Oxonium derivatives of *closo*-decaborate in reactions with sulfur-containing nucleophiles

E. Yu. Matveev,[a,b] G. A. Razgonyaeva,[a] V. N. Mustyatsa,[a] N. A. Votinova,[a,b] K. Yu. Zhizhin,[a,b] and N. T. Kuznetsov[a,b]*

[a]*N. S. Kurnakov Institute of General and Inorganic Chemistry Russian Academy of Sciences, 31 Leninsky prosp., 119991 Moscow, Russian Federation. E-mail: zhizhin@igic.ras.ru*

[b]*M. V. Lomonosov Moscow State Academy of Fine Chemical Technology, 86 prosp. Vernadskogo, 119571 Moscow, Russian Federation*

The reaction of the $[B_{10}H_9O_2C_4H_8]^-$, $[B_{10}H_9OC_4H_8]^-$, and $[B_{10}H_9OC_5H_{10}]^-$ anions with negatively charged S-nucleophiles, such as SH^-, SCN^-, and $S_2O_3^{2-}$, resulted in the ring opening of the cyclic substituent and the formation of derivatives with the terminal thiol, thiocyanate, and thiosulfate groups. The structures of the products were confirmed by the IR, mass, and ^1H, ^{11}B, and ^{13}C NMR spectra.

Key words: boron hydrides, *closo*-decaborate, ring opening, derivatives with terminal sulfur-containing group.

Derivatives of *closo*-borate anions with attached cyclic *exo*-polyhedral oxonium type substituents react with nucleophiles giving the compounds with functional group separated from the cluster by the alkoxy spacer.[1—7] This method for the boron clusters modification are of significant interest for the synthesis of novel boron-containing compounds for boron neutron capture therapy (BNCT), because the boron framework is separated from the functional groups and does not affect them. Therefore, ordinary chemical reactions can be used for the modifications of these functional groups. Thus, the *closo*-borate derivatives with terminal nucleophilic groups could be linked to biologically active substances (proteins, lipids, nucleotides), which will provide directed biological transport of boron-containing substances to the tumor cells.

It is known that sulfur-containing derivatives of *closo*-borates can be successfully used for BNCT.[8] The S-derivatives of *closo*-decaborates with functional groups separated from the boron cluster by the spacer could also be of large importance as the separation of the functional group significantly affected the reactivity of the $[B_{10}H_{10}]^{2-}$ derivatives.

The present work is devoted to study of the reactions of *closo*-decaborate oxonium derivatives with negatively charged S-nucleophiles, such as SH^-, SCN^-, $S_2O_3^{2-}$.

Results and discussion

The reactions of $[B_{10}H_9O_2C_4H_8]^-$, $[B_{10}H_9OC_4H_8]^-$, and $[B_{10}H_9OC_5H_{10}]^-$ with negatively charged S-nucleophiles resulted in derivatives **1**—**9** with attached nucleophilic group (see Experimental). On Scheme 1, these reactions are shown on the example of compound **10** (the $[B_{10}H_9O_2C_4H_8]^-$ anion). Sodium hydrosulfide, sodium thiosulfate and potassium thiocyanate were used as nucleophiles. In polar aprotic solvents with excellent metal-cation coordination ability, for example DMSO, these salts form very weakly solvated anions SH^-, $S_2O_3^{2-}$, and SCN^-, respectively, which are very effective nucleophiles.[9]

The resulting compounds with mixed cations (the compounds of the type **11**—**13**, see Scheme 1) were converted into water insoluble tetraphenylphosphonium salts. Thus, the thiol and thiosulfate derivatives were directly isolated from the reaction mixtures (compounds of the type **1** and **2**). In the case of thiocyanate derivatives, the treatment of the reaction mixtures with Ph_4PCl resulted in inseparable mixtures of the target compounds with tetraphenylphosphonium thiocyanate. Therefore, for the isolation of the target compounds, their cesium salts (compounds of the type **14**) were obtained, which were then converted to tetraphenylphosphonium salts. All reactions provided the target compounds in high yields (88—96%).

Thus, the derivatives with sulfur-containing substituents separated from the boron cluster by the alkoxy spacer were synthesized. The reactions were monitored by the IR spectroscopy. The IR spectra of the products exhibited the characteristic shift of the absorptions bands of the stretching vibrations of the C—O bonds to the shorter wavenumbers by 40—50 cm^{-1} due to the breaking of one of the C—O bonds in the oxonium substituent and the formation of the alkoxy chain. Moreover, the IR spectra of the isolated compounds contained the absorption bands charac-

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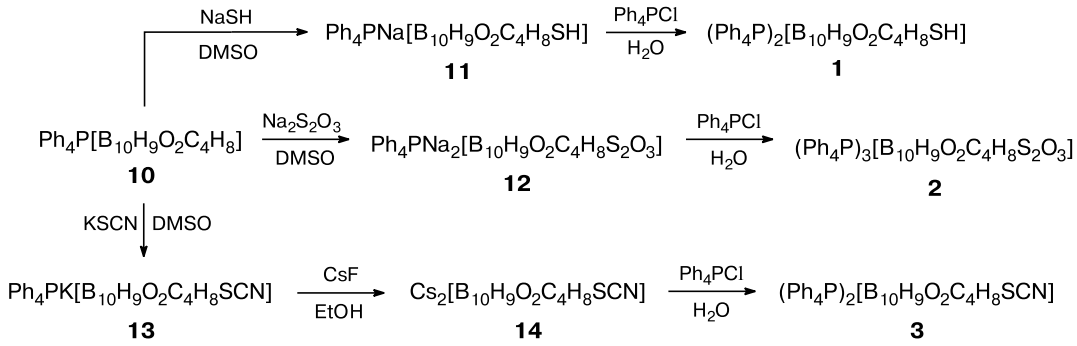
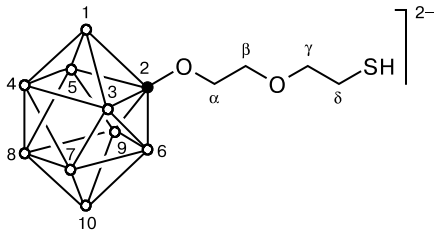
Scheme 1



teristic of the attached functional groups. For example, the IR spectra of the thiocyanate derivatives contained the absorption bands at 2150, 2128, and 2108 cm^{-1}, which were attributed to the stretching vibrations of the C≡N bond. This set of vibrations corresponded to the terminal thiocyanate group.[10]

The ring opening of the cyclic substituent was even more clearly demonstrated by ^{11}B NMR spectroscopy. The ^{11}B NMR spectra of all synthesized compounds are almost identical; the nature of the nucleophilic group has little effect on the pattern of the spectra. The change in the character of substituent on the equatorial boron atom upon the reaction led to the change in the positions of all signals in the spectra. The signal for the *ipso*-boron atom (structure **A**, atom B(2)), which was observed at δ 6.1 in the starting compound, shifted to the weaker field and nearly overlaps with the signal for the neighboring apical boron atom. The signal for another apical boron atom shifted to the stronger field. The spectral pattern in the strong fields was also changed: the ^{11}B NMR spectrum exhibited the separate signal, which was attributed to four boron atoms neighboring the substituted position (B(3), B(5), B(6), B(9)), and two signals for three opposite boron atoms (B(4), B(7), B(8)).



A

The structures of the synthesized compounds were also confirmed by the data from the ^1H NMR spectra. Thus the ^1H NMR spectra of the starting anion $[B_{10}H_9O_2C_4H_8]^-$ (compound **10**) contained two triplet signals for the α- and β-protons of the CH_2-groups at δ 4.6 and 4.2, respectively. The spectra of the synthesized compounds exhibited significant changes. Thus the ^1H NMR spectra of the $[B_{10}H_9OCH_2CH_2OCH_2CH_2SH]^{2-}$ anion (compound **1**), contained four triplet signals at δ 4.0 (α-CH_2), 3.9 (β-CH_2), 3.7 (γ-CH_2), and 3.2 (δ-CH_2) along with the broadened singlet signal for the proton of the SH-group at δ 2.9. The pattern of the ^{13}C NMR spectra of the compounds synthesized changed significantly as compared with that for the starting compounds. For example, the ^{13}C NMR spectra of the $[B_{10}H_9O_2C_4H_8]^-$ anion (compound **10**) exhibited two singlet signals for the α- and β-C atoms of the methylene groups at δ 58.2 and 80.8, respectively, while the ^{13}C NMR spectra of the thiol derivative (compound **2**) contained four singlet signals for the nonequivalent C atoms of the alkoxy chain at δ 38.3 (δ-CH_2), 68.6 (α-CH_2), 69.7 (γ-CH_2), and 72.7 (β-CH_2). The ^1H and ^{13}C spectra of the compounds synthesized are differ in the general pattern of the spectra and the chemical shifts due to the influence of the terminal nucleophilic groups.

The terminal functional groups were also indentified by the mass spectrometry (ESI/MS), which provided the molecular weights for all compounds synthesized. Typically, the anion part of the mass spectra contained the intensive peaks attributed to $[Ph_4P^+ + (B_{10}H_9O_2C_4H_8Nu)^{2-}]^-$ and $[H^+ + (B_{10}H_9O_2C_4H_8Nu)^{2-}]^-$.

In summary, it was shown that the negatively charged ions, SH^-, $S_2O_3^{2-}$, and SCN^-, can act as effective nucleophiles in the reactions with $[B_{10}H_9OC_4H_8]^-$, $[B_{10}H_9O_2C_4H_8]^-$, and $[B_{10}H_9OC_5H_{10}]^-$ in DMSO. The ring opening of the cyclic substituent and addition of the S-nucleophile could be regarded as a novel effective method for the functionalization of the *closo*-borates.

Experimental

The substituted derivatives of *closo*-decaborate **1**, $[Ph_4P]B_{10}H_9OC_4H_8$ (**15**), and $[Ph_4P]B_{10}H_9OC_5H_{10}$ (**16**) were prepared in accordance with the known methods.[4] 1,4-Dioxane and terahydrofuran were purified by the known procedure.[11] Potassium hydrosulfide was prepared by the known method.[12] DMSO, KOH, KSCN, $Na_2S_2O_3$, CsF, and Ph_4PCl with assay ≥99% were used as purchased.

The IR spectra were recorded on an Infralum FT-02 Fourier-transform IR spectrometer in the range of 7000—300 cm^{-1} with the resolution of 1 cm^{-1}. The samples were prepared as suspensions in Nujol (Aldrich) or fluorinated oil (Fluorolube, Merck). The ^1H, ^{13}C, and ^{11}B spectra were recorded on a Bruker AC-200 instrument employing the deuterium resonance of the solvent as the lock signal. The chemical shifts are given relative to $SiMe_4$ (^1H and ^{13}C) or boron trifluoride etherate (^{11}B). The mass spectra (ESI) were run on a Bruker Esquire 3000 plus mass spectrometer (Electrospray Voltage +(−)4500 V). Acetonitrile or a mixture acetonitrile—water (1 : 1) were used as solvents. Average analytical concentration of the sample was 1.00±0.20 mg mL^{-1}.

Tetraphenylphosphonium 2-[2-(2-mercaptoethoxy)ethoxy]-nonahydro-*closo*-decaborate (1) (the signs for the atoms in $[B_{10}HO_9(CH_2)_2O(CH_2)_2SH]^{2-}$ (**A**) are given above). A solution of compound **10** (1.09 g, 2 mmol) and NaSH (0.11 g, 2 mmol) in DMSO (20 mL) was shaken for 24 h. The resulting solution was poured into the aqueous solution of Ph_4PCl (0.75 g, 2 mmol), the precipitate that formed was filtered off and dried in desiccator over P_2O_5. Yield 1.67 g (96%). IR (KBr), ν/cm^{-1}: 2452 (ν(B—H)); 1104 (δ(B—B—H)); 697 (δ(B—B—B)); 1008 (ν(C—O)); 2686 (ν(C—H), S—CH_2); 1420 (δ(C—H), S—CH_2). ^1H NMR (CD_3CN), δ: 0.60—2.10 (m, 9 H, $B_{10}H_9$); 2.9 (s, SH); 3.2 (t, δ-CH_2); 3.7 (t, γ-CH_2); 3.9 (t, β-CH_2); 4.0 (t, α-CH_2). ^{13}C {^1H} NMR (CD_3CN), δ: 38.3 (δ-$\underline{C}H_2$); 68.6 (α-$\underline{C}H_2$); 69.7 (γ-$\underline{C}H_2$); 72.7 (β-$\underline{C}H_2$). ^{11}B NMR (CD_3CN), δ: −1.5 (s, B(2)); −2.5 (d, B(10)); −6.1 (d, B(1)); −23.7 (d, B(3), B(5), B(6), B(9)); −29.8 (d, B(7), B(8)); −33.9 (d, B(4)). MS (ESI), *m/z* (anion): 238.19 [M − 2 Ph_4P^+ + H^+]; 577.23 [M − Ph_4P^+]; *m/z* (cation): 339.10 [Ph_4P^+].

Tetraphenylphosphonium 2-[2-(2-thiosulfatoethoxy)ethoxy]-nonahydro-*closo*-decaborate (2). A solution of compound **10** (1.09 g, 2 mmol) and $Na_2S_2O_3$ (0.32 g, 2 mmol) in DMSO (20 mL) was shaken for 24 h. The resulting solution was poured into the aqueous solution of Ph_4PCl (1.5 g, 4 mmol), the precipitate that formed was filtered off and dried in desiccator over P_2O_5. Yield 2.17 r (89%). IR (KBr), ν/cm^{-1}: 2452 (ν(B—H)); 1110 (δ(B—B—H)); 695 (δ(B—B—B)); 1005 (ν(C—O)); 1378, 1160 (ν(S—O)). ^{11}B NMR (CD_3CN), δ: −1.8 (c, B(2)); −2.2 (d, B(10)); −6.4 (d, B(1)); −24.2 (d, B(3), B(5), B(6), B(9)); −29.6 (d, B(7), B(8)); −32.7 (d, B(4)).

Tetraphenylphosphonium 2-[2-(2-thiocyanatoethoxy)ethoxy] nonahydro-*closo*-decaborate (3). A solution of compound **10** (1.09 g, 2 mmol) and KSCN (0.19 g, 2 mmol) in DMSO (20 mL) was shaken for 24 h. The resulting solution was poured into a solution of CsF (0.61 g, 4 mmol) in MeOH, the precipitate that formed was filtered off and washed with MeOH (2S50 mL). The separated precipitate was dissolved in water and the resulting solution was poured into a solution of Ph_4PCl (1.5 g, 4 mmol) in water. The precipitate that formed was filtered off and dried in desiccator over P_2O_5. Yield 1.64 g (95%). IR (KBr), ν/cm^{-1}: 2452 (ν(B—H)); 1110 (δ(B—B—H)); 704 (δ(B—B—B)); 1009 (ν(C—O)); 2130, 2117, 2108 (ν(C—N)). ^{11}B NMR (CD_3CN), δ: −1.6 (s, B(2)); −2.4 (d, B(10)); −6.3 (d, B(1)); −23.7 (d, B(3), B(5), B(6), B(9)); −29.5 (d, B(7), B(8)); −33.2 (d, B(4)).

Tetraphenylphosphonium 2-[4-mercaptobutoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_2[B_{10}H_9O(CH_2)_4SH]$ (4) was synthesized analogously from $Ph_4P[B_{10}H_9OC_4H_8]$ (**15**) (1.06 g, 2 mmol) and NaSH (0.11 g, 2 mmol) in a yield of 1.62 g (95%). IR (KBr), ν/cm^{-1}: 2458 (ν(B—H)); 1106 (δ(B—B—H)); 701 (δ(B—B—B)); 1005 (ν(C—O)); 2690 (ν(C—H), S—CH_2); 1420 (δ(C—H), S—CH_2). ^1H NMR (CD_3CN), δ: 0.60—2.10 (m, 9 H, $B_{10}H_9$); 1.49 (s, SH); 2.53 (q, γ-CH_2); 2.77 (q, β-CH_2); 2.90 (t, δ-CH_2); 3.51 (t, α-CH_2). ^{13}C {^1H} NMR (CD_3CN), δ: 25.4 (γ-$\underline{C}H_2$); 28.3 (β-$\underline{C}H_2$); 38.5 (δ-$\underline{C}H_2$); 72.7 (α-$\underline{C}H_2$). ^{11}B NMR (CD_3CN), δ: −1.8 (s, B(2)); −3.2 (d, B(10)); −5.5 (d, B(1)); −23.7 (d, B(3), B(5), B(6), B(9)); −29.2 (d, B(7), B(8)); −34.2 (d, B(4)).

Tetraphenylphosphonium 2-[4-thiosulfatobutoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_3[B_{10}H_9O(CH_2)_4S_2O_3]$ (5) was synthesized analogously from salt **15** (1.06 g, 2 mmol) and $Na_2S_2O_3$ (0.32 g, 2 mmol) in a yield of 2.19 g (88%). IR (KBr), ν/cm^{-1}: 2450 (ν(B—H)); 1102 (δ(B—B—H)); 695 (δ(B—B—B)); 1005 (ν(C—O)); 1381, 1164 (ν(S—O)). ^1H NMR (CD_3CN), δ: 0.60—2.10 (m, 9 H, $B_{10}H_9$); 1.17 (q, δ-CH_2); 1.36 (q, β-CH_2); 2.70 (t, α-CH_2); 2.94 (t, δ-CH_2). ^{13}C {^1H} NMR (CD_3CN), δ: 29.4 (γ-$\underline{C}H_2$); 30.5 (β-$\underline{C}H_2$); 61.7 (α-$\underline{C}H_2$); 72.5 (β-$\underline{C}H_2$). ^{11}B NMR (CD_3CN), δ: −1.7 (s, B(2)); −3.0 (d, B(10)); −5.4 (d, B(1)); −23.5 (d, B(3), B(5), B(6), B(9)); −28.9 (d, B(7), B(8)); −34.1 (d, B(4)).

Tetraphenylphosphonium 2-[4-thiocyanatobutoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_2[B_{10}H_9O(CH_2)_4SCN]$ (6) was synthesized analogously from salt **15** (1.06 g, 2 mmol) and KSCN (0.19 g, 2 mmol) in a yield of 1.68 g (96%). IR (KBr), ν/cm^{-1}: 2452 (ν(B—H)); 1108 (δ(B—B—H)); 704 (δ(B—B—B)); 1009 (ν(C—O)); 2130, 2115, 2108 (ν(C≡N), S—C≡N). ^1H NMR (CD_3CN), δ: 0.60—2.10 (m, 9 H, $B_{10}H_9$); 1.17 (q, γ-CH_2); 1.36 (q, β-CH_2); 2.70 (t, α-CH_2), 2.94 (t, β-CH_2). ^{13}C {^1H} NMR (CD_3CN), δ: 31.2 (α-$\underline{C}H_2$); 35.8 (β-$\underline{C}H_2$); 58.0 (δ-$\underline{C}H_2$); 72.7 (γ-$\underline{C}H_2$); 100.3 (—S—$\underline{C}$≡N). ^{11}B NMR (CD_3CN), δ: −1.7 (s, B(2)); −3.0 (d, B(10)); −5.4 (d, B(1)); −23.5 (d, B(3), B(5), B(6), B(9)); −28.9 (d, B(7), B(8)); −34.1 (d, B(4)).

Tetraphenylphosphonium 2-[4-mercaptopentoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_2[B_{10}H_9O(CH_2)_5SH]$ (7) was synthesized analogously from $Ph_4P[B_{10}H_9OC_5H_{10}]$ (**16**) (1.09 g, 2 mmol) and NaSH (0.11 g, 2 mmol) in a yield of 1.56 g (93%). IR (KBr), ν/cm^{-1}: 2456 (ν(B-H)); 1106 (δ(B—B—H)); 701 (δ(B—B—B)); 1005 (ν(C—O)); 2690 (ν(C—H), S—CH_2); 1415 (δ(C—H), S—CH_2). ^{11}B NMR (CD_3CN), δ: −1.6 (s, B(2)); −3.0 (d, B(10)); −5.5 (d, B(1)); −23.8 (d, B(3), B(5), B(6), B(9)); −29.1 (d, B(7), B(8)); −34.4 (d, B(4)).

Tetraphenylphosphonium 2-[4-thiosulfatopentoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_3[B_{10}H_9O(CH_2)_5S_2O_3]$ (8) was synthesized analogously from salt **16** (1.09 g, 2 mmol) and $Na_2S_2O_3$ (0.32 g, 2 mmol) in a yield of 2.16 g (88%). IR (KBr), ν/cm^{-1}: 2450 (ν(B—H)); 1102 (δ(B—B—H)); 695 (δ(B—B—B)); 1005 (ν(C—O)); 1380, 1164 (ν(S—O)). ^{11}B NMR (CD_3CN), δ: −1.6 (s, B(2)); −3.2 (d, B(10)); −5.5 (d, B(1)); −23.6 (d, B(3), B(5), B(6), B(9)); −28.8 (d, B(7), B(8)); −34.1 (d, B(4)).

Tetraphenylphosphonium 2-[4-thiocyanatopentoxy]nonahydro-*closo*-decaborate, $(Ph_4P)_2[B_{10}H_9O(CH_2)_5SCN]$ (9) was synthesized analogously from salt **16** (1.09 g, 2 mmol) and KSCN (0.19 g, 2 mmol) in a yield of 1.63 g (94%). IR (KBr), ν/cm^{-1}: 2452 (ν(B—H)); 1108 (δ(B—B—H)); 704 (δ(B—B—B)); 995 (ν(C—O)); 2128, 2110, 2108 (ν(C≡N)). ^{11}B NMR (CD_3CN), δ: −1.6 (s, B(2)); −3.3 (d, B(10)); −5.5 (d, B(1)); −23.6 (d, B(3), B(5), B(6), B(9)); −28.8 (d, B(7), B(8)); −34.1 (d, B(4)).

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References

1. A. A. Semioshkin, I. B. Sivaev, V. I. Bregadze, *Dalton Trans.*, 2008, 977.
2. A. V. Orlova, N. N. Kondakov, B. G. Kimel, L. O. Kononov, E. G. Kononova, I. B. Sivaev, V. I. Bregadze, *Appl. Organometal. Chem.*, 2007, **21**, 98.
3. I. B. Sivaev, N. Yu. Kulikova, E. A. Nizhnik, M. V. Vichuzhanin, Z. A. Starikova, A. A. Semioshkin, V. I. Bregadze, *J. Organomet. Chem.*, 2008, **693**, 519.
4. I. B. Sivaev, A. A. Semioshkin, B. Brellochs, S. Sjöberg, V. I. Bregadze, *Polyhedron*, 2000, **19**, 627.
5. T. Peymann, K. Kück, D. Gabel, *Inorg. Chem.*, 1997, **36**, 5138.
6. K. Yu. Zhizhin, V. N. Mustyatsa, E. A. Malinina, E. Yu. Matveev, L. V. Goeva, I. N. Polyakova, N. T. Kusnetsov, *Zh. Neorg. Khim.*, 2005, **50**, 243 [*Russ. J. Inorg. Chem.* (*Engl. Transl.*), 2005, **50**, 203].
7. K. Yu. Zhizhin, V. N. Mustyatsa, E. A. Malinina, N. A. Votinova, E. Yu. Matveev, L. V. Goeva, I. N. Polyakova, N. T. Kusnetsov, *Zh. Neorg. Khim.*, 2004, **49**, 221 [*Russ. J. Inorg. Chem.* (*Engl. Transl.*), 2004, **49**, 180].
8. M. F. Hawthorne, *Angew. Chem., Int. Ed.*, 1993, **32**, 950.
9. J. March, *Advanced Organic Chemistry*, John Wiley and Sons, New York—Chichester—Brisbane—Toronto—Singapore, 1985.
10. K. Nakamoto, *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, Wiley Interscience, New York, 1986.
11. H. Becker, G. Domshke, E. Fanghanel, *Organikum*, VEB Deutscher Verlag der Wissenschaften, Berlin, 1990.
12. *Händbuch der präparativen anorganischen Chemie*, Ed. G. Brauer, Ferdinand Enker Verlag, Stuttgard, 1981.

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