Carboranes

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Nickel-Catalyzed Cross-Coupling Reactions of *o*-Carboranyl with Aryl Iodides: Facile Synthesis of 1-Aryl-*o*-Carboranes and 1,2-Diaryl-*o*-Carboranes**

*Cen Tang and Zuowei Xie**

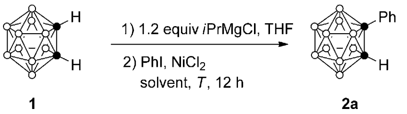
Abstract: *A nickel-catalyzed arylation at the carbon center of o-carborane cages has been developed, thus leading to the preparation of a series of 1-aryl-o-carboranes and 1,2-diaryl-o-carboranes in high yields upon isolation. This method represents the first example of transition metal catalyzed C,C′-diarylation by cross-coupling reactions of o-carboranyl with aryl iodides.*

Icosahedral carboranes (*closo*-$C_2B_{10}H_{12}$) have received increasing interest in medicine as boron neutron capture therapy agents,[1] in supramolecular design/nanomaterials as building blocks,[2] and in coordination/organometallic chemistry as ligands.[3] Recently, the discovery of very interesting photophysical properties of aryl-*o*-carboranes implies the existence of a unique role of *o*-carborane cages on the electronic systems.[4] However, the cage structure makes its derivatization difficult, thus resulting in a limited application scope. In general, 1-aryl-*o*-carboranes and 1,2-diaryl-*o*-carboranes are prepared from the condensation reaction of the corresponding aryl or diaryl acetylenes with decaborane,[4,5] and the yields of the desired products are variable. The hypertoxicity of decaborane also complicates this method. Obviously, a direct $C_{cage}-C_{sp2}$ bond formation by cross-coupling of an *o*-carboranyl and aryl is an attractive strategy for the synthesis of 1,2-(aryl)$_n$-*o*-carboranes ($n = 1, 2$). Unfortunately, direct nucleophilic substitution reaction of lithiocarboranes with aryl iodides does not proceed. In contrast, the reaction of 1-Cu-*o*-$C_2B_{10}H_{11}$ or 1,2-Cu_2-*o*-$C_2B_{10}H_{10}$ with aryl iodides affords 1-aryl-*o*-carboranes in moderate yields[6] and no 1,2-diaryl-*o*-carboranes are produced,[6,7] probably a result of steric reasons and the formation of the homocoupling product bis(carborane).[8]

Inspired by the transition metal catalyzed cross-coupling reaction of aryls,[9] we initiated a study to develop a transition metal catalyzed arylation of *o*-carboranes. Herein we report a nickel-catalyzed cross-coupling of carboranyls with aryls for the efficient and high-yielding synthesis of a variety of 1-aryl-*o*-carboranes and 1,2-diaryl-*o*-carboranes.

We commenced our studies by screening for a suitable temperature for the cross-coupling reaction of 1-MgCl-1,2-$C_2B_{10}H_{11}$ with phenyl iodide in THF under nickel catalysis. 1-MgCl-1,2-$C_2B_{10}H_{11}$ was conveniently prepared in situ from an equimolar reaction of *o*-carborane (**1**) with *i*PrMgCl in THF. Selected results are compiled in Table 1 (see the Supporting Information for a complete list). Of the factors examined, reaction temperature and solvent played the most important role. High temperatures facilitated the cross-coupling reaction. No obvious change in the yields of **2a** was observed when the catalyst loading was changed from 10 to 2 mol%. Accordingly, the reaction conditions of entry 11 (Table 1) were identified as the optimal reaction conditions. Under such reaction conditions, PhI offered the best yield of **2a** among all the PhX tested (X = I, Br, Cl; see Table S1 in the Supporting Information).

Table 1: Optimization of nickel-catalyzed cross-coupling reaction.[a]



Entry	PhI [equiv]	*T* [°C]	Solvent	NiCl$_2$ (mol%)	Yield [%][b]
1	1.0	RT	THF	10	n.r.
2	1.0	40	THF	10	5
3	1.0	70	THF	10	67
4	1.0	100	THF	10	88
5	1.0	100	THF	5	86
6	1.0	100	THF	2	86
7	1.1	100	THF	2	88
8	1.2	100	THF	2	91
9	1.2	60	Et_2O	2	n.r.
10	1.2	100	DME	2	–[c]
11	1.2	100	toluene	2	96
12	1.2	100	toluene	0	n.r.

[a] Reactions were conducted on 1.0 mmol scale of **1** in 5 mL of solvent in a closed flask for 12 h. [b] Determined by GC. [c] Complicated reaction mixture. DME = dimethoxyethane, n.r. = no reaction, THF = tetrahydrofuran.

Subsequently, the scope of this cross-coupling reaction was examined and the results were summarized in Table 2. In general, such a cross-coupling reaction was very efficient, thus giving 1-aryl-*o*-carboranes in high to excellent yields. It was tolerant of functional groups such as Cl, F, CF_3, OCH_3, and N-aryl carbazole. In addition, iodonaphthalene and iodophenanthrene were compatible with the reaction conditions, thus

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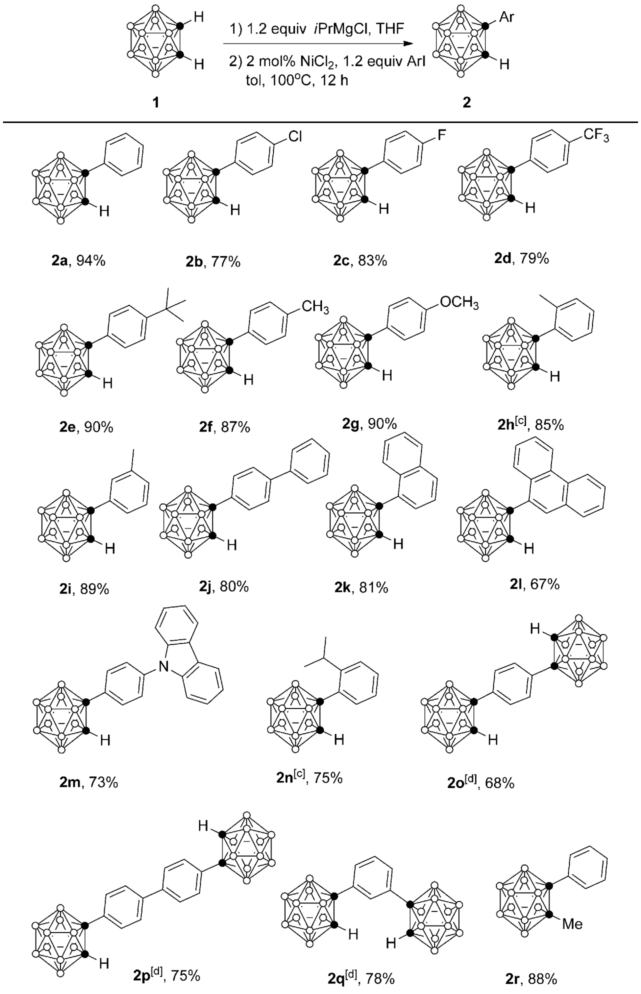
Table 2: Synthesis of 1-aryl-*o*-carboranes.[a,b]

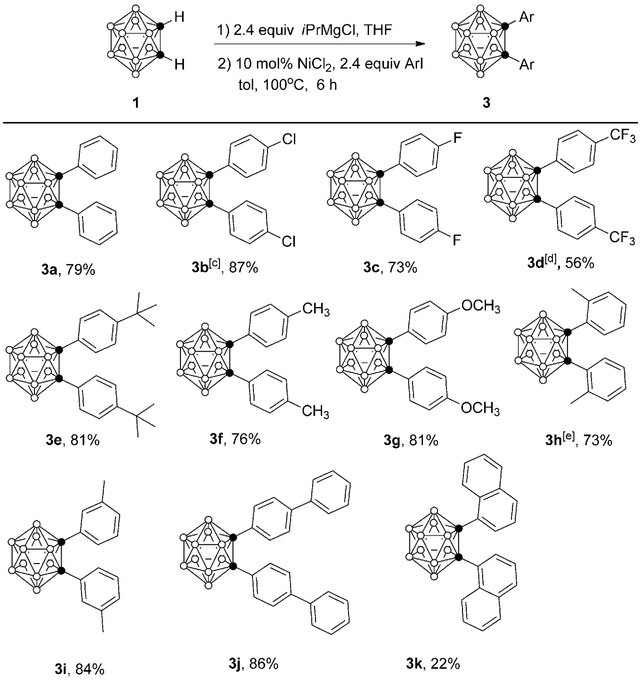


[a] Yield of isolated products. [b] Reactions were conducted at 1.0 mmol scale in 5 mL of toluene in a closed flask at 100 °C for 12 h. [c] Heated at 140 °C. [d] Used 0.6 equiv of either 1,4-diiodobenzene or 4,4′-diiodobiphenyl or 1,3-diiobenzene.

affording **2k** (81 %) and **2l** (67 %), respectively. For diiodobenzene and diiodobiphenyl, dicarboranylation proceeded to generate **2o**, **2p**, and **2q** in 68–78 % yields upon isolation. 1-Methyl-*o*-carborane also worked well to give **2r** in 88 % yield. For substrates with *ortho* substituents, a higher bath temperature (140 °C) was required to afford the desired products **2h** and **2n** in more than 75 % yield.

In contrast, during the isolation of **2a**, a trace amount of 1,2-diphenyl-*o*-carborane was detected by GC-MS, thus indicating that diarylation on both cage carbon atoms was possible. We then screened the reaction conditions and identified the optimal conditions as shown in Table 3 (see Table S2 for details). This reaction was compatible with a variety of aryl iodides, thus giving 1,2-diaryl-*o*-carboranes in 56–86 % yields, except for 1,2-dinaphthyl-*o*-carborane (**3k**). The low yield of **3k** was probably a result of poor reactivity of iodonaphthalene and steric reasons. A higher bath temperature (140 °C) was required for 1-iodo-2-methylphenyl to afford **3h** in 73 % yield. The more sterically demanding 1-iodo-2-isopropylphenyl produced only the monoarylated cage species **2n** (Table 2). For an aryl iodide with a strong electron-withdrawing group, such as CF_3, the diarylation product **3d** was obtained in a considerably reduced yield of 56 % (Table 3).

Table 3: Synthesis of 1,2-diaryl-*o*-carboranes.[a,b]



[a] Yield of isolated products. [b] Reactions were conducted at 1.0 mmol scale in 5 mL of toluene in a closed flask at 100 °C for 6 h. [c] Used 3 equiv of *p*-IC_6H_4Cl. [d] Reaction time was 8 h. [e] Reaction was performed at 140 °C (bath temperature).

The compounds **2** and **3** were fully characterized by ^1H, ^{13}C, and ^{11}B NMR spectroscopy as well as high-resolution mass spectrometry. The molecular structures of **2b**, **2d**, **2f**, **2g**, **2j**, **2l**, **2r** and **3a**, **3b**, **3c**, **3e**, **3f**, **3g** were further confirmed by single-crystal X-ray analyses. Figure 1 shows the representative structures of **2l** and **3g**.

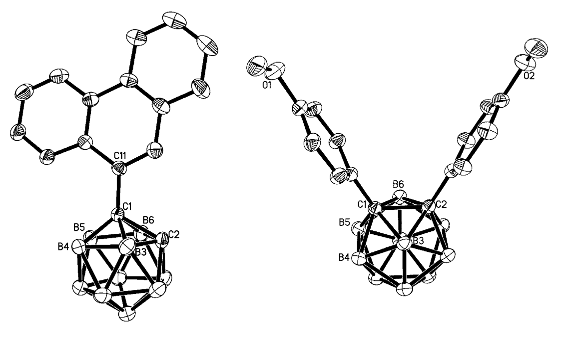


Figure 1. Molecular structures of **2l** (left) and **3g** (right).

To gain some insight into the reaction mechanism, the following control experiments were carried out. No reaction proceeded in the absence of $NiCl_2$, thus suggesting that the nickel catalyst was essential for such cross-coupling reactions. In addition, the yield of **2a** remained unchanged after addition of 1 equivalent of the radical trapping agent 1,1-diphenylethylene[10] to the reaction system, and thus ruled out the radical pathway. Under the similar reaction conditions, **3a** was obtained in 80% yield when using **2a** as the starting material. In contrast, an equimolar reaction of *trans*-(*p*-methoxyphenyl)iodobis(triethylphosphine)nickel(II)[11] with 1-MgCl-1,2-$C_2B_{10}H_{11}$ in 1,2-xylene at 150°C for 12 hours afforded **2g** in 46% yield upon isolation. These experimental data suggested that the aforementioned cross-coupling is a Kumada-type reaction.[12] Accordingly, a reaction mechanism is proposed as follows. The catalysis is initiated by a Ni^0 species which is generated in situ from the reaction of $NiCl_2$ with the Grignard reagent. Oxidative addition of ArI on Ni^0 results in the formation of [ArNiI(solvent)$_2$]. Transmetalation between [ArNiI(solvent)$_2$] and 1-MgCl-1,2-$C_2B_{10}H_{11}$ affords [ArNi(*o*-carboranyl)(solvent)$_2$]. Reductive elimination gives 1-aryl-*o*-carboranes and regenerates the catalyst Ni^0. Repeat of this catalytic cycle using 1-MgCl-2-aryl-1,2-$C_2B_{10}H_{10}$ as a starting material produces 1,2-diaryl-*o*-carboranes.

In summary, a nickel-catalyzed C_{cage}–C_{sp2} bond-forming reaction by the cross-coupling reaction of *o*-carboranyl with aryls has been developed for efficient and high-yield synthesis of 1-aryl-*o*-carboranes and 1,2-diaryl-*o*-carboranes. This method is general for the C-arylation of *o*-carboranes and represents the first transition metal catalyzed cage C,C′-diarylation of *o*-carboranes, as well as offers a facile and direct route for the incorporation of *o*-carborane unit into conjugated π systems.

Experimental Section

Typical procedure for the preparation of 1-aryl-*o*-carboranes (**2**): *i*PrMgCl (2.0 M in THF, 0.6 mL, 1.2 mmol) was slowly added to a THF solution (5 mL) of *o*-carborane (144 mg, 1.0 mmol) at 0°C, and the mixture was stirred at 0°C for 1 h. After replacement of THF with toluene (5 mL), and addition of aryl iodide (1.2 mmol) and $NiCl_2$ (2.6 mg, 0.02 mmol), the reaction mixture was heated at 100°C under stirring for 12 h in a closed flask. Then, the reaction was quenched with water (10 mL) and extracted with diethyl ether (20 mL × 3). The ether solutions were combined and concentrated to dryness in vacuo. The residue was subjected to flash column chromatography on silica gel (230–400 mesh) using *n*-hexane as eluent to give 1-aryl-*o*-carboranes (**2**).

Keywords: arylation · C–C formation · cross-coupling · homogeneous catalysis · nickel

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