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Nucleoside–Metallacarborane Conjugates for Base-Specific Metal Labeling of DNA

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Abstract: A general approach to the synthesis of nucleoside conjugates between derivatives of thymidine (T), 2′-*O*-deoxycytidine (dC), 2′-*O*-deoxyadenosine (dA), and 2′-*O*-deoxyguanosine (dG), and metallacarborane complexes is described. Metallacarborane–nucleoside derivatives are prepared by reaction of the dioxane–metallacarborane adduct with a base-activated 3′,5′-protected nucleoside. In the case of T and dG a mixture of regioisomers, which is easily separable by chromatographic methods, is obtained, thus yielding a series of modifications containing metallacarborane groups at the 2-*O*, 3-*N*, 4-*O* and 1-*N*, 2-*N*, 6-*O* locations, respectively; dC and dA are alkylated at the *exo*-amino function. The proposed methodology provides a route for the synthesis and study of nucleic acids modified with metallacarboranes at designated locations and a versatile approach to the incorporation of metals into DNA.

Keywords: alkylation · bioinorganic chemistry · materials science · metallacarboranes · nucleosides

Introduction

Contemporary technologies take advantage of the knowledge accumulated in different fields of science. The crossroads of biology and materials engineering and also biological and inorganic chemistry is a field that has yielded many fruitful interconnections, including new pharmaceuticals, diagnostic methods, and materials such as biological/non-biological conjugates.[1–3] Among this type of compounds, metal-bearing nucleosides are one of the most important representatives of molecular hybrids[4,5] as they can function as electrochemical and photoluminescent labels for nucleic acids,[6,7] infrared labels,[8,9] radioactive metal isotope carriers,[10] active centers of DNA-directed artificial chemical nucleases,[11] and metal-bearing components for the construction of probes for DNA-mediated electron transfer,[12] amongst others.

Metal centers are usually attached to the nucleoside unit in the form of a metal complex, and complex-containing nucleoside conjugates are predominantly constructed by one of two major pathways: a) the synthesis of a chelator-containing nucleoside followed by metal complexation, and b) the synthesis of a functionalized nucleoside to which a metal complex can be conjugated, although in the majority of cases chelators are used as vectors for metal ions. One of the few exceptions is metallocene-type complexes, of which the best known example is ferrocene.[13] Only the second example of nucleoside–metallocene-type conjugates described so far is the nucleoside–metallacarborane modifications reported by us recently[14] in which the metallacarborane modification is attached to the nucleoside component in a unique type of reaction between a dioxane–metallacarborane adduct and a base-activated nucleoside. This method, which was originally demonstrated for thymine nucleoside followed by incorporation of the obtained conjugate into a DNA-oligomer, can be considered as a third, direct pathway for the synthesis of metal-complex-containing nucleoside conjugates.[14]

Nucleosides and their analogues have great pharmacological potential as, for example, antiviral and antitumor drugs.[15,16] Metallacarboranes, after long neglect of the study of their biological properties, are presently being pursued by many investigators for their antiviral and antitumor activities.[17–19] It is therefore feasible that conjugates of nucleosides and metallacarboranes could exhibit useful biological characteristics. Another advantage of metallacarborane–nu-

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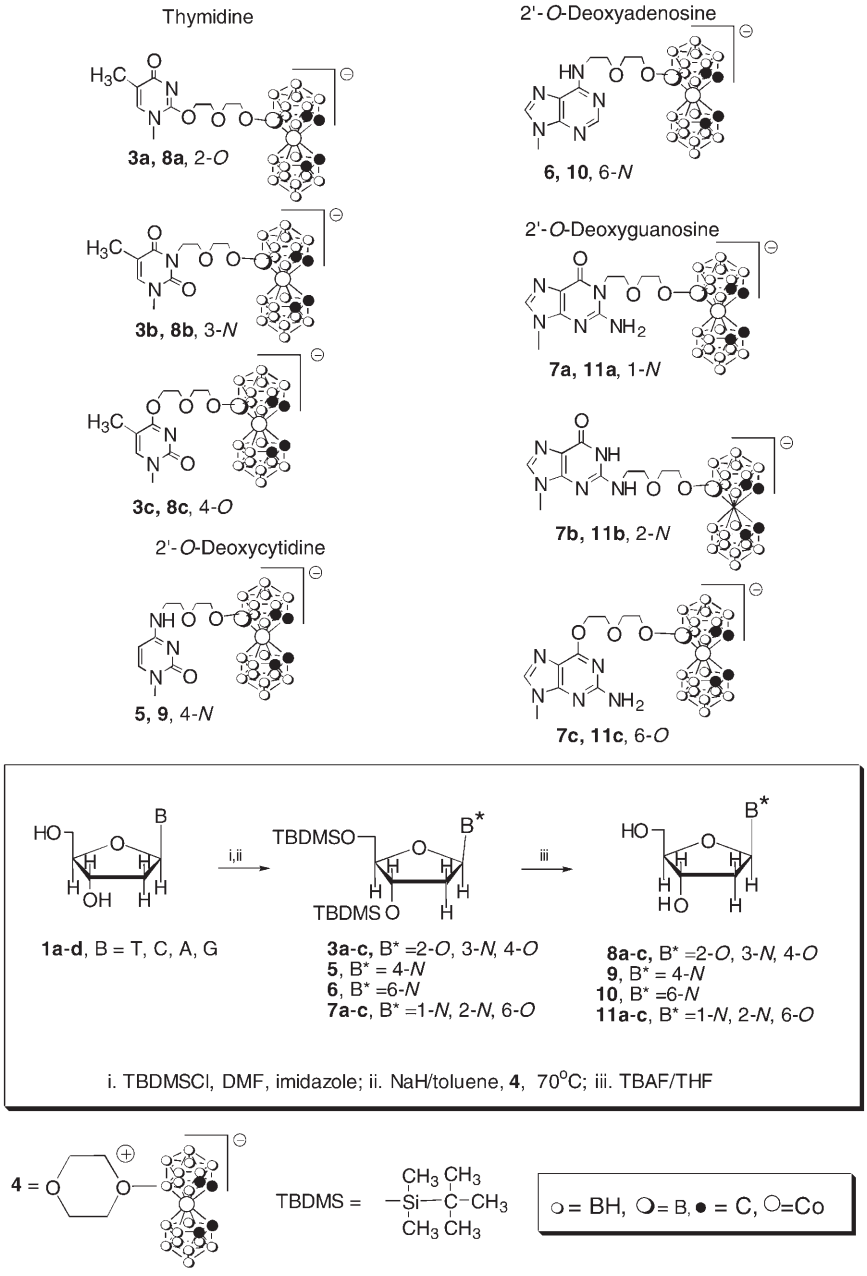
cleoside conjugates is their application as versatile synthons for the synthesis of metal-bearing DNA-oligomers for various applications.[5,14,20]

Here we describe a general method for the synthesis of metallacarborane derivatives of all four of the canonical nucleosides thymidine (T, **1a**), 2′-*O*-deoxycytidine (dC, **1b**), 2′-*O*-deoxyadenosine (dA, **1c**), and 2′-*O*-deoxyguanosine (dG, **1d**). The availability of this methodology makes studies of a broad spectrum of nucleoside conjugates bearing metals and incorporation of these metal centers into DNA-oligomers at designated locations possible. It also shows the versatility of nucleophilic ring opening in dioxane–metallacarborane adducts as a new approach for the attachment of metallacarboranes to biological molecules.

Results and Discussion

The target nucleoside–metallacarborane conjugates were obtained in a simple, three-step procedure. First, the 5′- and 3′-hydroxy functions of nucleosides **1a–d** were protected. For that purpose, instead of the monomethoxytrityl and acetyl groups used in our preliminary work for protection of 5′- and 3′-hydroxy functions, respectively,[14] *tert*-butyldimethylsilyl protection was used for both hydroxy groups. This change greatly simplified the protection and subsequent deprotection steps. The 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxynucleosides **2a–d** are easily available and can be prepared in high yield from suitable nucleosides following a literature procedure.[21] In the second step, each of the 3′,5′-protected nucleosides **2a–d** was activated with a 1.5 molar excess of sodium hydride then treated with a 1.5 molar excess of dioxane–metallacarborane adduct **4** in anhydrous toluene as reaction medium. In the third step, the *tert*-butyldimethylsilyl protection was removed by treatment with tetrabutylammonium fluoride to provide the metallacarborane–nucleoside conjugates **8a–c**, **9**, **10**, and **11a–c** containing metallacarborane modification at different locations within the nucleobase (Scheme 1). All the isolated intermediates and final products were fully characterized by UV, IR, and ^{1}H, ^{13}C, and ^{11}B NMR spectroscopy, FAB mass spectrometry, and chromatographic methods, and in the case of products **8–11** by circular dichroism (CD) measurements.

Ring opening in the cyclic ether attached to the [bis(1,2-dicarbollido)-3-cobalt(−1)] ion by simple nucleophiles has been described previously,[22–25] and recently the synthesis of a porphyrin-containing [bis(1,2-dicarbollido)-3-cobalt(−1)] ion was described, although application of the above method for complex biological molecules has not been pur-



Scheme 1. Synthesis of metallacarborane-substituted thymidines **8a** (2-*O*), **8b** (3-*N*), and **8c** (4-*O*), 2′-*O*-deoxycytidine **9** (4-*N*), 2′-*O*-deoxyadenosine **10** (6-*N*), and 2′-*O*-deoxyguanosines **11a** (2-*N*), **11b** (1-*N*), and **11c** (6-*O*).

sued.[26] Activation of the protected 2′-*O*-deoxynucleosides **2a–d** with sodium hydride results in deprotonation of thymine at the ring nitrogen 3-*N* and cytidine and adenine at 4-*N* and 6-*N* of the *exo*-amine group, respectively. Guanine can be deprotonated at either of the ring nitrogen atoms 1-*N* and 2-*N* of the *exo*-amino function, which leads to different products. The amide-like hydrogen atoms at 3-*N* of thymine and 1-*N* of guanine are rather acidic in character ($pK_a = 9.93$ and 9.42, respectively).[27] The *exo*-amino groups of cytidine, adenine, and guanine resemble aromatic amines containing electron-acceptor substituents (e.g. *para*-nitroaniline) in their rings. The pK_a values of the amino groups of the above heterocycles range from 2.5 to 4, which means that these groups can also be readily deprotonated.[28] In the case of protected thymidine (**2a**) and 2′-*O*-deoxyguanosine (**2c**), deprotonation at 3-*N* and 1-*N*, respectively, leads to ambident ion formation with the negative charge distributed over 2-*N*, 3-*N*, and 4-*O* for **2a** and 1-*N* and 6-*O* for **2c**. These ambident ions should react at the most nucleophilic site, which is the nitrogen atom, although in practice they react mostly at the oxygen atoms. The yields of the regioisomers isolated are as follows: **3a** (2-*O*) 30%, **3b** (3-*N*) 16%, **3c** (4-*O*) 30% (total yield of thymine alkylation: 76%), and **7a** (1-*N*) 5%, **7c** (6-*O*) 24% (along with 18% of the regioisomer **7b** alkylated at the *exo*-amino group 2-*N*; total yield of alkylation: 47%; see Table 1).

The N/O ratio for alkylation with the dioxane–metallacarborane adduct **4** of the ambident ion derived from **2a** is therefore 16/60 and for alkylation of **2c** 5/24, which means that factors other than the nucleophilicity of the reactive centers in ambident ion must therefore play a role. The most probable additional cause for the atypical pattern of alkylation of nucleosides **2a** and **2d** is the structure of the alkylating agent. A strong dependence of the specificity of alkylation on the nature of the alkylating species has been repeatedly found in early works on alkylation of nucleobases by carcinogens.[29–32] Agents that are not particularly ionic in nature mainly alkylate sites with a high relative nucleophilicity through a bimolecular displacement (S_N2) mechanism, whereas electrophiles with more ionic character prefer to react at the less nucleophilic sites. Owing to the presence of a positive charge on the oxygen atom of the dioxane moiety linked to B-8 of the metallacarborane complex, the electron density at C-1 of dioxane is strongly decreased. As a result, both reaction partners—the nucleophile and the electrophile—are in a highly polar state. This favors an S_N1 (O-alkylation preferred) rather than an S_N2 (N-alkylation preferred) mechanism and therefore O-alkylation of the nucleobase. An additional aspect which should be taken into consideration is the increase of the hardness of the electrophilic carbon center in dioxane due to the proximity of the oxonium oxygen atom and therefore preferential reaction with the harder oxygen ionic center of the thymine or guanine base than with the softer nitrogen one.[30–33] The site for base alkylation in the final products **8a–c** derived from **3a–c** was determined by comparing the UV spectra of **8a–c** (Table 2) with those of other alkylation products described in the literature,[29] and was subsequently confirmed by NMR spectroscopy using the HMBC technique to analyze the fully protected precursors **3a–c**. First, the signals of the methylene groups of the 3-oxapentoxy linker were assigned in the ^1H and ^{13}C NMR spectra using ^1H–^1H COSY and DEPT techniques for designating signals in the ^{13}C NMR spectrum. The DEPT procedure was applied to distinguish between CH (DEPT 90) and CH_2 (DEPT 135) groups.

Differentiation of the three possible alkylated forms (2-*O*, 3-*N*, and 4-*O*) in **3a–c** can be achieved by an HMBC experiment in the following way: for 2-*O* alkylation the NMR

Table 1. Yields of the alkylation reaction and chromatographic characteristics of the products **3–7**.

Compound	Yield [%]	TLC [R_f]
thymidine	total: 76	
3a (2-*O*)	30	0.14[a]
3b (3-*N*)	16	0.65[a]
3c (4-*O*)	30	0.29[a]
2′-*O*-deoxycytidine	[b]	[b]
5 (4-*N*)		
2′-*O*-deoxyadenosine	48	0.67[a]
6 (6-*N*)		
2′-*O*-deoxyguanosine	total: 47	
7a (1-*N*)	5	0.65[c]
7b (2-*N*)	18	0.20[c]
7c (6-*O*)	24	0.75[c]

[a] CH_2Cl_2/CH_3CN (3/1). [b] Deprotected without isolation to give **9** (4-*N*). [c] CH_2Cl_2/CH_3CN (3/2)

Table 2. Characteristics of metallacarborane-substituted thymidines **8a** (2-*O*), **8b** (3-*N*), and **8c** (4-*O*), 2′-*O*-deoxycytidine **9** (4-*N*), 2′-*O*-deoxyadenosine **10** (6-*N*), and 2′-*O*-deoxyguanosines **11a** (2-*N*), **11b** (1-*N*), and **11c** (6-*O*).

Compound	Molecular formula	MS[a] [M]	UV[b] [nm] λ_{min}	UV[b] [nm] λ_{max}	IR[c] [cm^{-1}] ν_{B-H}	TLC (R_f)
thymidine						
8a (2-*O*)	$C_{18}H_{42}B_{18}CoN_2O_7$	652.4	236 (sh), 284	259, 312	2556.2	0.29[d,e]
8b (3-*N*)	$C_{18}H_{42}B_{18}CoN_2O_7$	652.4	236, 294	271, 314	2539.60.35[d,e]	
8c (4-*O*)	$C_{18}H_{42}B_{18}CoN_2O_7$	652.4	241, 283 (sh)	278 (sh), 312	2540.6	0.32[d,e]
2′-*O*-deoxycytidine						
9 (4-*N*)	$C_{17}H_{41}B_{18}CoN_3O_6$	637.6	231, 294	275, 312	2539.50.32[f,g]	
2′-*O*-deoxyadenosine						
10 (6-*N*)	$C_{18}H_{41}B_{18}CoN_5O_5$	660.4	232, 284	260, 312	2539.50.14[e,f]	
2′-*O*-deoxyguanosine						
11a (1-*N*)	$C_{18}H_{41}B_{18}CoN_5O_6$	677.7	240, 291	279, 312	2555.60.67[d,g]	
11b (2-*N*)	$C_{18}H_{41}B_{18}CoN_5O_6$	677.3	227, 292	259, 312	2539.80.53[d,g]	
11c (6-*O*)	$C_{18}H_{41}B_{18}CoN_5O_6$	677.5	236, 262	251, 280 (sh), 312	2555.8	0.23[d,g]

[a] FAB-MS (negative, NBA); glycerin was used as matrix for **11c**. [b] In 95% C_2H_5OH. [c] In KBr. [d] 50 HPTLC plates, silica gel 60 F_{254}, Merck. [e] Eluting solvent system: CH_2Cl_2/CH_3OH (9/1). [f] Polygram Sil G/UV_{254}, Macherey–Nagel. [g] Eluting solvent system: CH_2Cl_2/CH_3OH (8/2).

spectrum should show one signal for the connecting C-2 of thymine and the protons of the α-methylene group of the 3-oxapentoxy linker, whereas for 3-*N* alkylation there should be two connectivities observable, namely C-2/α-H and C-4/α-H, and finally for 4-*O* alkylation one connectivity for C-4/α-H should again be observed.[34] In fact, all the expected correlations were detected (Figure 1), thus confirming the assignment made originally on the basis of UV spectroscopy.

The site for base alkylation in **11a–c** derived from **7a–c** was determined by comparing the UV spectra of **11a–c** (Figure 2, Table 2) with those of other alkylation products containing modifications at 1-*N*, 2-*N*, and 6-*O* of a guanine residue available in the literature.[31,33,35,36] In addition to nucleobase absorptions, the characteristic absorption of the metallacarborane moiety at $\lambda_{max}=312$ nm is observed for all nucleoside–metallacarborane conjugates **8–11**.

The physicochemical properties and biological activities of nucleosides are affected by their chemical structure, stereochemistry, and the conformation of the molecule. It was therefore interesting to test whether the metallacarborane modification affects the conformation of the metallacarborane–nucleoside conjugates, especially with respect to the rotation of the base about the N-glycosidic bond and the *syn*/*anti* preferences. Either form is allowed, although the *anti* conformation is more common for pyrimidine nucleosides while purine nucleosides are in a *syn* and *anti* conformational equilibrium.[37] Circular dichroism (CD) was used to compare the base conformation in metallacarborane–nucleoside conjugates **8–11** and their unmodified counterparts **2a–c**. In all cases the CD spectra of conjugates **8–11** recorded under the same conditions as for the unmodified nucleosides revealed a strong and diverse effect of the modification on conjugate conformation in terms of the spectral shapes and molecular ellipticity values in the recorded range 200–340 nm. The absorption maxima and minima in the CD spectra of modified thymidines **8a–c** are as follows: **8a** (2-*O*): $\lambda_{max}=260$ ($\Theta=-0.1$) and 232 ($\Theta=-4.2$), $\lambda_{min}=242$ (sh) ($\Theta=-3.0$) and 224 nm ($\Theta=-4.2$); **8b**: $\lambda_{max}=274$ ($\Theta=-1.8$), $\lambda_{min}=230$ nm ($\Theta=-5.0$); **8c**: $\lambda_{max}=285$ ($\Theta=0.4$) and 239 ($\Theta=-0.5$), $\lambda_{min}=252$ (sh) ($\Theta=-1.0$) and 218 nm ($\Theta=5.0$). The following values have been recorded for thymidine **1a**: $\lambda_{max}=274$ ($\Theta=3.2$) and 230 ($\Theta=-1.9$), $\lambda_{min}=242$ ($\Theta=-2.2$) and 218 nm ($\Theta=-4.2$). The most characteristic difference between **8a–c** and unmodified **1a** is a decrease in the molecular ellipticity for all regioisomers, a blue shift of the maximum for **8a** (2-*O*) at 260 nm, and a red shift of the maximum for **8c** (4-*O*) at 285 nm. The maximum at 274 nm for **8b** (3-*N*) is the same as for unmodified thymidine **1a**, but with lower intensity. The CD spectrum of **9** (4-*N*) changes drastically as it is flat, with Θ near to zero, in the range 240–340 nm, whereas unmodified 2′-*O*-deoxycitidine (**1b**) shows a strong, positive absorption with a maximum at $\lambda_{max}=274$ nm ($\Theta=7.2$) in the same range. The changes in the CD spectra of the modified purine nucleosides **10** (6-*N*) and **11a–c** are more consistent than for pyrimidine ones. In all cases the spectra of the modified nucleosides between

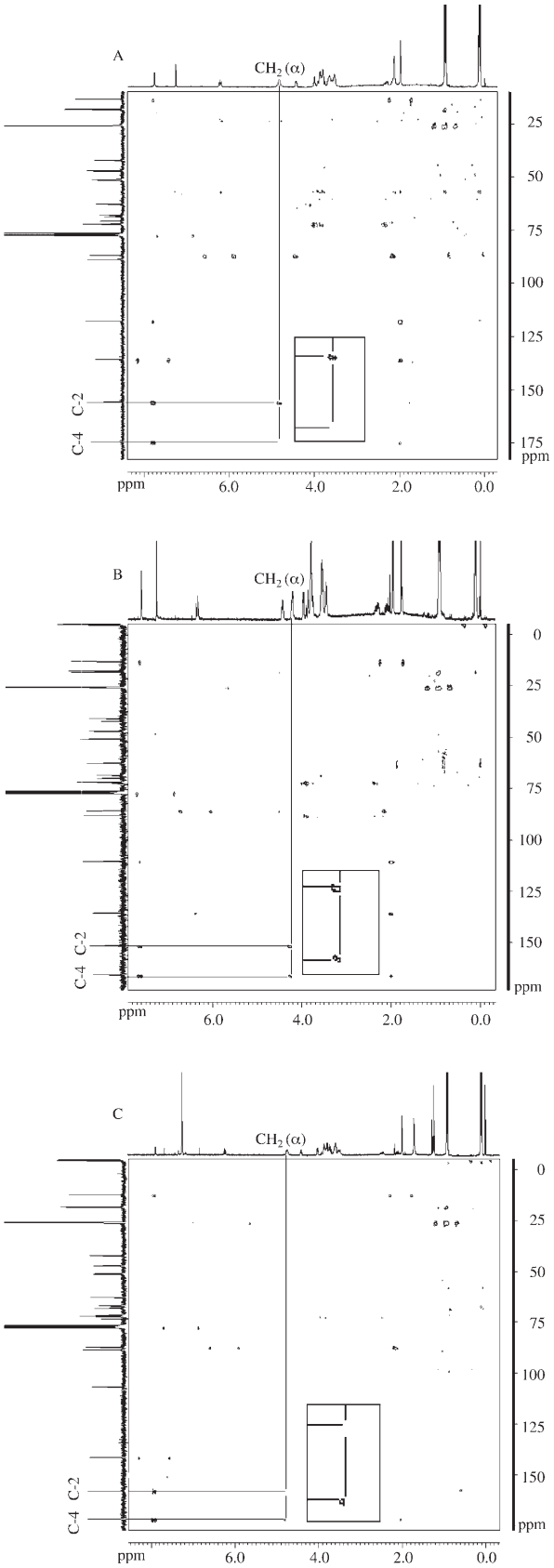


Figure 1. ^{1}H–^{13}C HMBC experiments (250 MHz) for analysis of the fully protected regioisomers of metallacarborane–thymidine conjugates A) **3a** (2-*O*), B) **3b** (3-*N*), and C) **3c** (4-*O*). The insets show a magnified part of the spectrum containing diagnostic cross-peaks between C-2 and/or C-4 and CH_2 (α).

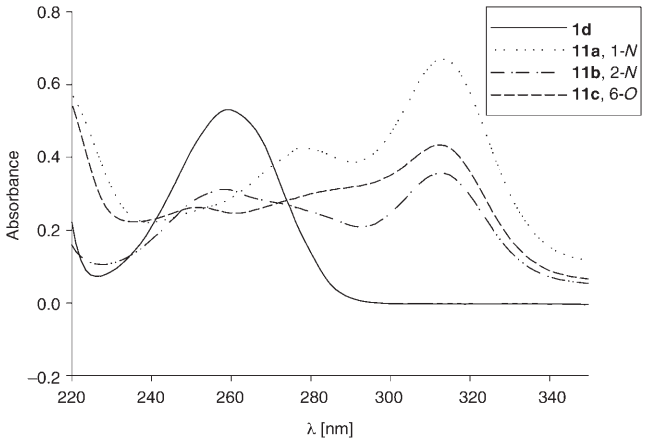


Figure 2. UV spectra of 2′-*O*-deoxyguanosine (**1d**) and deprotected derivatives of the 2′-*O*-deoxyguanosine containing a metallacarborane substituent attached to the nucleobase (**11a–c**).

240 and 340 nm, with λ_{max} around 285 nm, are a mirror-image of the spectra of the corresponding unmodified 2′-*O*-deoxyadenosine (**1c**) and 2′-*O*-deoxyguanosine (**1d**), respectively (Figure 2 and Scheme S6 in the Supporting Information). This suggests an opposite base conformation about the glycosidic bond in conjugates bearing metallacarborane modification (**10** and **11a–c**) to that in unmodified nucleosides **1c** and **1d**, respectively.

Finally, it should be pointed out that the effect of metallacarborane modification on the nucleoside conformation can manifest itself not only due to the presence of bulky substituents at the nucleobase itself but also due to the capacity of the ether linker to preorganize and favor chelation of cations such as Na^+ to produce a five-membered ring. Indeed, it has been shown that in the sodium salt [Na{3,3′-Co[8-$(CH_2CH_2O)_2CH_2CH_3$]-1,2-$C_2B_9H_{10}$}(1′,2′-$C_2B_9H_{11}$)] the chain contributes three oxygen atoms for coordination to Na^+ and that the metallacarborane cluster provides three extra B–H coordination sites.[38] Taking into consideration these observations one can contemplate similar structure formation in metallacarborane–nucleoside conjugates; the possibility of participation of additional coordination centers from the nucleobases can additionally amplify the effect of metallacarborane modification on the nucleoside conformation. Efforts towards crystallization of the conjugates **8–11** and their X-ray analysis as well as mass spectrometric and NMR studies aimed at elucidating this putative phenomenon are in progress in our laboratory.

In conclusion, a general method for the synthesis of cobalt-bearing metallacarborane–nucleoside conjugates has been proposed. The regioselectivity towards nucleobases of this unique alkylation reaction involving a metallacarborane–dioxane adduct as alkylating agent has been discussed. The present approach provides a route to nucleoside conjugates modified with metallacarboranes bearing different metals and different types of carborane cages as long as suitable adducts of the cyclic ether and boron cluster are available. Our method provides a route for the synthesis and study of nucleic acids modified with metallacarborane complexes at designated locations and of other biologically important derivatives of nucleosides.

Experimental Section

Materials: Thymidine, 2′-*O*-deoxycytidine, 2′-*O*-deoxyadenosine, and 2′-*O*-deoxyguanosine were purchased from Pharma-Waldhof GmbH (Düsseldorf, Germany). *tert*-Butyldimethylsilyl chloride was purchased from ABCR GmbH&Co.KG (Karlsruhe, Germany), 1 M tetrabutylammonium fluoride solution in THF was obtained from Sigma-Aldrich (Sp. z o.o. Poznan, Poland), and sodium hydride (60% suspension in mineral oil) was purchased from Lancaster Chemicals (Morecambe, England). Column chromatography was performed on silica gel 230–400 mesh from Sigma-Aldrich. (Steinheim, Germany). TLC was performed on silica gel F254 plates purchased from Sigma-Aldrich (Steinheim, Germany). Solvents were purchased with the highest available quality.

NMR spectroscopy: ^1H, ^{11}B, and ^{13}C NMR spectra were recorded with a Bruker Avance DPX 250 MHz spectrometer. The spectra were recorded at 250.13, 80.25, and 62.90 MHz, respectively. Tetramethylsilane and $BF_3/(C_2H_5)_2O$ were used as standards for $^1H/^{13}C$ and ^{11}B, respectively.

Mass spectrometry: FAB mass spectra were recorded with a Finnigan MAT spectrometer (Bremen, Germany) with nitrobenzyl alcohol (NBA) as matrix. The masses are those of negative ions. Although eleven isotopes of boron are known, boron exists naturally as a 19.9% ^{10}B isotope and 80.1% ^{11}B isotope mixture. A total of 18 boron atoms are present in the metallacarborane cage of compounds **3–11**. The mass spectra of these compounds correspond to all possible combinations of ^{10}B and ^{11}B isotope and give rise to multiple peaks for each specific molecule. In theory 18^2 combinations can exist, but the intensity of extreme peaks containing mostly ^{10}B or ^{11}B is low, therefore only peaks close to average, allowing natural boron isotopes′ abundance, are observable. Calculation of the theoretical molecular mass for compounds **3–11** was performed using the option "Analyze Structure" in the ChemDraw program. The calculated masses provided in the manuscript correspond to molecular weights based on the average mass of the elements consisting of natural isotopes. In practice, the most intense signal in the multiple peaks usually corresponds closely to the molecular weight.

UV spectroscopy: UV measurements were performed with a GBC Cintra10e UV-VIS spectrometer (Dandenong, Australia). Samples for UV experiments containing about 0.5 A_{260} ODU (ODU = optical density units) of **1a–d** and **8–11** were dissolved in 95% C_2H_5OH. The measurements were performed at ambient temperature.

IR spectroscopy: IR spectra were recorded with an ATI Mattson Infinity series MI-60 Fourier-transform IR spectrophotometer equipped with a silicon carbide (SiC) air-cooled source for the IR range, a cesium iodide beam-splitter, and DTGS (deuterated triglycine sulfate) detectors. Samples were prepared by diluting compounds with potassium bromide (70–140 mg of KBr per sample) and then pressing in a stainless-steel die to form discs of 0.8 cm diameter.

Circular dichroism (CD) of compounds 8–11 and their unmodified counterparts thymidine (T), 2′-*O*-deoxycytidine (dC), 2′-*O*-deoxyadenosine (dA), and 2′-*O*-deoxyguanosine (dG): CD spectra were recorded with a CD6 dichrograph (Jabin-Yvon, Longjumeau, France) in a cell with a 5-mm path length, 2-nm bandwidth, and 1–2-s integration time. The same molar extinction coefficients for modified nucleosides **8–11** and their unmodified counterparts were used: $\varepsilon = 8.8 \times 10^3$ (**8a–c** and T), $\varepsilon = 7.4 \times 10^3$ (**9** and dC), $\varepsilon = 15.2 \times 10^3$ (**10** and dA), and $\varepsilon = 11.8 \times 10^3\ M^{-1}cm^{-1}$ (**11a–c** and dG).[27] Samples for CD measurements were prepared by mixing 50-μL aliquots of concentrated stock solutions in methanol with 0.95 mL of 4 mM phosphate buffer (pH 7) containing KCl (0.9 mM), NaCl (100 mM), and EDTA (0.5 mM) (1 mL) to give a final concentration of compounds **4a–d** of between 1.6×10^{-5} and 1.6×10^{-4} M and 5% of CH_3OH. The spectra (200–350 nm) were recorded at 25 °C. Each spectrum was smoothed

with a 15- or 25-point algorithm (included in the manufacturer's software, version 2.2.1).

Synthesis of 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)thymidine (**2a**), 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxycytidine (**2b**), 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxyadenosine (**2c**), and 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxyguanosine (**2d**) was performed according to the literature procedure.[21] [8-Dioxane-3-cobalt bis(dicarbollide)]^0 (**4**) was obtained as described.[39]

General procedure for the synthesis of compounds 3–7: The procedure was performed under anhydrous conditions, with a positive pressure of argon. 3′,5′-*O*,*O*-Di(*tert*-butyldimethylsilyl)thymidine (**2a**), 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxycytidine (**2b**), 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxyadenosine (**2c**), or 3′,5′-*O*,*O*-di(*tert*-butyldimethylsilyl)-2′-*O*-deoxyguanosine (**2d**) (0.50–0.80 mmol) and 8-dioxane-[3-cobalt bis(1,2-dicarbollide)] zwitterion (**4**; 0.30–0.49 g, 0.75–1.20 mmol, 1.5 molar excess) were mixed together then dried over P_2O_5 under high vacuum for 24 h. NaH (60% suspension in mineral oil, 0.030–0.048 g, 0.75–1.20 mmol, 1.5 molar excess) was then added followed by anhydrous toluene (6–10 mL). The reaction mixture was stirred at 70°C for 2.0–5.5 h in an oil bath and then cooled to room temperature. Unreacted NaH was removed by centrifugation then the supernatant was evaporated to dryness to yield 0.5–1.0 g of crude compounds **3a** (2-*O*), **3b** (3-*N*), **3c** (4-*O*), **5** (4-*N*), **6** (6-*N*), **7a** (1-*N*), **7b** (2-*N*), and **7c** (6-*O*). The regioisomers of **3** and **7** were purified and separated, and compound **6** was purified, by silica gel column chromatography (15–30 g, 230–400 mesh). The following eluting solvent systems were used: a gradient of CH_3CN in CH_2Cl_2 (0–20%) for separation of regioisomers **3a–c**, 5% CH_3CN in CH_2Cl_2 for purification of **6**, and a gradient of CH_3CN in CH_2Cl_2 (0–30%) for separation and purification of regioisomers **7a–c**. Compound **5** (4-*N*) was transformed into **9** (4-*N*) directly without purification.

3a (2-*O*): Yield: 30%; R_f=0.14 (CH_3CN/CH_2Cl_2 1/3); ^{1}H NMR (250.13 MHz, $CDCl_3$, 25°C, TMS): δ=7.77 (s, 1H; H-6), 6.22 (t, $^3J_{H,H}$=6.69 Hz, 1H; H-1′), 4.81 (brs, 2H; CH_2-linker), 4.43 (m, 1H; H-3′), 4.00 (m, 1H; H-4′), 3.88–3.79 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.65 (m, 3H; 3×CH-metallacarborane), 3.53 (m, 3H; CH-metallacarborane and CH_2-linker), 2.37–2.10 (m, 2H; 2H-2′), 1.97 (s, 3H; CH_3–5), 1.00–3.00 (bm, 17H; BH-metallacarborane), 0.94 and 0.91 (2 s, 2×9H; -$C(CH_3)_3$ in TBDMS group at 3′ and 5′ positions), 0.13 and 0.11 ppm (2 s, 2×6H; CH_3-Si-CH_3 in TBDMS group at 3′ and 5′ positions); ^{11}B NMR (80.25 MHz, $CDCl_3$, 25°C, $BF_3/(C_2H_5)_2O$): δ=24.72 (B-8), −5.85 (B-8′, -10, -4, -7, -12, -10′, -4′, -7′, -12′), −18.26 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $CDCl_3$, 25°C, TMS): δ=174.49 (C-4), 155.83 (C-2), 135.79 (C-6), 117.79 (C-5), 88.70 (C-4′), 86.83 (C-1′), 72.41 (CH_2-linker), 72.06 (C-3′), 70.69 (CH_2-linker), 68.86 (CH_2-linker), 67.99 (CH_2-linker), 62.79 (C-5′), 51.32 (CH-metallacarborane), 41.07 (CH-metallacarborane), 42.17 (C-2′), 25.83, 25.70 (2×C of CH_3 in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 18.38, 17.94, (2×C-methylidene in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 13.39 (CH_3-5), −4.65, −4.86, −5.36, −5.42 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); UV/Vis (95% C_2H_5OH): λ_{min}=284.41, λ_{max}=256.32, 313.08 nm; MS (NBA, FAB): *m*/*z* (%): 880.1 (100) [*M*] ($C_{30}H_{70}B_{18}CoN_2O_7Si_2$=880.588).

3b (3-*N*): Yield: 16%; R_f=0.65 (CH_3CN/CH_2Cl_2 1/3); ^{1}H NMR (215.13 MHz, $CDCl_3$, 25°C, TMS): δ=7.60 (s, 1H; H-6), 6.35 (t, $^3J_{H,H}$=6.12 Hz, 1H; H-1′), 4.43 (m, 1H; H-3′), 4.21 (m, 2H; CH_2-linker), 3.97 (m, 1H; H-4′), 3.86–3.74 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.54 (m, 3H; 3×CH-metallacarborane), 3.45 (m, 3H; CH_2-linker and CH-metallacarborane), 2.31–2.02 (m, 2H; H-2′), 1.96 (s, 3H; CH_3–5), 2.50–1.00 (m, 17H; BH-metallacarborane), 0.93 and 0.9 (2 s, 2×9H; -$C(CH_3)_3$ in TBDMS group at 3′ and 5′ positions), 0.12 and 0.09 ppm (2 s, 2×6H; CH_3-Si-CH_3 in TBDMS group at 3′ and 5′ positions); ^{11}B NMR (80.25 MHz, $CDCl_3$, 25°C, $BF_3/(C_2H_5)_2O$): δ=25.61 (B-8), −5.77 (B-8′, -10, -4, -7, -9, -10′, -4′, -7′, -9′, -12′), −16.90 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $CDCl_3$, 25°C, TMS): δ=165.80 (C-4), 151.47 (C-2), 135.64 (C-6), 110.47 (C-5), 85.90 (C-1′), 72.33 (CH_2-linker), 71.79 (C-3′), 70.12 (CH_2-linker), 68.67 (CH_2-linker), 62.76 (C-5), 50.95 (CH-metallacarborane), 47.21 (CH-metallacarborane), 42.32 (CH_2-linker), 41.15 (C-2′), 25.94, 25.74 (2×C of CH_3 in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 18.42 and 18.00 (2×C-methylidene in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 13.33 (CH_3-5), −4.61, −4.87, −5.33 −5.40 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); UV/Vis (95% C_2H_5OH): λ_{min}=237.13 and 292.25, λ_{max}=270.42 and 314.05 nm; MS (NBA, FAB): *m*/*z* (%): 880.4 (100) [*M*] ($C_{30}H_{70}B_{18}CoN_2O_7Si_2$=880.588).

3c (4-*O*): Yield: 30%; R_f=0.29 (CH_3CN/CH_2Cl_2 1/3); ^{1}H NMR (215.13 MHz, $CDCl_3$, 25°C, TMS): δ=7.89 (s, 1H; H-6), 6.23 (t, $^3J_{H,H}$=6.42 Hz, 1H; H-1′), 4.47 (m, 2H; CH_2-linker), 4.39 (m, 1H; H-3′), 4.01 (q, $^3J_{H,H}$=2.85 Hz, $^3J_{H,H}$=2.47 Hz, 1H; H-4′), 3.86–3.58 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.52 (m, 3H; CH_2-linker and CH-metallacarborane), 3.47 (m, 3H, 3×CH-metallacarborane), 2.50–2.17 (m, 2H; 2H-2′), 1.99 (s, 3H; CH_3–5), 2.50–1.00 (m, 17H; BH-metallacarborane), 0.91 and 0.89 (2 s, 2×9H; -$C(CH_3)_3$ in TBDMS group at 3′ and 5′ positions), 0.11 and 0.09 ppm (2 s, 2×6H; CH_3-Si-CH_3 in TBDMS group at 3′ and 5′ positions); ^{11}B NMR (80.25 MHz, $CDCl_3$, 25°C, $BF_3/(C_2H_5)_2O$): δ=24.79 (B-8), −5.59 (B-8′, -10, -4, -7, -12, -10′, -4′, -7′, -12′), −15.67 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $CDCl_3$, 25°C, TMS): δ=171.52 (C-4), 157.77 (C-2), 141.30 (C-6), 106.69 (C-5), 88.44 (C-4′), 87.20 (C-1′), 73.14 (CH_2-linker), 72.08 (C-3′), 71.47 (CH_2-linker), 68.09 (CH_2-linker), 66.83 (CH_2-linker), 62.67 (C-5′), 51.27, 51.00, 47.08 (3×C; CH-metallacarborane), 42.21 (C-2′), 25.92, 25.74 (2×C of CH_3 in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 18.37, 17.89 (2×C-methylidene in -$C(CH_3)_3$ of TBDMS group at 3′ and 5′ positions), 12.23 (CH_3-5), −4.56, −4.85, −5.40 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); UV/Vis (95% C_2H_5OH): λ_{min}=237.44, λ_{max}=279.12 and 314.10 nm; MS (NBA, FAB): *m*/*z* (%): 880.4 (100) [*M*] ($C_{30}H_{70}B_{18}CoN_2O_7Si_2$=880.588).

6 (6-*N*): Yield: 48%; R_f=0.67 (CH_2Cl_2/CH_3CN 3/1); ^{1}H NMR (250.13 MHz, $CDCl_3$, 25°C, TMS): δ=8.46 (s, 1H; H-8), 8.04 (s, 1H; H-2), 6.42 (t, $^3J_{H,H}$=6.45 Hz, 1H; H-1′), 4.60 (m, 3H; H-3′ and CH_2-linker), 4.06 (m, 3H; H-4′ and CH_2-linker), 3.89–3.77 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.68–3.58 (m, 4H; 4×CH-metallacarborane), 2.50 (t, $^3J_{H,H}$=5.52 Hz, 2H; 2H-2′), 4.00–1.50 (bm, 17H; BH-metallacarborane), 0.93 and 0.92 (2 s, 2×9H; -$C(CH_3)_3$ in TBDMS group at 3′ and 5′ positions), 0.12 and 0.11 ppm (2 s, 2×6H; CH_3-Si-CH_3 in TBDMS group at 3′ and 5′ positions); ^{11}B NMR (80.25 MHz, $CDCl_3$, 25°C, $BF_3/(C_2H_5)_2O$): δ=24.89 (B-8), 7.69 (B-8′), −4.92 to −6.16 (B-10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′), −17.29 ppm (B-5, -11, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $CDCl_3$, 25°C, TMS): δ=151.89 (C-6), 145.96 (C-4), 145.50 (C-2), 142.73 (C-8), 120.00 (C-5), 88.49 (C-4′), 85.32 (C-1′), 74.41 (CH_2-linker), 71.44 (C-3′), 70.83 (CH_2-linker), 68.20 (CH_2-linker), 62.53 (C-5′), 53.17 (CH_2-linker), 51.40 and 47.07 (CH-metallacarborane), 41.95 (C-2′), 25.93, 25.69 (2×C of CH_3 in 3′- and 5′-$C(CH_3)_3$), 18.39, 17.93 (2×C-methylidene in 3′- and 5′-$C(CH_3)_3$), −4.65, −4.85, −5.39, −5.45 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); UV/Vis (95% C_2H_5OH): λ_{min}=232.42 and 284.38, λ_{max}=261.14 and 313.29 nm; MS (NBA, FAB): *m*/*z* (%): 889.6 (100) [*M*] ($C_{30}H_{69}B_{18}CoN_5O_5Si_2$=889.602).

7a (1-*N*): Yield: 5%; R_f=0.65 (CH_2Cl_2/CH_3CN 6/4); UV/Vis (95% C_2H_5OH): λ_{min}=237.35 and 268.14, λ_{max}=312.12 nm; MS (NBA, FAB): *m*/*z* (%): 905.7 (100) [*M*] ($C_{30}H_{69}B_{18}CoN_5O_6Si_2$=905.601).

7b (2-N): Yield: 18%; R_f=0.20 (CH_2Cl_2/CH_3CN 6/4); ^{1}H NMR (250.13 MHz, C_6D_6, 25°C, TMS): δ=8.25 (brs, 1H; H-8), 6.50 (brt, 1H; H-1′), 4.75 (brs, 1H; H-3′), 4.25 (brs, 1H; H-4′), 4.00–3.75 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.50–3.25 (m, 4H; 2×CH_2-linker), 3.25–3.10 (m, 3H; 3×CH-metallacarborane), 2.75 (brs, 1H; CH-metallacarborane), 2.75–2.50 (m, 2H; 2H-2′), 4.50–1.75 (m, 17H; BH-metallacarborane), 1.17 and 1.13 (2 s, 2×9H; -$C(CH_3)_3$ in TBDMS group at 3′ and 5′ positions), 0.32 and 0.30 ppm (2 s, 2×3H; CH_3 in -$Si(CH_3)_2$ at 3′ or 5′ position); ^{11}B NMR (80.25 MHz, C_6D_6, 25°C, $BF_3/(C_2H_5)_2O$): δ=25.8 (B-8), −2.5, −12.8 ppm (B-8′, -10, -4, -7, -9, -12, -10′, -4′, -7′, -12′, -5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, C_6D_6, 25°C, TMS): δ=160.6 (C-6), 152.6 (C-4), 149.7 (C-2), 138.4 (C-8), 117.8 (C-5), 88.4 (C-4′), 84.4 (C-1′), 72.7 (C-3′), 68.5 (C-5′), 63.6 (CH_2-linker), 51.2, 47.3, 42.9 (3×CH-metallacarborane), 41.3 (C-2), 26.2, 26.0 (2×C of CH_3 in 3′- and 5′-$C(CH_3)_3$), 18.6, 18.2 (2×C-methylidene in 3′- and 5′-$C(CH_3)_3$), −4.5, −4.7, −5.1, −5.2 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); UV/Vis (95% C_2H_5OH): λ_{min}=232.42 and 294.15, λ_{max}=259.18 and

314.12 nm; MS (NBA, FAB): *m/z* (%): 905.7 (100) [*M*] ($C_{30}H_{69}B_{18}CoN_5O_6Si_2$ = 905.601).

7c (6-*O*): Yield: 24%; R_f = 0.75 (CH_2Cl_2/CH_3CN 6/4); ^{1}H NMR (250.13 MHz, C_6D_6, 25°C, TMS): δ = 10.22 (br s, 1H; NH), 8.50 (s, 1H; H-8), 6.55 (t, $^3J_{H,H}$ = 5.75 Hz, 1H; H-1′), 4.90 (m, 1H; H-3′), 4.29 (m, 1H; H-4′), 4.11–3.99 (m, 6H; H-5′,5″ and 2×CH_2-linker), 3.73–3.61 (m, 4H; 2×CH_2-linker), 3.30 (br s, 1H; CH-metallacarborane), 3.19–3.10 (m, 2H; 2×CH-metallacarborane), 2.95 (br s, 1H; CH-metallacarborane), 2.76 (m, 2H; 2H-2′), 4.50–2.00 (m, 17H; BH-metallacarborane), 1.21 and 1.11 (2 s, 2×9H; -C(CH_3)$_3$ in TBDMS group at 3′ and 5′ positions), 0.41 and 0.39 (2 s, 2×3H; CH_3 in -Si(CH_3)$_2$ at 3′ or 5′ position), 0.31 and 0.29 ppm (2 s, 2×3H; CH_3 in -Si(CH_3)$_2$ at 3′ or 5′ position); ^{13}C NMR (62.90 MHz, C_6D_6, 25°C, TMS): δ = 154.88 (C-6), 152.27 (C-4), 149.63 (C-2), 136.63 (C-8), 107.34 (C-5), 89.40 (C-4′), 87.66 (C-1′), 72.90 (CH_2-linker), 72.27 (C-3′), 69.39 (C-5′), 67.55, 63.08 (2×CH_2-linker), 51.27, 50.68, (2×CH-metallacarborane), 49.10 (CH_2-linker), 47.78, 47.40 (2×CH-metallacarborane), 40.36 (C-2′), 26.07, 26.02 (2×C of CH_3 in 3′- and 5′-C(CH_3)$_3$), 18.56, 18.24 (2×C-methylidene in 3′- and 5′-C(CH_3)$_3$), −4.24, −4.48, −5.01, −5.12 ppm (4×C in CH_3-Si-CH_3 of TBDMS group at 3′ and 5′ positions); ^{11}B NMR (80.25 MHz, C_6D_6, 25°C, $BF_3/(C_2H_5)_2O$): δ = 25.92 (B-8), 5.00 to −35.00 ppm (br m, B-8′, -10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′, -5, -11, -6, -5′, -11′, -6′); UV/Vis (95% C_2H_5OH): λ_{min} = 246.29 and 270.33, λ_{max} = 258.41 and 310.13 nm; MS (NBA, FAB): *m/z* (%): 905.8 (100) [*M*] ($C_{30}H_{69}B_{18}CoN_5O_6Si_2$ = 905.601).

General procedure for the synthesis of compounds 8–11: Compound **3a–c**, **5**, **6**, or **7a–c** (0.10–0.35 mmol) was dried over P_2O_5 under high vacuum for 24 h. It was then dissolved in anhydrous THF (1.0–3.5 mL) and tetrabutylammonium fluoride was added (0.25–0.88 mL of a 1 M solution in THF; 0.25–0.88 mmol, 2.5 molar excess).[40] The reaction mixture was stirred at room temperature for 10–25 min whilst being protected against the introduction of moisture. After reaction completion a mixture of pyridine, methanol, and water (3/1/1, 2.5–10.0 mL) and Dowex 50W X 8 ion-exchange resin (pyridinium form, ca. 0.5–2.0 g wet weight) was added. After 30 min the ion-exchange resin was filtered off and washed with pyridine/methanol/water (2.5–10.0 mL). The filtrate and washings were combined then the solvents were evaporated under reduced pressure to yield an oily residue, which was co-evaporated with toluene (3×5 mL). The crude product was purified by silica gel column chromatography (6–12 g, 230–400 mesh). The following eluting solvent systems were used: a gradient of CH_3OH in CH_2Cl_2 (0–6%) for purification of **8a** (2-*O*), **8b** (3-*N*), and **8c** (4-*O*), a gradient of CH_3OH in CH_2Cl_2 (0–20%) for purification of **9**, (4-*N*), and 10% CH_3OH in CH_2Cl_2 for purification of **10** (6-*N*), **11a** (1-*N*), **11b** (2-*N*), and **11c** (6-*O*).

8a (2-*O*): Yield: 94%; R_f = 0.29 (CH_2Cl_2/CH_3OH 9/1); ^{1}H NMR (250.13 MHz, $(CD_3)_2CO$, 25°C, TMS): δ = 7.89 (s, 1H; H-6), 6.24 (t, $^3J_{H,H}$ = 6.37 Hz, 1H; H-1′), 4.49 (m, 3H; H-3′ and CH_2-linker), 4.27 (br s, 4H; 4×CH-metallacarborane), 3.96 (m, 1H; H-4′), 3.81 (m, 4H; H-5′,5″ and CH_2-linker), 3.59 (m, 4H; 2×CH_2-linker), 2.34 (m, 2H; 2H-2′), 1.83 (s, 3H; CH_3–5), 3.00–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, $[D_6](CD_3)_2CO$, 25°C, $BF_3/(C_2H_5)_2O$): δ = 23.09 (B-8), 4.87 to −8.12 (B-8′, -4, -7, -9, -10, -12, -4′, -7′, -9′, -10′, -12′), −16.58 to −27.31 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $(CD_3)_2CO$, 25°C, TMS): δ = 171.7 (C-4), 155.7 (C-2), 134.7 (C-6), 117.1 (C-5), 88.9 (C-4′), 87.2 (C-1′), 72.6 (CH_2-linker), 71.2 (C-3′), 69.2 (CH_2-linker), 68.3 (CH_2-linker), 62.2 (C-5′), 55.1 (CH-metallacarborane), 47.1 (CH-metallacarborane), 41.9 (C-2′), 13.8 ppm (CH_3-5); IR (KBr): $\tilde{\nu}$ = 2556 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 283.63, λ_{max} = 258.59 and 312.43 nm; MS (NBA, FAB): *m/z* (%): 652.4 (100) [*M*] ($C_{18}H_{42}B_{18}CoN_2O_7$ = 652.066).

8b (3-*N*): Yield: 83%, R_f = 0.3 (CH_2Cl_2/CH_3OH 9/1); ^{1}H NMR (250.13 MHz, $(CD_3)_2CO$, 25°C, TMS): δ = 7.79 (s, 1H; H-6), 6.34 (t, $^3J_{H,H}$ = 6.83 Hz, 1H; H-1′), 4.49 (m, 1H; H-3′), 4.29 (m, 4H; 2×CH-metallacarborane and CH_2-linker), 3.92 (m, 1H; H-4′), 3.79 (m, 2H; H-5′,5″), 3.53–3.46 (m, 8H; 2×CH-metallacarborane, 3×CH_2-linker), 2.27 (m, 2H; 2H-2′), 1.88 (s, 3H; CH_3–5), 3.00–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, $[D_6](CD_3)_2CO$, 25°C, $BF_3/(C_2H_5)_2O$): δ = 22.76 (B-8), 4.61 to −8.23 (B-8′, -4, -7, -9, -10, -12, -4′, -7′, -9′, -10′, -12′), −16.24 to −27.27 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $(CD_3)_2CO$, 25°C, TMS): δ = 163.4 (C-4), 151.3 (C-2), 135.2 (C-6), 109.2 (C-5), 88.2 (C-4′), 86.0 (C-1′), 73.7 (CH_2-linker), 71.6 (C-3′), 68.9 (CH_2-linker), 67.5 (CH_2-linker), 62.4 (C-5′), 59.0 (CH_2-linker), 55.1 and 46.9 (CH-metallacarborane), 40.8 (C-2′), 13.5 ppm (CH_3-5); IR (KBr): $\tilde{\nu}$ = 2540 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 236.05 and 293.65, λ_{max} = 271.11 and 313.69 nm; MS (NBA, FAB): *m/z* (%): 652.4 (100) [*M*] ($C_{18}H_{42}B_{18}CoN_2O_7$ = 652.066).

8c (4-*O*): Yield: 84%; R_f = 0.32 (CH_2Cl_2/CH_3OH 9/1); ^{1}H NMR (250.13 MHz, $(CD_3)_2CO$, 25°C, TMS): δ = 8.06 (s, 1H; H-6), 6.25 (t, $^3J_{H,H}$ = 6.57 Hz, 1H; H-1′), 4.42 (m, 3H; H-3′ and CH_2-linker), 4.28 (m, 2H; 2×CH-metallacarborane), 4.00 (m, 1H; H-4′), 3.80 (m, 4H; H-5′,5″ and CH_2-linker), 3.42 (m, 6H; 2×CH-metallacarborane and 2×CH_2-linker), 2.25 (m, 2H; 2H-2′), 1.94 (s, 3H; CH_3–5), 3.00–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, $(CD_3)_2CO$, 25°C, $BF_3/(C_2H_5)_2O$): δ = 23.02 (B-8), 5.00 to −7.27 (B-8′, -4, -7, -9, -10, -12, -4′, -7′, -9′, -10′, -12′), −16.0 to −27.5 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, $(CD_3)_2CO$), 25°C, TMS): δ = 170.9 (C-4), 156.1 (C-2), 141.8 (C-6), 104.5 (C-5), 88.8 (C-4′), 87.3 (C-1′), 72.6 (CH_2-linker), 71.5 (C-3′), 69.4 (CH_2-linker), 69.2 (CH_2-linker), 67.1 (CH_2-linker), 62.4 (C-5′), 55.1 and 47.1 (CH-metallacarborane), 41.8 (C-2′), 12.3 ppm (CH_3-5); IR (KBr): $\tilde{\nu}$ = 2541 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 241.06 and 292.40, λ_{max} = 312.43 nm; MS (NBA, FAB): *m/z* (%): 652.4 (100) [*M*] ($C_{18}H_{42}B_{18}CoN_2O_7$ = 652.066).

9 (4-*N*): Yield: 18% (calculated for two steps; crude **5** (4-N) was used without purification); R_f = 0.32 (CH_2Cl_2/CH_3OH 8/2); ^{1}H NMR (250.13 MHz, CD_3OD, 25°C, TMS): δ = 7.90 (d, $^3J_{H,H}$ = 7.59 Hz, 1H; H-6); 6.29 (t, $^3J_{H,H}$ = 6.56 Hz, 1H; H-1′), 5.98 (d, $^3J_{H,H}$ = 7.55 Hz, 1H; H-5), 4.35 (m, 1H; H-3′), 4.07 (m, 4H; 4×CH-metallacarborane), 3.91 (m, 1H; H-4′), 3.76–3.53 (m, 8H; H-5′,5″ and 3×CH_2-linker), 3.31–3.29 (m, 2H; CH_2-linker), 2.31–2.15(m, 2H; 2H-2′), 3.00–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, $CDCl_3$, 25°C, $BF_3/(C_2H_5)_2O$): δ = 24.9 (B-8), 5.9 (B-8′), −6.5 to −5.0 (B-10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′), −17.6 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, CD_3OD, 25°C, TMS): δ = 165.31 (C-4), 158.73 (C-2), 140.94 (C-6), 97.98 (C-5), 88.83 (C-4′), 87.33 (C-1′), 73.12 (CH_2-linker), 72.58 (C-3′), 72.16 (CH_2-linker), 62.89 (C-5′), 54.56, 49.68, and 48.16 (CH-metallacarborane), 41.81 ppm (C-2′); IR (KBr): $\tilde{\nu}$ = 2540 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 231.04 and 294.90 nm, λ_{max} = 274.87 and 312.43 nm; MS (NBA, FAB): *m/z* (%): 637.6 (100) [*M*] ($C_{17}H_{41}B_{18}CoN_3O_6$ = 637.055).

10 (6-*N*): Yield: 82%; R_f = 0.14 (CH_2Cl_2/CH_3OH 9/1), R_f = 0.46 (CH_3CN); ^{1}H NMR (250.13 MHz, CD_3OD, 25°C, TMS): δ = 8.55 (s, 1H; H-8); 8.46 (s, 1H; H-2), 6.47 (t, $^3J_{H,H}$ = 6.52 Hz, 1H; H-1′), 4.57 (m, 1H; H-3′), 4.48 (m, 2H; CH_2-linker), 4.03 (m, 1H; H-4′), 3.97–3.97 (m, 6H; CH_2-linker and 4×CH-metallacarborane), 3.80–3.75 (m, 2H, H-5′,5″), 3.61 (s, 4H; 2×CH_2-linker), 2.77–2.55 (m, 2H; 2H-2′), 2.50–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, CD_3OD, 25°C, $BF_3/(C_2H_5)_2O$): δ = 24.11 (B-8), 6.16 (B-8′), −5.90 (B-10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′), −18.11 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, CD_3OD, 25°C, TMS): δ = 152.4 (C-6), 149.0 (C-4), 147.8 (C-2), 69.8 and 68.8 (2×CH_2-linker), 143.8 (C-8), 121.1 (C-5), 89.6 (C-4′), 86.5 (C-1′), 73.6 (CH_2-linker), 72.3 (C-3′), 63.0 (C-5′), 54.1 (CH-metallacarborane), 52.0 (CH_2-linker), 48.0 (CH-metallacarborane), 41.9 ppm (C-2′); IR (KBr): $\tilde{\nu}$ = 2540 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 232.29 and 284.87, λ_{max} = 259.84, 266.10, and 312.43 nm; MS (NBA, FAB): *m/z* (%): 660.4 (100) [*M*−1] ($C_{18}H_{41}B_{18}CoN_5O_5$ = 661.079).

11a (1-*N*): Yield: 62%; R_f = 0.67 (CH_2Cl_2/CH_3OH 8/2); IR (KBr): ν = 2556 cm^{-1} (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 239.81 and 291.15, λ_{max} = 278.63 and 312.43 nm; MS (glycerin, FAB): *m/z* (%): 677.7 (100) [*M*] ($C_{18}H_{41}B_{18}CoN_5O_6$ = 677.079).

11b (2-*N*): Yield: 78%; R_f = 0.53 (CH_2Cl_2/CH_3OH 8/2); ^{1}H NMR (250.13 MHz, CD_3OD, 25°C, TMS): δ = 7.29 (s, 1H; H-8); 6.26 (t, $^3J_{H,H}$ = 6.00 Hz, 1H; H-1′), 4.52 (m, 1H; H-3′), 4.25 (m, 2H; CH_2-linker), 4.07–4.03 (m, 4H; 4×CH-metallacarborane), 3.92 (m, 1H; H-4′), 3.80 (m, 4H; H-5′,5″ and CH_2-linker), 3.70–3.55 (m, 4H; 2×CH_2-linker), 2.73, 2.35 (m, 2H; 2H-2′), 3.00–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, CD_3OD, 25°C, $BF_3/(C_2H_5)_2O$): δ = 23.5 (B-8), 5.9 (B-8′), −8.0 to −6.6 (B-10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′), −18.3 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, CD_3OD, 25°C, TMS): δ =

158.9 (C-6), 156.8 (C-4), 150.2 (C-2), 138.3 (C-8), 118.1 (C-5), 89.3 (C-4′), 85.9 (C-1′), 73.3 (CH_2-linker), 72.8 (C-3′), 71.3, 69.4 (2×CH_2-linker), 63.5 (C-5′), 54.7, 48.1 (CH-metallacarborane), 44.7 (CH_2-linker), 41.4 ppm (C-2′); IR (KBr): $\nu = 2540\ cm^{-1}$ (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 227.29 and 292.40, λ_{max} = 258.59 and 312.43 nm; MS (NBA, FAB): *m*/*z* (%): 677.3 (100) [*M*] ($C_{18}H_{41}B_{18}CoN_5O_6$ = 677.079).

11c (6-*O*): Yield: 66%; R_f = 0.23 (CH_2Cl_2/CH_3OH 8/2); ^1H NMR (250.13 MHz, CD_3OD, 25 °C, TMS): δ = 9.34 (s, 1H; NH), 6.39 (t, $^3J_{H,H}$ = 5.91 Hz, 1H; H-1′), 4.64 (m, 1H; H-3′), 4.09–3.60 (m, 15H; H-4′, H-5′,5″, 4×CH-metallacarborane, 4×CH_2-linker), 2.74–2.60 (m, 2H; 2H-2′), 3.10–1.00 ppm (m, 17H; BH-metallacarborane); ^{11}B NMR (80.25 MHz, CD_3OD, 25 °C, BF_3/$(C_2H_5)_2O$): δ = 23.8 (B-8), 5.0 (B-8′), −6.6 (B-10, -4, -7, -9, -12, -10′, -4′, -7′, -9′, -12′), −18.7 ppm (B-5, -11, -6, -5′, -11′, -6′); ^{13}C NMR (62.90 MHz, CD_3OD, 25 °C, TMS): δ = 156.4 (C-6), 155.3 (C-4), 152.5 (C-2), 140.7 (C-8), 106.2 (C-5), 88.2 (C-4′), 86.8 (C-1′), 73.2 (CH_2-linker), 72.8 (C-3′), 72.4 (C-5′), 69.9, 69.3 (2×CH_2-linker), 63.2 (CH_2-linker), 54.0, 50.0 (2×CH-metallacarborane), 49.7 (C-2′), 48.0 ppm (CH-metallacarborane); IR (KBr): $\tilde{\nu} = 2556\ cm^{-1}$ (B–H); UV/Vis (95% C_2H_5OH): λ_{min} = 236.05 and 262.35, λ_{max} = 251.08 and 312.43 nm; MS (NBA, FAB): *m*/*z* (%): 677.5 (90) [*M*], 809.6 (100) [$M^- + Cs^+ - H^+$] ($C_{18}H_{41}B_{18}CoN_5O_6$ = 677.079).

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