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Synthesis of functional derivatives of the $[3,3'\text{-Co}(1,2\text{-}C_2B_9H_{11})_2]^-$ anion

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Abstract

A series of various functional derivatives of the cobalt bis(1,2-dicarbollide) anion $[8\text{-}XCH_2CH_2OCH_2CH_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]^-$ (X = OH, NH_2, and $CH(NH_2)COOH$) were prepared by the ring-opening reactions of $[8\text{-}O(CH_2CH_2)_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]$ with different nucleophiles followed by functional group interconversion reactions. Acidic hydrolysis of $[8\text{-}NCCH_2CH_2OCH_2CH_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]^-$ resulted in the shorter-chain alcohol $[8\text{-}HOCH_2CH_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]^-$. Structures of $(Bu_4N)[8\text{-}AcNHC(COOEt)_2CH_2CH_2OCH_2CH_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]$ and $[8\text{-}(1\text{-}C_5H_5N)CH_2CH_2OCH_2CH_2O\text{-}3,3'\text{-}Co(1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]$ were determined by the single crystal X-ray diffraction method. Perspectives of application of functionalized cobalt bis(1,2-dicarbolide) derivatives in nuclear medicine are discussed.

Keywords: Cobalt bis(dicarbollide); Functional derivatives; Crystal structures; Nuclear medicine; Boron neutron capture therapy

1. Introduction

The current increase of interest in the chemistry of polyhedral boron hydride compounds is due to nice perspectives of their medical applications. The leading application of polyhedral boron hydrides in medicine belongs to boron neutron capture therapy—a binary cancer treatment based upon the interaction of two relatively harmless species, a ^{10}B nucleus and a thermal neutron, which results in the formation of the highly energetic ^4He and ^7Li as products. These fission products have an effective range of ~ 10 μm in tissue, thus, effectively limiting the extent of cellular damage to ca. one cell diameter. Therefore, the selective concentration of the ^{10}B nuclei within the tumor cells, followed by their capturing of thermal neutrons, should result in localized destruction of the malignant cells in the presence of the normal cells [1,2].

Polyhedral boron hydrides could also be used as linkers for the introduction of a radiohalogen label into biomolecules for radioimmunodiagnostics and radioimmuno-therapy. Radioactive halogen isotopes play an important role in nuclear medicine, however, there is a serious problem for the medical application of radiohalogens, which is 'dehalogenation', i.e. the relatively rapid release of radioactivity from the cells after intracellular processing of the labeled compound. The feasibility of labeling polyhedral boron hydride compounds with different radiohalogen isotopes has recently been shown and the high stability of the radiohalogen label in vivo has been demonstrated [3–5].

The three common commercially available isomeric dicarba-*closo*-dodecaborane(12) $C_2B_{10}H_{12}$-1,2-(*ortho*)-, -1,7-(*meta*), and -1,12-(*para*)-carboranes have been used for functionalization and connection to organic molecules via their carbon atoms which are available for normal organic chemistry [6,7]. However, the inherent drawback of carboranes is their extreme lipophilicity, which often renders the potentially bioactive structures contained within these clusters water-insoluble. Their isoelectronic and geometrical analogue, dodecahydro-*closo*-dodecaborate anion $[B_{12}H_{12}]^{2-}$ is, on the hand, water-soluble in the form of its alkali metal salts and is also extremely reactive in electrophilic substitution reactions such as halogenation, however,

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its functionalization is still relatively problematical [8–11].

Other attractive boron hydride compounds are the bis(dicarbollide) complexes of transition metals in which the metal ion is held between two η^5-bonding $[C_2B_9H_{11}]^{2-}$ ligands [12] (Fig. 1). The most studied complexes are bis(dicarbollides) of cobalt, nickel, and iron [13,14]. These complexes can easily be obtained starting from *ortho*-carborane [12] and one of them, namely Na[3,3′-Co(1,2-$C_2B_9H_{11})_2$], is now commercially available [15]. The bis(dicarbollide) complexes contain more boron atoms per molecule than either the carboranes or the *closo*-dodecaborate anion; and also display extraordinary stability due to the delocalized cluster bonding of the transition metal with ligand orbitals. The bis(dicarbollide) complexes are water soluble as sodium salts, and at the same time, are sufficiently hydrophobic to translocate across the phospholipid bilayer membranes [16,17] for delivery into the tumor cells. The boron atoms at the positions 8 and 8′ of the [3,3′-M(1,2-$C_2B_9H_{11})_2]^-$ cage easily undergo attack by electrophilic reagents making their functionalization possible.

Here, we describe the synthesis of various functional derivatives of the cobalt bis(1,2-dicarbollide) anion, [*commo*-3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$, by the nucleophilic ring-opening reaction in [8-O$(CH_2CH_2)_2$O-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)].

2. Results and discussion

The cobalt bis(1,2-dicarbollide) anion, [*commo*-3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$ (**1**), demonstrates extraordinary stability due to the delocalized cluster bonding of cobalt with the orbitals of the dicarbollide ligands. It is also promising candidate for boron neutron capture therapy for cancer and as a radiohalogen carrier for immunodiagnostics and immunotherapy of cancer. Boron atoms at the positions 8 and 8′ of the [3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$ cage readily undergo attack by electrophilic reagents giving the possibility to introduce various substituents [13]. However, this is complicated, since the substitution proceeds, as a rule, at both $[C_2B_9H_{11}]^{2-}$ ligands giving disubstituted derivatives.

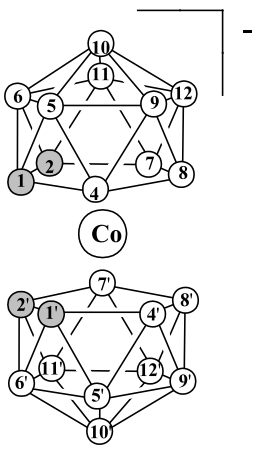


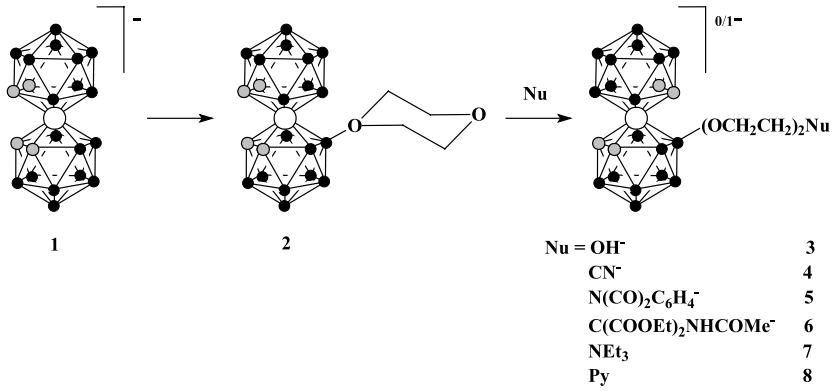
Fig. 1. Structure and numbering of atoms in the [3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$ anion.

By exploring the different possibilities of functionalization of the [3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$ anion we found that several approaches could be used. The first approach consists in the preliminary synthesis of a chain-linked bis(*o*-carboranes), followed by a partial degradation into the corresponding chain-linked bis(*nido*-7,8-dicarba-undecaborate) anions and subsequent metal trapping. Due to non-selective removal of one boron atom *o*-carborane cage during its degradation into *nido*-undecaborate this method gives mixtures of *meso*- and *dl*-isomers. This approach was originally realized for synthesis of [1,1′-(μ-TsN$(CH_2CH_2)_2$)-3,3′-Co(1,2-$C_2B_9H_{10})_2]^-$ [18].

The second approach consists in the synthesis of 8,8′-bridged derivatives followed by substitution in the bridge (e.g. [8,8′-μ-RS-3,3′-Co(1,2-$C_2B_9H_{10})_2$] (R=CH_2-CH=CH_2, CH_2COOMe, CH_2CH_2CN) [19] and [8,8′-μ-MeOC(O)CH_2NH-3,3′-Co(1,2-$C_2B_9H_{10})_2$] [20] were prepared by alkylation of the corresponding thio- and amino-bridged cobalt bis(dicarbollides)) or its asymmetric cleavage giving 8,8′-heterosubstituted derivatives (e.g. [8-H_3N-8′-I-3,3′-Co(1,2-$C_2B_9H_{10})_2$] [21] and [8-CH_2=CHRC(O)NH-8′-I-3,3′-Co(1,2-$C_2B_9H_{10})_2]^-$ [22] were prepared by treatment of the iodonium derivative [8,8′-μ-I-3,3′-Co(1,2-$C_2B_9H_{10})_2$] by ammonia or acrylonitrile, respectively, and [8-H_3N-8′-HO-3,3′-Co(1,2-$C_2B_9H_{10})_2$] [23] was prepared by reduction of the oxime-bridged derivative [8,8′-μ-NH_2O-3,3′-Co(1,2-$C_2B_9H_{10})_2$]). It should be noted that this approach mainly results in neutral charge-compensated derivatives of the [3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$ anion, which usually renders them water insoluble.

The third approach consists in controlled substitution at one of two equivalents $(C_2B_9H_{11})^{2-}$ ligands. It has been shown that electrophilic halogenation of **1** proceeds alternatively in both dicarbollide ligands [24]. However, examples of such alternating substitution are limited by halogenation reactions. Only monohalogen derivatives [8-X-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)]$^-$ (X = Cl, Br, I) can be used for subsequent functionalization by electrophilic attack at the second dicarbollide ligands or by cross-coupling reactions at the boron–halogen bond.

Another example of controlled substitution at one of the dicarbollide ligands is the formation of charge-compensated onium derivatives [8-L-3,3′-Co(1,2-$C_2B_9H_{10}$)-(1′,2′-$C_2B_9H_{11}$)] (L = SMe_2 [19], 1,4-dioxane [25]). Introduction of a strong electron-withdrawing substituent at position eight of one dicarbollide ligand results in a



Scheme 1.

significant redistribution of electron density in the metallacarborane cage and deactivation of the second dicarbollide ligand towards further electrophilic attack.

Recently, we proposed a new approach for the synthesis of functional derivatives of *closo*-dodecaborate anion $[B_{12}H_{12}]^{2-}$ based on the ring-opening reaction of its tetramethylene oxonium derivative [11]. Using different nucleophiles, various functional derivatives $[B_{12}H_{11}O(CH_2)_4X]^{2-}$, including alcohol, amine, acid, and amino acid, were prepared. Based on this experience and analysis of the literature we chose the dioxanium derivative [8-O(CH_2CH_2)$_2$O-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] (**2**) [25] as a precursor for the synthesis of functional derivatives of the [3,3′-Co(1,2-$C_2B_9H_{11}$)$_2$]$^-$ anion. It was shown earlier that treatment of the closely related compound [8-O(CH_2CH_2)$_2$O-8′-I-3,3′-Co(1,2-$C_2B_9H_{10}$)$_2$] with a nucleophilic agent, such as $C_5H_{11}ONa$, results in the ring opening reaction giving [8-$C_5H_{11}OCH_2CH_2OCH_2CH_2O$-8′-I-3,3′-Co(1,2-$C_2B_9H_{10}$)$_2$]$^-$ [26].

The dioxane ring in **2** was found to open easily at the oxonium oxygen atom under attack with various nucleophiles (Scheme 1). Its reaction with potassium hydroxide in biphasic water–benzene mixture in the presence of dibenzo-18-crown-6 under reflux conditions, as well as reaction with sodium hydroxide in water–diethyl ether mixture at room temperature resulted in its quantitative conversion to the corresponding alcohol **3**.

The reaction of **2** with potassium phthalimide in dimethylformamide at room temperature also proceeded smoothly giving the corresponding phthalimide derivative **5** which can easily be converted into the amine [8-$H_3NCH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] (**10**) and isolated as the intramolecular ammonium salt (Scheme 2). Formation of a similar intramolecular ammonium salt was previously observed in the case of $[B_{12}H_{11}O(CH_2)_4NH_3]^-$ [11].

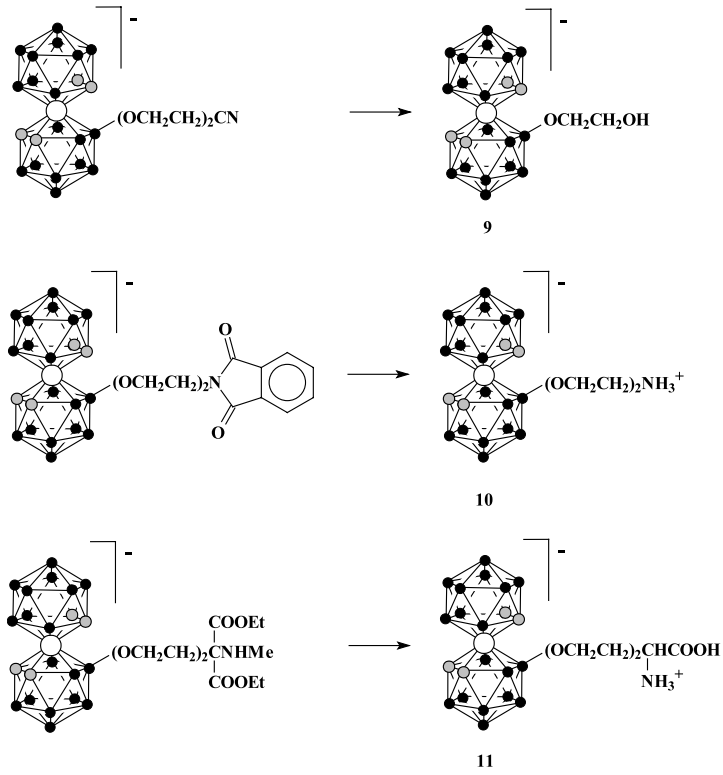
In planning to derive the carboxylic acid alkaline hydrolysis of the nitrile, as in the case of $[B_{12}H_{11}O(CH_2)_4COOH]^{2-}$ [11], we synthesized the corresponding nitrile [8-$NCCH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)]$^-$ (**4**) by the reaction of the oxonium derivative with tetrabutylammonium cyanide in dichloromethane (Scheme 1). However, the attempt to convert it to the acid resulted in elimination of acrylonitrile giving the short-chain alcohol [8-$HOCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)]$^-$ (**9**) (Scheme 2). This result was somewhat unexpected, but easy to explain. The 2-cyanoethyl group is known as one of the most common blocking groups in the nucleotide synthesis [27–29]. Recently this group was also proposed as effective protective group for the sulfur atom of the $[B_{12}H_{11}SH]^{2-}$ anion [8].

It should be noted that the alcohol **9** can be used as precursor for the synthesis of derivatives containing shorter spacers between the cobalt bis(dicarbollide) cage and various functional groups using traditional methods of organic chemistry.

The attempt to introduce the nitro group (for future reduction into the carboxylic function) by the reaction of **2** with the nitromethane anion which, was generated by addition of triethylamine or pyridine resulted in the corresponding intramolecular onium salts **7** and **8** in quantitative yield.

The reaction of **2** with diethyl acetamidomalonate (glycine anion equivalent for amino acid synthesis) in acetonitrile in the presence of potassium carbonate gives [8-$MeCONHC(COOEt)_2CH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)]$^-$ (**6**), which can be converted into the corresponding amino acid [8-$H_3NCH(COOH)CH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] (**11**) by acidic hydrolysis and decarboxylation (Schemes 1 and 2).

Crystal structures of (Bu_4N) (**6**) and **8** were determined by the single crystal X-ray diffraction method. The dicarbollide ligands in the structures of **6** (Fig. 2) and **8** (Fig. 3) are practically parallel and have the staggered *transoid* conformation that differs from the staggered *cisoid* conformation found in structures **1** [30] and **2** [25]. Similar *transoid* conformation was found



Scheme 2.

earlier in the structure of (Me_4N)[8-Ph-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] [23]. In all these structures, the C_2B_3 pentagonal planes of the dicarbollide ligands are nearly parallel to each other showing the dihedral angle of 0.8–3.8° (the interplane distance 2.938–2.956 Å) and are mutually rotated by 30–41° about their centroid–centroid axis. The selected bond distances for **6** and **8** are presented in Table 1.

These synthesized boron compounds can be delivered into tumor cells using different strategies for tumor targeting or can be used as building blocks for synthesis of boron-containing biomolecules. The presence of the unchanged BH group at position 8′ allows one to introduce various radiohalogen markers and using these compounds as prosthetic groups for radiohalogenation of biomolecules.

3. Experimental

NMR spectra were recorded on a Varian Gemini 200 and Varian Unity 400 spectrometers. Chemical shifts were referenced to $SiMe_4 = 0.00$ ppm for ^1H and ^{13}C and to $BF_3{\cdot}Et_2O = 0.0$ ppm for ^{11}B. Infrared spectra were recorded using a Perkin–Elmer 1760 FTIR spectrometer. Compound **2** was prepared as described in the literature [25].

3.1. Preparation of Cs(3)

(a) To a mixture of 0.500 g (1.2 mmol) **2** in 50 ml C_6H_6 and 50 ml 2 M aq. KOH was added 72 mg (0.2 mmol) dibenzo-18-crown-6. The reaction mixture was heated with intensive stirring under reflux for 4 h. The mixture was allowed to cool to room temperature (r.t.)

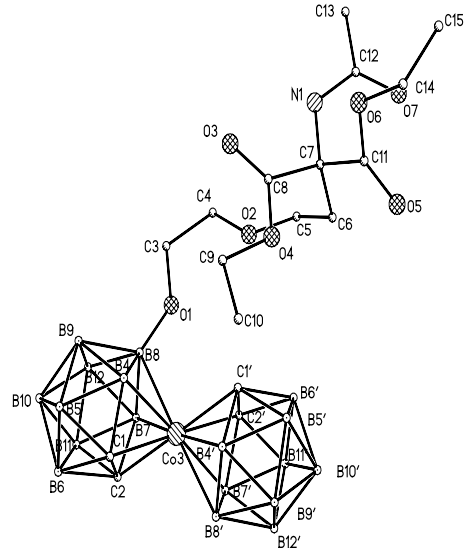


Fig. 2. Molecular structure of the [8-MeCONHC(COOEt)$_2$-$CH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)]$^-$ anion.

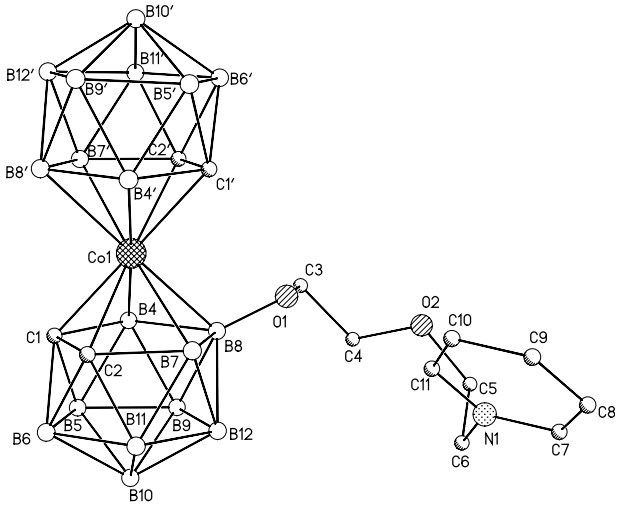


Fig. 3. Molecular structure of [8-(1-C_5H_5N)$CH_2CH_2OCH_2CH_2O$-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)].

where the organic layer was separated and the aqueous layer was washed twice with 50 ml of benzene. The organic layer and washings were combined, dried over anhydrous Na_2SO_4 and evaporated to dryness. The residue was dissolved in 100 ml of methanol and passed through Amberlite IR120(H^+) ion-exchange column. The acidic effluent was concentrated to 2 ml, diluted with 8 ml of water, and added to a solution of 1.0 g (3.0 mmol) Cs_2CO_3 in 10 ml of water. The yellow precipitate was filtered off, washed with 20 ml of cold water and dried over P_2O_5, giving 0.570 g (87%) of the product.

(b) A mixture of 0.205 g (0.5 mmol) **2** in 50 ml of Et_2O and 25 ml 1 M aq. KOH was stirred vigorously overnight at r.t. The organic layer was separated, washed with 25 ml of water, dried over anhydrous $MgSO_4$, and evaporated to dryness. The residue was dissolved in 5 ml of water and treated with a solution of 0.70 g (2.0 mmol) CsF in 2 ml of water. The precipitate was filtered off, washed with 2 ml of cold water, and

Table 1
Selected bond distances for **6** and **8**

	6	**8**		**6**	**8**
(a) *Bond distances in the cobaltacarborane cages of* **6** *and* **8** (Å)					
Co(3)–C(2)	2.010(2)	2.007(2)	Co(3)–C(2′)	2.013(2)	2.023(2)
Co(3)–C(1)	2.011(2)	2.015(2)	Co(3)–C(1′)	2.014(2)	2.022(2)
Co(3)–B(4)	2.099(2)	2.100(2)	Co(3)–B(4′)	2.090(2)	2.099(2)
Co(3)–B(7)	2.095(2)	2.099(2)	Co(3)–B(7′)	2.105(2)	2.103(2)
Co(3)–B(8)	2.157(2)	2.157(2)	Co(3)–B(8′)	2.151(2)	2.139(2)
C(1)–C(2)	1.640(3)	1.635(3)	C(1′)–C(2′)	1.623(2)	1.626(3)
C(1)–B(4)	1.701(3)	1.699(3)	C(1′)–B(4′)	1.710(3)	1.712(3)
C(2)–B(7)	1.699(3)	1.709(3)	C(2′)–B(7′)	1.707(3)	1.708(3)
B(4)–B(8)	1.818(3)	1.810(3)	B(4′)–B(8′)	1.793(3)	1.787(3)
B(7)–B(8)	1.796(3)	1.792(3)	B(7′)–B(8′)	1.781(3)	1.782(3)
C(1)–B(6)	1.724(3)	1.730(3)	C(1′)–B(6′)	1.724(3)	1.725(3)
C(2)–B(6)	1.726(3)	1.721(3)	C(2′)–B(6′)	1.716(3)	1.733(3)
C(1)–B(5)	1.699(3)	1.701(3)	C(1′)–B(5′)	1.696(3)	1.697(3)
C(2)–B(11)	1.698(3)	1.697(3)	C(2′)–B(11′)	1.706(3)	1.693(3)
B(4)–B(5)	1.795(3)	1.788(3)	B(4′)–B(5′)	1.795(3)	1.789(3)
B(7)–B(11)	1.789(3)	1.781(3)	B(7′)–B(11′)	1.795(3)	1.794(3)
B(4)–B(9)	1.787(3)	1.791(3)	B(4′)–B(9′)	1.784(3)	1.779(3)
B(7)–B(12)	1.783(3)	1.777(3)	B(7′)–B(12′)	1.785(3)	1.787(3)
B(8)–B(9)	1.808(3)	1.810(3)	B(8′)–B(9′)	1.795(3)	1.796(3)
B(8)–B(12)	1.814(3)	1.816(3)	B(8′)–B(12′)	1.791(3)	1.795(3)
B(6)–B(5)	1.768(3)	1.778(3)	B(6′)–B(5′)	1.761(3)	1.767(3)
B(6)–B(11)	1.771(3)	1.774(4)	B(6′)–B(11′)	1.769(3)	1.772(3)
B(5)–B(9)	1.772(3)	1.764(3)	B(5′)–B(9′)	1.773(3)	1.779(4)
B(11)–B(12)	1.772(3)	1.759(3)	B(11′)–B(12′)	1.776(3)	1.774(4)
B(9)–B(12)	1.792(3)	1.785(3)	B(9′)–B(12′)	1.781(3)	1.779(3)
B(6)–B(10)	1.771(3)	1.778(3)	B(6′)–B(10′)	1.766(3)	1.773(4)
B(5)–B(10)	1.781(3)	1.787(3)	B(5′)–B(10′)	1.785(3)	1.787(4)
B(11)–B(10)	1.781(3)	1.779(3)	B(11′)–B(10′)	1.777(3)	1.787(3)
B(9)–B(10)	1.787(3)	1.781(3)	B(9′)–B(10′)	1.782(3)	1.788(4)
B(12)–B(10)	1.789(3)	1.777(3)	B(12′)–B(10′)	1.783(3)	1.792(3)
(b) *Selected bond distances in the exo-polyhedral substituents in* **6** *and* **8** (Å)					
B(8)–O(1)	1.413(2)	1.416(3)	O(2)–C(5)	1.426(2)	1.415(3)
O(1)–C(3)	1.417(2)	1.429(2)	C(5)–C(6)	1.517(3)	1.508(3)
C(3)–C(4)	1.499(3)	1.510(3)	C(6)–C(7)	1.541(3)	–
C(4)–O(2)	1.430(2)	1.430(3)	C(6)–N(1)–	–	1.496(3)

dried over P_2O_5, giving 0.250 g (89%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 4.13 (2H, s), 4.02 (2H, s), 3.52 (2H, t), 3.44 (4H, m), 3.39 (2H, t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 72.4, 71.2, 68.0, 60.2, 52.0, 46.1. ^{11}B-NMR (acetone-d_6, ppm): δ 23.4 (1B, s), 4.8 (1B, d), 0.4 (1B, d), −2.4 (1B, d), −4.5 (2B, d), −7.1 (2B, d), −7.7 (2B, d), −8.4 (2B, d), −17.3 (2B, d), −20.4 (2B, d), −22.1 (1B, d), −28.6 (1B, d).

3.2. Preparation of (Bu_4N)(**4**)

To a solution of 205 mg (0.50 mmol) **2** in 50 ml CH_2Cl_2 was added 140 mg (0.52 mmol) tetrabutylammonium cyanide and was stirred overnight at r.t. The solvent was removed under reduced pressure leaving 330 mg (98%) of an orange oil. ^{1}H-NMR ($CDCl_3$, ppm): δ 4.19 (4H, s, CH_{carb}), 3.61 (2H, t), 3.54 (2H, t), 3.48 (2H, t), 3.19 (8H, m, Bu_4N^+), 2.54 (2H, t, CH_2CN), 1.58 (8H, m, Bu_4N^+), 1.37 (8H, m, Bu_4N^+), 0.95 (12H, t, Bu_4N^+); ^{13}C-NMR ($CDCl_3$, ppm): δ 118.1 (–CH_2CN), 72.0, 68.5, 65.5, 58.7 (Bu_4N^+), 54.6, 46.7, 23.8 (Bu_4N^+), 19.5 (Bu_4N^+), 18.7 (–CH_2CN), 13.5 (Bu_4N^+); ^{11}B-NMR ($CDCl_3$, ppm): δ 22.8 (1B, s), 3.5 (1B, d), 0.4 (1B, d), −2.2 (1B, d), −4.6 (2B, d), −8.1 (6B, d), −17.3 (2B, d), −20.3 (2B, d), −21.3 (1B, d), −28.3 (1B, d); IR (neat, cm^{-1}): 3053 (νCH_{carb}), 2558 (νBH), 2252 ($\nu C \equiv N$).

3.3. Preparation of Cs(**5**)

Potassium phthalimide (0.22 g, 1.2 mmol) was added to a solution of 0.41 g (1.0 mmol) **2** in 50 ml dimethylformamide and the reaction mixture was stirred overnight. The solution was concentrated under reduced pressure to dryness, the residue was dissolved in 30 ml of methanol and treated with 0.30 g (2.0 mmol) CsF in 10 ml of water. The solution was then concentrated to 5 ml under reduced pressure. Yellow-orange crystals formed and were filtered and dried in air giving 0.59 g (86%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 7.83 (4H, m), 4.10 (2H, s), 3.98 (2H, s), 3.71 (2H, t), 3.61 (2H, t), 3.46 (2H, t), 3.42 (2H, t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 167.7, 134.3, 131.5, 123.0, 70.7, 68.1, 67.0, 51.9, 46.0, 37.1; ^{11}B-NMR (C_3H_6O-d_6, ppm): δ 23.04 (1B, s), 4.13 (1B, d, $J = 116$ Hz), 0.47 (1B, d, $J = 143$ Hz), −2.48 (1B, d, $J = 151$ Hz), −4.24 (2B, d, $J = 159$ Hz), −7.31 (2B, d, $J = 125$ Hz), −8.19 (4B, d, $J = 122$ Hz), −17.25 (2B, d, $J = 153$ Hz), −20.37 (2B, d, $J = 159$ Hz), −22.03 (1B, d, $J = 192$ Hz), −28.41 (1B, d, $J = 140$ Hz).

3.4. Preparation of K(**6**)

Refluxed 0.41 g (1.0 mmol) 2, 0.25 g (1.15 mmol) diethylacetamidomalonate, and 1.38 g (10 mmol) K_2CO_3 in 50 ml acetonitrile overnight. The solution was cooled to r.t. and filtered. The solvent was evaporated in vacuo. The residue was dissolved in 30 ml of MeOH, 10 ml of water was added and the solution was concentrated to 5 ml under reduced pressure. The orange precipitate was filtered off and dried in air to give 0.50 g (76%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 8.17 (1H, s), 4.12 (2H, s), 4.08 (4H, m), 4.00 (2H, s), 3.45 (2H, t), 3.35 (2H, t), 3.30 (2H, t), 2.32 (2H, t), 1.31 (3H, s), 1.13 (6H, t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 169.0, 167.5, 71.0, 67.7, 65.3, 64.2, 61.4, 52.0, 46.0, 32.7, 22.1, 13.8; ^{11}B-NMR (Me_2SO-d_6, ppm): δ 24.0, 4.9, 0.0, −2.6, −7.3, −17.8, −20.0, −28.0.

3.5. Preparation of (Bu_4N)(**6**)

Refluxed 0.20 g (0.5 mmol) **2**, 0.12 g (0.55 mmol) diethylacetamidomalonate, 0.69 g (5 mmol) K_2CO_3, and 0.16 g (0.5 mmol) tetrabutylammonium bromide in 25 ml acetonitrile overnight. The solution was cooled to r.t. and filtered. The solvent was evaporated in vacuo. The residue was dissolved in 30 ml of MeOH, 10 ml of water was added and the solution was concentrated to 5 ml under reduced pressure. The precipitate was filtered off and dissolved in 2 ml dimethylsulfoxide. Slow evaporation of the solvent at r.t. gave orange needle-like crystals of (Bu_4N) (**6**) suitable for X-ray structure analysis.

3.6. Preparation of **7**

To 20 ml nitromethane was added 0.38 ml (5.0 mmol) triethylamine and stirred for 1 h at r.t. Then 205 mg (0.50 mmol) **2** was added to the solution and stirred at r.t. for 3 h. The solvent was removed under reduced pressure giving 250 mg (99%) of the product. ^{1}H-NMR ($CDCl_3$, ppm): δ 4.09 (2H, t), 3.93 (2H, s, CH_{carb}), 3.81 (2H, s, CH_{carb}), 3.70 (2H, t), 3.61 (2H, t), 3.47 (6H, q), 3.31 (2H, t), 1.36 (9H, t); ^{1}H-NMR (Me_2SO-d_6, ppm): δ 4.06 (2H, s, CH_{carb}), 3.91 (2H, s, CH_{carb}), 3.84 (2H, t), 3.59 (2H, t), 3.51 (2H, t), 3.39 (2H, t), 3.31 (6H, q), 1.16 (9H, t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 71.4, 68.6, 64.0, 56.1, 52.9, 50.9, 46.1, 7.3; ^{11}B-NMR (acetone-d_6, ppm): δ 24.3 (1B, s), 6.0 (1B, d), 0.4 (1B, d), −2.7 (1B, d), −4.7 (2B, d), −6.9 (2B, d), −7.5 (2B, d), −8.9 (2B, d), −17.4 (2B, d), −20.2 (2B, d), −22.5 (1B, d), −28.9 (1B, d). Orange crystals of **8** suitable for X-ray diffraction analysis were obtained by crystallization from warm (60 °C) dimethylsulfoxide.

3.7. Preparation of **8**

To 20 ml nitromethane was added 0.50 ml (6.0 mmol) pyridine and was stirred for 1 h at r.t. Added 205 mg (0.50 mmol) **2** to the solution and stirred at r.t. for 3 h. The solvent was removed under reduced pressure giving 240 mg (99%) of the product. ^{1}H-NMR

($CDCl_3$, ppm): δ 9.16 (2H, d), 8.50 (1H, t), 8.11 (2H, t), 4.84 (2H, t), 4.10 (2H, s), 3.80 (4H, m), 3.71 (2H, t), 3.67 (2H,t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 145.7, 145.3, 127.7, 71.5, 68.9, 68.5, 60.5, 50.8, 46.2.

3.8. Preparation of (Bu_4N)(9)

A solution of 0.270 g (0.40 mmol) **4** and 2.00 g NaOH in 50 ml EtOH was refluxed overnight. The reaction mixture was cooled to r.t., adjusted to pH 4 by addition of 2 M aqueous HCl and evaporated to dryness under reduced pressure. The residue was then treated with 50 ml of water and extracted twice with 50 ml of CH_2Cl_2. The organic layer was dried over $MgSO_4$ and the solvent was distilled off, giving 240 mg (96%) of the product. ^{1}H-NMR (CD_3OD, ppm): δ 4.07 (4H, s, CH_{carb}), 3.58 (4H, m, –OCH_2CH_2OH), 3.23 (8H, m, Bu_4N^+), 1.65 (8H, m, Bu_4N^+), 1.41 (8H, m, Bu_4N^+), 1.02 (12H, t, Bu_4N^+); ^{13}C-NMR (CD_3OD, ppm): δ 71.4, 63.6, 59.5 (Bu_4N^+), 54.3, 47.9, 24.7 (Bu_4N^+), 20.6 (Bu_4N^+), 14.0 (Bu_4N^+).

3.9. Preparation of Cs(9)

Dissolved 200 mg (0.32 mmol) (Bu_4N)(**9**) in 50 ml MeOH and passed through a column with Amberlite IR-120(H^+) ion-exchange resin. The effluent was concentrated to 20 ml, treated with 150 mg (0.46 mmol) Cs_2CO_3 and diluted with 50 ml of water. The solution was concentrated slowly under reduced pressure to 5 ml. The precipitate formed was filtered off, washed with 2 ml of cold water and dried over P_2O_5 giving 150 mg (91%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 4.05 (2H, s, CH_{carb}), 3.94 (2H, s, CH_{carb}), 3.42 (2H, t), 3.36 (2H, t); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 70.3, 61.7, 51.8, 46.1.

3.10. Preparation of 10

Refluxed 0.55 g (1.0 mmol) Cs(**5**) and 1.0 ml hydrazine hydrate in 50 ml of ethanol overnight. The solution was cooled to r.t. and 20 ml of water was added. The solution was then concentrated to 5 ml under reduced pressure. The precipitate that formed was filtered off and dried in air to give 0.30 g (71%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 7.71 (3H, s), 4.08 (2H, s), 3.94 (2H, s), 3.62 (4H, m), 3.52 (2H, t), 2.95 (2H, m); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 71.1, 68.3, 66.6, 51.1, 46.2, 38.8; ^{11}B-NMR (Me_2SO-d_6, ppm): δ 24.9, 6.4, −0.3, −3.3, −5.2, −7.0, −9.1, −17.6, −20.1, −22.1, −28.0.

3.11. Preparation of 11

Refluxed 0.33 g (0.5 mmol) K(**6**) in 130 ml 2 M aq. HCl overnight, the solution was then cooled and the solvent was distilled off. The residue was treated with 10 ml of water, the precipitate was filtered off and dried in air to give 0.18 g (75%) of the product. ^{1}H-NMR (Me_2SO-d_6, ppm): δ 8.11 (3H, s), 4.10 (2H, s), 3.97(2H, s), 3.56 (4H, m), 3.44 (4H, m), 1.99 (1H, m); ^{13}C-NMR (Me_2SO-d_6, ppm): δ 170.9, 70.9, 68.0, 66.0, 51.5, 50.2, 46.2, 29.9; ^{11}B-NMR (acetone-d_6, ppm): δ 24.4 (1B, s), 6.9 (1B, d), 0.7 (1B, d), −2.5 (1B, d), −4.9 (2B, d), −6.6 (4B, d), −9.2 (2B, d), −17.2 (2B, d), −20.3 (2B, d), −22.2 (1B, d), −28.5 (1B, d).

3.12. Crystal structure determination of (Bu_4N)(6) and 8

Crystal data: (Bu_4N)(**6**), $C_{33}H_{79}B_{18}CoN_2O_7$ (M = 869.49), triclinic, space group $P\bar{1}$ (No. 2), a = 10.786(1), b = 15.714(2), c = 16.201(2) Å, α = 93.330(2), β = 108.381(2), γ = 110.166(2)°, V = 2402.8(4)Å^3, Z = 2, D_{calc} = 1.202 g cm^{-3}, μ = 0.402 mm^{-1}, $F(000)$ = 928, crystal size 0.10 × 0.20 × 0.50 mm; **8**, $C_{13}H_{34}B_{18}CoNO_2$ (M = 489.92), triclinic, space group $P\bar{1}$ (No. 2), a = 7.312(1), b = 12.895(2), c = 14.809(3) Å, α = 69.184(4), β = 77.326(4), γ = 78.771(4)°, V = 1262.9(4) Å^3, Z = 2, D_{calc} = 1.288 g cm^{-3}, μ = 0.694 mm^{-1}, $F(000)$ = 504, crystal size 0.50 × 0.30 × 0.20 mm.

Single-crystal X-ray diffraction experiments were carried out with a Bruker SMART 1000 CCD area detector, using graphite monochromated Mo–K_α radiation (λ = 0.71073 Å, ω-scans with a 0.3° step in ω and 10 s per frame exposure, $2\theta < 60°$) at 110 K. The 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 [31] and semi-empirical method SADABS [32]. A total of 28159 ((Bu_4N)(**6**)) and 11345(**8**) reflections were measured, 13695 (R_{int} = 0.0330) and 5874 (R_{int} = 0.0291) independent reflections were used in further calculations and refinement. The structures were solved by direct method and refined by the full-matrix least-squares method against F^2 in anisotropic (for non-hydrogen atoms) and isotropic (for H atoms) approximation. All hydrogen atoms were located from the difference Fourier syntheses. The final refinements were converged to R_1 = 0.0832 (from 8492 unique reflections with $I > 2\sigma(I)$) and wR_2 = 0.1095 (from all 13695 unique reflections) for (Bu_4N) (**6**), 0.0511 (from 5276 unique reflections with $I > 2\sigma(I)$) and wR_2 = 0.1293 (from all 5855 unique reflections) for **8**; the number of the refined parameters is 866 and 452 for (Bu_4N) (**6**) and **8**, respectively. All calculations were performed on an IBM PC/AT using the SHELXTL software [33].

4. Supplementary material

Crystallographic data for (Bu_4N)(**6**) and **8** have been deposited with the Cambridge Crystallographic Data

Centre, CCDC-161935 and -161936, respectively. Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

5. Note added in proof

The first preliminary report on this subject was presented at the International Conference 'Organometallic Compounds—Materials for the Next Millenium' in Nizhnii Novgorod (May–June, 2000) [34]. At the same time completely independently the ring-opening reaction of [8-O(CH_2CH_2)$_2$O-3,3′-Co(1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] with phenolates and various phosphorus-containing nucleophiles was used by Plesek et al. for synthesis of extractants of radioniclides from nuclear wastes based on the cobalt bis(dicarbollide) anion [35]. This information was kindly reported us by Dr Bohumir Grüner at the 2nd European Symposium on Boron Chemistry in Dinard (September 2001).

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References

[1] M.F. Hawthorne, Angew. Chem. Int. Ed. Engl. 32 (1993) 950.
[2] A.H. Soloway, W. Tjarks, B.A. Barnum, F.-G. Rong, R.F. Barth, I.M. Codogni, J.G. Wilson, Chem. Rev. 98 (1998) 1515.
[3] M.F. Hawthorne, A. Maderna, Chem. Rev. 99 (1999) 3421.
[4] V. Tolmachev, H. Lundqvist, I. Sivaev, A. Orlova, S. Sjöberg, P. Olsson, L. Gedda, J. Labelled Compd. Radiopharm. 40 (1997) 122.
[5] V. Tolmachev, J. Koziorowski, I. Sivaev, H. Lundqvist, J. Carlsson, A. Orlova, L. Gedda, P. Olsson, S. Sjöberg, A. Sundin, Bioconjug. Chem. 10 (1999) 338.
[6] R.N. Grimes, Carboranes, Academic Press, NY, 1970.
[7] C. Morin, Tetrahedron 50 (1994) 12521.
[8] D. Gabel, D. Moller, S. Harfst, J. Röesler, H. Ketz, Inorg. Chem. 32 (1993) 2276.
[9] I.B. Sivaev, S. Sjöberg, V.I. Bregadze, D. Gabel, Tetrahedron Lett. 40 (1999) 3451.
[10] I.B. Sivaev, A.B. Bruskin, V.V. Nesterov, M.Yu. Antipin, V.I. Bregadze, S. Sjöberg, Inorg. Chem. 38 (1999) 5887.
[11] I.B. Sivaev, A.A. Semioshkin, B. Brellochs, S. Sjöberg, V.I. Bregadze, Polyhedron 19 (2000) 627.
[12] M.F. Hawthorne, D.C. Young, T.D. Andrews, D.V. Howe, R.L. Pilling, A.D. Pitts, M. Reintjes, L.F. Warren, P.A. Wegner, J. Am. Chem. Soc. 90 (1968) 879.
[13] I.B. Sivaev, V.I. Bregadze, Collect. Czech. Chem. Commun. 64 (1999) 783.
[14] I.B. Sivaev, V.I. Bregadze, J. Organomet. Chem. 614–615 (2000) 27.
[15] Aldrich, Handbook of Fine Chemicals and Laboratory Equipment, 2000–2001, p. 1545.
[16] B. Issaurat, G. Amblard, C. Gavach, Bioelectrochem. Bioenerg. 11 (1983) 37.
[17] R.J. Atwell, R. Sridharan, R. de Levie, Proc. Indian Acad. Sci. Chem. Sci. 97 (1986) 431.
[18] F.A. Gomez, S.E. Johnson, C.B. Knobler, M.F. Hawthorne, Inorg. Chem. 31 (1992) 3558.
[19] Z. Janousek, J. Plesek, S. Hermanek, K. Base, L.J. Todd, W.F. Wright, Collect. Czech. Chem. Commun. 46 (1981) 2818.
[20] A. Franken, J. Plesek, J. Fusek, M. Semrau, Collect. Czech. Chem. Commun. 62 (1997) 1070.
[21] J. Plesek, B. Štibr, S. Hermanek, Collect. Czech. Chem. Commun. 49 (1984) 1492.
[22] S.P. Knyazev, V.N. Kirin, E.E. Chernyshev, Doklady Chem. 350 (1996) 252.
[23] J. Plesek, F.H. Rajabi, V. Vangani, J. Fusek, Collect. Czech. Chem. Commun. 59 (1994) 1326.
[24] L. Matel, F. Macasek, P. Rajec, S. Hermanek, J. Plesek, Polyhedron 1 (1982) 511.
[25] J. Plesek, S. Hermanek, A. Franken, I. Cisarova, Ch. Nachtigal, Collect. Czech. Chem. Commun. 62 (1997) 47.
[26] P. Selucky, J. Plesek, J. Rais, M. Kyrs, L. Kadlecova, J. Radioanalyt. Nucl. Chem. 149 (1991) 131.
[27] G.M. Tener, J. Am. Chem. Soc. 83 (1961) 159.
[28] N.D. Sinha, J. Bierat, H. Köster, Tetrahedron Lett. 24 (1983) 5843.
[29] C. Merk, T. Reiner, E. Kvasyuk, W. Pfleiderer, Helv. Chim. Acta 83 (2000) 3198.
[30] L. Borodinsky, E. Sinn, R.N. Grimes, Inorg. Chem. 21 (1982) 1686.
[31] SMART V5.051 and SAINT V5.00. Area Detector Control and Integration Software; Bruker Analytical X-ray Systems, Inc.: Madison, WI-53719, USA, 1998.
[32] G.M. Sheldrick, SADABS. Bruker Analytical X-ray Systems, Inc.: Madison, WI-53719, USA, 1997.
[33] G.M. Sheldrick, SHELXTL-97, Version 5.10. Bruker Analytical X-ray Systems, Inc.: Madison, WI-53719, USA, 1997.
[34] I.B. Sivaev, S. Sjöberg, V.I. Bregadze, Abstr. Int. Conf. 'Organometallic Compounds—Materials for the Next Millenium', Nizhnii Novgorod, 2000. p. 142.
[35] J. Plesek, B. Grüner, J. Baca, P. Selucky, J. Rais, N.V. Šistková, B. Casensky, Proc. 6th Int. Inform. Exch. Meet. 'Nuclear Development, Actinide and Fission Products Partitioning and Transmutation' (Madrid, 2000), NEA OECD Publications, Paris Cedex 16, France 2001 paper No 43, p. 659.