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Regioselective synthesis of triiodo-*o*-carboranes and tetraiodo-*o*-carborane

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Abstract—3,6-Diiodo-*o*-carborane **3**, 3,6,9-triiodo-*o*-carborane **5**, 3,9,12-triiodo-*o*-carborane **6** and 3,6,9,12-tetraiodo-*o*-carborane **7**, which are suitable building blocks for supramolecular assemblies and carboracycles, were regioselectively synthesized by means of electrophilic iodination and introduction of iodine atoms via reconstruction of the *o*-carborane cage.
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The potential utilization of 1,2-dicarba-*closo*-dodecaborane, *o*-carborane **1**, as a building block for supramolecular assemblies and macrocyclic molecules containing carboranes (carboracycles) has recently been the subject of many reports.[1] The C–H protons of *o*-carborane are highly acidic (pK_a = 22.0) and consequently have the potential for hydrogen bonding.[2] Thus, supramolecular structures utilizing *o*-carborane are mainly generated by hydrogen bonding via the acidic *o*-carborane C–H vertices.[1b,3] It is important for the development of this field that a variety of functional substituents can be selectively introduced onto boron atoms of *o*-carborane.

Generally, B-iodinated *o*-carboranes react with a variety of Grignard reagents under Pd-catalyzed cross coupling conditions to form a B–C bond.[4] Thus, this reaction can be considered to be the most reliable method for preparing B-alkylated, B-arylated and B-ethynylated *o*-carboranes, which are the key molecules for construction of three-dimensional supramolecular assemblies and macrocyclic molecules based on spatial control by *o*-carborane. There are already two known methods for the introduction of iodine onto boron atoms of *o*-carborane (Chart 1). The two boron atoms closest to the carbon atoms (3- and 6-position) are the most electron-poor and are the most readily attacked by a variety of nucleophiles, such as alkoxide anion and fluoride anion. Consequently, a *nido*-carborane, *nido*-7,8-$C_2B_9H_{12}{}^-$, which lacks one boron atom adjacent to the two carbon atoms, is formed. This anionic *nido*-carborane is treated with *n*-BuLi to afford the corresponding dianion, *nido*-7,8-$C_2B_9H_{11}{}^{2-}$, followed by reaction with a boron triiodide, BI_3, to reconstruct 3-iodo-*o*-carborane, 3-I-1,2-$C_2B_{10}H_{11}$ **2**. The structural features,[5] reactivity[6] and the interactions[5] of acidic C–H protons of **2** were investigated in detail by Teixidor and co-workers. It is noteworthy that 3-iodo-*o*-carborane **2** builds up a supramolecular structure by self assembly.[5] On the other
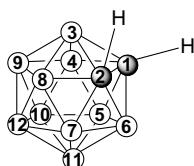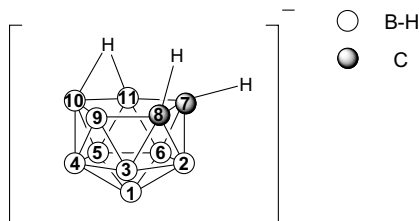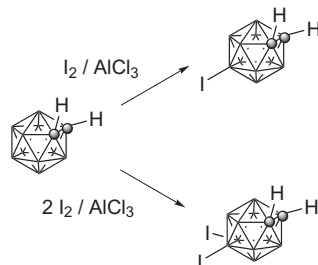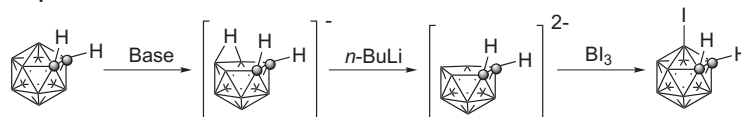

1,2-dicarba-*closo*-dodecaborane (*o*-carborane)   7,8-dicarba-*nido*-undecaborane

○ B-H
◉ C

Keywords: *o*-Carborane; Regioselective iodination; Supramolecules; Macromolecules.
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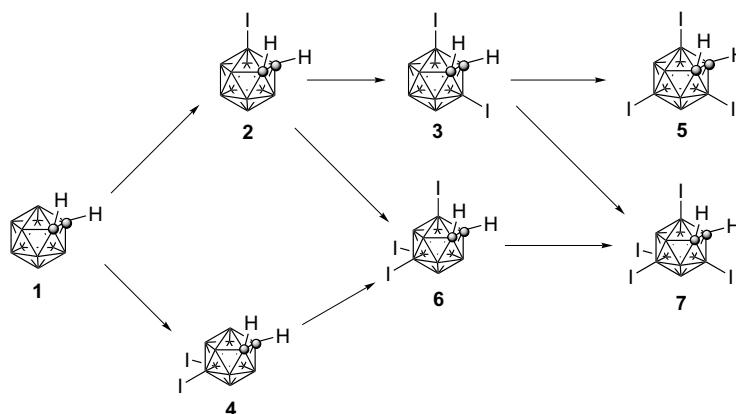
Electrophilic iodination

Nucleophilic deboronation and reconstruction of *o*-carborane

B-C Bond formation under Pd-catalyzed cross coupling conditions
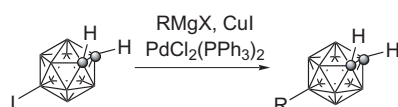
Chart 1. Alternative B-iodination of *o*-carborane and B–C bond formation employing a variety of Grignard reagents.

hand, the two boron atoms farthest from the two carbon atoms are the most electron-rich and undergo electrophilic substitution in the presence of a Lewis acid, such as AlCl$_3$, to afford 9-iodo- and/or 9,12-diiodo-*o*-carboranes.[7]

Several B-iodo-*o*-carboranes, such as 8-iodo-*o*-carborane[8] and polyiodo-*o*-carboranes (8,9,10,12-tetraiodo-*o*-carborane,[9] 4,5,7,8,9,10,11,12-octaiodo-*o*-carborane[10] and 3,4,5,7,8,9,10,11,12-nonaiodo-*o*-carborane[11]) have been reported. However, there are no reports on selective iodination of four characteristic boron atoms (3-, 6-, 9- and 12-positions) by using the combination of electrophilic reaction and reconstruction of the *o*-carborane cage. It seems likely that 3,6-diiodo-*o*-carborane **3**,[12] 3,6,9-triiodo-*o*-carborane **5**, 3,9,12-triiodo-*o*-carborane **6** and 3,6,9,12-tetraiodo-*o*-carborane **7** would be

very suitable as key intermediates for supramolecular and carboracyclic constructions utilizing the rigid three-dimensional nature of *o*-carborane.
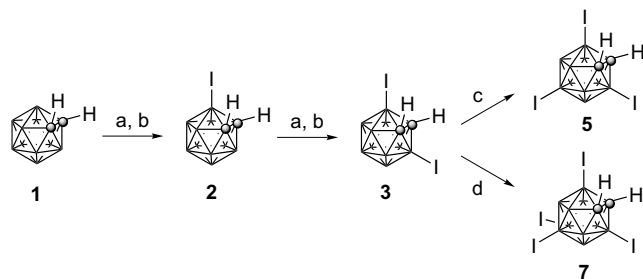
We framed a synthetic strategy for obtaining diiodo-*o*-carborane **3**, triiodo-*o*-carboranes **5**, **6** and tetraiodo-*o*-carborane **7** based on electrophilic iodination and introduction of iodine atoms by the reconstruction of *o*-carboranes (Chart 2). There is an alternative route in the first B-iodination of *o*-carborane **1**. That is to say, 3-iodo-*o*-carborane **2** can be synthesized by reconstruction of the *o*-carborane cage or by electrophilic iodination at the 9 and 12 positions of *o*-carborane. 3-Iodo-*o*-carborane **2** is converted into 3,6-diiodo-*o*-carborane **3** by reconstruction or 3,9,12-triiodo-*o*-carborane **6** by electrophilic iodination. Compound **6** can also be readily prepared from 9,12-diiodo-*o*-carborane under similar

Chart 2. Synthetic strategy for triiodo-(**5**, **6**) and tetraiodo-*o*-carboranes (**7**).

conditions to those used for 3-iodo-o-carborane. The electrophilic iodination of 3,6-diiodo-o-carborane **3** affords 3,6,9-triiodo-o-carborane **5** or 3,6,9,12-tetra-iodo-o-carborane **7**, which can also be prepared from 3,9,12-triiodo-o-carborane **6** by the usual B-iodination, depending on the amount of iodine used.
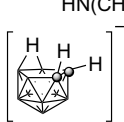
We initially investigated the synthetic route to 3,6,9-tri-iodo-o-carborane **5** and 3,6,9,12-tetraiodo-o-carborane **7** via 3,6-diiodo-o-carborane **3** (Scheme 1). o-Carborane **1** was deboronated with potassium hydroxide in ethanol, followed by treatment with trimethylammonium chloride to afford the trimethylammonium salt of the corresponding nido-compound, nido-7,8-$C_2B_9H_{12}^-$. The salt was refluxed with n-BuLi in ether for 6 h to afford a dianion, followed by reconstructive reaction with BI_3 to give 3-iodo-o-carborane **2**. In this reaction, we found that the yield was much lower than expected. n-Hexane is generally used as a solvent in reconstructive reactions, but the solubility of the dianion in n-hexane was extremely low, and this might have impeded the reconstructive reaction. Therefore, we investigated other solvents. We could obtain the desired compound in 74% yield by changing the solvent to toluene (Table 1). Comparing this with the results in the previous report,[7] it appears that toluene is a suitable solvent for reconstruction of o-carboranes.

Compound **2** was also deboronated to afford the corresponding nido-compound, 2-iodo-nido-7,8-$C_2B_9H_{11}^-$, and the synthesis of 3,6-diiodo-o-carborane **3**[13] was achieved in 52% yield under similar conditions to those

Table 2. Electrophilic iodination of 3,6-diiodo-o-carborane (**3**) with I_2 in the presence of $AlCl_3$

Entry	$AlCl_3$ (equiv)	I_2 (equiv)	Time (h)	**5** (%)	**7** (%)
1	0.2	1.1	6	88	8
2	0.2	2.2	6	20	Trace[a]
3	0.2	1.1+1.1	6+27	88	4
4	0.5	1.1	6	72	20
5	1.0	2.2	4	0	72
6	1.0	2.2	34	0	77

[a] Starting material was recovered in 77% yield.

used for 3-iodo-o-carborane. Compound **3** was iodinated at the 9 and/or 12 position(s) by electrophilic iodination in the presence of $AlCl_3$ in dichloromethane (Scheme 1). The selective preparation of mono- and dii-odo-o-carboranes was achieved as described in Table 2. The electrophilic monoiodination of **3** in the presence of a catalytic amount of $AlCl_3$ and equimolar iodine proceeded efficiently to afford 3,6,9-triiodo-o-carborane **5**[14] as the major product (88%) and 3,6,9,12-tetraiodo-o-carborane **7**[15] as a minor product (8%) (entry 1). Interestingly, in the electrophilic iodination of **3**, the use of excess iodine caused a decrease in the yield of **5** (20%) and **7** (trace amount), while the starting material **3** was recovered in 77% yield (entry 2). Addition of one more equivalent of iodine, after monoiodination of **3** under the conditions of entry 1, did not affect the product ratio (entry 3). Increase of $AlCl_3$ to 0.5 M affected the iodination, affording **5** in 72% yield and **7** in 20% yield (entry 4). Therefore, compound **3** was effectively iodinated in the presence of a stoichiometric amount of $AlCl_3$ and two equimolar iodine to afford 3,6,9,12-tetraiodo-o-carborane **7** as a sole product in high yield (entries 5 and 6).[16]

These results suggest that the introduction of three iodine atoms as electron-withdrawing groups at the 3, 6 and 9 positions decreased the electron density of the cage boron atoms sufficiently to suppress the fourth iodination. Therefore, control of the amount of $AlCl_3$ is effective for the selective synthesis of 3,6,9-triiodo-o-carborane **5** and 3,6,9,12-tetraiodo-o-carborane **7**.

We also investigated an alternative route for the synthesis of 3,6,9-triiodo-o-carborane **5** and 3,6,9,12-tetraiodo-o-carborane **7** (Schemes 2 and 3). Compound **2** was readily diiodinated at the 9 and 12 positions by two
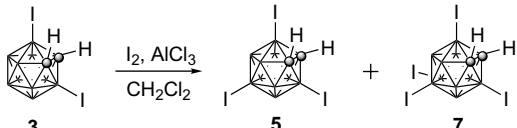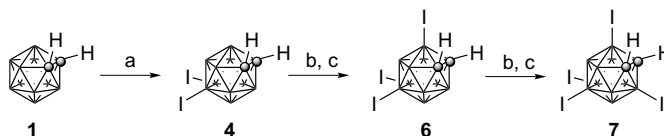

Scheme 1. Alternative synthesis of 3,6,9-triiodo-o-carborane (**5**) and 3,6,9,12-tetraiodo-o-carborane (**7**). (a) KOH, EtOH, trimethylammonium chloride; (b) n-BuLi, ether, then BI_3, toluene; (c) I_2, $AlCl_3$ (0.2 equiv), CH_2Cl_2; (d) I_2, $AlCl_3$(1.0 equiv), CH_2Cl_2.

Table 1. Reconstruction of o-carborane by reaction of the nido-cluster, nido-7,8-$C_2B_9H_{12}^-$ with BI_3

Entry	Solvent	Temp (°C)	Time (h)	Yield (%)
1	n-Hexane	rt	22	27 (68)[a]
2	Toluene	rt	37	74

[a] The yields reported by Li et al. are shown in parenthesis.[7]

Scheme 2. Synthesis of 3,9,12-triiodo-o-carborane (**6**) by electrophilic iodination. (a) I_2, $AlCl_3$ (0.2 equiv), CH_2Cl_2.

Scheme 3. Stepwise reconstructive synthesis of 3,9,12-triiodo-*o*-carborane (**6**) and 3,6,9,12-tetraiodo-*o*-carborane (**7**). (a) I$_2$, AlCl$_3$ (0.2 equiv), CH$_2$Cl$_2$; (b) KOH, EtOH, trimethylammonium chloride; (c) *n*-BuLi, ether, then BI$_3$, toluene.

equimolar iodine in the presence of a catalytic amount of AlCl$_3$ to afford 3,9,12-triiodo-*o*-carborane **6**[17] in 65% yield. The key intermediate **6** could also be obtained by deboronation and reconstruction of 9,12-diiodo-*o*-carborane **4**, prepared by the electrophilic substitution of *o*-carborane **1** with two equimolar iodine. Compound **4** was converted to the corresponding *nido*-compound, 4,5-diiodo-*nido*-7,8-C$_2$B$_9$H$_{10}^-$, by potassium hydroxide, followed by the reconstructive reaction with BI$_3$ in toluene to afford **6** in 55% yield. We also examined cyclohexane instead of toluene, but the solubility of the dianion in cyclohexane was very low, we could not get a satisfactory result (36% yield). Compound **6** was converted to 3,6,9,12-tetraiodo-*o*-carborane **7** in 29% yield via 2,4,5-triiodo-*nido*-7,8-C$_2$B$_9$H$_9^-$ under the conditions used for the preparation of **6**.

We achieved the regioselective synthesis of 3,6,9-triiodo-*o*-carborane **5**, 3,9,12-triiodo-*o*-carborane **6** and 3,6,9,12-tetraiodo-*o*-carborane **7** by the combination of electrophilic substitution for electron-rich boron atoms and nucleophilic substitution followed by reconstructive reaction for electron-poor boron atoms in *o*-carborane. The iodinated *o*-carboranes **3**, **5**, **6** and **7** could be useful as 'smart' building blocks to build up supramolecular structures through intermolecular C–H···I interactions in the fields of supramolecular chemistry and macromolecular chemistry utilizing *o*-carborane.

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13. 3,6-Diiodo-*o*-carborane **3**; colourless needles (recrystallized from *n*-hexane); mp 122–123 °C; ^{1}H NMR (270 MHz, CDCl$_3$) δ (ppm) 1.56–3.76 (br m, 8H), 4.12 (s, 2H); ^{13}C NMR (68 MHz, CDCl$_3$) δ (ppm) 64.20; ^{11}B NMR (192 MHz, CDCl$_3$, BF$_3$·OEt$_2$ external standard) δ (ppm) −28.02 (2B), −10.04 (4B), −8.98 (2B), −0.31 (2B); MS (EI) *m/z* 396 (M$^+$, 100%); Anal. Calcd for C$_2$H$_9$B$_{10}$I$_3$: C, 6.07; H, 2.55. Found: C, 6.15; H, 2.35.
14. 3,6,9-Triiodo-*o*-carborane **5**; colourless prisms (recrystallized from *n*-hexane and CH$_2$Cl$_2$); mp 140–142 ° C; ^{1}H NMR (270 MHz, CDCl$_3$) δ (ppm) 1.30–4.20 (br m, 7H), 4.23 (s, 1H), 4.38 (s, 1H); ^{13}C NMR (68 MHz, CDCl$_3$) δ (ppm) 60.20, 64.33; ^{11}B NMR (192 MHz, CDCl$_3$, BF$_3$·OEt$_2$ external standard) δ (ppm) −28.14 (2B), −15.44 (1B), −9.93 (2B), −9.48 (2B), −7.48 (2B), 0.89 (1H); MS (EI) *m/z* 522 (M$^+$, 100%); Anal. Calcd for C$_2$H$_9$B$_{10}$I$_3$: C, 4.60; H, 1.74. Found: C, 4.81; H, 1.70.
15. 3,6,9,12-Tetraiodo-*o*-carborane **7**; colourless cubes (recrystallized from *n*-hexane and CH$_2$Cl$_2$); mp 251–253 ° C; ^{1}H NMR (270 MHz, CDCl$_3$) δ (ppm) 2.00–4.40 (br m, 8H), 4.50 (s, 2H); ^{13}C NMR (68 MHz, CDCl$_3$) δ (ppm) 60.53; ^{11}B NMR (192 MHz, CDCl$_3$, BF$_3$·OEt$_2$ external standard) δ (ppm) −27.95 (2B), −13.10 (4B), −9.68 (2B), −5.94 (2B); MS (EI) *m/z* 648 (M$^+$), 127 (100%); Anal. Calcd for C$_2$H$_8$B$_{10}$I$_4$: C, 3.71; H, 1.24. Found: C, 4.01; H, 1.50.
16. 3,6,9-Triiodo-*o*-carborane **5** was also effectively iodinated in the presence of a stoichiometric amount of AlCl$_3$ and one equimolar iodine to afford 3,6,9,12-tetraiodo-*o*-carborane **7** in 76% yield.
17. 3,9,12-Triiodo-*o*-carborane **6**; colourless prisms (recrystallized from *n*-hexane and CH$_2$Cl$_2$); m.p. 198–200 °C; ^{1}H NMR (270 MHz, CDCl$_3$) δ (ppm) 0.60–4.65 (brm, 7H), 4.26 (s, 2H); ^{13}C NMR (68 MHz, CDCl$_3$) δ (ppm) 56.36; ^{11}B NMR (192 MHz, CDCl$_3$, BF$_3$·OEt$_2$ external standard) δ (ppm) −29.50 (1B), −13.77 (2B), −12.95 (1B), −12.01 (2B), −10.69 (2B), −7.66 (1B), −4.14 (1B); MS (EI) *m/z* 522 (M$^+$, 100%); Anal. Calcd for C$_2$H$_9$B$_{10}$I$_3$: C, 4.60; H, 1.74. Found: C, 4.83; H, 1.72.