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Synthesis and structure of novel *closo*-dodecaborate-based glycerols

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ABSTRACT

The reactions of oxonium derivatives of $[B_{12}H_{12}]^{2-}$ with different glycerol-based nucleophiles were studied. A series of novel *closo*-dodecaborate-based glycerols with different net charges on the molecules were prepared. A structure of {2-[2-(4-(2, 3-dihydroxypropyl)-dipiperazinium-1-yl)-ethoxy]-ethoxy}-undecahydro-*closo*-dodecaborate was determined and the existence of different intermolecular H-bonds was shown.

1. Introduction

Water-soluble functionalized derivatives of the dodecahydro-*closo*-dodecaborate anion are promising candidates for boron neutron capture therapy (BNCT) [1]. Our continuing interest in the chemistry of the dodecahydro-*closo*-dodecaborate anion $[B_{12}H_{12}]^{2-}$ aims toward facile, reliable and rational introduction of a broad variety of substituents. One of these methods consists of synthesis of its oxonium derivatives followed by their nucleophilic cleavage. This approach permits us to synthesize a range of $[B_{12}H_{12}]^{2-}$ derivatives with different active groups and them to various molecules [2]. Synthesis of *closo*-dodecaborate derivatives of glycerol is important because these compounds are standard starting materials for the preparation of lipids, precursors of liposomes. Liposomes are the smallest spherical lipid bilayers that can be produced from non-toxic phospholipids and cholesterol. These vesicles can be used as drug carriers and can be loaded with variety of molecules. The most commonly used lipids in preparation of liposomes are phosphatidylcholine, phosphatidylinositol and cholesterol which have limited intrinsic toxicity and are found abundantly as the components of cell membranes. Drugs with widely varying lipophilicities can be encapsulated in liposomes either in the phospholipid bilayer or in the entrapped aqueous core. Therefore, two approaches are possible when using liposomes in boron delivery: encapsulation of boron compounds in the aqueous core of the liposome, and incorporation of boron-containing lipids in the liposome bilayer. Both approaches, using different types of boron compounds, have been described and some results are summarized in reviews [3–5]. Boron-containing lipids constitute very interesting building blocks for the construction of boron-containing liposomes. A few approaches toward the synthesis of such lipids intended for incorporation into liposomes have been described in the literature. Synthesis of a *nido*-carborane lipid with a one-tailed moiety has been described, and the liposomal boron delivery using this compound and distearoylphosphatidylcholine (DSPC) has been examined in mice [6,7]. Later, Nakamura et al. designed a *nido*-carborane lipid with a double-tailed moiety for the purposes of high boron accumulation into liposomes [8]. More recently, Hawthorne et al. described a very similar lipid and investigated the *in vivo* toxicity of liposomes formed from the boron-containing lipid and helper lipids (DSPC, cholesterol (CHO)). They found that the liposomes were very toxic already at dosages of 6 mg boron per kg body weight [9]. Therefore, *nido*-carborane-based lipids might be problematic as agents for boron delivery in BNCT. Synthesis of the first ether lipid based on the *closo*-dodecaborate anion was reported by Sivaev et al. [10], some later ester lipids containing $[B_{12}H_{12}]^{2-}$ and $[B_{10}H_{10}]^{2-}$ anions were prepared by Lisovskii et al. [11]. A series of *closo*-dodecaborate-containing ester lipids was recently described by Nakamura and co-workers [12]. Synthesis of the double-tailed boron cluster lipids and, which have a $[B_{12}H_{11}S]$-moiety as a hydrophilic function, was achieved by S-alkylation of $[B_{12}H_{11}SH]^{2-}$ (BSH) with bromoacetyl and chloroacetocarbamate derivatives of diacylglycerols. A new class of lipids containing also BSH as hydrophilic lipid head group was synthesized by Gabel and co-workers [13]. Two lipids

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based on diethanolamine (*S*-(*N*,*N*-(2-dimyristoyloxyethyl)acetamido)thioundecahydro-*closo*-dodecaborate (2-) and *S*-(*N*,*N*-(2-dipalmitoyloxyethyl)acetamido)thioundecahydro-*closo*-dodecaborate (2-)) were described by them. One of these compounds was found to form liposomal vesicles without the addition of helper lipids, representing the first boron-containing lipid with this capability. Recently two more diethanolanine B_{12}-containig lipids were synthesized from the corresponding oxonium derivatives and their liposomal formation was studied as well by Gabel and co-workers [14]. In conclusion, till now B_{12}-based lipids were prepared either from BSH or from oxonium derivatives, but with a diethanolamine fragment.

It is to be mentioned that B_{12}-derivatives that contain the glycerol fragment, especially with free –OH groups, have not yet been described. However, preparation of such compounds is important because they seem to be rather attractive synthons for the preparation of various lipids by simple acylation reactions. Thus, in this paper we present easy and convenient methods of preparation of dodecaborate derivatives of glycerol in which the net charge on the products can be varied. The net charge of the corresponding lipids may influence the zeta potential of the liposomes and thus their biological properties, including the interaction with the negatively charged cell membranes.

2. Experimental

2.1. Materials and equipment

Chemicals were reagent grade and were used as received from commercial vendors. Acetonitrile was distilled from P_2O_5 and then from CaH_2. Oxonium derivative **1**, and ethyl 4-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]piperazine-1-carboxylate were prepared according to the described methods [15,16]. The ^1H, ^{13}C and ^{11}B NMR spectra were recorded at 400.13, 100.61 and 128.38 MHz, respectively, on a BRUKER-Avance-400 spectrometer. Tetramethylsilane and $BF_3/(C_2H_5)_2O$ were used as standards for ^1H and ^{13}C NMR, and ^{11}B NMR, respectively. All chemical shifts are reported in ppm (δ) relative to external standards. IR spectra were recorded on Infralum FT-801 FTIR spectrometer in nujol. Elemental analysis was performed in the Microanalytical laboratory of the A.N. Nesmeyanov Institute of Organoelement Compounds.

2.2. Synthesis of tetrabutylammonium sodium (2-{2-[(2,2-dimethyl-1,3-dioxolan-4-yl)methoxy]ethoxy}ethoxy)-undecahydro-closo-dodecaborate **2**

To the solution of 2.8 g (0.02 mol) of (2,2-dimethyl-1,3-dioxolan-4-yl)methanol (solketal) in 25 ml of dry CH_3CN was added 0,51 g (0.02 mol) of NaH and the mixture was stirred for 5 min until the evolution of H_2 was completed. Then 1 g of **1** (0.002 mol) was added and the mixture was refluxed for 10 h. Then the solid was filtered off and washed with 10 ml of CH_3CN. The solvent was evaporated and the rest was vacuum dried to afford pure **2** as colorless oil. Yield: 0.985 g (0.0016 mol, 74%). ^1H NMR (DMSO-d_6, δ, ppm): 4.14 (1H, m, HCO); 3.95, 3.54 (2H, 2 × m, CH_2OCH); 3.5–3.1 (10H, broad m, OCH_2); 3.13 (8H, m, $NCH_2CH_2CH_2CH_3$); 1.54 (8H, m, $NCH_2CH_2CH_2CH_3$); 1.31 (3H, s, CH_3); 1.28 (3H, s, CH_3); 1.27 (8H, m, $NCH_2CH_2CH_2CH_3$); 0.90 (12H, t, $NCH_2CH_2CH_2CH_3$, J = 7.3 Hz); 1.9–0.2 (11H, broad m, BH). ^{11}B NMR (DMSO-d_6, δ, ppm): 6.4 (1B, s, B(1)); −16.8 (5B, d, B(2–6), J = 128 Hz); −18.2 (5B, d, B(7–11), J = 127 Hz); −22.8 (1B, d, B(12), J = 128 Hz); ^{13}C NMR (DMSO-d_6, δ, ppm): 109.0 ($C(CH_3)_2$); 76.9 (CHO); 74.7, 72.1, 70.6, 69.9, 67.7, 66.5 (CH_2O); 58.0 ($NCH_2CH_2CH_2CH_3$); 27.1, 25.9 (CH_3); 23.5 ($NCH_2CH_2CH_2CH_3$); 19.7 ($NCH_2CH_2CH_2CH_3$); 13.8 ($NCH_2CH_2CH_2CH_3$). IR (ν, nujol, cm^{-1}): 2478 (BH).

2.3. Synthesis of dicesium {2-[2-(2,3-dihydroxypropoxy)ethoxy]ethoxy}-undecahydro-closo-dodecaborate **3**

Compound **2** (0.985 g) (0.0016 mol) was dissolved in 10 ml of MeOH and the solution of 0.65 g (0.00424 mol) of CsF in 10 ml of MeOH was added. A white precipitate was formed. It was filtered, washed with 10 ml of MeOH and vacuum dried. Then it was dissolved in 50 ml of H_2O, and 10 ml of HCl was added. After 4 h of stirring water was removed in vacuum, the rest was suspended in 20 ml of THF. The white precipitate was filtered, washed with 20 ml of THF and air dried. Yield: 0.870 g (0.0015 mol, 95%). M.p. >250 °C. *Anal.* Calc. For $C_7H_{26}B_{12}Cs_2O_5$: C, 14.35; H, 4.47. Found: C, 14.20; H, 4.45%. ^1H NMR (D_2O, δ, ppm): 3.85 (1H, m, HCO); 3.7–3.4 (12H, broad m, CH_2O); 2.2–0.1 (11H, broad m, BH). ^{11}B NMR (D_2O, δ, ppm): 4.64 (1B, s, B(1)); −17.0 (10B, m, B(2–11)); −21.2 (1B, d, B(12), J = 126 Hz). ^{13}C NMR (DMSO-d_6, δ, ppm): 71.7, 71.0, 70.3, 69.9, 69.3, 67.6, 62.6 (CH_2O). IR (ν, nujol, cm^{-1}): 3633, 3481 (OH), 2482 (BH).

2.4. Synthesis of tetrabutylammonium-{2-[2-(4-(2, 3-dihydroxypropyl)-dimethylammonium)-ethoxy]-ethoxy}-undecahydro-closo-dodecaborate **4**

The mixture of 1 g (0.002 mol) of **1** and 0.266 g (0.002 mol) of (2,3-dihydroxy)-propyl-dimethylamine was refluxed in 25 ml of CH_3CN for 24 h. Then the solvent was evaporated and 10 ml of H_2O was added to precipitate **4**. It was filtered off and vacuum dried. Yield: 0.787 g (0.0013 mol, 62%). M.p. = 117–118 °C. *Anal.* Calc. For $C_{25}H_{68}B_{12}N_2O_4$: C, 50.85; H, 11.61; N, 4.74. Found: C, 50.64; H, 11.48; N, 4.50%. ^1H NMR (DMSO-d_6, δ, ppm): 4.03 (1H, m, HCO); 3.87 (2H, m, CH_2O); 3.67 (2H, m, CH_2O); 3.61 (2H, m, CH_2N); 3.57 (2H, m, CH_2O); 3.48 (1H, dd, HOHCHCH, J = 8.9 Hz, J = 6.4 Hz); 3.42 (1H, dd, N-HCHCH, J = 7.4 Hz, J = 3.4 Hz); 3.33 (1H, dd, OHCHCH, J = 9.0 Hz, J = 6.4 Hz); 3.30 (1H, dd, N-HCHCH, J = 7.4 Hz, J = 3.4 Hz); 3.26 (6H, s, CH_3); 3.17 (8H, m, $NCH_2CH_2CH_2CH_3$); 1.56 (8H, m, $NCH_2CH_2CH_2CH_3$); 1.31 (8H, m, $NCH_2CH_2CH_2CH_3$); 0.93 (12H, t, $NCH_2CH_2CH_2CH_3$, J = 7.3 Hz); 1.9–0.2 (11H, broad m, BH). ^{11}B NMR (DMSO-d_6, δ, ppm): 5.2 (1B, s, B(1)); −16.9 (5B, d, B(2–6), J = 127 Hz); −17.6 (5B, d, B(7–11), J = 128 Hz); −21.8 (1B, d, B(12), J = 126 Hz); ^{13}C NMR (DMSO-d_6, δ, ppm): 70.2 (CHOH); 68.5, 67.9, 66.6, 64.6 (CH_2O); 64.2, 64.1 (CH_2N); 58.0 ($NCH_2CH_2CH_2CH_3$); 52.5 (CH_3); 23.5 ($NCH_2CH_2CH_2CH_3$); 19.6 ($NCH_2CH_2CH_2CH_3$); 13.7 ($NCH_2CH_2CH_2CH_3$). IR (ν, nujol, cm^{-1}): 3629, 3494 (OH), 2485 (BH).

2.5. Synthesis of 1-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]piperazine (**5**)

Ethyl 4-[(2,2-dimethyl-1,3-dioxolan-4-yl)methyl]piperazine-1-carboxylate was refluxed in 50 ml of EtOH with 16.8 g (0.3 mol) of KOH for 6 h, Then EtOH was evaporated, 50 ml of H_2O was added followed by extraction by Et_2O (2 × 10 ml). The organic layers were combined, dried over K_2CO_3, Et_2O was evaporated and the rest was vacuum distilled to give **5**. Yield: 7.4 g (0.037 mol, 73.8%). B.p. = 75 °C, 5×10^{-2} Torr. ^1H NMR ($CDCl_3$, δ, ppm): 4.33 (1H, m, CH–O); 4.10 (1H, m, O–HCH); 3.64 (1H, t, O–HCH, J = 10.7); 2.94 (4H, t, CH_2–N, J = 6.4); 2.50 (6H, m, CH_2–N); 1.64 (1H, s, NH); 1.46 (3H, s, CH_3); 1.40 (3H, s, CH_3). ^{13}C NMR ($CDCl_3$, δ, ppm): 108.8 (OCHO); 73.6 (CH–O); 68.1 (CH_2O); 55.0, 45.7 (CH_2N); 26.7, 25.4 (CH_3). IR (ν, nujol, cm^{-1}): 3271 (NH).

2.6. Synthesis of Cesium {2-[2-(methyl-(3-(2, 2,-dimethyl-1-3-dioxalanyl))-piperazinium-1-yl)-ethoxy]-ethoxy}-undecahydro-closo-dodecaborate **6**

The mixture of 1 g (0.002 mol) of **1** and 0.852 g (0.004 mol) of **5** in 50 ml of EtOH was refluxed for 4 h. Then the solvent was evaporated. The residue was washed with Et_2O (2 × 20 ml) and then recrystallized from 5 ml of EtOH. Compound **6** was filtered and vacuum dried. Yield: 1 g (0.0015 mol, 75%). M.p. = 170–172 °C. *Anal.* Calc. For $C_{30}H_{75}B_{12}N_3O_4$: C, 53.65; H, 11.25; N, 6.26. Found: C, 53.60; H, 11.18; N, 6.18%. ^{1}H NMR (DMSO-d_6, δ, ppm): 9.61 (1H, broad s, NH^+); 4.21 (1H, m, HCO); 4.01 (1H, m, O–HCH); 3.81 (2H, m, CH_2–O); 3.53 (7H, m, 2 × CH_2O, 2 × CH_2N^+ and OHCH); 3.30 (2H, m, CH_2N^+); 3.17 (8H, m, $NCH_2CH_2CH_2CH_3$); 3.05 (2H, m, CH_2N); 2.89 (2H, m, CH_2N); 2.55 (2H, m, CH_2N); 1.58 (8H, m, $NCH_2CH_2CH_2CH_3$); 1.33 (3H, s, CH_3); 1.31 (8H, m, $NCH_2CH_2CH_2CH_3$); 0.27 (3H, s, CH_3); 0.94 (12H, t, $NCH_2CH_2CH_2CH_3$, J = 4.9); 1.9–0.2 (11H, broad m, BH). ^{11}B NMR (DMSO-d_6, δ, ppm): 6.1 (1B, s, B(1)); −16.8 (5B, d, B(2-6), J = 127 Hz); −18.0 (5B, d, B(7–11), J = 128 Hz); −22.6 (1B, d, B(12), J = 126 Hz); ^{13}C NMR (DMSO-d_6, δ, ppm): 108.9 ($C(CH_3)_2$); 74.1, 68.8, 67.9, 64.1 (CH_2O); 71.5 (CH–O); 60.2, 54.3 (CH_2N^+); 58.0 ($NCH_2CH_2CH_2CH_3$); 51.6, 49.6 (CH_2N); 27.2, 26.0 (CH_3); 23.6 ($NCH_2CH_2CH_2CH_3$); 19.7 ($NCH_2CH_2CH_2CH_3$); 14.0 ($NCH_2CH_2CH_2CH_3$); IR (ν, nujol, cm^{-1}): 3133 (NH^+), 2485 (BH).

2.7. Synthesis of {2-[2-(4-(2, 3-dihydroxypropyl)-dipiperazinium-1-yl)-ethoxy]-ethoxy}-undecahydro-closo-dodecaborate (**7**)

One gram (0.0015 mol) of **6** was dissolved in 20 ml of 16% of aqueous HCl. Then the solvent was evaporated and the rest was recrystallized from the 5 ml of H_2O. Yield: 0.5 g (0.0013 mol, 64%). M.p. = 246 °C (dec). *Anal.* Calc. For $C_{11}H_{36}B_{12}N_2O_4{\cdot}3H_2O$: C, 29.74; H, 9.53; N, 6.31. Found: C, 29.09; H, 9.34; N, 6.15%. ^{1}H NMR (D_2O, δ, ppm): 9.91 (2H, broad s, NH (detected in DMSO-d_6)); 4.05 (1H, m, CH–O); 3.8–3.4 (18H, m, 4 × CH_2O and 5 × CH_2N^+); 3.23 (2H, m, CH_2N^+); 1.9–0.2 (11H, broad m, BH). ^{11}B NMR (D_2O): 6.2 (1B, s, B(1)); −16.5 (5B, d, B(2–6), J = 129 Hz); −18.3 (5B, d, B(7–11), J = 129 Hz); −23.1 (1B, d, B(12), J = 126 Hz). ^{13}C NMR (D_2O, δ, ppm): 74.1 (CHOH); 71.5, 68.7, 66.0, 64.0 (CH_2O); 55.2, 54.3 53.9, 52.1, 51.5, 49.9 (CH_2N^+). IR (ν, nujol, cm^{-1}): 3623, 3495 (OH), 3128 (NH^+), 2482 (BH).

2.8. X-ray diffraction data

Single-crystal X-ray diffraction experiment for **7**·3(H_2O) were carried out with a Bruker SMART 1000 CCD area detector, using graphite monochromated Mo Kα radiation (λ = 0.71073 Å, ω-scans with a 0.3° step in ω and 10 s per frame exposure, 2θ < 52°) at 120 K. Low temperature of the crystals was maintained with a Cryostream (Oxford Cryosystems) open-flow N_2 gas cryostat. Reflection intensities were integrated using SAINT software (SMART V5.051 and SAINT V5.00, area detector control and integration software and semi-empirical method SADABS [17]).

The colorless plate (0.45 × 0.35 × 0.20 mm) $C_{11}H_{36}B_{12}N_2O_4{\cdot}3(H_2O)$ is triclinic (M = 444.19), at 120 K a = 10.157(1) Å, b = 11.206(1) Å, c = 13.1420(15) Å, α = 102.949(3)°, β = 109.403(2)°, γ = 107.152(3)°, V = 1259.1(3) Å^3, space group $P\bar{1}$, Z = 2, D_{calc} = 1.172 g/Å^3.

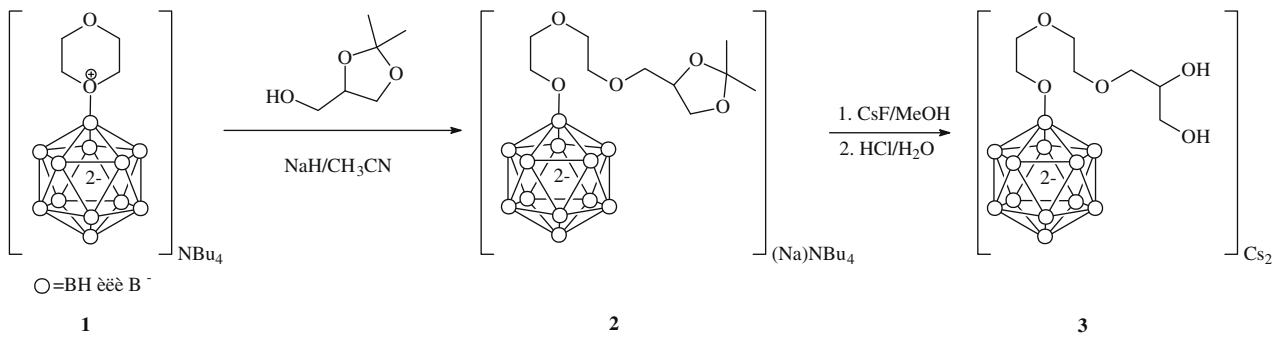
Intensities of 10962 reflections were measured and 4060 independent reflections (R_{int} = 0.0388) were used in further calculations and refinement. The structures were solved by direct method and refined by the full-matrix least-squares against F^2 in anisotropic (for no-hydrogen atoms) approximation. All carborane hydrogen atoms and, the H(N) atoms were located from the difference Fourier syntheses, the H(C) and H(OH) atoms were placed in geometrically calculated positions. All hydrogen atom positions were refined in isotropic approximation in riding model with the Uiso(H) parameters equal to 1.2 Ueq(Xi), where U(Xi) are the equivalent thermal parameters of the atoms to which corresponding H atoms are bonded. The refinement converged to wR_2 = 0.1625 and GOF = 1.013 for all 4860 independent reflections (R_1 = 0.0716 was calculated against F for the 2096 independent reflections with $I > 2\sigma(I)$). The number of the refined parameters was 336.

All calculations were performed on an IBM PC/AT using the SHELXTL software [17].

3. Results and discussion

Since different glycerol derivatives with O– or N′– single nucleophilic center are either commercially available or can be easily prepared, we have studied the reactions of some of these compounds with dioxonium derivative of *closo*-dodecaborate (**1**) to get its novel glycerol derivatives.

Previously we have shown that oxonium derivatives of $[B_{12}H_{12}]^{2-}$ do react with alcohols [18] and phenols [19] leading to corresponding ethers with good yields. Thus, we have run the reaction of oxoniun derivative **1** with solketal. We have found that this reaction, as expected, resulted in a novel cleavage product **2** as a mixed sodium and NBu_4 salt with a good yield. The structure of **2** was elucidated by NMR and microanalysis (cf. experimental). For example, in the ^{11}B NMR of **2** the signal of the substituted boron atom is shifted ca 2 ppm downfield compared to the starting material **1** [15]. This is typical for the transformation of BO^+R_2 system to B–OR. Compound **2** was transferred into its Cs-salt and then the ketal protection was removed, leading to a novel B_{12}-derivative with glycerol fragment **3** (Scheme 1). In the IR spectrum of **3** the absorbtion bands of OH-groups (3633 and 3481 sm^{-1}) were observed. The ^{11}B NMR of **3** was identical to **2**. In ^{1}H NMR, only signals of protons CH–OH, CH_2–O and BH groups were observed and there were no



Scheme 1.

signals of protons of methyl groups, detected in case of **2**. In ^{13}C NMR of **3**, seven signals of CH–OH, CH_2–OH and CH_2–O fragments were observed between 72 and 62 ppm. Compound **3** is a novel *closo*-dodecaborate cluster with glycerol fragment with (−2) charge on the molecule.

In our previous work [20] we have found that oxonium derivatives such as **1** react with various amines leading to corresponding cleavage products with excellent yields. Thus we have studied the reactions of **1** with amino derivatives of glycerol. We have found that oxonium derivative **1** reacts with 3-dimethylamino-propane-1,2-diole to give the ammonium derivative **4**, isolated as NBu_4-salt (Scheme 2). This (−1) charged *closo*-dodecaborate cluster with glycerol fragment was characterized by NMR and IR spectroscopy. In the IR spectrum of **4** the absorption band of OH-groups (3629 and 3494 sm^{-1}) were observed. In ^{11}B NMR of **4**, the signal of the substituted boron atom is shifted ca 2 ppm downfield compared to the starting material **1** as observed before for compound **2**. The ^1H NMR spectrum of **4** was rather complicated, but we succeeded in assigning the signals using ^1H-^1H COSY NMR (cf. experimental).

To obtain *closo*-dodecaborate cluster derivatives with glycerol fragment with no net charge of the molecule, we synthesized the piperazine derivative **5**. We found that **5** react with **1** to give the corresponding novel ammonium salt **6** (Scheme 3). This precursor was characterized by NMR spectroscopy. The signal of the acidic NH proton was observed at 9.61 ppm in the ^1H NMR spectrum.

Its acidic hydrolysis and quaternization of the second nitrogen afforded the goal product **7**, B_{12}-derivative of glycerol with no net charge. Compound **7** was characterized by IR and NMR spectroscopy and X-Ray diffraction (XRD) analysis. In the IR spectrum of **7** the absobtion bands of OH groups and water (3623 (free), 3495 (bonded) cm^{-1}) and NH^+(bonded) (3128 cm^{-1}) were observed. The ^{11}B NMR of **7** consisted of 4 signals with intensity ratio of 1:5:5:1 and their chemical shifts were typical for the mono-O-substituted B_{12} cluster. In ^1H NMR of **7**, besides the signals of CH–OH, CH_2–O and CH_2N^+ groups, the signals of two acidic protons at 8.91 ppm were detected.

Compound **7** was also studied by single X-ray diffraction analysis. The molecular structure of (2-{2-[4-(2,3-dihydroxypropyl) piperazinediium-1-yl]ethoxy}ethoxy)-undecahydro-*closo*-dodecaborate (**7**) is presented in Fig. 1. The 2, 3-dihydroxypropyl fragment is disordered over two positions with site occupancy factors equal to 0.632 and 0.368, respectively. This disorder is probably caused by incompactness of crystal packing that causes large displacement of disordered atoms. The geometric parameters of *closo*-dodecaborate cage are rather close to standard B–B bond distances values. Some of the bond lengths are presented in Table 1. The same bond distances were observed previously [20] for

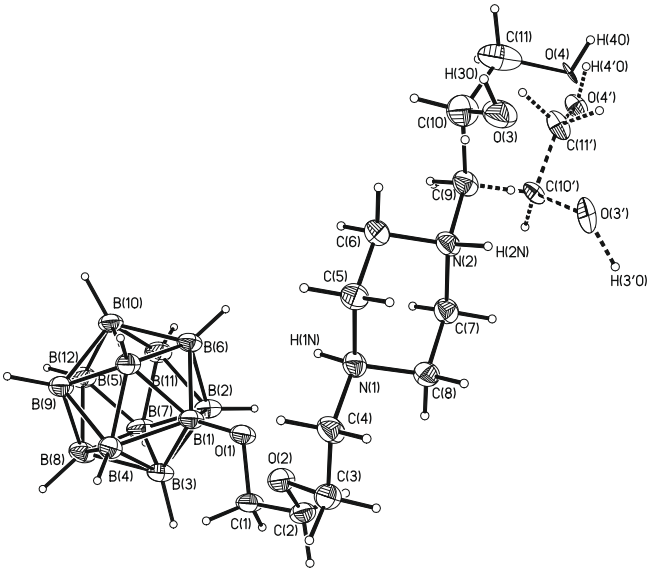
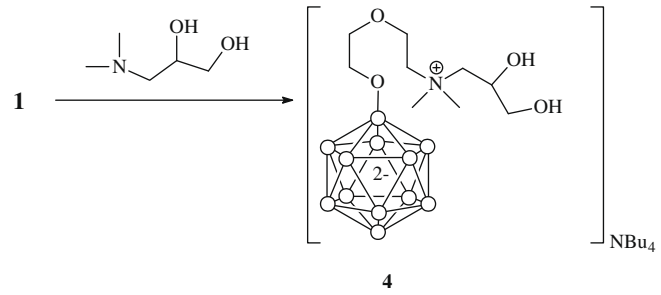


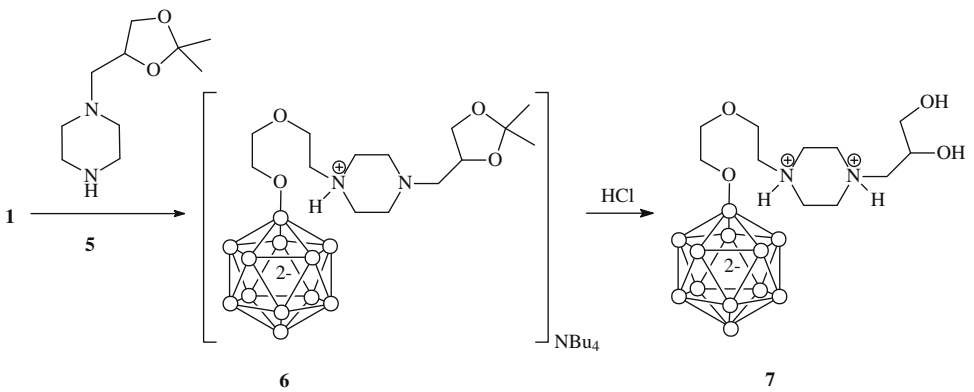
Fig. 1. The molecular structure of **7** with disordered 2,3-dihydroxypropyl fragment.

Table 1
Some elected bond lengths in **7**.

Bond	*d* (Å)	Bond	*d* (Å)
B(1)–O(1)	1.449(4)	C(2)–O(2)	1.421(4)
O(1)–C(1)	1.424(4)	O(2)–C(3)	1.438(4)
C(1)–C(2)	1.500(4)	C(3)–C(4)	1.499(4)
C(4)–N(1)	1.507(4)	O(1) ··N(1)	4.557
C(10)–O(3)	1.448(6)	C(11)–O(4)	1.394(6)
C(10′)–O(3′)	1.417(7)	C(11′)–O(4)	1.502(7)



Scheme 2.



Scheme 3.

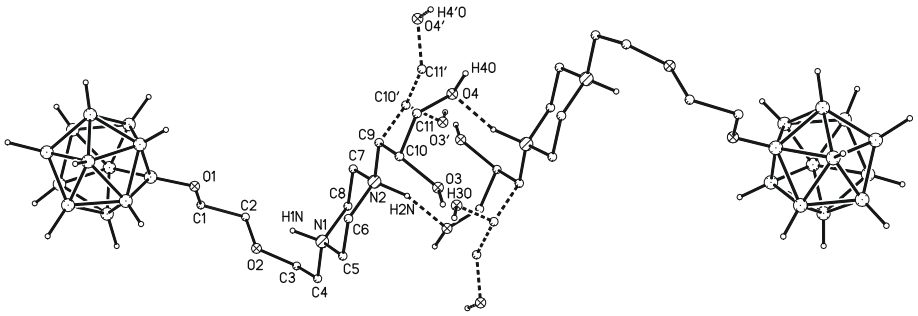


Fig. 2. Dimeric associates formed in the structure of **7** (alkyl H-atoms not displayed). H-bond N2–H2N···O4 parameters: distances N2···O4 and H2N···O4 are 2.843(4) Å and 1.80 Å, respectively; angle at H2N is 158°.

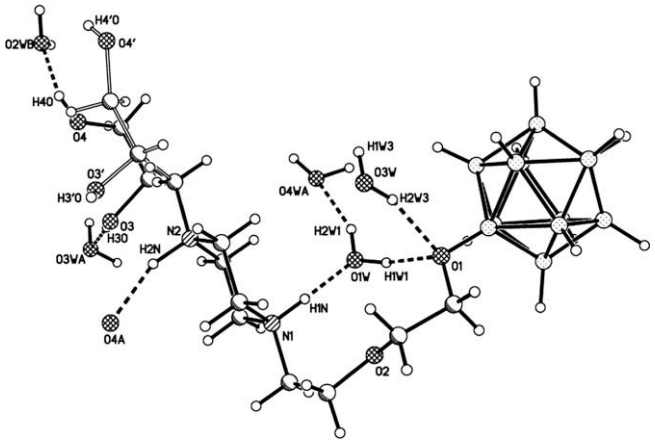


Fig. 3. The intermolecular hydrogen bonds formed in the structure **7**. The distances N(1)·· O1 W, O(1)···O1 W, O(1) ··O3 W, O(3) ··O3 W, O(4) ··O2 W and O1 W ··O4 W are 2.671(4), 2.804(3), 2.803(3), 2.703(5), 2.553(7) and 2.743(4) Å, respectively.

4-morpholino-(ethoxy}ethoxy)-undecahydro-*closo*-dodecaborate. In this molecule, the O(1)···N(1) chain has twisted conformation (O(1)···N(1) = 2.702 Å) due to the intermolecular hydrogen bond N(1)–H···O(1). In case of **7**, the conformation of this fragment is stretched and the distance O(1)···N(1) is much longer. An intramolecular hydrogen bond with the hydroxy group, N(1)–H1N···O(4)–H, is formed, rather than an intermolecular one.

In the structure of **7**, dimeric centeric symmetrical associates are formed due to a strong hydrogen bonding N2–H2N···O4 (Fig. 3). The second N1–H1N group and water molecules O1w and O3w form intramolecular H-bonds as well (Fig. 2).

Probably, the stretched conformation of 4-(2,3-dihydroxypropyl)piperazinediium-1-yl]ethoxy}ethoxy fragment in **7** is caused by crystal water that forms strong H-bond with the hydroxy groups (Fig. 3).

It is to be noticed that compound **7** is one of the rare examples of the neutral B_{12}-based species and the first one which is structurally characterized.

Thus, using facile cleavage reactions between the dioxanium derivative of the dodecaborate and O-and N-glycerol based nucleophiles, we have synthesized three novel compounds **3**, **4** and **7** in one or two steps with pretty good yields. These compounds contain on the one hand, a glucerol fragment with two free OH-groups and on the other hand, substituted *closo*-dodecaborate cluster unit. The obtained compounds differ by the net charge of the molecule (−2(**3**), −1(**4**) and 0(**7**)). The free –OH groups of these compounds can be easily acylated by fatty acids to give corresponding lipids. Therefore, a different boronated lipids based on these compounds can be prepared and the influence of the net charge of the lipids on zeta potential of the liposomes and thus their biological properties can be studied.

In conclusion, we have succeeded in developing effective approaches to *closo*-dodecaborate-based glycerols with different net charges on the molecules. The synthesis of lipids and liposomal studies based on these novel compounds will be continued in our laboratories.

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Appendix A. Supplementary data

CCDC 734889 contains the supplementary crystallographic data for compound **7**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.jorganchem.2009.10.038.

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