# *N*-substituted aminobiphenyl palladacycles stabilized by dialkylterphenyl phosphanes: preparation and applications in C-N cross-coupling reactions†

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**Abstract**

Neutral and cationic *N*-methyl- and *N*-phenyl-2-aminobiphenyl methanesulfonate palladacycles stabilized with dialkylterphenyl phosphanes has been prepared and characterized. Neutral structures are favored with the less bulky phosphane $PMe_2Ar^{Xyl2}$, **L1**, while more sterically demanding ligands $PiPr_2Ar^{Xyl2}$, **L3**, and $PCyp_2Ar^{Xyl2}$ (Cyp = cyclopentyl), **L4**, lead to cationic complexes in which the phosphane exhibits a bidentate $\kappa^1$-P, $\eta$-$C_{arene}$ coordination mode involving one of the *ipso* carbon atoms of a flanking terphenyl aryl ring. The complexes were evaluated for activity in C-N cross-coupling reactions and [Pd(*N*-methyl-2-aminobiphenyl)**L4**](OMs) (OMs = mesylate) was identified as the most efficient precatalyst, facilitating the coupling of aryl chlorides with secondary and primary amines and indoles.

**Keywords**

Cross-coupling, aryl amination, palladium catalysis, phosphane ligands, palladacycles

† Dedicated to Prof. Maurizio Peruzzini on the occasion of his 65th birthday.

## 1. Introduction

In modern synthetic chemistry, Pd-catalyzed cross-coupling methodologies are indispensable tools for building molecular complexity.[1] A range of specialized tertiary phosphanes[2] and, to a lesser degree, N-heterocyclic carbenes[3] have emerged as privileged ligand platforms to generate highly active palladium catalysts. Although structurally different, these ligands share the ability of stabilizing monoligated palladium(0) species LPd(0), which is proposed to be the true catalytically active species in most cross-coupling reactions.[4] Inefficient production of such LPd(0) intermediates under catalytic conditions result of a decrease in the activity and the selectivity of the catalyst system.[5] Despite the operational simplicity of in situ catalyst generation, i.e. by mixing the ligand of choice in excess with the appropriate palladium precursor, problems associated with formation of Pd(0) species with different composition and reactivity[6] make this procedure less appealing. Accordingly, the use of well-defined Pd precatalysts with the optimal palladium to ligand ratio (1:1) has proved to be a more convenient and cost-effective approach for the generation of the desired active monoligated LPd(0).[7] In recent years, several types of highly efficient Pd(II) precatalysts have been developed (Figure 1).[7b,7c]

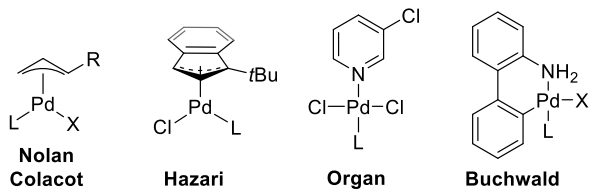
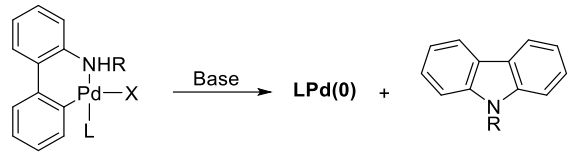



**Fig. 1.** Examples of outstanding Pd(II) coupling precatalysts.

Of these, stands out the family of 2-aminobiphenyl N,C-palladacycles introduced by Buchwald,[8] which has been applied to a wide variety of C-C and C-heteroatom cross-coupling reactions.[8d,9] The remarkable catalytic activity of these palladacycle precatalysts rely on facile activation, in the presence of base, to yield the desired monoligated palladium(0) species.[10] However, the activation reaction also produced catalytic amount of carbazole as by-product (Scheme 1). This NH-heterocycle is also susceptible of being arylated under reaction conditions, complicating product purification and diminishing the yield.[11] Moreover, it has been observed that carbazole can hinder catalyst performance due to coordination, as carbazolyl ligand, to in-cycle Pd(II) intermediates.[11] To address these shortcomings, palladacycle precatalysts with *N*-substituted 2-aminobiphenyl ligands have been described.[12] Their activation render the

formation of *N*-substituted carbazoles by-products that are unreactive towards further functionalization by cross-coupling. In addition, the absence of the NH-functionality in these molecules limits their coordination capabilities.




**Scheme 1.** Pathway for the activation of 2-aminobiphenyl palladacycles.

Very recently, we have reported on the preparation of 2-aminobiphenyl palladacycles supported by a variety of dialkylterphenyl phosphane ligands developed in our research group,[13] and demonstrated their competence as precatalysts in a variety of C-N cross-coupling reactions.[14] This work extends these studies to *N*-substituted 2-aminobiphenyl palladacycle analogues. Herein, we described the synthesis and the structural characterization of a series of *N*-methyl- and *N*-phenyl-substituted 2-aminobiphenyl palladacycle bearing terphenyl phosphanes. The catalytic activity of these precatalysts in the arylation of a range of *N*-nucleophiles including primary and secondary amines and indoles is also presented.

## 2. Experimental section

### *2.1. General considerations*

All preparations and manipulations were carried out under oxygen-free nitrogen, using conventional Schlenk techniques. Solvents were rigorously dried and degassed before use. Terphenyl phosphanes **L1**-**L4**,[13a,13b] and [Pd(*N*-R-2-aminobiphenyl)(μ-OMs)]$_2$ (R = Me, Ph)[12] were synthesized by following previously reported procedures. Reagents were purchased from commercial suppliers and used without further purification. Solvents were dried and degassed before use. Solution NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer. The $^{1}$H and $^{13}$C resonances of the solvent were used as the internal standard and the chemical shifts are reported relative to TMS while $^{31}$P was referenced to external $H_3PO_4$. Elemental analyses were performed by the Servicio de Microanálisis of Instituto de Investigaciones Químicas (IIQ). High resolution mass spectra were registered on Orbitrap Elite Mass Spectrometer at the Centro de Investigación Tecnología e Innovación, CITIUS (Universidad de Sevilla). X-ray diffraction studies were accomplished at CITIUS and Instituto de Investigaciones Químicas (IIQ).

*2.2. Synthesis of representative palladacycles*

***Pd(N-methyl-2-aminobiphenyl)(PMe$_2$Ar$^{Xyl2}$)(OMs),* 1·L1**.

$CH_2Cl_2$ (5 mL) was added to a mixture of [Pd(*N*-methyl-2-aminobiphenyl)(μ-OMs)]$_2$ (77.1 mg, 0.10 mmol) and $PMe_2Ar^{Xyl2}$ (69.1 mg, 0.20 mmol). The reaction mixture was stirred 2 h at room temperature. After filtration through a Celite plug, the solution was taken to dryness. The crude reaction product was purified by recrystallization from petroleum ether: $CH_2Cl_2$ (8:1) mixtures at 5 °C, rendering the title compound as yellow crystals. Yield: 98.7 mg (67%). $^1$H NMR (300 MHz, $CDCl_3$, 25 ºC): δ 7.59 (t, 1H, $J_{HH}$ = 7.1, C*H*$_{ar}$), 7.39-7.37 (m, 1H, C*H*$_{ar}$), 7.32-7.09 (m, 13H, C*H*$_{ar}$ and N*H*), 7.01 (t, 1H, $J_{HH}$ = 7.3 Hz, C*H*$_{ar}$), 6.73 (t, 1H, $J_{HH}$ = 7.3 Hz, C*H*$_{ar}$), 6.14 (t, 1H, $J_{HH}$ = 6.7 Hz, C*H*$_{ar}$), 2.58 (s, 3H, OMs), 2.40 (dd, 3H, $J_{HH}$ = 5.1 Hz, $J_{HP}$ = 2.7 Hz, C*H*$_3$N), 2.23 (s, 6H, C*H*$_3$), 2.17 (s, 6H, C*H*$_3$), 1.15 (d, 3H, $J_{HP}$ = 10.3 Hz, C*H*$_3$P), 0.73 (d, 3H, $J_{HP}$ = 10.0 Hz, C*H*$_3$P). $^{13}$C{$^1$H} NMR (75 MHz, $CDCl_3$, 25 ºC): δ 147.3 (d, $J_{CP}$ = 10 Hz, *C*$_q$), 144.3 (d, $J_{CP}$ = 3 Hz, *C*$_q$), 142.2 (d, $J_{CP}$ = 3 Hz, *C*$_q$), 141.0 (d, $J_{CP}$ = 4 Hz, *C*$_q$), 140.6 (*C*$_q$), 138.4 (*C*$_q$), 138.2 (*C*H$_{ar}$), 138.2 (*C*H$_{ar}$), 136.9 (*C*$_q$), 136.4 (*C*$_q$), 131.3 (*C*H$_{ar}$), 131.2 (*C*H$_{ar}$), 128.6 (*C*H$_{ar}$), 128.5 (*C*H$_{ar}$), 128.3 (*C*H$_{ar}$), 128.1 (*C*H$_{ar}$), 128.0 (*C*H$_{ar}$), 126.6 (*C*H$_{ar}$), 125.2 (*C*H$_{ar}$), 122.2 (*C*H$_{ar}$), 40.3 (*C*H$_3$N), 39.7 (OMs), 22.0 (*C*H$_3$), 22.0 (*C*H$_3$), 16.4 (d, $J_{CP}$ = 33 Hz, *C*H$_3$P), 15.1 (d, $J_{CP}$ = 29 Hz, *C*H$_3$P). $^{31}$P{$^1$H} NMR (121 MHz, $CDCl_3$, 25 ºC): δ 1.9. Anal. Calc. for $C_{38}H_{42}NO_3PPdS$·½ $CH_2Cl_2$: C, 59.85; H, 5.61; N, 1.81; S, 4.15. Found: C, 59.90; H, 5.89; N, 1.68; S, 4.20. ESI-MS (Orbitrap): *m/z* calculated for $C_{37}H_{39}NPPd^+$ [M – ($CH_3O_3S$)]$^+$ 634.1849. Found 634.1854.

***Pd(N-phenyl-2-aminobiphenyl)(PMe$_2$Ar$^{Xyl2}$)(OMs),* 2·L1**.

$CH_2Cl_2$ (5 mL) was added to a mixture of [Pd(*N*-phenyl-2-aminobiphenyl)(μ-OMs)]$_2$ (89.2 mg, 0.10 mmol) and $PMe_2Ar^{Xyl2}$ (69.1 mg, 0.20 mmol). The reaction mixture was stirred 2 h at room temperature. After filtration through a Celite plug, the solvent was evaporated under reduced pressure and the crude reaction product was purified by recrystallization from petroleum ether: $CH_2Cl_2$ (3:1) mixtures at 5 °C. Yield: 118.5 mg (76%). $^1$H NMR (300 MHz, $CDCl_3$, 25 ºC): δ 9.90 (d, 1H, $J_{HP}$ = 6.0 Hz, N*H*), 7.57 (td, 1H, $J_{HH}$ = 7.6, $J_{HP}$ = 2 Hz, C*H*$_{ar}$), 7.50 (dd, 1H, $J_{HH}$ = 7.4 Hz, $J_{HP}$ = 1.9 Hz, C*H*$_{ar}$), 7.37-7.27 (m, 2H, C*H*$_{ar}$), 7.24-7.17 (m, 4H, C*H*$_{ar}$), 7.11-7.00 (m, 8H, C*H*$_{ar}$), 6.95 (t, 2H, $J_{HH}$ = 7.3 Hz, C*H*$_{ar}$), 6.77 (d, 2H, $J_{HH}$ = 7.9 Hz, C*H*$_{ar}$), 6.55 (td, 1H, $J_{HH}$ = 7.5 Hz, $J_{HP}$ = 1.6 Hz, C*H*$_{ar}$), 5.95 (t, 1H, $J_{HH}$ = 6.9 Hz, C*H*$_{ar}$), 2.64 (s, 3H, OMs), 2.09 (s, 12H, C*H*$_3$), 1.29 (d, 3H, $J_{HP}$ = 10.8 Hz, C*H*$_3$P), 0.61 (d, 3H, $J_{HP}$ = 10.2 Hz, C*H*$_3$P). $^{13}$C{$^1$H} NMR (75

MHz, $CDCl_3$, 25 ºC): δ 147.5 (d, $J_{CP}$ = 10 Hz, $C_q$), 145.5 (d, $J_{CP}$ = 2 Hz, $C_q$), 143.6 (d, $J_{CP}$ = 3 Hz, $C_q$), 143.0 ($C_q$), 141.0 (d, $J_{CP}$ = 4 Hz, $C_q$), 138.7 ($C_q$), 138.4 (d, $J_{CP}$ = 3 Hz, $C_q$), 137.9 (d, $J_{CP}$ = 13 Hz, $CH_{ar}$), 136.8 ($C_q$), 136.5 ($C_q$), 131.4 ($CH_{ar}$), 131.3 ($CH_{ar}$), 131.2 (d, $J_{CP}$ = 2 Hz, $CH_{ar}$), 128.7 ($CH_{ar}$), 128.6 ($CH_{ar}$), 128.4 ($CH_{ar}$), 128.3 ($CH_{ar}$), 128.2 ($CH_{ar}$), 127.9 ($CH_{ar}$), 127.5 ($CH_{ar}$), 126.9 (d, $J_{CP}$ = 5 Hz, $CH_{ar}$), 125.2 ($CH_{ar}$), 124.6 (d, $J_{CP}$ = 2 Hz, $CH_{ar}$), 124.3 ($CH_{ar}$), 120.5 ($CH_{ar}$), 40.0 (OMs), 22.1 ($CH_3$), 21.9 ($CH_3$), 17.2 (d, $J_{CP}$ = 34 Hz, $CH_3P$), 15.6 (d, $J_{CP}$ = 29 Hz, $CH_3P$). $^{31}P\{^1H\}$ NMR (121 MHz, $CDCl_3$, 25 ºC): δ 2.0. Anal. Calc. for $C_{43}H_{44}NO_3PPdS$: C, 65.19; H, 5.60; N, 1.77; S, 4.05. Found: C, 65.23; H, 5.90; N, 1.53; S, 3.78. ESI-MS (Orbitrap): *m/z* calculated for $C_{42}H_{41}NPPd^+$ [M – $(CH_3O_3S)]^+$ 696.2006. Found 696.2015.

*2.3. General catalytic procedure for aryl amination reactions.*

The base was placed into a vial equipped with a J Young tap containing a magnetic bar. The aryl halide (0.5 mmol), the *N*-nucleophile (0.6 mmol), the GC internal standard (dodecane, 50 µL) and the solvent (0.5 mL) were added in turn, under a nitrogen atmosphere. The reaction mixture was placed in an oil bath at 110 °C and the precatalyst was added (0.5 mL, 0.01M in dioxane) under $N_2$ flow. The reaction mixture was stirred for 18 h in an oil bath at 110 °C. The reaction was allowed to cool to room temperature, diluted with ethyl acetate and filtered. The conversion was determined by GC analysis. Purification of products were attained by flash chromatography.

*2.4. X-ray crystallographic determinations.*

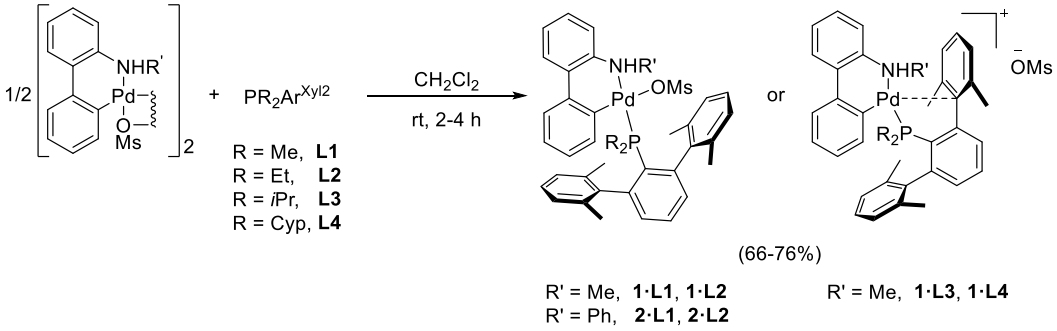
Suitable crystals for X-ray diffraction were coated with perfluoropolyether and mounted on a glass fibber and fixed in cold nitrogen stream to the goniometer head. Data collection have been performed on two difractometers: a Bruker-Nonius X8 Apex-II CCD diffractometer, using a graphite monochromator Mo radiation (λ=0.71073 Å) and fine-sliced ω and φ scans (scan widths 0.30° to 0.50°)[15a] under a flow of cold nitrogen (used with **1·L1**, **1·L2**, **1·L3**, **1·L4** and **3**) and a Bruker-AXSX8Kappa diffractometer equipped with an Apex-II CCD area detector, using a graphite monochromator Ag Kα1 (λ=0.56086 Å) and with a Bruker Cryo-Flex low-temperature device (used with **2·L1**). Data obtained were reduced (SAINT) and corrected for absorption effects by the multiscan method (SADABS).[15b] The structures were solved by direct methods (SIR2002,[16] SHELXS) and refined against all $F^2$ data by full-matrix least squares techniques (SHELXL-2018/3) minimizing $w[F_o^2-F_c^2]^2$.[17] All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions and

allowed to ride on their carrier atoms with the isotropic temperature factors $U_{iso}$ fixed at 1.2 times (1.5 times for methyl groups) of the $U_{eq}$ values of the respective carrier atoms. A summary of cell parameters, data collection, structures solution, and the refinement of crystal structures are provided in the Supporting Information (Tables S1 and S2). Atomic coordinates, anisotropic displacement parameters and bond lengths and angles can be found in the cif files which have been deposited in the Cambridge Crystallographic Data Centre with no. 2039701 (**1·L1**), 2039702 (**1·L2**), 2039703 (**1·L3**), 2039704 (**1·L4**), 2039457 (**2·L1**) and 2039705 (**3**). The data can be obtained free of charge via: https://www.ccdc.cam.ac.uk/structures/

## 3. Results and discussion

### *3.1. Synthesis and NMR characterization of palladacycles*

The synthesis of complexes **1** and **2** was accomplished by the equimolar reaction of *N*-substituted-2-aminobiphenyl-Pd methanesulfonate dimers with dialkylterphenyl phosphanes **L1**-**L4**, in dichloromethane at room temperature (Scheme 2).[12] For the less bulky phosphanes, i.e. those having methyl (**L1**) or ethyl substituents (**L2**) on the phosphorous, reactions proceeded smoothly furnishing *N*-methyl- and *N*-phenyl-2-aminobiphenyl palladacycles in high yields. Palladacycles **1·L1**, **2·L1**, **1·L2** and **2·L2** were isolated as air-stable, analytically pure pale-orange solids.




**Scheme 2**. General synthesis of palladacycles.

$^{31}P\{^{1}H\}$ NMR spectra of palladacycles **1·L1** and **2·L1** in $CDCl_3$ comprise a sharp singlet (δ 1.9 for **1·L1** and 2.0 for **2·L1**), which is shifted ca. 40 ppm to higher frequency relative to the free phosphane. Comparison with NMR data found for other transition metals terphenyl phosphanes complexes, including palladium,[13,14,18] suggests monodentate coordination of phosphane in **1·L1** and **2·L1**. Hence, it is safe to assume

that the mesylate anion is coordinated to the metal center in these two palladacycles. Room-temperature $^{1}H$ NMR spectra of these species are consistent with fast rotation of the phosphane around the P-$C_{aryl}$ bond, since only two resonances are observed for the four methyl substituents on the terphenyl moiety. In addition, the two P-Me groups give rise to differentiated doublets at 1.15 and 0.73 ppm ($^{2}J_{HP}$ = 10.2 Hz) for **1·L1** and 1.29 and 0.61 ppm ($^{2}J_{HP}$ = 10.5 Hz) for **2·L1**. Moreover, the methyl group bound to the N atom in palladacycle **1·L1** leads to a doublet of doublets centered at 2.40 ppm due to additional coupling with the $^{31}P$ nucleus ($^{4}J_{HP}$ = 2.7 Hz), in agreement with a mutually *trans* disposition of the phosphane and the amino group in this complex. Likewise, the resonance due to the NH group in complex **2·L1** is strongly deshielded and appears at 9.90 ppm as a doublet ($^{3}J_{HP}$ = 6.0 Hz).

Unlike the above, $^{31}P\{^{1}H\}$ NMR spectra in $CDCl_3$ of palladacycles **1·L2** and **2·L2**, bearing ethyl-substituted ligand $PEt_2Ar^{Xyl2}$ (**L2**), exhibit very broad resonances at room temperature, indicating that an exchange process is taking place in solution. Cooling the samples from 25 ºC to -30 ºC leads to the observation of two resonances at ca. 47 and 27 ppm (see Fig. S1 in the Supplementary Data), approximately at the same ratio. The $^{31}P$ chemical shift of the lower frequency resonance is indicative of a classical $\kappa^{1}$-P coordination of the phosphane ligand, whereas that of higher frequency signal ($\Delta\delta$ ca. 55 ppm with respect to free ligand) suggests a bidentate coordination mode of the phosphane, involving additional Pd···$C_{arene}$ interactions with one of the flanking ring of the terphenyl fragment.[13c,14] Presumably, they correspond to neutral and cationic palladacycles that interconvert each other by coordination/decoordination of the mesylate ligand. Accordingly, upon switching the original solvent ($CDCl_3$) to a less polar solvent such as $C_6D_6$, only the species with the lower frequency resonance ($\delta$ 26.8 and 26.4 for **1·L2** and **2·L2**, respectively) was observed in $^{31}P\{^{1}H\}$NMR spectra. Furthermore, both $^{1}H$ and $^{13}C\{^{1}H\}$ NMR spectra of these species recorded in $C_6D_6$ at room temperature resemble those corresponding to **1·L1** and **2·L1** described above, indicating that neutral palladacycles are favored in $C_6D_6$. Conversely, the more polar solvent $CD_3OD$ shifts the equilibrium mixture towards the cationic palladacycles [Pd(*N*-R-2-aminobiphenyl)($PEt_2Ar^{Xyl2}$)]$^{+}$ (see Supplementary Data). Unfortunately, solutions of these complexes in $CD_3OD$ were unstable preventing their full characterization. However, the most prominent NMR features of such cationic species with terphenyl phosphanes other than **L2** will be discussed below.

When reactions shown in Scheme 2 were undertaken using sterically crowded phosphanes P*i*Pr$_2$Ar$^{Xyl2}$ (**L3**) and PCyp$_2$Ar$^{Xyl2}$ (Cyp = cyclopentyl) (**L4**), only *N*-methyl-2-aminobiphenyl palladacycles **1·L3** and **1·L4** could be isolated, as air-stable, analytically pure solids in good yields. Both, in the $^{1}$H and $^{13}$C{$^{1}$H} NMR spectra of palladacycles **1·L3** and **1·L4** the non- equivalence of the two flanking rings of the terphenyl moieties is clearly observable. Thus, for complex **1·L3**, differentiated signals appear for the four methyl substituents of the xylyl rings in the aliphatic region of its $^{1}$H NMR spectrum recorded in $CDCl_3$ at room-temperature. In addition, distinctive pattern of signals for each of the *iso*-propyl groups bonded to phosphorus are found in the expected range. Moreover, $^{31}$P{$^{1}$H} NMR spectra of **1·L3** and **1·L4** show single resonances around 62.3 and 54.4 ppm, respectively, shifted by ca. 49 ppm to higher frequency values relative to uncoordinated phosphanes. Such a shift seems to be consistent with a bidentate binding mode of the phosphane in these complexes. Taken together, these observations support a cationic formulation for palladacycles **1·L3** and **1·L4**.

Reactions conducted to obtain *N*-phenyl-2-aminobiphenyl palladacycles with bulky ligands **L3** and **L4** led to the formation, in both instances, of a mixture of products consisting of two main components along with minor species. According to $^{31}$P{$^{1}$H} NMR spectroscopy recorded in $CDCl_3$, one of the major species seems to be the expected palladacycle, since its $^{31}$P{$^{1}$H} resonance appears at similar chemical shifts (ca. 65 and 55 ppm) to those found for the *N*-methyl analogues. The second main component of the mixture shows a single resonance at higher frequency, close to 80 ppm, which was tentatively attributed to a Pd(II)-phosphane complex bearing the *N*-phenyl 2-aminobiphenyl ligand solely bonded through the carbon atom. Unfortunately, the rapid degradation of the mixture in chlorinated solvents precluded further characterization. However, red crystals of a degradation product resulted from the reaction with phosphane **L4** could be isolated by layering a dichloromethane solution with petroleum ether. The X-ray diffraction analysis reveals this is a neutral Pd(II) complex of composition Pd(Cl)(OMs)(PCyp$_2$Ar$^{Xyl2}$), **3** (see Fig. S2, Supplementary Data), in which the loss of the *N*-phenyl-2-aminobiphenyl ligand is compensated by the adoption of a $\kappa^1$-P,$\eta^1$-C$_{arene}$ coordination mode of the terphenyl phosphane ligand. This finding appears to support that *N*-phenyl-2-aminobiphenyl platform cannot accommodate very large ligands such as P*i*Pr$_2$Ar$^{Xyl2}$, **L3** and PCyp$_2$Ar$^{Xyl2}$, **L4**. A similar remark has been reported for reactions of

*N*-phenyl-2-aminobiphenyl-palladacycles methanesulfonate dimers with sterically encumbered dialkylbiaryl phosphanes.[12]

*3.2. Molecular structures of palladacycles*

Neutral structures postulated for palladacycles **1·L1** and **2·L1** on the basis of NMR spectroscopy were confirmed by X-ray diffraction studies. The two complexes share akin structural features (Figure 2). Thus, in both species, the Pd center resides in a slightly distorted square-planar coordination geometry formed by the chelating *N*-substituted-2-aminobiphenyl ligand, the phosphane and the mesylate anion. The angle between the two planes defined by atoms N, Pd, OMs and P, Pd, C1, is actually of 8º for **1·L1** and 12º for **2·L1**. These notable distortions can be reasonably ascribed to the crowded coordination environment around the metal center. The phosphane lies opposite to the amino group of the chelating organic ligand, as usually encountered in analogous phosphane-stabilized N,C-palladacycles.[12,19] The mesylate ligand in these complexes is involved in intermolecular hydrogen bonding interactions with the NH function (NH···O 2.98 Å for **1·L1** and 2.82 Å for **2·L1**). Moreover, the terphenyl phosphane ligand adopts, in both complexes, a conformation[13b] in which one of the P-Me bonds is nearly coplanar with the central ring of the terphenyl moiety, resulting in two unequal P-C*ipso*-C*ortho* bond angles (average value: ca. 118 and 124°).

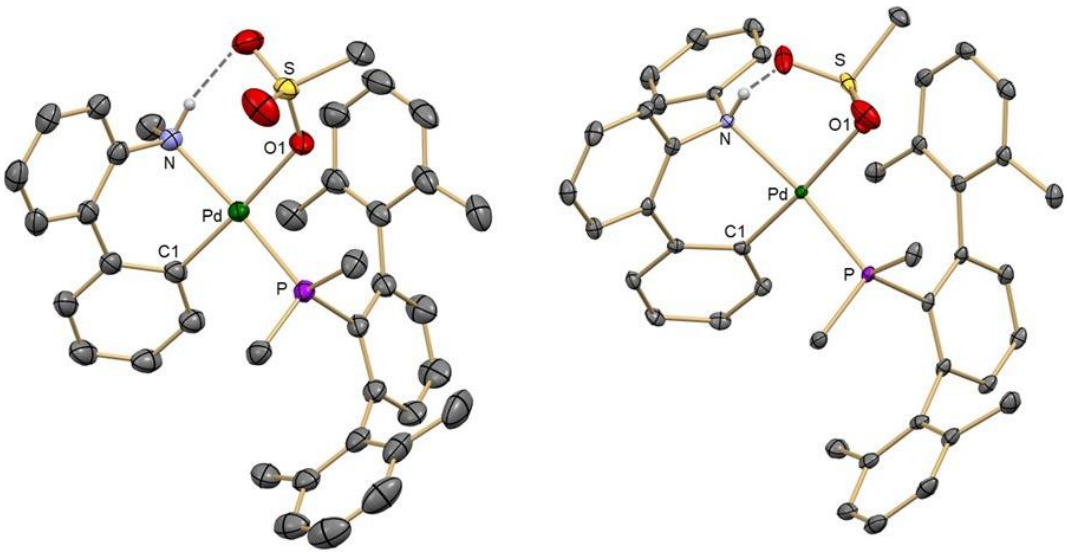



**Fig. 2.** Molecular structures of **1·L1** (left) and **2·L1** (right). Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability. Selected bond lengths (Å) and angles (°) for **1·L1**: Pd-P 2.2623(4), Pd-N 2.1156(12), Pd-C1 1.9898(15), Pd-O1 2.1558(12), N-Pd-P 172.59(4), C1-Pd-O1 176.00(6), C1-Pd-P, 92.11(4), P-Pd-O1 90.49(4), C1-Pd-N 86.82(6), N-Pd-O1 90.21(5); for **2·L1**: Pd-P 2.2545(6), Pd-N

2.1403(19), Pd-C1 1.990(2), Pd-O1 2.1670(16), N-Pd-P 167.79(6), C1-Pd-O1 175.43(7), C1-Pd-P, 91.93(6), P-Pd-O1 92.36(5), C1-Pd-N 87.00(8), N-Pd-O1 89.15(6).

Orange crystals of palladacyle **1·L2** suitable for single-crystal X-ray diffraction were obtained by layering a dichloromethane solution of **1·L2** with petroleum ether at 5 ºC. As shown in Fig. 3, in the solid-state the palladacycle adopts a four-coordinate distorted square-planar geometry in which the phosphane ligand is coordinated in a classical manner ( $\kappa^1$-P) and the mesylate anion is also bonded to the metal center. The structural properties of this complex are similar to those already described for palladacycles **1·L1** and **2·L1** and will not be further discussed.

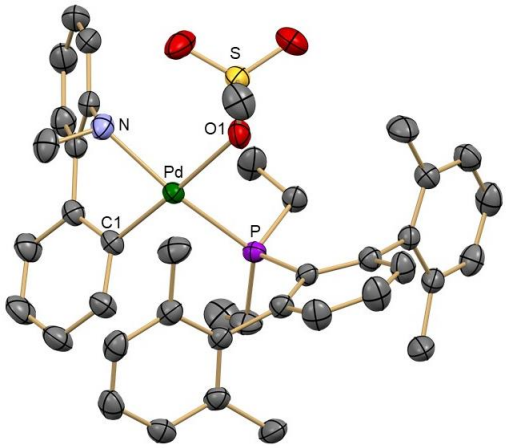



**Fig. 3.** Molecular structures of **1·L2**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability. Selected bond lengths (Å) and angles (°) for **1·L2**: Pd-P 2.2787(8), Pd-N 2.1200(14), Pd-C1 1.9807(15), Pd-O1 2.2019(13), N-Pd-P 167.02(4), C1-Pd-O1 177.49(6), C1-Pd-P, 94.04(5), P-Pd-O1 87.87(4), C1-Pd-N 85.72(6), N-Pd-O1 92.06(5).

For complexes **1·L3** and **1·L4** bearing larger phosphanes P*i*Pr$_2$Ar$^{Xyl2}$ and PCyp$_2$Ar$^{Xyl2}$, respectively, X-ray diffraction analyses reveal they are composed of a [Pd(*N*-methyl-2-aminobiphenyl)(PR$_2$Ar$^{Xyl2}$)]$^+$ cation with a mesylate counterion (Fig. 4 and Fig. S3). In the cationic complexes, the Pd(II) center is formally four-coordinate with the N,C-chelating ligand and the phosphane (in a bidentate $\kappa^1$-P,$\eta^1$-C$_{arene}$ bonding mode) forming the coordination sphere. The Pd···C$_{ipso}$ separation of ca. 2.40 Å for **1·L3** and 2.41 Å for **1·L4** suggests the existence of a weak bonding interaction between the two atoms involved,[20] and it is comparable to those of other known 2-aminobiphenyl palladacycles stabilized by biaryl phosphane[8c] or terphenyl phosphane ligands.[14] To facilitate this interaction, the central aryl ring of the terphenyl fragment bends towards the metal, resulting in a narrowing of the corresponding P-C$_{ipso}$-C$_{ortho}$ angle (114.4° and

115.8° for **1·L3** and **1·L4**, respectively) at the expense of the other (127.8° and 125.7° for **1·L3** and **1·L4**, respectively). Moreover, the two P-R groups are located at opposite sides with respect to the plane defined by the central aryl ring of the terphenyl moiety. The Pd-P and Pd-N bond lengths are within the range found for analogous cationic palladacycles.[8c,14]

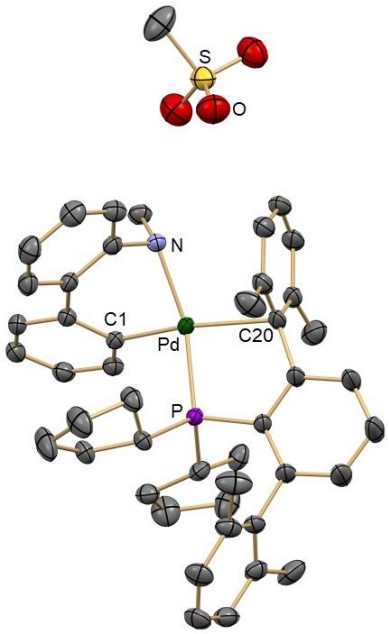



**Fig. 4.** Molecular structures of **1·L4**. Hydrogen atoms are omitted for clarity. Thermal ellipsoids are shown at 50% probability. Selected bond lengths (Å) and angles (°) for **1·L4**: Pd-P 2.2767(5), Pd-N 2.1587(16), Pd-C1 1.9982(19), Pd-C20 2.411(2), N-Pd-P 161.22(5), C1-Pd-C20 171.27(8), C1-Pd-P, 90.82(5), P-Pd-C20 83.97(5), C1-Pd-N 82.86(7), N-Pd-C20 104.22(7).

### *3.3. Catalytic applications in C-N cross-coupling reactions*

With a set of *N*-substituted-2-aminobiphenyl palladacycles in hand, their catalytic activity in the Buchwald-Hartwig reaction[21] was then assessed. The reaction between 4-chlorotoluene and morpholine was chosen as the model system to test precatalysts performance. We began applying the reaction conditions found for parent 2-aminobiphenyl palladacycle precatalysts, namely, NaO*t*Bu as the base, THF as the solvent, 0.5 mol% Pd loading and 80 °C as the reaction temperature.[14] The formation of the aryl amine was measured by GC after 18 h. For comparative purposes, the catalytic activity of [Pd(2-aminobiphenyl)($PCyp_2Ar^{Xyl2}$)](OMs), the best performing precatalyst of the unsubstituted 2-aminobiphenyl-derived series, was also included in this study. None of the *N*-substituted palladacycles promoted the C-N cross-coupling under these conditions. When rising the temperature up to 110 ºC the two precatalysts **1·L1** and **2·L1**

bearing the less sterically encumbered phosphane $PMe_2Ar^{Xyl2}$ displayed very low activity (Fig. 5). As expected, the catalytic performance improved significantly with increasing the ligand bulkiness and precatalyst **1·L4** demonstrated to be the most effective (Scheme 3), but in no case reaching or exceeding the yield found for the unsubstituted 2-aminobiphenyl palladacycle. Full conversions were attained with precatalyst **1·L4** when using 1 mol% catalyst loading. Interestingly, it was noted that precatalyst **2·L2** was more effective than precatalysts **1·L2** arising from the *N*-methyl-2-aminobiphenyl scaffold. Presumably, the larger size of the phenyl substituent as compare to the methyl could facilitate the precatalyst activation.

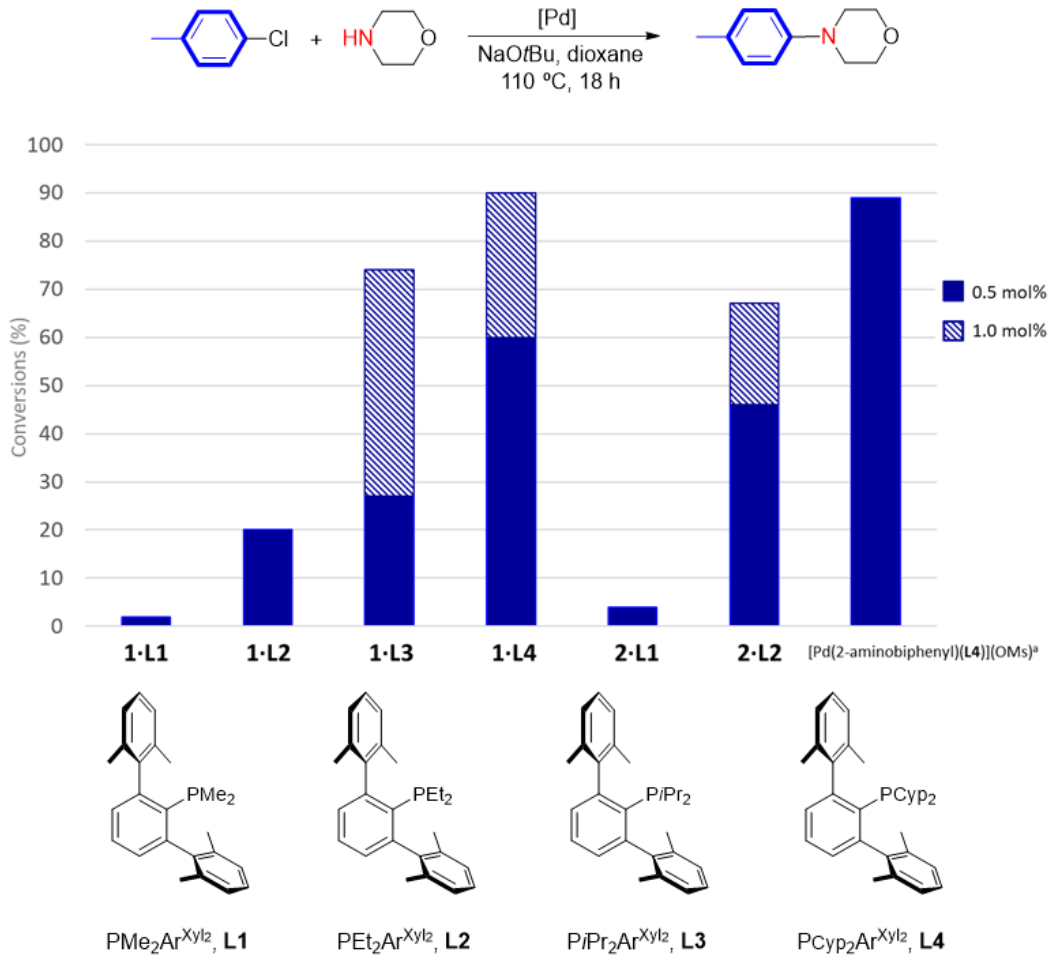
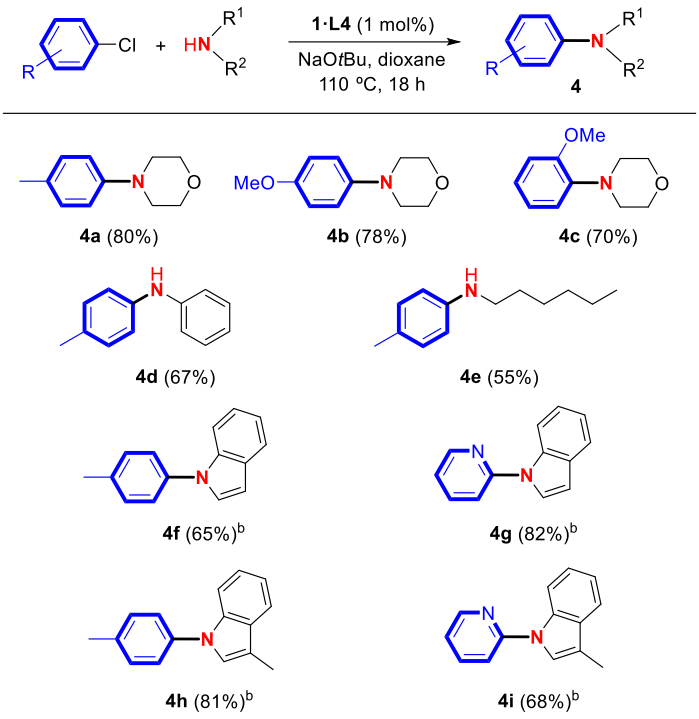



**Fig 5.** Catalytic performance of precatalysts **1** and **2** in the *N*-arylation of morpholine with 4-chlorotoluene. Reaction conditions: 4-chlorotoluene (0.5 mmol), morpholine (0.6 mmol), NaO*t*Bu (0.6 mmol), dioxane (1 mL), T = 110º C, reaction time 18 h. Conversions were determined by GC analysis of the reaction mixtures using dodecane as internal standard. [a]Isolated yield of product, see ref. 14.

Under the optimized reaction conditions, the competence of precatalyst **1·L4** was evaluated in various C-N cross-coupling reactions as illustrated in Table 1. The coupling of morpholine with electronically deactivated 4-chloroanisol and sterically hindered 2-

chloroanisol proceeded pleasingly, affording good yields of the corresponding products (Table 1, **4b** and **4c**). Anilines and primary alkyl amines were successfully arylated, providing the desired products in reasonable yields (Table 1, **4d** and **4e**). Moreover, **1·L4** promoted the efficient amination of aryl chlorides with indoles, which are difficult nucleophilic coupling partners due to their poor nucleophilicity, high acidity and strong coordination ability of the NH group.[22] The C-N coupling products were selectively[23] obtained in useful synthetic yields (Table 1, **4f** to **4i**). It is worth noting that all these catalytic reactions were conducted without adding excess ligand.

**Table 1.** Substrate scope for precatalyst **1·L4** in C-N cross-coupling reactions.[a]




[a]Reaction conditions: aryl chloride (0.5 mmol), *N*-nucleophile (0.6 mmol), NaO*t*Bu (0.6 mmol), dioxane (1 mL), T = 110 ° C, reaction time 18 h. Isolated yield of products. [b]Reaction performed in toluene.

The reduced catalytic activity observed for *N*-substituted-2-aminobiphenyl precatalysts, in comparison to that of the unsubstituted ones, was somewhat unexpected, especially in view that for analogous Pd(II) systems supported by biaryl phosphane ligands it has not been disclosed to make a difference.[12] From the above, it appears that free NH-carbazole produced during the activation of 2-aminobiphenyl palladacycles to

generate active LPd(0) species somehow contributes to stabilize low-coordinate palladium species preventing their deactivation. Ongoing work is aimed at ascertaining the role of NH-carbazole in C-N cross-coupling reactions mediated by 2-aminobiphenyl palladacycles.

## 4. Conclusions

A series of air and moisture stable *N*-methyl- and *N*-phenyl-2-aminobiphenyl methanesulfonate palladacycles stabilized by dialkylterphenyl phosphane ligands have been prepared. The complexes bearing the less sterically demanding phosphane $PMe_2Ar^{Xyl2}$ are neutral, both in solution and in the solid state. However, with increasing the steric bulk cationic structures are favored, in which the phosphane adopts a bidentate coordination mode ($\kappa^1$-P, $\eta$-$C_{arene}$) involving weak M···$C_{arene}$ interactions with one of the flanking aryl rings of the terphenyl fragment. Only palladacycle **1·L4** with the larger ligand $PCyp_2Ar^{Xyl2}$ has demonstrated competence in C-N cross-coupling of aryl chlorides with different *N*-nucleophiles including anilines, primary alkyl amines, secondary amines and indoles, albeit with significantly lower effectiveness compared with the non-substituted 2-aminobiphenyl palladacycle analogue.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Acknowledgements

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