Pergamon

PII: S0040-4039(97)00642-4

Tetrahedron Letters, Vol. 38, No. 19, pp. 3447-3450, 1997
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0040-4039/97 $17.00 + 0.00

Synthesis of Arylboronates *via* the Palladium(0)-Catalyzed Cross-Coupling Reaction of Tetra(alkoxo)diborons with Aryl Triflates

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Abstract: *The cross-coupling reaction of $(RO)_2BB(OR)_2$ (RO = methoxo and pinacolato) with aryl triflates to give arylboronates was carried out at 80 °C in the presence of $PdCl_2(dppf)$ (3 mol%), dppf (3 mol%) and KOAc (3 equivs) in dioxane. The reaction was available with various functional groups such as nitro, cyano, ester, and carbonyl groups.*
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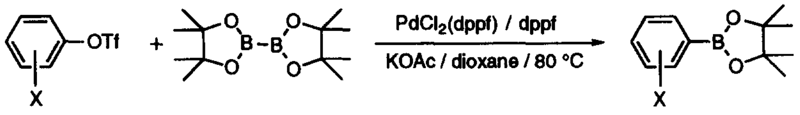
Recent studies on the addition and the cross-coupling reactions of tetra(alkoxo)diborons[1] (e.g., **2**, **4a**) by transition-metal catalyses provided a convenient method for the synthesis of organoboron compounds. The addition of **2** or bis(catecholato)diboron to alkynes,[2] 1,3-dienes,[3] and alkenes[4] with Pt(0), Rh(I), or Au(I) complexes has opened up a new access to stereodefined bis(boryl)alkenes and bis(boryl)alkanes. The Pd(0)-catalyzed cross-coupling reactions of **2** with haloarenes[5] and allyl acetates[6] afforded the corresponding aryl- and allylboronates. As a part of our program on the direct borylation of organic electrophiles with transition metal catalysts, we wish to report the Pd(0)-catalyzed cross-coupling reaction of aryl triflates with tetra(alkoxy)diboron (**2** or **4**) to give arylboronates (Eqs. 1 and 2).



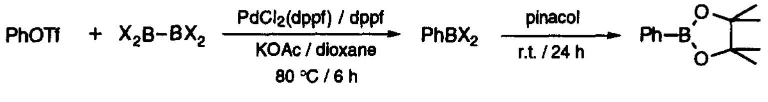
1 **2** **3**

(1)

The reaction between aryl triflates and **2** (1.1 equiv) was carried out at 80 °C using various catalysts, bases and solvents to optimize the reaction conditions. Phenyl triflate smoothly underwent the cross-coupling under similar conditions used for the synthesis of **3** from aryl halides: $PdCl_2(dppf)$ (3 mol%) (dppf abbreviate 1,1'-bis(diphenylphosphino)ferrocene) and KOAc (3 equivs) in DMSO at 80 °C.[5] However, relatively low yields resulted for other functionalized aryl triflates. The coupling with **1** having an electron-withdrawing group such as 4-acetylphenyl triflate gave only a 62% yield of **3** accompanying with 4-hydroxyacetophenone (29%) derived from the saponification of **1**.[7] On the other hand, the coupling with 4-methoxyphenyl triflate did not complete even on prolonged heating due to the catalyst decomposition precipitating palladium black (24 h, 64%).[8] Fortunately, the difficulties associated with the competitive saponification or the catalyst decomposition were easily overcome with the use of dioxane as the solvent and an additional 1 equivalent of dppf to the catalyst. The yields of both reactions with 4-acetyl- and 4-methoxyphenyl triflate were improved to

92% (6 h) and 93% (13 h), respectively. The addition of LiCl, which have been used for the Pd(0)-catalyzed cross-coupling of organostannanes with aryl and vinyl triflates, was ineffective.[9] KOAc can be the most suitable base because stronger bases such as K_3PO_4 and K_2CO_3 afford symmetrical biaryls resulting from the coupling between **3** and **1**.[5]

Although we used **2** which is thermally stable and inert to water and oxygen, thus allowing the handling without special precautions, the pinacol esters **3** thus obtained resist the hydrolysis to arylboronic acids. Alternatively, the methyl ester **4a** can be used for such purpose (Eq. 2). The cross-coupling of phenyl triflate with **4a** gave an 83% yield of **5a** along with biphenyl (14%), but the reaction with **4b** was relatively slow. For convenience of the GC analyses, the yields of **5** were estimated from the corresponding pinacol ester.

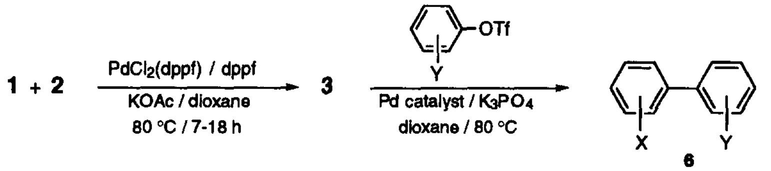


(2)

4a: X=OMe
4b: X=NMe$_2$

5a 83%
5b 48%

The representative results are summarized in Table 1. A variety of aryl triflates having an electron-withdrawing or -donating substituent can participate in the cross-coupling under the conditions optimized in the above.[10] Under these conditions, a wide variety of functional groups including nitro, cyano, ester, and carbonyl groups can be tolerated during the coupling (Entries 1-5). The reaction worked well for *ortho* monosubstituted aryl triflates (Entries 8 and 9), but all attempts at the coupling with mesityl triflate were unsuccessful. Heteroaryl triflates synthesized from 7-hydroxycoumarine and 8-hydroxyquinoline gave **3** without any difficulties (Entries 10 and 11), but a similar reaction with 2-quinolyl triflate failed. The protonolysis of the C-B bond is rather fast when the boron atom attached to the carbon adjacent to the heteroatom; thus, the protodeboration of **3** with the base afforded quinoline as the sole product.[11]



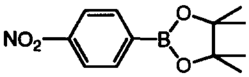
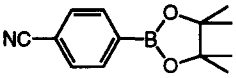
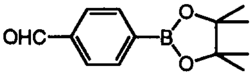
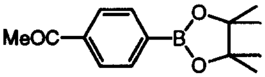
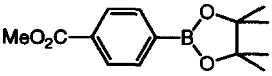
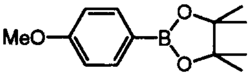
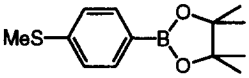
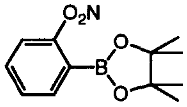
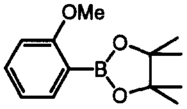
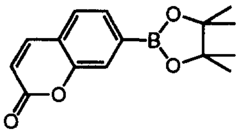
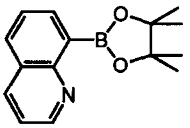
(3)[a]

Entry	X =	Y =	Pd catalyst	Time / h	Yield / %[b]
1	4-MeCO	4-NC	PdCl$_2$(dppf)	16	93
2	4-MeO	4-NC	PdCl$_2$(dppf)	24	81
3	4-MeO	4-MeS	PdCl$_2$(dppf) / dppf	24	65

[a]Experimental procedure, see Note 13. [b]Isolated yields based on the triflates used for the second coupling.

The direct preparation of arylboronic esters from aryl halides or triflates now allows a one-pot, two-step procedure for the synthesis of unsymmetrical biaryls (eq. 3).[12] The syntheses of three unsymmetrical

Table 1. The Synthesis of Arylboronates (Eq. 1)[a]

Entry	Triflate (**1**), Ar =	Product (**3**)	Time / h	Yield / %[b]
1	4-$O_2NC_6H_4$		6	86
2	4-NCC_6H_4		15	75
3	4-$HCOC_6H_4$		17	(91)
4	4-$MeCOC_6H_4$		6	(92)
5	4-$MeO_2CC_6H_4$		21	80
6	4-$MeOC_6H_4$		13	(93)
7	4-$MeSC_6H_4$		24	81
8	2-$O_2NC_6H_4$		21	(64)
9	2-$MeOC_6H_4$		16	(80)
10	7-coumaryl		17	84
11	8-quinolyl		39	65

[a] All reactions were carried out in dioxane (6 ml) at 80 °C using **2** (1.1 mmol), **1** (1.0 mmol), $PdCl_2(dppf)$ (3 mol%), dppf (3 mol%), and KOAc (3 mmol), see Note 10. [b] Isolated yields based on **1** and GLC yields are in parentheses.

biaryls were readily achieved in 93%, 81% and 65% yields when the cross-coupling reaction of the triflate with **2** was followed by the next reaction with another triflate in the presence of K_3PO_4.[13] Although both steps were efficiently catalyzed by $PdCl_2$(dppf), the addition of a fresh catalyst to the second coupling was advantageous to achieve high yields.[14]

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10. *The representative procedure for 3*: The flask was charged with $PdCl_2$(dppf) (0.03 mmol), dppf (0.03 mmol), KOAc (3 mmol) and **2** (1.1 mmol), and flushed with nitrogen. Dioxane (6 ml) and aryl triflate (1.0 mmol) were added, and the resulting mixture was then stirred at 80 °C for the period indicated in Table 1. The reaction mixture was diluted with benzene, washed with brine, and dried over $MgSO_4$. Kugelrohr distillation *in vacuo* gave **3**. GC analyses were carried out at 80-300 °C using a glass column (3 mm X 2 m) packed with 10% OV-17 on Uniport B.
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13. The solution of arylboronate, *in situ* prepared from **2** (1.1 mmol) and aryl triflate (1.1 mmol) following the procedure shown in Note 10, was directly used for the next cross-coupling with another triflate. K_3PO_4 (3 mmol), $PdCl_2$(dppf) (0.03 mmol), and aryl triflate (1.0 mmol) were added to the solution of **3**, and the mixture was heated to 80 °C for 16-24 h (entries 1 and 2). The second coupling with 4-methylthiophenyl triflate shown in entry 3 was incomplete due to the precipitation of palladium black; thus, 1 equivalent of dppf to $PdCl_2$(dppf) was added.
14. The sequential cross-couplings without an additional catalyst resulted in 50-70%.

(*Received in Japan* 12 *March* 1997; *revised* 31 *March* 1997; *accepted* 4 *April* 1997)