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Palladium-Catalyzed Aryl C−H Olefination with Unactivated, Aliphatic Alkenes

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Supporting Information

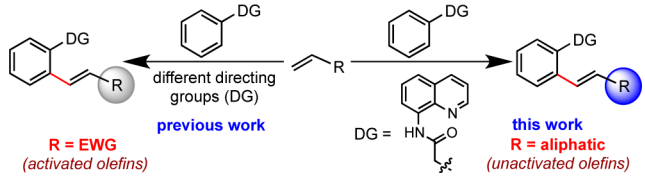
ABSTRACT: Palladium-catalyzed coupling between aryl halides and alkenes (Mizoroki−Heck reaction) is one of the most popular reactions for synthesizing complex organic molecules. The limited availability, problematic synthesis, and higher cost of aryl halide precursors (or their equivalents) have encouraged exploration of direct olefination of aryl carbon−hydrogen (C−H) bonds (Fujiwara−Moritani reaction). Despite significant progress, the restricted substrate scope, in particular noncompliance of unactivated aliphatic olefins, has discouraged the use of this greener alternative. Overcoming this serious limitation, we report here a palladium-catalyzed chelation-assisted ortho C−H bond olefination of phenylacetic acid derivatives with unactivated, aliphatic alkenes in good to excellent yields with high regio- and stereoselectivities. The versatility of this operationally simple method has been demonstrated through drug diversification and sequential C−H olefination for synthesizing divinylbenzene derivatives.

Unactivated carbon−hydrogen bonds (C−H) are present in every naturally occurring organic molecule. Functionalization of these C−H bonds is arguably of the highest synthetic importance. Due to the low reactivity, transition-metal catalysts have been extensively employed to convert them to carbon−heteroatom and carbon−carbon (C−C) bonds of interest.[1]

Palladium-catalyzed coupling between aryl halide and alkene (Mizoroki−Heck reaction) has traditionally been used for the C−C bond formation to synthesize arylated alkenes.[2] Given the importance of this reaction, introduction of alkene into the arene C−H bond (Fujiwara−Moritani reaction) to prepare the same carbogenic scaffolds offers an even more powerful strategy to access a wide array of pharmaceutical precursors and drug molecules.[3] However, the requirement of a large excess of the arene (often a solvent amount) and/or the regioselectivity issues have impeded the practicality of the Fujiwara−Moritani reaction. To address these issues, directing group assisted C(aryl)−H olefination reactions have been adopted in recent years. The usual approach is to use σ-chelating directing groups with a metal center,[4−8] which will lead to ortho selectivity through conformationally rigid five- to seven-membered rings. Very recently meta-selective C(aryl)−H bond activation and oxidative coupling with alkenes has also been reported for palladium catalysts.[10]

Despite significant efforts in alkenylation using palladium catalysts, previous reports have been limited to activated or electronically biased olefins such as acrylates and styrenes.[5−8] To achieve terminal insertion, preinstalled coordinating groups[11] have been found to be promising for selective cases but are limited in application. To date, unbiased alkenes remain the most challenging partner for C−H olefination reactions (Scheme 1).[7,9,12] In addition, regioselectivity issues due to lack

Scheme 1. Arene Ortho C−H Bond Olefination



of intrinsic bias in the aliphatic alkene and the migration of the C−C double bond along the aliphatic chain remain unsolved.[6k,8h]

Here we report a palladium-catalyzed chelation-assisted C−H olefination reaction between unactivated, aliphatic olefins and synthetically useful phenylacetic acid substrates. Notably, only activated olefins were used previously for oxidative Heck coupling of phenylacetic acids.[8h] The present alkenylation reaction has remarkably broad substrate scope, which is enabled by a bidentate directing group along with the use of the racemic 1,1′-binaphthyl-2,2′-diamine (*rac*-BINAM) ligand to enhance the catalytic activity of active Pd(II) species. The generality of this protocol is demonstrated here by preparing an exemplary set of alkenylated compounds (45 examples), most of which represent new chemical entities. The versatility of the protocol is shown by direct olefination of commercial drugs with aliphatic olefins.

Conventional monodentate directing groups are found to be ineffective in palladium-catalyzed C−H bond olefination with unactivated, aliphatic alkenes.[8] We reasoned that a rigid coordination to palladium with a bidentate directing group[13] and a six-membered palladacycle formation[14] during C−H olefination of the arene will help incorporating unactivated olefins as the coupling partner. Although benzoic or 3-phenylpropionic acid derived 8-aminoquinolinamide failed to provide expected olefination product,[15] the phenylacetic acid derivative **3a** gave the alkenylated product with 1-octene in 40%

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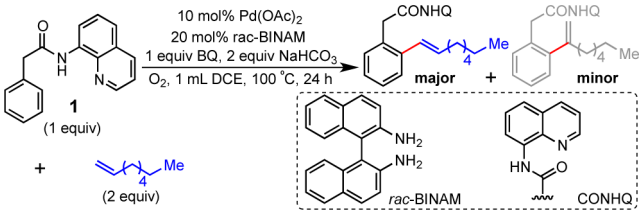
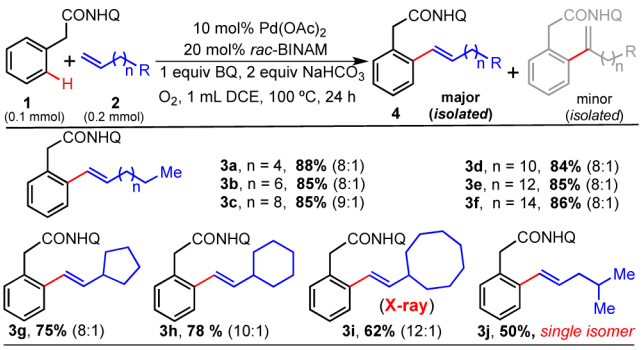
yield (linear/branched, 4/1) using silver acetate as co-oxidant. In order to increase the yield and to reduce the branched product, we thought to saturate the coordination sites of palladium by incorporating an auxiliary ligand. Interestingly, *rac*-BINAM provided 90% GC yield with 8/1 selectivity for linear/branched olefinated product with 1-octene (Scheme 2).

Scheme 2. Alkenylation with 1-Octene



We first tested different α-olefins (Table 1), which are important starting materials for synthetic lubricants, synthetic

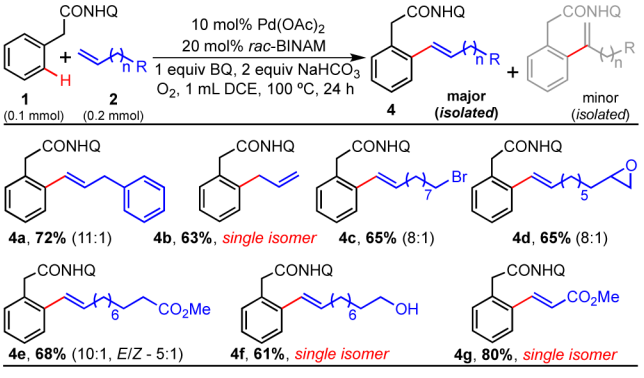
Table 1. Scope with Unactivated Aliphatic Olefins[15,16]



fatty acids, polymers, and plasticizers. Irrespective of the chain length of terminal aliphatic alkenes, excellent isolated yields (84–88%, **3a–f**) were obtained with high linear/branched selectivity. With different vinylcycloalkanes, the regioselectivity (linear/branched) improved with increasing cycloalkane ring size (**3g–i**). The olefination product with vinylcyclooctane was characterized by X-ray crystallography (**3i**), which further confirmed the trans geometry of the desired product.[15,16]

The scope of the position-selective alkenylation reaction was further extended to various functionalized aliphatic olefins (Table 2). Allylbenzene produced 72% yield (**4a**) with 11/1 selectivity for linear/branched products. An unconjugated terminal alkene moiety can be incorporated in the arene (**4b**)

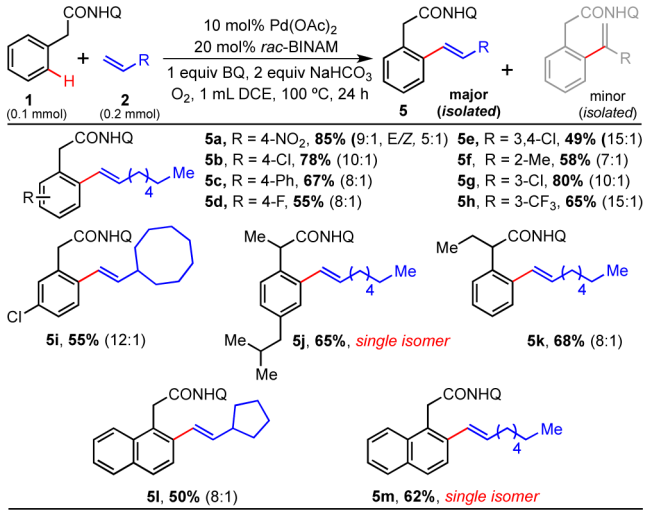
Table 2. Scope with Functionalized Unactivated Alkenes[15]



from allyl bromide. A bromo (**4c**), an epoxy (**4d**), an ester (**4e**), and a hydroxyl group (**4f**) containing alkenylated products were isolated in synthetically useful yields. Unfortunately, the present strategy failed to provide the desired product with different internal alkenes as well as 1,1-disubstituted alkenes.

To obtain insights into the electronic and steric effects on this direct oxidative coupling of C(aryl)–H bonds and olefins, 1-octene was reacted with a functionalized phenylacetamide of 8-aminoquinoline under the optimized reaction conditions (Table 3). Notably, meta-substituted phenylacetic acid

Table 3. Scope with Substituted Phenylacetic Acids[15]



derivatives employed in this study gave alkenylated products exclusively at the 6-position (**5g–l**). Halogenated arenes not only underwent coupling at the ortho position selectively and efficiently (**5b,d–g**) but also did not suffer any Heck coupling or protodehalogenation reactions. Complete selectivity for the 2-position vs the 8-position for 1-naphthylacetamide (**5l,m**) was noteworthy. Selectively linear olefinated products were also obtained for commercial drug ibuprofen (**5j**). Therefore, in combination with previous Rh-catalyzed methods,[7] this report demonstrates the use of a variety of unactivated aliphatic olefins for the generation of valuable linear alkenylated products.

In Tables 1–3, a variety of monoalkenylated products have been synthesized without any need for an ortho or meta substituent to prevent the bis-alkenylation. Encouraged by these results, we thought to provide divinylbenzene derivatives, since they are widely used as building blocks in synthetic chemistry and materials research.[17] Traditionally dihaloarenes were used (Mizoroki–Heck reaction) as the precursor for these commonly occurring carbogenic motifs.[18] In order to obtain sequential functionalization with unactivated olefins in a position-selective manner, mono-olefinated products have been utilized following the present method. A second olefination reaction[19] is expected to be problematic, since the electronic and steric properties of mono-olefinated species will be completely different from those of the starting materials.[8g]

Despite several potential challenges as outlined above, (homo)dialkenylated products[20] were obtained with 1-octene and styrene derivatives (Table 4, **6a–d**). The generation of unsymmetrical diolefinated products (Table 4) indicated that the present catalytic system is indeed very reactive and effective for both mono- and diolefination. With the preinstalled 1-

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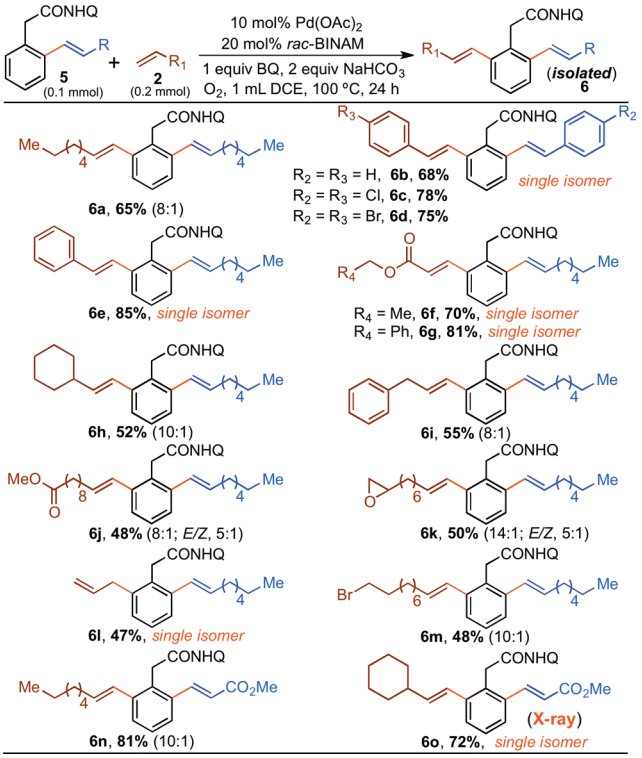
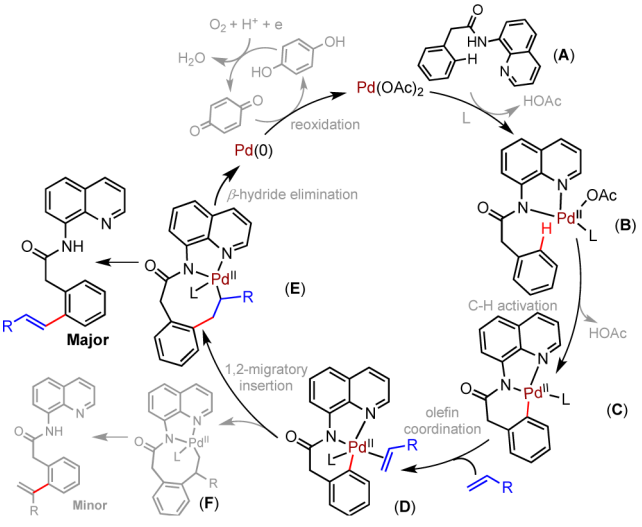
Table 4. Synthesis of Bis-Alkenylated Products[15,16]



octene olefinated product **3a**, styrene, ethyl acrylate, and benzyl acrylate were incorporated (**6e–g**, 70–85% yields). A variety of alkenes including α-olefin, α-branched olefin, allylbenzene, and aliphatic alkenes possessing bromo, ester, and epoxy groups were reacted with the 1-octene-olefinated product **3a** to produce unsymmetrical divinylbenzene compounds (**6h–o**, Table 4).

A stable six-membered palladacyclic intermediate (**C**) was proposed with chelating auxiliary 8-aminoquinoline through position-selective C–H activation (Scheme 3).[13,14a] Upon olefin coordination with **C**, intermediate **D** will be formed. BINAM (L) is unlikely to bind to the palladium center throughout the catalytic cycle in the presence of strongly coordinating substrates. Upon olefin binding in **D**, bidentate BINAM may act as a monodentate ligand in order to stabilize complex **D**.[21,22] These unsymmetrical ratios of olefinated product are likely due to the preferential attack of the C–Pd bond at the less hindered site of the olefin. Depending on preference, two eight-membered cyclometalated intermediates (**E** and **F**) have been proposed to form after 1,2-insertion. Finally, the N–H bond formation will generate Pd(0), which will be oxidized to Pd(II) with the help of benzoquinone and oxygen.

Scheme 3. Proposed Mechanism



The sequential olefinated product (e.g., **6g**) can be hydrogenated with Pd/C/H_2.[8g,15] Notably, the 8-aminoquinoline moiety can be easily removed by acid-catalyzed hydrolysis.[15]

In summary, we have developed an effective method of olefination for acetic acid derivatives by using palladium-catalyzed chelation-assisted ortho C–H bond functionalization techniques. The applicability of this present protocol was also demonstrated by a sequential bis-olefination reaction. Synthetic applications based on the present strategy and detailed mechanistic investigations are currently underway.

■ ASSOCIATED CONTENT

Supporting Information

Text, figures, tables, and CIF files giving experimental procedures, characterization data, and crystallographic data. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) For selected reviews on transition-metal-catalyzed C–C and C–heteroatom bond formation via C–H functionalization, see: (a) Dyker, G. *Handbook of C-H Transformations*; Wiley-VCH: Weinheim, Germany, 2005. (b) Alberico, D.; Scott, M. E.; Lautens, M. *Chem. Rev.* **2007**, *107*, 174. (c) Hartwig, J. F. *Nature* **2008**, *455*, 314. (d) Ackermann, L.; Vicente, R.; Kapdi, A. R. *Angew. Chem., Int. Ed.* **2009**, *48*, 9792. (e) Daugulis, O.; Do, H.-Q.; Shabashov, D. *Acc. Chem. Res.* **2009**, *42*, 1074. (f) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2009**, *110*, 624. (g) Chen, X.; Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094. (h) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (i) Sun, C.-L.; Li, B.-J.; Shi, Z.-J. *Chem. Rev.* **2010**, *111*, 1293. (j) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (k) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (l) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879.

(2) For selected references on the Mizoroki–Heck reaction, see: (a) Mizoroki, T.; Mori, K.; Ozaki, A. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Heck, R. F. *Acc. Chem. Res.* **1979**, *12*, 146. (c) Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009. (d) Dounay, A. B.; Overman, L. E. *Chem. Rev.* **2003**, *103*, 2945. (e) Nicolaou, K. C.;

Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442. (f) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170.

(3) For selected references on the Fujiwara−Moritani reaction, see: (a) Moritani, I.; Fujiwara, Y. *Tetrahedron Lett.* **1967**, 1119. (b) Jia, C. G.; Kitamura, T.; Fujiwara, Y. *Acc. Chem. Res.* **2001**, *34*, 844. (c) Zhou, L.; Lu, W. *Chem. Eur. J.* **2014**, *20*, 634.

(4) Yu, J.-Q.; Giri, R.; Chen, X. *Org. Biol. Chem.* **2006**, *4*, 4041.

(5) For selected examples of ruthenium-catalyzed C−H olefination, see: (a) Weissman, H.; Song, X. P.; Milstein, D. *J. Am. Chem. Soc.* **2001**, 123. (b) Kwon, K.-H.; Lee, D. W.; Yi, C. S. *Organomet.* **2010**, *29*, 5748. (c) Ackermann, L.; Pospech, J. *Org. Lett.* **2011**, *13*, 4153. (d) Padala, K.; Jeganmohan, M. *Org. Lett.* **2011**, *13*, 6144. (e) Arockiam, P. B.; Fischmeister, C.; Bruneau, C.; Dixneuf, P. H. *Green Chem.* **2011**, *13*, 3075. (f) Ackermann, L.; Wang, L.; Wolfram, R.; Lygin, A. V. *Org. Lett.* **2012**, *14*, 728. 337. (g) Li, B.; Ma, J.; Wang, N.; Feng, H.; Xu, S.; Wang, B. *Org. Lett.* **2012**, *14*, 736. (h) Padala, K.; Jeganmohan, M. *Org. Lett.* **2012**, *14*, 1134. (i) Kozhushkov, S. I.; Ackermann, L. *Chem. Sci.* **2013**, *4*, 886. (j) Li, B.; Ma, J.; Xie, W.; Song, H.; Xu, S.; Wang, B. *J. Org. Chem.* **2013**, *78*, 9345.

(6) For selected examples of rhodium-catalyzed C−H olefination, see: (a) Umeda, N.; Hirano, K.; Satoh, T.; Miura, M. *J. Org. Chem.* **2009**, *74*, 7094. (b) Wang, F.; Song, G.; Li, X. *Org. Lett.* **2010**, *12*, 5430. (c) Satoh, T.; Miura, M. *Chem. Eur. J.* **2010**, *16*, 11212. (d) Gong, T.-J.; Xiao, B.; Liu, Z.-J.; Wan, J.; Xu, J.; Luo, D.-F.; Fu, Y.; Liu, L. *Org. Lett.* **2011**, *13*, 3235. (e) Rakshit, S.; Grohmann, C.; Besset, T.; Glorius, F. *J. Am. Chem. Soc.* **2011**, *133*, 2350. (f) Li, H.; Li, Y.; Zhang, X.-S.; Chen, K.; Wang, X.; Shi, Z.-J. *J. Am. Chem. Soc.* **2011**, *133*, 15244. (g) Patureau, F. W.; Besset, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1064. (h) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett.* **2011**, *13*, 2372. (i) Wang, C.; Chen, H.; Wang, Z.; Chen, J.; Huang, Y. *Angew. Chem., Int. Ed.* **2012**, *51*, 7242. (j) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichim. Acta* **2012**, *45*, 31. (k) Liu, B.; Fan, Y.; Gao, Y.; Sun, C.; Xu, C.; Zhu, J. *J. Am. Chem. Soc.* **2013**, *135*, 468. (l) Zhou, J.; Li, B.; Hu, F.; Shi, B.-F. *Org. Lett.* **2013**, *15*, 3460. (m) Shen, Y.; Liu, G.; Zhou, Z.; Lu, X. *Org. Lett.* **2013**, *15*, 3366. (n) Feng, C.; Feng, D.; Loh, T.-P. *Org. Lett.* **2013**, *15*, 3670.

(7) Tsai, A. S.; Brasse, M.; Bergman, R. G.; Ellman, J. A. *Org. Lett.* **2011**, *13*, 540.

(8) For palladium-catalyzed C−H olefination, see: (a) Miura, M.; Tsuda, T.; Satoh, T.; Pivsa-Art, S.; Nomura, M. *J. Org. Chem.* **1998**, *63*, 5211. (b) Grimster, N. P.; Gauntlett, C.; Godfrey, C. R. A.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 3125. (c) Cai, G.; Fu, Y.; Li, Y.; Wan, X.; Shi, Z. *J. Am. Chem. Soc.* **2007**, *129*, 7666. (d) Cho, S. H.; Hwang, S. J.; Chang, S. *J. Am. Chem. Soc.* **2008**, *130*, 9254. (e) Zhang, Y.-H.; Shi, B.-F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2009**, *131*, 5072. (f) García-Rubia, A.; Arrayás, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511. (g) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 6169. (h) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315. (i) Wasa, M.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 3680. (j) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460. (k) Wang, L.; Liu, S.; Li, Z.; Yu, Y. *Org. Lett.* **2011**, *13*, 6137. (l) Garcia-Rubia, A.; Urones, B.; Gomez Arrayas, R.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 10927. (m) Huang, C.; Chattopadhyay, B.; Gevorgyan, V. *J. Am. Chem. Soc.* **2011**, *133*, 12406. (n) Wang, C.; Ge, H. *Chem. Eur. J.* **2011**, *17*, 14371. (o) Li, D.-D.; Yuan, T.-T.; Wang, G.-W. *Chem. Commun.* **2011**, *47*, 12789. (p) Liang, Z.; Ju, L.; Xie, Y.; Huang, L.; Zhang, Y. *Chem. Eur. J.* **2012**, *18*, 15816. (q) Wang, L.; Guo, W.; Zhang, X.-X.; Xia, X.-D.; Xiao, W.-J. *Org. Lett.* **2012**, *14*, 740. (r) Yu, M.; Xie, Y.; Xie, C.; Zhang, Y. *Org. Lett.* **2012**, *14*, 2164. (s) Liu, W.; Li, Y.; Xu, B.; Kuang, C. *Org. Lett.* **2013**, *15*, 2342. (t) Engle, K. M.; Yu, J.-Q. *J. Org. Chem.* **2013**, *78*, 8927. (u) Liu, Q.; Li, Q.; Ma, Y.; Jia, Y. *Org. Lett.* **2013**, *15*, 4528. (v) Nandi, D.; Ghosh, D.; Chen, S.-J.; Kuo, B.-C.; Wang, N. M.; Lee, H. M. *J. Org. Chem.* **2013**, *78*, 3445. (w) Wang, H.-L.; Hu, R.-B.; Zhang, H.; Zhou, A.-X.; Yang, S.-D. *Org. Lett.* **2013**, *15*, 5302. (x) Liu, B.; Jiang, H.-Z.; Shi, B.-F. *J. Org. Chem.* **2014**, *79*, 1521.

(9) Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10625.

(10) (a) Leow, D.; Li, G.; Mei, T.-S.; Yu, J.-Q. *Nature* **2012**, *486*, 518. (b) Dai, H.-X.; Li, G.; Zhang, X.-G.; Stepan, A. F.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 7567. (c) Wan, L.; Dastbaravardeh, N.; Li, G.; Yu, J.-Q. *J. Am. Chem. Soc.* **2013**, *135*, 18056. (d) Lee, S.; Lee, H.; Tan, K. L. *J. Am. Chem. Soc.* **2013**, *135*, 18778. (e) Tang, R.-Y.; Li, G.; Yu, J.-Q. *Nature* **2014**, *507*, 215.

(11) For examples of coordinating-group-containing olefins, see: (a) Delcamp, J. H.; White, M. C. *J. Am. Chem. Soc.* **2006**, *128*, 15076. (b) Delcamp, J. H.; Brucks, A. P.; White, M. C. *J. Am. Chem. Soc.* **2008**, *130*, 11270. (c) Su, Y.; Jiao, N. *Org. Lett.* **2009**, *11*, 2980. (d) Werner, E. W.; Sigman, M. S. *J. Am. Chem. Soc.* **2011**, *133*, 9692.

(12) (a) Daves, G. D.; Hallberg, A. *Chem. Rev.* **1989**, *89*, 1433. (b) Fall, Y.; Berthiol, F.; Doucet, H.; Santelli, M. *Synthesis* **2007**, 1683. (c) Qin, L.; Ren, X.; Lu, Y.; Li, Y.; Zhou, J. *Angew. Chem., Int. Ed.* **2012**, *51*, 5915. (d) Qin, L.; Hirao, H.; Zhou, J. *Chem. Commun.* **2013**, *49*, 10236.

(13) Rouquet, G.; Chatani, N. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726.

(14) (a) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154. (b) Gou, F.-R.; Wang, X.-C.; Huo, P.-F.; Bi, H.-P.; Guan, Z.-H.; Liang, Y.-M. *Org. Lett.* **2009**, *11*, 5726. (c) Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2010**, *132*, 3965. (d) Ano, Y.; Tobisu, M.; Chatani, N. *J. Am. Chem. Soc.* **2011**, *133*, 12984. (e) Ano, Y.; Tobisu, M.; Chatani, N. *Org. Lett.* **2011**, *14*, 354. (f) Tran, L. D.; Popov, I.; Daugulis, O. *J. Am. Chem. Soc.* **2012**, *134*, 18237. (g) Gutekunst, W. R.; Gianatassio, R.; Baran, P. S. *Angew. Chem., Int. Ed.* **2012**, *51*, 7507. (h) Aihara, Y.; Chatani, N. *Chem. Sci.* **2013**, *4*, 664. (i) Aihara, Y.; Chatani, N. *J. Am. Chem. Soc.* **2013**, *135*, 5308. (j) Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2013**, *135*, 17755. (k) Matsubara, T.; Asako, S.; Ilies, L.; Nakamura, E. *J. Am. Chem. Soc.* **2013**, *136*, 646. (l) Nishino, M.; Hirano, K.; Satoh, T.; Miura, M. *Angew. Chem., Int. Ed.* **2013**, *52*, 4457. (m) Rouquet, G.; Chatani, N. *Chem. Sci.* **2013**, *4*, 2201.

(15) See the Supporting Information for a detailed description. For linear olefins (entries **3a−f** and entries **5a−d**,**k**) 3−5% diolefinated product was detected.

(16) CCDC 1012625 (**3i**) and CCDC 1012626 (**6o**) can be obtained from http://www.ccdc.cam.ac.uk/data_request/cif.

(17) (a) Burroughes, J. H.; Bradley, D. D. C.; Brown, A. R.; Marks, R. N.; Mackay, K.; Friend, R. H.; Burns, P. L.; Holmes, A. B. *Nature* **1990**, *347*, 539. (b) Kraft, A.; Grimsdale, A. C.; Holmes, A. B. *Angew. Chem., Int. Ed.* **1998**, *37*, 402. (c) Grimsdale, A. C.; Chan, K. L.; Martin, R. E.; Jokisz, P. G.; Holmes, A. B. *Chem. Rev.* **2009**, *109*, 897.

(18) Plevyak, J. E.; Heck, R. F. *J. Org. Chem.* **1978**, *43*, 2454.

(19) For selected references on divinylbenzene, see: (a) Plevyak, J. E.; Dickerson, J. E.; Heck, R. F. *J. Org. Chem.* **1979**, *44*, 4078. (b) Spencer, A. *J. Organomet. Chem.* **1984**, *265*, 323. (c) Carlstrom, A. S.; Frejd, T. *J. Org. Chem.* **1991**, *56*, 1289. (d) Tao, W. J.; Nesbitt, S.; Heck, R. F. *J. Org. Chem.* **1990**, *55*, 63. (e) Sengupta, S.; Sadhukhan, S. K. *Tetrahedron Lett.* **1998**, *39*, 715. (f) Wang, C.; Tan, L. S.; He, J. P.; Hu, H. W.; Xu, J. H. *Synth. Commun.* **2003**, *33*, 773.

(20) For selected examples of trisubstituted arenes, see: (a) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 119. (b) Mariampillai, B.; Alliot, J.; Li, M.; Lautens, M. *J. Am. Chem. Soc.* **2007**, *129*, 15372. (c) Gericke, K. M.; Chai, D. I.; Bieler, N.; Lautens, M. *Angew. Chem., Int. Ed.* **2009**, *48*, 1447.

(21) (a) Denmark, S. E.; Stavenger, R. A.; Faucher, A. M.; Edwards, J. P. *J. Org. Chem.* **1997**, *62*, 3375. (b) Braunstein, P.; Naud. *F. Angew. Chem., Int. Ed.* **2001**, *40*, 680. (c) Lucas, H. R.; Meyer, G. J.; Karlin, K. D. *J. Am. Chem. Soc.* **2010**, *132*, 12927. (d) Ros, A.; Estepa, B.; Rodriguez, R. L.; Alvarez, E.; Fernandez, R.; Lassaletta, J. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 11724.

(22) A stoichiometric reaction under the experimental conditions was carried out in the absence of alkene. The ESI-MS indicated formation of intermediate **C** along with the features of **C** without BINAM. This Pd species (**C**) gave the desired product in 20% yield.