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Triarylphosphines as Aryl Donors for Pd(II)-Catalyzed Aromatic Coupling of Oxabenzonorbornadienes

Hui Zhou,[†,§] Jixing Li,[†,§] Huameng Yang,[†] Chungu Xia,*[,†] and Gaoxi Jiang*[,†,‡]

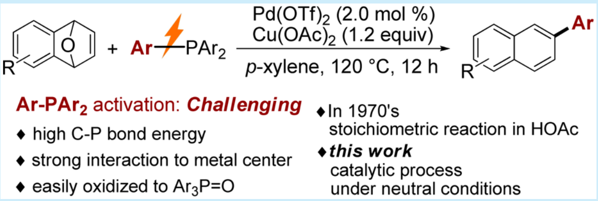
[†]State Key Laboratory for Oxo Synthesis and Selective Oxidation, Suzhou Research Institute of LICP, Lanzhou Institute of Chemical Physics (LICP), Chinese Academy of Sciences, Lanzhou 730000, P. R. China

[‡]Division of Advanced Nanomaterials, Suzhou Institute of Nano-Tech and Nano-Bionics, Chinese Academy of Sciences, Suzhou 215123, P. R. China

[§]University of Chinese Academy of Sciences, Beijing 100049, P. R. China

S *Supporting Information*

ABSTRACT: A new approach was developed for Pd(II)-catalyzed aromatic coupling of oxabenzonorbornadienes with triarylphosphines as both ligands and aryl donors. Diverse functional groups including halo- (F−, Cl−, and Br−), CF_3-, and furyl groups are well tolerated. For unsymmetrical triarylphosphines, the migration ability of aryls is consistent with the electronic property of substituents and maintains the order EDG−Ar > H−Ar > EWD−Ar (EDG means electron-donating group, EWG means electron-withdrawing group). A preliminary mechanistic study was also disclosed.



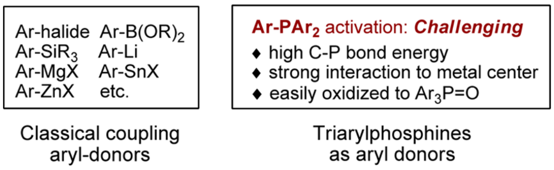
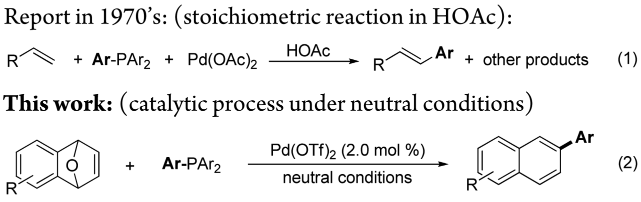


Figure 1. Typical aryl donors for coupling reaction.

Scheme 1. Ar_3P as Ar Donor in Pd-Catalysis


Report in 1970's: (stoichiometric reaction in HOAc):

This work: (catalytic process under neutral conditions)

Transition-metal catalyzed coupling reactions have emerged as the most reliable and powerful strategy for carbon−carbon bond formation.[1] Among these great achievements, coupling reactions, namely Heck, Negishi, and Suzuki reactions, were highlighted by the Nobel Prize in chemistry in 2010.[2] Conventionally, the current coupling aryl partners are usually limited in halides, organoboron, organosilane, and traditional organometallic (Li−, Mg−, Sn−, and Zn−) reagents (Figure 1, left). Despite these important advances, excavation of new surrogates to strengthen the extensive variations of coupling reactions is still in strong demand. Tertiary phosphines, containing three thermodynamically highly stable C−P bonds, are currently widely utilized in organic synthesis as reagents,[3] organocatalysts,[4] and supporting ligands in transition-metal catalysis,[5] but further exploitation of tertiary phosphine itself in the direct activation of the C−P bond remains unexplored yet of great interest and significance that may be due to its intrinsic characteristics: (i) possesses high C−P bond energy of around 513 kJ/mol,[6] (ii) exhibits strong interaction to metal catalysts, and (iii) is easily oxidized to $Ar_3P{=}O$ (Figure 1, right). The first report for arylation of olefins with triarylphosphines as aryl doners was given by Kikukawa and co-workers in 1972, wherein the use of stoichiometric amounts of $Pd(OAc)_2$ in acetic acid provoked the C−P bond cleavage (Scheme 1, eq 1).[7] Since then, considerable effort has been directed toward the challenging topic. Nevertheless, besides several reports in stoichiometric reactions with transition-metal compounds,[8] only a few catalytic processes were achieved, wherein triarylphosphines normally function as the diarylphosphinating agents.[9] A breakthrough in direct activation of a stable C−P bond was made by Oshima and co-workers in 2003.[10] They realized a $Pd(OAc)_2$-catalyzed oxidative Heck-type coupling reaction between olefins and arylphosphonic acids, in which the use of an overstoichiometric amount of tetrabutylammonium fluoride (TBAF) was crucial for the fission of a carbon−phosphorus bond. To the best of our knowledge, the success in using simple triarylphosphines as aryl donors for a catalytic cross-coupling reaction is unprecedented. Herein, we report the first example of a Pd(II)-catalyzed aromatic coupling of oxabenzonorbornadienes with triarylphosphines in the absence of any additional activators under neutral reaction conditions

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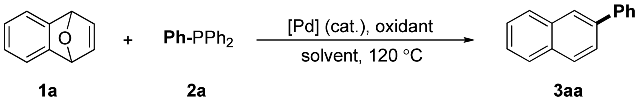
(Scheme 1, eq 2). Obviously, the process provided a catalytic method for the activation of a stable C−P bond and opened a new window for the application of phosphines.

Initially, we treated oxabenzonorbornadiene **1a**[11] with triphenylphosphine (PPh_3, 1.2 equiv) **2a** in the presence of 10 mol % of $Pd(OAc)_2$ under oxygen (1 atm) in *p*-xylene at 120 °C for 12 h (Table 1, entry 1). To our delight, about 5% of desired product 2-phenylnaphthalene **3aa** was detected by GC-MS. Encouraged by the rudimentary result, further optimization to improve the chemical yield was conducted. Examination of oxidants reveals that $Cu(OAc)_2$ is the best choice and provided **3aa** in 72% yield predominantly with the simultaneous formation of diphenylphosphinic acid after workup (entries 2−7). Changing the solvent gave comparable or worse yields than *p*-xylene (entries 8−13). Further screening of Pd(II)-catalysts revealed that $PdCl_2$ and $Pd(OTf)_2$ significantly improved the reaction, giving **3aa** in 77% and 80% yield, respectively (entries 14 and 15). Remarkably, even lowering the loading of $Pd(OTf)_2$ to 2.0 mol % also facilitated the adduct in 78% yield (entry 16). Increasing the amount of $Cu(OAc)_2$ to 1.2 equiv gave the best result, producing **3aa** in 80% isolated yield (entry 17). Control experiments that included changing the loading of PPh_3 (entries 18 and 19) and the reaction temperature (entries 20 and 21) proved to be less effective.

Table 1. Optimizaiton of Reaction Conditions[a]

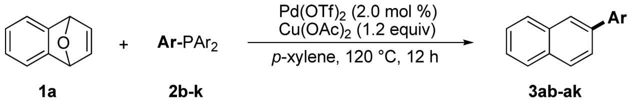


entry	[Pd] (mol %)	oxidant	solvent	yield (%)[b]
1	$Pd(OAc)_2$ (10)	O_2[c]	*p*-xylene	5
2	$Pd(OAc)_2$ (10)	Ag_2CO_3	*p*-xylene	n.d.[d]
3	$Pd(OAc)_2$ (10)	$K_2S_2O_8$	*p*-xylene	n.d.[d]
4	$Pd(OAc)_2$ (10)	TBHP	*p*-xylene	n.d.[d]
5	$Pd(OAc)_2$ (10)	DDQ	*p*-xylene	13
6	$Pd(OAc)_2$ (10)	BQ	*p*-xylene	40
7	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	*p*-xylene	72
8	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	toluene	70
9	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	dioxane	70
10	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	THF	66
11	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	CH_3CN	69
12	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	DMF	63
13	$Pd(OAc)_2$ (10)	$Cu(OAc)_2$	CH_2Cl_2	65
14	$PdCl_2$ (10)	$Cu(OAc)_2$	*p*-xylene	77
15	$Pd(OTf)_2$ (10)	$Cu(OAc)_2$	*p*-xylene	80
16	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	78
17[e]	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	85(80)
18[e,f]	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	75
19[e,g]	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	77
20[e,h]	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	80
21[e,i]	$Pd(OTf)_2$ (2.0)	$Cu(OAc)_2$	*p*-xylene	82

[a] Reaction conditions: **1a** (0.2 mmol), PPh_3 (1.2 equiv), oxidant (1.0 equiv), [Pd] (10−2.0 mol %), solvent (1.5 mL), 120 °C, 12 h. [b] Determined by GC-Mass using a standard. [c] O_2 (1 atm). [d] n.d. means not detected. [e] $Cu(OAc)_2$ (1.2 equiv); isolated yield is given in parentheses. [f] PPh_3 (1.5 equiv). [g] PPh_3 (1.0 equiv). [h] Reaction was performed at 100 °C. [i] Reaction was performed at 140 °C.

With the optimized conditions in hand, we next investigated the substrate scope with respect to both phosphines and oxabenzonorbornadienes to evaluate the generality of the reaction. First, a series of tri(homo)arylphosphines with different substitution patterns were employed to react with **1a** under the standard reaction conditions. As demonstrated in Table 2, several interesting functional groups, including electron-donating and -withdrawing substituents, were well tolerated, while the steric properties played a dramatic role in the reactivity. Using 4-position substituted triarylphosphines **2b−f** containing the CH_3O-, CH_3-, F-, Cl-, and even CF_3-group, the transformations afforded **3ab−af** in 84−48% yields smoothly (entries 1−5). Gratifyingly, **2g−i** bearing the CH_3O-, CH_3-, and Cl-group at the 3-position are well suitable for the aromatic coupling process and readily furnished the corresponding products **3ag−ai** in 73−81% yield (entries 6−8). In contrast to **2b** and **2g**, **2j** bearing a CH_3O group at the 2-position seems less reactive which may be due to the increased steric hindrance (entry 9).[12] Significantly, the relatively unstable trifurylphosphine **2k** is also compatible with this transformation, and the reaction enabled the formation of **3ak** in 30% yield predominantly (entry 10).

Table 2. Substrate Scope of Tri(homo)arylphosphines[a]

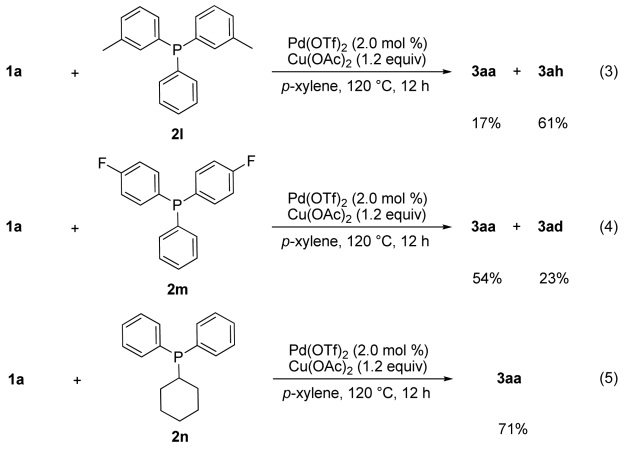


entry	Ar	3	yield (%)[b]
1	4-$CH_3OC_6H_4$	**3ab**	84
2	4-$CH_3C_6H_4$	**3ac**	82
3	4-FC_6H_4	**3ad**	70
4	4-ClC_6H_4	**3ae**	64
5	4-$CF_3C_6H_4$	**3af**	48
6	3-$CH_3OC_6H_4$	**3ag**	73
7	3-$CH_3C_6H_4$	**3ah**	80
8	3-ClC_6H_4	**3ai**	81
9	2-$CH_3OC_6H_4$	**3aj**	13
10	2-furyl	**3ak**	30

[a] Reaction conditions: **1a** (0.2 mmol), PAr_3 (1.2 equiv), $Pd(OTf)_2$ (2.0 mol %), $Cu(OAc)_2$ (1.2 equiv), *p*-xylene (1.5 mL), 120 °C, 12 h. [b] Yields of isolated products after column chromatography are given.

Remarkably, we were pleased to find that different kinds of tri(hetero)arylphosphines are also quite applicable to the transformation. As shown in Scheme 2, triarylphosphines **2l** and **2m** underwent the reaction to smoothly afford the mixtures of **3aa**/**3ah** and **3aa**/**3ad** in good yields (eqs 3 and 4). The

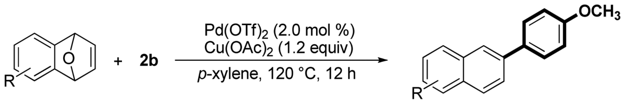
Scheme 2. Tri(hetero)arylphosphines as Substrates



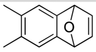
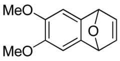
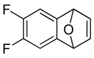
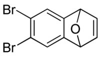
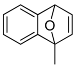
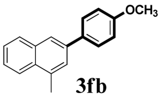
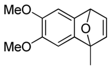
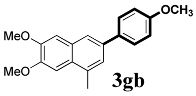
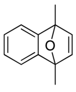
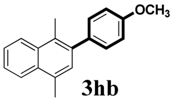
ratios of **3aa**/**3ah** and **3aa**/**3ad** indicate that electron-rich aryl groups migrated preferentially, which suggests that the migrating aryl group in the reaction has nucleophilic character. It is noteworthy that **3aa** was monitored exclusively and isolated in 71% yield with cyclohexyldiphenylphosphine **2n** as the starting material (eq 5).

Next the scope of oxabenzonorbornadienes for the new catalytic system was investigated (Table 3). It is found that oxabenzonorbornadienes possessing diverse substituents in different ring positions worked well. The treatment of **1b**−**h** with **2b** under the reaction conditions described above generated the corresponding products in good yields. Compounds **3bb** and **3cb** were obtained in 82% and 59% yield, respectively, when **1b** and **1c** were used as the substrates (entries 1−2). Symmetrically difluoro-substituted compound **1d** enabled the formation of **3db** in moderate yield readily (entry 3). Surprisingly, **1e** having a dibromo group undertook the reaction well, providing **3eb** in 48% yield predominantly (entry 4), which indicated that Pd(II) species rather than Pd(0) might be involved in the catalytic process.[12] Along with oxabenzonorbornadiene substrates with substituted benzenes, C1-substituted ones (**1f** and **1g**) were also employed and regioselectively produced **3fb** and **3gb** in 77% and 62% yields, respectively (entries 5 and 6). Even using highly sterically hindered C1, C4-disubstituted compound **1h** as the substrate, the reaction also effectively produced the corresponding adducts **3hb** in 73% yield (entry 7).

Table 3. Substrate Scope of Oxabenzonorbornadienes[a]



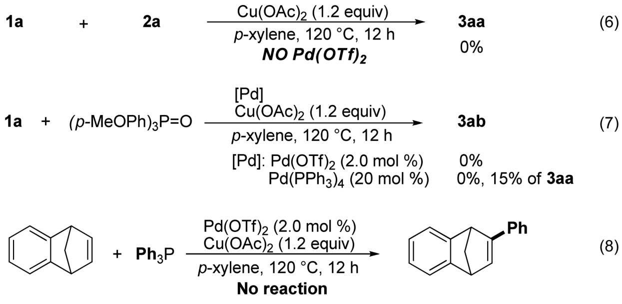
1b-h **3bb-hb**

entry	1	3	yield (%)[b]
1	 **1b**	**3bb**	82
2	 **1c**	**3cb**	59
3	 **1d**	**3db**	57
4	 **1e**	**3eb**	48
5	 **1f**	 **3fb**	77
6	 **1g**	 **3gb**	62
7	 **1h**	 **3hb**	73

[a] Reaction conditions: **1b**−**i** (0.2 mmol), **2b** (1.2 equiv), Pd(OTf)$_2$ (2.0 mol %), Cu(OAc)$_2$ (1.2 equiv), *p*-xylene (1.5 mL), 120 °C, 12 h. [b] All yields are isolated.

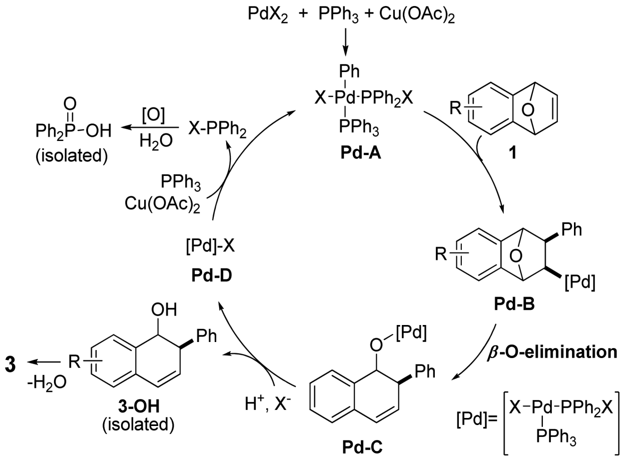
To explore the mechanism of this transformation, several control reactions were performed (Scheme 3). The C−P bond cleavage product was not monitored in the absence of the Pd-catalyst (eq 6). With tris(4-methoxyphenyl)phosphine oxide as the aryl donor under the identical conditions, the C−P bond cleavage was not observed and the oxide was recovered in >95% yield, while **3aa** was isolated in 15% yield with 20 mol % of $Pd(PPh_3)_4$ as the catalyst, indicating the phenyl transferred from the PPh_3 ligand (eq 7). When 1,4-methanonaphthalene was used instead of **1a**, no reaction occurred (eq 8).

Scheme 3. Control Experiments



Although the mechanism of this catalytic transformation is not completely clear yet, on the basis of previous reports[7,14] and the above-mentioned observations, a possible mechanism is proposed in Scheme 4. The reaction of the Pd(II) salt with PPh_3 and oxidant Cu(OAc)$_2$ gave the key active compound **Pd-A** reasonably that involved C−P bond cleavage of PPh_3 and the interchange between phenyl group and anion.[7] **Pd-A** reacted with **1** via oxidative addition to afford intermediate **Pd-B**, followed by β-O-elimination[15] to form **Pd-C**, and then compounds **3-OH**[16] and **Pd-D** were liberated after acidolysis. Dehydration of **3-OH** led to the desired product **3**. **Pd-A** was regenerated by the reaction of **Pd-D**, PPh_3, and Cu(OAc)$_2$ with the release of PPh_2X; the latter was hydrolyzed and oxidized to the isolated diphenylphosphinic acid.

Scheme 4. Plausible Mechanism



In summary, we developed the first catalytic approach for Pd(II)-catalyzed aromatic coupling of oxabenzonorbornadienes with triarylphosphines under neutral reaction conditions, in which triarylphosphines function as both ligands and aryl donors. The catalytic process underwent stable C−P bond cleavage and tolerated diverse functional groups, which allowed new potential in the application of phosphines. The preliminary mechanistic study reveals that the β-O-elimination of oxo-bridged dienes plays the key role for such a catalytic cycle. Further investigations to define the details of the mechanism and the scope of this catalyst system are currently in progress in our laboratory.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.5b02366.

Complete experimental details and characterization data for the compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: cgxia@lzb.ac.cn.
*E-mail: gxjiang2012@sinano.ac.cn.

Notes

The authors declare no competing financial interest.

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