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# Reactivity toward CO of Eight-Membered Palladacycles Derived from the Insertion of Alkenes into the Pd−C Bond of Cyclopalladated Primary Arylalkylamines of Pharmaceutical Interest. Synthesis of Tetrahydrobenzazocinones, Ortho-Functionalized Phenethylamines, Ureas, and an Isocyanate

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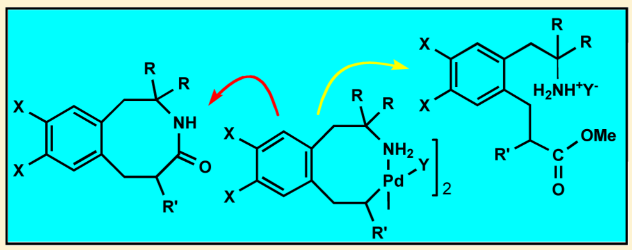
Supporting Information

**ABSTRACT:** The ortho-metalated complex $[Pd\{C,N\text{-}C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-}Br)]_2$ (**1a**) derived from homoveratrylamine reacts with ethyl acrylate, methyl vinyl ketone, or 2-norbornene to give the dimeric complex arising from the insertion of the alkene into the Pd−C bond, $[Pd\{C,N\text{-}CH(R)CH_2C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-}Br)]_2$ (R = $CO_2Et$ (**2a1**), C(O)Me (**2a2**)) or $[Pd\{C,N\text{-}CH(C_5H_8)\text{-}CHC_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-}Br)]_2$ (**2a3**). Complexes **2a** and the phentermine homologues **2b** react with CO to afford Pd(0) and (1) tetrahydrobenzazocinones, the heterocycles resulting from CO insertion into the Pd−C bond and C−N coupling, (2) unnatural amino acid derivatives, resulting from CO insertion and the reaction of the obtained acyl complex with the solvent (MeOH), or the product of protonolysis of the Pd−C bond, depending on the nature of the initial cyclopalladated compound, or (3) ureas, alone or mixed with an isocyanate, in the presence of a base. Phentermine derivatives **2b** react with HCl to give a dinuclear palladium complex $[PdCl(\mu\text{-}Cl)(L)]$, where L is the amine arising from the protonolysis of the Pd−C bond or the alkyl group resulting from Pd−N bond protonolysis, depending on the nature of the inserted alkene. The crystal structures of some palladium complexes and organic compounds have been determined by X-ray diffraction studies.




## INTRODUCTION

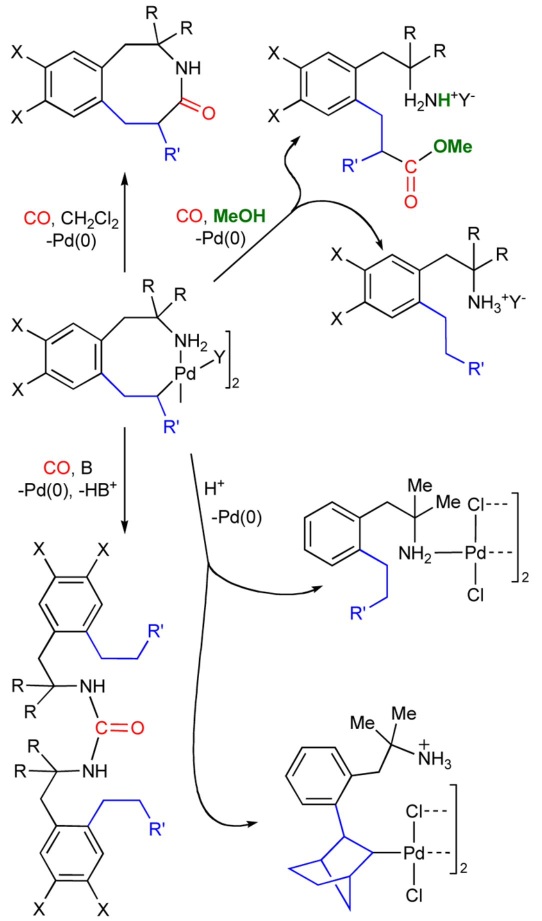
Alkenes such as 2-norbornene, ethyl acrylate, and methyl vinyl ketone insert into the Pd−$C_{aryl}$ bond of ortho-palladated complexes derived from primary phenethylamines, $[Pd(C,N\text{-}C_6H_4CH_2CR_2NH_2\text{-}2)(\mu\text{-}X)]_2$, to give surprisingly stable eight-membered palladacycles.[1] The singularity of these metallacycles emerges from two different features: (1) eight-membered palladacycles are rather scarce, and most of them arise from the insertion of one molecule of alkyne into the Pd−C bond of a six-membered ring,[2−4] and (2) palladacycles containing accessible $\beta$-hydrogen atoms are particularly rare, because they easily undergo the $\beta$-hydrogen elimination process to render Heck-type derivatives.[5] The stability of these eight-membered palladacycles has allowed us to study their reactions with RNC to obtain amidinium salts, which arise from decomposition of the organometallic complexes derived from the sequential insertion of an alkene and one isocyanide into the Pd−C bond of ortho-palladated primary phenethylamines.[1] These sequential insertions of unsaturated molecules into the Pd−C bond have a particular interest, as they are key steps in the palladium-catalyzed copolymerization reactions.[6]

In this article we report (1) the synthesis of eight-membered palladacycles containing accessible $\beta$-hydrogens derived from the insertion of an alkene into the Pd−$C_{aryl}$ bond of the orthopalladated homoveratrylamine (a hallucinogenic compound, closely related to the amphetamines family),[7] (2) the reactions of these complexes, and those of the previously reported analogous eight-membered palladacycles derived from phentermine,[1] with CO, which allows, depending on the reaction conditions, the synthesis of tetrahydrobenzazocinones, methyl or ethyl ester derivatives of unnatural N[7]-amino acids, or ureas (Scheme 1), and (3) the protonolysis reactions of some of the eight-membered palladacycles, which, depending on the inserted alkene, proceed via Pd−N or Pd−C bond breaking.

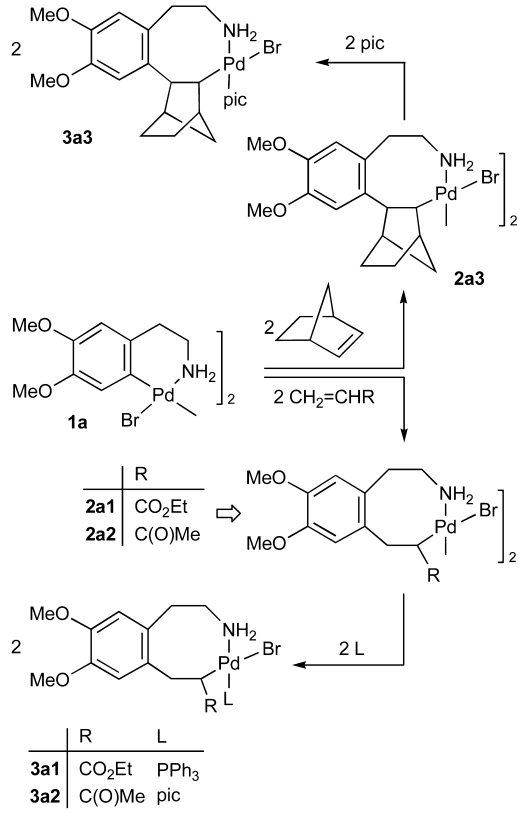
The reaction of eight-membered palladacycles with CO constitutes a new synthetic method to obtain eight-membered N-heterocycles, a type of compound that has addressed an increasing interest[8,9] because of their pharmacological proper-

**Received:** June 28, 2012
**Published:** August 16, 2012

**Scheme 1. Summary of the Reactivity of Eight-Membered Palladacycles toward CO and Acids**




**Scheme 2. Synthesis of Eight-Membered Palladacycles Derived from Homoveratrylamine**




ties. The benzazocine nucleus is particularly relevant because it can be found in biologically active molecules with analgesic,[10,11] antitumoral,[12] antihypertensive,[13] and antidepresive properties.[13] Generally, these derivatives are difficult to obtain because, due to unfavorable entropic and enthalpic factors, the traditional cyclization reactions cannot be applied to their synthesis.[8,14,15] Accordingly, there are relatively few general methods to prepare them.[9,10,14,16]

We have based the present study on the reactivity of cyclopalladated derivatives of primary amines of biological relevance,[1,2,17−21] such as homoveratrylamine and phentermine.

## ■ RESULTS AND DISCUSSION

**Synthesis and Structure of New Eight-Membered Palladacycles Derived from Homoveratrylamine.** The ortho-metalated complex derived from homoveratrylamine $[Pd\{C,N\text{-}C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-Br})]_2$ (**1a**) reacts with $CH_2{=}CHR$ (R = $CO_2Et$, C(O)Me) and norbornene ($C_7H_{10}$) in a 1:2 molar ratio, at room temperature, to give the dinuclear complexes $[Pd\{C,N\text{-}CH(R)CH_2C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-Br})]_2$ (R = $CO_2Et$ (**2a1**); C(O)Me (**2a2**)) and $[Pd\{C,N\text{-}CH(C_5H_8)CHC_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}(\mu\text{-Br})]_2$ (**2a3**), which contain the eight-membered palladacycles derived from the insertion of one molecule of the alkene into the Pd−C bond (Scheme 2). Only one set of signals is observed in the $^1$H NMR (DMSO-$d_6$) spectra of complexes **2a**, which indicates that the insertion is regiospecific. We have reported the synthesis of palladium complexes resulting from the insertion of alkenes (maleate and fumarate esters,[22] $CH_2{=}CHR$ (R = C(O)Me, $CO_2Et$),[1] norbornene,[1,23] 2,5-norbornadiene,[23] dicyclopentadiene[23]) into the Pd−C bond of aryl palladium complexes. As mentioned above, the scarce number of isolated products of this type of reaction is attributable to their tendency to decompose to afford the corresponding Heck arylated olefin. The few exceptions are those in which the required $\beta$-hydrogen elimination process cannot be achieved.[22,24] Since this was not the case of some of our complexes (R = C(O)Me, $CO_2Et$), we postulated that their stability was caused by the existence of the strong Pd−$NH_2$ bond, the electron-withdrawing nature of the R substituent, and the restricted flexibility of the eight-membered palladacycle because of the presence in solution of intramolecular hydrogen bonds (see below).[1]

Complexes **2a** react with neutral ligands in a 1:2 molar ratio to give the mononuclear derivatives $[Pd\{C,N\text{-}CH(R)\text{-}CH_2C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}Br(L)]$ (R = $CO_2Et$, L = $PPh_3$ (**3a1**); R = C(O)Me, L = 4-methylpyridine (pic) (**3a2**)) and $[Pd\{C,N\text{-}CH(C_5H_8)CHC_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_2\text{-}4,5\}Br(pic)]$ (**3a3**) (Scheme 2). The $^1$H NMR spectra of these monomeric complexes show the inequivalence of the $NH_2$ and $CH_2$ protons, caused by the presence of one or several chiral centers in the molecule, depending on the inserted alkene (see $^1$H NMR tables in the Supporting Information). For derivatives containing inserted methyl vinyl ketone or ethyl acrylate, the methine hydrogen atom is on $C^\alpha$, which is the most frequent regioisomer found in the insertion of electron-poor alkenes into the Pd−C bonds of neutral complexes.[25,26] We propose for all 2-norbornene derivatives structures arising from the syn addition of the Pd−C bond to the exo face of the olefin, according to a NOESY experiment carried out for complex **3a3** and in agreement with the results formerly observed for insertion of 2-norbornene in other six-membered palladacycles.[1]

The crystal structure of complex **3a2** has been solved by X-ray diffraction studies (Figure 1), confirming the proposed

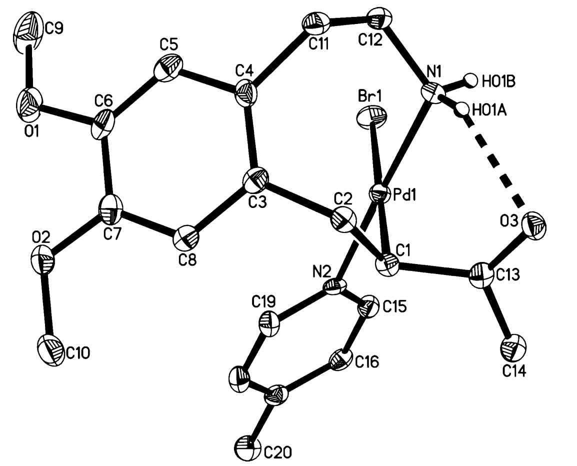



**Figure 1.** Thermal ellipsoid plot (50% probability) of complex **3a2** along with the labeling scheme. Hydrogen carbon atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Pd(1)−N(1) = 2.058(3), Pd(1)−N(2) = 2.037(3), Pd(1)−C(1) = 2.086(3), Pd(1)−Br(1) = 2.5085(5); C(1)−Pd(1)−N(1) = 90.11(13), N(1)−Pd(1)−Br(1) = 88.96(9), Br(1)−Pd(1)−N(2) = 90.05(9), N(2)−Pd(1)−C(1) = 90.90(13), Pd(1)−C(1)−C(2) = 112.2(2).

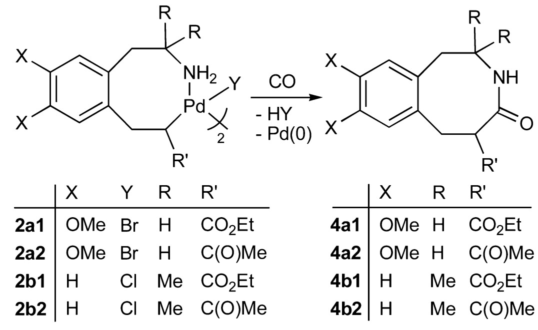
regiochemistry of the insertion reaction. The palladium atom is in an almost perfect square-planar environment (mean deviation of the plane Pd(1)−C(1)−N(1)−Br(1)−N(2) 0.0216 Å), and it forms part of an eight-membered ring that adopts a boat-chair conformation. There is an intramolecular hydrogen bond between the oxygen atom of the carbonyl group and one of the hydrogen atoms of the $NH_2$ group, while the other hydrogen is interacting with the carbonyl group of another molecule, giving rise to dimers (see Supporting Information).

We propose for all the other mononuclear complexes that the monodentated ligands ($PPh_3$, pic) are trans to the $NH_2$ group, because this is the expected geometry according to the greater transphobia between C-/P- and C-/N-donor than N-/P-donor and N-/N-donor pairs of ligands, respectively.[27] In addition, the X-ray crystal structures of related complexes have shown these geometries.[1,2,18,28,29]

**Reactivity of the Eight-Membered Palladacycles toward CO. Synthesis and Characterization of Tetrahydrobenzazocinones and Esters.** The isolation of complexes **2a** gave us the chance to explore their reactivity toward CO. We have as well extended this study to their previously reported phentermine homologues **2b** (Scheme 3).[1]

Complexes **2a** or **2b** react with CO at 65 °C or room temperature, respectively, to afford Pd(0) and the corresponding tetrahydrobenzazocinones **4a** or **4b** (Scheme 3), respectively. Formation of these lactams can be explained according to the generally accepted mechanism for the insertion of CO into the Pd−C bond of five- and six-membered palladacycles,[26,30,31] that is, (1) coordination of CO to the metal center, (2) migratory insertion of the organyl group to the coordinated CO, and (3) depalladation of the acyl complex

**Scheme 3. Synthesis of Tetrahydrobenzazocinones**




| | X | Y | R | R' |
|---|---|---|---|---|
| **2a1** | OMe | Br | H | $CO_2Et$ |
| **2a2** | OMe | Br | H | C(O)Me |
| **2b1** | H | Cl | Me | $CO_2Et$ |
| **2b2** | H | Cl | Me | C(O)Me |

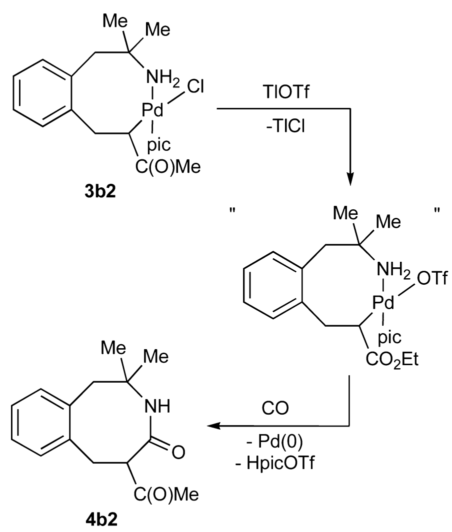
| | X | R | R' |
|---|---|---|---|
| **4a1** | OMe | H | $CO_2Et$ |
| **4a2** | OMe | H | C(O)Me |
| **4b1** | H | Me | $CO_2Et$ |
| **4b2** | H | Me | C(O)Me |

| | X | Y | R |
|---|---|---|---|
| **2a3** | OMe | Br | H |
| **2b3** | H | Cl | Me |

| | X | R |
|---|---|---|
| **4a3** | OMe | H |
| **4b3** | H | Me |

through a C−N coupling. Lactam **4b2** can be obtained in better yield by reacting the previously reported mononuclear derivative **3b2**[1] with CO in the presence of TlOTf (Scheme 4). Generally, the generation of cationic palladacycles facilitates

**Scheme 4. Improved Synthesis of the Tetrahydrobenzazocinone Derived from Phentermine and Methyl Vinyl Ketone**

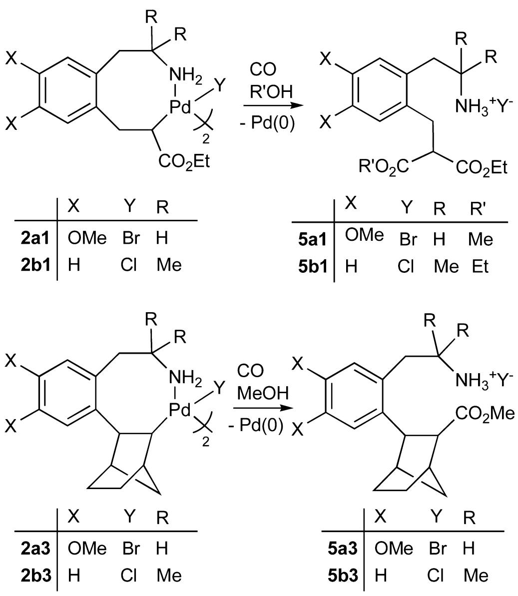



the insertion process of unsaturated ligands into the Pd−C bond and the decomposition of the resulting complex.[1,20,32]

The synthesis of the eight-membered lactams **4** resulting from alkene/CO sequential insertions into the Pd−C bond have no precedents. We have reported (1) the synthesis of tetrahydroisoquinolones or tetrahydrocarbolinones by reacting CO with six-membered palladacycles obtained by cyclopalladation of some primary amines,[19−21] (2) a few examples of the reverse CO/alkene insertion process giving products resulting from the polyinsertion of the alkene,[23] and (3) sequential alkyne/CO insertion reactions into the Pd−C bond of cationic eight-membered *C,O*-palladacycles to give eight-membered benzo[*d*]-azocine-2,4(1*H*,3*H*)-diones.[3]

The nature of the products obtained through CO insertion into palladacycles depends greatly on the solvent, and thus it has been reported that esters or amides can be obtained in the presence of alcohols or amines, respectively.[31,33,34] When the reactions of the complexes **2** with CO were carried out in ethanol or methanol, decomposition to metallic palladium took place, and the corresponding methyl or ethyl ester derivatives of unnatural $N^7$-amino acids **5** (Scheme 5) were isolated in moderate to good yields (48−88%).

**Scheme 5. Synthesis of Esters Derived from Homoveratrylamine and Phentermine**




| | X | Y | R |
|---|---|---|---|
| 2a1 | OMe | Br | H |
| 2b1 | H | Cl | Me |

| | X | Y | R | R' |
|---|---|---|---|---|
| 5a1 | OMe | Br | H | Me |
| 5b1 | H | Cl | Me | Et |

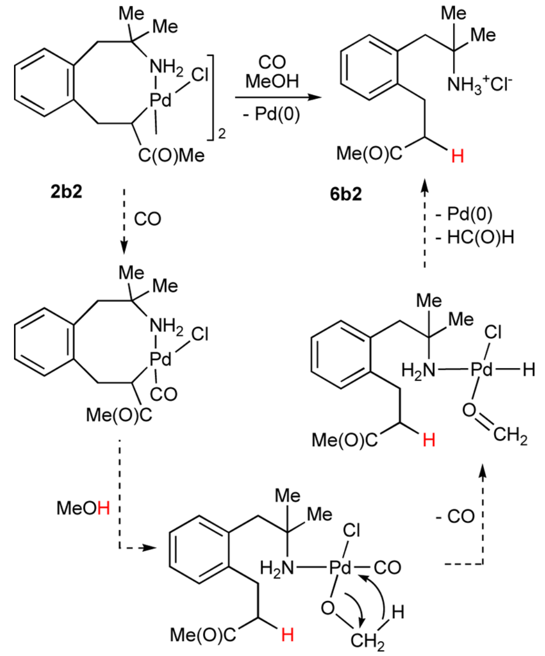
| | X | Y | R |
|---|---|---|---|
| 2a3 | OMe | Br | H |
| 2b3 | H | Cl | Me |

| | X | Y | R |
|---|---|---|---|
| 5a3 | OMe | Br | H |
| 5b3 | H | Cl | Me |

**Synthesis of Ortho-Alkylated Amines and Ureas.** Surprisingly, the reaction of complex **2b2** and CO in methanol did not afford the lactam nor the ester. Instead, the ortho-alkylated ammonium salt **6b2** was obtained, resulting from protonolysis of the Pd−C bond (Scheme 6). Taking into account that complex **2b2** is very insoluble in methanol, that when a suspension of **2b2** in this solvent was stirred at room temperature for 12 h no reaction occurred, and that CO does not appear in product **6b2**, the role of CO could be its coordination to Pd: (1) to render a soluble monomeric complex, which would undergo the reaction with methanol, or (2) to modify the electronic properties and/or the strength of the Pd−C bond, making its protonolysis easier. In the first case, the protonolysis would take place in the presence of any ligand that reacted with the dimer to afford a soluble complex. However, when a solution of complex **2b2** in a mixture of acetonitrile/methanol (3:1) was stirred at room temperature for 12 h, no decomposition to Pd(0) was observed and complex **2b2** was recovered. Therefore, the simple formation of a soluble product cannot justify the obtention of the salt **6b2**.

A possible reaction pathway to explain the formation of this ammonium salt would involve: (1) CO coordination, to give a soluble mononuclear derivative, (2) protonolysis of the Pd−C bond (probably assisted by the oxygen atom of the carbonyl group in $\alpha$-position), to render an alcoxo complex, and (3) a $\beta$-elimination process, to give a Pd(II) hydrido complex that would decompose generating Pd(0) and HCl.[35] This reaction

**Scheme 6. Proposed Pathway for the Synthesis of Compound 6b2**

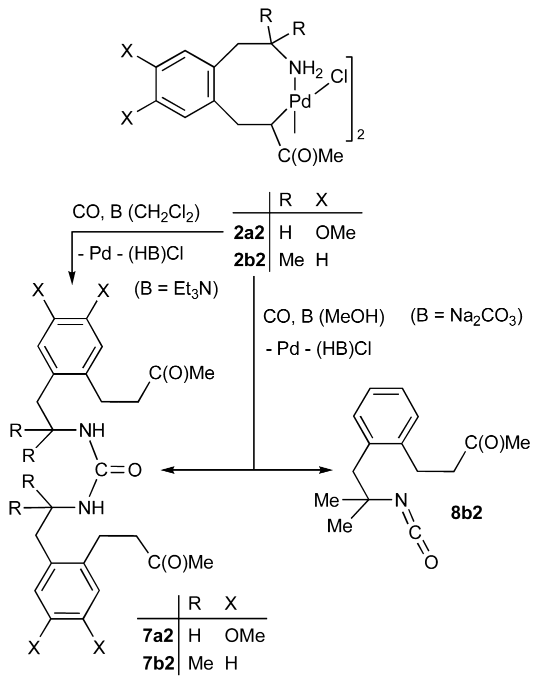



mechanism is consistent with the experimental isolation of the ammonium chloride intead of the free amine as the reaction product (Scheme 6). Moreover, when the reaction is carried out in MeOD, the isolated ammonium chloride (**6b2-*d*$_1$**; ESI-HRMS) contains a deuterium atom in $\alpha$-position to the carbonyl group, as shown by its $^1$H NMR spectrum. The protonolysis of the Pd−C bond has been postulated as one of the steps in some Pd(II)-catalyzed C−C and C−N coupling reactions.[28,36]

Trying to avoid the protonolysis process, we carried out these reactions in the presence of a base. The reaction of **2a2**, CO, and $NEt_3$ in $CH_2Cl_2$ rendered the urea **7a2**, along with metallic palladium and $(HNEt_3)Br$. Likewise, the reaction of **2b2**, CO, and $Na_2CO_3$ in MeOH afforded a mixture of the urea **7b2** and the isocyanate **8b2** (Scheme 7). Palladium catalysts have been widely used for the synthesis of ureas by oxidative carbonylation of primary amines.[37] In the catalytic cycle, isocyanates were proposed as intermediates[38] and in some cases detected.[39] The isolation of **8b2** gives additional support to this proposal.

To explain these results, we propose the reaction pathway depicted in Scheme 8. The first step is the coordination of CO to Pd(II), to give a mononuclear complex **A**, which undergoes two different reactions: (1) the base deprotonates the coordinated $NH_2$ group to give **B**, favoring the insertion of CO into the Pd−N bond to give an organometallic carbamoyl intermediate **C**,[38] which evolves through a $\beta$-hydride elimination process to give the isocyanate **D** (**8b2**); (2) the Pd−C bond in **A** undergoes a protonolysis by reaction with MeOH (see above) or $Et_3NH^+$ to render the cationic complex **E**, which decomposes to give the free amine **F** and a cationic Pd(II) complex **G**, which is reduced to Pd(0) by MeOH, as shown above, or by CO. The hydroamination of the isocyanate by the amine affords the ureas **7**. The isolation of isocyanate **8b2** means that when $Na_2CO_3$ is used as a base in MeOH, the reaction route (1) is faster than that of (2). Similar steps have

**Scheme 7. Synthesis of Ureas 7a2 and 7b2 and Isocyanate 8b2**



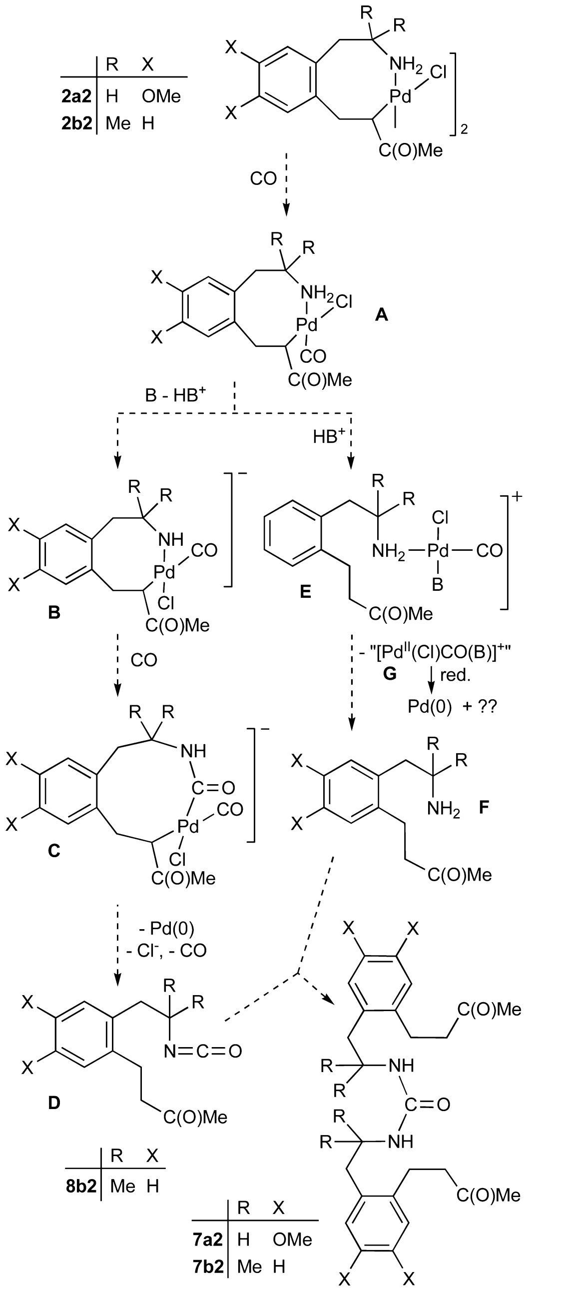

been proposed for the catalytic formation of ureas by oxidative carbonylation of primary amines.[38,40]

The facile protonolysis of the Pd−C bond in complex **2b2** in the presence of CO and a weak acid moved us to try its reaction with strong acids. Thus, when HCl was bubbled through a suspension of **2b2** in $CH_2Cl_2$, the dimeric complex **9b2** was obtained (Scheme 9). In this case, the presence of the auxiliary ligand CO was unnecessary to induce the protonolysis process.

The crystal structure of complex **9b2** has been determined by X-ray diffraction studies (Figure 2) and shows a centrosymmetric molecule with the palladium atoms in a slightly distorted square-planar geometry (mean deviation of the plane Pd(1)−N(1)−Cl(1)−Cl(2A)−Cl(2) 0.0629 Å). The coordination planes of both palladium atoms form an angle of 147.1°. Two molecules of complex **9b2** are stacked together, connected through hydrogen bond interactions, giving a dimer in which the palladium and chloro atoms are eclipsed and the terminal chains alternate (Figure 3).

The reaction of palladacycle **2b1** with HCl led to intractable mixtures. Palladacycle **2b3** reacted with HCl to give an orange solid **9b3**, which analyzes as **2b3**·HCl but whose insolubility prevented its characterization by NMR spectroscopy. The reaction of **9b3** with an excess of XyNC afforded the soluble complex **10b3**, which contains an inserted and two coordinated molecules of the isocyanide, and an $NH_3^+$ group (Scheme 10), according to its IR, $^1H$ and $^{13}C$ NMR spectra, and elemental analysis. Therefore, it is reasonable to assume that complex **9b3** also contains an $NH_3^+$ group, and thus we propose for it the zwitterionic structure depicted in Scheme 10. A similar Pd−N bond dissociation in acidic media was reported by Ryabov for five-membered palladacyles.[41] In summary, when treated with HCl, complex **2b2** undergoes Pd−C bond protonolysis, while complex **2b3** a Pd−$NH_2$ protonolysis. It is difficult to explain this different behavior that may be attributed to the steric influence of the bulky inserted norbornene and/or to the electron-withdrawing nature of the C(O)Me group.

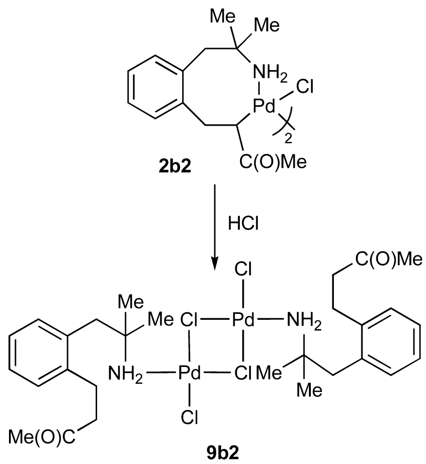
**Scheme 8. Proposed Pathway for the Synthesis of Ureas 7 and Isocyanate 8b2**




In order to obtain an amide derivative, analogous to the ester **5b1**, the reaction of complex **2b1** and CO in $CH_2Cl_2$ was carried out in the presence of $NH_3$ or $NHEt_2$ instead of MeOH or EtOH.[34] However, the reaction did not render the expected amide but the previously described[1] complex **3b1** or **3b1′**, respectively, which contains a coordinated $NHR_2$ molecule (R = H, Et; Scheme 11). It is reasonable to assume that CO cannot displace the amino ligand from the coordination sphere of palladium(II), and consequently, the insertion reaction of CO into the Pd−C bond does not take place. When an excess of $NHEt_2$ (molar ratio = 1:4) was added to a suspension of the palladacycle **2b2** in $CH_2Cl_2$ and the mixture was stirred for 24 h under a CO atmosphere, decomposition to metallic palladium took place and a mixture of the nonsymmetric urea **7b2′** and the previously reported isoquinoline **11b2**[1] (ca. 2:1 ratio),


dx.doi.org/10.1021/om300593x | Organometallics 2012, 31, 6351−6364

Scheme 9. Synthesis of Complex 9b2



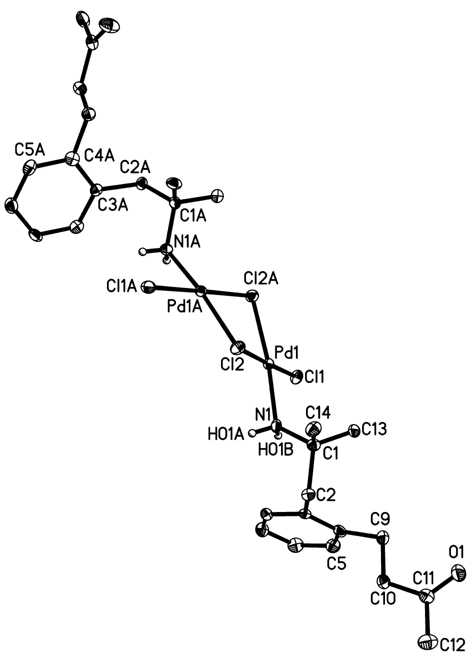




Figure 2. Thermal ellipsoid plot (50% probability) of complex **9b2** along with the labeling scheme. Hydrogen carbon atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Pd(1)–N(1) = 2.019(3), Pd(1)–Cl(1) = 2.2904(9), Pd(1)–Cl(2) = 2.3324(9), Pd(1)–Cl(2A) = 2.3296(9), C(9)–C(10) = 1.529(5); N(1)–Pd(1)–Cl(1) = 87.37(10), Cl(1)–Pd(1)–Cl(2A) = 92.92(3), Cl(2)–Pd(1)–Cl(2A) = 85.81(3), N(1)–Pd(1)–Cl(2) = 93.93(10).

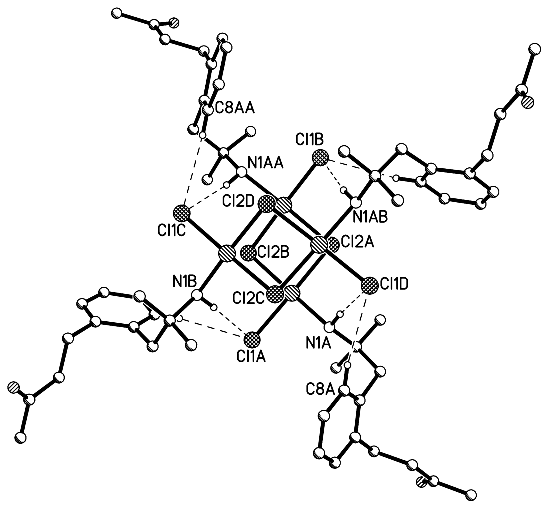
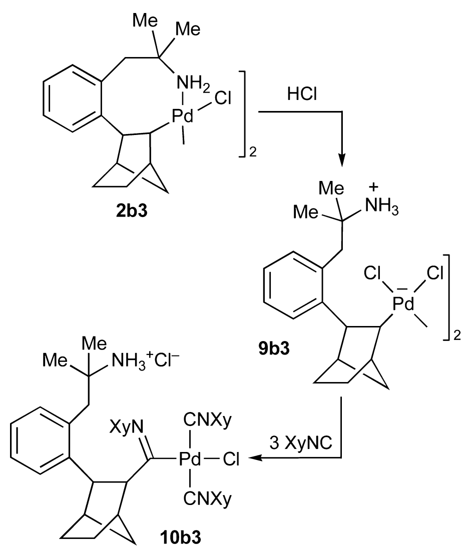



Figure 3. X-ray packing view of compound **9b2** (50% probability) showing the dimer generated by the hydrogen bond interactions. Details (including symmetry operators) are given in the Supporting Information.

Scheme 10. Reaction of Complex 2b3 with HCl and XyNC




which arised from a $\beta$-hydrogen elimination/hydroamination process (Scheme 11). The obtention of the urea **7b2′** can be easily explained by reaction of $NHEt_2$ with the isocyanate **8b2**, which can be formed following pathway (1) proposed in Scheme 8. Again, it is difficult to explain the different behavior of both palladacycles derived from the insertion of ethyl acrylate and methyl vinyl ketone. Nevertheless, it must be related with the different steric and/or electronic properties of the $CO_2Et$ and C(O)Me substituent on the carbon atom in $\alpha$-position to the Pd(II).

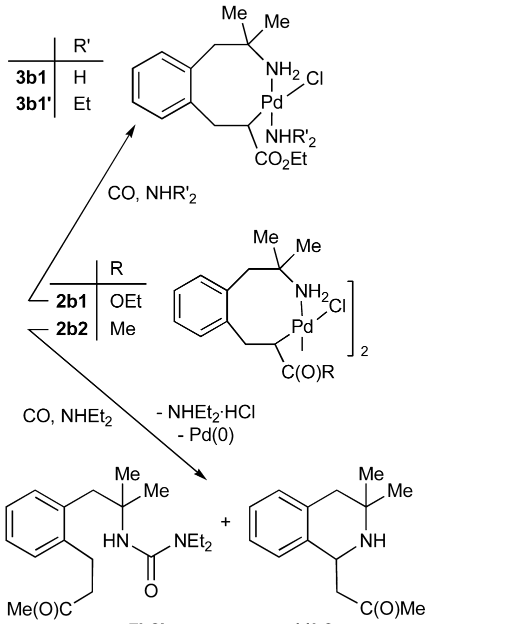
**Structure of Organic Derivatives Obtained by Carbonylation.** All the organic derivatives obtained by reaction of eight-membered palladacycles and CO have been characterized by IR and NMR spectroscopy and elemental analysis or exact mass. In addition, the crystal structures of compounds **4b1**, **4b2**, **5b3**, and **6b2** have been determined by X-ray diffraction studies. Data on these structures and selected $^1$H NMR data (hydrogen of NH or $NH_2$ groups and those related to the inserted alkene moiety) for tetrahydrobenzazocinones, esters, alkylated amines, ureas, and isocyanates obtained from phentermine and homoveratryl amine can be found in the Supporting Information.

The salts **5a1**, **5a3**, **5b1**, **5b3**, and **6b2** exhibit very low molar conductivities in acetone (6–12 $\Omega^{-1}$ $cm^2$ $mol^{-1}$), less than that expected for 1:1 electrolytes,[42] which could be due to the existence of hydrogen bonds in solution, as shown in the crystal structures of **5b3** and **6b2** (see Supporting Information).

## ■ CONCLUSION

The ortho-palladated complex derived from homoveratrylamine undergoes the insertion of ethyl acrylate, methyl vinyl ketone, or 2-norbornene, leading to the formation of stable dimeric eight-membered palladacycles, in spite of being $\sigma$-alkyl

**Scheme 11. Reaction of Palladacycles Derived from Phentermine with CO in the Presence of Amines**



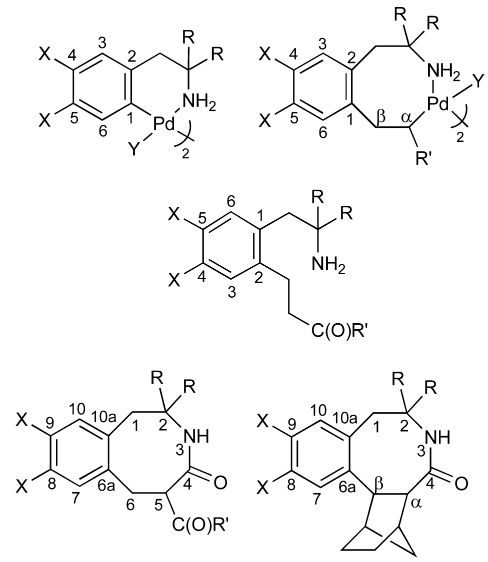

complexes containing accessible hydrogen atoms in $\beta$-position to the palladium atom. Mononuclear complexes can be easily obtained by their reaction with neutral ligands such as phosphines or pyridines. The eight-membered palladacycles undergo CO insertion into the Pd−C bond to render, depending on the experimental conditions, Pd(0) and either (1) hexahydrobenzazocinones, through an intramolecular C−N coupling process, or (2) esters, when the reactions are carried out in the presence of alcohols. The complexes arising from the insertion of methyl vinyl ketone into the six-membered palladacycles undergo protonolysis of the Pd−C bond under mild conditions to produce (1) dinuclear complexes containing the alkyl-substituted amine (in the presence of HCl) or (2) the ortho-alkylated amine derivarives (in the presence of methanol). When the protonolysis reactions are carried out in the presence of $Na_2CO_3$, the urea derived from the ortho-alkylated amine is obtained. In contrast, the reaction of the eight-membered palladacycle arising from the insertion of 2-norbornene with acids renders an organometallic complex where the Pd−N bond has been dissociated.

## ■ EXPERIMENTAL SECTION

**General Procedures.** Infrared spectra were recorded on a Perkin-Elmer 16F-PC-FT spectrometer. C, H, N, and S analyses, conductance measurements, and melting point determinations were carried out as described elsewhere.[21] Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in Bruker Avance 300, 400, or 600 spectrometers. Chemical shifts were referenced to TMS ($^1$H, $^{13}$C{$^1$H}) or $H_3PO_4$ ($^{31}$P{$^1$H}). Signals in the $^1$H and $^{13}$C NMR spectra of all complexes were assigned with the help of HMQC and HMBC techniques. Mass spectra and exact masses were recorded on an AUTOSPEC 5000 VG mass spectrometer. Reactions were carried out at room temperature without special precautions against moisture unless otherwise specified.

The complexes [Pd{*C,N*-$C_6H_2CH_2CH_2NH_2$-2,$(MeO)_2$-4,5)($\mu$-Br)]$_2$ (**1a**),[21] [Pd{(*C,N*)-CH($CO_2$Et)$CH_2C_6H_4(CH_2CMe_2NH_2)$-2}($\mu$-Cl)]$_2$ (**2b1**), [Pd{(*C,N*)-CH(COMe)-$CH_2C_6H_4(CH_2CMe_2NH_2)$-2}($\mu$-Cl)]$_2$·1/4$CH_2Cl_2$ (**2b2**·1/4$CH_2Cl_2$), [Pd{(*C,N*)-CH($C_5H_8$)$CHC_6H_4(CH_2CMe_2NH_2)$-2}($\mu$-Cl)]$_2$ (**2b3**), and [Pd{(*C,N*)-CH(COMe)$CH_2C_6H_4(CH_2CMe_2NH_2)$-2}Cl-($NC_5H_4$Me-4)] (**3b2**) were prepared as previously reported.[1] Ethyl acrylate (Merck), methyl vinyl ketone, 2-norbornene, 4-methylpyridine (4-picoline), $NHEt_2$, $PPh_3$, $^t$BuNC, XyNC, HOTf ($HSO_3CF_3$) (Fluka), $NEt_3$ (Sigma-Aldrich), $NH_3$ (gas, Air Products), and $Na_2CO_3$ (Baker) were used as received. HCl gas was generated *in situ* by reaction of NaCl and $H_2SO_4$. TlOTf was prepared by reaction of $Tl_2CO_3$ and $HO_3SCF_3$ (1:2) in water and recrystallized from acetone/$Et_2O$. Chart 1 gives the numbering schemes for the new palladacycles and the organic compounds.

**Chart 1. Numbering Schemes for the New Palladacycles and the Organic Compounds**



**Synthesis of [$Pd_2${*C,N*-CH($CO_2$Et)$CH_2C_6H_2CH_2CH_2NH_2$-2, $(OMe)_2$-4,5}$_2$($\mu$-Br)$_2$] (2a1).** Ethyl acrylate (0.059 mL, 0.545 mmol) was added to a suspension of complex [$Pd_2${*C,N*-$C_6H_2CH_2CH_2NH_2$-2, $(OMe)_2$-4,5}$_2$($\mu$-Br)$_2$] (**1a**; 200 mg, 0.273 mmol) in $CH_2Cl_2$ (20 mL), and the mixture was stirred for 30 min. Formation of a small amount of palladium(0) was observed. The resulting solution 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 × 5 mL) and air-dried to afford a first crop of **2a1** as a yellow solid (162 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **2a1** as a yellow solid (40 mg). Yield: 202 mg, 0.216 mmol, 79%. Mp: 137 °C. Anal. Calcd for $C_{30}H_{44}Br_2N_2O_8Pd_2$ (942.344): C, 38.24; H, 4.81; N, 2.97. Found: C, 37.91; H, 4.87; N, 3.08. IR (cm$^{-1}$): $\nu$(NH) 3239 m; $\nu$(CO) 1665 m. $^1$H NMR (300.1 MHz, DMSO-$d_6$): $\delta$ 1.20 (t, 3 H, Me, $^3J_{HH}$ = 7.2 Hz), 2.14 (dd, 1 H, $C^{\beta}H_2$, $^2J_{HH}$ = 13.8 Hz, $^3J_{HH}$ = 6.9 Hz), 2.66 (br d, 2 H, $CH_2$Ar, $^2J_{HH}$ = 10.2 Hz), 2.95−3.20 (m, 3 H, $CH_2$N + 1 H of $C^{\beta}H_2$), 3.68 (m, partially obscured by the MeO signal, 2 H, $C^{\alpha}$H + 1 H of $NH_2$), 3.72 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 4.03 (m, 2 H, $CH_2$O), 4.79 (br d, 1 H, $NH_2$, $^2J_{HH}$ = 10.2 Hz), 6.69 (s, 1 H, H6), 6.88 (s, 1 H, H3). $^{13}$C{$^1$H} NMR (75.45 MHz, DMSO-$d_6$): $\delta$ 14.4 (s, Me), 31.9 (s, $C^{\beta}H_2$), 32.0 (s, $CH_2$Ar), 41.2 (s, $C^{\alpha}$H), 41.5 (s, $CH_2$N), 55.0 (s, MeO), 55.9 (s, MeO), 59.2 (s, $CH_2$O), 112.0 (s, CH, C6), 114.4 (s, CH, C3), 129.0 (s, C2), 133.7 (s, C1), 147.0 (s, C5), 147.3 (s, C4), 176.1 (s, CO).

**Synthesis of [$Pd_2${*C,N*-CH(COMe)$CH_2C_6H_2CH_2CH_2NH_2$-2, $(OMe)_2$-4,5}$_2$($\mu$-Br)$_2$] (2a2).** Methyl vinyl ketone (0.045 mL, 0.546 mmol) was added to a suspension of complex **1a** (200 mg, 0.273 mmol) in $CH_2Cl_2$ (25 mL), and the mixture was stirred for 1 h. Formation of a small amount of palladium(0) was observed. The resulting suspension 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 × 5 mL) and air-dried to afford a first crop of **2a2** as a yellow solid (163 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **2a2** as a yellow solid (31 mg). Yield: 194 mg, 0.222 mmol, 81%. Mp: 126 °C. Anal. Calcd for $C_{28}H_{40}Br_2N_2O_6Pd_2$ (873.283): C, 38.51; H, 4.62; N, 3.21. Found: C, 38.61; H, 4.66; N, 3.28. IR ($cm^{-1}$): $\nu$(NH) 3271 s, 3152 m; $\nu$(CO) 1633 vs. $^1$H NMR (400.91 MHz, DMSO-$d_6$): $\delta$ 1.99 (dd, 1 H, $C^{\beta}H_2$, $^2J_{HH}$ = 13.6, $^3J_{HH}$ = 6.4 Hz), 2.08 (s, 3 H, Me), 2.09−2.14 (m, partially obscured by the Me signal, 1 H, $NH_2$), 2.63 (br d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.0 Hz), 2.87−2.95 (m, 1 H, $CH_2Ar$), 3.05−3.14 (m, 2 H, $CH_2N$), 3.23 (m, 1 H, $C^{\beta}H_2$), 3.72 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 4.16 (dd, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 11.2, $^3J_{HH}$ = 6.4 Hz), 4.88 (br d, 1 H, $NH_2$, $^2J_{HH}$ = 10.8 Hz), 6.73 (s, 1 H, H6), 6.87 (s, 1 H, H3). $^{13}C\{^1H\}$ NMR (75.45 MHz, DMSO-$d_6$): $\delta$ 28.9 (s, Me), 30.1 (s, $C^{\beta}H_2$), 31.9 (s, $CH_2Ar$), 47.6 (s, $CH_2N$), 54.7 (s, $C^{\alpha}H$), 55.1 (s, MeO), 56.0 (s, MeO), 111.9 (s, CH, C6), 114.5 (s, CH, C3), 129.1 (s, C2), 133.4 (s, C1), 147.0 (s, C5), 147.4 (s, C4), 203.1 (s, CO).

**Synthesis of [$Pd_2${*C*,*N*-CH($C_5H_8$)CH$C_6H_2CH_2CH_2NH_2$-2,(OMe)$_2$-4,5}$_2$($\mu$-Br)$_2$] (2a3).** 2-Norbornene (50 mg, 0.546 mmol) was added to a suspension of complex **1a** (200 mg, 0.273 mmol) in $CH_2Cl_2$ (25 mL), and the mixture was stirred for 1 h. Formation of a small amount of palladium(0) was observed. The resulting suspension 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 × 5 mL) and air-dried to afford a first crop of **2a3** as a yellow solid (105 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **2a3** as a yellow solid (54 mg). Yield: 159 mg, 0.173 mmol, 63%. Mp: 152 °C. Anal. Calcd for $C_{34}H_{48}Br_2N_2O_4Pd_2$ (921.414): C, 44.32; H, 5.25; N, 3.04. Found: C, 44.53; H, 5.43; N, 3.02. IR ($cm^{-1}$): $\nu$(NH) 3546 s, 3465 s, 3412 s, 3229 m. $^1$H NMR (400.91 MHz, DMSO-$d_6$): $\delta$ 1.07−1.40 (m, 4 H, $CH_2$ nor + $CH_2$ nor), 1.50−1.62 (m, 2 H, $CH_2$ nor), 2.14−2.26 (m, 3 H, CH nor + $C^{\alpha}H$ + 1 H of $CH_2Ar$), 2.47−2.83 (m, 6 H, $C^{\beta}H$ + CH nor + $CH_2N$ + 1 H of $CH_2Ar$ + 1 H of $NH_2$), 3.06−3.14 (m, 1 H, $NH_2$), 3.70 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 6.77 (s, 1 H, H3), 6.92 (s, 1 H, H6). $^{13}C\{^1H\}$ NMR (100.81 MHz, DMSO-$d_6$): $\delta$ 30.1 (s, $CH_2$), 30.5 (s, $CH_2$), 30.9 (s, $CH_2$), 31.7 (s, $CH_2$), 32.2 (s, $CH_2$), 38.5 (s, $CH_2$), 40.9 (s, CH nor), 41.2 (s, CH nor), 42.2 (s, CH nor), 45.4 (s, $CH_2$), 45.6 (s, CH nor), 46.2 (s, $CH_2$), 46.5 (s, CH nor), 50.9 (s, CH nor), 51.2 (s, CH nor), 51.7 (s, CH nor), 55.3 (s, MeO), 55.5 (s, MeO), 55.9 (s, MeO), 55.9 (s, MeO), 108.9 (s, CH), 111.0 (s, CH), 112.8 (s, CH), 114.9 (s, CH), 131.0 (s, C), 131.1 (s, C), 135.3 (s, C), 135.5 (s, C), 146.7 (s, C), 147.1 (s, C). The $^{13}$C NMR spectrum of complex **2a3** in DMSO-$d_6$ is more complicated than expected. We attribute it to the existence in solution of a mixture of two compounds: the dimer **2a3** and the monomer **2a3-DMSO**, in which the solvent has split the bromo bridges. The reaction of this mixture with 4-picoline affords only complex **3a3**.

**Synthesis of [Pd{*C*,*N*-CH($CO_2$Et)$CH_2C_6H_2CH_2CH_2NH_2$-2,(OMe)$_2$-4,5}Br($PPh_3$)] (3a1).** $PPh_3$ (56 mg, 0.214 mmol) was added to a solution of complex **2a1** (100 mg, 0.107 mmol) in $CH_2Cl_2$ (20 mL), and the resulting solution was stirred for 30 min. 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 × 5 mL) and air-dried to afford **3a1** as a yellow solid. Yield: 112 mg, 0.154 mmol, 72%. Mp: 134 °C. Anal. Calcd for $C_{33}H_{37}BrNO_4Pd$ (728.960): C, 54.37; H, 5.12; N, 1.92. Found: C, 54.28; H, 5.23; N, 1.91. IR ($cm^{-1}$): $\nu$(NH) 3267 m, 3195 m, 3132 m; $\nu$(CO) 1660 s. $^1$H NMR (300.1 MHz): $\delta$ 1.04 (t, 3 H, Me, $^3J_{HH}$ = 6.9 Hz), 2.18 (dd, 1 H, $C^{\beta}H_2$, $^2J_{HH}$ = 11.1 Hz, $^3J_{HH}$ = 6.6 Hz), 2.74 (br d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.4 Hz), 2.94 (dd, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 10.8 Hz, $^3J_{HH}$ = 6.9 Hz), 3.11 (m, 1 H, $CH_2Ar$), 3.24 (m, 2 H, 1 H of $NH_2$ + 1 H of $C^{\beta}H_2$), 3.40−3.48 (m, 2 H, 1 H of $CH_2N$ + 1 H of $NH_2$), 3.59 (s, 3 H, MeO), 3.59−3.63 (m, partially obscured by the MeO signal, 1 H, $CH_2N$), 3.93−4.00 (m, partially obscured by the MeO signal, 2 H, $CH_2O$), 4.02 (s, 3 H, MeO), 6.12 (s, 1 H, H6), 6.84 (s, 1 H, H3), 7.28−7.37 (m, 6 H, *m*-H, $PPh_3$), 7.39−7.48 (m, 9 H, *o*-H + *p*-H, $PPh_3$). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 14.1 (s, Me), 32.6 (s, $C^{\beta}H_2$), 33.5 (s, $CH_2Ar$), 36.9 (s, $C^{\alpha}H$), 46.8 (s, $CH_2N$), 55.9 (s, MeO), 55.9 (s, MeO), 59.6 (s, $CH_2O$), 112.3 (s, CH, C6), 113.4 (s, CH, C3), 127.9 (d, *m*-CH, $PPh_3$, $^3J_{CP}$ = 10.7 Hz), 129.3 (s, C2), 130.4 (d, *p*-CH, $PPh_3$, $^4J_{CP}$ = 2.0 Hz), 131.2 (d, *i*-C, $PPh_3$, $^1J_{CP}$ = 50.7 Hz), 134.5 (s, C1), 135.1 (d, *o*-CH, $PPh_3$, $^2J_{CP}$ = 11.4 Hz), 147.8 (s, C5), 148.0 (s, C4), 177.6 (s, CO). $^{31}$P NMR (121.5 MHz): $\delta$ 35.3 (s).

**Synthesis of [Pd{*C*,*N*-CH(COMe)$CH_2C_6H_2CH_2CH_2NH_2$-2,(OMe)$_2$-4,5}Br($NC_5H_4$Me-4)] (3a2).** 4-Picoline (0.018 mL, 0.183 mmol) was added to a solution of complex **2a2** (80 mg, 0.092 mmol) in $CH_2Cl_2$ (20 mL), and the resulting solution was stirred for 30 min. 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 × 5 mL) and air-dried to afford **3a2** as a yellow solid. Yield: 74 mg, 0.140 mmol, 76%. Mp: 118 °C. Anal. Calcd for $C_{20}H_{27}BrN_2O_3Pd$ (529.770): C, 45.34; H, 5.14; N, 5.29. Found: C, 45.28; H, 4.99; N, 5.27. IR ($cm^{-1}$): $\nu$(NH) 3220 w, 3173 w, 3135 w; $\nu$(CN) 1601 s; $\nu$(CO) 1511 s. $^1$H NMR (400.91 MHz): $\delta$ 2.02 (dd, 1 H, $C^{\beta}H_2$, $^2J_{HH}$ = 14.0, $^3J_{HH}$ = 6.0 Hz), 2.14 (s, 3 H, MeCO), 2.36 (s, 3 H, Me, pic), 2.38 (m, partially obscured by the Me signal, 1 H, $NH_2$), 2.76 (br d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.8 Hz), 3.07 (br d, 1 H, $NH_2$ $^2J_{HH}$ = 14.0 Hz), 3.12−3.19 (m, 2 H, 1 H of $CH_2N$ + 1 H of $CH_2Ar$), 3.34−3.43 (m, 2 H, 1 H of $CH_2N$ + 1 H of $C^{\beta}H_2$), 3.63 (dd, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 11.2, $^3J_{HH}$ = 6.0 Hz), 3.85 (s, 3 H, MeO), 3.96 (s, 3 H, MeO), 6.57 (s, 1 H, H6), 6.90 (s, 1 H, H3), 7.07 ("d", 2 H, *m*-H, pic, $^3J_{HH}$ = 6.4 Hz), 7.07 ("d", 2 H, *o*-H, pic, $^3J_{HH}$ = 6.4 Hz). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 0.6 (s, Me, pic), 29.2 (s, *Me*CO), 30.9 (s, $C^{\beta}H_2$), 32.4 (s, $CH_2Ar$), 47.0 (s, $C^{\alpha}H$), 47.8 (s, $CH_2N$), 55.4 (s, MeO), 55.5 (s, MeO), 111.0 (s, CH, C6), 113.7 (s, CH, C3), 125.5 (s, *m*-CH, pic), 129.3 (s, C2), 133.3 (s, C1), 146.9 (s, C4 + C5), 149.4 (s, *p*-C, pic), 151.4 (s, *o*-CH, pic). The $^{13}$C NMR resonance corresponding to the CO group was not observed. Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of $Et_2O$ into a solution of **3a2** in $CH_2Cl_2$.

**Synthesis of [Pd{*C*,*N*-CH($C_5H_8$)CH$C_6H_2CH_2CH_2NH_2$-2,(OMe)$_2$-4,5}Br($NC_5H_4$Me-4)]·$H_2O$ (3a3·$H_2O$).** 4-Picoline (12.4 $\mu$L, 0.127 mmol) was added to a solution of complex **2a3** (60 mg, 0.064 mmol) in $CH_2Cl_2$ (20 mL), and the resulting solution was stirred for 30 min. 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 × 5 mL) and air-dried to afford a first crop of **3a3**·$H_2O$ as a yellow solid (52 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **3a3**·$H_2O$ as a yellow solid (10 mg). Yield: 62 mg, 0.108 mmol, 85%. Mp: 125 °C. Anal. Calcd for $C_{23}H_{31}BrN_2O_2Pd\cdot H_2O$ (571.837): C, 48.31; H, 5.82; N, 4.90. Found: C, 47.90; H, 5.67; N, 4.81. IR ($cm^{-1}$): $\nu$(NH) 3299 m, 3249 m, 3206 w; $\nu$(CN) 1614 s. $^1$H NMR (400.91 MHz): $\delta$ 0.56 (d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 9.6 Hz), 0.83 (d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 9.6 Hz), 1.23−1.29 (m, 2 H, 1 H of $CH_2$ nor + 1 H of $CH_2$ nor), 1.37−1.43 (m, 1 H, $CH_2$ nor), 1.37−1.43 (m, 1 H, $CH_2$ nor), 1.59−1.63 (m, partially obscured by the $H_2O$ signal, 1 H, $CH_2$ nor), 2.08 (d, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 3.6 Hz), 2.23 (d, 1 H, CH nor, $^3J_{HH}$ = 8.8 Hz), 2.30 (s, 3 H, Me, pic), 2.41 (d, 1 H, $C^{\beta}H$, $^3J_{HH}$ = 3.6 Hz), 2.66 (m, 1 H, $CH_2Ar$), 2.76 (d, 1 H, CH nor, $^3J_{HH}$ = 8.8 Hz), 2.83 (dd, 1 H, $CH_2Ar$, $^2J_{HH}$ = 16.0, $^3J_{HH}$ = 4.0 Hz), 3.29−3.41 (m, 3 H, $CH_2N$ + 1 H of $NH_2$), 3.60 (br s, 1 H, $NH_2$), 3.85 (s, 3 H, MeO), 3.96 (s, 3 H, MeO), 6.71 (s, 1 H, H6), 6.88 (s, 1 H, H3), 7.07 (d, 2 H, *m*-H, pic, $^3J_{HH}$ = 4.4 Hz), 8.05 (br s, 2 H, *o*-H, pic). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 21.1 (s, Me, pic), 30.2 (s, $CH_2$ nor), 31.1 (s, $CH_2$ nor), 33.0 (s, $CH_2Ar$), 36.2 (s, $CH_2$ nor), 40.9 (s, CH nor), 42.9 (s, CH nor), 46.1 (s, $C^{\alpha}H$), 47.0 (s, $CH_2N$), 51.4 (s, $C^{\beta}H$), 55.9 (s, MeO), 56.0 (s, MeO), 108.3 (s, CH, C6), 113.8 (s, CH, C3), 125.3 (s, *m*-CH, pic), 124.9 (s, *o*-CH, pic), 131.5 (s, C2), 137.1 (s, C1), 146.4 (s, C5), 147.0 (s, C5), 148.7 (s, *p*-C, pic).

**Synthesis of 5-Ethoxycarbonyl-8,9-dimethoxy-1,2,5,6-tetrahydro-3-benzazocin-4-one (4a1).** CO was bubbled for 5 min through a solution of complex **2a1** (75 mg, 0.080 mmol) in $CHCl_3$ (30 mL), and the resulting mixture was heated at 65 °C for 16 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting mixture was slowly 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 × 5 mL) and air-dried to afford a first crop of **4a1** as an off-white solid (15 mg). The solvent was removed from the filtrate, and the residue was vigorously stirred in *n*-pentane (3 mL). The suspension was filtered, and the solid was air-dried to afford a second crop of **4a1** as an off-white solid (18 mg). Yield: 33 mg, 0.107 mmol, 67%. Mp: 93 °C. ESI-HRMS: exact mass calcd for $C_{16}H_{22}NO_5$ 308.1498 [$(M + H)^+$]; found 308.1499 [$(M + H)^+$]; Δ = 0.0001. IR ($cm^{-1}$): $\nu$(NH) 3333 m; $\nu$(CO) 1740 m; $\nu(CO_{NH})$ 1655 m. $^1H$ NMR (400.91 MHz): δ 1.31 (t, 3 H, Me, $^3J_{HH}$ = 7.2 Hz), 2.96−3.04 (m, 2 H, $CH_2Ar$), 3.14 (m, 1 H, $CH_2CH$), 3.40 (m, 1 H, $CH_2CH$), 3.47−3.53 (m, 1 H, $CH_2N$), 3.71−3.77 (m, 1 H, $CH_2N$), 3.84 (s, 3 H, MeO), 3.86 (s, 3 H, MeO), 3.88 (m, partially obscured by the MeO signal, 1 H, CH), 4.27 (q, 2 H, $CH_2O$, $^3J_{HH}$ = 7.2 Hz), 5.54 (br s, 1 H, NH), 6.56 (s, 1 H, H10), 6.75 (s, 1 H, H7). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 14.1 (s, Me), 32.9 (s, $CH_2CH$), 35.2 (s, $CH_2Ar$), 40.4 (s, $CH_2N$), 53.2 (s, CH), 55.9 (s, MeO), 61.7 (s, $CH_2O$), 113.8 (s, CH, C10), 114.2 (s, CH, C7), 128.2 (s, C10a), 128.8 (s, C6a), 147.7 (s, C9), 147.9 (s, C8), 169.9 (s, $CO_2Et$). The $^{13}C$ NMR resonance corresponding to the CO group was not observed. Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of *n*-pentane into a solution of **4a1** in $CHCl_3$.

**Synthesis of 5-Acetyl-8,9-dimethoxy-1,2,5,6-tetrahydro-3-benzazocin-4-one (4a2).** CO was bubbled for 5 min through a solution of complex **2a2** (75 mg, 0.086 mmol) in $CHCl_3$ (30 mL), and the resulting mixture was heated at 65 °C for 16 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting suspension 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 × 5 mL) and air-dried to afford a first crop of **4a2** as a pale yellow solid (18 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **4a2** as a pale yellow solid (16 mg). Yield: 34 mg, 0.123 mmol, 72%. Mp: 112 °C. ESI-HRMS: exact mass calcd for $C_{15}H_{20}NO_4$ 278.1392 [$(M + H)^+$]; found 278.1395; Δ = 0.0003. IR ($cm^{-1}$): $\nu$(NH) 3277 w, 3196 m; $\nu$(CO) 1721 vs; $\nu(CO_{NH})$ 1646 vs. $^1H$ NMR (400.91 MHz): δ 2.14 (s, 3 H, Me), 2.90−2.97 (m, 2 H, 1 H of $CH_2CH$ + 1 H of $CH_2Ar$), 3.07−3.12 (m, 1 H, $CH_2CH$), 3.37−3.44 (s, 2 H, 1 H of $CH_2Ar$ + 1 H of $CH_2N$), 3.80−3.74 (m, 1 H, $CH_2N$), 3.84 (s, 3 H, MeO), 3.85 (s, 3 H, MeO), 3.92 (m, 1 H, CH), 5.51 (br s, 1 H, NH), 6.56 (s, 1 H, H7), 6.70 (s, 1 H, H10). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 29.32 (s, Me), 31.0 (s, $CH_2Ar$), 40.1 (s, $CH_2CH$), 40.2 (s, $CH_2N$), 55.9 (s, MeO), 55.9 (s, MeO), 61.9 (s, CH), 113.7 (s, CH, C10), 114.4 (s, CH, C7), 128.2 (s, C6a), 128.8 (s, C10a), 147.7 (s, C8), 147.8 (s, C9), 171.8 (s, CONH), 203.1 (s, COMe).

**Synthesis of 5,6-(Cyclopenta-1,3-diyl)-8,9-dimethoxy-1,2,5,6-tetrahydro-3-benzazocin-4-one (4a3).** CO was bubbled for 5 min through a suspension of complex **2a3** (60 mg, 0.065 mmol) and $Na_2CO_3$ (28 mg, 0.260 mmol) in $CHCl_3$ (30 mL), and the resulting mixture was heated at 65 °C for 16 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting suspension 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 × 5 mL) and air-dried to afford a first crop of **4a3** as a colorless solid (13 mg). The filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The resulting suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford a second crop of **4a3** as a colorless solid (21 mg). Yield: 34 mg, 0.165 mmol, 98%. Mp: 117 °C. ESI-HRMS: exact mass calcd for $C_{18}H_{24}NO_3$ 302.1753 [$(M + H)^+$]; found 302.1755 [$(M + H)^+$]; Δ = 0.0002. IR ($cm^{-1}$): $\nu$(NH) 3362 m; $\nu$(CO) 1646 s. $^1H$ NMR (400.91 MHz): δ 1.30−1.43 (m, 2 H, 1 H of $CH_2$ nor + 1 H of $CH_2$ nor), 2.34 (br d, 1 H, 1 H of $CH_2$ nor, $^3J_{HH}$ = 10.0 Hz), 1.61−1.79 (m, 2 H, 1 H of $CH_2$ nor + 1 H of $CH_2$ nor), 2.10 (br d, 1 H, 1 H of $CH_2$ nor, $^3J_{HH}$ = 9.6 Hz), 2.66 (m, 2 H, CH nor + CH nor), 2.74−2.80 (m, 1 H, 1 H of $CH_2Ar$), 2.08 (d, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 10.0 Hz), 3.19−3.29 (m, 3 H, 1 H of $CH_2Ar$ + 1 H of $CH_2N$ + $C^{\beta}H$), 3.68−3.75 (m, 1 H, 1 H of $CH_2Ar$), 3.83 (s, 3 H, MeO), 3.85 (s, 3 H, MeO), 5.15 (m, 1 H, NH), 6.56 (s, 1 H, H10), 6.85 (s, 1 H, H7). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 29.0 (s, $CH_2$ nor), 30.3 (s, $CH_2$ nor), 32.2 (s, $CH_2Ar$), 36.9 (s, $CH_2$ nor), 38.9 (s, $CH_2N$), 39.4 (s, CH nor), 39.5 (s, CH nor), 49.2 (s, $C^{\beta}H$), 52.2 (s, $C^{\alpha}H$), 55.9 (s, MeO), 55.9 (s, MeO), 109.7 (s, CH, C7), 113.7 (s, CH, C10), 1278.4 (s, C10a), 133.0 (s, C6a), 147.4 (s, C9), 147.8 (s, C8), 175.8 (s, CO).

**Synthesis of 2,2-Dimethyl-5-ethoxycarbonyl-1,2,5,6-tetrahydro-3-benzazocin-4-one (4b1).** CO was bubbled for 5 min through a solution of complex **2b1** (150 mg, 0.192 mmol) in $CH_2Cl_2$ (15 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 3 mL, and $Et_2O$ (15 mL) was added. The resulting suspension was filtered through a plug of Celite, the filtrate was concentrated to ca. 4 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford **4b1** as a colorless solid (64 mg, 0.232 mmol). In the mother liquors, more solid crystallized. The suspension was filtered, and the solid was washed with *n*-pentane (5 mL) and air-dried to give a second crop of **4b1** (13 mg, 0.047 mmol). Yield: 78 mg, 0.279 mmol, 73%. Mp: 160 °C. Anal. Calcd for $C_{16}H_{21}NO_3$ (275.152): C, 69.79; H, 7.69; N, 5.09. Found: C, 69.85; H, 8.00; N, 5.11. IR ($cm^{-1}$): $\nu$(NH) 3289 w, 3205 s, 3068 s; $\nu(CO_2R)$ 1732 vs; $\nu(CO_{NH})$ 1651 vs. $^1H$ NMR (400.91 MHz): δ 1.26 (s, 3 H, Me, $CMe_2$), 1.30 ($X_3$ part of an $ABX_3$ system, 3 H, $MeCH_2$, $^3J_{AX}$ = $^3J_{BX}$ = 7.2 Hz), 1.60 (s, 3 H, Me, $CMe_2$), 2.68 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.4 Hz), 3.29 (dd, 1 H, $CH_2CH$, $^2J_{HH}$ = 15.6, $^3J_{HH}$ = 8.4 Hz), 3.32 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 15.2 Hz), 3.52 (dd, 1 H, $CH_2CH$, $^2J_{HH}$ = 15.6, $^3J_{HH}$ = 11.2 Hz), 4.24 (m, 1 H, CH, partially obscured by the resonance of $CH_2O$), 4.26 (AB part of an $ABX_3$ system, 2 H, $CH_2O$, $^2J_{AB}$ = 2.8 Hz), 5.16 (s, 1 H, NH), 7.02−7.05 (m, 1 H, H10), 7.17− 7.20 (m, 2 H, H8 + H9), 7.23 −7.25 (m, 1 H, H7). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 14.21 (s, $MeCH_2$), 30.0 (s, Me, $CMe_2$), 30.1 (s, Me, $CMe_2$), 33.7 (s, $CH_2CH$), 45.7 (s, $CH_2Ar$), 49.2 (s, CH), 53.2 (s, $CMe_2$), 61.5 (s, $CH_2O$), 126.8 (s, CH, C9), 127.5 (s, CH, C8), 130.9 (s, CH, C10), 131.5 (s, CH, C7), 135.2 (s, C10a), 137.0 (s, C6a), 169.3 (s, $CO_2R$), 170.4 (s, CONH). Single crystals suitable for an X-ray diffraction study were obtained by slow evaporation of the solvent from a solution of **4b1** in $CHCl_3$.

**Synthesis of 2,2-Dimethyl-5-acetyl-1,2,5,6-tetrahydro-3-benzazocin-4-one (4b2).** Method A: CO was bubbled for 5 min through a solution of complex **2b2** (125 mg, 0.168 mmol) in $CH_3CN$ (15 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, and the solvent was removed from the filtrate. $CH_2Cl_2$ (2 mL) and $Et_2O$ (15 mL) were added, the resulting suspension was filtered, the filtrate was concentrated to ca. 2 mL, and *n*-pentane (20 mL) was added. The suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to afford **4b2** as a colorless solid. Yield: 19 mg, 0.08 mmol, 24%. Method B: TlOTf (118 mg, 0.333 mmol) was added to a solution of complex **3b2** (150 mg, 0.330 mmol) in $CH_2Cl_2$ (15 mL), the resulting suspension was stirred for 3 h, CO was bubbled for 5 min through the suspension, and the mixture was stirred for 12 h under a CO atmosphere (1 atm). 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 $Et_2O$ (20 mL) was added. The suspension was filtered to remove the picolinium triflate formed. The solvent was removed from the filtrate, the residue was dissolved in $CH_2Cl_2$ (20 mL), $Na_2CO_3$ (200 mg, 1.89 mmol) was added, and the mixture was stirred for 3 h. The suspension was filtered, the solvent was removed from the filtrate, and $Et_2O$ (15 mL) was added. The suspension was filtered, and the solid was washed with $Et_2O$ (2 × 5 mL) and air-dried to afford **4b2** as a colorless solid (30 mg). When the mother liquors were cooled in an ice bath, a solid crystallized in the mixture, which was filtered and washed with cold $Et_2O$ (5 mL) and air-dried to give a second crop of **4b2** as a colorless solid (12 mg). Yield: 42 mg, 0.171 mmol, 52%. Mp: 196−198 °C. ESI-HRMS: exact mass calcd for $C_{15}H_{19}NO_2$ 245.1416; found 245.1426; Δ = 0.001. IR ($cm^{-1}$): ν(NH) 3283 w, 3209 m; ν(CO) 1727 vs; ν($CO_{NH}$) 1652 vs. $^1H$ NMR (400.91 MHz): δ 1.30 (s, 3 H, Me, $CMe_2$), 1.62 (s, 3 H, Me, $CMe_2$), 2.27 (s, 3 H, COMe), 2.70 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.4 Hz), 3.16 (dd, 1 H, $CH_2CH$, $^2J_{HH}$ = 15.6 Hz, $^3J_{HH}$ = 8.8 Hz), 3.31 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.4 Hz), 3.46 (dd, 1 H, $CH_2CH$, $^2J_{HH}$ = 15.6 Hz, $^3J_{HH}$ = 10.8 Hz), 4.20 (t, 1 H, CH, $^3J_{HH}$ = 9.6 Hz), 5.29 (br s, 1 H, NH), 7.03−7.06 (m, 1 H, H10), 7.17−7.19 (m, 2 H, H8 + H9), 7.20−7.24 (m, 1 H, H7). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 29.2 (s, CO*Me*), 30.0 (s, Me, $CMe_2$), 30.4 (s, Me, $CMe_2$), 32.3 (s, $CH_2CH$), 45.6 (s, $CH_2Ar$), 53.3 (s, $CMe_2$), 56.53 (s, CH), 126.7 (s, CH, C9), 127.5 (s, CH, C8), 130.8 (s, CH, C10), 131.5 (s, CH, C7), 135.1 (s, C10a), 137.4 (s, C6a), 171.1 (s, CONH), 201.6 (s, CO). Single crystals suitable for an X-ray diffraction study were obtained by slow evaporation of a solution of **4b2** in $CHCl_3$.

**Synthesis of 2,2-Dimethyl-5,6-(cyclopenta-1,3-diyl)-1,2,5,6-tetrahydro-3-benzazocin-4-one (4b3).** CO was bubbled for 5 min through a suspension of complex **2b3** (160 mg, 0.208 mmol) in $CH_2Cl_2$ (15 mL), and the resulting mixture was stirred for 24 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 3 mL, and $Et_2O$ (15 mL) was added. The resulting suspension was filtered through a plug of Celite, the solvent was removed from the filtrate, and $Et_2O$ (10 mL) was added. The suspension was filtered, and the solid was washed with $Et_2O$ (5 mL) and air-dried to afford **4b3** as a colorless solid. Yield: 75 mg, 0.278 mmol, 67%. Mp: 169 °C. ESI-HRMS: exact mass calcd for $C_{18}H_{23}NO$ 269.1780; found 269.1784; Δ = 0.0004. IR ($cm^{-1}$): ν(NH) 3282 w, 3210 m; ν(CO) 1653 vs. $^1H$ NMR (300.1 MHz): δ 1.25 (s, 3 H, Me, $CMe_2$), 1.30−1.43 (m partially obscured by the resonance of $CMe_2$, 2 H, $CH_2$ nor), 1.47 (d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 8.7 Hz), 1.54 (s, 3 H, Me, $CMe_2$), 1.65−1.79 (m, 2 H, $CH_2$ nor), 2.08 (d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 8.4 Hz), 2.60 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 13.8 Hz), 2.73 (br s, 2 H, CH nor + CH nor), 2.89 (br d, 1 H, $C^{\alpha}H$, $^3J_{HH}$ = 9.6 Hz), 3.55 (d, 1 H, $C^{\beta}H$, $^3J_{HH}$ = 9.9 Hz), 3.28 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 13.8 Hz), 4.87 (br s, 1 H, NH), 7.06 (d, 1 H, H10, $^3J_{HH}$ = 6.9 Hz), 7.15 (t, 1 H, H9, $^3J_{HH}$ = 6.9 Hz), 7.21 (t, 1 H, H8, $^3J_{HH}$ = 7.2 Hz), 7.31 (d, 1 H, H7, $^3J_{HH}$ = 7.2 Hz). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 28.0 (s, $CH_2$ nor), 30.0 (s, Me, $CMe_2$), 30.9 (s, $CH_2$ nor), 31.2 (s, Me, $CMe_2$), 37.4 (s, $CH_2$ nor), 38.2 (s, CH nor), 41.1 (s, CH nor), 44.0 (s, $CH_2Ar$), 50.0 (s, $C^{\beta}H$), 52.2 (s, $CMe_2$), 53.6 (s, $C^{\alpha}H$), 125.2 (s, CH, C7), 125.9 (s, CH, C9), 127.2 (s, CH, C8), 129.3 (s, CH, C10), 136.5 (s, C10a), 140.8 (s, C6a), 174.2 (s, CO).

**Synthesis of 2-(1-Methoxycarbonyl-1-ethoxycarbonylethyl)-homoveratrylamine Hydrobromide (5a1).** CO was bubbled for 5 min through a solution of complex **2a1** (90 mg, 0.096 mmol) in MeOH (30 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting suspension was filtered through a plug of Celite, and the solvent was removed from the filtrate. The residue was vigorously stirred in $Et_2O$ (30 mL), and the solid was filtered, washed with $Et_2O$ (2 × 5 mL), and dried under nitrogen to afford **5a1** as a colorless solid. Yield: 55 mg, 0.142 mmol, 73%. Mp: 105 °C. ESI-HRMS: exact mass calcd for $C_{17}H_{26}NO_6$ 340.1760 [(M − Br)$^+$]; found 340.1777 [(M − Br)$^+$]; Δ = 0.0017. $\Lambda_M$ ($\Omega^{-1}$ $cm^2$ $mol^{-1}$): 11 (5.10 × $10^{-4}$ M). IR ($cm^{-1}$): ν(NH) 3452 w, 3366 w, 3173 w, 3187 w; ν(CO) 1747 s, 1735 s. $^1H$ NMR (400.91 MHz): δ 1.58 (t, 3 H, Me, $^3J_{HH}$ = 7.2 Hz), 3.21 (m, 4 H, $CH_2CH$ + $CH_2Ar$), 3.32 (m, 2 H, $CH_2N$), 3.66 (s, 3 H, MeO, $CO_2Me$), 3.67−3.72 (m, partially obscured by the MeO signal, 1 H, CH), 3.80 (s, 3 H, MeO), 3.86 (s, 3 H, MeO), 4.10 (q, 2 H, $CH_2O$, $^3J_{HH}$ = 6.6 Hz), 6.64 (s, 1 H, H3), 6.82 (s, 1 H, H6), 7.36 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 13.9 (s, Me), 29.9 (s, $CH_2Ar$), 31.0 (s, $CH_2CH$), 41.1 (s, $CH_2N$), 52.7 (s, MeO, $CO_2$*Me*), 53.1 (s, CH), 55.9 (s, MeO), 56.1 (s, MeO), 61.8 (s, $CH_2O$), 112.8 (s, CH, C3), 113.2 (s, CH, C6), 127.0 (s, C1), 127.9 (s, C2), 147.9 (s, C4), 148.0 (s, C5), 169.1 (s, $CO_2Et$), 169.6 (s, $CO_2Me$).

**Synthesis of 2-(1-Methoxycarbonylnorbornyl)-homoveratrylamine Hydrobromide (5a3).** CO was bubbled for 5 min through a solution of complex **2a3** (80 mg, 0.087 mmol) in MeOH (20 mL), and the resulting mixture was stirred for 16 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting suspension was filtered through a plug of Celite, and the solvent was removed from the filtrate. The residue was vigorously stirred in *n*-pentane (30 mL), and the solid was filtered, washed with *n*-pentane (2 × 5 mL), and dried under nitrogen to afford **5a3** as a colorless solid. Yield: 50 mg, 0.121 mmol, 70%. Mp: 79 °C. ESI-HRMS: exact mass calcd for $C_{19}H_{28}NO_4$ 334.2018 [(M − Br)$^+$]; found 334.2015 [(M − Br)$^+$]; Δ = 0.0003. $\Lambda_M$ ($\Omega^{-1}$ $cm^2$ $mol^{-1}$): 12 (5.02 × $10^{-4}$ M). IR ($cm^{-1}$): ν(NH) 3366 br w; ν(CO) 1719 s. $^1H$ NMR (200.13 MHz): δ 1.28−1.73 (m, 5 H, $CH_2$ nor + $CH_2$ nor + 1 H of $CH_2$ nor), 2.34 (br s, 1 H, 1 H of $CH_2$ nor), 2.42 (br s, 1 H, CH nor), 2.56 (br s, 1 H, CH nor), 3.13 (s, 3 H, MeO), 3.17−3.45 (m, 6 H, $CH_2Ar$ + $CH_2N$ + $C^{\alpha}H$ + $C^{\beta}H$), 3.82 (s, 3 H, MeO), 3.86 (s, 3 H, MeO), 6.75 (s, 1 H, H6), 6.78 (s, 1 H, H3), 8.12 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 27.9 (s, $CH_2$ nor), 30.4 (s, $CH_2Ar$), 31.4 (s, $CH_2$ nor), 38.5 (s, $CH_2$ nor), 39.2 (s, CH nor), 41.2 (s, $CH_2N$), 42.1 (s, CH nor), 47.0 (s, $C^{\beta}H$), 51.3 (s, MeO), 55.4 (s, $C^{\alpha}H$), 55.9 (s, MeO), 56.1 (s, MeO), 110.2 (s, CH, C3), 112.8 (s, CH, C6), 127.0 (s, C1), 133.1 (s, C2), 147.4 (s, C5), 147.8 (s, C4), 174.4 (s, CO).

**Synthesis of 2-(1,1-Di(ethoxycarbonyl)ethyl)phentermine Hydrochloride (5b1).** CO was bubbled for 5 min through a suspension of complex **2b1** (150 mg, 0.192 mmol) in EtOH (15 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The suspension was filtered through a plug of Celite, the solvent was removed from the filtrate, $Et_2O$ (10 mL) was added to the residue, and the mixture was vigorously stirred. The resulting suspension was filtered, and the solid was washed with $Et_2O$ (2 × 5 mL) and air-dried to give a first crop of **5b1** as a colorless solid (39 mg). The mother liquors were concentrated to ca. 3 mL, *n*-pentane (20 mL) was added, the suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to give a second crop of **5b1** as a colorless solid (27 mg). Yield: 66 mg, 0.184 mmol, 48%. Mp: 103 °C. $\Lambda_M$ ($\Omega^{-1}$ $cm^2$ $mol^{-1}$): 6 (5.20 × $10^{-4}$ M). Anal. Calcd for $C_{18}H_{28}ClNO_4$ (357.872): C, 60.41; H, 7.89; N, 3.9. Found: C, 60.56; H, 8.27; N, 3.90. IR ($cm^{-1}$): bands corresponding to the $NH_3$ group were not observed; ν($CO_2R$) 1747 s, 1731 s. $^1H$ NMR (400.91 MHz): δ 1.17 (br t, 6 H, *Me*$CH_2$, $^3J_{HH}$ = 6.0 Hz), 1.50 (s, 6 H, $CMe_2$), 3.20 (s, 2 H, $CH_2Ar$), 3.31 (br d, 2 H, $CH_2CH$, $^3J_{HH}$ = 5.2 Hz), 3.64 (br s, 1 H, CH), 4.12 (br q, 4 H, $CH_2O$, $^3J_{HH}$ = 6.4 Hz), 7.19 (br s, 3 H, H3 + H4 + H5), 7.32 (br s, 1 H, H6), 8.52 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 14.0 (s, *Me*$CH_2$), 25.8 (s, C*Me*$_2$), 31.7 (s, $CH_2CH$), 41.7 (s, $CH_2Ar$), 53.4 (s, CH), 56.4 (s, $CMe_2$), 61.6 (s, $CH_2O$), 127.3 (s, CH, C4), 127.7 (s, CH, C5), 129.7 (s, CH, C3), 132.2 (s, CH, C6), 133.2 (s, C1), 137.0 (s, C2), 168.7 (s, CO).

**Synthesis of 2-(1-Methoxycarbonylnorbornyl)phentermine Hydrochloride (5b3).** CO was bubbled for 5 min through a suspension of complex **2b3** (200 mg, 0.260 mmol) in MeOH (15 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The suspension was filtered through a plug of Celite, the filtrate was concentrated to ca. 1 mL, and $Et_2O$ (25 mL) was added. The resulting suspension was filtered, and the solid was washed with $Et_2O$ (2 × 5 mL) and air-dried to afford compound **5b3** as a colorless solid. Yield: 154 mg, 0.456 mmol, 88%. Mp: 238 °C. $\Lambda_M$ ($\Omega^{-1}$ $cm^2$ $mol^{-1}$): 6 (4.70 × $10^{-4}$ M). Anal. Calcd for $C_{19}H_{28}ClNO_2$ (337.884): C, 67.54; H, 8.35; N, 4.15. Found: C, 67.59; H, 8.37; N, 4.11. IR ($cm^{-1}$): bands corresponding to the $NH_3$ group were not observed; ν($CO_2R$) = 1737 vs. $^1H$ NMR (400.91 MHz): δ 1.48 (s, 3 H, Me, $CMe_2$), 1.48−1.56 (m, partially obscured by the resonance of $CMe_2$, 3 H, $CH_2$ nor), 1.53 (s, 3 H, Me, $CMe_2$), 1.62−1.64 (m, 2 H, $CH_2$ nor), 2.40 (d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 10.0 Hz), 2.47 (s, 1 H, CH nor), 2.52 (s, 1 H, CH nor), 2.91 (s, MeO), 3.05 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 14.0 Hz), 3.16 (d, 1 H,

$C^{\alpha}H$, $^3J_{HH}$ = 9.6 Hz), 3.50 (d, partially obscured by the resonance of $C^{\beta}H$, 1 H, $CH_2Ar$), 3.55 (d, 1 H, $C^{\beta}H$, $^3J_{HH}$ = 9.6 Hz), 7.07−7.19 (m, 3 H, H4 + H5 + H6), 7.29 (d, 1 H, H3, $^3J_{HH}$ = 8.0 Hz), 8.69 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 24.7 (s, Me, $CMe_2$), 25.9 (s, Me, $CMe_2$), 27.7 (s, $CH_2$ nor), 31.3 (s, $CH_2$ nor), 38.2 (s, $CH_2$ nor), 39.5 (s, CH nor), 41.4 (s, CH nor), 41.7 (s, $CH_2Ar$), 47.7 (s, $C^{\beta}H$), 50.5 (s, MeO), 54.2 (s, $C^{\alpha}H$), 56.6 (s, $CMe_2$), 125.9 (s, CH, C5), 127.0 (s, CH, C3), 127.2 (s, CH, C4), 130.9 (s, CH, C6), 134.0 (s, C1), 141.6 (s, C2), 173.3 (s, CO). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of $Et_2O$ into a solution of **5b3** in $CHCl_3$.

**Synthesis of 2-(Acetylethyl)phentermine Hydrochloride (6b2).** CO was bubbled for 5 min through a suspension of complex **2b2**·1/4$CH_2Cl_2$ (160 mg, 0.216 mmol) in MeOH (15 mL), and the resulting mixture was stirred for 48 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The suspension was filtered through a plug of Celite, and the solvent was removed from the filtrate. The residue was dissolved in $CH_2Cl_2$ (1 mL), and $Et_2O$ (20 mL) was added. The resulting suspension was filtered, and the solid was washed with $Et_2O$ (2 × 5 mL) and air-dried to afford **6b2** as a colorless solid. Yield: 102 mg, 0.399 mmol, 92%. Mp: 133 °C. $\Lambda_M$ ($\Omega^{-1}$ cm$^2$ mol$^{-1}$): 8 (5.43 × $10^{-4}$ M). Anal. Calcd for $C_{14}H_{22}ClNO$ (255.784): C, 65.74; H, 8.67; N, 5.48. Found: C, 65.56; H, 8.75; N, 5.43. IR (cm$^{-1}$): $\nu$(NH) 3392 w; $\nu$(CO) 1703 vs. $^1H$ NMR (400.91 MHz): $\delta$ 1.48 (s, 6 H, $CMe_2$), 2.11 (s, 3 H, COMe), 2.71 (t, 2 H, $CH_2CO$, $^3J_{HH}$ = 7.2 Hz), 3.00 (t, 2 H, Ar$CH_2$CH$_2$, $^3J_{HH}$ = 7.6 Hz), 3.20 (s, 2 H, $CH_2CMe_2$), 7.13−7.21 (m, 3 H, H3 + H4 + H5), 7.24 (d, 1 H, H6, $^3J_{HH}$ = 7.6 Hz), 8.60 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 25.5 (s, C*Me*$_2$), 26.9 (s, $CH_2Ar$), 30.2 (s, CO*Me*), 41.6 (s, $CH_2CMe_2$), 44.8 (s, $CH_2CO$), 56.6 (s, $CMe_2$), 126.4 (s, CH, C5), 127.7 (s, CH, C4), 129.5 (s, CH, C3), 131.9 (s, CH, C6), 132.8 (s, C1), 140.3 (s, C2), 207.8 (s, CO). Data corresponding to the deuterated product **6b2-*d*$_1$** (obtained when the reaction was carried out using MeOD as solvent): ESI-HRMS exact mass calcd for $C_{14}H_{21}DNO$, 221.1764 [M$^+$]; found 221.1771 [M$^+$]; Δ = 0.0007. $^1H$ NMR (300.1 MHz): $\delta$ 1.48 (s, 6 H, $CMe_2$), 2.11 (s, 3 H, COMe), 2.70 (m, 1 H, CHDCO), 3.00 (d, 2 H, $CH_2Ar$, $^3J_{HH}$ = 7.5 Hz), 3.20 (s, 2 H, $CH_2CMe_2$), 7.13−7.21 (m, 3 H, H3 + H4 + H5), 7.24 (d, 1 H, H6, $^3J_{HH}$ = 7.6 Hz), 8.6 (br s, 3 H, $NH_3$). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of $Et_2O$ into a solution of **6b2** in $CH_2Cl_2$.

**Synthesis of 1,3-Bis(4,5-Dimethoxy-2-(3-oxobutyl)-phenethyl)urea (7a2).** CO was bubbled for 5 min through a solution of complex **2a2** (80 mg, 0.092 mmol) and $NEt_3$ (0.026 mL, 0.183 mmol) in $CH_2Cl_2$ (20 mL), and the resulting mixture was stirred for 12 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The resulting suspension was filtered through a plug of Celite, and the solvent was removed from the filtrate. The residue was vigorously stirred in $Et_2O$ (30 mL), and the solid was filtered, washed with $Et_2O$ (2 × 5 mL), and air-dried to afford a mixture of compound **7a2** and $NHEt_3Br$. This solid was dissolved in $CH_2Cl_2$ (20 mL), and $Na_2CO_3$ was added (100 mg, 0.943 mmol). The resulting suspension was stirred for 6 h and then 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 × 5 mL) and air-dried to afford **7a2** as a colorless solid. Yield: 32 mg, 0.115 mmol, 63%. Mp: 107 °C. ESI-HRMS: exact mass calcd for $C_{29}H_{41}N_4O_7$ 529.2914 [(M + 1)$^+$]; found 529.2913; Δ = 0.0001. IR (cm$^{-1}$): $\nu$(NH) 3363 s; $\nu$(CO) 1713 s; $\nu$(CO$_{NH}$) 1626. $^1H$ NMR (400.91 MHz): $\delta$ 2.14 (s, 3 H, Me), 2.76 (m, 4 H, $CH_2CO$ + $CH_2Ar$), 2.83 (m, 2 H, $CH_2CH_2CO$), 3.39 ("t", 2 H, $CH_2N$, $^3J_{HH}$ = 6.4 Hz), 3.82 (s, 3 H, MeO), 3.83 (s, 3 H, MeO), 4.81 (br s, 1 H, NH), 6.63 (s, 1 H, H3), 6.67 (s, 1 H, H6). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 25.8 (s, $CH_2CH_2CO$), 30.2 (s, Me), 32.6 (s, $CH_2Ar$), 41.6 (s, $CH_2N$), 44.7 (s, $CH_2CO$), 55.9 (s, MeO), 55.9 (s, MeO), 112.0 (s, CH, C3), 112.9 (s, CH, C6), 128.9 (s, C1), 131.0 (s, C2), 147.4 (s, C5), 147.5 (s, C4), 158.2 (s, CONH), 208.6 (s, CO).

**Synthesis of 1,3-Bis(2-methyl-1-(2-(3-oxobutyl)phenyl)-propan-2-yl)urea (7b2).** $Na_2CO_3$ (100 mg, 0.943 mmol) was added to a suspension of complex **2b2**·1/4$CH_2Cl_2$ (150 mg, 0.202 mmol) in MeOH (10 mL), and the mixture was stirred for 24 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, and the solvent was removed from the filtrate. The residue was taken in $CH_2Cl_2$ (30 mL), and the mixture was filtered through a plug of Celite. The solvent was removed from the filtrate, and $Et_2O$ (5 mL) was added. The suspension was filtered, and the solid was washed with $Et_2O$ (2 mL) and air-dried to give a first crop of **7b2** as a colorless solid (12 mg). The mother liquors were concentrated to ca. 1 mL, *n*-pentane (15 mL) was added, and the resulting suspension was cooled in an ice-bath and filtered. The solid was washed with *n*-pentane (5 mL) and air-dried to give a second crop of **7b2** (10 mg) as a colorless solid. The solvent was evaporated from the filtrate, and the residue was vacuum-dried to give **8b2** as a colorless oil (36 mg, 0.146 mmol).

**Data of the Urea 7b2.** Yield: 22 mg, 0.047 mmol, 23%. Mp: 166 °C. ESI-HRMS: exact mass calcd for $C_{29}H_{41}N_2O_3$, 465.3112 [(M + 1)$^+$]; found 465.3137 [(M + 1)$^+$]; Δ = 0.0025. Anal. Calcd for $C_{29}H_{40}N_2O_3$ (464.693): C, 74.96; H, 8.68; N, 6.03. Found: C, 74.73; H, 9.02; N, 6.06. IR (cm$^{-1}$): $\nu$(NH) 3363 s; $\nu$(CO) 1714 s; $\nu$(CO$_{NH}$) 1633 s. $^1H$ NMR (400.91 MHz): $\delta$ 1.33 (s, 6 H, $CMe_2$), 2.12 (s, 3 H, COMe), 2.73 (t, 2 H, $CH_2CO$, $^3J_{HH}$ = 7.2 Hz), 2.96 (t, 2 H, Ar$CH_2$CH$_2$, $^3J_{HH}$ = 7.2 Hz), 3.06 (s, 2 H, $CH_2CMe_2$), 4.29 (s, 1 H, NH), 7.07−7.16 (m, 3 H, H3 + H4 + H5), 7.20 (d, 1 H, H6, $^3J_{HH}$ = 7.6 Hz). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 26.6 (s, Ar$CH_2CH_2$), 28.1 (s, C*Me*$_2$), 30.0 (s, CO*Me*), 41.4 (s, $CH_2CMe_2$), 44.4 (s, $CH_2CO$), 53.8 (s, $CMe_2$), 125.6 (s, CH, C5), 126.5 (s, CH, C4), 128.2 (s, CH, C3), 136.3 (s, C1), 139.9 (s, C2), 157.0 (s, CONH), 208.3 (s, CO).

**Data of the Isocyanate 8b2.** Yield: 36 mg, 0.146 mmol, 34%. IR (cm$^{-1}$): $\nu$(NCO) 2255 s; $\nu$(CO) = 1714 s. $^1H$ NMR (400.91 MHz): $\delta$ 1.39 (s, 6 H, $CMe_2$), 2.20 (s, 3 H, COMe), 2.72 ("t", 2 H, $CH_2CO$, $^3J_{HH}$ = 7.2 Hz), 2.86 (s, 2 H, $CH_2CMe_2$), 2.98 ("t", 2 H, Ar$CH_2$CH$_2$, $^3J_{HH}$ = 7.2 Hz), 7.15−7.23 (m, 4 H, H3 + H4 + H5 + H6). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 26.9 (s, Ar$CH_2CH_2$), 30.0 (s, CO*Me*), 30.6 (s, C*Me*$_2$), 42.0 (s, $CH_2CMe_2$), 45.4 (s, $CH_2CO$), 59.4 (s, $CMe_2$), 125.8 (s, CH, Ar), 127.3 (s, CH, Ar), 129.0 (s, CH, Ar), 131.8 (s, CH, Ar), 134.9 (s, C1), 140.6 (s, C2), 208.2 (s, CO). The $^{13}C$ NMR signal corresponding to the NCO group was not observed.

**Synthesis of 1,1-Diethyl-3-(2-methyl-1-(2-(3-oxobutyl)-phenyl)propan-2-yl)urea (7b2′).** $Et_2NH$ (70 $\mu$L, 0.673 mmol) was added to a suspension of complex **2b2**·1/4$CH_2Cl_2$ (120 mg, 0.166 mmol) in $CH_2Cl_2$ (15 mL), and the mixture was stirred for 24 h under a CO atmosphere (1 atm). Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 1 mL, and *n*-pentane (25 mL) was added. The resulting suspension was filtered to remove the $Et_2NH_2Cl$ formed and other impurities. The solvent was removed from the filtrate to give an oily residue (80 mg), whose $^1H$ NMR spectrum corresponds to a mixture ca. 2:1 of the urea **7b2′** and the isoquinoline **11b2** depicted in Scheme 11. The residue was dissolved in $Et_2O$ (10 mL), and HCl was bubbled through the solution for 1 min. The solvent was concentrated to ca. 2 mL, and *n*-pentane (15 mL) was added. The resulting suspension was filtered, and the solvent was removed to dryness from the filtrate to afford the urea **7b2′** as a pale yellow oil. Yield: 45 mg, 0.141 mmol, 42%. ESI-HRMS: exact mass calcd for $C_{19}H_{31}N_2O_2$, 319.2380 [(M + H)$^+$]; found 419.2396 ; Δ = 0.0016. IR (cm$^{-1}$): $\nu$(NH) 3360 s; $\nu$(CO) 1715 s; $\nu$(CO$_{NH}$) 1634 s. $^1H$ NMR (400.91 MHz): $\delta$ 1.08 (t, 6 H, N(CH$_2$*Me*)$_2$, $^3J_{HH}$ = 7.6 Hz), 1.34 (s, 6 H, $CMe_2$), 2.14 (s, 3 H, COMe), 2.68 (t, 2 H, $CH_2CO$, $^3J_{HH}$ = 7.2 Hz), 2.96 (t, 2 H, $CH_2Ar$, $^3J_{HH}$ = 7.2 Hz), 3.09 (s, 2 H, $CH_2CMe_2$), 3.19 (q, 4 H, N($CH_2$Me)$_2$, $^3J_{HH}$ = 7.6 Hz), 4.01 (s, 1 H, NH), 7.09−7.15 (m, 4 H, Ar). $^{13}C\{^1H\}$ NMR (100.81 MHz): $\delta$ 13.8 (s, N(CH$_2$*Me*)$_2$), 26.9 (s, $CH_2Ar$), 28.2 (s, C*Me*$_2$), 29.9 (s, CO*Me*), 40.7 (s, $CH_2CMe_2$), 41.1 (s, N($CH_2$Me)$_2$), 45.2 (s, $CH_2CO$), 54.0 (s, $CMe_2$), 125.7 (s, CH, C5), 126.5 (s, CH, C4), 128.9 (s, CH, C3), 131.7 (s, CH, C6), 136.3 (s, C1), 140.2 (s, C2), 156.5 (s, CONH), 207.9 (s, CO).

**Synthesis of [$Pd_2Cl_2\{NH_2CMe_2CH_2C_6H_4(CH_2CH_2COMe)\text{-}2\}_2(\mu\text{-}Cl)_2$] (9b2).** HCl was bubbled through a suspension of complex **2b2**·1/4$CH_2Cl_2$ (105 mg, 0.142 mmol) in $CH_2Cl_2$ (15 mL) for 5 min. The suspension became an orange solution, which was concentrated to ca. 2 mL. $Et_2O$ (20 mL) was added, the suspension was filtered, the filtrate was concentrated to ca. 3 mL, and *n*-pentane (15 mL) was added. The resulting suspension was filtered, and the solid was washed with *n*-pentane (2 × 5 mL) and air-dried to give **9b2** as an orange solid. Yield: 81 mg, 0.102 mmol, 72%. Mp: 126 °C. Anal. Calcd for $C_{28}H_{42}Cl_4N_2O_2Pd_2$ (793.297): C, 42.39; H, 5.34; N, 3.53. Found: C, 42.19; H, 5.52; N, 3.51. IR ($cm^{-1}$): $\nu$(NH) 3262 m, 3168 m; $\nu$(CO) 1721 s. $^1$H NMR (300.1 MHz): $\delta$ 1.33 (s, 6 H, $CMe_2$), 2.14 (s, 3 H, COMe), 2.67 (t, 2 H, $CH_2CO$, $^3J_{HH}$ = 7.2 Hz), 2.92 (t, partially obscured by the resonance of $CH_2CMe_2$, 2 H, $CH_2Ar$, $^3J_{HH}$ = 7.2 Hz), 2.96 (s, 2 H, $CH_2CMe_2$), 4.15 (br s, 2 H, $NH_2$), 7.14 (m, 4 H, H3 + H4 + H5 + H6). $^{13}C\{^1H\}$ NMR (75.45 MHz): $\delta$ 27.1 (s, $CH_2Ar$), 28.4 (s, $CMe_2$), 30.1 (s, COMe), 44.4 (s, $CH_2CMe_2$), 45.0 (s, $CH_2CO$), 58.5 (s, $CMe_2$), 126.1 (s, CH, C5), 127.4 (s, CH, C4), 129.6 (s, CH, C3), 131.5 (s, CH, C6), 134.0 (s, C1), 140.2 (s, C2), 207.7 (s, CO). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of *n*-pentane into a solution of **9b2** in $CH_2Cl_2$.

**Synthesis of $[Pd_2Cl_2\{CH(C_5H_8)CHC_6H_4(CH_2CMe_2NH_3)\text{-}2\}_2(\mu\text{-}Cl)_2]\cdot CH_2Cl_2$ (9b3·$CH_2Cl_2$).** HCl was bubbled through a suspension of complex **2b3** (150 mg, 0.195 mmol) in $CH_2Cl_2$ (15 mL) for 5 min. The suspension became an orange solution, and then a yellow solid precipitated in the reaction mixture. The suspension was stirred for 20 min and filtered. The solid was washed with $CH_2Cl_2$ (2 × 5 mL) and air-dried to give **9b3**·$CH_2Cl_2$ as a yellow solid. Yield: 146 mg, 0.157 mmol, 81%. Dec: 172 °C. Anal. Calcd for $C_{34}H_{50}Cl_4N_2Pd_2\cdot CH_2Cl_2$ (926.367): C, 45.38; H, 5.66; N, 3.02. Found: C, 45.17; H, 5.87; N, 3.03. IR ($cm^{-1}$): $\nu$(NH) 3397 (br). The presence of the crystallization solvent was confirmed by reacting **9b3**·$CH_2Cl_2$ with XyNC (molar ratio 1:6) in DMSO-$d_6$ in an NMR tube. The $^1$H spectra of the formed solution corresponds to a 1:0.5 mixture of **10b3**:$CH_2Cl_2$, that is, a half a molecule of $CH_2Cl_2$ per palladium.

**Synthesis of $[PdCl\{C({=}NXy)CH(C_5H_8)CHC_6H_4CH_2CMe_2NH_3\}(CNXy)_2]Cl\cdot H_2O$ (10b3·$H_2O$).** XyNC (150 mg, 1.143 mmol) was added to a suspension of **9b3**·$CH_2Cl_2$ (120 mg, 0.129 mmol) in $CH_2Cl_2$ (15 mL). An orange solution formed, and then a yellow solid precipitated in the reaction mixture. The suspension was stirred for 1 h and filtered. The solid was washed with $CH_2Cl_2$ (2 × 5 mL) and $Et_2O$ (5 mL) and air-dried to give complex **10b3**·$H_2O$ as a yellow solid. Yield: 160 mg, 0.192 mmol, 74%. Mp: 201 °C. Anal. Calcd for $C_{44}H_{52}Cl_2N_4Pd\cdot H_2O$ (832.264): C, 63.50 ; H, 6.54; N, 6.73. Found: C, 63.25; H, 6.71; N, 6.69. IR ($cm^{-1}$): $\nu$(NH) = 3447 w, 3366 w; $\nu$(C≡N) = 2171 vs; $\nu$(C=N) = 1647 s. $^1$H NMR (400.91 MHz, DMSO-$d_6$): $\delta$ 1.18 (s, 3 H, Me, $CMe_2$), 1.24 (s, 3 H, Me, $CMe_2$), 1.45 (br d, 1 H, $CH_2$ nor, $^2J_{HH}$ = 9.2 Hz), 1.55−1.67 (m, 4 H, $CH_2$ nor), 1.74 (s, 3 H, Me, C=NXy), 2.03 (s, 3 H, Me, C=NXy), 2.31 (s, 12 H, Me, C≡NXy), 2.33 (m partially obscured by the resonance of Me group, 1 H, $CH_2$ nor), 2.42 (br s, 1 H, CH nor), 2.93 (d, 1 H, $CH_2Ar$, $^2J_{HH}$ = 13.6 Hz), 3.19 (br d, 1 H, CH nor, $^3J_{HH}$ = 3.6 Hz), 3.62−3.72 (m, 3 H, 1 H from $CH_2Ar$ + $CH^{\alpha}$ + $CH^{\beta}$), 6.50 (br d, 1 H, *m*-H, C=NXy, $^3J_{HH}$ = 7.2 Hz), 6.55 (t, 1 H, *p*-H, C=NXy, $^3J_{HH}$ = 7.2 Hz), 6.85 (br d, 1 H, *m*-H, C=NXy, $^3J_{HH}$ = 6.8 Hz), 7.00 (t, 1 H, H4, $^3J_{HH}$ = 7.6 Hz), 7.03 (br d, 1 H, H3, $^3J_{HH}$ = 7.6 Hz), 7.15 (t, 1 H, H5, $^3J_{HH}$ = 7.2 Hz), 7.24 (d, 4 H, *m*-H, C≡NXy, $^3J_{HH}$ = 7.6 Hz), 7.36 (m, 2 H, *p*-H, C≡NXy), 7.40 (d, 1 H, H6, $^3J_{HH}$ = 8.0 Hz), 8.20 (br s, 3 H, $NH_3$). $^{13}C\{^1H\}$ NMR (75.45 MHz, DMSO-$d_6$): $\delta$ 18.4 (s, Me, C≡NXy), 19.0 (s, Me, C=NXy), 24.1 (s, Me, $CMe_2$), 25.3 (s, Me, $CMe_2$), 27.9 (s, $CH_2$ nor), 31.2 (s, $CH_2$ nor), 37.4 (s, $CH_2$ nor), 41.7 (s, $CH_2Ar$), 41.9 (s, CH nor), 43.7 (s, CH nor), 47.6 (s, $C^{\beta}$H), 54.6 (s, $CMe_2$), 69.6 (s, $C^{\alpha}$H), 122.1 (s, *p*-CH, C=NXy), 125.0 (s, *i*-C, C≡NXy), 125.33 (s, CH, C4), 125.36 (s, *o*-CH, C=NXy), 126.2 (s, *o*-CH, C=NXy), 126.8 (s, CH, C5), 127.1 (s, *m*-CH, C=NXy), 127.3 (s, CH, C6), 127.8 (s, *m*-CH, C=NXy), 128.1 (s, *m*-CH, C≡NXy), 130.2 (s, *p*-CH, C≡NXy), 131.4 (s, CH, C3), 134.2 (s, C2), 135.4 (s, *o*-C, C≡NXy), 143.8 (s, C1), 145.4 (s, C≡N), 149.3 (s, *i*-C, C=NXy), 176.7 (s, C=N).

**Single-Crystal X-ray Structure Determinations.** Relevant crystallographic data and details of the refinements for the structures of compounds **3a2**, **4a1**, **4b1**, **4b2**, **5b3**, **6b2**, and **9b2** are summarized in the Supporting Information. *Data Collection.* Crystals suitable for X-ray diffraction were mounted in inert oil on a glass fiber and transferred to a SuperNova, Dual, Cu at zero, Atlas (**3a2**), a Bruker SMART (**4a1**, **4b1**, **4b2**, **6b2**, and **9b2**), or an Oxford Diffraction Nova O (**5b3**) diffractometer. Data were recorded at 100(2) (**3a2**, **4a1**, **4b1**, **4b2**, **9b2**), 103(2) (**5b3**), or 293(2) K (**6b2**), using mirror- (**3a2**) or graphite-monochromated (**4a1**, **4b1**, **4b2**, **6b2**, and **9b2**) Mo K$\alpha$ radiation ($\lambda$ = 0.71073 Å) or mirror-monochromated Cu K$\alpha$ radiation ($\lambda$ = 1.54184 Å; **5b3**) and $\omega$-scan mode. An analytical numeric absorption correction using a multifaceted crystal model based on expresion derived by Clark and Reid[43] was applied for complex **3a2**. Multiscan absorption corrections were applied for compounds **4a1**, **4b2**, **5b3**, and **9b2**. *Structure Solution and Refinements.* Crystal structures were solved by the direct (**3a2**, **4a1**, **4b1**, **4b2**, **5b3**, and **6b2**) or Patterson method (**9b2**), and all non-hydrogen atoms refined anisotropically on $F^2$ using the program SHELXL-97.[44] Hydrogen atoms were refined as follows. Compounds **3a2** and **6b2**: $NH_2$ or $NH_3$, free with SADI; methyl, rigid group; all others, riding. Compound **4a1**: NH, free with DFIX; methyl, rigid groups; all others, riding. Compound **4b1**: NH, free; ordered methyl, rigid group; all others, riding. Compounds **4b2**, **5b3**, and **9b2**: NH, $NH_2$, or $NH_3$, free; methyl, rigid group; all others, riding. Special features: Compounds **4a1** and **4b1**: non-centrosymmetric structures without heavy atoms (just C, H, N, O). With Mo radiation there are usually no significant Friedel differences, and thus the Friedel opposite reflections become exactly equivalent in intensity. Because of that, MERG 3 was used in the refinement of the structures. Compound **4b1**: the OEt group of one of the two independent molecules is disordered over two positions with a ca. 76:24 occupancy distribution. Complex **9b2**: Absolute structure (Flack)[45] parameter is 0.00(3).

## ■ ASSOCIATED CONTENT

### Supporting Information

Selected $^1$H NMR data for the new compounds, details (including symmetry operators) of hydrogen bondings, listing of all refined and calculated atomic coordinates, anisotropic thermal parameters, bond lengths and angles, crystallographic data, and CIF files for compounds **3a2**, **4a1**, **4b1**, **4b2**, **5b3**, **6b2**, and **9b2**. This material is available free of charge via the Internet at http://pubs.acs.org.

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### Notes

The authors declare no competing financial interest.

## ■ ACKNOWLEDGMENTS


We thank Ministerio de Educación y Ciencia (Spain), FEDER (CTQ2007-60808/BQU), and Fundación Séneca (04539/GERM/06) for financial support. J.-A.G.-L. and M.-J.O.-M. are grateful to the Fundación Séneca (CARM, Spain) and Ministerio de Educación y Ciencia (Spain), respectively, for their research grants. We thank Dr. Alexandra Griffin (Agilent Technologies) and Dr. Peter G. Jones (Technische Universität Braunschweig) for X-ray measurements for compounds **3a1** and **5b3**, respectively.


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