Carbon-substituted 9,12-dimercapto-1,2-dicarba-closo-dodecaboranes via a 9,12-bis(methoxy-methylthio)-1,2-dicarba-closo-dodecaborane precursor

Abstract

Dithiolated derivatives of 1,2-dicarba-closo-dodecaboranes are common ligands to be used for self-assembling monolayers, nanoparticles or transition metal complexes due to their robust molecular structure. The 9,12-Dimercapto-1,2-dicarba-closo-dodecaborane, a derivative with two SH-groups in neighbored positions is an interesting unit for the preparation of in positions 1 and 2 functionalized derivatives. In this contribution, we report a convenient synthesis of 1,2-disubstituted 9,12-dimercapto-1,2-dicarba-closo-dodecaboranes via a with the methoxy-methyl group (MOM) S-protected precursor in good yields. All compounds are well characterized via HiRes-mass spectroscopy, proton, carbon and boron nmr-spectroscopy and infrared spectroscopy. The precursor 9,12-Bis(methoxy-methylthio)-1,2-dicarba-closo-dodecaborane was proved via a X-Ray-crystal structure.

Keywords: Carborane, Dicarba-closo-dodecaborane, Dimercapto-carborane, Surfactant, protecting group, Dithiolcarborane

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Introduction

1,2-Dicarba-closo-dodecaboranes ($C_2B_{10}H_{12}$)—often abbreviated as ortho- or o-carboranes—are due to their wide applicability an intensively investigated research field of boron chemistry[1, 2, 3, 4]. Mono- or multithiolated o-carborane derivatives are often used as ligands in transition metal complex chemistry or in self assembling monolayers (SAMs)[5, 6, 7]. Their ball like shape leads to the formation of two dimensional highly packed quasi crystalline monolayers on metal surfaces like gold, silver or copper. The most often investigated thiolated o-carborane derivative is the 1,2-dimercapto-o-carborane ($1,2-(HS)_2C_2B_{10}H_{10}$).

The less common isomer 9,12-dimercapto-o-carborane 2 ($9,12-(HS)_2C_2B_{10}H_{10}$) is differing not only in the position of the SH-groups but also in several properties such as dipol moment or pk-values[5, 8]. One interesting aspect of the 9,12-isomer is, that the dipol moment in protonated (($HS)_2C_2B_{10}H_{10}$) state points in the same direction as in deprotonated (($C_2B_{10}H_{10}S_2^2$) state. In case of the 1,2-isomer the dipole moment turns to the opposite direction after deprotonation of the SH-groups.

As up to now research has been done only on unmodified 9,12-dimercapto-o-carborane 2, we were interested in the influence of substituents on the properties on 1,2-disubstituted 9,12-dimercapto-o-carboranes. The positions one and two of the o-carborane cluster are the most reactive and are the positive charge extrema of the dipol. A substitution at these positions is easiest to perform and will have the strongest influence on the dipole and hence to the properties of the carborane cluster.

o-Carborane is synthesized by reaction of acetylene with decaborane. The same approach can be used to obtain 1,2-disubstituted o-carboranes just by using correspondingly substituted acetylene derivatives[9, 10, 11]. Introduction of mercapto groups in positions nine and twelve of o-carborane to synthesize 9,12-dimercapto-o-carborane is performed under harsh conditions with elemental sulfur in a aluminium chloride melt at 160–180°C and affords the product in good yields[12]. In case of 1-mono- or 1,2-disubstituted o-carboranes the same

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1Substitution of positions 9 and 12 as the most negative part of cause too, but they are already substituted by the SH-groups.
conditions will lead to monothiolation of the o-carborane cluster in position nine or twelve only[13]. Furthermore these conditions will lead to degradation of structural more complex substituents and hence impedes a broader applicability.

Another method for introducing substituents into unsubstituted o-carboranes at the carbon positions is to deprotonate the cluster at these positions with strong bases such as sodium amide or butyl lithium followed by reaction with electrophilic agents f.e. alkylants like alkyl bromides or iodides[14, 15], ether groups[16], carbonyl compounds like aldehydes[17, 18], ketones[19, 20], chloroformates[14] or carbon dioxide[21, 22, 23], michael acceptors[24], silanes[14, 25], amino groups [23] or elements sulfur[26, 7], selenium and tellurium[7]. This method of substituent introduction was never used for 9,12-dimercapto-o-carborane and its derivatives. In this contribution we describe a convenient way for the synthesis of 1,2-disubstituted 9,12-dimercapto-o-carboranes by introduction of an easy obtainable 9,12-dithiolated o-carborane precursor. Recently a similar approach has been described independently by Hey-HAWKINS and coworkers. This study provides us with a basis for comparison of both synthetic routes.[27]

Figure 1 shows a general approach. The key molecule in this approach is the precursor for the introduction of the 9,12-dithiolated o-carborane unit. To avoid undesired attack of the sulfur atoms, a protection group for the sulfur atoms is necessary which is stable against strong basic conditions and cleavable under mild conditions without degrading the carborane cluster or attached structures. The methoxy-methyl-group seems to be ideal for this purpose. Its easy introducability, broad stability against various conditions especially from strong basic and acidic conditions, non-oxidative character and easy cleavability from thiols with mercury(II)-salts makes it the protecting group of choice for mercapto functionalities[28].

In a first experiment, we checked whether a quantitative lithiation at positions one and two of the 9,12-bis(methoxy-methylthio)-o-carborane precursor 2 is possible. This can be done via a deuteration (R=D in figure 1) through deu-
terium oxide of the dilithiated species. Additionally, we followed the mercuration of the icosahedral carbons as an unwanted side reaction of the deprotection of the mercapto groups by mercury(II)-salts.

The second step is the introduction of the substituents in positions one and two, analogously to the synthesis of 1,2-disubstituted o-carboranes starting from plain o-carborane. The precursor 9,12-bis(methoxy-methylthio)-o-carborane is lithiated in positions one and two quantitatively by n-butyl lithium followed by addition of the alkyl halogenide.

**Synthesis**

*Analytical equipment.* NMR-spectra were acquired on Varian MercuryPlus or Bruker Avance400 spectrometer with 400 MHz in proton, 100 MHz in carbon and 128 MHz in boron-11 channel at room temperature. Infrared spectra were measured with a Nicolet Nexus 670-FT-Infrared Spectrometer as film or KBr tablet in a range of 4000–400 cm\(^{-1}\). Mass analysis was made with a Thermo-Finnigan LQC-Fleet Ion Trap spectrometer in negative mode using electro spray ionisation (ESI). Concentration \(\approx 100 \text{ ng·mL}^{-1}\), injection volume 5 μL·min\(^{-1}\), source voltage 5.48 kV, tube lens voltage –124.67 V, capillary voltage –11.05 V. HiRes mass spectroscopy was measured using a TQ Orbitrap Velos (Thermo Scientific) spectrometer in negative mode with a mass accuracy better than 3 ppm. Solvent: acetonitrile, vaporizer temperature 350°C, capillary temperature 300°C.

*Chemicals.* Deuterium oxide, n-butyl lithium, n-heptylbromide, ethylbromide and bromomethyl methylether were purchased from Sigma Aldrich chemicals and used as received. 9,12-Dimercapto-o-carborane was obtained from Katchem and recrystallized prior use. Solvents like THF and Ether were dried over sodium metal/benzophenone and distilled before use.

**Synthesis of 9,12-Bis(methoxy-methylthio)-o-carborane** 2. 9,12-Dimercapto-o-carborane (500 mg, 2.4 mmol, 1 eq.) is dissolved in dry and degassed THF under inert atmosphere at rt. potassium tert-butanolate (592.4 mg, 5.3 mmol, 2.2 eq) is added and a cream white solid precipitates immediately. The suspension is stirred for further 1 h at rt followed by the addition of bromomethyl methylether.
(719.7 mg, 5.76 mmol, 2.4 eq). The color switches from cream white to lime white directly (formation of KBr). The suspension is stirred for 3 h.

A saturated aqueous NaCl-solution (20 mL) is added and the two-phase system stirred vigorously for 30 min. The organic phase is separated, dried over Na₂SO₄, filtered and the solvent removed under reduced pressure. The residue is dissolved in ether (20 mL) and washed 2× with water (20 mL). The phases are separated, the organic phase is dried over Na₂SO₄ and the solution evaporated to dryness.

The remaining solid is purified via column chromatography on silica gel. First with chloroform as eluent to remove remaining tert-butanol, then switching to chloroform/acetoni trile (4:1; v/v, R_f=0.62) to elute the product.

Smaller amounts (<500 mg) can be recrystallized from cyclohexane or cyclohexane/toluene (9:1 v/v).

9,12-Bis(methoxy-methylthio)-o-carborane is obtained in 61% yield (434 mg).

¹H-NMR (CDCl₃): δ = 4.68 (s, 4H, SCH₂O), 3.61 (s, 2H, Borane-CH), 3.33 (s, 6H, OCH₃), 3.2–1.04 (m, 8H, BH).

¹³C-NMR (CDCl₃): δ = 75.1 (SCH₂O), 55.7 (OCH₃), 48.1 (icosahedral-CH).

¹¹B-NMR (CDCl₃): δ = 14.65, –0.87, –6.65, –8.9.

HiRes-MS: m/z = 296.190 (100%,M⁻), 299.182 (8%, cut-off-peak).

_Synthesis of 9,12-bis(methoxy-methylthio)-1,2-dideutero-o-carborane 3a._ 9,12-bis(methoxy-methylthio)-o-carborane (201.9 mg, 0.681 mmol, 1 eq) is dissolved in abs. diethylether (10 mL) under argon atmosphere. The solution is cooled to 0°C (ice bath). A solution of 2.5 M n-Buli in hexane (0.85 mL, 0.135 mmol, 2 eq.) is added dropwise with a syringe and a white precipitate is formed immediately. The suspension is stirred for further 15 min at this temperature, followed by the addition of deuteriomoxide (5 mL, 250 mmol, 370 eq.) and stirred for 1 h at rt. The phases are separated and the aqueous phase is extracted 2× with diethylether (10 mL). The combined organic phases are dried over Na₂SO₄ and the solvent is evaporated. The resulting oil is allowed to crystallize and the solid recrystallized from cyclohexane/toluene (9:1).

Yield 100%.

¹H-NMR (CDCl₃): δ = 4.68 (s, 4H, SCH₂O), 3.34 (s, 6H, OCH₃), 3.2–1.04 (m, 8H, BH).
\(^{13}\)C-NMR (CDCl\(_3\)): \(\delta = 75.1\) (SCH\(_2\)O), 55.7 (OCH\(_3\)), 47.8 (triplet, borane-CH).

\(^{11}\)B-NMR (CDCl\(_3\)): \(\delta = 7.02, -8.42, -14.27, -16.53\).

HiRes-MS: \(m/z = 298.202\) (100%, M\(^+\)), 301.194 (7%, cut-off-peak).

9,12-dimercapto-1,2-dideutero-o-carborane \(4a\). 9,12-Bis(methoxy-methylthio)-1,2-dideutero-o-carborane (150 mg, 0.5 mmol, 1 eq.) is dissolved in 10 mL acetonitrile/water (4:1) and a solution of mercury(II)-chloride (220.2 mg, 1 mmol, 2 eq.) in acetonitrile/water (4:1, 5 mL) is added. The mercury-carborane complex precipitates as a white solid after a few seconds. For completion of the reaction, the mixture is allowed to stir for additional 2 h. The mercury complex is collected and washed 2× with acetonitrile/water (4:1, 5 mL), suspended in ethanol (10 mL) and \(\text{H}_2\text{S}\) is bubbled through the suspension for 4 h. The carborane dissolves and a black precipitate is formed. The black mercury sulfide removed by filtration and the solvent is evaporated. The synthesis affords 26.2 mg (98%) of 9,12-dithio-1,2-dideutero-o-carborane.

\(^{1}\)H-NMR (CDCl\(_3\)): \(\delta = 3.23–1.33\) (m, 8H, BH), 0.59 (s, 2H, SH).

\(^{13}\)C-NMR (CDCl\(_3\)): \(\delta = 47.0\) (t, CD).

\(^{11}\)B-NMR (CDCl\(_3\)): \(\delta = 5.38, -6.40, -13.80, -16.30\).

HiRes-MS: \(m/z = 210.150\) (100%, M\(^+\)), 213.142 (9%, cut-off-peak).

9,12-dimercapto-1,2-dideutero-o-carborane \(4c\). 9,12-Bis(methoxy-methylthio)-1,2-o-carborane (110,1 mg, 0.37 mmol, 1 eq.) is dissolved in abs. THF (2.5 mL) and cooled to 0°C (ice bath) under nitrogen atmosphere. \(n\)-BuLi (0.47 mL, 1.6 M in hexane, 0.75 mmol, 2.03 eq.) is added dropwise with a syringe. The solution is stirred for 30 minutes at 0°C. After this period, ethylbromide (88.7 mg, 0.81 mmol, 2.2 eq.) is added and the ice bath is removed. The solution is allowed to stir overnight. The solvent is removed, the residue dissolved in methylenechloride (5 mL) and washed 2× with water (5 mL). After drying over Na\(_2\)SO\(_4\), the solvent is evaporated.

The resulting solid is dissolved in acetonitrile/water (4:1, 10 mL). Mercury(II)-chloride (201 mg, 0.74 mmol) in acetonitrile/water (4:1, 1 mL) is added and the formed white suspension is stirred for further two hours. The solid is collected and washed 2× with of acetonitrile/water (4:1, 5 mL). The solid is suspended
in ethanol and H_2S is bubbled through. The white precipitate dissolves and black mercurysulfide is formed. After two hours, the solid is removed by filtration and the solution evaporated to dryness. The resulting solid is sublimed at 140℃ (oil bath temperature) at 2*10^{-2} mbar. 85 mg of 9,12-dithio-1,2-diethyl-1,2-carborane were obtained (87%).

^1H-NMR (CDCl_3): δ = 3.25–1.59 (m, 8H, BH), 2.23 (q, 4H, CH_2, ^3J=7.50 Hz), 1.17 (t, 6H, CH_3, ^3J=7.50 Hz).

^13C-NMR (CDCl_3): δ = 73.9 (Borane-C), 27.6 (CH_2), 14.2 (CH_3).

^11B-NMR (CDCl_3): δ = 3.34 (B-S), –5.00– –11.19 (m).

GC-MS (EI): m/z = 263 (M+1, 100%), 236, 209, 183, 156, 131, 114.

**Synthesis of 9,12-bis(methoxy-methylthio)-1,2-diheptyl-o-carborane 3b.** A solution of 9,12-Bis(methoxy-methylthio)-o-carborane (274 mg, 0.92 mmol, 1 eq.) in absolute THF (100 mL) is cooled to 0℃ under inert atmosphere. n-BuLi (0.74 mL, 1.86 mmol, 2,5M in hexane, 2.02 eq.) are added with a syringe. The solution is stirred for further 15 minutes at 0℃. After that period, 1-bromo-n-heptane (362.5 mg, 2.024 mmol, 2.2 eq) is added dropwise and the mixture is stirred at 0℃ for 30 minutes and at room temperature overnight.

The solvent is removed, the residue dissolved in 10 mL ether and washed 2× with water (10 mL). After separation of the organic layer, drying over sodium sulfate, the mixture is passed through a pad of silica gel with ether as eluent. The mixture is stirred at 0℃ for 30 minutes and at room temperature overnight.

After removal of the ether, the product 364 mg 9,12-bis(methoxy-methylthio)-1,2-diheptyl-o-carborane is obtained (80%).

^1H-NMR (CDCl_3): δ = 4.68 (s, 4H, S–CH_2–O), 3.35 (s, 6H, CH_3O), 3.14–1.63 (m, 8H, BH), 2.13 (t, 4H, B–C–CH_2, ^3J=8.7 Hz), 1.53 (m, 4H, B–C–CH_2–CH_2), 1.28 (m, 16H, (CH_2)_4–CH_3), 0.86 (t, 6H, CH_3, ^3J=7.25 Hz).

^13C-NMR (CDCl_3): δ = 75.1 (S–CH_2–O), 75.54 (icosahedral-C), 55.60 (CH_3O), 34.10 (icosahedral-C–CH_2), 31.47 ((CH_2)_4–CH_3), 29.78 (icosahedral-C–CH_2–CH_2), 29.10 ((CH_2)_4–CH_3), 28.7 ((CH_2)_4–CH_3), 22.43 ((CH_2)_4–CH_4), 13.93 (CH_4).

^11B-NMR ((CDCl3)): δ = 12.51 (B-S), 4.82– –13.16 (BH).

HiRes-MS: m/z = 492.408 (100%, M^+), 495.401 (10%, cut-off-peak).
Synthesis of 9,12-dimercapto-1,2-diheptyl-o-carborane 4b. To a solution of 9,12-
bis(methoxy-methylthio)-1,2-diheptyl-o-carborane (589 mg, 1.2 mmol, 1 eq.) in
10 mL acetonitrile are added a solution of mercury(II)-chloride (651.6 mg, 2.4 mmol,
2 eq.) in acetonitrile (2 mL). After a few seconds, a white precipitate is formed,
separated via centrifugation and the solid washed 2× with acetonitrile (5 mL).
The residue is dissolved in chloroform and \( \text{H}_2\text{S} \) is bubbled through and after
a while, a black precipitate of mercursulfide is formed. For completion of the
reaction \( \text{H}_2\text{S} \) is passed though for further two hours. The black suspension is
filtered and the clear colorless solution is evaporated to dryness.
The 9,12-dimercapto-1,2-diheptyl-o-carborane is obtained in 69% yield (335 mg)

\[ ^1\text{H}-\text{NMR (CDCl}_3\text{):} \delta = 3.24-1.66 \text{ (m, 8H, BH),} 2.20-2.05 \text{ (t, 4H, B–C–CH}_2, \]
\[ ^3\text{J}=8.54 \text{ Hz), 1.53 (m, 4H, B–C–CH}_2–CH}_2, 1.28 (m, 16H, (CH}_2\text{)_4–CH}_3), \]
\[ 0.88 (t, 6H, CH}_3, ^3\text{J}=6.63 \text{ Hz).} \]

\[ ^{13}\text{C}-\text{NMR (CDCl}_3\text{):} \delta = 73.11 \text{ (icosahedral–C), 34.04 (B–C–CH}_2, 31.54 \]
\[ ((CH}_2\text{)_4–CH}_3, 29.89 (B–C–CH}_2–CH}_2), 29.14 ((CH}_2\text{)_4–CH}_3), 28.77 ((CH}_2\text{)_4–CH}_3), \]
\[ 22.53 ((CH}_2\text{)_4–CH}_3), 14.04 (CH}_3). \]

\[ ^{11}\text{B}-\text{NMR: (CDCl}_3\text{):} \delta = 11.10 \text{ (B–S),} -0.07 \text{ (BH),} -3.48 \text{ (BH).} \]

HiRes-MS: \( m/z = 404.356 \) (100%, M ), 407.358 (8%, cut-off-peak).

Results and Discussion

Precursor 9,12-bis(methoxy-methylthio)-o-carborane 2
The synthesis of the key precursor 9,12-bis(methoxy-methylthio)-o-carborane
2 starts from commercially available 9,12-dimercapto-o-carborane 1. The methoxy-
methyl-protecting group is introduced by deprotonation of the SH-groups by
potassium tert-butanolate and addition of bromomethyl-methyl ether to the
formed suspension. Attempts to replace tert-butanolates by potassium car-
bonate or butyl lithium led to much lower yields. To avoid oxidative degra-
dation the reaction must be performed under Schlenk conditions, the use of
balloon techniques is insufficient. Purification is done by column chromatogra-
phy. Impurities and remaining tert-butanol are first washed off with chloroform

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and the product eluated with chloroform/acetonitrile afterwards. Alternatively, the product can also be recrystallized from a cyclohexane/toluene 9:1. The 9,12-bis(methoxy-methylthio)-o-carborane 2 does not easily crystallize from the mother liquor, it rather separates as an insoluble oil layer which subsequently solidifies. This happens mainly when the compound is dissolved f.e. in toluene, THF or chloroform, and cyclohexane or hexane is added for precipitation. Recrystallization is not recommended for amounts >500 mg as the precursor suffers from thermal degradation when molten. This decreases the yield in the extent as more substance is to be recrystallized. For purification of amounts greater than 500 mg of precursor, column chromatography is more appropriate.

[Figure 2 about here.]

[Figure 3 about here.]

In the proton nmr spectrum (figure 2) of the compound two singlets at 4.68 (methylene) and 3.33 ppm (methoxy) can be seen and furthermore the absence of the SH-signal at 0.59 ppm. The signals at 3.61 ppm (CH) and from 3.2 to 1.04 ppm (BH) belong to the carborane icosahedron. In the $^{13}\text{C}$-NMR (figure 3) the three expected signals occur at 75.1 ppm for the methylene groups, at 55.7 ppm for the methoxy groups and at 48.1 ppm for the icosahedral carbons. The proton decoupled B-11 nmr spectrum signals shows the typical o-carborane pattern with signals at 14.65, −0.87, −6.65 and −8.9 ppm.

[Figure 4 about here.]

A comparison of the single crystal X-ray-structures of 9,12-Bis(methoxy-methylthio)-o-carborane 2 (figure 4) and 9,12-Dimercapto-o-carborane[5] shows by 0.005 Å shorter boron-boron distances in 2. On icosahedral carbon-boron bonds this is a more distinct effect than on the other (boron-boron) cluster bonds. This bond length enlargement corresponds with the electron density in the carborane cluster. An explanations of this effect is the assumption, that in 2 the electron density of the etherified sulfur is lower compared to the SH-groups of the 9,12-dimercapto-o-carborane and thus a decreased electron density inside the carborane cluster. The shortening of the distance of the etherified sulfur atoms of about 0.25Å supports this estimation whereas the increased dihedral
angle of about 1 degree can be explained by the higher sterical demand of the MOM-group.

The infrared spectrum of compound 2 (figure 5) shows an intense valence C-H vibration band in the range 3080–2750 cm\(^{-1}\). The intense band at 2600 cm\(^{-1}\) belongs to the borane BH-vibrations. The shoulder at 2812 cm\(^{-1}\) is a typical band of the methoxy group and is visible only in the S-MOM-protected o-carborane species.

Despite the strong Raman activity of the mercapto group, the attachment and detachment of the MOM-groups onto the mercapto functionality of the carborane cluster can not be followed by Raman spectroscopy. The thiol band at about 2600 cm\(^{-1}\) is overlapping with the bands of the boron cluster. Chemical modification of the mercapto functionality results only in a slight intensity change.

9,12-Bis(methoxy-methylthio)-1,2-dideutero-o-carborane 3a and 9,12-dimercapto-1,2-dideutero-o-carborane 4a

A lithiation/deuteration of 9,12-bis(methoxy-methylthio)-o-carborane 2 at the icosahedral carbon atoms proved, that substitution of CH protons proceeds analogously to unmodified o-carborane.[23, 26] The synthesis was performed according to typical procedures by dissolving the carborane derivative in dry ether and using \(n\)-butyl lithium for deprotonation of the carbon atoms. In contrast to the lithiation of unfunctionalized o-carborane, where only the dilithiated o-carborane species precipitates, monolithiated 2 precipitates directly. This may be caused by complexation of the lithium by the SMOM-groups. The free carborane anion formed is then insoluble in ether. After the addition of two equivalents of butyl lithium the obtained dilithiated carborane species is quenched with deuterium oxide. After work up the product was obtained in quantitative yield.

The 100% conversion is proved by proton and carbon NMR. The signal at 3.61 ppm in the proton spectrum disappears (figure 2) and the signal at 48.1 ppm in the carbon spectrum turns into a triplet (figure 3). In the HiRes-mass spectrum the signals are by two units shifted to higher mass from 296.19 to
This and the complete absence of any proton related signals reveals a quantitative deuteration of both carbon anions.

Cleavage of the MOM-group is achieved under mild conditions with mercury(II)-chloride in acetonitrile/water mixture as solvent. The 9,12-dimercapto-1,2-dideutero-o-carborane mercury complex precipitates immediately after addition of the HgCl$_2$ solution as a white solid. After a couple of minutes, the precipitate is isolated and suspended in ethanol. 4a is released from mercury by bubbling H$_2$S through the suspension of the mercury complex and can be obtained in 75% yield.

In the proton nmr the resonance of the thiol proton occurs at 0.39 ppm. In the carbon nmr, the C-D triplet undergoes a slight shift to lower frequencies of about 2 ppm. No evidence for a reprotonation of icosahedral carbon through mercury reagents used can be found under the given reaction conditions, neither in the proton spectra nor in the carbon spectra (see below).

The infrared spectra of 4a and 3a are identical to their protonated counterparts except the expected shift of the icosahedral hydrocarbon bands from 3043 cm$^{-1}$ (3014 cm$^{-1}$) to 2272 cm$^{-1}$ (2260 cm$^{-1}$) after deuteration (figure 5). The immediate separation of the mercury complex of 3a from excess mercury(II)-chloride is necessary to avoid metallization of the icosahedral carbon atoms, which has been described in the literature[29, 30, 31]. A reaction time of 10 h with mercury(II) chloride leads together with the release by H$_2$S to a reprotonation of the icosahedral carbon atoms. This reprotonation is shown by a comparison of the proton spectra of 9,12-dimercapto-1,2-dideutero-o-carborane 4a and its reactant 9,12-bis(methoxy-methylthio)-1,2-dideutero-o-carborane 3a (figure 6). It shows an increased C-H signal at 3.6 ppm which indicates a reprotonation of about 18% of the deuterated carbon atoms.

[Figure 6 about here.]

Alkylation of 9,12-bis(methoxy-methylthio)-o-carborane 2 and release of the thiol

After the evidence of a quantitative lithiation of both icosahedral carbons of 2 was achieved by complete deuteration as described above, the feasibility of the thereby formed dianion for a nucleophilic substitution with alkyl halogenides was investigated.
To attach alkylchains—ethyl and heptyl for the herein described derivatives—onto the carbon positions, 2 was lithiated analogously to the deuteration reaction described above, using THF as solvent instead of ether for better support of Sn-reactions. The dianion is then allowed to react with two equivalents of the corresponding alkylhalogenide.

For the heptyl derivative 3b the solvent was removed and yellowish impurities were easily removed via filtration over silica gel with diethyl ether as eluent. The MOM groups were cleaved with mercury(II) chloride whereby the mercapto-carborane mercury complex separated as a waxy solid. Product 4b was obtained after passing H₂S through a solution of the mercury complex and removal of precipitating mercury sulfide. The 9,12-dimercapto-1,2-diheptyl-o-carborane 4b incurs as a colorless oil.

The ethyl substituted compound was worked up differently. It was roughly separated from reactants and solvent and the raw product 3c was used without further purification for the synthesis of 4c by cleaving the protecting groups with mercury(II) chloride. The final product was released by passing H₂S gas into a ethanolic suspension of the mercury-product complex and purified by sublimation.

In the proton spectra of 3b and 4b the resonance of the icosahedral C-H at 3.61 ppm is missing. The signals of the alkyl chains occur at typical ranges from 2.12 to 0.86 ppm (heptyl).

The icosahedral carbon interestingly undergoes a strong shift to higher frequencies—even when alkylated with simple alkyl groups—of about 30 ppm. The successful attachment of the alkyl substituents is proved by a HMBC correlation spectrum of 3b (figure 7). It shows a cross peak between the resonances at 73 ppm (icosahedral carbon) and 2.12 ppm (first CH₂ side chain).

In a decoupled boron NMR-spectrum of 3b, alkylation of the icosahedral carbons results in a shift of the hydrogen bound from three distinct signals to one overlapping peak with two maxima at −2.02 and −3.62 ppm. The SH-bound borons undergo a slight shift from 14.62 ppm before to 12.43 ppm after alkylation.
The spectra—proton and carbon—of 4b show the expected amount of resonances with almost same chemical shifts as 3b. In both carbon and proton NMR spectra, the signals of the MOM-group are missing and the typical SH-proton resonance at 0.39 ppm occurs in the proton spectra. In contrast, the boron spectrum of 4b shows a more complex pattern compared to 3b with distinct signals for B-S (11.06 ppm) and borons in positions 8 and 10. All other borons are summarized below one broad peak at ~3.51 ppm.

In the infrared spectrum, both derivatives 3b and 4b show next to the typical boron-vibrations at 2600 cm\(^{-1}\) strong C-H valence and deformation bands at 3080–2750 cm\(^{-1}\) and 1460 cm\(^{-1}\) respectively. The MOM-protected derivative has the typical methoxy band, which occurs at 2812 cm\(^{-1}\). The strong resonances at 3043 cm\(^{-1}\) which belongs to the icosahedral CH-vibrations, are missing.

The proton spectrum of 9,12-dimercapto-1,2-diethyl-o-carborane 4c shows the expected ethyl pattern at 1.17 (CH\(_3\)) and 2.23 ppm (CH\(_2\)) next to the boron and mercapto proton resonances (figure 8). The carbon spectrum shows three signals. The resonance of the icosahedral carbon encounters with 74 ppm in the same shift after alkylation as in case of 4b.

Conclusion

We described a new synthetic pathway to 1,2-dialkylated 9,12-dimercapto-o-carboranes through a 9,12-methoxy-methylthio (MOM) substituted o-carborane precursor. This 9,12-bis(methoxy-methylthio)-o-carborane was prepared using potassium tert-butanolate and bromomethyl-methyl ether with a reasonable yield of about 60–65% and purity.

Deuteration experiments of the 9,12-bis(methoxy-methylthio)-o-carborane precursor showed a 100% proton-deuterion exchange in the positions one and two and hence revealed a quantitative lithiation at these positions.

The corresponding alkylated derivatives were synthesized by lithiation with n-BuLi followed by reaction with alkyl halides and were obtained in good yields of about 60–65%.

Prior to alkylation experiments, deuteration experiments revealed a 100% proton-lithiation exchange at positions 1 and 2 of the S-protected mercapto-
o-carborane icosahedron. Cleavage of the MOM-groups was achieved using mercury(II)-chloride followed by release of the mercapto-compound by \( \text{H}_2\text{S} \) in almost quantitative yields. In case of the 1,2-dideuterated compound, longer reaction times with \( \text{HgCl}_2 \) led to a metallization of the o-carborane cluster and thereby to a reprotonation at the carbon positions during release with \( \text{H}_2\text{S} \).

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Supplementary data

Crystallographic data for compound 2 can be obtained . . . Complete spectral data can be found in a separate supplementary data file.

References


Figure 1: General scheme of substitution of 9,12-bis(methoxy-methylthio)-o-carborane 2. Conditions a) K-\textit{\textit{o-}}-tert-butanol in abs. THF, then MOM-bromide b) \textit{\textit{n-}}-bali, then D$_2$O or R–X c) HgCl$_2$ then H$_2$S. For description of R see table 1.
Figure 2: $^1$H-NMR spectra of the 9,12-dimercapto-o-carborane derivatives: a) 1, b) 2, c) 3a, d) 4a. Signal 1a and 1b: MOM-group, signal 2: icosahedral CH, 3 BH, 4: SH.
Figure 3: $^{13}$C-NMR spectra of the 9,12-Bis(methoxy-methylthio)-$o$-carborane precursor and of the products of the deuteration reaction sequence. a) 1, b) 2, c) 3, d) 4.
Figure 4: ORTEP model of the 9,12-bis(methoxy-methylthio)-o-carborane 2. The ellipsoids are displayed with a probability of 50% at a temperature of 293 K.
Figure 5: Infrared spectra of 1, 2, 3a and 4a. Assigned resonances: a) CH (icosaeder), b) CH (MOM, stretch), c) BH, d) CD, e) C-C (stretch, icosaeder), f) CH (MOM, deformation).
Figure 6: Details of the NMR spectra of 9,12-dimercapto-1,2-dideutero-o-carborane and 9,12-bis(methoxy-methylthio)-1,2-dideutero-o-carborane. The reprotonation at the carbon atoms is displayed by the increase of the signal at 3.55/3.6 ppm.
Figure 7: HMBC-correlation spectrum of 9,12-bis(methoxy-methyl-thio)-1,2-diheptyl-o-carborane. The displayed correlations reveals the successful substitution of the icosahedral carbons.
Figure 8: Proton spectrum of 4c.
<table>
<thead>
<tr>
<th>Number</th>
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<tbody>
<tr>
<td>3a/4a</td>
<td>Deuterium</td>
</tr>
<tr>
<td>3b/4b</td>
<td>Heptyl</td>
</tr>
<tr>
<td>3c/4c</td>
<td>Ethyl</td>
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Table 1: List of derivatives of compound 3.