO), 27.8 (s, *Me*CO), 39.8 (s, CH_2Ar), 40.9 (s, CH_2N), 55.7 (s, OMe), 56.1 (s, OMe), 100.1 (s, CH), 110.6 (s, CH, C2), 115.4 (s, CH, C5), 128.2 (s, C6), 130.1 (s, C1), 145.0 (s, C4, *C*-OMe), 146.2 (s, C3, *C*-OMe), 186.9 (s, CO), 187.2 (s, CO).

Synthesis of (*S*)-[Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}Br(PPh_3)] (3a-Br). PPh_3 (55.1 mg, 0.21 mmol) was added to a suspension of complex **1a-Br** (80 mg, 0.11 mmol) in CH_2Cl_2 (20 mL), and the resulting solution was stirred for 30 min. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and *n*-pentane (15 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give complex **3a-Br** as a yellow solid. Yield: 73.7 mg, 0.12 mmol, 55%. Mp: 135 °C. Anal. Calcd for $C_{28}H_{27}BrNO_3PPd$ (642.817): C, 52.32; H, 4.23; N, 2.18. Found: C, 52.03; H, 4.23; N, 2.23. IR (cm^{-1}): ν(NH) 3320 m 3252 w; ν(CO) 1737 m. ^{1}H NMR (400.91 MHz): δ 3.23 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 3.2 Hz), 3.66 (dd, partially obscured by the signal of OMe, 1 H, CH_2, $^2J_{HH}$ = 13.2, $^3J_{HH}$ = 5.6 Hz), 3.70 (s, 3 H, OMe), 3.88 (br s, 1 H, CH), 3.93 (br s, 1 H, NH_2), 4.05 (br s, 1 H, NH_2), 5.84 (dd, 1 H, H5, $^4J_{HP}$ = 5.2, $^4J_{HH}$ = 2.4 Hz), 6.23 (dd, 1 H, H3, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 2.4 Hz), 6.62 (d, 1 H, H2, $^3J_{HH}$ = 8.0 Hz), 7.29–7.34 (m, 6 H, *m*-H, PPh_3), 7.38–7.42 (m, 4 H, OH + *p*-H of PPh_3), 7.53–7.58 (m, 6 H, *o*-H, PPh_3). ^{13}C NMR (75.45 MHz): δ 45.5

(s, CH_2), 50.4 (s, CH), 52.9 (s, OMe), 110.8 (s, CH, C3), 123.3 (d, CH, C5, $^3J_{CP}$ = 9.9 Hz), 126.8 (s, CH, C2), 127.6 (s, C1), 128.0 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 10.8 Hz), 130.7 (s, *p*-CH, PPh_3), 131.0 (d, *i*-C, PPh_3, $^1J_{CP}$ = 51.0 Hz), 134.8 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 11.5 Hz), 152.6 (s, C4, C–OH), 155.1 (s, C6, C–Pd), 172.6 (s, CO). ^{31}P NMR (162.29 MHz): δ 35.9 (s, PPh_3). $[\alpha]_D^{20}$ = +49.54 (c = 0.20, CH_2Cl_2).

Synthesis of (*S*)-[Pd{*C*,*N*-$C_6H_3CH_2CH(CO_2Me)NH_2$-2,(OH)-4}(OAc)PPh_3]·H_2O (3a-OAc·H_2O). PPh_3 (73 mg, 0.28 mmol) was added to a suspension of complex **1a-OAc** (150 mg, 0.21 mmol) in CH_2Cl_2 (20 mL), and the resulting solution was stirred for 2 h. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (15 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **3a-OAc**·H_2O as a yellow solid. Yield: 153 mg, 0.24 mmol, 57%. Mp: 181 °C. Anal. Calcd for $C_{30}H_{30}NO_5PPd·H_2O$ (639.972): C, 56.30; H, 5.04; N, 2.19. Found: C, 56.16; H, 4.86; N, 2.28. IR (cm^{-1}): ν(NH) 3319 m, 3262 m; ν(CO) 1736 s; $\nu(CO)_{OAc}$ 1572 br s. ^{1}H NMR (300.1 MHz): δ 1.45 (s, 3 H, Me, OAc), 1.86 (br s, 2 H, H_2O), 3.25 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.5, $^3J_{HH}$ = 3.6 Hz), 3.62 (dd, partially obscured by the signal of OMe, 1 H, CH_2, $^3J_{HH}$ = 4.8 Hz), 3.65 (s, 3 H, OMe), 3.72 (br s, 1 H, CH), 3.86 (br s, 1 H, NH_2), 5.21 (br s, 1 H, NH_2), 5.72 (dd, 1 H, H5, $^4J_{HP}$ = 5.1, $^4J_{HH}$ = 2.1 Hz), 6.37 (dd, 1 H, H3, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.8 Hz), 6.63 (br s, 1 H, OH), 6.69 (d, 1 H, H2, $^3J_{HH}$ = 7.8 Hz), 7.24–7.31 (m, 6 H, *m*-H, PPh_3), 7.34–7.46 (m, 9 H, *o*-H + *p*-H, PPh_3). ^{13}C NMR (75.45 MHz): δ 24.2 (s, Me, OAc), 46.1 (s, CH_2), 50.5 (s, CH), 52.7 (s, OMe), 111.2 (s, CH, C3), 124.3 (d, CH, C5, $^3J_{CP}$ = 10.9 Hz), 126.7 (s, CH, C2), 127.9 (s, C1), 128.2 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 10.6 Hz), 130.2 (d, *i*-C, PPh_3, $^1J_{CP}$ = 49.1 Hz), 130.3 (s, *p*-CH, PPh_3), 134.5 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 11.8 Hz), 146.9 (s, C6, C–Pd), 152.9 (d, C5, $^4J_{CP}$ = 4.6 Hz), 172.9 (s, CO_2Me), 179.3 (s, CO, OAc). ^{31}P NMR (121.5 MHz): δ 33.6 (s, PPh_3). $[\alpha]_D^{20}$ = +3.38 (c = 0.20, MeOH). Single crystals of **3a-OAc**, suitable for X-ray diffraction study, were obtained by slow diffusion of *n*-pentane into a solution of **3a-OAc**·H_2O in $CHCl_3$.

Synthesis of [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}Br(PPh_3)] (3b-Br). Method A. PPh_3 (107 mg, 0.41 mmol) was added to a suspension of complex **1b-Br**·H_2O (150 mg, 0.20 mmol) in CH_2Cl_2 (30

mL), and the resulting solution was stirred for 1 h. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give a first crop of complex **3b-Br** (63 mg). The filtrate was concentrated to ca. 2 mL and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give a second crop of complex **3b-Br** as a yellow solid (73 mg). Yield: 136 mg, 0.22 mmol, 54%. **Method B.** PPh_3 (54.3 mg, 0.21 mmol) was added to a suspension of complex **9b** (100 mg, 0.21 mmol) in CH_2Cl_2 (25 mL), and the resulting solution was stirred for 3 h. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 1 mL, and Et_2O (15 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **3b-Br** as a pale yellow solid. Yield: 75.3 mg, 0.12 mmol, 58%. Mp: 147 °C. Anal. Calcd for $C_{28}H_{29}BrNO_2PPd$ (628.833): C, 53.48; H, 4.65; N, 2.23. Found: C, 53.42; H, 4.69; N, 2.39. IR (cm^{-1}): ν(NH) 3259 m, 3210 m. ^{1}H NMR (400.91 MHz): δ 2.77 (br s, 2 H, CH_2N), 3.12 (s, 3 H, OMe), 3.13 (m, partially obscured by the signal of OMe, 2 H, CH_2Ar), 3.39 (br s, 2 H, NH_2), 3.77 (s, 3 H, OMe), 5.99 (d, 1 H, H5, $^4J_{HP}$ = 4.8 Hz), 6.54 (s, 1 H, H2), 7.28–7.33 (m, 6 H, *m*-H, PPh_3), 7.36–7.41 (m, 3 H, *p*-H, PPh_3), 7.49–7.55 (m, 6 H, *o*-H, PPh_3). ^{13}C NMR (100.81 MHz): δ 37.7 (s, CH_2N), 42.5 (s, CH_2Ar), 55.0 (s, OMe), 56.0 (s, OMe), 110.4 (s, CH, C2), 118.7 (d, CH, C5, $^3J_{CP}$ = 11.9 Hz), 128.1 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 10.6 Hz), 130.4 (d, *p*-CH, PPh_3, $^4J_{CP}$ = 2.2 Hz), 131.4 (d, *i*-C, PPh_3, $^1J_{CP}$ = 49.8 Hz), 134.8 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 11.5 Hz), 142.2 (s, C6), 145.5 (d, C4, $^4J_{CP}$ = 4.8 Hz), 146.1 (s, C3). The C1 resonance was not observed. ^{31}P NMR (81.01 MHz): δ 35.5 (s, PPh_3).

Synthesis of [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(OAc)PPh_3]·0.25H_2O (3b-OAc·0.25H_2O). PPh_3 (61 mg, 0.23 mmol) was added to a solution of complex **1b-OAc**·H_2O (80 mg, 0.11 mmol) in CH_2Cl_2 (30 mL), and the resulting mixture was stirred for 30 min and then filtered through a plug of Celite. The filtrate was concentrated to ca. 2 mL, and *n*-pentane (15 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give complex **3b-**

OAc·0.25H_2O as a pale yellow solid. Yield: 110 mg, 0.18 mmol, 79%. Mp: 170 °C. Anal. Calcd for $C_{30}H_{32}NO_4PPd$·1/4H_2O (612.467): C, 58.83; H, 5.35; N, 2.29. Found: C, 58.44; H, 5.70; N, 2.67. IR (cm^{-1}): ν(NH) 3278 w; $\nu(CO)_{OAc}$ 1572 br s. ^{1}H NMR (300.1 MHz): δ 1.46 (s, 3 H, Me), 1.84 (s, 0.5 H, H_2O), 2.73 (br s, 2 H, CH_2N), 3.02 (s, 3 H, OMe), 3.14 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 5.4 0 Hz), 3.78 (s, 3 H, OMe), 4.12 (br s, 2 H, NH_2), 6.01 (d, 1 H, H5, $^4J_{HP}$ = 4.5 Hz), 6.60 (s, 1 H, H2), 7.30–7.36 (m, 6 H, *m*-H, PPh_3), 7.39–7.51 (m, 9 H, *p*-H + *o*-H, PPh_3). ^{13}C NMR (75.45 MHz): δ 24.1 (s, Me), 37.5 (s, CH_2N), 43.2 (s, CH_2Ar), 54.8 (s, OMe), 55.9 (s, OMe), 110.7 (s, CH, C2), 118.9 (d, CH, C5, $^3J_{CP}$ = 11.7 Hz), 128.3 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 10.6 Hz), 130.4 (s, *p*-CH, PPh_3), 130.5 (d, *i*-C, PPh_3, $^1J_{CP}$ = 48.4 Hz), 131.7 (s, C1), 133.4 (s, C6), 134.6 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 12.2 Hz), 144.9 (s, C4), 146.0 (s, C3). The CO resonance was not observed. ^{31}P NMR (121.5 MHz): δ 34.2 (s, PPh_3).

Synthesis of [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}Br{P(*p*-To)$_3$}] (3b'-Br). P(*p*-To)$_3$ (83 mg, 0.27 mmol) was added to a suspension of complex **1b-Br**·H_2O (100 mg, 0.13 mmol) in CH_2Cl_2 (30 mL), and the resulting solution was stirred for 1 h. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and n-*p*entane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give complex **3b'-Br** as an off-white solid. Yield: 132 mg, 0.197 mmol, 74%. Mp: 147 °C. Anal. Calcd for $C_{31}H_{35}BrNO_2PPd$ (670.924): C, 55.50; H, 5.26; N, 2.09. Found: C, 55.35; H, 5.32; N, 2.10. IR (cm^{-1}): ν(NH) 3550 m, 3470 m, 3411 m, 3254 w. ^{1}H NMR (300.1 MHz): δ 2.33 (s, 9 H, Me), 2.76 (br s, 2 H, CH_2N), 3.12 (s, 3 H, OMe), 3.14 (m, partially obscured by the signal of OMe, 2 H, CH_2Ar), 3.36 (br s, 2 H, NH_2), 3.77 (s, 3 H, OMe), 5.98 (d, 1 H, H5, $^4J_{HP}$ = 4.8 Hz), 6.54 (s, 1 H, H2), 7.10 (br d, 6 H, *m*-H, P(*p*-To)$_3$, $^3J_{HH}$ = 6.6 Hz), 7.38 (dd, 6 H, *o*-H, P(*p*-To)$_3$, $^3J_{HP}$ = 11.4, $^3J_{HH}$ = 8.1 Hz). ^{13}C NMR (75.45 MHz): δ 21.4 (s, Me), 37.6 (d, CH_2N, $^3J_{CP}$ = 2.3 Hz), 42.5 (s, CH_2Ar), 54.9 (s, OMe), 56.0 (s, OMe), 110.3 (s, CH, C2), 118.8 (d, CH, C5, $^3J_{CP}$ = 11.8 Hz), 128.0 (d, one-half of the doublet was obscured by the *m*-CH signal, *i*-C), 128.8 (d, *m*-CH, P(*p*-To)$_3$, $^3J_{CP}$ = 11.0 Hz), 130.5 (s, C1), 134.7 (d, *o*-CH, P(*p*-To)$_3$, $^2J_{CP}$ = 11.8 Hz),

140.4 (d, *C*–Me, P(*p*-To)$_3$, $^4J_{CP}$ = 2.4 Hz), 142.1 (br s, C6), 145.4 (d, C4, *C*–OMe, $^4J_{CP}$ = 4.9 Hz), 146.0 (s, C3, *C*–OMe). ^{31}P NMR (121.50 MHz): δ 33.6 (s, P(*p*-To)$_3$).

Synthesis of (*S*)-[Pd{*C*,*N*-C$_6$H$_3$CH$_2$CH(CO$_2$Me)NH$_2$-2,(OH)-4}Br(CNXy)] (4a). XyNC (34.5 mg, 0.26 mmol) was added to a suspension of complex **1a-Br** (100 mg, 0.13 mmol) in CH_2Cl_2 (25 ml), and the resulting solution was was stirred for 2 h. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (15 ml) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL), and air-dried to give a first crop of complex **4a** as a yellow solid (30 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (15 ml) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL), and air-dried to give a second crop of complex **4a** as a pale yellow solid (72 mg). Yield: 102 mg, 0.20 mmol, 76%. Mp: 115 °C. Anal. Calcd for $C_{19}H_{21}BrN_2O_3Pd$ (511.712): C, 44.60; H, 4.14; N, 5.47. Found: C, 44.97; H, 3.89; N, 5.49. IR (cm^{-1}): ν(NH) 3304 v br; ν(CN) 2189 s; ν(CO) 1735 s. ^{1}H NMR (400.91 MHz): δ 2.40 (s, 6 H, Me, Xy), 3.15 (dd, 1 H, CH$_2$, $^2J_{HH}$ = 14.0, $^3J_{HH}$ = 4.8 Hz), 3.37 (dd, 1 H, CH$_2$, $^2J_{HH}$ = 14.0, $^3J_{HH}$ = 4.0 Hz), 3.63 (br m, 1 H, CH), 3.71 (s, 3 H, OMe), 3.88 (br m, 1 H, NH$_2$), 4.20 (br m, 1 H, NH$_2$), 5.20 (br s, 1 H, OH), 6.51 (dd, 1 H, H3, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 2.8 Hz), 6.84 (d, 1 H, H2, $^3J_{HH}$ = 8.0 Hz), 7.07 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.09 (d, 1 H, H5, $^4J_{HH}$ = 2.4 Hz), 7.21 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz). ^{13}C NMR (75.45 MHz): δ 18.9 (s, Me, Xy), 44.3 (s, CH$_2$), 50.2 (s, CH), 53.1 (s, OMe), 112.1 (s, CH, C3), 125.0 (s, CH, C5), 127.9 (s, C1), 128.0 (s, *m*-CH, Xy), 128.5 (s, CH, C2), 129.7 (s, *p*-CH, Xy), 136.0 (s, *o*-C, Xy), 146.5 (s, C6, C–Pd), 152.6 (s, C4, C–OH), 172.0 (s, CO). The resonances of the *i*-C of Xy and CN were not observed. $[\alpha]_D^{20}$ = +5.36 (c = 0.20, CH_2Cl_2).

Synthesis of [Pd{*C*,*N*-C(=NXy)-C$_6$H$_2$CH$_2$CH$_2$NH$_2$-6,(OMe)$_2$-3,4}Br(CNXy)] (5b). XyNC (71.6 mg, 0.55 mmol) was added to a suspension of complex **1b-Br**·H_2O (100 mg, 0.13 mmol) in CH_2Cl_2 (25 ml), and the resulting solution was was stirred for 4 h. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (15 ml) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give a first crop of complex **5b** (83 mg). The

filtrate was concentrated to ca. 2 mL, and *n*-pentane (15 ml) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give a second crop of complex **5b** (27 mg). Yield: 110 mg, 0.18 mmol, 66%. Mp: 165 °C. Anal. Calcd for $C_{28}H_{32}BrN_3O_2Pd$ (628.905): C, 53.47; H, 5.13; N, 6.68. Found: C, 53.37; H, 5.03; N, 6.93. IR (cm^{-1}): ν(NH) 3263 m, 3228 m, 3153 w; ν(CN) 2177 s; ν(C=N) 1629 s. ^{1}H NMR (400.91 MHz): δ 2.16 (s, 6 H, Me, Xy), 2.18 (s, 6 H, Me, Xy), 2.93 (br s, 2 H, NH_2), 3.24 (quint, 1 H, CH_2N, $^3J_{HH}$ = 6.0 Hz), 3.80 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 5.6 Hz), 3.91 (s, 3 H, OMe), 3.94 (s, 3 H, OMe), 6.68 (s, 1 H, H2), 6.79 (dd, 1 H, *p*-H, coordinated Xy, $^3J_{HH}$ = 8.0, $^3J_{HH}$ = 6.4 Hz), 6.87 (d, 2 H, *m*-H, coordinated Xy, $^3J_{HH}$ = 7.6 Hz), 7.02 (d, 2 H, *m*-H, inserted Xy, $^3J_{HH}$ = 7.6 Hz), 7.17 (t, 1 H, *p*-H, inserted Xy, $^3J_{HH}$ = 7.6 Hz), 7.60 (s, 1 H, H5), ^{13}C NMR (100.81 MHz): δ 18.7 (s, Me, Xy), 19.4 (s, Me, Xy), 37.2 (s, CH_2Ar), 43.3 (s, CH_2N), 56.0 (s, OMe), 56.1 (s, OMe), 110.7 (s, CH, C5), 113.0 (s, CH, C2), 123.1 (s, *p*-CH, coordinated Xy), 126.5 (s, *o*-C, coordinated Xy), 127.5 (s, *m*-CH, inserted Xy), 128.0 (s, *m*-CH, coordinated Xy), 129.3 (s, *p*-CH, inserted Xy), 129.4 (s, C1), 132.0 (s, C6), 135.1 (s, *o*-C, inserted Xy), 148.0 (s, C4), 150.5 (s, C3), 151.4 (s, *i*-C, coordinated Xy), 174.9 (s, CN, inserted Xy). The ^{13}C resonances corresponding to *i*-C of the inserted Xy and CN of the coordinated Xy were not observed.

Synthesis of [Pd(OAc)$_2${NH$_2$CH$_2$CH$_2$C$_6$H$_3$(OMe)$_2$-3,4}$_2$] (6b-OAc). Homoveratrylamine (1 mL, 6.02 mmol) was added to a suspension of $Pd(OAc)_2$ (675.6 mg, 3.01 mmol) in acetone (50 mL), and the resulting mixture was stirred for 16 h. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **6b-OAc**·H_2O as a yellow solid (1415 mg). Yield: 1415.1 mg, 2.34 mmol, 78%. The crystallization water can be removed by heating the sample at 60 ºC for 2 h in a vacuum oven. Mp: 145 °C. Anal. Calcd for $C_{24}H_{36}N_2O_8Pd$ (586.971): C, 49.11; H, 6.18; N, 4.77. Found: C, 48.92; H, 6.22; N, 4.92. IR (cm^{-1}): ν(NH) 3244 m, 3200 m, 3119 m; $\nu(CO)_{OAc}$ 1566 s. ^{1}H NMR (200.13 MHz): δ 1.86 (s, 3 H, Me, OAc), 2.79 (quint, 2 H, CH_2N, $^3J_{HH}$ = 6.8 Hz), 2.92 ("t", 2 H, NH_2Ar, $^3J_{HH}$ = 6.8 Hz), 3.67 (m, 2 H, NH_2), 3.86 (s, 3 H, OMe), 3.88 (s, 3 H, OMe), 6.72 (A part of an ABC system, 1 H, H2, $^4J_{AB}$ = 2.0 Hz), 6.75 (B part of an ABC system, 1 H, H6, $^3J_{BC}$ = 8.0, $^4J_{AB}$ = 2.0 Hz), 6.80

(C part of an ABC system, 1 H, H5, $^{3}J_{BC}$ = 8.0 Hz). ^{13}C NMR (50.3 MHz): δ 23.4 (s, Me, OAc), 36.5 (s, CH_2Ar), 44.7 (s, CH_2N), 55.8 (s, OMe), 55.9 (s, OMe), 111.4 (s, CH, C5), 111.8 (s, CH, C2), 120.7 (s, CH, C6), 130.0 (s, C1), 147.8 (s, C4, *C*-OMe), 149.1 (s, C3, *C*-OMe), 179.9 (s, CO). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of *n*-pentane into a solution of **6b-OAc**·H_2O in CH_2Cl_2.

Synthesis of [$PdBr_2${$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$_2$] (6b-Br). NaBr (500 mg, 4.859 mmol) was added to a suspension of complex **6b-OAc**·H_2O (500 mg, 0.826 mmol) in acetone (50 ml), and the resulting suspension was stirred for 16 h. The solvent was removed, CH_2Cl_2 (40 mL) was added, and the mixture was filtered through a plug of Celite. The filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **6b-Br** as a yellow solid. Yield: 479 mg, 0.76 mmol, 92%. Mp: 148 °C. Anal. Calcd for $C_{20}H_{30}Br_2N_2O_4Pd$ (628.698): C, 38.21; H, 4.81; N, 4.46. Found: C, 38.18; H, 5.00; N, 4.34. IR (cm^{-1}): ν(NH) 3275 s, 3213 s, 3213 m. ^{1}H NMR (400.91 MHz): δ 2.63 (br t, 2 H, NH_2, $^{3}J_{HH}$ = 6.8 Hz), 2.83 (t, 2 H, CH_2Ar, $^{3}J_{HH}$ = 6.8 Hz), 3.08 (quint, 2 H, CH_2N, $^{3}J_{HH}$ = 6.8 Hz), 3.86 (s, 3 H, OMe), 3.90 (s, 3 H, OMe), 6.73 (A part of an ABC system, 1 H, H2, $^{4}J_{AB}$ = 2.0 Hz), 6.73 (B part of an ABC system, 1 H, H6, $^{3}J_{BC}$ = 8.0, $^{4}J_{AB}$ = 2.0 Hz), 6.81 (C part of an ABC system, 1 H, H5, $^{3}J_{BC}$ = 8.0 Hz). ^{13}C NMR (100.81 MHz): δ 37.1 (s, CH_2Ar), 44.7 (s, CH_2N), 55.9 (s, OMe), 55.9 (s, OMe), 111.5 (s, CH, C_6H_3), 111.6 (s, CH, C_6H_3), 120.9 (s, CH, C_6H_3), 129.1 (s, C1), 148.0 (s, *C*-OMe), 149.2 (s, *C*-OMe). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of Et_2O into a solution of **6b-Br** in CH_2Cl_2.

Synthesis of [$Pd(OAc)_2${$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$PPh_3$]·$H_2O$ (7b-OAc·H_2O). Method A. PPh_3 (89 mg, 0.34 mmol) was added to a suspension of complex **6b-OAc**·H_2O (200 mg, 0.33 mmol) in CH_2Cl_2 (30 mL), and the resulting solution was stirred for 1 h. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give complex **7b-**

OAc·H_2O as a yellow solid. Yield: 121 mg, 0.18 mmol, 53%. **Method B.** PPh_3 (129 mg, 0.49 mmol) was added to a solution of complex **8b** (100 mg, 0.25 mmol) in CH_2Cl_2 (30 mL), and the resulting solution was stirred for 1 h. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and Et_2O (15 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give a first crop of complex **7b-OAc**·H_2O (153 mg). The filtrate was concentrated to ca. 2 mL and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give a second crop of complex **7b-OAc**·H_2O (48 mg). Yield: 201 mg, 0.29 mmol, 60%. Mp: 126 °C. Anal. Calcd for $C_{32}H_{36}NO_6PPd·H_2O$ (686.03): C, 56.02; H, 5.58; N, 2.04. Found: C, 56.12; H, 5.54; N, 2.14. IR (cm^{-1}): ν(NH) 3229 m, 3139 m; $\nu(CO)_{OAc}$ 1633 vs. ^{1}H NMR (400.91 MHz): δ 1.42 (s, 6 H, Me, OAc), 1.86 (br s, 2 H, H_2O), 2.90 ("t", 2 H, CH_2Ar, $^3J_{HP}$ = 6.4 Hz), 2.97 (m, 2 H, CH_2N), 3.79 (m, 2 H, NH_2), 3.84 (s, 3 H, OMe), 3.85 (s, 3 H, OMe), 6.72 (C part of an ABC system, 1 H, H2, $^4J_{BC}$ = 1.8 Hz), 6.74 (B part of an ABC system, 1 H, H6, $^3J_{AB}$ = 7.9, $^4J_{BC}$ = 1.8 Hz), 6.78 (A part of an ABC system, 1 H, H5, $^3J_{AB}$ = 7.9 Hz), 7.39–7.44 (m, 6 H, *m*-H, PPh_3), 7.48–7.52 (m, 3 H, *p*-H, PPh_3), 7.69–7.75 (m, 6 H, *o*-H, PPh_3). ^{13}C NMR (75.45 MHz): δ 22.8 (s, Me, OAc), 37.4 (s, CH_2Ar), 44.3 (s, CH_2N), 55.7 (s, OMe), 55.8 (s, OMe), 111.2 (s, CH, C5), 111.8 (s, CH, C2), 120.7 (s, CH, C6), 127.7 (d, *i*-C, PPh_3, $^1J_{CP}$ = 52.1 Hz), 128.4 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 11.0 Hz), 130.9 (d, *p*-CH, PPh_3, $^4J_{CP}$ = 2.7 Hz), 130.5 (s, C1), 134.3 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 11.0 Hz), 147.6 (s, *C*–OMe), 148.9 (s, *C*–OMe), 178.1 (s, CO). ^{31}P NMR (121.5 MHz): δ 21.3 (s, PPh_3). Single crystals of **7b-OAc**, suitable for an X-ray diffraction study, were obtained by slow diffusion of Et_2O into a solution of **7b-OAc**·H_2O in $CHCl_3$.

Synthesis of [$PdBr_2${$NH_2CH_2CH_2C_6H_3(OMe)_2$-3,4}$PPh_3$] (7b-Br). PPh_3 (42 mg, 0.16 mmol) was added to a suspension of complex **6b-Br** (100 mg, 0.16 mmol) in CH_2Cl_2 (30 mL), and the resulting solution was stirred for 1 h. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give a first crop of complex **7b-Br** as an orange solid (48

mg). The filtrate was concentrated to ca. 2 mL and *n*-pentane (30 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give a second crop of complex **7b-Br** as an orange solid (53 mg). Yield: 101 mg, 0.14 mmol, 89%. Mp: 163 °C. Anal. Calcd for $C_{28}H_{30}Br_2NO_2PPd$ (709.755): C, 47.38; H, 4.26; N, 1.97. Found: C, 47.30; H, 4.13; N, 2.01. IR (cm^{-1}): ν(NH) 3283 s, 3240 s, 3146 m. ^{1}H NMR (400.91 MHz): δ 2.76 (m, 2 H, NH_2), 2.88 ("t", 2 H, CH_2Ar, $^3J_{HP}$ = 6.8 Hz), 3.33 (m, 2 H, CH_2N), 3.85 (s, 3 H, OMe), 3.87 (s, 3 H, OMe), 6.76 (B part of an ABC system, 1 H, H6, $^3J_{AB}$ = 8.0, $^4J_{BC}$ = 1.8 Hz), 6.76 (A part of an ABC system, 1 H, H2, $^4J_{AB}$ = 1.8 Hz), 6.80 (C part of an ABC system, 1 H, H5, $^3J_{BC}$ = 8.0 Hz), 7.38–7.48 (m, 9 H, *m*-H + *p*-H, PPh_3), 7.69–7.74 (m, 6 H, *o*-H, PPh_3). ^{13}C NMR (75.45 MHz): δ 37.8 (d, CH_2Ar, $^3J_{CP}$ = 3.2 Hz), 44.8 (d, CH_2N, $^3J_{CP}$ = 2.6 Hz), 55.9 (s, OMe), 56.0 (s, OMe), 111.4 (s, CH, C5), 111.7 (s, CH, C2), 121.0 (s, CH, C6), 128.0 (d, *m*-CH, PPh_3, $^3J_{CP}$ = 11.2 Hz), 129.7 (s, C1), 130.7 (d, one-half of the doublet was obscured by the *p*-CH signal), 130.9 (d, *p*-CH, PPh_3, $^4J_{CP}$ = 2.5 Hz), 134.8 (d, *o*-CH, PPh_3, $^2J_{CP}$ = 10.5 Hz), 147.9 (s, *C*–OMe), 149.2 (s, *C*–OMe). ^{31}P NMR (162.29 MHz): δ 28.0 (s, PPh_3).

Synthesis of $[Pd_2(\mu\text{-}OAc)_2(OAc)_2\{NH_2CH_2CH_2C_6H_3(OMe)_2\text{-}3,4\}_2]$ (8b). Homoveratrylamine (273 mg, 1.51 mmol) was added to a suspension of $Pd(OAc)_2$ (338 mg, 1.51 mmol) in CH_2Cl_2 (30 mL), and the mixture was stirred for 1 h. The resulting solution was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) and air-dried to give complex **6b-OAc** as a yellow solid (179 mg, 0.31 mmol, 40%). The filtrate was concentrated to ca. 4 mL and *n*-hexane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-hexane (2 x 5 mL) and air-dried to give complex **8b** (214 mg, 0.26 mmol) as an orange solid (214 mg). Yield: 214 mg, 0.26 mmol, 35%. Mp: 50 °C. Anal. Calcd for $C_{28}H_{42}N_2O_{12}Pd_2$ (881.486): C, 41.44; H, 5.22; N, 3.45. Found: C, 41.44; H, 5.41; N, 3.49. IR (cm^{-1}): $\nu(CO)_{OAc}$ 1631 br, 1567 br. ^{1}H NMR (400.91 MHz): δ 1.88 (s, 3 H, Me, OAc), 1.89 (s, 3 H, Me, OAc), 2.57 (quint, 1 H, CH_2N, $^3J_{HH}$ = 6.4 Hz), 2.71 (quint, 1 H, CH_2N, $^3J_{HH}$ = 6.4 Hz), 3.19 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 6.8 Hz), 3.86 (br m, 1 H, NH_2), 3.86 (s, 3 H, OMe), 3.91 (s, 3 H, OMe), 5.09 (br m, 1 H, NH_2), 6.84 (C part of an ABC system, 1

H, H5, $^3J_{BC}$ = 8.0 Hz), 6.89 (B part of an ABC system, 1 H, H6, $^3J_{AB}$ = 8.0, $^4J_{BC}$ = 1.6 Hz), 6.91 (A part of an ABC system, 1 H, H2, $^4J_{AB}$ = 1.6 Hz). ^{13}C NMR (100.81 MHz): δ 22.6 (s, Me, OAc), 22.8 (s, Me, OAc), 35.5 (s, CH_2Ar), 44.4 (s, CH_2N), 55.5 (s, OMe), 55.6 (s, OMe), 111.2 (s, CH, C5), 111.9 (s, CH, C2), 120.6 (s, CH, C6), 129.8 (s, C1), 147.6 (s, C4, *C*–OMe), 148.8 (s, C3, *C*–OMe), 179.3 (s, CO), 185.2 (s, CO).

Synthesis of [Pd{*C*,*N*-$C_6H_2CH_2CH_2NH_2$-6,$(OMe)_2$-3,4}(tmeda)]Br (9b). To a suspension of $Pd(dba)_2$ (552.6 mg, 0.96 mmol) in dry toluene (20 mL) was added tmeda (111.7 mg, 0.96 mmol), and the mixture was stirred for 10 min under a N_2 atmosphere. 6-Bromo-3,4-dimethoxyphenethylemine (250 mg, 0.96 mmol) was then added, and the stirring was continued for 24 h. The resulting suspension was filtered, and the solid was washed with Et_2O (3 x 5 mL) and air-dried to give complex **9b** as an ochre solid, which is contaminated with traces of metallic palladium. Complex **9b** cannot be recrystallized to obtain a satisfactory elemental analysis, because it is very insoluble in most common solvents. Yield: 333.1 mg, 0.69 mmol, 72%. Mp: 173–176 °C. Anal. Calcd for $C_{16}H_{30}BrN_3O_2Pd$ (482.752): C, 39.81; H, 6.26; N, 8.70. Found: C, 39.34; H, 5.99; N, 7.68. IR (cm^{-1}): *ν*(NH) 3185 m, 3086 s. ^{1}H NMR (400.91 MHz, DMSO-d_6): δ 2.53 (s, 6 H, MeN), 2.59 (s, 6 H, MeN), 2.63 (m, 2 H, CH_2, tmeda), 2.81 (m, 2 H, CH_2, tmeda), 3.06 (m, 2 H, CH_2Ar), 3.65 (s, 3 H, OMe), 3.66 (m, partially obscured by the signal of OMe, 2 H, CH_2N), 3.74 (s, 3 H, OMe), 4.30 (m, 2 H, NH_2), 6.62 (s, 1 H, H2), 6.77 (s, 1 H, H5). ^{13}C NMR (50.30 MHz, DMSO-d_6): δ 38.4 (s, CH_2Ar), 41.2 (s, CH_2N), 47.4 (s, MeN), 50.2 (s, MeN), 55.7 (s, OMe), 55.9 (s, OMe), 58.1 (s, CH_2, tmeda), 62.2 (s, CH_2, tmeda), 110.9 (s, CH, C2), 115.9 (s, CH, C5), 132.2 (s, C1), 139.8 (s, C6), 145.2 (s, C4), 146.3 (s, C3).

Synthesis of (*S*)-7-Hydroxy-3-(methoxycarbonyl)-3,4-dihydroisoquinolin-1(2*H*)-one (10a). CO was bubbled through a suspension of complex **1a-Br** (150 mg, 0.20 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred under a CO atmosphere for 16 h. Decomposition to metallic palladium was observed. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5

mL) and air-dried to give crude compound **10a** as a pale yellow solid. Yield: 37 mg, 0.17 mmol, 43%. A spectroscopically pure sample of **10a** was obtained by recrystallization from CH_2Cl_2/Et_2O. Mp: 143 °C dec. IR (cm^{-1}): ν(NH) 3302 w; ν(CO) 1722 m; $\nu(CO)_{CON}$ 1667 m. ^1H NMR (300.1 MHz, acetone-d_6): δ 3.13, 3.29 (part AB of an ABX system, 2 H, CH_2, $^2J_{AB}$ = 15.8, $^3J_{AX}$ = 6.1, $^3J_{BX}$ = 5.3 Hz), 3.64 (s, 3 H, OMe), 4.42 (part X of an ABX system, 1 H, CH), 6.94 (dd, 1 H, H6, $^3J_{HH}$ = 8.1, $^4J_{HH}$ = 2.7 Hz), 7.07 (br s, 1 H, NH), 7.12 (d, 1 H, H5, $^3J_{HH}$ = 8.1 Hz), 7.45 (d, 1 H, H8, $^4J_{HH}$ = 2.7 Hz), 8.50 (s, 1 H, OH). ^{13}C NMR (75.45 MHz, acetone-d_6): δ 30.8 (s, CH_2), 52.6 (s, OMe), 53.9 (s, CH), 114.5 (s, CH, C8), 120.1 (s, CH, C6), 128.0 (s, C4a), 129.6 (s, CH, C5), 130.9 (s, C8a), 157.4 (s, C7), 165.3 (s, CO), 172.7 (s, *C*O_2Me). ESI-HRMS: exact mass calcd for $C_{11}H_{11}NO_4$ 221.0685; found 221.0688. $[\alpha]_D^{20}$ = +26.86 (c = 0.20, MeOH).

Synthesis of 6,7-Dimethoxy-3,4-dihydroisoquinolin-1(2*H*)-one (10b). CO was bubbled through a suspension of complex **1b-Br**·H_2O (145 mg, 0.19 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred under a CO atmosphere for 16 h. Decomposition to metallic palladium was observed. The mixture was filtered through a plug of $MgSO_4$, the filtrate was concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, and the solid was washed with Et_2O (2 x 5 mL) to give compound **10b** pale yellow solid. Yield: 47 mg, 0.23 mmol, 59%. IR (cm^{-1}): ν(NH) 3176 m; ν(CO) 1655 s. ^1H NMR (200.13 MHz): δ 2.94 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 6.6 Hz), 3.56 ("td", 2 H, CH_2N, $^3J_{HH}$ = 6.6, $^3J_{HH}$ = 2.4 Hz), 3.93 (s, 6 H, Me, OMe), 5.97 (br s, 1 H, NH), 6.68 (s, 1 H, H5), 7.57 (s, 1 H, H8). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 28.0 (s, CH_2Ar), 40.5 (s, CH_2N), 56.0 (s, OMe), 56.1 (s, OMe), 109.5 (s, CH, C5), 110.1 (s, CH, C8), 121.3 (s, C8a), 132.6 (s, C4a), 148.0 (s, C7), 152.1 (s, C6), 166.3 (s, CO). Spectroscopic data are in agreement to those in the literature (^1H and ^{13}C NMR).[53]

Single-Crystal X-ray Structure Determinations. Relevant crystallographic data and details of the refinement for the structures of compounds **Ia**·2MeCN, **3a-OAc**, **6b-Br**, **6b-OAc**·H_2O and **7b-OAc** are summarized in the Supplementary Material. Data Collection: Crystals suitable for X-ray diffraction were mounted in inert oil on a glass fiber and transferred to a Bruker SMART APEX diffractometer.

Data were recorded at 100(2)K using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å) and *ω*-scan mode. Multiscan absorption corrections were applied. Solution and Refinements: Crystal structures were solved by Patterson (**6b-OAc**·H_2O) or direct method (**Ia**·2MeCN, **3a-OAc**, **6b-Br** and **7b-OAc**) and all nonhydrogen atoms refined anisotropically on F^2 using the program SHELXL-97.[58] Hydrogen atoms were refined as follows: Complexes **Ia**·2MeCN: NH_2 and OH, free with DFIX; ordered methyl, rigid group; all others, riding. Complex **3a-OAc**: NH_2 and OH, free with DFIX; methyl, rigid group; all others, riding. Complex **6b-Br**: NH_2, free with SADI; methyl, rigid group; all others, riding. Complex **6b-OAc**·H_2O: H_2O, free with SADI; NH_2, free; methyl, rigid group; all others, riding. Complex **7b-OAc**: NH_2, free with SADI; ordered methyl, rigid group; all others, riding. Special features: Complex **Ia**·2MeCN: C10 is disordered over two positions, with a ca. 53:47% occupancy distribution. Complex **3a-OAc**: A region of residual electron density could not be interpreted in terms of realistic solvent molecules, even allowing for possible disorder. For this reason the program SQUEEZE, which is part of the PLATON system,[59] was employed to remove mathematically the effects of the solvent. Standard deviations of refined parameters should be interpreted with caution. The void volume per cell was 250 $Å^3$, with a void electron count per cell of 83. This solvent was not taken into account when calculating derived parameters such as the formula weight, because the nature of the solvent was uncertain. The CO_2Me group is disordered over two positions with a ca. 52:48% occupancy distribution. Complex **7b-OAc**: A region of residual electron density could not be interpreted in terms of realistic solvent molecules, even allowing for possible disorder. For this reason the program SQUEEZE, which is part of the PLATON system, was employed to remove mathematically the effects of the solvent. Standard deviations of refined parameters should be interpreted with caution. The void volume per cell was 184 $Å^3$, with a void electron count per cell of 46. This solvent was not taken into account when calculating derived parameters such as the formula weight, because the nature of the solvent was uncertain. One OMe goup is disordered over two positions with a ca. 55:45% occupancy distribution.

CONCLUSION

Ortho-palladated complexes derived from homoveratrylamine and L-tyrosine methyl ester, both biologically relevant arylalkylamines, can be easily prepared by reacting their corresponding triflates and $Pd(OAc)_2$, in a 1:1 molar ratio, in acetonitrile at 78 ºC. In this conditions, ortho-palladation of the homoveratrylamine occurs regiospecifically at C6 position. The use of the triflate salts instead of the free arylalkylamines as starting materials in the ortho-palladation reactions offers evident advantages: (1) it avoids the formation of undesirable by-products, which in the case of L-tyrosine methyl ester derive from its acidic OH group and (2) the ortho-palladated complexes are obtained in better yields. These cyclopalladated complexes can be used as intermediates in organic synthesis, as proved by the fact that their reactions with CO render the corresponding tetrahydroisoquinolones. We have investigated the published ortho-palladation of homoveratrylamine and found that, in our hands, instead of palladation at C2 a mixture containing coordination and cyclopalladated complexes at C6 were obtained.

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Supporting Information Available: Experimental details for the synthesis of 2-bromo-3,4-dimethoxyphenethylamine, details (including symmetry operators) of hydrogen bondings and listing of all refined and calculated atomic coordinates, anisotropic thermal parameters, bond lengths and angles, CIF files for complexes, table of crystallographic data of **Ia**·2MeCN, **3a-OAc**, **6b-Br**, **6b-OAc**·H_2O and **7b-OAc**. This material is available free of charge via the Internet at http://pubs.acs.org.

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