N,*N*-Dialkyl-2-iodoanilines: A versatile source for the synthesis of Pd(II) complexes. Synthesis of novel OCP- and CCN-pincer palladium complexes†

Daniel Solé,*[a] Xavier Solans[b] and Mercé Font-Bardia[b]

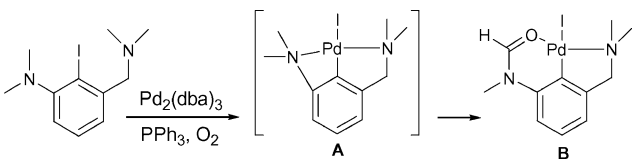
Received 1st June 2007, Accepted 27th July 2007
First published as an Advance Article on the web 15th August 2007
DOI: 10.1039/b708306h

The reactivity of a series of *N*,*N*-dimethyl-2-iodoanilines bearing different chelating "arms" at the 3-position with $Pd_2(dba)_3$ has been explored. 3-[(Diphenylphosphino)methyl]-2-iodo-*N*,*N*-dimethylaniline (**1**) reacted with $Pd_2(dba)_3$ and PPh_3 under aerobic conditions to give the OCP-pincer complex **4**, which was formed by sequential C(sp^3)–H activation/oxidation at the α-position of the aniline N atom. On the other hand, under similar reaction conditions, 3-[2-(dimethylamino)ethyl]-2-iodo-*N*,*N*-dimethylaniline (**2**) afforded the CCN-pincer complex **5**, after a second C–H activation process at the formyl group of the initially formed OCN-pincer complex. In contrast, 2-iodo-3-(1*H*-1,2,4-triazol-1-ylmethyl)-*N*,*N*-dimethylaniline (**3a**) and 2-iodo-3-(pyrazol-1-ylmethyl)-*N*,*N*-dimethylaniline (**3b**) reacted with $Pd_2(dba)_3$ and PPh_3, respectively, to give the 6-membered azapalladacycles **6a** and **6b**, in which the aniline nitrogen is merely a spectator substituent. Finally, treatment of iodide complex **6a** with Tl(TfO) afforded the CN-bidentate cationic complex **8**. Solid-state structures of palladium complexes **4**, **5**, and **8**·CH_2Cl_2·3CH_3OH·5H_2O were determined by X-ray analysis.

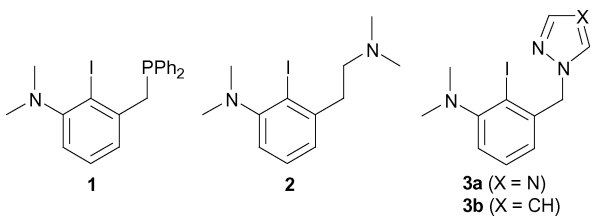
Introduction

Pincer complexes containing tridentate monoanionic ligands (LCL′), which are connected to the metal *via* an anionic aryl carbon atom and two mutually *trans*-chelating donor sites at the 2,6-positions of the aromatic ring, have attracted considerable attention since their first appearance in the late 1970s.[1] The majority of investigations have been carried out with symmetrical pincer-type complexes bearing two equivalent chelate rings (usually five-membered or less commonly six-membered). In contrast, asymmetrical pincer complexes with mixed donor atoms or ring sizes have been scarcely studied.[2]

In the context of our studies about the introduction of four-membered azapalladacycles into tridentate palladium complexes,[3] we have recently reported the synthesis of palladium OCN-pincer complexes (*i.e.*, **B**) derived from *N*,*N*-dialkyl-3-[(dialkylamino)-methyl]-2-iodoanilines by means of an unprecedented oxidation process (Scheme 1).[4] During this work, we realized that the initially formed NCN′-pincer complex **A**, having simultaneously a 4- and a 5-membered chelate ring, would have severe bond angle strain around the metal centre, which could be responsible for the intramolecular alkylamino C–H activation and subsequent aerobic oxidation leading to **B**. Hoping to gain more information about this process, we decided to synthesize some *N*,*N*-dimethyl-2-iodoanilines bearing different chelating "arms" at the 3-position, and study their reaction with $Pd_2(dba)_3$. In this context, in order to evaluate if the different electron-donor properties of the phosphine and the amine ligands could modify the course of the oxidation process, iodoaniline **1** bearing a P donor instead of the N donor has been studied. On the other hand, we considered that it would also be interesting to attempt the synthesis of less strained pincer complexes. To this end, we have focused on the reactions of substrates **2** and **3a**,**b**, which would afford palladium pincer complexes bearing a six-membered metallacycle instead of the five-membered chelate. We report here that the reactivity of the *N*,*N*-dimethyl-2-iodoanilines bearing chelating "arms" at the 3-position with $Pd_2(dba)_3$ is strongly dependent on the nature of the "arm", which obliges the aniline nitrogen atom to act as a spectator substituent or as a participant in metal-centred reactions such as the previously reported C–H activation/oxidation sequence.



Scheme 1 Synthesis of OCN-pincer complexes.



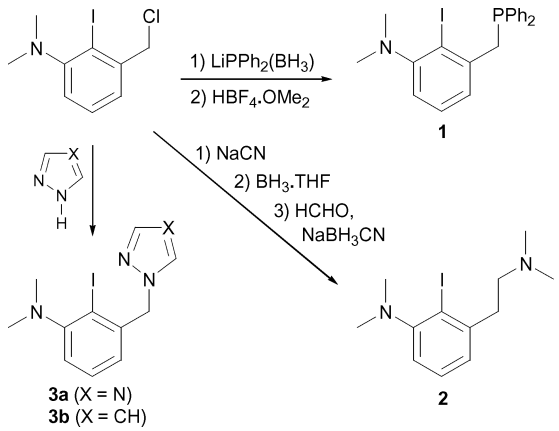
Results

Synthesis of iodoanilines 1, 2, and 3a,b

The new iodoanilines were prepared from 3-(dimethylamino)-2-iodobenzyl chloride (Scheme 2). Phosphine **1** was prepared from

[a]*Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, Av. Joan XXIII s/n, 08028, Barcelona, Spain. E-mail: dsole@ub.edu; Fax: +34 93 402 45 39; Tel: +34 93 402 45 40*
[b]*Departament de Cristal·lografia, Mineralogia i Dipòsits Minerals, Universitat de Barcelona, Martí i Franquès s/n, 08028, Barcelona, Spain*

† CCDC reference numbers 649320–649322. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b708306h

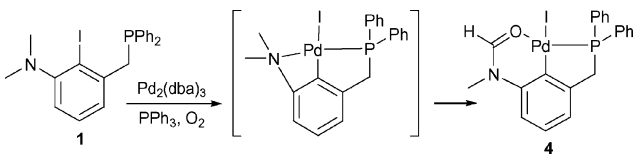


Scheme 2 Synthesis of 2-iodoanilines **1**, **2**, and **3a**,**b**.

the latter following the protocol developed by Zhang *et al.*,[5] which involves a nucleophilic attack with $LiPPh_2(BH_3)$ and subsequent removal of the BH_3 group. On the other hand, iodoaniline **2** was synthesized from the benzyl chloride by a sequence of reactions involving treatment with sodium cyanide, reduction of the nitrile with the BH_3·THF complex, and finally methylation of the resulting primary amine. Finally, reaction of the benzyl chloride with 1,2,4-triazole sodium salt and with pyrazole afforded iodoanilines **3a** and **3b**, respectively.

Synthesis and characterization of palladium complexes

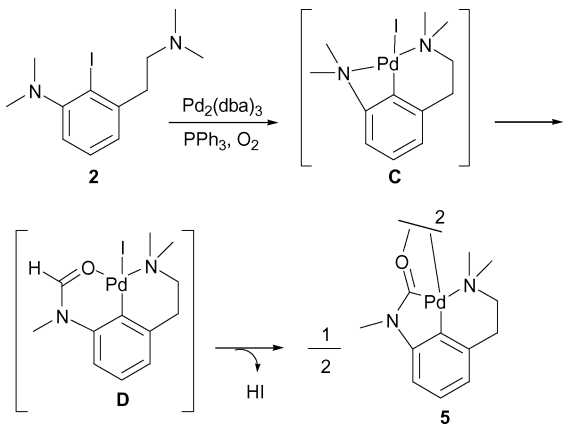
The studies were begun with iodoaniline **1** bearing a P donor connected to the aromatic ring by a methylene unit. Treatment of **1** with $Pd_2(dba)_3$ and PPh_3 (0.6 : 1 molar ratio) in open air afforded OCP-pincer complex **4** (47%), resulting from the sequential $C(sp^3)$–H activation[6] and aerobic oxidation at the α-position of the aniline N atom (Scheme 3).[4]



Scheme 3

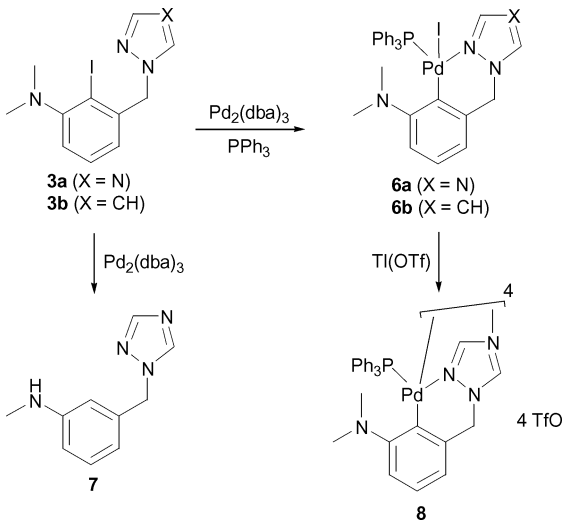
Iodoaniline **2** bearing a dimethylene unit as the connector of the aromatic ring and the amine chelating site behaved very differently from the previously studied systems. We expected that both the flexibility of the aliphatic chain and the increased size of one of the rings would decrease the strain around the palladium atom and allow the [4,6]-NCN′-pincer complex **C** to be isolated. However, all the attempts to prepare this target were unsuccessful. Thus, the reaction of **2** with $Pd_2(dba)_3$ (benzene, rt) under an argon atmosphere resulted in the formation of a complex reaction mixture and the deposition of the Pd metal. On the other hand, under aerobic reaction conditions [$Pd_2(dba)_3$ and PPh_3 (0.6 : 1 molar ratio), benzene, rt, open air] iodoaniline **2** afforded binuclear palladium(II) complex **5** (85% yield) instead of the expected palladium OCN-pincer complex **D** (Scheme 4). The structure of complex **5** was confirmed by X-ray crystallography (Fig. 2).

Finally, we studied iodoanilines **3a**,**b**, bearing a nitrogen heterocycle as the pendant ligand. Under aerobic reaction



Scheme 4

conditions and in the presence of PPh_3 (1 equiv.), iodoaniline **3a** afforded palladium complex **6a**[7] in 31% yield (Scheme 5). When the reaction was carried out under an argon atmosphere a cleaner mixture was obtained and the yield of **6a** increased to 67%. A similar reaction was observed starting from iodoaniline **3b**, which on treatment with $Pd_2(dba)_3$ and PPh_3 (0.6 : 1 molar ratio) under argon afforded palladium complex **6b**[8] in 75% yield. Palladium complexes **6a**,**b** are robust compounds that can be purified by flash chromatography without decomposition and were characterized by elemental analysis and ^1H, ^{13}C, and ^{31}P NMR spectra. It is noteworthy that pincer complexes could not be obtained either from anilines **3a**,**b** or palladium complexes **6a**,**b**. Thus, treatment of **3a** with $Pd_2(dba)_3$ in the absence of PPh_3 under an argon atmosphere afforded aniline **7** (47%), resulting from the hydrodehalogenation and demethylation of the starting material.[4] On the other hand, when palladium complex **6a** was treated with Tl(TfO) to remove the iodo ligand and facilitate the coordination of the dimethylamino group, the vacant coordination site was occupied by the N-4 of a different triazole unit and cationic azapalladacycle **8** was obtained instead (60%).



Scheme 5 Synthesis of palladium complexes **6a**,**b** and **8**.

The molecular structures of complexes **4**, **5**, and **8**·CH_2Cl_2·$3CH_3OH$·$5H_2O$ have been determined by X-ray diffraction studies and are shown in Fig. 1–3, respectively.

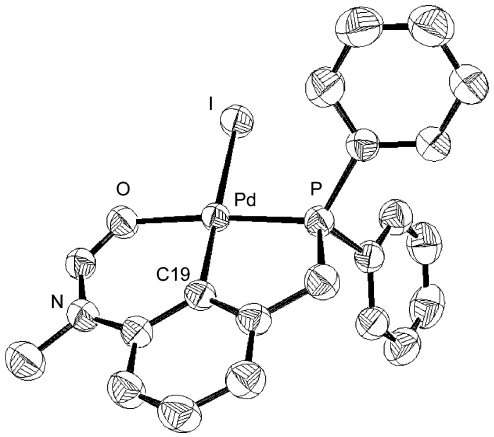


Fig. 1 Thermal ellipsoid representation (50%) of the molecular structure of **4**. Hydrogen atoms are omitted for clarity. Selected distances (Å) and angles (°): Pd–I = 2.6858(10), Pd–P = 2.1908(8), Pd–O = 2.039(2), Pd–C19 = 2.009(3); C19–Pd–O = 91.15(10), C19–Pd–P = 84.96(8), O–Pd–I = 89.71(6), P–Pd–I = 94.19(3).

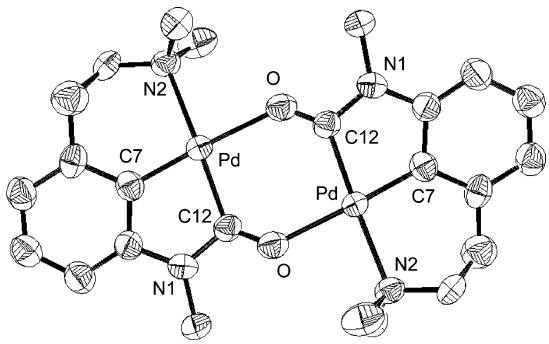


Fig. 2 Thermal ellipsoid representation (50%) of the molecular structure of **5**. Hydrogen atoms are omitted for clarity. Selected distances (Å) and angles (°): Pd–O = 2.171(3), Pd–N = 2.184(4), Pd–C7 = 1.865(5), Pd–C12 = 2.002(4); C7–Pd–C12 = 80.87(19), C12–Pd–O = 96.70(14), C7–Pd–N = 97.14(17), O–Pd–N = 85.41(13).

In OCN-pincer palladium complex **4** the palladium atom shows a square-planar coordination, the largest deviation from the main plane being in the C atom [deviation 0.034(2) Å]. The six-membered [C,O] chelate ring is planar while the five-membered [C,P] chelate ring has an envelope form with the phosphorus being the out-of-plane atom.

Binuclear palladium complex **5** has a crystallographic centre that relates two asymmetric units [κ^3N,C,C-$C_6H_3\{CH_2$-$CH_2NMe_2\}$-2-{N(Me)C(O)}-6] through two acyl bridges. The oxygen atom of the acyl ligand of one palladium centre is bonded to the second palladium atom. This arrangement results in a planar form for the six-membered ring formed by the two palladium atoms and two CO bridges, which leads to a Pd–Pd distance of 3.923(3) Å, significantly greater than those found in related compounds.[9] The six-membered [C,N] chelate ring has a screw-boat form and the five-membered [C,C] chelate ring has an envelope form with the palladium atom being the out-of-plane atom. The palladium atom shows a square-planar coordination, the largest deviation from the main plane being in the C atom [deviation 0.084(4) Å].

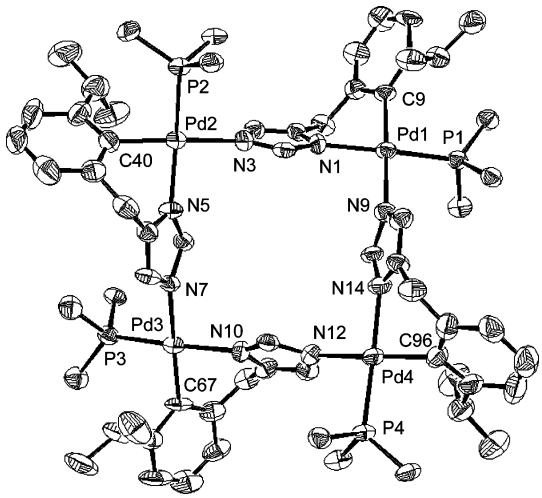


Fig. 3 View of tetrameric cation from crystal structure of **8**·CH_2Cl_2·$3CH_3OH$·$5H_2O$. Hydrogen atoms and the phenyl groups of PPh_3 ligands are omitted for clarity. Selected distances (Å) and angles (°): Pd1–P1 = 2.2678(12), Pd1–N1 = 2.087(3), Pd1–N9 = 2.178(4), Pd1–C9 = 1.995(4), P1–Pd1–N9 = 92.07(11), N1–Pd1–N9 = 92.61(15), N1–Pd1–C9 = 85.82(17), P1–Pd1–C9 = 90.26(13), Pd2–P2 = 2.2671(13), Pd2–N5 = 2.101(4), Pd2–N3 = 2.155(4), Pd2–C40 = 2.019(5), P2–Pd2–N3 = 93.72(11), N3–Pd2–N5 = 92.26(16), N5–Pd2–C40 = 85.61(18), P2–Pd2–C40 = 89.76(14), Pd3–P3 = 2.2749(14), Pd3–N10 = 2.103(4), Pd3–N7 = 2.136(3), Pd3–C67 = 1.985(4), P3–Pd3–N7 = 93.08(10), N7–Pd3–N10 = 91.14(14), N10–Pd3–C67 = 85.64(19), P3–Pd3–C67 = 91.37(16), Pd4–P4 = 2.2836(13), Pd4–N14 = 2.103(4), Pd4–N12 = 2.157(4), Pd4–C96 = 2.011(5), P4–Pd4–N12 = 91.97(12), N12–Pd4–N14 = 93.16(16), N14–Pd4–C96 = 84.76(19), P4–Pd4–C96 = 91.58(15).

The structure of complex **8**·CH_2Cl_2·$3CH_3OH$·$5H_2O$ consists of a tetranuclear cluster of palladium atoms where each 1,2,4-triazole "arm" acts as a bidentate ligand bridging two palladium centres. This arrangement of the tetrameric cation results in a "four-membered ring" with a palladium atom in each vertex, which adopts a CR form and has a pseudo twofold axis. The four trifluoromethanesulfonate ions are non-equivalent by crystallographic symmetry and play different roles in the crystal structure. Thus, while two trifluoromethanesulfonate ions make π-ring interactions with two vicinal triazole rings [distance of S(1)–O(103) to the aromatic centroid of N(5)–N(7) triazole ring = 2.971(6) Å and distance of S(2)–O(203) to the aromatic centroid of N(1)–N(3) triazole ring = 3.025(5) Å] and are hydrogen bonded to the solvate molecules, the other two trifluoromethanesulfonate ions are only hydrogen bonded to the solvates. The palladium atoms show a tetrahedral distorted square-planar coordination, the largest deviation from the main plane being in the C atom of the aromatic ring [deviation of 0.151(4) Å for Pd(1), 0.193(5) Å for Pd(2), 0.179(5) Å for Pd(3), and 0.195(5) Å for Pd(4)]. The six-membered chelate ring has a boat form and the plane of the aromatic ring is twisted out of the coordination plane [58.4(2)° for Pd(1), 59.7(2)° for Pd(2), 58.1(2)° for Pd(3), and 56.8(2)° for Pd(4)].

Discussion

Among the different iodoanilines explored in this work, only the NCP-based system **1** showed a similar behaviour to those

previously studied by us[4] and afforded the expected OCL-pincer complex (**4**). Thus, it becomes clear that the robust coordination of the phosphine "arm" with the palladium atom in the initially formed NCP-pincer complex can not overcome the high strain associated with the simultaneous presence of a 4- and 5-membered chelate ring, which is the origin of the C(sp^3)–H activation/oxidation process leading to **4**.

On the other hand, the formation of palladium complex **5** in the reaction of "long arm" iodoaniline **2** with $Pd_2(dba)_3$ is expected to proceed *via* intramolecular C–H activation of the formyl group[10] in the initially formed OCN-pincer complex **D**. It is worth noting that this activation reaction was not observed either in the OCN-pincer complexes previously reported by us (*i.e.*, **B**) or in the OCP-pincer complex **4**, both bearing a methylene unit as a connector of the aromatic ring and donor group. Although the precise mechanism of this C–H activation has not been established, the different behaviour could be understood taking into account that the longer amine "arm" provides additional reactivity possibilities, since its labile coordination could assist the facile generation of the vacant site required for the C–H activation process in palladium complex **D**.[11] On the other hand, although not incorporated in the final products, PPh_3 has an active role in the oxidation reactions leading to OCP-pincer complex **4** and CCN-pincer complex **5** (Schemes 3 and 4), as we have demonstrated in our reported synthesis of the OCN-pincer complex **B**.[4]

Finally, the different behaviour of anilines **3a**,**b** is probably a consequence of the chelate stability of six-membered metallacycles with coordination of heterocyclic nitrogens being higher than that of the "long arm" aliphatic amine. Moreover, although we failed to obtain single crystals of **6a** and **6b** suitable for X-ray analysis, it is expected that, as in the case of cationic complex **8** and as is usual for this kind of complex,[7a,8a] the six-membered metallacycle adopts a boat conformation, in which the plane of coordination is twisted out of the plane of the benzene ring. For instance, in cationic complex **8** the planes of coordination of the Pd atoms are twisted 56.8(2)–59.7(2)° out of the planes of the arene rings. In complexes **6a**,**b** this twisting, which is much greater than that observed in similar six-membered palladacycles lacking the dimethylamino substituent,[7a,8a] avoids the severe steric interactions with the dimethylamino group and allows the PPh_3 ligand to occupy the fourth coordination site.

It should be noted, however, that in the absence of PPh_3, the C(sp^3)–H activation process at the N-methyl group of **3a** did take place, as evidenced by the isolation of aniline **7** (*vide supra*). We have previously observed the formation of such hydrodehalogenation-dealkylation products in the reactions of *N*,*N*-dialkyl-3-[(dialkylamino)methyl]-2-iodoanilines with $Pd_2(dba)_3$ in the absence of PPh_3, in a process in which the alkyl group is removed as the respective aldehyde.[4]

Experimental

Procedures for the synthesis of the starting iodoanilines

3-(Dimethylamino)-2-iodobenzyl alcohol. A mixture of 3-amino-2-iodobenzyl alcohol[12] (0.85 g, 3.43 mmol), K_2CO_3 (0.97 g, 6.99 mmol), and CH_3I (1.33 mL, 21 mmol) in CH_3CN (15 mL) was stirred at 50 °C in a sealed tube for 24 h. The solvent was evaporated and the residue was partitioned between water and dichloromethane. The organic layer was washed with brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, from hexanes to 8 : 2 hexanes–EtOAc) to give 3-(dimethylamino)-2-iodobenzyl alcohol (0.76 g, 80%). ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.75 (s, 6H), 4.73 (s, 2H), 7.06 (dd, J = 7.8 and 1.8 Hz, 1H), 7.18 (dd, J = 7.8 and 1.8 Hz, 1H), 7.32 (t, J = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 50 MHz): δ 45.3 (CH_3), 70.4 (CH_2), 101.8 (C), 119.9 (CH), 123.8 (CH), 128.9 (CH), 144.4 (C), 155.2 (C). Anal. calc. for $C_9H_{12}INO$: C, 39.01; H, 4.36; N, 5.05%. Found: C, 38.67; H, 4.36; N, 5.00%.

3-(Dimethylamino)-2-iodobenzyl chloride. A solution of 3-(dimethylamino)-2-iodobenzyl alcohol (0.57 g, 2.06 mmol) and triethylamine (1.6 mL, 11.3 mmol) in dichloromethane (15 mL) was cooled to 0 °C under argon, and methanesulfonyl chloride (0.8 mL, 10.3 mmol) was added dropwise. The solution was stirred at room temperature for 3 d. The mixture was poured into saturated aqueous $NaHCO_3$ solution and extracted with dichloromethane. The organic layer was dried and concentrated to give 3-(dimethylamino)-2-iodobenzyl chloride (0.6 g, quantitative), which was used in the next step without purification. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.75 (s, 6H), 4.78 (s, 2H), 7.08 (dd, J = 7.8 and 1.5 Hz, 1H), 7.20 (dd, J = 7.8 and 1.5 Hz, 1H), 7.30 (t, J = 7.8 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 45.1 (CH_3), 52.6 (CH_2), 103.9 (C), 120.6 (CH), 125.3 (CH), 128.9 (CH), 141.4 (C), 155.9 (C).

[3-(Dimethylamino)-2-iodobenzyl]diphenylphosphino-borane. A solution of $HPPh_2(BH_3)$ (220 mg, 1.1 mmol) in THF (3 mL) was cooled to −78 °C, and a 1.6 M solution of n-BuLi in hexane (0.63 mL, 1 mmol) was added dropwise. The resulting solution was brought slowly to room temperature and then added dropwise to a cooled (−20 °C) solution of 3-(dimethylamino)-2-iodobenzyl chloride (270 mg, 0.9 mmol) in THF (3 mL). The reaction was maintained at −20 °C for 20 h and then warmed to room temperature. The mixture was poured into water and extracted with Et_2O. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO_2, from hexanes to 1 : 1 hexanes–EtOAc) to give [3-(dimethylamino)-2-iodobenzyl]diphenylphosphino-borane (334 mg, 81%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.59 (s, 6H), 4.03 (d, J = 11.7 Hz, 2H), 6.98 (dt, J = 7.5 and 1.5 Hz, 1H), 7.11 (dt, J = 7.5 and 1.5 Hz, 1H), 7.21 (t, J = 7.5 Hz, 1H), 7.38–7.72 (m, 10H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 39.5 (d, J = 31.1 Hz, CH_2), 45.0 (s, CH_3), 107.7 (d, J = 5.7 Hz, C), 119.1 (d, J = 2.9 Hz, CH), 126.1 (d, J = 4.0 Hz, CH), 127.7 (d, J = 56.5 Hz, C), 128.3 (d, J = 9.8 Hz, CH), 128.6 (d, J = 4.0 Hz, CH), 131.1 (d, J = 2.3 Hz, CH), 132.8 (d, J = 8.7 Hz, CH), 137.3 (d, J = 4.6 Hz, C), 155.5 (d, J = 2.3 Hz, C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 36.5. HRMS (ESI-TOF): m/z 460.0843 $(M + H)^+$.

3-[(Diphenylphosphino)methyl]-2-iodo-*N*,*N*-dimethylaniline (1). To a solution of [3-(dimethylamino)-2-iodobenzyl]diphenylphosphino-borane (325 mg, 0.7 mmol) in dichloromethane (5 mL) at −5 °C was added $HBF_4{\cdot}OMe_2$ (0.17 mL, 1.4 mmol). The reaction was warmed slowly to room temperature and stirred for 18 h. Dichloromethane (5 mL) was added and the resulting solution was transferred into a degassed saturated aqueous $NaHCO_3$ solution *via* cannula. The resulting mixture was stirred and the organic layer was removed *via* cannula. The $NaHCO_3$ phase was extracted twice

with dichloromethane. The combined organic layers were washed with brine, dried, and concentrated to give [3-(dimethylamino)-2-iodobenzyl]diphenylphosphine (280 mg, 90%), which was used in the next step without purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.69 (s, 6H), 3.68 (s, 2H), 6.51 (dt, J = 7.5 and 1.5 Hz, 1H), 6.85 (dt, J = 7.5 and 1.5 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H), 7.26–7.32 (m, 6H), 7.38–7.50 (m, 6H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 42.6 (d, J = 16.7 Hz, CH_2), 45.3 (s, CH_3), 106.3 (d, J = 5.2 Hz, C), 118.1 (d, J = 2.9 Hz, CH), 125.5 (d, J = 8.0 Hz, CH), 127.9 (d, J = 1.1 Hz, CH), 128.2 (d, J = 6.9 Hz, CH), 128.6 (s, CH), 133.0 (d, J = 18.4 Hz, CH), 137.8 (d, J = 16.1 Hz, C), 142.0 (d, J = 7.5 Hz, C), 155.6 (d, J = 1.7 Hz, C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 5.8. HRMS (ESI-TOF): m/z 446.0529 $(M + H)^+$.

[3-(Dimethylamino)-2-iodophenyl]acetonitrile. A mixture of 3-(dimethylamino)-2-iodobenzyl chloride (425 mg, 1.44 mmol) and NaCN (78 mg) in DMSO was stirred at 80 °C overnight. The mixture was diluted with Et_2O and washed with brine. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO_2, CH_2Cl_2) to give [3-(dimethylamino)-2-iodophenyl]acetonitrile (250 mg, 61%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.75 (s, 6H), 3.90 (s, 2H), 7.08 (dd, J = 7.5 and 1.5 Hz, 1H), 7.26 (dd, J = 7.5 and 1.5 Hz, 1H), 7.34 (t, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 31.6 (CH_2), 45.1 (CH_3), 103.6 (C), 117.5 (C), 120.3 (CH), 124.2 (CH), 129.3 (CH), 135.0 (C), 156.3 (C).

2-[3-(Dimethylamino)-2-iodophenyl]ethylamine. To a solution of [3-(dimethylamino)-2-iodophenyl]acetonitrile (250 mg, 0.87 mmol) in THF (6 mL) at 0 °C was added dropwise a 1 M solution of BH_3·THF in THF (4.37 mL, 4.37 mmol), and was stirred at room temperature for 24 h. The mixture was cooled to 0 °C, and 6 M HCl (0.5 mL) was added. The mixture was then made basic with 1 M NaOH solution and extracted with dichloromethane. The organic layer was washed with water, dried, and then concentrated to give 2-[3-(dimethylamino)-2-iodophenyl]ethylamine (255 mg, quantitative), which was used in the next step without purification. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.73 (s, 8H), 2.98 (s, 2H), 6.98 (m, 2H), 7.21 (t, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 42.1 (CH_2), 45.4 (CH_3), 45.6 (CH_2), 105.4 (C), 118.7 (CH), 125.3 (CH), 128.5 (CH), 144.0 (C), 155.7 (C).

3-[2-(Dimethylamino)ethyl]-2-iodo-*N*,*N*-dimethylaniline (2). To a solution of 2-[3-(dimethylamino)-2-iodophenyl]ethylamine (255 mg, 0.87 mmol) in acetonitrile (5 mL) were added a 37% aqueous solution of formaldehyde (1.43 mL), $NaBH_3CN$ (273 mg, 4.35 mmol), and acetic acid (0.22 mL, 3.92 mmol). The mixture was stirred at room temperature for 2 h, then acetic acid (0.22 mL, 3.92 mmol) was added, and the stirring was maintained for 30 min. The reaction mixture was diluted with dichloromethane and water, and was made basic with 2 M NaOH. The organic layer was concentrated; the residue was dissolved in a mixture of MeOH (5 mL) and 2 M NaOH (5 mL), and was refluxed overnight. The solvent was removed *in vacuo*, the residue was dissolved in dichloromethane and washed with water. The organic layer was dried and concentrated. The residue was purified by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 10%) to give amine **2** (165 mg, 60%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.37 (s, 6H), 2.55 (m, 2H), 2.73 (s, 6H), 3.03 (m, 2H), 6.95 (dd, J = 7.5 and 1.5 Hz, 1H), 6.99 (dd, J = 7.5 and 1.5 Hz, 1H), 7.22 (t, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 40.2 (CH_2), 45.3 (CH_3), 45.4 (CH_3), 59.8 (CH_2), 105.3 (C), 118.4 (CH), 125.0 (CH), 128.5 (CH), 144.9 (C), 155.6 (C). Anal. calc. for $C_{12}H_{19}IN_2$: C, 45.30; H, 6.02; N, 8.80%. Found: C, 45.37; H, 5.94; N, 8.68%.

2-Iodo-3-(1*H*-1,2,4-triazol-1-ylmethyl)-*N*,*N*-dimethylaniline (3a). To a solution of 3-(dimethylamino)-2-iodobenzyl chloride (180 mg, 0.61 mmol) in acetonitrile (10 mL) was added 1,2,4-triazole sodium salt (124 mg, 1.36 mmol). The mixture was stirred at 50 °C for 5 h. The solvent was evaporated and the residue was partitioned between saturated aqueous $NaHCO_3$ solution and dichloromethane. The organic layer was washed with brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 1%) to give triazole **3a** (138 mg, 69%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.74 (s, 6H), 5.49 (s, 2H), 6.76 (dd, J = 7.8 and 1.5 Hz, 1H), 7.09 (dd, J = 8.1 and 1.5 Hz, 1H), 7.28 (dd, J = 8.1 and 7.8 Hz, 1H), 7.99 (s, 1H), 8.18 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 45.2 (CH_3), 59.3 (CH_2), 103.2 (C), 120.8 (CH), 124.7 (CH), 129.2 (CH), 138.9 (C), 143.7 (CH), 152.0 (CH), 156.1 (C). Anal. calc. for $C_{11}H_{13}IN_4$: C, 40.26; H, 3.99; N, 17.07%. Found: C, 40.33; H, 3.86; N, 16.93%.

2-Iodo-3-(pyrazol-1-ylmethyl)-*N*,*N*-dimethylaniline (3b). A mixture of 3-(dimethylamino)-2-iodobenzyl chloride (250 mg, 0.86 mmol), pyrazole (88 mg, 1.3 mmol), and NaI (142 mg, 0.95 mmol) in acetone (10 mL) was stirred at reflux for 5 h. The solvent was evaporated and the residue was partitioned between saturated aqueous $NaHCO_3$ solution and dichloromethane. The organic layer was washed with brine, dried, and concentrated. The residue was purified by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 1%) to give pyrazole **3b** (190 mg, 68%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.74 (s, 6H), 5.45 (s, 2H), 6.31 (t, J = 2.1 Hz, 1H), 6.47 (dm, J = 7.5 Hz, 1H), 7.04 (dd, J = 7.8 and 1.5 Hz, 1H), 7.21 (dd, J = 7.8 and 7.5 Hz, 1H), 7.48 (dd, J = 2.1 and 0.6 Hz, 1H), 7.59 (dd, J = 2.1 and 0.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 45.2 (CH_3), 61.6 (CH_2), 102.3 (C), 105.8 (CH), 120.1 (CH), 123.8 (CH), 129.0 (CH), 129.9 (CH), 139.6 (CH), 141.1 (C), 155.6 (C). Anal. calc. for $C_{12}H_{14}IN_3$: C, 44.05; H, 4.31; N, 12.84%. Found: C, 43.71; H, 4.47; N, 12.39%.

Synthesis of palladium complexes

[OCP]PdI complex 4. To a solution of iodoaniline **1** (25 mg, 0.056 mmol) in dry benzene (5 mL) were added PPh_3 (15 mg, 0.056 mmol) and $Pd_2(dba)_3$ (31 mg, 0.034 mmol). The solution was stirred at room temperature under an open atmosphere for 22 h. The reaction mixture was filtered through Celite, washing carefully with benzene. The filtrate was evaporated to dryness to give a residue that was purified by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 4%) to give **4** as a brown solid. Yield: 15 mg, 47%. Single crystals of complex **4** were grown by slowly evaporating a dichloromethane solution. Mp: 210–213 °C. ν_{max}/cm^{-1} (KBr) 1628 (CO). ^{1}H NMR (CD_2Cl_2, 300 MHz): δ 3.52 (s, 3H), 3.94 (d, J = 12.6 Hz, 2H), 7.02 (m, 1H), 7.12–7.20 (m, 2H); 7.32–7.46 (m, 6H), 7.73–7.82 (m, 4H), 8.24 (d, J = 12 Hz, 1H). ^{13}C NMR (CD_2Cl_2, 75.4 MHz): δ 39.2 (CH_3), 46.0 (d, J = 35.7 Hz, CH_2), 113.8 (CH), 122.2 (d, J = 23.1 Hz, CH), 126.5 (CH), 128.7 (d, J = 11.5 Hz, CH), 131.4 (d, J = 2.9 Hz, CH), 131.4 (d, J = 54.7 Hz, C), 133.5 (d, J = 10.9 Hz, CH), 136.9 (C), 148.7 (d,

J = 15.5 Hz, C), 159.6 (CH). One C was not observed. ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 56.7. Anal. calc. for $C_{21}H_{19}INOPPd$: C, 44.59; H, 3.39; N, 2.48%. Found: C, 44.45; H, 3.54; N, 2.36%.

[CCN]-Palladium pincer complex 5. To a solution of iodoaniline **2** (20 mg, 0.063 mmol) in dry benzene (5 mL) were added PPh_3 (16 mg, 0.06 mmol) and $Pd_2(dba)_3$ (35 mg, 0.038 mmol). The solution was stirred at room temperature under an open atmosphere for 24 h. The solvent was removed *in vacuo* and the residue was triturated with diethyl ether. The mixture was filtered through Celite, washing carefully with diethyl ether. The ether filtrate was discarded, and then the washing was continued with dichloromethane. The dichloromethane filtrate was evaporated to dryness to give a residue that was purified by chromatography (SiO_2, CH_2Cl_2) to give **5** as a yellow solid. Yield: 17 mg, 85%. Single crystals of complex **5** were grown by slowly evaporating a dichloromethane–diethyl ether solution. Mp: 146 °C (decomp.). ν_{max}/cm^{-1} (KBr) 1543 (CO). ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.67 (s, 6H), 2.72 (dd, J = 5.7 and 5.4 Hz, 2H), 2.95 (dd, J = 5.7 and 5.4 Hz, 2H), 3.03 (s, 3H), 6.49 (dd, J = 7.5 and 1 Hz, 1H), 6.54 (d, J = 7.5 Hz, 1H), 6.97 (t, J = 7.5 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 26.9 (CH_3), 33.9 (CH_2), 47.9 (CH_3), 63.2 (CH_2), 106.8 (CH), 120.1 (CH), 124.6 (CH), 141.9 (C), 153.4 (C), 207.7 (C). One C was not observed. Anal. calc. for $C_{24}H_{32}N_4O_2Pd_2$: C, 46.39; H, 5.19; N, 9.02%. Found: C, 46.34; H, 5.19; N, 8.88%.

Azapalladacycle 6a. To a solution of iodoaniline **3a** (21 mg, 0.064 mmol) in dry benzene (5 mL) were added PPh_3 (17 mg, 0.064 mmol) and $Pd_2(dba)_3$ (35 mg, 0.038 mmol). The solution was stirred at room temperature under an argon atmosphere for 20 h. The reaction mixture was filtered through Celite, washing carefully with benzene. The filtrate was evaporated to dryness to give a residue that was purified by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 1%) to give **6a** as a white solid. Yield: 30 mg, 67%. ^{1}H NMR ($CDCl_3$, 200 MHz): δ 2.66 (s, 6H), 5.22 (d, J = 13.4 Hz, 1H), 5.88 (d, J = 13.4 Hz, 1H), 6.12 (broad d, J = 7.8 Hz, 1H), 6.73 (d, J = 7.8 Hz, 1H), 6.81 (t, J = 7.8 Hz, 1H), 7.16–7.52 (m, 15H), 8.28 (s, 1H), 8.66 (s, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 46.9 (broad, CH_3), 57.8 (CH_2), 118.5 (CH), 120.2 (CH), 125.1 (CH), 127.4 (d, J = 10.9 Hz, CH), 129.8 (d, J = 2.3 Hz, CH), 132.6 (d, J = 52.4 Hz, C), 134.5 (d, J = 10.9 Hz, CH), 135.8 (C), 143.0 (CH), 151.3 (d, J = 5.7 Hz, C), 155.8 (CH), 157.3 (d, J = 4.6 Hz, C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 32.8. Anal. calc. for $C_{29}H_{28}IN_4PPd$: C, 49.98; H, 4.05; N, 8.04%. Found: C, 50.19; H, 4.08; N, 7.63%.

Azapalladacycle 6b. Using the same procedure as for the synthesis of **6a** and starting from iodoaniline **3b** (25 mg, 0.076 mmol), palladium complex **6b** was obtained as a white solid after purification by chromatography (SiO_2, from hexane to hexane–EtOAc 40%). Yield: 40 mg, 75%. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.66 (broad s, 6H), 5.03 (d, J = 13.6 Hz, 1H), 5.93 (d, J = 13.6 Hz, 1H), 6.06 (dt, J = 7.6 and 1.6 Hz, 1H), 6.24 (m, 1H), 6.70 (dd, J = 7.6 and 1.2 Hz, 1H), 6.77 (t, J = 7.6 Hz, 1H), 7.15–7.35 (m, 9H), 7.45 (broad, 6H), 7.56 (d, J = 2.4 Hz. 1H), 8.25 (d, J = 1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75.4 MHz): δ 46.6 (broad, CH_3), 60.5 (CH_2), 106.3 (d, J = 3.5 Hz, CH), 117.9 (CH), 119.8 (CH), 124.6 (CH), 127.3 (d, J = 10.3 Hz, CH), 129.6 (CH), 130.5 (CH), 133.0 (d, J = 51.8 Hz, C), 134.5 (d, J = 10.3 Hz, CH), 137.3 (C), 144.6 (CH), 151.6 (d, J = 5.2 Hz, C), 157.1 (d, J = 4.6 Hz, C). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 31.7. Anal. calc. for $C_{30}H_{29}IN_3PPd$·EtOAc: C, 52.13; H, 4.76; N, 5.36%. Found: C, 52.59; H, 4.72; N, 5.57%.

1-[3-(Methylamino)benzyl]-1,2,4-triazole (7). Using the same procedure as for the synthesis of **6a**, but without the addition of PPh_3, aniline **7** was obtained as an oil after purification by chromatography (SiO_2, from CH_2Cl_2 to CH_2Cl_2–MeOH 10%). Yield: 7 mg, 47%. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.81 (s, 3H), 3.80 (broad, 1H), 5.26 (s, 2H), 6.46 (broad s, 1H), 6.55–6.61 (m, 2H), 7.18 (t, J = 7.8 Hz, 1H), 7.96 (s, 1H), 8.04 (s, 1H). HRMS (ESI-TOF): m/z 189.1126 $(M + H)^+$.

Azapalladacycle 8. To a solution of palladium complex **6a** (34 mg, 0.049 mmol) in dry THF (10 mL) was added Tl(TfO) (19 mg, 0.054 mmol). The mixture was stirred at room temperature

Table 1 Selected crystallographic data for complexes **4**, **5**, and **8**·CH_2Cl_2·3CH_3OH·5H_2O

	4	**5**	**8**·CH_2Cl_2·3CH_3OH·5H_2O
Formula	$C_{21}H_{19}INOPPd$	$C_{24}H_{32}N_4O_2Pd_2$	$C_{124}H_{136}Cl_2F_{12}N_{16}O_{20}P_4Pd_4S_4$
M_r	565.64	621.34	3147.22
Crystal system	Monoclinic	Orthorhombic	Triclinic
Space group	$P2_1/c$	$Pbca$	$P\bar{1}$
a/Å	10.477(4)	7.688(5)	14.493(4)
b/Å	10.940(3)	11.928(7)	14.905(2)
c/Å	18.559(3)	25.540(8)	33.266(7)
α/°	90	90	90.80(2)
β/°	106.32(2)	90	96.83(2)
γ/°	90	90	91.37(2)
V/Å^3	2041.5(10)	2342(2)	7132(3)
Z	4	4	2
D_c/Mg m^{-3}	1.840	1.762	1.464
F(000)	1096	1248	3198
Crystal size/mm	0.2 × 0.1 × 0.1	0.2 × 0.1 × 0.1	0.21 × 0.15 × 0.1
θ range/°	3.46–30.00	3.09–28.51	2.58–32.34
Reflections collected	19826	1741	72516
Independent reflections (R_{int})	5467 (0.0324)	1741 (0.0570)	37777 (0.0437)
$R1$ [$I>2\sigma(I)$]	0.0338	0.0539	0.0777
$wR2$ [$I>2\sigma(I)$]	0.0882	0.1261	0.2372
Goodness-of-fit on F^2	1.239	1.219	1.028

for 24 h. A pale yellow precipitate formed that was collected by filtration and then triturated with MeOH. The resulting solid was filtered off and dried to give **8** as a yellow solid. Yield: 21 mg, 60%. Single crystals of complex **8** were grown by slowly evaporating a dichloromethane–diethyl ether–MeOH solution under an open atmosphere. Mp: decomposition of the crystal when heating. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.45 (broad, 6H), 5.21 (d, $J = 14.4$ Hz, 1H), 6.15 (d, $J = 14.4$ Hz, 1H), 6.17 (d, $J = 6$ Hz, 1H), 6.89 (d, $J =$ 7.2 Hz, 1H), 6.95–7.10 (m, 10H), 7.26–7.32 (m, 6H), 7.76 (s, 1H), 8.41 (s, 1H). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 41.0 (broad, CH_3), 58.8 (CH_2), 119.2 (CH), 122.8 (CH), 125.3 (CH), 128.7 (d, $J =$ 10.1 Hz, CH), 128.9 (d, $J = 55.0$ Hz, C), 131.0 (CH), 132.8 (d, $J =$ 10.9 Hz, CH), 136.3 (C), 140.6 (C), 144.5 (CH), 150.7 (C), 157.4 (CH). ^{31}P NMR ($CDCl_3$, 121.5 MHz): δ 28.6. HRMS (ESI-TOF): m/z 569.1090 $(M)^+$.

X-Ray crystallography

Intensities for complexes **4**, **5**, and **8**·CH_2Cl_2·$3CH_3OH$·$5H_2O$ were collected with a MAR345 diffractometer. The structures were solved by direct methods, using the SHELXS97 computer program. All the structures were refined by full-matrix least-squares methods with the SHELXL97 computer program.[13] A summary of the crystallographic data and refinement parameters for **4**, **5**, and **8**·CH_2Cl_2·$3CH_3OH$·$5H_2O$ is given in Table 1. ORTEP[14] plots for complexes **4**, **5**, and the cation of **8** are shown in Fig. 1–3, respectively.

Conclusions

The *N*,*N*-dimethyl-2-iodoanilines with chelating "arms" at the 3-position have proved to be a versatile source of Pd(II) complexes when reacting with $Pd_2(dba)_3$. The nature of the complex obtained strongly depends on the type of chelating "arm". Thus, from iodoanilines bearing $-CH_2PR_2$ and $-CH_2NR_2$ units, [OCL]PdI complexes (L = P, N respectively) were obtained by means of a sequential C(sp^3)–H activation/oxidation process at the α-position of the aniline N atom. On the other hand, the iodoaniline with the long "arm" $-CH_2CH_2NR_2$ afforded a [CCN]Pd complex, resulting from a multistep process in which a new C–H activation reaction takes place after the initial C(sp^3)–H activation/oxidation sequence. Finally, the iodoanilines based on triazole and pyrazole "arms" afforded simple 6-membered azapalladacycles in which the aniline N is merely a spectator. From the results obtained in this work and in previous studies we can conclude that the four-membered cyclopalladated framework cannot fit into stable [NCL]PdI pincer complexes. Further investigation will be conducted to establish the mechanisms of the activation/oxidation sequences observed.

Acknowledgements

This work was supported by MEC (Spain)-FEDER (Project CTQ2004-04701/BQU) and DURSI-Catalonia (Grant 2005SGR-00442). D. S. thanks the DURSI for "Distinció per a la Promoció de la Recerca Universitària".

Notes and references

1 M. Albrecht and G. van Koten, *Angew. Chem., Int. Ed.*, 2001, **40**, 3751–3781; J. T. Singleton, *Tetrahedron*, 2003, **59**, 1837–1857; J. Dupont, C. S. Consorti and J. Spencer, *Chem. Rev.*, 2005, **105**, 2527–2572.
2 See, for example: B. Rybtchinski, S. Oevers, M. Montag, A. Vigalok, H. Rozenberg, J. M. L. Martin and D. Milstein, *J. Am. Chem. Soc.*, 2001, **123**, 9064–9077; E. Poverenov, M. Gandelman, L. J. W. Shimon, H. Rozenberg, Y. Ben-David and D. Milstein, *Chem.–Eur. J.*, 2004, **10**, 4673–4684; E. Poverenov, M. Gandelman, L. J. W. Shimon, H. Rozenberg, Y. Ben-David and D. Milstein, *Organometallics*, 2005, **24**, 1082–1090; E. Poverenov, G. Leitus, L. J. W. Shimon and D. Milstein, *Organometallics*, 2005, **24**, 5937–5944; J. Fischer, M. Schürmann, M. Mehring, U. Zachwieja and K. Jurkschat, *Organometallics*, 2006, **25**, 2886–2893 and references therein.
3 D. Solé, S. Díaz, X. Solans and M. Font-Bardia, *Organometallics*, 2006, **25**, 1995–2001.
4 D. Solé, L. Vallverdú, X. Solans and M. Font-Bardia, *Chem. Commun.*, 2005, 2738–2740.
5 J. M. Longmire, X. Zhang and M. Shang, *Organometallics*, 1998, **17**, 4374–4379.
6 For a related C–H activation process, see: J. A. M. Brandts, E. Kruiswijk, J. Boersma, A. L. Spek and G. van Koten, *J. Organomet. Chem.*, 1999, **585**, 93–99.
7 For 1,2,4-triazole-based pincer complexes, see: (*a*) E. Díez-Barra, J. Guerra, I. López-Solera, S. Merino, J. Rodríguez-López, P. Sánchez-Verdú and J. Tejeda, *Organometallics*, 2003, **22**, 541–547; (*b*) E. Díez-Barra, J. Guerra, V. Hornillos, S. Merino and J. Tejeda, *Organometallics*, 2003, **22**, 4610–4612.
8 For pyrazole-based pincer complexes, see: (*a*) C. M. Hartshorn and P. J. Steel, *Organometallics*, 1998, **17**, 3487–3496; (*b*) H. P. Dijkstra, M. D. Meijer, J. Patel, R. Kreiter, G. P. M. van Klink, M. Lutz, A. L. Spek, A. J. Canty and G. van Koten, *Organometallics*, 2001, **20**, 3159–3168; (*c*) F. Churruca, R. SanMartín, I. Tellitu and E. Domínguez, *Synlett*, 2005, 3116–3120.
9 J. Dupont, M. Pfeffer, J. C. Daran and Y. Jeannin, *Organometallics*, 1987, **6**, 899–901 and references therein.
10 K. Hosoi, K. Nozaki and T. Hiyama, *Org. Lett.*, 2002, **4**, 2849–2851.
11 The C–H activation reaction probably involves the formation of an organopalladium(IV) complex intermediate. A. J. Canty, *Acc. Chem. Res.*, 1992, **25**, 83–90.
12 K. Koerber-Plé and G. Massiot, *Synlett*, 1994, 759–760.
13 G. M. Sheldrick, *SHELXS97 and SHELXL97*, University of Göttingen, Göttingen, Germany, 1997.
14 ORTEP drawings were generated by ORTEP-3 1.074.L. J. Farrugia, *J. Appl. Crystallogr.*, 1997, **30**, 565.

