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

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ABSTRACT

The ortho-metalated complex $[\text{Pd}\{C,N\text{-}C_6\text{H}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{-}2,(\text{OMe})_{2-4,5}\}(\mu\text{-Br})_2]$ (**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, $[\text{Pd}\{C,N\text{-CH(R)CH}_2\text{C}_6\text{H}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{-}2,(\text{OMe})_{2-4,5}\}(\mu\text{-Br})_2]$ (R = CO₂Et (**2a1**), C(O)Me (**2a2**)) or $[\text{Pd}\{C,N\text{-CH(C}_5\text{H}_8)\text{CHC}_6\text{H}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{-}2,(\text{OMe})_{2-4,5}\}(\mu\text{-Br})_2]$ (**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 aminoacid 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 $[\text{PdCl}(\mu\text{-Cl})(\text{L})]$, 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.

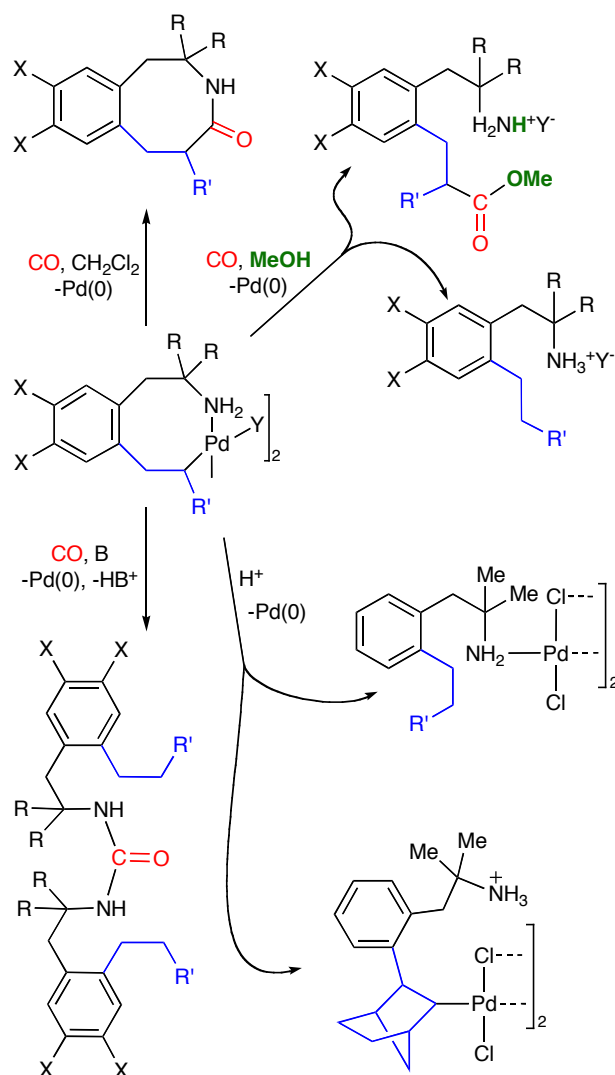
INTRODUCTION

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, $[\text{Pd}(C,N\text{-}C_6\text{H}_4\text{CH}_2\text{CR}_2\text{NH}_2\text{-}2)(\mu\text{-X})_2]$, 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 β -hydrogen atoms are particularly rare, because they easily undergo the β -hydrogen elimination process to render the 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 orthopalladated 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 co-polymerization reactions.⁶

In this article we report (1) the synthesis of eight-membered palladacycles containing accessible β -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 N⁷-amino acids, or ureas (Scheme 1), and (3) the protonolysis reactions of some of the eight-membered palladacycles, which, depending on the inserted alkene, proceeds *via* Pd–N or Pd–C bond breaking.

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



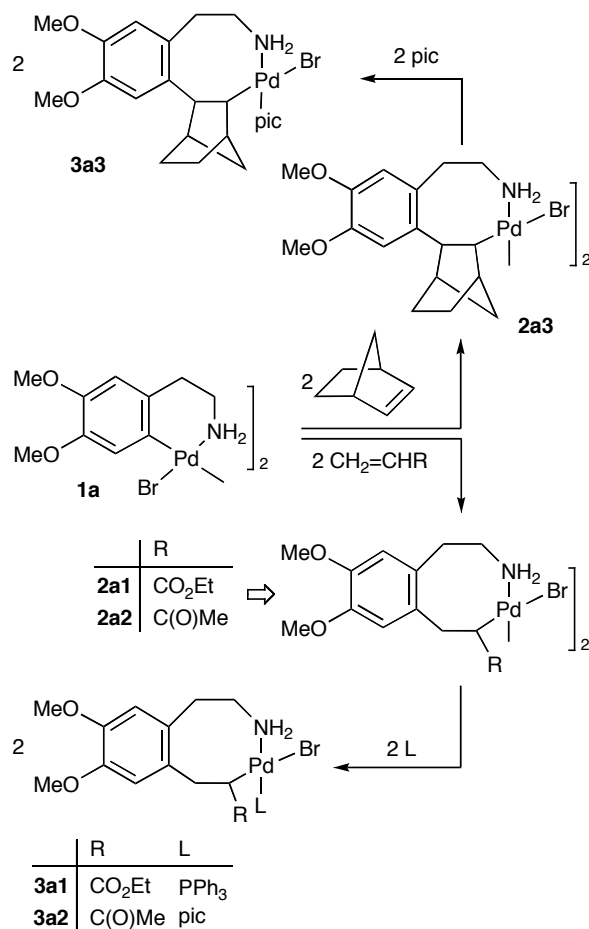
The reaction of eight-membered palladacycles with CO constitutes a new synthetic method to obtain eight-membered *N*-heterocycles, a type of compounds which have addressed an increasing interest^{8,9} because of their pharmacological properties. The benzazocine nucleus is particularly relevant because it can be found in biologically active molecules with analgesic,^{10,11} antitumoral,¹² antihypertensive¹³ and antidepressive properties.¹³ Generally, these derivatives are difficult to obtain because, due to unfavourable 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 $[\text{Pd}\{C,N\text{-}C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_{2-4,5}\}(\mu\text{-}Br)]_2$ (**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 $[\text{Pd}\{C,N\text{-}CH(R)CH_2C_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_{2-4,5}\}(\mu\text{-}Br)]_2$ ($R = CO_2Et$ (**2a1**); $C(O)Me$ (**2a2**)) and $[\text{Pd}\{C,N\text{-}CH(C_5H_8)CHC_6H_2CH_2CH_2NH_2\text{-}2,(OMe)_{2-4,5}\}(\mu\text{-}Br)]_2$ (**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 1H NMR ($DMSO\text{-}d_6$) 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 , norbornene),^{1,23} 2,5-norbornadiene, dicyclopentadiene)²³ into the C–Pd bond of aryl palladium complexes. As mentioned above, the scarce number of isolated products of this type of reactions is attributable to their tendency to decompose to afford the corresponding Heck arylated olefin. The few exceptions are those in which the required β -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–NH₂ 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 the intramolecular hydrogen bonds (see below).¹

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



Complexes **2a** react with neutral ligands in a 1:2 molar ratio, to give the mononuclear derivatives $[\text{Pd}\{C,N\text{-CH(R)CH}_2\text{C}_6\text{H}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{-2, (OMe)}_{2-4,5}\}\text{Br(L)}]$ ($R = \text{CO}_2\text{Et}$, $L = \text{PPh}_3$ (**3a1**); $R = \text{C(O)Me}$, $L = 4\text{-methylpyridine (pic)}$ (**3a2**)) and $[\text{Pd}\{C,N\text{-CH(C}_5\text{H}_8)\text{CHC}_6\text{H}_2\text{CH}_2\text{CH}_2\text{NH}_2\text{-2, (OMe)}_{2-4,5}\}\text{Br(pic)}]$ (**3a3**) (Scheme 2). The ^1H 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 ^1H NMR Tables in the Supporting Information). For derivatives containing inserted methyl vinyl ketone or ethyl acrylate, the methine hydrogen atom is on C^α , 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 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 hydrogen atoms of the NH₂ group, while the other hydrogen is interacting with the carbonyl group of another molecule giving rise to dimers (see Supporting Information).

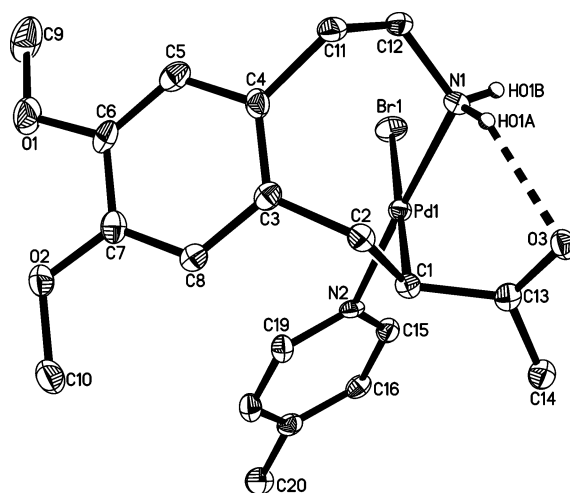


Figure 1. Thermal ellipsoid plot (50% probability) of complex **3a2** along with the labelling scheme. Hydrogen carbon atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Pd(1)–N(1) = 2.058(3), Pd(1)–N(2) = 2.037(3), Pd(1)–C(1) = 2.086(3), Pd(1)–Br(1) = 2.5085(5); C(1)–Pd(1)–N(1)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

We propose for all the other mononuclear complexes that the monodentated ligands (PPh₃, pic) are trans to the NH₂ group, because this is the expected geometry according to the great

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}

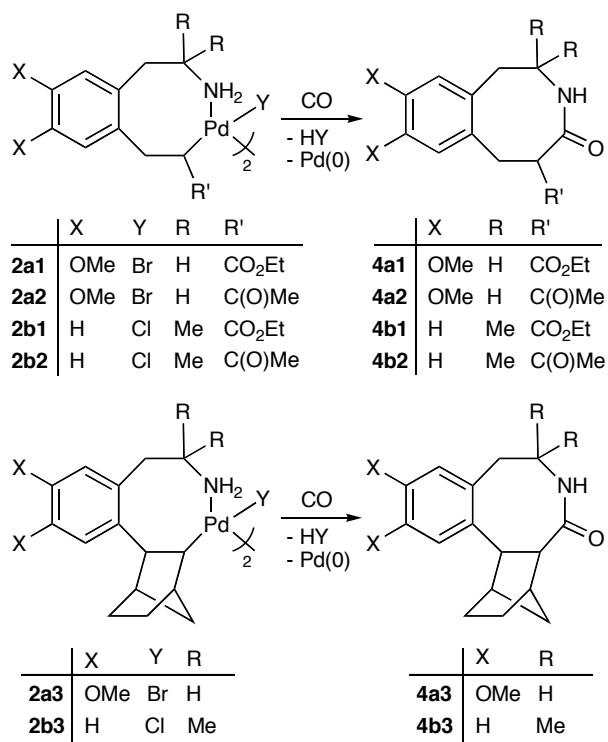
Reactivity of the Eight-membered Palladacycles towards CO. Synthesis and Characterization of Tetrahydrobenzazocinones and Esters. The isolation of complexes **2a** gave us the chance to explore their reactivity towards CO. We have as well extended this study to their previously reported phentermine homologues **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 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 the insertion process of unsaturated ligands into the Pd–C bond and the decomposition of the resulting complex.^{1,20,32}

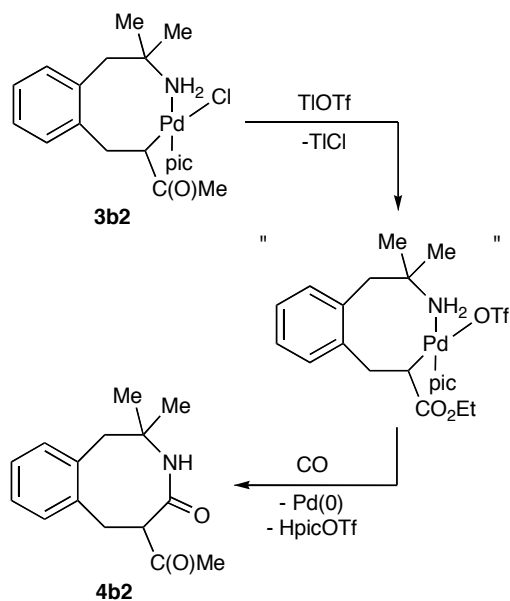
The synthesis of the eight-membered lactams **4** resulting from alkene/CO sequential insertions into the Pd–C bond have no precedents. We have reported (1) the synthesis of tetrahydroisoquinolones or tetrahydrocarbolinones by reacting CO with six membered palladacycles obtained by cyclopalladation of some primary amines,¹⁹⁻²¹ (2) a few examples of the reverse CO/alkene insertion process giving products resulting from the polyinsertion of the alkene²³ 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(*1H,3H*)-diones.³

Scheme 3. Synthesis of Tetrahydrobenzazocinones

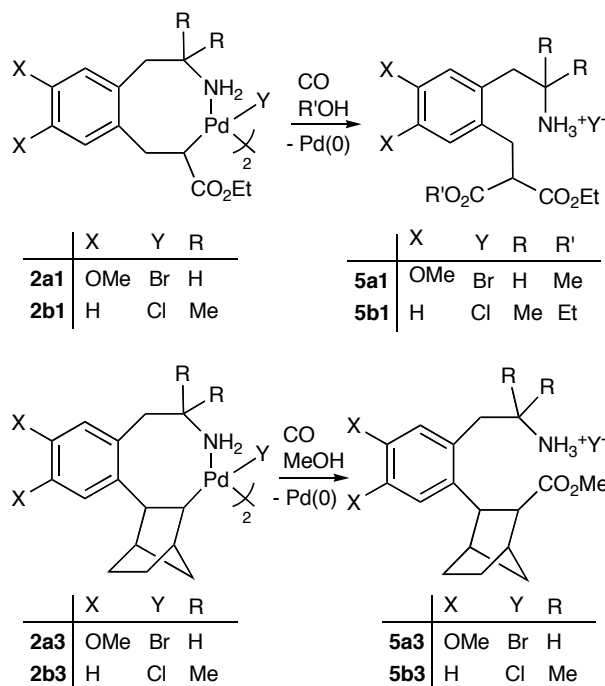


Scheme 4. Improved Synthesis of the Tetrahydrobenzazocinone Derived from Phentermine and Methyl Vinyl Ketone



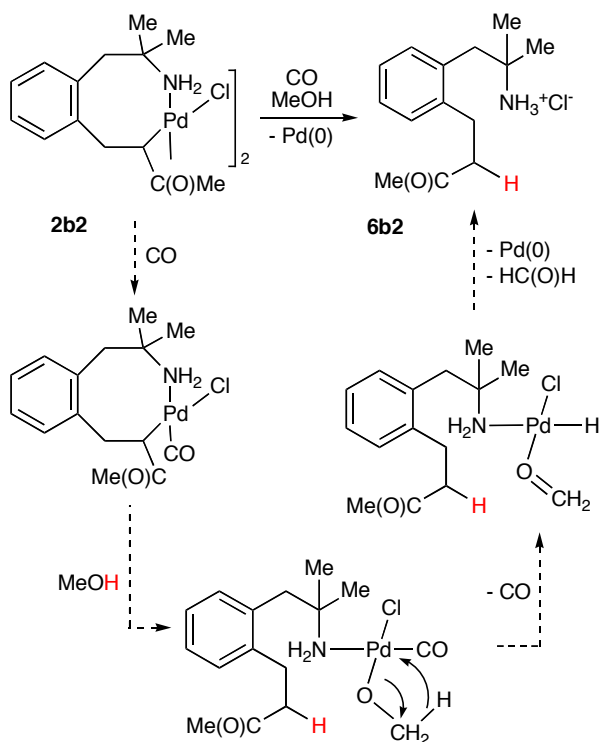
The nature of the products obtained through CO insertion into palladacycles depends greatly on the solvent, and thus it has been reported that esters or amides can be obtained in the presence of alcohols or amines, respectively.^{31,33,34} When the reactions of the complexes **2** with CO were carried out in ethanol or methanol, decomposition to metallic palladium took place, and the corresponding methyl or ethyl ester derivatives of unnatural N⁷-amino acids **5** (Scheme 5) were isolated in moderate to good yields (48–88%).

Scheme 5. Synthesis of Esters Derived from Homoveratrylamine and Phentermine



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 C–Pd 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 which 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**.

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

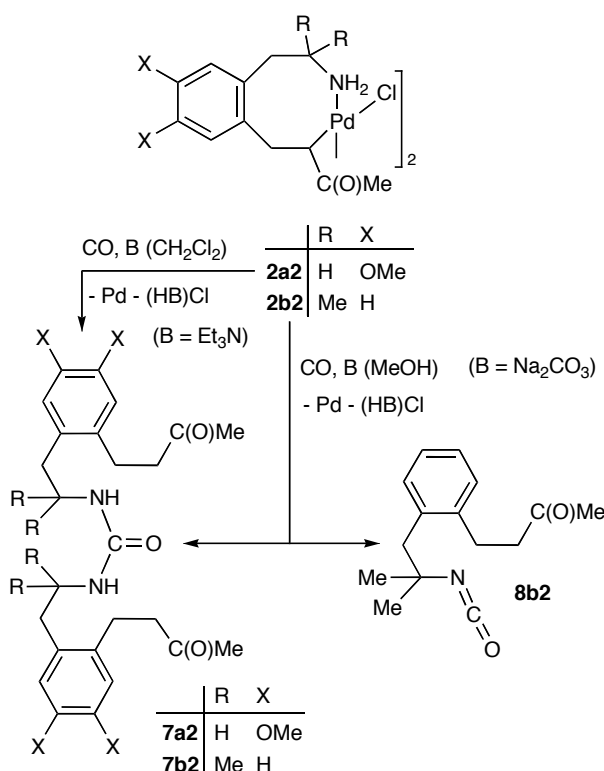


A possible reaction pathway to explain the formation of this ammonium salt would involve: (1) CO coordinación, to give a soluble mononuclear derivative, (2) protonolysis of the C–Pd bond (probably assisted by the oxygen atom of the carbonyl group in α -position), to render an alcoxocomplex, and (3) a β -elimination process, to give a Pd(II) hydrido-complex that would decompose generating Pd(0) and HCl.³⁵ This reaction mechanism is consistent with the experimental isolation of the ammonium chloride instead of the free amine as the reaction product (Scheme 6). Moreover, when the reaction is carried out in MeOD, the isolated ammonium chloride (**6b2-d₁**; ESI-HRMS) contains a deuterium atom in α -position to the carbonyl group, as shown by its ¹H NMR spectrum. The protonolysis of the C–Pd 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 NEt₃ in CH₂Cl₂ rendered the urea **7a2**, along with metallic palladium and (HNEt₃)Br. Likewise, the reaction of **2b2**, CO and Na₂CO₃ 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 intermediates³⁸ and in some cases detected.³⁹ The isolation of **8b2** gives additional support to this proposal.

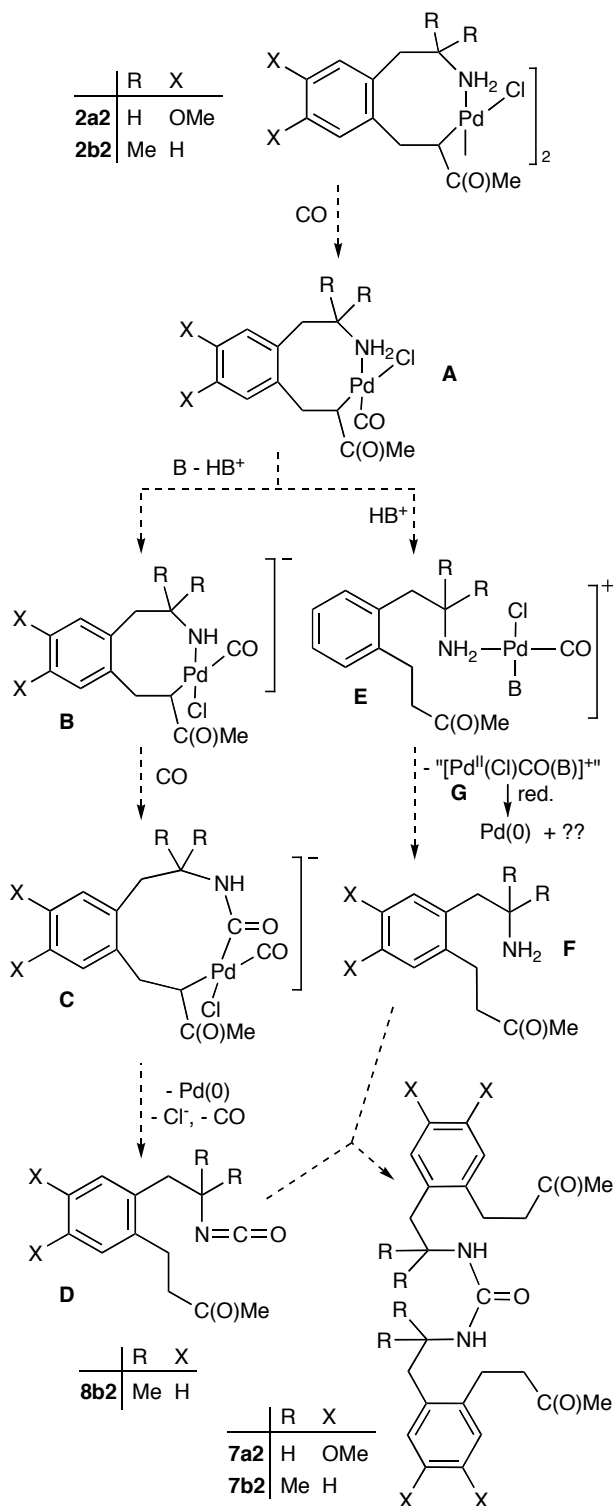
Scheme 7. Synthesis of Ureas **7a2** and **7b2** and isocyanate **8b2**



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 NH₂ 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 β -hydride elimination process to give the isocyanate **D** (**8b2**); and (2) the Pd–C bond in **A** undergoes a protonolysis by reaction with MeOH (see above) or Et₃NH⁺ to render the cationic complex **E** that decomposes to give the free amine **F** and a cationic Pd(II) complex **G** that 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 way (1) is faster than that of (2). Similar steps have been proposed for the catalytic formation of ureas by oxidative carbonylation of primary amines.^{38,40}

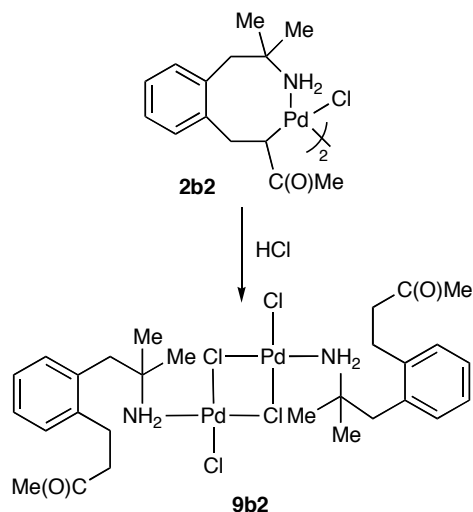
Scheme 8. Proposed Pathway for the Synthesis of Ureas **7** and Isocyanate **8b2**



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 necessary to induce the protonolysis process but the reduction step did not take place.

Scheme 9. Synthesis of Complex **9b2**



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).

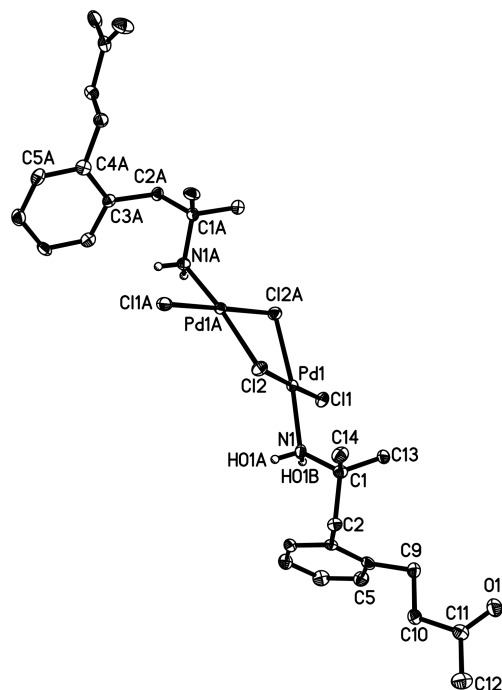


Figure 2. Thermal ellipsoid plot (50% probability) of complex **9b2** along with the labelling scheme. Hydrogen carbon atoms have been omitted for clarity. Selected bond lengths (Å) and angles (deg): Pd(1)–N(1) = 2.019(3), Pd(1)–Cl(1) = 2.2904(9), Pd(1)–Cl(2) = 2.3324(9), Pd(1)–Cl(2A) = 2.3296(9), C(9)–C(10)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

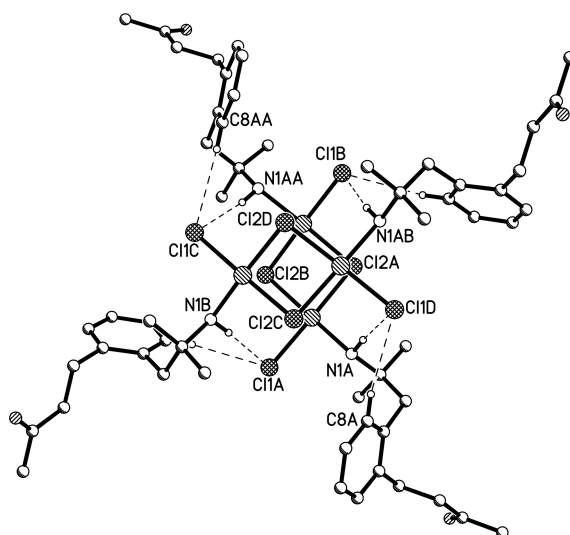
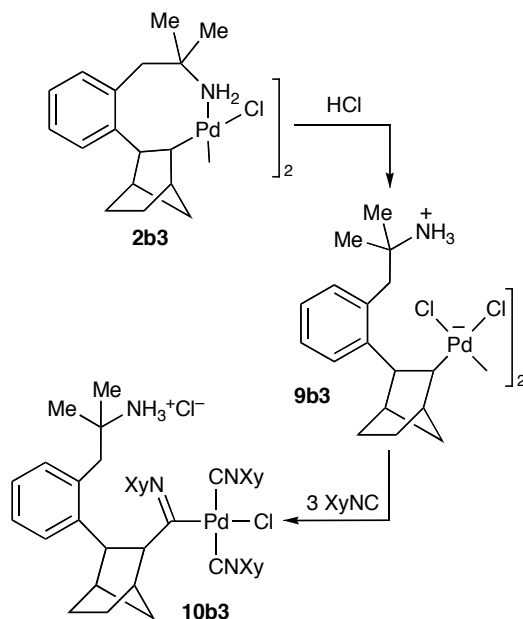


Figure 3. X-ray packing view of compound **9b2** (50% probability) showing the dimer generated by the hydrogen bond interactions. Details (including symmetry operators) are given in the Supporting Information.

The reaction of palladacycle **2b1** with HCl led to intractable mixtures. Palladacycle **2b3** reacted with HCl to give an orange solid **9b3** that analyzes as **2b3**·HCl but which 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 palladacycles.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 behaviour that may be attributed to the steric influence of the bulky inserted norbornene or/and to the electron withdrawing nature of the C(O)Me group.

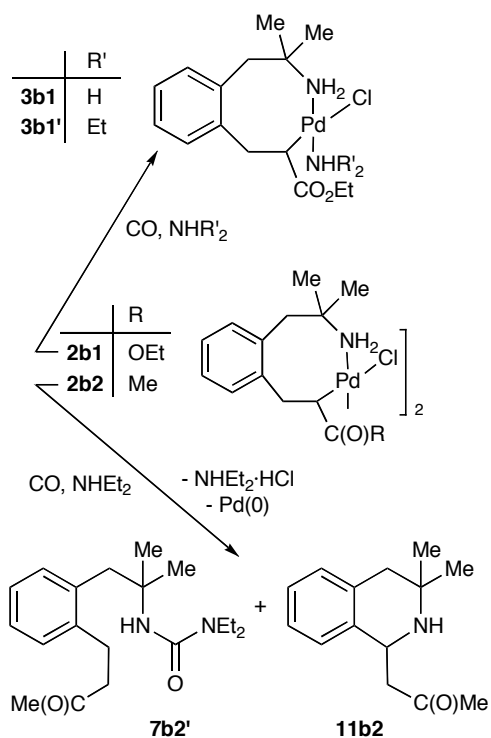
Scheme 10. Reaction of Complex **2b3** with HCl and XyNC



In order to obtain an amide derivative, analogous to the ester **5b1**, the reaction of complex **2b1** and CO in CH₂Cl₂ was carried out in the presence of NH₃ or NHEt₂ instead of MeOH or EtOH.³⁴ However, the reaction did not render the expected amide but the previously described¹ complex **3b1** or **3b1'**, respectively, which contains a coordinated NHR₂ 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 NHEt₂ (molar ratio = 1:4) was added to a suspension of the palladacycle **2b2** in CH₂Cl₂, and the mixture was stirred for 24 h under a CO atmosphere, decomposition to metallic palladium took place, and a mixture of the non-symmetric urea **7b2'** and the previously reported isoquinoline **11b2**¹ (ca. 2:1 ratio), which arises from a β-hydrogen elimination/hydroamination process (Scheme 11). The obtention of the urea **7b2'** can be easily explained by reaction of NHEt₂ with the isocyanate **8b2**, which can be formed following the pathway (1) proposed in Scheme 8. Again, it is difficult to explain the different behaviour 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 CO₂Et and C(O)Me substituent on the carbon atom in α -position to the Pd(II).

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



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 ¹H NMR data (hydrogen of NH or NH₂ 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 $\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) 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 σ -alkyl complexes containing accessible hydrogen atoms in β 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: (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 C–Pd 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 derivatives (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 N–Pd bond has been dissociated.

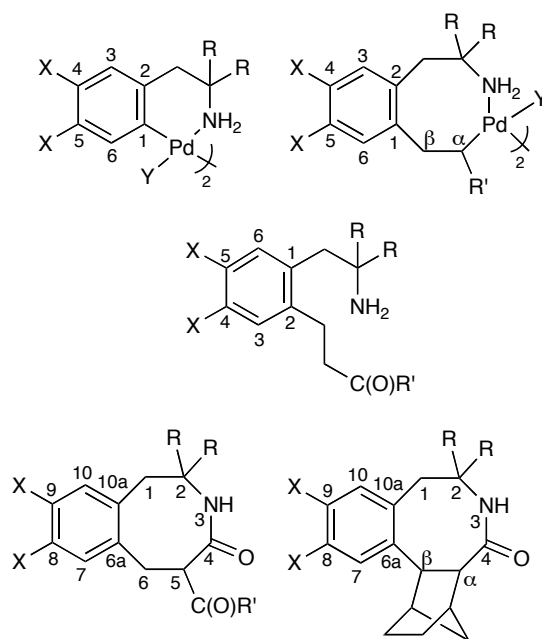
EXPERIMENTAL SECTION

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 CDCl₃ in Bruker Avance 300, 400 or 600 spectrometers. Chemical shifts were referenced to TMS (¹H, ¹³C{¹H}) or H₃PO₄ (³¹P{¹H}). Signals in the ¹H and ¹³C 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 other specification.

The complexes [Pd{*C,N*-C₆H₂CH₂CH₂NH₂-2,(MeO)₂-4,5}(μ-Br)]₂ (**1a**),²¹ [Pd{κ²(*C,N*)-CH(CO₂Et)CH₂C₆H₄(CH₂CMe₂NH₂)-2}(μ-Cl)]₂ (**2b1**), [Pd{κ²(*C,N*)-CH(COMe)CH₂C₆H₄(CH₂CMe₂NH₂)-2}(μ-Cl)]₂·1/4CH₂Cl₂ (**2b-2·1/4CH₂Cl₂**), [Pd{κ²(*C,N*)-CH(C₅H₈)CHC₆H₄(CH₂CMe₂NH₂)-2}(μ-Cl)]₂ (**2b3**) and [Pd{κ²(*C,N*)-CH(COMe)CH₂C₆H₄(CH₂CMe₂NH₂)-2}Cl(NC₅H₄Me-4)] (**3b2**) were prepared as previously reported.¹ Ethyl acrylate (Merck), methyl vinyl ketone, 2-norbornene, 4-methylpyridine (4-picoline), NHEt₂, PPh₃, ^tBuNC, XyNC, HOTf (HSO₃CF₃) (Fluka), NEt₃ (Sigma-Aldrich), NH₃ (gas, Air Products) and Na₂CO₃ (Baker) were used as received. HCl gas was generated *in situ* by reaction of NaCl and H₂SO₄. TlOTf was prepared by reaction of Tl₂CO₃ and HO₃SCF₃ (1:2) in water, and recrystallized from acetone/Et₂O. 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 [Pd₂{C,N-CH(CO₂Et)CH₂C₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}₂(μ-Br)₂] (2a1**).**

Ethyl acrylate (0.059 mL, 0.545 mmol) was added to a suspension of complex [Pd₂{C,N-C₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}₂(μ-Br)₂] (**1a**; 200 mg, 0.273 mmol) in CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 x 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 C₃₀H₄₄Br₂N₂O₈Pd₂ (942.344): C, 38.24; H, 4.81; N, 2.97. Found: C, 37.91; H, 4.87; N, 3.08. IR (cm⁻¹): ν(NH) 3239 m; ν(CO) 1665 m. ¹H NMR (300.1 MHz, DMSO-*d*₆): δ 1.20 (t, 3 H, Me, ³J_{HH} = 7.2 Hz), 2.14 (dd, 1 H, C^βH₂, ²J_{HH} = 13.8 Hz, ³J_{HH} = 6.9 Hz), 2.66 (br d, 2 H, CH₂Ar, ²J_{HH} = 10.2 Hz), 2.95–3.20 (m, 3 H, CH₂N + 1 H of C^βH₂), 3.68 (m, partially obscured by the MeO signal, 2 H, C^αH + 1 H of NH₂), 3.72 (s, 3 H, MeO),

3.73 (s, 3 H, MeO), 4.03 (m, 2 H, CH₂O), 4.79 (br d, 1 H, NH₂, ²J_{HH} = 10.2 Hz), 6.69 (s, 1 H, H6), 6.88 (s, 1 H, H3). ¹³C{¹H} NMR (75.45 MHz, DMSO-*d*₆): δ 14.4 (s, Me), 31.9 (s, C^βH₂), 32.0 (s, CH₂Ar), 41.2 (s, C^αH), 41.5 (s, CH₂N), 55.0 (s, MeO), 55.9 (s, MeO), 59.2 (s, CH₂O), 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 [Pd₂{C,N-CH(COMe)CH₂C₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}₂(μ-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 CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 x 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 C₂₈H₄₀Br₂N₂O₆Pd₂ (873.283): C, 38.51; H, 4.62; N, 3.21. Found: C, 38.61; H, 4.66; N, 3.28. IR (cm⁻¹): ν(NH) 3271 s, 3152 m; ν(CO) 1633 vs. ¹H NMR (400.91 MHz, DMSO-*d*₆): δ 1.99 (dd, 1 H, C^βH₂, 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, NH₂), 2.63 (br d, 1 H, CH₂Ar, ²J_{HH} = 14.0 Hz), 2.87–2.95 (m, 1 H, CH₂Ar), 3.05–3.14 (m, 2 H, CH₂N), 3.23 (m, 1 H, C^βH₂), 3.72 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 4.16 (dd, 1 H, C^αH, ³J_{HH} = 11.2, ³J_{HH} = 6.4 Hz), 4.88 (br d, 1 H, NH₂, ²J_{HH} = 10.8 Hz), 6.73 (s, 1 H, H6), 6.87 (s, 1 H, H3). ¹³C{¹H} NMR (75.45 MHz, DMSO-*d*₆): δ 28.9 (s, Me), 30.1 (s, C^βH₂), 31.9 (s, CH₂Ar), 47.6 (s, CH₂N), 54.7 (s, C^αH), 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 [Pd₂{C,N-CH(C₅H₈)CHC₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}₂(μ-Br)₂] (2a3). 2-Norbornene (50 mg, 0.546 mmol) was added to a suspension of complex **1a** (200 mg, 0.273 mmol) in CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 x 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 C₃₄H₄₈Br₂N₂O₄Pd₂ (921.414): C, 44.32; H, 5.25; N, 3.04. Found: C, 44.53; H, 5.43; N, 3.02. IR (cm⁻¹): ν(NH) 3546 s, 3465 s, 3412 s, 3229 m. ¹H NMR (400.91 MHz, DMSO-*d*₆): δ 1.07–1.40 (m, 4 H, CH₂ nor + CH₂ nor), 1.50–1.62 (m, 2 H, CH₂ nor), 2.14–2.26 (m, 3 H, CH nor + C^αH + 1 H of CH₂Ar), 2.47–2.83 (m, 6 H, C^βH + CH nor + CH₂N + 1 H of CH₂Ar + 1 H of NH₂), 3.06–3.14 (m, 1 H, NH₂), 3.70 (s, 3 H, MeO), 3.73 (s, 3 H, MeO), 6.77 (s, 1 H, H3), 6.92 (s, 1 H, H6). ¹³C {¹H} NMR (100.81 MHz, DMSO-*d*₆): δ 30.1 (s, CH₂), 30.5 (s, CH₂), 30.9 (s, CH₂), 31.7 (s, CH₂), 32.2 (s, CH₂), 38.5 (s, CH₂), 40.9 (s, CH nor), 41.2 (s, CH nor), 42.2 (s, CH nor), 45.4 (s, CH₂), 45.6 (s, CH nor), 46.2 (s, CH₂), 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 ¹³C 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 splitted the bromo-bridges. The reaction of this mixture with 4-picoline affords only complex **3a3**.

Synthesis of [Pd{C,N-CH(CO₂Et)CH₂C₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}Br(PPh₃)] (3a1**).** PPh₃ (56 mg, 0.214 mmol) was added to a solution of complex **2a1** (100 mg, 0.107 mmol) in CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 C₃₃H₃₇BrNO₄Pd (728.960): C, 54.37; H, 5.12; N, 1.92. Found: C, 54.28; H, 5.23; N, 1.91. IR (cm⁻¹): ν(NH) 3267 m, 3195 m, 3132 m; ν(CO) 1660 s. ¹H NMR (300.1 MHz): δ 1.04 (t, 3 H, Me, ³J_{HH} = 6.9 Hz), 2.18 (dd, 1 H, C^βH₂, ²J_{HH} = 11.1 Hz, ³J_{HH} = 6.6 Hz), 2.74 (br d, 1 H, CH₂Ar, ²J_{HH} = 14.4 Hz), 2.94 (dd, 1 H, C^αH, ³J_{HH} = 10.8 Hz, ³J_{HH} = 6.9 Hz), 3.11 (m, 1 H, CH₂Ar), 3.24 (m, 2 H, 1 H of NH₂ + 1 H of C^βH₂), 3.40–3.48 (m, 2 H, 1 H of CH₂N + 1 H of NH₂), 3.59 (s, 3 H, MeO), 3.59–3.63 (m, partially obscured by the MeO signal, 1 H, CH₂N), 3.93–4.00 (m, partially obscured by the MeO signal, 2 H, CH₂O), 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, PPh₃), 7.39–7.48 (m, 9 H, *o*-H + *p*-H, PPh₃). ¹³C{¹H} NMR (100.81 MHz): δ 14.1 (s, Me), 32.6 (s, C^βH₂), 33.5 (s, CH₂Ar), 36.9 (s, C^αH), 46.8 (s, CH₂N), 55.9 (s, MeO), 55.9 (s, MeO), 59.6 (s, CH₂O), 112.3 (s, CH, C₆), 113.4 (s, CH, C₃), 127.9 (d, *m*-CH, PPh₃, ³J_{CP} = 10.7 Hz), 129.3 (s, C₂), 130.4 (d, *p*-CH, PPh₃, ⁴J_{CP} = 2.0 Hz), 131.2 (d, *i*-C, PPh₃, ¹J_{CP} = 50.7 Hz), 134.5 (s, C₁), 135.1 (d, *o*-CH, PPh₃, ²J_{CP} = 11.4 Hz), 147.8 (s, C₅), 148.0 (s, C₄), 177.6 (s, CO). ³¹P NMR (121.5 MHz): 35.3 (s).

Synthesis of [Pd{C,N-CH(COMe)CH₂C₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}Br(NC₅H₄Me-4)] (3a2**).** 4-Picoline (0.018 mL, 0.183 mmol) was added to a solution of complex **2a2** (80 mg, 0.092 mmol) in CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 C₂₀H₂₇BrN₂O₃Pd (529.770): C, 45.34; H, 5.14; N, 5.29. Found: C, 45.28; H, 4.99; N, 5.27. IR (cm⁻¹): ν(NH) 3220 w, 3173 w, 3135 w; ν(CN) 1601 s; ν(CO) 1511 s. ¹H NMR (400.91 MHz): δ 2.02 (dd, 1 H, C^βH₂, 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, NH₂), 2.76 (br d, 1 H, CH₂Ar, ²J_{HH} = 14.8 Hz), 3.07 (br d, 1 H, NH₂, ²J_{HH} = 14.0 Hz), 3.12–3.19 (m, 2 H, 1 H of CH₂N + 1 H of CH₂Ar), 3.34–3.43 (m, 2 H, 1 H of CH₂N + 1 H of C^βH₂), 3.63 (dd, 1 H, C^αH, 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). ¹³C {¹H} NMR (100.81 MHz): δ 0.6 (s, Me, pic), 29.2 (s, MeCO), 30.9 (s, C^βH₂), 32.4 (s, CH₂Ar), 47.0 (s, C^αH), 47.8 (s, CH₂N), 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 ¹³C 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 Et₂O into a solution of **3a2** in CH₂Cl₂.

Synthesis of [Pd{C,N-CH(C₅H₈)CHC₆H₂CH₂CH₂NH₂-2,(OMe)₂-4,5}Br(NC₅H₄Me-4)]·H₂O (3a3**·H₂O).** 4-Picoline (12.4 μL, 0.127 mmol) was added to a solution of complex **2a3** (60 mg, 0.064 mmol) in CH₂Cl₂ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 5 mL) and air-dried to afford a first crop of **3a3**·H₂O 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 x 5 mL) and air-dried to afford a second crop of **3a3**·H₂O as a yellow solid (10 mg). Yield: 62 mg, 0.108 mmol, 85%. Mp: 125 °C. Anal. Calcd for C₂₃H₃₁BrN₂O₂Pd·H₂O (571.837): C, 48.31; H, 5.82; N, 4.90. Found: C, 47.90; H, 5.67; N, 4.81. IR (cm⁻¹): ν(NH) 3299 m, 3249 m, 3206 w; ν(CN) 1614 s. ¹H NMR (400.91 MHz): δ 0.56 (d, 1 H, CH₂ nor, ²J_{HH} = 9.6 Hz), 0.83 (d, 1 H, CH₂ nor, ²J_{HH} = 9.6 Hz), 1.23–1.29 (m, 2 H, 1 H of CH₂ nor + 1 H of CH₂ nor), 1.37–1.43 (m, 1 H, CH₂ nor), 1.37–1.43 (m, 1 H, CH₂ nor), 1.59–1.63 (m, partially obscured by the H₂O signal, 1 H, CH₂ nor), 2.08 (d, 1 H, C^αH, 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^βH, ³J_{HH} = 3.6 Hz), 2.66 (m, 1 H, CH₂Ar), 2.76 (d, 1 H, CH nor, ³J_{HH} = 8.8 Hz), 2.83 (dd, 1 H, CH₂Ar, ²J_{HH} = 16.0, ³J_{HH} = 4.0 Hz), 3.29–3.41 (m, 3 H, CH₂N + 1 H of NH₂), 3.60 (br s, 1 H, NH₂), 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). ¹³C{¹H} NMR (100.81 MHz): δ 21.1 (s, Me, pic), 30.2 (s, CH₂ nor), 31.1 (s, CH₂ nor), 33.0 (s, CH₂Ar), 36.2 (s, CH₂ nor), 40.9 (s, CH nor), 42.9 (s, CH nor), 46.1 (s, C^αH), 47.0 (s, CH₂N), 51.4 (s, C^βH), 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 CHCl₃ (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 x 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 C₁₆H₂₂NO₅ 308.1498 [(M+H)⁺]; found 308.1499 [(M+H)⁺]; Δ = 0.0001. IR (cm⁻¹): ν(NH) 3333 m; ν(CO) 1740 m; ν(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, CH₂Ar), 3.14 (m, 1 H, CH₂CH), 3.40 (m, 1 H, CH₂CH), 3.47–3.53 (m, 1 H, CH₂N), 3.71–3.77 (m, 1 H, CH₂N), 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, CH₂O, ³J_{HH} = 7.2 Hz), 5.54 (br s, 1 H, NH), 6.56 (s, 1 H, H10), 6.75 (s, 1 H, H7). ¹³C {¹H} NMR (100.81 MHz): δ 14.1 (s, Me), 32.9 (s, CH₂CH), 35.2 (s, CH₂Ar), 40.4 (s, CH₂N), 53.2 (s, CH), 55.9 (s, MeO), 61.7 (s, CH₂O), 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, CO₂Et). The ¹³C 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 CHCl₃.

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 CHCl₃ (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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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 x 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 C₁₅H₂₀NO₄ 278.1392 [(M+H)⁺]; found 278.1395; Δ = 0.0003. IR (cm⁻¹): ν(NH)

3277 w, 3196 m; $\nu(\text{CO})$ 1721 vs; $\nu(\text{CO}_{\text{NH}})$ 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). $^{13}\text{C}\{^1\text{H}\}$ 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-diy1)-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 x 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 x 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 $\text{C}_{18}\text{H}_{24}\text{NO}_3$ 302.1753 $[(\text{M}+\text{H})^+]$; found 302.1755 $[(\text{M}+\text{H})^+]$; $\Delta = 0.0002$. IR (cm^{-1}): $\nu(\text{NH})$ 3362 m; $\nu(\text{CO})$ 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, $^3J_{\text{HH}} = 10.0$ 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, $^3J_{\text{HH}} = 9.6$ 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^αH , $^3J_{\text{HH}} = 10.0$ Hz), 3.19–3.29 (m, 3 H, 1 H of CH_2Ar

+ 1 H of CH₂N + C^βH), 3.68–3.75 (m, 1 H, 1 H of CH₂Ar), 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). ¹³C{¹H} NMR (100.81 MHz): δ 29.0 (s, CH₂ nor), 30.3 (s, CH₂ nor), 32.2 (s, CH₂Ar), 36.9 (s, CH₂ nor), 38.9 (s, CH₂N), 39.4 (s, CH nor), 39.5 (s, CH nor), 49.2 (s, C^βH), 52.2 (s, C^αH), 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 CH₂Cl₂ (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 Et₂O (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 x 5 mL) and air-dried to afford **4b1** as a colorless solid (64 mg, 0.232 mmol). In the mother liquors, some 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 C₁₆H₂₁NO₃ (275.152): C, 69.79; H, 7.69; N, 5.09. Found: C, 69.85; H, 8.00; N, 5.11. IR (cm⁻¹): ν(NH) 3289 w, 3205 s, 3068 s; ν(CO₂R) 1732 vs; ν(CO_{NH}) 1651 vs. ¹H NMR (400.91 MHz): δ 1.26 (s, 3 H, Me, CMe₂), 1.30 (X₃ part of an ABX₃ system, 3 H, MeCH₂, ³J_{AX} = ³J_{BX} = 7.2 Hz), 1.60 (s, 3 H, Me, CMe₂), 2.68 (d, 1 H, CH₂Ar, ²J_{HH} = 14.4 Hz), 3.29 (dd, 1 H, CH₂CH, ²J_{HH} = 15.6, ³J_{HH} = 8.4 Hz), 3.32 (d, 1 H, CH₂Ar, ²J_{HH} = 15.2 Hz), 3.52 (dd, 1 H, CH₂CH, ²J_{HH} = 15.6, ³J_{HH} = 11.2 Hz), 4.24 (m, 1 H, CH, partially obscured by the resonance of CH₂O), 4.26 (AB part of an ABX₃ system, 2 H, CH₂O, 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). $^{13}\text{C}\{^1\text{H}\}$ NMR (100.81 MHz): δ 14.21 (s, *Me*CH₂), 30.0 (s, Me, CMe₂), 30.1 (s, Me, CMe₂), 33.7 (s, CH₂CH), 45.7 (s, CH₂Ar), 49.2 (s, CH), 53.2 (s, CMe₂), 61.5 (s, CH₂O), 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, CO₂R), 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 CHCl₃.

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 CH₃CN (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. CH₂Cl₂ (2 mL) and Et₂O (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 x 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 CH₂Cl₂ (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 MgSO₄, the filtrate was concentrated to ca. 2 mL, and Et₂O (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 CH₂Cl₂ (20 mL), Na₂CO₃ (200 mg, 1.89 mmol) was added, and mixture was stirred for 3 h. The suspension was filtered, the solvent was removed from the filtrate, and Et₂O (15 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2

x 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 Et₂O (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 C₁₅H₁₉NO₂ 245.1416; found 245.1426; $\Delta = 0.001$. IR (cm⁻¹): ν (NH) 3283 w, 3209 m; ν (CO) 1727 vs; ν (CONH) 1652 vs. ¹H NMR (400.91 MHz): δ 1.30 (s, 3 H, Me, CMe₂), 1.62 (s, 3 H, Me, CMe₂), 2.27 (s, 3 H, COMe), 2.70 (d, 1 H, CH₂Ar, ²J_{HH} = 14.4 Hz), 3.16 (dd, 1 H, CH₂CH, ²J_{HH} = 15.6 Hz, ³J_{HH} = 8.8 Hz), 3.31 (d, 1 H, CH₂Ar, ²J_{HH} = 14.4 Hz), 3.46 (dd, 1 H, CH₂CH, 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). ¹³C{¹H} NMR (100.81 MHz): δ 29.2 (s, COMe), 30.0 (s, Me, CMe₂), 30.4 (s, Me, CMe₂), 32.3 (s, CH₂CH), 45.6 (s, CH₂Ar), 53.3 (s, CMe₂), 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 CHCl₃.

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 CH₂Cl₂ (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 Et₂O (15 mL) was added. The resulting suspension was filtered through a plug of Celite, the solvent was removed from the filtrate, and Et₂O (10 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (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 C₁₈H₂₃NO 269.1780;

found 269.1784; $\Delta = 0.0004$. IR (cm^{-1}): $\nu(\text{NH})$ 3282 w, 3210 m; $\nu(\text{CO})$ 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, $^2J_{\text{HH}} = 8.7$ 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, $^2J_{\text{HH}} = 8.4$ Hz), 2.60 (d, 1 H, CH_2Ar , $^2J_{\text{HH}} = 13.8$ Hz), 2.73 (br s, 2 H, CH nor + CH nor), 2.89 (br d, 1 H, C^αH , $^3J_{\text{HH}} = 9.6$ Hz), 3.55 (d, 1 H, C^βH , $^3J_{\text{HH}} = 9.9$ Hz), 3.28 (d, 1 H, CH_2Ar , $^2J_{\text{HH}} = 13.8$ Hz), 4.87 (br s, 1 H, NH), 7.06 (d, 1 H, H10, $^3J_{\text{HH}} = 6.9$ Hz), 7.15 (t, 1 H, H9, $^3J_{\text{HH}} = 6.9$ Hz), 7.21 (t, 1 H, H8, $^3J_{\text{HH}} = 7.2$ Hz), 7.31 (d, 1 H, H7, $^3J_{\text{HH}} = 7.2$ Hz). $^{13}\text{C}\{^1\text{H}\}$ 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^βH), 52.2 (s, CMe_2), 53.6 (s, C^αH), 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-ethoxycarbonylmethyl) 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 x 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 $\text{C}_{17}\text{H}_{26}\text{NO}_6$ 340.1760 [(M-Br) $^+$]; found 340.1777 [(M-Br) $^+$]; $\Delta = 0.0017$. Λ_{M} ($\Omega^{-1} \text{cm}^2 \text{mol}^{-1}$) = 11 (5.10×10^{-4} M). IR (cm^{-1}): $\nu(\text{NH})$ 3452 w, 3366 w, 3173 w, 3187 w; $\nu(\text{CO})$ 1747 s, 1735 s. ^1H NMR (400.91 MHz): δ 1.58 (t, 3 H, Me, $^3J_{\text{HH}} = 7.2$ Hz), 3.21 (m, 4 H, $\text{CH}_2\text{CH} + \text{CH}_2\text{Ar}$), 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, CH₂O, $^3J_{\text{HH}} = 6.6$ Hz), 6.64 (s, 1 H, H3), 6.82 (s, 1 H, H6), 7.36 (br s, 3 H, NH₃). $^{13}\text{C}\{^1\text{H}\}$ NMR (75.45 MHz): δ 13.9 (s, Me), 29.9 (s, CH₂Ar), 31.0 (s, CH₂CH), 41.1 (s, CH₂N), 52.7 (s, MeO, CO₂Me), 53.1 (s, CH), 55.9 (s, MeO), 56.1 (s, MeO), 61.8 (s, CH₂O), 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, CO₂Et), 169.6 (s, CO₂Me).

Synthesis of 2-(1-Methoxycarbonyl-norbornyl) 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 x 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 C₁₉H₂₈NO₄ 334.2018 [(M-Br)⁺]; found 334.2015 [(M-Br)⁺]; $\Delta = 0.0003$. $\Lambda_{\text{M}} (\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}) = 12 (5.02 \times 10^{-4} \text{ M})$. IR (cm⁻¹): $\nu(\text{NH})$ 3366 br w; $\nu(\text{CO})$ 1719 s. ^1H NMR (200.13 MHz): δ 1.28–1.73 (m, 5 H, CH₂ nor + CH₂ nor + 1 H of CH₂ nor), 2.34 (br s, 1 H, 1 H of CH₂ 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, CH₂Ar + CH₂N + C ^{α} H + C ^{β} 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, NH₃). $^{13}\text{C}\{^1\text{H}\}$ NMR (75.45 MHz): δ 27.9 (s, CH₂ nor), 30.4 (s, CH₂Ar), 31.4 (s, CH₂ nor), 38.5 (s, CH₂ nor), 39.2 (s, CH nor), 41.2 (s, CH₂N), 42.1 (s, CH nor), 47.0 (s, C ^{β} H), 51.3 (s, MeO), 55.4 (s, C ^{α} 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-Diethoxycarbonylmethyl 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, Et₂O (10 mL) was added to the residue, and the mixture was vigorously stirred. The resulting suspension was filtered, and the solid was washed with Et₂O (2 x 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 x 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. Λ_M ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$): 6 ($5.20 \times 10^{-4} \text{ M}$). Anal. Calcd for C₁₈H₂₈ClNO₄ (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 NH₃ group were not observed; $\nu(\text{CO}_2\text{R})$ 1747 s, 1731 s. ¹H NMR (400.91 MHz): δ 1.17 (br t, 6 H, MeCH₂, ³J_{HH} = 6.0 Hz), 1.50 (s, 6 H, CMe₂), 3.20 (s, 2 H, CH₂Ar), 3.31 (br d, 2 H, CH₂CH, ³J_{HH} = 5.2 Hz), 3.64 (br s, 1 H, CH), 4.12 (br q, 4 H, CH₂O, 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, NH₃). ¹³C{¹H} NMR (100.81 MHz): δ 14.0 (s, MeCH₂), 25.8 (s, CMe₂), 31.7 (s, CH₂CH), 41.7 (s, CH₂Ar), 53.4 (s, CH), 56.4 (s, CMe₂), 61.6 (s, CH₂O), 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-Methoxycarbonyl-norbornyl) 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 Et₂O (25 mL) was added. The resulting suspension was filtered, and the solid was washed with Et₂O (2 x 5 mL) and air-dried to afford compound **5b3** as a colorless solid. Yield: 154 mg, 0.456 mmol, 88%. Mp: 238

°C. Λ_M ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$) = 6 ($4.70 \times 10^{-4} \text{ M}$). Anal. Calcd for $\text{C}_{19}\text{H}_{28}\text{ClNO}_2$ (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; $\nu(\text{CO}_2\text{R}) = 1737$ 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, $^2J_{\text{HH}} = 10.0$ 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 , $^2J_{\text{HH}} = 14.0$ Hz), 3.16 (d, 1 H, C^αH , $^3J_{\text{HH}} = 9.6$ Hz), 3.50 (d, partially obscured by the resonance of C^βH , 1 H, CH_2Ar), 3.55 (d, 1 H, C^βH , $^3J_{\text{HH}} = 9.6$ Hz), 7.07–7.19 (m, 3 H, H4 + H5 + H6), 7.29 (d, 1 H, H3, $^3J_{\text{HH}} = 8.0$ Hz), 8.69 (br s, 3 H, NH_3). $^{13}\text{C}\{^1\text{H}\}$ NMR (100.81 MHz): δ 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^βH), 50.5 (s, MeO), 54.2 (s, C^αH), 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-acetylmethyl phentermine hydrochloride (6b2). CO was bubbled for 5 min through a suspension of complex **2b2**· $1/4\text{CH}_2\text{Cl}_2$ (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 x 5 mL) and air-dried to afford **6b2** as a colorless solid. Yield: 102 mg, 0.399 mmol, 92%. Mp: 133 °C. Λ_M ($\Omega^{-1} \text{ cm}^2 \text{ mol}^{-1}$): 8 ($5.43 \times 10^{-4} \text{ M}$). Anal. Calcd for $\text{C}_{14}\text{H}_{22}\text{ClNO}$ (255.784): C, 65.74; H, 8.67; N, 5.48. Found: C, 65.56; H, 8.75; N, 5.43. IR (cm^{-1}): $\nu(\text{NH})$ 3392 w; $\nu(\text{CO})$ 1703 vs. ^1H NMR (400.91 MHz): δ 1.48 (s, 6 H, CMe_2), 2.11

(s, 3 H, COMe), 2.71 (t, 2 H, CH₂CO, ³J_{HH} = 7.2 Hz), 3.00 (t, 2 H, ArCH₂CH₂, ³J_{HH} = 7.6 Hz), 3.20 (s, 2 H, CH₂CMe₂), 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, NH₃). ¹³C{¹H} NMR (100.81 MHz): δ 25.5 (s, CMe₂), 26.9 (s, CH₂Ar), 30.2 (s, COMe), 41.6 (s, CH₂CMe₂), 44.8 (s, CH₂CO), 56.6 (s, CMe₂), 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-d₁** (obtained when the reaction was carried out using MeOD as solvent): ESI-HRMS exact mass calcd for C₁₄H₂₁DNO, 221.1764 [M⁺]; found 221.1771 [M⁺]; Δ = 0.0007. ¹H NMR (300.1 MHz): δ 1.48 (s, 6 H, CMe₂), 2.11 (s, 3 H, COMe), 2.70 (m, 1 H, CHDCO), 3.00 (d, 2 H, CH₂Ar, ³J_{HH} = 7.5 Hz), 3.20 (s, 2 H, CH₂CMe₂), 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, NH₃). Single crystals suitable for an X-ray diffraction study were obtained by slow diffusion of Et₂O into a solution of **6b2** in CH₂Cl₂.

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 NEt₃ (0.026 mL, 0.183 mmol) in CH₂Cl₂ (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 Et₂O (30 mL), and the solid was filtered, washed with Et₂O (2 x 5 mL) and air-dried to afford a mixture of compound **7a2** and NHEt₃Br. This solid was dissolved in CH₂Cl₂ (20 mL), and Na₂CO₃ 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 Et₂O (30 mL) was added. The suspension was filtered, and the solid was washed with Et₂O (2 x 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; $\Delta = 0.0001$. IR (cm^{-1}): $\nu(NH)$ 3363 s; $\nu(CO)$ 1713 s; $\nu(CO_{NH})$ 1626. 1H NMR (400.91 MHz): δ 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): δ 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**· $1/4CH_2Cl_2$ (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 $[(M+1)^+]$; $\Delta = 0.0025$. 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}): $\nu(\text{NH})$ 3363 s; $\nu(\text{CO})$ 1714 s; $\nu(\text{CONH})$ 1633 s. ^1H NMR (400.91 MHz): δ 1.33 (s, 6 H, CMe_2), 2.12 (s, 3 H, COMe), 2.73 (t, 2 H, CH_2CO , $^3J_{\text{HH}} = 7.2$ Hz), 2.96 (t, 2 H, ArCH_2CH_2 , $^3J_{\text{HH}} = 7.2$ 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, $^3J_{\text{HH}} = 7.6$ Hz). $^{13}\text{C}\{^1\text{H}\}$ NMR (100.81 MHz): δ 26.6 (s, ArCH_2CH_2), 28.1 (s, CMe_2), 30.0 (s, COMe), 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}): $\nu(\text{NCO})$ 2255 s; $\nu(\text{CO}) = 1714$ s. ^1H NMR (400.91 MHz): δ 1.39 (s, 6 H, CMe_2), 2.20 (s, 3 H, COMe), 2.72 ("t", 2 H, CH_2CO , $^3J_{\text{HH}} = 7.2$ Hz), 2.86 (s, 2 H, CH_2CMe_2), 2.98 ("t", 2 H, ArCH_2CH_2 , $^3J_{\text{HH}} = 7.2$ Hz), 7.15–7.23 (m, 4 H, H3 + H4 + H5 + H6). $^{13}\text{C}\{^1\text{H}\}$ NMR (100.81 MHz): δ 26.9 (s, ArCH_2CH_2), 30.0 (s, COMe), 30.6 (s, CMe_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-methyl-1-(2-(3-oxobutyl)phenyl)propan-2-yl)urea (7b2'). Et_2NH (70 μL , 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 $\text{Et}_2\text{NH}_2\text{Cl}$ formed and other impurities. The solvent was removed from the filtrate to give an oily residue (80 mg) which ^1H -NMR correspond 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 C₁₉H₃₁N₂O₂, 319.2380 [(M+H)⁺]; found 419.2396 ; Δ = 0.0016. IR (cm⁻¹): ν(NH) 3360 s; ν(CO) 1715 s; ν(CO_{NH}) 1634 s. ¹H NMR (400.91 MHz): δ 1.08 (t, 6 H, N(CH₂Me)₂, ³J_{HH} = 7.6 Hz), 1.34 (s, 6 H, CMe₂), 2.14 (s, 3 H, COMe), 2.68 (t, 2 H, CH₂CO, ³J_{HH} = 7.2 Hz), 2.96 (t, 2 H, CH₂Ar, ³J_{HH} = 7.2 Hz), 3.09 (s, 2 H, CH₂CMe₂), 3.19 (q, 4 H, N(CH₂Me)₂, ³J_{HH} = 7.6 Hz), 4.01 (s, 1 H, NH), 7.09–7.15 (m, 4 H, Ar). ¹³C{¹H} NMR (100.81 MHz): δ 13.8 (s, N(CH₂Me)₂), 26.9 (s, CH₂Ar), 28.2 (s, CMe₂), 29.9 (s, COMe), 40.7 (s, CH₂CMe₂), 41.1 (s, N(CH₂Me)₂), 45.2 (s, CH₂CO), 54.0 (s, CMe₂), 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 [Pd₂Cl₂{NH₂CMe₂CH₂C₆H₄(CH₂CH₂COMe)-2}₂(μ-Cl)₂] (9b2**).** HCl was bubbled through a suspension of complex **2b2**·1/4CH₂Cl₂ (105 mg, 0.142 mmol) in CH₂Cl₂ (15 mL) for 5 min. The suspension became an orange solution, which was concentrated to ca. 2 mL. Et₂O (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 x 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 C₂₈H₄₂Cl₄N₂O₂Pd₂ (793.297): C, 42.39; H, 5.34; N, 3.53. Found: C, 42.19; H, 5.52; N, 3.51. IR (cm⁻¹): ν(NH) 3262 m, 3168 m; ν(CO) 1721 s. ¹H NMR (300.1 MHz): δ 1.33 (s, 6 H, CMe₂), 2.14 (s, 3 H, COMe), 2.67 (t, 2 H, CH₂CO, ³J_{HH} = 7.2 Hz), 2.92 (t, partially obscured by the resonance of CH₂CMe₂, 2 H, CH₂Ar, ³J_{HH} = 7.2 Hz), 2.96 (s, 2 H, CH₂CMe₂), 4.15 (br s, 2 H, NH₂), 7.14 (m, 4 H, H3 + H4 + H5 + H6). ¹³C{¹H} NMR (75.45 MHz): δ 27.1 (s, CH₂Ar), 28.4 (s, CMe₂), 30.1 (s, COMe),

44.4 (s, CH₂CMe₂), 45.0 (s, CH₂CO), 58.5 (s, CMe₂), 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 CH₂Cl₂.

Synthesis of [Pd₂Cl₂{CH(C₅H₈)CHC₆H₄(CH₂CMe₂NH₃)-2}₂(μ-Cl)₂]-CH₂Cl₂ (9b3**·CH₂Cl₂).** HCl was bubbled through a suspension of complex **2b3** (150 mg, 0.195 mmol) in CH₂Cl₂ (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 CH₂Cl₂ (2 x 5 mL) and air-dried to give **9b3**·CH₂Cl₂ as a yellow solid. Yield: 146 mg, 0.157 mmol, 81%. Dec.: 172 °C. Anal. Calcd for C₃₄H₅₀Cl₄N₂Pd₂·CH₂Cl₂ (926.367): C, 45.38; H, 5.66; N, 3.02. Found: C, 45.17; H, 5.87; N, 3.03. IR (cm⁻¹): ν(NH) 3397 (br). The presence of the crystallization solvent was confirmed by reacting **9b3**·CH₂Cl₂ with XyNC (molar ratio 1:6) in DMSO-*d*₆ in an NMR tube. The ¹H spectra of the formed solution corresponds to a 1:0.5 mixture of **10b3**:CH₂Cl₂, that is a half a molecule of CH₂Cl₂ per palladium.

Synthesis of [PdCl{C(=NXy)CH(C₅H₈)CHC₆H₄CH₂CMe₂NH₃}(CNXy)₂]Cl·H₂O (10b3**·H₂O).** XyNC (150 mg, 1.143 mmol) was added to a suspension of **9b3**·CH₂Cl₂ (120 mg, 0.129 mmol) in CH₂Cl₂ (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 CH₂Cl₂ (2 x 5 mL) and Et₂O (5 mL) and air-dried to give complex **10b3**·H₂O as a yellow solid. Yield: 160 mg, 0.192 mmol, 74 %. Mp: 201 °C. Anal. Calcd for C₄₄H₅₂Cl₂N₄Pd·H₂O (832.264): C, 63.50 ; H, 6.54; N, 6.73. Found: C, 63.25; H, 6.71; N, 6.69. IR (cm⁻¹): ν(NH) = 3447 w, 3366 w; ν(C≡N) = 2171 vs; ν(C=N) = 1647 s. ¹H NMR (400.91 MHz, DMSO-*d*₆): δ 1.18 (s, 3 H, Me, CMe₂), 1.24 (s, 3 H, Me, CMe₂), 1.45 (br d, 1 H, CH₂

nor, $^2J_{\text{HH}} = 9.2$ Hz), 1.55–1.67 (m, 4 H, CH₂ 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, CH₂ nor), 2.42 (br s, 1 H, CH nor), 2.93 (d, 1 H, CH₂Ar, $^2J_{\text{HH}} = 13.6$ Hz), 3.19 (br d, 1 H, CH nor, $^3J_{\text{HH}} = 3.6$ Hz), 3.62–3.72 (m, 3 H, 1 H from CH₂Ar + CH^α + CH^β), 6.50 (br d, 1 H, *m*-H, C=NXY, $^3J_{\text{HH}} = 7.2$ Hz), 6.55 (t, 1 H, *p*-H, C=NXY, $^3J_{\text{HH}} = 7.2$ Hz), 6.85 (br d, 1 H, *m*-H, C=NXY, $^3J_{\text{HH}} = 6.8$ Hz), 7.00 (t, 1 H, H4, $^3J_{\text{HH}} = 7.6$ Hz), 7.03 (br d, 1 H, H3, $^3J_{\text{HH}} = 7.6$ Hz), 7.15 (t, 1 H, H5, $^3J_{\text{HH}} = 7.2$ Hz), 7.24 (d, 4 H, *m*-H, C≡NXY, $^3J_{\text{HH}} = 7.6$ Hz), 7.36 (m, 2 H, *p*-H, C≡NXY), 7.40 (d, 1 H, H6, $^3J_{\text{HH}} = 8.0$ Hz), 8.20 (br s, 3 H, NH₃). ¹³C{¹H} NMR (75.45 MHz, DMSO-*d*₆): δ 18.4 (s, Me, C≡NXY), 19.0 (s, Me, C=NXY), 24.1 (s, Me, CMe₂), 25.3 (s, Me, CMe₂), 27.9 (s, CH₂ nor), 31.2 (s, CH₂ nor), 37.4 (s, CH₂ nor), 41.7 (s, CH₂Ar), 41.9 (s, CH nor), 43.7 (s, CH nor), 47.6 (s, C^βH), 54.6 (s, CMe₂), 69.6 (s, C^αH), 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 α radiation ($\lambda = 0.71073$ Å), or mirror-monochromated Cu-K α

radiation ($\lambda = 1.54184 \text{ \AA}$; **5b3**) and ω -scan mode. Analytical numeric absorption correction using a multifaceted crystal model based on expression derived by Clark and Reid⁴³ was applied for complex **3a2**. Multi-scan absorption corrections were applied for compounds **4a1**, **4b2**, **5b3** and **9b2**. *Structure Solution and Refinements*. Crystal Structures were solved by 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**: NH₂ or NH₃, 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, NH₂ or NH₃, 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: 0.00(3).

ASSOCIATED CONTENT

Supporting Information Available: Selected ¹H NMR data for the new compounds, details (including symmetry operators) of hydrogen bondings and 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.

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For the Table of contents

