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Stereoselective Synthesis of Polyenes via Heck Coupling of Vinylboronate Esters.

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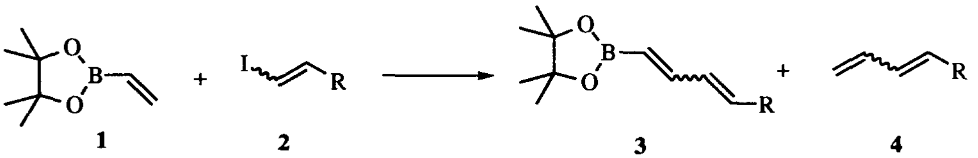
Abstract: *E*- and *Z*-1-alkenyl iodides react with vinylboronate pinacol ester **1** under palladium(0) catalysed, Heck conditions to provide polyenylboronates in moderate yields after purification. The addition of either silver(I) or thallium(I) salts to the reaction mixture is essential. Alkenyl bromides are unreactive under identical reaction conditions.

Palladium catalysed cross-coupling reactions have become one of the most widely used procedures for synthesising new carbon-carbon bonds[1]. One reaction in particular, the palladium catalysed cross-coupling of organoboron derivatives has become extensively used for the synthesis of a wide range of carbon skeletons[2]. Due to interests in polyene containing natural products and related molecules[3] we began to consider alkenylboronate **1** as a potential vinyl dianion equivalent since it could react by either a Heck[4] or a Suzuki[5]-type pathway. Preliminary results[6] from these laboratories have shown that Heck reactions of vinylboronate **1** can be achieved with arylbromides or iodides in the presence of palladium(0). In this communication, we report the Heck reaction of boronate **1** with alkenyliodides, and the utility of this chemistry for the stereoselective synthesis of polyenes.

Initial attempts to accomplish Heck reactions of vinylboronate **1** with various alkenyl bromides were completely unsuccessful. However, 1-alkenyl iodides react with vinylboronate **1**, though only in the presence of silver(I) or thallium(I) salts, as shown in **Equation 1** and **Table 1.**

eq. 1

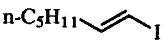
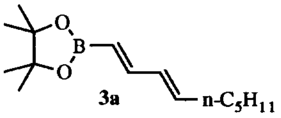
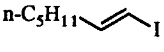
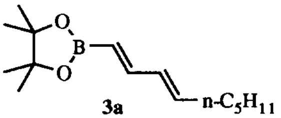
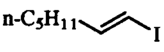
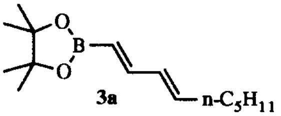
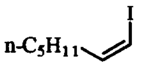
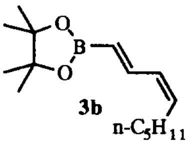
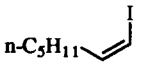
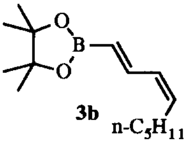
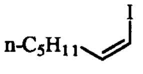
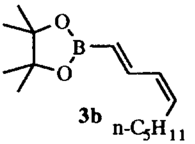
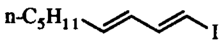
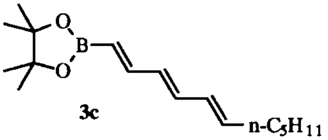


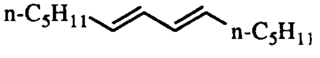
1 **2** **3** **4**

Heck product Suzuki product

Reaction of boronate **1** with *E*-iodide **2a**[7] using catalytic palladium(0) and silver(I) acetate gave dienylboronate **3a** in 56 % yield, after silica gel chromatograpy[8,9] (entry 1). Repeating the same reaction as shown in entry 3 with thallium(I) acetate under identical reaction conditions, also afforded diene **3a**, but in only 29 % isolated yield and accompanied by diene **5** in 27 % yield. However, this reaction failed completely when neither silver nor thallium salts were added (entry 2), which contrasts with the corresponding Heck reactions of aryl bromides and iodides with boronate 1[6].

Table 1.

Entry	Iodide 2	Conditions	Heck product 3	Ratio 3:4	Yield 3
1	 **2a**	cat. Pd(OAc)$_2$, PPh$_3$, AgOAc, Et$_3$N, MeCN, Δ	 **3a**	100:0	56
2	 **2a**	cat. Pd(OAc)$_2$, PPh$_3$, Et$_3$N, MeCN, Δ	 **3a**	No reaction	-
3	 **2a**	cat. Pd(OAc)$_2$, PPh$_3$, TlOAc, Et$_3$N, MeCN, Δ	 **3a**	100:0	29
4	 **2b**	cat. Pd(OAc)$_2$, PPh$_3$, TlOAc, Et$_3$N, MeCN, Δ	 **3b**	100:0	10
5	 **2b**	cat. Pd(OAc)$_2$, PPh$_3$, Et$_3$N, MeCN, Δ	 **3b**	No reaction	-
6	 **2b**	cat. Pd(OAc)$_2$, PPh$_3$, AgOAc, Et$_3$N, MeCN, Δ	 **3b**	Iodide consumed	0
7	 **2c**	cat. Pd(OAc)$_2$, PPh$_3$, AgOAc, Et$_3$N, MeCN, Δ	 **3c**	66:34	56



5

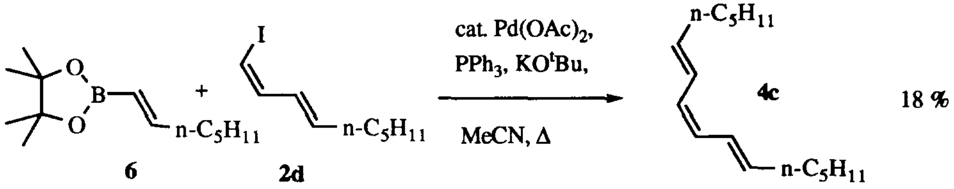
Heck reactions of Z-iodide **2b**[7] with vinylboronate **1** proved much more difficult to perform; for example, silver(I) mediated reaction conditions (entry 6) proved far too destructive for the iodide **2b**. Rapid decomposition of the iodide **2b** occurred, without reaction with the boronate **1**. Indeed, iodide **2b** rapidly decomposes in the presence of silver(I) acetate alone. However, use of thallium(I) acetate in place of silver(I) solved this problem of iodide decomposition (entry 4), but dienylboronate **3b** was only isolated in 10 %

unoptimised yield[8,9]. Again, on omission of the silver or thallium salts; this reaction failed to give any coupled products at all (entry 5).

Further demonstration of the utility of these Heck reactions for the synthesis of functionalised polyenes came from the preparation of a trienylboronate **3c**. Reaction of the highly light sensitive dienyl iodide **2c**[7] with boronate **1** in the presence of silver(I) acetate under the reaction conditions shown (entry 7), gave trienylboronate **3c** in 56 % unoptimised yield after silica gel purification[8,9].

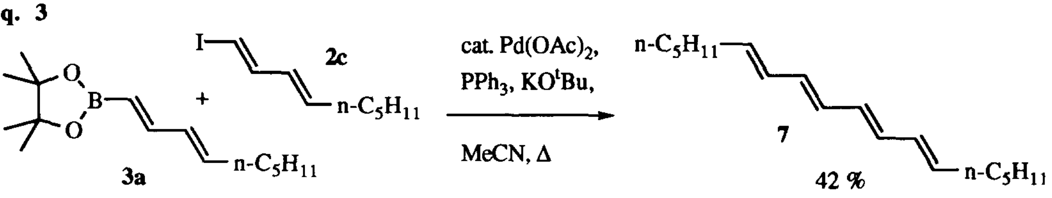
In order to demonstrate the utility of these boronates for the synthesis of polyenes, boronate **6**[10] was subjected to Suzuki coupling[11] with *cis*-dienyl iodide **2d**[7] (the iodide used was an 87:13 mixture of *cis*:*trans*) (**equation 2**). The major product obtained was *E,Z,E*-triene **4c**, albeit in only 18 % yield after chromatography.

eq. 2



Similarly, dienylboronate **3a** was subjected to coupling with dienyliodide **2c**[7] under Suzuki conditions[11] as shown in **eq. 3**. The hindered pinacol boronate ester **3a** was cleanly converted to the tetraene **7**[9] in 42 % unoptimised yield after purification.

eq. 3



We have shown that the hindered pinacol vinylboronate **1** can be used as a vinyl dianion equivalent, *via* sequential Heck and Suzuki coupling reactions, allowing access to polyene derivatives. Further studies and application of this strategy for the preparation of complex polyene systems is underway and will be reported in due course.

Acknowledgements.

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References and Notes.

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3. a) Birge, R.R.; *Ann. Rev. Phys. Chem.*, **1990**, *41*, 683; b) Kiehl, A.; Eberhardt, A.; Adam, M.; Enkelmann, V.; and Müller, K.; *Angew. Chem., Int. Edn.Engl.*, **1992**, *31*, 1588; c) Babadri, F.; Fiandanese, V.; Naso, F.; *J. Org. Chem.*, **1991**, *56*, 6245.
4. Heck reactions on vinylsilanes have been reported; Yamashita, H.; Roan, B.L.; and Tanaka, M.; *Chem. Letters*, **1990**, 2175.
5. a) Hyuga, S.; Yamashina, N.; Hara, S.; and Suzuki, A.; *Chem. Letters*, **1988**, 809; b) Ogima, M.; Hyuga, S.; Hara, S.; Suzuki, A.; *ibid*, **1989**, 1959.
6. Hunt, A.R.; Stewart, S.K.; and Whiting, A.;*Tetrahedron Lett.*, **1993**, *34*, 3599.
7. See following communication.
8. Typical Heck procedure: A mixture of AgOAc (or TlOAc) (4.81 mmol), $Pd(OAc)_2$ (0.14 mmol) and PPh_3 (0.28 mmol) was suspended in dry MeCN (25 ml) under Ar. The alkenyl iodide (4.81 mmol), Et_3N (5.78 mmol) and vinylboronate **1** (5.78 mmol) were then added and the mixture was heated at 75 °C for 1.5 h. After cooling, the mixture was diluted with CH_2Cl_2, filtered, washed with 5% HCl, H_2O and satd. NaCl soln., dried ($MgSO_4$) and evaporated to give a yellow oil. The crude products were purified by SiO_2 chromatography.
9. All new compounds had satisfactory spectroscopic and analytical properties. Selected ^1H n.m.r. data (300 MHz, $CDCl_3$): Boronate **3a**, 5.41 (1H, d, J = 17.7 Hz, CHB), 5.83-5.93 (1H, m, $CH_2.C\underline{H}:CH$), 6.12 (1H, dd, J = 10.3 and 15.1 Hz, $C\underline{H}.CH:CHB$), and 6.98 (1H, dd, J = 10.3 and 17.7 Hz, $C\underline{H}:CHB$); Boronate **3b**, 5.52 (1H, d, J = 17.5 Hz, CHB), 5.59 (1H, dt, J = 10.8 and 7.7 Hz,$CH_2.C\underline{H}:CH$), 6.06 (1H, t, J = 10.8 Hz, $C\underline{H}.CH:CHB$), and 7.30 (1H, dd, J = 11.0 and 17.5 Hz, $C\underline{H}:CHB$); Boronate **3c**, 5.50 (1H, d, J = 17.6 Hz, CHB), 5.76-5.87 (1H, m, $CH_2.C\underline{H}:CH$), 6.08, 6.18 and 6.33 (each 1H, dd, J = 10.5 and 14.8 Hz, $CH:C\underline{H}.C\underline{H}:C\underline{H}.CH:CHB$), and 7.02 (1H, dd, J = 10.5 and 17.6 Hz, $C\underline{H}:CHB$); Triene **4c**, 5.69 (2H, dt, J = 7.3 and 15.0 Hz, 2 x $CH_2.C\underline{H}:CH.CH$), 5.85 (2H, d, J = 8.7 Hz, 2 x $CH_2.CH:CH.C\underline{H}$), and 6.48 (2H, dd, J = 8.7 and 15.0 Hz, 2 x $CH_2.CH:C\underline{H}.CH$); Tetraene **7**, 5.64-5.74 (2H, m, 2 x $CH_2.C\underline{H}:CH$), and 6.03-6.21 (6H, m, 2 x $CH_2.CH:C\underline{H}.C\underline{H}:C\underline{H}$).
10. Boronate **6** was prepared from the catechol ester[a], by trans-esterification with pinacol (in a mixture of chloroform and satd. $NaHCO_3$ soln.); a) Brown, H.C.; and Gupta, S.K.; *J. Am. Chem. Soc.*, **1972**, *94*, 4370.
11. Suzuki procedure: KO^tBu (0.33 mmol), $Pd(OAc)_2$ (0.001 mmol) and PPh_3 were suspended in dry MeCN (2 ml) under Ar. The iodide (0.16 mmol) and boronate (0.197 mmol) were added and the mixture heated at 70 °C for 1 h. The mixture was diluted with Et_2O, washed with 5% HCl, H_2O and satd. NaCl soln., dried ($MgSO_4$) and evaporated to give a brown oil. Purification by SiO_2 chromatography (hexane as eluant) gave the polyene.

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