

## Novel Approach to Aminocarboranes by Mild Amidation of Selected Iodo-carboranes

Yulia Sevryugina, Richard L. Julius, and M. Frederick Hawthorne\*

International Institute of Nano and Molecular Medicine, School of Medicine, University of Missouri, 1514 Research Park Drive, Columbia, Missouri 65211-3450, United States

Received August 10, 2010

A mild protocol for the palladium-catalyzed Buchwald–Hartwig amidation of icosahedral carboranes is described. Employing 2-dicyclohexylphosphino-2'-(*N,N*-dimethylamino)biphenyl (**1**) as a ligand and  $K_3PO_4$  as a base, benzamide, trifluoroacetamide, acetamide, and formamide were coupled to a series of mono- and di-iodo carboranes furnishing the respective carborane derivatives in good to excellent yields. Subsequent base-mediated saponification of the trifluoroacetamide derivatives was shown to provide the free aminocarboranes. The structures of *N*-(1,7-dicarba-*closo*-dodecaboran-9-yl)-benzamide (**8a**), *N*-(1,7-dicarba-*closo*-dodecaboran-9-yl)trifluoroacetamide (**8b**), *N*-(1,12-dicarba-*closo*-dodecaboran-2-yl)-benzamide (**10a**), *N*-(1,2-dicarba-*closo*-dodecaboran-9-yl)benzamide (**12a**), *N*-(1,2-dicarba-*closo*-dodecaboran-9-yl)acetamide (**12c**), *N*-(1,2-dicarba-*closo*-dodecaboran-9-yl)formamide (**12d**), *N*-(1,2-dicarba-*closo*-dodecaboran-3-yl)benzamide (**13a**), *N,N'*-(1,7-dicarba-*closo*-dodecaboran-9,10-diyl)dibenzamide (**15a**), and *N,N'*-(1,7-dicarba-*closo*-dodecaboran-9,10-diyl)bis(trifluoroacetamide) (**15b**) have been established through X-ray single-crystal diffraction studies.

### Introduction

The icosahedral carboranes, *closo*-1,2- $C_2B_{10}H_{12}$  (*o*-carborane), *closo*-1,7- $C_2B_{10}H_{12}$  (*m*-carborane), and *closo*-1,12- $C_2B_{10}H_{12}$  (*p*-carborane), have been the subject of investigation in areas as diverse as host–guest chemistry,<sup>1</sup> catalysis,<sup>2</sup> ion sensing,<sup>3</sup> and materials science<sup>4</sup> as well as medicinal chemistry

applications.<sup>5</sup> Key to this variety of applications is the unique properties of carboranes, such as resistance to catabolism, kinetic inertness to reagents, rigidity, and strong hydrophobicity. Critical for exploiting these properties is the facile and well-defined derivative chemistry of carborane compounds. Substitution at the C–H vertices is easily accomplished through deprotonation by a strong base (alkyllithium reagents, Grignard reagents, etc.) affording a strong nucleophilic carboranyl anion capable of reaction with a wide range of electrophiles including alkyl halides, carbonyl derivatives, and chlorosilanes, to mention only a few examples.<sup>6</sup> Conversely, the B–H vertices permit derivatization by reactive electrophiles, leading, for example, to B-iodo derivatives. The latter, in combination with Pd-catalyzed cross-coupling reactions, facilitate synthesis of a diverse range of B-derivatives.

The most prominent of Pd-catalyzed aryl/alkenyl-heteroatom coupling reactions is the Buchwald–Hartwig coupling. The first coupling reaction between an aryl halide and amino stannane was reported by Migita et al. in 1983 but stayed unreferenced for a decade.<sup>8</sup> Hartwig and Buchwald further expanded the reaction scope by independently demonstrating the use of milder bases ( $K_3PO_4$ ,  $CS_2CO_3$ , KOH, etc.) to deprotonate the amine after complexation to the palladium center.<sup>9</sup>

\*To whom correspondence should be addressed. E-mail: hawthornem@missouri.edu.

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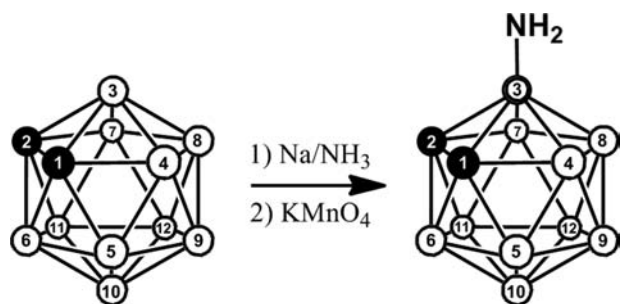
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Scheme 1. Amination of *o*-Carborane in the 3-Position<sup>a</sup>

<sup>a</sup> In all icosahedral cage structures solid sphere represents CH; hollow sphere represents BH; bolded hollow sphere represents B.

While Buchwald–Hartwig coupling has facilitated the synthesis of a great diversity of compounds, introduction of an amino functionality at the boron atom of a carborane cage remains challenging.

Reduction of *o*-carborane with sodium in liquid ammonia leads to the 3-amino-*o*-carborane dianion derivative that may then be oxidized to the neutral species with potassium permanganate,<sup>10</sup> as shown in Scheme 1. In a similar fashion the *N*-piperidyl derivative of *o*-carborane has been obtained.<sup>11</sup> However, this reaction has proven to be difficult because of the potential for fire and/or explosion, particularly during the oxidation step.<sup>12</sup> Additionally, only the 3-amino-*o*-carborane isomer may be synthesized through this method because of isomerization of both *m*- and *p*-carboranes under these reaction conditions.<sup>11</sup>

Amino derivatives of *m*-carboranes may be produced through insertion of diphenylaminodichloroborane into dicarbollide ion [*m*-C<sub>2</sub>B<sub>9</sub>H<sub>11</sub>]<sup>2-</sup><sup>13</sup> or by the reaction of 2-carboxy-*m*-carborane, C<sub>2</sub>B<sub>10</sub>H<sub>11</sub>(2-COOH), with HN<sub>3</sub> in H<sub>2</sub>SO<sub>4</sub>,<sup>14</sup> the latter method also furnishing the *p*-carborane derivative, 2-amino-*p*-carborane.<sup>15</sup> However, given the ease of the high-yield, regioselective synthesis of a large variety of iodo-carborane derivatives and the ubiquity of the Buchwald–Hartwig coupling reaction in organic synthesis, Pd-catalyzed coupling reactions would seem an ideal route to the previously uncommon B–N carborane derivatives.

Numerous examples of B–C bond-forming palladium-catalyzed coupling exist in iodo-carborane chemistry.<sup>16</sup> However, many of these reactions suffer from the need for strong nucleophilic reaction partners as well as long reaction times at elevated temperatures. One significant contributing factor necessitating such forcing conditions, in all probability, is the sluggish reactivity of the B–I bond toward oxidative addition to a palladium center, presumably the first step in any Pd-catalyzed coupling reaction.<sup>17</sup> However, previous studies had shown that judicious choice of ligand, base, and palladium source exert significant influence on the kinetics of coupling reactions.<sup>18</sup> We wish to leverage the recent advances in coupling reaction design to extend the B-coupling of carboranes to include nitrogen nucleophiles with a minimum of both harsh reaction conditions and extended reaction times.

Recently, two reports appeared which describe the catalytic coupling of amines with 2-iodo-*p*-carborane<sup>19</sup> and amides with both 9-iodo-*m*-carborane and 2-iodo-*p*-carborane.<sup>20</sup> In the first instance,<sup>19</sup> a variety of aliphatic and aromatic amines are reacted with 2-iodo-*p*-carborane using a 5% BINAP/Pd(dba)<sub>2</sub> catalytic system (BINAP = 2,2'-bis(diphenylphosphino)-1,1'-binaphthyl, dba = dibenzylideneacetone) and employing <sup>t</sup>BuONa as a base. The resulting aminocarboranes are formed in moderate to good yields with the major side-products being either *p*-carborane or the 2-hydroxy-*p*-carborane compound. While this method furnishes the desired coupling products, it is significantly limited by the use of <sup>t</sup>BuONa as a base. Though <sup>t</sup>BuONa is both economical and easily obtained, use of a strong base precludes the use of many functional groups and significantly restricts the scope of the reaction. Additionally, <sup>t</sup>BuONa is capable of deboronating both *o*- and *m*-carboranes to the corresponding *nido*-species, ruling out its use in the majority of carborane applications.

Further investigations of carborane-based Buchwald–Hartwig coupling describe the coupling of amides to both 9-iodo-*m*-carborane and 2-iodo-*p*-carborane in moderate to good isolated yields.<sup>20</sup> The key step in this reaction is the formation of metalloamide nucleophile through deprotonation with NaH in dioxane. Once again, the use of a strong base (NaH) precludes the use of a wide variety of functional groups in this reaction. The continuing studies we report here describe the development of a facile, inexpensive, and mild protocol for the Pd-catalyzed coupling of a variety of nitrogen-nucleophiles with *ortho*-, *meta*-, and *para*-carboranes.

## Experimental Section

**General Procedures.** All coupling reactions were carried out under argon using Schlenk techniques. Toluene was freshly distilled from CaH<sub>2</sub> prior to use, and tetrahydrofuran (THF) was dried by distillation over sodium metal. All other solvents were used as purchased from commercial sources. Benzamide, 2,2,2-trifluoroacetamide, 2-dicyclohexylphosphino-2-(*N,N*-dimethylamino)biphenyl (DavePhos) (**1**), (2-biphenyl)dicyclohexylphosphine (**2**),

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(2-biphenyl)di-*tert*-butylphosphine (**3**), ethylenebis(diphenylphosphine) (**4**), 2-dicyclohexylphosphino-2,6-dimethoxybiphenyl (**5**), 2-dicyclohexylphosphino-2,4,6-triisopropylbiphenyl (**6**), 2-di-*tert*-butylphosphino-2,4,6-triisopropylbiphenyl (**7**), sodium hydroxide, and tris(dibenzylideneacetone)dipalladium were used as purchased (Sigma-Aldrich, St.-Louis, MO). 9-Iodo-*o*-carborane<sup>21</sup> and 3-iodo-*o*-carborane<sup>22</sup> were prepared according to the procedures described by Jones et al. 2-Iodo-*p*-carborane and 9-iodo-*m*-carborane were prepared analogous to earlier report.<sup>23</sup> All iodo-carboranes as well as formamide were azeotropically dried with benzene to remove any trace of water. Tribasic potassium phosphate was ground to a fine powder and then dried thoroughly by heating under vacuum at 105 °C. All solids (with the exception of sodium hydroxide) were stored in an argon-filled glovebox. Silica gel was used as purchased (63–200  $\mu\text{m}$ , Sorbent Technologies, Inc.). Analytical thin-layer chromatography (TLC) for carborane identification was performed by using precoated silica-gel XHL plates (Sorbent Technologies, Inc.) and visualized by dipping into an acidified (hydrochloric acid) solution of PdCl<sub>2</sub> followed by heating. <sup>11</sup>B, <sup>13</sup>C, and <sup>1</sup>H NMR spectra were obtained using Bruker DRX 500, DRX 300, Bruker Avance 400 and Avance 500 spectrometers. <sup>19</sup>F NMR spectra were acquired on Bruker Avance 400 (376.5 MHz). <sup>11</sup>B and <sup>19</sup>F NMR spectra were externally referenced to BF<sub>3</sub>·Et<sub>2</sub>O ( $\delta = 0$  ppm for <sup>11</sup>B NMR and  $-153.0$  ppm for <sup>19</sup>F NMR). <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were internally referenced to residual solvent signals (CDCl<sub>3</sub>,  $\delta = 7.24$  ppm for <sup>1</sup>H NMR and 77.0 ppm for <sup>13</sup>C NMR). All NMR spectra were recorded from CDCl<sub>3</sub> solutions. All here reported coupling constants *J* are in hertz (Hz). Mass spectra were obtained on an ABI QSTAR and Mariner Biospectrometry Workstation by PerSeptive Biosystems. Melting points were obtained using an automated melting point system OptiMelt (Stanford research system).

**Test Reactions.** In a glovebox, dry test tubes were charged with 50 mg (0.18 mmol) of 9-iodo-*m*-carborane, 3 equiv (118 mg, 0.54 mmol) of K<sub>3</sub>PO<sub>4</sub>, 5 equiv (112 mg, 0.90 mmol) of benzamide, 2.5 mol % (4 mg, 0.005 mmol) of Pd<sub>2</sub>(dba)<sub>3</sub>, and 5 mol % of the respective ligand **1–7**. The tubes were then sealed with a latex cap, approximately 2 mL of dry toluene was added via syringe, and the tubes were then suspended in a 100 °C oil bath. The reaction was monitored via thin layer chromatography (TLC).

**General Procedure for Coupling of Compounds 8, 10, 12, 13, 15.** Into an argon-filled glovebox was brought a dry 25 mL Schlenk flask, where was added 500 mg (1.85 mmol) of the appropriate iodo-carborane, 3 equiv (5.54 mmol) of the appropriate nitrogen nucleophile, 5 equiv (1.96 g, 9.23 mmol) of K<sub>3</sub>PO<sub>4</sub>, 5 mol % (36 mg, 0.09 mmol) of **1**, 2.5 mol % (42 mg, 0.046 mmol) of Pd<sub>2</sub>(dba)<sub>3</sub>, and a Teflon-coated magnetic stir bar. The flask was then capped with a stopper, removed from the glovebox, and approximately 8 mL of dry toluene was added by syringe. The amount of toluene should be minimal, just enough to cover the base so that reaction mixture looks as a thick slurry. The flask was then placed in a 100 °C oil bath for 2 h during which the color changed from purple to orange. After 2 h, the flask was removed from the oil bath and reaction mixture filtered. The filtrate was evaporated to leave orange-to-red oily residue. The residue was then dissolved in dichloromethane and evaporated with about 3 mL of SiO<sub>2</sub> (63–200  $\mu\text{m}$ ) and then twice coevaporated with a small amount of hexane. The solid was added directly to the top of a silica column and eluted beginning with 0:100 dichloromethane/hexane mixture and continuously increasing the concentration of dichloromethane. It is important to move quickly from reaction to column. This is especially needed for the *ortho*-carborane and trifluoroacetamide derivatives reactions. Once the compound was isolated from a column, the volatiles were removed by rotary evaporator to provide

the product in yields given below. Further purification may be accomplished by passing through active carbon column or by recrystallization from hexane or mixtures of diethyl ether/hexane and dichloromethane/hexane. The alternative synthetic routes using THF as a solvent generally lead to lower yields and are provided in the Supporting Information.

***N*-(1,7-Dicarba-closo-dodecaboran-9-yl)benzamide (8a).** According to the general procedure, 449 mg (92%) of compound **8a** were obtained as a white solid: mp 155.7–157.6 °C. <sup>1</sup>H NMR (300 MHz):  $\delta$  7.90 (m, 2H, C<sub>arom</sub>-H), 7.41 (m, 3H, C<sub>arom</sub>-H), 5.97 (s, 1H, NH), 2.90 (s, 2H, C<sub>carborane</sub>-H), 3.8–1.2 (m, 9H, BH). <sup>13</sup>C NMR (75 MHz):  $\delta$  169.5 (C=O), 135.4, 131.3, 128.4, 127.2 (C<sub>arom</sub>), 52.0 (C<sub>carborane</sub>). <sup>11</sup>B NMR (160.4 MHz):  $\delta$  -0.6 (1B, s), -7.1 (2B, d, *J* 162), -11.2 (1B, d, *J* 151), -14.1 (2B, d, *J* 170), -15.6 (2B, d, *J* 168), -18.8 (1B, d, *J* 180), -22.1 (1B, d, *J* 162). HRMS (ESIMS) *m/z* for C<sub>9</sub>H<sub>16</sub>NOB<sub>10</sub> [M-H]<sup>-</sup> calcd 262.2239, found 262.1726.

***N*-(1,7-Dicarba-closo-dodecaboran-9-yl)trifluoroacetamide (8b).** According to the general procedure, 394 mg (89%) of compound **8b** were obtained as a slightly off-white solid. <sup>1</sup>H NMR (400 MHz):  $\delta$  5.77 (s, 1H, NH), 2.80 (s, 2H, C<sub>carborane</sub>-H), 3.4–1.4 (m, 9H, BH). <sup>13</sup>C NMR (125.8 MHz):  $\delta$  159.4 (q, *J*<sub>F</sub> 36.4, C=O), 115.8 (q, *J*<sub>F</sub> 292.5, CF<sub>3</sub>), 52.5 (C<sub>carborane</sub>). <sup>19</sup>F NMR:  $\delta$  -75.7 (CF<sub>3</sub>). <sup>11</sup>B NMR (128.4 MHz):  $\delta$  -1.6 (1B, s), -6.8 (2B, d, *J* 164), -10.4 (1B, d, *J* 152), -13.7 (2B, d, *J* 154), -14.8 (2B, d, *J* 161), -18.2 (1B, d, *J* 182), -20.9 (1B, d, *J* 182). HRMS (APCI) *m/z* for C<sub>4</sub>H<sub>12</sub>NOB<sub>10</sub>F<sub>3</sub> [M]<sup>+</sup> calcd 255.1876, found 255.1667.

***N*-(1,12-Dicarba-closo-dodecaboran-2-yl)benzamide (10a).** According to the general procedure, 407 mg (83%) of compound **10a** were obtained as a white solid: mp 141.6–143.6 °C. <sup>1</sup>H NMR (500 MHz):  $\delta$  7.82 (m, 2H, C<sub>arom</sub>-H), 7.53 (m, 1H, C<sub>arom</sub>-H), 7.45 (m, 2H, C<sub>arom</sub>-H), 6.18 (s, 1H, NH), 3.84 (s, 1H, C<sub>carborane</sub>-H), 2.77 (s, 1H, C<sub>carborane</sub>-H), 3.2–1.4 (m, 9H, BH). <sup>13</sup>C NMR (125.8 MHz):  $\delta$  169.88 (C=O), 134.8, 131.7, 128.5, 127.1 (C<sub>arom</sub>), 65.2, 60.6 (C<sub>carborane</sub>). <sup>11</sup>B NMR (160.4 MHz):  $\delta$  -5.4 (1B, s), -14.2 (2B, d, *J* 172), -15.7 (4B, d, *J* 164), -16.6 (2B, d, *J* 159), -19.8 (1B, d, *J* 178). HRMS (ESIMS) *m/z* for C<sub>9</sub>H<sub>16</sub>NOB<sub>10</sub> [M-H]<sup>-</sup> calcd 262.2239, found 262.1666.

***N*-(1,12-Dicarba-closo-dodecaboran-2-yl)trifluoroacetamide (10b).** According to the general procedure, 363 mg (82%) of compound **10b** were obtained as a slightly off-white solid: mp 79.6–81.9 °C. <sup>1</sup>H NMR (500 MHz):  $\delta$  6.36 (s, 1H, NH), 3.61 (s, 1H, C<sub>carborane</sub>-H), 2.82 (s, 1H, C<sub>carborane</sub>-H), 3.2–1.6 (m, 9H, BH). <sup>13</sup>C NMR (125.8 MHz):  $\delta$  159.8 (q, *J*<sub>F</sub> 37.5, C=O), 116.2 (q, *J*<sub>F</sub> 296.0, CF<sub>3</sub>), 64.9, 61.6 (C<sub>carborane</sub>). <sup>11</sup>B NMR (160.4 MHz):  $\delta$  -6.7 (1B, s), -14.4 (2B, d, *J* 176), -15.5 (4B, d, *J* 152), -16.3 (2B, d, *J* 144), -19.0 (1B, d, *J* 167). HRMS (APCI) *m/z* for C<sub>4</sub>H<sub>11</sub>NOB<sub>10</sub>F<sub>3</sub> [M-H]<sup>-</sup> calcd 254.1798, found 254.1197.

***N*-(1,2-Dicarba-closo-dodecaboran-9-yl)benzamide (12a).** According to the general procedure, 440 mg (90%) of compound **12a** were obtained as a slightly off-white solid: mp 181.9–182.5 °C. <sup>1</sup>H NMR (400 MHz):  $\delta$  7.76 (m, 1H, C<sub>arom</sub>-H), 7.74 (m, 1H, C<sub>arom</sub>-H), 7.41 (m, 3H, C<sub>arom</sub>-H), 5.73 (s, 1H, NH), 3.54 (s, 1H, C<sub>carborane</sub>-H), 3.49 (s, 1H, C<sub>carborane</sub>-H), 3.4–1.4 (m, 9H, BH). <sup>13</sup>C NMR (125.8 MHz):  $\delta$  168.9 (C=O), 135.6, 131.2, 128.4, 127.1 (C<sub>arom</sub>), 51.2, 45.6 (C<sub>carborane</sub>). <sup>11</sup>B NMR (160.4 MHz):  $\delta$  5.9 (1B, s), -3.5 (1B, d, *J* 148), -9.7 (2B, d, *J* 149), -14.5 (2B, d, *J* 175), -16.1 (2B, d, *J* 159), -16.7 (2B, d, *J* 130). HRMS (APCI) *m/z* for C<sub>9</sub>H<sub>16</sub>NOB<sub>10</sub> [M-H]<sup>-</sup> calcd 262.2239, found 262.1984.

***N*-(1,2-Dicarba-closo-dodecaboran-9-yl)trifluoroacetamide (12b).** According to the general procedure, 423 mg (90%) of compound **12b** were obtained as a pale yellow solid, which was further recrystallized from hexane to yield 197 mg of off-white crystals (yield 42%): mp 96.1–96.6 °C. <sup>1</sup>H NMR (400 MHz):  $\delta$  5.63 (s, 1H, NH), 3.57 (s, 1H, C<sub>carborane</sub>-H), 3.55 (s, 1H, C<sub>carborane</sub>-H), 3.2–1.4 (m, 9H, BH). <sup>13</sup>C NMR (125.8 MHz):  $\delta$  158.7 (q, *J*<sub>F</sub> 36.3, C=O), 115.8 (q, *J*<sub>F</sub> 300.0, CF<sub>3</sub>), 51.9, 47.2 (C<sub>carborane</sub>). <sup>19</sup>F NMR:  $\delta$  -76.2 (CF<sub>3</sub>). <sup>11</sup>B NMR (128.4 MHz):  $\delta$  4.4 (1B, s), -3.4 (1B, d, *J* 150), -9.8 (2B, d, *J* 152), -14.7 (2B, d, *J* 150), -15.7 (2B, d, *J* 140), -16.6 (2B, d,

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*J* 181). HRMS (APCI)  $m/z$  for  $C_4H_{12}NOB_{10}F_3$   $[M+H]^+$  calcd 255.1876, found 255.1176.

***N*-(1,2-Dicarba-closo-dodecaboran-9-yl)acetamide (12c).** To a mixture of 9-iodo-*o*-carborane (1.90 g, 7.04 mmol), acetamide (1.25 g, 21.2 mmol),  $Pd_2(dba)_3$  (0.161 g, 0.176 mmol), **1** (0.138 g, 0.352 mmol) and  $K_3PO_4$  (7.47 g, 35.2 mmol) was added freshly distilled THF (20 mL), and the reaction mixture was stirred at room temperature for 48 h. After this time starting material was still present in the reaction mixture, so it was heated to 40 °C for another 24 h. The reaction mixture was filtered and coevaporated with 30 mL of  $SiO_2$  (63–200  $\mu m$ ), which was put on the top of the chromatography column (120 mL, 63–200  $\mu m$ ). It was chromatographed using ethyl acetate gradient in hexanes (0 to 55%) to give after evaporation 0.780 g (55%) of white crystalline solid: mp 155.8–157.0 °C.  $^1H$  NMR (500 MHz):  $\delta$  5.21 (br s, 1H, NH), 3.55 (s, 1H,  $C_{carborane}-H$ ), 3.51 (s, 1H,  $C_{carborane}-H$ ), 2.8–1.6 (m, 9H, BH), 1.97 (s, 3H,  $CH_3$ ).  $^{13}C$  NMR (125.8 MHz):  $\delta$  172.8 (C=O), 51.4, 45.8 ( $C_{carborane}$ ), 25.1 ( $CH_3$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  5.5 (1B, s), –3.5 (1B, d, *J* 147), –9.7 (2B, d, *J* 151), –14.5 (2B, d, *J* 163), –15.9 (2B, d, *J* 131), –16.6 (2B, d, *J* 179). HRMS (APCI)  $m/z$  for  $C_4H_{17}NOB_{10}$   $[M+2H]^+$  calcd 203.2315, found 203.1816;  $m/z$  for  $C_4H_{14}NOB_{10}$   $[M-H]^-$  calcd 200.2080, found 200.2106.

***N*-(1,2-Dicarba-closo-dodecaboran-9-yl)formamide (12d).** A 250 mL Schlenk flask was charged with 9-iodo-*o*-carborane (7.5 g, 27.6 mmol),  $Pd_2(dba)_3$  (0.632 g, 0.69 mmol), **1** (0.543 g, 1.38 mmol),  $K_3PO_4$  (29.3 g, 138 mmol), formamide (3.73 g, 82.8 mmol), and 35 mL of THF. The reaction mixture was heated at 60 °C for 3 h under argon atmosphere. After cooling to room temperature, the solvent was dried under vacuum, redissolved in dichloromethane, and run onto a small silica plug, washed, and dried under vacuum. The product was isolated by silica gel column chromatography as a white solid: 2.61 g (50%).  $^1H$  NMR (500 MHz):  $\delta$  7.96 (d, 1H, CH), 5.55 (s, 1H, NH), 3.52 (s, 1H,  $C_{carborane}-H$ ), 3.43 (s, 1H,  $C_{carborane}-H$ ), 3.0–0.7 (m, 9H, BH).  $^{13}C$  NMR (125.8 MHz):  $\delta$  166.1 (C=O), 51.3, 44.9 ( $C_{carborane}$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  5.9 (1B, s), –4.1 (1B, d, *J* 149), –10.4 (2B, d, *J* 151), –15.6 (2B, d, *J* 162), –16.0 (2B, d, *J* 162), –17.1 (2B, d, *J* 184). HRMS (TOF MS)  $m/z$  for  $C_3H_{12}NOB_{10}$   $[M-H]^-$  calcd 186.1923, found 186.1937.

***N*-(1,2-Dicarba-closo-dodecaboran-3-yl)benzamide (13a).** According to the general procedure, 440 mg (90%) of compound **13a** were obtained as a slightly off-white solid.  $^1H$  NMR (500 MHz):  $\delta$  7.82 (m, 2H,  $C_{arom}-H$ ), 7.59 (m, 1H,  $C_{arom}-H$ ), 7.51 (m, 2H,  $C_{arom}-H$ ), 6.39 (s, 1H, NH), 4.62 (s, 2H,  $C_{carborane}-H$ ), 3.1–1.5 (m, 9H, BH).  $^{13}C$  NMR (125.8 MHz):  $\delta$  171.3 (C=O), 133.6, 132.5, 128.8, 127.1 ( $C_{arom}$ ), 54.8 ( $C_{carborane}$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  –4.5 (2B, d, *J* 149), –6.7 (1B, s), –11.0 (1B, d, *J* 151), –12.7 (2B, d, *J* 167), –14.4 (2B, d, *J* 132), –15.1 (2B, d, *J* 146). HRMS (ESIMS)  $m/z$  for  $C_9H_{17}NOB_{10}$   $[M]$  calcd 263.2317, found 263.1584.

***N*-(1,2-Dicarba-closo-dodecaboran-3-yl)trifluoroacetamide (13b).** According to the general procedure, 240 mg (51%) of compound **13b** were obtained as an off-white crystalline solid: mp 80.3–81.3 °C.  $^1H$  NMR (500 MHz):  $\delta$  6.46 (s, 1H, NH), 4.41 (s, 2H,  $C_{carborane}-H$ ), 3.1–1.6 (m, 9H, BH).  $^{13}C$  NMR (125.8 MHz):  $\delta$  160.5 (q,  $J_F$  37.5, C=O), 115.2 (q,  $J_F$  286.3,  $CF_3$ ), 54.7 ( $C_{carborane}$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  –3.8 (2B, d, *J* 151), –8.2 (1B, s), –10.7 (1B, d, *J* 151), –13.1 (3B, d, *J* 175), –14.6 (3B, d, *J* 181). HRMS (APCI)  $m/z$  for  $C_4H_{12}NOB_{10}F_3$   $[M+H]^+$  calcd 255.1876, found 255.1189.

***N,N'*-(1,7-dicarba-closo-dodecaboran-9,10-diyl)dibenzamide (15a).** Into an argon-filled glovebox was brought a dry 25 mL round-bottom flask into which was added 1.00 g (2.52 mmol) of 9,10-diiodo-*m*-carborane. To this was added 4 equiv (1.22 g, 10.08 mmol) of benzamide, 5 equiv (2.67 g, 12.6 mmol) of  $K_3PO_4$ , 5 mol % (50 mg, 0.13 mmol) of **1**, 2.5 mol % (58 mg, 0.06 mmol) of  $Pd_2(dba)_3$ , and a Teflon-coated magnetic stir bar. The flask was then capped with a latex stopper, removed from

the glovebox, and approximately 8 mL of dry toluene was added by syringe. The flask was then placed in a 100 °C oil bath for 12 h during which the color changed from purple to orange. After 12 h, the flask was removed from the oil bath and approximately 2 g of silica gel was added to the reaction mixture. The volatiles were then removed, and the remaining solid was added directly to the top of a silica column. The product was then eluted beginning with a 0:100 diethyl ether/hexane mixture and finishing in a 100:0 diethyl ether/hexane mixture while increasing diethyl ether concentration 10% at a time stepwise. The volatiles were then removed under reduced pressure by rotary evaporator to provide 848 mg (88%) of product **15a** as a white solid: mp 225.6–228.1 °C.  $^1H$  NMR (500 MHz):  $\delta$  7.91 (4H, m,  $C_{arom}-H$ ), 7.46 (6H, m,  $C_{arom}-H$ ), 7.05 (2H, s, NH), 2.88 (2H, s,  $C_{carborane}-H$ ), 3.5–1.5 (8H, m, BH).  $^{13}C$  NMR (100.6 MHz):  $\delta$  171.3 (C=O), 135.0, 131.4, 128.4, 127.3 ( $C_{arom}$ ), 48.2 ( $C_{carborane}$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  –1.8 (2B, s), –7.6 (2B, d, *J* 140), –15.8 (4B, d, *J* 140), –23.7 (2B, d, *J* 152). HRMS (APCI)  $m/z$  for  $C_{16}H_{21}N_2O_2B_{10}$   $[M-H]^-$  calcd 381.2614, found 381.1670.

***N,N'*-(1,7-dicarba-closo-dodecaboran-9,10-diyl)bis(trifluoroacetamide) (15b).** Following the synthetic procedure for **15a** but using 1.14 g (10.08 mmol) of trifluoroacetamide, 775 mg (84%) of compound **15b** were obtained as an off-white solid: mp 165.1–167.2 °C.  $^1H$  NMR (500 MHz):  $\delta$  6.63 (2H, s, NH), 2.98 (2H, s,  $C_{carborane}-H$ ), 3.5–1.7 (8H, m, BH).  $^{13}C$  NMR (100.6 MHz):  $\delta$  160.3 (C=O), 117.3, 114.4 ( $CF_3$ ), 49.2 ( $C_{carborane}$ ).  $^{19}F$  NMR:  $\delta$  –76.1 ( $CF_3$ ).  $^{11}B$  NMR (160.4 MHz):  $\delta$  –3.0 (2B, s), –7.8 (2B, d, *J* 164), –15.4 (4B, d, *J* 152), –22.7 (2B, d, *J* 197). HRMS (APCI)  $m/z$  for  $C_6H_{11}N_2O_2B_{10}F_6$   $[M-H]^-$  calcd 365.1731, found 365.0845.

**General Procedure for the Hydrolysis of Compounds 8b, 10b, and 13b (Compounds 9b, 11b, 14b).** In a round-bottom flask equipped with a magnetic stir bar was added 300 mg (1.18 mmol) of the appropriate trifluoroacetamide derivative (**8b**, **10b**, or **13b**) along with 1.5 g of NaOH, 10 mL of distilled water, 3 mL of THF, 3 mL of MeOH, and 3 mL of  $^iPrOH$ . The mixture was then allowed to stir at room temperature. Reaction was completed after 3 days for **9b**, 7 days for **11b**, and 6 days for **14b**. It is recommended to monitor the reaction progress by TLC. For **11b** an additional 1 g of NaOH dissolved in 5 mL of water was introduced after 3 days from the reaction start, and the stirring was resumed. Upon completion, to the reaction mixture was added approximately 15 mL of distilled water. The solution was then extracted with dichloromethane (3  $\times$  15 mL), the organic fractions were combined, dried over  $Na_2SO_4$ , and all volatiles were removed by rotary evaporator. For **11b** even after 7 days of stirring at room temperature some of starting material was still present in the reaction mixture. Therefore, the product was further purified by silica-gel column chromatography. Compounds **9b**, **11b**, **14b** were obtained as white powders.

**9-Amino-1,7-dicarba-closo-dodecaborane (9b).** According to the general procedure, 166 mg (89%) of compound **9b** were obtained as a white solid: mp 165.0–166.7 °C.  $^1H$  NMR (400 MHz):  $\delta$  2.71 (s, 2H,  $C_{carborane}-H$ ), 0.71 (s, 2H,  $NH_2$ ), 3.2–1.1 (m, 9H, BH).  $^{13}C$  NMR (100.6 MHz):  $\delta$  50.8 ( $C_{carborane}$ ).  $^{11}B$  NMR (128.4 MHz):  $\delta$  5.1 (1B, s), –7.5 (2B, d, *J* 161), –10.7 (1B, d, *J* 149), –14.2 (2B, d, *J* 163), –16.0 (2B, d, *J* 166), –19.5 (1B, d, *J* 180), –25.5 (1B, d, *J* 181). HRMS (APCI)  $m/z$  for  $C_2H_{14}NB_{10}$   $[M+H]^+$  calcd 160.2130, found 160.2390.

**2-Amino-1,12-dicarba-closo-dodecaborane (11b).** Product **11b** was purified by column chromatography eluted beginning with dichloromethane and then slowly increasing concentration of 5%  $Et_2NH/MeOH$  solution in dichloromethane to 7%. First was eluted the starting material **10b** still present in the reaction mixture (42 mg, 14% of the initial load). Product **11b** was isolated as a white powder (142 mg, 76% yield). The product (**11b**) has a strong and distinct odor as well as high volatility, which results in the here reported yield being lower than the actual one. The compound sublimates before melting at atmospheric pressure:  $T_{subl}$  is 163.4–166.4 °C.  $^1H$  NMR

(400 MHz):  $\delta$  2.95 (s, 1H,  $C_{\text{carborane}}-H$ ), 2.77 (s, 1H,  $C_{\text{carborane}}-H$ ), 1.07 (s, 2H,  $NH_2$ ), 3.3–0.9 (m, 9H,  $BH$ ).  $^{13}C$  NMR (100.6 MHz):  $\delta$  68.5, 62.7 ( $C_{\text{carborane}}$ ).  $^{11}B$  NMR (128.4 MHz):  $\delta$  -0.8 (1B, s), -14.7 (2B, d,  $J$  158), -15.9 (4B, d,  $J$  164), -17.9 (2B, d,  $J$  167), -23.2 (1B, d,  $J$  166). HRMS (APCI)  $m/z$  for  $C_2H_{14}NB_{10} [M+H]^+$  calcd 160.2130, found 160.2323.

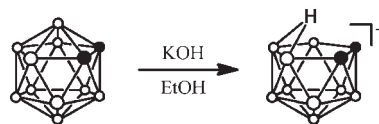
**3-Amino-1,2-dicarba-closo-dodecaborane (14b).** According to the general procedure, 185 mg (99%) of compound **14b** was obtained as a white solid.  $^1H$  NMR (400 MHz):  $\delta$  3.52 (2H, s,  $C_{\text{carborane}}-H$ ), 1.38 (2H, s,  $NH_2$ ), 3.2–0.7 (9H,  $BH$ ).  $^{13}C$  NMR (100.6 MHz):  $\delta$  58.0 ( $C_{\text{carborane}}$ ).  $^{11}B$  NMR (128.4 MHz):  $\delta$  0.3 (1B, s), -4.4 (2B, d,  $J$  148), -9.7 (1B, d,  $J$  149), -14.1 (1B, d,  $J$  182), -14.8 (2B, d,  $J$  155), -15.4 (2B, d,  $J$  163), -18.6 (1B, d,  $J$  152). HRMS (APCI)  $m/z$  for  $C_2H_{14}NB_{10} [M+H]^+$  calcd 160.2130, found 160.2039; for  $C_2H_{12}NB_{10} [M-H]^-$  calcd 158.1974, found 158.1949.

**X-ray Diffraction Studies.** The X-ray quality crystals were obtained upon slow evaporation of diethyl ether/hexane mixtures, except for crystals of **15b<sub>O</sub>**, which were grown from dichloromethane/hexane. Data collection for the studied crystals was carried out at -100 °C on a Bruker SMART 1000 CCD area detector system using the  $\omega$  scan technique with Mo  $K\alpha$  radiation ( $\lambda = 0.71073$  Å) from a graphite monochromator. Data reduction and integration were performed with the software package SAINT.<sup>24</sup> Data were corrected for absorption using SADABS.<sup>25</sup> The crystal structures were solved with the direct methods program SHELXS-97 and were refined by full matrix least-squares techniques with the SHELXTL<sup>26</sup> suite of programs. All non-hydrogen atoms were refined with anisotropic thermal parameters, except for the three disordered  $CF_3$ -groups in crystal structures of **8b**, four in **15b<sub>M</sub>** and one in **15b<sub>O</sub>**, for which disorder was modeled over three rotational orientations. The hydrogen atoms were located in difference Fourier maps and refined individually. For **8a** and **12c**, some hydrogens were included at geometrically idealized positions and refinement was mixed. Crystallographic data and details of data collection and structure refinements of **8a,b**, **10a**, **12a,c,d**, **13a**, **15a,b** are provided in Supporting Information, Table S2.

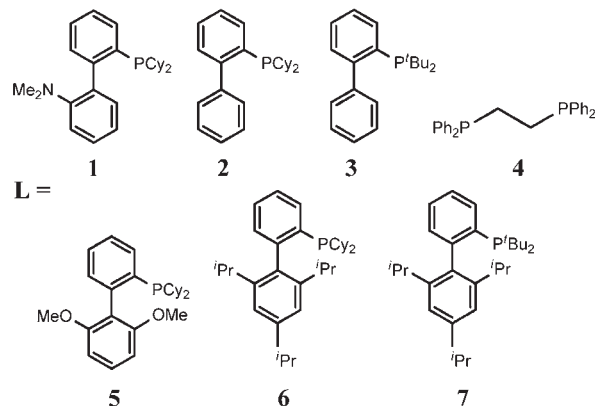
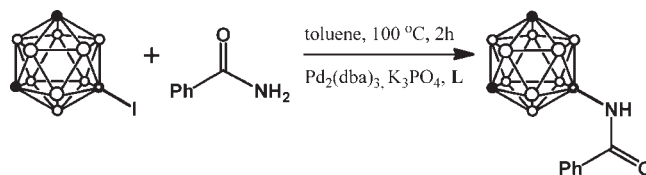
## Results and Discussion

**Test Reactions.** Key to successful Buchwald–Hartwig coupling reactions is careful selection of both ligand and base.<sup>27</sup> Carboranes exhibit a nonuniform electron density pointing toward the boron atoms furthest away from the carbons,<sup>28</sup> which is most pronounced in *ortho*-carborane. In the latter, the most electron poor boron atoms nearest

**Scheme 2.** Deboronation of *o*-Carborane to 7,8-Dicarba-*nido*-undecaborate



**Scheme 3.** Phosphine Ligands Screening Test Reactions



Cy = cyclohexyl; <sup>t</sup>Bu = *tert*-butyl; <sup>i</sup>Pr = *iso*-propyl

to the carbon vertices are susceptible to attack by nucleophilic bases leading to loss of a BH vertex from the cage and formation of the *nido*- $C_2B_9H_{12}^-$  structure (Scheme 2).<sup>29</sup>

Tribasic potassium phosphate, commonly employed in Buchwald–Hartwig coupling, was selected to circumvent this undesired side reaction. Many Buchwald-type biaryl phosphine ligands are commercially available and possess excellent substrate tolerance and versatility. A selection of ligands **1**–**7** was chosen to be screened in test reactions involving the coupling of benzamide to 9-iodo-*m*-carborane (Scheme 3). As 9-iodo-*m*-carborane was shown to be less reactive in cross-coupling reactions than 2-iodo-*p*-carborane<sup>30</sup> and its deboronation to occur under more drastic conditions comparing to *o*-carborane, it was chosen as a test-substrate. Reactions were carried out at the 50 mg scale (0.18 mmol of iodo-carborane) and monitored by TLC.

After 2 h, the reaction using catalyst ligand **1** showed complete consumption of starting 9-iodo-*m*-carborane and presence of substituted 9-amido-*m*-carborane, while other reaction mixtures exhibited substantial amounts of unreacted starting material, particularly the *tert*-butyl substituted phosphines.

**Coupling Reactions of 9-Iodo-*m*-carborane.** In an effort to fully characterize and quantify reaction products, the reaction shown in Scheme 3 with phosphine ligand **1** was attempted on a larger scale. After 2 h, TLC analysis

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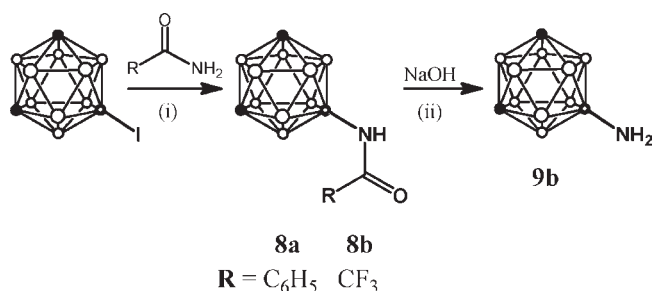
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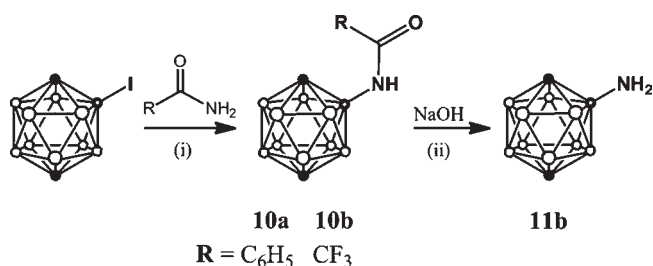
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**Scheme 4.** Synthetic Route to 9-Amino-*m*-carborane (**9b**)<sup>a</sup>

<sup>a</sup> (i) Toluene, 100 °C, 2 h, 2.5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>, 5 equiv of K<sub>3</sub>PO<sub>4</sub>, 5 mol % **1**; (ii) rt, 3 d, H<sub>2</sub>O, THF, MeOH, <sup>t</sup>PrOH.

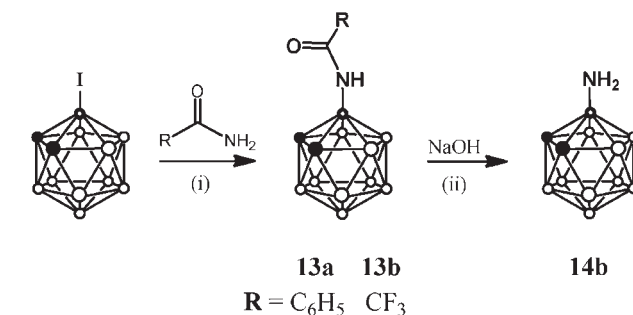
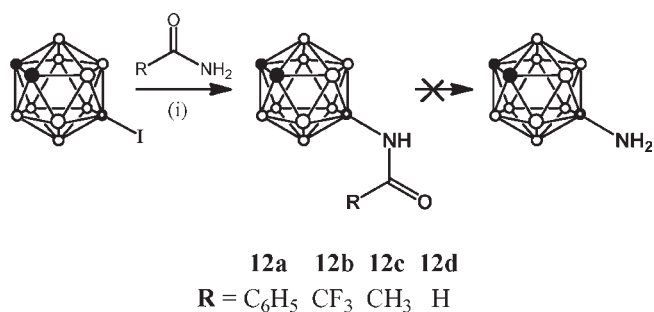
**Scheme 5.** Synthetic Route to 2-Amino-*p*-carborane (**11b**)<sup>a</sup>

<sup>a</sup> (i) Toluene, 100 °C, 2 h, 2.5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>, 5 equiv of K<sub>3</sub>PO<sub>4</sub>, 5 mol % **1**; (ii) rt, 7 d, H<sub>2</sub>O, THF, MeOH, <sup>t</sup>PrOH.

indicated the consumption of the starting 9-iodo-*m*-carborane. Following silica-gel chromatography, the product, *N*-(1,7-dicarba-*closo*-dodecaboran-9-yl)benzamide (**8a**) was isolated in 92% yield. The facile conjugation of benzamide to the cage accomplished above prompted further exploration into the coupling of other amides that would provide the free aminocarboranes after deprotection. While benzamide itself presents a possible route to aminocarborane products through acid-catalyzed hydrolysis, this technique generally involves prolonged heating, which may lead to degradation of the cage to the *nido*-structure through nucleophilic attack by the now deprotected amine. As a result, it was decided to attempt the coupling of trifluoroacetamide to the respective iodo-carborane. The resulting *N*-carboranyltrifluoroacetamide derivative could then be easily hydrolyzed under basic conditions at room temperature.<sup>31</sup> Using a protocol similar to that which furnished the *N*-benzamide derivative, *N*-(1,7-dicarba-*closo*-dodecaboran-9-yl)trifluoroacetamide (**8b**) was produced in 89% yield. A subsequent base-mediated saponification of **8b** leads to the corresponding 9-amino-*m*-carborane (**9b**) in 89% yield (Scheme 4).

**Coupling reactions of 2-iodo-*p*-carborane.** Using these optimized reaction conditions, we have carried out the amidation of 2-iodo-*p*-carborane to produce *N*-(1,12-dicarba-*closo*-dodecaboran-2-yl)benzamide (**10a**) and *N*-(1,12-dicarba-*closo*-dodecaboran-2-yl)trifluoroacetamide (**10b**) in 83% and 82% yields, respectively. A subsequent base-mediated saponification of **10b** leads to the 2-amino-*p*-carborane (**11b**) in 76% yield (Scheme 5).

**Coupling Reactions of *o*-Carboranes.** The above reaction conditions were explored for the synthesis of *o*-carboranylbenzamides. As mentioned above,<sup>29</sup> the reaction of

**Scheme 6.** Synthetic Route to Amino-*o*-carboranes<sup>a</sup>

<sup>a</sup> (i) Toluene, 100 °C, 2 h, 2.5 mol % Pd<sub>2</sub>(dba)<sub>3</sub>, 5 equiv of K<sub>3</sub>PO<sub>4</sub>, 5 mol % **1**; (ii) rt, 6 d, H<sub>2</sub>O, THF, MeOH, <sup>t</sup>PrOH.

*ortho*-carborane and Lewis base, such as alkoxides, amines, and fluoride commonly results in deboronation of the icosahedral [C<sub>2</sub>B<sub>10</sub>]-cage affording a *nido*-anion [7,8-C<sub>2</sub>B<sub>9</sub>-H<sub>12</sub>]<sup>-</sup>. However, the mild reaction conditions reported here successfully produced *closo-ortho*-carborane derivatives bearing benzamido (**12a** and **13a**), trifluoroacetamido (**12b** and **13b**), acetamido (**12c**) and formamido (**12d**) groups (Scheme 6). It is notable, that this is the first time when amidation of *ortho*-carborane is achieved directly from the parent iodo-carborane. The previously known *o*-carborane derivatives, all being substituted at the B(3)-position, were obtained from the 3-amino-*o*-carborane. The latter was prepared following Zakharkin's procedure or its successful modification by Kasar.<sup>10–12</sup> In fact, compounds **12a–d** are the first 9-substituted *ortho*-carboranyl amides reported.

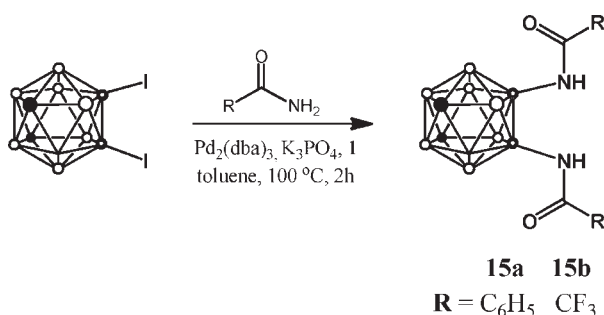
A subsequent base-mediated saponification of 3-trifluoroacetamido-*o*-carborane (**13b**) leads to the almost quantitative yield (99%) of 3-amino-*o*-carborane (**14b**). Although the *o*-carborane is known to be susceptible to the alcoholic base degradation to the *nido*-monoanion [7,8-C<sub>2</sub>B<sub>9</sub>H<sub>12</sub>]<sup>-</sup>, we observed no deboronation of the [C<sub>2</sub>B<sub>10</sub>]-cage when using NaOH/MeOH/THF/<sup>t</sup>PrOH/H<sub>2</sub>O route for synthesis of **14b**. On the other hand, hydrolysis of 9-trifluoroacetamido-*o*-carborane (**12b**) using either base or acid-mediated hydrolysis leads to cage deboronation and formation of a 5(6)-ammonium-7,8-dicarba-*nido*-undecaborate. Moreover, the treatment of 3-trifluoroacetamido-*o*-carborane (**13b**) in strongly acidic medium (hydrochloric acid) also resulted in *closo*-cage degradation to the *nido*-anion. While the mechanisms of deboronation upon acidic hydrolysis for both trifluoroacetamido-*ortho*-carboranes (**12b** and **13b**) are not emphasized in this paper, it needs to be mentioned that similar precedents have been reported in literature. Levit et al. described the deboronation of *N*-tosyl-(*S*)-prolyl- and

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**Table 1.** Selected Bond Lengths (Å) and Bond Angles (deg) for **8a,b**, **10a**, **12a,c,d**, **13a**, **15a,b** of General Formula  $a\text{-C}_2\text{B}_{10-n}(\text{B}(b)\text{NHCOR})_n\text{H}_{12-m}$ ,<sup>a</sup>

|  | <i>a</i> | <i>b</i> | R                             | <i>n</i> | B–N        | N–C        | C=O        | B–C <sup>c</sup> | B–B <sup>c</sup> | B–N–C      |
|--|----------|----------|-------------------------------|----------|------------|------------|------------|------------------|------------------|------------|
| <b>8a<sup>b</sup></b>                  | <i>m</i> | 9        | C <sub>6</sub> H <sub>5</sub> | 1        | 1.487(5)   | 1.347(5)   | 1.235(4)   | 1.698(7)         | 1.767(7)         | 125.8(3)   |
| <b>8b<sup>b</sup></b>                  | <i>m</i> | 9        | CF <sub>3</sub>               | 1        | 1.495(5)   | 1.328(4)   | 1.219(4)   | 1.704(6)         | 1.772(7)         | 125.5(3)   |
| <b>10a</b>                             | <i>p</i> | 2        | C <sub>6</sub> H <sub>5</sub> | 1        | 1.475(4)   | 1.350(4)   | 1.237(3)   | 1.705(5)         | 1.770(5)         | 126.8(3)   |
| <b>12a<sup>b</sup></b>                 | <i>o</i> | 9        | C <sub>6</sub> H <sub>5</sub> | 1        | 1.492(3)   | 1.349(3)   | 1.238(3)   | 1.702(4)         | 1.778(4)         | 125.95(19) |
| <b>12c</b>                             | <i>o</i> | 9        | CH <sub>3</sub>               | 1        | 1.4926(15) | 1.3437(15) | 1.2353(15) | 1.708(2)         | 1.7829(19)       | 127.36(10) |
| <b>12d</b>                             | <i>o</i> | 9        | H                             | 1        | 1.4914(18) | 1.3216(18) | 1.2337(18) | 1.705(2)         | 1.780(2)         | 126.64(13) |
| <b>13a</b>                             | <i>o</i> | 3        | C <sub>6</sub> H <sub>5</sub> | 1        | 1.4601(13) | 1.3633(12) | 1.2275(12) | 1.7144(14)       | 1.782(16)        | 126.46(8)  |
| <b>15a<sup>d</sup></b>                 | <i>m</i> | 9,10     | C <sub>6</sub> H <sub>5</sub> | 2        | 1.480(3)   | 1.343(3)   | 1.235(3)   | 1.703(4)         | 1.784(3)         | 127.41(18) |
| <b>15b<sup>M</sup><sub>b,d,e</sub></b> | <i>m</i> | 9,10     | CF <sub>3</sub>               | 2        | 1.486(6)   | 1.328(5)   | 1.218(5)   | 1.699(7)         | 1.778(8)         | 127.3(4)   |
| <b>15b<sup>O</sup><sub>d,e</sub></b>   | <i>m</i> | 9,10     | CF <sub>3</sub>               | 2        | 1.494(3)   | 1.337(3)   | 1.219(3)   | 1.704(3)         | 1.781(4)         | 126.50(19) |

<sup>a</sup> *a* = *o*-, *m*-, or *p*-; *b* is a substitution position; *n* = 1 or 2; R = C<sub>6</sub>H<sub>5</sub>, CF<sub>3</sub>, CH<sub>3</sub> or H. <sup>b</sup> Averaged for several crystallographically independent molecules. <sup>c</sup> Averaged for all distances. <sup>d</sup> Averaged for both amido-groups. <sup>e</sup> Compound **15b** crystallized in two different crystal forms: monoclinic, **15b<sub>M</sub>**, and orthorhombic, **15b<sub>O</sub>**.

**Scheme 7.** Amidation of 9,10-Diiodo-*m*-carborane

*N*-phthaloyl-*(S)*-alanyl amides of 3-amino-1-phenyl-1,2-dicarba-*closo*-dodecaborane under reflux in a mixture of glacial acetic acid and concentrated HCl.<sup>32</sup>

Aminocarboranes would be an excellent source of new B-derivatives if they were easy to obtain. Herein, we have successfully realized the base-mediated hydrolysis of carboranyl trifluoroacetamides to afford the 9-amino-*m*- (**9b**), 2-amino-*p*- (**11b**), and 3-amino-*o*- (**14b**) carboranes in 89%, 76%, and 99% isolated yields, respectively.

To broaden the scope of this chemistry, the amidation of 9,10-diiodo-*m*-carborane by benzamide and trifluoroacetamide were investigated and found to result in high yields (88% for **15a** and 84% for **15b**) of disubstituted amido-derivatives of *m*-carborane (Scheme 7).

**Structural Characterization.** Structural determinations using X-ray diffraction of compounds **8a,b**, **10a**, **12a,c,d**, **13a**, **15a,b** confirm the assignments of their structures from spectroscopic data. Their molecular structures along with the atom numbering schemes, are given in Supporting Information, Figures S1–S10. Selected bond distances and angles are given in Table 1.

The carborane cage displays B–B and B–C bond lengths of 1.767(7)–1.784(3) and 1.698(7)–1.7144(14) Å, respectively, which are within the expected values for carborane cage.<sup>33</sup> Similarly, the N–C and C=O bonds are within the predicted range for their parent amides.<sup>34</sup> All bond lengths and angles are within the range of distances reported

for other carboranyl amides<sup>20,35</sup> (Supporting Information, Table S3). Despite no significant discrepancies in the majority of bond lengths and angles, the B–N bond lengths vary with respect to the electron density at the B-atom of the corresponding carborane: 3-*o*-Cb ≪ 2-*p*-Cb < 9-*m*-Cb < 9-*o*-Cb.<sup>36</sup>

Free rotation of the amide moiety with respect to the carborane cage in solution results in dihedral angles around the B–N bond ranging from 3.0(2) to 174.6(2)° upon crystallization (Supporting Information, Table S4). On the contrary, the rotation around the N–C bond is significantly more hindered (the reported rotation barrier is 75–84 kJ/mol)<sup>37</sup> and the B–N–C=O angles range from 0.0(6) to 19.2(3)°. It is only in **12d**, 9-formamido-*o*-carborane, that this angle is 179.74(16)°, the carborane being oriented *trans*- to the formamide oxygen and **12d** thus being the first carboranyl amide found to crystallize as the *E*-isomer.

**Conclusions**

Four monoiodo-carborane compounds, 9-iodo-*m*-carborane, 2-iodo-*p*-carborane, 9-iodo-*o*-carborane, and 3-iodo-*o*-carborane have been successfully coupled through Pd-catalyzed reactions to both benzamide and trifluoroacetamide. Also, 9-iodo-*o*-carborane was coupled to acetamide and formamide. In addition to mono-, bis(2,2,2-trifluoroacetamide), and dibenzamide derivatives have been successfully synthesized. Crucial to this effort was the proper choice of a highly active phosphine ligand, 2-dicyclohexylphosphino-2'-(*N*,*N*-dimethylamino)biphenyl (**1**) and a mild base K<sub>3</sub>PO<sub>4</sub>, both of which significantly expand the scope of substrates amenable to such coupling reactions. In the course of this study we were able to obtain single crystals of compounds **8a,b**, **10a**, **12a,c,d**, **13a**, **15a,b** and confirm their molecular structures by X-ray crystallography. The trifluoroacetamide derivatives facilitated the synthesis of the respective aminocarboranes through base-mediated saponification. Aminocarboranes are important reactive synthons, and it is encouraging that the protocol developed here allows the introduction of amino groups at various

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reactive positions of the carborane cage. In the future, it is hoped to extend this protocol to include other coupling partners, including oxygen containing nucleophiles<sup>38</sup> and enolates.<sup>39</sup>

**Acknowledgment.** We gratefully acknowledge the National Science Foundation (CHE-0702774) for the financial support of this work. We are very grateful to Dr. Alexander Safronov for the synthesis of 9-acetamido-*o*-carborane and Dr. Radha Kishan Motkuri for the synthesis of

9-formamido-*o*-carborane and crystals of 9-acetamido-*o*-carborane and 9-formamido-*o*-carborane. The authors thank Dr. Satish S. Jalisatgi, Dr. Mark W. Lee, and Dr. Charles Barnes for helpful discussions. The authors also thank Dr. Oscar Tutusaus for in-house mass spectrum analysis program “MS Simulator” and Dr. Ilia Guzei (UW-Madison) for in-house crystallographic program “ModiCIFer”.

**Supporting Information Available:** X-ray crystallographic files in CIF format for compounds **8a,b**, **10a**, **12a,c,d**, **13a**, **15a**, **b**, the molecular structures of studied compounds, packing diagrams, details of structures refinement, and scrupulous analysis of hydrogen bonding. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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