# Oxovanadium(V)-catalyzed oxidative biaryl synthesis from organoborate under $O_2$†

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**Oxidative ligand coupling of organoborates was catalyzed by $VO(OEt)Cl_2$ under oxygen atmosphere, which provides a versatile method for the selective synthesis of symmetrical or unsymmetrical biaryls.**

Oxidative coupling of organometallic nucleophiles leads to the formation of a new carbon–carbon bond, which is considered to be a complementary method for the conventional nucleophile–electrophile coupling. The oxidative homo-coupling of aryl-metal reagents by transition-metal oxidants has been widely studied to offer a useful method for the construction of symmetrical biaryl backbones.[1] However, oxidative cross-coupling is usually difficult to perform because of the lack of selectivity.[2] We have previously reported the selective carbon–carbon bond formation of main-group organometallics, such as organoaluminiums,[3] organoborons,[4] organozincs,[5] and their ate complexes using oxovanadium(V) compounds as a stoichiometric oxidant. From a synthetic viewpoint, a catalytic method for oxidative coupling needs to be developed. Although tetraarylborates are transformed to biaryls by photochemical,[6] electrochemical[7] or chemical oxidation,[8] there has been no report on the formation of biaryls from tetraarylborates using a catalytic amount of a metallic oxidant. In this paper, we wish to report a first example of the catalytic ligand coupling of organoborates induced by $VO(OEt)Cl_2$ under oxygen atmosphere. The chemoselective ligand coupling was accomplished by the oxidation of unsymmetrical tetraarylborates.

Sodium tetraphenylborate (**1a**) was treated with a series of high-valent vanadium compounds **3** (0.1 molar equivalents to **1a**) in acetonitrile under oxygen atmosphere (Table 1).[9] No catalytic activity was observed with vanadium(IV) compounds, like $VO(acac)_2$, $VO(hfac)_2$ (hfac = hexafluoroacetylacetonate) and $Cp_2VCl_2$ (entries 1–3). Among five-valent vanadiums, although $V_2O_5$ exhibited no catalytic activity (entry 4), a catalytic reaction occurred with $VOCl_3$ (33% yield, entry 5). A better result was obtained when $VO(OEt)Cl_2$ was used (52% yield, entry 6).

**Table 1** Oxidative ligand coupling of $NaBPh_4$ with a catalytic amount of vanadium compound

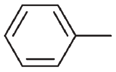
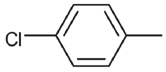
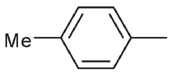
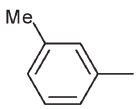
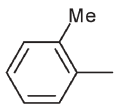
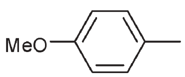
$$\underset{\mathbf{1a}}{NaBPh_4} \xrightarrow[\text{MeCN, O}_2\text{, rt, 12 h}]{\text{vanadium catalyst (0.1 molar equivalents to }\mathbf{1a}\text{)}} \underset{\mathbf{2a}}{Ph-Ph}$$

| Entry | Vanadium catalyst **3** | Yield of **2a** (%) |
|---|---|---|
| 1 | $VO(acac)_2$ | trace |
| 2 | $VO(hfac)_2$ | trace |
| 3 | $Cp_2VCl_2$ | 9 |
| 4 | $V_2O_5$ | 5 |
| 5 | $VOCl_3$ | 33 |
| 6 | $VO(OEt)Cl_2$ | 52 |

The present method was successfully extended to the catalytic ligand coupling of various symmetrical tetraarylborates **1** with $VO(OEt)Cl_2$ (Table 2).‡ Use of 0.2 molar equivalents of $VO(OEt)Cl_2$ to **1** gave the corresponding biaryls **2** in satisfactory yields (85–90%) for almost all borates (entries 1, 3, 4, 5 and 6). The catalytic reaction also proceeded with 0.1 molar equivalents of $VO(OEt)Cl_2$ to **1** (entry 7). In the case of sodium tetrakis(4-chlorophenyl)borate (**1b**), however, the yield of 4,4′-dichlorobiphenyl (**2b**) was low (entry 2). Thus, the higher π-electron density on the aromatic ring is considered to permit more facile oxidation, suggesting that the ligand coupling is controlled by the electronic properties of the aryl groups.

**Table 2** Catalytic oxidative ligand coupling of $NaBAr_4$ with $VO(OEt)Cl_2$

$$\underset{\mathbf{1}}{NaBAr_4} \xrightarrow[\text{MeCN/CH}_2\text{Cl}_2\text{ = 2/1, O}_2\text{, rt, 20 h}]{\text{VO(OEt)Cl}_2\text{ (0.2 molar equivalents to }\mathbf{1}\text{)}} \underset{\mathbf{2}}{Ar-Ar}$$

| Entry | Ar | **1** | Yield of **2** (%) |
|---|---|---|---|
| 1 |  | **1a** | 87 |
| 2 |  | **1b** | 20 |
| 3 |  | **1c** | 90 |
| 4 |  | **1d** | 85 |
| 5 |  | **1e** | 87 |
| 6 |  | **1f** | 90 |
| 7 | | **1f** | 70[a] |

[a] 0.1 molar equivalents of $VO(OEt)Cl_2$ to **1** were used.

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† Electronic supplementary information (ESI) available: Compound characterization data ($^1H$, $^{13}C$, $^{11}B$ NMR and ESR) for selected compounds. See DOI: 10.1039/b610731a

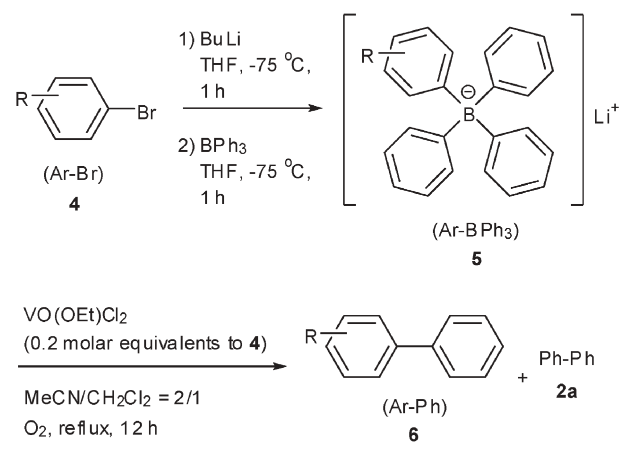
To obtain further insight into the ligand coupling, a crossover experiment was conducted. Two different borates, sodium tetraphenylborate (**1a**) and sodium tetrakis(4-methoxyphenyl)borate (**1f**), were treated with two molar equivalents of $VO(OEt)Cl_2$ (a molar equivalent for each substrate) in one pot (Scheme 1). The products were found to be biphenyl (**2a**) and 4,4′-bismethoxybiphenyl (**2f**), and the formation of 4-methoxybiphenyl (**6f**) was not detected at all. These findings indicate that the ligand coupling proceeds only intramolecularly.

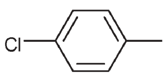
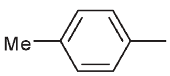
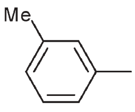
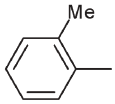
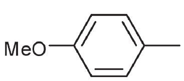
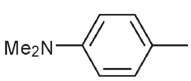
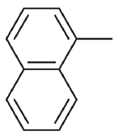
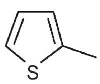
The different reactivities based on the electronic properties of the aryl groups and the intramolecular coupling mode permitted a selective carbon–carbon bond formation in the reaction of the unsymmetrical borates **5**. A variety of **5** were prepared from the corresponding aryl bromide **4**, BuLi and $BPh_3$ *in situ*. With use of the electron-rich aryl bromide as a starting substrate, the unsymmetrical biaryl was obtained as a major product by the treatment of 0.2 molar equivalents of $VO(OEt)Cl_2$ to **4** (Table 3, entries 2–8).§ The coupling of methyl-substituted aryl bromides **4c–e** was revealed to depend on the substituent position. Use of 4-methylphenyl bromide (**4c**) resulted in 4-methylbiphenyl (**6c**) in 60% yield (entry 2). However, starting from 2-methylphenyl bromide (**4e**), both yield and selectivity were lowered (entry 4). Since a similar low reactivity was observed with the naphthyl derivative (entry 7), a steric effect appears to operate in the coupling in addition to the electronic effect. In the case of 4-chlorophenyl bromide (**4b**), the cross-coupling product, 4-chlorobiphenyl (**6b**) was obtained only in 10% yield, while biphenyl (**2a**) was predominantly produced in 45% yield (entry 1). This method was applied to the coupling of the heterocyclic group to give the unsymmetrical biaryl *via* selective carbon–carbon bond formation (entry 8).

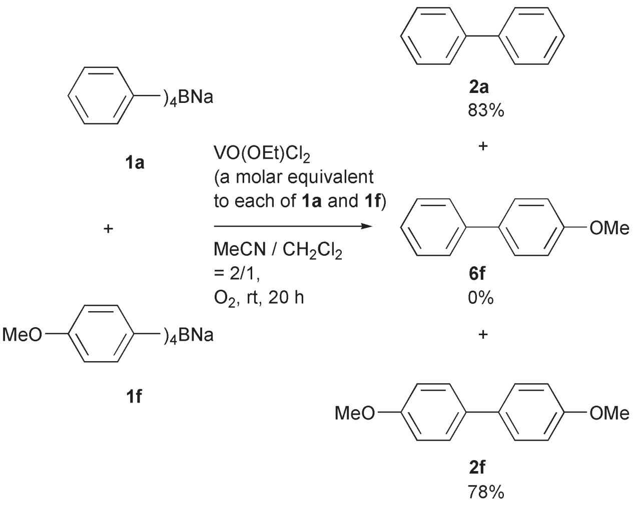
A similar mechanism seems to operate as proposed in the stoichiometric reaction.[4] During the ligand coupling reaction, the vanadium(V) species is reduced to a vanadium(IV) one, which was detected in the ESR spectrum of the reaction mixture. Thus-obtained V(IV) species might be reoxidized to a vanadium(V) one with molecular oxygen, forming a catalytic redox cycle.[10]

To develop an atom economical process, potassium diphenyldifluoroborate (**7a**)[11] was employed in the ligand coupling. Although the reactivity was lower, the ligand coupling proceeded at 70 °C as shown in Scheme 2.

**Table 3** Ligand coupling of unsymmetrical borate **5**



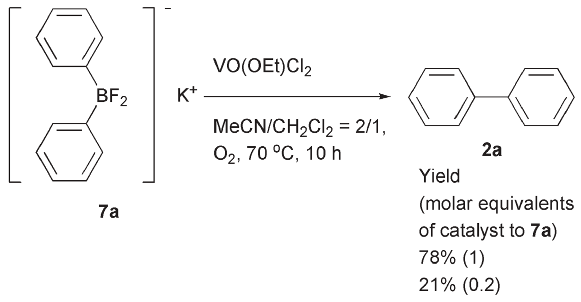
| Entry | Ar | 4 | Yield (%) 6 | Yield (%) 2a | Selectivity 6 : 2a |
|---|---|---|---|---|---|
| 1 |  | **4b** | 10 | 45 | 18 : 82 |
| 2 |  | **4c** | 60 | 9 | 87 : 13 |
| 3 |  | **4d** | 47 | 9 | 84 : 16 |
| 4 |  | **4e** | 14 | 8 | 64 : 36 |
| 5 |  | **4f** | 70 | 9 | 89 : 11 |
| 6 |  | **4g** | 58 | 7 | 89 : 11 |
| 7 |  | **4h** | 30 | 8 | 79 : 21 |
| 8 |  | **4i** | 62 | 8 | 89 : 11 |



**Scheme 1** Crossover experiment.

In conclusion, the oxovanadium-catalyzed ligand coupling of the organoborates was demonstrated to provide a versatile method for the selective oxidative coupling between two aryl nucleophiles on boron. It should be noted that the ligand coupling to unsymmetrical biaryls was achieved with *in situ* generated unsymmetrical borates.

Thanks are due to the Analytical Center, Graduate School of Engineering, Osaka University, for the measurement of the $^{11}B$ NMR and ESR spectra. This work was supported by a



**Scheme 2** Ligand coupling of diphenyldifluoroborate (**7a**).

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## Notes and references

‡ General procedure for symmetrical biaryls **2**. In a 2-necked 20 mL round-bottom flask, a stirring bar and sodium tetraarylborate (**1**, 0.20 mmol) were placed and dried. Under an oxygen atmosphere, acetonitrile (2 mL) and dichloromethane (0.95 mL) were added into the flask, followed by the addition of $VO(OEt)Cl_2$ (0.80 M solution in dichloromethane, 0.05 mL, 0.040 mmol). The mixture was stirred for 20 h at room temperature, and then quenched by the addition of 3 mL of pH 7 buffer ($KH_2PO_4$–$Na_2HPO_4$). After extraction with $Et_2O$ (3 × 10 mL), the combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The resulting crude product was purified with preparative TLC (hexane) to afford the corresponding biaryl **2** (Table 2).

§ General procedure for unsymmetrical biaryls **6**. To a 2-necked 20 mL round-bottom flask equipped with a reflux condenser and a stirring bar, aryl bromide (0.20 mmol) in THF (1 mL) was added. The mixture was cooled to −75 °C (ethanol–dry ice). BuLi (1.35 M solution in hexane, 0.148 mL, 0.20 mmol) was added, and the mixture was stirred for 1 h at the same temperature. A THF (1 mL) solution of $BPh_3$ (48.4 mg, 0.20 mmol) was added at −75 °C. After stirring for 1 h, the reaction flask was allowed to reach room temperature and the solvent was exchanged from THF to acetonitrile (2 mL)–dichloromethane (0.95 mL). Under an oxygen atmosphere, $VO(OEt)Cl_2$ (0.80 M solution in dichloromethane, 0.05 mL, 0.040 mmol) was added, and the reaction mixture was stirred for 12 h under reflux. The reaction was quenched by the addition of pH 7 buffer (3 mL). After extraction with $Et_2O$ (10 mL × 3), the combined organic layer was washed with brine, dried over $MgSO_4$, and evaporated. The purification of the crude product with preparative TLC (hexane–dichloromethane = 3 : 2) gave the corresponding unsymmetrical biaryl **6** (Table 3).

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