

Improved methods for the halogenation of the $[\text{HCB}_{11}\text{H}_{11}]^-$ anion[†]

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Expedient and economical methods for the synthesis of undeca-halogenated carborane anions have been developed.

The monocarba-*closo*-dodecaborate anion $[\text{HCB}_{11}\text{H}_{11}]^-$ (Fig. 1) and its derivatives $[\text{HCB}_{11}\text{X}_{11}]^-$ (from here on: carborane anions; X = H, Me, Hal) are a potentially very advantageous class of weakly coordinating anions (WCA).^{1,2} While other types of WCA (most common are probably the fluorinated tetraarylborates)³ possess similarly weak basicity and nucleophilicity,⁴ carborane anions are inimitable in their robustness. The combination of these properties uniquely empowers carboranes to sustain both the integrity and the reactivity of even the most potent Lewis or Brønsted acids.^{5–7} The acid $\text{H}[\text{HCB}_{11}\text{Cl}_{11}]$ is the strongest reported Brønsted acid to date, yet it is stable to sublimation at 200 °C.⁸ Carborane anions allowed isolation of discrete salts of vinyl,⁹ *tert*-butyl,¹⁰ and fullerene¹¹ cations. The $\text{Me}[\text{HCB}_{11}\text{Me}_5\text{Br}_6]$ reagent is several orders of magnitude more reactive than methyl triflate.¹² Carborane anions have allowed for solution chemistry of silylium (R_3Si^+) cations^{5,13,14} and even for the isolation of a discrete silylium cation in the solid state.¹⁵ Our interest in carborane anions stems from their matchless performance in silylium- and aluminium-catalyzed¹⁶ C–F activation.¹⁷

In spite of their advantages, carborane anions are still in the process of making the transition “from exotica to specialty chemicals” as formulated by Reed in 1998.² A major obstacle to wider adoption of carborane anions as WCA’s of choice have been the arduous synthetic routes. In this communication, we report dramatically simplified syntheses of undeca-halogenated

carborane anions, arguably the most desirable members of the family because of their highest robustness and least basicity.⁴

Syntheses of fluorinated (or trifluoromethyl-substituted) carboranes require the use of F_2 gas, which involves non-trivial setup and training.^{18,19} Chlorination, bromination, and iodination of carboranes are also accomplished using elemental halogens (or ICl).¹ The heavier halogens are progressively less hazardous, however brominated and especially iodinated carboranes suffer from poor solubility and are more coordinating than their chlorinated analogs. $[\text{HCB}_{11}\text{H}_{11}]^-$ has been described as aromatic in three dimensions.²⁰ Its halogenation has been mechanistically likened to classical electrophilic aromatic substitution and proceeds first at the “*para*” position, followed by the “*meta*” belt, and finally, by the “*ortho*” belt.¹ Hexahalogenation (Cl, Br, I) can be performed selectively.^{2,21} However, successful execution of the hexahalogenation syntheses requires real-time monitoring of the reaction by ^{11}B NMR for hours or days, while, especially in the case of hexachlorination, deviations from the scale and conditions of the optimized procedure often result in loss of selectivity and overhalogenation. Undecachlorination takes place with ICl in triflic acid after several days at > 200 °C.^{8,22} This is a consistently reproducible synthesis, but it requires a \$3000 pressure- and reagent-resistant reactor for a 2 g batch capacity, and a rather extensive workup. Undecabromination has been reported to take place under similarly harsh conditions on a small scale in a sealed tube with Br_2 in triflic acid.²² Undecachlorination of $[\text{MeCB}_{11}\text{H}_{11}]^-$ proceeded under less draconian conditions with Cl_2 in hot glacial acetic acid after a week,²² but it required the extra methylation step which furthermore precludes the potentially attractive subsequent functionalization at the carbon site.

We were interested in developing methods for halogenation that ideally (a) are reproducible and insensitive to minor variations in conditions, *i.e.*, “foolproof”; (b) are scalable; (c) do not require monitoring of the course of the reaction; (d) do not involve elemental halogens, especially Cl_2 gas; (e) proceed under atmospheric pressure and without specialty apparatus; (f) use inexpensive reagents; (g) proceed to completion preferably in one day or less.

We focused our attention on element chlorides that are known to be oxidizing/chlorinating agents and zeroed in on SO_2Cl_2 and SbCl_5 . These reagents are inexpensive,²³ of relatively low toxicity, and are liquids that possess volatility that allows for a respectable reflux temperature but relative ease of removal of the excess of reagent under vacuum. Although SO_2Cl_2 and SbCl_5 are aggressive reagents, they can be handled in the laboratory under standard safety precautions. SO_2Cl_2 has the added advantage of presumably generating only gaseous by-products (SO_2 and HCl). Both

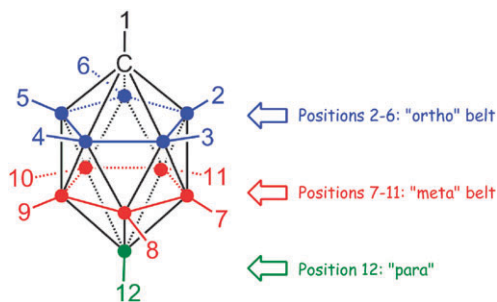
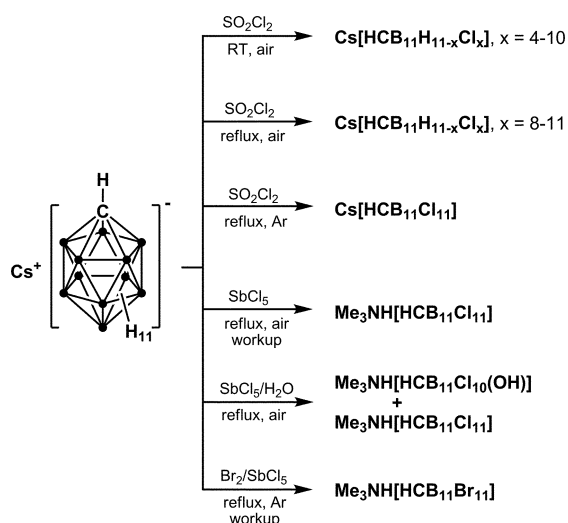


Fig. 1 Representation of the monocarba-*closo*-dodecaborate(–) $[\text{HCB}_{11}\text{H}_{11}]^-$ anion, or carborane (dots at vertices 2–12 represent boron atoms; each vertex is capped with a hydrogen atom).

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[†] Electronic supplementary information (ESI) available: Experimental details, NMR and mass-spectra, as well as the details of the crystallographic study. CCDC 763177 contains crystallographic data for $\text{Ph}_3\text{C}[\text{HCB}_{11}\text{Br}_{11}]$. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c001555e



Scheme 1 New synthetic routes to polyhalogenated carboranes.

SO_2Cl_2 and SbCl_5 have been used for chlorination in organic synthesis, including aromatic chlorination.^{24,25} SbF_5 was also reported to react with *o*-(di)carborane ($1,2\text{-C}_2\text{B}_{10}\text{H}_{12}$) to give partially fluorinated products.²⁶

Direct reaction (Scheme 1) of 1 g $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ with refluxing neat SbCl_5 led to a clean formation of $[\text{HCB}_{11}\text{Cl}_{11}]^-$ in 24 h (negative-ion MALDI-MS evidence)[‡] [Caution: violent reaction ensues upon addition of SbCl_5 to $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$]. After workup, the carborane anion was isolated as a Me_3NH^+ salt in 81% yield. While we have not been able to obtain fully satisfactory elemental analysis data, the NMR data are consistent with those previously reported. MS analysis also showed essentially only the expected $[\text{HCB}_{11}\text{Cl}_{11}]^-$ isotope pattern. Treatment with refluxing SbCl_5 also converts mixtures of partially chlorinated carboranes to $[\text{HCB}_{11}\text{Cl}_{11}]^-$ (MS evidence). The workup in this procedure is complicated by the presence of Sb by-products of low volatility (presumably, SbCl_3), however, they are successfully removed as elemental analysis of the isolated product showed Sb levels below detection limit of 0.17%. Repeats of this procedure on a 5–10 g scale occasionally led to the detection (by MS) of an impurity. We assign the impurity to be $[\text{HCB}_{11}\text{Cl}_{10}(\text{OH})]^-$ based on the observed isotope pattern and on that refluxing of a mixture containing this impurity with $(\text{Me}_3\text{Si})_2\text{NH}$ resulted in the observation of a new MS pattern consistent with $[\text{HCB}_{11}\text{Cl}_{10}(\text{OSiMe}_3)]^-$. The culprit in the hydroxylation is most likely adventitious water—the fraction of this impurity increased dramatically when 5 equiv. of water was added at the beginning of the reaction. $[\text{HCB}_{11}\text{Cl}_{10}(\text{OH})]^-$ can no longer be detected by MS if an isolated mixture is additionally refluxed with SbCl_5 or SO_2Cl_2 .

Treatment of $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ with neat SO_2Cl_2 at ambient temperature for 24 h without preventing contact with air led to a mixture of various partially chlorinated products ($[\text{HCB}_{11}\text{H}_{11-x}\text{Cl}_x]^-$ with $x = 4\text{--}10$ after 24 h). Analysis of aliquots by MALDI-MS during this reaction did not show a single dominant product at any point in the reaction. Heating $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ in SO_2Cl_2 at refluxing temperature for 1 day led to a mixture of mostly octa-, nona-, deca-, and undecachloro-carborane anions $[\text{HCB}_{11}\text{H}_{11-x}\text{Cl}_x]^-$ ($x = 8\text{--}11$), and subsequent

heating for another 4 days led to only minor changes in the composition of the mixture. Performing the reaction in the presence of Lewis acids AlCl_3 or TiCl_4 did not lead to exhaustive chlorination. In contrast, refluxing $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ in SO_2Cl_2 under dry argon for 24 h led to complete conversion to $\text{Cs}[\text{HCB}_{11}\text{Cl}_{11}]$ (MS evidence), which was isolated upon recrystallization from water. We were able to obtain 84–87% yields of $\text{Cs}[\text{HCB}_{11}\text{Cl}_{11}]$ starting with 0.1, 1, or 5 g of $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ and it was characterized by ^1H , ^{11}B , ^{13}C NMR and elemental analysis. This procedure handily satisfies the conditions (a)–(g) we outlined above for an “ideal” protocol.

The retardation of chlorination by SO_2Cl_2 in reactions without argon protection is likely owing to the slow absorption of water from air. Intentional addition of water (2% mol *vs.* SO_2Cl_2 , 3.4 equiv. *vs.* carborane) to the reaction mixture at the start of the reaction severely retarded the chlorination, resulting in no more than quadruple chlorination after 1 d of reflux.

Encouraged by the success in chlorination, we have turned our attention to bromination. Bromine, in general, is a thermodynamically weaker oxidant than chlorine. High oxidation state element bromides that could be conceivable brominating agents are not stable with respect to release of Br_2 either at even room temperature (*e.g.*, SO_2Br_2 or SbBr_5) or at a temperature not too far from the boiling point of Br_2 (*e.g.*, PBr_5). Because of this, solutions for avoiding the use of Br_2 in undecabromination (which clearly requires forcing conditions) were not apparent to us. Nonetheless, we were delighted to discover that treating $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ with Br_2 followed by SbCl_5 and heating at 150°C for only 1 h led to the complete conversion of the anion to $[\text{HCB}_{11}\text{Br}_{11}]^-$ (MS evidence). Upon workup, $\text{Me}_3\text{NH}[\text{HCB}_{11}\text{Br}_{11}]$ was isolated in 77% yield and characterized by ^1H , ^{11}B , ^{13}C NMR, and MALDI MS. The reaction generates a mixture of $[\text{HCB}_{11}\text{HBr}_{10}]$ and $[\text{HCB}_{11}\text{Br}_{11}]$ anions already at room temperature, but short thermolysis is needed to complete the bromination.

We found it important to add Br_2 to $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ first, followed by SbCl_5 . When $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ was treated with a ready mixture of Br_2 and SbCl_5 , formation of the $[\text{HCB}_{11}\text{Br}_{10}\text{Cl}]^-$ impurity along with $[\text{HCB}_{11}\text{Br}_{11}]^-$ was detected by MS. Addition of neat Br_2 to $\text{Cs}[\text{HCB}_{11}\text{H}_{11}]$ results in a violent reaction. The reaction is much more subdued if CH_2Cl_2 is used as solvent for the initial bromination with Br_2 alone. Evidently, it is important to “prebrominate” the more reactive positions in the parent carborane anion to preclude competitive chlorination.

Using the standard cation exchange procedures for carborane salts,^{2,5,7} we obtained the triphenylmethyl salt of $[\text{HCB}_{11}\text{Br}_{11}]^-$ and studied it by single-crystal X-ray diffraction methods.[§] The corresponding ORTEP plot is presented in Fig. 2. The central carbon of the trityl cation (C1) comes closest to one of the Br atoms of the “meta” belt, but the separation is $>3.4\text{ \AA}$. The sum of angles about C1 is essentially 360° . The B–Br distances vary in a narrow range between $1.910(7)$ and $1.950(6)\text{ \AA}$ with the B–Br bond distance to the Br atom closest to C1 (Br5) being an unremarkable $1.938(6)\text{ \AA}$. These data are consistent with the lack of covalent interaction between the ions.

In summary, we report new, straightforward methods for the formation of valuable $[\text{HCB}_{11}\text{Cl}_{11}]^-$ and $[\text{HCB}_{11}\text{Br}_{11}]^-$

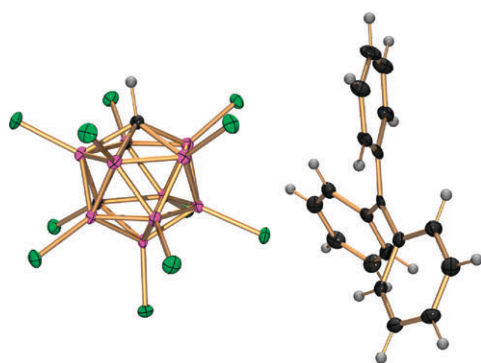


Fig. 2 POV-Ray²⁷ rendition of the ORTEP²⁸ drawing (50% thermal ellipsoids) of $\text{Ph}_3\text{C}[\text{HCB}_{11}\text{Br}_{11}]$ showing selected atom labelling. The toluene solvent molecule is omitted for clarity.

anions. While the involved synthesis or the relatively high cost²⁹ of the requisite parent anion $[\text{HCB}_{11}\text{H}_{11}]^-$ remains an issue, the syntheses we report here make the subsequent halogenation expedient, economical, and readily available to chemists at large without the need for specialized training or equipment.

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Notes and references

† In this work, we have relied on negative-ion MALDI mass-spectrometric analyses to gauge the composition of mixtures of carborane anions. Mass-spectrometry is much more apt at identifying the components of mixtures than ^{11}B NMR or elemental analysis. While MS data here cannot characterize the ratios in a rigorously quantitative fashion, it is reasonable to assume that structurally very similar anions should provide similar response in the mass-spectra. Thus, MS is useful for approximate assessment of compositions but especially for identification of components and detection of small amounts of impurities. For example, ^{11}B NMR or elemental analysis would not allow to detect 5–10% impurity of $[\text{HCB}_{11}\text{HCl}_{10}]^-$ in $[\text{HCB}_{11}\text{Cl}_{11}]^-$ nor would they allow for deconvolution of the composition of mixtures.

§ Crystal data for $\text{Ph}_3\text{C}[\text{HCB}_{11}\text{Br}_{11}]$: $\text{C}_{27}\text{H}_{24}\text{B}_{11}\text{Br}_{11}$, $M = 1346.38$, pale yellow needle, $0.30 \times 0.10 \times 0.10$ mm, monoclinic, space group $P2_1/c$ (No. 14), $a = 13.968(5)$, $b = 21.852(5)$, $c = 13.127(5)$ Å, $\beta = 96.936(5)^\circ$, $V = 3977(2)$ Å³, $Z = 4$, $D_c = 2.248$ g cm⁻³, $F_{000} = 2504$, Bruker APEX-II CCD, MoK α radiation, $\lambda = 0.71069$ Å, $T = 70(2)$ K, $2\theta_{\text{max}} = 50.0^\circ$, 23 031 reflections collected, 6468 unique ($R_{\text{int}} = 0.0457$). Final $\text{Goof} = 1.015$, $R_1 = 0.0350$, $wR_2 = 0.0767$, R indices

based on 4956 reflections with $I > 2\sigma(I)$ (refinement on F^2), 442 parameters, 447 restraints. Lp and absorption corrections applied, $\mu = 11.103$ mm⁻¹.

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