

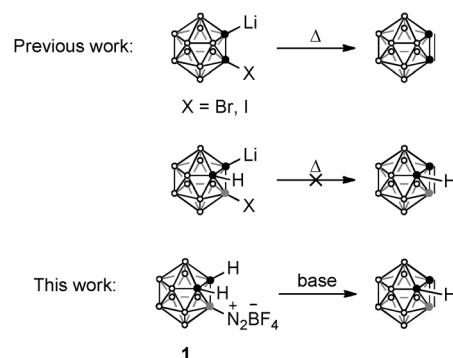
1,3-Dehydro-*o*-Carborane: Generation and Reaction with Arenes**

Da Zhao, Jiji Zhang, and Zuowei Xie*

Abstract: Like the importance of benzyne, witnessed in modern arene chemistry for decades, 1,2-dehydro-*o*-carborane (*o*-carboryne), a three-dimensional relative of benzyne, has been used as a synthon for generating a wide range of cage, carbon-functionalized carboranes over the past 20 years. However, the selective B functionalization of the cage still represents a challenging task. Disclosed herein is the first example of 1,3-dehydro-*o*-carborane featuring a cage C–B bond having multiple bonding characters, and is successfully generated by treatment of 3-diazonium-*o*-carborane tetrafluoroborate with non-nucleophilic bases. This presents a new methodology for simultaneous functionalization of both cage carbon and boron vertices.

Icosahedral carborane has superaromatic character exhibiting extraordinary thermal stability and unusual chemical reactivity such as aromatic substitution, similar to that of benzene.^[1] 1,2-Dehydro-*o*-carborane (*o*-carboryne) is a very reactive intermediate, which can be regarded as a three-dimensional relative of 1,2-dehydrobenzene (benzyne) (Figure 1).^[2] They share some common features, however, *o*-

a cage compound having C–B bonds with multiple bonding characters, would be a reactive intermediate for simultaneous functionalization of both cage carbon and boron vertices. Such a species might be generated in a similar manner to that of *o*-carboryne, which can be produced from 1-X-2-Li-*o*-C₂B₁₀H₁₀ by LiX salt elimination (X = Br,^[2a] I^[2c]; Scheme 1).



Scheme 1. Generation of *o*-carboryne and 1,3-dehydro-*o*-carborane.

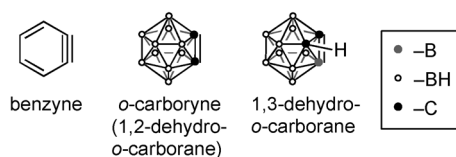


Figure 1. Benzyne, *o*-carboryne, and 1,3-dehydro-*o*-carborane.

carboryne has its own unique properties resulting mainly from steric/electronic features.^[3] It can undergo [4+2] and [2+2] cycloadditions,^[2a,4] ene reactions,^[5] and C–H bond-insertion reactions^[6] with a variety of organic molecules to afford a large class of *o*-carborane derivatives. Thus, *o*-carboryne is a very useful synthon for generating a wide range of cage, carbon-functionalized carboranes which may have potential applications in medicine,^[7] materials science,^[8] and organometallic/coordination chemistry.^[9] With this in mind, we speculated that 1,3-dehydro-*o*-carborane (Figure 1), featuring

Our initial attempts to obtain 1,3-dehydro-*o*-carborane from 1-Li-3-X-*o*-C₂B₁₀H₁₀ (X = Br, I) by LiX elimination failed since 1-Li-3-X-*o*-C₂B₁₀H₁₀ was thermally stable, even under forced reaction conditions, owing to a very strong B–X bond.^[10] In view of the properties of diazonium salts of carboranes,^[11] we thought that 3-(N₂⁺BF₄[−])-*o*-C₂B₁₀H₁₁ (**1**) may serve as a good precursor for 1,3-dehydro-*o*-carborane as dinitrogen is an excellent leaving group after deprotonation of the cage C–H (Scheme 1). Indeed, this is an efficient method to generate previously unknown 1,3-dehydro-*o*-carborane. Its generation and chemical properties are reported herein.

3-Diazonium-*o*-carborane tetrafluoroborate (**1**) was prepared in 70% yield upon isolation, by treatment of 3-amino-*o*-carborane^[12] with 1.2 equivalents of in situ generated nitrosyl fluoride in the presence of boron trifluoride.^[13] It was noted that the stability of **1** is dependent upon the counterion used and BF₄[−] offers the highest thermal stability of the salt among the anions, such as PF₆[−] and Cl[−], examined.

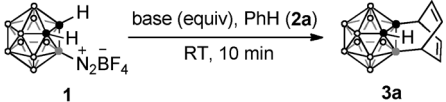
To test our hypothesis, a benzene suspension of **1** was treated with 1 equivalent of *n*BuLi at room temperature for 10 minutes to give the expected [4+2] cycloaddition product **3a** in 38% yield upon isolation (entry 1, Table 1). The low yield resulted from the formation of 3-*n*Bu-*o*-C₂B₁₀H₁₁, which was generated from the nucleophilic attack of *n*BuLi.^[14] When the non-nucleophilic base lithium diisopropylamide (LDA) was used, **3a** was obtained in 72% yield (entry 2). Other less-nucleophilic bases gave relatively lower yields (entries 3–5). Increasing the amount of base did not improve the yield (entry 6). The reaction also proceeded well in the

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Table 1: Screening of reaction conditions.

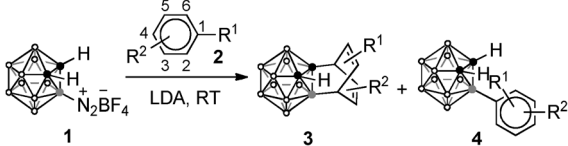


Entry	Base (equiv)	Yield [%] ^[a]
1	<i>n</i> BuLi (1.0)	38
2	LDA (1.0)	72
3	NaH (1.0)	55
4	NaNH ₂ (1.0)	61
5	LiHMDS (1.0)	66
6	LDA (2.0)	72
7 ^[b]	LDA (1.0)	72

[a] Yield of isolated product. [b] The reaction was performed in the dark. LDA = lithium diisopropylamide, LiHMDS = lithium bis(trimethylsilyl)-amide.

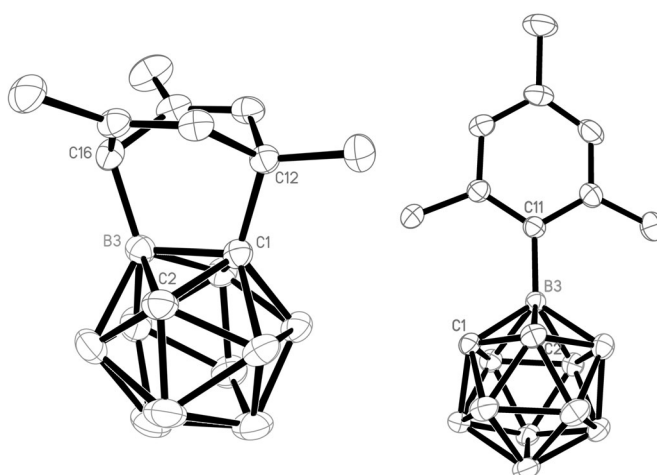
dark (entry 7). These results suggest that **1** is a good precursor of 1,3-dehydro-*o*-carborane and its reaction with benzene is more efficient than that of *o*-carboryne.^[4g]

Under the optimal reaction conditions (entry 2, Table 1), various arenes with different substituents, such as trimethylsilyl, halo, and alkyl groups, were examined. The results are compiled in Table 2. In general, the reaction efficiency of 1,3-dehydro-*o*-carborane with arenes was much higher than that of *o*-carboryne. For the methyl-substituted arenes **2i–m**, the corresponding aromatic ene reaction products,^[15] 3-aryl-*o*-carborane (**4**), were also isolated and became the major product in cases of **2k** and **2m** (entries 11 and 13). Representative molecular structures of the [4+2] cycloadduct and the aromatic ene reaction product are shown in Figure 2.

Table 2: Reaction of arenes with 1,3-dehydro-*o*-carborane.^[a]


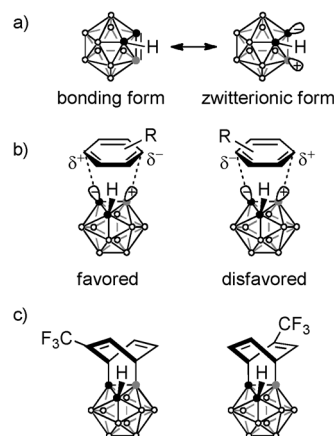
Entry	R ¹ /R ² (2)	Yield [%] ^[b]	3 (regioselectivity) ^[c]	4
1	H/H (2a)	72 (–)	–	–
2 ^[d]	F/2,3,4,5,6-F ₅ (2b)	25 (–)	–	–
3	F/H (2c)	64 (91:9)	–	–
4	Cl/H (2d)	67 (68:32)	–	–
5	Cl/2-Cl (2e)	55 (–)	–	–
6	CF ₃ /H (2f)	53 (100:0)	–	–
7	TMS/H (2g)	52 (71:29)	–	–
8	<i>t</i> Bu/H (2h)	67 (62:38)	–	–
9	Me/H (2i)	55 (73:27)	–	27
10	Me/2-Me (2j)	47 (–)	–	39
11	Me/3-Me (2k)	26 (79:21)	–	53
12	Me/4-Me (2l)	39 (–)	–	41
13	Me/3,5-Me ₂ (2m)	24 (89:11)	–	69

[a] Reaction conditions: LDA (1.0 equiv), arenes **2** (40.0 equiv), room temperature, 10 min. [b] Yield of isolated products. [c] Determined by ¹H NMR spectra. Regioselectivity refers to the ratios of favoured addition fashion over disfavoured one. [d] The low yield resulted from the high volatility of **3b**. TMS = trimethylsilyl.

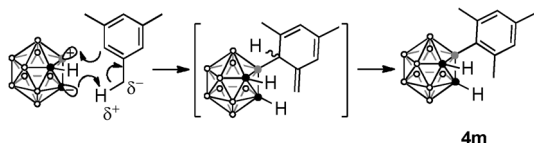

Figure 2. Molecular structures of **3m** (left) and **4m** (right).^[19] Thermal ellipsoids shown at 35% probability.

Since carbon and boron atoms are different in nature and the cage C–B bonds are polarized, the reactive intermediate, 1,3-dehydro-*o*-carborane, is best described as a resonance hybrid of both bonding and zwitterionic forms (Scheme 2a). Thus, the regioselectivity of the [4+2] cycloaddition of 1,3-dehydro-*o*-carborane with substituted arenes is governed by electronic factors, though steric factors may also play a role, and is similar to that of hetero-Diels–Alder reactions^[16] or the reactions of distorted arynes.^[17] Scheme 2b shows both the electronically favored and disfavored [4+2] cycloadditions of 1,3-dehydro-*o*-carborane with substituted arenes.

For arenes having more-evenly distributed electron density, two or more [4+2] cycloaddition modes were observed (see the Supporting Information). However in the case of **2f**, only one [4+2] cycloaddition mode was observed, probably owing to the strong inductive effect imparted by the CF₃ group. As 1,3-dehydro-*o*-carborane is an unsymmetrical species, it is expected that its reaction with substituted arenes affords structural isomers of the products. For instance, two structural isomers were isolated in the reaction of **2f** (Scheme 2c).

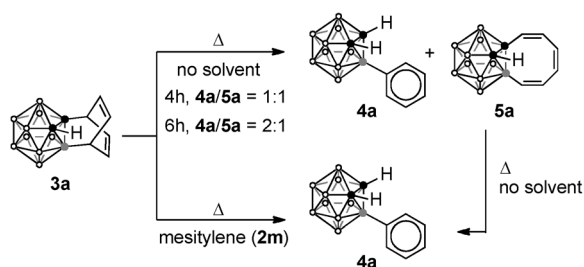

Scheme 2. a) Two resonance forms of 1,3-dehydro-*o*-carborane. b) The [4+2] cycloaddition modes. c) Two structural isomers generated from **2f**.

Remarkably different from that of *o*-carboryne, the reactions with toluene and its derivatives, **2i–m**, also gave the aromatic ene reaction products^[15] **4** in 27–69 % yields in addition to the [4+2] cycloadducts. The ratio of ene product to [4+2] cycloadducts increased with the number of the benzylic C–H bonds (entries 9–13, Table 2). In case of the reaction of **2m**, an intermediate of the aromatic ene reaction was observed in the ¹H NMR spectrum of the crude reaction mixture (see the Supporting Information) and it rearomatized to **4m** within 30 minutes. It is noteworthy that such an aromatic ene reaction proceeded with excellent regioselectivity, thus giving only the cage B3-substituted products 3-aryl-*o*-C₂B₁₀H₁₁ (**4**). This selectivity can be ascribed to the zwitterionic nature of 1,3-dehydro-*o*-carborane as illustrated in Scheme 3.



Scheme 3. Aromatic ene reaction of 1,3-dehydro-*o*-carborane.

It is documented that the [4+2] cycloadducts of *o*-carboryne with arenes can undergo thermal retro-Diels–Alder reaction to produce the homo-Diels–Alder products in almost quantitative yield.^[4c] To explore the possibility of cycloadducts as a new source of 1,3-dehydro-*o*-carborane through retro-Diels–Alder reaction, pyrolysis of the Diels–Alder adducts of 1,3-dehydro-*o*-carborane was conducted. Heating of a solid of the [4+2] cycloadduct **3a** at 250 °C for 6 hours in a sealed tube gave a 2:1 mixture of **4a** and the 1,3-cyclooctatetraenocarborane **5a** in 80 % yield (Scheme 4),



Scheme 4. Pyrolysis of the cycloadduct **3a**.

a reaction which is unprecedented. The molecular structure of **5a** was confirmed by single-crystal X-ray analyses (Figure 3). The compound **5a** was completely converted into **4a** with heating at 250 °C for 6 hours, thus indicating that **4a** is a thermodynamically more stable product. In contrast, heating of a mesitylene (**2m**) solution of **3a** at 250 °C for 6 hours in a sealed tube afforded **4a** in quantitative yield (Scheme 4). Neither the [4+2] cycloadduct **3m** nor the aromatic ene reaction product **4m** were observed. These results indicate that the cage B–C bond does not break in such reactions and the transformations are intramolecular.

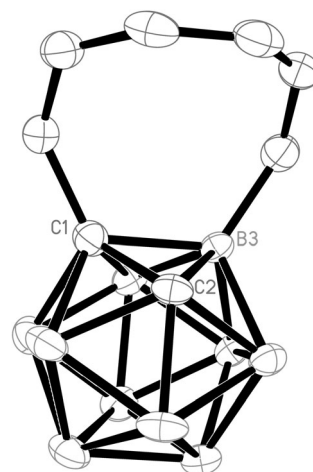
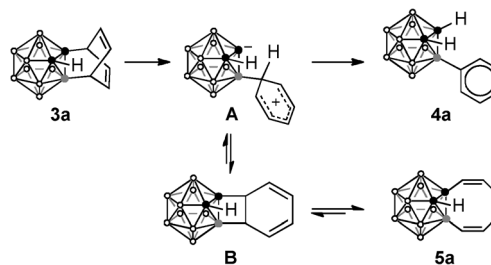


Figure 3. Molecular structure of **5a**.^[19] Thermal ellipsoids shown at 35 % probability.

To understand these processes, DFT calculations were performed (see the Supporting Information). The results show that breaking of the cage C–C(sp³) bond is energetically favored over that of the cage B–C(sp³), and **4a** is thermodynamically more stable than **5a** by 42.1 kcal mol^{–1}. Accordingly, a reaction mechanism is proposed in Scheme 5. Heterolytic cleavage of the cage C–C(sp³) bond in **3a** generates the intermediate **A**. Migration of a proton in **A** gives the thermodynamic product **4a**. Alternatively, the formation of a cage C–C(sp³) bond affords another intermediate, **B** (formally [2+2] cycloadduct), which undergoes sigmatropic rearrangement to yield the kinetic product **5a**.



Scheme 5. Proposed mechanism for thermal rearrangement.

In conclusion, we report, for the first time, the generation of 1,3-dehydro-*o*-carborane bearing cage C–B bonds having multiple bonding characters. It undergoes Diels–Alder reactions with arenes to give [4+2] cycloadducts, in which electronic factors govern the regioselectivity. Meanwhile, for arenes bearing benzylic C–H bonds, a highly regioselective aromatic ene reaction was also observed and the product ratio of [4+2] cycloaddition adduct to the ene reaction adduct depends on the number of benzylic protons. These results suggest that 1,3-dehydro-*o*-carborane is best described as a resonance hybrid of a bonding form and a zwitterionic form as shown in Scheme 2a. Thus, it shares some chemical properties with those of *o*-carboryne. In contrast, it also has

its own unique properties which result from the polarized cage C–B bond. The present work demonstrates that 1,3-dehydro-*o*-carborane is a useful synthon for simultaneous C,B functionalization of *o*-carboranes.^[18]

Experimental Section

Typical procedure: Benzene (**2a**; 1 mL) was added to a mixture of **1** (51.6 mg, 0.2 mmol) and LDA (0.2 mmol) under an atmosphere of dry argon. The resulting mixture was stirred at room temperature for 10 min and quenched by wet *n*-hexane. After removal of solvents in vacuo, the residue was examined by ¹H NMR spectroscopy and then subjected to flash column chromatography on silica gel (230–400 mesh) using *n*-hexane as the eluent to give **3a** (32 mg, 72 %) as colorless crystals. ¹H NMR (400 MHz, CDCl₃): δ = 6.83 (m, 2H), 6.37 (t, *J* = 6.4 Hz, 1H), 6.26 (t, *J* = 6.8 Hz, 1H) (olefinic CH), 4.07 (t, *J* = 6.0 Hz, 1H) (CH), 3.85 (br, 1H) (cage CH), 3.64 ppm (t, *J* = 6.0 Hz, 1H) (BCH). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ = 143.3, 142.7, 134.4, 132.6, 82.0 (cage C), 70.8 (cage C), 45.2, 34.8 ppm. ¹¹B{¹H} NMR (128 MHz, CDCl₃): δ = −3.5 (1B), −4.9 (1B), −6.4 (1B), −7.6 (1B), −10.3 (2B), −12.3 (1B), −14.6 (2B), −16.2 ppm (1B). HRMS (EI) calcd for C₈H₁₆¹¹B₈¹⁰B₂⁺ 220.2254, found 220.2250.

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