Regiospecific Functionalization of Pharmaceuticals and Other Biologically Active Molecules through Cyclopalladated Compounds. 2-Iodination of Phentermine and L-Tryptophan Methyl Ester†

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Phentermine hydrochloride ($(PhCH_2CMe_2NH_3)Cl$) or L-tryptophan methyl ester hydrochloride ($[C_8H_6NCH_2CH(CO_2Me)NH_3]Cl$) reacts with $Pd(OAc)_2$ in a 1:1 molar ratio to give the cyclometalated complex $[Pd_2(\kappa^2\text{-}C,N\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2)_2(\mu\text{-}Cl)_2]$ (**1**) or (*S,S*)-$[Pd_2\{\kappa^2\text{-}C,N\text{-}C_8H_5NCH_2CH(CO_2Me)NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**2**), respectively. Reaction of **1** or **2** with iodine affords *trans*-$[PdCl_2(NH_2CMe_2CH_2C_6H_4I\text{-}2)_2]$ (**3**) or *trans*-(*S,S*)-$[PdCl_2\{NH_2CH(CO_2Me)CH_2C_8H_5NI\text{-}2\}_2]$ (**4**), which further reacts with 1,10-phenanthroline to give $[PdCl_2(phen)]$ and the free amine 2-I-phentermine (**5**) or (*S*)-2-I-tryptophan methyl ester (**6**) (overall yields 44 and 51%, respectively, considering phentermine and L-tryptophan methyl ester as starting materials). The crystal structure of complex **3** has been determined by X-ray diffraction studies.

Introduction

We have recently proved that, contrary to previous studies,[1] it is possible to *ortho*-palladate primary amines, such as benzylamines and phenethylamines, even if they lead to six-membered palladacycles.[2] Since a considerable number of drugs and biologically active molecules are related to primary amines (e.g., amphetamines such as phentermine are used as anorexics; neurotransmitters such as dopamine and amino acids such as tryptophan are used to treat depression, schizophrenia, and other neuropsychiatric disorders),[3] we decided to synthesize C-palladated biomolecules (i.e., phentermine and L-tryptophan methyl ester) through direct metalation reactions. Not only have analogous bio-organometallic complexes attracted great interest,[4,5] but this type of compounds can act as precursors of new derivatives potentially relevant from a biological point of view. Among the possible derivatives, the *ortho*-iodinated aryl-substituted alkylamines are particularly interesting, as they are not easily prepared by other methods, such as direct electrophilic substitution. *Ortho*-iodination extends the reactivity of organic molecules[6] and makes amines such as the ones used in this work suitable for the palladium-mediated synthesis of six-membered N-heterocycles.[7] In addition, iodination of amino acids can be a convenient approach for the direct labeling of small peptides. Barluenga et al. have recently reported a regioselective method to prepare *ortho*-iodinated phenylalanine-containig peptide sequences,[8] but the method cannot be applied to the amino acid itself.[9] Some of the results reported here were presented at a conference.[10]

Results and Discussion

Phentermine hydrochloride ($(PhCH_2CMe_2NH_3)Cl$) or L-tryptophan methyl ester hydrochloride ($[C_8H_6NCH_2CH(CO_2Me)NH_3]Cl$) reacted with $Pd(OAc)_2$ in a 1:1 molar ratio, in acetonitrile, at 80 °C or room temperature, respectively, to give the cyclometalated complex $[Pd_2(\kappa^2\text{-}C,N\text{-}C_6H_4CH_2CMe_2NH_2\text{-}2)_2(\mu\text{-}Cl)_2]$ (**1**) or (*S,S*)-$[Pd_2\{\kappa^2\text{-}C,N\text{-}C_8H_5NCH_2CH(CO_2Me)NH_2\text{-}2\}_2(\mu\text{-}Cl)_2]$ (**2**) (Scheme 1).

† Dedicated to Dr. José-Antonio Abad on the occasion of his retirement in recognition of his outstanding contributions to our research group.

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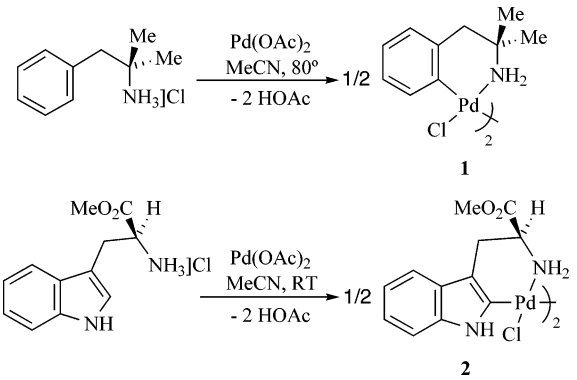
Scheme 1. Cyclometalation of Phentermine Hydrochloride and L-Tryptophan Methyl Ester Hydrochloride



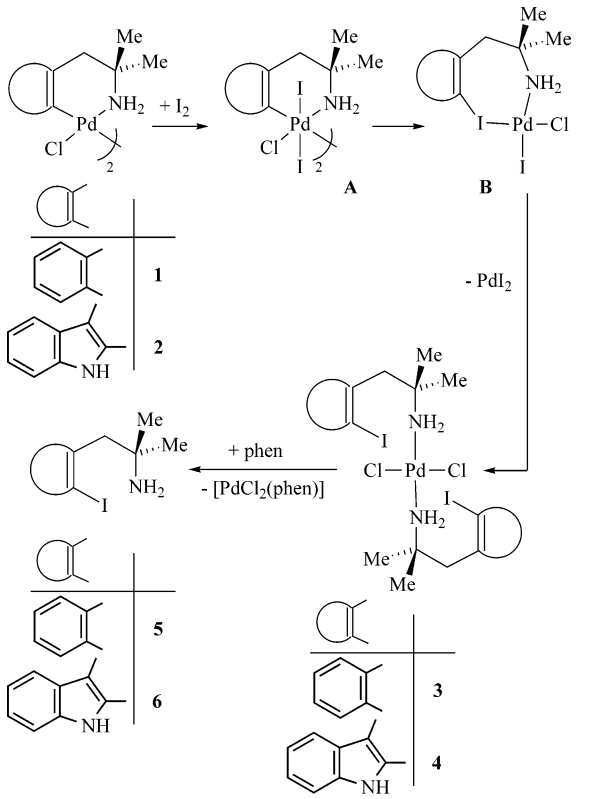
The first product isolated from the reaction of L-tryptophan methyl ester hydrochloride and $Pd(OAc)_2$ is a yellow solid that precipitates from the reaction mixture. Its elemental analysis and IR spectrum (with two weak bands at 2312 and 2284 cm^{-1} that can be assigned to acetonitrile) suggest the formulation [PdCl{κ^2-*C*,*N*-$C_8H_5NCH_2CH(CO_2Me)NH_2$-2}(NCMe)]. Attempts to obtain crystals suitable for X-ray diffraction failed, and in the absence of crystallographic evidence, other formulations such as [Pd_2{κ^2-*C*,*N*-$C_8H_5NCH_2CH(CO_2Me)NH_2$-2}$_2$($\mu$-Cl)$_2$]·2MeCN (**2**·2MeCN) cannot be ruled out. However, the product was used as the starting material for the synthesis of **4** (see below) and could be recrystallized from acetone to give complex **2**.

It is interesting to note that complexes containig *ortho*-metalated α-amino acid derivatives are rare.[5,11] Kaminskaia et al. have reported the cyclopalladation of indenil derivatives, which are analogous to tryptophanyl-(amino acid) dipeptides.[12]

The ^1H and ^{13}C NMR spectra of complexes **1** and **2** clearly show that cyclometalation has taken place. Whereas a multiplet corresponding to five aromatic protons is observed in the ^1H NMR spectrum of free phentermine, a set of four different signals, corresponding to the four remaining protons in the *ortho*-metalated ring, is found for **1**. In the case of L-tryptophan methyl ester, the ^1H NMR signal corresponding to H(2) of the free ligand disappears upon metalation. In both cases, the resonance due to the carbon bonded to Pd shifts downfield with respect to that of the corresponding free ligand, as observed in other cyclopalladated complexes.[13]

The reaction of complex **1** or **2** with I_2, in CH_2Cl_2 at room temperature, afforded *trans*-[$PdCl_2(NH_2CMe_2CH_2C_6H_4I$-2)$_2$] (**3**) or *trans*-(*S*,*S*)-[$PdCl_2${$NH_2CH(CO_2Me)CH_2C_8H_5NI$-2}$_2$] (**4**), respectively, in good yield (Scheme 2).[14] For these reactions, we propose an initial step involving the oxidative addition of iodine to give a Pd(IV) complex (see **A** in Scheme 2). This would then undergo a reductive elimination followed by a symmetrization process, leading to **3** or **4** and PdI_2. In fact, palladium iodide was isolated quantitatively from the reaction mixture by filtration as a dark brown solid. This was then reacted with PPh_3 (1:2) to give [$PdI_2(PPh_3)_2$], which was characterized by ^{31}P NMR.

Scheme 2. Proposed Reaction Pathway for the Synthesis of 3 and 4 and the Synthesis of 5 and 6



The symmetrization reaction involves formation of a complex containing two ligands on the same palladium atom from a dinuclear precursor having only one ligand per palladium atom. If the symmetrization were an intramolecular process, an equimolecular mixture of complexes **1** and **2** would react with I_2 to give only **3** and **4**. However, if it were an intermolecular reaction, it would afford a mixture of **3**, **4**, and the mixed complex [$PdCl_2(L_I)(L'_I)$], where L_I and L'_I are the *ortho*-iodinated ligands. To clarify the mechanism of this reaction, complexes **1** and **2** were treated with I_2 (molar ratio 1:1:4) in CH_2Cl_2 for 2.5 h. The ^1H NMR spectrum of the resulting mixture showed complexes **3** and **4** and another set of signals that could be assigned to a complex containing the two different iodinated amines bonded to the same palladium atom, thus suggesting that the symmetrization reaction occurs via an intermolecular process. This was further confirmed by the fact that a mixture of **3** and **4** did not give the mixed complex, but remained unaltered after 2.5 h in CH_2Cl_2.

Espinet et al. have reported a similar reaction between [Pd(Fmes)(κ^2-*C*,*N*-$C_6H_4CH_2NMe_2$-2)(OH_2)] (Fmes = 2,4,6-tris(trifluoromethyl)phenyl) and I_2, but in this case the *ortho*-iodinated benzylamine ligand remains coordinated to the Pd atom through both the nitrogen and the iodine atoms to form [Pd(Fmes)(κ^2-*I*,*N*-$IC_6H_4CH_2NMe_2$-2)(OH_2)].[15] Probably, an analogous complex

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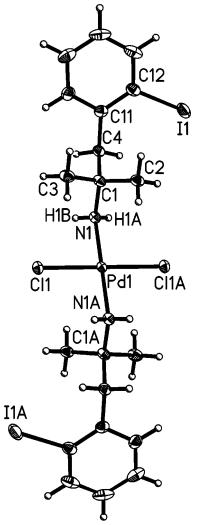


Figure 1. Thermal ellipsoid plot (50% probability) of **3** along with the labeling scheme. Selected bond lenghs (Å) and angles (deg): Pd(1)−N(1) 2.063(3), Pd(1)−Cl(1) 2.3129(7), N(1)−C(1) 1.503(4), I(1)−C(12) 2.111(4), N(1)−Pd(1)−Cl(1) 89.46(8), N(1)−Pd(1)−Cl(1A) 90.54(8).

(see **B** in Scheme 2) is an intermediate in the synthesis of **3** or **4**. Its seven-membered ring structure, less stable than the six-membered ring present in the benzylamine derivative, would facilitate the intermolecular process leading to **3** and **4**.

2-I-Phentermine (**5**) and (*S*)-2-I-tryptophan methyl ester (**6**) were conveniently prepared in high yield by reacting complexes **3** and **4** with 1,10-phenanthroline (phen). The byproduct in these reactions, [$PdCl_2$(phen)], precipitates from the mixtures and can be easily separated from the final amines by filtration.

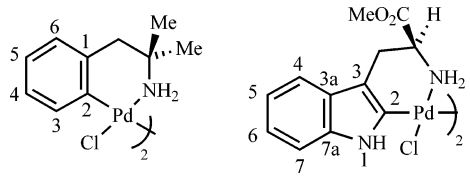
Substitution of the Pd atom by iodine was confirmed by ^{13}C NMR spectroscopy. The resonance due to the carbon atom bonded to iodine shifts upfield with respect to the corresponding signals in both the cyclometalated complexes (**1** and **2**) and the free ligands. This is a well-known effect.[16] In addition, the ^1H NMR spectra of the iodo-amines **5** and **6** show the signals corresponding to the NH_2 groups shifted upfield with respect to those in complexes **3** and **4**, as expected upon decoordination.

The crystal structure of complex **3** (Figure 1) has been determined by X-ray diffraction and shows the palladium atom coordinated to two chlorine atoms and two nitrogen atoms in an almost perfect square planar geometry [angles N(1)−Pd(1)−Cl(1) 89.46(8)°, N(1)−Pd(1)−Cl(1A) 90.54(8)°]. The amine ligands adopt a *trans* disposition, which is the same for all other bis(amino)-dihalopalladium(II) complexes.[17]

Conclusions

We report for the first time the cyclometalation of biologically active primary amines, phentermine and L-tryptophan methyl ester, and their 2-iodination. The latter occurs through *trans*-[$PdCl_2L_2$], where L is the 2-iodinated amine. The crystal structure of the phentermine derivative has been determined by X-ray diffraction. The 2-iodo amines have been isolated and characterized by reacting the corresponding *trans*-[$PdCl_2L_2$] complexes with 1,10-phenanthroline.

Chart 1. Numbering Scheme for the NMR Assignment of Complexes 1 and 2



1 **2**

Experimental Section

General Procedures. Infrared spectra were recorded on a Perkin-Elmer 16F-PC-FT spectrometer. C, H, and N analyses, conductance measurements in acetone, and melting point determinations were carried out as described elsewhere.[18] Unless otherwise stated, NMR spectra were recorded in $CDCl_3$ in Bruker Avance 300 or 400 spectrometers. Chemical shifts are referenced to TMS [^1H and $^{13}C\{^1H\}$]. Signals in the ^1H and ^{13}C NMR spectra of all complexes were assigned with the help of HSQC and HMBC techniques. Reactions were carried out at room temperature without special precautions against moisture. Phentermine (α,α-dimethylphenethylamine) hydrochloride (Aldrich), L-tryptophan methyl ester hydrochloride, PPh_3 (Fluka), 1,10-phenanthroline monohydrate (Merck), and palladium acetate (Johnson Matthey) were used as received.

Synthesis of [Pd_2(κ^2-*C*,*N*-$C_6H_4CH_2CMe_2NH_2$-2)$_2$(μ-Cl)$_2$] (1). Phentermine hydrochloride (500 mg, 2.69 mmol) was added to a solution of $Pd(OAc)_2$ (605 mg, 2.69 mmol) in acetonitrile (40 mL), and the resulting mixture was heated at 80 °C for 4 h. The resulting suspension was filtered through a plug of $MgSO_4$, the filtrate was concentrated to dryness, the residue was dissolved in CH_2Cl_2 (5 mL), and *n*-hexane (30 mL) was added to give an oily precipitate. The solvent was removed, the residue taken in CH_2Cl_2 (5 mL), the suspension filtered out, and the solid washed with CH_2Cl_2 (2 × 1 mL) and air-dried to give **1** as a yellow solid. Yield: 583 mg, 1.00 mmol, 75%. Dec pt: 179 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 5 (6.96×10^{-4} M). Anal. Calcd for $C_{20}H_{28}Cl_2N_2$ (580.164): C, 41.40; H, 4,86; N, 4.83. Found: C, 41.23; H, 5.11; N, 4.75. IR (cm^{-1}): ν(NH) = 3306, 3236. ^1H NMR (300 MHz): δ 1.20 (s, 6 H, Me), 2.96 (b s, 2 H, NH_2), 3.04 (s, 2 H, CH_2), 6.75 (dd, 1 H, H6, C_6H_4, $^3J_{HH}$ = 7.0, $^4J_{HH}$ = 1.8 Hz), 6.82 (td, 1 H, H4, C_6H_4, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.8 Hz), 6.91 (td, 1 H, H5, C_6H_4, $^3J_{HH}$ = 7.2, $^4J_{HH}$ = 1.2 Hz), 7.26 (dd, 1 H, H3, C_6H_4, $^3J_{HH}$ = 7.5, $^4J_{HH}$ = 1.2 Hz). $^{13}C\{^1H\}$ NMR (75.45 MHz): δ 29.0 (s, Me), 49.4 (s, *C*-Me_2), 54.4 (s, CH_2), 124.5 (s, CH, C5, C_6H_4), 124.9 (s, CH, C4, C_6H_4), 128.0 (s, CH, C6, C_6H_4), 135.5 (s, CH, C3, C_6H_4), 136.9 (s, C1, C_6H_4), 139.6 (s, C−Pd, C2, C_6H_4).

Synthesis of (*S*,*S*)-[Pd_2\{κ^2-*C*,*N*-$C_8H_5NCH_2CH(CO_2Me)$-NH_2-2\}$_2$(μ-Cl)$_2$] (2). L-Tryptophan methyl ester hydrochloride (908 mg, 3.56 mmol) was added to a solution of $Pd(OAc)_2$ (800 mg, 3.56 mmol) in acetonitrile (60 mL), and the resulting mixture was stirred at room temperature for 48 h. A yellow solid formed, which was filtered out, washed with MeCN (2 × 3 mL) and diethyl ether (2 × 5 mL), and air-dried to give complex **2**·2MeCN (1203 mg, 1.50 mmol, 84%) as a yellow solid. Anal. Calcd for $C_{28}H_{32}Cl_2N_6O_4Pd_2$ (800.308): C, 42.02; H, 4.03; N, 10.50. Found: C, 42.17; H, 3.98; N, 10.40. IR (cm^{-1}): ν(NH) = 3422, 3296, 3188, 3116; ν(CN) = 2312, 2284; ν(CO) = 1730.

Complex **2**·2MeCN (250 mg, 0.312 mmol) was taken up in acetone (75 mL), the resulting mixture was filtered through a

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plug of $MgSO_4$, and the yellow solution obtained was concentrated to ca. 8 mL. A yellow solid formed, which was filtered out, washed with acetone (2 × 3 mL) and diethyl ether (2 × 5 mL), and air-dried to give complex **2** (127 mg, 0.177 mmol, 57%). Dec pt: 198 °C. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 0 (5.18×10^{-4} M). Anal. Calcd for $C_{24}H_{26}Cl_2N_4O_4Pd_2$ (718.202): C, 40.14; H, 3.65; N, 7.80. Found: C, 40.25; H, 3.60; N, 7.67. IR (cm^{-1}): ν(NH) = 3432, 3415, 3303, 3225; ν(CO) = 1729. ^{1}H NMR [400 MHz, $(CD_3)_2SO$]: δ 3.03 ("dd", 1 H, CH_2, $^2J_{HH}$ = 15.5, $^3J_{HH}$ = 9.0 Hz), 3.17 ("dd", 2 H, CH_2, $^2J_{HH}$ = 15.5, $^3J_{HH}$ = 3.6 Hz), 3.60 (m, 1 H, CH), 3.63 (s, 3 H, OMe), 5.14−5.22 (m, 2 H, NH_2), 6.87 (m, 2 H, H5 + H6, C_8H_5N), 7.23 (m, 1 H, H4, C_8H_5N), 7.31 (m, 1 H, H7, C_8H_5N), 10.48 (s, 1 H, NH). ^{13}C{^{1}H} NMR [100.81 MHz, $(CD_3)_2SO$]: δ 27.1 (s, CH_2), 52.1 (s, OMe), 52.8 (s, CH), 106.4 (s, C3, C_8H_5N), 109.8 (s, CH, C7, C_8H_5N), 116.1 (s, CH, C4, C_8H_5N), 117.7 (s, CH, C5, C_8H_5N), 119.2 (s, CH, C6, C_8H_5N), 127.9 (s, C3a, C_8H_5N), 130.0 (s, C2, C_8H_5N), 135.4 (s, C7a, C_8H_5N), 172.0 (s, CO).

Synthesis of *trans*-[PdCl$_2$(NH$_2$CMe$_2$CH$_2$C$_6$H$_4$-I-2)$_2$] (3). I_2 (140 mg, 0.552 mmol) was added to a solution of complex **1** (160 mg, 0.276 mmol) in CH_2Cl_2 (35 mL), and the resulting mixture was stirred for 2.5 h. A dark brown solid was formed. The suspension was filtered through a plug of $MgSO_4$; solvent was removed until ca. 2 mL. A yellow solid was formed, which was filtered out, washed with CH_2Cl_2 (5 mL) and diethyl ether (5 mL), and air-dried to give compound **3**. Yield: 141 mg, 0.194 mmol, 70%. Mp: 202 °C dec. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 0 (5.45×10^{-4} M). Anal. Calcd for $C_{20}H_{28}Cl_2I_2N_2Pd$ (727.564): C, 33.02; H, 3.88; N, 3.85. Found: C, 32.87; H, 3.99; N, 3.85. IR (cm^{-1}): ν(NH) = 3281, 3228. ^{1}H NMR (400 MHz): δ 1.57 (s, 6 H, Me), 2.92 (s, 2 H, NH_2), 3.16 (s, 2 H, CH_2), 6.94 (ddd, 1 H, H5, C_6H_4, $^3J_{HH}$ = 7.8, $^3J_{HH}$ = 7.1, $^4J_{HH}$ = 2.0 Hz), 7.26 (dd, 1 H, H3, C_6H_4, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 2.0 Hz), 7.28 (td, 1 H, H4, $^3J_{HH}$ = 7.8, $^4J_{HH}$ = 1.2 Hz), 7.86 (dd, 1 H, H6, $^3J_{HH}$ = 8.0, $^4J_{HH}$ = 1.2 Hz). ^{13}C{^{1}H} NMR (100.81 MHz): δ 29.9 (s, Me), 52.3 (s, CH_2), 57.7 (s, *C*-Me$_2$), 102.9 (s, C2, C−I, C_6H_4), 128.4 (s, CH, C5, C_6H_4), 129.0 (s, CH, C4, C_6H_4), 131.2 (s, CH, C6, C_6H_4), 139.4 (s, C1, *C*-CH_2, C_6H_4), 140.4 (s, CH, C3, C_6H_4).

Synthesis of *trans*-(*S*,*S*)-[PdCl$_2${NH$_2$CH(CO$_2$Me)CH$_2$C$_8$H$_5$N-I-2}$_2$] (4). I_2 (159 mg, 0.626 mmol) was added to a supension of complex **2**·2MeCN (250 mg, 0.312 mmol) in CH_2Cl_2 (35 mL), and the resulting mixture was stirred for 2.5 h. A dark brown solid was formed. The suspension was filtered through a plug of $MgSO_4$, solvent was removed until ca. 2 mL, and *n*-hexane (30 mL) was added to precipitate a yellow solid, which was filtered out, washed with *n*-hexane (2 × 5 mL), and air-dried to give compound **4**. Yield: 169.8 mg, 0.196 mmol, 63%. Mp: 129 °C dec. Λ_M (Ω^{-1} cm^2 mol^{-1}) = 2 (4.99×10^{-4} M). Anal. Calcd for $C_{24}H_{26}Cl_2I_2N_4O_4Pd$ (865.602): C, 33.30; H, 3.03; N, 6.47. Found: C, 33.27; H, 3.07; N, 6.26. IR (cm^{-1}): ν(NH) = 3371, 3282, 3227; ν(CO) = 1736. ^{1}H NMR (400 MHz): δ 3.10 (dd, 1 H, CH_2, $^2J_{HH}$ = 14.7, $^3J_{HH}$ = 7.3 Hz), 3.31 (dd, 1 H, NH_2, $^2J_{HH}$ = 11.0, $^3J_{HH}$ = 5.9 Hz), 3.40 (dd, 1 H, CH_2, $^2J_{HH}$ = 14.7, $^3J_{HH}$ = 7.1 Hz), 3.59 (m, 1 H, NH_2, partially obscured by the OMe), 3.62 (s, 3 H, OMe), 4.12 (q, 1 H, CH, $^3J_{HH}$ = 6.8 Hz), 7.10 (m, 2 H, H5 + H6, C_8H_5N), 7.25 (m, 1 H, H7, C_8H_5N), 7.57 (m, 1 H, H4, C_8H_5N), 8.21 (s, 1 H, NH). ^{13}C{^{1}H} NMR (100.81 MHz): δ 31.7 (s, CH_2), 52.9 (s, OMe), 56.8 (s, CH), 80.6 (s, C−I, C_8H_5N), 110.7 (s, CH, C7, C_8H_5N), 115.3 (s, C3, C_8H_5N), 117.9 (s, CH, C4, C_8H_5N), 120.3 (s, CH, C5, C_8H_5N), 122.6 (s, CH, C6, C_8H_5N), 127.1 (s, C3a, C_8H_5N), 138.9 (s, C7a, C_8H_5N), 171.6 (s, CO).

Synthesis of 2-I-C$_6$H$_4$CH$_2$CMe$_2$NH$_2$ (5). 1,10-Phenanthroline monohydrate (38.1 mg, 0.192 mmol) was added to a suspension of complex **3** (140 mg, 0.192 mmol) in CH_2Cl_2 (40 mL), and the resulting mixture was stirred for 4 h. A yellow solid precipitated (60.8 mg, 0.170 mmol, 89%), which was filtered out and identified as [$PdCl_2$(phen)] by IR spectroscopy. Solvent was removed, diethyl ether (10 mL) was added to the residue, the resulting suspension was filtered through a plug of Celite, and solvent was removed from the filtrate under vacuum to give compound **5** as a yellow liquid. Yield: 88.8 mg, 0.323 mmol, 84%. Anal. Calcd for $C_{10}H_{14}IN$ (275.129): C, 43.66; H, 5.13; N, 5.09. Found: C, 43.31; H, 5.17; N, 5.17. ^{1}H NMR (300 MHz): δ 1.19 (s, 6 H, Me), 1.29 (s, 2 H, NH_2), 2.92 (s, 2 H, CH_2), 6.90 (m, 1 H, H5, C_6H_4), 7.28 (m, 2 H, H3 + H4, C_6H_4), 7.86 ("d", 1 H, H6, C_6H_4). ^{13}C{^{1}H} NMR (75.45 MHz): δ 30.7 (s, Me), 51.5 (s, *C*-Me$_2$), 53.3 (s, CH_2), 103.0 (s, C2, C−I, C_6H_4), 127.7 (s, CH, C5, C_6H_4), 128.0 (s, CH, C4, C_6H_4), 130.9 (s, CH, C6, C_6H_4), 139.9 (s, CH, C3, C_6H_4), 141.6 (s, C1, *C*-CH_2, C_6H_4). FAB$^+$-MS: *m/z* 276 [(M + 1)$^+$].

Synthesis of (*S*)-2-I-C$_8$H$_5$N-CH$_2$CH(CO$_2$Me)NH$_2$ (6). 1,10-Phenanthroline monohydrate (35 mg, 0.177 mmol) was added to a solution of complex **4** (150 mg, 0.173 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was stirred for 4 h. A dark yellow solid precipitated (52.4 mg, 0.163 mmol, 94%), which was filtered out and identified as [$PdCl_2$(phen)] by IR spectroscopy. Solvent was removed, diethyl ether (10 mL) was added to the residue, the resulting suspension was filtered through a plug of Celite, and solvent was removed from the filtrate under vacuum to give compound **6** as a waxy off-white solid. Yield: 115.1 mg, 0.334 mmol, 97%. Anal. Calcd for $C_{12}H_{13}IN_2O_2$ (344.148): C, 41.88; H, 3.81; N, 8.14. Found: C, 42.17; H, 3.89; N, 8.13. ^{1}H NMR (300 MHz): δ 1.72 (s, 2 H, NH2), 2.95 ("dd", 1 H, CH_2, $^2J_{HH}$ = 14.4, $^3J_{HH}$ = 8.4 Hz), 3.24 ("dd", 1 H, CH_2, $^2J_{HH}$ = 14.4, $^3J_{HH}$ = 5.1 Hz), 3.71 (s, 3 H, OMe), 3.90 ("dd", 1 H, CH, $^3J_{HH}$ = 8.4, $^3J_{HH}$ = 5.1 Hz), 7.06 (m, 2 H, H5 + H6, C_8H_5N), 7.18 (m, 1 H, H7, C_8H_5N), 7.52 (m, 1 H, H4, C_8H_5N), 9.17 (s, 1 H, NH). ^{13}C{^{1}H} NMR (75.45 MHz): δ 32.6 (s, CH_2), 52.6 (s, OMe), 55.0 (s, CH), 79.8 (s, C2, C_8H_5N), 110.6 (s, CH, C7, C_8H_5N), 116.8 (s, C3, C_8H_5N), 117.6 (s, CH, C4, C_8H_5N), 119.7 (s, CH, C5, C_8H_5N), 122.2 (s, CH, C6, C_8H_5N), 127.4 (s, C3a, C_8H_5N), 138.8 (s, C7a, C_8H_5N), 175.3 (s, CO). FAB$^+$-MS: *m/z* 345 [(M + 1)$^+$].

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Supporting Information Available: Listing of all refined and calculated atomic coordinates, anisotropic thermal parameters, bond lengths and angles and a CIF file for complex **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

OM0506522

Table 1. Crystal Data and Structure Refinement for Complex 3

formula	$C_{20}H_{28}Cl_2I_2N_2Pd$
fw	727.54
cryst syst	monoclinic
space group	*P*2(1)/*c*
temperature (K)	100(2)
a (Å)	17.4596(7)
b (Å)	10.3359(4)
c (Å)	6.5904(3)
α (deg)	90
β (deg)	93.156(2)
γ (deg)	90
volume (Å^3)	1187.50(9)
Z	2
ρ_{calcd} (Mg m^{-3})	2.035
μ(Mo Kα) (mm^{-1})	3.615
F(000)	696
cryst size (mm)	0.42 × 0.19 × 0.11
θ range (deg)	2.29 to 26.37
no. of reflns coll	12 654
no. of indep reflns	2428
R_{int}	0.0213
max. and min. transmsn	0.6919 and 0.3121
no of data/restraints/params	2428/1/134
goodness-of-fit on F^2	1.157
R1 [$I > 2\sigma(I)$]	0.0252
wR2 (all reflns)	0.0558
largest diff peak and hole (e Å^3)	1.318 and −0.984