ORGANIC LETTERS

2003
Vol. 5, No. 6
893−895

Rhodium-Catalyzed Cross-Coupling of Allyl Alcohols with Aryl- and Vinylboronic Acids in Ionic Liquids

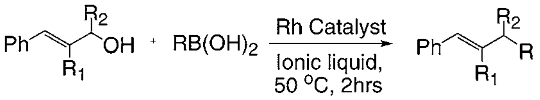
George W. Kabalka,* Gang Dong, and Bollu Venkataiah

*Departments of Chemistry and Radiology, The University of Tennessee,
Knoxville, Tennessee 37996-1600*

kabalka@utk.edu

Received January 14, 2003

ABSTRACT



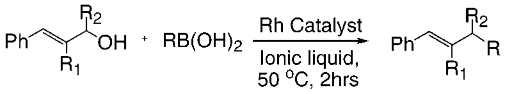
The direct coupling of aryl- and vinylboronic acids with allylic alcohols has been achieved in ionic liquids using a rhodium catalyst.

Ionic liquids, especially ambient-temperature ionic liquids consisting of 1,3-dialkylimidazolium cations, have shown great promise as environmentally benign reaction media because of their negligible vapor pressure, as well as their excellent chemical and thermal stabilities.[1] Furthermore, their compatibility with transition-metal catalysts and limited miscibility with common solvents simplifies catalyst recycling.

Transition-metal-catalyzed allylic alkylation using π-allyl complexes represents an important carbon−carbon bond-forming reaction that is widely used for constructing complex organic molecules.[2] Allylic halides,[3] carboxylates,[4] carbonates,[5] phosphates,[6] and related compounds are generally utilized as allylation reagents. On the basis of the viewpoint of atom economy,[7] the ability to use allylic alcohols in allylation reactions would be highly beneficial. However, they are rarely used because hydroxide is a poor leaving group. A few approaches have been reported, but they require either severe reaction conditions or unique ligands.[8]

Boronic acids are widely used reagents in organic synthesis because they are commercially available, stable, generally nontoxic, and compatible with a variety of functional groups. Coupling reactions of boronic acids with allyl halides[3c] and esters[4c] are well-known, but to the best of our knowledge, the direct coupling of boronic acids with allylic alcohols has not been reported. In a continuation of our studies of boron chemistry in ionic liquids,[9] we wish to report the direct allylation of cinnamyl alcohols using boronic acids catalyzed by ligandless rhodium catalysts (Scheme 1).

Scheme 1. Cross-Coupling of Boronic Acid and Cinnamyl Alcohol



R = aryl, alkenyl, heteroaryl
R_1 = H, CH_3
R_2 = H, Ph

Various rhodium catalysts, solvents, and reaction conditions were examined using *p*-tolylboronic acid and cinnamyl

---

* To whom correspondence should be addressed.

(1) (a) Dupont, J.; Souza, R. F.; Suarez, A. Z. *Chem. Rev.* **2002**, *102*, 3667. (b) Welton, T. *Chem. Rev.* **1999**, *99*, 2071. (c) Sheldon, R. *Chem. Commun.* **2001**, 2399. (d) Wasserscheid, P.; Keim, W. *Angew. Chem., Int. Ed.* **2000**, *39*, 3773.

(2) Tsuji, J. *Transition Metal Reagents and Catalysts*; Wiley: New York, 2000.

(3) (a) Sheffy, F. K.; Godschalx, J. P.; Stille, J. K. *J. Am. Chem. Soc.* **1984**, *106*, 4833. (b) Godschalx, J. P.; Stille, J. K. *Tetrahedron Lett.* **1980**, *21*, 2599. (c) Moreno-Nanas, M.; Pajuelo, F.; Pleixats, R. *J. Org. Chem.* **1995**, *60*, 2396.

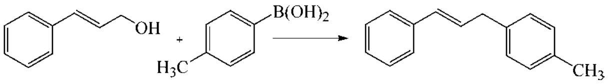
(4) (a) Hayashi, T.; Kawasura, T.; Uozumi, Y. *Chem. Commun.* **1997**, 561. (b) Miyaura, N.; Yamada, K.; Suginome, H.; Suzuki, A. *J. Am. Chem. Soc.* **1985**, *107*, 972.

(5) Evans, P. A.; Nelson, J. D. *J. Am. Chem. Soc.* **1998**, *120*, 5581.

(6) (a) Okude, Y.; Hirano, S.; Hiyama, T.; Nozaki, H. *J. Am. Chem. Soc.* **1977**, *99*, 3179. (b) Tanigawa, Y.; Nishimura, K.; Kawasaki, A.; Murahashi, S. *Tetrahedron Lett.* **1982**, *23*, 5549.

10.1021/ol034067d CCC: $25.00

Table 1. Effect of Catalysts and Solvents on the Reaction of Cinnamyl Alcohol with *p*-Tolylboronic Acid



entry	catalyst[a]	reaction media	T (°C)	reaction time (h)	isolated yield (%)
1	$RhCl_3 \cdot xH_2O$	CH_2Cl_2	50	5	10
2	$RhCl_3 \cdot xH_2O$	toluene	50	12	10
3	$RhCl_3 \cdot xH_2O$	$BmimBF_4$	50	5	trace
4	$RhCl_3 \cdot xH_2O$	$BmimPF_6$	50	2	62
5	$RhCl_3 \cdot xH_2O$	$BmimPF_6$	rt	12	0
6	Rh(acac)(1,5-cyclooctadiene)Cl	$BmimPF_6$	50	2	62
7	$Rh(PPh_3)_3Cl$	$BmimPF_6$	50	2	61
8	$RhCl_3 \cdot xH_2O$ and KOAc (10 mol %)	$BmimPF_6$	50	2	0
9	$RhCl_3 \cdot xH_2O$ and CH_3COOH (10 mol %)	$BmimPF_6$	50	1.5	66
10	$RhCl_3 \cdot xH_2O$ and HF[b]	$BmimBF_4$	50	2	59
11	$RhCl_3 \cdot xH_2O$, CuI (10 mol %)	$BmimPF_6$	50	2	67
12	$RhCl_3 \cdot xH_2O$, $Cu(OAc)_2$ (10 mol %)	$BmimPF_6$	50	2	72

[a] 3 mol % of Rh catalyst used. [b] One equivalent of aqueous HF (48%) used.

alcohol as model substrates (Table 1). Dramatic differences in yields were observed (Table 1, entries 1−4). 1-Butyl-3-methylimidazolium hexafluorophosphate ($BmimPF_6$) was found to be the most effective solvent. No reaction was observed in polar solvents such as water and DMF. Three common rhodium catalysts were evaluated (Table 1, entries 4−7), and both Rh(I) and Rh(III) were found to be effective. Although bases are commonly used in transition-metal-catalyzed coupling reactions,[10] they inhibited this reaction (Table 1, entry 8). However, acids increased the reaction rate (Table 1, entries 9 and 10). The addition of copper salts such as cupric acetate enhanced reaction yields by approximately 10%. This effect has been observed previously.[11] The highest yields were obtained using a mixture of $RhCl_3 \cdot xH_2O$ (3 mol %) and $Cu(OAc)_2$ (10 mol %) in $BmimPF_6$ at 50 °C for 2 h.

To enhance the utility of the reaction, we evaluated a variety of organoboronic acids (aryl, alkenyl, heteroaryl) and allylic alcohols[12] (Table 2). Electron-rich boronic acids generated higher yields than electron-deficient boronic acids. Steric factors also affected the yield. Ortho- and meta-substituted arylboronic acids (Table 2, entries 9 and 10) typically gave lower yields than the para-substituted arylboronic acids. Sterically hindered alcohols (Table 2, entries 12 and 13) also led to lower yields. Aliphatic alcohols were found to be unreactive. It is noteworthy that the catalyst system can be recycled with no significant loss in reaction yields (Table 3).

Table 2. Coupling of Organoboronic Acids with Allylic Alcohols[a]

entry	boronic acid	alcohol	yield[b] (%)
1	*p*-tolyl	cinnamyl	72
2	phenyl	cinnamyl	65
3	*p*-methoxyphenyl	cinnamyl	76
4	*p*-chlorophenyl	cinnamyl	41
5	*p*-methylthiophenyl	cinnamyl	78
6	*p*-acylphenyl	cinnamyl	0
7	*trans*-β-styrenyl	cinnamyl	50
8	2-thiophene	cinnamyl	33
9	*o*-tolyl	cinnamyl	55
10	*m*-tolyl	cinnamyl	61
11	1-naphthyl	α-methylcinnamyl	52
12	*p*-tolyl	1,3-diphenyl-2-propen-1-ol	60
13	*p*-methoxyphenyl	1,3-diphenyl-2-propen-1-ol	65

[a] Reactions were carried out using $RhCl_3 \cdot xH_2O$ (3 mol %) and $Cu(OAc)_2$ (10 mol %) in $BmimPF_6$ at 50 °C for 2 h. [b] Isolated yields.

Although a detailed mechanistic study has not been undertaken, the reaction most likely proceeds via the pathway outlined in Scheme 2. Oxidative addition of cinnamyl alcohol

---

(7) Trost, B. M. *Science* **1991**, *254*, 1471.

(8) (a) Fumiyuki, O.; Hideyuki, O.; Seiji, K.; Shogo, Y.; Tatsuya, M.; Masaaki, Y. *J. Am. Chem. Soc.* **2002**, *124*, 10968. (b) Bricout, H.; Carpentier, J. F.; Mortreux, A. *J. Mol. Catal. A* **1998**, *136*, 243. (c) Sakakibara, M.; Ogawa, A. *Tetrahedron Lett.* **1994**, *35*, 8013. (d) Bergbreiter, D. E.; Weatherford, D. A. *Chem. Commun.* **1989**, 883. (e) Haudegond, J.-P.; Chauvin, Y.; Commeureuc, D. *J. Org. Chem.* **1979**, *44*, 3063. (f) Atkins, K. E.; Walker, W. E.; Manyik, R. M. *Tetrahedron Lett.* **1970**, 3821. (g) Hata, G.; Takashi, K.; Miyake, A. *Chem. Commun.* **1970**, 1392.

(9) (a) Kabalka, G. W.; Malladi, R. R. *Chem. Commun.* **2000**, 2191. (b) Kabalka, G. W.; Venkataiah, B. *Tetrahedron Lett.* **2002**, *43*, 3703.

(10) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Suzuki, A. *J. Organomet. Chem.* **1998**, *576*, 147. (c) Stanforth, S. P. *Tetrahedron* **1998**, *54*, 263.

(11) (a) Savarin, C.; Srogl, J.; Liebeskind, L. S. *Org. Lett.* **2001**, *3*, 91. (b) Du, X.; Suguro, M.; Hirabayashi, K.; Mori, A. *Org. Lett.* **2001**, *3*, 3313. (c) Chan, D. M. T.; Monaco, K. L.; Wang, R.; Winters, M. P. *Tetrahedron Lett.* **1998**, *39*, 2933. (d) Evans, D. A.; Katz, J. L.; West, T. R. *Tetrahedron Lett.* **1998**, *39*, 2937.

(12) **General Procedure:** allylic alcohol (1 mmol) and boronic acid (1.2 mmol) are dissolved in $BmimPF_6$ (1.5 mL) contained in a two-necked round-bottomed flask and $RhCl_3 \cdot xH_2O$ (3 mol %) along with $Cu(OAc)_2$(1mole%) are added. The reaction mixture is allowed to stir for 2 h at 5 °C under a N_2 atmosphere. The product can then be isolated by distillation. For convenience, the product is extracted into diethyl ether (4 × 3 mL). The combined extracts are dried over anhydrous $MgSO_4$, concentrated and purified by flash chromatography using silica gel.

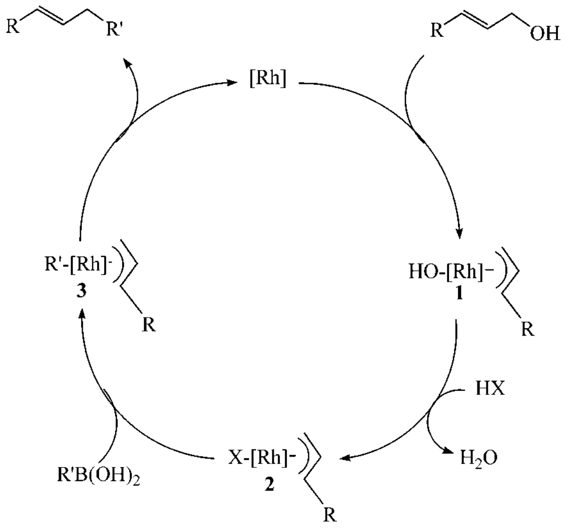
Table 3. Reaction of *p*-Tolylboronic Acid with Cinnamyl Alcohol Using Recycled Catalytic System[a]

entry	isolated yield (%)
first cycle	70
second cycle	72
third cycle	73
fourth cycle	71
fifth cycle	68

[a] Catalyst was recovered by filtration and utilized in subsequent experiment (cycle).

to rhodium would generate π-allylrhodium intermediate **1**. The formation of intermediate **2** drives the reaction by elimination of water in the presence of HF that is present in $BmimPF_6$ due to the relatively facile decomposition of PF_6 anion in the presence of trace amounts of water.[13] Subsequently, the transmetalation of **2** by boronic acid produces intermediate **3**. Reductive elimination of rhodium then generates the product. It is noteworthy that the reaction does not occur in $BmimBF_4$ (Table 1, entry 3) unless HF is added to the reaction media (Table 1, entry 10). At this time, it is not possible to rule out a mechanism involving the conversion of the allylic alcohol to the corresponding halide or phosphate. However, control experiments in which cinnamyl alcohol was heated in $BmimPF_6$ at 50 °C for 2 h led to recovery of only the alcohol. In addition, an experiment carried out using toluene (which would obviate the formation of a halo or phosphate intermediate) in place of $BmimPF_6$ produced a 10% yield of the coupled product.

Scheme 2



In summary, the coupling reactions of a wide variety of boronic acids with cinnamyl alcohols have been studied. The protocol is applicable to aryl, vinyl, and heteroarylboronic acids and aromatic allyl alcohols. The catalyst system and the ionic liquid can be recycled several times without significant loss in product yield.

Acknowledgment. We wish to thank the U.S. Department of Energy and the Robert H. Cole Foundation for support of this research.

Supporting Information Available: Experimental procedures and analytical data. This material is available free of charge via the Internet at http://pub.acs.org.

OL034067D

---

(13) Dupont, J.; Silva, S. M.; de Souza, R. F. *Catal. Lett.* **2001**, *77*, 131.