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Intermolecular Heck-Type Coupling of Aryl Iodides and Allylic Acetates

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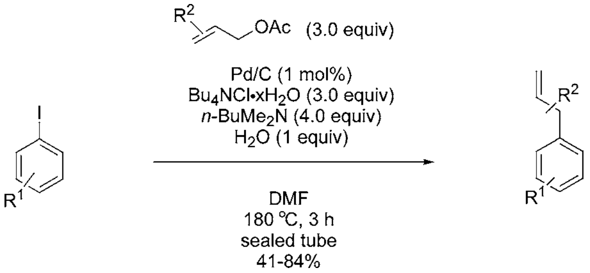
ABSTRACT



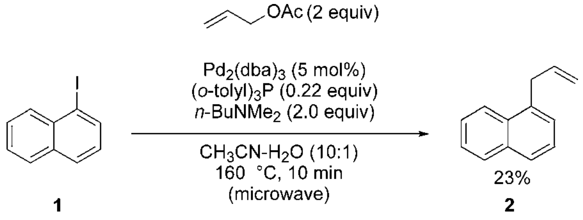
A palladium-catalyzed arylation of allylic acetates followed by β-acetoxy elimination was shown to produce Heck-type coupling products. Optimal reaction conditions employed ligand-free palladium on carbon in the presence of tetrabutylammonium chloride, a trialkylamine base, and water.

Palladium-catalyzed coupling reactions are among the most useful synthetic methods for the formation of carbon−carbon and carbon−heteroatom bonds.[1] Included within this general class is the Heck reaction,[2] which has received a substantial amount of interest since its initial report.[3] Recently, we reported the intramolecular Heck-type coupling of aryl iodides and allylic acetates/carbonates.[4] β-Acetoxy elimination occurs preferentially over β-hydride elimination, producing olefinic products. Methods for the intermolecular coupling of allylic acetates and aryl iodides have been previously reported; however, these methods require stoichiometric amounts of metal additives to form nucleophilic reagents *in situ*.[5] Herein, we report a method for aryl−allyl intermolecular coupling between aryl iodides and allylic acetates.

1-Iodonaphthalene **1** and allyl acetate were reacted with use of our previously optimized conditions for the intramolecular reaction (Scheme 1).

While a low yield of the desired product **2** was obtained, examination of other allyl leaving groups gave even poorer results (Table 1). We then examined the effect of the catalyst and additives.

Scheme 1. Initial Coupling Experiments



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(1) Tsuji, J. *Palladium Reagents and Catalysts: New Perspectives for the 21st Century*; Wiley: Chichester, UK, 2004.

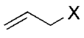
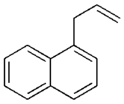
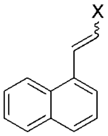
(2) (a) Mizoroki, T.; Mori, K. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 581. (b) Mizoroki, T.; Mori, K. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1505−1508. (c) Heck, R. F.; Nolley, J. P., Jr. *J. Org. Chem.* **1972**, *37*, 2320−2322. (d) Dieck, H. A.; Heck, R. F. *J. Am. Chem. Soc.* **1974**, *96*, 1133−1136.

(3) (a) Heck, R. F. *Palladium Reagents in Organic Synthesis*; Academic Press: New York, 1985. (b) Trost, B. M.; Verhoeven, T. R. In *Comprehensive* Organometallic Chemistry; Wilkinson, G., Stone, F. G., Abel, E. W., Eds.; Pergamon: Oxford, UK, 1982; Vol. 8, pp 799−938. (c) Farina, V. In *Comprehensive Organometallic Chemistry II*; Wilkinson, G., Stone, F. G., Abel, E. W., Eds.; Pergamon: Oxford, UK, 1995; Vol. 12, pp 161−240. (d) *Metal-Catalyzed Cross-coupling Reactions*; Diederich, F., Stang, P. J., Eds.; Wiley-VCH: Weinheim, Germany, 1998. (e) Hegedus, L. S. In *Organometallics in Synthesis: A Manual*; Schlosser, M., Ed.; Wiley: Chichester, UK, 1994; Chapter 5. (f) Link, J. T. In *Organic Reactions*; Overman, L. E., Ed.; Wiley: Hoboken, NJ, 2002; Vol. 60, pp 157−534 and references therein.

(4) Lautens, M.; Tayama, E.; Herse, C. *J. Am. Chem. Soc.* **2005**, *127*, 72−73.

10.1021/ol051947e CCC: $30.25

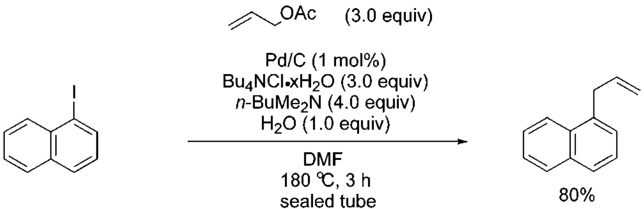
Table 1. Investigation of Leaving Groups for the Intermolecular Heck-Type Coupling Reaction[a]

entry	 (2.0 equiv)		
		yield (%)[b]	yield (%)[b]
1	**X** = OAc	23%	38% (*E/Z*= 13/1)
2	Br	33%	traces
3	OCO_2Et	29%	traces
4	OTs	10%	traces
5	$OP(O)(OEt)_2$	traces	traces

[a] Conditions: aryl iodide (1.0 equiv), allylic acetate (2.0 equiv), $Pd_2(dba)_3$ (5 mol %), (*o*-tolyl)$_3$P (22 mol %), *n*-$BuMe_2N$ (2.0 equiv), CH_3CN-H_2O, 10:1, 160 °C in microwave reactor. [b] NMR yield, mesitylene used as internal standard.

Optimization of the palladium catalyst showed palladium on carbon to be the catalyst of choice (Scheme 2). The use of phosphine ligands in the reaction provided low yields of **2**; however, other ligand free palladium sources such as palladium acetate led to complete conversion of the starting material.

Scheme 2. Optimized Coupling Conditions



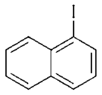
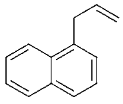
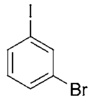
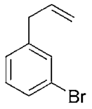
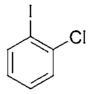
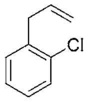
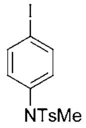
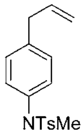
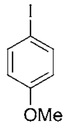
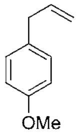
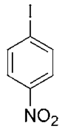
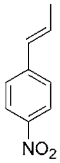
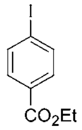
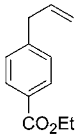
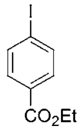
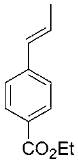
1

80%
2

A number of tetrabutylammonium salts were also screened as additives for the reaction. It was found that tetrabutylammonium chloride increased the conversion of the reaction similarly to the ligand-free Heck coupling reported by Jeffery.[6]

The reaction scope was explored under the optimized conditions. We began by examining the aryl iodide partner (Table 2). Electron donating groups (entry 5) led to increased reaction times, presumably due to slower oxidative addition of palladium into the aryl iodine bond.[1] Substrates bearing electron withdrawing substituents required shorter reaction times. However, in these cases rapid isomerization of the alkene to the thermodynamically more stable styrenyl system occurred under the reaction conditions (entries 6 and 8). In the case of an ester in the *para* position **13** (entry 7) the terminal olefin **14** could be isolated when 5 mol % of palladium was used. Both aryl chlorides and bromides (entries 2 and 3) were stable under the reaction conditions, providing a useful handle for further functionalization of the products.

Table 2. Heck-Type Coupling of Allyl Acetate with Various Aryl Iodides[a]

entry	aryl iodide	product	yield (%)[b]
1	 **1**	 **2**	80
2	 **3**	 **4**	79
3	 **5**	 **6**	54
4	 **7**	 **8**	71
5[c]	 **9**	 **10**	58
6	 **11**	 **12**	67
7[d]	 **13**	 **14**	58[e]
8	 **13**	 **15**	85

[a] Conditions: aryl iodide (1.0 equiv), allylic acetate (3.0 equiv), $Bu_4NCl{\cdot}xH_2O$ (3.0 equiv), *n*-$BuMe_2N$ (4.0 equiv), 10% Pd/carbon (1 mol %), H_2O (1.0 equiv), DMF, 180 °C sealed tube, 3 h except as noted. [b] All yields refer to isolated, pure products. [c] Reaction heated for 8 h. [d] Reaction heated for 1 h with 10% Pd/carbon (5 mol %). [e] 18% of internal olefin observed.

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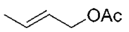
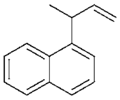
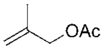
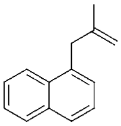
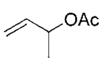
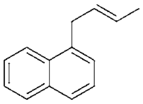
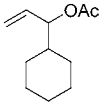
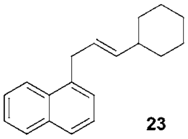
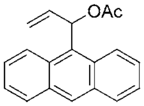
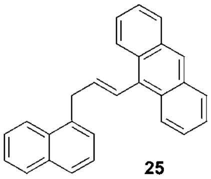
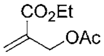
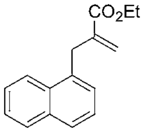
(5) (a) Yokoyama, Y.; Ito, S.; Takahashi, Y.; Murakami, Y. *Tetrahedron Lett.* **1985**, *26*, 6457−6460. (b) Trost, B. M.; Walchli, R. *J. Am. Chem. Soc.* **1987**, *109*, 3487−3488. (c) Ikegami, R.; Koresawa, A.; Shibata, T.; Takagi, K. *J. Org. Chem.* **2003**, *68*, 2195−2199. (d) Lee, P. H.; Sung, S.-Y.; Lee, K. *Org. Lett.* **2001**, *3*, 3201−3204.

(6) Jeffery, T. *Tetrahedron* **1996**, *52*, 10113−10130.

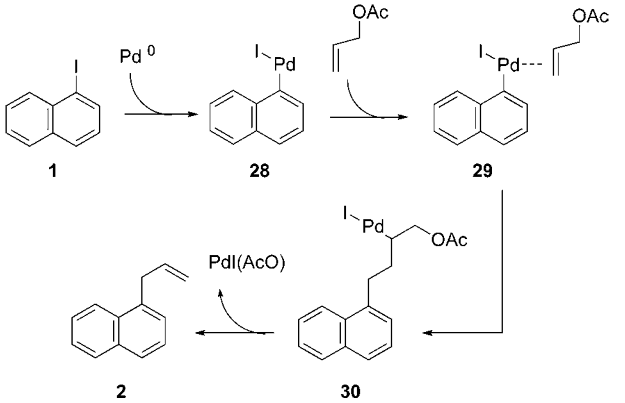
We next turned our attention to the range of allylic acetates that participate in the reaction (Table 3). As with most Heck reactions, substitution on the olefin led to slower reaction rates and lower yields.[1] Interestingly, use of a 1,2-disubstituted olefin (entry 1) led to the formation of a tertiary center, which offers the possibility of developing an asymmetric method. Substitution at the position α to the acetate was also tolerated and afforded the desired products in good yields (entries 3−5). Olefin selectivity was dependent upon the size of the substituent, with larger substituents leading to the less sterically hindered trans product.

Table 3. Heck-Type Coupling of 1-Iodonaphthalene with Various Allylic Acetates[a]

entry	allylic acetate	product	yield (%)[b]
1[c]	 **16**	 **17**	51
2[d]	 **18**	 **19**	41
3	 **20**	 **21**	83 (E/Z=2/1)
4	 **22**	 **23**	84 (E/Z=12/1)
5	 **24**	 **25**	64 (E/Z> 20:1)
6	 **26**	 **27**	43

[a] Conditions: aryl iodide (1.0 equiv), allylic acetate (3.0 equiv), $Bu_4NCl \cdot xH_2O$ (3.0 equiv), n-$BuMe_2N$ (4.0 equiv), 10% Pd/carbon (1 mol %), H_2O (1.0 equiv), DMF, 180 °C sealed tube, 3 h except as noted. [b] All yields refer to isolated, pure products. [c] Reaction heated for 12 h. [d] 10% Pd/carbon (10 mol %).

Scheme 3. Proposed Mechanism for the Heck-Type Coupling Reaction



A possible mechanism (Scheme 3) for this reaction involves initial oxidative insertion of palladium into the aryl−iodine bond of **1** to give **28**, followed by carbopalladation of olefin **29** to give intermediate **30**. Intermediate **30** then undergoes β-acetoxy elimination to give **2**. Reduction of Pd(II) to Pd(0) is then most likely achieved by coordination of an amine base followed by β-hydride transfer and reductive elimination of hydrogen iodide. While a π-allyl-type intermediate could also be postulated, the formation of isomeric products from isomeric starting materials (entries 1 vs 3) suggests this is not a dominant process.

In summary, we have developed an intermolecular coupling of aryl iodides and allylic acetates *via* a Heck-type coupling under low palladium catalyst loadings. This procedure gives rapid access to a range of both terminal and internal olefins, which can easily be further functionalized.

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Supporting Information Available: Experimental procedures and full characterization of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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