Electrochemistry of different boranes, carbaboranes and their *exo*-skeletal hydroxy derivatives at the graphite carbon electrode in aqueous phosphate buffers

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ABSTRACT

Electrochemical behavior of four cluster boranes and nine derivatives of ten- and eleven-vertex cluster boranes has been studied in phosphate buffers. These compounds show promising applications in biological sciences and in biomedicine and, therefore, analytical techniques developed for their determination and analysis of their bioconjugates should be compatible with aqueous media. Results presented herein show that both *endo*- and *exo*-skeletal substitutions of cluster boranes significantly influence their electrochemical responses, such as the shape of voltammetric curves, the position of the current maximum in a potential scale, and the peak current density. Selected substitutions can be utilized to tune electrochemical properties of the boron cluster compounds in order to optimize their responses for their electroanalytical determination and their usage as labels for biopolymers.

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1. Introduction

Synthetic cluster boranes (boron cluster compounds, BCC) and compounds formally derivable from them differ principally from compounds, which occur in nature, and from their synthetic organic analogues [1,2]. The idea of electron deficient chemical bond has been developed in order to explain the sterical structure of these clusters, where two electrons occupy three-center orbital belonging to three neighboring boron atoms in a triangular facet. The electron delocalization over all three center orbitals leads to aromaticity of the polyhedra [3] and causes its specific geometric shape composed of triangular facets. The three-dimensional architecture, delocalized charge of anionic clusters, and a partial hydridic character of terminal B-H (two electron) bonds, never seen in organic species, resulted in potential applications of boranes, carbaboranes and their derivatives in several diverse areas such as low nucleophilic anions, solid electrolytes, catalysis and material chemistry [4,5]. Among these applications, the medical and pharmaceutical use [5–11] has attracted a wide attention. Over two last decades the main focus in this area has turned from boron carriers applied in boron neutron capture

therapy [9] towards compounds designed to treat various therapeutically relevant targets. In the majority of cases, icosahedral carboranes have been incorporated as hydrophobic pharmacophores into structures of various therapeutically relevant organic drugs. It has been demonstrated that they may increase binding affinities [7,8]. Certain, but still limited examples cover the use of other available boron cages in this area. Smaller metallacarborane cages proved anticancer activity [12,13]. The icosahedral anionic metallacarboranes can act as specific inhibitors of HIV-Protease enzyme [10,11] or can be used for sensing or as biomarkers [14]. Recently, a specific action of substituted [*nido*-$C_2B_9H_{12}$]$^-$ anion as Carbonic Anhydrase IX inhibitor was demonstrated [15]. In addition, it was demonstrated recently that boron cluster compounds are promising for studies on labeling nucleic acids [16].

Until recently, electrochemical studies of various cluster boranes and their simple derivatives have been carried out mainly in solvents where cluster boranes easily dissolve [4,17,18]. However, biological and medicinal application of these compounds, including strategies involving preparation of various bioconjugates such as BCC-labeled oligonucleotides, require analytical methods compatible with aqueous media. Electrochemistry proved to be powerful technique for detection of various biopolymers, including nucleic acids [19], proteins [20] and others. Therefore, we started the systematic electrochemical

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Table 1

Peak positions and heights with simple characteristics of used BCCs and some BCCs used in our previous works [21,22] on stationary GCE (inside the paper [21] data for rotating GCE and concentration of 200 μM), pH = 8, concentration of BCCs 1 mM. * Uncharged $B_{18}H_{22}$ changed spontaneously to $B_{18}H_{21}^-$, and, simultaneously become stable by dissolution in PB.

Systematic formula	Charge of the boron anion	Label in the text	Molecular weight of the boron cluster	Peak position/V	Peak height/ μA cm^{-2}
Electrochemical parameters of BCCs obtained in this study					
nido-$B_{11}H_{14}$(Et$_3$NH)	1-	*B11*	133.03	0.21; 1.25; 1.70	1.37; 3.03; 15.37
nido-7-$CB_{10}H_{13}$Cs	1-	*CB10*	133.23	1.21; 1.47	251.18; 35.05
nido-7,8-$C_2B_9H_{12}$(Me$_3$NH)	1-	*7,8C2B9*	133.41	0.63	308.22
nido-7,9-$C_2B_9H_{12}$(Me$_3$NH)	1-	*7,9C2B9*	133.41	0.86; 1.25	124.24; 23.39
nido-7-$SB_{10}H_{11}$(Me$_4$N)	1-	*SB10*	151.26	0.96; 1.25; 1.71	1.46; 1.41; 9.76
nido-7-$PB_{10}H_{12}$(1,8-dimethylammonium-naftalen)	1-	*PB10*	151.17	0.19; 0.91; 1.33; 1.71;	1.23; 0.17; 0.38; 12.85;
9-OH-*nido*-7,8-$C_2B_9H_{11}$(Me$_4$N)	1-	*9OH7,8C2B9*	149.20	0.21; 0.32; 0.45; 0.85	17.34; 9.53; 6.51; 1.04
10-OH-*nido*-7,8-$C_2B_9H_{11}$(Me$_4$N)	1-	*10OH7,8C2B9*	149.20	0.45	110.67
arachno-6-CB_9H_{14}(Me$_4$N)	1-	*CB9*	144.22	0.58; 0.99; 1.29	21.89; 127.83; 22.02
arachno-6-SB_9H_{12}Cs	1-	*SB9*	274.37	0.50; 0.75;	17.41; 5.10
closo-$B_{10}H_{10}$(Et$_3$NH)$_2$	2-	*B10*	118.18	0.49; 0.79; 0.93; 1.03; 1.16	23.24; 83.30; 103.42; 67.42; 28.57
B_3H_8(Bu$_4$N)	1-	*B3*	40.49	0.47; 1.20	3.46; 13.70
syn-$B_{18}H_{22}$ *	1-	*B18*	216.77	0.62; 0.73; 0.99; 1.11	77.38; 56.05; 25.21; 16.14
Electrochemical parameters of some BCCs obtained in previous studies [21,22]					
closo-$B_{12}H_{12}$(Et$_3$NH)$_2$	2-	*B12*	141.82	1.58	282.00
1-OH-*closo*-$B_{12}H_{11}$Cs$_2$	2-	*B12OH*	157.82	1.17	327.00
1-*closo*-$CB_{11}H_{12}$(Me$_3$NH)	2-	*CB11*	143.02	1.75	7.80
7,12-(OH)$_2$-1-*closo*-$CB_{11}H_{10}$(Bu$_4$N)	1-	*CB11OH2*	175.02	1.65	475.00

investigation, strictly in the aqueous solutions, of the simplest cluster boranes, which can be considered as basic building units in the synthesis of bioconjugation functionalized compounds that are suitable for electrochemical tracing. In the first two studies [21,22], we focused on twelve vertex cluster series anions and their simple *exo*- and *endo*-skeletal derivatives due to their easier dissolution in solvents capable of proton solvation. The phosphate buffers and glassy carbon electrodes (GCEs) have been used in these studies. Smooth surface of the polished GCE seems to be the best choice for the BCCs characterization as we showed previously [21]. On the contrary the surface morphology could play very important role for the electrochemical behavior of organic molecules, particularly the planar ones [23]. The electrochemical responses on GCE depend on the structure, position and number of *exo*-skeletal substituents, and on the number and positions of carbon atoms in carbaboranes. The most pronouncing compounds of our previous study [21] were the BCCs with hydrophilic *exo*-skeletal substituents, like 1-OH-*closo*-$B_{12}H_{11}$ or 12-OH-1-*closo*-$CB_{11}H_{11}$. Therefore we decided to extend our study towards BCCs composed of different number of boron atoms along with their *endo*- and *exo*-skeletal derivatives. For this study we selected clusters with numbers of cluster atoms differing 12 that belong to various structural types (see Table 1 and for schematic structure Fig. 1).

2. Experimental

All electrochemical experiments were performed at the room temperature using Autolab 302 potentiostat (Ecochemie, The Netherlands) connected to the conventional electrochemical cell with three-electrode system. An Ag|AgCl|3 M KCl reference electrode and a platinum wire (1 mm diameter) counter electrode were used. The differential pulse voltammetry (DPV) was applied with the pulse amplitude of 0.025 V, pulse width of 50 ms, and scan rate of 0.008 V s^{-1}. Glassy carbon electrode (GCE, 2 mm diameter, Metrohm, Switzerland) was used as the working electrode. Measured current values were normalized to the geometrical surface area of used electrodes. Prior electrochemical measurements, GCE was mechanically polished using silicon carbide papers (SiC polishing papers, Struers, Denmark) and the polishing was finalized using the 1 μm diamond particles in spray on Lecloth B

polishing cloth (Leco, USA). GCE was sonicated for 5 min just before use. For electrochemical measurements, phosphate buffers (PB), of various pH values have been mixed from NaH$_2$PO$_4$ and Na$_2$HPO$_4$. The concentration of phosphate anions was kept at 0.2 M in all buffers.

Salts of boron cluster anions investigated in this study are listed in Table 1. These salts are laboratory samples synthesized by previously published methods [24–26], except the compounds $CB_{10}H_{13}$Cs and *syn*-$B_{18}H_{22}$, which were purchased from Katchem (Praha, Czech Republic). Cations in the salts specified in Table 1, which served for the precipitation of the anions in the last synthesis step, were exchanged for sodium cation using Amberlite CG-120 (Fluka) to increase their solubility in water, and to avoid contingent effects of different cations on electrochemical experiments. Uncharged $B_{18}H_{22}$ is ionized spontaneously to $B_{18}H_{21}^-$ upon dissolution in water. It has been simultaneously stabilized by its dissolution in phosphate buffer, which eliminated the split protons from solution. It is possible that in the case of *B3,CB9* and *B11* the ion exchange may cause partial dissipation of the BCC structure. All BCCs used in his study were prepared as 1 mM solutions according to weighting. All other chemicals were purchased from Sigma-Aldrich and were of the highest available purity.

3. Results and discussion

BCCs used in this study can be divided into 2 groups according to the number of vertexes in their cage: the first group contains compounds comprising 11 vertexes; the second group contains anions with 3, 10 and 18 vertexes (5 compounds). The electrochemical current density responses of all investigated BCCs, shown on Fig. 2, consist mainly from several overlapping current density peaks. Their computer deconvolution to individual peaks have not been applied for the sake of simplicity considering the aim of this study. The term peak is used in this article only for symmetrical responses, which have only one current density maximum at a particular electrochemical potential. The current density maxima of investigated specimens and their corresponding applied potentials are summarized in Table 1. Data for the twelve-vertex species investigated earlier [21,22] are included for comparison.