Activation of Alkynes by a Redox-Active Carboranyl Diphosphine and Formation of Boron-Containing Phosphacycles

Gayathri B. Gage, Amanda L. Humphries, Mark D. Smith, and Dmitry V. Peryshkov

ABSTRACT: In this work, we report the reactivity of the carboranyl diphosphine, 1-PBu$_2$–2-PPr$_2$–C$_{10}$B$_{10}$H$_{12}$, with terminal alkynes, resulting in the formation of boron-containing phosphacycles. The reported system combines the nucleophilic activation of electron-deficient terminal alkynes via electron-rich phosphine groups with the redox behavior of carborane clusters to promote a sequence of metal-free intramolecular B–H bond activation and cyclization, creating an alkenylphosphonium cycle fused with a reduced open nido-carborane cluster.

INTRODUCTION

Icosahedral boron clusters have attracted renewed attention for their potential utilization in several key fields, including medicinal chemistry, ligand design and catalysis, luminescent materials, supramolecular chemistry, and battery electrolytes. These clusters possess remarkable stability due to their unusual electronic structure, which features a high degree of electron delocalization that is often described as 3D aromaticity. Neutral C$_{10}$B$_{10}$H$_{12}$ carborane clusters contain both C–H and B–H vertices, with the C–H bonds being weakly acidic ($p_K_a$ of ortho-C$_{10}$B$_{10}$H$_{12}$ is ca. 23). Thus, carbon vertex derivatization of these molecules largely relies on the deprotonation of cluster C–H bonds with strong bases followed by reactions with organic or inorganic electrophiles. The relative ease of functionalization of carbon vertices results in the library of carborane derivatives being largely dominated by C-substituted clusters. In contrast, the borane B–H bonds are rather strong, with a bond dissociation energy estimated at 118 kcal/mol (comparable to aromatic C–H bonds). The chemistry of these boron vertices shares similarities with arenene chemistry, and the functionalization usually proceeds through electrophilic substitution promoted by Lewis acids or by oxidative addition to electron-rich late transition metal centers. Recently, the development of new transition metal-catalyzed coupling methods has significantly expanded the library of B-substituted carboranyl derivatives. In addition to closo–{C$_{2}$B$_{10}$} cages, there has been a significant progress in the selective B–H bond functionalization for nido–{C$_{2}$B$_{10}$} clusters.

Metal-free bond activation, including organocatalysis, is emerging as a powerful method for the construction of new complex molecules. For example, electron-rich phosphines have been recognized as efficient nucleophilic organocatalysts for the derivatization of electron-deficient alkynes. Recently, the triarylphtosine-catalyzed C-alkenylation of C$_{6}$B$_{9}$H$_{11}$ has been reported by Xie and co-workers (Scheme 1a). A related, intramolecular cyclization of a carborane-supported phosphine with an alkene fragment, resulting in a carborane-fused phosphole, has been reported by Duan and co-workers (Scheme 1b). This group also reported the intermolecular activation of electron-deficient alkynes by carboranyl monophosphines, which resulted in the deprotonation and subsequent derivatization of the remaining carborane C-vertex to form a five-member phosphacycle (Scheme 1c).

In all literature examples, functionalization of the remaining unsubstituted cluster C–H vertex was reported, in some cases, accompanied by deboronation of the cluster and conversion from a closo–{C$_{2}$B$_{10}$} to a nido–{C$_{2}$B$_{10}$} cage.

Recently, we reported an example of metal-free bond activation by the carboranyl diphosphine 1-PBu$_2$–2-PPr$_2$–C$_{10}$B$_{10}$H$_{12}$ (1). This main group element system utilizes two basic phosphine sites and has the ability to cycle through the two-electron redox states of the carborane cluster to afford the ability to both donate electrons through the nucleophilic phosphine groups and accept electrons through cluster opening resulting in a concomitant increase in the C–P bond order.

In our initial communication, we reported the reactivity of the redox-active carboranyl diphosphine system with main group hydrides and alcohols. The closo-carborane cage accepts two electrons and becomes a diatomic nido–{C$_{2}$B$_{10}$} cluster, and the two phosphines convert to phosphonium cations.

Received: August 14, 2022
Published: November 9, 2022
Scheme 1. Reactivity of Carboranyl Phosphines with Alkynes

Previous work:
(a) phosphine-catalyzed cluster C-H bond alkenylation

(b) phosphine-centered cyclization and deboronation

(c) phosphine-centered cluster C-H bond activation, cyclization, and deboronation

This work:
B-H bond activation and alkenylation driven by redox-active carboranyl diphosphine

Overall reactivity may be described as the oxidative addition of the substrate to the whole molecule of 1. In this work, we explored the reactivity of carboranyl diphosphine 1 with alkynes. We found that the synergy between the two electron-rich phosphine groups and the electron-accepting cluster leads to a cascade process, resulting in metal-free cage B−H bond activation and the formation of boron-containing fused phosphole-type zwitterionic cyclic products (Scheme 2).

Scheme 2. Reactivity of 1 with Phenylacetylene (Ar = Ph) and 2-Ethynylpyridine (Ar = 2-Py). Unlabeled Cluster Vertices = BH

RESULTS AND DISCUSSION

Carboranyl diphosphine 1 reacts with one equivalent of phenylacetylene at 70 °C to form a single product in 76% yield. The $^{31}$P($^1$H) nuclear magnetic resonance (NMR) spectrum of the product features two singlets, indicating an open cluster. A single crystal X-ray diffraction study revealed the structure of P(Ph)($^1$Pr$_2$)P(CHCPh)(Bu$_2$)(C$_9$B$_{10}$H$_{10}$) (2) (Figure 1) and confirmed the carborane cage is an open 12-vertex *nido*-cluster, which is reduced by two electrons. The cluster is C$_2$-symmetric, giving rise to two enantiomers of 2 that co-crystallized as a racemate. The P($^1$Pr$_2$) group is protonated, and the P(Bu$_2$) group is converted to an alkynylphosphonium center through the attachment of phenylacetylene. The β-carbon of the alkynylphosphonium forms a bond with the carborane boron atom that was adjacent to the cluster carbon atoms in the parent *closo*-form. Structural metrics of 2 are consistent with a zwitterionic and an alkenylphosphonium structure. When more than one equivalent of phenylacetylene was added to the reaction mixture, the formation of a different single product was observed by *in situ* NMR spectroscopy. Other disubstituted alkynes, such as diphenylacetylene did not react with 1. Alkyl-substituted terminal alkynes, such as 1-hexyne or 1-phenyl-2-trimethylsilylacetylene did not react with 1. Alkyl-substituted terminal alkynes, such as 1-heyne or trimethylsilylacetylene did not react with 1. When more than one equivalent of phenylacetylene was present, the formation of a different single product was observed by *in situ* NMR spectroscopy. The structure of the product was established by single crystal X-ray diffraction study as P(CHCPh)(Ph)$_2$P(Ph)$_2$Bu$_2$(C$_9$B$_{10}$H$_{10}$) (4) (Figure 2). One phenylacetylene molecule was activated analogously to 2, forming a B−C bond with the cluster and completing the five-membered cycle, and an additional alkynyl fragment connected to the P($^1$Pr$_2$) group as a phosphinoalkenyl moiety, with the substituents adopting a trans-orientation around the double bond. The structural metrics of the phosphole-like part of 4 are analogous to those of 2. Compound 4 slowly converts to a cascade process, resulting in metal-free cage B−H bond activation and the formation of boron-containing fused phosphole-type zwitterionic cyclic products (Scheme 2).

Figure 1. Displacement ellipsoid plot (50% probability) of the zwitterionic product P(H)($^1$Pr$_2$)P(CHCPh)(Bu$_2$)(C$_9$B$_{10}$H$_{10}$) (2). Hydrogen atoms of alkyl groups are not shown. Selected distances (Å): C1−C1 = 1.757(2), C2−C2 = 1.763(2), C3−C3 = 1.787(2), C3−C4 = 1.355(2).

Figure 2. One phenylacetylene molecule was activated analogously to 2, forming a B−C bond with the cluster and completing the five-membered cycle, and an additional alkynyl fragment connected to the P($^1$Pr$_2$) group as a phosphinoalkenyl moiety, with the substituents adopting a trans-orientation around the double bond. The structural metrics of the phosphole-like part of 4 are analogous to those of 2. Compound 4 slowly converts to a cascade process, resulting in metal-free cage B−H bond activation and the formation of boron-containing fused phosphole-type zwitterionic cyclic products (Scheme 2).
to 2 upon standing in solution at room temperature, but 2 does not convert to 4 in the presence of additional phenylacetylene (Scheme 2). Analogously, the reaction of 2.1 equiv of 2-ethynylpyridine and 1 at 70 °C produced the product (5), which is isostructural to 4. Like compound 4, compound 5 similarly slowly converts to 3 upon standing in solution, which precluded its isolation in the pure form (ca. 95% purity according to NMR spectroscopy). Nevertheless, we have been able to determine its crystal structure (see the Supporting Information), which is analogous to 4.

Phosphines have been known to attack electron-deficient alkynes, leading to the formation of vinylphosphonium intermediates. Recently, the reaction of carboranyl monoalkynes and acetylenedicarboxylates was reported, wherein the remaining relatively acidic C–H bond of the cluster was deprotonated and a new C–C bond between the alkyne and carborane was formed. Although the outcome of that reaction was complicated by the loss of one boron vertex and the eventual formation of an 11-vertex nido-cluster, the overall transformation is conceptually analogous to the activation of alkynes by electron-rich phosphines for subsequent reactions with nucleophiles. In the case presented herein, the synergy between the redox capability of carborane and the electronically conjugated phosphine groups at each cluster carbon atom was utilized in reactions with electron-deficient alkynes, ultimately leading to the activation of the B–H bond of the cluster. Importantly, the observed reactivity is completely analogous to our recently reported examples of bond-activation of main group hydrides and alcohols by 1, which also led to the formation of zwitterions with two phosphonium centers and a dianionic cluster. The synthesis of 2–5 features regioselective metal-free B–H bond activation with the formation of a direct C–B bond. Notably, the carborane cluster retained all its 12 vertices and was converted to its C2-symmetric nido-form through two-electron reduction.

We propose that the following sequence of steps leads to the observed formation of 2–5 by combining nucleophilic organocatalytic reactivity and the redox behavior of the inorganic cluster (Scheme 3). The first step of this transformation can be considered as phosphate-promoted activation of the alkyne, where the more electron-rich P(Bu)3 group acts as a nucleophile to attack the alkyne, forming the P–C bond and the carbanionic intermediate A. Notably, this regioselectivity with respect to the phosphate groups was observed in all cases. The nucleophilic, geometrically constrained intermediate then attacks the proximal B–H bond of the cluster, forming the C–B bond. The attack occurs at the boron atom that is adjacent to the two carbon atoms, as this is the most electron-deficient B-vertex. We found that the formation of 2 proceeds slightly faster for 4-methoxyphenylacetylene than for phenylacetylene, which is, in turn, significantly faster than 4-fluorophenylacetylene. This behavior may be caused by stronger nucleophilicity of the intermediate A when the alkyne substituent cannot efficiently stabilize the carbanion, thus promoting the attack on the B–H bond of the cluster. The closo-carborane cluster receives two electrons from the B–H bond, oxidizing the formally hydridic (B)H hydrogen atom to a proton, forming the intermediate B. This proton eventually migrates to the remaining basic P(Pr)3 group, forming another phosphonium center. Importantly, when the deuterium-labeled phenylacetylene, PhCCD, was used in the reaction with 1, the P(Pr)3 group in the product 2 contained a P–H instead of a P–D bond. This observation confirms that this proton originates from the cluster B–H bond and not from deprotonation of the alkyne. The ultimate results of these steps are B–H bond activation, formation of two phosphonium cations, and the cluster-opening two-electron reduction of carborane.

In the presence of excess phenylacetylene, the final step of the reaction (protonation of the second phosphate group) is in competition with the nucleophilic attack of the phosphorous atom on the alkyne to form a phosphinoalkenyl moiety instead. This proposed reaction sequence is supported by the fact that the addition of phenylacetylene to 2 does not result in the conversion to 4, an observation which can be explained by the fact that 2 already contains two phosphonium cations, and therefore possesses no nucleophilic centers to activate another equivalent of alkyne. Furthermore, the formation of 4 is facilitated in the presence of an external base (triethylamine), which presumably binds the proton formed in the B–H bond activation. The reverse transformation of 4 to 2 occurs slowly (several weeks), possibly through alkyne elimination from the phosphonium alkynyl fragment, generating free phenylacetylene and a protonated P(Pr)3 group.

The simultaneous presence of two electron-rich phosphate groups on the redox-active carborane cluster is crucial for the observed B–H bond activation and cyclization. If the phosphate group is not attached to the cluster, as in the
Inorganic Chemistry

observed apparent isomerization instead. This peculiar outcome prompted us to estimate the relative stability of isomers 2 and 6. The density function theory calculations, with the PBE0 hybrid functional and TZP basis set revealed that the compound 6 is more stable than 2 by only 0.3 kcal/mol. It is possible that the oxidation of 2 is an initial step of the isomerization transformation.

**CONCLUSIONS**

In summary, we demonstrated the activation of electron-deficient alkynes by a redox-active carborane cluster possessing two electron-rich phosphine groups. The observed transformation is an interplay of the nucleophilic reactivity of phosphines coupled with the electron-accepting ability of the carborane cluster, resulting in B–H bond activation and the formation of phosphine- and boron-containing heterocycles.

**MATERIALS AND METHODS**

All synthetic manipulations, unless stated otherwise, were carried out either in a nitrogen-filled Vacuum Atmospheres (VAC) drybox or on a dual manifold Schlenk-style vacuum line. The solvents were sparged with nitrogen, passed through activated alumina, and stored over activated 4 Å Linde-type molecular sieves. Benzene-d6, CDC13, and CD2Cl2 were degassed and stored over activated 4 Å Linde-type molecular sieves. NMR spectra were recorded using Varian spectrometers at 400 (1H), 100 (13C), and 128 (11B) MHz, reported in δ (parts per million) and referenced to the residual 1H/13C signals of the deuterated solvent or an external BF4(Ph3P)2 (0.0 ppm) standard. J values are given in Hz. Elemental analysis was provided by Midwest Microlab.

(PBu4)2[P(CH2Ph)2] (1) was prepared according to a previously reported literature procedure. Ortho-carborane C2B10H12 (Boron Specialties), n-butylamine solution (n-BuLi, 2.5 M solution in hexane), phenylacetylene, and 2-ethynylpyridine were used as received.

**Synthesis of P(H)(Pr2)[P(CH2Ph)2]B2(H)(C2B10H12) (2).** A portion of 1 (0.050 g, 0.124 mmol) was dissolved in 1 mL of benzene and phenylacetylene (0.014 g, 0.136 mmol, 1.1 equiv) was added. The reaction mixture was stirred for 5 days at 70 °C. The sample was dried under vacuum and washed with hexanes (2 mL × 3) resulting in a light brown solid (yield: 0.047 g, 76%).

31P{1H} NMR (CDCl3): δ 65.0 (s, 1P, (C(CH2)3)3), 34.3 (s, 1P, P(CH(C3H3))2), 45.7 (s, 1P, P(CH(C3H3))2). 31P NMR (CD2Cl2): δ 66.9 (s, 1P, P(CH(C3H3))2). 1H NMR (CDCl3): δ 7.51–7.30 (m, 5H, PhC=CPh), 2.62 (m, 1H, P-(CH2Ph)2), 2.48 (m, 1H, P-(CH2Ph)2), 1.46 (d, 18H, P(CH2CH2)2), 1.39 (m, 12H, P(CH2CH2)2). 11B{1H} NMR (CD2Cl2): δ 26.00 (BH), 22.6 (BH), 21.1 (BH), 1.2 (BH), –8.6 (BC), –9.4 (BH), –16.1 (BH), –17.3 (BH). 13C NMR (CD2Cl2): δ 141.4 (d, JCP = 20 Hz, PhC=CH), 127.9 (s, PCH2), 127.7 (s, PhC=CH), 127.6 (s, PhC=CH), 116.8 (d, JCP = 82 Hz, PhC=CH), 35.8 (d, JCP = 44 Hz, P(CH2CH2)2), 35.8 (d, JCP = 37 Hz, P(CH2CH2)2), 29.0 (s, P(CH2CH2)2). 1H NMR (CDCl3): δ 7.4 (d, JCP = 46 Hz, P(CH2CH2)2), 2.86 (d, JCP = 47 Hz, P(CH2CH2)2). Anal. calcd for C44H38B2P2: C, 65.89; H, 9.55. Found: C, 65.64; H, 9.89.

**Synthesis of P(H)(Pr2)[P(CH2Ph)2]B2(H)(C2B10H12) (3).** A portion of compound 1 (0.050 g, 0.12 mmol) was dissolved in 1 mL of benzene and 2-ethynylpyridine was added (11 μL, 0.11 mmol, 0.9 equiv). The reaction mixture was heated for 4 h at 70 °C. Volatiles were removed under vacuum, and the solid was washed with 5 mL hexanes and 5 mL diethyl ether. The product was extracted with 3 mL DCM and dried under vacuum, yielding an orange/brown solid. Yield: 0.024 g, 42%.
Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.inorgchem.2c02919.

Characterization data (NMR spectra and crystallographic details), displacement ellipsoid plots, and computational method details (PDF)

### Accession Codes

CCDC 2084267 and 2193431–2193444 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 369333.

### AUTHOR INFORMATION

#### Corresponding Author

Dmitry V. Peryshkov — Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States; orcid.org/0000-0002-5653-9502; Email: peryshkov@sc.edu

#### Authors

Gayathri B. Gange — Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States

Amanda L. Humphries — Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States

Mark D. Smith — Department of Chemistry and Biochemistry, University of South Carolina, Columbia, South Carolina 29208, United States

Complete contact information is available at: https://pubs.acs.org/doi/10.1021/acs.inorgchem.2c02919

#### Author Contributions

G.B.G. and A.L.H. contributed to the work equally.

#### Notes

The authors declare no competing financial interest.

### ACKNOWLEDGMENTS

This material is based upon work supported by the National Science Foundation under grants CHE-1654301 and CHE-2154828.

### REFERENCES


(28) Wong, Y. O.; Smith, M. D.; Peryshkov, D. V. Reversible Water Activation Driven by Contraction and Expansion of a 12-Vertex-


