Heterogeneous & Homogeneous & Bio- & Nano-

CHEMCATCHEM

CATALYSIS

Accepted Article

Title: Palladium-catalyzed C2-H arylation of unprotected (N-H)-indoles "on water" using primary diamantyl phosphine oxides as a new class of PPO ligands

Authors: Oana Moncea, Didier Poinsot, Andrey A Fokin, Peter R Schreiner, and Jean Cyrille Hierso

To be cited as: *ChemCatChem* 10.1002/cctc.201800187

Link to VoR: http://dx.doi.org/10.1002/cctc.201800187

A Journal of

ChemPubSoc Europe

WILEY-VCH

www.chemcatchem.org

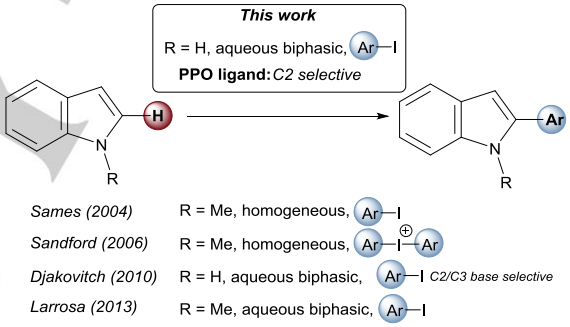
Palladium-catalyzed *C2*–H arylation of unprotected (*N*–H)-indoles "on water" using primary diamantyl phosphine oxides as a new class of PPO ligands

Oana Moncea,[a, b] Didier Poinsot,[b] Andrey A. Fokin,[b, c] Peter R. Schreiner,*[b] and Jean-Cyrille Hierso*[a, d]

Abstract: We present the palladium-catalyzed arylation of (*N*–H)-indoles with functionalized haloarenes "on water" using hitherto untested primary diamantyl phosphine oxides (PPO) as ligands. Remarkable *C2*–H arylation selectivity was achieved employing functionalized iodoarenes and *N*-unprotected indoles. We provide evidence that the *in situ* generated oxide of (9-hydroxydiamant-4-yl)phosphine **L1** is key for the reaction efficiency by comparison of a set of diamantane-based compounds structurally related to **L1**. Our results demonstrate the power of the new PPO ligands for the C–H functionalization of unprotected (*N*–H)-heterocycles.

Introduction

Heterocycles are building blocks in biologically active compounds and in molecular materials with valuable electronic or optical properties.[1] Because of the necessity to provide cleaner, more convergent, and less costly heterocycle syntheses, catalytic systems based on transition metals have been developed.[2] Palladium catalysis has especially contributed to the straightforward synthesis and functionalization of indoles.[1, 3] Arylindoles are recurrent motifs in biologically active molecules as well as pharmaceuticals[2k, 4] and have traditionally been prepared using cross-coupling strategies. Development of C–H arylation allows the direct functionalization of indoles thus enabling the simple synthesis of aryl-substituted indoles.[5] An important breakthrough in the selective *C2*–H functionalization of indoles (**Scheme 1**) was the use of (*N*)-protected indoles in organic solvents at temperatures higher than 120 °C.[5a] The use of highly reactive bisaryl salts[5c] or large amounts of silver additives such as Ag_2O[5h] or silver carboxylate salts[6] enables (*C*–H)-arylation at room temperature and in water. Djakovitch's group further developed this approach under heterogeneous conditions with a Pd/zeolite supported system in dioxane[7] and "on water" after careful screening of organophosphine ligands and bases for mastering *C2*- and *C3*-arylation selectivity.[8] The current state-of-the art indicates sustainable conditions are actively being explored,[5c, 9] but limitations clearly remain and concern most often (*N*)-protection,[9a, 9c] the need for addition of over stoichiometric amounts of metal additives and/or surfactants,[9b, 9c] and the impracticable use of oxidation reagents such as diaryliodonium salts in excess.[5c, 9d] In this context, further development of sustainable catalytic systems available for arylating unprotected indoles selectively among *N*–H, *C2*–H, and *C3*–H bonds is clearly desirable, and may rely on a new generation of ligand supported palladium catalysts.



Scheme 1. Palladium catalyzed (*N*–H)-indole *C2*-arylation.

Ackermann's group reported palladium complexes derived from secondary adamantyl phosphine oxide (SPO) $(1\text{-Ad})_2P(O)H$ (**A**, **Figure 1**) as air stable catalysts for *C*–H arylation and benzylation of electron-deficient oxazole or oxazoline heterocycles.[10] Unfortunately, for the indole moiety this catalyst was found ineffective although other highly hindered heteroatom-substituted SPOs (**B**, **Figure 1**) combined with palladium allowed *C3*-arylation of (*N*–H)-indoles with aryl bromides at fairly moderate temperature without additives.[11] Lately, bis(diamantyl)-based SPO ligands (**C**, **Figure 1**) enabled the C–H functionalization of electron rich oxazolines from aryl halides.[12]

We have previously reported synthetic access to structurally related primary diamantyl phosphines $(4\text{-DiAd})PH_2$ from the facile reduction of phosphonic dichlorides with $LiAlH_4$.[13] The reaction tolerates the presence of 9-chloro or 9-hydroxy groups on the diamondoid scaffold, and the resulting functionalized primary diamantyl phosphines (9-hydroxydiamant-4-yl)phosphine (**L1)** and (9-chlorodiamant-4-yl)phosphine (**L6**) (**Figure 1**) were found to be reasonably air-stable, rendering them potentially useful as ligands for transition metal catalysis.

Herein, we present the use of such preligands in palladium catalysis for unprotected (*N*–H)-indoles C–H arylation under aqueous conditions.

[a] *Institut de Chimie Moléculaire de l'Université de Bourgogne (ICMUB), UMR-CNRS 6302, Université de Bourgogne Franche-Comté, 9 avenue Alain Savary, 21078 Dijon, France*

[b] *Institute of Organic Chemistry, Justus-Liebig-University, Heinrich-Buff-Ring 17, 35392 Giessen, Germany*

[c] *Department of Organic Chemistry, Igor Sikorsky Kiev Polytechnic Institute, Prospekt. Pobedy 37, 03056 Kiev, Ukraine*

[d] *Institut Universitaire de France (IUF), 103 Bd. Saint Michel, 75005 Paris Cedex 5, France*

Supporting information for this article is given via a link at the end of the document.

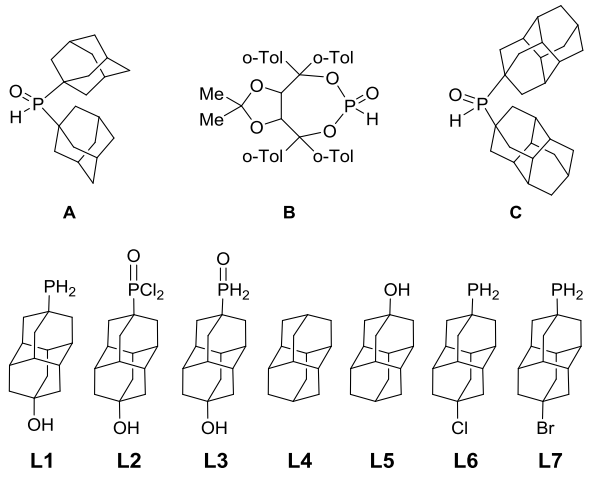


Figure 1. Known SPO ligands (**A**–**C**), together with diamantyl derivatives used herein as ligands in palladium catalysis (**L1**–**L7**).

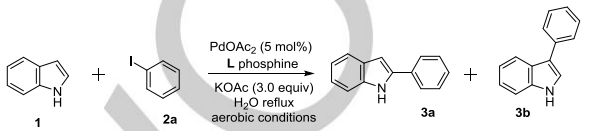
Results and Discussion

We investigated the selective C–H arylation reaction of unprotected (*N*–H)-indole with palladium acetate and **L1** under aqueous conditions. The use of water as a solvent for C–H arylation reactions can result in an increase in chemoselectivity as well as rates, and may be advantageous from a sustainable chemistry perspective.[14] When reactants are water insoluble, the "on-water" concept –often associated with the contributions of Sharpless–[15] applies, and the hydrogen-bonding across the phase tends to increase the reaction rate.[16] Palladium acetate together with **L1** in aqueous conditions are expected to form a palladium phosphinous acid complex similar to the one described with adamantyl based SPO ligands.[3c]

We initiated our screening by coupling the unprotected indole **1** with iodobenzene **2** in the presence of $Pd(OAc)_2$. In this case, regioselectivity concerns *N*–H, *C2*–H, and *C3*–H functionalization but the reaction conditions can be tuned in order to selectively obtain one of the products[8] and for all our experiments, no *N*–H coupling product was observed by ^{1}H NMR or GC-MS. We used KOAc as a cheap base and water under reflux conditions to examine the performance of **L1** (**Table 1**). Previously, ligands like PPh_3 (10 mol%) and chelating diphosphine bis(diphenylphosphino)methane (dppm, 5 mol%) combined with palladium gave *C2*–H coupling in indole arylations with good yields;[8] these are currently the best ligands under biphasic catalytic conditions. Therefore, we also compared **L1** with PPh_3 and chelating diphosphine bis(diphenylphosphino)propane (dppp). In the absence of palladium but with **L1** no reaction occurred. In the presence of palladium without ligand, the yield was limited to 30% (**Table 1**, entry 1).

Good *C2*–H arylation selectivity for product **3a** was obtained with KOAc at 5 to 10 mol% ligand loading. While PPh_3 (**Table 1** entry 2) and the chelating diphosphine dppp (**Table 1** entry 3), provided coupling with 68% and 42% yield, respectively, 10 mol% of **L1** gave 81% yield (entry 4). These results were confirmed by experiments in which the amount of phosphine ligand was decreased to 5.0 mol% (entries 5–7) and 2.5 mol% (entries 8–10). At this lower amount, **3a** formed in 80% yield showing no efficiency decrease. We optimized the amount of **L1** needed in the reaction by monitoring phosphine/palladium molar ratio (**Figure S1**).

Table 1 Screening of primary diamantyl phosphine **L1** for indole C–H arylation.



Entry	Ligand	mol%	Yield (%)[a]	Selectivity[c]
1	—	—	30	19:1
2	PPh_3	10	68	>20:1
3	dppp	10	42	9:1
4	**L1**	10	81	19:1
5	PPh_3	5	59	>20:1
6	dppp	5	59	19:1
7	**L1**	5	83	>20:1
8	PPh_3	2.5	60	19:1
9	dppp	2.5	48	19:1
10	**L1**	2.5	80 (72)[b]	>20:1

Conditions: **1** (0.4 mmol, 50 mg), **2a** (0.5 mmol, 102 mg), base (3 equiv.), [Pd] (5 mol%), H_2O (1 mL), 100 °C, 30 h. [a] Yield from standardized ^{1}H NMR; [b] Yield of isolated product; [c] **3a**:**3b** selectivity determined by GC;

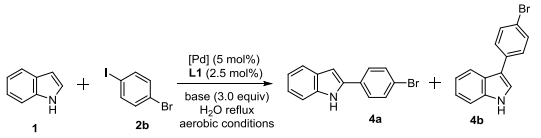
With these preliminary conditions in hand, we considered the effects of the palladium source and the base (**Table 2**). We also included the coupling of 1-bromo-4-iodobenzene **2b** to assess chemoselectivity: no coupling product at the bromine function was observed. Various Pd(II) sources were used: $PdCl_2$, [Pd(η^3-C_3H_5)(η^5-C_5H_5)], and [Pd(η^3-C_3H_5)Cl]$_2$). They did not affect the yields much (79–87%, **Table 2** entries 1–4). The use of $Pd(OAc)_2$ is preferred owing to its availability and low cost. From the various bases explored (CsOAc, KOH, K_2CO_3, $KHCO_3$, NaOH and LiOH, **Table 2** entries 5–10, respectively) the most effective was $KHCO_3$ for which full conversion to *C2*-arylation product was achieved leading to 92% yield of isolated **4a** (entry 10).

Although $KHCO_3$ has been reported to be responsible for loss in *C2*-arylation/*C3*-arylation selectivity in other indole arylation,[8] this was not the case with L1. "On water" reactions usually occur when substrates are poorly soluble in this solvent. Accordingly, we measured palladium leakage into water by ICP-MS after the reaction (**Table S1**). Using LiOH as base resulted in significant palladium leakage but with the other bases, the amount of palladium was less than 5 ppm.

We further examined which features of **L1** play a critical role for efficient coupling. We focused our attention on (*1*) whether the primary phosphine function is essential or could be advantageously substituted by other groups, (*2*) if the hydroxy group was necessary because of strong hydrogen bonding in

water, (*3*) if the diamantane framework alone (or hydroxylated) plays a role beyond the phosphine donor atom, and (*4*) what the effect of oxidation of the $–PH_2$ group would be. The last issue is important since during our optimization studies we observed that aerobic conditions are preferable (**Tables S2** and **S3**) while degassed solvent and reactions under inert atmosphere were found much less effective. These questions could be answered by using a specifically chosen set of diamantane-based compounds, as shown in **Table 3**.

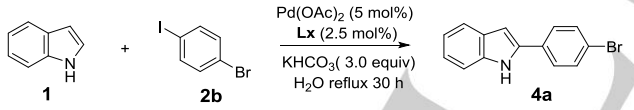
Table 2 Screening of palladium sources and bases for coupling **1** and **2b** using **L1**.



Entry	Pd source	Base	Yield (%)[a]	Selectivity[c]
1	$Pd(OAc)_2$	KOAc	86 (80)[b]	15:1
2	$PdCl_2$	KOAc	87	>20:1
3	$[Pd(\eta^3\text{-}C_3H_5)(\eta^5\text{-}C_5H_5)]$	KOAc	81	>20:1
4	$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$	KOAc	79	>20:1
5	$Pd(OAc)_2$	CsOAc	84	>20:1
6	$Pd(OAc)_2$	KOH	25	1:4
7	$Pd(OAc)_2$	K_2CO_3	55	1.5:1
8	$Pd(OAc)_2$	NaOH	44	>20:1
9	$Pd(OAc)_2$	LiOH	34	1:1
10	$Pd(OAc)_2$	$KHCO_3$	98 (92)[b]	17:1

Conditions: **1** (0.4 mmol, 50 mg), **2b** (0.5 mmol, 150 mg), base (3 equiv.), [Pd] (5 mol%), **L1** (2.5 mol%), H_2O (1 mL), 100 °C, 30 h. [a] Yield from standardized ^{1}H NMR; [b] Yield of isolated product; [c] **4a**:**4b** selectivity

Table 3 Influence of diamantane derivatives in the direct *C2*-arylation of unprotected indoles.

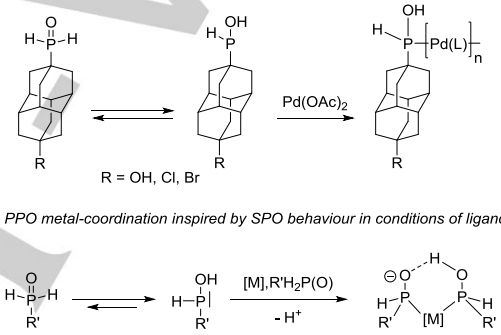


Entry	Ligand (2.5 mol%)	Yield **4a** (%)[a]
1	—	45[c]
2	**L1**	94 (88)[b]
3	**L2**	48
4	**L3**	89 (82)[b]
5	**L4**	45
6	**L5**	45
7	**L6**	90
8	**L7**	90

Conditions: **1** (2.0 mmol), **2b** (2.4 mmol), $Pd(OAc)_2$ (5 mol%), $KHCO_3$ (6.0 mmol), distilled water (2 mL) in a sealed screw cap vial of 5 mL at 100 °C during 30 h under air. [a] Yields determined by standardized NMR ^{1}H; [b] Yield of isolated product; [c] 48 h reaction time.

We also tested diamantyl dichlorophosphonate **L2**, which is the precursor for **L1**. Only 48% yield of **4a** was obtained indicating that **L2** does not interfere with this reaction (**Table 3**, entry 3). Unsurprisingly it is neither ligand nor preligand for palladium catalysts.

Phosphine oxide **L3** is the oxidation product of **L1** and can be readily obtained by bubbling air in a dichloromethane solution of **L1** at room temperature.[17] Because of the aerobic conditions used in refluxing water, we assume that **L3** forms *in situ* from **L1**. This assumption is somewhat corroborated by the results obtained when using **L3** as a ligand (**Table 3**, entry 4) which are in the same range of values as for **L1**. This oxide is likely to be the efficient ligand for palladium catalysis since our experiments have shown that using **L1** under strictly anaerobic conditions performs poorly (**Table S2**). A tautomeric equilibrium between pentavalent and trivalent phosphorus species has been described previously for diamondoid SPO ligands.[10a, 12] We assume that this equilibrium can take place also for **L3** (**Scheme 2**) and in the presence of late transition metals that coordinate to trivalent phosphorus.



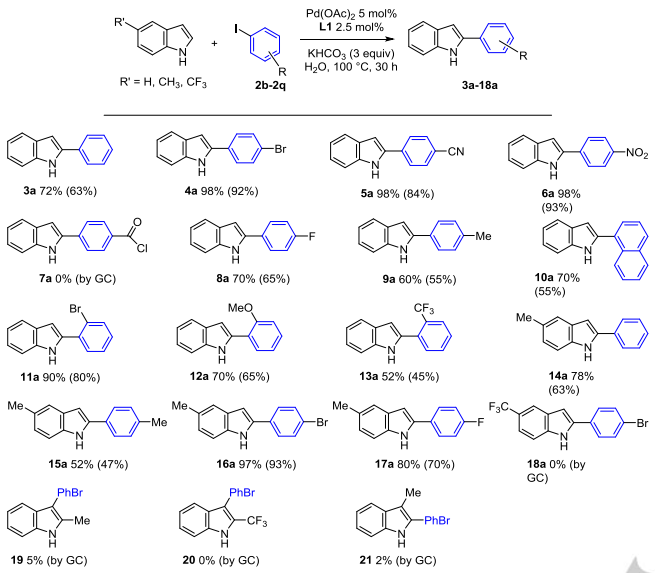
Scheme 2. Tautomeric forms of diamantane phosphine oxide **L3** and suggested coordination to palladium.

NMR solution studies using the reaction conditions or pure D_2O could not be employed to provide evidence for this equilibrium because of solubility issues. We thus isolated the palladium complexes that form upon reaction of **L1** or **L3** with ¼$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$. The coordinated species were found to be mostly insoluble in $CDCl_3$, CD_2Cl_2, CD_3OD, D_2O, $(CD_2)_4O$, CD_3CN, and $(CD_3)_2SO$ supporting a polymeric nature of the complex (**Scheme 2**). The preparation and characterization by FT-IR and ICP-MS of these complexes is detailed in the ESI. ICP-MS analysis indicates an expected molar ratio of 2:1 for Pd:P in agreement with our catalytic conditions. The data collected might be associated with an oligomeric form of the complex which still remains to be clarified.

Further screening of related preligands demonstrated that the presence of trivalent phosphorus (belonging to PH_2 from **L1** or to PH(OH) from **L3**) is essential for the reaction to proceed efficiently. This was confirmed by the poor results obtained with diamantane **L4** and hydroxydiamantane **L5**, which add nothing to *C2*–arylation reaction (**Table 3** entries 5–6, respectively). Conversely, primary diamantyl phosphines **L6** and **L7** displayed an activity comparable to that of **L1**. We already reported that electron-withdrawing functions at remote positions of the

diamantane cage are essential for enhancing air-stability in the solid state of primary diamantyl phosphines.[13]

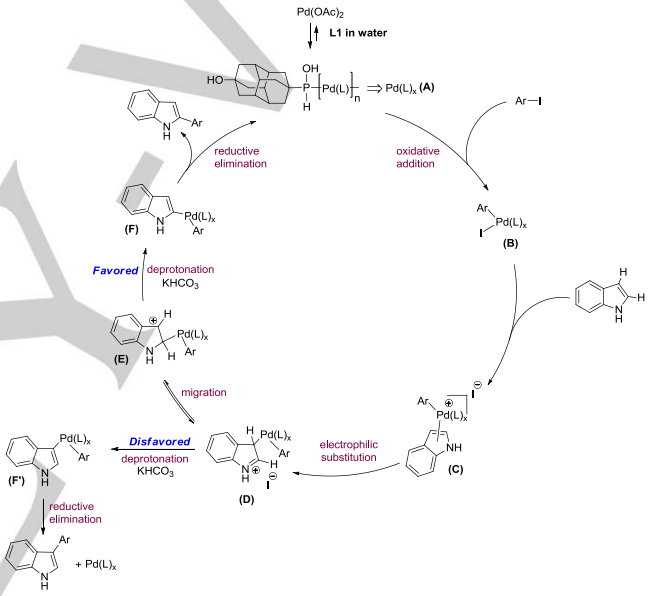
Having established that **L1** oxidizes quickly under the catalytic conditions to **L3**, thereby promoting the formation of **3a** and **4a**, we further explored the scope of the coupling reaction (**Scheme 3**).



Scheme 3. *C2*-arylation of unprotected indole using primary diamondoid phosphines as ligands. Conditions: indole (2.0 mmol), aryl iodide (2.4 mmol), $Pd(OAc)_2$ (0.05 mmol), **L1** (0.025 mmol), $KHCO_3$ (6.0 mmol), H_2O (2 mL) at 100 °C during 30 h; NMR ^1H yields and yields of isolated products in brackets.

At 2.0 mmol scale, aryl iodides incorporating various electron-withdrawing (bromo, fluoro, cyano, and nitro), or electron-donating (methyl, naphthyl) groups in the *para*-position provided good yields of the desired *C2* products. The catalytic coupling system did not tolerate chloro acetyl group (**7a** does not form). More challenging *ortho*-substituted aryl iodides[18] could also be successfully coupled, tolerating bromide (**11a**, 80%), methoxy (**12a**, 65%), and trifluoromethyl (**13a**, 45%) functions. Functionalized indole moiety with methyl group at *C5* was coupled successfully with electron deficient and electron rich aryl iodides. Conversely, the electron-withdrawing trifluoromethyl group at *C5* was found unfavorable for *C2*–H indole arylation with electron deficient aryl iodides(**18a**). Bromoarenes were also tested as coupling partners for this reaction (**Table S5**). Using the same catalytic conditions we achieved arylindole formation in 5–80% yields with *para*-substituted bromoarenes, but we observed a loss of the *C2*/*C3* selectivity. Notably, Manabe's group reported recently ligand-directed *C3*-arylation selectivity by tuning biphenyl phosphines design with a remote intervening OH group.[19]

Detailed mechanistic studies rationalizing *C2* vs *C3* regioselectivity in palladium-catalyzed C–H arylation of indoles have been reported for systems using $Pd(OAc)_2$ and PPh_3 ligands in organic solvents.[20] On this basis we propose a mechanism depicted in **Scheme 4** in which electrophilic substitution at *C3* is achieved by a cationic palladium catalyst holding an aryl substituent (from intermediate **C** in **Scheme 4**). Intermediate **D** is expected to follow two different pathways: (a) a *C3*–C2 migration of the palladium center favored by weak bases such as $KHCO_3$, affording complex (**E**) that leads to the C2-regioisomer; (b) a re-aromatisation preferred in the presence of strong bases such as OH^- affording complex (**F'**) that leads to the C3-regioisomer. Compared to a direct carbometallation mechanism via neutral species, this pathway justifies the formation of both the *C2* and *C3* products observed (**Table 1**).[20a] In addition, formation of cationic species are favored in water. Thereby, the combination of $KHCO_3$ and the bulky alkyl diamantyl-based PPO ligand would much favor the deprotonation step from **E** *vs* deprotonation from **D**, and thus a reductive elimination towards the *C2* arylated product.



Scheme 4. Proposed mechanism for the *C2*-arylation of unprotected indole using diamantyl PPO as ligand.

We investigated this mechanism by blocking the *C2*–H or *C3*–H positions on the indole ring. Blocking the *C2*–H position first with an electron-donating (**19**) and then with an electron withdrawing (**20**) group shows very limited conversion (5% in the case of electron rich indole moiety) towards the *C3*-regioisomer. This also correlates with the absence of diarylation products at both *C2* and *C3* under the present catalytic conditions. When blocking the *C3*-position on the indole ring with an electron-donating group, we were expecting full conversion into **21** but only 2% conversion was achieved. This result strongly supports the idea that a palladium-*C3* to *C2* migration followed by deprotonation process has to take place but is inhibited by the presence of methyl group in the *C3* position.

Conclusions

We describe the direct C–H arylation of unprotected indoles "on water" under aerobic conditions using new primary phosphine oxide ligands. High *C2*-selectivity was achieved with bulky primary diamantyl phosphine **L1** and $Pd(OAc)_2$. Excellent functional group tolerance was observed with aryl iodides as coupling partners. Electron-donating and electron-withdrawing groups were tolerated at *para* and *ortho*-positions on the iodoarenes. Control investigations of related ligands established the superior efficiency of **L1** in its *in situ* oxidized primary phosphine oxide form. The trivalent phosphorus atom of **L1** or **L3** and the presence of the OH group are necessary for achieving superior performances in *C2*-arylation of (*N*–H)-indoles "on water". $KHCO_3$ as base allows the migration step to take place thus favoring *C2*-arylation process. The efficient use of primary phosphines (often assumed to be pyrophoric) as ligands in metal catalysis, under aerobic conditions in water, is quite unusual and will be the subject of further investigations with other branched alkyl diamondoid cages.

Experimental Section

Synthesis of functionalized diamantanes.

L5: 4-Hydroxydiamantane. Obtained analytical data were identical to literature data.[21]

L2: (9-Hydroxydiamant-4-yl)phosphonic dichloride. Obtained analytical data were identical to literature data.[13]

L7': (9-Bromodiamant-4-yl)phosphonic dichloride. 9-Hydroxydiamant-4-yl phosphonic dichloride (**L2**) (0.470 g, 1.47 mmol) was placed in a 20 mL round bottom flask and cooled to a temperature between 0 and −10 °C while 15 mL DCM were added followed by a solution of thionyl bromide (0.5 mL, 5.88 mmol) in DCM. The solution was stirred at r. t. for 72 h and afterwards poured on 40 mL water with 10 mL DCM. The mixture was stirred until it became colorless (30 min). The phases were separated and the aqueous phase was extracted with DCM (3 × 10 mL) and the combined extracts were dried over $MgSO_4$. The solvent was removed in vacuo, affording (9-bromodiamant-4-yl) phosphonic dichloride (**L3'**) (0.510 g, 90%) as a white powder.^{1}H NMR (300 MHz, $CDCl_3$): *δ*= 2.28−2.23 (m, 6H), 1.99−1.92 (m, 9H), 1.86−1.80 (m, 3H);^{13}C NMR (75 MHz, $CDCl_3$): *δ* = 62.2 (s, C), 48.6 (d, J = 2.5 Hz, CH_2), 44.4 (d, J = 92.5 Hz, C), 39.8 (d, J = 2.5 Hz, CH), 34.9 (d, J = 16.0 Hz, CH), 34.9 (d, J = 3.5 Hz, CH_2);^{31}P{^{1}H} NMR (121 MHz, $CDCl_3$): *δ*= 64.63 ppm. HRMS (ESI) $([M+Na])^+$ calcd. for $C_{14}H_{18}BrCl_2NaOP$ 404.9547; found: 404.9552.

L3: (9-Hydroxydiamant-4-yl)phosphine oxide. Obtained analytical data were identical to literature data.[17]

L7: (9-Bromodiamant-4-yl)phosphine. 9-Bromodiamant-4-yl phosphonic dichloride (**L7'**) (0.054 g, 0.14 mmol) was placed in a 5 mL two-neck flask under argon and cooled to a temperature between −78 and −60 °C while 1 mL dry THF was added. To the colorless solution, a $LiAlH_4$ solution (0.18 mL, 1 M in THF, 0.18 mmol, 1.3 equiv) was added dropwise over the course of 10 min. The mixture was stirred at −10 °C for 5 h. The reaction was quenched with HCl (5%, 0.1 mL) followed by extraction with cold dichloromethane (3 × 3 mL) and was dried over $MgSO_4$. The solvent was removed in vacuo, affording (9-bromodiamant-4-yl) phosphine (**L4**) (0.038 g, 79%) as a white powder. ^{1}H NMR (600 MHz, $CDCl_3$): *δ*= 2.90 (d, 2H, J_{P-H} = 164.4 Hz), 2.37−2.27 (m, 6H), 1.89−1.73 (m, 12H);^{13}C NMR (150 MHz, $CDCl_3$): *δ*= 64.7 (s, C), 49.2 (s, CH_2), 44.6 (s, CH_2), 40.3 (s, CH), 36.5 (s, CH), 26.7 (s, C);^{31}P{^{1}H} NMR (242 MHz, $CDCl_3$): *δ*= −85.9 ppm. HRMS (ESI) $([M+H])^+$ calcd. for $C_{14}H_{21}BrP$ 299.0558; found: 299.0552.

L6: (9-Chlorodiamant-4-yl)phosphine and **L1: (9-hydroxydiamant-4-yl)phosphine** were synthesized according to the procedure described in the literature; obtained analytical data were identical to literature data.[13]

General procedure for the direct *C2*-arylation of unprotected indole.

Indole (2.0 mmol, 0.234 g), aryl iodide (2.4 mmol), $Pd(OAc)_2$ (0.05 mmol), ligand **Lx** (0.025 mmol), $KHCO_3$ (6.0 mmol) and H_2O (2 mL) were introduced in screw cap vial (5 mL). The resulting biphasic mixture was heated at 100 °C for 30 h. After this time, the mixture was cooled to room temperature and the excess of base was neutralized with HCl solution (1M). Ethyl acetate was added (5 mL) and the phases were separated. The aqueous phase was further extracted with ethyl acetate (3 x 10 mL) and the organic phases were dried over $MgSO_4$ and concentrated. The residue was dissolved in dichloromethane together with Celite® to form a solid deposit for column chromatography (hexane/ethyl acetate: 95/5) that afforded the desired product.

3a: 2-Phenylindole. Beige solid, ^{1}H NMR (500 MHz, DMSO-d^6) *δ*= 11.52 (s, 1H), 7.87 (d, ^{3}J = 7.4 Hz, 2H), 7.54 (d, ^{3}J = 7.8 Hz, 1H), 7.47 (t, ^{3}J = 7.8 Hz, 2H), 7.41 (d, ^{3}J = 8.1 Hz, 1H), 7.32 (t, ^{3}J = 7.4 Hz, 1H), 7.11 (ddd, ^{3}J = 7.9 and 7.1 Hz, ^{4}J = 0.9 Hz, 1H), 7.00 (ddd, ^{3}J = 7.7 and 7.1 Hz, ^{4}J = 0.6 Hz, 1H), 6.90 (d, ^{4}J = 1.6 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) *δ*= 137.6 (C), 137.1 (C), 132.2 (C), 129.0 (CH), 128.6 (C), 127.4 (CH), 125.0 (CH), 121.6 (CH), 120.1 (CH), 119.4 (CH), 111.3 (CH), 98.7 (CH); HRMS (ESI) ($[M+Na]^+$) calcd. for $C_{14}H_{11}NNa$: 216.0783; found: 216.0780.

4a: **2-(4-Bromophenyl)-indole.** Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) *δ*= 11.58 (s, 1H), 7.81 (d, ^{3}J = 10.0 Hz, 2H), 7.65 (d, ^{3}J = 10.0 Hz, 2H), 7.53 (d, ^{3}J = 10.0 Hz, 1H), 7.39 (d, ^{3}J = 10.0 Hz, 1H), 7.11 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J = 1.0 Hz, 1H), 7.00 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J = 1.0 Hz, 1H), 6.94 (d, J = 1.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) *δ*= 137.2 (C), 136.4 (C), 131.8 (CH), 131.5 (C), 128.5 (C), 126.9 (CH), 121.9 (CH), 120.3 (C), 120.2 (CH), 119.5 (CH), 111.3 (CH), 99.3 (CH); HRMS (ESI) ($[M]^+$) calcd. for $C_{14}H_{10}BrN$: 270.9991; found: 270.9994.

5a: 2-(4-Benzonitrile)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) *δ*= 11.84 (s, 1H), 8.31 (td, ^{3}J = 10.0 Hz, 2H), 8.11 (td, ^{3}J = 10.0 Hz, 2H), 7.60 (d, ^{3}J = 5.0 Hz, 1H), 7.45 (dd, ^{3}J = 5.0 and ^{4}J = 1.0 Hz, 1H), 7.18 (m, 2H), 7.04 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J = 1.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) *δ*= 142.6 (C), 137.7 (C), 136.5 (C), 135.6 (C) 132.8 (CH), 128.3 (d, J = 34.0 Hz, C), 125.3 (CH), 122.7 (CH), 120.6 (CH), 119.8 (CH), 118.9 (C), 111.6 (CH), 109.1 (C), 101.5 (CH); HRMS (ESI) ($[M]^+$) calcd. for $C_{15}H_{10}N_2$: 218.0838; found: 218.0836.

6a: 2-(4-Nitrophenyl)-indole. Yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) *δ*= 11.84 (s, 1H), 8.31 (td, ^{3}J = 10.0 Hz, 2H), 8.11 (td, ^{3}J = 10.0 Hz, 2H), 7.60 (d, ^{3}J = 5.0 Hz, 1H), 7.45 (dd, ^{3}J = 5.0 and ^{4}J = 1.0 Hz, 1H), 7.18 (m, 2H), 7.04 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J = 1.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) *δ*= 145.8 (C), 138.6 (C), 137.9 (C), 135.2 (C), 128.7 (d, J = 41.0 Hz, C), 125.5 (CH), 124.3 (CH), 124.2 (CH), 123.1 (CH), 120.8 (CH) 119.9 (CH), 111.7 (CH), 102.4 (CH); HRMS (ESI) ($[M]^+$) calcd. for $C_{14}H_{10}N_2O_2$: 238.0736; found: 238.0735.

8a: 2-(4-Fluorophenyl)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) δ= 11.52 (s, 1H), 7.90 (m, 2H), 7.52 (d, ^{3}J = 5.0 Hz, 1H), 7.39 (dd, ^{3}J = 10.0 and 5.0 Hz, 1H), 7.31 (t, ^{3}J = 5.0 Hz, 2H), 7.09 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J =1.0 Hz, 1H), 7.00 (ddd, ^{3}J = 10.0 and 5.0 Hz, ^{4}J = 1.0 Hz, 1H), 6.87 (d, J = 5.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) δ= 162.5 (C), 160.6 (C), 137.1 (C), 136.7 (C), 128.9 (C), 128.6 (CH), 126.9 (d, J = 9 Hz, CH), 121.5 (CH), 120.0 (CH), 119.4 (CH), 115.9 (CH), 115.73 (CH), 111.3 (CH), 98.7 (CH); HRMS (ESI) ([M+H]$^+$) calcd. for $C_{14}H_{11}FN$: 212.0870; found: 212.0869.

9a: 2-(4-Methylphenyl)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) δ= 11.45 (s, 1H), 7.75 (d, ^{3}J = 5.0 Hz, 2H), 7.49 (d, ^{3}J = 10.0 Hz, 2H), 7.38 (d, ^{3}J = 10.0 Hz, 1H), 7.26 (d, ^{3}J = 10.0 Hz, 1H), 7.06 (t, ^{3}J = 7.4 Hz, 1H), 6.97 (t, ^{3}J = 7.9 Hz, 1H), 6.80 (s, 1H), 2.34 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d^6) δ= 137.8 (C), 136.9 (C), 136.7 (C), 129.4 (CH), 128.7 (C), 124.9 (CH), 121.3 (CH), 119.8 (CH), 119.3 (CH), 119.4 (CH), 111.2 (CH), 98.0 (CH), 20.8 (CH_3); HRMS (ESI) ([M+H]$^+$) calcd. for $C_{15}H_{14}N$: 208.1169; found: 208.1121.

10a:2-(1-Naphthyl)-indole. Pale yellow solid, ^{1}H NMR (400 MHz, DMSO-d^6) δ= 11.57 (s, 1H), 8.31-8.35 (m, 1H), 7.97-8.04 (m, 2H), 7.72 (d, ^{3}J = 8.0 Hz, 1H), 7.45-7.64 (m, 4H), 7.46 (d, ^{3}J = 8.0 Hz, 1H), 7.16 (t, ^{3}J = 8.0 Hz, 1H), 7.07 (t, ^{3}J = 8.0 Hz, 1H), 6.74 (s, 1H); ^{13}C NMR (100 MHz, DMSO-d^6) δ= 136.7 (C), 136.4 (C), 133.5(C), 130.9 (C), 130.8 (C), 128.4 (CH), 128.3 (C), 128.1 (CH), 127.2 (CH), 126.7 (CH), 126.1 (CH), 125.5 (CH), 125.4 (CH), 121.4 (CH), 119.9 (CH), 119.2 (CH), 111.3 (CH), 102.4 (CH); HRMS (ESI) ([M+Na]$^+$) calcd. for $C_{18}H_{13}NNa$: 266.0940; found: 266.0940.

11a: 2-(2-Bromophenyl)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) δ= 11.40 (s, 1H), 7.77 (dd, ^{3}J = 8.0 Hz, ^{4}J = 1.0 Hz, 1H), 7.65 (dd, ^{3}J = 7.5 Hz, ^{4}J = 1.5 Hz, 1H), 7.58 (d, ^{3}J = 7.5 Hz, 1H), 7.52-7.48 (m, 1H), 7.41 (dd, ^{3}J = 8.0 Hz, ^{4}J = 1.0 Hz, 1H), 7.32 (td, ^{3}J = 7.5 Hz, ^{4}J = 1.5 Hz, 1H), 7.15- 7.10 (m, 1H), 7.04- 7.00 (m, 1H), 6.80 (d, ^{3}J = 2.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) δ= 136.4 (C), 135.8 (C), 133.7 (C), 133.6 (C), 131.3 (CH), 129.4 (CH), 127.9 (CH), 127.8 (C), 121.7 (CH), 121.5 (CH), 120.2 (CH), 119.3 (CH), 111.4 (CH), 102.7 (CH); HRMS (ESI) ([M+H]$^+$) calcd. for $C_{14}H_{11}BrN$: 272.0069; found: 272.0069.

12a: 2-(2-Methoxyphenyl)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) δ= 11.17 (s, 1H), 7.80 (dd, ^{3}J = 8.0 Hz, ^{4}J = 2.0 Hz, 1H), 7.52 (d, ^{3}J = 8.0 Hz, 1H), 7.44 (dd, ^{3}J = 8.0 Hz, ^{4}J = 0.5 Hz, 1H), 7.34-7.29 (m, 1H), 7.15 (m, 1H), 7.09-7.04 (m, 2H), 6.99-6.96 (m, 1H), 6.94 (br s,1H), 3.94 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d^6) δ= 156.0 (C), 136.3 (C), 134.5 (C), 128.6 (CH), 128.1 (C), 127.7 (CH), 121.2 (CH), 120.7 (CH), 120.6 (C), 119.8 (CH), 119.0 (CH), 112.0 (CH), 111.3 (CH), 101.5 (CH), 55.5 (CH_3); HRMS (ESI) ([M+H]$^+$) calcd. for $C_{15}H_{14}NO$: 224.1069; found: 224.1067.

13a: 2-(2-Trifluoromethylphenyl)-indole. Pale yellow solid, ^{1}H NMR (500 MHz, DMSO-d^6) δ= 11.43 (s, 1H), 7.88 (d, ^{3}J = 5.0 Hz, 1H), 7.78 (t, ^{3}J = 5.0 Hz, 1H), 7.69 (d, ^{3}J = 5.0 Hz, 1H), 7.64 (t, ^{3}J = 5.0 Hz, 1H), 7.57 (d, ^{3}J = 5.0 Hz, 1H), 7.41 (d, ^{3}J = 10.0 Hz, 1H), 7.14 (t, ^{3}J = 5 Hz, 1H), 7.03 (t, ^{3}J = 10.0 Hz, 1H), 6.56 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d^6) δ= 136.5 (C), 134.4 (C), 132.4 (CH), 132.3 (CH), 128.5 (CH), 127.9 (C), 127.2 (d, J = 30 Hz, C), 126.3 (d, J = 5Hz, CH), 125.2 (C), 123.0 (C), 121.6 (CH), 120.2 (CH), 119.3 (CH), 111.3 (CH), 102.6 (CH); HRMS (ESI) ([M+H]$^+$) calcd. for $C_{15}H_{11}F_3N$: 262.0838; found: 262.0834.

14a: 2-(4-phenyl)-5-methylindole. Pale yellow solid, ^{1}H NMR (400 MHz, DMSO-d^6) δ = 11.37 (s, 1H), 7.83 (d, ^{3}J = 8.0 Hz, 2H), 7.44 (t, ^{3}J = 8.0 Hz, 2H), 7.29 (m, 3H), 6.93 (dd, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 1H), 6.80 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d^6) δ = 137.6 (C), 135.5 (C), 132.3 (C), 128.9 (CH), 128.8 (C), 127.7 (CH), 127.2 (CH), 124.6 (CH), 123.1 (CH), 119.5 (CH), 110.9 (CH), 98.8 (CH), 21.2 (CH_3); HRMS (ESI) ([M-H]$^+$) calcd. for $C_{15}H_{12}N$: 206.0975; found:206.0976.

15a: 2-(4-Methylphenyl)-5-methylindole. Pale yellow solid, ^{1}H NMR (400 MHz, DMSO-d^6) δ = 11.30 (s, 1H), 7.72 (d, ^{3}J = 8.0 Hz, 2H), 7.26 (m, 4H), 6.89 (dd, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 1H), 6.73 (m, 1H), 2.34 (d, 6H); ^{13}C NMR (100 MHz, DMSO-d^6) δ = 137.7 (C), 136.5 (C), 135.3 (C), 129.5 (C), 129.3 (CH), 128.9 (C), 127.6 (C), 124.8 (CH), 122.9 (CH), 119.4 (CH), 110.8 (CH), 97.5 (CH), 21.1 (CH_3), 20.1 (CH_3) ; HRMS (ESI) ([M-H]$^+$) calcd. for $C_{16}H_{14}N$: 220.1131; found: 220.1132.

16a: 2-(4-Bromophenyl)-5-methylindole. Pale yellow solid, ^{1}H NMR (400 MHz, DMSO-d^6) δ = 11.42 (s, 1H), 7.79 (dt, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 2H), 7.63 (dt, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 2H), 7.31 (br s, 1H), 7.28 (d, ^{3}J = 8.0 Hz, 1H), 6.94 (dd, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 1H), 6.84 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d^6) δ = 136.3 (C), 135.6 (C), 131.7 (CH), 128.7 (C), 127.9 (C), 126.7 (CH), 123.5 (CH), 120.0 (C), 119.7 (C), 111.2 (CH), 111.0 (CH), 98.8 (CH), 21.2 (CH_3); HRMS (ESI) ([M-H]$^+$) calcd. for $C_{15}H_{11}BrN$: 284.0075; found:284.0080.

17a: 2-(4-Fluorophenyl)-5-methylindole. Pale yellow solid, ^{1}H NMR (400 MHz, DMSO-d^6) δ = 11.37 (s, 1H), 7.87 (dd, ^{3}J = 8.0 Hz, ^{4}J = 4.0 Hz, 2H), 7.28 (m, 4H), 6.92 (d, ^{3}J = 8.0 Hz, 1H), 6.77 (m, 1H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d^6) δ = 162.6 (C), 160.2 (C), 136.6 (C), 135.5 (C), 128.9 (C), 127.8 (C), 126.8 (d, ^{3}J = 8.0 Hz, 2 CH), 123.1 (CH), 119.5 (CH), 115.8 (CH), 115.5 (CH), 110.9 (CH), 98.1 (CH), 21.1 (CH_3); HRMS (ESI) ([M-H]$^+$) calcd. for $C_{15}H_{11}FN$: 224.0881; found: 224.0885.

Acknowledgments

This work was supported by the ANR–DFG program (**Hybridiams** ANR-16-CE92-0037-01 and Schr 597/31-1), Conseil Régional de Bourgogne through the plan d'actions régional pour l'innovation (PARI: projects CDEA for OM and 3MIM-P4) and the fonds européen de développement regional (FEDER). The work in Giessen was supported in part (for OM and PRS) by the US Department of Energy, Office of Science, Basic Energy Sciences, Materials Sciences and Engineering Division, under contract DE-AC02-76SF00515.

Keywords: C–H arylation • diamondoid • indole • primary phosphine ligand • water catalysis

[1] a) J. Roger, A. L. Gottumukkala, H. Doucet, *ChemCatChem* **2010**, *2*, 20-40; b) M. Platon, R. Amardeil, L. Djakovitch, J.-C. Hierso, *Chem. Soc. Rev.* **2012**, *41*, 3929-3968.

[2] a) J. J. L. a. G. W. Gribble, *Palladium in Heterocyclic Chemistry: A Guide for the Synthetic Chemist, Vol. 20*, Elsevier, **2000**; b) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127-2198; c) F. Alonso, I. P. Beletskaya, M. Yus, *Chem. Rev.* **2004**, *104*, 3079-3160; d) G. Zeni, R. C. Larock, *Chem. Rev.* **2004**, *104*, 2285-2310; e) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644-4680; f) K. Undheim, in *Handbook of Organopalladium Chemistry for Organic Synthesis*, Wiley, **2002**, pp. 409-492; g) G. Kirsch, S. Hesse, A. Comel, *Curr. Org. Synth.* **2004**, *1*, 47-63; h) Y.-J. Cheng, S.-H. Yang, C.-S. Hsu, *Chem. Rev.* **2009**, *109*, 5868-5923; i) I. K.

Moon, J.-W. Oh, N. Kim, *J. Photochem. Photobiol., A* **2008**, *194*, 351-355; j) J. Li, A. C. Grimsdale, *Chem. Soc. Rev.* **2010**, *39*, 2399-2410; k) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2011**, *111*, PR215-PR283; l) J. V. Grazulevicius, P. Strohriegl, J. Pielichowski, K. Pielichowski, *Prog. Polym. Sci.* **2003**, *28*, 1297-1353.

[3] a) S. Cacchi, G. Fabrizi, *Chem. Rev.* **2005**, *105*, 2873-2920; b) G. R. Humphrey, J. T. Kuethe, *Chem. Rev.* **2006**, *106*, 2875-2911; c) L. Ackermann, *Synlett* **2007**, *2007*, 0507-0526; d) K. Krüger, A. Tillack, M. Beller, *Adv. Synth. Catal.* **2008**, *350*, 2153-2167; e) R. Vicente, *Org. Biomol. Chem.* **2011**, *9*, 6469-6480.

[4] J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem. Int. Ed.* **2012**, *51*, 8960-9009.

[5] a) B. S. Lane, D. Sames, *Org. Lett.* **2004**, *6*, 2897-2900; b) X. Wang, B. S. Lane, D. Sames, *J. Am. Chem. Soc.* **2005**, *127*, 4996-4997; c) N. R. Deprez, D. Kalyani, A. Krause, M. S. Sanford, *J. Am. Chem. Soc.* **2006**, *128*, 4972-4973; d) C. Bressy, D. Alberico, M. Lautens, *J. Am. Chem. Soc.* **2005**, *127*, 13148-13149; e) D. R. Stuart, K. Fagnou, *Science* **2007**, *316*, 1172; f) S.-D. Yang, C.-L. Sun, Z. Fang, B.-J. Li, Y.-Z. Li, Z.-J. Shi, *Angew. Chem. Int. Ed.* **2008**, *47*, 1473-1476; g) R. J. Phipps, N. P. Grimster, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 8172-8174; h) N. Lebrasseur, I. Larrosa, *J. Am. Chem. Soc.* **2008**, *130*, 2926-2927; i) J. Cornella, P. Lu, I. Larrosa, *Org. Lett.* **2009**, *11*, 5506-5509; j) T. Dröge, A. Notzon, R. Fröhlich, F. Glorius, *Chem. Eur. J.* **2011**, *17*, 11974-11977; k) S. G. Modha, M. F. Greaney, *J. Am. Chem. Soc.* **2015**, *137*, 1416-1419.

[6] S. Islam, I. Larrosa, *Chem. Eur. J.* **2013**, *19*, 15093-15096.

[7] G. Cusati, L. Djakovitch, *Tetrahedron Lett.* **2008**, *49*, 2499-2502.

[8] L. Joucla, N. Batail, L. Djakovitch, *Adv. Synth. Catal.* **2010**, *352*, 2929-2936.

[9] a) Y. Huang, Z. Lin, R. Cao, *Chem. Eur. J.* **2011**, *17*, 12706-12712; b) G.-p. Lu, C. Cai, *Synlett* **2012**, *23*, 2992-2996; c) Z. Xu, Y. Xu, H. Lu, T. Yang, X. Lin, L. Shao, F. Ren, *Tetrahedron* **2015**, *71*, 2616-2621; d) L. Duan, R. Fu, B. Zhang, W. Shi, S. Chen, Y. Wan, *ACS Catal.* **2016**, *6*, 1062-1074; e) A. H. Sandtorv, *Adv. Synth. Catal.* **2015**, *357*, 2403-2435; f) H. P. L. Gemoets, I. Kalvet, A. V. Nyuchev, N. Erdmann, V. Hessel, F. Schoenebeck, T. Noel, *Chem. Sci.* **2017**, *8*, 1046-1055.

[10] a) L. Ackermann, *Synthesis* **2006**, *2006*, 1557-1571; b) L. Ackermann, S. Barfüsser, C. Kornhaass, A. R. Kapdi, *Org. Lett.* **2011**, *13*, 3082-3085.

[11] L. Ackermann, S. Barfüßer, *Synlett* **2009**, *2009*, 808-812.

[12] D. Ghorai, V. Müller, H. Keil, D. Stalke, G. Zanoni, B. A. Tkachenko, P. R. Schreiner, L. Ackermann, *Adv. Synth. Catal.* **2017**, *359*, 3137-3141.

[13] O. Moncea, M. A. Gunawan, D. Poinsot, H. Cattey, J. Becker, R. I. Yurchenko, E. D. Butova, H. Hausmann, M. Šekutor, A. A. Fokin, J.-C. Hierso, P. R. Schreiner, *J. Org. Chem.* **2016**, *81*, 8759-8769.

[14] R. N. Butler, A. G. Coyne, *Chem. Rev.* **2010**, *110*, 6302-6337.

[15] S. Narayan, J. Muldoon, M. G. Finn, V. V. Fokin, H. C. Kolb, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2005**, *44*, 3275-3279.

[16] Y. Jung, R. A. Marcus, *J. Am. Chem. Soc.* **2007**, *129*, 5492-5502.

[17] M. A. Gunawan, O. Moncea, D. Poinsot, M. Keskes, B. Domenichini, O. Heintz, R. Chassagnon, F. Herbst, R. M. K. Carlson, J. E. P. Dahl, A. A. Fokin, P. R. Schreiner, J.-C. Hierso, *Adv. Funct. Mater.* **2018**, *doi.org/10.1002/adfm.201705786.*

[18] a) D. Roy, S. Mom, D. Lucas, H. Cattey, J.-C. Hierso, H. Doucet, *Chem. Eur. J.* **2011**, *17*, 6453-6461; b) N. Dwadnia, J. Roger, N. Pirio, H. Cattey, R. Ben Salem, J.-C. Hierso, *Chem. Asian J.* **2017**, *12*, 459-464.

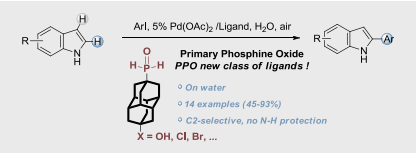
[19] M. Yamaguchi, K. Suzuki, Y. Sato, K. Manabe, *Org. Lett.* **2017**, *19*, 5388-5391.

[20] a) B. S. Lane, M. A. Brown, D. Sames, *J. Am. Chem. Soc.* **2005**, *127*, 8050-8057; b) L. Joucla, L. Djakovitch, *Adv. Synth. Catal.* **2009**, *351*, 673-714; c) T. C. Boorman, I. Larrosa, in *Progress in Heterocyclic Chemistry, Vol. 22* (Eds.: G. Gribble, J. A. Joule), Elsevier, **2011**, pp. 1-20; d) Y. Li, W.-H. Wang, K.-H. He, Z.-J. Shi, *Organometallics* **2012**, *31*, 4397-4400.

[21] N. A. Fokina, B. A. Tkachenko, A. Merz, M. Serafin, J. E. P. Dahl, R. M. K. Carlson, A. A. Fokin, P. R. Schreiner, *Eur. J. Org. Chem.* **2007**, *2007*, 4738-4745.

FULL PAPER

(9-Hydroxydiamant-4-yl) phosphine is key for the aerobic Pd-catalyzed *C2*-arylation of unprotected (*N*–H)-indoles with functionalized haloarenes “on water”. Our results demonstrate the power of the new primary phosphine oxide (PPO) ligands for the C–H functionalization of unprotected (*N*–H)-heterocycles.



Oana Moncea, Didier Poinsot, Andrey A. Fokin, Peter R. Schreiner, and Jean-Cyrille Hierso**

Page No. – Page No.

Palladium-catalyzed *C2*–H arylation of unprotected (*N*–H)-indoles “on water” using primary diamantyl phosphine oxides as a new class of PPO ligands