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ARYLATION REACTIONS OF MONOCARBA-*CLOSO*-DODECABORATE AT THE BORON VERTICES

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Abstract – We have developed two methods for aryl group introduction at the boron vertices of monocarba-*closo*-dodecaborate under palladium catalysis. Details of reaction development, as well as mechanistic insights, are described.

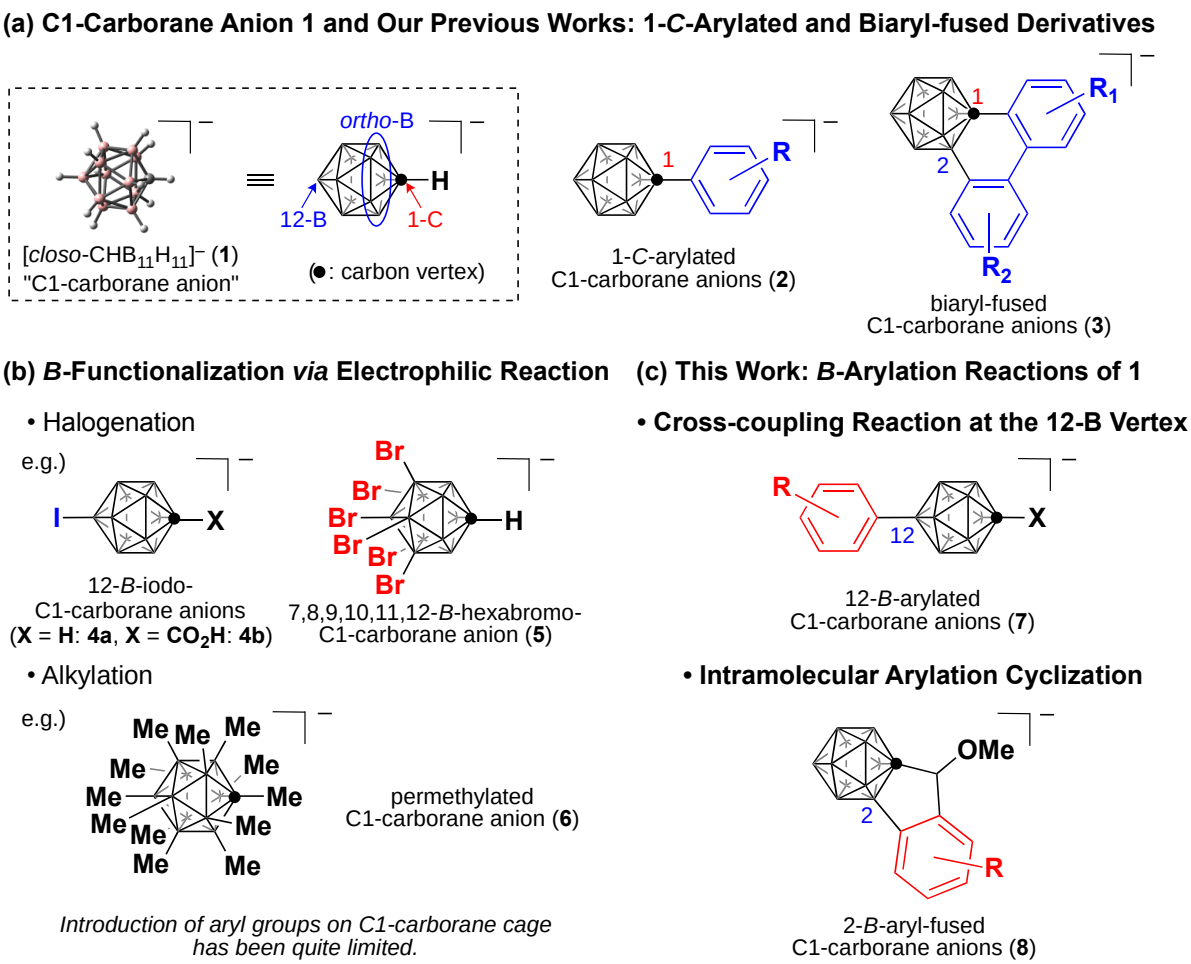
This paper is dedicated to Prof. Kiyoshi Tomioka on the occasion of his 70th birthday.

INTRODUCTION

Monocarba-*closo*-dodecaborate [*closo*-$CHB_{11}H_{11}]^-$ (**1**; denoted here as C1-carborane anion, Scheme 1a) is an anionic stable icosahedral cluster, composed of one carbon and eleven boron atoms.[1] The unique features of this molecule include the excellent anion stability with extremely low nucleophilicity and basicity.[2] Further, the three-dimensional aromaticity (σ-aromaticity),[3] which is the similar molecular properties to ordinary π-aromatic compounds, such as electronic delocalization, reactivity, and stability, makes this molecule fascinating as a core of molecular functions. However, the application of this molecule as functional molecules has been quite limited, which is in contrast to the fact that the structurally-related electronically-neutral (C2-)carborane compound ([*closo*-$C_2B_{10}H_{12}$]) has been broadly utilized based on reliable synthetic methodologies.[4] The contrast situation is mostly because of the dearth of efficient functionalization methods on the cage of C1-carborane anion.

Given the importance of aromatic component in a broad range of functional molecules, development of efficient methods for aryl group introduction should be significant. We previously developed the

cross-coupling reaction of C1-carborane anion at the 1-C vertex.[5] We found that a series of 1-*C*-arylated C1-carborane anions **2** thus obtained showed "σ-π conjugation," which is a conjugation behavior between σ-aromatic cage of **1** and π-arene moiety in **2**.[6] While the boron vertices of the cage of **1** are amenable to electrophilic reactions such as halogenation and alkylation (Scheme 1b),[1] a reliable aryl group on the boron vertices has not been available. Only (unsubstituted) phenyl group introduction was reported with Kumada-Tamao-Corriu-type cross-coupling reactions of 12-iodo derivatives.[7,8] We report herein two types of aryl group introduction on the boron vertices. Negishi-type cross-coupling reaction of 12-iodo derivatives was developed with the expectation that the organozinc-mediated reaction should show a substrate scope. The development of palladium-catalyzed intramolecular arylation cyclization to afford 2-*B*-arylated derivatives **8** is also described (Scheme 1c). Some mechanistic insights including the results DFT calculations are described.

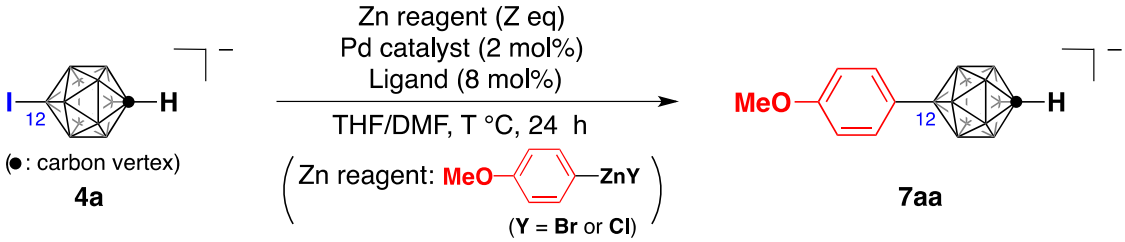


Scheme 1. C1-carborane anion **1** and its functionalization

RESULTS AND DISCUSSION

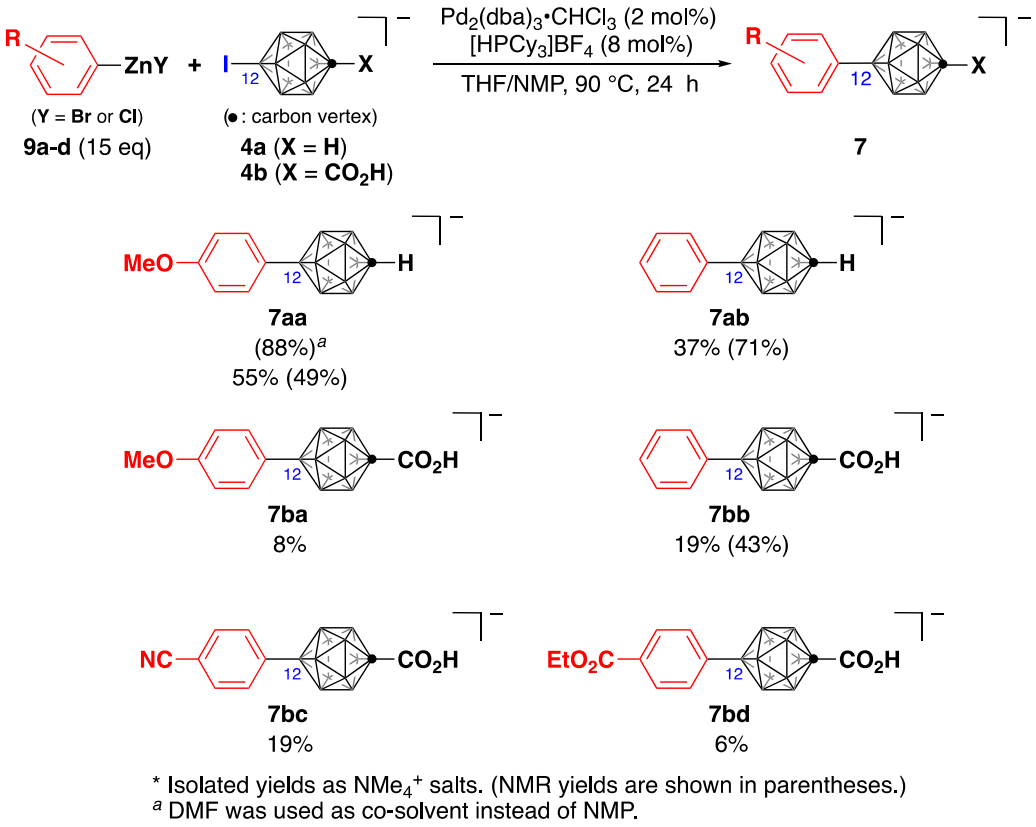
We commenced our studies to develop Negishi-type cross-coupling reaction at the 12-B vertex by screening suitable reaction conditions.[9] Thus, the cross-coupling reaction of 12-iodo C1-carborane anion (**4a**, 1.0 eq) with the excess arylzinc reagent prepared from *p*-$MeOC_6H_4MgBr$ and $ZnCl_2$ was examined as model reaction using palladium catalysts in a mixture of THF and DMF as the solvent (Table 1). While $Pd(OAc)_2$/P(*o*-$MeOC_6H_4)_3$ system was optimal in the cross-coupling reaction at the 1-C vertex, the combination of $Pd_2(dba)_3$•$CHCl_3$ and PPh_3 gave the better chemical yield of **7aa** at 70 °C (Entry 1,2). the use of BINAP or P^{t}Bu$_3$ (from [HP^{t}Bu$_3$]BF_4) showed the poor reactivity (Entry 3,4), PCy_3 (from [$HPCy_3$]BF_4) was found to be a ligand of choice. The desired cross-coupled product **7aa** was obtained in 58% NMR yield. The use of excess amount of arylzinc reagent was crucial, and the reactivity was decreased with the reduced amount of zinc reagent (Entry 6). In addition, the direct use of parent reagent (*i.e.* without the addition of $ZnCl_2$) did not promote this reaction at all under these conditions 7). Finally, the effects of temperature were examined (Entry 8,9). The raised temperature to 90 °C the reaction outcome, and the chemical yield of **7aa** was increased to 88%. In some cases, NMP was used a co-solvent instead of DMF.

Table 1. Conditions optimization of Negishi-type cross-coupling reaction of **4a**



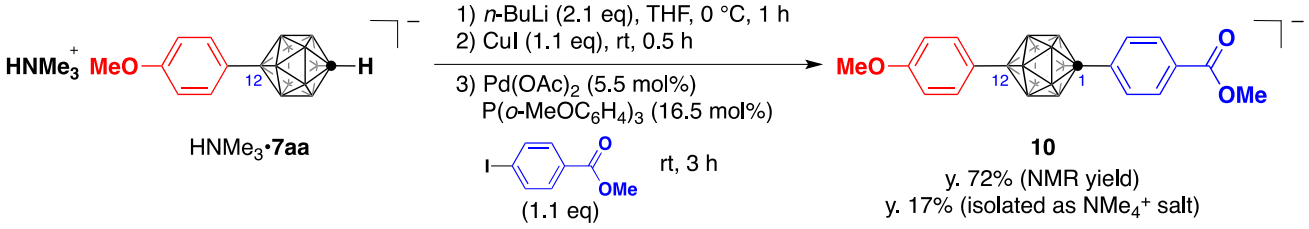
Entry	Pd catalyst	Ligand	Z [eq]	T [°C]	NMR yield [%]
1	$Pd(OAc)_2$	PAr_3	15[a]	70	25
2	$Pd_2(dba)_3$•$CHCl_3$	PPh_3	15[a]	70	31
3	$Pd_2(dba)_3$•$CHCl_3$	BINAP	15[a]	70	0
4	$Pd_2(dba)_3$•$CHCl_3$	[HP^{t}Bu$_3$]BF_4	15[a]	70	trace
5	$Pd_2(dba)_3$•$CHCl_3$	[$HPCy_3$]BF_4	15[a]	70	58
6	$Pd_2(dba)_3$•$CHCl_3$	[$HPCy_3$]BF_4	5[b]	70	43
7	$Pd_2(dba)_3$•$CHCl_3$	[$HPCy_3$]BF_4	(5)[c]	70	0
8	$Pd_2(dba)_3$•$CHCl_3$	[$HPCy_3$]BF_4	15[a]	50	52
9	$Pd_2(dba)_3$•$CHCl_3$	[$HPCy_3$]BF_4	15[a]	90	88

PAr_3 = Tris(*o*-methoxyphenyl)phosphine
[a] *p*-$MeOC_6H_4MgBr$ (15 eq) + $ZnCl_2$ (16.3 eq).
[b] *p*-$MeOC_6H_4MgBr$ (5 eq) + $ZnCl_2$ (5.4 eq). The reaction time was 48 h.
[c] *p*-$MeOC_6H_4MgBr$ (5 eq) in the absence of $ZnCl_2$.



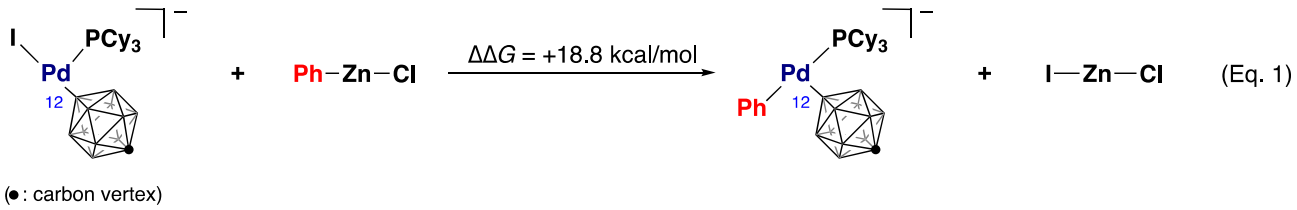
Scheme 2. Cross-coupling reaction of C1-carborane anion at the 12-B vertex

This cross-coupling reaction afforded several 12-*B*-arylated derivatives **7** as presented in Scheme 2. The methoxy derivative **7aa** was isolated as NMe_4^+ salt in 55% yield. The unsubstituted derivative **7ab** was similarly obtained. Further, these reaction conditions were applicable to the 1-carboxylic acid derivative and thus, several 12-*B*-arylated C1-carboranyl acid derivatives (**7ba**-**7bd**) were produced for the first time. The base sensitive cyano and ester functionality, as well as carboxylic acid moiety, are compatible under organozinc cross-coupling reaction conditions. As a preliminary result, the substituent effects on the of these derivatives were observed,[10,11] suggesting the effective electronic interaction among π-arene moiety, σ-aromatic C1-carborane cage, and carboxyl group. In addition, a 1,12-bisarylated C1-carborane anion derivative was also synthesized by utilizing two cross-coupling strategies (Scheme 3).



Scheme 3. Synthesis of 1,12-bisarylated C1-carborane anion derivative **10**

Several mechanistic insights should be considered. Firstly, DFT calculation at the B3LYP/SDD&6-31+G* levels of theory suggested that the oxidative addition of **4a** to $Pd(PMe_3)_2$ (as a model complex of $Pd(PCy_3)_2$) should require the high activation energy ($\Delta G^{\ddagger}$ = +31.8 kcal/mol).[11,12] Experimentally, the reaction of NMe_4•**4a** (0.06 mmol) with $Pd(PCy_3)_2$ (0.05 mmol) in THF at 50 °C for overnight showed very poor conversion on ^{31}P NMR spectrum even in the presence of Ag^+ salt.[13] Second, the large excess amount of organozinc reagent is needed for the reasonable conversion. The modelled transmetalation event (Eq. 1) revealed that this process is rather endothermic ($\Delta\Delta G$ = +18.8 kcal/mol), consistent with the requirement of excess amount of zinc reagent to displace the equilibrium to the product side. These points should be the keys in order to further improve this cross-coupling reaction.

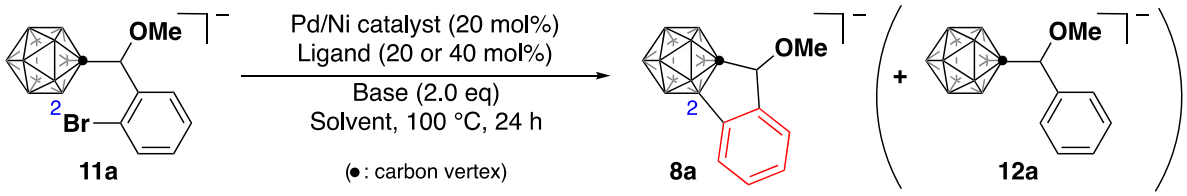


Among the boron vertices on the C1-carborane anion cage, *ortho*-boron vertices are least reactive and the selective functionalization is particularly difficult. The selective functionalization reactions have been developed very recently,[8] all of which require the directed metalation group at the 1-carbon vertex. We have recently reported the one-pot annulation to afford the biaryl-fused C1-carborane anions **3** (Scheme 1a) using cyclic biaryliodonium reagents.[14] The selective disconnection of *ortho* B–H bonds was realized in an intramolecular manner by palladium catalysis. To further apply this strategy, we investigated the intramolecular arylation cyclization to demonstrate *B*-arylation of C1-carborane anion at the *ortho*-boron vertices.

The starting compound **11a** was prepared very easily by the reaction of 1-*C*-lithiated C1-carborane anion with 2-bromobenzaldehyde, followed by the quenching with excess amount of iodomethane (see Experimental section). The conditions screening for the desired intramolecular arylation cyclization was performed as summarized in Table 2. Given the σ-aromaticity of C1-carborane cage, we examined the related conditions to those employed for palladium-catalyzed direct arylation reactions of π-aromatic compounds.[15] Thus, we found that the use of catalytic amount of $Pd(OAc)_2$ and RuPhos in the presence of Ag_2CO_3 as a base in DMF at 100 °C promoted the desired arylation cyclization to afford 2-*B*-arylated product **8a** albeit the low yield (16%, Entry 1). The major by-product was the de-brominated (uncyclized) compound **12a** determined by ESI-MS analysis. The use of nickel acetate as a catalyst precursor instead of $Pd(OAc)_2$ did not promote the C–B bond formation (Entry 2). The ligand effects were tested (Entry 3,4), and we found that Xantphos was suitable among them and **8a** was obtained in 54% yield. Changing

the base to Cs_2CO_3 decreased the reactivity (Entry 5), and among the solvents screened, DMF gave the optimal reaction outcome (Entries 6, 7). The structure of **8a** was determined by means of NMR (^{1}H, ^{1}H{^{11}B}, ^{11}B, ^{11}B{^{1}H}, ^{13}C{^{1}H}, *etc.*) and ESI-MS analyses. Further, the 2-*B*-arylated structure of **8a** through the C–B bond formation was unequivocally established by single-crystal X-ray diffraction analysis (Figure 1).[16] Under the identical reaction conditions, the substituted derivatives **8b** and **8c** were obtained with a similar efficiency.

Table 2. Conditions optimization of intramolecular arylation cyclization of **11a**



Entry	Pd/Ni catalyst	Ligand	Base	Solvent	NMR yield of **8a** [%]
1	$Pd(OAc)_2$	RuPhos (40 mol%)	Ag_2CO_3	DMF	16
2	$Ni(OAc)_2{\cdot}4H_2O$	RuPhos (40 mol%)	Ag_2CO_3	DMF	0
3	$Pd(OAc)_2$	DavePhos (40 mol%)	Ag_2CO_3	DMF	16
4	$Pd(OAc)_2$	Xantphos (20 mol%)	Ag_2CO_3	DMF	54
5	$Pd(OAc)_2$	Xantphos (20 mol%)	Cs_2CO_3	DMF	4
6	$Pd(OAc)_2$	Xantphos (20 mol%)	Ag_2CO_3	THF	28
7	$Pd(OAc)_2$	Xantphos (20 mol%)	Ag_2CO_3	MeCN	14

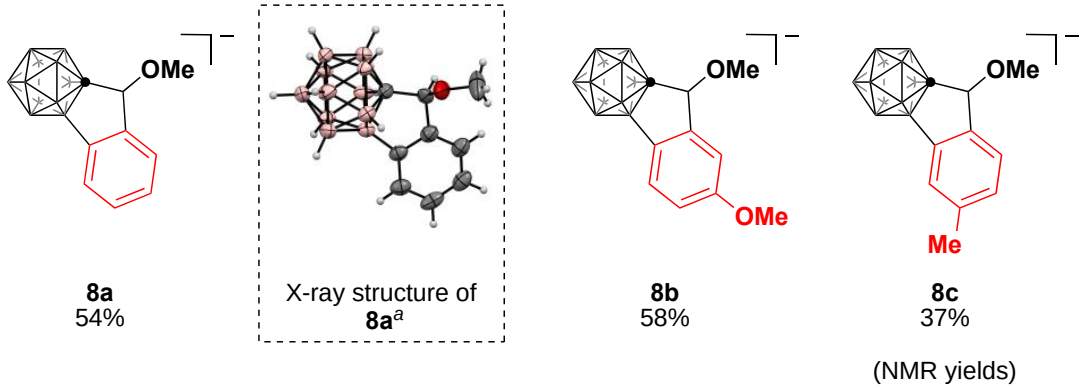


Figure 1. Palladium-catalyzed 2-*B*-arylation cyclization

[a] ORTEP of **8a** with 50% probability ellipsoids. The tetraphenylphosphonium counterion is omitted for clarity. One of two orientationally disordered molecules is described.

To get insight into the reaction mechanism, we carried out the DFT calculation on the arylation cyclization step at the B3LYP/SDD&6-31+G* levels of theory (Figure 2). **INT1** was identified as the

starting complex that should be derived from the oxidative addition of **11a** to a Pd(0) complex, followed by counter anion exchange. Before the metalation event, a minor conformation change from **INT1** to **INT1'** was necessary. The rather strong agostic interaction between the *ortho* B–H bond and the palladium center[8a] was observed in **INT1'**. Thus, the B–H bond disconnection from this complex selectively took place *via* **TS1** with an activation barrier of +24.6 kcal/mol to afford **INT2** having both aryl and carboranyl ligands on palladium. The subsequent reductive elimination smoothly proceeded ($\Delta G^{\ddagger}$ = +9.7 kcal/mol), and **INT3** having the newly formed C–B bond was generated with a large exothermicity.

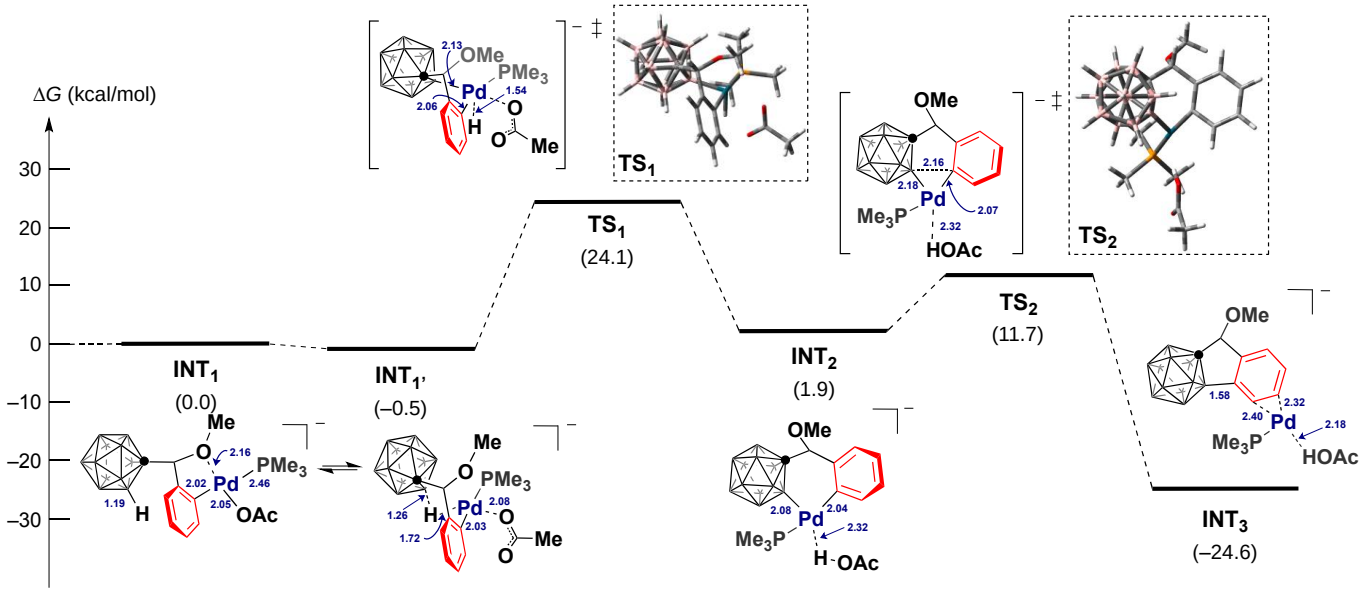


Figure 2. Modeled reaction pathway of the arylation cyclization step

Energy changes and bond lengths at the B3LYP/SDD (for Pd) and 6-31+G* (for the other atoms) levels of theory are shown in kcal/mol and Å, respectively. Insets represent the structures of **TS1** and **TS2**.

In conclusion, we have developed the arylation reactions of monocarba-*closo*-dodecaborate at the boron vertices. Cross-coupling reaction of 12-iodo derivatives with arylzinc reagents afforded a variety of 12-*B*-arylated C1-carborane anions. The mechanistic investigations suggested some keys to be improved in the oxidative addition and transmetalation steps. The intramolecular arylation cyclization was also developed to give 2-*B*-arylated derivatives **8** under palladium catalysis. DFT calculation revealed the agostic interaction between the *ortho* B–H bond and the palladium center was crucial for the selective B–H bond disconnection. Effective "σ-π conjugation" behavior was preliminarily suggested with these *B*-arylated C1-carborane anions by the acidity measurement of carboxylic acid derivatives and DFT calculations. The detailed investigations of unique properties of arylated C1-carborane anions, as well as further development of aryl group introductions, are subjects of ongoing research in our laboratory.

EXPERIMENTAL

General: NMR spectra were obtained on a Bruker AVANCE III HD 500 or a JEOL ECX-500 spectrometers. Chemical shifts are expressed in δ (ppm) values, and coupling constants are expressed in hertz (Hz). The following abbreviations are used: s = singlet, d = doublet, t = triplet, m = multiplet, and bs = broad singlet. Melting points were determined with a Yanaco micro melting point apparatus. IR spectra were obtained on a JASCO FT/IR-4700. ESI mass spectra were measured on a Bruker micrOTOF-II or micrOTOF-QIII spectrometer.

General procedure for the cross-coupling reaction at the 12-boron vertex:

Et_2O solution of $ZnCl_2$ (1.0 M, 24.4 mL, 24.4 mmol) was charged in a Schlenk flask and cooled to 0 ºC. To the solution of 4-methoxyphenylmagnesium bromide (0.5 M in THF, 45 mL, 22.5 mmol) was added and stirred for 15 min. Then $[HNMe_3]^+[closo\text{-}CHB_{11}H_{10}I]^-$ ([$HNMe_3$]•**4a)** (493.5 mg, 1.5 mmol) in 5.0 mL THF, $Pd_2(dba)_3$•$CHCl_3$ (31.2mg, 0.03 mmol), and $[HPCy_3]BF_4$ (44.4 mg, 0.12 mmol) in 7.6 mL NMP were added to the solution. The reaction mixture was heated to 90 ºC. After stirred for 24 h, NH_4Cl aq. was added to the reaction mixture and extracted with AcOEt. The generation of the desired compound was checked by ESI-MS analysis, and the determination of chemical yield was carried out by ^1H NMR analysis using 1,3,5-trimethoxybenzene (33.6 mg 0.20 mmol) as an internal standard. The NMR yield was determined as 49% with this procedure. The solvent was removed in vacuo, and the obtained material was purified by silica gel flash column chromatography (eluent: AcOEt/*n*-hexane, then MeOH). Further purification by reverse-phase column chromatography gave **7aa** (the counter cation(s) were not determined).

The counter cation exchange to NMe_4 was performed as follows: NMe_4Cl solution was added to the water solution of **7aa**, and then extracted by AcOEt. NMe_4•**7aa** was obtained in 55% yield based on the starting material.

Tetramethylammonium 12-(4-methoxyphenyl)carba-*closo*-dodecaborate, [NMe_4][12-(4-MeO-C_6H_4)-$CHB_{11}H_{10}$] (NMe_4•7aa): [1356030-23-3 for **7aa**].

According to the general procedure, the anionic species **7aa** was obtained in 49% NMR yield. NMe_4•**7aa** was isolated in 55% yield. $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.71 (bs, 5H), 1.78 (bs, 5H), 2.18 (bs, 1H), 3.43 (s, 12H), 3.66 (s, 3H), 6.57 (d, J = 8.5 Hz, 2H), 7.28 (d, J = 8.5 Hz, 2H); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6)□δ□–16.63 (bs, 5B, B2,3,4,5,6), –12.47 (bs, 5B, B7,8,9,10,11), 2.74 (bs, 1B, B12) ; MS (ESI (–)) *m/z* calcd for $C_8H_{18}B_{11}O$ $[M–NMe_4]^-$ 249.2454, found 249.2475.

Tetramethylammonium 12-phenylcarba-*closo*-dodecaborate,

[NMe_4][12-C_6H_5-$CHB_{11}H_{10}$] (NMe_4•7ab): [223548-02-5 for **7ab**].

According to the general procedure, the anionic species **7ab** was obtained in 71% NMR yield, 37% isolated yield. NMe_4•**7ab** was isolated as a white solid: $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.72 (bs, 5H), 1.79 (bs, 5H), 2.21 (s, 1H), 3.43 (s, 12H), 6.92 (m, 1H), 6.98 (m, 2H), 7.39 (m, 2H); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6)□δ□–16.55 (bs, 5B, B2,3,4,5,6), –12.45 (bs, 5B, B7,8,9,10,11), 2.70 (bs, 1B, B12); MS (ESI (–)) *m/z* calcd for $C_7H_{16}B_{11}$ $[M–NMe_4]^-$ 219.2348, found 219.2370.

Tetramethylammonium 1-carboxy-12-(4-methoxyphenyl)carba-*closo*-dodecaborate,
[NMe_4][1-CO_2H-12-(4-MeO-C_6H_4)-$CB_{11}H_{10}$] (NMe_4•7ba).

According to the general procedure, the anionic species **7ba** was obtained in 8% isolated yield. NMe_4•**7ba** was isolated as a white solid: mp 209-210 ºC; ATR-FTIR (neat) ν 413, 423, 457, 483, 526, 568, 616, 669, 728, 793, 831, 860, 945, 1038, 1131, 1181, 1218, 1274, 1306, 1365, 1418, 1446, 1481, 1506, 1599, 1633, 1698, 1740, 2005, 2362, 2525, 2571, 2970 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.29 (bs, 5H), 1.84, (bs, 5H), 3.45 (s, 12H), 3.67 (s, 3H), 6.59 (d, J = 8.5 Hz, 2H), 7.26 (d, J = 8.5 Hz, 2H); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6)□δ□–14.41 (bs, 5B, B2,3,4,5,6), –12.68 (bs, 5B, B7,8,9,10,11), 2.52 (bs, 1B, B12) ; MS (ESI (–)) *m/z* calcd for $C_9H_{18}B_{11}O_3$ $[M–NMe_4]^-$ 293.2352, found 293.2377.

Tetramethylammonium 1-carboxy-12-phenylcarba-*closo*-dodecaborate,
[NMe_4][1-CO_2H-12-C_6H_5-$CB_{11}H_{10}$] (NMe_4•7bb).

According to the general procedure, the anionic species **7bb** was obtained in 43% NMR yield, 19% isolated yield. NMe_4•**7bb** was isolated as a yellow solid: mp 186-187 ºC; ATR-FTIR (neat) ν 410, 459, 671, 706, 746, 853, 947, 1039, 1217, 1375, 1482, 1704, 2527, 2922 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.86 (bs, 5H), 2.05 (bs, 5H) 6.93 (m, 1H), 6.98 (m, 2H), 7.37 (m, 2H); ^{13}C NMR (125.77 MHz, acetone-d_6) δ 55.2 (t, J = 3.8 Hz), 124.5 (s), 126.0 (s), 132.8 (s), 168.3 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6)□δ□–14.23 (bs, 5B, B2,3,4,5,6), –12.45 (bs, 5B, B7,8,9,10,11), 3.03 (bs, 1B, B12) ; MS (ESI (–)) *m/z* calcd for $C_8H_{16}B_{11}O_2$ $[M–NMe_4]^-$ 263.2247, found 263.2269.

Tetramethylammonium 1-CO_2H-12-(4-cyanophenyl)carba-*closo*-dodecaborate,
[NMe_4][1-CO_2H-12-(4-CN-C_6H_4)-$CB_{11}H_{10}$] (NMe_4•7bc).

According to the general procedure, the anionic species **7bc** was obtained in 19% isolated yield. NMe_4•**7bc** was isolated as a yellow solid: mp 105-106 ºC; ATR-FTIR (neat) ν 409, 419, 462, 502, 552, 660, 714, 837, 947, 1033, 1238, 1482, 1597, 1715, 2226, 2531 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz,

acetone-d_6) δ 1.84 (bs, 5H), 2.05 (bs, 5H), 3.46 (s, 12H), 7.37 (d, J = 8.0 Hz, 2H), 7.51 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125.77 MHz, acetone-d_6) δ 55.2 (t, J = 3.8 Hz), 108.2 (s), 119.6 (s), 129.5 (s), 133.3 (s), 167.7 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); ^{11}B{^{1}H} NMR (160.46 MHz, acetone-d_6)□δ□–14.08 (bs, 5B), –12.48 (bs, 5B), 2.05 (bs, 1B); MS (ESI (–)) *m/z* calcd for $C_{11}H_{20}B_{11}O_4$ $[M–NMe_4]^-$ 288.2199, found 288.2219.

Tetramethylammonium 1-CO_2H-12-(4-ethoxycarbonylphenyl)carba-*closo*-dodecaborate, [NMe_4][1-CO_2H-12-(4-CO_2Et-C_6H_4)-$CB_{11}H_{10}$] (NMe_4•7bd).

According to the general procedure, the anionic species **7bd** was obtained in 6% isolated yield. NMe_4•**7bd** was isolated as a yellow solid: mp 152-153 ºC; ATR-FTIR (neat) ν 414, 425, 449, 457, 470, 483, 492, 521, 584, 621, 643, 683, 712, 759, 823, 847, 870, 900, 947, 1031, 1076, 1111, 1127, 1178, 1217, 1289, 1313, 1369, 1395, 1445, 1483, 1551, 1599, 1664, 1723, 2359, 2536, 2970, 3361 cm^{-1}; ^{1}H{^{11}B} NMR (500.13 MHz, acetone-d_6) δ 1.32 (t, J = 7.0 Hz, 3H), 1.86 (bs, 5H), 2.09 (bs, 5H), 3.45 (s, 12H), 4.27 (q, J = 7.0 Hz, 2H), 7.48 (d, J = 8.0 Hz, 2H), 7.68 (d, J = 8.0 Hz, 2H); ^{13}C NMR (125.77 MHz, acetone-d_6) δ 13.8 (s), 55.1 (t, J = 3.8 Hz), 59.8 (s), 127.0 (s), 127.0 (s), 132.7 (s), 166.7 (s), 167.8 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); ^{11}B{^{1}H} NMR (160.46 MHz, acetone-d_6)□δ□–14.12 (bs, 5B), –12.42 (bs, 5B), 2.49 (bs, 1B); MS (ESI (–)) *m/z* calcd for $C_{11}H_{20}B_{11}O_4$ $[M–NMe_4]^-$ 335.2458, found 335.2478.

Tetramethylammonium1-(4-methoxycarbonylphenyl)-12-(4-methoxyphenyl)carba-*closo*-dodecaborate, [NMe_4][1-(4-CO_2Me-C_6H_4)-12-(4-MeO-C_6H_4)-$CB_{11}H_{10}$] (NMe_4•10).

1-*C*-Cross-coupling reaction of **7aa** was conducted with the reported procedure in Ref. 5. **10** was obtained in 72% NMR yield, 17% isolated yield. NMe_4•**10** was isolated as a gray solid: mp 228-229 ºC; ATR-FTIR (neat) ν 425, 457, 470, 503, 528, 566, 585, 661, 692, 734, 756, 817, 849, 870, 900, 948, 1022, 1041, 1076, 1114, 1177, 1217, 1231, 1280, 1371, 1407, 1436, 1482, 1505, 1595, 1609, 1704, 1733, 2360, 2523, 2970, 3649 cm^{-1}; ^{1}H{^{11}B} NMR (500.13 MHz, acetone-d_6) δ 1.95 (bs, 5H), 2.11 (bs, 5H), 3.45 (s, 12H), 3.68 (s, 3H), 3.83 (s, 3H), 6.60 (d, J = 8.5 Hz, 2H), 7.31 (d, J = 9.0 Hz, 2H), 7.65 (d, J = 9.0 Hz, 2H), 7.78 (d, J = 8.5 Hz, 2H); ^{13}C NMR (125.77 MHz, acetone-d_6) δ 51.2 (s), 54.2 (s), 55.1 (d, J = 3.8 Hz), 111.8 (s), 128.1 (s), 128.2 (s), 128.7 (s) 133.6 (s), 147.4 (s), 157.8 (s), 166.2 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); ^{11}B{^{1}H} NMR (160.46 MHz, acetone-d_6)□δ□–13.32 (bs, 5B, B2,3,4,5,6), –11.68 (bs, 5B, B7,8,9,10,11), 2.87 (bs, 1B, B12) ; MS (ESI (–)) *m/z* calcd for $C_{16}H_{24}B_{11}O_3$ $[M–NMe_4]^-$ 383.2822, found 383.2844.

Preparation of 11a:

$[Cs]^+[closo\text{-}CHB_{11}H_{11}]^-$ ([Cs]•**1**) (551.2 mg 2.0 mmol) was charged in a Schlenk flask and dried under reduced pressure at 120 ºC for 1 h. The flask was charged with argon, and 16 mL of anhydrous THF was added at room temperature. The solution was cooled to –78 ºC and *n*-BuLi (2.14 M in *n*-hexane, 1.9 mmol) was added. The mixture was stirred at the same temperature for 10 min and then at 0 ºC for 1 h. 2-Bromobenzaldehyde (0.25 mL 2.2 mmol) was added at 0 ºC, and the reaction mixture was warmed to room temperature and stirred for 2 h. To the reaction mixture was added MeI (0.65 mL 10mmol) at that temperature. After stirred at room temperature for 1 h, K_2CO_3 (1.4 g, 10 mmol) was added to the reaction mixture and stirred at that temperature overnight. Then the reaction mixture was poured into distilled water and extracted with AcOEt. The generation of the desired compound was checked by ESI-MS analysis, and the determination of chemical yield was carried out by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (33.6 mg, 0.20 mmol) as an internal standard. The NMR yield was determined as 83% with this procedure. The solvent was removed in vacuo, and the obtained material was purified by silica gel flash column chromatography (eluent: AcOEt/*n*-hexane, then MeOH). Further purification by reverse-phase column chromatography gave **11a** (the counter cation(s) were not determined).

The counter cation exchange to NMe_4 was performed as follows: NMe_4Cl solution was added to the water solution of **11a**, and then collected the precipitate by filtration. The white solid was washed with water, and dried under vacuum (overnight) to afford pure NMe_4•**11a** (284.8 mg, 34% yield based on the starting material).

NMe_4•**11a** was isolated as a white solid: mp 137-138 ˚C; ATR-FTIR (neat) ν 418, 448, 458, 467, 522, 607, 671, 702, 725, 760, 850, 947, 988, 1024, 1040, 1090, 1161, 1205, 1364, 1433, 1480, 1739, 2017, 2361, 2523, 2822, 2971, 3566 cm^{-1}; ^{1}H{^{11}B} NMR (500.13 MHz, acetone-d_6) δ 1.54 (bs, 5H), 1.72 (bs, 1H), 2.04 (bs, 5H), 3.00 (s, 3H), 3.46 (s, 12H), 4.86 (s, 1H), 7.12 (m, 1H), 7.29 (m, 1H) 7.46 (m, 2H); ^{13}C{^{1}H} NMR (125.77 MHz, acetone-d_6) δ 55.2 (t, J = 3.8 Hz), 56.6 (s), 83.9 (s), 124.8 (s), 126.4 (s), 128.8 (s), 130.7 (s), 131.6 (s), 140.8 (s); ^{11}B{^{1}H} NMR (160.46 MHz, acetone-d_6) δ –14.18 (bs, 5B, B2,3,4,5,6), –13.36 (bs, 5B, B7,8,9,10,11), –7.37 (bs, 1B, B12); MS (ESI (–)) *m/z* calcd for $C_9H_{18}B_{11}O$ $[M–NMe_4]^-$ 342.1679, found 342.1702.

Tetramethylammonium 1-[(2-bromo-5-methoxyphenyl)(methoxy)methyl]carba-*closo*-dodecaborate, [NMe_4][1-CH(2-Br-5-MeOC_6H_4)(OMe)-$CB_{11}H_{11}$] (NMe_4•11b)

According to the above mentioned procedure using 2-bromo-5-methoxybenzaldehyde, **11b** was obtained in 80% NMR yield. NMe_4•**11b** was isolated as a white solid: mp 203-204 ˚C; ATR-FTIR (neat) ν 412, 423, 439, 456, 468, 484, 514, 558, 597, 625, 634, 678, 722, 757, 797, 827, 883, 904, 951, 987, 1015, 1040, 1052, 1091, 1125, 1154, 1170, 1200, 1227, 1279, 1349, 1415, 1441, 1479, 1568, 1597, 1741, 2016, 2148, 2359, 2528, 2819, 2932, 3621 cm^{-1}; ^{1}H{^{11}B} NMR (500.13 MHz, acetone-d_6) δ 1.55 (bs, 5H), 1.72 (bs,

1H), 2.04 (bs, 5H), 3.02 (s, 3H), 3.46 (s, 12H), 3.77 (s, 3H), 4.80 (s, 1H), 6.74 (m, 1H), 7.05 (d, J = 3.5 Hz, 1H), 7.04 (m, 1H); $^{13}C\{^{1}H\}$ NMR (125.77 MHz, acetone-d_6) δ 54.9 (s), 55.3 (s), 56.7 (s), 73.2 (s), 83.9 (s), 115.2 (s), 115.3 (s), 115.6 (s), 115.7 (s), 132.2 (s), 141.8 (s), 158.5 (s); $^{11}B\{^{1}H\}$ NMR (160.46 MHz, acetone-d_6) δ –14.17 (bs, 5B, B2,3,4,5,6), –13.36 (bs, 5B, B7,8,9,10,11), –7.33 (bs, 1B, B12); MS (ESI (–)) *m/z* calcd for $C_{10}H_{21}B_{11}BrO_2$ $[M–NMe_4]^-$ 372.1837, found 372.1893.

Tetramethylammonium 1-[(2-bromo-4-methylphenyl)(methoxy)methyl]carba-*closo*-dodecaborate, [NMe_4][1-CH(2-Br-4-MeC_6H_4)(Me)-$CB_{11}H_{11}$] (NMe_4•11c)

According to the general procedure using 2-bromo-4-methylbenzaldehyde, **11c** was obtained in 78% NMR yield. NMe_4•**11c** was isolated as a white solid: mp 202-203 ˚C; ATR-FTIR (neat) ν 430, 443, 581, 671, 701, 725, 820, 842, 865, 948, 990, 1038, 1093, 1160, 1207, 1479, 1604, 2530 cm^{-1}; $^{1}H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.54 (bs, 5H), 1.71 (bs, 1H), 2.04 (bs, 5H), 2.08 (s, 3H), 2.98 (s, 3H), 3.46 (s, 12H), 4.81 (s, 1H), 7.10 (d, J = 8.0 Hz, 1H), 7.27 (s, 1H), 7.32 (d, J = 8.0 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (125.77 MHz, acetone-d_6) δ 19.7 (s), 55.2 (t, J = 3.8 Hz), 56.5 (s), 83.7 (s), 124.6 (s), 127.3 (s), 130.4 (s), 131.8 (s), 137.8 (s), 138.8 (s); $^{11}B\{^{1}H\}$ NMR (160.46 MHz, acetone-d_6) δ –14.17 (bs, 5B, B2,3,4,5,6), –13.38 (bs, 5B, B7,8,9,10,11), –7.41 (bs, 1B, B12); MS (ESI (–)) *m/z* calcd for $C_{10}H_{21}B_{11}BrO$ $[M–NMe_4]^-$ 356.1888, found 356.1908.

General procedure for the intramolecular arylation cyclization:

[NMe_4]•**11a** (233.8 mg 0.56 mmol), $Pd(OAc)_2$ (24.7 mg 0.11 mmol), XantPhos (63.6 mg 0.11 mmol), Ag_2CO_3 (303.6 mg 1.1 mmol) were charged in a Schlenk flask under argon atmosphere. Then, 5.6 mL of anhydrous DMF was added at room temperature. The solution was heated to 100 ºC and the mixture was stirred at that temperature for 24 h. The reaction mixture was poured into distilled water, filtrated by a Celite® pad, and extracted with AcOEt. The generation of the desired compound was checked by ESI-MS analysis, and the determination of chemical yield was carried out by ^{1}H NMR analysis using 1,3,5-trimethoxybenzene (33.6 mg, 0.20 mmol) as an internal standard. The NMR yield was determined as 54% with this procedure. The solvent was removed in vacuo, and the obtained material was purified by silica gel flash column chromatography (eluent: AcOEt/*n*-hexane, then MeOH). Further purification by reverse-phase column chromatography gave **8a** (the counter cation(s) were not determined).

The counter cation exchange to NMe_4 was performed as follows: NMe_4Cl solution was added to the water solution of **8a**, and then collected the precipitate by filtration. The white solid was washed with water, and dried under vacuum (overnight) to afford pure NMe_4•**8a** (41.6 mg, 22% yield based on the starting material).

NMe_4•**8a** was isolated as a white solid: mp 183-184 ˚C; ATR-FTIR (neat) ν 426, 436, 457, 484, 541, 578, 607, 662, 681, 717, 748, 834, 867, 948, 989, 1038, 1088, 1109, 1164, 1178, 1203, 1308, 1362, 1414, 1442, 1479, 1638, 1740, 2359, 2520, 2825, 2920, 2981 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.53 (bs, 1H), 1.58 (bs, 1H), 1.72 (bs, 4H), 1.78 (bs, 1H), 1.82 (bs, 1H), 2.00 (bs, 1H), 2.14 (bs, 1H), 3.46 (s, 12H), 3.53 (s, 3H), 4.47 (s, 1H), 7.00 (m, 2H), 7.06 (m, 1H), 7.30 (m, 1H); $^{13}C\{^1H\}$ NMR (125.77 MHz, acetone-d_6) δ 55.2 (t, J = 3.8 Hz), 58.8 (s), 76.2 (s) 88.4 (s), 124.8 (s), 124.9 (s), 126.5 (s), 127.3 (s), 152.9 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6) δ –15.53 (m, 2B), –14.04 (bs, 2B), –11.95 (m, 3B), –10.94 (bs, 1B), –9.01 (bs, 1B), -3.73 (bs, 2B); MS (ESI (–)) *m/z* calcd for $C_9H_{18}B_{11}O$ $[M–NMe_4]^–$ 261.2454, found 261.2522.

NMe_4•**8b:** According to the general procedure using **11b**, **8b** was obtained in 58% NMR yield. NMe_4•**8b** was isolated as a white solid: mp 190-191 ˚C; ATR-FTIR (neat) ν 415, 426, 457, 469, 483, 523, 552, 580, 655, 683, 719, 851, 946, 986, 1036, 1089, 1111, 1148, 1193, 1237, 1284, 1310, 1350, 1414, 1479, 1566, 1603, 1741, 2359, 2519, 2829, 2936 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.50 (bs, 1H), 1.60 (bs, 1H), 1.70 (m, 3H), 1.77 (bs, 1H), 1.79 (bs, 1H), 1.98 (bs, 1H), 2.13 (bs, 1H), 3.45 (s, 12H), 3.52 (s, 3H), 3.69 (s, 3H), 4.43 (s, 1H), 6.61 (dd, J = 8.0 Hz, J = 2.0 Hz, 1H), 6.67 (d, J = 2.0 Hz, 1H), 7.17 (d, J = 8.0 Hz, 1H); $^{13}C\{^1H\}$ NMR (125.77 MHz, acetone-d_6) δ 54.4 (s) 55.2 (s), 58.8 (s), 76.4 (s), 88.3 (s), 110.8 (s), 112.5 (s), 127.7 (s), 154.4 (s), 158.4 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.): $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6) δ –16.31 (bs, 1B), –15.71 (bs, 1B), –15.12 (bs, 1B), –14.19 (bs, 2B), –12.66 (bs, 1B), –11.92 (bs, 1B), –10.81 (bs, 1B), –9.07 (bs, 1B), –3.68 (bs, 1B); MS (ESI (–)) *m/z* calcd for $C_{10}H_{20}B_{11}O_2$ $[M–NMe_4]^–$ 291.2560, found 291.2578.

NMe_4•**8c:** According to the general procedure using **11c**, **8c** was obtained in 37% NMR yield. NMe_4•**8c** was isolated as a white solid: mp 107-108 ˚C; ATR-FTIR (neat) ν 403, 424, 446, 466, 485, 504, 553, 572, 671, 727, 819, 946, 982, 1037, 1089, 1161, 1191, 1307, 1346, 1416, 1481, 2360, 2527 cm^{-1}; $^1H\{^{11}B\}$ NMR (500.13 MHz, acetone-d_6) δ 1.52 (bs, 1H), 1.57 (bs, 1H), 1.71 (m, 3H), 1.72 (bs 1H), 1.81 (bs, 1H), 1.98 (bs, 1H), 2.13 (bs, 1H), 2.23 (s, 3H), 3.43 (s, 12H), 3.50 (s, 3H), 4.43 (s, 1H), 6.81 (d, J = 7.5 Hz, 1H), 6.93 (d, J = 7.5 Hz, 1H), 7.12 (s, 1H); $^{13}C\{^1H\}$ NMR (125.77 MHz, acetone-d_6) δ 20.5 (s), 55.2 (t, J = 3.8 Hz), 58.7 (s), 76.5 (s), 88.3 (s), 124.5 (s), 125.6 (s), 128.2 (s), 135.5 (s), 150.1 (s) (The carbon directly attached to the boron atom was not detected, likely due to quadrupolar relaxation.); $^{11}B\{^1H\}$ NMR (160.46 MHz, acetone-d_6) δ –16.04 (m, 3B), –14.15 (m, 3B), –12.60 (bs, 1B), –11.99 (bs, 1B), –

10.91 (bs, 1B), –9.08 (bs, 1B), –3.72 (bs, 1B); MS (ESI (–)) *m/z* calcd for $C_{10}H_{20}B_{11}O$ $[M–NMe_4]^-$ 275.2610, found 275.2704.

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11. For details, see Supporting Information.
12. The calculated activation energy of oxidative addition of iodobenzene to $Pd(PMe_3)_2$ complex at the same level of theory was + 17.2 kcal/mol (see Supporting Information).
13. As a preliminary experiment, the use of DMF instead of THF gave a new peak (at 37 ppm) in an almost 1:1 ratio with the peak of $Pd(PCy_3)_2$ complex in ^{31}P NMR spectrum. ^{11}B NMR spectrum also showed the decrease of **4a**. These results implied the faster oxidative addition in DMF and the requirement of such highly polar co-solvent.
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16. Crystallographic data have been deposited with the Cambridge Crystallographic Data Centre: Deposition code CCDC-1823927. This material can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.