OL | Organic Letters

pubs.acs.org/OrgLett

Letter

Late-Stage Diversification of Biarylphosphines through Rhodium(I)-Catalyzed C−H Bond Alkenylation with Internal Alkynes

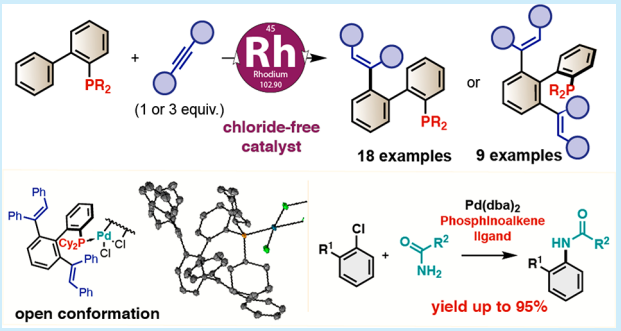
Zhuan Zhang, Marie Cordier, Pierre H. Dixneuf, and Jean-François Soulé*

Cite This: https://dx.doi.org/10.1021/acs.orglett.0c02023

Read Online

ACCESS | Metrics & More | Article Recommendations | Supporting Information

ABSTRACT: We report herein P(III)-directed C−H bond alkenylation of (dialkyl)- and (diaryl)biarylphosphines using internal alkynes. Chloride-free $[Rh(OAc)(COD)]_2$ acts as a better catalyst than commercially available $[RhCl(COD)]_2$. Conditions were developed to control the mono- and difunctionalization depending on the alkyne stoichiometry. One of these novel bisalkenylated (dialkyl)biarylphosphines was employed for the preparation of a palladium(II) complex, and some of these functionalized ligands outperformed their corresponding unfunctionalized phosphines in Pd-catalyzed amidation with sterically hindered aryl chlorides.



Phosphine ligands play a significant role in catalysis, tuning the reactivity at the metal center through their modulable steric and electronic properties.[1] (Dialkyl)- or (diaryl)-biarylphosphines such as JohnPhos and XPhos ligands are widely employed in transition-metal (e.g., Pd or Au) catalysis because of their unique structural features displaying weak metal−arene interactions.[2] The presence of bulky substituents (i.e., *i*Pr) at both *ortho′* positions avoids cyclometalation and leads to more active catalysts (Figure 1). However, the traditional synthetic approaches for biarylphosphines involve multiple steps with polar organometallic reagents, making it challenging to produce banks of multifunctional ligands to search for optimal catalytic activities. Recently, late-stage diversification via C−H bond functionalization has been comfortably ensconced to optimize the design of pharmaceuticals[3] and organic materials,[4] but it has barely been employed for generation of ligand banks.[5] Since the discovery by Hartwig that regioselective C−H bond functionalization can be directed by P(III) atom,[6] this strategy has been applied to quickly modify biaryl phosphines by C−H bond borylation[7] arylation,[8] and silylation.[9] In 2019, our group reported *ortho′*-C−H bond alkylation of biarylphosphines, allowing the preparation of 40 multifunctional phosphines with unique efficiency for catalytic carboxylation reactions (Figure 2a).[10] At the same time, Shi's group reported similar reactions, albeit using $[RhCl(COD)]_2$.[11] They also showed that terminal alkynes can be

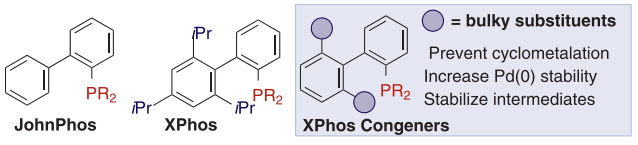


Figure 1. Relevant and structural features of biarylphosphines.

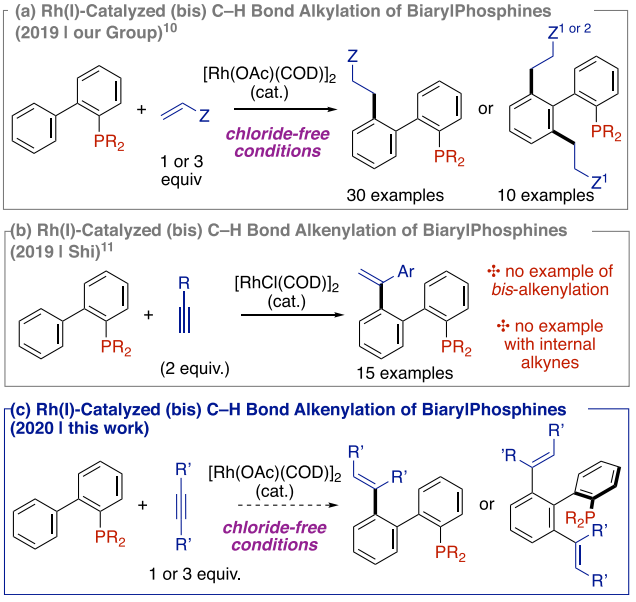


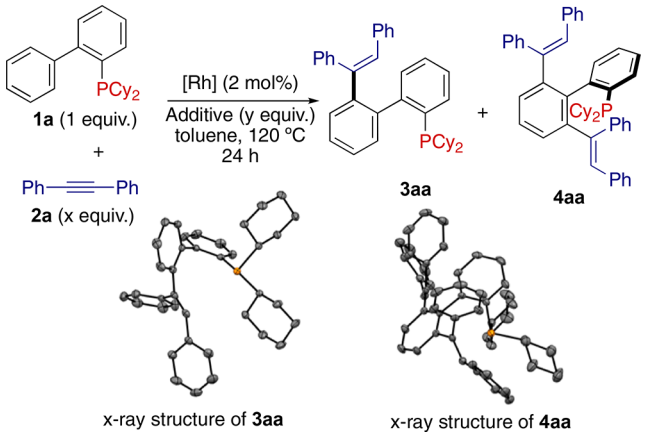
Figure 2. Late-stage diversification of biarylphosphines.

Received: June 18, 2020

employed, leading to *ortho′*-monoalkenylated biarylphosphines (Figure 2b).[11] In contrast to alkenes, with which bis-*ortho′*-dialkylation easily occurs, only monoalkenylation happened with terminal alkynes. As there was no example of mono- or dialkenylation with internal alkynes, we investigated Rh(III) and Rh(I) catalytic systems to reach this target (Figure 2c).

We selected Cy-JohnPhos (**1a**) and diphenylacetylene (**2a**) as model substrates to investigate the C−H bond alkenylation directed by the P(III) atom (Table 1). As the first attempt, we

Table 1. Optimization of the Reaction Conditions



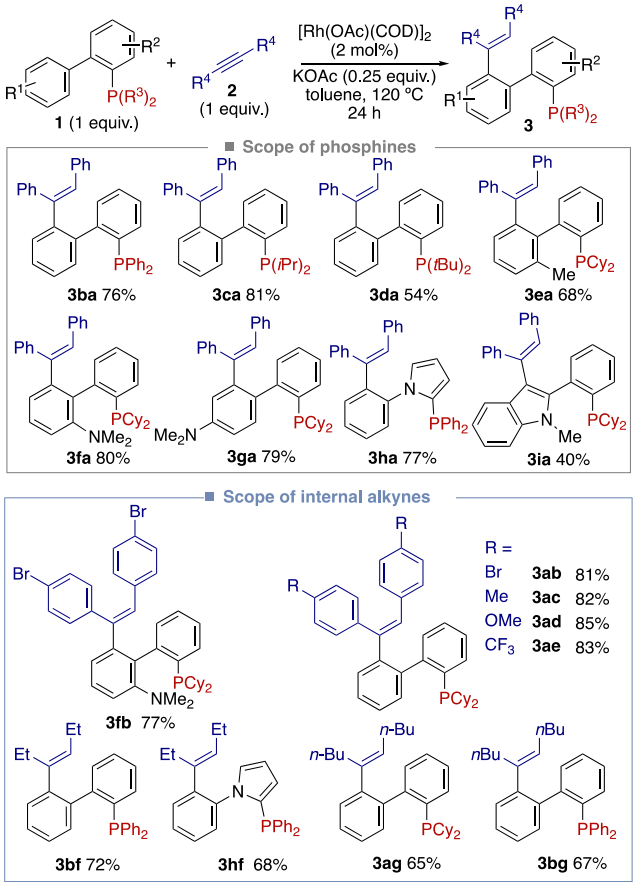
	[Rh]	Additive	3aa (%)	4aa (%)
1	$Cp^*Rh(CH_3CN)_3(SbF_6)_2$	PivOH (5)	0	0
2	$[Cp^*RhCl_2]_2$	–	0	0
3	$[RhCl(COD)]_2$	–	23	0
4	$RhCl(PPh_3)_3$	–	10	0
5	$[Rh(OAc)(COD)]_2$	–	71	21
6	$[Rh(OAc)(COD)]_2$	K_2CO_3 (0.25)	75	18
7	$[Rh(OAc)(COD)]_2$	K_3PO_4 (0.25)	32	3
8	$[Rh(OAc)(COD)]_2$	KOAc (0.25)	86	8
9	$[Rh(OAc)(COD)]_2$	AcONa (0.25)	84	11
10	$[Rh(OAc)(COD)]_2$	PivOK (0.25)	72	18
11[a]	$[Rh(OAc)(COD)]_2$	KOAc (0.25)	55	43
12[b]	$[Rh(OAc)(COD)]_2$	KOAc (0.25)	30	62
13[b,c]	$[Rh(OAc)(COD)]_2$	KOAc (0.25)	15	75
14[b,c]	$[Rh(OAc)(COD)]_2$	KOAc (0.5)	10	78

[a] 2 equiv. of **2a**; [b] 3 equiv. of **2a** , [c] 4 mol% of Rh catalyst

evaluated the conditions described by Fagnou for the hydroarylation of internal alkynes (i.e., 2 mol % $Cp^*Rh(CH_3CN)_3(SbF_6)_2$ associated with PivOH in toluene),[12] but no reaction occurred (entry 1). The use of $[Cp^*RhCl_2]_2$ as the catalyst also failed to deliver the functionalized phosphine **3aa** or **4aa** (entry 2), likely because of strong P(III)−Rh(III) bonds. We then evaluated Rh(I) catalysts, as we and others previously demonstrated their efficiency in P(III)-directed C−H bond activation/functionalization.[7d,8,10,11] Moreover, Rh(I) catalysts have also been employed in alkenylations of arene $C(sp^2)$−H bonds with alkynes using a bidentate directing group[13] or a nitrogen group.[14] Shi's conditions for alkenylation with terminal alkyne afforded **3aa** in only 23% yield (entry 3). The use of Wilkinson's catalyst $[RhCl(PPh_3)_3]$ gave a lower yield (entry 4). However, higher activity was observed using 2 mol % chloride-free $[Rh(OAc)(COD)]_2$ as the catalyst, which afforded monoalkenylated phosphine **3aa** in 71% yield along with a 21% yield of bisalkenylated phosphine **4aa** (entry 5). Interestingly, in the presence of a base the formation of the bis-*ortho′*-alkenylated phosphine **4aa** decreased, and the best result was obtained using 0.25 equiv of KOAc, which afforded **3aa** in 86% isolated yield (entries 6−10). To get the bis-*ortho′*-alkenylated phosphine **4aa** selectively, we increased the amount of **2a** (entries 11 and 12). In the presence of 3 equiv of **2a** and 4 mol % Rh catalyst, **4aa** was isolated in 75% yield (entry 13). With 0.5 equiv of KOAc, the isolated yield can rise up to 78% (entry 14).

Having determined the best reaction conditions for the mono- and dialkenylnation of biarylphosphines through P(III)-assisted C−H bond cleavage, we turned our attention to the scope of the reaction. First, we investigated the monofunctionalization using 2 mol % $[Rh(OAc)(COD)]_2$ with 25 mol % KOAc in toluene at 120 °C, and biarylphophine/alkyne ratio of 1:1 (Scheme 1). The reaction of diphenylacetylene with

Scheme 1. Scope of Rhodium(I)-Catalyzed *ortho′*-C−H Bond Alkenylation of Biarylphosphines with Alkynes



biphenyls bearing a diphenylphosphino or diisopropylphosphino group afforded the corresponding phosphine−alkene ligands **3ba** and **3ca** in 76% and 81% yield, respectively. In contrast to the previous report on Rh(I)-catalyzed hydroarylation of terminal alkynes,[11] in which sterically hindered *t*-Bu-JohnPhos (**1d**) is not reactive, the reaction with diphenylacetylene led to the formation of monoalkenylated phosphine **3da** in 54% yield. *Ortho′*-substituted biarylphosphines such as MePhos (**1e**) and DavePhos (**1f**) also underwent C−H bond alkenylation at the *ortho′* position to afford phosphines **3ea** and **3fa** in good yields. Rh(I)-catalyzed *ortho′*-C−H bond alkenylation of 2-dicyclohexylphosphino-4-(*N*,*N*-dimethylamino)-1,1′-biphenyl (**1g**) afforded **3ga** in 79% yield. These reaction conditions are tolerant of heteroaromatic

https://dx.doi.org/10.1021/acs.orglett.0c02023
Org. Lett. XXXX, XXX, XXX−XXX

moieties. Indeed, cataCXium PCy with an *N*-phenylpyrrole scaffold—developed by Beller's group for cross-couplings of aryl chlorides[15]— is alkenylated on the phenyl ring to provide phosphine−alkene **3ha** in 77% yield. CM-Phos—developed by Kwong for cross-coupling reactions with aryl mesylates[16]—undergoes indolinyl C3−H bond alkenylation to afford **3ia** in moderate yield.

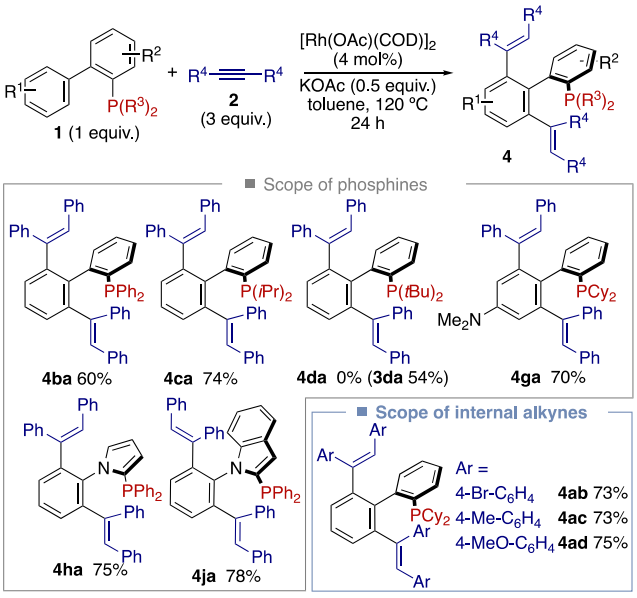
Next, we investigated the reactivity of other internal alkynes. The functionalization of DavePhos (**1f**) with 1,2-bis(4-bromophenyl)ethyne afforded phosphine **3fb** in 77% yield without cleavage of the C−Br bonds, which could be further employed to generate more diversity via cross-coupling reactions. Hydroarylation of 1,2-bis(4-bromophenyl)ethyne, 1,2-di-*p*-tolylethyne, 1,2-bis(4-methoxyphenyl)ethyne, and 1,2-bis(4-(trifluoromethyl)phenyl)ethyne with JohnPhos (**1a**) efficiently occurred to produce **3ab**−**ae** in good yields. Less reactive hex-3-yne (**2f**) and dec-5-yne (**2g**) were also suitable substrates in C−H bond alkenylation, affording the novel phosphine−alkene ligands **3bf**, **3hf**, **3ag**, and **3bg** in good yields. However, the use of nonsymmetrical alkynes (e.g., ethyl 3-phenylpropiolate or 1-phenyl-1-propyne) led to nonharvestable mixtures of isomers.

We then explored the difunctionalization of biarylphosphine *ortho*′-C−H bonds using an excess amount of internal alkyne and 4 mol % $[Rh(OAc)(COD)]_2$ with 50 mol % KOAc in toluene at 120 °C (Scheme 2). The steric factor of the phosphorus substituent appears to be critical. The diphenylphosphino and diisopropylphosphino groups were efficient directing groups in the bis-*ortho*′-alkenylation, affording **4ba** and **4ca** in 60% and 74% yield, respectively. In contrast, the reaction with *t*Bu-JohnPhos (**1d**) failed to deliver the difunctionalized phosphine **4da**, and we observed only the formation of monofunctionalized phosphine **3da** in 54% yield. The introduction of a strong electron-donating group such as NMe_2 did not affect the reactivity, as the dialkenylated product **4ga** was isolated in 70% yield. The twofold C−H bond activation/functionalization of cataCXium PCy (**1h**) afforded **4ha** in 75% yield. CataCXium PInCy with the *N*,*N*-phenylindole scaffold **1j** was bisalkenylated on the phenyl unit to provide phosphine−bisalkene **4ja** in 78% yield. Bis-C−H bond alkenylations of **1a** were also carried out with other symmetrical *para*-substituted diarylacetylenes (i.e., R = Br, Me, OMe), affording **4ab**−**ad** in 73−75% yield.

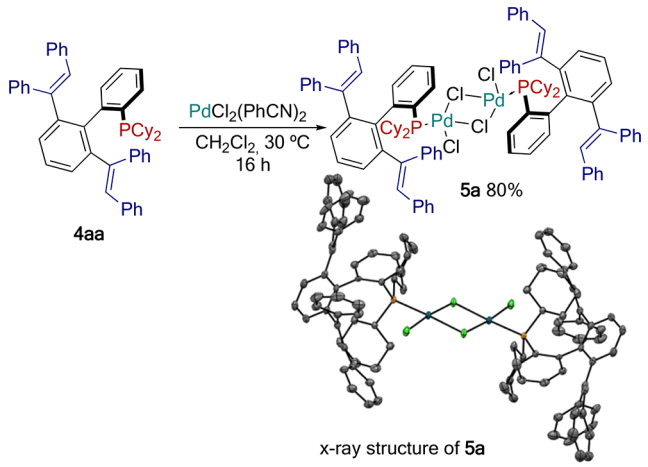
To estimate the coordination ability of phosphine **4aa**, we prepared palladium(II) complex **5a** (Scheme 3). Mixing ligand **4aa** and $PdCl_2(PhCN)_2$ in CH_2Cl_2 at room temperature led to the complete formation of complex **5a**, as indicated by $^{31}P\{^1H\}$ NMR spectroscopy with a downfield shift of the phosphorus atom from δ = −7.7 ppm for the free phosphine to δ = 67.0 ppm for the complex. In the X-ray crystallographic structure, complex **5a** was found to have a dimeric structure with a chloro bridge unit and a distorted square-planar coordination geometry. The Pd−Pd distance of 3.50 Å was somewhat longer than that in the corresponding SPhos−palladium compound (2.24 Å), and the Pd−P distance of 2.26 Å was similar to that in the SPhos−palladium compound (2.25 Å). In contrast to JohnPhos and SPhos, which adopted a closed conformation,[17] **5a** presents an open conformation, i.e., the secondary aryl ring points away from the metal center, avoiding a metal−arene interaction. This conformation switch might be due to the introduction of the very bulky 1,2-diphenylvinyl substituents.

Finally, we demonstrated the positive effect of the introduction of the alkenyl group on biarylphosphines by comparing the catalytic activities of a couple of these novel (bis)alkenylated (dialkyl)biarylphosphines with their parent phosphines that are often used in Pd-catalyzed cross-coupling reactions. Aryl chlorides are much less reactive substrates in Pd-catalyzed cross-coupling reactions, but they are more abundant and less expensive than the bromide or iodide equivalents. Their cross-coupling with amides remains challenging, as specific phosphine ligands have to be designed to promote the oxidative addition to the aryl chloride and reductive elimination of an amidate ligand from the Pd(II) center, which can generate κ^2-amidate palladium intermediate complexes (**A** in Scheme 4), resulting in inhibition of the reductive elimination and thus the catalytic efficiency.[18] We selected electron-rich and sterically hindered 2-chlorotoluene and acetamide as model substrates to evaluate the potential of our bifunctional biarylphosphines in Pd-catalyzed amidation

Scheme 2. Scope of Rhodium(I)-Catalyzed Twofold *ortho*′,*ortho*′-C−H Bond Alkenylation of Biarylphosphines with Alkynes

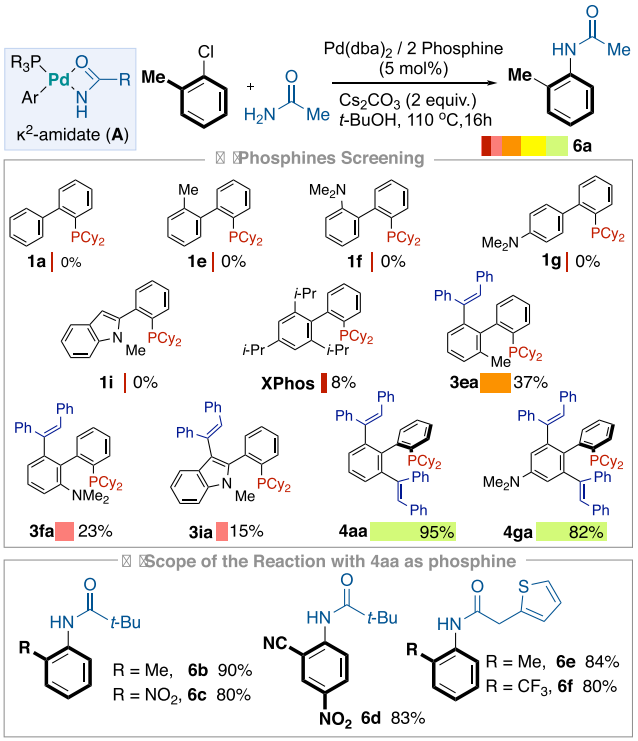


Scheme 3. Stabilization of Pd(II) with Bulky Phosphine Ligand 4aa



https://dx.doi.org/10.1021/acs.orglett.0c02023
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 4. Application of Bisalkenylated (Dialkyl)biarylphosphines in the Pd-Catalyzed Amidation of Aryl Chlorides



(Scheme 4). In the presence of 2.5 mol % $Pd(dbda)_2$/2 phosphine and 2 equiv of Cs_2CO_3 in *t*-BuOH, the commercially available (dicyclohexyl)biarylphosphines [JohnPhos (**1a**), MePhos (**1e**), DavePhos (**1f**), DavePhos analogue **1g**, cataCXium PInCy (**1i**), and XPhos] were almost inactive. Interestingly, the use of phosphine−alkene hybrid ligands **3ea**, **3fa**, and **3ia** gave the desired *N*-arylamide **6a** in 15−37% yield. Surprisingly higher yields were observed using the phosphines **4aa** and **4ga** bearing two alkenyl units, leading to the formation of **6a** in 95% and 82% yield, respectively. This positive rise of activity is expected to arise from the presence of the very bulky alkenyl group at both *ortho′* positions, which might stabilize Pd intermediates by non-covalent interactions[19] or/and may avoid the formation of κ^2-amidate palladium intermediate complexes (**A**). Using the most active bifunctional phosphine, **4aa**, we confirmed that C−N bond cross-coupling nicely occurred, affording arylamides **6b−f** in high yields (Scheme 4, bottom).

In summary, we have reported the first example of C−H bond alkenylation of aromatic C−H bonds of biarylphosphines with internal alkynes through P(III)-directed C−H bond cleavage with $Rh^I(OAc)$ catalysts. The use of KOAc in association with the chloride-free Rh(I) catalyst allowed monofunctionalization or difunctionalization depending on the stoichiometry of the reaction. A new class of phosphine−alkene ligands with different steric and electronic properties were obtained in good yields. The introduction of these very bulky vinyl substituents induces a conformation switch of the palladium complex from a closed form to an open form. A significant consequence for the catalytic performance is that monophosphines that have typically been ineffective in the amidation of aryl chlorides were morphed into ligands that create highly active palladium catalysts in amidation of *ortho*-substituted aryl chlorides. Applications of the developed ligand libraries and more detailed coordination studies are currently ongoing in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c02023.

Additional procedures and data, including characterizations, crystal structures, and NMR results (PDF)

Accession Codes

CCDC 1968419, 1968421, and 1982983 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

Jean-François Soulé − *Univ Rennes, CNRS, ISCR UMR 6226, F-35000 Rennes, France;* orcid.org/0000-0002-6593-1995; Email: jean-francois.soule@univ-rennes1.fr

Authors

Zhuan Zhang − *Univ Rennes, CNRS, ISCR UMR 6226, F-35000 Rennes, France;* orcid.org/0000-0003-4841-4109

Marie Cordier − *Univ Rennes, CNRS, ISCR UMR 6226, F-35000 Rennes, France*

Pierre H. Dixneuf − *Univ Rennes, CNRS, ISCR UMR 6226, F-35000 Rennes, France*

Complete contact information is available at: https://pubs.acs.org/10.1021/acs.orglett.0c02023

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the CNRS, UR1 for providing financial support. Z.Z. acknowledges the China Scholarship Council (CSC) for his Ph.D. grant (201706780007).

■ REFERENCES

(1) (a) Berrisford, D. J.; Bolm, C.; Sharpless, K. B. Ligand-Accelerated Catalysis. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1059−1070. (b) Crabtree, R. H. Multifunctional Ligands in Transition Metal Catalysis. *New J. Chem.* **2011**, *35*, 18−23.

(2) (a) Martin, R.; Buchwald, S. L. Palladium-Catalyzed Suzuki−Miyaura Cross-Coupling Reactions Employing Dialkylbiaryl Phosphine Ligands. *Acc. Chem. Res.* **2008**, *41*, 1461−1473. (b) Ruiz-Castillo, P.; Buchwald, S. L. Applications of Palladium-Catalyzed C−N Cross-Coupling Reactions. *Chem. Rev.* **2016**, *116*, 12564−12649. (c) Zuccarello, G.; Zanini, M.; Echavarren, A. M. Buchwald-Type Ligands on Gold(I) Catalysis. *Isr. J. Chem.* **2020**, *60*, 360−372.

(3) (a) Yamaguchi, J.; Yamaguchi, A. D.; Itami, K. C−H Bond Functionalization: Emerging Synthetic Tools for Natural Products and Pharmaceuticals. *Angew. Chem., Int. Ed.* **2012**, *51*, 8960−9009. (b) Wang, W.; Lorion, M. M.; Shah, J.; Kapdi, A. R.; Ackermann, L. Late-Stage Peptide Diversification by Position-Selective C-H Activation. *Angew. Chem., Int. Ed.* **2018**, *57*, 14700−14717.

(4) (a) Wencel-Delord, J.; Glorius, F. C−H Bond Activation Enables the Rapid Construction and Late-Stage Diversification of Functional

https://dx.doi.org/10.1021/acs.orglett.0c02023
Org. Lett. XXXX, XXX, XXX−XXX

Molecules. *Nat. Chem.* **2013**, *5*, 369−375. (b) Hagui, W.; Doucet, H.; Soulé, J.-F. Application of Palladium-Catalyzed C(sp2)−H Bond Arylation to the Synthesis of Polycyclic (Hetero)Aromatics. *Chem.* **2019**, *5*, 2006−2078.

(5) Zhang, Z.; Dixneuf, P. H.; Soulé, J.-F. Late Stage Modifications of P-containing Ligands using Transition-Metal-Catalyzed C-H Bond Functionalisation. *Chem. Commun.* **2018**, *54*, 7265−7280.

(6) (a) Shelby, Q.; Kataoka, N.; Mann, G.; Hartwig, J. Unusual in Situ Ligand Modification to Generate a Catalyst for Room Temperature Aromatic C−O Bond Formation. *J. Am. Chem. Soc.* **2000**, *122*, 10718−10719. (b) Bedford, R. B.; Coles, S. J.; Hursthouse, M. B.; Limmert, M. E. The Catalytic Intermolecular Orthoarylation of Phenols. *Angew. Chem., Int. Ed.* **2003**, *42*, 112−114.

(7) (a) Crawford, K. M.; Ramseyer, T. R.; Daley, C. J.; Clark, T. B. Phosphine-Directed C−H Borylation Reactions: Facile and Selective Access to Ambiphilic Phosphine Boronate Esters. *Angew. Chem., Int. Ed.* **2014**, *53*, 7589−7593. (b) Wright, S. E.; Richardson-Solorzano, S.; Stewart, T. N.; Miller, C. D.; Morris, K. C.; Daley, C. J. A.; Clark, T. B. Accessing Ambiphilic Phosphine Boronates through C−H Borylation by an Unforeseen Cationic Iridium Complex. *Angew. Chem., Int. Ed.* **2019**, *58*, 2834−2838. (c) Fukuda, K.; Iwasawa, N.; Takaya, J. Ruthenium-Catalyzed ortho C−H Borylation of Arylphosphines. *Angew. Chem., Int. Ed.* **2019**, *58*, 2850−2853. (d) Wen, J.; Wang, D.; Qian, J.; Wang, D.; Zhu, C.; Zhao, Y.; Shi, Z. Rhodium-Catalyzed PIII-Directed ortho-C−H Borylation of Arylphosphines. *Angew. Chem., Int. Ed.* **2019**, *58*, 2078−2082.

(8) Qiu, X.; Wang, M.; Zhao, Y.; Shi, Z. Rhodium(I)-Catalyzed Tertiary Phosphine Directed C−H Arylation: Rapid Construction of Ligand Libraries. *Angew. Chem., Int. Ed.* **2017**, *56*, 7233−7237.

(9) Wang, D.; Zhao, Y.; Yuan, C.; Wen, J.; Zhao, Y.; Shi, Z. Rhodium(II)-Catalyzed Dehydrogenative Silylation of Biaryl-Type Monophosphines with Hydrosilanes. *Angew. Chem., Int. Ed.* **2019**, *58*, 12529−12533.

(10) Zhang, Z.; Roisnel, T.; Dixneuf, P. H.; Soulé, J.-F. Rh(I)-Catalyzed P(III) -Directed C-H Bond Alkylation: Design of Multifunctional Phosphines for Carboxylation of Aryl Bromides with Carbon Dioxide. *Angew. Chem., Int. Ed.* **2019**, *58*, 14110−14114.

(11) Wang, D.; Dong, B.; Wang, Y.; Qian, J.; Zhu, J.; Zhao, Y.; Shi, Z. Rhodium-Catalyzed Direct Hydroarylation of Alkenes and Alkynes with Phosphines Through Phosphorous-Assisted C−H Activation. *Nat. Commun.* **2019**, *10*, 3539.

(12) Schipper, D. J.; Hutchinson, M.; Fagnou, K. Rhodium(III)-Catalyzed Intermolecular Hydroarylation of Alkynes. *J. Am. Chem. Soc.* **2010**, *132*, 6910−6911.

(13) Shibata, K.; Natsui, S.; Chatani, N. Rhodium-Catalyzed Alkenylation of C−H Bonds in Aromatic Amides with Alkynes. *Org. Lett.* **2017**, *19*, 2234−2237.

(14) (a) Lim, Y.-G.; Lee, K.-H.; Koo, B. T.; Kang, J.-B. Rhodium(I)-Catalyzed *ortho*-Alkenylation of 2-Phenylpyridines with Alkynes. *Tetrahedron Lett.* **2001**, *42*, 7609−7612. (b) Shibata, Y.; Otake, Y.; Hirano, M.; Tanaka, K. Amide-Directed Alkenylation of sp2 C−H Bonds Catalyzed by a Cationic Rh(I)/BIPHEP Complex Under Mild Conditions: Dramatic Rate Acceleration by a 1-Pyrrolidinecarbonyl Group. *Org. Lett.* **2009**, *11*, 689−692. (c) Parthasarathy, K.; Jeganmohan, M.; Cheng, C.-H. Rhodium-Catalyzed One-Pot Synthesis of Substituted Pyridine Derivatives from α,β-Unsaturated Ketoximes and Alkynes. *Org. Lett.* **2008**, *10*, 325−328.

(15) (a) Rataboul, F.; Zapf, A.; Jackstell, R.; Harkal, S.; Riermeier, T.; Monsees, A.; Dingerdissen, U.; Beller, M. New Ligands for a General Palladium-Catalyzed Amination of Aryl and Heteroaryl Chlorides. *Chem. - Eur. J.* **2004**, *10*, 2983−2990. (b) Zapf, A.; Jackstell, R.; Rataboul, F.; Riermeier, T.; Monsees, A.; Fuhrmann, C.; Shaikh, N.; Dingerdissen, U.; Beller, M. Practical Synthesis of New and Highly Efficient Ligands for the Suzuki Reaction of Aryl Chlorides. *Chem. Commun.* **2004**, 38−39. (c) Li, H.; Dong, K.; Jiao, H.; Neumann, H.; Jackstell, R.; Beller, M. The Scope and Mechanism of Palladium-Catalyzed Markovnikov Alkoxycarbonylation of Alkenes. *Nat. Chem.* **2016**, *8*, 1159−1166.

(16) So, C. M.; Zhou, Z.; Lau, C. P.; Kwong, F. Y. Palladium-Catalyzed Amination of Aryl Mesylates. *Angew. Chem., Int. Ed.* **2008**, *47*, 6402−6406.

(17) (a) Schmid, T. E.; Jones, D. C.; Songis, O.; Diebolt, O.; Furst, M. R. L.; Slawin, A. M. Z.; Cazin, C. S. J. Mixed Phosphine/N-Heterocyclic Carbene Palladium Complexes: Synthesis, Characterization and Catalytic Use in Aqueous Suzuki−Miyaura Reactions. *Dalton Trans.* **2013**, *42*, 7345−7353. (b) Vuoti, S.; Haukka, M.; Pursiainen, J. Mono and Dinuclear Palladium Complexes of *o*-Alkyl Substituted Arylphosphane Ligands: Solvent-Dependent Syntheses, NMR-sSpectroscopic Characterization and X-ray Crystallographic Studies. *J. Organomet. Chem.* **2007**, *692*, 5044−5052.

(18) Ikawa, T.; Barder, T. E.; Biscoe, M. R.; Buchwald, S. L. Pd-Catalyzed Amidations of Aryl Chlorides Using Monodentate Biaryl Phosphine Ligands: A Kinetic, Computational, and Synthetic Investigation. *J. Am. Chem. Soc.* **2007**, *129*, 13001−13007.

(19) Mahmudov, K. T.; Gurbanov, A. V.; Guseinov, F. I.; Guedes da Silva, M. F. C. Noncovalent Interactions in Metal Complex Catalysis. *Coord. Chem. Rev.* **2019**, *387*, 32−46.

https://dx.doi.org/10.1021/acs.orglett.0c02023
Org. Lett. XXXX, XXX, XXX−XXX