Article

Insertion of Carbenes into Deprotonated
nido-Undecaborane, B_{11}H_{13}(2-)

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Abstract: We have examined the insertion of carbenes carrying leaving groups into the [nido-B_{11}H_{13}]^{2-} dianion to form the [closo-1-CB_{11}H_{12}]^{-} anion. The best procedure uses CF_{3}SiMe_{3} and LiCl as the source of CF_{2}. It is simple, convenient and scalable and proceeds with 70–90% yield. Density functional calculations have been used to develop a mechanistic proposal that accounts for the different behavior of CF_{2}, requiring only one equivalent of base for successful conversion of Na[nido-B_{11}H_{14}]^{-} to [closo-1-CB_{11}H_{12}]^{-}, and CCl_{2} and CBr_{2}, which require more.

Keywords: carboranes; [closo-1-CB_{11}H_{12}]^{-} anion; difluorocarbene

1. Introduction

The [closo-1-CB_{11}H_{12}]^{-} anion [1] (1) is a member of a broad class of compounds called carboranes [2]. They are derived from three-dimensional polyhedral boron hydrides in which at least at one vertex, a boron atom has been replaced with a carbon atom. These unusual structures are characterized by high thermal and chemical stability attributable to σ-electron delocalization. The monocarba-closo-dodecaborate(−) anion and its derivatives are of special interest as they are one of the most weakly-coordinating anions [3,4] and have a high positive redox potential [5]. The solubility of their salts in water and the possibility of functionalization at boron and carbon vertices make them suitable agents for boron neutron capture therapy [6]. The anion 1 has also been found to be an effective building block for highly polar liquid crystals [7–9] and functionalized carbaborates serve as counterions in ionic liquids [10,11].

Several methods of synthesis of cluster 1 are known and each has its advantages. The first preparation (Scheme 1) was reported by Knoth [12,13] and relied on thermolysis of a salt of the [nido-7-CB_{10}H_{13}]^{-} anion (2). The precursor 2 was generated from decaborane, B_{10}H_{14} (3) by treatment with sodium cyanide to give [arachno-6-CN-B_{10}H_{13}]^{2-} (4), which was then hydrolyzed using HCl to yield [nido-7-H_{2}N-7-CB_{10}H_{12}] (5). The zwitterion 5 was methylated with Me_{2}SO_{4} to give [nido-7-Me_{2}N-7-CB_{10}H_{13}]^{-} (6), which was then deaminated with sodium in liquid ammonia to give 2. Thermolysis yielded a mixture of 1 and [closo-1-CB_{9}H_{10}]^{−} (7). Treatment of 2 with BH_{3}:NEt_{3} also led to the formation of 1.
double boron vertex insertion to yield the desired 1 in 65% overall yield (Scheme 4).

The method was modified and made somewhat safer by Heřmánek [14] (Scheme 2).

The synthesis still starts with decaborane. Only one equivalent of sodium cyanide is required to convert 3 into 4 and HCl is used in place of an ion exchange resin. Further steps include methylation of 5, boron vertex insertion into 6, remethylation of the amino group in 8 and deamination using sodium.

The method developed by Fox and Hughes [15] eliminated the use of the toxic cyanide and took advantage of the facile conversion of 3 to 9 with isocyanides, similar to that with cyanide. Further steps resemble those in Knoth’s and Heřmánek’s methods (Scheme 3).

A more convenient route, which still requires the use of decaborane (3), was developed by Kennedy [16]. In this process, 3 is converted into [arachno-6-CB$_9$H$_{14}$]$^-$ (10), which then undergoes a double boron vertex insertion to yield the desired 1 in 65% overall yield (Scheme 4).
An attempt to use iodoform led only to the oxidation product. (trifluoromethyl)trimethylsilane in our procedure allowed us to work under conditions that are more convenient and we avoid the use of a glove-box and of pressure.

Reactions using the phosphonates were reproducible but poorly scalable. Rh-catalyzed reaction to insertion of dihalocarbenes into 1 resulted in a convenient procedure that affords a nearly quantitative yield. Our results are accompanied by a computational study of the mechanism. The overall yield of the easy two-step preparation of 1 from NaBH4 and BF3·Et2O now is 45–60%, making this desirable anion inexpensively accessible.

Over the years, we have attempted to improve the yield of 1 by varying the nature of the carbene and the reaction conditions extensively. Presently, we report the details of our investigations, which resulted in a convenient procedure that affords a nearly quantitative yield. Our results are accompanied by a computational study of the mechanism. The overall yield of the easy two-step preparation of 1 from NaBH4 and BF3·Et2O now is 45–60%, making this desirable anion inexpensively accessible.

Surprisingly to us, the key to success was to use difluorocarbene. The same discovery was made independently by Leito and collaborators [19], who used a pressure vessel and reported their results earlier this year. The use of an initiator [20,21] for the formation of difluorocarbene from (trifluoromethyl)trimethylsilane in our procedure allowed us to work under conditions that are more convenient and we avoid the use of a glove-box and of pressure.

2. Results

2.1. Synthesis

Our initial extensive attempts to optimize and scale up the previously reported conditions for insertion of dihalocarbenes into 11, using haloforms as the source of dichlorocarbene and dibromocarbene, proved unsuccessful. We turned to diethyl (dichloromethyl)phosphonate and tetraethyl (chloromethylene)bisphosphonate as the carbene source (Table 1, entries 1 and 2). The former was found to be effective in yielding 1 in 65% yield. The latter gave a 50% yield of the desired product, contaminated with significant amounts of the oxidation product, [nido-7-OH-B11H13]−. Reactions using the phosphonates were reproducible but poorly scalable. Rh-catalyzed reaction to generate a carbene from tetraethyl diposphonodiazomethane only resulted in a complex mixture of unidentified products (Table 1, entry 3).
Table 1. Carbene insertion into 11 a.

| Entry | Carbene Source | Solvent | Volume [mL] | Temp [°C] | Yield of 1 [%] |
|-------|----------------|---------|-------------|-----------|---------------|
| 1     | CHCl_3P(O)(OEt)_2 | THF     | 20          | rt        | 65            |
| 2     | CHCl_2[P(O)(OEt)]_2 | THF     | 20          | rt        | 50 b          |
| 3     | CN_2P(O)(OEt)_2 | THF     | 20          | rt        | 0 c           |
| 4     | CCl_3COONa          | Diglyme | 10          | 150       | 0 c           |
| 5     | CF_3COONa            | Diglyme | 10          | 165       | 0 c           |
| 6     | CF_3COOLi            | Diglyme | 10          | 165       | 0 c           |

a Experiments run on 250 mg of [NHMe_3][B_11H_14]; with 2.5 equiv of carbene source. b Combined yield of 1 and [nido-7-OH-B_{11}H_{13}]−. c Boron cluster decomposition.

Attempts to obtain 1 with dichlorocarbene to be generated from sodium trichloroacetate (Table 1, entry 4) or with difluorocarbene, whose generation from sodium chlorodifluoroacetate was sought similarly (Table 1, entries 5 and 6), were unsuccessful. The high temperature required for carbene generation caused cluster decomposition and poor recovery of the starting material. Carefully dried lithium trifluoroacetate also proved not to be a good source of difluorocarbene at temperatures tolerated by the boron cluster.

Attempts using trimethyl(trifluoromethyl)silane as difluorocarbene source and NBu_4Br as the initiator (Table 2, entries 1, 3–5) gave the desired product in high yields but the degree of conversion was poorly reproducible. Further attempts to modify the experimental conditions to yield 1 gave only the starting material or a mixture of the starting material and the desired product (Table 2, entries 2, 6–8). Interestingly, lowering the reaction temperature to 70 °C resulted mostly in the formation of the oxidation product, [nido-7-OH-B_{11}H_{13}]− (Table 2, entry 8).

Table 2. Optimization of the reaction conditions using TMS-CF_3 as the source of carbene a.

| No. | TMS-CF_3 (equiv) | Solvent | Volume [mL] | Initiator [mol%] | Temp [°C] | Yield of 1 [%] |
|-----|-----------------|---------|-------------|------------------|-----------|---------------|
| 1   | 2.5             | DME     | 20          | TBAB [5]         | 85        | 67            |
| 2   | 2.5             | DME     | 10          | TBAB [5]         | 85        | 0 b           |
| 3   | 2.5             | THF     | 20          | TBAB [5]         | 66        | 78            |
| 4   | 2.5             | THF     | 10          | TBAB [5]         | 66        | 75            |
| 5   | 4.0             | DME     | 20          | TBAB [5]         | 85        | 85            |
| 6   | 2.5             | Diglyme | 10          | TBAB [5]         | 120       | 0 b           |
| 7   | 4.0             | DME     | 10          | TBAF [5]         | 85        | 0 b           |
| 8   | 2.5             | DME     | 10          | TBAF [5]         | 70        | 0 c           |

a Experiments run on 250 mg of [NHMe_3][B_{11}H_{14}]. b Starting material was recovered. c [nido-7-OH-B_{11}H_{13}]− was the major product; TBAB = tetrabutylammonium bromide; TBAF = tetrabutylammonium fluoride, 1.0 M in THF.

The addition of various lithium halides as a co-initiator for the reaction of 11 with TMS-CF_3 proved to be successful in making the reaction reproducible. The desired product was obtained in 94% and 78% yield (Table 3, entry 1) using a combination of LiCl and TBAB. Two more runs using the same conditions gave 1 in 78% yield. Interestingly, changing the reaction solvent to 1,2-dimethoxyethane (higher boiling point) appeared to have a significant effect on the reaction outcome. Starting material recovery was poor and cluster decomposition was observed (Table 3 entries 2, 3 and 5). Increasing the volume of THF (Table 3, entry 4), changing the ratio of LiCl to TBAB (Table 3, entry 6) or increasing the number of equivalents of TMS-CF_3 (Table 3, entry 7) did not improve the yield of 1. The product was obtained in 69% yield when higher concentration of the dianion was used (Table 3, entry 6). Lowering the reaction temperature to 60 °C (Table 3, entry 9) also decreased the yield of 1. Replacement of LiCl with LiBr (Table 3, entries 10 and 12) or LiI (Table 3, entry 11) in a combination with TBAB produced 1 in lower yields. The highest reproducible yield, 78%, based on three runs was achieved when TMS-CF_3 (2.5 equiv) was used in the presence of LiCl (15 mol%) as the initiator in refluxing THF (10 mL) (Table 3, entry 14). A combination of LiCl and LiBr (Table 3, entry 13) afforded 1 in a
comparable yield. Doubling the number of equivalents of TMS-CF\(_{3}\) (Table 3, entry 15) did not improve the yield. A simultaneous increase of the amount of TMS-CF\(_{3}\) and the initiator (Table 3, entries 16 and 17) surprisingly gave 1 in lower yields. When lithium bromide was employed as the initiator in place of lithium chloride (Table 3, entry 18), the desired product was afforded in a slightly lower yield (72%). Lowering the reaction temperature by a few degrees and using lithium bromide (Table 3, entry 19) caused a significant decrease in the yield (45%). That result is consistent with lower yields, 54% of 1, when a lower temperature of 50 °C (Table 3, entry 28) was used, or 52% of 1, when the reaction was performed at room temperature (Table 3, entry 29). The latter experiment also required longer stirring time (2 days). Higher loads of the initiator, 50 and 100 mol% of LiBr (Table 3, entries 20 and 21) did not offer any improvement in the yield. Lithium iodide, unlike chloride and bromide, gave rather moderate yields (Table 3, entries 23 and 24) of 1, in two different runs, 62% and 67%, respectively. Lower initiator loads, 5 mol%, (Table 3, entry 25), along with a decrease in the solvent volume to 5 mL (Table 3, entry 27) afforded 1 in much lower yields, 60% and 40%, respectively. This is consistent with the result obtained when the solvent volume was decreased to 5 mL (Table 3, entry 26) and 1 was produced in 56% yield. That suggests that under these conditions, significant cluster decomposition occurs. Surprisingly, the desired product can also be obtained in the absence of an initiator (Table 3, entry 30) but in rather moderate yield (40%). Diglyme was found to be inferior to tetrahydrofuran as the reaction solvent. The cluster 1 was afforded in only 50% yield (Table 3, entry 31) when the reaction was run at 100 °C but only the starting material was recovered when the temperature was lowered to 66 °C (Table 3, entry 32).

Our previous work involving dichlorocarbene generated from chloroform indicated that excess sodium hydride was required for the reaction to proceed. Our new method uses only 3.5 equivalents of NaH. The first equivalent is needed to convert the NMe\(_3\)H\(^+\) salt of 12 to its Na\(^+\) salt and the second is needed to convert 12 to the dianion 11. An excess of NaH, used as insurance against any adventitious moisture or carbon dioxide, is filtered off. In three parallel experiments, run in tetrahydrofuran, 1,2-dimethoxyethane and diglyme, excess sodium hydride (6 equivalents total) was not filtered off. All three experiments produced the product but they required three days to complete (Table 3, entries 33–35). This is consistent with recently published results [19] where excess sodium hydride is used and is not filtered off and the experiments are reported to be complete in nearly 70 h. A larger scale experiment, using 5 g of [NHMe\(_3\)][B\(_{12}\)H\(_{14}\)], gave 1 in 77% yield (Table 3, entry 37), proving that the reaction is scalable.

It appears that contrary to our initial impression, the presence of the lithium cation is not necessary for the reaction to proceed readily. Other halide anion sources were examined as initiators for the generation of difluorocarbene from TMS-CF\(_{3}\). Alkali metal halides and alkaline earth metal halides (Table 4, entries 1–5 and 7–10) all afforded 1 in good and very good yields. Interestingly, the use of zinc chloride only led to cluster decomposition and no desired product (Table 4, entry 6). The desired 1 was obtained even when less usual halides were employed as the initiators. Palladium (II) chloride, gadolinium (III) fluoride and indium (III) chloride were effective in producing 1 (Table 4, entries 11–13). However, the experiments required two days to run to completion and the yields were not improved.

Other sources of dihalocarbenes, analogous to TMS-CF\(_{3}\), were also examined. When TMS-CCl\(_{3}\) and TMS-CCl\(_{2}\)Br were employed using the standard procedure (Table 5, entries 1, 2 and 5), no product was produced, suggesting that an additional equivalent of a base, expected from the stoichiometry, was necessary. When additional insoluble base, NaH, was present in the solution (Table 5, entries 4 and 7), the product 1 was produced in poor or trace quantities, respectively. However, when EtONa, a THF-soluble additional base, was present, 1 was formed but along with significant amounts of the [2-EtO-closo-1-CB\(_{12}\)H\(_{11}\)]\(^-\) byproduct (Table 5, entry 3), already familiar from earlier work in which CCl\(_2\) was generated from chloroform and base in the presence of EtONa [17]. TMS-CCl\(_{2}\)Br appeared to be less efficient than TMS-CCl\(_{3}\) in producing 1 even in the presence of EtONa and led to a mixture of products after prolonged heating (Table 5, entry 6). In contrast, known difluorocarbene sources,
TMS-CF₂Br and TMS-CF₂Cl, did afford the desired 1 even in the absence of additional base but not in very good yields and the experiments required two days to complete (Table 5, entries 8 and 9).

| No. | TMS-CF₃ (equiv) | Solvent | Volume [mL] | Initiator [mol%] | Temp [°C] | Yield of 1 [%] |
|-----|----------------|---------|-------------|------------------|-----------|---------------|
| 1   | 2.5            | THF     | 10          | LiCl [10]/TBAB [5] | 66        | 94 b         |
| 2   | 2.5            | DME     | 10          | LiCl [10]/TBAB [5] | 85        | 0 c          |
| 3   | 2.5            | DME     | 20          | LiCl [10]/TBAB [10]  | 70        | 0 c          |
| 4   | 2.5            | THF     | 20          | LiCl [10]/TBAB [5] | 66        | 76           |
| 5   | 2.5            | DME     | 20          | LiCl [10]/TBAB [5] | 85        | 0 c          |
| 6   | 2.5            | THF     | 10          | LiCl [10]/TBAB [10]  | 66        | 67 d         |
| 7   | 3.5            | THF     | 10          | LiCl [10]/TBAB [5] | 66        | 68           |
| 8   | 2.5            | THF     | 10          | LiCl [10]/TBAB [5] | 66        | 69 e         |
| 9   | 2.5            | THF     | 10          | LiCl [10]/TBAB [5] | 60        | 61           |
| 10  | 2.5            | THF     | 10          | LiBr [10]/TBAB [5] | 66        | 62           |
| 11  | 2.5            | THF     | 10          | LiI [10]/TBAB [5]  | 66         | 50           |
| 12  | 3.5            | THF     | 10          | LiBr [10]/TBAB [5] | 66        | 65           |
| 13  | 5.0            | THF     | 10          | LiCl [10]/LiBr [10] | 66        | 76           |
| 14  | 2.5            | THF     | 10          | LiCl [15]        | 66        | 78 f         |
| 15  | 5.0            | THF     | 10          | LiCl [15]        | 66        | 78           |
| 16  | 5.0            | THF     | 10          | LiCl [25]        | 66        | 68           |
| 17  | 5.0            | THF     | 10          | LiCl [50]        | 66        | 73           |
| 18  | 2.5            | THF     | 10          | LiBr [15]        | 66         | 72           |
| 19  | 3.5            | THF     | 10          | LiBr [15]        | 60         | 45           |
| 20  | 3.5            | THF     | 10          | LiBr [50]        | 66         | 74           |
| 21  | 3.5            | THF     | 10          | LiBr [100]       | 66        | 77           |
| 22  | 3.5            | THF     | 20          | LiBr [15]        | 66         | 61           |
| 23  | 2.5            | THF     | 10          | LiI [15]         | 66         | 62           |
| 24  | 5.0            | THF     | 10          | LiI [15]         | 66         | 67           |
| 25  | 2.5            | THF     | 10          | LiCl [5]         | 66         | 60           |
| 26  | 2.5            | THF     | 5           | LiCl [15]        | 66         | 56           |
| 27  | 2.5            | THF     | 5           | LiCl [5]         | 66         | 40           |
| 28  | 2.5            | THF     | 10          | LiCl [15]        | 50         | 54           |
| 29  | 2.5            | THF     | 10          | LiCl [15]        | rt         | 52 g         |
| 30  | 2.5            | THF     | 10          | -                | 66         | 40           |
| 31  | 2.5            | Diglyme | 10          | LiCl [15]        | 100        | 50           |
| 32  | 2.5            | Diglyme | 10          | LiCl [15]        | 66         | 0 h          |
| 33  | 2.5            | THF     | 10          | LiCl [15]        | 66         | 77 i         |
| 34  | 2.5            | DME     | 10          | LiCl [15]        | 85         | 52 i         |
| 35  | 2.5            | Diglyme | 10          | LiCl [15]        | 100        | 25 i         |
| 36  | 2.5            | THF     | 10          | LiCl [15]        | 66         | 56 j         |
| 37  | 2.5            | THF     | 200         | LiCl [15]        | 66         | 77 k         |

* Experiments run on 250 mg of [NHMe₃][B₁₁H₁₄]. b Two more runs gave 78% yield. c Decomposition of starting material. d Based on three runs. e 500 mg of [NHMe₃][B₁₁H₁₄] was used. f Based on three runs. g Reaction mixture stirred for 2 days. h Starting material recovered. i Six equiv. of NaH, no filtration, stirred for three days. j Solvent evaporated after deprotonation, residue redissolved in THF. k 5.0 g of [NHMe₃][B₁₁H₁₄] was used. TBAB = tetrabutylammonium bromide.
Table 4. Optimization of the reaction conditions using various metal halides as initiators and TMS-CF\(_3\) as the carbene source \(^a\).

| No. | TMS-CF\(_3\) (equiv) | Solvent | Volume [mL] | Initiator [mol\%] | Temp [°C] | Yield of 1 [%] |
|-----|----------------------|---------|-------------|-------------------|-----------|----------------|
| 1   | 2.5                  | THF     | 10          | KF [15]           | 66        | 53             |
| 2   | 2.5                  | THF     | 10          | NaCl [15]         | 66        | 65             |
| 3   | 2.5                  | THF     | 10          | KCl [15]          | 66        | 54             |
| 4   | 2.5                  | THF     | 10          | CsCl [15]         | 66        | 71             |
| 5   | 2.5                  | THF     | 10          | MgCl\(_2\) [15]   | 66        | 64             |
| 6   | 2.5                  | THF     | 10          | ZnCl\(_2\) [15]   | 66        | 0 \(^b\)       |
| 7   | 2.5                  | THF     | 10          | NaI [15]          | 66        | 60             |
| 8   | 2.5                  | THF     | 10          | KI [15]           | 66        | 70             |
| 9   | 2.5                  | THF     | 10          | CsI [15]          | 66        | 57             |
| 10  | 2.5                  | THF     | 10          | KBr [15]          | 66        | 54             |
| 11  | 2.5                  | THF     | 10          | PdCl\(_2\) [15]   | 66        | 76 \(^c\)      |
| 12  | 2.5                  | THF     | 10          | GdF\(_3\) [15]    | 66        | 59 \(^c\)      |
| 13  | 2.5                  | HF      | 10          | InCl\(_3\) [15]   | 66        | 65 \(^c\)      |

\(^a\) Experiments run on 250 mg of [NHMe\(_3\)][B\(_{11}\)H\(_{14}\)]. \(^b\) Cluster decomposition. \(^c\) Reaction mixture was stirred for two days.

Table 5. Other dihalocarbene sources \(^a\).

| No. | Reagent (equiv) | Solvent | Volume [mL] | Initiator | Temp [°C] | Yield of 1 [%] |
|-----|-----------------|---------|-------------|-----------|-----------|----------------|
| 1   | TMS-CCl\(_3\) (2.5) | THF     | 10          | LiCl      | 66        | 0 \(^b\)       |
| 2   | TMS-CCl\(_3\) (2.5) | diglyme | 10          | LiCl      | 120       | 0 \(^b\)       |
| 3   | TMS-CCl\(_3\) (2.5) | THF     | 10          | LiCl      | 66        | 21 \(^c,d,e\)  |
| 4   | TMS-CCl\(_3\) (3.5) | THF     | 10          | LiCl      | 66        | 5 \(^c,d,g\)   |
| 5   | TMS-CBr\(_3\) (2.5) | THF     | 10          | LiCl      | 66        | 0 \(^b\)       |
| 6   | TMS-CBr\(_3\) (2.5) | THF     | 10          | LiCl      | 66        | 40 \(^c,d,h\)  |
| 7   | TMS-CBr\(_3\) (3.5) | THF     | 10          | LiCl      | 66        | Traces \(^c,f,i\) |
| 8   | TMS-CF\(_2\)Br (2.5) | THF     | 10          | LiCl      | 66        | 71 \(^c\)      |
| 9   | TMS-CF\(_2\)Cl (2.5) | THF     | 10          | LiCl      | 66        | 47 \(^c\)      |

\(^a\) Experiments run on 250 mg of [NHMe\(_3\)][B\(_{11}\)H\(_{14}\)]; 15 mol\% of LiCl. \(^b\) Starting material was recovered. \(^c\) Reaction mixture stirred for two days. \(^d\) Two equiv. of EtONa added. \(^e\) Also a 6\% yield of [closo-2-EtO-1-CB\(_{11}\)H\(_{11}\)]. \(^f\) 4 eq. of NaH (no filtration). \(^g\) 5\% yield of 1 and 40\% recovered 12. \(^h\) Approximately 40\% 1, 40\% of [closo-2-EtO-1-CB\(_{11}\)H\(_{11}\)] and 20\% recovered 12. \(^i\) Traces of 1 and 35\% recovery of 12.

2.2. Mechanism

The mechanism of dichlorocarbene insertion into [nido-B\(_{11}\)H\(_{14}\)]\(^−\) was investigated computationally before \([17,22]\) and our results are similar. The results for difluorocarbene and dibromocarbene are new.

In Figure 1, we present an updated and expanded calculation of possible pathways for the insertion of difluorocarbene, dichlorocarbene and dibromocarbene. After proton abstraction from 12, the resulting 11 is attacked by the dihalocarbene, resulting in a barrierless formation of 13. After the dianion 13 loses a halide, a branching of the reaction path occurs, leading to 14 (upper pathway, \(E_a(F) = 6.7; E_a(Cl) = 3.6; E_a(Br) = 3.6 \text{ kcal/mol}\)) and to 15 (lower pathway, \(E_a(F) = 1.8; E_a(Cl) = 2.1; E_a(Br) = 1.7 \text{ kcal/mol}\)). Compound 14 can undergo deprotonation to form the dianion 16, which could lose the second halide in a process that involves a high barrier in case of F (27.2 kcal/mol) and a lower one for Cl and Br (14.5 and 15.7 kcal/mol, respectively) to form 18.
The upper pentagon to the side of the cage and forming 19. This reaction has the highest barrier on the minimum energy path that leads to 1 (21.1 kcal/mol for F, 13.4 for Cl and 14.9 for Br). Compound 19 virtually immediately rearranges to 18, which transforms to 20 by deprotonation (which closes the cage), followed by protonation resulting in the final product 1.

Figure 1. Calculated reaction energies and barriers for conversion of 12 to 1. Bold: highest barrier in a branch. Red arrows: minimum energy path. Bottom left: pathways for halogenation in position 2. The -H⁺ sign: deprotonation by an added base (e.g. NaH or NaOEt). Asterisk at $E_a$ (conversion of 19 to 18): without zero-point vibrational energy, 0.01 kcal/mol.
In the preferred lower pathway, compound 15 can undergo halogenation (eventually producing the side product 21) or deprotonation (resulting in 17 and subsequently leading to 1). The attack of the halide nucleophile at a boron vertex that is a next nearest neighbor to carbon is the most probable, and results in 22b. The barriers are similar for both F and Cl (∼15 kcal/mol) and slightly lower for Br (13 kcal/mol).

Formation of 17 by deprotonation of 15 is interesting—in the anhydrous medium, fluoride (F⁻) can act as a base, easily (5.6 kcal/mol barrier) abstracting a hydrogen from 15. The deprotonation by chloride and bromide has a much higher barrier (19.0 and 18.5 kcal/mol, respectively) and a significantly less favorable equilibrium (16.7 and 20.8 kcal/mol for Cl⁻ and Br⁻, respectively, vs. 2.9 for F⁻), implying that the reaction of 15 and Cl⁻ or Br⁻ is more likely to result in the formation of the halogenated side-product 22b. Since chloride and bromide do not deprotonate 17, the presence of an additional equivalent of strong base is required (NaH or preferably the soluble EtONa).

In 17, the transfer of the final bridged hydrogen to the carbon and the dissociation of the halide could result in the immediate formation of 1 but this reaction has relatively high barriers (28 kcal/mol in both cases). Instead, the halide can leave, which results in the carbon displacing a BH group from the upper pentagon to the side of the cage and forming 19. This reaction has the highest barrier on the minimum energy path that leads to 1 (21.1 kcal/mol for F, 13.4 for Cl and 14.9 for Br). Compound 19 virtually immediately rearranges to 18, which transforms to 20 by deprotonation (which closes the cage), followed by protonation resulting in the final product 1.

3. Discussion

Two related mechanistic aspects of this primarily synthetic study appear noteworthy to us. First, not counting the base needed to convert the initial NMe3H⁺ salt of 12 into its sodium salt, only one equivalent of base, used to convert 12 to 11, is needed for the reaction with CF₂. Yet, at first sight stoichiometry suggests that two will be necessary to neutralize the HF formed:

\[ \text{B}_{11}\text{H}_{14}^- + \text{CF}_2 = \text{CB}_{11}\text{H}_{12}^- + 2\text{HF}. \]

Removing possibly present excess NaH from 11 by filtration does not hinder the reaction with difluorocarbene in the least and it appears that a large excess of NaH actually hinders it. Reluctantly, we conclude that one equivalent of HF is eliminated spontaneously and absorbed in the glassware. Otherwise stated, in the anhydrous environment the fluoride anion is acting as a base. In contrast, the less basic chloride and bromide anions do not and work with CCl₂ and CBr₂ requires additional base.

The second noteworthy observation is that against our original expectations based on the known affinity of fluorine for boron, difluorocarbene is greatly superior to other halocarbenes. We were initially reluctant to even try it for fear that one or both fluorine atoms will end up on boron vertices. In actual fact, this is not observed at all and CF₂ is vastly superior to both CCl₂ and CBr₂. We attribute the difference to the ability of the fluoride anion to act as a strong base. This view is supported by the density functional theory (DFT) results for the conversion of 15 to 17 (Figure 1), which document the role that the much higher strength of the HF bond compared to the HCl and HBr bonds plays in permitting the removal of a proton from the cluster anion. When the reaction is performed with CCl₂ or CBr₂ instead of CF₂, 15 is much more easily diverted toward other products, especially those with a nucleophile in position 2. This type of byproduct has not been observed at all when CF₂ is used.

4. Materials and Methods

4.1. General Information

Tetrahydrofuran, 1,2-dimethoxyethane and diglyme were dried and distilled from sodium/benzophenone under Ar. Reagents were used as supplied without purification unless stated otherwise. All operations were performed under argon using Schlenk techniques unless stated otherwise. Sodium hydride (60% oil dispersion) was washed with hexane three times under Ar before use. (Trifluoromethyl)trimethylsilane was purchased from Oakwood Chemical (Estill,
SC, USA). (Difluoromethyl)trimethylsilane [23], (bromodifluoromethyl)trimethylsilane [24], (chlorodifluoromethyl)trimethylsilane [25], (tribromomethyl)trimethylsilane [26] and (trichloromethyl)trimethylsilane [27] were prepared according to reported procedures. $^1$H, $^{13}$B and $^{19}$F NMR spectra were recorded on Bruker Avance-III 300 MHz instrument in CDCl$_3$ or CDC$_3$N. Chemical shifts are reported in ppm.

4.2. Calculations

All density functional theory (DFT) calculations were done using the B3LYP functional, which has previously been used for the description of carborane reactions [22,28]. Long-range interactions were corrected using Grimme’s dispersion scheme with Becke-Johnson damping (D3BJ) [29]. Solvent effects were modelled using Truhlar’s SMD implicit solvent model [30]. All optimizations were followed by harmonic frequency calculations and all reported numbers include zero-point vibrational energy. Gaussian09B01 [31] was used for all calculations.

4.3. Procedures

**General procedure for preparation of [NEt$_4$][CB$_3$H$_{12}$]** (1). A solution of [NHMe$_3$][B$_{11}$H$_{14}$] [18] (250 mg, 1.29 mmol) in freshly-distilled THF (5 mL) was added dropwise to a suspension of NaH (109 mg, 4.53 mmol) in THF (5 mL) cooled to $-40$ °C under Ar. The reaction mixture was stirred at $-40$ °C for 15 min, allowed to warm to room temperature and stirred for 30 min. Gas evolution was observed during warming up. The formation of the dianion, [2Na][B$_{11}$H$_{13}$], was confirmed by $^{13}$B-NMR (Figure 2): $^{13}$B$^1$H NMR (96 MHz, CD$_3$CN) $d$ = -20.8 (10B), -31.5 (1B). The solution was then filtered through a cotton plug under Ar into an oven-dried flask charged with carefully dried LiCl (8.23 mg, 0.194 mmol, 10 mol%). The reaction mixture was heated to reflux and (trifluoromethyl)trimethylsilane (460 mg, 3.24 mmol, 0.48 mL) was added dropwise to the reaction flask. The solution turned yellow and then orange. The reaction mixture was refluxed for 16 h, cooled to room temperature and quenched with water (2 mL). The solvents were evaporated under reduced pressure, water (25 mL) was added to the residue and the solution was acidified with 10% aqueous HCl. The aqueous layer was extracted with Et$_2$O (3 x 30 mL). The combined organic layers were transferred to a flask, water (30 mL) was added and the organic solvent was removed under reduced pressure. The resulting aqueous solution was filtered through a cotton plug and treated with solid NEt$_3$Br (408 mg, 1.94 mmol). The precipitate was filtered and dried to give 276 mg (78% yield) of [NEt$_4$][CB$_3$H$_{12}$] as a white solid (65% yield): $^1$H-NMR (300 MHz, CD$_3$CN) $d$ br m 0.4–2.5 (11H), 2.82 (s, 9H); $^{13}$B$^1$H NMR (96 MHz, CD$_3$CN) $d$ = -14.2 (1B), -16.1 (5B), -16.7 (5B).
5. Summary

We have developed a simple and efficient method for the preparation of the \([\text{closo-1-CB}_{11}H_{12}]^−\) cluster anion from cheap and commonly available reagents, NaBH₄, BF₃·Et₂O, TMS-CF₃ and NaH in only two steps in a 45–60% overall yield. Unlike other published protocols, our method requires only a simple experimental setup and commonly available glassware and it does not require toxic and expensive decaborane, excess reagents or glove-box and pressure vessels. Manual operations are simple and can be easily performed in a hood and the process is easily scalable. Moreover, in contrast to other methods, the product is afforded in just 16 hours. We have performed DFT calculations to develop a mechanistic proposal for the carbene insertion process and to account for the remarkable differences between various carbenes.

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Sample Availability: Samples of the compounds are not available from the authors. A salt of the [closo-1-CB11H12-anion can probably be purchased from Boron Specialties LLC.

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