

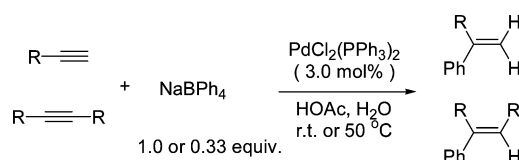
Palladium-Catalyzed Hydrophenylation of Alkynes with Sodium Tetrphenylborate under Mild Conditions

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In an aqueous solution of acetic acid, $\text{PdCl}_2(\text{PPh}_3)_2$ showed high catalytic activity for the hydrophenylation of both terminal and internal alkynes with sodium tetrphenylborate (NaBPh_4) under mild conditions, affording phenyl alkenes in moderate to excellent yields.

Introduction

Catalytic hydroarylation of multiple carbon–carbon bonds is an important method for constructing complex molecules from relatively simple precursors. Although transition metal complex¹ or Lewis acid² catalyzed hydroarylations by direct activation of a C–H bond of arenes have been intensively studied, most research so far has focused only on the electron-rich arenes, and the control of regioselectivity is still difficult. The use of organoheteroatom compounds has also been described in hydroarylation with high selectivity, such as diphenylantimony chloride³ and tetraphenyltin.⁴ In particular, arylboron drew a lot of attention recently, due to its high functional group compatibility, ready availability, and stability. Miyaura and co-workers reported the first rhodium-catalyzed addition of arylboronic acid to α,β -unsaturated ketones in 1997.⁵ After that, great effort was made in this rhodium-catalyzed asymmetric 1,4-addition by applying a variety of appropriate chiral ligands.⁶ The hydroarylation of alkynes with arylboronic acid has also

been described,⁷ and the reaction has been extended to the arylation cyclization of alkyne-tethered olefins and aldehydes.⁸ However, the reaction of hydroarylation with sodium tetrphenylborate, which is a stable and inexpensive phenylating reagent, has rarely been reported.⁹ In this paper, we wish to develop an efficient palladium-catalyzed hydrophenylation of alkynes with sodium tetrphenylborate under mild conditions.

Results and Discussion

The reaction of 1-octyne (**1a**) with sodium tetrphenylborate was first investigated to optimize reaction conditions, and a variety of acids and palladium catalysts were examined (Table 1). When a mixture of **1a** (0.5 mmol), NaBPh_4 (0.5 mmol), and $\text{PdCl}_2(\text{PPh}_3)_2$ (0.005 mmol) was stirred at room temperature in glacial acetic acid or H_2O for 6 h (entries 1 and 2), only a small

(1) Selected examples: (a) Jia, C.; Piao, D.; Oyamada, J.; Lu, W.; Kitamura, T.; Fujiwara, Y. *Science* **2000**, *287*, 1992–1995. (b) Lim, Y.-G.; Lee, K.-H.; Koo, B. T.; Kang, J.-B. *Tetrahedron Lett.* **2001**, *42*, 7609–7612. (c) Tsukada, N.; Mitsuboshi, T.; Setoguchi, H.; Inoue, Y. *J. Am. Chem. Soc.* **2003**, *125*, 12102–12103. (d) Karshedt, D.; Bell, A. T.; Tilley, T. D. *Organometallics* **2004**, *23*, 4169–4171.

(2) Selected examples: (a) Yamaguchi, M.; Kido, Y.; Hayashi, A.; Hirama, M. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1313–1315. (b) Yonehara, F.; Kido, Y.; Yamaguchi, M. *Chem. Commun.* **2000**, 1189–1190. (c) Reetz, M. T.; Sommer, K. *Eur. J. Org. Chem.* **2003**, 3485–3496.

(3) Matoba, K.; Motofusa, S.-i.; Cho, C. S.; Ohe, K.; Uemura, S. *J. Organomet. Chem.* **1999**, *574*, 3–10.

(4) Ohe, T.; Uemura, S. *Tetrahedron Lett.* **2002**, *43*, 1269–1271.

(5) Sakai, M.; Hayashi, H.; Miyaura, N. *Organometallics* **1997**, *16*, 4229–4231.

(6) Selected examples: (a) Takaya, Y.; Ogasawara, M.; Hayashi, T. *J. Am. Chem. Soc.* **1998**, *120*, 5579–5580. (b) Takaya, Y.; Ogasawara, M.; Hayashi, T. *Tetrahedron Lett.* **1999**, *40*, 6957–6961. (c) Hayashi, T.; Senda, T.; Takaya, Y.; Ogasawara, M. *J. Am. Chem. Soc.* **1999**, *121*, 11591–11592. (d) Senda, T.; Ogasawara, M.; Hayashi, T. *J. Org. Chem.* **2001**, *66*, 6852–6856. (e) Hayashi, T.; Ueyama, K.; Tokunaga, N.; Yoshida, K. *J. Am. Chem. Soc.* **2003**, *125*, 11508–11509. (f) Otomaru, Y.; Kina, A.; Shintani, R.; Hayashi, T. *Tetrahedron: Asymmetry* **2005**, *16*, 1673–1679. (g) Chen, F.-X.; Kina, A.; Hayashi, T. *Org. Lett.* **2006**, *8*, 341–344.

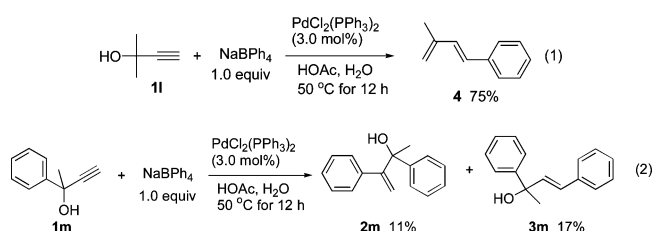
(7) (a) Hayashi, T.; Inoue, K.; Taniguchi, N.; Ogasawara, M. *J. Am. Chem. Soc.* **2001**, *123*, 9918–9919. (b) Shirakawa, E.; Takahashi, G.; Tsuchimoto, T.; Kawakami, Y. *Chem. Commun.* **2001**, 2688–2689.

(8) (a) Shintani, R.; Okamoto, K.; Otomaru, Y.; Ueyama, K.; Hayashi, T. *J. Am. Chem. Soc.* **2004**, *127*, 54–55. (b) Shintani, R.; Tsurusaki, A.; Okamoto, K.; Hayashi, T. *Angew. Chem., Int. Ed.* **2005**, *44*, 3909–3912.

(9) (a) Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1994**, *465*, 85–92. (b) Cho, C. S.; Motofusa, S.-i.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 883–888.

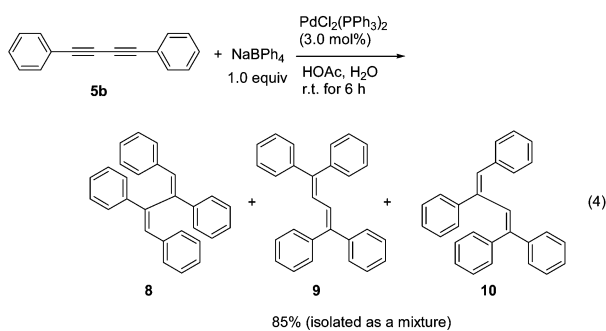
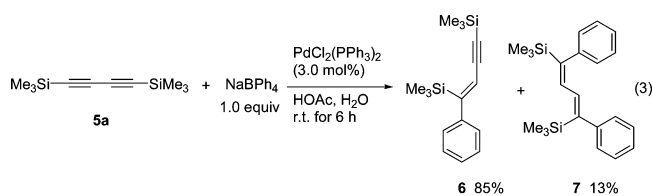
(2k) in excellent yield and regioselectivity, indicating that the phenyl group was almost exclusively introduced at the position β to the ester group (entry 10).

Although the reaction of 2-methylbut-3-yn-2-ol (**1l**) with sodium tetraphenylborate at room temperature afforded a complicated mixture, in which the formation of corresponding adduct could be determined by GC and GC-MS, when the same reaction was performed at 50 °C for 12 h, interestingly, (*E*)-2-methyl-4-phenylbuta-1,3-diene (**4**) was obtained in 75% isolated yield (eq 1). These results indicated that, in contrast to linear terminal alkynes, the use of sterically congested **1l** resulted in selective formation of the *anti*-Markovnikov adduct, which underwent dehydration to give **4** under the reaction conditions. Since many alkynols are relatively easy to access, this process could be used as a practical method for the synthesis of conjugated dienes.



However, when 2-phenylbut-3-yn-2-ol (**1m**) was employed, no expected products of dehydration could be obtained, and the corresponding Markovnikov adduct **2m** and *trans anti*-Markovnikov adduct **3m** were isolated in low yields (eq 2). Likewise, as a result of the steric hindrance of substituents, the formation of the *anti*-Markovnikov adduct was favored.

The hydrophenylations of 1,3-diyne were also examined, and the reactions took place smoothly under the same conditions. The conversion of 1,4-bis(trimethylsilyl)buta-1,3-diyne (**5a**) was almost quantitative, affording both singly and doubly phenylated products **6** and **7** in 85% and 13% yields, respectively (eq 3). In the case of 1,4-diphenylbuta-1,3-diyne (**5b**), the reaction gave three doubly phenylated products that were isolated in 85% as a mixture (eq 4). Attempts to separate these adducts were not successful, and only **8** was isolated in analytical purity with low yield (15%).



SCHEME 1. Proposed Mechanism for Palladium(II)-Catalyzed Hydrophenylation of Alkynes with NaBPh₄

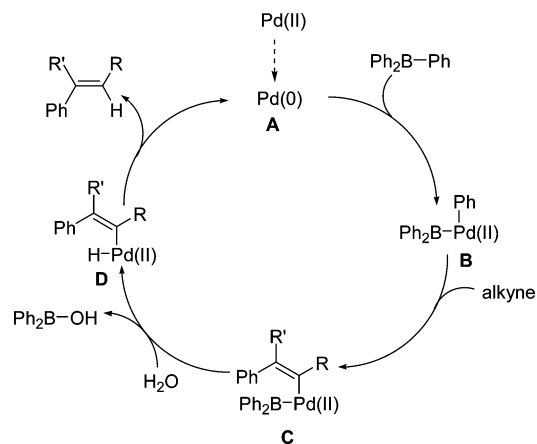


TABLE 4. Palladium-Catalyzed Reactions of Alkynes with Sodium Tetraphenylborate^a

entry	alkyne	main adduct	yield(%) ^b	2:3 ^c
1	1a	2a	51	92:8
2	<i>n</i> -C ₅ H ₁₁ ≡COOEt 1n	<i>n</i> -C ₅ H ₁₁ COOEt Ph 2n	87	92:8
3	Ph≡COOEt 1o	Ph Ph COOEt 2o	>99	>99:1
4	<i>n</i> -C ₄ H ₉ ≡Ph 1p	<i>n</i> -C ₄ H ₉ Ph Ph 2p	70	66:34 ^d

^a Reactions were carried out using alkyne (1.0 mmol), NaBPh₄ (0.3 mmol), HOAc (2.0 mmol), and PdCl₂(PPh₃)₂ (0.03 mmol) in H₂O (2.0 mL) in a sealed tube at 50 °C for 12 h. ^b Isolated yield based on alkyne used. ^c Determined by GC. ^d Determined by ¹H NMR.

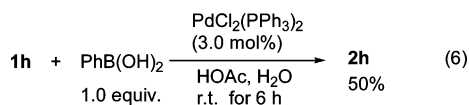
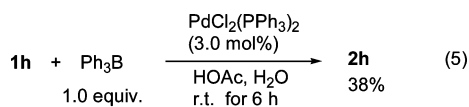
In previous reports on the hydrophenylation of alkenes with NaBPh₄⁹ and coupling reaction of NaBPh₄ with aryl halides,¹⁰ usually only one or two phenyl groups could be transferred. As shown in Table 2, entry 7, the reaction of diphenylacetylene (**1h**) with NaBPh₄ afforded the adduct **2h** in quantitative yield. In order to explore the possibility for further efficient transfer of phenyl groups in NaBPh₄, we examined the reaction of **1h** with 0.33 or 0.25 equiv of NaBPh₄ again under different conditions. As summarized in Table 3, either increasing reaction temperature or prolonging reaction time could promote the reaction, and a satisfactory result could be achieved when the reaction was performed at 50 °C for 12 h with 0.33 equiv of NaBPh₄, indicating that at most three phenyl groups could be efficiently utilized (entries 3 and 4).

To demonstrate the generality and efficiency of the above process, we carried out the reaction of 0.33 equiv of NaBPh₄ with several other alkynes at 50 °C (Table 4). Although the reaction of **1a** with 0.33 equiv of NaBPh₄ afforded adducts in 51% yield (entry 1), similar to the result by using 0.5 equiv of

(10) Wang, J.-X.; Yang, Y.; Wei, B. *Synth. Commun.* **2004**, *34*, 2063–2069.

NaBPh₄ at room temperature as indicated in entry 6 of Table 1, the internal alkynes underwent the hydrophenylation smoothly to give corresponding products in good to high yields (entries 2–4). Both yields of adducts and the selectivities of reactions are comparable to the results summarized in Table 2.

It is known that NaBPh₄ can react with acetic acid to give Ph₃B, benzene, and sodium acetate, and Ph₃B can be further hydrolyzed into di- and monophenylboronic acid.⁹ Therefore, we also examined the reactivity of Ph₃B and PhB(OH)₂ with alkyne at room temperature. As shown in eqs 5 and 6, the reactions of **1h** with Ph₃B or PhB(OH)₂ also afforded **2h** in moderate yields.

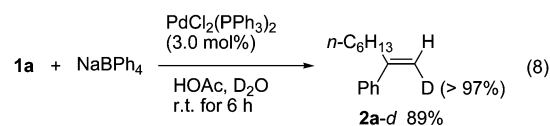
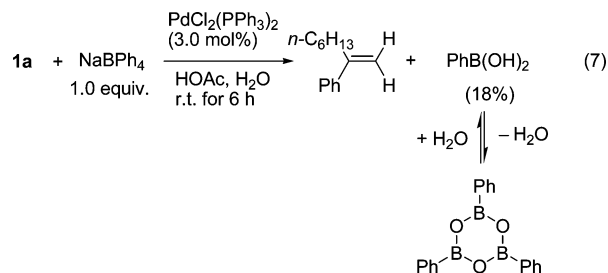


On the basis of the above observations, we proposed a possible mechanism for the present hydrophenylation in Scheme 1. It includes the oxidative addition of the C–B bond to Pd(0) species to give intermediate **B**¹¹ and selective insertion of alkyne into Pd–C to give **C**. Hydrolysis of **C** followed by reductive elimination of the C–C bond finally gives the hydrophenylating products and regenerates the Pd(0) species. Ph₃B, Ph₂B(OH), and PhB(OH)₂ should be the possible phenylating intermediates in the reaction system.

The results obtained in this work can be rationally explained by this proposed mechanism: (1) the formation of benzene was found in all the reactions confirmed by GC and GC-MS, and thus only three phenyl groups in NaBPh₄ could be maximally efficiently used; (2) the dominant formation of Markovnikov-type adduct in the hydrophenylation of terminal alkynes is due to the selective insertion of a terminal alkyne (R = H) into Pd–C bonds with the R' group away from the metal center to give the less steric repulsion intermediate **C**; (3) the regioselectivity of the phenyl group attached to the position β to the ester group in the reactions of propiolates **1k**, **1n**, and **1o** (R = COOR'') is possibly resulted from the interaction of palladium and ester group.¹²

In addition, the careful analyses of the reaction mixture indicated in entry 5 of Table 1 disclosed the formation of mono- and diphenylboronic acids, and we have also successfully isolated PhB(OH)₂ from the reaction mixture and found that PhB(OH)₂ is in equilibrium with triphenylboroxin in CDCl₃ (eq 7).¹³ Moreover, as shown in eq 8, the reaction of **1a** in D₂O afforded selectively deuterated product **2a-d**, which again confirmed the *cis*-type addition manner. These findings gave direct evidence to support our proposed mechanism. More interestingly, in Hayashi's Rh-catalyzed hydroarylation system,

a similar reaction as eq 8 gave the product with deuterium incorporated at the ortho position of the phenyl group, which was caused by 1,4-rearrangement of rhodium in intermediate **C**.^{7a} Larock has also reported similar behavior in the Pd-catalyzed reaction of alkynes and aryl iodide.¹⁴ However, possibly as a result of milder reaction conditions, no migration was observed in the present catalysis system.



Conclusions

In summary, we have developed a palladium-catalyzed hydrophenylation of alkynes with sodium tetraphenylborate with improved utilization efficiency of the reagent. From a synthetic point of view, the present catalytic procedure to produce arylalkenes has advantages over other methods in that it took place in an aqueous solution under mild conditions with high regio- and stereoselectivity and several functional groups were tolerated.

Experimental Section

Typical Procedure for Hydrophenylation of 1-Octyne (1a) with Sodium Tetraphenylborate To Afford 2-Phenyl-1-octene (2a) (Table 1, entry 5). A mixture of 1-octyne (**1a**) (74.0 μL, 0.5 mmol), NaBPh₄ (171.1 mg, 0.5 mmol), HOAc (58.0 μL, 1.0 mmol), PdCl₂(PPh₃)₂ (10.5 mg, 0.015 mmol), and H₂O (1.0 mL) was stirred under nitrogen in a sealed tube at room temperature for 6 h. After reaction, the mixture was first subjected to a short silica column chromatography (ca. 5 cm of silica gel, eluted with CH₂Cl₂) to remove the water. Then octadecane (92.5 mg, 0.36 mmol) was added in the elution as internal standard for GC analysis. After GC and GC-MS analysis, the solvents and volatiles were removed under vacuum, and the residue was then subjected to preparative TLC isolation (silica, eluted with petroleum ether). Compound **2a** was obtained in 84.7 mg (0.45 mmol, 90%) as a yellow oil. The result of GC analysis of the reaction mixture revealed that **2a** and **3a** were formed in a total of 98% yield with a ratio of 93:7. **Data for 2a:** ¹H NMR (300 MHz, CDCl₃) δ 7.39–7.21 (m, 5H), 5.24 (d, 1H, *J* = 1.5 Hz), 5.03 (d, 1H, *J* = 1.5 Hz), 2.48 (t, 2H, *J* = 7.4 Hz), 1.48–1.23 (m, 8H), 0.86 (t, 3H, *J* = 6.9 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 148.8, 141.5, 128.2, 127.2, 126.1, 112.0, 35.4, 31.7, 29.1, 28.3, 22.7, 14.1; GC-MS *m/z* 188 (M⁺).

Hydrophenylation of Diphenylacetylene (1h) with Sodium Tetraphenylborate To Afford Triphenylethene (2h)¹⁶ at Elevated Temperature (Table 3, entry 3). A mixture of diphenyl-

(11) Oxidative addition of a carbon-boron bond to Pd(0) has so far been proposed in several cases: (a) Ohe, T.; Ohe, K.; Uemura, S.; Sugita, N. *J. Organomet. Chem.* **1988**, *344*, C5. (b) Cho, C. S.; Uemura, S. *J. Organomet. Chem.* **1994**, *465*, 85–92. (c) Cho, C. S.; Motofusa, S.-i.; Ohe, K.; Uemura, S. *J. Org. Chem.* **1995**, *60*, 883–888.

(12) The interaction of carbonyl group and transition metal complex has been previously reported in catalyzed 1,4-additions. See refs 5 and 8.

(13) For review, see: Lappert, M. F. *Chem. Rev.* **1956**, *56*, 959–1064.

(14) Tian, Q.; Larock, C. L. *Org. Lett.* **2000**, *2*, 3329–3332.

(15) Yoshida, K.; Hayashi, T. *J. Am. Chem. Soc.* **2003**, *125*, 2872–2873.

(16) Song, C. E.; Jung, D.-u.; Choung, S. Y.; Roh, E. J.; Lee, S.-g.; *Angew. Chem., Int. Ed.* **2004**, *43*, 6183–6185.

acetylene (**1h**) (178.2 mg, 1.0 mmol), NaBPh₄ (112.9 mg, 0.33 mmol), HOAc (116.0 μ L, 2.0 mmol), PdCl₂(PPh₃)₂ (21.0 mg, 0.03 mmol), and H₂O (2.0 mL) was heated in a sealed tube under nitrogen at 50 °C for 12 h. After reaction, the mixture was first subjected to a short silica column chromatography (ca. 5 cm of silica gel, eluted with CH₂Cl₂) to remove the water. The elution was condensed and subjected to GC and GC-MS analysis. After that, the solvents and volatiles were removed under vacuum, and the residue was then subjected to preparative TLC isolation (silica, eluted with petroleum ether). Compound **2h** was obtained in 245.9 mg (0.96 mmol, 96%) as a pale yellow oil. **Data for 2h:** ¹H NMR

(300 MHz, CDCl₃) δ 7.33–6.95 (m, 16H); ¹³C NMR (75 MHz, CDCl₃) δ 143.4, 142.5, 140.3, 137.3, 130.3, 129.5, 128.6, 128.2, 128.1, 127.9, 127.6, 127.5, 127.4, 126.7; GC-MS *m/z* 256 (M⁺).

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Supporting Information Available: General method, characterization data and charts of ¹H and ¹³C NMR for all products. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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