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Novel motif for bidentate P,N ligands. Application to Pd-catalyzed Suzuki cross-coupling reactions

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ABSTRACT

A library of novel C_2-symmetric P,N ligands based on a Tröger's base backbone was prepared via a concise two-step synthesis starting from a commercially available aniline derivative. X-ray crystallography and ^{31}P NMR studies confirm that a single ligand molecule can accommodate two palladium atoms via coordination to nitrogen and phosphorus. Preliminary results proved the synthetic potential of this species in Suzuki cross-coupling reactions of aryl bromides with arylboronic acids.

1. Introduction

Metal-catalyzed cross-coupling reactions have matured over the years into an incredibly powerful tool in the hands of synthetic chemists [1]. The broad spectrum of protocols covers cross-coupling reactions basically of all types of hybridized carbons [2] with carbon, nitrogen [3], oxygen [4], sulfur [5] and phosphorus [6] atoms. Besides countless applications in academic research [7], these types of transformations have attracted also the attention of industrial chemists as demonstrated by scientific reports on their use in the synthesis of pharmaceuticals and agrochemicals [8]. This galore of cross-coupling reactions was possible due to the detailed understanding of the reaction mechanism, extensive screening of reaction conditions and sophisticated design of ligands [9]. As environmental and economic needs evolve with time, ligand evolution is imperative. Employment of new structural motifs into rational ligand design appears to be an attractive approach for the development of new ligands.

Tröger's base[10] is a textbook example of a molecule containing stable stereogenic nitrogen atoms [11]. The pyramidal inversion at nitrogen centers is hindered due to the presence of the methylene bridge between the nitrogen atoms thereby preventing the racemization of enantiomerically pure Tröger's base derivatives under non-acidic conditions even at elevated temperature. This feature together with a unique V-shape of the Tröger's base scaffold has inspired numerous scientists to exploit this motif in various fields such as molecular recognition, bioorganic chemistry and supramolecular chemistry [12]. Its implementation in the ligand design is, however, scarce [13]. Despite the fact that the Tröger's base skeleton represents an easily accessible, rigid, chiral moiety, the design of ligands profiting from the presence of this unit is rather underdeveloped [14]. We have recently reported a straightforward synthesis of new S,N and Se,N doubly bidentate ligands based on Tröger's base backbone [15]. Their coordination properties in Ag(I)-complexes were studied by NMR spectroscopy as well as X-ray diffraction crystallography and it was shown that a single molecule of the ligand can accommodate two silver atoms via coordination to chalcogen and nitrogen atoms. Herein, we would like to expand our approach to a new class of P,N ligands.

2. Results and discussion

2.1. Ligand synthesis

The synthesis starts with the formation of 4,10-dibromo Tröger's base (**1**) by the condensation of 2-bromo-4-methylaniline with paraformaldehyde in trifluoroacetic acid [16]. Compound **1** was formed in a highly efficient manner and the crystallization of the partially concentrated organic extracts after an aqueous work-up was fully sufficient for the isolation of a pure product (97% yield). Two strategies were applied for the installment of the phosphane moieties. Typically, the lithium–bromine exchange followed by the

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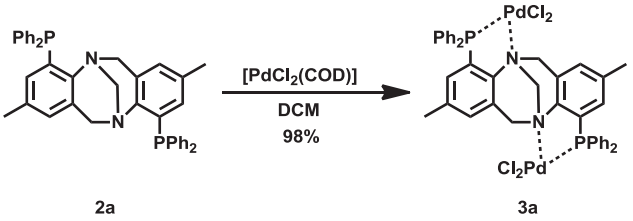
quenching with a chlorophosphane gave the corresponding P,N ligands **2a**–**c** (Scheme 1).

We have observed throughout different projects that the stability of the dilithiated species (upon lithium–bromine exchange of **1**) is somewhat limited and only reactive electrophiles yielded the corresponding products in high yields [17]. This tendency was also observed in the present case. The reaction proceeded with satisfactory yields when the substituents on chlorophosphanes were phenyl or 4-methylphenyl. The increased steric hindrance in the case of bulkier chlorodialkylphosphanes resulted in prolonged reaction time during which the dilithiated species deteriorated and the anticipated phosphanes were obtained only in low (**2c**) or no (**2d**) yields. Furthermore, the dicyclohexylphosphane ligand proved extremely sensitive towards oxidation rendering its isolation and purification exceedingly cumbersome. We have thus treated the crude reaction mixture with an excess of borane tetrahydrofuran complex (5 equiv) and isolated the ligand as its borane adduct **2c′**. The deprotection was achieved by an action of diethylamine and the crude phosphane ligand **2c** was directly used in catalysis. Dissatisfied with the poor outcome of the synthesis of *t*Bu-phosphane **2d**, we have attempted an alternative synthesis via palladium-catalyzed phosphanation. To our delight, **2d** was obtained in 26% yield. In general, the presented approach represents a concise two-step strategy for the preparation of a library of new P,N ligands. The introduction of the phosphane moiety in the last step allows for a high modularity of this protocol.

2.2. Coordination properties

We have studied the coordination properties of the new ligands upon complexation with palladium. The solution of ligand **2a** in DCM was added to the solution of 2 equivalents of [$PdCl_2$(COD)] in DCM and the resulting solution was stirred for 1 h at RT. The analysis of the reaction mixture by ^{31}P NMR revealed that the signal for the free ligand at −15.1 ppm disappeared and single phosphine species was detected at 36.1 ppm as a doublet ($J_{H-P} = 10.9$ Hz) which was assigned to the dipalladium complex **3a** (Scheme 2). Similarly, the NMR experiment with the cyclohexyl analogue **2c** revealed the complete disappearance of the ^{31}P NMR signal of the free ligand upon addition of 2 equivalents of [$PdCl_2$(COD)]. The coordination resulted again in single phosphine species at 62.4 ppm (proton decoupled ^{31}P NMR).



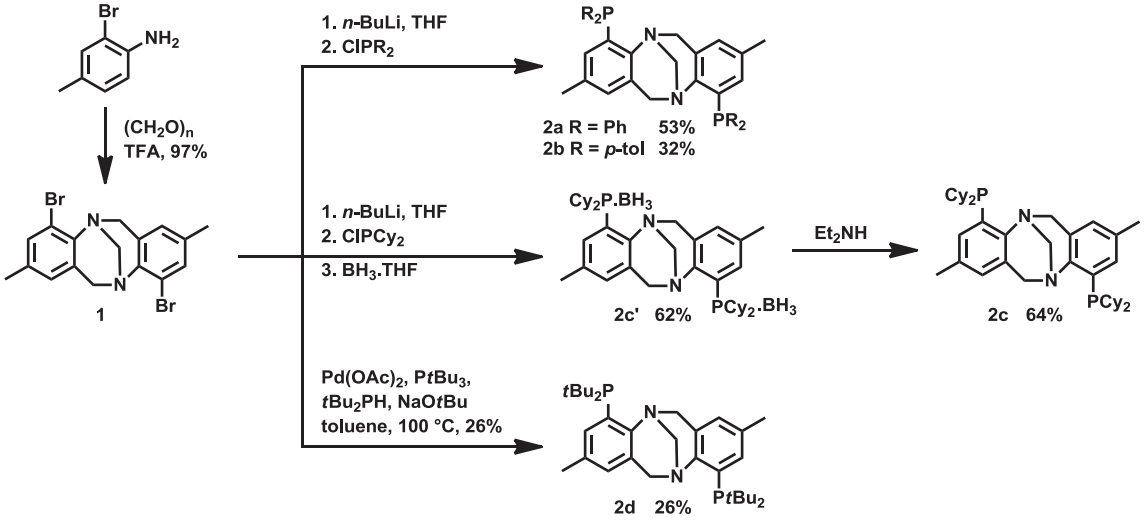
Scheme 2. Coordination of **2a** to palladium.

We were able to grow single crystals of **3a** by vapor diffusion of pentane into a dichloromethane solution. The ORTEP view of **3a** is shown in Fig. 1. Two molecules of dichloromethane are present in the crystal structure. The chlorine atoms (Cl5 and Cl6) in the dichloromethane molecule closer to the ligand are disordered over two sites with site occupancy factors of 0.56 and 0.44. As a consequence, one of the chlorine atoms (Cl1) at Pd(1) is disordered over two sites with site occupancy factors of 0.58 and 0.42.

The X-ray analysis confirmed that a single molecule of ligand **2a** is able to accommodate two palladium atoms resulting in dipalladium complex **3a**. Both palladium atoms coordinate in the same fashion with square-planar geometry around palladium. The complex **3a** thus retains the C_2-symmetry of the parent ligand. Nitrogen and phosphorus atoms replaced COD as ligands in the coordination sphere of palladium. The bond lengths between palladium and phosphorus are 2.1868(10) Å and 2.1996(11) Å, respectively, which corresponds to the bond lengths in other palladium containing five-membered cycles. The same goes for the bonds between palladium and nitrogen (2.123(3) Å and 2.122(3) Å). The values for the P–Pd–N angles (85.75(9)° and 86.37(9)°) are in agreement with values reported for other five-membered palladacycles with this ligand set. The phosphorus and nitrogen atoms are located out of plane of the aromatic rings. The torsion angle defined by P(1)–C(1)–C(14)–N(1) is −8.7(5)° and −14.3(5)° in the case of N(2)–C(7)–C(8)–P(2). The dihedral angle between the aromatic planes is 102.56(12)°.

2.3. Catalysis

With a small library of ligands in our hands we have performed some initial tests to evaluate their catalytic properties in palladium-



Scheme 1. Synthesis of P,N ligands **2a**–**d**.

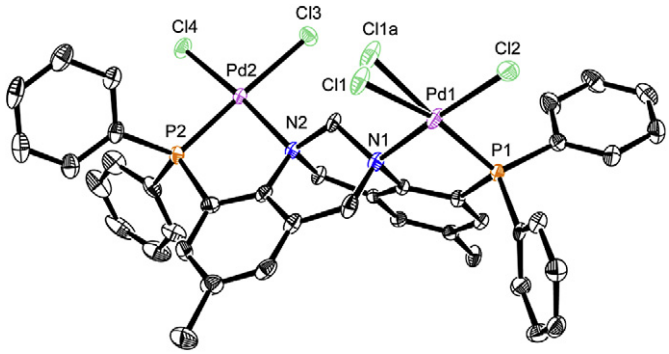


Fig. 1. ORTEP representation of complex **3a**. Hydrogen atoms and solvent molecules are omitted for clarity. Thermal ellipsoids are set to 50% probability. Selected bond lengths (Å) and bond angles (°): Pd1–N1 2.123(3), Pd2–N2 2.122(3), Pd1–P1 2.1868(10), Pd2–P2 2.1996(11), Pd1–Cl1 2.424(3), Pd1–Cl1A 2.332(3), Pd1–Cl2 2.2584(11), Pd2–Cl3 2.3640(11), Pd2–Cl4 2.2693(10), N1–Pd1–P1 85.75(9), N2–Pd2–P2 86.37(9).

catalyzed C–C cross-coupling reactions. A fast screening revealed that $Pd(OAc)_2$ is superior to $Pd_2(dba)_3$ as the palladium source for the reaction between bromobenzene and phenylboronic acid (Table 1, Entries 1 and 2). The use of potassium triphosphate resulted in shorter reaction time compared to cesium carbonate (Entries 2 and 3). THF proved to be the most suitable solvent resulting in the lowest temperature and the highest reaction rate (Entries 2, 4–7). Finally, we evaluated the potential of other synthesized ligands. The *p*-tolyl analogue **2b** gave basically same result as **2a** yielding the product in 99% yield (Entry 8). Interestingly, the electron-rich bulky ligands **2c** and **2d** turned out to be completely inactive even after a prolonged reaction time (Entries 9 and 10).

Applying the most suitable conditions, we checked a few substrates to briefly evaluate the scope and limitation of the catalyst (Table 2). The presence of the electron-withdrawing substituent facilitates the oxidative addition of palladium into the carbon–bromine bond resulting in shorter reaction times (Entry 1). Interestingly, one or two substituents in the vicinity of the bromine atom are tolerated (Entries 2 and 3). *Ortho*-substituted boronic acid can be also efficiently applied under these conditions (Entry 4). Unfortunately, the presented catalytic system completely failed to involve aryl chlorides in the Suzuki cross-coupling. The above-mentioned results suggest that a few sophisticated changes have to be done regarding the catalyst design.

3. Conclusion

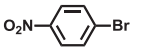
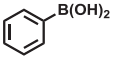
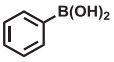
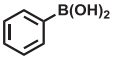
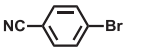
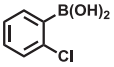
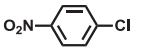
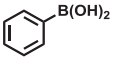
We have demonstrated that the Tröger's base scaffold can be efficiently used as a backbone for new class of P,N ligands. ^{31}P NMR and X-ray crystallographic studies of the corresponding Pd(II)-complex **3a** confirmed that a single ligand acts as doubly bidentate and can thus accommodate two palladium atoms via coordination to nitrogen and phosphorus. Preliminary tests of the catalytic activity revealed that the diarylphosphane ligands **2a** and **2b** catalyze the Suzuki cross-coupling of aryl bromides with boronic acids. We are currently trying to modify the design of Tröger's base derived ligands in order to improve their catalytic performance as well as to test the enantiomerically pure ligands in asymmetric catalysis.

Table 1
Screening of the reaction conditions (Pd-source, ligand, base, solvent, temperature) for the Suzuki cross-coupling.

Entry	Catalyst	Ligand	Base	Solvent	Temperature (°C)	Time (h)	Yield (%)[a]
1	$Pd_2(dba)_3$	**2a**	K_3PO_4	THF	70	19	33
2	$Pd(OAc)_2$	**2a**	K_3PO_4	THF	70	4	99
3	$Pd(OAc)_2$	**2a**	Cs_2CO_3	THF	70	22	68
4	$Pd(OAc)_2$	**2a**	K_3PO_4	Toluene	90	24	48
5	$Pd(OAc)_2$	**2a**	K_3PO_4	EtOH	75	17	88
6	$Pd(OAc)_2$	**2a**	K_3PO_4	DMF	100	5	73
7	$Pd(OAc)_2$	**2a**	K_3PO_4	Dioxane	90	17	45
8	$Pd(OAc)_2$	**2b**	K_3PO_4	THF	70	4	99
9	$Pd(OAc)_2$	**2c**	K_3PO_4	THF	70	18	0
10	$Pd(OAc)_2$	**2d**	K_3PO_4	THF	70	18	0

[a] Isolated yields after column chromatography.

Table 2
Suzuki cross-coupling of aryl halides with arylboronic acids.[a]

Entry	Ligand	Aryl halide	Boronic acid	Time (h)	Yield (%)[b]
1	**2a**			1.5	92
2	**2a**			7	79
3	**2a**			7	91
4	**2b**			1.5	90
5	**2a**			22	0

[a] Reaction conditions: 1.5 mmol aryl halide, 2.25 mmol arylboronic acid, 3 mmol K_3PO_4, $Pd(OAc)_2$ (2 mol%), ligand (1 mol%), 3 mL THF, 70 °C.
[b] Isolated yields after column chromatography.

4. Experimental

4.1. General

The reactions were carried out in oven-dried glassware under argon using Schlenk techniques. All solvents were freshly distilled under argon from an appropriate drying agent before use. Flash chromatography was performed with Fluka silica gel 60. NMR spectra were measured on Bruker Avance DPX-300, DPX-400, III HD Nanobay-300 and III HD Nanobay-400 spectrometers. The chemical shifts are recorded in ppm and are referenced to 85% H_3PO_4 (for ^{31}P) and to tetramethylsilane (^1H and ^{13}C). The ^2D lock frequency of $CDCl_3$ was used as the internal secondary reference in all cases. High-resolution mass spectra were measured by the MS-Service of the "Laboratorium für Organische Chemie der ETH" on a Bruker Daltonics maXis ESI-QTOF. The X-ray structure was measured on a Bruker APEX2 diffractometer with CCD area detector and Mo-K_α radiation. Single crystals were coated at room temperature with perfluoroalkylether oil and mounted on a 0.1 mm glass capillary. The structures were solved by direct methods in SHELXTL and successive interpretation of the different Fourier maps, followed by full-matrix least-squares refinement (against F^2).

4.2. Ligand synthesis

4.2.1. Synthesis of rac-4,10-bis(diphenylphosphino)-2,8-dimethyl-6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine [2a]

A Schlenk flask was charged with **1** (0.82 g, 2 mmol) under argon and THF (20 mL) was added. Then it was cooled down to −78 °C and *n*-BuLi (1.6 M in hexane, 2.8 mL, 4.4 mmol, 2.2 equiv) was added dropwise to form a pale yellow suspension. After

10 min, chlorodiphenylphosphane (0.78 mL, 4.4 mmol, 2.2 equiv) was added dropwise and the suspension turned clear again. The stirring was continued overnight at ambient temperature. Sat. NH_4Cl solution (20 mL) was added and it was extracted with DCM (3 × 20 mL). Combined org. layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash column chromatography (SiO_2 (40 g); DCM/hexane 4:1) to give **2a** as a white solid (640 mg, 53%).

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.08 (s, 6H, CH_3), 4.18 (s, 2H, NCH_2N), 4.32 (d, ^3J = 17.3 Hz, 2H, endo CH_2N), 4.55 (d, ^3J = 17.3 Hz, 2H, exo CH_2N), 6.50 (s, 2H, Ar–*H*), 6.60 (s, 2H, Ar–*H*), 7.25–1.39 (m, 20H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 21.4 (*C*H$_3$), 57.7 (d, J_{C-P} = 9.7 Hz, *C*H$_2$N), 67.9 (NCH$_2$N), 128.6, 128.7, 128.8, 128.9, 129.0, 129.1, 133.1 (d, J_{C-P} = 11.7 Hz), 133.5 (d, J_{C-P} = 19.3 Hz), 133.9, 134.4, 134.9 (d, J_{C-P} = 20.4 Hz), 137.8 (d, J_{C-P} = 11.2 Hz), 138.3 (d, J_{C-P} = 11.0 Hz), 149.3 (d, J_{C-P} = 21.1 Hz); ^{31}P NMR (162 MHz, $CDCl_3$): −15.1; HRMS (ESI): *m*/*z* [MH]$^+$ calcd for $C_{41}H_{37}N_2P_2$: 619.2420; found: 619.2426.

4.2.2. Synthesis of rac-4,10-bis(di-p-tolylphosphino)-2,8-dimethyl-6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine [2b]

The title compound was synthesized in analogy to the abovementioned procedure for **2a** starting from **1** (650 mg, 1.6 mmol). A solution of chlorobis(4-methylphenyl)phosphine (880 mg, 3.52 mmol) in THF (5 mL) was used to quench the lithiated species. The crude product was purified by flash column chromatography (SiO_2; hexane/ethyl acetate 10:1 to 2:1 containing 0.1% Et_3N) to give a yellowish-white solid which was further purified via re-precipitation from a mixture of DCM/hexane to give **2b** as a white solid (354 mg, 32%). ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.08 (s, 6H, CH_3), 2.35 (s, 6H, CH_3), 2.40 (s, 6H, CH_3), 4.16 (s, 2H, NCH_2N) 4.32 (d, ^3J = 17.4 Hz, 2H, endo CH_2N), 4.52(d, ^3J = 17.4 Hz, 2H, exo CH_2N), 6.51 (s, 2H, Ar–*H*), 6.59 (s, 2H, Ar–*H*), 7.12 (m, 8H, Ar–*H*), 7.18 (m, 4H, Ar–*H*), 7.25 (m, 4H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 21.0 (*C*H$_3$), 21.3 (*C*H$_3$), 21.4 (*C*H$_3$), 57.2 (d, J_{C-P} = 10.5 Hz, *C*H$_2$N), 67.5 (NCH$_2$N), 128.3, 128.5 (d, J_{C-P} = 4.9 Hz), 129.0 (d, J_{C-P} = 7.0 Hz), 129.3 (d, J_{C-P} = 7.3 Hz), 133.1 (d, J_{C-P} = 19.5 Hz), 133.0, 133.3, 133.7, 134.0 (d, J_{C-P} = 10.1 Hz), 134.4 (d, J_{C-P} = 20.7 Hz), 134.6 (d, J_{C-P} = 9.8 Hz), 137.9, 138.5, 149.3 (d, J_{C-P} = 21.1 Hz); ^{31}P NMR (121 MHz, $CDCl_3$): δ [ppm] = −17.8; HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{45}H_{45}N_2P_2$: 675.3052; found: 675.3042.

4.2.3. Synthesis of rac-4,10-bis(dicyclohexylphosphino)-2,8-dimethyl-6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine [2c]

The title compound was synthesized in analogy to the abovementioned procedure for **2a** starting from **1** (200 mg, 0.5 mmol). A solution of chlorodicyclohexylphosphane (256 mg, 1.1 mmol) in THF (5 mL) was used to quench the lithiated species. The reaction was allowed to reach room temperature overnight. It was then cooled to 0 °C and BH_3.THF (10 mL, 10 mmol of a 1 M solution in THF) was added. The reaction mixture was allowed to reach room temperature and then it was stirred for additional 6 hours. The reaction was then transferred into a saturated solution of NH_4Cl (20 mL) under argon and it was stirred for 5 min. It was extracted with DCM (3 × 30 mL). Combined organic layers were dried over $MgSO_4$ and concentrated. The crude product was purified by flash column chromatography (SiO_2 (30 g); hexane/ethyl acetate 4:1 containing 0.1% Et_3N) to give a pale yellow solid as the borane protected phosphane **2c′** (307 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 0.23–1.02 (br, 6H, BH_3), 1.16–1.97 (m, 38H, *Cy*), 2.07 (d, ^2J = 13.3 Hz, 2H, *Cy*), 2.30 (s, 6H, CH_3), 2.36–2.47 (m, 2H, *Cy*), 2.68–2.78 (m, 2H, *Cy*), 3.94 (d, ^2J = 17.1 Hz, 2H, endo CH_2N), 4.20 (s, 2H, NCH_2N), 4.69 (d, ^2J = 17.1 Hz, 2H, exo CH_2N), 6.81(s, 2H, Ar–*H*), 7.36 (d, J_{H-P} = 12.9 Hz 2H, Ar–*H*); ^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 21.0 (Ar–*C*H$_3$), 25.9 (d, J_{C-P} = 13.6 Hz), 26.8 (d, J_{C-P} = 11.2 Hz), 27.0 (d, J_{C-P} = 2.5 Hz), 27.1 (d, J_{C-P} = 1.9 Hz), 27.2 (d, J_{C-P} = 11.2 Hz), 28.0 (d, J_{C-P} = 36.5 Hz), 28.5 (d, J_{C-P} = 35.5 Hz), 33.2 (d, J_{C-P} = 33.9 Hz), 34.1 (d, J_{C-P} = 32.4 Hz), 57.4 (*C*H$_2$N), 66.0 (NCH$_2$N), 122.9 (d, J_{C-P} = 44.1 Hz), 129.0 (d, J_{C-P} = 5.7 Hz), 130.6 (d, J_{C-P} = 2.1 Hz), 134.8 (d, J_{C-P} = 11.5 Hz), 137.1 (d, J_{C-P} = 12.7 Hz), 149.3; ^{31}P NMR (162 MHz, $CDCl_3$): δ [ppm] = 32.1; HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{41}H_{67}N_2P_2B_2$: 671.4974 (100.0%); found: 671.4977 (100.0%).

Prior to the catalytic test, the borane protected phosphane **2c′** (50 mg, 0.075 mmol) was placed into a J Young flask under argon. Dry DCM (3 mL) and diethylamine (5 mL) were added and the flask was sealed. The reaction mixture was stirred at 50 °C for 24 h. It was cooled down, silica (2 g) was added and the volatiles were removed. The residue was placed at the top of a short silica column (6 g) and eluted with hexane/EtOAc 4:1 + 0.1% Et_3N to give a white solid (30 mg, 64%) which was briefly checked by ^{1}H and ^{31}P NMR and immediately used in catalysis. ^{1}H NMR (300 MHz, CD_2Cl_2): 0.75–2.04 (m, 44H, *Cy*), 2.14 (s, 6H, CH_3), 4.09 (s, 2H, NCH_2N) 4.25 (d, ^3J = 16.7 Hz, 2H, endo CH_2N), 4.39 (d, ^3J = 16.6 Hz, 2H, exo CH_2N), 6.61 (s, 2H, Ar–*H*), 6.93 (s, 2H, Ar–*H*); ^{31}P NMR (121 MHz, CD_2Cl_2): δ [ppm] = −14.9.

4.2.4. Synthesis of rac-4,10-bis(di-tert-butylphosphino)-2,8-dimethyl-6,12-dihydro-5,11-methanodibenzo[b,f][1,5]diazocine [2d]

In the glove-box, a Schlenk flask was charged with **1** (204 mg mg, 0.5 mmol), $Pd(OAc)_2$ (9.5 mg, 4.2 mmol, 4.2 mol%), NaO*t*-Bu (115 mg, 1.2 mmol, 2.4 equiv), (*t*Bu)$_3$P (10.2 mg, 5 mmol, 5 mol%) and (*t*Bu)$_2$PH (146.2 mg, 1.0 mmol, 2 equiv). Schlenk flask was taken out of the glove-box, dry toluene (2 mL) was added and the reaction mixture was stirred at 100 °C for 24 h under argon. It was then cooled down to room temperature and Et_2O (10 mL) was added and the mixture was transferred into a separate funnel. The reaction vessel was rinsed with diethyl ether (2 × 20 mL). The combined ether layers were washed with water (2 × 10 mL) and brine (2 × 10 mL). The aqueous layers were back extracted with ether (20 mL). The combined ether layers were dried over $MgSO_4$ and the organic solvent was removed under reduced pressure. The crude material was purified via recrystalization (hexane/ethyl acetate, 1:1) to give a white solid (75 mg, 26%).

^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 1.17 (d, $^3J_{H-P}$ = 11.4 Hz, 18H, (CH_3)$_3$), 1.36 (d, $^3J_{H-P}$ = 11.7 Hz, 18H, (CH_3)$_3$), 2.25 (s, 6H, CH_3), 4.16 (s, 2H, NCH_2N) 4.36 (d, ^3J = 17.1 Hz, 2H, endo CH_2N), 4.61 (d, ^3J = 17.1 Hz, 2H, exo CH_2N), 6.72(s, 2H, Ar–*H*), 7.36 (s, 2H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 21.1 (Ar–*C*H$_3$), 29.8 (d, J_{C-P} = 14.3 Hz, C(*C*H$_3$)$_3$), 31.5 (d, J_{C-P} = 24.9 Hz, *C*(CH$_3$)$_3$), 31.8 (d, J_{C-P} = 16.2 Hz, C(*C*H$_3$)$_3$), 33.3 (d, J_{C-P} = 23.9 Hz, *C*(CH$_3$)$_3$), 58.6 (d, J_{C-P} = 11.7 Hz, *C*H$_2$N), 67.4 (NCH$_2$N), 128.4, 128.8 (d, J_{C-P} = 5.9 Hz), 131.8, 132.5 (d, J_{C-P} = 24.5 Hz), 134.8 (d, J_{C-P} = 4.0 Hz), 151.2; ^{31}P NMR (121.5 MHz, $CDCl_3$): δ [ppm] = 15.9; HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{33}H_{53}N_2P_2$: 539.3678; found: 539.3692.

4.3. Synthesis of $(PdCl_2)_2$(2a) [3a]

A Schlenk flask was charged with ligand **2a** (31 mg, 0.05 mmol) and [$PdCl_2$(cod)] (28.6 mg, 0.10 mmol, 2 equiv) under argon. DCM (5 mL) was added and the resulting mixture was stirred for 4 h at RT. It was filtered through a pad of celite and pentane was added. The precipitation was filtered off, washed with pentane and dried to give **3a** as a yellow solid (48 mg, 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ [ppm] = 2.26 (s, 6H, CH_3), 4.15 (d, ^3J = 16.6 Hz, 2H, endo CH_2N), 5.99 (d, ^3J = 16.6 Hz, 2H, exo CH_2N), 6.12 (s, 2H, NCH_2N), 6.82 (s, 2H, Ar–*H*), 7.12 (d, ^3J = 10.5 Hz, 2H, Ar–*H*), 7.48–7.53 (m, 4H, Ar–*H*), 7.62–7.73 (m, 10H, Ar–*H*), 7.78–7.82 (m, 2H, Ar–*H*), 8.09–8.14 (m, 4H, Ar–*H*); ^{13}C NMR (101 MHz, $CDCl_3$): δ [ppm] = 20.5 (*C*H$_3$), 63.5 (*C*H$_2$N), 72.5 (NCH$_2$N), 117.2, 126.2 (d, J_{C-P} = 18.0 Hz), 126.3

(d, $J_{C-P} = 9.5$ Hz), 126.7, 127.0, 128.2, 128.7, 129.0 (d, $J_{C-P} = 12.9$ Hz), 129.8 (d, $J_{C-P} = 11.7$ Hz), 131.9, 132.6 (d, $J_{C-P} = 2.9$ Hz), 132.9 (d, $J_{C-P} = 2.7$ Hz), 133.6 (d, $J_{C-P} = 10.7$ Hz), 134.0 (d, $J_{C-P} = 11.8$ Hz), 134.7, 141.8 (d, $J_{C-P} = 7.2$ Hz), 149.5 (d, $J_{C-P} = 16.1$ Hz); ^{31}P NMR (162 MHz, $CDCl_3$): 36.1 (d, $J_{H-P} = 10.9$ Hz); HRMS (ESI): *m/z* $[M + NH_4]^+$ calcd for $C_{41}H_{40}$ $Cl_4N_3P_2Pd_2$: 991.9508; found: 991.9489.

4.4. General procedure for Suzuki cross-coupling

A Schlenk flask was charged with aryl halide (1.5 mmol), arylboronic acid (2.25 mmol, 1.5 equiv), K_3PO_4 (3.0 mmol, 2 equiv), $Pd(OAc)_2$ (0.03 mmol, 2 mol%), ligand (0.015 mmol, 1 mol%), evacuated and back filled with argon (3×). Dry THF (3.0 mL) was then added. The resulting mixture was stirred at 70 °C under argon for a specified time and then cooled down to room temperature. It was diluted with DCM (50 mL), filtered over a celite plug and evaporated under reduced pressure to give a crude material which was purified via column chromatography on silica gel.

4.4.1. 1,1′-Biphenyl

White solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.37(m, 2H, Ar–*H*), 7.47 (m, 4H, Ar–*H*), 7.62 (m, 4H, Ar–*H*), ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 127.2, 127.3, 128.9, 141.3, MS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_{10}$: 154.07; found: 154.0.

4.4.2. 4-Nitro-1,1′-biphenyl

White solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.43–7.53 (m, 3H), 7.63 (dd, $^3J = 8.1$ Hz, $^4J = 1.4$ Hz, 2H), 7.74 (d, $^3J = 8.7$ Hz, 2H), 8.30 (d, $^3J = 8.7$ Hz, 2H); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 124.1, 127.4, 127.8, 128.9, 129.2, 138.8, 147.6; MS (EI): *m/z* $[M]^+$ calcd for $C_{12}H_9NO_2$: 199.0; found: 199.0.

4.4.3. 2-Methyl-1,1′-biphenyl

White solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.33(s, 3H, CH_3), 7.27–7.33 (m, 4H, Ar–*H*), 7.35–7.40 (m, 3H, Ar–*H*), 7.42–7.47 (m, 2H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 20.5, 125.8, 126.8, 127.3, 128.1, 129.2, 129.8, 130.3, 135.4, 141.9, 142.0; MS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_{12}$: 168.1; found: 168.1.

4.4.4. 2,6-Dimethyl-1,1′-biphenyl

Colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 2.07(s, 6H, CH_3-*H*) 7.11–7.20 (m, 5H, Ar–*H*), 7.33–7.38 (m, 1H, Ar–*H*), 7.42–7.47 (m, 2H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 20.8, 126.6, 127.0, 127.3, 128.4, 129.0, 136.1, 141.1, 141.9; MS (EI): *m/z* $[M]^+$ calcd for $C_{14}H_{14}$: 182.1; found: 182.1.

4.4.5. 2′-Chloro-[1,1′-biphenyl]-4-carbonitrile

White solid; ^{1}H NMR (300 MHz, $CDCl_3$): δ [ppm] = 7.32–7.39 (m, 3H), 7.49–7.54 (m, 1H), 7.56 (d, $^3J = 8.2$ Hz, 2H, Ar–*H*), 7.75 (d, $^3J = 8.2$ Hz, 2H, Ar–*H*); ^{13}C NMR (75 MHz, $CDCl_3$): δ [ppm] = 111.5, 118.8, 127.2, 129.6, 130.3, 130.3, 131.0, 131.9, 132.2, 132.7, 133.4, 138.7, 144.0. MS (EI): *m/z* $[M]^+$ calcd for $C_{13}H_8NCl$: 213.0; found: 213.0.

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Appendix A. Supplementary material

CCDC 912274 (Pd-complex **3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif and are also available in the supporting information for this article.

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