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Insertion of Isocyanides, Isothiocyanates and Carbon Monoxide into the Pd–C Bond of Cyclopalladated Complexes Containing Primary Aryl-Alkylamines of Biological and Pharmaceutical Significance. Synthesis of Lactams and Cyclic Amidinium Salts Related to the Isoquinoline, Benzo[*g*]isoquinoline and β-Carboline Nuclei

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Keywords

Primary amines, cyclopalladation, ortho-palladated complexes, carbon monoxide insertion reactions, isocyanides and isothiocyanates, 1-oxo-isoquinolines, 1-oxo-β-carbolines, cyclic amidines, amidinium salts

Summary

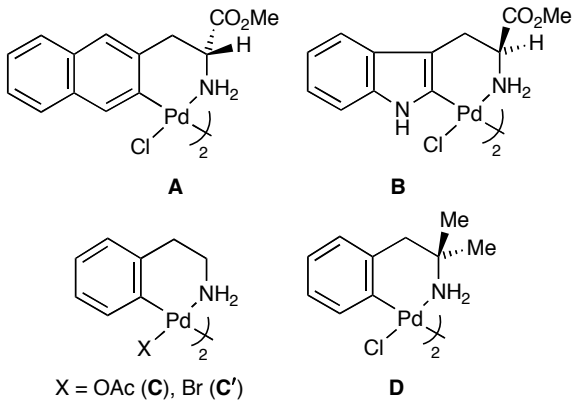
Cyclometalation of 3-(2-naphthyl)-D-alanine methyl ester is achieved by reacting the corresponding hydrochloride salt and $Pd(OAc)_2$ in a 1:1 molar ratio (acetonitrile, room temperature, 6 days). Although the chloro-bridged dimer (**A**) cannot be isolated in a pure form, addition of RNC to the reaction mixture affords the mononuclear derivatives (*R*)-[Pd{κ^2(*C*,*N*)-$C_{10}H_6CH_2CH(CO_2Me)NH_2$-2}Cl(CNR)] (R = ^{t}Bu, **1a-^{t}Bu**; Xy ($C_6H_3Me_2$-2,6), **1a-Xy**). Similar complexes (*S*)-[Pd{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}Cl(CNR)] (R = ^{t}Bu, **1b-^{t}Bu**; Xy, **1b-Xy**) are prepared from RNC and the previously reported cyclometalated derivative of L-tryptophan methyl ester, (*S*,*S*)-[Pd_2{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}$_2$($\mu$-Cl)$_2$] (**B**). Compound **1b-Xy** reacts with XyNC to give the iminoacyl complex (*S*)-[Pd{κ^2(*C*,*N*)-$C(=NXy)C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}Cl(CNXy)] (**2b**), which crystal structure has been determined by X-ray diffraction studies. The cyclopalladated dimer **B** or those containing phenethylamine (**C**) or phentermine (**D**; see Chart 1) reacts with RNC (R = ^{t}Bu, Xy) in refluxing chloroform or toluene to render, depending on the reaction conditions, the cyclic amidines (**3c-^{t}Bu**, **3d-Xy**) or the amidinium salts (**4b-^{t}Bu**, **4c-^{t}Bu, 4c-Xy, 4d-^{t}Bu, 4d-Xy**). The amidines **3a-^{t}Bu** and **3a-Xy** and the amidinium salts **4a-^{t}Bu** and **4a-Xy** are synthesized from complexes **1a-^{t}Bu** and **1a-Xy**. When **D** reacts with isothiocyanates RNCS (R = Me, To (C_6H_4Me-4)), the cyclic amidinium salts **4d-Me** and **4d-To** are isolated. Amidinium triflates derived from phentermine with an aryl substituent at the exocyclic nitrogen atom (**4d-Xy**, **4d-To**) present *E*/*Z* isomerism in $CHCl_3$ or CH_2Cl_2 solution. CO reacts with **A**–**D** to give, after depalladation, the corresponding lactams: (*R*)-1-oxo-3-(methoxycarbonyl)-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (**5a**), (*S*)-1-oxo-3-(methoxycarbonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (**5b**), 1-oxo-1,2,3,4-tetrahydroisoquinoline (**5c**), or 1-oxo-3,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (**5d**). The

crystal structures of compounds **4b-^{t}Bu**, **4c-^{t}Bu**, **4d-^{t}Bu**,**Xy**,**Me**,**To** and **5a–d**, have been determined by X-ray diffraction studies.

Introduction

It is well known that carbon monoxide and isocyanides insert into the Pd–C bond of aryl complexes to afford acyl[1-5] or iminoacyl derivatives.[4-17] These reactions have been extensively studied as they are involved in many stoichiometric and catalytic palladium–mediated organic transformations.[5,10,18-21] Particularly, when ortho-metalated tertiary benzylamines are used as starting materials, depalladation of the organometallic intermediates allows the synthesis of N-heterocycles.[22] Nevertheless, only a few examples involving cyclopalladated primary amines have been reported,[14,21,23-25] probably due to the scarce number of these complexes reported in the literature.[21,26]

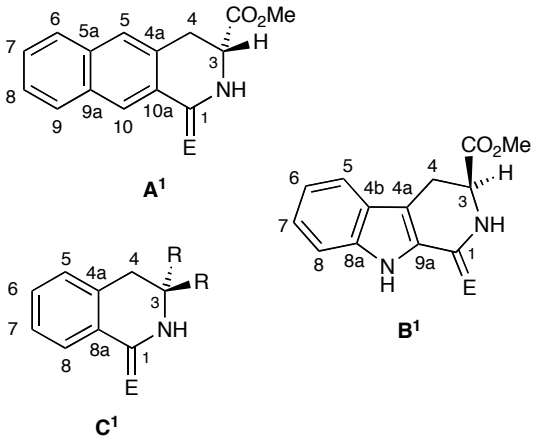
Chart 1. Cyclometalated Complexes Derived from 3-(2-Naphthyl)-D-alanine Methyl Ester (**A**), L-tryptophan Methyl Ester (**B**), Phenethylamine (**C, C′**) and Phentermine (**D**). See reference [30] for compound numbering



We report in this article: (1) the regiospecific cyclopalladation of the non-natural occuring aminoacid derivative 3-(2-naphthyl)-D-alanine methyl ester; (2) the insertion reactions of RNC, RNCS and CO into the Pd–C bond in this cyclopalladated complex as well

as in others containing primary aryl-alkylamines (Chart 1) of biological or/and pharmaceutical relevance as phenethylamine,[27] phentermine,[28] or L-tryptophan methyl ester,[29] which afford the corresponding lactams or cyclic amidine-derivatives related to the isoquinoline, and β-carboline nuclei (Chart 2); and, (3) the isomeric equilibria of the amidinium salts derived from phentermine and XyNC or ToNCS.

Chart 2. Lactams (E = O) and Amidines (E = NR) Containing the 3,4-Dihydrobenzo[*g*]isoquinoline (**A**[1]), 2,3,4,9-Tetrahydro-β-carboline (**B**[1]) and 3,4-Dihydroisoquinoline (**C**[1]) Nuclei and their Numbering Schemes



The 1,2,3,4-tetrahydroisoquinolin-1-one and 2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indol-1-one (tetrahydro-β-carbolinone) rings are structural units found in natural products.[31] Both nuclei possess significant bioactivities (e.g., central nervous system,[32] antiviral,[33] antithrombotic,[34] or cytotoxic activity[35]), and have served as important intermediates for the synthesis of more complex alkaloids and further functionalized polycyclic systems of biological interest.[36-39] The wide variety of pharmacological activity associated with cyclic amidines has also been very well documented and includes antitumoral,[40] anticoagulant,[41] antiinflammatory,[42,43] antihypertensive,[44] and hypoglycemic activities.[45] Besides, they can act as potent inhibitors of human nitric oxide synthase (NOS),[46,47] and glycosidases.[48] Because of

it, significant efforts have been made to construct both lactams[19,49-52] and cyclic amidines skeletons[41,43,47,53] over recent years.

Results and Discussion

Synthesis and Structure of New Cyclometalated Complexes. When 3-(2-naphthyl)-D-alanine (D-naphthylalanine) methyl ester hydrochloride reacted with $Pd(OAc)_2$ in a 1:1 molar ratio in acetonitrile for 6 days, an orange solid **I** (Scheme 1) was isolated from the reaction mixture, which ^{1}H NMR showed very broad signals that could not be easily assigned. Nevertheless, the aromatic region of the spectrum showed signals corresponding to the metalated and the non-metalated naphthyl ring of the starting amino acid derivative. There were also two resonances in the region corresponding to the OMe groups (one very sharp and other very strong and broad), but they overlapped and their relative ratio was difficult to evaluate. Besides, no acetate signals were present. The mixture could not be separated by fractional crystallization or by chromatography, although its reactivity showed that the cyclometalated complex (*R,R*)-[$Pd_2\{\kappa^2(C,N)$-$C_{10}H_6CH_2CH(CO_2Me)NH_2-2\}_2(\mu$-Cl$)_2$] (**A**) was the main component (Scheme 1). Thus, this mixture **I** was successfully used as starting material to synthesize other D-naphthylalanine methyl ester derivatives (see below).

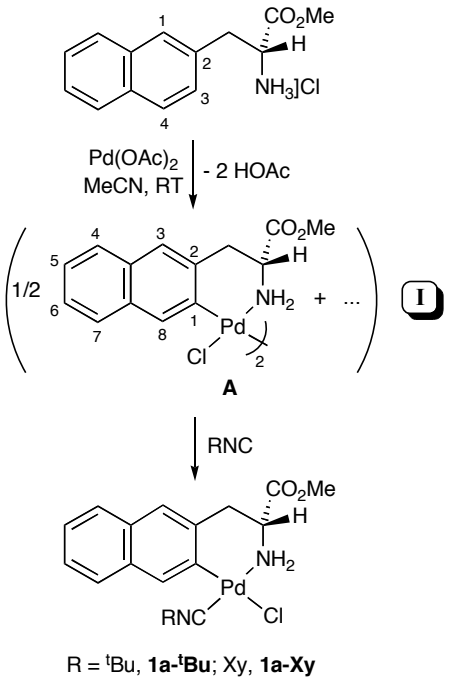
Other reaction conditions (acetonitrile at 80 ºC for 4–8 h, or toluene at 60 or 75 ºC for 12 h) were tested to cyclopalladate the D-naphthylalanine methyl ester hydrochloride. In all cases, decomposition to metallic palladium was observed and the yield of the cyclometalated material **A** in the mixture **I** did not improved (tested by ^{1}H NMR).

Addition of ^{t}BuNC or XyNC to a solution of the mixture **I** in CH_2Cl_2 allowed the isolation of the mononuclear isocyanide complex (*R*)-[Pd$\{\kappa^2(C,N)$-$C_{10}H_6CH_2CH(CO_2Me)NH_2-2\}$Cl(CNR)] (R = ^{t}Bu (**1a-^{t}Bu)**, Xy (**1a-Xy**), Scheme 1). **I** was

assumed to be pure complex **A** to calculate the required amount of the isocyanide to prepared these complexes, which means that an excess of the ligands was used.

There are two possible sites for metalation of naphthylalanine methyl ester: the C1 and C3 atoms of the naphthyl ring (see Scheme 1 for numbering diagram). The ^{1}H and ^{13}C NMR spectra of complexes **1a-^{t}Bu** and **1a-Xy** showed only one set of signals and thus, one isomer was formed. This isomer agreed with C–H activation at C3 position, as the resonance for H3 in the free ligand (7.39 ppm in DMSO-d_6) disappeared upon metalation. Besides, the ^{1}H NMR spectra of complexes **1a-^{t}Bu,Xy** showed two sharp singlets in the aromatic region, assigned to the H3 and H8 protons of the cyclometalated ring (**1a-^{t}Bu**: 7.43, 7.70 ppm; **1a-Xy**: 7.47, 7.90 ppm). In the ^{13}C NMR spectra of both complexes, the resonances due to C1 (**1a-^{t}Bu**: 140.8 ppm; **1a-Xy**: 140.6 ppm) were deshielded with respect to that of the corresponding free ligand (127.4 ppm in DMSO-d_6) as observed in other cyclopalladated complexes.[21,54]

Scheme 1. Synthesis of Cyclometalated Derivatives of D-Naphthylalanine Methyl Ester



R = ^{t}Bu, **1a-^{t}Bu**; Xy, **1a-Xy**

We could not discard the presence of the other regioisomer (emerging from C–H activation at C1 position of the free ligand) in the mixture **I**, but none of its derivatives was

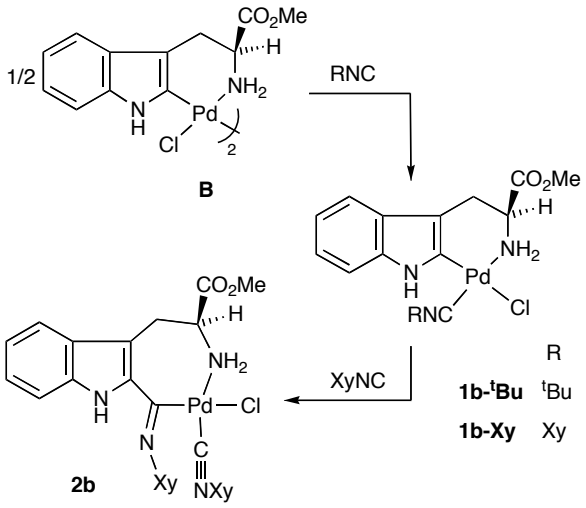
detected, neither in the reactions with isocyanides, nor in the reaction of **I** with CO (see below).

Direct palladation of *N,N*-dimethyl-(2-naphthyl)methylamine,[55] *N,N*-dimethyl(1-(2-naphthyl)ethyl)amine,[56] and 2-(2′-naphthyl)pyridine[57] have also been reported to occur regiospecifically at C3 position,[55] and this fact has been explained in terms of different steric constrains for the 1- and the 3-metalated transition states.[55]

Cyclopalladated L-tryptophan methyl ester complex (*S,S*)-[$Pd_2\{\kappa^2$-*C,N*-$C_8H_5NCH_2CH(CO_2Me)NH_2-2\}_2(\mu$-Cl$)_2$] (**B**, Chart 1)[58] also reacted in a 1:2 molar ratio with RNC to give (*S*)-[Pd$\{\kappa^2$(*C,N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)-2\}$Cl(CNR)] (R = ^{t}Bu (**1b-^{t}Bu)**, Xy (**1b-Xy**), Scheme 2). When XyNC was used, a small amount of the aminoacyl complex (*S*)-[Pd$\{\kappa^2$(*C,N*)-C(=NXy)$C_8H_5N(CH_2CH(CO_2Me)NH_2)-2\}$Cl(CNXy)] (**2b**) was isolated from the reaction mixture. Complex **2b** was independently prepared in excellent yield by reaction of complex **1b-Xy** and XyNC in a 1:1 molar ratio. Under the same conditions, ^{t}BuNC did not insert into the Pd–C bond, which was not surprising because this reaction becomes more difficult for isocyanides having electron-donating groups.[16,17] The behavior of **B** contrasts with that of **A**, which does not insert XyNC even when using an excess of this isocyanide (see below).

The ^{1}H and ^{13}C NMR spectra of complexes **1b-^{t}Bu**,**Xy** and **2b** are in agreement with the proposed structures. In complex **2b**, prevented rotation around the Xy–N bond of the inserted isocyanide fragment, due to sterical hindrance, makes inequivalent the two Me groups, as well as the meta protons and carbons and ortho carbons of the xylyl ring, as observed in the ^{1}H and ^{13}C NMR spectra (^{1}H NMR: Me, 1.87 and 2.48 ppm; *m*-H, 6.54 and 7.16 ppm. ^{13}C NMR: Me, 18.6 and 20.1 ppm; *o*-C, 126.5, 127.8 ppm; *m*-CH, 126.9, 128.8 ppm).

Scheme 2. Reactions of the Cyclopalladated Complexes Derived from Tryptophan Methyl Ester with Isocyanides



In complex **2b**, the coordinated isocyanide is located in trans position to the amine group. We propose the same geometry for complexes **1a-^{t}Bu,Xy**, and **1b-^{t}Bu,Xy** because this is the normal behavior for benzylamine palladacycles,[1,8,14,15,17] and it is in agreement with the well-established *transphobia* between C-donor ligands.[11,12,20,59]

The crystal structure of complex **2b** has been determined by X-ray diffraction (Figure 1) and shows the palladium atom coordinated to Cl(1), N(2), the terminal carbon atom of the isocyanide ligand (C15), and the carbon atom of the inserted isocyanide (C12) in a square-planar geometry (mean deviation from the plane Pd(1), Cl(1), N(2), C(12), C(15) = 0.0324 Å). The seven-membered metallacycle adopts a boat conformation, defined by three planes: (1) C(12)–Pd(1)–N(2), (2) C(2)–C(3)–C(10)–N(2) (mean deviation 0.055 Å), and (3) C(3)–C(11)–C(10). The angle between planes (1) and (2) is 69.8º, while that between planes (2) and (3) is 50.6º. Both Xy rings are nearly parallel (dihedral angle between the two Xy rings = 15.7º) and nearly perpendicular to the Pd-coordination plane (angles of 72.3 and 70.1º, respectively), thus avoiding steric hindrance. Similar features have been observed in related structures.[11,15,60] Each molecule of complex **2b** is connected to two others through hydrogen

bonds (involving the NH group of the indol rings and the chlorine atoms), giving infinite chains along the *a* axis.

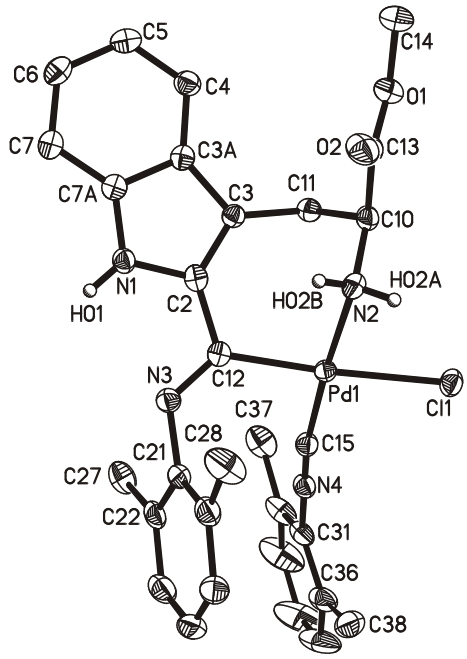
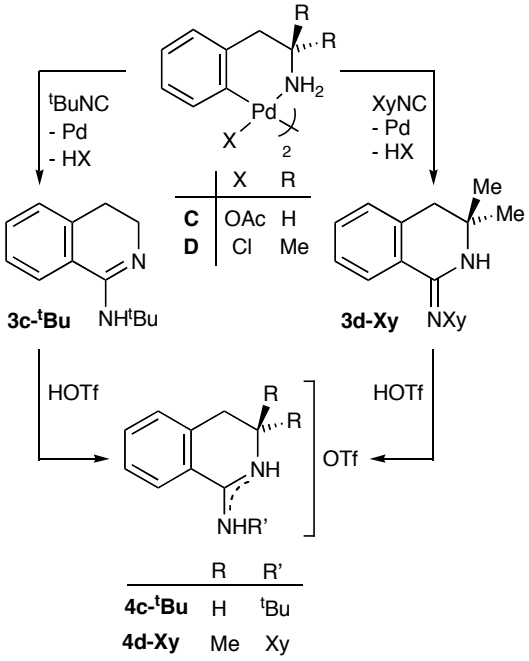


Figure 1. Thermal ellipsoid plot (50% probability) of **2b** along with the labeling scheme. Selected bond lengths (Å) and angles (deg): Pd(1)–Cl(1) = 2.4138(5), Pd(1)–N(2) = 2.1067(16), Pd(1)–C(12) = 2.0154(18), Pd(1)–C(15) = 1.9222(19), C(12)–N(3) = 1.278(2), C(15)–N(4) = 1.151(2); Cl(1)–Pd(1)–N(2) = 86.78(4), N(2)–Pd(1)–C(12) = 91.37(7), C(12)–Pd(1)–C(15) = 92.02(8), C(15)–Pd(1)–Cl(1) = 89.84(6), C(12)–N(3)–C(21) = 124.47(16), Pd(1)–C(15)–N(4) = 171.91(17), C(15)–N(4)–C(31) = 178.8(2).

Synthesis of Amidines and Amidinium Salts through Insertion of Isocyanides into the Pd–C Bond of Cyclopalladated Complexes. When **C** or **D** was treated with RNC (1:2.2 or 1:2 molar ratio, respectively) in refluxing toluene, formation of Pd(0) was observed and from the reaction mixture, crude 3,4-dihydroisoquinoline **3c-^{t}Bu** or **3d-Xy** was isolated as a pale yellow liquid or colorless solid, respectively (Scheme 3). These amidines were very

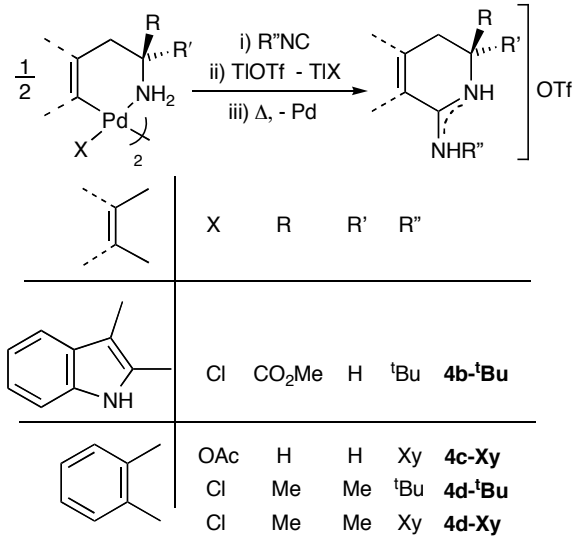
difficult to purify by fractional crystallization, because they were very soluble in organic solvents (including *n*-pentane), or by chromatography, as they got retained even in deactivated silica gel or alumina. The few previous related studies on the reactivity of cyclopalladated primary amines towards isocyanides always reported the synthesis of the corresponding amidinium salts,[14,21,23] or complexes $[PdX_2L_2]$ where L is the amidine.[14]

Scheme 3. Synthesis and Protonation of Amidines **3c-^{t}Bu** and **3d-Xy**



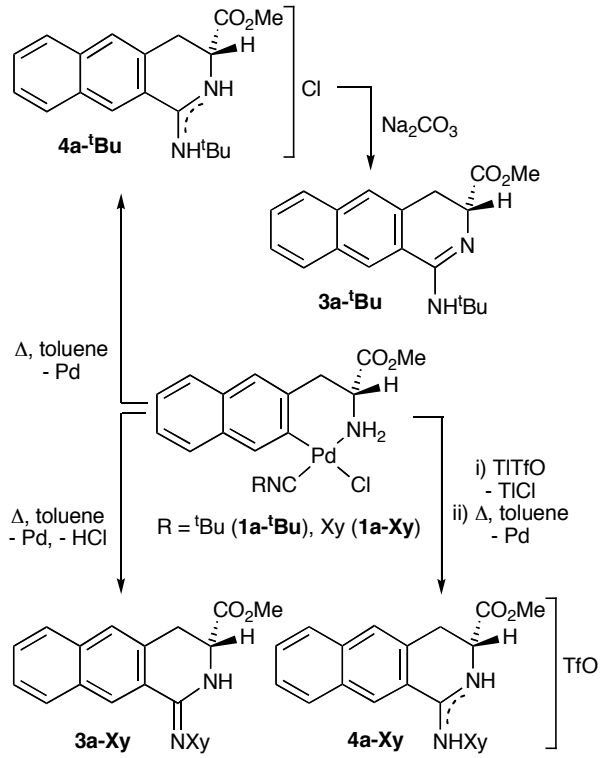
In order to get more easily isolable amidine derivatives, the corresponding salts were obtained by reacting **3c-^{t}Bu** or **3d-Xy** with triflic acid in Et_2O. The cyclic amidinium triflate **4c-^{t}Bu** or **4d-Xy** precipitated in the reaction mixture and was isolated as a colorless powder (Scheme 3). Salt **4d-Xy** was a mixture of two isomers, the nature of which will be discussed in the last part of this Section. Whitby et al. have reported the palladium-catalyzed synthesis of cyclic amidines, starting from 2-bromobenzylamine or 2-bromophenethylamine, ^{t}BuNC and Cs_2CO_3.[61] Nevertheless, it is necessary to point out the restricted availability of the required 2-haloarenes and the limitations of the process, which seems to give only good yields for *tert*-alkyl-isonitriles.

Scheme 4. Synthesis of Cyclic Amidinium Salts Containing the Isoquinoline and β-Carboline Nuclei



Following a method we have previously used with other cyclopalladated derivatives,[14,21] the amidinium salt **4d-Xy** was also prepared by reacting the ortho-metalated derivative **D** with XyNC and TlOTf (OTf = O_3SCF_3, Scheme 4) but, surprisingly, the same method did not afford **4c-^{t}Bu** starting from **C′**. Instead, an unidentified product was obtained, which showed no ^{t}Bu resonance in its ^{1}H NMR spectrum. This one pot synthesis allows to prepare with moderate to good yields (47–66%) other amidinium salts, **4b-^{t}Bu, 4c-Xy** and **4d-^{t}Bu** (Scheme 4), but no **4a** salts using the mixture **I**, because they could not be separated from other products. However, refluxing in toluene **1a-^{t}Bu** yielded the amidinium chloride **4a-^{t}Bu**, along with a small amount of the amidine **3a-^{t}Bu** (Scheme 5) that can be prepared by treatment of salt **4a-^{t}Bu** with Na_2CO_3. Contrarily, when **1a-Xy** was heated in toluene, the amidine **3a-Xy** was isolated instead the salt **4a-Xy** that can be obtained if complex **1a-Xy** is treated with thallium triflate and heated up in toluene.

Scheme 5. Synthesis of Cyclic Amidines and Amidinium Salts Containing the Benzo[g]isoquinoline Nucleus



In agreement with the previous studies on the reactivity of cyclopalladated complexes towards isocyanides,[1,4-6,8-17] we propose that the first step in the synthesis of amidines and their salts is the coordination of the isocyanide to afford complexes **1** (Scheme 5). In fact, complexes **3a-Xy** and **4a-^{t}Bu** could be prepared starting from **1a-Xy** and **1a-^{t}Bu**, respectively. Under thermal conditions, insertion of the isocyanide into the Pd–C bond to give an iminoacyl complex **II** is proposed (Scheme 6).[7,8,13,14] Although such an intermediate has not been isolated, we have reported the synthesis of a related complex by refluxing a solution of [Pd{$C_6H_4CH_2NH_2$-2}Br(CNXy)] in toluene.[14] Depalladation and C–N coupling from the iminoacyl complex **II** will give the corresponding amidinium salt (compounds **4**), which in the case of X = Cl can afford an amidine (compounds **3**) after HCl elimination. The additional

use of TlOTf hinders the last step, leading always to amidinium salts. In fact, when **1a-Xy** was refluxed in toluene with or without TlOTf, the salt **4a-Xy** or, respectively, the amidine **3a-Xy** was obtained. However, contrarily to **1a-Xy**, when complex **1a-^{t}Bu** was refluxed in toluene the amidinium chloride **4a-^{t}Bu** was formed, along with only a small amount of the amidine **3a-^{t}Bu** (Scheme 5), which must be attributed to the more acidic character of **4a-Xy** than **4a-^{t}Bu**.[62]

The migration rate of the aryl group to the coordinated isocyanide increases when increasing the electrophilicity of the isocyanide and the nucleophilicity of the carbon atom bonded to palladium(II).[16] Thus, aryl-isocyanides react faster than alkyl-isocyanides. Besides, insertion reactions into the Pd–C bond of the cyclometalated tryptophan derivatives (complexes **b**) should be faster than reactions on cyclometalated phenethyl derivatives as the indol ring is strongly activated towards electrophilic reagents due to the effect of the lone pair at the nitrogen atom.[63] Moreover, the smaller steric requirements of the indol nucleus compared to the phenyl ring would also accelerate the reaction. These trends explain the following experimental observations: (1) the preparation of compound **4b-^{t}Bu** required milder conditions than the synthesis of the other amidinium salts; (2) insertion of isocyanide at room temperature was only observed when XyNC and the cyclometalated tryptophan derivative were used; and (3) the amidinium salt derived from tryptophan methyl ester and XyNC was not obtained when the standard procedure (cationic intermediate and refluxing toluene) was used, probably because the insertion reaction is so favored that polyinserted derivatives are formed.[2,12,64]

Synthesis of Amidinium Salts through Insertion of Isothiocyanates into the Pd–C Bond of Cyclopalladated Complexes. There are only a few examples of the insertion of isothiocyanates into a σ M–C bond (M = Mg,[65] Al,[66] Zr,[67] Nb,[68] Ta,[68] Re,[69] Fe,[70] Co,[71] Ni,[72]

and Pd[73]). In most cases, the heterocumullene inserts to form an *N*-alkyl or *N*-aryl thioamidato ligand which binds to the metal in a $\kappa^2(N,S)$ (Chart 3) fashion, although examples of κ^1 bonding through the sulfur or the nitrogen atom have also been reported.

Scheme 6. Proposed Reaction Pathway for the Synthesis of Amidinium Salts through Isocyanide Insertion

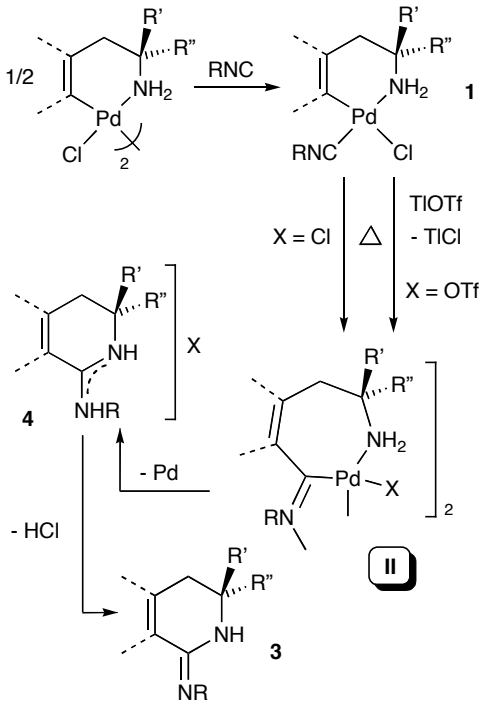
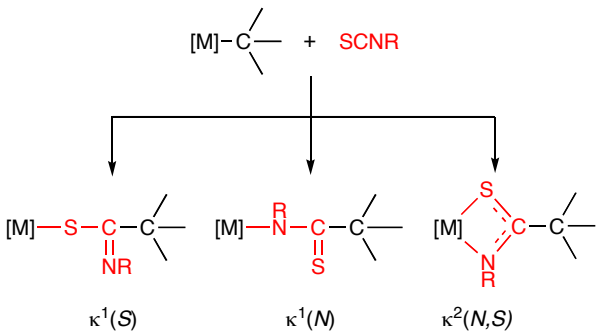


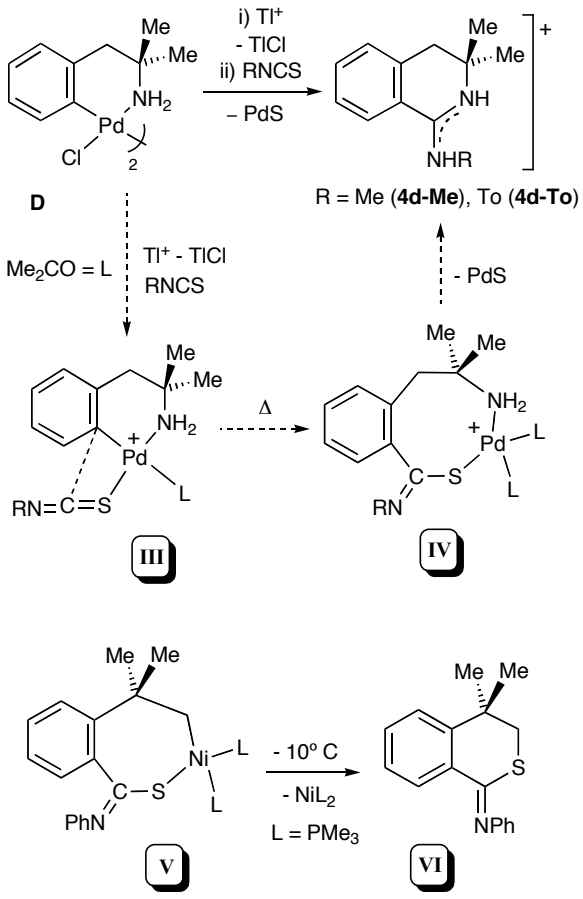
Chart 3. Products of the insertion reactions of isothiocyanates into M–C bonds



Reactions of RNCS (R = Me, To) with cyclometalated primary aryl-alkylamines, were attempted with **B**, **C** and **D**. The reactions were carried out in one pot/two steps process involving addition of TlOTf to an acetone solution (**C**, **D**) or suspension (**B**) of the

cyclopalladated complex to generate a cationic derivative, which would be more reactive towards insertion reactions.[9] After removing TlCl, RNCS was added, the suspension was refluxed in toluene and the crystalline black solid formed during the reaction was removed. However, only from **D**, amidinium salts **4d-Me** and **4d-To** could be isolated in pure form and in moderate yields (41–67%; Scheme 7). Other reactions conditions were also unsuccessfully attempted with **C** and **D**. The isolated salts **4** would have been the products obtained from insertion of MeNC and ToNC into the C–Pd bond of **D**. To confirm that the formation of the isocyanide fragment does not arise from decomposition of the isothiocyanate prior to the insertion reaction, ToNCS was heated in toluene at 110 ºC for 4 h. Unaltered ToNCS was recovered (by ^{1}H NMR).

Scheme 7. Synthesis and Proposed Reaction Pathway for the Synthesis of Amidinium Salts **4d-Me,To**



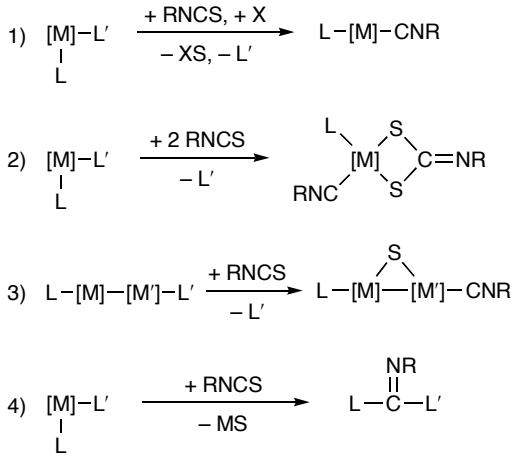
The black solid formed contained C, H and S (by elemental analysis), did not react with PPh_3 to afford $SPPh_3$, and it was only partially soluble in aqua regia. When treated with concentrated HNO_3, a small fraction of the solid dissolved. This fraction was diluted with distilled water and treated with $AgNO_3$ to precipitate a dark gray solid. All this data move us to propose that the black solid is PdS, along with some ocluded organic compounds and not a mixture of Pd(0) and sulfur.

The proposed reaction pathway for the synthesis of **4d-Me,To** is shown in Scheme 7. Removing the chloro ligand in **D** allows coordination of the isothiocyanate, probably via the sulfur atom (**III**).[74] Insertion of the isothiocyanate into the Pd–C bond, affords an unstable eight-membered palladacycle (**IV**) that may be a solvento-complex, as shown in Scheme 7, or a dimer, as both the imino N and the endocyclic S atoms support lone pairs. A Ni(II) intermediate of this type (**V)**, isolated at –80 ºC, decomposes at –10 ºC, rendering the coupling product of the two atoms bonded to palladium (C and S). However, the loss of the metal from our intermediate **IV** does not occur in the same way and the most thermodynamically favored C–N coupling and PdS precipitation are observed.

It has been described that the reactions of metal complexes with isothiocyanates frequently involve the cleavage of the S–C bond to afford products containing the degradation fragments of the RNCS.[75] These reactions normally require the presence of: (1) a sulfur abstracting ligand, such as phosphine, to render the metal isocyanide and the corresponding sulfide;[76] (2) an excess of isothiocyanate, to yield, through a disproportionation reaction, an isocyanide and a dithiocarbimato group;[77] or (3) a bimetallic system, to render an isocyanide ligand and a bridging-sulfide group.[78] Non of these routes corresponds with the reaction

described in this paper (Scheme 8, reaction 4), which seems to be a new path for activation of the S–C bond of isothiocyanates through coordination to metal complexes.

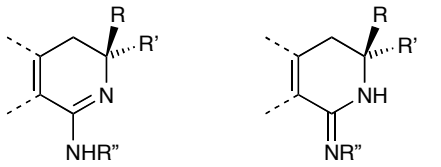
Scheme 8. Model Reactions for Activation of RNCS through Metal-Complexes



Structure of Amidines and Amidinium Salts. *N*,*N*′-Disubstituted amidines RN=C(R')–NHR" can show prototropic tautomerism (Chart 4). This equilibrium is displaced in favor of the tautomer containing the proton at the N atom with the weeker electron-withdrawing group.[79] In our case, the ^{1}H NMR and ^{13}C NMR spectra of crude **3a-^{t}Bu,Xy**, **3c-^{t}Bu** and **3d-Xy** show one set of signals and thus, for each amidine, only one tautomer is observed in solution. For amidines **3a-^{t}Bu** and **3c-^{t}Bu** (R′ = ^{t}Bu), the proton chemical shift of the *tert*-butyl group (**3a-^{t}Bu**: 1.54 ppm; **3c-^{t}Bu**: 1.46 ppm) shows that the isomer with the endocyclic C=N bond (Chart 4) was formed. Whitby et al. have found that the proton shift of this group in a variety of amidines Ar–C(=N^{t}Bu)NR$_2$ and Ar–C(=NR)NH^{t}Bu was 1.00–1.26 ppm in the former and 1.41–1.45 ppm in the latter,[61,80] including **3c-^{t}Bu**.[61] For amidines **3a-Xy** and **3d-Xy** (Chart 4), the resonances corresponding to the *p*-H of the xylyl group (**3a-Xy**: 6.93 ppm; **3d-Xy**: 6.88 ppm) and *p*-C (**3a-Xy**: 122.8 ppm; **3d-Xy**: 122.2 ppm) appear in their

NMR spectra strongly shielded with respect to those of the free isocyanide. This fact has been used to assing an exocyclic imino tautomeric form to similar amidines.[81]

Chart 4. Tautomeric Forms for Cyclic Amidines

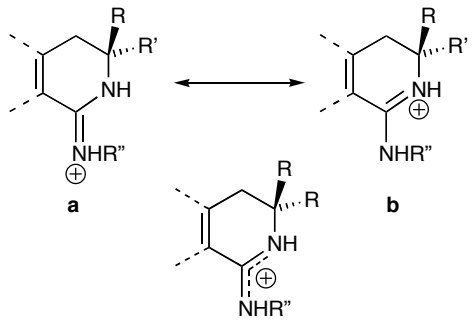


endocyclic imino isomer — **3a-^{t}Bu**, **3c-^{t}Bu**

exocyclic imino isomer — **3a-Xy**, **3d-Xy**

In general, protonation of amidines occurs at the imino nitrogen, rather than the amino one, because the new cation is thus stabilized by resonance (Chart 5).[82] Therefore, both tautomeric forms of *N*,*N*′-disubstituted amidines must lead to only one amidinium tautomer.

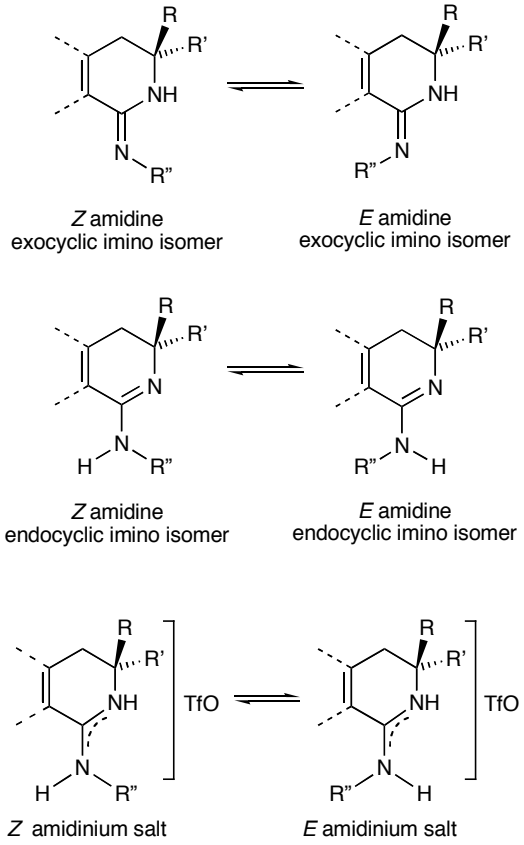
Chart 5. Resonance Forms for Cyclic Amidinium Salts



Because of the double or partially-double character of the exocyclic C–N bond in amidines and amidinium salts, *E*/*Z* isomerism around this bond is possible (Chart 6). Variable temperature ^{1}H NMR spectra of compounds **4d-^{t}Bu,Xy,Me,To** were recorded (CD_2Cl_2, from –80 to 20 ºC; $CDCl_3$, from 20 to 60 ºC). The ^{1}H NMR spectrum of **4d-Xy** at –60 ºC showed two sets of signals, accounting for two isomers, in a molar ratio 9:1 (determined by the NH integral ratios). Its ^{1}H-^{15}N HMQC spectrum confirmed the presence of two sets of two single protonated, anisocronous nitrogen nuclei, which were assigned to the *E*- and *Z*-isomers. The ^{1}H NMR signals of the *Z*-isomer (the major isomer) were easily distinguished by the resonance corresponding to H8 of the isoquinoline nucleus (8.54 ppm), as it showed a NOE to

the exocyclic NH signal (XyN*H*). The composition of the mixture was temperature dependent. Thus, at 25 ºC in $CDCl_3$, a mixture 3:1 (***Z*-4d-Xy**:***E*-4d-Xy)** was obtained, while at 60 ºC in $CDCl_3$ the ratio between isomers was 3:2 (***Z*-4d-Xy**:***E*-4d-Xy**). Amidinium salt **4d-To** also exhibits dinamic behaviour in $CDCl_3$ solution, although in this case, only at –60 ºC the *E*/*Z* equilibrium is slow enough to observe both isomers. At this temperature, the *Z*-isomer was the major component (***Z*-4d-To**:***E*-4d-To** = 7:1), as proved by ^{1}H NMR (H8, 8.26 ppm).

Chart 6. *E*/*Z* Isomerism for Cyclic Amidines and Amidinium Salts



Above this temperature, all the NH and the aromatic signals became broader, until they nearly dissappear at 60 ºC. The ^{1}H NMR spectra of amidinium salts **4d-^{t}Bu** and **4d-Me**, recorded at different temperatures in CD_2Cl_2 or $CDCl_3$, showed only one set of resonances, assigned to the *Z*-isomers (in both cases, H8 of the isoquinoline nucleus showed a NOE to the exocyclic NH signal). The ^{1}H NMR spectra of amidinium triflates **4d** were also recorded in DMSO-d_6

solutions and they showed exclusively the presence of the *Z*-isomer, which proves that the equilibrium observed for **4d-Xy,To** is also solvent dependent, as described for other amidinium salts.[83]For the remaining amidinium triflates **4a-^{t}Bu,Xy**, **4b-^{t}Bu** and **4c-^{t}Bu** and amidines **3a-^{t}Bu,Xy**, **3c-^{t}Bu** and **3d-Xy**, although no variable temperature NMR studies have been carried out, the chemical shifts of the only set of signals observed in solution at room temperature corresponds to a unique isomer (and not to an average situation emerging from an equilibrium, as observed for **4d-To**). We propose a *Z*-stereochemistry based on the following facts: (1) this is the geometry showed in solid state by all the amidinium salts synthetized whose crystal structures have been solved (**4b-^{t}Bu**, **4c-^{t}Bu**, **4d-^{t}Bu,Xy,Me,To**; see below) and by other aryl-amidines similar to **3d-Xy**;[84] (2) this geometry minimizes steric hindrance, as the most bulky substituent at the exocyclic nitrogen and its nearest aromatic hydrogen atom are situated in trans position; (3) for amidines **3a-^{t}Bu,Xy**, **3c-^{t}Bu** and **3d-Xy**, DFT calculations estimate the difference of stability between the *Z*/*E*-isomers (see Supporting Information) to be around 23 kJ/mol, which is comparable to that in **4d-^{t}Bu**,**Xy**,**Me**,**To** (34.8–21.6 kJ/mol).

The different behavior in solution of **4d-Xy**,**To** (equilibrium between *Z*/*E*-isomers) and the other amidinium salts (only *Z*-isomers) arises from the nature of the substituents at both nitrogen atoms: in the formers the most electron-withdrawing group is bonded to the exocyclic nitrogen atom (R" = To, Xy) and the most electron-releasing group to the endocyclic nitrogen atom (R = R' = Me), which increases the contribution of resonace form **b** (Chart 5). In addition, the lower rotational energy around the exocyclic C–N bond when R" = To than Xy is due to a stronger –I effect and smaller steric demand of To than Xy.

Other authors observed *E*/*Z*-isomerism in solution for semicyclic amidinium salts derived from 2-[(2-cyclohexylcyclopentyl)imino]hexahydroazepin,[83] and related the greater

amount of the *E*-isomers in equilibrium to the larger steric demand of the substituent at the exocyclic nitrogen atom. This is not our case as isomerization is not observed for amidinium salt **4d-^{t}Bu**, with the largest substituent at the exocyclic nitrogen atom.

The crystal structures of amidinium salts **4b-^{t}Bu** (Figure 2), **4c-^{t}Bu** (see Supporting Information) and **4d-^{t}Bu** (Figure 3), **4d-Xy** (Figure 4), **4d-Me**, **4d-To** (see Supporting Information) have been determined by X-ray diffraction. For each salt, the lengths of the $N_{exocyclic}$–C and $N_{endocyclic}$–C bonds are nearly identical (around 1.32 Å; see Supporting Information), and the C–C(–N)–N atoms are coplanar. These values indicate delocalized bonding within the amidinium groups. All the crystal structures correspond to *Z*-isomers, reflecting the thermodynamic stability of this geometry. For compounds **4d-Xy** and **4d-To**, the angle between the Xy or To plane and the above defined plane is 75 or 129º, respectively. All these features are similar to those reported for analogous amidinium triflates.[14,58]

In all the compounds, the cationic units are connected to the triflate groups through hydrogen bonds (**4b-^{t}Bu** and **4d-To**: for each cation, five interactions with three different triflates; **4c-^{t}Bu**: three interactions with two different triflates; **4d-^{t}Bu,Xy**: two interactions with two different triflates; **4d-Me**: three interactions with three different triflates), generating single (**4b-^{t}Bu**, **4c-^{t}Bu**, **4d-^{t}Bu,Xy**) or double chains (**4d-Me,To**).

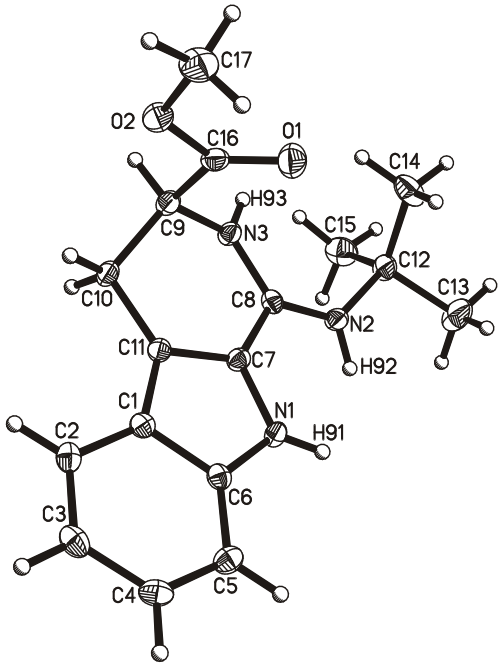


Figure 2. Thermal ellipsoid plot (50% probability) of the cation of **4b-^{t}Bu** along with the labeling scheme. Selected bond lengths (Å) and angles (deg): N2–C12 = 1.498(2), N2–C8 = 1.315(2), N3–C8 = 1.339(2), N3–C9 = 1.461(2), C7–C8 = 1.446(2); C8–N2–C12 = 129.49(16), C8–N3–C9 = 121.51(15), N3–C8–N2 = 123.40(16), N3–C8–C7 = 115.41(15), N2–C8–C7 = 121.11(16).

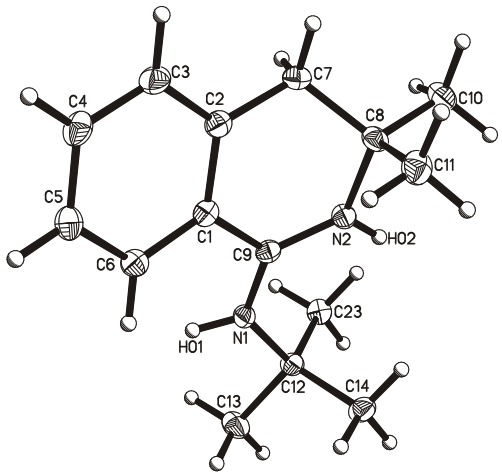


Figure 3. Thermal ellipsoid plot (50% probability) of the cation of **4d-^{t}Bu** along with the labeling scheme. Selected bond lengths (Å) and angles (deg): N1–C12 = 1.4943(18), N1–C9 = 1.3225(18), N2–C9 = 1.3249(19), N2–C8 = 1.4952(18), C1–C9 = 1.4835(19); C9–N1–C12 = 128.95(12), C9–N2–C8 = 123.58(12), N2–C9–N1 = 123.71(13), N2–C9–C1 = 117.86(13), N1–C9–C1 = 118.43(13).

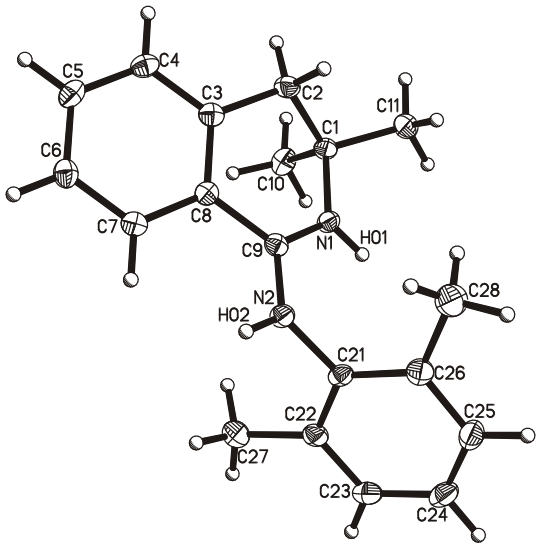


Figure 4. Thermal ellipsoid plot (50% probability) of the cation of **4d-Xy** along with the labeling scheme. Selected bond lengths (Å) and angles (deg): N2–C21 = 1.4413(17), N2–C9 = 1.3227(17), N1–C9 = 1.3182(17), N1–C1 = 1.4897(16), C8–C9 = 1.4785(18); C9–N2–C21 = 125.78(11), C9–N1–C1 = 124.63(11), N1–C9–N2 = 121.13(12), N1–C9–C8 = 119.36(12), N2–C9–C8 = 119.49(12).

Synthesis of Lactams through Insertion of Carbon Monoxide into the Pd–C Bond of Cyclopalladated Complexes. Insertion of CO into the Pd–C bond of cyclopalladated tertiary aryl-alkylamines and related compounds is a well-known process that,[22,85] depending on the reaction conditions, allows the synthesis of esters[63,86] or *N*-heterocycles.[7,15,24,87] Palladium complexes have been used to prepare lactams, (1) through a catalytic oxidative

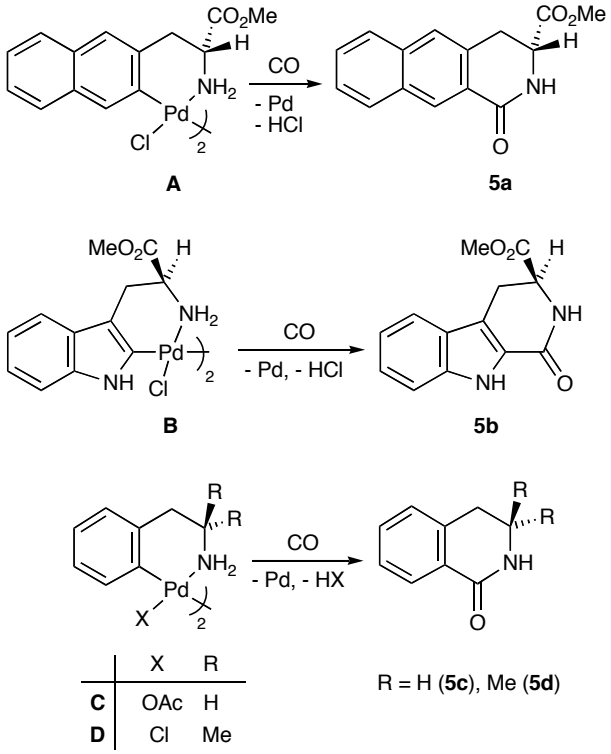
addition process using bromo- or iodo-aryl-alkylamines with CO in the presence of catalytic amounts of Pd(0),[19] or (2) via orthopalladation of the amine. This second way can be a catalytic or stoichiometric process depending on the nature of the amine. Thus, *N*-alkyl-*ω*-aryl-alkylamines react with CO using $Pd(OAc)_2$ as catalyst and $Cu(OAc)_2/O_2$ as reoxidant affording benzolactams;[52,88] however, primary amines lead to ureas, certainly because ortho palladation of these amines, required to give lactams, does not occur when an excess of the amine is present.[89,90] Therefore, to prepare lactams from primary amines it is required the stoichiometric carbonylation of their orthopalladated derivatives.[14,21,23,24] Thus, the reaction of **A**–**C** with CO in $CHCl_3$ or CH_2Cl_2 at room temperature gave palladium(0) and lactames **5a–c** (Scheme 9). The yield of **5a** (48% with respect to the used D-naphthylalanine methyl ester hydrochloride) proves that the cyclometalated complex $[Pd_2\{\kappa^2(C,N)\text{-}C_{10}H_6CH_2CH(CO_2Me)NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**A**) is the main component of mixture **I**.

Previous reports on the synthesis of compounds **5b**–**d** involve: (1) the ring closure of isocyanates or isothiocyanates with polyphosphoric acid (PPA; for **5c**, **5d**),[37,91,92] trifluoroacetic acid (TFA; for **5b**),[93] a mixture of HBr and HOAc (for **5b**),[94] and $AlCl_3$ (for **5b**);[39] (2) cyclization of phenethylcarbamates with PPA (for **5c**,**d**),[91,95] and a mixture of P_2O_5 and $POCl_3$ (for **5c**);[38,50] and (3) Bischler-Napieralski reactions from ortho-substituted-*N*-acyl-2-phenethylamines[92,96] and subsequently reduction of the imide formed (for **5c**). None of these methods have been successfully applied to the preparation of the three lactams and, in most cases, yields are from low to moderate and several steps are involved in the synthesis. To our knowledge, no synthesis of compound **5a** has been reported, although some derivatives are known.[51]

^1H and ^{13}C NMR spectra of compounds **5b**–**d** are in agreement with the reported data.[39,92,97] For lactam **5a**, the ^1H and ^{13}C NMR spectra correspond with the proposed

structure. Protons H8 of the isoquinoline nucleus and H10 of the naphthylalanine fragment appear deshielded, probably due to the anisotropic influence of the C=O double bond (**5a**: H10, 8.65 ppm; **5c**: H8, 8.04 ppm; **5d**: H8, 8.07 ppm).

Scheme 9. Synthesis of Lactams **5a**–**d**



The crystal structures of the lactams **5a**–**d** have been determined by X-ray diffraction studies (see Figures 5 (**5a**), 6 (**5b**) and Supporting Information for **5c** and **5d**). In all cases, the discrete molecules are associated through hydrogen bonds giving dimers (**5d**), infinite double chains (**5a**, **5c**) or layers (**5b**). For compounds **5a**,**b** there are two independent molecules in the asymmetric unit, which are also connected through hydrogen bonds.

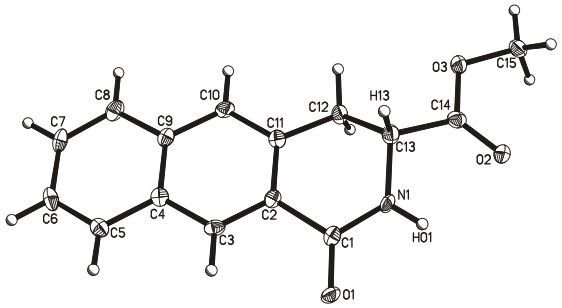


Figure 5. Thermal ellipsoid plot (50% probability) of one of the independent molecules of **5a** along with the labeling scheme. Selected bond lengths (Å) and angles (deg) are given for both independent molecules. (A) C(1)–O(1) = 1.232(3), C(1)–N(1) = 1.339(4), N(1)–C(13) = 1.461(4), C(1)–C(2) = 1.496(4); C(2)–C(1)–O(1) = 121.2(3), C(2)–C(1)–N(1) = 116.9(3), O(1)–C(1)–N(1) = 121.9(3), C(1)–N(1)–C(13) = 123.5(2). (B) C(21)–O(4) = 1.243(3), C(21)–N(2) = 1.343(4), N(2)–C(33) = 1.464(3), C(21)–C(22) = 1.488(4); C(22)–C(21)–O(4) = 121.2(3), C(22)–C(21)–N(2) = 116.8(2), O(4)–C(21)–N(2) = 122.0(3), C(21)–N(2)–C(33) = 122.6(2).

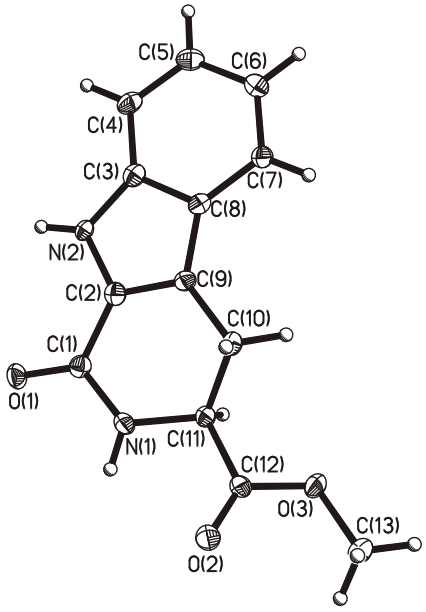


Figure 6. Thermal ellipsoid plot (50% probability) of one of the independent molecules of **5b** along with the labeling scheme. Selected bond lengths (Å) and angles (deg) are given for both

independent molecules (A) C(1)–O(1) = 1.238(3), C(1)–N(1) = 1.363(3), N(1)–C(11) = 1.458(3), C(1)–C(2) = 1.460(3); C(2)–C(1)–O(1) = 124.0(2), C(2)–C(1)–N(1) = 113.5(2), O(1)–C(1)–N(1) = 122.4(2), C(1)–N(1)–C(11) = 122.4(2). (B) C(21)–O(4) = 1.235(3), C(21)–N(3) = 1.356(3), N(3)–C(31) = 1.469(3), C(21)–C(22) = 1.464(3); C(22)–C(21)–O(4) = 123.9(2), C(22)–C(21)–N(3) = 113.2(2), O(4)–C(21)–N(3) = 122.9(2), C(21)–N(3)–C(31) = 122.5(2).

Conclusions

Cyclometalation of 3-(2-naphthyl)-D-alanine methyl ester is achieved by reacting the corresponding hydrochloride salt and $Pd(OAc)_2$. Regiospecific functionalization of the resulting cyclopalladated complex as well as those derived from other primary aryl-alkylamines of pharmaceutical and biological relevance (phenethylamine, phentermine, L-tryptophan methyl ester) can be achieved through insertion reactions of RNC, RNCS and CO into the Pd–C bond of the appropriate cyclometalated complexes. Thus, isocyanides or isothiocyanates afford the corresponding cyclic amidines or amidinium salts. The reaction with RNCS involves a new path for activation of the S–C bond of isothiocyanates through coordination to metal complexes. *E*/*Z* isomerism is observed in those amidinium salts supporting an electron-withdrawing group at the exocyclic nitrogen atom and an electron-releasing group at the endocyclic nitrogen atom, that is, amidinium salts derived from phentermine and XyNC or ToNCS. Reactions of the cyclometalated complexes with CO afford 1-oxo-3,4-dihydroisoquinolines and 1-oxo-2,3,4,9-tetrahydro-β-carbolines.

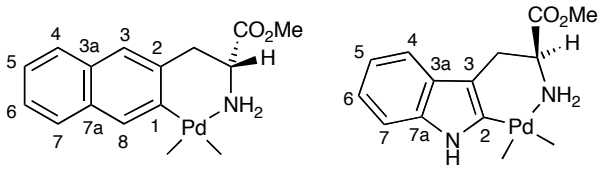
Experimental Section

Caution! *Special precautions should be taken when handling thallium(I) compounds because of their toxicity.*

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.[98] Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in Bruker Avance 300, 400 or 600 spectrometers. Chemical shifts are referenced to TMS [^{1}H and $^{13}C\{^1H\}$]. 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.

^{t}BuNC, XyNC, MeNCS (Fluka), ToNCS (Aldrich), and $Pd(OAc)_2$ (Johnson Matthey) were used as received. 3-(2-Naphthyl)-D-alanine (Degussa) was converted to 3-(2-naphthyl)-D-alanine methyl ester hydrochloride by treatment with 2,2-dimethoxypropane and concentrated hydrochloric acid (see Supporting Information), using Rache1e's procedure.[99] (*S,S*)-$[Pd_2\{\kappa^2(C,N)\text{-}C_8H_5N(CH_2CH(CO_2Me)NH_2)\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**B**) and $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**D**) were prepared as previously reported.[58] $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CH_2NH_2\text{-}2\}_2(\mu\text{-}OAc)_2]$ (**C**) was prepared from $Pd(OAc)_2$ and phenethylamine (acetonitrile, 78 ºC, 6 h) following a similar procedure to that reported for $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CH_2NH_2\text{-}2\}_2(\mu\text{-}Br)_2]$ (**C′**).[89] TlOTf was prepared by reaction of Tl_2CO_3 and HO_3SCF_3 (1:2) in water, and recrystallized from acetone/Et_2O. Charts 2 and 7 give the numbering schemes for the organic compounds and the new palladacycles, respectively.

Chart 7. Numbering Schemes for Cyclometalated Fragments Containing (*R*)-Naphthylalanine Methyl Ester and (*S*)-Tryptophan Methyl Ester



Ortho metalation of 3-(2-Naphthyl)-D-alanine methyl ester. 3-(2-Naphthyl)-D-alanine methyl ester hydrochloride (500 mg, 1.88 mmol) was added to a solution of $Pd(OAc)_2$ (423 mg, 1.88 mmol) in acetonitrile (60 mL), and the resulting solution was stirred at room temperature for 6 days. A small amount of metallic palladium was formed. The solvent was evaporated, CH_2Cl_2 (15 mL) added and the suspension was filtered through a plug of Celite. The filtrate was concentrated ca. 2 mL, and Et_2O (30 mL) was added and the resulting suspension was filtered, washed with Et_2O (2 x 3 mL) and air-dried to give mixture **I** (537 mg) as an orange solid. ^1H NMR of this solid in $CDCl_3$ showed very broad peaks, difficult to assign, but the analysis of the aromatic region indicated a mixture of the cyclometalated complex $[Pd_2\{\kappa^2\text{-}C,N\text{-}C_{10}H_6CH_2CH(CO_2Me)NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**A**) and other non-cyclometalated species such as $[Pd_2(\mu\text{-}Cl)Cl\{NH_2CH(CO_2Me)CH_2C_{10}H_7\}_2]$ or $[Pd_2Cl_2\{NH_2CH(CO_2Me)CH_2C_{10}H_7\}_2]$. This mixture could not be separated neither by fractional crystallization nor by chromatography.

Mixture **I** was used as the starting material to synthesize complexes **1a-^{t}Bu,Xy** and **5a**.

Synthesis of (*R*)-[Pd{κ^2(*C,N*)-$C_{10}H_6CH_2CH(CO_2Me)NH_2$-2}Cl($CN^tBu$)] (1a-^{t}Bu). ^{t}BuNC (80 μl, 0.708 mmol) was added to a solution of mixture **I** (250 mg of the crude product, obtained from 233 mg, 0.876 mmol of D-naphthylalanine methyl ester hydrochloride) in CH_2Cl_2 (15 mL). The resulting solution was stirred for 30 min, then concentrated to ca. 1 mL and Et_2O (30 mL) added and the suspension was filtered to give and the solid washed with Et_2O (2 x 5 mL), and air-dried to afford complex **1a-^{t}Bu** (93 mg, 0.205

mmol) as a yellow solid. The filtrate was cooled at 0 ºC, the suspension was filtered, and the solid washed with Et_2O (2 x 5 mL) and air-dried to afford a second crop of analytically pure **1a-^{t}Bu** (95 mg, 0.210 mmol). Yield: 188 mg, 0.415 mmol, 47%. Mp: 190 °C. Anal. Calcd for $C_{19}H_{23}ClN_2O_2Pd$ (453.258): C, 50.35; H, 5.11; N, 6.18. Found: C, 49.90; H, 5.12; N, 6.35. IR (cm^{-1}): ν(NH) = 3105; ν(CN) = 2212; ν(CO) = 1739. ^{1}H NMR (400 MHz): δ 1.48 (s, 9 H, ^{t}Bu), 3.35 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.8, $^3J_{HH}$ = 5.3 Hz), 3.59 (dd, 1 H, CH_2, $^2J_{HH}$ = 13.8, $^3J_{HH}$ = 4.4 Hz), 3.70 (s, 3 H, OMe), 3.76 (m, 1 H, CH), 3.96 (m, 1 H, NH_2), 4.20 (m, 1 H, NH_2), 7.37 (m, 2 H, H5 + H6), 7.43 (s, 1 H, H3), 7.65 (d, 1 H, H7, $^3J_{HH}$ = 7.8 Hz), 7.69–7.70 (m, 2 H, H4 + H8). ^{13}C{^{1}H} NMR (100.81 MHz): δ 30.0 (s, C*Me*$_3$), 45.6 (s, CH_2), 50.8 (s, CH), 53.1 (s, OMe), 58.1 (s, *C*Me$_3$), 124.7 (s, CH, C6), 125.4 (s, CH, C5), 125.7 (s, CH, C3), 126.4 (s, CH, C4), 127.2 (s, CH, C7), 130.4 (t, C≡N, $^1J_{CN}$ = 19.0 Hz), 131.7 (s, C3a), 132.2 (s, C7a), 135.5 (s, C2), 136.3 (s, CH, C8), 140.8 (s, C–Pd), 171.8 (s, CO).

Synthesis of (*R*)-[Pd{κ^2(*C*,*N*)-$C_{10}H_6CH_2CH(CO_2Me)NH_2$-2}Cl(CNXy)] (1a-Xy). XyNC (54 mg, 0.411 mmol) was added to a solution of mixture **I** (150 mg of the crude product, obtained from 140 mg, 0.527 mmol of D-naphthylalanine methyl ester hydrochloride) in CH_2Cl_2 (20 mL). The resulting solution was stirred for 1 h, then concentrated to ca. 1 mL and Et_2O (20 mL) was added to give a suspension which was filtered, washed with Et_2O (2 x 2 mL) and air-dried to afford analytically pure complex **1a-Xy** as a yellow solid. The filtrate was concentrated to ca. 5 mL, *n*-hexane was added and the suspension filtered off, the solid washed with *n*-hexane (2 x 3 mL) and air-dried to give a second crop of complex **1a-Xy**. Yield: 149 mg, 0.297 mmol, 56%. Mp: 158 °C dec. Anal. Calcd for $C_{23}H_{23}ClN_2O_2Pd$ (501.302): C, 55.11; H, 4.62; N, 5.59. Found: C, 54.89; H, 4.61; N, 5.86. IR (cm^{-1}): ν(NH) = 3167, 3093; ν(CN) = 2195; ν(CO) = 1738. ^{1}H NMR (400

MHz): δ 2.39 (s, 6 H, Me, Xy), 3.40 (A part of a ABMXY system, 1 H, CH_2, $^2J_{AB}$ = 13.8, $^3J_{AM}$ = 5.4 Hz), 3.71 (s, 3 H, OMe), 3.65 (B part of a ABMXY system, 1 H, CH_2, $^2J_{AB}$ = 13.8, $^3J_{BM}$ = 4.4 Hz), 3.81 (M part of a ABMXY system, 1 H, CH), 4.11 (X part of a ABMXY system, 1 H, NH_2, $^2J_{XY}$ = 11.0, $^3J_{XM}$ = 10.0 Hz), 4.33 (Y part of a ABMXY system, 1 H, NH_2, $^2J_{XY}$ = 11.0, $^3J_{YM}$ = 4.9 Hz), 7.06 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.20 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.35 (m, 2 H, H5 + H6), 7.47 (s, 1 H, H3), 7.61 (m, 1 H, H4), 7.69 (m, 1 H, H7), 7.90 (s, 1 H, H8). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 18.7 (s, Me, Xy), 45.7 (s, CH_2), 50.9 (s, CH), 53.1 (s, OMe), 124.8 (s, CH, C6), 125.4 (s, CH, C5), 126.0 (s, CH, C3), 126.3 (s, CH, C4), 127.2 (s, CH, C7), 128.0 (s, *m*-CH, Xy), 129.7 (s, *p*-CH, Xy), 131.8 (s, C3a), 132.1 (s, C7a), 135.5 (s, C2), 135.9 (s, *o*-C, Xy), 137.0 (s, CH, C8), 140.6 (s, C–Pd), 171.6 (s, CO). The ^{13}C NMR resonances corresponding to the *i*-C of Xy and the C≡N group (both carbon atoms bonded to N) were not observed.

Synthesis of (*S*)-[Pd{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}Cl($CN^tBu$)] (1b-^{t}Bu). ^{t}BuNC (150 μL, 1.328 mmol) was added to a suspension of complex (*S*,*S*)-[Pd_2{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}$_2$(μ-Cl)$_2$]·2MeCN (**B**·2MeCN; 500 mg, 0.625 mmol) in CH_2Cl_2 (20 mL). The mixture was stirred for 45 min and then filtered through a plug of $MgSO_4$. The filtrate was concentrated to ca. 2 mL and Et_2O (20 mL) was added to give a suspension which was filtered, the solid washed with Et_2O (2 x 3 mL) and air-dried to give complex **1b-^{t}Bu** as a yellow solid. Yield: 385 mg, 0.871 mmol, 70%. Dec pt: 160 °C. Anal. Calcd for $C_{17}H_{22}ClN_3O_2Pd$ (442.235): C, 46.17; H, 5.01; N, 9.50. Found: C, 45.67; H, 5.08; N, 9.49. IR (cm^{-1}): ν(NH) = 3294, 3184, 3112; ν(CN) = 2214; ν(CO) = 1740. ^1H NMR (300 MHz,): δ 1.47 (s, 9 H, ^{t}Bu), 2.77 (dd, 1 H, CH_2, $^2J_{HH}$ = 15.6, $^3J_{HH}$ = 11.1 Hz), 2.98 (m, 1 H, CH), 3.23-3.33 (m, 1 H of CH_2 + 1 H of NH_2), 3.61 (s, 3 H, OMe), 3.65 (br s, 1 H, NH_2),

7.03 (m, 2 H, H5 + H6), 7.31 (dd, 1 H, H7, $^3J_{HH}$ = 8.1, $^4J_{HH}$ = 1.2 Hz), 7.37 (dd, 1 H, H4, $^3J_{HH}$ = 8.1, $^4J_{HH}$ = 1.2 Hz), 8.35 (s, 1 H, NH, C_8H_5N). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 28.9 (s, CH_2), 29.7 (s, C*Me*$_3$), 52.7 (s, OMe), 53.2 (s, CH), 59.0 (s, *C*Me$_3$), 108.8 (s, C3), 109.8 (s, CH, C7), 116.6 (s, CH, C4), 119.0 (s, CH, C5), 120.3 (s, CH, C6), 126.8 (s, C3a), 127.2 (t, C≡N, $^1J_{CN}$ = 20.0 Hz), 134.3 (s, C–Pd), 137.1 (s, C7a), 172.0 (s, CO).

Synthesis of (*S*)-[Pd{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}Cl(CNXy)] (1b-Xy). XyNC (82 mg, 0.625 mmol) was added to a suspension of complex (*S*,*S*)-[Pd_2{κ^2(*C*,*N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2}$_2$(μ-Cl)$_2$]·2MeCN (**B**·2MeCN)(250 mg, 0.312 mmol) in CH_2Cl_2 (25 mL). The mixture was stirred for 15 min and then filtered through a plug of $MgSO_4$. The filtrate was concentrated to ca. 2 mL, Et_2O (25 mL) was added and the suspension was filtered, the solid washed with Et_2O (2 x 3 mL) and air-dried to give yellow complex **1b-Xy**. Yield: 179 mg, 0.365 mmol, 58%. Dec pt: 176 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 0 (8.8 x 10^{-4} M). Anal. Calcd for $C_{21}H_{22}ClN_3O_2Pd$ (490.279): C, 51.45; H, 4.52; N, 8.57. Found: C, 51.47; H, 4.55; N, 8.45. IR (cm^{-1}): ν(NH) = 3284, 3230; ν(CN) = 2196; ν(CO) = 1744, 1735. ^{1}H NMR (400 MHz): δ 2.30 (s, 6 H, Me, Xy), 2.99 (dd, 1 H, CH_2, $^2J_{HH}$ = 15.0, $^3J_{HH}$ = 10.4 Hz), 3.24–3.34 (m, 2 H, CH + 1 H of CH_2), 3.65 (s, 3 H, OMe), 3.73 (br d, 1 H, NH_2, $^3J_{HH}$ = 10.7 Hz), 3.94 ("t", 1 H, NH_2, $^2J_{HH}$ = $^3J_{HH}$ = 10.9 Hz), 6.82 (td, 1 H, H5, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 0.9 Hz), 6.91 (td, 1 H, H6, $^3J_{HH}$ = 7.1, $^3J_{HH}$ = 1.0 Hz), 7.01 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.17–7.22 (m, 3 H, H4 + H7 + *p*-H of Xy), 8.36 (s, 1 H, NH, C_8H_5N). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 18.7 (s, Me, Xy), 28.6 (s, CH_2), 52.7 (s, OMe), 53.5 (s, CH), 108.9 (s, C3), 109.5 (s, CH, C7), 116.4 (s, CH, C4), 118.9 (s, CH, C5), 120.3 (s, CH, C6), 125.7 (s, *i*-C, Xy), 126.7 (s, C3a), 128.1 (s, *m*-CH, Xy), 129.9 (s, *p*-CH, Xy), 134.3 (s, C–Pd), 135.9 (s, *o*-C, Xy), 137.4 (s, C7a), 140.6 (br s, C≡N), 171.9 (s, CO).

Synthesis of (*S*)-[Pd{κ^2(*C*,*N*)-C(=NXy)C_8H_5N($CH_2CH(CO_2Me)NH_2$)-2}Cl(CNXy)] (2b). XyNC (42 mg, 0.318 mmol) was added to a suspension of complex **1b-Xy** (150 mg, 0.306 mmol) in $CHCl_3$ (30 mL). The mixture was stirred for 18 h and then filtered through a plug of $MgSO_4$; the filtrate was concentrated to ca. 2 mL, *n*-pentane (25 mL) was added and the suspension was filtered, the solid was washed with *n*-pentane (2 x 3 mL) and air-dried to give yellow complex **2b**. Yield: 126.6 mg, 0.204 mmol, 67%. Mp: 213 °C dec. Anal. Calcd for $C_{30}H_{31}ClN_4O_2Pd$ (621.457): C, 57.98; H, 5.03; N, 9.02. Found: C, 57.94; H, 5.16; N, 9.00. IR (cm^{-1}): ν(NH) = 3328, 3314, 3272; ν(C≡N) = 2199; ν(CO) = 1730; ν(C=N) = 1577. ^{1}H NMR (400 MHz): δ 1.87 (s, 3 H, Me, inserted Xy), 2.09 (s, 6 H, Me, coordinated Xy), 2.48 (s, 3 H, Me, inserted Xy), 3.26 ("t", 1 H, NH_2, $^2J_{HH}$ = $^3J_{HH}$ = 10.6 Hz), 3.52 (m, 1 H, NH_2), 3.70 (s, 3 H, OMe), 3.97 (br d, 1 H, CH_2, $^2J_{HH}$ = 15.0 Hz), 4.47 (m, 1 H, CH), 4.98 (dd, 1 H, CH_2, $^2J_{HH}$ = 15.0, $^3J_{HH}$ = 6.4 Hz), 6.54 (d, 1 H, *m*-H, inserted Xy, $^3J_{HH}$ = 7.4 Hz), 6.82 (t, 1 H, *p*-H, inserted Xy, $^3J_{HH}$ = 7.5 Hz), 7.01 (d, 2 H, *m*-H, coordinated Xy, $^3J_{HH}$ = 7.6 Hz), 7.12 (ddd, 1 H, H5, $^3J_{HH}$ = 8.0, $^3J_{HH}$ = 7.0, $^4J_{HH}$ = 0.9 Hz), 7.16 (d, 1 H, *m*-H, inserted Xy, $^3J_{HH}$ = 7.6 Hz), 7.17 (t, 1 H, *p*-H, coordinated Xy, $^3J_{HH}$ = 7.6 Hz), 7.28 (ddd, 1 H, H6, $^3J_{HH}$ = 8.0, $^3J_{HH}$ = 7.0, $^4J_{HH}$ = 1.0 Hz), 7.37 (d, 1 H, H7, $^3J_{HH}$ = 8.1 Hz), 7.56 (d, 1 H, H4, $^3J_{HH}$ = 8.1 Hz), 9.25 (s, 1 H, NH, C_8H_5N). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 18.6 (s, Me, coordinated + inserted Xy), 20.1 (s, Me, inserted Xy), 30.0 (s, CH_2), 53.0 (s, OMe), 53.6 (s, CH), 111.5 (s, CH, C7), 118.9 (s, CH, C4), 120.0 (s, CH, C5), 123.4 (s, *p*-CH, inserted Xy), 124.9 (s, CH, C6), 125.8 (s, *i*-C, coordinated Xy), 126.5 (s, *o*-C, inserted Xy), 126.9 (s, *m*-CH, inserted Xy), 127.7 (s, *m*-CH, coordinated Xy), 127.8 (s, *o*-C, inserted Xy), 128.8 (s, *m*-CH, inserted Xy), 128.0 (s, C3a), 129.5 (s, *p*-CH, coordinated Xy), 133.1 (s, C2), 135.2 (s, *o*-C, coordinated

Xy), 135.5 (s, C7a), 139.0 (br s, C≡N), 151.9 (s, *i*-C, inserted Xy), 164.0 (s, C–Pd), 172.4 (s, CO). The ^{13}C NMR resonance corresponding to C3 was not observed.

Single crystals of **2b**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-hexane into a solution of **2b** in $CHCl_3$.

Synthesis of (*R*)-1-(*tert*-Butylamino)-3-(methoxycarbonyl)-3,4-dihydrobenzo[*g*]isoquinoline (3a-^{t}Bu) and *Z*-(*R*)-1-(*tert*-Butylamino)-3-(methoxycarbonyl)-3,4-dihydrobenzo[*g*]isoquinolinium Chloride (4a-^{t}Bu). Complex **1a-^{t}Bu** (140 mg, 0.309 mmol) was dissolved in toluene (15 mL), and the solution was refluxed for 7 h. Decomposition to metallic palladium was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added and the resulting suspension was filtered through a plug of Celite. The filtrate was concentrated to ca. 2 mL, and Et_2O (25 mL) was added, the suspension was filtered, the solid washed with Et_2O (2 x 5 mL) and air-dried to give the pale yellow amidinium salt **4a-^{t}Bu** (72 mg, 0.207 mmol, 67%). ^{1}H NMR (400 MHz): δ 1.80 (s, 9 H, ^{t}Bu), 3.39 (m, 2 H, CH_2), 3.65 (s, 3 H, OMe), 5.21 (br s, 1 H, CH), 7.56 (t, 1 H, H8, $^3J_{HH}$ = 7.7 Hz), 7.65 (t, 1 H, H7, $^3J_{HH}$ = 7.9 Hz), 7.70 (s, 1 H, H5), 7.81 (d, 1 H, H6, $^3J_{HH}$ = 8.2 Hz), 8.08 (d, 1 H, H9, $^3J_{HH}$ = 8.2 Hz), 8.33 (br s, 1 H, CHN*H*), 8.78 (s, 1 H, H10), 10.02 (br s, 1 H, ^{t}BuN*H*).

A small amount of crude amidine **3a-^{t}Bu** was isolated after the Et_2O filtrate was concentrated to dryness and the residue was dried under vacuum.

Solid **4a-^{t}Bu** (72 mg, 0.207 mmol) was suspended in acetone (15 mL), Na_2CO_3 (150 mg, 1.41 mmol) was added, and the mixture was stirred for 12 h. The suspension was filtered through a plug of $MgSO_4$ and the solvent evaporated. Et_2O (25 mL) was added and the suspension was filtered to remove solid impurities. The filtrate was concentrated to dryness to give compound **3a-^{t}Bu** as a pale yellow solid. Yield: 34 mg, 0.109 mmol, 53%. Mp: 152 °C.

IR (cm^{-1}): ν(NH) = 3429; ν(CO) = 1735; ν(CN) = 1615, 1526. ^{1}H NMR (300 MHz): δ 1.54 (s, 9 H, ^{t}Bu), 3.04–3.17 (m, 2 H, CH_2), 3.70 (s, 3 H, OMe), 4.35 (m, 1 H, CH), 4.64 (br s, 1 H, CHN*H*), 7.41–7.52 (m, 2 H, H7 + H8), 7.61 (s, 1 H, H5), 7.76 (m, 1 H, H6), 7.82 (s, 1 H, H10), 7.84 (m, 1 H, H9). ^{13}C{^{1}H} NMR (75.45 MHz): δ 29.0 (s, C*Me*$_3$), 30.9 (s, CH_2), 51.4 (s, *C*Me$_3$), 51.9 (s, OMe), 58.2 (s, CH), 121.9 (s, CH, C10), 125.6 (s, C10a), 125.8 (s, CH, C8), 126.0 (s, CH, C5), 127.1 (s, CH, C6), 127.2 (s, CH, C7), 128.5 (s, CH, C9), 132.2 (s, C9a), 133.3 (s, C4a + C5a), 154.3 (s, C1), 174.6 (s, CO). FAB$^+$-MS: *m/z* 311.0 [(M+1)+]. EI-HRMS: exact mass calcd for $C_{19}H_{22}N_2O_2$ 310.1681; found 310.1670; Δ = 0.0011.

Synthesis of (*R*)-1-((2,6-Dimethylphenyl)amino)-3-(methoxycarbonyl)-3,4-dihydrobenzo[*g*]isoquinoline (3a-Xy). Complex **1a-Xy** (100 mg, 0.199 mmol) was dissolved in toluene (15 mL), and the solution was refluxed for 7 h. Decomposition to metallic palladium was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added and the resulting suspension was filtered through a plug of Celite. The filtrate was concentrated to ca. 1 mL, *n*-pentane (15 mL) was added and the suspension was filtered. The solid was washed with *n*-pentane (2 x 5 mL) and air-dried to give crude **3a-Xy**. Yield: 40 mg, 0.112 mmol, 56%. Crude **3a-Xy** was dissolved in CH_2Cl_2 (1 mL) and subjected to silica gel preparative TLC. Elution with CH_2Cl_2 gave a yellow band (R_f = 0.7) which was collected and extracted with methanol; the solution was filtered through a plug of Celite and the filtrate was concentrated to dryness to give spectroscopically pure compound **3a-Xy** as a yellow solid (11 mg, 0.031 mmol; purification yield: 28%). Mp: 75 °C. IR (cm^{-1}): ν(NH) = 3381; ν(CO) = 1743; ν(CN) = 1645, 1626. ^{1}H NMR (400 MHz): δ 2.17 (s, 3 H, Me, Xy), 2.25 (s, 3 H, Me, Xy), 3.36, 3.50 (AB part of an ABMX system, 2 H, CH_2, $^2J_{AB}$ = 15.1, $^3J_{AM}$ = 6.8, $^3J_{BM}$ = 4.8 Hz), 3.64 (s, 3 H, OMe), 4.21 (m, M part of an ABMX system, 1 H, CH), 5.16 (br s, 1 H,

NH), 6.93 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.08 (d, 1 H, *m*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.11 (d, 1 H, *m*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.46–7.54 (m, 2 H, H7 + H8), 7.67 (s, 1 H, H5), 7.80 (d, 1 H, H6, $^3J_{HH}$ = 8.1 Hz), 7.97 (d, 1 H, H9, $^3J_{HH}$ = 7.9 Hz), 8.98 (s, 1 H, H10). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 17.8 (s, Me, Xy), 17.9 (s, Me, Xy), 32.5 (s, CH_2), 52.9 (s, CH), 52.5 (s, OMe), 122.8 (s, *p*-CH, Xy), 126.0 (s, CH, C8), 126.1 (s, CH, C5), 127.0 (s, CH, C6), 127.3 (s, C10a), 127.4 (s, CH, C7 + C10), 128.1 (s, *m*-CH, Xy), 128.3 (s, *m*-CH, Xy), 128.9 (s, *o*-C, Xy), 129.2 (s, CH, H9), 129.3 (s, *o*-C, Xy), 131.0 (s, C4a), 132.5 (s, C9a), 134.3 (s, C5a), 145.9 (s, *i*-C, Xy), 148.6 (s, C1), 171.9 (s, CO). FAB^+-MS: *m/z* 359.2 $[(M+1)^+]$. EI-HRMS: exact mass calcd for $C_{23}H_{22}N_2O_3$ 358.1681; found 358.1705; Δ = 0.0024.

Synthesis of 1-(*tert*-Butylamino)-3,4-dihydroisoquinoline (3c-^{t}Bu) and *Z*-1-(*tert*-Butylamino)-3,4-dihydroisoquinolinium Triflate (4c-^{t}Bu). ^{t}BuNC (65 μL, 0.575 mmol) was added to a suspension of complex $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CH_2NH_2\text{-}2\}_2(\mu\text{-}OAc)_2]$ (**C**; 150 mg, 0.262 mmol) in toluene (15 mL), and the mixture was refluxed for 7 h. Decomposition to metallic palladium was observed. The suspension was concentrated to dryness, Et_2O (30 mL) was added, and the suspension was filtered through a plug of Celite. The solvent was evaporated, *n*-pentane (30 mL) was added, and the resulting suspension was filtered to remove solid impurities. The filtrate was concentrated to dryness to give compound **3c-^{t}Bu** as a pale yellow liquid. Yield: 98 mg, 0.484 mmol, 92%. ^1H NMR (400 MHz): δ 1.46 (s, 9 H, ^{t}Bu), 2.63 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 6.8 Hz), 3.48 ("t", 2 H, CH_2N, $^3J_{HH}$ = 6.8 Hz), 4.30 (br s, 1 H, NH), 7.17 (br d, 1 H, H5, $^3J_{HH}$ = 7.2 Hz), 7.23–7.32 (m, 3 H, H6 + H7 + H8). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 27.7 (s, CH_2Ar), 29.0 (s, CMe_3), 44.8 (s, CH_2N), 50.8 (s, CMe_3), 122.2 (s, CH, C8), 126.4 (s, CH, C7), 127.5 (s, CH, C5), 127.7 (s, C8a), 129.4 (s, CH, C6), 139.8 (s, C4a), 153.9 (s, C1). ESI-MS: *m/z* 203.1 $[(M+1)^+]$.

HOTf (0.1 mL, 1.13 mmol) was added to a solution of compound **3c-^{t}Bu** (98 mg, 0.484 mmol) in Et_2O (10 mL). The resulting suspension was stirred for 15 min, and then filtered off, the solid washed with *n*-pentane (2 x 5 mL) and air-dried to give compound **4c-^{t}Bu** as a colorless solid. Yield: 78 mg, 0.221 mmol, 46%. Mp: 153 °C. Anal. Calcd for $C_{14}H_{19}F_3N_2O_3S$ (352.375): C, 47.72; H, 5.44; N, 7.95; S, 9.10. Found: C, 47.76; H, 5.62; N, 8.03; S, 8.86. IR (cm^{-1}): ν(NH) = 3323 s; ν(CN) = 1651, 1575. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 137 (5.11 x 10^{-4} M). ^{1}H NMR (400 MHz): δ 1.58 (s, 9 H, ^{t}Bu), 2.96 (t, 2 H, CH_2Ar, $^3J_{HH}$ = 6.5 Hz), 3.72 (td, 2 H, C*H*$_2$NH, $^3J_{HH}$ = 6.5, $^3J_{HH}$ = 3.5 Hz), 7.32 (d, 1 H, H5, $^3J_{HH}$ = 7.5 Hz), 7.45 (t, 1 H, H7, $^3J_{HH}$ = 7.6 Hz), 7.57 (td, 1 H, H6, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.0 Hz), 7.62 (br s, 1 H, ^{t}BuN*H*), 7.95 (d, 1 H, H8, $^3J_{HH}$ = 7.7 Hz), 8.37 (br s, 1 H, CH_2N*H*). ^{13}C{^{1}H} NMR (100.81 MHz): δ 27.3 (s, CH_2Ar), 28.2 (s, C*Me*$_3$), 39.7 (s, CH_2NH), 54.6 (s, *C*Me$_3$), 120.4 (q, CF_3, $^1J_{CF}$ = 319.7 Hz), 122.6 (s, C8a), 126.9 (s, CH, C8), 128.2 (s, CH, C7), 128.5 (s, CH, C5), 134.3 (s, CH, C6), 138.3 (s, C4a), 156.3 (s, C1).

Single crystals of **4c-^{t}Bu**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-hexane into a solution of **4c-^{t}Bu** in $CHCl_3$.

Synthesis of 1-((2,6-Dimethylphenyl)imino)-3,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (3d-Xy). XyNC (68 mg, 0.518 mmol) was added to a suspension of complex [$Pd_2\{\kappa^2(C,N)$-$C_6H_4CH_2CMe_2NH_2$-2$\}_2(\mu$-Cl$)_2$] (150 mg, 0.258 mmol) in acetone (20 mL), and the mixture was stirred for 10 min. TlOTf (183 mg, 0.518 mmol) was added, and the resulting suspension was further stirred for 15 min and filtered through a plug of Celite. The filtrate was concentrated to dryness and the residue was suspended in toluene (20 mL) and refluxed for 7 h. Decomposition to metallic palladium was observed. The solvent was evaporated, the residue was taken up in acetone (25 mL), filtered through a plug of Celite, and

Na_2CO_3 (100 mg, 0.943 mmol) was added to the filtrate. The mixture was stirred for 3 h and then filtered through a plug of Celite. The filtrate was concentrated to dryness, the residue was dissolved in CH_2Cl_2 (2 x 10 mL) and the mixture filtered through a plug of Celite. The solvent was evaporated and the solid was dried under vacuum to give compound **3d-Xy** as a colorless solid. Yield: 118 mg, 0.422 mmol, 82%. Mp: 88–90 °C. Anal. Calcd for $C_{19}H_{22}N_2$ (278.399): C, 81.97; H, 7.97; N, 10.06. Found: C, 82.16; H, 8.25; N, 10.00. IR (cm^{-1}): ν(NH) = 3368; ν(CN) = 1628, 1574. ^{1}H NMR (300 MHz): δ 1.13 (s, 6 H, CMe_2), 2.11 (s, 6 H, Me, Xy), 2.85 (s, 2 H, CH_2), 4.31 (br s, 1 H, NH), 6.88 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.06 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.16 (dd, 1 H, H5, $^3J_{HH}$ = 6.6, $^4J_{HH}$ = 0.9 Hz), 7.35 (m, 2 H, H6 + H7), 8.43 (dd, 1 H, H8, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 1.6 Hz). ^{13}C{^{1}H} NMR (75.45 MHz): δ 17.8 (s, Me, Xy), 29.0 (s, C*Me*$_2$), 42.1 (s, CH_2), 50.7 (s, *C*Me_2), 122.2 (s, *p*-CH, Xy), 126.5 (s, CH, C7), 126.7 (s, CH, C8), 128.0 (s, CH, C5), 128.0 (s, *m*-CH, Xy), 128.8 (s, *o*-C, Xy), 128.9 (s, C8a), 130.0 (s, CH, C6), 135.8 (s, C4a), 146.2 (s, *i*-C, Xy), 148.7 (s, C1). FAB$^+$-MS: *m/z* 279.1 [$(M+1)^+$].

Synthesis of *Z*-(*R*)-1-((2,6-Dimethylphenyl)amino)-3-(methoxycarbonyl)-3,4-dihydrobenzo[*g*]isoquinolinium Triflate (4a-Xy). Complex **1b** (170 mg, 0.339 mmol) was dissolved in CH_2Cl_2, TlOTf (245 mg, 0.69 mmol) was added, the resulting suspension was stirred for 4 h, filtered through a plug of Celite and the filtrate was concentrated to dryness. The residue was dissolved in toluene (15 mL), and the solution was refluxed for 7 h. Decomposition to metallic palladium was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added and the resulting suspension was filtered through a plug of Celite. The filtrate was concentrated to ca. 3 mL, Et_2O (15 mL) was added and the suspension was filtered to remove a black solid. The solvent was evaporated to give crude **4a-Xy**. Yield: 84.0 mg, 0.165

mmol, 49%. Crude **4a-Xy** was dissolved in CH_2Cl_2 (1 mL) and *n*-pentane (20 mL) was added. A colorless suspension formed, which was stirred at 0 ºC for 30 min, and filtered, (17 mg, 0.033 mmol; recrystallization yield: 20%). Mp: 167 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 114 (4.95 x 10^{-4} M). Anal. Calcd for $C_{24}H_{23}F_3N_2O_5S$ (508.515): C, 56.69; H, 4.56; N, 5.51; S, 6.31. Found: C, 56.23; H, 4.75; N, 5.41; S, 6.04. IR (cm^{-1}): ν(NH) = 3190; ν(CO) = 1747; ν(CN) = 1644, 1626. ^{1}H NMR (400 MHz): δ 2.21 (s, 3 H, Me, Xy), 2.32 (s, 3 H, Me, Xy), 3.41, 3.52 (AB part of an ABX system, 2 H, CH_2, $^2J_{AB}$ = 16.3, $^3J_{AX}$ = 5.7, $^3J_{BX}$ = 5.1 Hz), 3.63 (s, 3 H, OMe), 4.62 (m, X part of an ABX system, 1 H, CH), 7.09 (d, 1 H, *m*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.11 (d, 1 H, *m*-H, Xy, $^3J_{HH}$ = 7.2 Hz), 7.18 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.52 (br d, 1 H, CHN*H*, $^3J_{HH}$ = 4.0 Hz), 7.56 (t, 1 H, H8, $^3J_{HH}$ = 8.0 Hz), 7.68 (t, 1 H, H7, $^3J_{HH}$ = 8.0 Hz), 7.76 (s, 1 H, H5), 7.83 (d, 1 H, H6, $^3J_{HH}$ = 8.0 Hz), 8.23 (d, 1 H, H9, $^3J_{HH}$ = 8.4 Hz), 9.15 (s, 1 H, H10), 10.92 (s, 1 H, XyN*H*). ^{13}C{^{1}H} NMR (100.81 MHz): δ 17.4 (s, Me, Xy), 17.7 (s, Me, Xy), 30.9 (s, CH_2), 52.3 (s, CH), 53.3 (s, OMe), 117.9 (s, C10a), 120.3 (q, CF_3, $^1J_{CF}$ = 317.0 Hz), 127.1 (s, CH, C6), 127.6 (s, CH, C8), 127.7 (s, CH, C5), 128.7 (s, C4a), 129.4 (s, *m*-CH, Xy), 129.5 (s, *m*-CH, Xy), 130.1 (s, *p*-CH, Xy), 130.5 (s, CH, C7), 130.7 (s, CH, C9), 130.8 (s, CH, C10), 135.9 (s, *o*-C, Xy), 136.0 (s, C5a), 136.1 (s, *o*-C, Xy), 132.3 (s, C9a), 158.4 (s, C1), 169.4 (s, CO). The ^{13}C NMR resonance corresponding to the *i*-C of Xy was not observed.

Synthesis of *Z*-(*S*)-1-(*tert*-Butylamino)-3-(methoxycarbonyl)-4,9-dihydro-3*H*-β-carbolin-2-ium Triflate (4b-^{t}Bu). ^{t}BuNC (71 μL, 0.628 mmol) was added to a suspension of complex (*S,S*)-[Pd_2\{κ^2(*C,N*)-$C_8H_5N(CH_2CH(CO_2Me)NH_2)$-2\}$_2$(μ-Cl)$_2$]·2$CH_3CN$ (**B**·2MeCN; 250 mg, 0.312 mmol) in acetone (30 mL), and the mixture was stirred for 5 min. TlOTf (220 mg, 0.622 mmol) was added and the resulting suspension was further stirred for 15 min and then filtered through a plug of Celite. The solvent was evaporated, $CHCl_3$ (30 ml) added, and

the resulting solution was refluxed for 8 h. Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, the solvent was evaporated, and the oily residue was vigorously stirred in *n*-hexane to give a dark yellow solid, which was filtered, washed with *n*-hexane (2 x 5 mL) and air-dried. This solid was chromatographed on deactivated silica gel, using Et_2O as eluent and then acetone. The acetone effluent was collected, the solvent evaporated and the solid was recrystallized from CH_2Cl_2/Et_2O to give **4b-^{t}Bu** as a colorless solid Yield: 184 mg, 0.493 mmol, 66%. Mp: 187–189 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 121 (5.25 x 10^{-4} M). Anal. Calcd for $C_{18}H_{22}F_3N_3O_5S$ (449.448): C, 48.10; H, 4.93; N, 9.35; S, 7.13 Found: C, 47.94; H, 5.07; N, 9.17; S, 6.87. IR (cm^{-1}): ν(NH) = 3304 br, s; ν(CO) = 1746; ν(CN) = 1636, 1590. ^{1}H NMR (300 MHz): δ 1.64 (s, 9 H, ^{t}Bu), 3.41, 3.52 (AB part of an ABMX system, 2 H, CH_2, $^2J_{AB}$ = 17.1, $^3J_{AM}$ = 4.4, $^3J_{BM}$ = 7.1 Hz), 3.71 (s, 3 H, OMe), 4.89 (m, M part of an ABMX system, 1 H, CH), 7.16 (td, 1 H, H6, $^3J_{HH}$ = 7.3, $^4J_{HH}$ = 0.9 Hz), 7.35 (td, 1 H, H7, $^3J_{HH}$ = 7.2, $^4J_{HH}$ = 1.2 Hz), 7.52–7.61 (m, 3 H, H5 + H8 + CHN*H*), 8.32 (s, 1 H, ^{t}BuN*H*), 10.88 (s, 1 H, NH, C_8H_5N). ^{13}C{^{1}H} NMR (75.45 MHz): δ 22.8 (s, CH_2), 28.6 (s, C*Me*$_3$), 53.4 (s, OMe), 54.0 (s, CH), 55.3 (s, *C*Me$_3$), 113.5 (s, CH, C8), 119.4 (s, C9a), 120.1 (s, C4a), 120.2 (q, CF_3, $^1J_{CF}$ = 318.9 Hz), 120.3 (s, CH, C5), 121.4 (s, CH, C6), 124.3 (s, C4b), 127.6 (s, CH, C7), 139.3 (s, C8a), 151.6 (s, C1), 170.5 (s, CO).

Single crystals of **4b-^{t}Bu**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-hexane into a solution of **4b-^{t}Bu** in CH_2Cl_2.

Synthesis of *Z*-1-((2,6-Dimethylphenyl)amino)-3,4-dihydroisoquinolinium Triflate (4c-Xy). XyNC (78 mg, 0.595 mmol) was added to a suspension of complex [$Pd_2\{\kappa^2(C,N)$-$C_6H_4CH_2CH_2NH_2$-2$\}_2(\mu$-OAc$)_2$] (**C**; 170 mg, 0.298 mmol) in acetone (20 mL), and the mixture was stirred for 10 min. TlOTf (210 mg, 0.595 mmol) was added and the mixture was

stirred for 15 min. The solvent was evaporated, CH_2Cl_2 (20 mL) was added, and the suspension was filtered through a plug of Celite. The filtrate was concentrated to dryness, toluene (25 mL) was added and the mixture was refluxed for 7 h. Decomposition to metallic palladium was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added, the suspension filtered through a plug of $MgSO_4$, the filtrate concentrated to ca. 2 mL, and Et_2O (30 mL) was added. The suspension was filtered, the solid washed with Et_2O (2 x 5 mL) and air-dried to give crude **4c-Xy**. Yield: 112 mg, 0.280 mmol, 47%. An analytically pure sample of the off-colorless **4c-Xy** was obtained by recrystallization from acetone/Et_2O (38 mg, 0.095 mmol; recrystallization yield: 34%). Mp: 172 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 125 (5.80 x 10^{-4} M). Anal. Calcd for $C_{18}H_{19}F_3N_2O_3S$ (400.419): C, 53.99; H, 4.78; N, 6.99; S, 8.01. Found: C, 53.63; H, 4.72; N, 6.82; S, 7.63. IR (cm^{-1}): ν(NH) = 3202 br, s; ν(CN) = 1646, 1572. ^{1}H NMR (400 MHz): δ 2.17 (s, 6 H, Me, Xy), 2.97 ("t", 2 H, CH_2Ar, $^3J_{HH}$ = 6.8 Hz), 3.53 ("t", 2 H, C*H*$_2$NH, $^3J_{HH}$ = 6.8 Hz), 7.07 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.14 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.5 Hz), 7.38 (d, 1 H, H5, $^3J_{HH}$ = 7.4 Hz), 7.49 (t, 1 H, H7, $^3J_{HH}$ = 7.5 Hz), 7.57 (br s, 1 H, CH$_2$N*H*), 7.65 (td, 1 H, H6, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 1.0 Hz), 8.36 (d, 1 H, H8, $^3J_{HH}$ = 7.6 Hz), 10.22 (br s, 1 H, XyN*H*). ^{13}C{^{1}H} NMR (100.81 MHz): δ 17.6 (s, Me, Xy), 27.3 (s, CH_2Ar), 39.5 (s, CH_2NH), 120.2 (q, CF_3, $^1J_{CF}$ = 319.6 Hz), 121.2 (s, C8a), 127.6 (s, CH, C8), 128.6 (s, CH, C5), 128.6 (s, CH, C7), 129.3 (s, *m*-CH, Xy), 129.7 (s, *p*-CH, Xy), 129.7 (s, *i*-C, Xy), 135.0 (s, CH, C6), 135.8 (s, *o*-C, Xy), 138.3 (s, C4a), 157.6 (s, C1).

Synthesis of *Z*-1-(*tert*-Butylamino)-3,3-dimethyl-3,4-dihydroisoquinolinium Triflate (4d-^{t}Bu). ^{t}BuNC (70 μL, 0.619 mmol) was added to a suspension of complex [Pd$_2${κ^2(*C*,*N*)-$C_6H_4CH_2CMe_2NH_2$-2}$_2$(μ-Cl)$_2$] (**D**; 180 mg, 0.310 mmol) in acetone (20 mL), and the mixture stirred for 5 min. TlOTf (220 mg, 0.622 mmol) was added, and the resulting

suspension was further stirred for 15 min and filtered through a plug of $MgSO_4$. The solvent was evaporated, toluene (30 mL) was added, and the mixture was refluxed for 6 h. Decomposition to metallic palladium was observed. The mixture was filtered through a plug of $MgSO_4$, toluene was evaporated and the oily residue was vigorously stirred in Et_2O to give a suspension, which was filtered, the solid washed with Et_2O (2 x 5 mL) and air-dried to give compound **4d-^{t}Bu** as an off-colorless solid. Yield: 153.9 mg, 0.402 mmol, 65%. Mp: 137 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 143 (5.33 x 10^{-4} M). Anal. Calcd for $C_{16}H_{23}F_3N_2O_3S$ (380.429): C, 50.52; H, 6.09; N, 7.36; S, 8.43. Found: C, 50.35; H, 6.40; N, 7.32; S, 8.35. IR (cm^{-1}): ν(NH) = 3353 s, 3315 s; ν(CN) = 1636, 1561. ^{1}H NMR (400 MHz): δ 1.45 (s, 6 H, CMe_2), 1.61 (s, 9 H, ^{t}Bu), 2.96 (s, 2 H, CH_2), 7.16 (br s, 1 H, $CMe_2N\mathit{H}$), 7.28 (d, 1 H, H5, $^3J_{HH}$ = 7.3 Hz), 7.47 (t, 1 H, H7, $^3J_{HH}$ = 7.5 Hz), 7.59 (t, 1 H, H6, $^3J_{HH}$ = 7.5 Hz), 7.98 (br s, 1 H, ^{t}Bu$N\mathit{H}$), 8.08 (d, 1 H, H8, $^3J_{HH}$ = 7.9 Hz). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 27.1 (s, $C\mathit{Me}_2$), 28.6 (s, $C\mathit{Me}_3$), 41.0 (s, CH_2), 54.1 (s, $\mathit{C}Me_2$), 54.9 (s, $\mathit{C}Me_3$), 120.5 (q, CF_3, $^1J_{CF}$ = 320.1 Hz), 121.5 (s, C8a), 127.4 (s, CH, C8), 128.4 (s, CH, C7), 129.0 (s, CH, C5), 134.7 (s, CH, C6), 136.4 (s, C4a), 156.1 (s, C1).

Single crystals of **4d-^{t}Bu**, suitable for an X-ray diffraction study, were obtained by slow diffusion of Et_2O into a solution of **4d-^{t}Bu** in CH_2Cl_2.

Synthesis of *Z*/*E*-1-((2,6-Dimethylphenyl)amino)-3,3-dimethyl-3,4-dihydroisoquinolium Triflate (*Z*/*E*-4d-Xy). XyNC (107 mg, 0.816 mmol) was added to a suspension of complex $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**D**; 237 mg, 0.408 mmol) in acetone (15 mL), and the mixture was stirred for 10 min. TlOTf (288 mg, 0.815 mmol) was added, and the resulting suspension was further stirred for 15 min and then filtered through a plug of $MgSO_4$. The solvent was evaporated, toluene (20 mL) was added and the

mixture refluxed for 7 h. Decomposition to metallic palladium was observed. Toluene was evaporated, CH_2Cl_2 (25 mL) was added, the suspension filtered through a plug of Celite and the filtrate concentrated to ca. 2 mL. Et_2O (15 mL) was added to afford a suspension, which was filtered to afford a *Z*/*E*-**4d-Xy** as a colorless solid. Yield: 218 mg, 0.509 mmol, 62%. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 137 (5.13 x 10^{-4} M). Anal. Calcd for $C_{20}H_{23}F_3N_2SO_3$ (428.473): C, 56.06; H, 5.41; N, 6.54; S, 7.48. Found: C, 56.25; H, 5.56; N, 6.68; S, 7.03. IR (cm^{-1}): ν(NH) = 3192 vs; ν(CN) = 1644, 1578. ^{1}H NMR (25 ºC, $CDCl_3$, 600 MHz): ***Z*-4d-Xy**: δ 1.31 (s, 6 H, CMe_2), 2.23 (s, 6 H, Me, Xy), 3.03 (s, 2 H, CH_2), 6.30 (br s, 1 H, CMe_2NH), 7.20 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.8 Hz), 7.28 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.8 Hz), 7.38 (d, 1 H, H5, $^3J_{HH}$ = 7.8 Hz), 7.58 (t, 1 H, H7, $^3J_{HH}$ = 7.8 Hz), 7.70 (t, 1 H, H6, $^3J_{HH}$ = 7.8 Hz), 8.54 (d, 1 H, H8, $^3J_{HH}$ = 7.8 Hz), 10.77 (br s, 1 H, XyN*H*); ***E*-4d-Xy**: δ 1.41 (s, 6 H, CMe_2), 2.15 (s, 6 H, Me, Xy), 3.02 (s, 2 H, CH_2), 6.89 (d, 1 H, CH, $^3J_{HH}$ = 7.8 Hz), 7.02 (t, 1 H, CH, $^3J_{HH}$ = 7.8 Hz), 7.07 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.8 Hz), 7.19 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.8 Hz; partially obscured by *m*-H of Xy of *Z* isomer), 7.34 (d, 1 H, CH, $^3J_{HH}$ = 7.8 Hz), 7.51 (dt, 1 H, CH, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.2 Hz), 9.71 (br s, 1 H, CMe_2NH), 9.99 (br s, 1 H, XyN*H*). Low temperature ^{1}H NMR (–60 ºC, CD_2Cl_2, 400 MHz): ***Z*-4d-Xy**: δ 1.26 (s, 6 H, CMe_2), 2.19 (s, 6 H, Me, Xy), 3.02 (s, 2 H, CH_2), 6.18 (s, 1 H, CMe_2NH), 7.22 (d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.2 Hz), 7.32 (t, 1 H, *p*-H, Xy, $^3J_{HH}$ = 7.6 Hz), 7.41 (d, 1 H, H5, $^3J_{HH}$ = 7.6 Hz), 7.53 (t, 1 H, H7, $^3J_{HH}$ = 7.6 Hz), 7.72 (t, 1 H, H6, $^3J_{HH}$ = 7.6 Hz), 8.34 (d, 1 H, H8, $^3J_{HH}$ = 8.0 Hz), 10.51 (s, 1 H, XyN*H*). ^{1}H NMR (DMSO-d_6, 400 MHz; only the isomer ***Z*-4d-Xy** was observed): δ 1.23 (s, 6 H, CMe_2), 2.21 (s, 6 H, Me, Xy), 3.09 (s, 2 H, CH_2), 7.29 (br d, 2 H, *m*-H, Xy, $^3J_{HH}$ = 7.2 Hz), 7.36 (dd, 1 H, *p*-H, Xy, $^3J_{HH}$ = 8.8, $^3J_{HH}$ = 6.4 Hz), 7.52 (d, 1 H, H5, $^3J_{HH}$ = 7.6 Hz), 7.61 (t, 1 H, H7, $^3J_{HH}$ = 7.6 Hz), 7.78 (dt, 1 H, H6, $^3J_{HH}$ = 7.6, $^4J_{HH}$ = 0.8 Hz), 8.25 (d, 1 H, H8, $^3J_{HH}$ = 7.6 Hz), 8.92 (s, 1 H, CMe_2NH), 10.91 (s, 1 H, XyN*H*). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 100.81 MHz; only the

isomer ***Z*-4d-Xy** was observed): δ 17.44 (s, Me, Xy), 26.6 (s, C*Me*$_2$), 39.8 (s, CH_2), 53.1 (s, *C*Me$_2$), 121.0 (s, C8a), 126.6 (s, CH, C8), 127.8 (s, CH, C7), 128.9 (s, *m*-CH, Xy), 129.3 (s, CH, C5), 129.5 (s, *p*-CH, Xy), 135.0 (s, CH, C6), 135.8 (s, *o*-C, Xy), 137.8 (s, C4a), 155.7 (s, C1). The ^{13}C NMR resonances corresponding to the *i*-C of Xy and the CF_3 of triflate were not observed.

Single crystals of ***Z*-4d-Xy**, suitable for an X-ray diffraction study, were obtained by slow diffusion of Et_2O into a solution of **4d-Xy** in CH_2Cl_2.

Synthesis of *Z*-1-(Methylamino)-3,3-dimethyl-3,4-dihydroisoquinolinium Triflate (4d-Me). TlOTf (245 mg, 0.693 mmol) was added to a solution of [Pd_2{κ^2(*C*,*N*)-$C_6H_4CH_2CMe_2NH_2$-2}$_2$(μ-Cl)$_2$] (**D**; 200 mg, 0.344 mmol) in acetone (15 mL). The resulting suspension was stirred for 15 min and filtered through a plug of Celite. MeNCS (60 mg, 0.820 mmol) was added to the filtrate and the mixture stirred for 1 h. The solvent was evaporated and the residue was suspended in toluene (25 mL) and refluxed for 7 h. Formation of a black solid was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added and the mixture was filtered though a plug of $MgSO_4$. The filtrate was concentrated to ca. 2 mL, Et_2O (20 mL) was added and the suspension filtered off. The solid was washed with Et_2O (2 x 5 mL) and air-dried to give crude **4d-Me**. Yield: 96 mg, 0.284 mmol, 41%. Crude **4d-Me** was recrystallized from $CHCl_3$/Et_2O to give anallytically pure **4d-Me** as a colorless solid (76 mg, 0.225 mmol, recrystallization yield: 79%). Mp: 131 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 135 (5.09 x 10^{-4} M). Anal. Calcd for $C_{13}H_{17}F_3N_2O_3S$ (338.348): C, 46.15; H, 5.06; N, 8.28; S, 9.48. Found: C, 46.09; H, 5.24; N, 8.56; S, 9.17. IR (cm^{-1}): ν(NH) = 3317 s; ν(CN) = 1658, 1556. ^{1}H NMR (400 MHz): δ 1.43 (s, 6 H, CMe_2), 2.94 (s, 2 H, CH_2), 3.20 (d, 3 H, *Me*NH, $^3J_{HH}$ = 5.04 Hz), 7.28 (d, 1 H, H5, $^3J_{HH}$ = 7.5 Hz), 7.44 (t, 1 H, H7, $^3J_{HH}$ = 7.5 Hz), 7.58 (td, 1 H, H6, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.1

Hz), 8.01 (d, 1 H, H8, $^3J_{HH}$ = 7.9 Hz), 8.10 (br s, 1 H, $CMe_2N\mathit{H}$), 8.77 (m, 1 H, Me$N\mathit{H}$). $^{13}C\{^1H\}$ NMR (100.81 MHz): δ 27.1 (s, $C\mathit{Me}_2$), 29.1 (s, MeNH), 41.2 (s, CH_2), 53.5 (s, $\mathit{C}Me_2$), 120.4 (q, CF_3, $^1J_{CF}$ = 318.7 Hz), 121.2 (s, C8a), 126.3 (s, CH, C8), 128.3 (s, CH, C7), 129.1 (s, CH, C5), 134.5 (s, CH, C6), 136.5 (s, C4a), 157.2 (s, C1).

Single crystals of **4d-Me**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-hexane into a solution of **4d-Me** in CH_2Cl_2.

Synthesis of *Z*-1-(*p*-Tolylamino)-3,3-dimethyl-3,4-dihydroisoquinolinium Triflate (4d-To). TlOTf (194 mg, 0.55 mmol) was added to a solution of $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (160 mg, 0. 275 mmol) in acetone (15 mL). The mixture was stirred for 15 min and filtered through a plug of Celite. *p*-ToNCS (90 μl, 0.66 mmol) was added to the filtrate and the resulting mixture was stirred for 1 h. The solvent was evaporated and the remaining residue was suspended in toluene (25 mL) and refluxed for 8 h. Formation of a black solid was observed. Toluene was evaporated, CH_2Cl_2 (30 mL) was added and the mixture was filtered though a plug of Celite. The solvent was concentrated to ca. 2 mL, Et_2O (20 mL) was added and the suspension filtered off. The solid was washed with Et_2O (2 x 5 mL) and air-dried to give colorless **4d-To**. Yield: 153 mg, 0.369 mmol, 67%. Mp: 155 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 161 (4.92 x 10^{-4} M). Anal. Calcd for $C_{19}H_{21}F_3N_2O_3S$ (414.446): C, 55.06; H, 5.11; N, 6.76; S, 7.74. Found: C, 55.00; H, 5.25; N, 6.83; S, 7.56. IR (cm^{-1}): ν(NH) = 3242 br, s; ν(CN) = 1634, 1574. ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.24 (s, 6 H, CMe_2), 2.38 (s, 3 H, Me, To), 3.07 (s, 2 H, CH_2), 7.33–5.40 (m, 4 H, *m*-H + *o*-H, To), 7.49 (d, 1 H, H5, $^3J_{HH}$ = 7.5 Hz), 7.57 (t, 1 H, H7, $^3J_{HH}$ = 7.5 Hz), 7.75 (dt, 1 H, H6, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 0.9 Hz), 8.18 (d, 1 H, H8, $^3J_{HH}$ = 7.5 Hz), 9.15 (s, 1 H, $CMe_2N\mathit{H}$), 11.05 (s, 1 H, To$N\mathit{H}$). $^{13}C\{^1H\}$ NMR (DMSO-d_6, 75.45 MHz): δ 20.8 (s, Me, To), 26.3 (s, $C\mathit{Me}_2$), 53.0 (s, $\mathit{C}Me_2$), 121.5 (s, C8a),

126.1 (s, *o*-CH, To), 126.7 (s, CH, C8), 127.5 (s, CH, C7), 129.3 (s, CH, C5), 130.5 (s, *m*-CH, To), 131.7 (s, *i*-C, To), 134.8 (s, CH, C6), 137.8 (s, C4a), 138.0 (s, *p*-C, To), 155.9 (s, C1). The resonances corresponding to the CH_2 group (obscured by the DMSO) and the CF_3 of triflate were not observed. Low temperature NMR: ^{1}H NMR (–60 ºC, $CDCl_3$, 400 MHz): δ 1.40 (s, 6 H, CMe_2), 2.38 (s, 3 H, Me, To), 3.06 (s, 2 H, CH_2), 7.84 (s, 1 H, CMe_2N*H*), 7.27 ("d", 2 H, *m*-H, To, $^3J_{HH}$ = 8.3 Hz), 7.33 ("d", 2 H, *o*-H, To, $^3J_{HH}$ = 9.0 Hz), 7.41 (d, 1 H, H5, $^3J_{HH}$ = 7.6 Hz), 7.55 (t, 1 H, H7, $^3J_{HH}$ = 7.8 Hz), 7.76 (t, 1 H, H6, $^3J_{HH}$ = 7.5 Hz), 8.26 (d, 1 H, H8, $^3J_{HH}$ = 7.9 Hz), 10.75 (s, 1 H, ToN*H*). $^{13}C\{^1H\}$ NMR (–60 ºC, $CDCl_3$, 100.81 MHz): δ 21.2 (s, Me, To), 27.1 (s, C*Me*$_2$), 40.2 (s, CH_2), 53.3 (s, *C*Me$_2$), 119.6 (q, CF_3, $^1J_{CF}$ = 319.0 Hz), 119.6 (s, C8a), 125.0 (s, *o*-CH, To), 127.3 (s, CH, C8), 128.3 (s, CH, C7), 129.1 (s, CH, C5), 129.1 (s, *i*-C, To), 131.1 (s, *m*-CH, To), 135.4 (s, CH, C6), 136.6 (s, C4a), 139.4 (s, *p*-C, To), 156.8 (s, C1).

Single crystals of **4d-To**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-pentane into a solution of **4d-To** in $CHCl_3$.

Synthesis of (*R*)-1-Oxo-3-(methoxycarbonyl)-1,2,3,4-tetrahydrobenzo[*g*]isoquinoline (5a). CO was bubbled for 10 min through a suspension of 200 mg of the mixture **I** (obtained from 186 mg, 0.700 mmol of D-naphthylalanine methyl ester hydrochloride) in $CHCl_3$ (15 mL). The resulting mixture was stirred under a CO atmosphere for 12 h. Decomposition to metallic palladium was observed. The mixture was filtered through a plug of Celite, the filtrate was concentrated to ca. 1 mL and Et_2O (15 mL) was added. The suspension was filtered and the solid washed with Et_2O (2 x 5 mL) and air-dried to afford crude off-colorless **5a**. Yield: 86 mg, 0.337 mmol, 48%. Crude **5a** was recrystallized from $CHCl_3/Et_2O$ to give pure **5a** as colorless solid (51 mg, 0.200 mmol;

recrystallization yield: 59%). Mp: 183 °C. Anal. Calcd for $C_{15}H_{13}NO_3$ (255.273): C, 70.58; H, 5.13; N, 5.49. Found: C, 70.19; H, 5.52; N, 5.40. IR (cm^{-1}): ν(NH) = 3209; ν(CO) = 1745, 1662. ^{1}H NMR (300 MHz): δ 3.51, 3.36 (AB part of an ABMX system, 2 H, CH_2, $^2J_{AB}$ = 15.4, $^3J_{AM}$ = 9.4, $^3J_{BM}$ = 4.6 Hz), 3.79 (s, 3 H, OMe), 4.47 (m, M part of an ABMX system, 1 H, CH), 6.77 (br s, 1 H, NH), 7.47–7.59 (m, 2 H, H7 + H8), 7.67 (s, 1 H, H5), 7.81 (d, 1 H, H6, $^3J_{HH}$ = 8.2 Hz), 7.95 (d, 1 H, H9, $^3J_{HH}$ = 8.0 Hz), 8.65 (s, 1 H, H10). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 31.6 (s, CH_2), 52.9 (s, OMe), 53.2 (s, CH), 126.0 (s, CH, C5), 126.1 (s, C10a), 126.3 (s, CH, C8), 127.2 (s, CH, C6), 128.3 (s, CH, C7), 129.4 (s, CH, C9), 129.5 (s, CH, C10), 131.8 (s, C4a), 132.2 (s, C9a), 135.2 (s, C5a), 165.4 (s, CONH), 170.9 (s, *C*O_2Me). FAB$^+$-MS: *m/z* 256.1 [$(M+1)^+$]. EI-HRMS: exact mass calcd for $C_{15}H_{13}NO_3$ 255.0895; found 255.0913; Δ = 0.0018.

Single crystals of **5a**, suitable for an X-ray diffraction study, were obtained by slow evaporation of a solution of **5a** in $CHCl_3$.

Synthesis of (*S*)-1-Oxo-3-(methoxycarbonyl)-2,3,4,9-tetrahydro-1*H*-pyrido[3,4-*b*]indole (5b). CO was bubbled through a suspension of complex (*S*,*S*)-[$Pd_2\{\kappa^2(C,N)$-$C_8H_5N(CH_2CH(CO_2Me)NH_2)-2\}_2(\mu$-Cl$)_2$]·2$CH_3CN$ (**B**·2MeCN; 250 mg, 0.312 mmol) in $CHCl_3$ (30 mL), and the resulting mixture was stirred under a CO atmosphere for 24 h. Decomposition to metallic palladium was observed. The mixture was filtered and the filtrate was concentrated to dryness, CH_2Cl_2 (20 ml) was added and the resulting suspension was filtered through a plug of $MgSO_4$. The solvent was evaporated, the residue was vigorously stirred with *n*-pentane, the suspension was filtered and thes solid was washed with *n*-pentane (2 x 2 mL) and air-dried to give compound **5b** as a creamy solid. Yield: 110 mg, 0.448 mmol, 72%. Mp: 178 °C dec (lit.[94] 178–179 ºC). IR (cm^{-1}): ν(NH) = 3251, 3212; ν(CO) = 1732,

1665. ^{1}H NMR (300 MHz): δ 3.32, 3.46 (AB part of an ABMX system, 2 H, CH_2, $^{2}J_{AB}$ = 16.1, $^{3}J_{BM}$ = 9.7, $^{3}J_{AM}$ = 6.2 Hz), 3.79 (s, 3 H, OMe), 4.58 (M part of an ABMX system, 1 H, CH, $^{3}J_{MX}$ = 2.1 Hz), 6.65 (s, 1 H, CON*H*), 7.13 (td, 1 H, H6, $^{3}J_{HH}$ = 7.8, $^{4}J_{HH}$ = 0.9 Hz), 7.29 (td, 1 H, H7, $^{3}J_{HH}$ = 8.1, $^{4}J_{HH}$ = 1.2 Hz), 7.49 (d, 1 H, H8, $^{3}J_{HH}$ = 8.1 Hz), 7.58 (d, 1 H, H5, $^{3}J_{HH}$ = 8.1 Hz), 10.48 (br s, 1 H, NH, C_8H_5N). ^{13}C{^{1}H} NMR (100.81 MHz): δ 24.0 (s, CH_2), 52.9 (s, OMe), 55.0 (s, CH), 112.9 (s, CH, C8), 117.6 (s, C4a), 120.2 (s, CH, C5), 120.3 (s, CH, C6), 124.9 (s, C4b), 125.4 (s, CH, C7), 125.9 (s, C9a), 137.9 (s, C8a), 162.4 (s, CONH), 171.3 (s, *C*O_2Me). FAB^{+}-MS: *m/z* 245.0 [(M+1)$^{+}$]. EI-HRMS: exact mass calcd for $C_{13}H_{12}N_2O_3$ 244.0848; found 244.0850; Δ = 0.0002. Spectroscopic data are in accordance with the data available in the literature (^{1}H and ^{13}C NMR in DMSO-d_6).[39]

Single crystals of **5b**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-hexane into a solution of **5b** in CH_2Cl_2.

Synthesis of 1-Oxo-1,2,3,4-tetrahydroisoquinoline (5c). CO was bubbled through a suspension of complex [Pd_2{κ^2(*C*,*N*)-$C_6H_4CH_2CH_2NH_2$-2}$_2$(μ-OAc)$_2$] (**C**; 170 mg, 0.298 mmol) in CH_2Cl_2 (20 mL), and the resulting mixture was stirred under a CO atmosphere for 3 h. Decomposition to metallic palladium was observed. The solvent was evaporated, Et_2O (45 mL) was added, and the mixture was filtered through a plug of $MgSO_4$. The filtrate was concentrated to dryness to give compound **5c** as a colorless liquid. When stored, thin needles of solid **5c** appeared in the walls of the vial. Yield: 74 mg, 0.502 mmol, 84%. IR (cm^{-1}): ν(NH) = 3242; ν(CO) = 1666. ^{1}H NMR (200 MHz): δ 2.97 (t, 2 H, CH_2Ar, $^{3}J_{HH}$ = 6.8 Hz), 3.56 (td, 2 H, C*H*$_2$NH, $^{3}J_{HH}$ = 6.8, $^{3}J_{HH}$ = 3.0 Hz), 7.21 (d, 1 H, H5, $^{3}J_{HH}$ = 7.4 Hz), 7.33 (t, 1 H, H7, $^{3}J_{HH}$ = 7.4 Hz), 7.44 (td, 1 H, H6, $^{3}J_{HH}$ = 7.4, $^{4}J_{HH}$ = 1.4 Hz), 7.88 (br s, 1 H, NH), 8.04 (dd, 1 H, H8, $^{3}J_{HH}$ = 7.6, $^{4}J_{HH}$ = 1.4 Hz). ^{13}C{^{1}H} NMR (50.30 MHz): δ 28.5 (s, CH_2Ar), 40.4

(s, CH_2NH), 127.5 (s, CH, C7), 127.7 (s, CH, C5), 128.3 (s, CH, C8), 129.1 (s, C8a), 132.7 (s, CH, C6), 139.4 (s, C4a), 167.8 (s, CO). EI-MS: *m/z* 147.1 [M]. EI-HRMS: exact mass calcd for C_9H_9NO 147.0684; found 147.0682; Δ = 0.0002. Spectroscopic data are in accordance with the data available in the literature (^{1}H and ^{13}C NMR).[97]

Single crystals of **5c**, suitable for an X-ray diffraction study, growed in the vial where compound **5c** was stored.

Synthesis of 1-Oxo-3,3-dimethyl-1,2,3,4-tetrahydroisoquinoline (5d). CO was bubbled through a suspension of complex $[Pd_2\{\kappa^2(C,N)\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**D**; 200 mg, 0.344 mmol) in CH_2Cl_2 (25 mL), and the resulting mixture was stirred under a CO atmosphere for 2.5 h. Decomposition to metallic palladium was observed. The solvent was evaporated and acetone (10 mL) and NEt_3 (95 μL, 0.688 mmol) were added. The resulting suspension was stirred for 15 min and then acetone was evaporated, Et_2O (10 mL) was added, and the suspension was filtered to remove metallic palladium and $NHEt_3Cl$. The filtrate was concentrated to dryness to give compound **5d** as a colorless solid. Yield: 118 mg, 0.676 mmol, 98%. Mp: 148 °C (lit.[92] 146–148 °C). IR (cm^{-1}): ν(NH) = 3179, 3043; ν(CO) = 1666. ^{1}H NMR (300 MHz): δ 1.32 (s, 6 H, Me), 2.92 (s, 2 H, CH_2), 6.58 (br s, 1 H, NH), 7.18 (dd, 1 H, H5, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 0.9 Hz), 7.34 ("t", 1 H, H7, $^3J_{HH}$ = 7.5 Hz), 7.45 (td, 1 H, H6, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.5 Hz), 8.07 (dd, 1 H, H8, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.5 Hz). ^{13}C{^{1}H} NMR (75.45 MHz): δ 28.8 (s, Me), 41.5 (s, CH_2), 51.9 (s, *C*Me_2), 126.9 (s, CH, C7), 127.7 (s, CH, C8), 127.8 (s, CH, C5), 127.9 (s, C8a), 132.2 (s, CH, C6), 137.5 (s, C4a), 165.6 (s, CO). FAB$^+$-MS: *m/z* 176.1 [$(M+1)^+$]. Spectroscopic data are in accordance with the data available in the literature (^{1}H NMR).[92]

Single crystals of **5d**, suitable for an X-ray diffraction study, were obtained by slow diffusion of *n*-pentane into a solution of **5d** in CH_2Cl_2.

X-ray Structure Determinations. X-ray data for compounds **2b**, **4b-^{t}Bu**, **4c-^{t}Bu**, **4d-^{t}Bu,Xy,Me,To** and **5a**–**d** are summarized in Tables 1 and 2. Data Collection. Crystals were mounted in inert oil on a glass fiber and transferred to a Bruker SMART APEX diffractometer. Data were recorded at low temperature and using ω scans. Multiscan absorption corrections were applied for compounds **2b**, **4c-^{t}Bu**, **4d-^{t}Bu,Xy,Me** and **5d**. Structure Solution and Refinements. Structures were solved by direct method and refined anisotropically on F2 using the program SHELX-97.[100] Hydrogen atoms were refined as follows: NH, free; NH_2, free with SADI; methyl, rigid group; all others, riding. *Special features*: Complex **2b**: Absolute structure (Flack) parameter:[101] –0.006(16). Compound **4b-^{t}Bu**: Flack parameter: –0.02(6). Compounds **5a,b**: They present 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.

Computational Details. Density funtional calculations were carried out using the GAUSSIAN-03 program package.[102] The hybrid density functional B3LYP method was applied,[103] employing 6-31G* as the basis set.[104] After geometry optimizations, analytical frequency calculations were carried out to confirm that all of them correspond with a minimum.

Acknowledgement. We thank Ministerio de Educación y Ciencia (Spain) and FEDER (CTQ2004-05396) for financial support. J.-A. G.-L. is grateful to the Ministerio de Educación y Ciencia and the University of Murcia (Spain) for consecutively research grants.

Supporting Information Available. Total energies and total energies differences (hartrees/molecule) calculated for the *E*/*Z*-isomer of compounds **3a-^{t}Bu,Xy**, **3c-^{t}Bu**, **3d-Xy** and **4d-^{t}Bu**,**Xy**,**Me**,**To**, experimental details for 3-(2-naphthyl)-D-alanine methyl ester hydrochloride, ^{1}H and ^{13}C NMR tables 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 and CIF files for compounds **2b, 4b-^{t}Bu**, **4c-^{t}Bu**, **4d-^{t}Bu,Xy,Me,To** and **5a**–**d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Table 1. Crystal Data and Structure Refinement for Complex **2b** and Lactams **5a–d**.

	2b	**5a**	**5b**	**5c**	**5d**
formula	$C_{30}H_{31}ClN_4O_2Pd$	$C_{15}H_{13}NO_3$	$C_{13}H_{12}N_2O_3$	C_9H_9NO	$C_{11}H_{13}NO$
fw	621.44	255.26	244.25	147.17	175.22
temperature	100(2) K	100(2) K	100(2) K	100(2) K	100(2) K
crystal syst	orthorhombic	orthorhombic	triclinic	monoclinic	monoclinic
space group	$P2_12_12_1$	$P2_12_12_1$	$P1$	$P2_1/c$	$C2/c$
a (Å)	12.9743(10)	6.0656(3)	5.8964(4)	11.3470(11)	19.8437(12)
b (Å)	14.5650(11)	15.6690(8)	8.3010(5)	5.2078(5)	5.5447(3)
c (Å)	15.1878(12)	25.2834(14)	11.9991(8)	13.5158(12)	17.6217(11)
α (deg)	90	90	72.139(2)	90	90
β (deg)	90	90	81.825(2)	113.083(2)	103.851(2)
γ (deg)	90	90	86.683(2)	90	90
V (Å^3)	2870.0(4)	2403.0(2)	553.26(6)	734.74(12)	1882.49(19)
Z	4	8	2	4	8
ρ_{calcd} (Mg m^{-3})	1.438	1.411	1.466	1.330	1.237
μ (Mo, Kα) (mm^{-1})	0.773	0.099	0.106	0.088	0.079
F(000)	1272	1072	256	312	752
cryst size (mm)	0.21 x 0.20 x 0.19	0.31 x 0.12 x 0.07	0.43 x 0.17 x 0.10	0.34 x 0.12 x 0.09	0.32 x 0.20 x 0.14
θ range (deg)	1.94 to 28.26	2.07 to 28.14	1.80 to 26.37	1.95 to 27.10	2.11 to 28.07
reflns coll	33299	27919	6159	5726	10312
independent reflns	6678	3268	2262	1616	2188
R_{int}	0.0239	0.0728	0.0197	0.0439	0.0221
max. and min. transmsn	0.867 and 0.855	—	—	—	0.989 and 0.975
restraints/params	1/360	1/353	3/343	0/104	0/124
goodness-of-fit on F^2	1.062	1.049	1.068	1.065	1.088
R1 [$I > 2\sigma(I)$]	0.0218	0.0534	0.0331	0.0636	0.0448
wR2 (all reflns)	0.0545	0.1005	0.0838	0.1787	0.1171
largest diff. peak and hole (e Å^{-3})	0.510 and –0.219	0.296 and –0.342	0.257 and –0.279	0.784 and –0.357	0.339 and –0.240

Table 2. Crystal Data and Structure Refinement for Amidinium Salts **4b-^{t}Bu, 4c-^{t}Bu, and 4d-^{t}Bu,Xy,Me,To**.

	4b-^{t}Bu	**4c-^{t}Bu**	**4d-^{t}Bu**	**4d-Xy**	**4d-Me**	**4d-To**
formula	$C_{18}H_{22}F_3N_3O_5S$	$C_{14}H_{19}F_3N_2O_3S$	$C_{16}H_{23}F_3N_2O_3S$	$C_{20}H_{23}F_3N_2O_3S$	$C_{13}H_{17}F_3N_2O_3S$	$C_{19}H_{21}F_3N_2O_3S$
fw	449.45	352.37	380.42	428.46	338.35	414.44
temperature	100(2) K	100(2) K	100(2) K	100(2) K	293(2) K	100(2) K
crystal syst	orthorhombic	monoclinic	orthorhombic	monoclinic	monoclinic	triclinic
space group	$P2_12_12_1$	$P2_1/c$	$Pbca$	$C2/c$	$P2_1/c$	$P\bar{1}$
a (Å)	9.436(4)	9.7404(7)	11.5966(5)	15.5438(6)	10.5365(5)	9.2550(6)
b (Å)	10.310(5)	9.1752(7)	15.1252(7)	19.1839(7)	16.8639(8)	10.3129(7)
c (Å)	21.063(10)	18.1889(13)	20.7926(11)	15.5671(6)	8.6326(4)	11.2789(8)
α (deg)	90	90	90	90	90	103.744(2)
β (deg)	90	98.581(2)	90	117.576(2)	102.701(2)	109.012(2)
γ (deg)	90	90	90	90	90	91.426(2)
V (Å^3)	2049.2(16)	1607.3(2)	3647.0(3)	4114.6(3)	1496.36(12)	982.51(12)
Z	4	4	8	8	4	2
ρ_{calcd} (Mg m^{-3})	1.457	1.456	1.386	1.383	1.502	1.401
μ (Mo, Kα) (mm^{-1})	0.220	0.248	0.244	0.208	0.236	0.215
F(000)	936	736	1600	1792	704	432
cryst size (mm)	0.29 x 0.22 x 0.09	0.36 x 0.32 x 0.09	0.25 x 0.24 x 0.11	0.34 x 0.14 x 0.12	0.23 x 0.15 x 0.10	0.22 x 0.13 x 0.11
θ range (deg)	1.93 to 27.11	2.11 to 26.37	1.96 to 26.37	1.82 to 26.37	1.98 to 26.37	1.98 to 28.18
reflns coll	12636	17044	37842	22478	16171	11471
independent reflns	4428	3287	3728	4211	3050	4407
R_{int}	0.0412	0.0237	0.0300	0.0237	0.0269	0.0393
max. and min. transmsn	——	0.978 and 0.916	0.976 and 0.946	0.976 and 0.933	0.974 and 0.942	——
restraints/params	5/287	0/219	0/239	11/274	0/210	0/264
goodness-of-fit on F^2	1.074	1.047	1.068	1.020	1.051	1.026
R1 [$I > 2\sigma(I)$]	0.0374	0.0348	0.0355	0.0345	0.0334	0.0429
wR2 (all reflns)	0.0932	0.0929	0.0886	0.0910	0.0855	0.1093
largest diff. peak and hole (e Å^{-3})	0.321 and –0.338	0.524 and –0.253	0.398 and –0.336	0.421 and –0.322	0.518 and –0.314	0.406 and –0.335