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Palladium-Catalyzed Cross-Coupling Reactions of Vinyl and Aryl Triflates with Tetraarylborates

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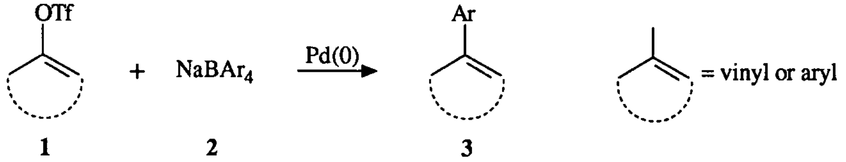
Abstract: *Sodium tetraarylborates 2 have been found to couple efficiently with vinyl and aryl triflates 1 in the presence of a palladium(0) catalyst to afford arylalkenes and biaryls 3 in good yields and under mild conditions.*

The palladium-catalyzed cross coupling reactions of vinyl and aryl triflates with organometallic reagents have emerged during the past few years as versatile methods for carbon-carbon bond formation. A variety of organometallics such as organotin,[1] zinc,[2] boron,[3] aluminium,[4] and silicon[5] reagents have been used as coupling partners, the organoboron compounds being one of the most recently studied. Specifically, the coupling reactions of vinyl and aryl triflates with trivalent organoboron compounds in the presence of a base have been reported to take place readily to furnish alkenes, 1,3-alkadienes, arylalkenes, and biaryls in high yields and under relatively mild conditions.[3]

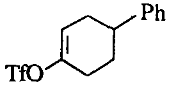
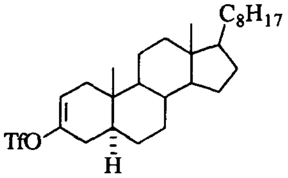
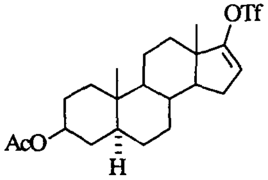
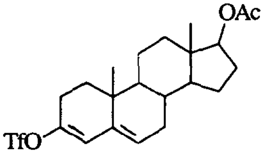
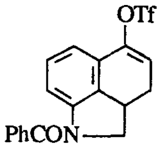
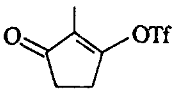
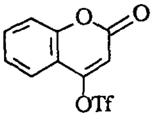
Since the use of tetravalent organoboron compounds has not been explored, we decided to investigate the as yet unknown reaction of vinyl and aryl triflates with tetraarylborates. Herein we disclose our results which suggest broad utility of this variation for the synthesis of arylalkenes and biaryls, according to the following equation.



Representative results are summarized in the Table. Our initial experiments have been carried out with vinyl triflates **1a** and **1b** as model substrates and commercially available and inexpensive sodium tetraphenylborate ($NaBPh_4$) as phenyl transfer agent. $NaBPh_4$ has been used recently as a phenylating agent in palladium-catalyzed processes such as substitution of allylic chlorides[6] and acetates[7] and coupling with aryl bromides.[8]

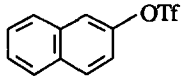
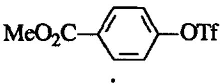
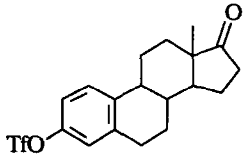
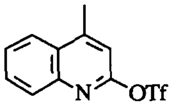
Reaction of **1a** (1 mmol) with $NaBPh_4$ (1 mmol) in DMF in the presence of $Pd(PPh_3)_4$ as the catalyst and in the absence of a base proceeded even at room temperature to produce **3** in useful yield (Entry 1). As expected, the reaction rate turned out to be higher at 60 °C (Entry 2). Analogously, **1b** reacted completely at 60 °C within 1 h (entry 4). Use of 0.5 mmol of $NaBPh_4$ stopped the conversions of **1a** and **1b** to about 50%. Subsequent addition of 1 mmol of Et_3N allowed however the reactions to proceed to completion. Complete conversions were also achieved with 0.5 mmol of borate when Et_3N was added from the beginning of the reaction (entries 3 and 5). An appreciable yield of **3** was obtained from **1b** even with 0.25 mmol of $NaBPh_4$ in the presence of 2 mmol of base (entry 6), indicating that more than two phenyl groups were available for transfer to the vinylic moiety. Indeed, triphenylboron BPh_3 (0.5 mmol) was a phenylating agent under these conditions and provided **3** in 53% yield from **1b** after 24 h at 60 °C. However, since the use of 0.25 mmol of $NaBPh_4$ was ac-

Table. Palladium-Catalyzed Cross-Coupling of Vinyl and Aryl Triflates with Tetraarylborates[a]

Entry	Vinyl or Aryl Triflate **1**[b]	Ar in $NaBAr_4$[c] (borate/triflate molar ratio)	Reaction time (h)	Yield (%)[d] of Product **3**
1	 **a**	Ph (1)[e]	24	65
2		Ph (1)	2	73
3		Ph (0.5)	3	68
4	 **b**	Ph (1)	1	73
5		Ph (0.5)	2.5	73
6		Ph (0.25)[f]	24	64
7		4-MeC_6H_4 (0.5)	2.5	71
8		4-FC_6H_4 (0.5)	1.5	77
9	 **c**	Ph (0.5)	3	72
10		4-MeC_6H_4 (0.5)	2.5	68
11	 **d**	Ph (0.5)	3.5	67
12	 **e**	Ph (0.5)	4.5	56
13	 **f**	Ph (0.5)	3	53
14	 **g**	Ph (0.5)	24	41
15		Ph (0.5)[g]	4	55

(continued)

Table. (continued)

Entry	Vinyl or Aryl Triflate 1^b	Ar in $NaBAr_4^c$ (borate/triflate molar ratio)	Reaction time (h)	Yield (%)^d of Product 3
16	 **h**	Ph (0.5)	3	81
17		$4\text{-}MeC_6H_4$ (0.5)	3	73
18	 **i**	Ph (1)	2	88
19		Ph (0.5)	3	84
20		$4\text{-}FC_6H_4$ (0.5)	4	89
21	 **j**	Ph $(0.5)^h$	7	69
22		Ph $(0.5)^{g,h}$	3	84
23		$4\text{-}MeC_6H_4$ $(0.5)^{g,h}$	3	83
24	 **k**	Ph $(0.5)^{g,h}$	3	91

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[a] All reactions were carried out in the same manner as described in the text, unless otherwise noted. Addition of Et_3N was omitted in the reactions with 1 mmol of borate. Disappearance of the starting material was monitored by TLC. [b] Triflates **1a-i, k** were prepared according to: Cacchi, S.; Morera, E.; Ortar, G. *Synthesis* **1986**, 320-322. Aryl triflate **1j** was prepared according to: Kiesewetter, D. O.; Katzenellenbogen, J. A.; Kilbourn, M. R.; Welch, M. J. *J. Org. Chem.* **1984**, *49*, 4900-4905. [c] Sodium tetraphenylborate and sodium tetrakis(4-fluorophenyl)borate were commercial products (Aldrich). Sodium tetrakis(4-tolyl)borate was prepared according to: Köster, R. in: *Houben-Weyl Methoden der Organischen Chemie*, 4th Ed., Vol. 13/3b, Thieme, Stuttgart, **1983**, p. 767. [d] Yields of isolated material. All the products were adequately characterized spectroscopically. [e] Reaction carried out at room temperature. [f] 2 mmol of Et_3N were used. [g] Reaction performed at 80 °C. [h] Toluene and $K_3PO_4{\cdot}3H_2O$ (1 mmol) were used as the solvent and as the base, respectively.

companied with a much lower reaction rate and a decrease of the yield, all subsequent reactions of tetraarylborates with vinyl triflates have been conducted with a borate:triflate molar ratio of 0.5:1.

In a typical procedure (entry 9), a mixture of 3β-acetoxy-5α-androst-16-en-17-yl triflate (**1c**, 464 mg, 1 mmol), $NaBPh_4$ (171 mg, 0.5 mmol), Et_3N (0.14 mL, 1 mmol), and $Pd(PPh_3)_4$ (35 mg, 0.03 mmol) in DMF (4 mL) was stirred at 60 °C for 3 h under nitrogen. The reaction mixture was then diluted with brine and extracted with ether. The organic phase was washed twice with brine, dried (Na_2SO_4), and evaporated. Chromatography of the residue (506 mg) on silica gel (20 g) using hexane-AcOEt (95:5) as eluent afforded 284 mg (72%) of 3β-acetoxy-17-phenyl-5α-androst-16-ene: mp 146.5-148 °C (hexane); $[\alpha]_D$ +21° ($CHCl_3$, 1%); ^1H NMR ($CDCl_3$) δ 0.85 (3H, s, 10-Me), 0.98 (3H, s, 13-Me), 1.97 (3H, s, 3β-OAc), 4.70 (1H, m, 3α-H), 5.88 (1H, m, C-16 H), 7.2-7.5 (5H, m, aromatics).

The procedure was then extended to aryl triflates. While **1h** and **1i** reacted smoothly to produce the expected arylated products in good yields (entries 16-20), the reaction of aryl triflates **1j** and **1k** with $NaBPh_4$ was sluggish and incomplete. After considerable experimentation,[9] we have found that the cross-coupling reaction worked satisfactorily with these triflates as well under heterogeneous conditions *i.e.* by using $K_3PO_4 \cdot 3H_2O$ (1 mmol) as the base in toluene (entries 21-24). The use of K_3PO_4 suspended in dioxane or THF has already been reported by Suzuki to be effective for the coupling of vinyl and aryl triflates with a variety of trivalent organoboron reagents.[3c]

In conclusion, the reactions of vinyl and aryl triflates with tetraarylborates appear to constitute a valuable and flexible supplement to the known arylation procedures, in particular to those employing organic triflates as substrates and arylboronic acids as aryl transfer agents. At least two aryl groups are readily available for transfer. The transfer of a third aryl moiety, although less effective under the conditions examined, is also feasible. The arylation scheme can be described by the following set of consecutive reactions.

$$\text{R-OTf} + \text{NaBAr}_4 \xrightarrow{\text{Pd(0)}} \text{R-Ar} + \text{BAr}_3 \qquad \text{(a)}$$

$$\text{R-OTf} + \text{BAr}_3 \xrightarrow[\text{base}]{\text{Pd(0)}} \text{R-Ar} + \text{" TfOBAr}_2\text{"} \qquad \text{(b)}$$

$$\text{R-OTf} + \text{" TfOBAr}_2\text{"} \xrightarrow[\text{base}]{\text{Pd(0)}} \text{R-Ar} + \text{" (TfO)}_2\text{BAr "} \qquad \text{(c)}$$

According to Suzuki,[3c] the role of the base can be attributed to the increase in the nucleophilicity of BAr_3 and " $TfOBAr_2$ " formed in steps (a) and (b), respectively, by coordination with the boron atom, thus allowing the transfer of the aryl group from boron to palladium in the transmetallation process involving these species.

The presence of a base is generally not essential for the reactions to proceed to completion, provided that an equimolar amount of borate is used, and this fact may well prove useful in the case of chiral triflates prone to undergo some base-catalyzed racemization during reaction.[3a]

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9. The following conditions have been attempted with **1j**: $Pd(PPh_3)_4/Et_3N/DMF/80$ °C; $Pd(PPh_3)_4/Et_3N/LiCl/DMF/60$ °C; $Pd_2(dba)_3/Et_3N/DMF/60$ °C; $Pd_2(dba)_3/dppf/Et_3N/60$ °C; $Pd(PPh_3)_4/Et_3N$/toluene/80 °C; $Pd(PPh_3)_4/K_2CO_3/DMF/60$ °C; $Pd(PPh_3)_4/K_2CO_3$/dioxane or toluene/80 °C. Under all these reaction conditions, either no reaction or a largely incomplete conversion of **1j** were observed.

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