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Syntheses and chemistry of bis- and tris-mercaptoborates*

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Abstract: The preparation and chemistry of bis- and tris-mercaptoborates based on *closo*-B_{12} and *closo*-B_{10} structures is described. These species undergo a number of reactions such as halogenation and alkylation without changing the *closo*-borane core. Addition of the third dimethylsulfide substituent to the *closo*-boranes is thought to proceed via an unusual cationic intermediate.

Keywords: mercaptoborates; polyhedral boranes; synthesis; structures; clusters.

INTRODUCTION

In recent years, we have been developing synthetic routes to bis- and tris-mecaptoborate salts based on *closo*-B_{12} and *closo*-B_{10} structures. Some of the compounds may ultimately have potential for use in boron neutron capture therapy (BNCT) of tumors. Syntheses of the icosahedral B_{12} species start from the monoboron species $BH_3{\cdot}SMe_2$, and proceed via the inner sulfonium salts 1,7-$(SMe_2)_2$-$B_{12}H_{10}$ (and its 1,12- and 1,2-isomers) and the $[B_{12}H_{11}(SMe)_2]^-$ monoanion. This is especially advantageous from the standpoint of ease of potential ^{10}B enrichment for BNCT applications. These species undergo a number of reactions without changing the *closo*-borane core. Reaction with nucleophiles has been shown to produce thioether anions, and reduction by alkali metals in liquid ammonia also produces thioethers. The compounds are also amenable to selective halogenation, providing a simple route into boron–carbon cross-coupling reactions with Grignard reagents.

Reaction of 1,7-$(SMe_2)_2$-$B_{12}H_{10}$ with dimethylsulfoxide (DMSO) in acid solution allows introduction of a third sulfur substituent to the cluster, forming 1,7-$(SMe_2)_2$-9-SMe-$B_{12}H_9$.

The analogous tris-substituted *closo*-decaborate species 1,10-$(SMe_2)_2$-2-SMe-$B_{10}H_7$ is prepared from $[B_{10}H_{10}]^{2-}$. The suggestion that this neutral species was formed via a cationic [1,2,10-$(Me_2S)_3B_{10}H_7]^+$ intermediate is supported by the results of methylation of 1,10-$(SMe_2)_2$-2-SMe-$B_{10}H_7$ by $[Me_3O]^+$ BF_4^-. [1,2,10-$(Me_2S)_3B_{10}H_7]^+$ BF_4^- is isolated from this reaction and has been characterized by X-ray diffraction.

PREPARATION OF $B_{12}H_{10}(SMe_2)_2$ ISOMERS AND $[Me_3S][B_{12}H_{11}(SMe)_2]$

$B_{12}H_{10}(SMe_2)_2$ and the $[B_{12}H_{11}(SMe_2)]^-$ anion have been known for many years, and a number of reasonably high-yield syntheses have been developed [1–5]. However, full spectral and structural characterization of all three possible isomers of the disubstituted neutral complexes as well as the mono-

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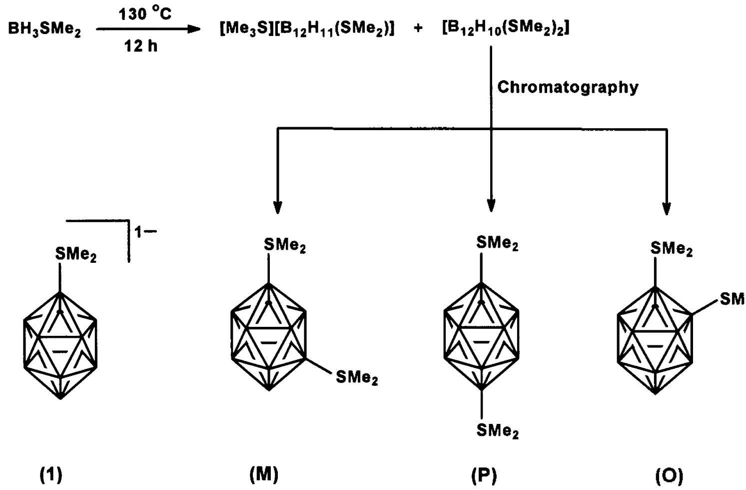
substituted anion has only more recently been performed [6,7]. We have developed a simple, one-step procedure using dimethylsulfide-borane complex, $BH_3{\cdot}SMe_2$, that yields predominantly the neutral disubstituted compound as the 1,7-$(SMe_2)_2$-$B_{12}H_{10}$ isomer, along with smaller quantities of the 1,12- and 1,2-species (Scheme 1).



Scheme 1 Production of inner sulfonium salts of *closo*-dodecaborane via pyrolysis of methylsulfide-borane.

Heating of commercially obtained $BH_3{\cdot}SMe_2$ at 130 °C for several hours in a stainless steel pressure vessel results in a series of condensation reactions to eliminate hydrogen gas and build polyborane species [8]. Our procedure is of significant utility in preparation of pure 1,7-$(SMe_2)_2$-$B_{12}H_{10}$, and also leads to lower-yield or slow syntheses of 1,12-$(SMe_2)_2$-$B_{12}H_{10}$, 1,2-$(SMe_2)_2$-$B_{12}H_{10}$, and $[SMe_3]^+[B_{12}H_{11}(SMe_2)]^-$, and in addition circumvents the need to handle relatively hazardous B_2H_6.

SYNTHESIS OF THIOETHER ANIONS BY REACTION OF SULFONIUM SALTS WITH NUCLEOPHILES AND BY ALKALI METAL REDUCTION

Following isolation and characterization of the inner sulfonium salts $[Me_2SB_{12}H_{11}]^-$ and $(Me_2S)_2$-$B_{12}H_{10}$ above [9], it was decided to study their reactions with nucleophiles to produce thioethers [13]. Soloway et al. [14] previously used potassium phthalimide in dimethylformamide (DMF) to synthesize $[(MeS)(Me_2S)B_{12}H_{10}]^-$ from a mixture of isomers of $(Me_2S)_2B_{12}H_{10}$, and the dianions $[MeSB_{12}H_{11}]^{2-}$ and $[(MeS)_2B_{12}H_{10}]^{2-}$ have also been isolated from the reaction of $[B_{12}H_{12}]^{2-}$ and dimethyl disulfide [3].

The 1,2-, 1,7-, and 1,12-isomers of $B_{12}H_{10}(SMe_2)_2$ (**O**, **M**, and **P**) react with potassium phthalimide in DMF or EtSNa in CH_3CN/EtOH upon reflux, producing the corresponding isomers of $[(MeS)(Me_2S)B_{12}H_{10}]^-$ (**O**$^{1-}$, **M**$^{1-}$, **P**$^{1-}$). If excess of either nucleophile is used, $[Me_2SB_{12}H_{11}]^-$ (**1**) and **O**, **M**, **P** can be converted into dianions $[MeSB_{12}H_{11}]^{2-}$ (**2**) and $[(MeS)_2B_{12}H_{10}]^{2-}$ (**O**$^{2-}$, **M**$^{2-}$, **P**$^{2-}$).

When **1** or **O**, **M**, **P** are treated with an excess of an alkali metal (Na, K) in liquid ammonia at –40 °C, sulfide **2** or bissulfide dianions **O**$^{2-}$, **M**$^{2-}$, **P**$^{2-}$ are obtained cleanly and almost instantly. While both the reaction with nucleophiles and alkali metal reduction methods are useful for the synthesis of dianions **2**, **O**$^{2-}$, **M**$^{2-}$, and **P**$^{2-}$, only the former method is suitable for the synthesis of the mixed sulfide-sulfonium anions **O**$^{1-}$, **M**$^{1-}$, **P**$^{1-}$.

SYNTHESIS OF HALOGENATED BISSULFONIUM-*CLOSO*-DODECABORATES 9-X-1,7-(SMe_2)$_2B_{12}H_9$, 9,10-X_2-1,7-(Me_2S)$_2B_{12}H_8$ AND BORON–CARBON CROSS-COUPLING REACTIONS OF IODIDES WITH GRIGNARD REAGENTS

Construction of carbon–carbon bonds via palladium-catalyzed cross-coupling reactions has become a routine synthetic tool of modern organic synthesis [15]. On the other hand, examples of substitution in carborane and borane clusters based on similar boron–carbon cross-coupling reactions are still relatively scarce [16–22].

Our interest in this methodology has led to the preparation and characterization of halogenated derivatives of 1,2-, 1,7-, and 1,12-(Me_2S)$_2$-$B_{12}H_{10}$ (**O**, **M**, **P**) [23]. Reactions of the resulting iodides with Grignard reagents leads to B-alkyl and -aryl derivatives.

Two series of compounds, 9-X-1,7-(Me_2S)$_2B_{12}H_9$ and 9,10-X_2-1,7-(Me_2S)$_2B_{12}H_8$ (X = Cl, Br, I), have been synthesized from reactions of 1,7-(Me_2S)$_2B_{12}H_{10}$ with various halogenating reagents. Electrophilic substitution in 1,7-(Me_2S)$_2B_{12}H_{10}$ takes place at positions 9 and 10. The X-ray structure of 9-I-1,7-(Me_2S)$_2B_{12}H_9$ is shown in Fig. 1.

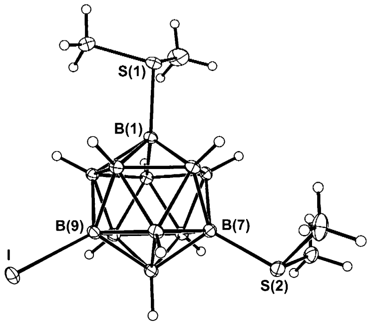


Fig. 1 Structure of 9-I-1,7-(Me_2S)$_2B_{12}H_9$.

In the presence of 5 mol % (PPh_3)$_2PdCl_2$, the iodides 9-I-1,7-(Me_2S)$_2B_{12}H_9$, 2-I-1,12-(Me_2S)$_2B_{12}H_9$, and 9,10-I_2-1,7-(Me_2S)$_2B_{12}H_8$ react with RMgX (R = Me, Ph, Bn; X = Cl, Br) in tetrahydrofuran (THF) to yield the corresponding B-alkyl- and B-aryl-substituted products in good yields without using CuI as a cocatalyst [23]. The molecular structures of 9-R-1,7-(Me_2S)$_2B_{12}H_9$ (R = Ph, Bn) and 2-Bn-1,12-(Me_2S)$_2B_{12}H_9$ have been obtained by single-crystal X-ray analysis. The structure of 9-Bn-1,7-(Me_2S)$_2B_{12}H_9$ is shown in Fig. 2.

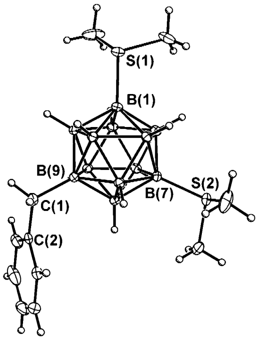


Fig. 2 Structure of 9-Bn-1,7-(Me_2S)$_2B_{12}H_9$.

SYNTHESIS AND CHARACTERIZATION OF 9-(2',4'-$(NO_2)_2C_6H_3S$)-1,7-$(Me_2S)_2B_{12}H_9$ AND 1,7-$(SMe_2)_2$-9-SMe-$B_{12}H_9$

Additional substitution of the icosahedral framework by sulfur-based moieties was the next goal of this work. Muetterties and coworkers [3] reported a low yield preparation of $[(MeS)_3B_{12}H_9]^{2-}$, the first icosahedral *closo*-dodecaborane species bearing 3 exopolyhedral sulfur substituents.

To further explore the possibility of tris-substitution of *closo*-dodecaboranes, the reaction between 1,7-$(Me_2S)_2B_{12}H_{10}$ and 2,4-$(NO_2)_2C_6H_3SCl$ was performed [23]. The chief product obtained was 9-(2',4'-$(NO_2)_2C_6H_3S$)-1,7-$(Me_2S)_2B_{12}H_9$, even when an excess of the sulfur electrophile was used. Its structure is shown in Fig. 3. When an analogous procedure was attempted using the isomeric 1,12-$(Me_2S)_2B_{12}H_{10}$, no reaction was observed.

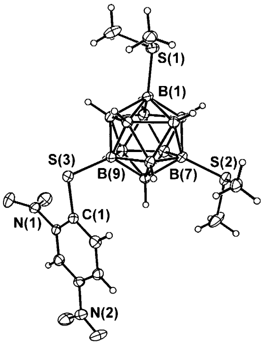


Fig. 3 Structure of 9-(2',4'-$(NO_2)_2C_6H_3S$)-1,7-$(Me_2S)_2B_{12}H_9$.

In related work [24], 1,7-$(Me_2S)_2B_{12}H_{10}$ reacts with DMSO within an hour upon heating in acidic solution. Following aqueous work-up, 1,7-$(Me_2S)_2$-9-(MeS)-$B_{12}H_9$ was isolated. The product was characterized by single-crystal X-ray diffraction, and its structure is shown in Fig. 4.

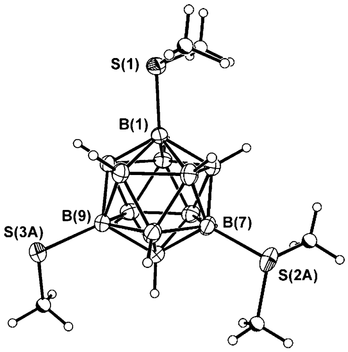


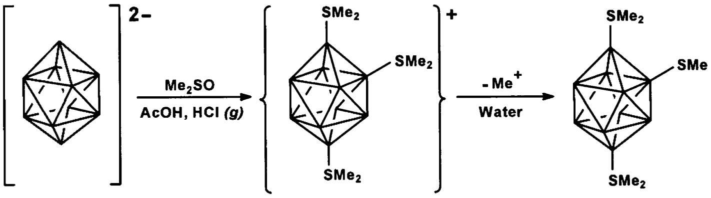
Fig. 4 Structure of 1,7-$(Me_2S)_2$-9-(MeS)-$B_{12}H_9$.

The species appears to be obtained as a result of loss of the methyl cation, $\{Me\}^+$, during the aqueous work-up. The ^{11}B spectrum of the reaction mixture appears to support the presence of the cationic intermediate $[1,7,9\text{-}(Me_2S)_3\text{-}B_{12}H_9]^+$, which has higher (3-fold) symmetry than the isolated neutral product.

IMPROVED SYNTHESIS OF 1,10-$(Me_2S)_2$-2-MeS-$B_{10}H_7$ AND ISOLATION AND X-RAY STRUCTURAL CHARACTERIZATION OF $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$ BF_4^-

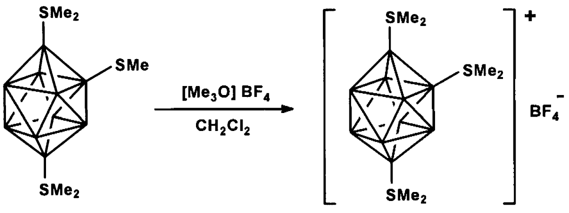
In addition to the disubstituted *closo*-dodecaboranes mentioned above, the related *closo*-decaborane species $(Me_2S)_2B_{10}H_8$ was first synthesized by Muetterties and coworkers in the mid-1960s [10]. A small number of neutral tris-substituted *closo*-B_{10} species exist in the literature, but these feature only two charge-compensated substituents [25]. Consistent with this, our research group previously reported the isolation and characterization of neutral 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$ [26].

This previously reported (14 % yield) synthesis of 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$ in acetic acid relied solely on an initial spike of temperature, which proved difficult to control, given the exothermic nature of the reaction. By extending the reaction time to 3 h, the yield of 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$ was increased to as much as 60 %. NMR evidence suggests that the reaction proceeds via a cationic intermediate, $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$, as illustrated in Scheme 2.



Scheme 2 Suggested mechanism of formation of 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$.

This intermediate cannot be isolated directly, as the equilibrium favors the cation only in acetic acid solution. Addition of water precipitates the neutral species, 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$. In order to isolate the cationic species, a reverse reaction was performed on 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$ using $[Me_3O]^+$ BF_4^- as the methylating agent. This reaction cleanly afforded $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$ BF_4^- (Scheme 3).



Scheme 3 Production of $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$ via methylation of 1,10-$(Me_2S)_2$-2-(MeS)-$B_{10}H_7$.

The $^{11}B\{^1H\}$ NMR spectrum of this species in acetonitrile is identical to that of the acetic acid reaction solution above. In this case, the conditions employed enabled isolation of the cationic tris-substituted cluster. Diffraction quality crystals of the tetrafluoroborate salt were obtained, and the structure of the cation is shown in Fig. 5.

Isolation and characterization of $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$ also lends support to the suggestion of an analogous $[1,7,9\text{-}(Me_2S)_3B_{12}H_9]^+$ intermediate species in the preparation of 1,7-$(Me_2S)_2$-9-$MeSB_{12}H_9$ from 1,7-$(Me_2S)_2B_{12}H_{10}$, above.

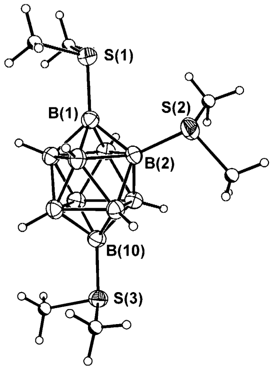


Fig. 5 Structure of the $[1,2,10\text{-}(Me_2S)_3B_{10}H_7]^+$ cation.

CONCLUSION

We have developed a series of simple routes to bis- and tris-substituted *closo* borates with $-SMe_2$ and –SMe substituents, and have investigated some reactions possible at the sulfur atoms, with no disruption of the *closo* architecture. This work is continuing with a view to production of species with potential therapeutic applications.

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8. Dimethylsulfide-borane complex was purchased from Aldrich Chemical Company, Milwaukee, WI, and contains 5–10 % excess dimethylsulfide to stabilize the complex. The reagent was used as supplied.
9. The term "inner- onium salt" was used by Muetterties and Knoth [10,11] for partially or fully charge-compensated [12] *closo*-borane polyhedrons substituted with one or two molecules of a neutral two-electron donor such as R_2S, R_3N, N_2.
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