Heck Reaction

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Intermolecular Mizoroki–Heck Reaction of Aliphatic Olefins with High Selectivity for Substitution at the Internal Position**

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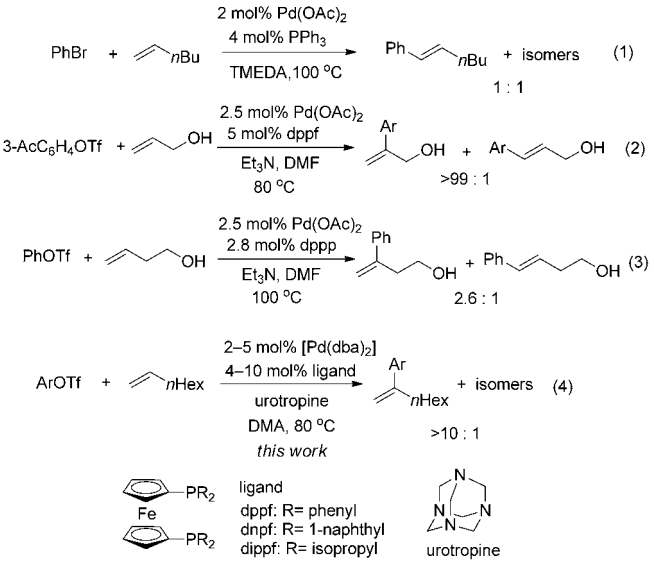
The Mizoroki–Heck reaction generally refers to Pd-catalyzed C–C bond formation between organic (pseudo)halides and olefins. Today, it has become a powerful tool to prepare substituted olefins.[1] A key issue in intermolecular Heck reactions is the control of the site where aryl groups insert into olefins. High regioselectivity can be easily achieved for olefins carrying substituents with a significant electronic difference at the two olefinic sites,[2] such as acrylates[3] and vinyl ethers.[4]

Aliphatic olefins, however, generally lack intrinsic electronic differentiation between two olefinic positions and it has been challenging to achieve good regiocontrol [Eq. (1), Scheme 1].[5,6] To induce terminal insertion, coordinating groups are often present on olefins to serve as chelates.[7] The chelation strategy was also used in oxidative[8] and decarboxylative[9] Heck reactions to achieve regioselectivity. Recently, Sigman and Werner reported high terminal selectivity even for olefins without chelating groups.[10] For aliphatic olefins, high internal selectivity also proved very difficult to achieve, except a few special cases.[11] For example, Cabri et al. reported that olefin insertion into cationic aryl–Pd intermediates can be biased toward the internal position, but the selectivity was too low to be synthetically useful.[12] As a special case, allylic alcohol gave excellent internal selectivity, because owing to the inductive effect of its hydroxy group the electronic density on the internal carbon atom is decreased [Eq. (2), Scheme 1]. The inductive effect quickly diminishes over several bonds. Thus, for homoallylic alcohol the selectivity dropped drastically [Eq. (3), Scheme 1]. Herein, we report a general method for Heck reactions of aliphatic olefins in high internal selectivity, by using a set of ferrocene-based bisphosphine ligands [Eq. (4), Scheme 1].

The Heck products, α-alkylstyrenes can be readily converted to various chiral building blocks by asymmetric catalytic processes.[13] They are also intermediates in the synthesis of bioactive natural products[14] and drug candidates.[15] The α-alkylstyrenes used to be prepared by cross-couplings of 2-alkenyl electrophiles or 2-alkenyl metallic reagents. Our new method directly uses simple olefins and does not require preactivation of olefin substrates.



Scheme 1. Intermolecular Heck reactions of aliphatic olefins. TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine, Tf = trifluoromethanesulfonyl, dppp = 1,3-bis(diphenylphosphino)propan, dba = dibenzylideneacetone, DMA = dimethylacetamide.

Initially, we used a model reaction of 1-naphthyl triflate and 1-octene and dppf as supporting ligand for the palladium catalyst (Figure 1). To our surprise, a dramatic effect of bases was observed (Figure 1). In particular, when trialkylamines, such as triethylamine and Hünig's base, were used, significant reduction of aryl triflate was observed, and the corresponding reduction product was obtained in up to 50% yield.[16] In contrast, when urotropine was used, no reduction byproduct was detected and Heck products were formed in almost quantitative yield. The ratio of the desired isomer, 2-aryl-1-octene versus all other isomers was 13:1, determined by GC.[17] It is worth pointing out that this ratio is not equivalent to regioselectivity. Urotropine is a relatively weak Lewis base,[18] and it does not compete strongly for the vacant site on a cationic (dppf)Pd(Ar) intermediate. Furthermore, its β-hydrogen atom cannot eliminate to donate a hydride to palladium, according to Bredt's rule. In comparison, when the more basic and donating bases DBU and DABCO were used, only small amounts of Heck products were formed. Other bases such as 2,6-lutidine, proton sponge, and Li_2CO_3 gave much lower yields than urotropine.

In the model reaction of 1-naphthyl triflate and 1-octene, we have screened many bisphosphine ligands to improve the

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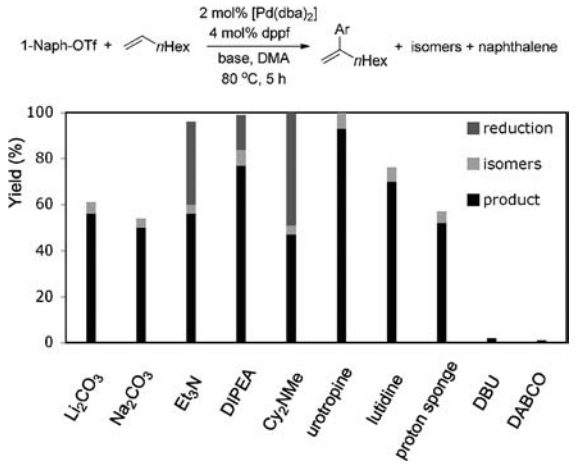
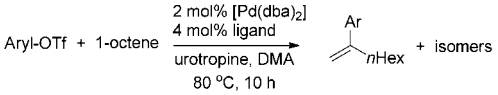


Figure 1. Effect of bases on the formation of different products of the model reaction. In addition to the formation of the Heck product (black bars) and isomers (light gray), reduction of the aryl triflate (dark gray) was also observed. DIPEA = diisopropylethylamine, Cy = cyclohexyl, DBU = 1,8-diazabicyclo[5.4.0]undec-7-ene, DABCO = 1,4-diazabicyclo[2.2.2]octane.

selectivity. To our delight, ferrocene-derived 1,1′-bisphosphine ligands were particularly selective in delivering the branched product (Figure 2). For example, when the ligand dippf was used, the selectivity was improved to 57:1 in the presence of 2 mol% palladium catalyst (for details, see the Supporting Information).



Aryl	dnpf	dppf	dippf
phenyl[a]	11:1	4:1	(complex)
1-naphthyl	18:1	13:1	57:1
o-*t*-butylphenyl	2:1	50:1	22:1

Figure 2. Interplay between ligands and aryl triflates on selectivity. The ratios of the branched Heck product to all other isomers are shown. [a] 5 mol% [Pd(dba)$_2$] and 10 mol% ligand were used.

Later, we found that the selectivity was highly dependent on the aryl electrophiles. For example, if the aryl triflate contained a large *ortho*-*tert*-butyl group, the ligand dppf was very selective and gave a selectivity of 50:1 (Figure 2). In general, we found it very difficult to achieve high selectivity for aryl triflates without an *ortho* group. In model reactions with phenyl triflate, the ligand dppf only afforded 4:1 selectivity, and the ligand dippf gave a complex mixture of product isomers. After examination of a dozen of bisphosphine ligands, we found that the new ligand 1,1′-bis[di(1-naphthyl)phosphino]ferrocene (dnpf) can give a good selectivity of 11:1 (Figure 3; dnpf = d(1-naph)pf in Figure 3).[19]

After establishing suitable conditions for each subclass of aryl triflates, we examined the scope of aryl triflates with 1-octene as model olefin (Scheme 2). Some observations are noteworthy. a) For aryl electrophiles without *ortho* groups,

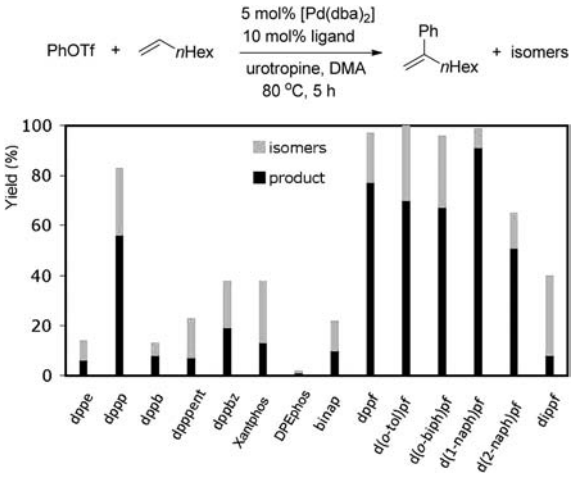
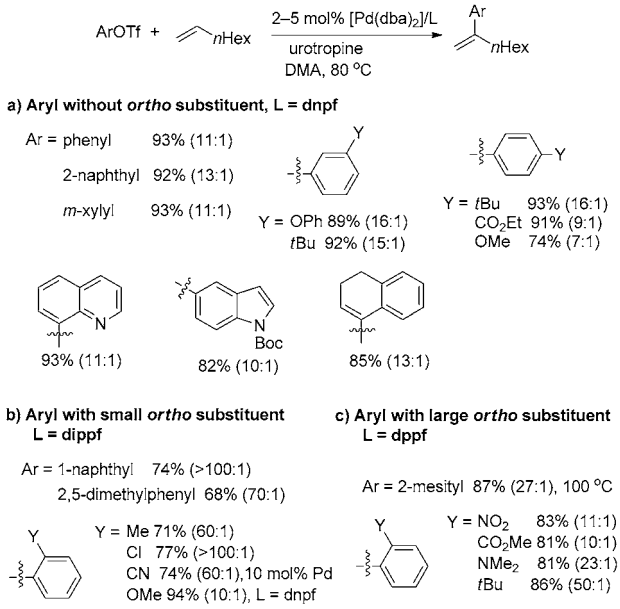


Figure 3. Effect of ligands in the Heck reaction of phenyl triflate. dppe, dppb, dpppent, and dppbz are typical bisphosphine ligands.[19]

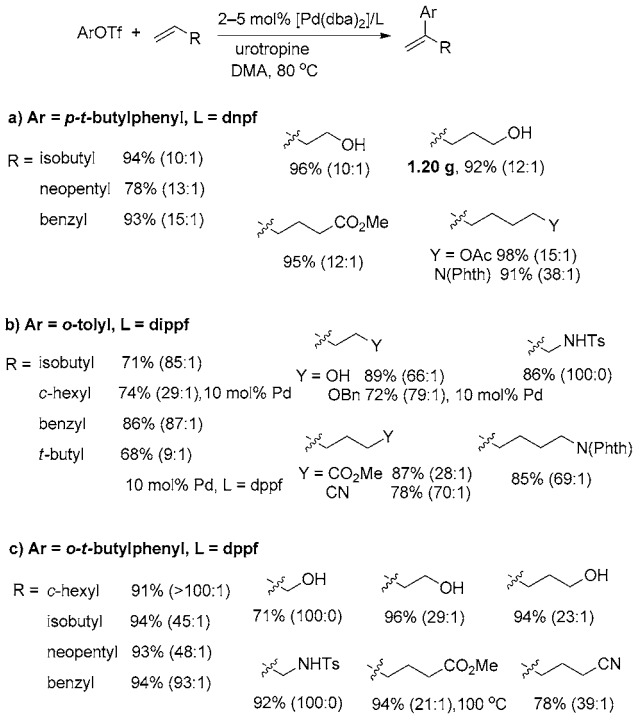


Scheme 2. Scope of organic triflates in the Heck reaction of 1-octene. The ratios of the Heck product shown in the scheme to all other isomers are given in brackets.

the ligand dnpf gave a selectivity above 10:1 for most substrates. For aryl triflates substituted with either electron-donating or electron-withdrawing groups at the *para* position, the selectivity dropped slightly. Some heteroaryl triflates, derived from indole and quinoline, worked well. One example of a vinyl electrophile is also included. b) For aryl electrophiles carrying small *ortho* substituents, the dippf ligand afforded 2-aryl-1-octenes almost exclusively in most cases. Both aromatic chloride and nitrile were tolerated under the catalytic condition. For *o*-anisyl triflate, the ligand dnpf was found to be more selective than dippf. c) For aryl electrophiles carrying large *ortho* groups, the dppf ligand gave good to excellent selectivity. Even sterically demanding 2-mesityl triflate can give high selectivity at 100 °C. Some polar *ortho*

subtituents such as nitro, ester, and dimethylamino substituents did not interfere with the catalytic cycle.

Next, we studied the scope of terminal olefins with each subclass of aryl triflates (Scheme 3). Many polar groups on olefins are compatible, such as ester, nitrile, phthalimide,

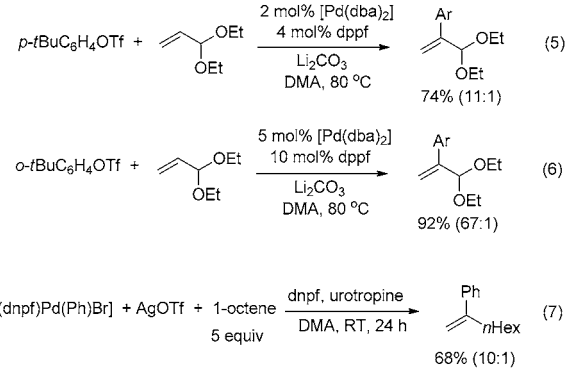


Scheme 3. Scope of olefins in Heck reactions of model aryl triflates. The ratios of the Heck product shown in the scheme to all other isomers are given in brackets. Phth = phthaloyl, Ts = *p*-toluenesulfonyl.

sulfonamide, and even alcohol groups. Most reactions provided good internal selectivity. For example, homoallylic and bishomoallylic alcohols coupled with aryl triflates carrying no *ortho* substituents in more than 10:1 selectivity, which is unprecedented.[12] Some very hindered olefins can also be used. In a reaction of *tert*-butylethylene, the aryl group added preferentially to the more hindered internal position in 9:1 selectivity, in the presence of the dppf ligand. Furthermore, allylbenzene reacted smoothly, although it is prone to undergo facile olefin isomerization catalyzed by palladium hydride.[20] One example, with 5-hydroxy-1-pentene as olefin substrate, was scaled up to produce 1.2 g of the Heck product without loss of selectivity (12:1). The desired isomer can be separated from other isomers by flash chromatography.

In Heck reactions of α,β-unsaturated carbonyl compounds, there is a strong bias for aryl groups to insert at the electron-poor β position.[21] Thus, to introduce aryl groups at the α position, cross-couplings of α-halogenated or α-metallated acrylates are often employed.[22] Interestingly, our Heck condition can be applied to perform selective α arylation of acrolein diethyl acetal [Eqs. (5)–(6), Scheme 4].[23]

To determine the origin of high selectivity from the dnpf ligand, we have prepared its oxidative addition complex with PhBr. Treatment of [(dnpf)Pd(Ph)Br] with 1-octene in the



Scheme 4. α Arylation of acrolein diethyl acetal [Eqs. (5) and (6)] and treatment of the [(dnpf)Pd(Ph)Br] complex with 1-octene [Eq. (7)].

presence of AgOTf gave the Heck product in 68% yield and 10:1 selectivity [Eq. (7), Scheme 4].[24] The selectivity is very similar to that observed under catalytic conditions. Single-crystal X-ray diffraction analysis of the complex showed some unusual structural features.[25] First, the backbone of dnpf adopts an almost eclipsed ferrocene conformation, unlike staggered ones in related dppf complexes.[26] Edge-to-edge interactions between two neighboring *P*-naphthyl groups were identified to enforce this unusual conformation. Second, the coordination geometry is significantly distorted from square planarity. For example, the bond angles ∡P2-Pd-C(phenyl) and ∡P1-Pd-Br are deviated from linearity by more than 10 degrees (Figure 4). Furthermore, both the *Pd*-phenyl group and bromine atom are forced substantially out of the plane defined by P1-Pd-P2; this kind of distorted geometry is absent in dppf complexes.[26] The distortion is caused by steric repulsion with neighboring *P*-naphthyl groups of the ligand. In the terminal insertion mode, the olefinic substituent will experience severe steric repulsion with the ligand. Thus, terminal insertion is greatly disfavored.

We have also conducted DFT calculations (PBE1PBE) on the insertion step using propene as model olefin. The purpose is to understand the effect of both ligands and *ortho* groups on *Pd*-phenyl groups on regioselectivity. Assuming fast equilibrium among olefin conformers of each complex, regioselectivity will be dictated by relative energy (ΔE) of transition

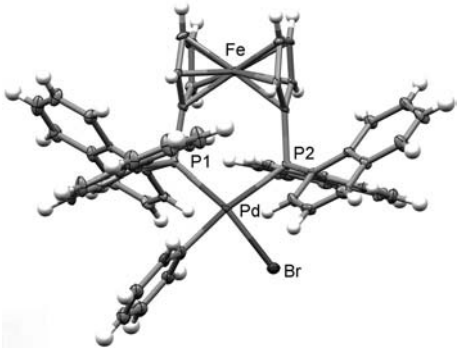


Figure 4. ORTEP representation of the [(dnpf)Pd(Ph)Br] complex with 50% thermal ellipsoid probability. Important bond angles: ∡Br-Pd-C(phenyl) = 84°; ∡P1-Pd-P2 = 103°; ∡P2-Pd-C(phenyl) = 168°; ∡P1-Pd-Br = 166°.

states (TSs). From the cationic (dppf)Pd(Ph)(propene), ΔE between the predominant TS(terminal) and TS(internal) was calculated to be 2 kcal mol^{-1}. From the corresponding *ortho-tert*-butylphenyl complex, ΔE increased to 4.5 kcal mol^{-1}. The reason is that the TS of terminal insertion is more sensitive to steric influence than that of internal insertion. Moreover, when the ligand was switched from dppf to dnpf in the cationic (ligand)Pd(Ph)(propene) complex, ΔE was raised to 2.3 kcal mol^{-1}, which is in agreement with observed trends of selectivity.

In summary, we have realized a general method for Heck reaction of terminal aliphatic olefins with high internal selectivity. The ratio of the desired products, 2-aryl-1-alkenes versus the sum of all other isomers is generally higher than 10:1. When aryl triflates contain *ortho* substituents, the selectivity is even higher, up to 100:0. The synthetic usefulness of the method was further augmented by the fact that trace amounts of minor isomers can be readily removed from the desired isomers by flash chromatography in most cases. Our experimental and computational studies indicate that the dnpf ligand improved selectivity by inhibiting the minor pathway of terminal insertion owing to steric effects. Furthermore, the (dnpf)Pd catalyst was successfully applied to a regioselective Heck reaction of aromatic olefins by us recently.[27] Application of the catalyst to similar Heck reactions of aryl halides is ongoing.

Experimental Section

In air, a 100 mL dry Schlenk tube containing a magnetic stir bar was charged with [Pd(dba)$_2$] (172 mg, 0.30 mmol) and 1,1′-bis[di(1-naphthyl)phosphino]ferrocene, dnpf (453 mg, 0.60 mmol). The atmosphere was switched to argon after three cycles of evacuation and refilling. Degassed DMA (30 mL) was then added. After stirring for 10 min at room temperature, the mixture was treated with *p-tert*-butylphenyl triflate (1.69 g, 6.0 mmol), 4-pentene-1-ol (2 equiv, 1.03 g, 12.0 mmol), and urotropine (2 equiv, 1.68 g, 12.0 mmol). The reaction tube was capped tightly and the mixture was heated with vigorous stirring in an oil bath at 80 °C (external temperature). The aryl triflate was fully consumed after seven hours (monitored by GC). The ratio of the desired isomer versus all other isomers combined was determined to be 12:1 by GC. After routine workup and flash chromatography, the Heck product was obtained as colorless oil (1.20 g, 92 % combined yield). The desired isomer was separated from other minor isomers by flash chromatography.

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[1] Reviews: a) R. F. Heck, *Acc. Chem. Res.* **1979**, *12*, 146; b) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009; c) K. C. Nicolaou, P. G. Bulger, D. Sarlah, *Angew. Chem.* **2005**, *117*, 4516; *Angew. Chem. Int. Ed.* **2005**, *44*, 4442; d) S. Bräse, A. de Meijere, *Metal-Catalyzed Cross-coupling Reactions* (Eds.: A. de Meijere, F. Diederich), Wiley-VCH, Weinheim, **2004**, pp. 217–316; e) G. Zeni, R. C. Larock, *Chem. Rev.* **2006**, *106*, 4644.

[2] Reviews: a) W. Cabri, I. Candiani, *Acc. Chem. Res.* **1995**, *28*, 2; b) G. D. Daves, A. Hallberg, *Chem. Rev.* **1989**, *89*, 1433; c) P. Nilsson, K. Olofsson, M. Larhed, *The Mizoroki-Heck Reaction* (Ed.: M. Oestreich), Wiley, New York, **2009**, pp. 133.

[3] Examples: a) A. F. Littke, G. C. Fu, *J. Am. Chem. Soc.* **2001**, *123*, 6989; b) B. P. Carrow, J. F. Hartwig, *J. Am. Chem. Soc.* **2010**, *132*, 79.

[4] Examples: a) W. Cabri, I. Candiani, A. Bedeschi, R. Santi, *J. Org. Chem.* **1990**, *55*, 3654; b) K. S. A. Vallin, M. Larhed, A. Hallberg, *J. Org. Chem.* **2001**, *66*, 4340; c) T. M. Gøgsig, A. T. Lindhardt, M. Dekhane, J. Grouleff, T. Skrydstrup, *Chem. Eur. J.* **2009**, *15*, 5950; d) J. Ruan, J. Xiao, *Acc. Chem. Res.* **2011**, *44*, 614.

[5] Examples: a) H. A. Dieck, R. F. Heck, *J. Am. Chem. Soc.* **1974**, *96*, 1133; b) S. Bräse, M. Schroen, *Angew. Chem.* **1999**, *111*, 1139; *Angew. Chem. Int. Ed.* **1999**, *38*, 1071; c) A. C. Albéniz, P. Espinet, B. Martín-Ruiz, D. Milstein, *J. Am. Chem. Soc.* **2001**, *123*, 11504; d) S. P. Mabic, L. Vaysse, C. Benezra, J.-P. Lepoittevin, *Synthesis* **1999**, 1127; e) Y. Fall, F. Berthiol, H. Doucet, M. Santelli, *Synthesis* **2007**, 1683; f) In the reaction of PhBr and vinylcyclohexane under the ligand-free condition, we determined selectivity to be 5:1 favoring terminal insertion: Q. Yao, E. P. Kinney, Z. Yang, *J. Org. Chem.* **2003**, *68*, 7528; g) V. Calò, A. Nacci, A. Monopoli, P. Cotugno, *Angew. Chem.* **2009**, *121*, 6217; *Angew. Chem. Int. Ed.* **2009**, *48*, 6101.

[6] Computational studies: a) R. J. Deeth, A. Smith, J. M. Brown, *J. Am. Chem. Soc.* **2004**, *126*, 7144; b) H. von Schenck, B. Åkermark, M. Svensson, *J. Am. Chem. Soc.* **2003**, *125*, 3503.

[7] Examples: a) F. Berthiol, H. Doucet, M. Santelli, *Synthesis* **2006**, 1518; b) D. Pan, A. Chen, Y. Su, W. Zhou, S. Li, W. Jia, J. Xiao, Q. Liu, L. Zhang, N. Jiao, *Angew. Chem.* **2008**, *120*, 4807; *Angew. Chem. Int. Ed.* **2008**, *47*, 4729.

[8] a) Terminal-selective oxidative Heck reaction of aliphatic olefins carrying directing groups: J. H. Delcamp, M. C. White, *J. Am. Chem. Soc.* **2006**, *128*, 15076; b) Y. Su, N. Jiao, *Org. Lett.* **2009**, *11*, 2980; c) J. H. Delcamp, A. P. Brucks, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 11270; d) E. W. Werner, M. S. Sigman, *J. Am. Chem. Soc.* **2010**, *132*, 13981.

[9] Terminal-selective decarboxylative Heck reaction of aliphatic olefins carrying directing groups: P. Hu, J. Kan, W. Su, M. Hong, *Org. Lett.* **2009**, *11*, 2341.

[10] E. W. Werner, M. S. Sigman, *J. Am. Chem. Soc.* **2011**, *133*, 9692.

[11] Ni-catalyzed internal-selective Heck reactions of benzyl chlorides: R. Matsubara, A. C. Gutierrez, T. F. Jamison, *J. Am. Chem. Soc.* **2011**, *133*, 19020.

[12] A Pd/dppp catalyst gave good internal selectivity (19:1) in reactions of homoallylic alcohol with 1-naphthyl electrophiles (special case). The high selectivty was not observed with other aryl electrophiles; a) W. Cabri, I. Candiani, A. Bedeschi, R. Santi, *J. Org. Chem.* **1992**, *57*, 3558; b) One example of 9:1 selectivity favoring internal insertion was reported for a special pair of substrates: J. Ruan, J. A. Iggo, N. G. Berry, J. Xiao, *J. Am. Chem. Soc.* **2010**, *132*, 16689; c) J. Mo, L. Xu, J. Ruan, S. Liu, J. Xiao, *Chem. Commun.* **2006**, 3591.

[13] Asymmetric hydrogenation: a) S. J. Roseblade, A. Pfaltz, *Acc. Chem. Res.* **2007**, *40*, 1402; b) J. Mazuela, P.-O. Norrby, P. G. Andersson, O. Pamies, M. Dieguez, *J. Am. Chem. Soc.* **2011**, *133*, 13634; c) J. Mazuela, J. J. Verendel, M. Coll, B. Schaffner, A. Borner, P. G. Andersson, O. Pamies, M. Dieguez, *J. Am. Chem. Soc.* **2009**, *131*, 12344; d) Sharpless dihydroxylation: H. C. Kolb, M. S. VanNieuwenhze, K. B. Sharpless, *Chem. Rev.* **1994**, *94*, 2483; Epoxidation: e) Z. Li, H. Yamamoto, *J. Am. Chem. Soc.* **2010**, *132*, 7878; Hydroboration: f) R. Corberán, N. W. Mszar, A. H. Hoveyda, *Angew. Chem.* **2011**, *123*, 7217; *Angew. Chem. Int. Ed.* **2011**, *50*, 7079; g) C. Mazet, D. Gérard, *Chem. Commun.* **2011**, *47*, 298; Hydroacylation: h) I. Piel, M. Steinmetz, K. Hirano, R. Froehlich, S. Grimme, F. Glorius, *Angew. Chem.* **2011**, *123*, 5087; *Angew. Chem. Int. Ed.* **2011**, *50*, 4983; i) K. Kundu,

J. V. McCullagh, A. T. Morehead, Jr., *J. Am. Chem. Soc.* **2005**, *127*, 16042.

[14] Examples: a) S. P. Cook, A. Polara, S. J. Danishefsky, *J. Am. Chem. Soc.* **2006**, *128*, 16440; b) G. Li, A. Padwa, *Org. Lett.* **2011**, *13*, 3767; c) A. Padwa, M. A. Brodney, M. Dimitroff, B. Liu, T. Wu, *J. Org. Chem.* **2001**, *66*, 3119; d) J. R. Vyvyan, C. Loitz, R. E. Looper, C. S. Mattingly, E. A. Peterson, S. T. Staben, *J. Org. Chem.* **2004**, *69*, 2461.

[15] Examples: a) L. Zhou, C. K. Tan, X. Jiang, F. Chen, Y.-Y. Yeung, *J. Am. Chem. Soc.* **2010**, *132*, 15474; b) L. J. Farmer, L. Zhi, S. Jeong, W. W. Lamph, D. L. Osburn, G. Croston, K. S. Flatten, R. A. Heyman, A. M. Nadzan, *Bioorg. Med. Chem. Lett.* **2003**, *13*, 261; c) T. Nishi, K. Ishibashi, K. Nakajima, Y. Iio, T. Fukazawa, *Tetrahedron: Asymmetry* **1998**, *9*, 3251; d) A. P. Truong, et al., *Bioorg. Med. Chem. Lett.* **2010**, *20*, 4789; e) N. Charrier, et al., *Bioorg. Med. Chem. Lett.* **2009**, *19*, 3664 For authors of references [15d,e] see the Supporting Information.

[16] Examples of Pd-catalyzed reduction of aryl triflates by trialkylamines: a) J. M. Saa, M. Dopico, G. Martorell, A. Garcia-Raso, *J. Org. Chem.* **1990**, *55*, 991; b) W. Cabri, I. Candiani, S. DeBernardinis, F. Francalanci, S. Penco, R. Santo, *J. Org. Chem.* **1991**, *56*, 5796.

[17] As many as six minor isomers of the Heck product were detected by GC. Integration of the signals in the ^{1}H NMR spectrum was not suitable for determination of selectivity in these reactions owing to low signal intensity of the minor isomers.

[18] The pK_a values of conjugate acids in water: urotropine, 5.1; DBU, 12; DABCO, 8.8; 2,6-lutidine, 6.8; proton sponge, 12.

[19] Ligands d(*o*-tol)pf, d(*o*-biph)pf, d(1-naph)pf, and d(2-naph)pf are 1,1′-ferrocene bisphosphines carrying *o*-tolyl, *o*-biphenyl, 1-naphthyl, and 2-naphthyl groups on the phosphorus atom, respectively.

[20] Example: D. Gauthier, A. T. Lindhardt, E. P. K. Olsen, J. Overgaard, T. Skrydstrup, *J. Am. Chem. Soc.* **2010**, *132*, 7998.

[21] A single example of α-selective Heck reaction between PhI and methyl acrylate was reported, using Pd nanoparticles as catalyst in supercritical CO_2: L. K. Yeung, C. T. Lee, K. P. Johnston, R. M. Crooks, *Chem. Commun.* **2001**, 2290.

[22] Examples: a) F. Berthiol, H. Doucet, M. Santelli, *Eur. J. Org. Chem.* **2003**, 1091; b) B. H. Lipshutz, Ž. V. Bošković, D. H. Aue, *Angew. Chem.* **2008**, *120*, 10337; *Angew. Chem. Int. Ed.* **2008**, *47*, 10183; c) L. Jeremy I, *Tetrahedron Lett.* **1993**, *34*, 6211; d) Coupling of α-diazocarbonyl compounds: C. Peng, G. Yan, Y. Wang, Y. Jiang, Y. Zhang, J. Wang, *Synthesis* **2010**, 4154; e) Coupling of tosylhydrazides: J. Barluenga, M. Tomás-Gamasa, F. Aznar, C. Valdés, *Chem. Eur. J.* **2010**, *16*, 12801.

[23] α-Arylacroleins can be obtained after hydrolysis of the acetals, but the former are unstable at room temperature: I. Crossland, *Org. Synth.* **1981**, *60*, 6.

[24] The stoichiometric reaction of $[(PMe_3)_2PdPh]^+BF_4^-$ and 1-octene gave 2:1 selectivity favoring terminal insertion: F. Kawataka, I. Shimizu, A. Yamamoto, *Bull. Chem. Soc. Jpn.* **1995**, *68*, 654.

[25] CCDC 870134 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[26] Examples of [(dppf)Pd(Ar)X] complexes: a) A. G. Sergeev, G. A. Artamkina, V. N. Khrustalev, M. Y. Antipin, I. P. Beletskaya, *Mendeleev Commun.* **2007**, *17*, 142; b) C. Czauderna, H. Wurziger, Y. Sun, W. R. Thiel, *Z. Anorg. Allg. Chem.* **2008**, *634*, 2380.

[27] Y. Zou, L. Qin, X. Ren, Y. Lu, Y. Li, J. Zhou, unpublished results.

