Universitat de Girona

Facultat de Ciències | Memòria del Treball Final de Grau

Synthesis of new Cobalt complexes with carborane-type ligands for its potential application in BNCT (Boron Neutron Capture Therapy)

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AGRAÏMENTS

A la Doctora Marisa Romero, tutora del treball de fi de grau, per la seva exigència, orientació i la confiança d'acompanyar-me durant la trajectòria del projecte. Gràcies al conjunt de l'equip de recerca, Catàlisi i Sostenibilitat, en especial a l'Ester Manrique per la seva dedicació i el seu continu suport en tot moment del projecte. Gràcies als altres estudiants de treball de final de grau, companys de classe i a l'hora amics per fer que les moltes hores de laboratori i de despatx fossin més amenes.

RESUM

En aquest treball de final de grau s'ha desenvolupat i optimitzat una ruta sintètica per obtenir diferents complexos de cobalt amb lligands de tipus carborà, amb la idea d'obtenir compostos d'alt contingut en bor que presentin bona solubilitat en aigua per a la seva posterior aplicació en el camp de la medicina, ja que l'ús principal dels clústers de bor està en el tractament del càncer mitjançant la teràpia de captura d'electrons o BNCT (teràpia de captura de neutrons de bor).

La primera secció del treball s'ha centrat en la síntesi d'aquests complexos de cobalt. En primer lloc s'han sintetitzat les sals sòdiques (benzoat sòdic i 1-COONa-p-$C_2B_{10}H_{11}$) per a ser utilitzades com a nucleòfils en la síntesi d'algun dels compostos. S'ha sintetitzat el compost [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **2**, que hem utilitzat com a compost de partida per sintetitzar la resta dels compostos metallacarborans. Aquest complex mononuclear **2** reacciona amb els corresponents àcids o sals per formar els següents compostos: [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **3,** K_2[1'',4''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-C_6H_4] **4**, Na[3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5** i K_2[1'',12''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$] **6**.

La segona secció del treball es centra en la caracterització de tots els nous complexos que contenen lligands de tipus carboxílics i carboranilcarboxílics. Els complexos s'han sintetitzat i caracteritzat en estat sòlid mitjançant tècniques analítiques i en dissolució mitjançant tècniques espectroscòpiques (RMN, IR, UV-visible i ESI-MS).

Finalment, s'han estudiat les propietats redox de dos dels compostos sintetitzats **5** i **6**, mitjançant voltametria cíclica.

RESUMEN

En este trabajo de final de grado se ha desarrollado y optimizado una ruta sintética para obtener diferentes complejos de cobalto con ligandos tipo carborano, con la idea de obtener compuestos de alto contenido en boro que presenten buena solubilidad en agua para su posterior aplicación en el campo de la medicina, ya que el uso principal de los clústeres de boro está en el tratamiento del cáncer mediante la terapia de captura de electrones o BNCT (Terapia de captura de neutrones de boro).

La primera sección del trabajo se ha centrado en la síntesis de estos complejos de cobalto. En primer lugar, se han sintetizado las sales sódicas (benzoato sódico y 1-COONa-p-$C_2B_{10}H_{11}$) para ser utilizadas como nucleófilos en la síntesis de alguno de los compuestos. Se ha sintetizado el compuesto [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **2**, que hemos utilizado como compuesto de partida para sintetizar el resto de los compuestos metallacarboranos. Este complejo mononuclear **2** reacciona con los correspondientes ácidos o sales para formar los siguientes compuestos: [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **3,** K_2[1'',4''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-C_6H_4] **4**, Na[3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5** y K_2[1'',12''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$] **6**.

La segunda sección del trabajo se centra en la caracterización de todos los nuevos complejos que contienen ligandos de tipo carboxílicos y carboranilcarboxylicos. Los complejos se han sintetizado y caracterizado en estado sólido mediante técnicas analíticas y en disolución mediante técnicas espectroscópicas (RMN, IR, UV-visible y ESI-MS).

Finalmente, se han estudiado las propiedades redox de dos de los compuestos sintetizados **5** y **6** mediante voltametría cíclica.

SUMMARY

In this dissertation work we have developed and optimized a synthetic route to obtain different cobalt complexes with carborane-type ligands, with the idea to obtaining high boron compounds that present a good solubility in water for its application in the medicine field, since the main use of the boron clusters is in the cancer treatment by electron capture therapy or BNCT (Boron Neutron Capture Therapy).

The first section of the dissertation is focused on the synthesis of this cobalt complexes. First of all, sodium salts (sodium benzoate and 1-COONa-p-$C_2B_{10}H_{11}$) have been synthesized to be used as nucleophiles in the synthesis of some of the compounds. The compound [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **2** has been synthesized, which we have used as a starting compound to synthesize the rest of the compounds metallacarboranes. This mononuclear complex **2** reacts with the corresponding acids or salts to form the following compounds: [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **3,** K_2[1'',4''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-C_6H_4] **4**, Na[3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5**, K_2[1'',12''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$] **6**.

The second section of the dissertation is focused on the characterization of all new complexes that contain carboxylic and carboranylcarboxylic ligands. Complexes have been synthesized and characterized in the solid state by analytical techniques and in dissolution using spectroscopic techniques (NMR, IR, UV-visible and ESI-MS).

Finally, redox properties of two of the synthesized compounds **5** and **6** have been studied by cyclic voltammetry.

GLOSSARY OF TERMS AND ABBREVIATIONS

Abs	Absorbance
abs.	Absolute
acetone-d_6	Deuterated acetone
Anal. Found (Calc.)	Analysis found (analysis calculated)
B_c	Carborane boron
BNCT	Boron Neutron Capture Therapy
br	Broad
C_c	Carborane carbon
Cl	Cloride
CV	Cyclic voltammetry
DCM	Methylene chloride
DME	1,2-Dimethoxyethane
d	Doblet
ε	Extinction coefficient
E	Potential
$E_{1/2}$	Half-wave potential
eq	Equivalents
ESI-MS	Electrospray ionization mass spectrometry
h	Hours
IR	Infra Red
J	Coupling constant
M	Metal
m	Multiplet
MHz	Megahertz
MeOH	Methanol
m/z	Mass-to-charge ratio
NMR	Nuclear magnetic resonance
ppm	Parts per million
S	Sulfur
S	Singlet
SCE	Saturated calomel electrode
RT	Room Temperature
T	Temperature
t	Triplet
TBAP	Tetrabutylammonium perchlorate
UV-Vis	Ultraviolet-visible spectroscopy
vs	Versus
λ	Wavelength
ν	Wavenumber
δ	Chemical shift

CHAPTER 1. INTRODUCTION

1.1 Boranes and carboranes

Boron clusters chemistry is currently contemplate as a bridge between organic, inorganic and organometallic chemistry, with some theoretic chemistry, polymers and medicine influences. Boranes are neutral or anionic compounds with empirical formula $[B_nH_n]^{x-}$. Their structure is based on triangular face polyhedral with a B-H unit in each vertex. There are a large number of boranes in which one or more of the boron vertexes have been substituted by heteroatoms such as C, P, Al or S giving rise to a variety of compounds called heteroboranes.[1] The most studied among them are the carboranes in which one or two of the boron atoms have been replaced by carbon atoms. The empiric formula of these compounds is: $[C_nB_mH_{n+m+p}]^{x-} = [(CH)_n(BH)_mH_p]^{x-}$, where *n* represents the number of C atoms within the vertices of the cluster, *m* is the number of B atoms within the cluster and *p* the number of bridging H (bridge H).

The electronic requirements of boranes were studied by Wade, Milngos, Rudolph and Williams and obey the classic Wade's rules.[2] These electron-counting rules allow the prediction of the shape of the cluster structure taking into account the number of occupied vertices and the number of electron pairs required to form the cluster skeleton. Thus, being *n* the number of polyhedral vertexes (B atoms or different heteroatoms), if the number of electrons joining the cluster is n+1, the compound presents a *closo* structure; if it is n+2, the compound is *nido* and if it is n+3 the cluster is *arachno*. To make the skeletal electron counts is considered that each B-H unit gives two electrons to the cluster, from the boron atom; each C-H ó C-R unit contribute with three electrons from the carbon atom and each bridge hydrogen atom provides one electron to the cluster.

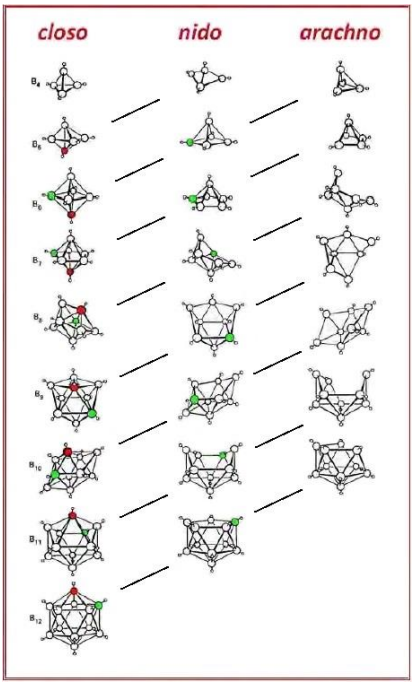


Figure 1. Structural relationship between closo, nido and arachno boranes and hetero -substituted boranes.

Figure 1 shows the structural relationship between *closo*, *nido* and *arachno* boranes as well as hetero-substituted boranes.[2b] The diagonal lines connect species that have the same number of skeletal

electron pairs. Hydrogen atoms except those of the B-H framework have been omitted for clarity. Thus, when one vertex of the *closo* structure is removed (red atom in Figure 1), the *nido* is obtained and if a second vertex is removed of this structure (green vertex in Figure 1), the *arachno* cluster is obtained.

As can be observed, the boron clusters are electron deficient due to their peculiar molecular architecture and type of bond (3 centres-2 electrons),[3] which provide to the cluster particular properties that cannot be found in their organic analogous.[4]

The most studied boranes are the carboranes and among them, the more known are the icosahedral clusters that possesses two carbon atoms, named dicarba-*closo*-dodecaboranes, which corresponds to the empirical formula $C_2B_{10}H_{12}$.

1.2 Closo-carboranes

The dicarba-*closo*-dodecarboranes, *closo*-$C_2B_{10}R_{12}$, are the most studied of all the carboranes due to their high thermic stability[4a,5] and their high chemical resistance.[1a,1d] These properties are because of the electronic delocalization present in the structure.

Depending on the relative position of the carbon atoms in the cluster there are three isomers (*Figure 2*: 1,2-dicarba-*closo*-dodecaborane (*o*-carborane), 1,7-dicarba-*closo*-dodecaborane (*m*-carborane) and 1,12-dicarba-*closo*-dodecaborane (*p*-carborane). The *o*-carborane is stable till temperatures around 460 ºC, over this temperature it isomerizes becoming *m*-carborane and that one, between 600 and 700 ºC, turns into *p*-carborane[1a,6] As can be seen, the thermal isomerization process gives rise to the more stable isomer, which is the one with the carbon atoms opposite within the cluster.[7]

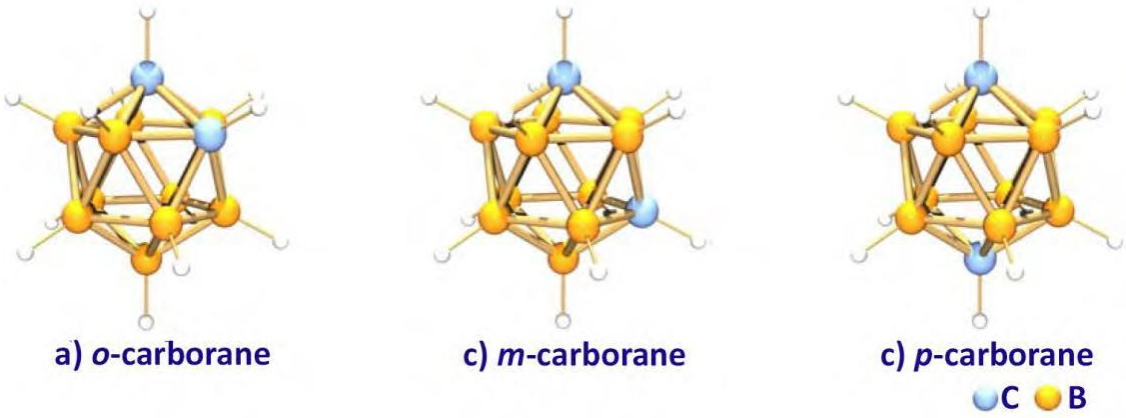


Figure 2. Positional isomers of the dicarba-*closo*-dodecaborane, *closo*-$C_2B_{10}H_{12}$

These dicarba-*closo*-dodecaborane compounds are really interesting due to their facility to change their behaviour according to the exo-cluster groups bond to the boron or carbon atoms.

1.3 Applications of the *o*-carboranes

The 1,2-dicarba-closo-dodecaboranes, 1,2-closo-$C_2B_{10}H_{12}$, and its derivatives are clusters with structures that present uncommon characteristics such as low nucleophilicity, chemical inertness,[1a,1d] thermal stability, electron-withdrawing properties, and stability and low toxicity in biological systems that have stimulated the development of a wide range of potential applications based on a molecular approach for the preparation of materials such as, polymer synthesis, ceramic precursors, nonlinear optics, selective ion-exchange sensors, microelectrodes and gold nanoparticles monolayers modification, as well as applications in catalysis, medicine and in wastewater treatment for nuclear power plants.

In the medicine field, the main use of the boron clusters is in the cancer treatment by electron capture therapy or BNCT (Boron Neutron Capture Therapy) which is based on the use of complexes with a large content of the ^{10}B isotope[8] thus, looking for complexes with a large number of clusters which afford to have a molecule with a large number of boron atoms per molecule.[4a,9] Moreover, other applications of boron clusters are seen such as the use of iodinated boron clusters as contrast agents in the X-Ray technic[10] or the use of cobalt metallacarboranes as proteins inhibitors.[11]

1.4 Cosan as a molecular imaging platform

The inorganic, boron-based molecule cobaltabisdicarbollide, [3,3'-Co(1,2-$C_2B_9H_{11})_2]^-$, commonly known as cosan, is a stable complex in which the cobalt atom is sandwiched between two η^5-bonding $[C_2B_9H_{11}]^{2-}$ moieties. While showing differentiated properties from lipid molecules (e.g. amphiphilic character in water), cosan has the ability to assemble into monolayer vesicles. As recently demonstrated, cosan can cross through synthetic lipid membranes without disrupting membrane integrity [12] and accumulates in vitro within living cells.[13] Additionally, it can be readily multi-decorated by incorporation of functional groups into the different vertices. These properties, together with its high boron content, chemical stability and solubility under physiologic conditions, make cosan a suitable building block for the preparation of boron carrier drugs.

Despite the large variety of cosan derivatives being described in the literature with potential application in BNCT, the transition from bench to bed (even in the preclinical

setting) has been only occasionally approached. The main reason behind this fact still remains the lack of techniques able to determine, in vivo and in real time, the accumulation of boron in the tumour and surrounding tissues, allowing a candidate-by-candidate screening and prediction of therapeutic efficacy. Nuclear imaging techniques such as Positron Emission Tomography (PET) and Single Photon Emission Computerized Tomography (SPECT) in combination with X-ray Computed Tomography (CT) are valuable tools for the in vivo assessment of pharmacokinetic properties of new chemical entities; they are thus anticipated to be suitable methods for determining boron accumulation in the tumour and surrounding tissues. Nonetheless, application of nuclear imaging requires radiolabelling of the molecule under investigation with a positron or a gamma emitter. To date radiolabelling of polyhedral boranes and heteroboranes with the radionuclide covalently attached to the cluster cage has been restricted to nido and closo derivatives.[14]

1.5 Metallacarboranes as building blocks for BNCT techniques

Compound [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **2** has been shown to be susceptible to nucleophilic attack at the dioxane carbon adjacent to the positively charged oxygen atom by a variety of nucleophile agents containing oxygen, nitrogen, phosphorus and carbon, resulting in one anionic species formed by the opening of the dioxane ring. Recent reviews cover the known scope of reactions of different oxonium derivatives of polyhedral boron hydrides.

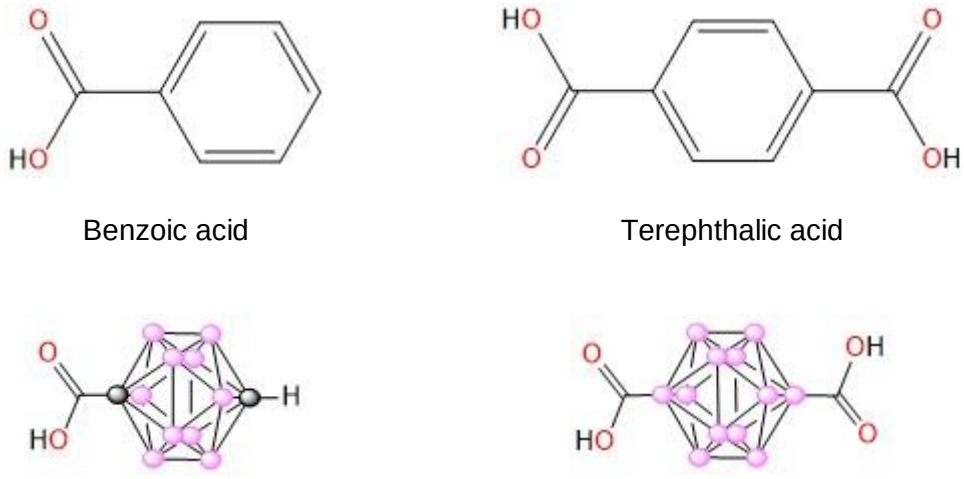
In this dissertation work we used carboranylcarboxylic acids as nucleophiles to attack the dioxane ring. We generate new compound with mono and dicarboranylcarboxylic acids to improve the solubility in water for its potential application in BNCT.

CHAPTER 2. OBJECTIVES

The aims of this work are the ones following:

- To learn the techniques of synthesis and spectroscopic and electrochemical characterization, which are characteristic of a research laboratory.

- The synthesis of new metallacarboranes complexes derived from the cyclic oxonium [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **2**, by using carboxylic and carboranylcarboxylic acids as nucleophiles (ligands). The ligands used in this work are the ones following in the *Figure 3*.



Benzoic acid

Terephthalic acid

1-COOH-p-$C_2B_{10}H_{11}$ acid

1,12-$(COOH)_2$-$C_2B_{10}H_{10}$ acid

Figure 3. Plot for ligands used in this work

- The analytical, spectroscopic characterization of the complexes synthesized and the electrochemical characterization of two of these compounds (**5** and **6**).

CHAPTER 3. EXPERIMENTAL SECTION

3.1 Instrumentation and measurements

- *UV-Vis*

UV-Vis spectroscopy was performed on a Cary 50 Scan (Varian) UV-Vis spectrophotometer with 1 cm quartz cells.

- *Cyclic voltammetry (CV)*

CV experiment was performed in an IJ-Cambria IH-660 potentiostat using a three electrode cell. Glassy carbon electrode (3 mm diameter) from BAS was used as working electrode, platinum wire as auxiliary and SCE as the reference electrode. The complexes were dissolved in solvents containing the necessary amount of n-Bu_4NPF_6 (TBAH) as supporting electrolyte to yield a 0.1 M ionic strength solution. All $E_{1/2}$ values reported in this work were estimated from cyclic voltammetry experiments as the average of the oxidative and reductive peak potentials $(E_{p,a}+E_{p,c})/_2$.

- *IR*

IR spectroscopy was performed on an Agilent Technologies, Cary 630 FTIR equipped with an ATR system, directly on the samples without any previous treatment.

- *NMR spectra*

NMR spectra have been recorded with a Bruker av 300 MHz, Bruker av 400 MHz and Bruker 400 MHz ascent instruments equipped with the appropriate decoupling accessories ^{1}H and $^{1}H\{^{11}B\}$ NMR (300.13/400.13 MHz), $^{13}C\{^{1}H\}$ NMR (75.47/100.62 MHz) and ^{11}B and $^{11}B\{^{1}H\}$ NMR (96.29/128.37 MHz) in acetone-d_6 as solvent. Chemical shift values for ^{11}B NMR spectra were referenced to external $BF_3{\leftarrow}OEt_2$ and those for ^{1}H, $^{1}H\{^{11}B\}$ and $^{13}C\{^{1}H\}$ NMR spectra were referenced to $SiMe_4$. Chemical shifts are reported in units of parts per million downfield from reference, and all coupling constants in Hz. For the NMR assignments, we used the same labeling scheme as for the structures described in the text.

- *Mass spectra*

The mass spectra were recorded in the negative ion mode using a Bruker Daltonics esquire6000 ESI-MS (N_2 laser; λ_{exe} 337nm, 0.5 ns pulses; Skimmer voltage 40 V). Samples were run using deuterated acetone (CD_3COCD_3) as the solvent.

3.2 Synthesis of compounds

Materials. All reagents used in the present work were obtained from Aldrich Chemical Co. in the highest commercially available purity grade and were used without further purification. Reagent grade organic solvents were obtained from SDS and high purity deionized water was obtained by passing distilled water through a nanopore Mili-Q water purification system.

Synthesis. Ligand 1-COOH-p-$C_2B_{10}H_{11}$ and 1,12-$(COOH)_2$-$C_2B_{10}H_{10}$ [15] , Cs[3,3'-Co($C_2B_9H_{11}$)$_2$] (**1**) [16] , [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] (**2**) [17, 18] and [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] (**3**) [19] complexes and ligands were prepared according to the literature. All synthetic manipulations were routinely performed under dinitrogen atmosphere using standard Schlenk tubes and vacuum line techniques.

Synthesis of the ligand 1-COONa-p-$C_2B_{10}H_{11}$

This ligand was prepared by neutralization of the 1-COOH-p-$C_2B_{10}H_{11}$ acid. Dried sodium carbonate (17 mg, 0.16 mmol) and 1-COOH-p-$C_2B_{10}H_{11}$ (60 mg, 0.319 mmol) were dissolved in 15 mL of distilled water at room temperature. After stirring 2 hours, the solvent was removed. The resulting solid was filtered off and dried in vacuum. Yield: 65 mg (97 %) of pure 1-COONa-p-$C_2B_{10}H_{11}$ (sodium salt) was obtained. **IR ν(cm^{-1})**: 3306 (O-Na), 3053 (C_c-H), 2888 (C-H)$_{alkyl}$, 2600 (B-H), 1626 (C=O), 1347 δ(CH). **^{1}H NMR (400 MHz, $(CD_3)_2CO$)**: δ 3.35 (s, 1H, C-H), 3.10-1.4 (m, 10H, B-H). **^{1}H{^{11}B} NMR (400 MHz, $(CD_3)_2CO$)**: δ 3.35 (s, 1H, C-H), 2.40 (s, 5H, B-H), 2.13 (s, 5H, B-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ -12.56 (t, ^{1}J(B,H) = 376Hz, ^{2}J(B,H) = 180Hz, 10B). **^{11}B{^{1}H} NMR (96.3 MHz, $(CD_3)_2CO$)**: δ -11.36 (d, ^{1}J(B,H) = 213Hz, 10B).

Synthesis of [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], (2)

Under an inert atmosphere, a mixture of dried commercial cesium salt of cobaltabisdicarbollide **1** (1.5 g, 3.28 mmol) and 3.33 mL of $BF_3{\cdot}Et_2O$ (8 eq, 26.27 mmol) were refluxed in 150 mL of dry dioxane. The mixture was refluxed at 125ºC for 5 hours. After cooling down, the solution was filtered to eliminate the remaining borates formed during the reaction. The filtrated liquid was evaporated at the rotary evaporator.

The remaining solid was passed through column chromatography on silica gel and the product was eluted with methylene chloride (SiO_2). The first orange fraction obtained correspond to **2**. The solvent was evaporated, washed twice with 10 mL of diethyl ether and dried in vacuum. Yield: 0.684 g (51 %) of pure complex **2** was obtained. **IR ν(cm$^{-$**

^{1}): 3038 (C_c-H), 2959, 2918, 2866 (C-H)$_{alkyl}$, 2529 (B-H), 1444 δ(CH_2), 1255 δ(CH), 1129, 1094 (C-O-C). **^{1}H NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.71 (t, ^{3}J(H,H) = 4Hz, ^{2}J(H,H) = 8Hz, 4H, OCH_2CH_2), 4.41 (br s, 2H, C_c-H), 4.07 (t, ^{3}J(H,H) = 4Hz, ^{2}J(H,H) = 8Hz, 4H, OCH_2CH_2), 4.03 (br s, 2H, C_c-H), 3.45-1.20 (m, 17H, B-H). **^{1}H{^{11}B} NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.71 (t, ^{3}J(H,H) = 4Hz, ^{2}J(H,H) = 8Hz, 4H, OCH_2CH_2), 4.41 (br s, 2H, C_c-H), 4.07 (t, ^{3}J(H,H) = 4Hz, ^{2}J(H,H) = 8Hz, 4H, OCH_2CH_2), 4.03 (br s, 2H, C_c-H), 3.21 (s, 3H, B-H), 2.91 (s, 4H, B-H), 2.32 (s, 2H, B-H), 2.17 (s, 1H, B-H), 1.77 (s, 3H, B-H), 1.68 (s, 2H, B-H), 1.54 (s, 1H, B-H), 1.29 (s, 1H, B-H). **^{13}C{^{1}H} NMR (75.5 MHz, $(CD_3)_2CO$)**: δ 83.96 (s, OCH_2CH_2), 66.26 (s, OCH_2CH_2), 55.13 (s, C_c-H), 48.85 (s, C_c-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 24.25 (s, 1B, B(8)), 8.07 (d, ^{1}J(B,H) = 135Hz, 1B, B(8')), 4.45 (d, ^{1}J(B,H) = 142Hz, 1B, B(10)), -2.24 (s, 1B, B(10')), -4.48 (d, ^{1}J(B,H) = 144Hz, 4B, B(4,4',7,7')), -9.04 (t, ^{1}J(B,H) = 275Hz, ^{2}J(B,H) = 137Hz, 4B, B(9,9',12,12')), -15.23 (d, ^{1}J(B,H) = 161Hz, 2B, B(5',11')), -18.75 (d, ^{1}J(B,H) = 163Hz, 2B, B(5,11)), -22.04 (s, 1B, B(6)), -26.81 (d, ^{1}J(B,H) = 170Hz, 1B, B(6')). **^{11}B{^{1}H} NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 24.63 (s, 1B, B(8)), 8.34 (s, 1B, B(8')), 4.70 (s, 1B, B(10)), -2.92 (s, 1B, B(10')), -4.34 (s, 2B, B(4',7')), -8.26 (s, 2B, B(4,7)), -9.58 (s, 4B, B(9,9',12,12')), -15.26 (s, 2B, B(5',11')), -18.80 (s, 2B, B(5,11)), -21.21 (s, 1B, B(6)), -26.89 (s, 1B, B(6')).

Synthesis of $[N(CH_3)_4][3,3'\text{-}Co(8\text{-}O(CH_2CH_2O)_2C(O)C_6H_5\text{-}1,2\text{-}C_2B_9H_{10})(1',2'\text{-}C_2B_9H_{11})]$, (3)

Under an inert atmosphere, dried sodium benzoate (18 mg, 0.122 mmol) and **2** (50 mg, 0.122 mmol) were dissolved in 10 mL of anhydrous DME. After stirring overnight, the solvent was removed. The product was redissolved in the minimum volume of ethanol, and an aqueous solution containing an excess of $[N(CH_3)_4]Cl$ was added, resulting in the formation of an orange precipitate. This was filtered off, washed with water and petroleum ether, and dried in vacuum. Yield: 63.7 mg (86%) of pure **3** complex was obtained. **Anal. calcd** for $C_{19}H_{46}B_{18}CoNO_4$: C, 37.65; H, 7.65; N, 2.31. Found: C, 36.94; H, 7.63; N, 2.31. **IR ν(cm^{-1})**: 3035 (C_c-H), 2961, 2920, 2868 (C-H)$_{alkyl}$, 2528 (B-H), 1706 (C=O), 1483, 1450 δ(CH_2), 1273 δ(CH), 1180, 1118 (C-O-C), 943 (C-N). **^{1}H NMR (400 MHz, $(CD_3)_2CO$)**: δ 8.04 (d, ^{3}J(H,H) = 8Hz, 2H, C_6H_5), 7.62 (t, ^{3}J(H,H) = 15Hz, ^{4}J(H,H) = 8Hz, 1H, C_6H_5), 7.51 (t, ^{3}J(H,H) = 15Hz, ^{4}J(H,H) = 7Hz, 2H, C_6H_5), 4.43 (t, ^{2}J(H,H) = 10Hz, ^{3}J(H,H) = 5Hz, 2H, OCH_2CH_2), 4.28 (br s, 4H, C_c-H), 3.83 (t, ^{2}J(H,H) = 10Hz, ^{3}J(H,H) = 5Hz, 2H, OCH_2CH_2), 3.60 (s, 4H, OCH_2CH_2), 3.45 (s, 12H, $N(CH_3)_4$), 2.91-1.49 (m, 17H, B-H). **^{1}H{^{11}B} NMR (400 MHz, $(CD_3)_2CO$)**: δ 8.04 (d, ^{3}J(H,H) = 8Hz, 2H, C_6H_5), 7.62 (t, ^{3}J(H,H) = 15Hz, ^{4}J(H,H) = 8Hz, 1H, C_6H_5), 7.51 (t, ^{3}J(H,H) = 15Hz, ^{4}J(H,H) = 8Hz, 2H, C_6H_5), 4.43 (t, ^{2}J(H,H) = 10Hz, ^{3}J(H,H) = 5Hz, 2H, OCH_2CH_2), 4.28 (br s, 4H, C_c-H), 3.83 (t, ^{2}J(H,H) = 10Hz, ^{3}J(H,H) = 5Hz, 2H, OCH_2CH_2), 3.62-3.57 (m,

4H, OCH_2CH_2), 3.46 (s, 12H, $N(CH_3)_4$), 2.91 (s, 3H, B-H), 2.00 (s, 2H, B-H), 1.79 (s, 2H, B-H), 1.66 (s, 2H, B-H), 1.57 (s, 2H, B-H). 1.47 (s, 2H, B-H), 1.29 (s, 4H, B-H). **$^{13}C\{^1H\}$ NMR (75.5 MHz, $(CD_3)_2CO$)**: δ 165.87 (s, COO), 132.88 (s, C_6H_5), 129.39 (s, C_6H_5), 128.45 (s, C_6H_5), 71.89 (s, OCH_2), 68.78 (s, OCH_2), 68.49 (s, OCH_2), 64.30 (s, OCH_2), 54.48 (s, C_c-H), 46.38 (s, C_c-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 23.01 (s, 1B, B(8)), 3.90 (d, $^1J(B,H)$ = 140Hz, 1B, B(8')), 0.41 (d, $^1J(B,H)$ = 137Hz, 1B, B(10)), -1.68 (s, 1B, B(10')), -4.21 (d, $^1J(B,H)$ = 156Hz, 4B, B(4,4',7,7')), -7.66 (t, $^1J(B,H)$ = 216Hz, $^2J(B,H)$ = 121Hz, 4B, B(9,9',12,12')), -17.20 (d, $^1J(B,H)$ = 151Hz, 2B, B(5',11')), -20.34 (d, $^1J(B,H)$ = 151Hz, 2B, B(5,11)), -22.81 (s, 1B, B(6)), -28.49 (d, $^1J(B,H)$ = 151Hz, 1B, B(6')). **$^{11}B\{^1H\}$ NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 23.01 (s, 1B, B(8)), 4.01 (s, 1B, B(8')), 0.44 (s, 1B, B(10)), -2.42 (s, 1B, B(10')), -4.11 (s, 2B, B(4',7')), -7.39 (s, 2B, B(4,7)), -8.26 (s, 4B, B(9,9',12,12')), -17.21 (s, 2B, B(5',11')), -20.34 (s, 2B, B(5,11)), -21.92 (s, 1B, B(6)), -28.48 (s, 1B, B(6')). **ESI-MS (m/z)**: 532.2 (M, 100%); 546.45 (M – $C_4H_8O_2$, 17%).

Synthesis of $K_2[1'',4''-\{3,3'-Co(8-O(CH_2CH_2O)_2CO-1,2-C_2B_9H_{10})(1',2'-C_2B_9H_{11})\}_2-C_6H_4]$, (**4**)

Under an inert atmosphere, a mixture of dried terephthalic acid (10.1 mg, 0.061 mmol) and potassium carbonate (67.4 mg, 0.487 mmol) were refluxed in 10 mL of anhydrous acetone at 100 ºC for 2 hours. Then, a solution of **2** (50 mg, 0.122 mmol) in 5 mL of anhydrous acetone was added dropwise in the solution. After stirring overnight, the excess of potassium carbonate was filtered off and discarded. The solvent was removed, washed with petroleum ether and dried in vacuum. Yield: 58.1 mg (90%).

Column chromatography on silica was carried out (SiO_2, CH_2Cl_2/MeOH 9:1), the first orange fraction containing compound **2** was discarded. The second yellow-orange fraction containing **4** was obtained. The volume of the later fraction was reduced to dryness. Finally, the solid was washed twice with 10 mL of diethyl ether and dried in vacuum. Yield: 16.2 mg (25 %) of pure **4** complex was obtained. **Anal. calcd** for $C_{24}H_{62}B_{36}Co_2O_8K_2$: C, 27.08; H, 5.82. Found: C, 26.96; H, 5.65. **IR ν(cm^{-1})**: 3038 (C_c-H), 2959, 2919, 2879 $(C\text{-}H)_{alkyl}$, 2533 (B-H), 1702 (C=O), 1446, 1408 δ(CH_2), 1257 δ(CH), 1105, 1020 (C-O-C). **^1H NMR (400 MHz, $(CD_3)_2CO$)**: δ 8.16 (s, 4H, C_6H_4), 4.47 (t, $^2J(H,H)$ = 10Hz, $^3J(H,H)$ = 5Hz, 4H, OCH_2CH_2), 4.26 (br s, 8H, C_c-H), 3.85 (t, $^2J(H,H)$ = 10Hz, $^3J(H,H)$ = 5Hz, 4H, OCH_2CH_2), 3.60 (m, 8H, OCH_2CH_2), 2.74-1.46 (m, 34H, B-H). **$^1H\{^{11}B\}$ NMR (400 MHz, $(CD_3)_2CO$)**: δ 8.16 (s, 4H, C_6H_4), 4.47 (t, $^2J(H,H)$= 10Hz, $^3J(H,H)$= 5Hz, 4H, OCH_2CH_2), 4.27 (br s, 8H, Cc-H), 3.85 (t, $^2J(H,H)$= 10Hz, $^3J(H,H)$= 5Hz, 4H, OCH_2CH_2), 3.63-3.58 (m, 8H, OCH_2CH_2), 2.74 (s, 6H, B-H), 2.00 (s, 4H, B-H),

1.79 (s, 6H, B-H), 1.64 (s, 6H, B-H), 1.56 (s, 6H, B-H), 1.46 (s, 6H, B-H). **$^{13}C\{^{1}H\}$ NMR (75.5 MHz, $(CD_3)_2CO$)**: δ 166.09 (s, COO), 134.96 (s, C_6H_4), 130.37 (s, C_6H_4), 72.71 (s, OCH_2), 71.76 (s, OCH_2), 69.51 (s, OCH_2), 65.50 (s, OCH_2), 55.19 (s, C_c-H), 47.22 (s, C_c-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 21.22 (s, 2B, B(8)), 2.76 (s, 2B, B(8')), -1.53 (s, 2B, B(10)), -3.79 (d, $^{1}J(B,H)$ = 143Hz, 2B, B(10')), -6.23 (m, 8B, B(4,4',7,7')), -9.88 (t, $^{1}J(B,H)$ = 220Hz, $^{2}J(B,H)$ = 117Hz, 8B, B(9,9',12,12')), -19.22 (d, $^{1}J(B,H)$ = 150Hz, 4B, B(5',11')), -22.26 (d, $^{1}J(B,H)$ = 138Hz, 4B, B(5,11)), 24.48 (s, 2B, B(6)), -31.04 (d, $^{1}J(B,H)$ = 147Hz, 2B, B(6')). **$^{11}B\{^{1}H\}$ NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 24.11 (s, 2B, B(8)), 5.07 (s, 2B, B(8')), 1.29 (s, 2B, B(10)), -1.64 (s, 2B, B(10')), -3.54 (s, 4B, B(4',7')), -6.47 (s, 4B, B(4,7)), -7.37 (s, 8B, B(9,9',12,12')), -16.46 (s, 4B, B(5',11')), -19.60 (s, 4B, B(5,11)), -20.88 (s, 2B, B(6)), -28.26 (s, 2B, B(6')). **ESI-MS (m/z)**: 493.2 (M, 100%)/2; 506.7 ((M + N_2)/2, 40%).

Synthesis of Na[3,3'-Co(8-O(CH_2CH_2O)$_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], (**5**)

Under an inert atmosphere, dried 1-COONa-p-$C_2B_{10}H_{11}$ (26 mg, 0.122 mmol) and **2** (50 mg, 0.122 mmol) were refluxed in 10 mL of anhydrous DME at 150 ºC. After stirring overnight, the solvent was removed. This was filtered off, washed with petroleum ether and dried in vacuum. Yield: 49.3 mg (60%) of pure **5** was obtained. **Anal. calcd** for $C_{11}H_{40}B_{28}CoO_4K$: C, 21.27; H, 6.49. Found: C, 21.13; H, 6.22. **IR v(cm^{-1})**: 3054 (C_c-H), 2959, 2918, 2866 (C-H)$_{alkyl}$, 2536 (B-H), 1717 (C=O), 1456 δ(CH_2), 1265 δ(CH), 1188, 1121 (C-O-C). **^{1}H NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.25 (br s, 4H, C_c-H), 4.14 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.62 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.56 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.49 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 2.84 (br s, 1H, C-H), 2.54 (s, 10H, B_c-H), 2.00-0.80 (m, 17H, B-H). **$^{1}H\{^{11}B\}$ NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.25 (br s, 4H, C_c-H), 4.14 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.62 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.56 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 3.49 (t, $^{2}J(H,H)$= 10Hz, $^{3}J(H,H)$= 5Hz, 2H, OCH_2CH_2), 2.82 (br s, 1H, C-H), 2.54 (s, 10H, B_c-H), 2.41 (s, 4H, B-H), 2.20 (s, 4H, B-H), 1.99 (br s, 2H, B-H), 1.78 (br s, 2H, B-H), 1.66 (br s, 3H, B-H), 1.56 (br s, 2H, B-H). **$^{13}C\{^{1}H\}$ NMR (75.5 MHz, $(CD_3)_2CO$)**: δ 162.36 (s, COO), 72.78 (s, C-COO), 70.65 (s, OCH_2), 69.41 (s, OCH_2), 69.05 (s, OCH_2), 67.63 (s, OCH_2), 55.31 (s, C_c-H), 47.30 (s, C_c-H), 41.32 (s, C-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 22.67 (s, 1B, B(8)), 3.51 (d, $^{1}J(B,H)$ = 130Hz, 1B, B(8')), 0.17 (d, $^{1}J(B,H)$ = 136Hz, 1B, B(10)), -2.11 (s, 1B, B(10')), -4.60 (d, $^{1}J(B,H)$ = 162Hz, 4B, B(4,4',7,7')), -8.14 (t, $^{1}J(B,H)$ = 221Hz, $^{2}J(B,H)$ = 103Hz, 4B, B(9,9',12,12')), -14.72 (t, $^{1}J(B,H)$ = 352Hz, $^{2}J(B,H)$ = 171Hz, 10B, B_c-H) -19.25 (d, $^{1}J(B,H)$ = 146Hz, 2B, B(5',11')), -21.64 (s, 2B,

B(5,11)), -23.15 (s, 1B, B(6)), -28.96 (d, ^{1}J(B,H) = 158Hz, 1B, B(6')). **$^{11}B\{^{1}H\}$ NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 22.63 (s, 1B, B(8)), 3.68 (s, 1B, B(8')), 0.10 (s, 1B, B(10)), -2.79 (s, 1B, B(10')), -4.58 (s, 2B, B(4',7')), -7.77 (s, 2B, B(4,7)), -8.63 (s, 4B, B(9,9',12,12')), -14.69 (d, ^{1}J(B,H) = 176Hz, 10B, B_c-H) -17.66 (s, 2B, B(5',11')), -20.82 (s, 2B, B(5,11)), -22.32 (s, 1B, B(6)), -28.96 (s, 1B, B(6')). **ESI-MS (m/z)**: 598.4 (M, 100%); 627.4 (M + H^+ + N_2), 3%).

Synthesis of K_2[1'',12''-{3,3'-Co(8-O(CH_2CH_2O)$_2$CO-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$], (6)

Under an inert atmosphere, a mixture of dried 1,12-$(COOH)_2$-$C_2B_{10}H_{10}$ (23 mg, 0.1 mmol) and potassium carbonate (107 mg, 0.775 mmol) were refluxed in 10 mL of anhydrous acetone at 100 ºC for 2 hours. Then, a solution of **2** (80 mg, 0.195 mmol) in 5 mL of anhydrous acetone was added dropwise in the solution. After stirring overnight, the excess of potassium carbonate was filtered off and discarded. The solvent was removed, washed with petroleum ether and dried in vacuum. Yield: 103 mg (94%) of pure **6** was obtained. **Anal. calcd** for $C_{20}H_{68}B_{46}Co_2O_8K_2$: C, 21.26; H, 6.06. Found: C, 21.11; H, 6.27. **IR ν(cm^{-1})**: 3039 (C_c-H), 2961, 2921, 2881 (C-H)$_{alkyl}$, 2532 (B-H), 1702 (C=O), 1440, 1411 δ(CH_2), 1257 δ(CH), 1105, 1020 (C-O-C). **^{1}H NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.25 (br s, 8H, C_c-H), 4.16 (m, 4H, OCH_2CH_2), 3.63 (m, 4H, OCH_2CH_2), 3.57 (m, 4H, OCH_2CH_2), 3.50 (m, 4H, OCH_2CH_2), 2.75-2.35 (m, 17H, B-H), 2.09 (s, 10H, B_c-H), 2.02-1.43 (m, 17H, B-H). **$^{1}H\{^{11}B\}$ NMR (400 MHz, $(CD_3)_2CO$)**: δ 4.25 (br s, 8H, C_c-H), 4.16 (m, 4H, OCH_2CH_2), 3.63 (m, 4H, OCH_2CH_2), 3.57 (m, 4H, OCH_2CH_2), 3.50 (m, 4H, OCH_2CH_2), 2.75 (s, 6H, B-H), 2.47 (s, 4H, B-H), 2.42 (s, 4H, B-H), 2.39 (s, 4H, B-H), 2.09 (s, 10H, B-H), 2.00 (s, 2H, B-H), 1.79 (s, 3H, B-H), 1.65 (s, 6H, B-H), 1.56 (s, 3H, B-H), 1.47 (s, 2H, B-H). **$^{13}C\{^{1}H\}$ NMR (75.5 MHz, $(CD_3)_2CO$)**: δ 163.81 (s, COO), 72.86 (s, C-COO), 69.48 (s, OCH_2), 69.10 (s, OCH_2), 67.81 (s, OCH_2), 67.65 (s, OCH_2), 55.25 (s, C_c-H), 47.35 (s, C_c-H). **^{11}B NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 22.95 (s, 2B, B(8)), 4.00 (d, ^{1}J(B,H) = 130Hz, 2B, B(8')), 0.44 (d, ^{1}J(B,H) = 144Hz, 2B, B(10)), -1.74 (s, 2B, B(10')), -4.31 (d, ^{1}J(B,H) = 162Hz, 4B, B(4',7')), -7.80 (t, ^{1}J(B,H) = 215Hz, ^{2}J(B,H) = 109Hz, 12B, B(4,7,9,9',12,12')), -14.72 (d, ^{1}J(B,H) = 169Hz, 10B, B_c-H) -17.28 (d, ^{1}J(B,H) = 162Hz, 4B, B(5',11')), -20.31 (d, ^{1}J(B,H) = 152Hz, 4B, B(5,11)), -22.71 (s, 2B, B(6)), -28.42 (d, ^{1}J(B,H) = 141Hz, 2B, B(6')). **$^{11}B\{^{1}H\}$ NMR (96.3 MHz, $(CD_3)_2CO$)**: δ 24.16 (s, 2B, B(8)), 5.14 (s, 2B, B(8')), 1.51 (s, 2B, B(10)), -1.38 (s, 2B, B(10')), -3.22 (s, 4B, B(4',7')), -6.26 (s, 4B, B(4,7)), -7.20 (s, 8B, B(9,9',12,12')), -12.89 (s, 10B, B_c-H) -16.24 (s, 4B, B(5',11')), -19.39 (s, 4B, B(5,11)), -20.97 (s, 2B, B(6)), -27.60 (s, 2B, B(6')). **ESI-MS (m/z)**: 1091.7 (M + K^+, 57%); 1075.7 (M + Na^+, 10%); 642.3 (M + K^+ + H^+ - [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], 73%); 525.8 (M/2,

100%), 540.8 ($M + 2H^+ + N_2$)/2, 7%).

3.3 Ethical and sustainability criteria

Due to the experimental processes carried out in a synthetic laboratory, sometimes large quantities of solvent were need, especially in processes of purification of products. However, the waste generated residues were stored properly, in containers intended for properly labeled purpose. It has been tried to work maximizing the atomic economy, but sometimes it has not been possible because the reactions gave some byproducts.

CHAPTER 4. RESULTS AND DISCUSSION

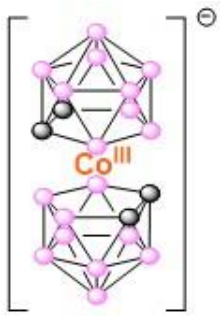
4.1 Synthesis

The synthetic strategies followed for the preparation of the Co (III) compounds **3** - **6** are outlined in *Scheme 2*. The reaction of Cs[3,3'-Co($C_2B_9H_{11}$)$_2$], **1** with dioxane generates the complex [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], **2**[4.5]. This mononuclear complex has been proven to be susceptible to nucleophilic attack on the positively charged oxygen atom, then reacts further with compounds that have nucleophilic character like organic and inorganic carboxylic acids. Therefore, the salts from the organic and inorganic carboxylic acids, were used as nucleophiles. In the case of the monoacid ligands (benzoic acid and 1-COOH-p-$C_2B_{10}H_{11}$), we used the sodium salt as nucleophile to obtaining the mono-anionic compounds [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **3** and Na[3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5**. In the case of the dicarboxylic acids we have used potassium carbonate salt to generate *in situ* the nucleophile that permit to obtain the di-anionic compound K_2[1'',4''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-C_6H_4] **4** and K_2[1'',12''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$] **6**. After stirring overnight, the compounds **3** – **6** were isolated by evaporation of the solvent or by a cationic exchange in the case of compound **3** using tetramethylammonium salt. The complexes **2** and **4** were separated and purified through column chromatography in silica. For all the cases, orange solids were obtained as the final product. The nucleophilic reaction generates new high-boron-content compounds. The nucleophilic character of carboxylic acids in the ring-opening reaction of cyclic oxonium [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], **2**, leads to new compounds incorporating the $(OCH_2CH_2)_2OC(O)$-R chain (R= C_6H_5 (**3**), C_6H_4COOH (**4**), $C_2B_{10}H_{11}$ (**5**), $C_2B_{10}H_{10}COOH$ (**6**)) and the [3,3′-Co(1,2-$C_2B_9H_{11}$)$_2$]$^-$ moiety. Our interest lies in obtaining novel high boron content polyanionic species with enhanced water solubility.

Scheme 1. Opening of the exo-Cluster Dioxanate Ring Reaction by Nucleophilic Attack with the respective salts of organic carboxylic acids.

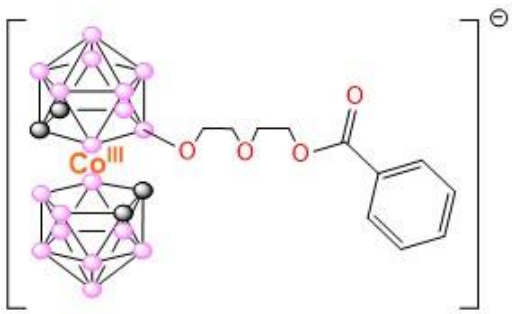
Chart 1 shows the anionic species synthesized from the zwitterionic **2** according to *Scheme 1*.

Chart 1. Monosubstituted **2** - **6** Anions [a].

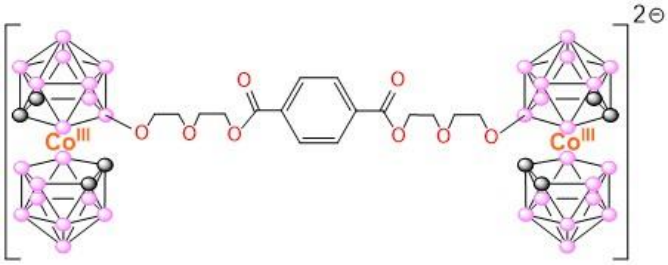


(**1**)

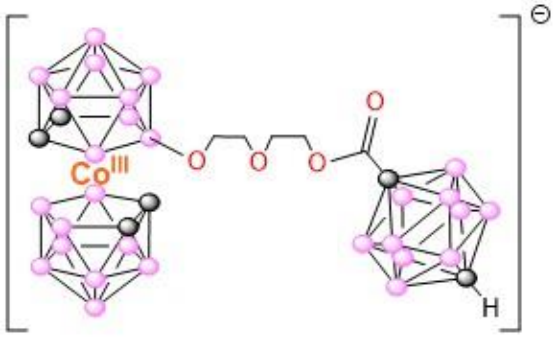
(**2**)



(**3**)



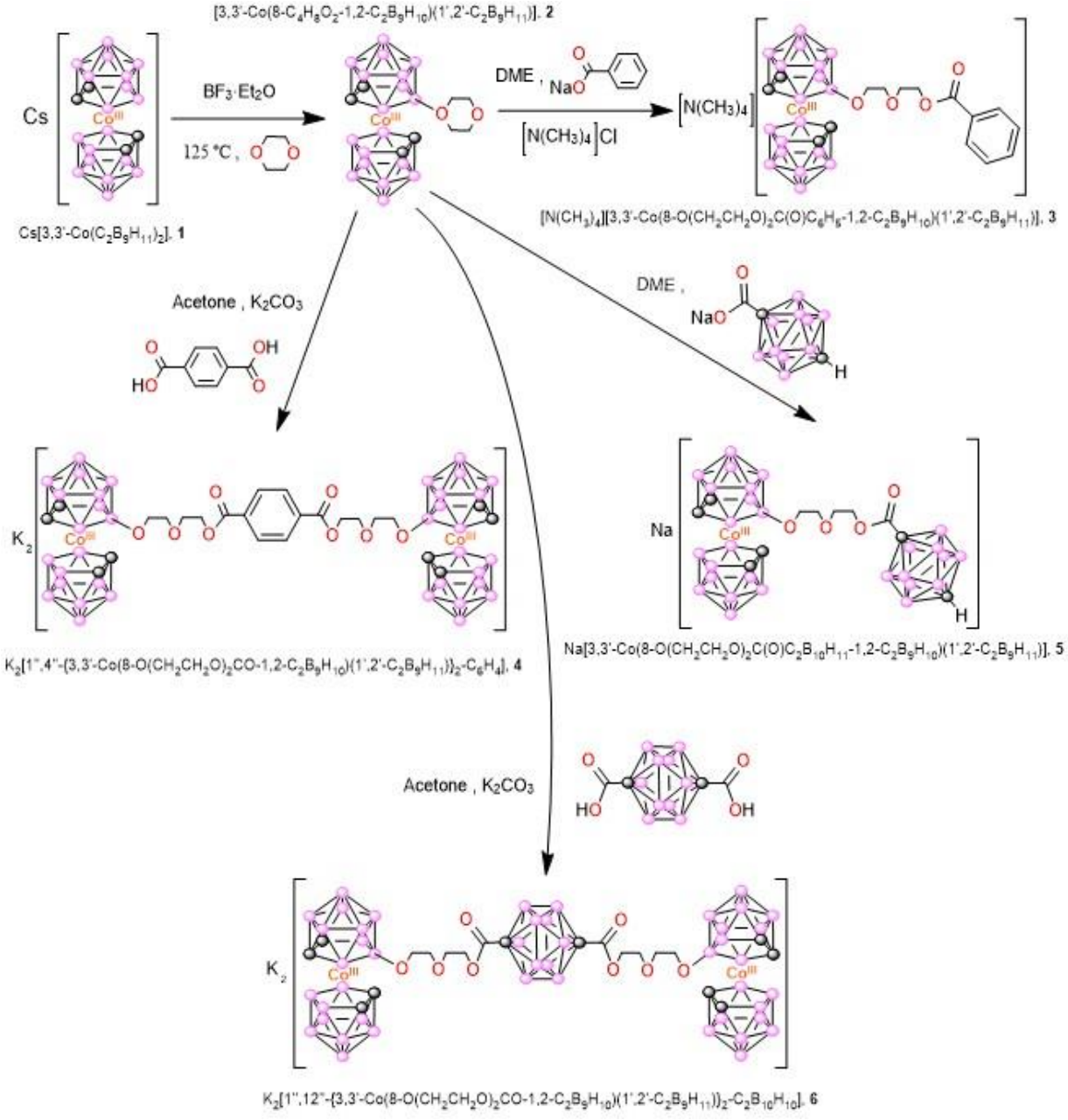
(**4**)



(**5**)

(**6**)

[a] Atoms in black are CH vertexes, the rest of the vertices in the clusters are BH.



Scheme 2. Synthetic strategies and ligands used in this work.

4.2 Spectroscopic properties

4.2.1 IR spectroscopy

Figures 4 and 5 show the IR spectra corresponding to two representative compounds **3** and **6**, respectively. All compounds show peaks around 3030, 2990, 2530, 1700, 1450, 1260, 1100 cm^{-1}.

The IR spectra of all complexes described display typical $\nu(C_c\text{-}H)$ absorption at frequencies around 3030 cm^{-1}, assigned to the stretching vibrations of the carbons in the cluster of cobaltabisdicarbollide. Also all the compounds show the typical ν(B-H) absorption around 2530 cm^{-1}.

The bands observed over 2960-2860 cm^{-1} can be assigned to $\nu(C\text{-}H)_{alkyl}$ stretching modes of the chain of the dioxane opened ring. In the region of 1100 cm^{-1} and 1450 cm^{-1} can be found ν(C-O-C) stretching and $\delta(CH_2)$ bending of the same carbon chain.

All compounds show a strong band at 1700 cm^{-1} that corresponds to the ν(C=O) stretching from the carboxyl group present in the ligands.

In the case of compound **3**, the band observed at 943 cm^{-1} corresponds to ν(C-N) stretching of the tetramethylammonium counterion.

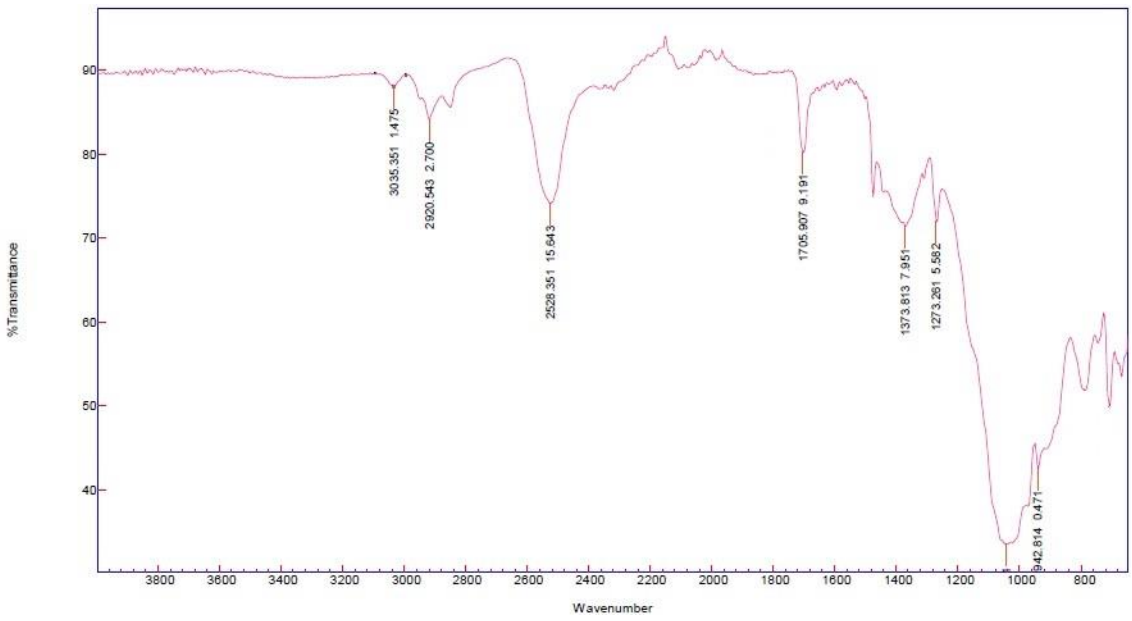


Figure 4. FTIR spectra of compound **3**.

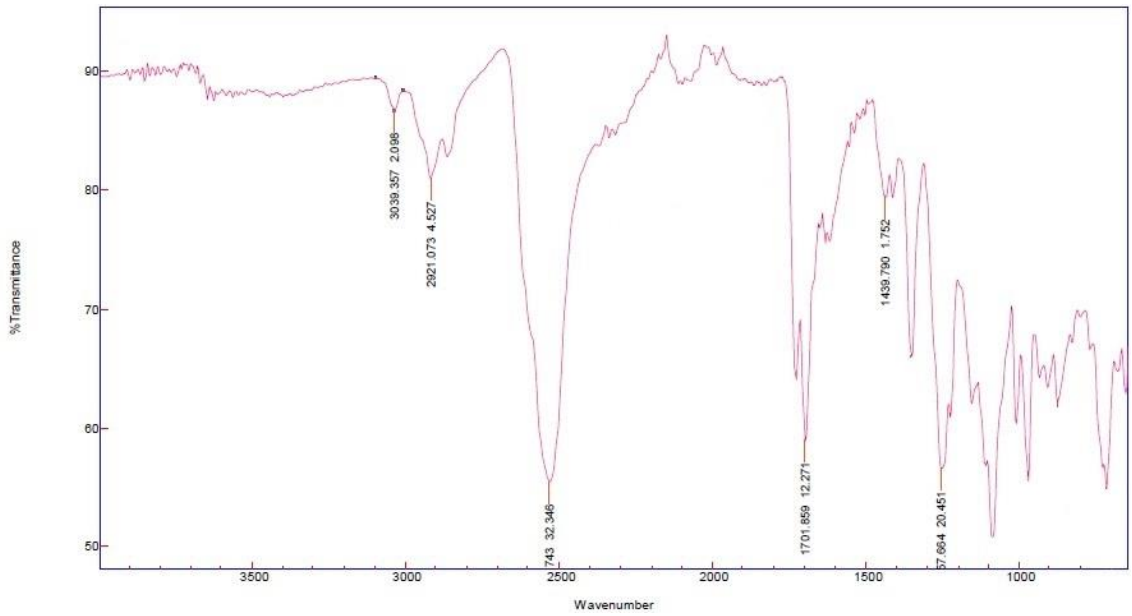


Figure 5. FTIR spectra of compound **6**.

4.2.2 NMR spectroscopy

The structures of all compounds isolated have been solved by NMR, $^{1}H\{^{11}B\}$, ^{11}B, $^{11}B\{^{1}H\}$ and $^{13}C\{^{1}H\}$ NMR spectra and mass spectrometry. The one-dimensional (1D) NMR spectra of complex **3 – 6** were recorded in acetone-d_6. *Figure 6 and 7* show the $^{1}H\{^{11}B\}$ NMR spectra of compounds **5** and **6**.

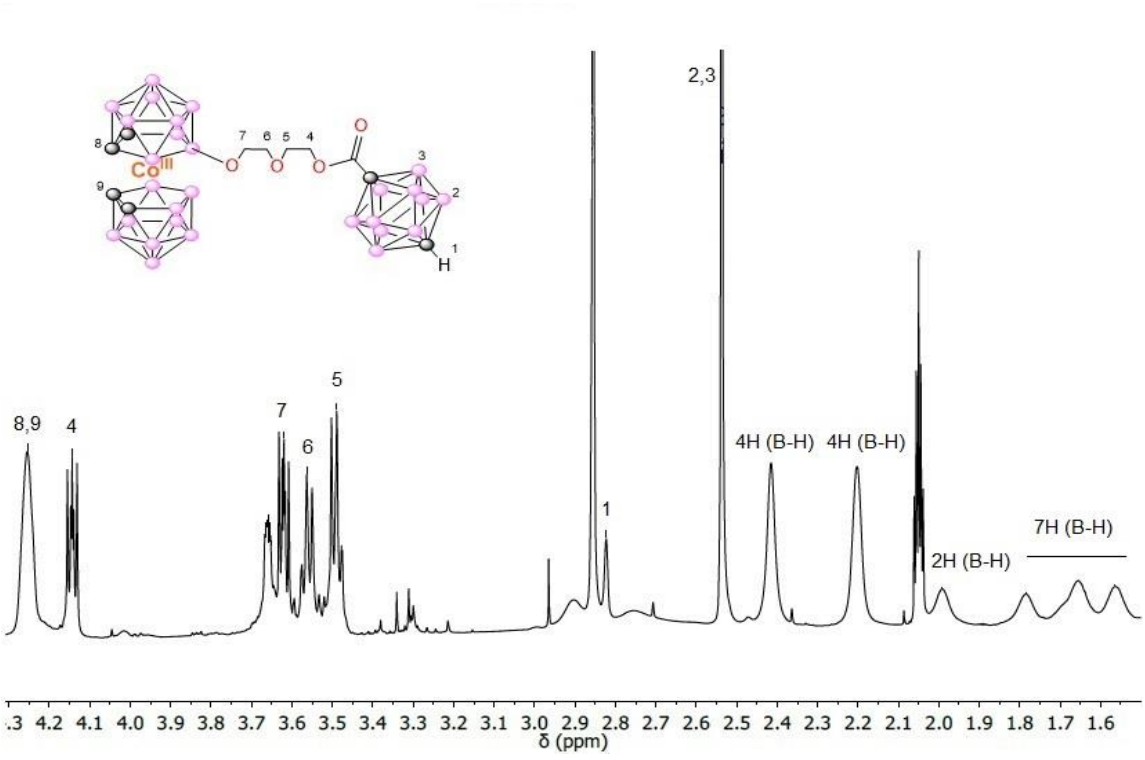


Figure 6. $^{1}H\{^{11}B\}$ RMN spectra of compound **5**.

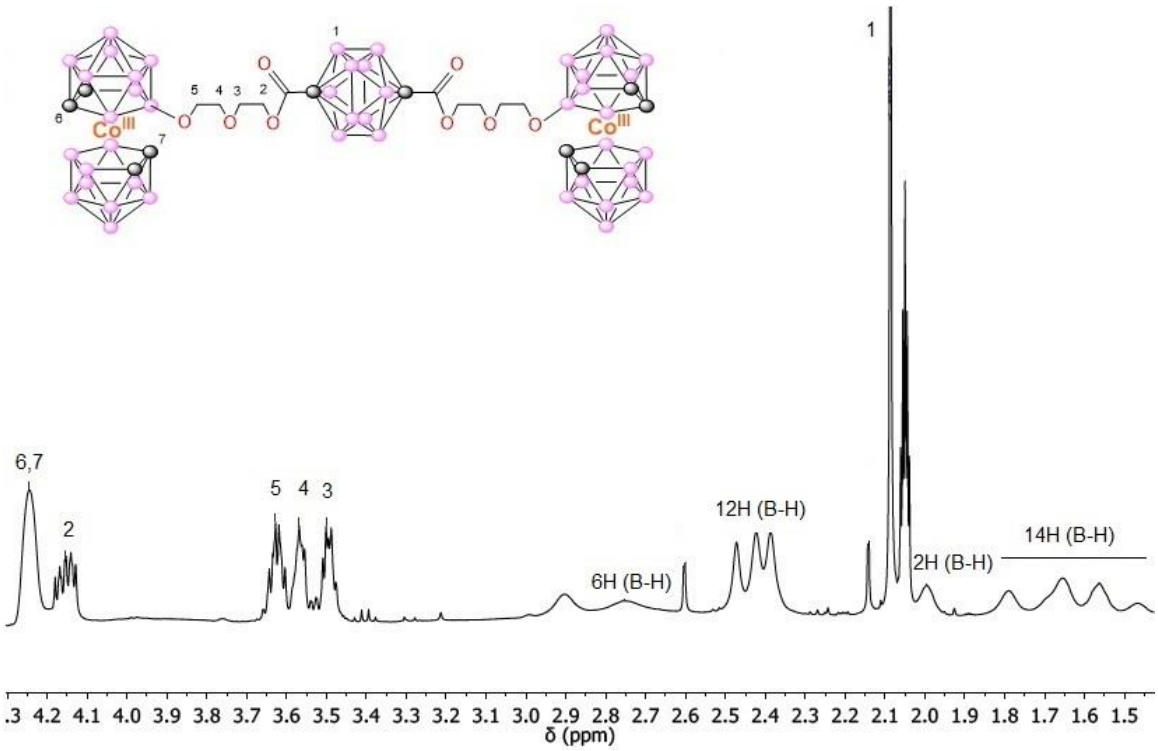


Figure 7. $^{1}H\{^{11}B\}$ RMN spectra of compound **6**.

It can be observed that the $^{1}H\{^{11}B\}$ NMR spectra of compounds **3** and **4** exhibit signals in the aromatic region associated with the presence of benzene. The most interesting feature of the spectra in all the complexes are the protons of the 1,4-dioxane chain. In all of them, the signals of the B(8)-OCH_2-, -CH_2OCH_2- and CH_2- were observed in the range δ= 4.4 – 3.5 ppm. The presence of C_c-H signals corresponding to the [3,3'-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)$^-$ unit appear as a signal around 4.25 ppm that integrates 4 protons; the one carbon CH resonance of the coordinated ligand 1-COOH-p-$C_2B_{10}H_{11}$ in compound **5** appears at 2.9 ppm. correspond to the carbons (C_c-H) in the borate cluster. Finally, others signals in the range of 3 – 1.2 ppm correspond to B-H atoms.

The $^{11}B\{^{1}H\}$ NMR spectra of anions **3** - **6** featured an identical 1:1:1:1:2:2:4:2:2:1:1 pattern ranging from +25 to -29 ppm. *Table 1* shows the main δ values of the $^{11}B\{^{1}H\}$ NMR spectra of **2** and monosubstituted **3** - **6** anions and *Figures 8 and 9* show the spectra of complexes **5** and **6**, respectively. *Figure 10* show comparative spectra of ^{11}B and $^{11}B\{^{1}H\}$ RMN of compound **4**.

The resonance at the lowest field remains as a singlet in the ^{11}B NMR spectrum, corresponding to the B(8) substituted boron atom.

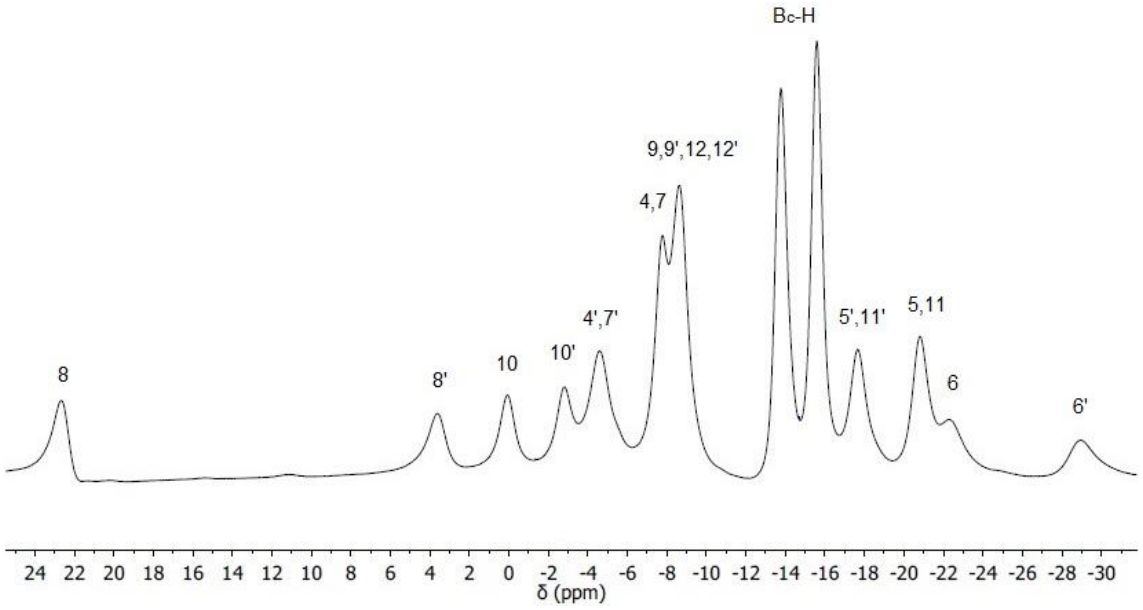


Figure 8. $^{11}B\{^{1}H\}$ RMN spectra of compound **5**.

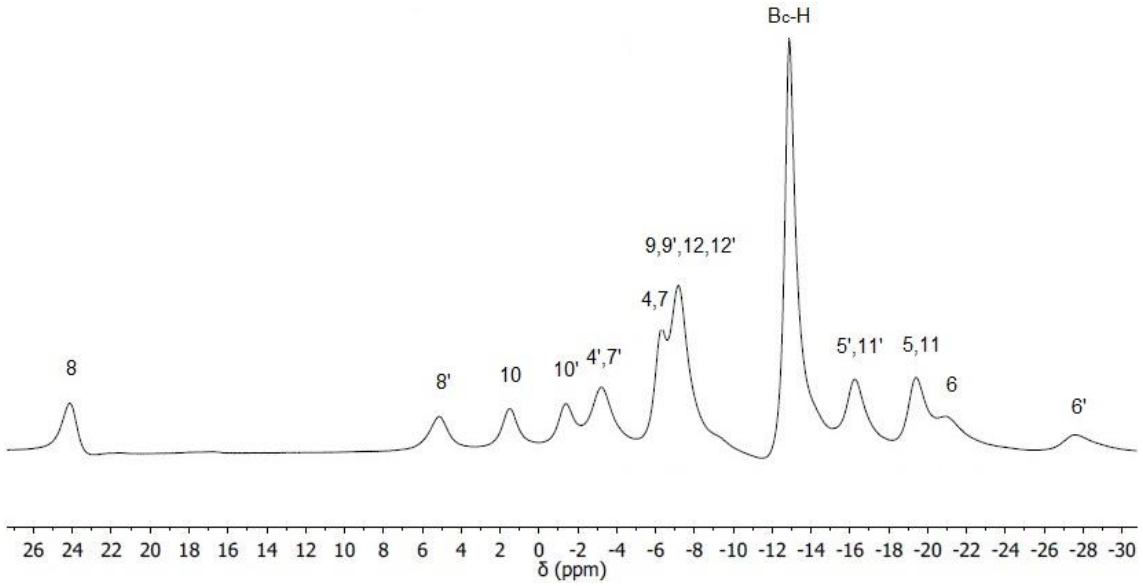


Figure 9. $^{1}H\{^{11}B\}$-RMN spectra of compound **6**.

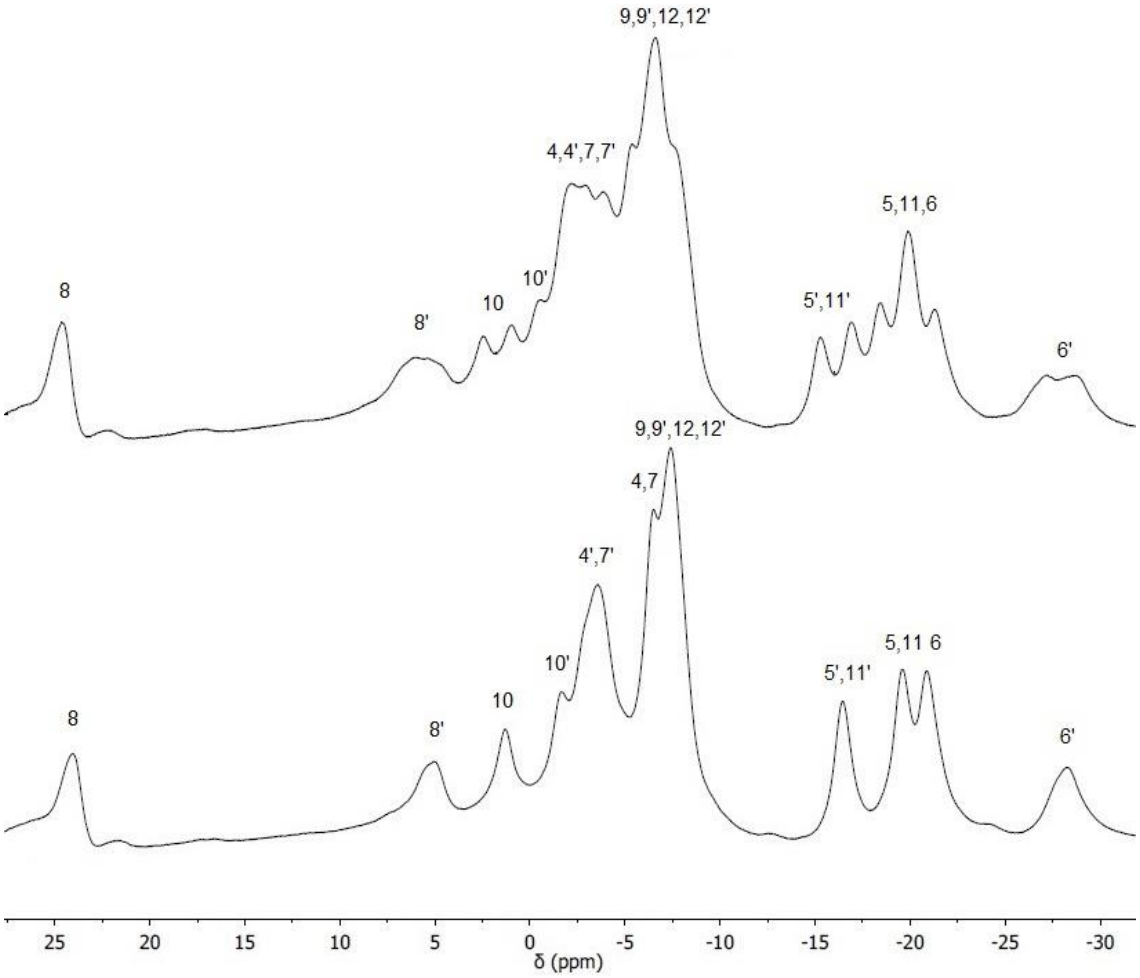


Figure 10. Comparative of ^{11}B and $^{11}B\{^1H\}$ RMN spectra of compound **4**.

Table 1. $^{11}B\{^1H\}$ NMR Spectra (all in ppm) of B(8) Monosubstituted Derivatives of [3,3′-Co(1,2-$C_2B_9H_{11})_2]^-$. [a]

1	6.5 B(8,8')		1.4 B(10,10′)		-6.0 B(4,4′,7,7′,9,9′,12,12′)			-17.2 B(5,5′,11,11′)		-22.7 B(6,6′)	
	24.6	8.3	4.7	-2.9	-4.3	-8.3	-9.6	-15.3	-18.8	-21.2	-26.9
2	B(8)	B(8′)	B(10)	B(10′)	B(4′,7′)	B(4,7)	B(9,9',12,12')	B(5′,11′)	B(5,11)	B(6)	B(6′)
3	*23.0*	4.0	0.5	-2.4	-4.1	-7.4	-8.3	-17.2	-20.3	-21.9	-28.5
4	*24.1*	5.1	1.3	-1.6	-3.5	-6.5	-7.4	-16.5	-19.6	-20.9	-28.3
5	*22.6*	3.7	0.1	-2.8	-4.6	-7.8	-8.6	-17.7	-20.8	-22.3	-29.0
6	*24.2*	5.1	1.5	-1.4	-3.2	-6.3	-7.2	-16.2	-19.4	-21.0	-27.6

[a] In each column, the number of boron atoms is preserved. In italics are represented the resonances due to B-O.

The $^{11}B\{^{1}H\}$-NMR resonance featured patterns in the range from δ= 15 to -22 ppm that agree with these carborane clusters. [20] The observed ^{11}B NMR pattern, 1:1:1:1:2:2:4:2:2:1:1, reflects the C_s symmetry of the molecules (12 different signals). The boron resonance with a relative intensity of 4 is due to a coincidental overlap of two resonances with a 2:2 relative intensity. The $^{11}B\{^{1}H\}$ NMR of [3,3′-Co(1,2-$C_2B_9H_{11})_2$]$^-$ displays five resonances in the range +6.5 to -22.7 ppm with a 2:2:8:4:2 pattern, in agreement with an averaged C_{2V} symmetry. The incorporation of one substituent at position B(8) lowers the symmetry to Cs, maintaining only one symmetry plane and making the two dicarbollide moieties no longer equivalent.

The $^{11}B\{^{1}H\}$ NMR spectrum of monosubstituted derivatives of [3,3′-Co(1,2-$C_2B_9H_{11})_2$]$^-$ is the result of the plain addition of the two individual halves, as schematized in *Figure 11*.

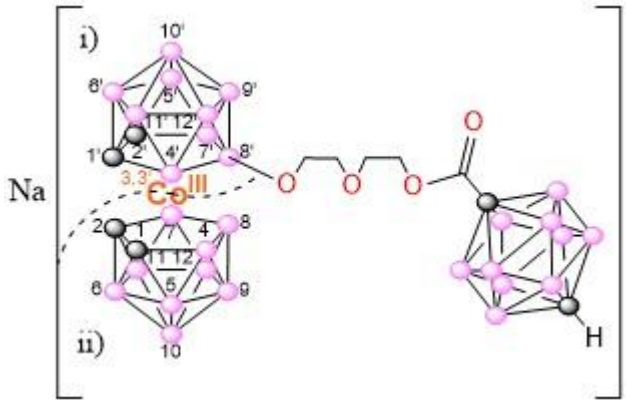


Figure 11. The $^{11}B\{^{1}H\}$ NMR spectrum of **5** is the result of the addition of the two individual halves. Example of vertex numbering for Na[3,3'-Co(8-O($CH_2CH_2O)_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)], **5**.

As an example, the $^{11}B\{^{1}H\}$ NMR of Na[3,3'-Co(8-O($CH_2CH_2O)_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5** is the addition of the $^{11}B\{^{1}H\}$ NMR of the parent Cs[3,3′-Co(1,2-$C_2B_9H_{11})_2$] plus the spectrum of [3,3'-Co(8-O($CH_2CH_2O)_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)]$^-$. The spectrum of Cs[3,3′-Co(1,2-$C_2B_9H_{11})_2$] displays resonances at 6.5(1), 1.4(1), -6.0(4), -17.2(2), and -22.7(1) ppm, and the spectrum of Na[3,3'-Co(8-O($CH_2CH_2O)_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5** displays resonances at 22.6(1), 3.7(1), 0.1(1), -2.8(1), -4.6(2), -7.8(2), -8.6(4), -17.7(2), -20.8(2), -22.3(1), and -29.0(1) ppm.

If resonances attributable to the unsubstituted ligand, showing only minor shifts in respect to parent Cs[3,3′-Co(1,2-$C_2B_9H_{11})_2$], are removed, the resonances of the unknown disubstituted [3,3'-Co(8-O($CH_2CH_2O)_2$C(O)$C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-

$C_2B_9H_{11})]^-$ ligand could be clearly distinguished and assigned at 22.6(1), -2.8(1), -4.6(2), -7.8(2), -17.7(2), and -22.3(1) ppm. The 1:1:2:2:2:1 pattern is consistent with a C_s fragment symmetry, and the high chemical shift value at 22.6 strongly supports assignment to B(8)-O-.

4.2.3 UV-Vis spectroscopy

The UV-Vis spectra of complex **6** is displayed in *Figure 12* whereas their main features are presented in the experimental section. The electronic UV-vis spectrum of **6** shows one strong absorption band at 305 nm with others at 362 and 454 nm in agreement with the report by Matel[21] and the visible spectrum was interpreted on the basis of ligand field theory.[22]

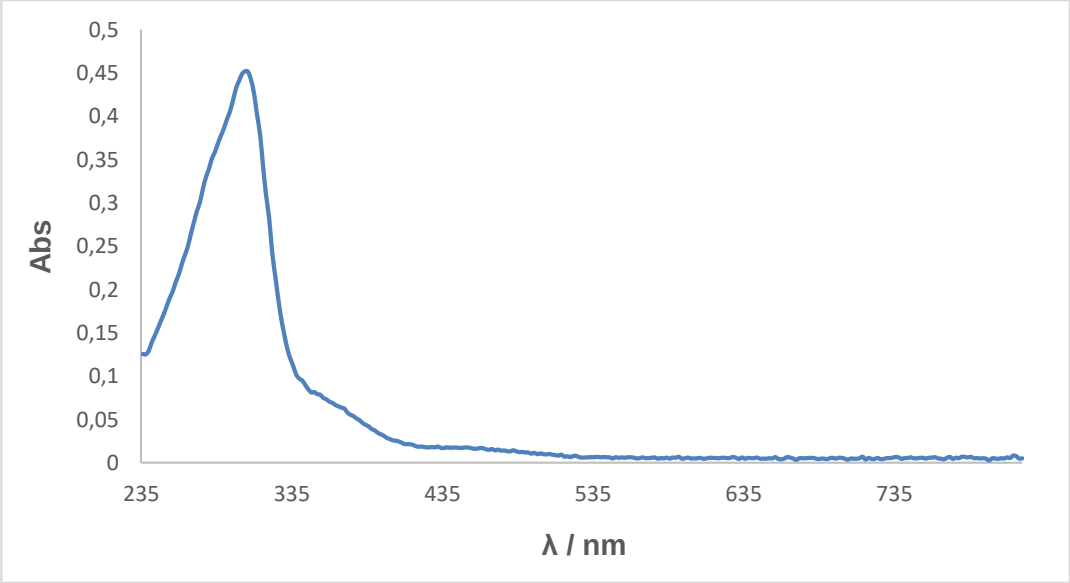


Figure 12. UV/Vis spectra of **6** in DCM.

4.2.4 Mass spectroscopy

Compounds **3** - **6** were studied by the ESI-MS technique at the negative ion mode without the use of matrices. The lack of matrices aids the interpretation of the primary and secondary mechanisms. We understand as a “primary” mechanism the separation of the anionic cobaltabisdicarbollide derivatives from the bonded cation. The “secondary” mechanism can give some clues about the nucleophilic character of the electron-rich oxygen atom directly bonded to the cluster B(8) boron atom. *Figure 13* shows the ESI-MS spectra of all the compounds as a representative example.

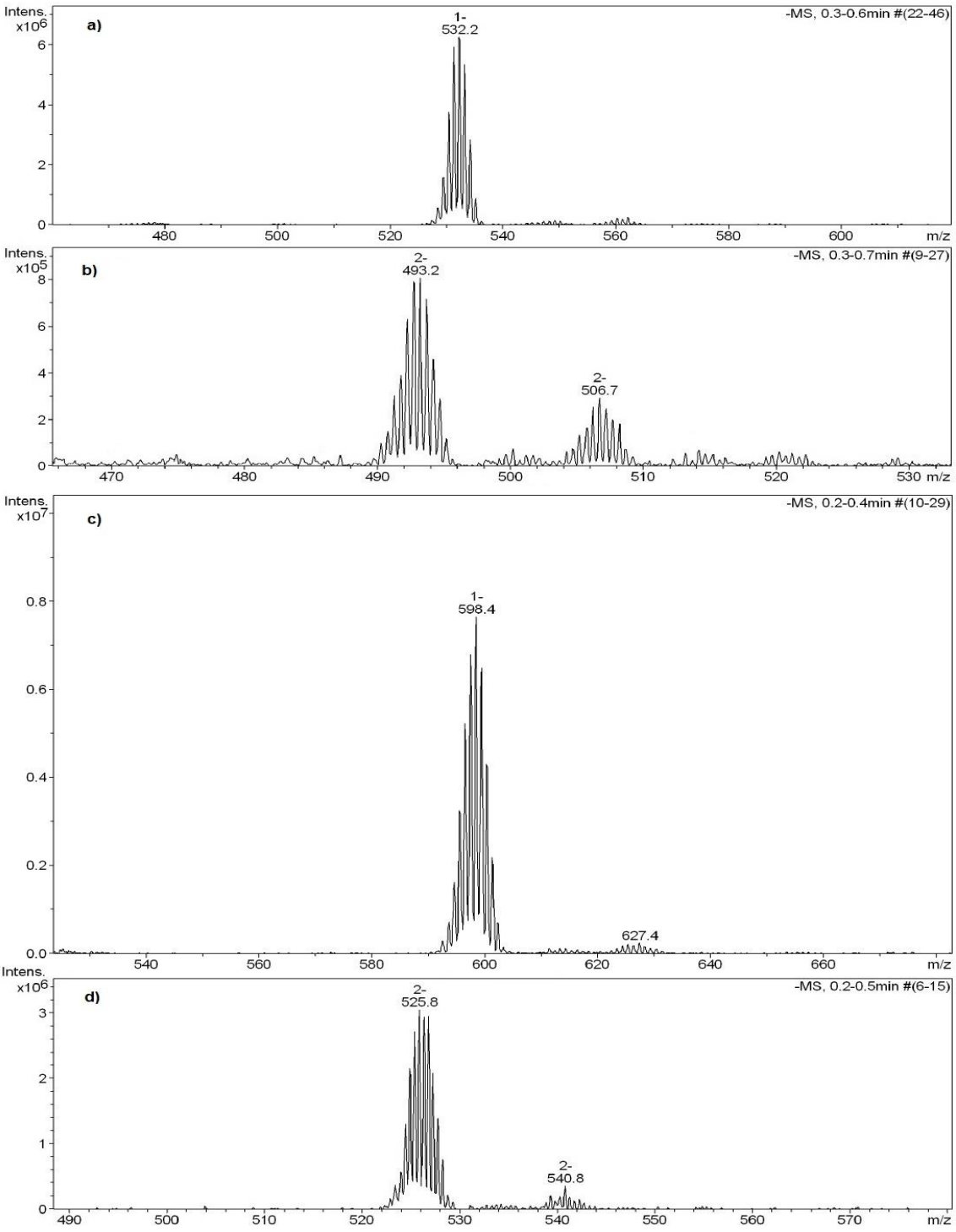


Figure 13. ESI-MS spectra of all the compounds (**3** (a), **4** (b), **5** (c) and **6** (d)). See the Experimental Section for the fragmentation.

For spectra a) peak with an ion at 532.2 correspond to the molecular ion peak of the compound **3**. Compound **4** (b) with a peak at 493.2, correspond to the molecular ion peak. Other peak at 506.2 correspond to molecular ion peak plus N_2 ($M + N_2$)/2. In compound **5** (c), molecular ion peak appears at 598.4 and other peak at 627.4 correspond to molecular ion peak with H^+ plus N_2 ($M + H^+ + N_2$). Finally, as compound

5, compound **6** (d) has a peak at 525.8 correspond to the molecular ion peak and at 540.8 with $2H^+$ plus N_2 $(M + 2H^+ + N_2)/2$.

4.3 Electrochemical properties

The redox properties of the compounds 5 and 6 described in the present work were investigated by means of cyclic voltammetry (CV) and are summarized in *Table 2*. *Figure 14* shows the CVs for 5 (a) and 6 (b). The redox potential for the couple [3,3'-Co_x(8-O(CH_2CH_2O)$_2$C(O)-R-1,2-$C_2B_9H_{10}$)$_n$(1',2'-$C_2B_9H_{11}$)]$^{-1/-2}$, (x = 1 and n =1 for compound **5** and x = 2 and n = 2 for compound **6**) is in both cases -1.37 V, all vs SCE. The process is reversible in the case of compound **6**, but unlike of **5** that shows a quasireversible process. We can conclude that in the [Co-Co] compound **6**, no exists electronic communication between the two metal atoms since the same $1e^-$ curve were found for two chemically equivalent Co atoms. If electronic communication had existed two distinct ET processes should be observed.

Table 2. Electrochemical data (CH_2Cl_2 + 0.1 M TBAP, $E_{1/2}$ in V vs SCE) for complexes **5** and **6**.

Compound	E_{pc} (Co(III) → Co(II))	E_{pa} (Co(II) → Co(III))
5	-1.69	-1.06
6	-1.42	-1.32

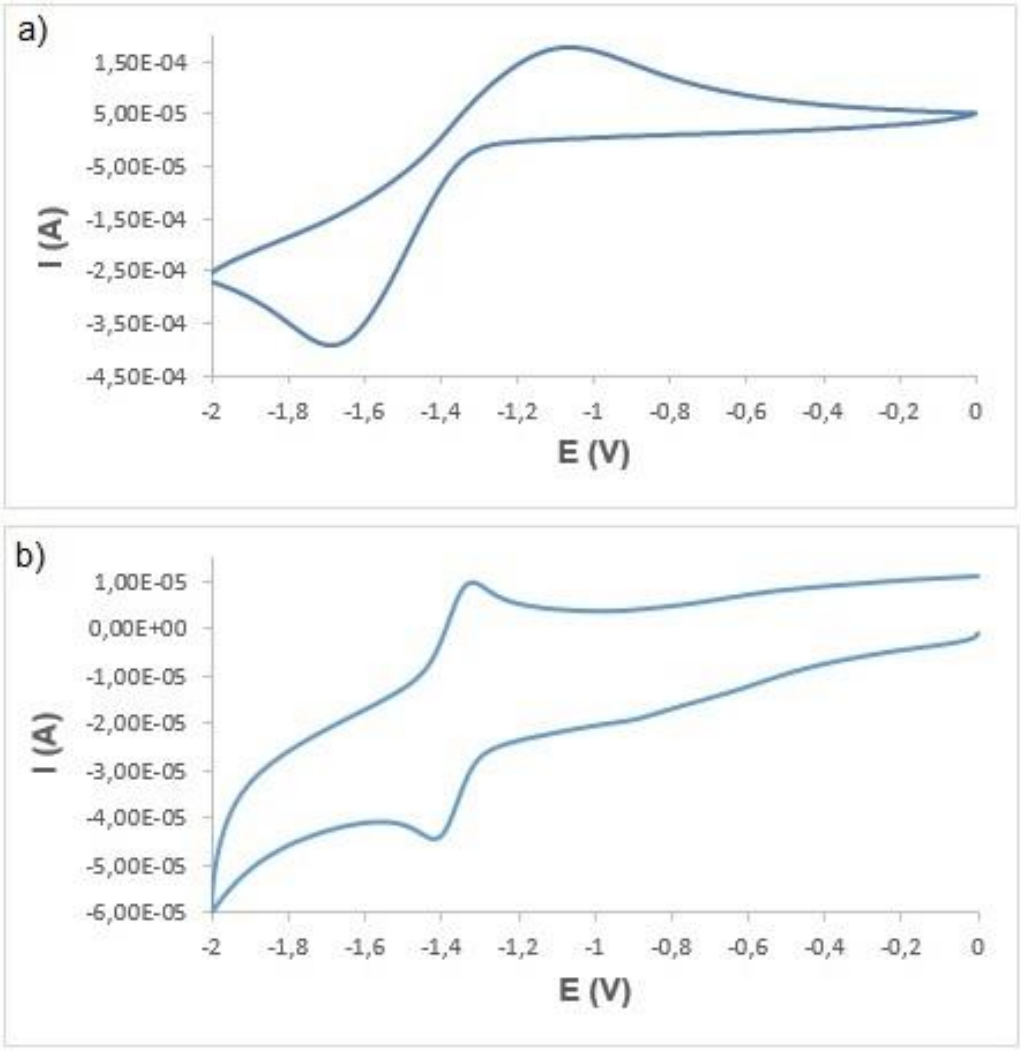


Figure 14. CV for complexes a) **5** and b) **6** in CH_2Cl_2.

CHAPTER 5. CONCLUSIONS

In this final degree work has been synthetized new metallacarboranes compounds through ring-opening reaction of cyclic oxonium [3,3′-Co(8-$C_4H_8O_2$-1,2-$C_2B_9H_{10}$)(1′,2′-$C_2B_9H_{11}$)] (**2**) by using carboxylic and carboranylcarboxylic acids, as nucleophiles. It has shown that polyanionic species of high-boron-content molecules, can be obtained in high-yield synthesis, in some cases.

1. Four cobalt complexes have been synthesized containing, in the case of mono-anionic compounds we used benzoic and 1-COOH-p-$C_2B_{10}H_{11}$ acid as ligands to obtain [$N(CH_3)_4$][3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_6H_5$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **3** and Na[3,3'-Co(8-$O(CH_2CH_2O)_2C(O)C_2B_{10}H_{11}$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)] **5**. In the case of the di-anionic compounds we used terephthalic and 1,12-$(COOH)_2$-$C_2B_{10}H_{10}$ acid to obtain K_2[1'',4''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-C_6H_4] **4** and K_2[1'',12''-{3,3'-Co(8-$O(CH_2CH_2O)_2CO$-1,2-$C_2B_9H_{10}$)(1',2'-$C_2B_9H_{11}$)}$_2$-$C_2B_{10}H_{10}$] **6**. The **4** and **6** cobalt complexes were obtained with a similar synthesis method but using its respective ligands (potassium salt generate in situ of the reaction) as nucleophiles. Also come with the **3** and **5** cobalt complexes but the its respective ligands were sodium salts and its generate before of the nucleophilic reaction.

2. The exhaustive spectroscopic characterization of the complexes by $^1H\{^{11}B\}$ NMR, $^{11}B\{^1H\}$ NMR and ESI-MS confirms the structural presence of the corresponding compounds show the molecular ion peaks of all the compounds.

3. The redox behavior shows that compound **6** displays a reversible redox process corresponding to the couple Co(III)/Co(II) but in the case of compound **5** this process is quasireversible. In the case of [Co-Co] **6** complex, the CV shows that there isn't communication between the two metal centres.

4. The relative good solubility of the synthetized compounds in water opens the possibility to be able to use these compounds as potential candidates for application in BNCT.

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