Communication

Palladium Catalyzed Aryl C–H Olefination with Unactivated, Aliphatic Alkenes

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Palladium Catalyzed Aryl C–H Olefination with Unactivated, Aliphatic Alkenes

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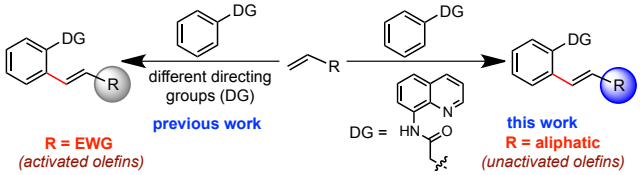
Supporting Information

ABSTRACT: Palladium catalyzed coupling between aryl halides and alkenes (Mizoroki-Heck reaction) is one of the most popular reactions for synthesizing complex organic molecules. 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, restricted substrate scope in particular noncompliance of unactivated aliphatic olefins restricted the usage of this greener alternative. Overcoming this serious limitation, we report here a palladium-catalyzed chelation-assisted *ortho*-C–H bond olefination of phenyl acetic 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 divinyl benzene derivatives.

Unactivated carbon-hydrogen bonds (C–H) are present in every naturally occurring organic molecules. Functionalization of these C–H bonds is arguably of 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 arene C–H bond (Fujiwara-Moritani reaction) to prepare the same carbogenic scaffolds offers even more powerful strategy to access wide array of pharmaceutical precursors and drug molecules.[3] However, requirement of large excess of the arene (often solvent amount) and/or the regioselectivity issues has impeded the practicality of the Fujiwara-Moritani reaction. To address these issues, directing group assisted C(aryl)–H olefination reactions are 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 5-7 membered rings. Very recently *meta*-selective C(aryl)–H bond activation and oxidative coupling with alkenes has also been reported by palladium catalyst.[10]

Scheme 1. Arene *Ortho* C–H Bond Olefination



Despite significant efforts for alkenylation using palladium catalysts, previous reports are limited to activated or electronically biased olefins like acrylates and styrenes.[5-8] To achieve terminal insertion, pre-installed coordinating groups[11] have been found to be promising for selective cases, but are limited in application. Till date, unbiased alkenes remain the most challenging partner for C–H olefination reaction (Scheme 1).[7, 9, 12] In addition, regioselectivity issues due to lack of intrinsic biasness in aliphatic alkene and the migration of C–C double bond along the aliphatic chain remain unsolved.[6k, 8h]

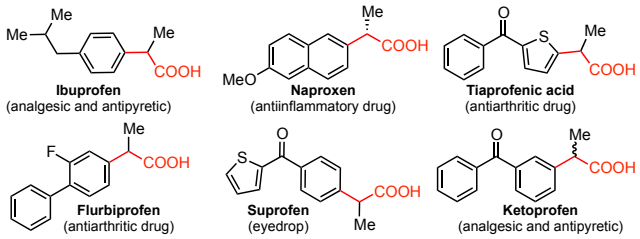
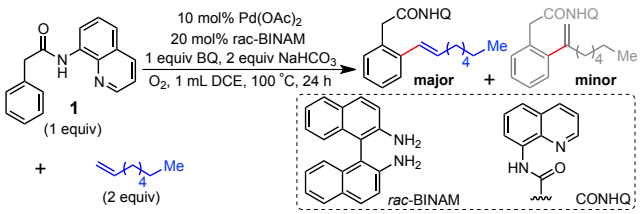


Figure 1. Commercial drugs with aryl acetic acid motif

Here we report a palladium catalyzed chelation-assisted C–H olefination reaction between unactivated, aliphatic olefins and synthetically useful phenyl acetic acid substrates. Notably, only activated olefins were used previously for oxidative Heck coupling of phenyl acetic acids.[8h] The present alkenylation reaction has remarkably broad substrate scope, which is enabled by bidentate directing group along with the use of 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 (Figure 1) with aliphatic olefins.

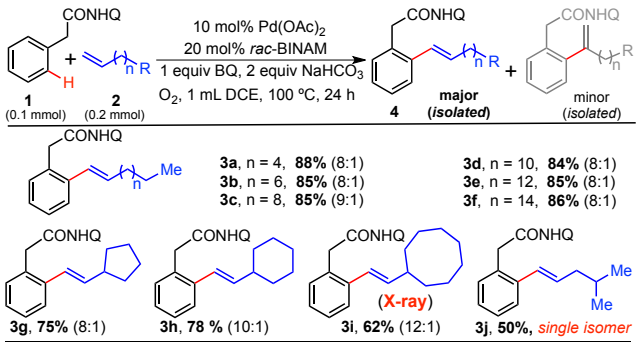
Scheme 2. Alkenylation with 1-octene



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 groups[13] and a six-membered palladacycle formation[14] during C–H olefination of arene will help incorporating unactivated olefins as the coupling partner. Although benzoic or 3-

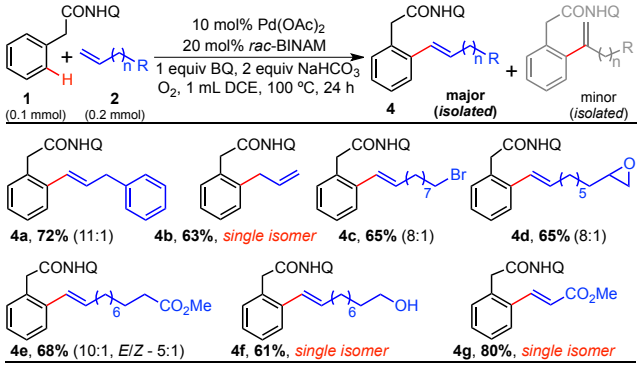
phenylpropionic acid derived 8-amino quinolinamide failed to provide expected olefination product,[15] phenyl acetic acid derivative (**3a**) gave the alkenylated product with 1-octene in 40% yield (linear/branched, 4:1) using silver acetate as co-oxidant. In order to increase the yield and to reduce the branched product, we thought to saturate the coordination sites of palladium by incorporating auxiliary ligand. Interestingly, *rac*-BINAM provided 90% GC yield with 8:1 selectivity for linear/branched olefinated product with 1-octene (Scheme 2).

Table 1. Scope with Unactivated Aliphatic Olefins[15]



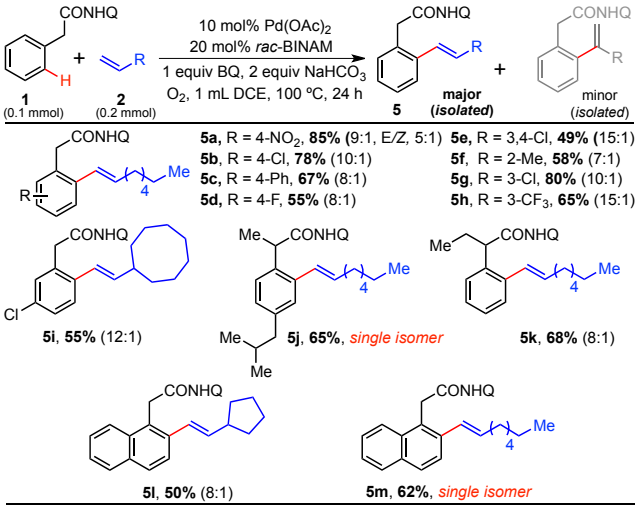
We first tested different alpha olefins (Table 1), which are important starting materials for synthetic lubricants, synthetic fatty acids, polymers and plasticizers. Irrespective of the chain length of terminal aliphatic alkenes, excellent isolated yields (84-88%, **3a**-**3f**) were obtained with high linear/branched selectivity. With different vinyl cycloalkanes, regioselectivity (linear/branched) was improved with increasing cycloalkane ring size (**3g**-**3i**). Such observations may be attributed to the preferred migratory insertion towards linear product formation with α-branched olefins. Olefination product with vinyl cyclooctane was characterized by X-ray crystallography (**3i**), which further confirmed the *trans*-geometry of the desired product.[15, 16]

Table 2. Scope with Functionalized Unactivated Alkenes



The scope of the position-selective alkenylation reaction was further extended to various functionalized aliphatic olefins (Table 2). Allyl benzene produced 72% yield (**4a**) with 11:1 selectivity for linear/branched products. An unconjugated terminal alkene moiety can be incorporated in arene (**4b**) from allyl bromide *via* a concerted elimination upon insertion of alkene in the initially generated palladium-aryl species. Arene C–H bond can be selectively reacted with aliphatic alkene bearing bromo substituent (**4c**). An epoxy (**4d**), an ester (**4e**) and a hydroxyl group (**4f**) containing alkenylated products were isolated in synthetically useful yields. Unfortunately, present strategy failed to provide desired product with different internal alkenes (*e.g.* (*E*)-hex-2-ene, cyclohexene, 1H-indene *etc.*) as well as 1,1-disubstituted alkenes (*e.g.* β-pinene).

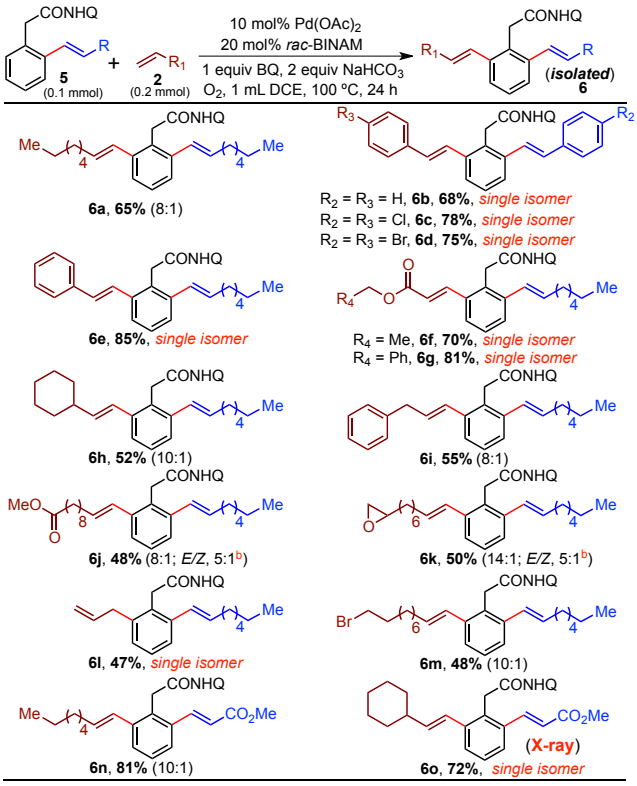
Table 3. Scope with Substituted Phenylacetic Acids[15]



To obtain insights into the electronic and steric effect on this direct oxidative coupling of C(aryl)–H bonds and olefins, 1-octene was reacted with functionalized phenylacetamide of 8-aminoquinoline under the optimized reaction conditions (Table 3). Notably, *meta* substituted phenyl acetic acid derivatives employed in this study gave alkenylated product exclusively at the 6-position (**5f**-**5h**). Halogenated arenes not only underwent coupling at the *ortho* position selectively and efficiently (**5b**, and **5d**-**5g**), but also did not suffer any Heck coupling or protodehalogenation reactions. Although a moderate yield of olefin insertion into 1-naphthylacetamide was attained (**5l** and **5m**), complete selectivity for 2-position *vs.* 8-position was noteworthy. Further no branched alkenylated product was detected for this case. This olefination reaction was also successfully extended to α-substituted phenyl acetic acid substrate (**5k**). Selectively linear olefinated product was also obtained for commercial drugs (Figure 1), such as Ibuprofen (**5j**) and Naproxen (**5n**). Therefore, in combination with previous Rh-catalyzed method,[7] this report demonstrated the use of a variety of unactivated aliphatic olefins for the generation of valuable linear alkenylated products.

In Tables 1-3, a variety of mono-alkenylated products have been synthesized without any need for *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 occuring carbogenic motifs.[18] In order to obtain sequential functionalization with unactivated olefins by position selective manner, mono-olefinated products have been utilized following the present method. Second olefination reaction is expected to be problematic since electronic and steric properties of mono olefinated species will be completely different than the starting materials.[8g] Further, the ability of the monoalkenylated product to coordinate with the palladium centers may hinder the catalyst to achieve the second alkenylation.[19]

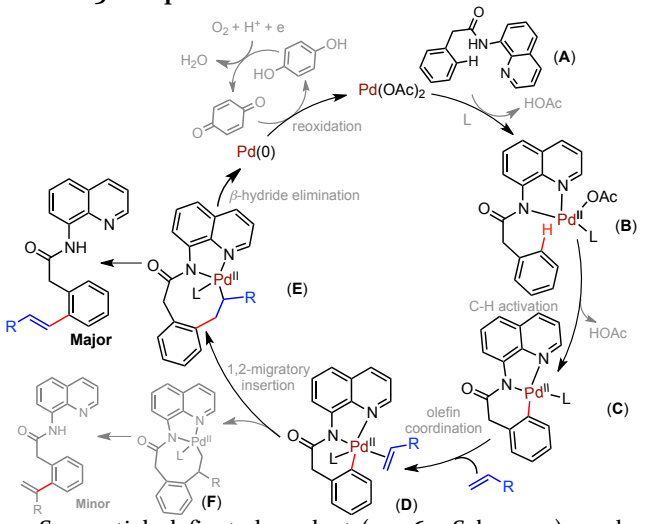
Table 4. Synthesis of Bis-alkenylated Products



Despite several potential challenges as outlined above, (homo)di-alkenylated products[20] were obtained with 1-octene and styrene derivatives (Table 4, **6a-6d**). Subsequently, we focused on synthesizing differentially substituted diolefinated compounds. Generation of unsymmetrical diolefinated products (Table 4) indicated that the present catalytic system is indeed very reactive and effective for both mono- and di-olefination. With pre-installed 1-octene olefinated product **3a**, styrene, ethyl acrylate and benzyl acrylate were incorporated (**6e-6g**, 70-85% yields). A variety of alkenes including alpha olefin, α-branched olefin, allyl benzene, aliphatic alkene possessing bromo, ester and epoxy groups were reacted with 1-octene-olefinated product **3a** to produce unsymmetrical divinylbenzene compounds (**6h-6o**, Table 4).

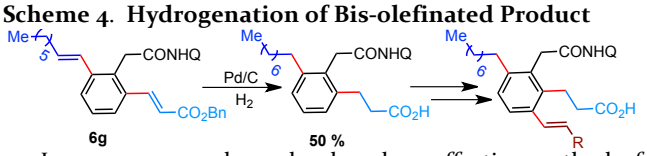
A stable six-membered palladacycle intermediate (**C**) was proposed with chelating auxiliary 8-aminoquinoline through position-selective C–H activation (Scheme 3).[13, 14a] Upon olefin coordination with **C**, intermediate **D** will be formed. BINAM (L) is unlikely to bind to the palladium center throughout the catalytic cycle in presence of strongly coordinating substrates. Upon olefin binding in **D**, bidentate BINAM may act as monodentate ligand in order to stabilize complex **D**.[21] Unlike activated or electronically biased olefins, migratory insertion may occur to both sides of aliphatic alkene. Nonetheless, linear olefinated product was obtained in major quantity compared to branched product. These unsymmetrical ratios of olefinated product are likely due to the preferential attack by C–Pd bond to the less hindered site of olefin. Depending on preference, two eight membered cyclometallated intermediate (**E** or **F**) has 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



Sequential olefinated product (*e.g.* **6g**, Scheme 4) can be hydrogenated with Pd/C/H_2. In this way, different long chain alkyl groups can be incorporated to arene. The resulting product may further be applied for iterative olefination.[8g] Notably, the 8-aminoquinoline moiety can be easily removed by acid catalyzed hydrolysis.[15]

Scheme 4. Hydrogenation of Bis-olefinated Product



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 technique. The applicability of this present protocol was also demonstarted by the sequential bis-olefination reaction. Synthetic applications based on present strategy and detailed mechanistic investigations are currently underway.

ASSOCIATED CONTENT

Supporting Information

Experimental procedures and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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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,* **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 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 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) For a recent review on σ-chelating directing groups, see: Yu, J.-Q.; Giri, R.; Chen, X. *Org. Bio. 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. *Aldrichimica 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) For linear olefinated product formation with unactivated aliphatic olefin using rhodium catalyst, see: 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) For Ir-catalyzed vinylfuran synthesis from unactivated alkenes, see: Sevov, C. S.; Hartwig, J. F. *J. Am. Chem. Soc.* **2014**, *136*, 10625.

(10) For palladium catalyzed *meta*-selective arene C–H functionalization, see: (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) For chelation assisted C–H functionalization using 8-aminoquinoline, see: (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 Supporting Information for detailed description. For linear olefins (entries **3a**-**3f**, and entries **5a**-**5d** and **5k**) 3-5% diolefinated product was detected. We could not isolate these compounds in pure form. For all other entries, we could not detect the diolefination product.

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

(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.

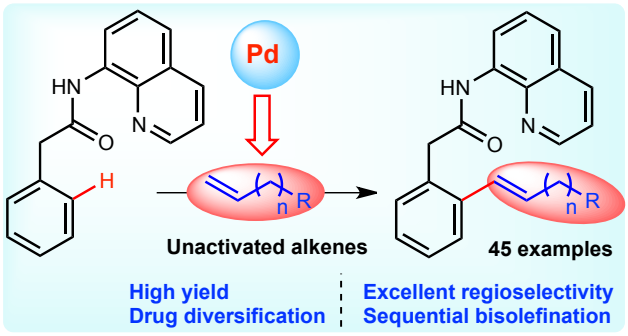
(19) For selected references of divinyl benzene, see: (a) Plevyak, J. E.; Dickerson, J. E.; Heck, R. F. *J. Org. Chem.* **1979**, *44*, 4078. (b) Spencer, A. *J. Organomet. Chem.* **1984**, *265*, 323. (c) Carlstrom, A. S.; Frejd, T. *J. Org. Chem.* **1991**, *56*, 1289. (d) Tao, W. J.; Nesbitt, S.; 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 arene, see: (a) Catellani, M.; Frignani, F.; Rangoni, A. *Angew. Chem. Int. Ed. Eng.* **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) For selected examples of the competition between coordination of incoming ligand (*e.g.* olefin, CO, CH_3CN *etc.*) and decoordination of one arm of the multidentate chelate, see: (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 condition 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 (Scheme 2) with 1-octene along with five other inseparable mixtures of compounds.

TOC Graphic :


HN
O
N
H
Pd
n R
Unactivated alkenes
HN
O
N
n R
45 examples
High yield
Drug diversification
Excellent regioselectivity
Sequential bisolefination