

Copper-Promoted Cyanation of a Boron Cluster: Synthesis, X-ray Structure, and Reactivity of 12-CN-*closo*-CHB₁₁H₁₀[−]Aaron J. Rosenbaum,[†] Douglas H. Juers,[‡] and Marcus A. Juhasz^{*,†}[†]Department of Chemistry and [‡]Department of Physics, Whitman College, 345 Boyer Avenue, Walla Walla, Washington 99362, United States

S Supporting Information

ABSTRACT: Microwave-assisted cross-coupling reactions of boron-iodinated derivatives of 1-carba-*closo*-dodecaborate(1[−]) (**1**) with CuCN is shown to cyanate boron vertices of this anion. Clusters with one or two CN groups can be prepared: syntheses of 12-CN-CHB₁₁H₁₀[−] (**3**) and 7,12-(CN)₂-CHB₁₁H₉[−] (**6**) gave yields of 80% and 81%, respectively. The [Et₄N]⁺ salts of **3** and **6** were characterized by NMR, IR, and mass spectroscopies, and the crystal structure of [Et₄N]**3** was determined by single-crystal X-ray diffraction. Hydrolysis of **3** gave the carboxylic acid 12-COOH-CHB₁₁H₁₀[−] (**7**).

Anions based on 1-carba-*closo*-dodecaborate(1[−]) (**1**, i.e., *closo*-CHB₁₁H₁₁[−]; Figure 1), have received much recent

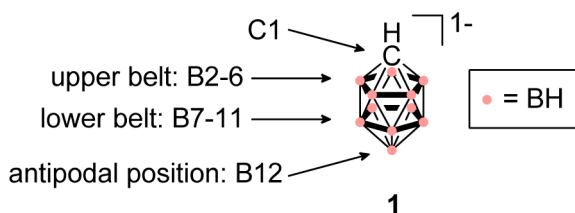


Figure 1. Numbering scheme for **1**.

attention because their use has increased in practical applications. The low nucleophilicity and exceptional stability of this cluster make it an ideal counterion for extreme electrophiles,¹ and its low basicity allowed for the preparation of the strongest Brønsted acid ever isolated.² Applications of this cluster in catalysis,^{3–5} ionic liquids,^{6,7} liquid crystals,⁸ and pharmaceuticals^{9,10} have been described. **1** is an attractive moiety for use in boron neutron capture therapy because it is boron-rich and stable under physiological conditions. However, the development of drugs that utilize the CB₁₁ cluster is hindered, in part, by a lack of synthetic methods for attaching the cluster to biologically active molecules.

Existing synthetic routes for modifying **1** generally give substitution of groups either at the carbon or at borons of the cluster. A number of derivatives of **1** bearing groups at C1 have been prepared by deprotonation of the carbon vertex and subsequent reaction with a variety of electrophiles. However, routes for introducing substituents at boron vertices are more limited.^{11,12} Cyanation of **1** would provide two potential benefits. Because CN groups can be converted into a variety of other

functional groups, including carboxylic acids, amides, and amines, cyanation opens a variety of synthetic possibilities. In addition, electron-withdrawing substituents such as CN are known to improve **1** as a weakly coordinating anion¹ and a superweak base.² Superacids derived from cyanated derivatives of **1** were postulated in DFT calculations over a decade ago,¹³ and recent studies suggest that the conjugate acids of heavily cyanated clusters would surpass the strongest isolable Brønsted acid, H(CHB₁₁Cl₁₁).¹⁴ The least basic anions require CN groups at multiple boron vertices, but no method has been reported for cyanating borons of the CB₁₁ cage. To date, the only reported cyanated derivative of **1** is 1-CN-CHB₁₁H₁₀[−], which bears a single CN group at the carbon of the cluster.¹⁵

Electrophilic substitution is an established method for derivatizing borons of the CB₁₁ cluster,¹¹ and the introduction of a CN group using electrophilic sources of CN (e.g., CNBr) was explored. However, our attempts to cyanate **1** directly using cyanogen bromide gave bromination in all cases, and 12-Br-CHB₁₁H₁₀[−], a previously reported compound,¹⁶ was consistently identified as the product.

Transition-metal-promoted cross-coupling reactions have been developed for converting aryl halides to aryl nitriles in organic synthesis,^{17,18} and reactions involving a cyanide source with catalytic palladium or nickel, as well as reactions that use stoichiometric CuCN (i.e., the Rosenmund–von Braun reaction),¹⁹ represent alternative methods for cyanation. A cross-coupling cyanation strategy is attractive in light of the straightforward synthesis of iodinated derivatives of **1** and their success as substrates for palladium-catalyzed cross-coupling reactions,²⁰ especially under microwave irradiation.²¹ We report here a microwave-assisted copper-promoted cyanation method for the CB₁₁ cluster and the preparation of the only examples known of boron-cyanated derivatives of **1**.

Microwave irradiation of 12-I-CHB₁₁H₁₀[−] (**2**)²⁰ with CuCN gave 12-CN-CHB₁₁H₁₀[−] (**3**), which was isolated as a white crystalline tetraethylammonium salt in 80% yield.²² A mass at *m/z* = 168 in the negative-ion mass spectrum and a downfield ¹¹B NMR shift from −17.8 ppm for **2** to −12.3 ppm for **3** for the antipodal boron (B12) resonance indicated the substitution of iodine with CN. A new resonance at 130 ppm in the ¹³C NMR spectrum of [Et₄N]**3** can be assigned to C_{CN}; broadening of this peak due to one-bond coupling with a quadrupolar ¹¹B nucleus is consistent with the attachment of the CN group to boron. The IR spectrum of [Et₄N]**3** showed a band at 2208 cm^{−1}, consistent

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with a $\text{C}\equiv\text{N}$ stretching mode and in agreement with a value of 2216 cm^{-1} calculated for **3** in the gas phase at the B3LYP/6-31+G(d) level.²³

Evaporation of an acetonitrile/water solution of $[\text{Et}_4\text{N}]\text{3}$ gave crystals suitable for X-ray diffraction, and the crystal structure²⁴ confirmed the identity of the monocyanoanion (Figure 2). In

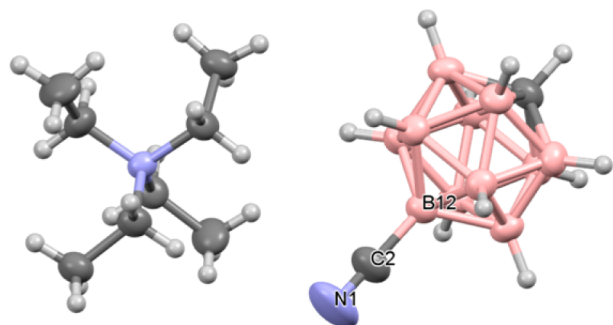


Figure 2. Molecular structure of $[\text{Et}_4\text{N}]\text{3}$. (Displacement ellipsoids are at the 40% probability level.) Selected bond lengths [pm]: B12–C2, 155.0(3); C2≡N1, 113.3(4). Selected bond angle [deg]: B12–C2–N1, 178.4(3).

the solid state, **3** has a nearly C_{5v} -symmetric structure, consistent with the gas-phase geometry predicted by DFT calculations. The B–C_{CN} bond length of 155.0 pm is similar to that for alkyne-substituted CB_{11} cages (156.8 pm for 12- $\text{HC}\equiv\text{C}-\text{CHB}_{11}\text{H}_{10}^-$),¹³ and the $\text{C}\equiv\text{N}$ distance of 113.3 pm matches the bond length in organic nitriles.

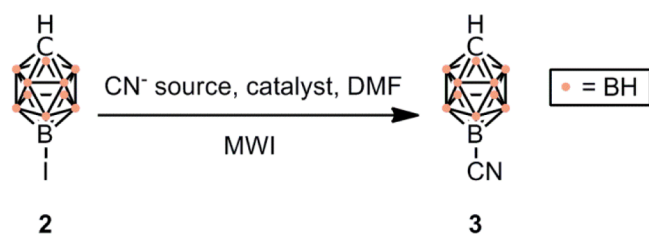
Several parameters in the synthesis of **3** were investigated (Table 1). Initial reactions were performed using $[\text{Cs}]\text{2}$ with a cyanide source and 10 mol% $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ in DMF. The reaction was sensitive to the cyanide source, and attempts that used NaCN or KCN were unsuccessful. Only reactions containing CuCN proceeded, and the role of copper in the reaction was explored briefly. Attempts to use catalytic CuI with stoichiometric NaCN or KCN failed, suggesting that copper is not catalytic in the reaction. Stoichiometric CuCN was required for cyanation, and a moderate excess (1.5 equiv) was found to give shorter and more consistent reaction times.

In reactions containing $\text{Pd}(\text{Ph}_3)_2\text{Cl}_2$, the inner salt 12- $\text{Ph}_3\text{P}-\text{CHB}_{11}\text{H}_{10}$ (**4**) was observed as a side product, consistent with other cross-coupling reactions of **2** that employ this as the catalyst.²⁵ The removal of **4** is problematic, and reducing the amount of $\text{Pd}(\text{Ph}_3)_2\text{Cl}_2$ was explored as a way to minimize this impurity. However, reactions slowed when less $\text{Pd}(\text{Ph}_3)_2\text{Cl}_2$ was used. Changing the palladium catalyst to 10 mol% $\text{Pd}(\text{OAc})_2$ avoided the formation of **4**, but a slightly higher temperature was required. Since copper(I) is known to promote cyanation reactions of inorganic molecules,²⁶ the possibility of a palladium-free, copper-promoted cyanation route was explored. Reactions containing an excess of CuCN were found to proceed without palladium; however, these reactions required longer heating, and their reaction times were variable (2–8 h).

The reaction of 7,12- $\text{I}_2-\text{CHB}_{11}\text{H}_9^-$ (**5**) under conditions similar for those used to prepare **3** gave 7,12- $(\text{CN})_2-\text{CHB}_{11}\text{H}_9^-$ (**6**) in 81% yield.²⁷ The IR spectrum of **5** showed a single band at 2214 cm^{-1} , which can be attributed to an unresolved pair of bands for the two $\text{C}\equiv\text{N}$ stretching modes. This assignment agrees with DFT calculations at the B3LYP/6-31+G(d) level, which give values of 2224.5 cm^{-1} (asymmetric $\text{C}\equiv\text{N}$ stretch) and 2224.7 cm^{-1} (symmetric $\text{C}\equiv\text{N}$ stretch) for **5**.

Conversion of the cyano group in **3** into other functional groups was explored. ^{11}B NMR monitoring of the acid-catalyzed hydrolysis of **3** indicated conversion to a new compound with a downfield-shifted resonance at -4.4 ppm for the B12 position (Figure 3). This compound was isolated as a $[\text{Et}_4\text{N}]^+$ salt and identified as 12- $\text{COOH}-\text{CHB}_{11}\text{H}_{10}^-$ (**7**). The identity of **7** was supported by negative-ion MS,²⁸ a ^{13}C resonance at 188.2 ppm [$q, {}^1J(^{13}\text{C}, {}^{11}\text{B}) = 95\text{ Hz}$, $^{13}\text{C}=\text{O}$], the disappearance of the CN band in the IR, and the appearance of bands at 1653 cm^{-1} (strong, $\text{C}=\text{O}$ stretch) and 3131 cm^{-1} (v br, OH stretch). To confirm the formation of a carboxylic acid group during hydrolysis and to rule out the primary amide 12- $\text{CONH}_2-\text{CHB}_{11}\text{H}_{10}^-$ (**8**), NaOH was added to **7** with monitoring by ^{11}B NMR. The response of the B12 resonance (Figure 3) is consistent with titration of the monoprotic acid **7** to give the carboxylate ion 12- $\text{COO}-\text{CHB}_{11}\text{H}_{10}^{2-}$ (**9**): Less than 1 equiv of base broadens and shifts this resonance slightly downfield, and slightly more than 1 equiv of base shifts this peak to -1.3 ppm .

Table 1. Summary of the Reaction Conditions for Monocyanoanion

						
entry	scale (mg of $[\text{Cs}]\text{2}$)	CN [−] source ^a	Pd catalyst ^b	time (min)	temp (°C)	conversion (%) ^c /yield (%) ^d
1	10	NaCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$	30	200	0 ^c
2	10	NaCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2 + \text{CuI}$ (18 mol%)	30	200	0 ^c
3	10	KCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$	30	200	0 ^c
4	10	KCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2 + \text{CuI}$ (18 mol%)	30	200	0 ^c
5	25/250	CuCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$	15	180	100 ^c /80 ^d
6	25	CuCN	$\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (2 mol%)	120	220	100 ^c
7	25/250	CuCN	$\text{Pd}(\text{OAc})_2$	15	250	100 ^c /72 ^d
8	25/250	CuCN	none	120	250	100 ^c /80 ^d

^aA total of 1.5 equiv of CN^- was used. ^bA total of 10 mol% Pd was used for all reactions, unless otherwise noted. ^cSmall-scale reactions were monitored by ^{11}B NMR analysis of the crude reaction mixture. ^dIsolated yield after purification.

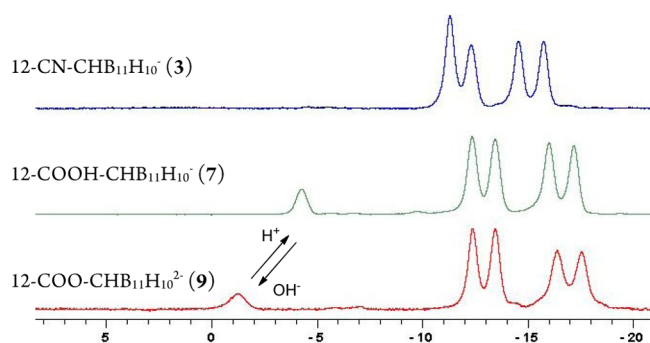


Figure 3. ^{11}B NMR spectra of 3, 7, and 9 in acetone.

Additional base beyond 2 equiv gives no further change, but acidification reverts the spectrum to that of 7.

In summary, we have shown that microwave-assisted cyanation using CuCN , with or without a palladium catalyst, is a convenient method for attaching CN groups to **1** and have prepared two new compounds by this route: **3** and **6**. These are the first examples of **1** bearing CN groups at boron vertices. A new carboxylic acid derivative, **7**, resulting from acid-catalyzed hydrolysis of **3**, represents the first of many compounds that could be prepared by reactions of the CN group.

■ ASSOCIATED CONTENT

■ Supporting Information

Experimental procedures, spectroscopic data, X-ray crystallographic data including a CIF file. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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Notes

The authors declare no competing financial interest.

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(22) Characterization for $[\text{Et}_4\text{N}]3$. Anal. Calcd for $(\text{C}_{10}\text{H}_{31}\text{B}_{11}\text{N}_2)$: C, 40.27; H, 10.48; N, 9.39. Found: C, 39.83; H, 10.58; N, 9.27. ESI-MS for **3** (m/z , isotopic abundance >50): 167 (75), 168 (100), 169 (84) [calcd for $\text{C}_2\text{B}_{11}\text{H}_{10}\text{N}^-$ (**3**): 167 (74), 168 (100), 169 (82)].

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(27) Characterization for $[\text{Et}_4\text{N}]6$. ^{11}B NMR (acetone, ppm): δ -11.78 [s, 1B, B12], -12.31 [d, 4B, B2–6], -15.83 [d, 5B, B8–11], -17.51 [s, 1B, B7]. MS (m/z , isotopic abundance >50): 192 (68), 193 (100), 194 (70) [calcd for $\text{C}_3\text{B}_{10}\text{H}_{10}\text{N}_2$] (**6**): 192 (74), 193 (100), 194 (82)]. Anal. Calcd for $\text{C}_{11}\text{H}_{30}\text{B}_{11}\text{N}_3$: C, 40.87; H, 9.35; N, 12.99. Found: C, 39.87; H, 9.08; N, 12.66.

(28) Characterization for $[\text{Et}_4\text{N}]7$. MS (m/z , isotopic abundance >50): 186 (73), 187 (100), 188 (83) [calcd for $\text{C}_2\text{B}_{11}\text{H}_{13}\text{NO}^-$ (**7**): 185 (74), 186 (100), 187 (82)]. Anal. Calcd for $\text{C}_{10}\text{H}_{32}\text{B}_{11}\text{NO}_2$: C, 37.85; H, 10.17; N, 4.42. Found: C, 37.59; H, 10.94; N, 4.40.