ORGANIC
LETTERS

2008
Vol. 10, No. 5
973−976

Suzuki-Miyaura Coupling of Diarylmethyl Carbonates with Arylboronic Acids: A New Access to Triarylmethanes

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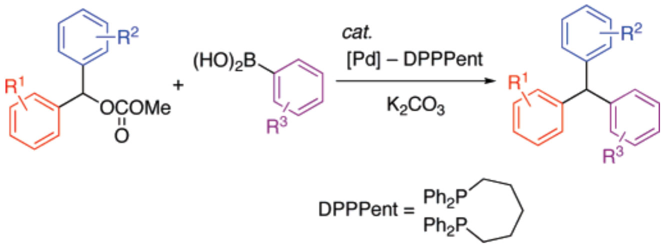
Received January 12, 2008

ABSTRACT



Suzuki-Miyaura coupling of diarylmethyl carbonates with arylboronic acids proceeded in the presence of $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$–DPPPent (1,5-bis(diphenylphosphino)pentane) catalyst, yielding a variety of triarylmethanes.

The triarylmethane framework is often found in various attractive molecules, for example, leuco dyes[1] and some candidates for molecular magnets.[2] The framework appears in a flavonoid isolated from a cajeput tree, melanervin.[3] Recently, it was reported that triarylmethanes containing a thiophenyl group exhibit antitubercular activity.[4] Triarylmethanes are typically synthesized by Friedel−Crafts arylation of diarylmethanols or by reduction of triarylmethanols, which are prepared by nucleophilic addition of aryl metal compounds to carbonyl.[5,6]

Meanwhile, the Suzuki-Miyaura reaction is widely utilized for selective C−C bond formation in organic synthesis.[7] No diarylmethyl halides, however, have been utilized as electrophilic substrates for the cross-coupling, which will provide a straightforward approach to triarylmethanes. Recently, Molander attempted the cross-coupling of bromodiphenylmethane with an aryltrifluoroborate but failed to obtain the desired triarylmethane in pure form.[8] This paper discloses that the cross-coupling of diarylmethyl carbonates with arylboronic acids proceeded with success in the presence of a palladium catalyst.

Recently, we and others reported the cross-coupling of benzylic carbonates[8−11] and phosphates[12] with organometallic compounds. The reports stimulated us to develop the cross-

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(1) (a) Duxbury, D. F. *Chem. Rev.* **1993**, *93*, 381−433. (b) Guinot, S. G. R.; Hepworth, J. D.; Wainwright, M. *J. Chem. Soc., Perkin Trans. 2* **1998**, 297−303. (c) Lewis, E. S.; Perry, J. M.; Grinstein, R. H. *J. Am. Chem. Soc.* **1970**, *92*, 899−905.

(2) (a) Schlenk, W.; Brauns, M. *Ber. Deutsch. Chem. Ges.* **1915**, *48*, 661−669. (b) Seitz, G.; Mönnighoff, H. *Angew. Chem., Int. Ed. Engl.* **1970**, *9*, 906−907.

(3) Antus, S.; Schindlbeck, E.; Ahmad, S.; Seligmann, O.; Chari, V. M.; Wagner, H. *Tetrahedron* **1982**, *38*, 133−137.

(4) Parai, M. K.; Panda, G.; Chaturvedi, V.; Manju, Y. K.; Sinha, S. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 289−292.

(5) (a) Nair, V.; Vidya, N.; Abhilash, K. G. *Synthesis* **2006**, 3647−3653. (b) Katritzky, A. R.; Toader, D. *J. Org. Chem.* **1997**, *62*, 4137−4141. (c) Muthyala, R.; Katritzky, A. R.; Lan, X. *Dyes Pigm.* **1994**, *25*, 303−324 and references cited therein.

(6) Recently, Yorimitsu and Oshima reported a palladium-catalyzed synthesis of triarylmethanes containing an azaaryl, see: Niwa, T.; Yorimitsu, H.; Oshima, K. *Org. Lett.* **2007**, *9*, 2373−2375.

(7) Representative reviews: (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457−2483. (b) Miyaura, N. *Top. Curr. Chem.* **2002**, *219*, 11−59. (c) Bellina, F.; Carpita, A.; Rossi, R. *Synthesis* **2004**, 2419−2440.

(8) Molander, G. A.; Elia, M. D. *J. Org. Chem.* **2006**, *71*, 9198−9202.

(9) Kuwano, R.; Yokogi, M. *Org. Lett.* **2005**, *7*, 945−947.

(10) Stille coupling of a (4-oxazolyl)methyl carbonate, see: Lindsey, C. C.; O'Boyle, B. M.; Mercede, S. J.; Pettus, T. R. R. *Tetrahedron Lett.* **2004**, *45*, 867−868.

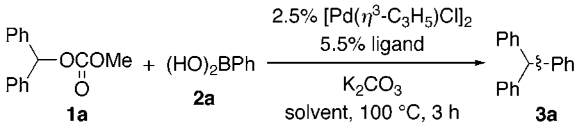
(11) Hiyama coupling of benzylic carbonates, see: Nakao, Y.; Ebata, S.; Chen, J.; Imanaka, H.; Hiyama, T. *Chem. Lett.* **2007**, *36*, 606−607.

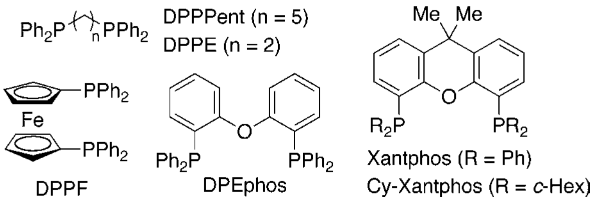
(12) McLaughlin, M. *Org. Lett.* **2005**, *7*, 4875−4878.

10.1021/ol800078j CCC: $40.75

coupling of arylboronic acids with diarylmethyl carbonates, which are a type of benzylic carbonates. Thus, the reaction of diphenylmethyl methyl carbonate (**1a**) with phenylboronic acid (**2a**) was attempted under the conditions optimized in the previous work, that is, using $[Pd(\eta^3\text{-}C_3H_5)Cl]_2$−DPPPent[13] catalyst in DMF at 80 °C, but resulted in no formation of triphenylmethane **3a**. Elevating the reaction temperature led to the production of **3a** but in low yield (Table 1,[14] entry 1). Solvent strongly affected the reaction rate (entries 2−4). The desired cross-coupling product **3a** was obtained in high yield when *tert*-amyl alcohol was used as a solvent. As with other palladium-catalyzed reactions involved with benzylic C−O bond cleavage, the choice of phosphine ligand was crucial for the palladium catalysis (entries 5−10). In this case, DPPF was comparable to DPPPent.[15] However, employment of other phosphine ligands, including monophosphines, caused a significant decrease in the catalytic activity. To our surprise, the formation of **3a** was scarcely observed in the reaction using Cy-Xantphos

Table 1. Effect of Ligand and Solvent on the Cross-Coupling of Diphenylmethyl Carbonate (**1a**) with Phenylboronic Acid (**2a**)[a]

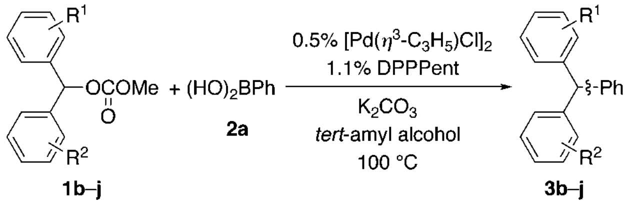


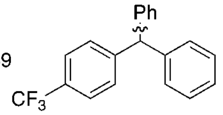
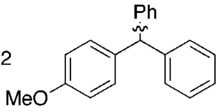
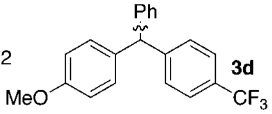
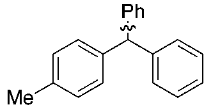
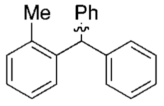
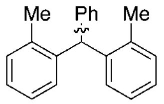
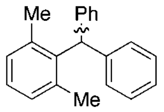
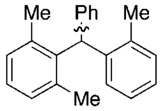
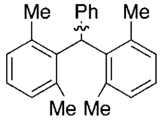


entry	ligand	solvent	yield, %[b,c]
1	DPPPent	DMF	15
2	DPPPent	Toluene	35
3	DPPPent	1,4-dioxane	36
4	DPPPent	*tert*-amyl alcohol	76 (87)[d]
5	PPh_3[e]	*tert*-amyl alcohol	14
6	DPPE	*tert*-amyl alcohol	1
7	DPPF	*tert*-amyl alcohol	87 (90)[e]
8	DPEphos	*tert*-amyl alcohol	16
9	Xantphos	*tert*-amyl alcohol	1
10	Cy-Xantphos	*tert*-amyl alcohol	1
11[f]	DPPPent	*tert*-amyl alcohol	1

[a] Reactions were conducted on a 0.2 mmol scale in 1.0 mL of solvent at 100 °C for 3 h. The ratio of **1a**:**2a**:K_2CO_3:$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$:ligand was 20:30:60:0.5:1.1. [b] GC yield (average of two runs). [c] The yields in parentheses were isolated yields in a 1 mmol scale with 1.0 mol % palladium. [d] The reaction was conducted for 48 h. [e] The reaction was conducted for 27 h. [f] Diphenylmethyl acetate was used in place of **1a**.

Table 2. Reactions of Diarylmethyl Carbonates **1** with **2a**[a]



entry	R^1	R^2	**1**	time, h	product (**3**)	yield, %[b]
1	4-CF_3	H	**1b**	49	 **3b**	64
2[c]	4-MeO	H	**1c**	72	 **3c**	72
3	4-MeO	4-CF_3	**1d**	72	 **3d**	77
4	4-Me	H	**1e**	24	 **3e**	87
5	2-Me	H	**1f**	49	 **3f**	88
6	2-Me	2-Me	**1g**	72	 **3g**	39
7	2,6-Me_2	H	**1h**	72	 **3h**	11
8	2,6-Me_2	2-Me	**1i**	72	 **3i**	30
9	2,6-Me_2	2,6-Me_2	**1j**	24	 **3j**	11

[a] Reactions were conducted on a 1.0 mmol scale in *tert*-amyl alcohol (1.0 mL) at 100 °C. The ratio of **1**:**2a**:K_2CO_3:$[Pd(\eta^3\text{-}C_3H_5)Cl]_2$:DPPPent was 100:110:220:0.5:1.1. [b] Isolated yield. [c] The reaction was conducted with 5 mol % palladium.

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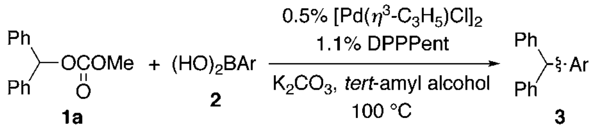
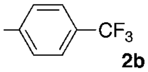
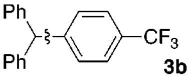
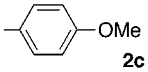
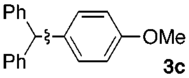
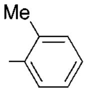
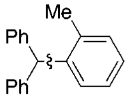
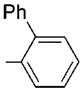
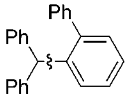
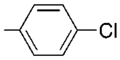
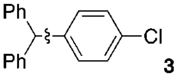
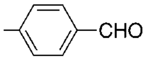
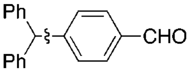
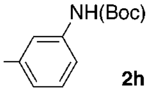
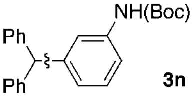
(13) DPPPent = 1,5-bis(diphenylphosphino)pentane: Sacconi, L.; Gelsomini, J. *Inorg. Chem.* **1968**, *7*, 291−294.

(14) Bidentate phosphine ligands in Table 1 were abbreviated as follows: (a) DPPE = 1,2-bis(diphenylphosphino)ethane: Issleib, K.; Müller, D.-W. *Chem. Ber.* **1959**, *92*, 3175−3182. (b) DPPF = 1,1′-bis(diphenylphosphino)ferrocene: Bishop, J. J.; Davison, A.; Katcher, M. L.; Lichtenberg, D. W.; Merrill, R. E.; Smart, J. C. *J. Organomet. Chem.* **1971**, *27*, 241−249. (c) DPEphos = bis[2-(diphenylphosphino)phenyl]ether, Xantphos = 9,9-dimethyl-4,6-bis(diphenylphosphino)xanthene: Kranenburg, M.; van der Burgt, Y. E. M.; Kamer, P. C. J.; van Leeuwen, P. W. N. M.; Goubitz, K.; Fraanje, J. *Organometallics* **1995**, *14*, 3081−3089. (d) Cy-Xantphos = 4,5-bis(dicyclohexylphosphino)-9,9-dimethylxanthene: Kuwano, R.; Kusano, H. *Chem. Lett.* **2007**, *36*, 528−529.

(15) As with the Suzuki-Miyaura reaction of benzylic carbonate, the production of triphenylmethane might significantly be affected by the bite angle of the chelate bisphosphine. Our speculation about the effect was mentioned in ref 9.

Table 3. Cross-Couplings of **1a** with Arylboronic Acids **2**[a]



entry	Ar (**2**)	time, h	product (**3**)	yield, %[b]
1	 **2b**	24	 **3b**	93
2	 **2c**	48	 **3c**	97
3	 **2d**	48	 **3f**	86
4	 **2e**	48	 **3k**	77
5	 **2f**	72	 **3l**	60
6	 **2g**	72	 **3m**	61
7	 **2h**	72	 **3n**	97

[a] Reactions were conducted on a 1.0 mmol scale in *tert*-amyl alcohol (1.0 mL) at 100 °C for 24 h. The ratio of **1a**:**2**:K_2CO_3:[Pd(η^3-C_3H_5)Cl]$_2$:DPPPent was 100:110:220:0.5:1.1. [b] Isolated yield.

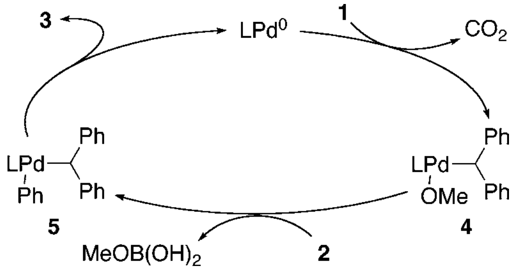
ligand, which was the most effective for the palladium-catalyzed nucleophilic substitution of **1a** with malonate carbanions.[14d] The reaction using acetate in place of carbonate resulted in a trace yield of **3a** (entry 11).[16] The loading of the DPPPent− or DPPF−palladium catalyst was reduced to 1% without a significant loss of yield of **3a** (entries 4 and 7). DPPF was slightly superior to DPPPent for the reaction of **1a** with **2a**.

The effect of the substituent on the aromatic ring of the diarylmethyl carbonate was investigated for the cross-coupling with phenylboronic acid (Table 2). The reaction of electron-deficient **1b** gave the desired product **3b** in good yield (entry 1). In contrast, the electron-donating methoxy group of **1c** caused significant deterioration of the yield of triarylmethane **3c** (13%) due to formation of α-methoxy-α-(*p*-methoxylphenyl)toluene through palladium-catalyzed decarboxylative etherification. Efficient production of **3c** required an increase of the catalyst loading (entry 2). In the above two reactions, DPPPent ligand was preferable to DPPF. Electrophilic substrate **1d** bearing both electron-rich and -poor aryl groups was converted into **3d** in 77% yield (entry 3). The electron-withdrawing trifluoromethyl group might cancel the undesirable effect of methoxy group. Subsequently, the Suzuki-Miyaura coupling was applied to a series of ortho-substituted diarylmethyl carbonates **1f**−**j**. The reactivity of mono-methylated substrate **1f** was comparable to that of the para-isomer **1e** (entry 5). However, a second ortho-methyl substituent caused significant obstruction of the cross-coupling with **2a**. As a matter of fact, the reactions of diarylmethyl carbonates **1g** and **1h** failed to react with **2a** in good yields (entries 6 and 7). The additional methyl may sterically obstruct the attack of DPPPent−palladium on the diarylmethyl substrates. More congested triarylmethanes **3i** and **3j** could be obtained by means of DPPPent−palladium catalysis but in low yield (entries 8 and 9). The low yields of **3g**−**j** were hardly improved when the catalyst loading increased to 5%.

A range of arylboronic acids worked as coupling partners of diphenylmethyl carbonate **1a** as shown in Table 3. The catalytic cross-coupling was scarcely affected by the electronic property of the para-substituent of the arylboronic acid (entries 1, 2). An interesting discrepancy has been observed: triarylmethane **3c** was obtained in high yield from the reaction of **2c**, whereas the cross-coupling of **1c** with **2a** was shown to be less effective. Whereas the ortho-substituents of **2d** and **2e** slightly hindered the catalytic reaction, coupling products **3f** and **3k** were obtained in good yields (entries 3, 4). The Suzuki-Miyaura coupling of diphenylmethyl carbonate was compatible with chloro, aldehyde, and Boc-protected amino groups (entries 5−7). However, nitro and hydroxyl groups obstructed the conversion of the starting materials. The DPPPent−palladium did not work well for the reaction of 2-phenylethenylboronic acid, giving the cross-coupling product in only 15% yield.

The Suzuki-Miyaura reaction of diarylmethyl carbonates **1** would proceed like that of benzylic carbonates (Scheme 1).[9] DPPPent−palladium(0) cleaves the benzylic C−O bond of **1** to form (diarylmethyl)palladium intermediate **4**. The alkoxo ligand on **4** undergoes transmetalation with an arylboronic acid. Reductive elimination of the resulting (aryl)(diarylmethyl)palladium(II) **5** yields the desired triarylmethane **3** and regenerates palladium(0).

Scheme 1. Probable Pathway of the Suzuki-Miyaura Coupling of Diphenylmethyl Carbonates **1**



We developed the Suzuki-Miyaura coupling of diarylmethyl carbonates. The reaction proceeds well by using [Pd(η^3-C_3H_5)Cl]$_2$−DPPPent or −DPPF as catalyst. The former catalyst was applied to the synthesis of a wide range

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[16] Kuwano, R.; Yokogi, M. *Chem. Commun.* **2005**, 5899−5901.

of triarylmethanes. The method disclosed here will be useful for constructing various triarylmethane frameworks in organic synthesis.

Acknowledgment. This work was supported by Tokuyama Science Foundation, Iketani Science and Technology Foundation, KAKENHI (No. 16685011 and 19020051), and a Grant-in-Aid for the Global COE Program, “Science for Future Molecular Systems” from MEXT. This paper is dedicated to the memory of Professor Yoshihiro Matsumura.

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

OL800078J