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A convenient synthetic route to useful monobranched polyethoxylated halogen terminated $[3,3\text{-Co}(1,2\text{-C}_2\text{B}_9\text{H}_{11})_2]^-$ synthons

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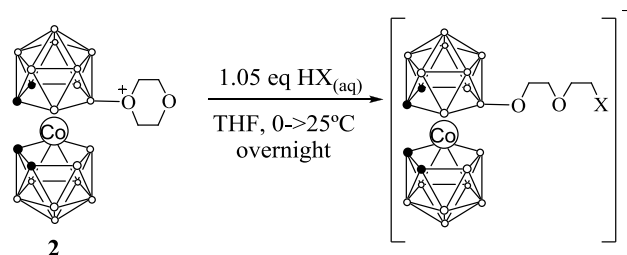
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An atom efficient and environmentally friendly route has been developed to obtain a new range of reagents in metallocarborane chemistry having monobranched polyethoxylated cobaltabisdicarbollide synthons.

10 Cobaltabisdicarbollide, $[3,3'\text{-Co}(1,2\text{-C}_2\text{B}_9\text{H}_{11})_2]^-$ (**[1]**), is a sandwich complex electronically similar to ferrocene but with distinctive properties. **[1]** has been proposed in some applications such as extraction of radionuclides,¹ in materials^{1a,2} or medicine.^{1a,3} **[1]** has 18 boron and four carbon positions to be substituted. This great capacity of substitution is one of the strengths of **[1]**, but is largely unexplored. As a result, the derivative chemistry of **[1]** is far from having been as investigated as this of ferrocene. Since 1997, when $[3,3'\text{-Co}(8\text{-C}_4\text{H}_8\text{O}_2\text{-}1,2\text{-C}_2\text{B}_9\text{H}_{10})(1',2'\text{-C}_2\text{B}_9\text{H}_{11})]$ (**[2]**) was first described,⁴ it has become the most popular reagent to bind **[1]** on platforms for different purposes, and it has been possible thanks to its easy reaction with nucleophiles. **[2]** can be prepared easily and in high yield.⁴ On the other hand alkyl halides, mainly R-Cl, R-Br and R-I, are reagents for a wide range of reactions: in substitution and elimination reactions, in the preparation of lithium reagents, or in malonic and acetoacetic synthesis, just to mention some of the most common synthetic uses of alkyl halides. With the objective to have easily accessible reagents of the alkyl halide type that incorporate **[1]**, we focused on **[2]** as an appropriate and readily available material. The necessary requirement was that the haloalkylmetallocarborane preparation had to be high yield. This would be an atom efficient, and environmentally friendly transformation.^{5,6}

35 It was of notice that despite the large number of derivatives of **[2]**, none contained a terminal halide.⁷ Our first attempts to achieve so were done in organic solvents and with soluble halides as nucleophiles, but the results were unfruitful. Things were different when haloacids were used in organic solvents. These conditions led to the sought compounds. Interestingly, it was noticed that rigorous conditions of solvent dryness and air exclusion were not necessary.

With no atmosphere special conditions, in a typical experiment for the synthesis of $[3,3'\text{-Co}(8\text{-}(\text{OCH}_2\text{CH}_2)_2\text{F}\text{-}1,2\text{-C}_2\text{B}_9\text{H}_{10})(1',2'\text{-C}_2\text{B}_9\text{H}_{11})]^-$, **[3]**, see Scheme 1 for a representation of this terminal fluoride, 200 mg of **[2]** (0.488 mmol) were dissolved in 10 mL of reagent grade THF. The solution was cooled with an ice/water bath and 7.8 μL of 26M HF(aq) were added dropwise. Following the addition, stirring was continued overnight while the temperature raised to normal room conditions. The solvent was removed and 10 mL



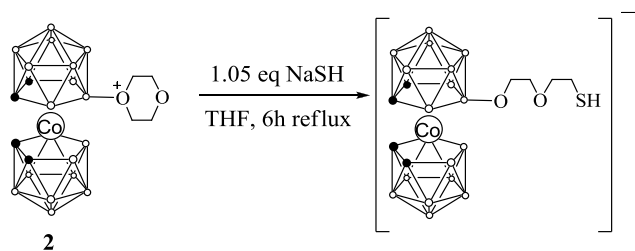
Scheme 1 Schematic synthesis of anions **3-6**. X = F (**[3]**), Cl (**[4]**), Br (**[5]**), I (**[6]**)

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of diethyl ether was added. The ether was neutralized with saturated $\text{NaHCO}_3(\text{aq})$, rinsed with aqueous NaCl solution and evaporation of the organic phase led to $\text{Na}[\mathbf{3}]\cdot 2\text{Et}_2\text{O}$ in 80% yield. The ^{11}B -NMR displayed resonances at 24.5 (1B, s), 5.9 (1B, d), 1.3 (1B, d), -1.6 (1B, d), -3.7 (2B, d), -6.3 (4B, d), -7.4 (2B, d), -16.4 (2B, d), -19.5 (2B, d), -21.2 (1B, d) and -27.7 (1B, d). The ^1H -NMR displayed resonances at 4.16 (2H, br s, C_c-H), 4.13 (2H, br s, C_c-H), 3.67 (2H, m, OCH_2CH_2), 3.55 (2H, t, OCH_2CH_2), 3.27 (4H, m, OCH_2CH_2) and 2.88-1.43 (17H, m, B-H). The ^{11}B -NMR indicated that no cluster substitution had taken place neither by F⁻ nor by OH⁻. This was confirmed by the MALDI-TOF analysis in which signals at 456.2, 442.2, 428.2, 338.6 and 323.5 m/z were observed corresponding to M+2CH₂, M+CH₂, M, M-C₄H₈OF and M-C₄H₈O₂F. The IR displays bands at 3043, 2870, 2568, 1453 and 1099 cm⁻¹ corresponding to C_c-H, C_{alkyl}-H, B-H, CH₂, C-O-C, respectively. A signal at 1056 cm⁻¹ has been attributed to the stretching C-F. The chemical analysis are in agreement with the formula indicated with two solvating diethyl ether molecules. The Cs⁺ and N(CH₃)₄⁺ salts were precipitated directly from the non-neutralized solution upon the addition of CsCl or N(CH₃)₄Cl, respectively.

The same conditions were used to prepare the anions $[3,3'\text{-Co}(8\text{-}(\text{OCH}_2\text{CH}_2)_2\text{X}\text{-}1,2\text{-C}_2\text{B}_9\text{H}_{10})(1',2'\text{-C}_2\text{B}_9\text{H}_{11})]^-$, (X=Cl (**[4]**), Br (**[5]**), I (**[6]**)). Details for their synthesis and their salts can be found in the supplementary section. Salts of Cs**[4]**, N(CH₃)₄**[5]** and N(CH₃)₄**[6]** have been produced in good yields, 88%, 81%, 80%, respectively.

Thiol terminated organic molecules are of interest for the functionalization of surfaces, in particular gold surfaces.⁸ As we have done with halogen terminated molecules incorporating **[1]**, we thought it would be convenient to have an adequate reagent that could be easily prepared terminated with a -SH moiety. Again we considered, as before, that the reagent had to



Scheme 2 Schematic synthesis of anion **9**.

be obtained in a simple way and in good yield. The reaction is shown in Scheme 2.

In a typical experiment for the synthesis of $[3,3'\text{-Co}(8\text{-(OCH}_2\text{CH}_2)_2\text{SH-1,2-C}_2\text{B}_9\text{H}_{10})(1',2'\text{-C}_2\text{B}_9\text{H}_{11})]^-$, (**9**), 100 mg of **[2]** (0.244 mmol) were dissolved in 10 mL of reagent grade THF. Next, 15 mg of sodium hydrosulfide (0.244 mmol) were added and the reaction mixture was stirred overnight. Then, the mixture was refluxed for 6h. The solvent was removed and the residue was extracted with diethyl ether and 1M HCl. After solvent evaporation, the residue was dissolved in the minimum volume of ethanol and a saturated aqueous solution of $\text{N}(\text{CH}_3)_4\text{Cl}$ was added resulting in the formation of an orange precipitate, namely $\text{N}(\text{CH}_3)_4[\mathbf{9}]$, in 85% yield. The ^{11}B -NMR displayed resonances at 22.8 (1B, s), 3.7 (1B, d), 0.5 (1B, d), -2.4 (1B, d), -4.1 (2B, d), -7.5 (2B, d), -8.2 (4B, d), -17.2 (2B, d), -20.4 (2B, d), -21.8 (1B, d) and -28.4 (1B, d). The ^1H -NMR displayed resonances at 4.27 (4H, br s, $\text{C}_c\text{-H}$), 3.70 (2H, t, OCH_2CH_2), 3.58 (2H, m, OCH_2CH_2), 3.50 (2H, m, OCH_2CH_2), 3.44 (12H, s, $\text{N}(\text{CH}_3)_4$), 2.91 (2H, t, OCH_2CH_2), 2.92-1.46 (17H, m, B-H) and 1.39 (1H, s, S-H). The MALDI-TOF analysis showed the desired molecular peak as well as fragmentation signals at 458.7, 444.7, 410.6, 382.6, 366.5, 337.5 and 324.5 m/z corresponding to $\text{M}+\text{CH}_2$, M , M-SH , $\text{M-C}_2\text{H}_4\text{SH}$, $\text{M-OC}_2\text{H}_4\text{SH}$, $\text{M-OC}_4\text{H}_8\text{SH}$ and $\text{M-O}_2\text{C}_4\text{H}_8\text{SH}$, respectively.

The formation of a B-C bond on the boron cluster is not simple and well understood. Up to today very few methods have proven reliable. Of the conventional methods for C-C coupling only the modified Kumada cross-coupling reaction has been shown to behave well for the B-C coupling. It is based on the reaction of a cluster B-I with a Grignard reagent in the presence of a "Pd" catalyst and CuI as a co-catalyst.⁹

With the aim to keep this route of functionalization on **[1]**, in addition to the haloalkyl substitution, we considered the possibility to generate mixed doubly functionalized derivatives of **[1]**. The reaction is shown in Scheme 3, for the syntheses of **[7]** and **[8]**, and as there can be seen, two markedly different reactive sites have been generated. In a typical experiment for the preparation of $[3,3'\text{-Co}(8\text{-(OCH}_2\text{CH}_2)_2\text{Br-1,2-C}_2\text{B}_9\text{H}_{10})(8'\text{-I-1',2'-C}_2\text{B}_9\text{H}_{11})]^-$, (**7**), 29 mg of $\text{N}(\text{CH}_3)_4[\mathbf{5}]$ (0.05 mmol) were dissolved in 5 mL of reagent grade EtOH. Then, 26 mg of iodine (0.103 mmol) were added. The reaction mixture was left to stand overnight at room temperature and was then heated under reflux for 1.5h. The excess iodine was decomposed by the addition of a solution of Na_2SO_3 in water and the resulting mixture was evaporated. This was washed with water and the product was redissolved in the minimum volume of ethanol and an aqueous solution containing an

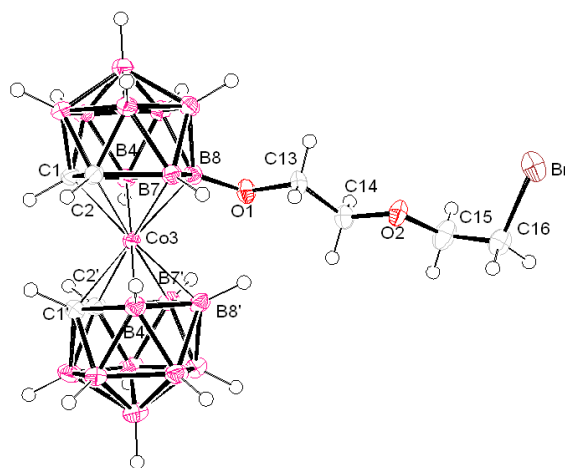
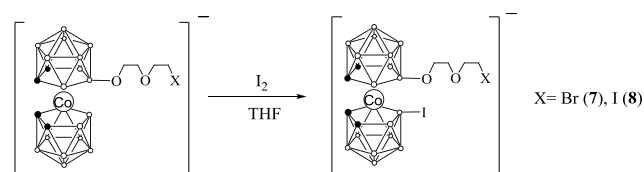


Figure 1 Molecular structure of $\text{N}(\text{CH}_3)_4[\mathbf{5}]$. The thermal ellipsoids are set at 30% probability.

excess of $\text{N}(\text{CH}_3)_4\text{Cl}$ was added, resulting in the formation of an orange precipitate, namely $\text{N}(\text{CH}_3)_4[\mathbf{7}]$, in 81% yield. The ^{11}B -NMR displayed resonances at 22.4 (1B, s), 0.3 (2B, d), -3.8 (2B, d), -4.9 (4B, d), -6.5 (2B, d), -6.5 (1B, s), -17.1 (2B, d), -19.2 (2B, d), -22.4 (1B, d) and -26.6 (1B, d). The ^1H -NMR displayed resonances at 4.49 (2H, br s, $\text{C}_c\text{-H}$), 4.19 (2H, br s, $\text{C}_c\text{-H}$), 3.73 (2H, t, OCH_2CH_2), 3.56 (4H, t, OCH_2CH_2), 3.53 (2H, m, OCH_2CH_2), 3.45 (12H, s, $\text{N}(\text{CH}_3)_4$) and 3.16-1.66 (16H, m). The MALDI-TOF analysis showed the desired molecular weight as well as fragmentation signals at 617.6, 570.4, 537.4 and 492.2 m/z corresponding to M , $\text{M-I}+2\text{Br}$, M-I and M-I-Br , respectively. Preparation of **[8]** was done in a like manner starting from $\text{N}(\text{CH}_3)_4[\mathbf{6}]$. Details are in the supplementary section.

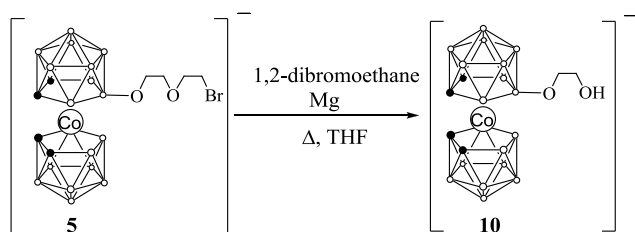
As described, the reaction conditions leading to these reagents are very simple: they do not require controlled conditions of humidity, they use aqueous hydric acids or NaHS and reagent grade THF instead of anhydrous THF or DME.



Scheme 3 Schematic synthesis of anions **7** and **8**.

All derivatives of **[2]** do contain the group $-\text{OCH}_2\text{CH}_2\text{OCH}_2\text{CH}_2-$ as a consequence of the nucleophilic attack. By reaction of $\text{N}(\text{CH}_3)_4[\mathbf{5}]$ with Mg and 1,2-dibromoethane, the cobaltabisdicarbollide farthest ether group is split generating an alcoholate moiety that is later hydrolyzed to the alcohol $[3,3'\text{-Co}(8\text{-(OCH}_2\text{CH}_2\text{OH)-1,2-C}_2\text{B}_9\text{H}_{10})(1',2'\text{-C}_2\text{B}_9\text{H}_{11})]^-$, (**10**). The reaction is exemplified in Scheme 4. Anion **[10]** becomes itself a reagent ready to generate a new set of haloalkylcobaltabisdicarbollide reagents in which the halide, or the adequate leaving group is at 3 bonds of the cluster. In a typical experiment leading to **[10]**, Mg turnings (45 mg, 1.85 mmol) were added to 2 mL of anhydrous THF. Then, a solution of $\text{N}(\text{CH}_3)_4[\mathbf{5}]$ (50 mg, 0.09 mmol) in THF and dibromoethane (0.05 mL, 0.12 mmol) were added

dropwise, at the same time, to the Mg suspension. Once the addition was completed the reaction mixture was left refluxing due to the exothermic reaction. When it returns to room temperature, water is added to quench the reaction. The solution is evaporated. The resulting residue is dissolved in Et₂O and extracted 3x HCl (1M). The product was redissolved in the minimum volume of ethanol and an aqueous solution containing an excess of N(CH₃)₄Cl was added, resulting in the formation of an orange precipitate, namely N(CH₃)₄[**10**], in 76% yield. The ¹¹B-NMR displayed resonances at 24.31 (1B, s), 5.45 (1B, d), 1.07 (1B, d), -1.84 (1B, d), -3.69 (2B, d), -6.57 (2B, d), -7.30 (4B, d), -16.57 (2B, d), -19.57 (2B, d), -21.40 (1B, d) and -27.94 (1B, d). The ¹H-NMR displayed resonances at 4.18 (4H, br s, C_c-H), 3.5 (4H, m, OCH₂CH₂), 3.44 (12H, s, N(CH₃)₄), 2.94 (1H, br s, O-H) and 2.88-1.44 (17H, m, B-H). The MALDI-TOF analysis showed the desired molecular peak at 384.31 m/z corresponding to M. No fragmentation peaks were observed in this case. The IR has shown bands at 3524, 3038, 2925, 2556, 1482 and 946 cm⁻¹ corresponding to O-H, C_c-H, C_{alkyl}-H, B-H, CH₃ and C-N, respectively.



Scheme 4 Schematic synthesis of anion **10**.

The nature of some of these reagents, particularly N(CH₃)₄[**5**] and N(CH₃)₄[**6**] has been clearly established by X-ray structural analysis. Good quality crystals of N(CH₃)₄[**5**] and N(CH₃)₄[**6**] were grown by slow evaporation of a hexane layered dichloromethane solution. The analysis confirmed the monobranched polyethoxylated brominated and iodinated terminated cobaltabisdicarbollide anions, respectively (see Figures 1 and 2).¹⁰ The structure of compound N(CH₃)₄[**10**] was also verified by a single-crystal X-ray measurement. However, due to bad quality of the crystals, the obtained R-value is of 14%, do not allow the full publication of the structure.

As a summary, new reagents for the incorporation of cobaltabisdicarbollide into different platforms have been synthesized. These reagents are of the type R-X, X = halogen or SH, and can be easily and in good yields generated from the readily available [3,3'-Co(8-C₄H₈O₂-1,2-C₂B₉H₁₀)(1',2'-C₂B₉H₁₁)]. These reagents contain the branch -O(CH₂)₂O(CH₂)₂X, but also a parent reagent with the branch O(CH₂)₂OH has been obtained. It is expected that these reagents will facilitate the applicability of metallacarboranes in a variety of different fields.

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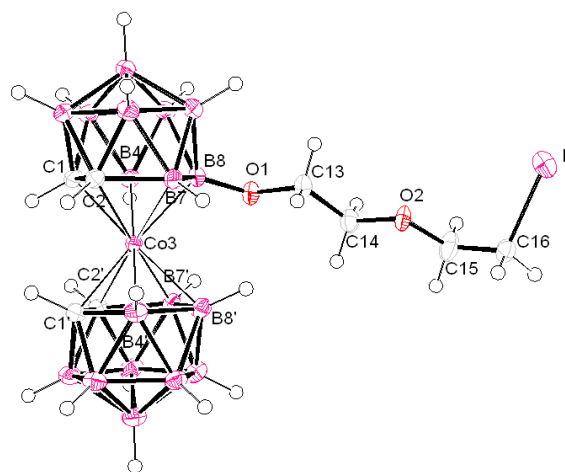


Figure 2 Molecular structure of N(CH₃)₄[**6**]. The thermal ellipsoids are set at 30% probability.

Notes and references

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- † Electronic Supplementary Information (ESI) available: [Synthesis and characterization of **3-10** and crystal structure of compounds N(CH₃)₄[**5**] and N(CH₃)₄[**6**]]. See DOI: 10.1039/b000000x/
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