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High Yielding Preparation of Dicarba-*closo*-dodecaboranes Using a Silver(I) Mediated Dehydrogenative Alkyne-Insertion Reaction

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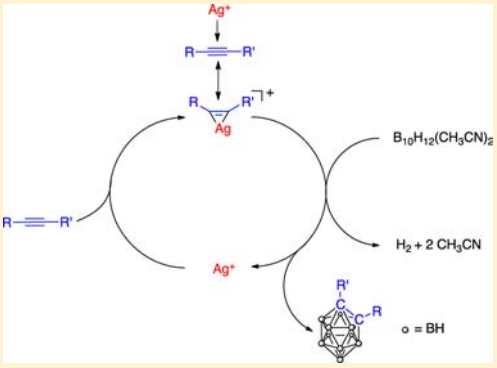
Supporting Information

ABSTRACT: The synthesis of 1,2-dicarba-*closo*-dodecaboranes (*ortho*-carboranes) is often low yielding which is a critical issue given the increasing use of boron clusters in material science and medicinal chemistry. To address this barrier, a series of Cu, Ag, and Au salts were screened to identify compounds that would enhance the yields of *ortho*-caboranes produced when treating alkynes with $B_{10}H_{12}(CH_3CN)_2$. Using a variety of functionalized ligands including mono- and polyfunctional internal and terminal alkynes, significant increases in yield were observed when $AgNO_3$ was used in catalytic amounts. $AgNO_3$ appears to prevent unwanted reduction/hydroboration of the alkyne prior to carborane formation, and the process is compatible with aryl, halo, hydroxy, nitrile, carbamate, and carbonyl functionalized alkynes.



INTRODUCTION

1,2-Dicarba-*closo*-dodecaboranes (*ortho*-carboranes) are polyhedral clusters of boron and carbon atoms that were first reported in the early 1960s.[1] There has been renewed interest in carboranes for both materials[2] and medicinal chemistry applications[3] which exploit the unique architecture and physical and chemical properties of the cluster.[4] Carboranes are being used as hydrophobic pharmacophores for developing new inorganic pharmaceuticals,[5] molecular imaging probes, and radiotherapeutics[6] while for material science applications they offer a platform for creating electronically tunable building blocks.[7]

One of the longstanding challenges associated with carborane chemistry is that the general method used to prepare them often produces products in modest to very low yield. Traditionally, carboranes are made by combining decaborane ($B_{10}H_{14}$) with a Lewis base such as acetonitrile or dialkylsulfides to create a reactive complex ($B_{10}H_{12}L_2$) (Figure 1a)[8] which is then treated with an alkyne to give the desired product. Yields of carboranes prepared in this manner vary significantly and can produce complex mixtures particularly for hindered alkynes which require lengthy reaction times (24−48 h) and elevated temperatures.[1,9] An alternative route is to functionalize *ortho*-carborane directly. However, this approach requires a strong base where the resulting anion is hindered, necessitating the use of reactive electrophiles to produce products in acceptable yield.[10]

Sneddon and co-workers recently introduced an alternative strategy for the preparation of carboranes where enhanced yields and shorter reaction times were observed.[11] The method

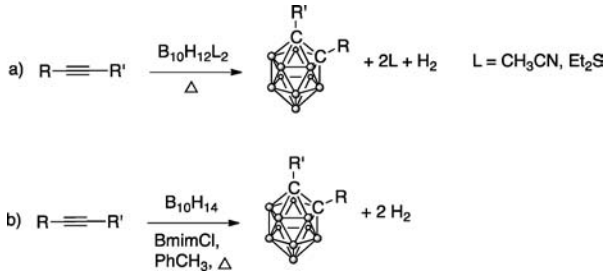


Figure 1. Methods for the preparation of 1,2-dicarba-*closo*-dodecaboranes.

utilizes ionic liquids (Figure 1b) and decaborane, which was successful in increasing yields for reactions involving terminal and internal alkynes where products could be produced in under an hour. The most effective method employed a catalytic amount of the ionic liquid 1-butyl-3-methyl-imidazolium chloride (bmimCl) in toluene.

It has been reported that the yields of carboranes from less basic acetylenes such as propargyl bromide are generally greater than those from more basic acetylenes.[12] This is somewhat counterintuitive since less basic acetylenes introduce higher activation enthalpies. The observed difference in yield is believed to be due to the fact that less basic alkynes do not readily undergo degradative hydroboration reactions which compete with carborane formation. We hypothesized that it may be possible to enhance carborane formation using

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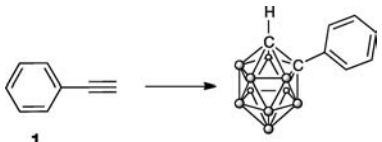
transition metals to mediate the basicity of alkynes thereby preventing premature degradation. To test this concept, a screening study was initiated using Lewis acids including a library of group 11(1B) metal salts that are known to coordinate to alkynes.[13] From this study we found that silver(I) significantly enhanced the yield of carboranes derived from both terminal and internal alkynes.

RESULTS AND DISCUSSION

Coinage metals have long been used to moderate the activity of alkynes.[14] Consequently, using phenyl acetylene as a model system, a series of simple Lewis acids focusing mainly on Au(III), Ag(I), and Cu(I) were screened for their ability to promote carborane formation (Table 1). Initially, reactions

Table 1. Conditions, Reagents, and Results from Lewis Acid Screening Experiments[a]



1 2

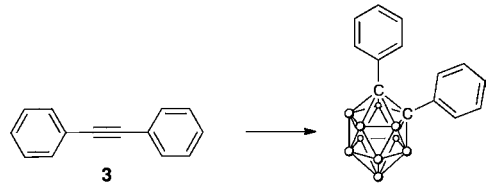
entry	Lewis acid	solvent	temp (°C)	time	yield (%)
1	$AuCl_3$	DCM	25	16 h	65
2	$AuCl_3$	toluene	40	16 h	77
3	AgOTf	DCM	25	4 days	55
4	AgCl	DCM	25	4 days	57
5	CuCl	DCM	25	2 days	80
6	CuCl	toluene	45	16 h	67
7	$AlCl_3$	DCM	25	2 days	70
8	$AlCl_3$	toluene	45	16 h	70
9	CuI	DCM	25	2 days	55
10	CuI	toluene	45	16 h	73
11	CuBr	DCM	50	16 h	70
12	CuBr	toluene	50	16 h	74
13	AgI	DCM	40	2 days	56
14	$AgNO_3$	DCM	50	16 h	80
15	$AgNO_3$	toluene	50	16 h	76
16	$AgSbF_6$	DCM	25	16h	58
17	$AgSbF_6$	toluene	50	16 h	43
18	$PdCl_2$	DCM	25	16h	42
19	$AgSbF_6/AuCl_3$	toluene	50	16 h	84
20	$AgSbF_6/AuCl_3$	DCM	25	16 h	56
21	$AgNO_3$, 2 equiv	toluene	100	1.5 h	80
22	$AgNO_3$	toluene	100	16 h	93
23	$AgNO_3$	toluene	100	16 h	93
24	$AgNO_3$	toluene	100	16 h	92
av/std	$AgNO_3$	toluene	100	16 h	93 ± 1
	no Lewis acid	toluene	120	10 h	65−68
	(Bmim)Cl	toluene	120	7 min	71

[a]Reactions were performed using a 2:1 mol ratio of phenylacetylene to $B_{10}H_{12}(CH_3CN)_2$ and 4 mol % of the Lewis acid with respect to the amount of the alkyne. The grey spheres represent B−H vertices.

were performed in dichloromethane or toluene between room temperature and 50 °C using 4 mol % of the Lewis acid with respect to the amount of alkyne. As a control, reactions with $B_{10}H_{12}(CH_3CN)_2$ alone were run under identical conditions. Initial results showed increased yield for $AuCl_3$, CuCl, and $AgNO_3$ both in dichloromethane and toluene. A mixed catalyst system consisting of $AgSbF_6/AuCl_3$ in toluene also demonstrated improved yield over the uncatalyzed reaction. As a comparison, reactions involving $PdCl_2$ and $AlCl_3$, which are both reported to activate alkynes,[15] were also run. The reaction with Pd(II) showed no improvement in yield while the reaction with $AlCl_3$ increased the yield; however, isolation of the product was not trivial and required extensive chromatography.

The Lewis acid and conditions which showed positive impact with phenylacetylene were applied to the internal alkyne diphenylacetylene (Table 2) in a second series of screening

Table 2. Lewis Acid Screening Studies for an Internal Alkyne[a]



3 4

entry	Lewis acid	solvent	temp (°C)	time	yield (%)
1	$AgSbF_6/AuCl_3$	toluene	50	16 h	40
2	CuCl	DCM	25	16 h	45
3	$AgNO_3$	DCM	25	16 h	47
4	$AgNO_3$, 2 equiv	toluene	100	5 h	80
5	$AgNO_3$	toluene	100	16 h	82
6	$AgNO_3$	toluene	100	16 h	83
7	$AgNO_3$	toluene	100	16 h	80
8	$AgNO_3$	toluene	100	16 h	81
9	$AgNO_3$	toluene	100	16 h	83
av/std	$AgNO_3$	toluene	100	16 h	81 ± 2
	no Lewis acid	toluene	120	16 h	41
	(Bmim)Cl	toluene	120	2 h	34

[a]Reactions involved a 2:1 ratio of diphenylacetylene and $B_{10}H_{12}(CH_3CN)_2$ and 4 mol % of the Lewis acid compared to the amount of the alkyne. The grey spheres represent B−H vertices.

tests. Without Lewis acid, the yield of 1,2-diphenylcarborane was 41%. When silver nitrate was combined with diphenylacetylene and $B_{10}H_{12}(CH_3CN)_2$ and the reaction heated for 16 h, the yield nearly doubled. This increase is significant considering that hindered and internal alkynes typically produce clusters in low yield but are nonetheless important for the formation of boron-based bioactive compounds, radiopharmaceuticals, and BNCT agents.[4d,16]

Further optimization focused on the silver nitrate system because of the positive initial results and the availability, solubility, and low-cost of the reagent. With phenylacetylene, the reaction conditions were varied, and it was noted that when the temperature was increased to 100 °C and reaction time extended to 16 h, the isolated yield of **2** increased to 93%. This exceeded both the yield with no Lewis acid (65−68%) and the reaction run in ionic liquid (71%). There was no evidence of residual silver in the product, and the ^{11}B NMR and MS data confirmed that the product was the *closo*- and not the corresponding *nido*-carborane.

The silver mediated reaction was subsequently applied to a series of functionalized alkynes that can be used to build up an array of carborane-derived materials (Table 3). All reactions were performed in triplicate and repeated independently by different members of the laboratory to assess the consistency of the methodology.

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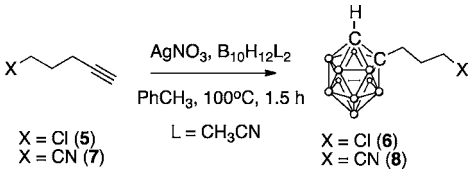
Table 3. Comparison of Conventional, Silver Nitrate Mediated, and Ionic Liquid Reactions for the Preparation of a Variety of Carborane Derivatives[a]

	yield (%)		
compd	conventional method	Ag method	ionic liquid
2	52[25a]/279	93 ± 1	71[11c]
4	41	81 ± 2	34
6	62[27]	77 ± 1	
8	74[28]	84 ± 2	65[11c]
10	67	88 ± 1	
12	90[29]	89 ± 7	
14	50	84 ± 4	
16	40, 59[17]	84 ± 3	55[23]
18	4	52 ± 6	35[32]
22	10	59 ± 4	25

[a]Select reactions were performed in head-to-head comparisons while others were compared to literature yields. Reaction conditions and ratios of reagents can be found in the Experimental Section and Supporting Information.

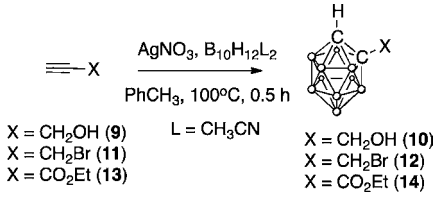
The yield of **6** prepared from 5-chloropentyne (Scheme 1) increased by 15% over that from the conventional synthesis

Scheme 1



method where the yield reached a maximum in 2 h rather than 16 h observed for the arylacetylene derivatives. This same trend was also observed for 5-hexynenitrile where without the addition of silver nitrate, the preparation of **8** required five days to achieve 70% yield. One concern was that $AgNO_3$ at the elevated reaction temperature might cause degradation of the nitrile. The melting point of the isolated product was 81−82 °C, and a CN stretch was observed in the IR (2250 cm^{-1}) which matched the associated literature values while the ^{13}C NMR showed a peak at 118.07 ppm which corresponded to the chemical shift for the nitrile group observed in the spectrum of an authentic standard of **8**. The $AgNO_3$ method also worked effectively with propargyl alcohol (Scheme 2) where the yield

Scheme 2



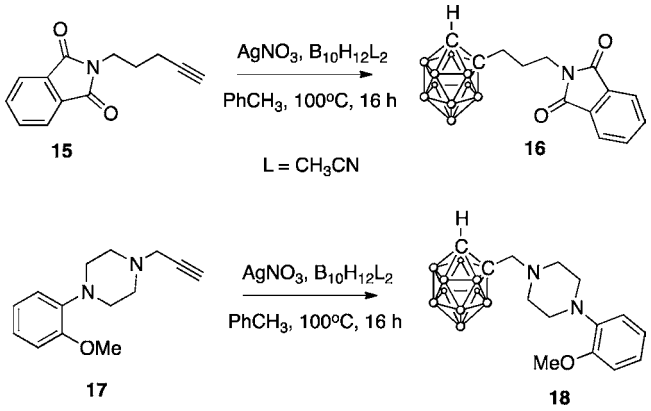
of **10** increased by 21% for the same reaction with no Lewis acid (88% versus 67%). The literature method for preparing **10** generally involved the use of a protected (acetylated) propargyl alcohol prior to carborane formation, thus requiring a subsequent deprotection step. With $AgNO_3$ present, it was possible to prepare the product in a single step in high yield using a facile purification method. The melting point, NMR, and MS data of the isolated product were consistent with literature values.

The preparation of the carborane **12** from propargyl bromide in the presence of $AgNO_3$ produced the desired compound in 89% yield which is comparable to yields following the conventional method; however, the reaction was complete in one-quarter the amount of time (30 min versus 2 h). The reaction with propargyl bromide was one of the few examples that had a large standard deviation in yield (89 ± 7). We believe this to be due to the reactivity of the starting material toward moisture as opposed to variability in the silver mediated reaction, which was not observed for other alkynes. All characterization data for the isolated product matched that in the literature, and there was no evidence of hydrolysis or reduction of **12**; reactions which could potentially be promoted by $AgNO_3$. This is consistent with the chloropentyne derivative **6** which was also stable and showed no signs of silver halide formation under the reported conditions.

Carborane carboxylic acid derivatives are useful synthons for a variety of applications including the preparation of inorganic analogues of pharmaceuticals.[5c,18] The ethyl ester **14** was successfully prepared from ethyl propiolate in greater than 80% yield in 30 min which was a similar time employed for the hydroxymethyl and bromomethyl derivatives **10** and **12**. There was no evidence of hydrolysis or decarboxylation based on the mass spectrum of the product. The presence of a unique triplet and quartet in the ^1H NMR and a peak at 161.04 ppm in the ^{13}C NMR spectrum confirmed the presence of the ester.

Focus shifted to alkynes which in our hands produced carboranes in very low yield (Scheme 3). *N*-Pentylphthalimide

Scheme 3



15 is a useful precursor for the preparation of hetero-difunctionalized carborane derivatives. Under standard conditions the yield of **16** was 40% in our hands, and the reaction mixture contained multiple impurities which made purification challenging. With $AgNO_3$, the reaction yield was greater than 80%, and purification was achieved by simple silica gel chromatography with a single solvent mixture. A second challenging construct was the alkyne **17** derived from phenyl piperazine. Metal complexes of this class of compounds have shown high affinity for α-adrenergic receptors; however, preparation of the ligand is hampered by low yield of the carborane. Without $AgNO_3$, the yield of **18** was 4% after 24 h while with the ionic liquid method the yield was 35%. With $AgNO_3$, the yield increased further to 52%.

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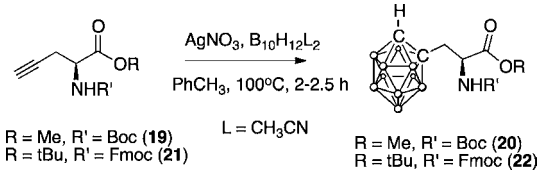
Carborane amino acid derivatives[19] are particularly useful for the preparation of high affinity and metabolically resistant peptides[3b] but can be difficult to synthesize in high yield. Amino acid analogues like **20** and **22** (Scheme 4) which have

Scheme 4



orthogonal protecting groups can be used to prepare carborane derived peptides via solid-phase synthesis. Using the conventional synthetic approach, compound **22** was isolated in less than 10% yield. When $AgNO_3$ was used the yields remained poor; however, when the amount of Lewis acid was increased 2-fold, the yield of **22** rose to nearly 60% and isolation of the product from impurities was much simpler. ^{11}B NMR of the products showed a typical pattern for substituted *ortho*-carboranes, and there was no evidence of *nido*-carborane formation. The MS spectra were consistent with the desired products and show no evidence of silver being coordinated to the ligands which was an initial concern given the potential to form a coordination complex with the amino acid.

In general, the silver mediated reaction works effectively using an excess of $B_{10}H_{12}(CH_3CN)_2$ or the alkyne. The ratio selected for each reaction, which was typically 2:1 alkyne:decaborane, was based on the one that required the simplest purification protocol, which largely depended on the R_f of the alkyne compared to that for the product. Reaction times varied from 30 min to 16 h, and all reactions could easily be followed by TLC. It should also be noted that when the reaction scale for compounds **4** and **6** was increased by an order of magnitude, the observed yields increased further (see Supporting Information).

Having identified significant benefit to adding $AgNO_3$, attention shifted to proposing a possible reaction pathway and potential basis for the observed yield enhancements. Hill et al. demonstrated that the rate-determining step in carborane formation is the addition of the alkyne to $B_{10}H_{12}L_2$.[20] A competing reaction is hydroboration of the alkyne, which prevents carborane formation. Strongly basic alkynes are more susceptible to this side reaction (and related processes associated with alkyne degradation); consequently, inhibiting the pathway by moderating the reactivity of the alkyne would lead to increased yield of the desired carborane products.

Under the current reaction conditions, which do not involve the addition of base, the silver likely forms an intermediate π-complex (Figure 2),[21] decreasing Lewis basicity of the alkyne, thereby preventing the unwanted hydroboration and related alkyne degradation pathways. Following formation of the carborane, which does not readily coordinate the metal, the silver is liberated to coordinate to another alkyne, hence the need to use only catalytic amounts of the metal. As an initial probe of the reaction pathway, a mixture of **7** and $AgNO_3$ were combined at room temperature, and a mass spectrum was taken after 5 min at room temperature and periodically after the mixture was heated to 100 °C in toluene. The results showed evidence of the Ag complex of **7** for the room temperature samples and those during the initial heating periods which is in

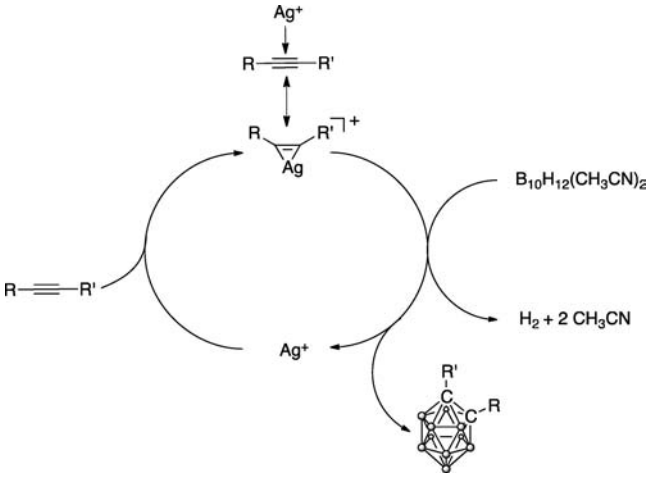


Figure 2. Interaction of Ag(I) with alkynes and a possible pathway for the formation of *ortho*-carborane derivatives.

agreement with the literature for silver(I) interactions with alkynes.[21a] When $B_{10}H_{12}(CH_3CN)_2$ was added the spectra became much more complex, and there was significant overlap with the Ag−alkyne complex. However, there was no evidence of Ag complexes of the boron starting material or Ag−carborane complexes of **8** indicating that the primary interaction is likely between silver(I) and the alkyne. On the basis of the literature and preliminary experimental evidence, rather than simply catalyzing carborane formation, $AgNO_3$ may in fact be preventing unwanted side reactions from occurring leaving the alkyne available to form the desired cluster. Clearly, more detailed theoretical studies will be required to map out changes in activation energy barriers akin to what was elegantly done to probe the mechanism associated with the ionic liquid promoted reactions.[22] In the interim, $AgNO_3$ can be used to enhance the yield of carborane formation where our current focus involves evaluating the methodology with an even broader spectrum of substrates. Studies will include adding various Ag(I) ligand complexes as opposed to the free metal to determine if it is possible to increase yield further while reducing reaction temperatures and times.

■ CONCLUSION

A series of Cu, Ag, and Au salts were evaluated for their ability to enhance the yields of carboranes when added to mixtures of different alkynes and $B_{10}H_{12}(CH_3CN)_2$. Using a variety of functionalized alkynes including mono- and polyfunctional internal and terminal alkynes, significant increases in yield were observed when $AgNO_3$ was used in catalytic amounts. Products were isolated using simple chromatographic methods and structures confirmed spectroscopically and through comparison to authentic standards.

■ EXPERIMENTAL SECTION

General. Unless otherwise stated, all chemical reagents were purchased and used as received from Sigma-Aldrich without further purification. Solvents were purchased from Caledon. Decaborane was purchased and used as received from Katchem (Czech Republic). H-Pra−OH·HCl and Fmoc-L-Pra−OH were purchased and used as received from Advanced Chemtech. *N*-(4-Pentynyl)phthalimide,[23] Boc-Pra-OMe,[24] and $B_{10}H_{12}(CH_3CN)_2$[8] were synthesized according to literature procedures. Reactions were monitored using Alugram Sil G/UV_{254} thin layer chromatography (TLC) plates. Carborane-containing species were visualized with 0.2% $PdCl_2$ in hydrochloric

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acid (3.0 M) which, upon heating, gave dark brown spots. Column chromatography was accomplished with Silica Gel 60 (EMD Chemical Inc.) or ultrapure silica gel (Silicycle).

^{1}H, ^{13}C, and ^{11}B NMR spectra were recorded on Bruker AV700, AV600, or AV200 spectrometers. ^{1}H chemical shifts are reported in ppm relative to the residual proton signal of the NMR solvents. Coupling constants (J) are reported in Hertz (Hz). The ^{1}H NMR spectra of carboranes typically exhibit a broad signal between 3.00 and −0.75 ppm arising from the protons attached to the boron atoms of the cage, which were not reported separately in the ensuing assignments. ^{13}C chemical shifts are reported in ppm relative to the carbon signal of the NMR solvents. ^{11}B chemical shifts are reported in ppm relative to an external standard of $BF_3{\cdot}Et_2O$. Microwave reactions were performed using a Biotage initiator microwave. Low resolution mass spectra were obtained on a Waters/Micromass GCT-ToF instrument using electron impact ionization or a Waters/Micromass Quattro Ultima spectrometer using electrospray type ionization. High resolution mass spectra were obtained on a Waters/Micromass Q-ToF Ultimaglobal spectrometer. Infrared spectra were obtained on a Bruker Tensor 27 FTIR spectrometer. Optical rotations were obtained using an Atago Polax-2L polarimeter.

General Synthetic Procedure: Lewis Acid Screening (Method A). In a dried 5 mL Emry's microwave vial, the Lewis acid was combined with the alkyne and $B_{10}H_{12}(CH_3CN)_2$ in the indicated amounts. The reaction vessel was sealed and kept under high vacuum for several minutes prior to flushing with Ar. Anhydrous toluene was added, and the resulting reaction mixture was stirred at 100 °C under Ar for the indicated time. After cooling to room temperature the solvent was removed under reduced pressure and the desired product isolated by silica gel chromatography using the solvent system indicated below.

General Synthetic Procedure: Conventional Method (Method B). In a dried 5 mL Emry's microwave vial, $B_{10}H_{12}(CH_3CN)_2$ was combined with the alkyne in the indicated amounts. The reaction vessel was sealed and kept under high vacuum for few minutes prior to flushing with Ar. Dry toluene was added, and the resulting mixture was stirred at 100 °C under Ar for the indicated time. After cooling to room temperature the solvent was removed under reduced pressure, and the desired product was isolated by silica gel chromatography.

General Synthetic Procedure: Ionic Liquid (Method C). In a dried 5 mL Emry's microwave vial, 1-butyl-3-methylimidazolium chloride and decaborane were combined in the indicated amounts. The reaction vessel was sealed and kept under high vacuum for a few minutes prior to flushing with Ar. The alkyne was dissolved in dry toluene and added, and then the mixture was stirred at 100 °C under Ar for the indicated time. After cooling to room temperature the solvent was removed under reduced pressure, and the desired product was isolated by silica gel chromatography.

1-Phenyl-1,2-dicarba-*closo*-dodecaborane (2). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (53 mg, 0.26 mmol) and phenylacetylene (53 mg, 0.52 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. Purification by silica gel chromatography with hexane gave 53 mg (93%) of compound **1** as a white solid. The reaction was repeated three times affording an average yield of 93 ± 1%. Mp: 66−67 °C. HRMS (TOF ES) calcd for $C_8H_{15}B_{10}$: 219.2181. Found: 219.2172 [M^-]. The acquired characterization data was consistent with literature values.[25]

1,2-Diphenyl-1,2-dicarba-*closo*-dodecaborane (4). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (52 mg, 0.26 mmol) and diphenylacetylene (91 mg, 0.51 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. Purification by silica gel chromatography with hexane gave 63 mg (82%) of compound **2** as a white solid. The reaction was repeated three times affording an average yield of 81 ± 2%. Mp: 148−149 °C. HRMS (TOF EI) calcd for $C_{14}H_{20}B_{10}$: 296.2615. Found: 296.2615 [M^+]. The acquired characterization data was consistent with literature values.[1,26]

1-(3-Chloropropyl)-1,2-dicarba-*closo*-dodecaborane (6). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (58 mg, 0.29 mmol) and 5-chloropentyne (58 mg, 0.57 mmol) were combined in the presence of $AgNO_3$ (5 mg, 0.03 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 2 h. The solution was cooled to room temperature, diluted with 10 mL of toluene, and filtered through Celite. The resulting solution was concentrated under reduced pressure and purified by silica gel chromatography (hexane:diethyl ether 5:1, R_f = 0.25), (48 mg, 76%) of compound **4** as a white solid. The reaction was repeated three times affording an average yield of 77 ± 1%. Mp: 50−51 °C. HRMS (EI) calcd for $C_5H_{17}B_{10}Cl$: 222.1949. Found: 222.1950 [M^+]. The acquired characterization data was consistent with literature values.[27]

1-(3-Cyanopropyl)-1,2-dicarba-*closo*-dodecaborane (8). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (50 mg, 0.25 mmol) and 5-hexynenitrile (46 mg, 0.49 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 1.5 h. The solution was cooled to room temperature, diluted with 10 mL of toluene, and filtered through Celite. The resulting solution was concentrated under reduced pressure and purified by silica gel chromatography (3:1 hexane:diethyl ether, R_f = 0.43) (45 mg, 87%) of compound **3** as a white solid. The reaction was repeated three times affording an average yield of 84 ± 2%. Mp: 81−82 °C. HRMS (TOF EI) calcd for $C_6H_{17}B_{10}N$: 213.2303. Found: 213.2434 [M^+]. The acquired characterization data was consistent with literature values.[28]

1-(Hydroxymethyl)-1,2-dicarba-*closo*-dodecaborane (10).[29] *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (300 mg, 1.48 mmol) and propargyl alcohol (42 mg, 0.75 mmol) were combined in the presence of $AgNO_3$ (12 mg, 0.07 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 0.5 h. The solution was cooled to room temperature, diluted with 10 mL of toluene, and filtered through Celite. The resulting solution was concentrated under reduced pressure and purified by silica gel chromatography (hexane:ethyl acetate 8:1, R_f = 0.30) and gave 112 mg (0.64 mmol, 86%) of compound **7** as a white solid. The reaction was repeated three times affording an average yield of 88 ± 1%. Mp: 230−232 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.10 (s, 2H, CH_2OH), 3.91 (s, 1H, $C_{carborane}H$). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 74.8, 65.1, 57.6. $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$) δ −2.7, −4.9, −9.0, −11.8, −13.2. FTIR (KBr, cm^{-1}): ν 3059, 2959, 2593, 1342. HRMS (TOF EI) calcd for $C_3H_{14}B_{10}O$: 174.2050. Found: 174.2018 [M^+].

Method B. $B_{10}H_{12}(CH_3CN)_2$ (150 mg, 0.74 mmol) and propargyl alcohol (83 mg, 1.48 mmol) were combined in 3 mL of anhydrous toluene and heated at 100 °C for 2 h. Purification by silica gel chromatography with diethyl ether gave 86 mg (0.49 mmol, 66%) of compound **7** as a white solid.

1-(Bromomethyl)-1,2-dicarba-*closo*-dodecaborane (12)..[9,30] *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (55 mg, 0.27 mmol) and propargyl bromide (80 wt % in toluene, 76 mg, 0.52 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 0.5 h. The solution was cooled to room temperature, diluted with 10 mL of toluene, and filtered through Celite. The resulting solution was concentrated under reduced pressure, purified by silica gel chromatography (hexane, R_f = 0.25), and gave 61 mg (0.26 mmol, 96%) of compound **8** as a white solid. The reaction was repeated three times affording an average yield of 89 ± 7%. Mp: 30−31 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.01 (s, 1H, $C_{carborane}H$), 3.97 (s, 2H, CH_2Br). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 71.2, 61.0, 32.2. $^{11}B\{^{1}H\}$ NMR (192 MHz, $CDCl_3$) δ −2.4, −5.0, −8.6, −10.5, −12.4, −12.9. FTIR (neat, cm^{-1}): ν 3067, 2616, 1429. HRMS (TOF EI) calcd for $C_3H_{13}B_{10}Br$: 237.1191. Found: 237.1185 [M^+].

Ethyl(1,2-dicarba-*closo*-dodecaborane)-1-carboxylate (14).[31] *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (162 mg, 0.80 mmol) and ethyl propriolate (39 mg, 0.40 mmol) were combined in the presence of $AgNO_3$ (7 mg, 0.04 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 0.5 h. Purification by silica gel chromatography with diethyl ether gave 64 mg (0.30 mmol, 74%) of compound **9** as a white solid. The reaction was repeated three times affording an average yield of 84 ± 4%. Mp: 54−56 °C. ^{1}H NMR (600 MHz, $CDCl_3$) δ 4.29 (q, 2H, J = 6.0 Hz, CH_2CH_3), 4.08 (s, 1H, $C_{carborane}H$), 1.32 (t, 3H, CH_2CH_3). $^{13}C\{^{1}H\}$ NMR (150 MHz, $CDCl_3$) δ 161.0, 69.0, 64.9,

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56.9, 13.8. $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$) δ −2.6, −8.9, −12.0, −13.6. FTIR (KBr, cm^{-1}): ν 3079, 2603, 2582, 1743. HRMS (TOF EI) calcd for $C_5H_{16}B_{10}O_2$: 216.2156. Found: 216.2198 $[M^+]$.

1-(3-Phthalimidopropyl)-1,2-dicarba-*closo*-dodecaborane (16). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (51 mg, 0.25 mmol) and *N*-(4-pentynyl)phthalimide (107 mg, 0.50 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. Purification by recrystallization (slow evaporation of hexane−dichloromethane at room temperature) gave 71 mg (85%) of compound **5** as a white solid (hexane:ethyl acetate 1:1, R_f = 0.46). The reaction was repeated three times affording an average yield of 84 ± 3%. Mp: 120−122 °C. HRMS (TOF EI) calcd for $C_{13}H_{21}B_{10}NO_2$: 333.2525; Found: 333.2649 $[M^+]$. The acquired characterization data was consistent with literature values.[23]

1-[(4-(2-Methoxyphenyl)piperazin-1-yl)methyl]-1,2-dicarba-*closo*-dodecaborane (18). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (52 mg, 0.26 mmol) and 1-(2-methoxyphenyl)-4-(prop-2-ynyl)piperazine (118 mg, 0.52 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. The solution was cooled to room temperature, diluted with 10 mL of toluene, and filtered through Celite. The resulting solution was concentrated under reduced pressure, purified by silica gel chromatography (hexane:dichloromethane 4:1, R_f = 0.29), and gave 52 mg (0.15 mmol, 58%) of compound **6** as a white solid. The reaction was repeated three times affording an average yield of 52 ± 6%. Mp: 133−135 °C. HRMS (TOF CI) calcd for $C_{14}H_{28}B_{10}N_2O$: 348.3212, Found: 348.3200 $[M^+]$. The acquired characterization data was consistent with literature values.[32]

Boc-L-Carb-OMe (20).[33] *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (100 mg, 0.50 mmol) and Boc-Pra-OMe (56 mg, 0.25 mmol) were combined in the presence of $AgNO_3$ (4 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 2.5 h. Purification by silica gel chromatography (ethyl acetate:hexane; 1:3; R_f = 0.37) gave 50 mg (58%) of compound **10** as a white solid. The reaction was repeated three times affording an average yield of 60 ± 4%. Mp: 129−130 °C. $[\alpha]^{26}$ −14°. ^1H NMR (600 MHz, $CDCl_3$) δ 5.02 (bs, 1H, N*H*), 4.28 (bs, 1H, CH_2CHNH), 3.99 (bs, 1H, $C_{carborane}H$), 3.77 (s, 3H, OCH_3), 2.93 (dd, 1H, J = 6 Hz, J = 18 Hz, CH_2CHNH), 2.61 (m, 1H, CH_2CHNH), 1.45 (s, 9H, $(CH_3)_3$). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 170.8, 155.1, 81.2, 71.7, 60.6, 53.1, 39.6, 28.2. $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$) δ −2.2, −5.0, −9.0, −10.4, −11.1, 12.9. FTIR (KBr, cm^{-1}): ν 3360, 3216, 3057, 2580, 1738, 1703. HRMS (TOF ES) calcd for $C_{11}H_{27}B_{10}NO_4Na$: 368.2847. Found: 368.2847 $[M + Na]^+$.

Method B. $B_{10}H_{12}(CH_3CN)_2$ (150 mg, 0.75 mmol) and Boc-Pra-OMe (252 mg, 1.11 mmol) were combined in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. Purification by silica gel chromatography (ethyl acetate:hexane; 3:1) gave 98 mg (0.28 mmol, 38%) of compound **10** as a white solid.

Method C. $B_{10}H_{14}$ (61 mg, 0.50 mmol) and 1-butyl-3-methylimidazolium chloride (50 mg, 0.29 mmol) were combined, and Boc-Pra-OMe (228 mg, 1.00 mmol) dissolved in anhydrous toluene (3 mL) was added. The resulting mixture was heated at 100 °C for 2 h. Purification by silica gel chromatography (ethyl acetate:hexane; 3:1) gave 60 mg (0.17 mmol, 35%) of compound **10** as a white solid.

Fmoc-L-Pra-O*t*-butyl (21). Following a literature procedure,[34] Fmoc-L-propargylglycine (2.00 g, 5.96 mmol) and *tert*-butyl 2,2,2-trichloroacetimidate (5.40 g, 24.7 mmol) were combined in a 50 mL round-bottom flask and dissolved in a mixture of anhydrous dichloromethane and tetrahydrofuran (4:1 v/v, 50 mL). The resulting mixture was stirred at room temperature overnight under argon. The solvent was subsequently evaporated under reduced pressure, the residue dissolved in ethyl acetate (50 mL) and the solution extracted with 10% sodium bicarbonate (2 × 100 mL), brine (1× 100 mL), and water (1× 100 mL). The organic layer was dried using sodium sulfate and evaporated under reduced pressure. The desired product was isolated by silica gel chromatography (hexane:ethyl acetate; 3:1) affording **1a** (1.53 g, 65%) as a white solid. Mp: 57−58 °C. $[\alpha]^{26}$ −6°. ^1H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, 2H, J = 12 Hz, Ar*H*), 7.64 (d, 2H, J = 12 Hz, Ar*H*), 7.41 (m, 2H, Ar*H*), 7.33 (m, 2H, Ar*H*), 5.82 (d, 1H, J = 7.86 Hz, N*H*), 4.48 (m, 1H, NHC*H*CO), 4.41 (m, 1H, C*H*CH_2O), 4.26 (m, 2H, $CHCH_2O$), 2.80 (m, 2H, CH_2CCH), 2.09 (m, 1H, CH_2CCH), 1.53 (s, 9H, CH_3). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 169.4, 155.7, 143.9, 143.8, 141.3, 127.8, 127.1, 125.2, 120.0, 82.8, 78.6, 71.6, 67.2, 52.7, 47.2, 28.0, 23.0. FTIR (KBr, cm^{-1}): ν 3300, 2978, 1717, 1506. HRMS (TOF ES) calcd for $C_{24}H_{25}NO_4Na$: 414.1681. Found: 414.1676 $[M + Na]^+$.

Fmoc-L-Car-O*t*-butyl (22). *Method A.* $B_{10}H_{12}(CH_3CN)_2$ (64 mg, 0.32 mmol) and Fmoc-Pra-O*t*Butyl (62 mg, 0.16 mmol) were combined in the presence of $AgNO_3$ (3 mg, 0.02 mmol) in anhydrous toluene (3 mL) and heated at 100 °C for 2 h. Purification by silica gel chromatography (ethyl acetate:hexane; 1:2; R_f = 0.65) gave 47 mg (59%) of compound **11** as a white solid. The reaction was repeated three times affording an average yield of 59 ± 4%. Mp: 93−95 °C. $[\alpha]^{26}$ −25°. ^1H NMR (600 MHz, $CDCl_3$) δ 7.77 (d, 2H, J = 6 Hz, Ar*H*), 7.58 (d, 2H, J = 6 Hz, Ar*H*), 7.42 (m, 2H, Ar*H*), 7.33 (m, 2H, Ar*H*), 5.23 (bs, 1H, N*H*), 4.50 (m, 1H, $CHCH_2O$), 4.43 (m, 1H, $CHCH_2O$), 4.22 (m, 1H, C*H*CH_2O), 4.21 (m, 1H, NHC*H*CO), 3.90 (s, 1H, $C_{carborane}H$), 2.88 (m, 1H, $C_{carborane}CH_2CHNH$), 2.60 (m, 1H, $C_{carborane}CH_2CHNH$), 1.47 (s, 9H, $(CH_3)_3$). $^{13}C\{^1H\}$ NMR (150 MHz, $CDCl_3$) δ 169.0, 155.7, 143.6, 141.4, 127.9, 127.2, 124.9, 120.1, 83.9, 72.0, 67.2, 60.6, 54.2, 47.1, 39.6, 27.8. $^{11}B\{^1H\}$ NMR (192 MHz, $CDCl_3$) δ −2.06, −5.02, −9.17, −11.06, −12.79. FTIR (KBr, cm^{-1}): ν 3326, 2584, 1716. HRMS (TOF ES) calcd for $C_{24}H_{36}B_{10}NO_4$: 510.3660. Found: 510.3655 $[M + H]^+$.

Method B. $B_{10}H_{12}(CH_3CN)_2$ (50 mg, 0.25 mmol) and Fmoc-Pra-O*t*Butyl (194 mg, 0.50 mmol) were combined in anhydrous toluene (3 mL) and heated at 100 °C for 16 h. Purification by silica gel chromatography (petroleum ether:diethyl ether; 3:2) gave 13 mg (0.03 mmol, 10%) of compound **11** as a white solid.

Method C. $B_{10}H_{14}$ (63 mg, 0.52 mmol) and 1-butyl-3-methylimidazolium chloride (50 mg, 0.29 mmol) were combined, and Fmoc-Pra-O*t*Butyl (405 mg, 1.03 mmol) dissolved in anhydrous toluene (3 mL) was added. The resulting mixture was heated at 100 °C for 16 h. Purification by silica gel chromatography (petroleum ether:diethyl ether; 3:2) gave 65 mg (0.13 mmol, 25%) of compound **11** as a white solid.

MS Reaction Monitoring Experiments. 5-Hexynenitrile (0.5 mmol) was dissolved in toluene, giving a 1 M solution. Silver nitrate (0.5 equiv) was added and the reaction mixture heated to 100 °C, and samples were taken diluted by 1:1000 in MeCN. Spectra were collected in positive mode at select time points. The process was repeated in the presence of 0.5 mmol of $B_{10}H_{12}(CH_3CN)_2$.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^1H, ^{13}C, ^{11}B, IR, and HRMS spectra for reported compounds, additional experimental methods, and tables of reaction yields and conditions. 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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