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Selective Oxidative Ligand Coupling of Organoborates Bearing an Alkynyl Group

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Dedicated to Professor Armin de Meijere on the occasion of his 70th birthday.

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Abstract: Selective oxidative ligand coupling of alkynyl(triaryl)borates was achieved by treatment with ethoxyvanadyl dichloride [VO(OEt)Cl_2] to form the *sp–sp*^{2} carbon-carbon bond. A one-pot procedure through the *in situ* preparation of the borate was demonstrated using triphenylborane and 1-ethynyl-4-methoxybenzene.

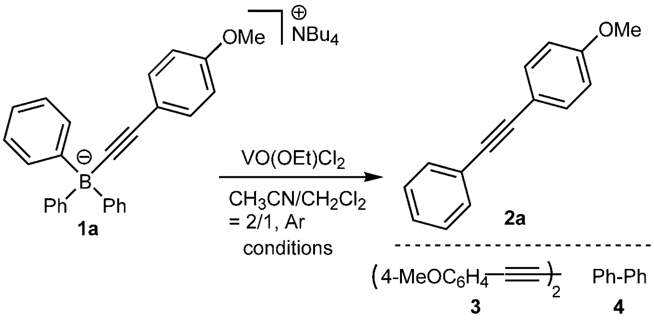
Keywords: borates; cross-coupling; ligand coupling; oxidation; vanadium

The *sp–sp*^{2} carbon-carbon bond forming reaction is one of the most important reactions to produce ubiquitous compounds with a triple bond as pharmaceutical intermediates, liquid crystals, polymers and materials with specialized optical and electronic properties. The palladium-catalyzed cross-coupling of a terminal alkyne with a vinyl or aryl halide, as typified by the Sonogashira reaction,[1] can provide a direct route to the formation of an *sp–sp*^{2} carbon-carbon bond.[2] On the other hand, oxidative cross-coupling of organometallic nucleophiles leads to the formation of a carbon-carbon bond, which is considered to be a complementary method for the conventional nucleophile-electrophile coupling.[3] However, oxidative cross-coupling is usually difficult to achieve because of the lack of selectivity,[4] although many studies have been recently performed for the oxidative homo-coupling reaction of organometallic aryl nucleophiles.[5] As for the oxidative cross-coupling of alkynyl and aryl nucleophiles, there are very limited examples.[6–8] Iodine-induced oxidative coupling based on the activation of a triple bond in alkynyltriorganoborates was reported by Suzuki, Brown and co-workers.[6] Recently, Knochel and co-workers demonstrated the copper(I)-mediated oxidative cross-coupling between alkynyllithiums and arylmagnesiums by the subsequent treatment with chloranil.[7] We have also achieved the selective oxovanadium(V)-induced oxidative cross-coupling of organoaluminium ate complexes generated *in situ* from alkynyl- or aryllithiums,[8] as well as the selective oxidative carbon-carbon bond forming reaction of main group organometallics, such as organozirconocenes,[9] organoborons,[10] organozincs,[11] and their ate complexes using oxovanadium(V) compounds as a stoichiometric oxidant. The selective ligand coupling between two aryl nucleophiles on boron using the vanadium(V)-catalyzed oxidation of borates under molecular oxygen was also developed.[12] Organoborates are convenient reagents as a nucleophile due to their stability towards air and moisture, however the stability does not hamper their high reactivity in a large variety of reactions.[13] This motivated us to investigate the oxidative cross-coupling between the alkynyl and aryl ligands of the borates. Herein, we report the selective oxidative ligand coupling of alkynyl(triaryl)borates by treatment with VO(OEt)Cl_2, forming the *sp–sp*^{2} carbon-carbon bond.

Triphenylborane was easily coupled with [(4-methoxyphenyl)ethynyl]lithium at $-78\,^{\circ}C$ for 1 h. After the thus-obtained mixture had been concentrated, the addition of methanol and tetrabutylammonium bromide to the mixture caused a precipitation. The suspension was filtered, and the residue was washed with methanol to give tetrabutylammonium [(4-methoxyphenylethynyl)triphenyl]borate (**1a**) in 96% yield. Other borates were prepared similarly.

The oxidative ligand coupling of the borate **1a** with VO(OEt)Cl_2 was investigated as summarized in Table 1. In the reaction at room temperature for 2 h, the use of 4 molar equivalents of VO(OEt)Cl_2 to **1a**

Table 1. Oxidative ligand coupling of the borate **1a** using $VO(OEt)Cl_2$.



Entry	$VO(OEt)Cl_2$ [equiv.]	Time [h]	Temp. [°C]	Isolated yield of **2a** [%]
1	4	2	r.t.	89
2	4	0.033	r.t.	79
3	4	2	−42	62
4	2	2	r.t.	84
5	1	2	r.t.	52[a]
6	0.5	2	r.t.	18[a]
7	0.1	2	r.t.	2[a]
8[b]	0.1	2	r.t.	6[a]

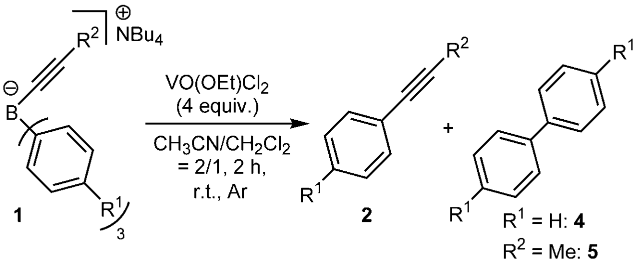
[a] Determined by ^1H NMR.

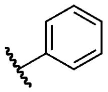
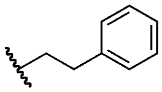
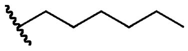
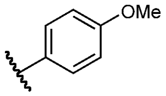
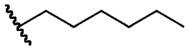
[b] Under molecular oxygen.

selectively afforded the hetero-coupling product **2a** in 89% yield (Table 1, entry 1), where no homo-coupling product diyne **3** and a trace amount of biphenyl (**4**) were observed. According to our previous study, **1a** is likely to couple intramolecularly.[12] This reaction was quite fast in that it proceeded within 2 min to give **2a** in 79% yield (Table 1, entry 2). Even at −42 °C, this ligand coupling provided **2a** in 62% yield (Table 1, entry 3). Reducing the amount of $VO(OEt)Cl_2$ to 2 molar equivalents did not decrease the yield (84%, Table 1, entry 4). However, lower equivalents resulted in a significant decrease of yields (52, 18, and 2% for 1, 0.5, and 0.1 molar equivalents, respectively, Table 1, entries 5–7). An improvement was observed in the reaction under an oxygen atmosphere (Table 1, entry 8).

To investigate the vanadium species in this reaction, the changes in the vanadium species with the addition of the borate were monitored by ^{51}V NMR experiment. It was conducted with $VOCl_3$ as an external standard (0 ppm), which was also used as a standard for the quantitative evaluation in this reaction. First, $VO(OEt)Cl_2$ was measured in THF-d_8 using an NMR tube with a resealable J-Young valve attached under a nitrogen atmosphere. The peak at −326 ppm was observed for $VO(OEt)Cl_2$. Addition of 0.1 molar equivalents of the borate **1a** [referred to $VO(OEt)Cl_2$] to this solution resulted in a decrease of $VO(OEt)Cl_2$. Finally, $VO(OEt)Cl_2$ was completely consumed after the addition of a total of 0.5 molar equivalents of **1a**. This decrease is probably due to the conversion from V(V) to V(IV). The reaction was similarly worked up and purified. The isolated yield of **2a** in this NMR experiment was 72% with >99% selectivity. These results clearly suggest that $VO(OEt)Cl_2$ contributes to this coupling reaction as an oxidant.

Table 2. Oxidative ligand coupling of various borates **1b–f** using $VO(OEt)Cl_2$.



	R^1	R^2	Yield [%][a]	
			2	**4 or 5**
1b	H		11, 19[b]	trace
1c[c]	H		72	12
1d[c]	H		66	10
1e	Me	 OMe	72	8
1f[c]	Me		79	6

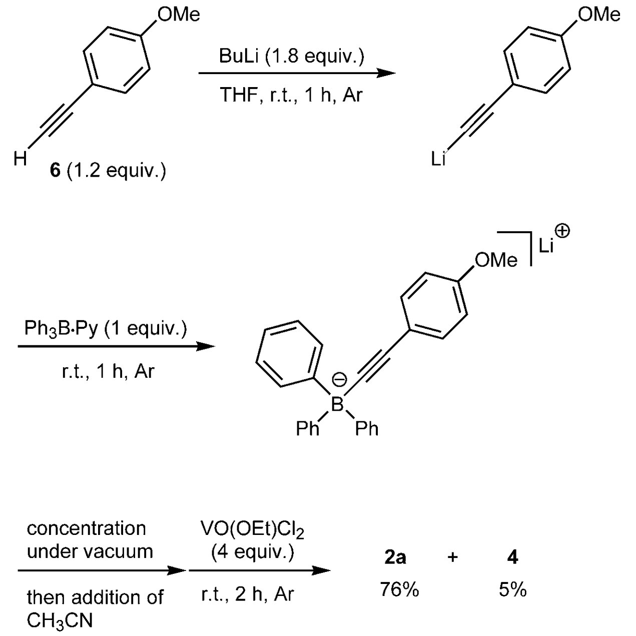
[a] Determined by ^1H NMR.

[b] 1,1,2-Triphenylethene.

[c] The counter ammonium cation is Me_4N^+.

The scope of the oxidative ligand coupling of various borates **1b–f** using $VO(OEt)Cl_2$ was investigated as summarized in Table 2. Phenylethynyl(triphenyl)-borate **1b** reacted to give **2b** in 11% yield as well as a trace amount of **4**, where the hydrophenylated product of **2b**, 1,1,2-triphenylethene, was also observed (19%).[14] When R is a phenethyl or a hexyl group, the corresponding hetero-coupling product was obtained mainly (72 and 66% yields, respectively), while around 10% of the homo-coupling product **4** was also formed in each case. The ligand coupling reaction using the borates **1e** and **1f**, prepared from tris(4-tolyl)borane, also afforded the corresponding hetero-coupling products **2e** and **2f** mainly (72 and 79% yields, respectively). An ionic mechanism has been proposed in the iodine-induced coupling of alkynyl-triorganoborates.[6] The homo-coupling product is observed in the present case, but was not found in the iodine-induced one. Another reaction path *via* an electron transfer mechanism[15] may be operating in our case as reported in our previous study of the oxovanadium-induced coupling of borates.[10]

A one-pot procedure through the *in situ* preparation of the borate was demonstrated using triphenylborane and 1-ethynyl-4-methoxybenzene (**5**; Scheme 1). Lithiation of **6** by the treatment with BuLi, followed by the addition of triphenylborane, generated the corresponding borate. Then, the evaporation of THF was carried out to replace the solvent by CH$_3$CN. To the reaction mixture was added 4 molar equivalents of VO(OEt)Cl$_2$ to afford the desired **2a** in 76% yield together with a small amount of **4** (5%). The homo-coupled diyne **3** was not obtained in this reaction.



Scheme 1. One-pot oxidative ligand coupling of the borate through its *in situ* preparation.

In conclusion, the chemoselective oxidative ligand coupling of alkynyl(triaryl)borates is achieved by the treatment with VO(OEt)Cl$_2$, forming the *sp–sp*^{2} carbon-carbon bond. A one-pot procedure through the *in situ* preparation of the borate was demonstrated. Further investigations on the catalytic system are now underway.

Experimental Section

Typical Procedure for the Preparation of the Borate 1

In a 3-necked, 100-mL round-bottom flask fitted with a dropping funnel, was placed a stirring bar and the system was dried by heating under reduced pressure. Under an argon atmosphere, THF (20 mL) and alkynyl compound (12 mmol) were added into the flask, and the mixture was cooled to −78 °C. To the mixture was dropwise added 1.59 M BuLi hexane solution (6.92 mL, 11 mmol) over 30 min at the same temperature. After 1 h, the triarylborane pyridine complex (10 mmol) was added to the reaction mixture at the same temperature. The reaction mixture was allowed to warm to room temperature. After 1 h, a small amount of methanol was added to quench the reaction. After concentration, the residue was dissolved in methanol. To the solution, tetrabutyl- or tetramethylammonium halide (10 mmol) was added, and the resulted white precipitate was filtered and washed with cold methanol to give the desired borate **1**.

General Procedure for the Oxidative Coupling of the Borate 1 using VO(OEt)Cl$_2$

In a 2-necked, 20-mL round-bottom flask was placed a stirring bar and the apparatus was dried by heating under reduced pressure. Under an argon atmosphere, acetonitrile (2 mL), dichloromethane (1 mL), and the borate **1** (0.30 mmol) were added into the flask, followed by the addition of VO(OEt)Cl$_2$ (2.0 M solution in dichloromethane, 0.6 mL, 1.2 mmol) at room temperature. The mixture was stirred for 2 h at room temperature, then quenched by the addition of a pH 7 aqueous buffer solution (KH$_2$PO$_4$/Na$_2$HPO$_4$). After extraction with Et$_2$O three times, the combined organic layer was washed with brine, dried over MgSO$_4$, and evaporated. The resulting crude product was purified by preparative TLC (hexane) to afford the corresponding coupling product **2**.

One-Pot Procedure for the Oxidative Coupling using VO(OEt)Cl$_2$

In a 2-necked, 20-mL round-bottom flask was placed a stirring bar and the apparatus was dried by heating under reduced pressure. Under an argon atmosphere, THF (5 mL) and 1-ethynyl-4-methoxybenzene **6** (48 mg, 0.36 mmol) were added into the flask. To the mixture was dropwise added 1.59 M BuLi hexane solution (0.34 mL, 0.54 mmol) over 30 min at room temperature. After 1 h, the triphenylborane pyridine complex (96 mg, 0.3 mmol) was added to the reaction mixture. After 1 h, the reaction mixture was slowly concentrated and dried under reduced pressure, then acetonitrile (5 mL) was added, followed by the addition of VO(OEt)Cl$_2$ (2.0 M solution in dichloromethane, 0.6 mL, 1.2 mmol) at room temperature. The mixture was stirred for 2 h, then quenched by the addition of a pH 7 aqueous buffer solution (KH$_2$PO$_4$/Na$_2$HPO$_4$). After extraction with Et$_2$O three times, the combined organic layer was washed with brine, dried over MgSO$_4$, and evaporated. The resulting crude product was purified by preparative TLC (hexane) to afford the corresponding coupling product **2a**.

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