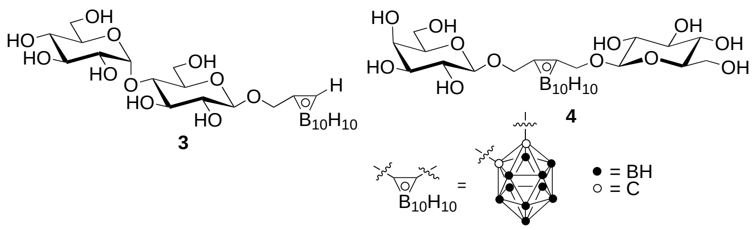
Novel Carboranyl *C*-Glycosides for the Treatment of Cancer by Boron Neutron Capture Therapy

Lutz F. Tietze,*[a] Ulrich Griesbach,[a] Ingrid Schuberth,[a] Ulrich Bothe,[a] Alberto Marra,[b] and Alessandro Dondoni*[b]

Abstract: The synthesis of the novel unprotected carboranyl *C*-glycosides **2** and **20**–**24** starting from ethynyl *C*-glycosides **1**, **5**–**8**, **10**, and **13** is described. The new compounds are highly water-soluble and display only a very low cytotoxicity, which makes them promising candidates for use in boron neutron capture therapy for the treatment of cancer.

Keywords: alkynes · antitumor agents · boron neutron capture therapy · carboranes · drug research · *C*-glycosides

Introduction



Boron neutron capture therapy (BNCT) is a binary system used for the treatment of cancer, which involves administration of a boron compound and subsequent irradiation with slow neutrons. It relies on the specific ability of the isotope ^{10}B to react with thermic neutrons to give an α particle and a $^{7}Li^{3+}$ ion in a nuclear reaction. If boron is present in a tumor cell, irradiation with a beam of slow neutrons will cause destruction of the malign tissue.[1] However, there are several problems associated with this approach, such as the need to introduce high levels of boron into the cancer cells. The stable *ortho*-carboranes[2] are therefore used as the boron source, which allow the transport of ten boron atoms per molecule into the cancer cells. However, the poor solubility in water and distinct cytotoxicity of most of these compounds has limited their use in BNCT. In view of their excellent water solubilities, negligible toxicities, and high rates of uptake into cancer cells, we have focused our interest on carboranyl *O*-glycosides such as maltoside **3** for use in BNCT.[3] Mixed carboranediyl *O*-bisglycosides such as **4** show almost no uptake into tumor cells due to their enhanced hydrophilicities. They may therefore be used for a selective delivery into malignant cells by employing glycohydrolases connected to monoclonal antibodies that bind to tumor-associated antigens. These glycohydrolases can transform the bisglycosides into lipophilic compounds.[4]

A possible disadvantage of *O*-glycosylated carboranes might be the enzymatic cleavage of such compounds by glycohydrolases. This problem would not arise with *C*-glycosylated carboranes, although, to date, there has been only one example of a carborane unit connected to the anomeric carbon atom of a tetrahydropyran ring with the anomeric carbon atom still bearing a hydroxy group, as reported by Dahlhoff et al.[5] Such *C*-linked compounds were obtained as anomeric mixtures by the addition of monolithio *meta*-carborane to trimethylsilyl-protected D-glucono-1,5-lactone or analogous 1,4-lactones.

Herein, we describe the stereoselective synthesis of novel *C*-glycosylated carboranes for use in BNCT by reaction of decaborane(14) with alkynyl *C*-glycosides, and their biological evaluation. We expected the biological and chemical properties of this new class of configurationally stable carboranyl *C*-glycosides to be as good as those of their *O*-glycosidic analogues. As already mentioned, the novel *C*-glycosides should not be affected by the action of any glycohydrolase.

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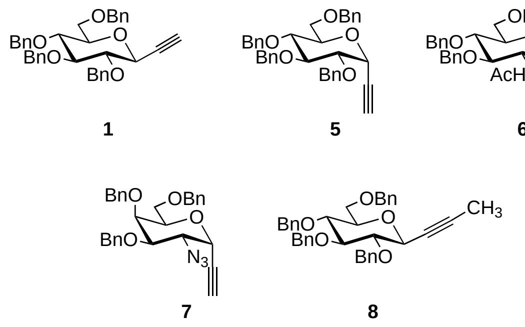
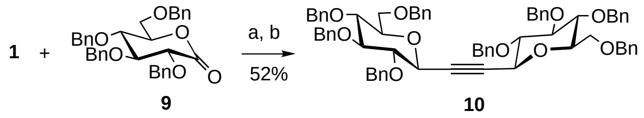
Results and Discussion

The carboranyl-*C*-glycosides **2**, **20**–**24** were synthesized by a well-established procedure involving addition of the $B_{10}H_{12} \cdot 2CH_3CN$ complex to the triple bond of the perbenzylated ethynyl *C*-glycosides **1**, **5**–**8**, **10**, and **13**, followed by hydrogenolytic cleavage of the benzyl protecting groups.

Synthesis of *C*-glycosyl acetylenes: The known perbenzylated ethynyl β-*C*-glycoside **1** was readily prepared[6, 7] by a sequence of addition of cerium TMS-acetylide to the corresponding gluconolactone, deoxygenation with triethylsilane

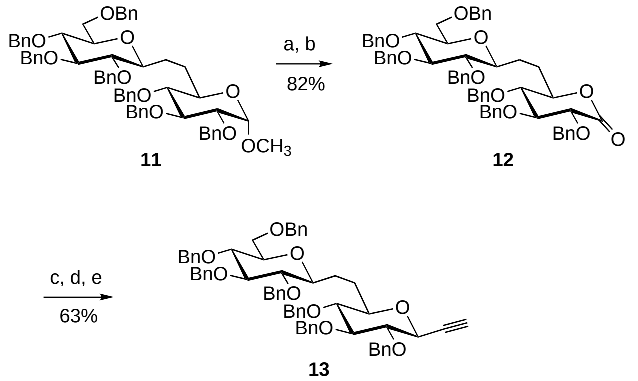


and boron trifluoride etherate ($Et_3SiH/BF_3 \cdot Et_2O$), and cleavage of the TMS group with sodium hydroxide.[6, 7] The α-linked derivatives **5**–**7** were also obtained as described previously,[7] by *C*-glycosidation (ethynylation) of the corresponding sugar acetates using tributylstannyl(trimethylsilyl)-ethyne (nBu$_3$SnC≡CSiMe$_3$) in the presence of trimethylsilyl triflate (TMSOTf), followed by desilylation. The 1-propynyl *C*-glucoside **8** was synthesized in high yield (90%) in one step by methylation of the lithio derivative of **1** using methyl triflate as the alkylating agent.[8] The stereointegrity of the β-linkage at the pseudoanomeric center of **8**, as in the precursor *C*-glycoside **1**, was confirmed by ^{1}H NMR spectroscopy; the signal of the pseudoanomeric proton (4-H), observed at δ = 4.06 ppm, shows a coupling constant of $J_{4,5} = 9.5$ Hz, which is typical for a *trans*-diaxial arrangement. The bisglycosylated ethyne **10** was also prepared in good yield (52%) in a straightforward manner by addition of the lithio derivative of **1** to the gluconolactone **9** and deoxygenation with $Et_3SiH/BF_3 \cdot Et_2O$ (Scheme 1). The β-linkage at the anomeric centers of the two glycoside residues was again confirmed by the vicinal coupling constant of the anomeric proton (9.2 Hz).



Scheme 1. Synthesis of **10**. a) BuLi, THF, −70 °C, 1.5 h; b) Et_3SiH, $BF_3 \cdot Et_2O$, CH_3CN/CH_2Cl_2, −10 °C, 1 h.

The synthesis of the ethynyl *C*-gentiobioside **13** was more laborious because it involved the stereoselective formation of two *C*-glycosidic bonds, one in the assembly of the two sugar residues, and the other in installing the ethynyl group into the resulting *C*-disaccharide. The methyl *O*-glycoside **11** (Scheme 2) had already been prepared in one of our



Scheme 2. Synthesis of **13**. a) AcOH, H_2SO_4, 100 °C, 75 min; PCC, CH_2Cl_2, RT, 1 h; c) TMS-ethyne, BuLi, $CeCl_3$, THF, −78 °C, 2 h; d) Et_3SiH, $BF_3 \cdot Et_2O$, CH_3CN/CH_2Cl_2, −10 °C, 1 h; e) aq. NaOH, CH_3OH/THF, RT, 1 h.

laboratories by Wittig coupling of a sugar aldehyde and a sugar phosphorane.[9] Acid-catalyzed hydrolysis of the anomeric methoxy group in **11**, followed by oxidation of the corresponding hemiacetal with pyridinium chlorochromate (PCC) afforded the *C*-gentiobionolactone **12** in very good overall yield (82%). The ethynyl group was introduced by following the same reaction sequence as employed for the ethynylation of monosaccharides, that is addition of cerium TMS-acetylide, deoxygenation with $Et_3SiH/BF_3 \cdot Et_2O$, and desilylation with NaOH. Compound **13** was obtained in 63% overall yield according to this three-step reaction sequence. The β-linkage at the anomeric center of **13** was confirmed by the vicinal coupling constant of $J = 9.7$ Hz for the signal at δ = 3.96 ppm attributable to the pseudoanomeric proton (3-H).

Synthesis of carboranyl *C*-glycosides: To prepare the carboranyl *C*-glycosides, decaborane(14) ($B_{10}H_{14}$) was heated in acetonitrile under reflux for 1 h to give the $B_{10}H_{12} \cdot 2CH_3CN$ adduct,[10] which was then treated with the ethynyl *C*-glycosides **1, 5**–**8**, **10**, and **13** in toluene to give the benzyl-protected carboranyl *C*-glycosides **14**–**19** in moderate to excellent

Abstract in German: *Die Synthese der neuartigen ungeschützten Carboranyl-C-Glycoside **2** und **20**–**24** ausgehend von Ethinyl-C-Glycosiden wie **1, 5**–**8, 10** und **13** wird beschrieben. Die neuen Verbindungen sind wasserlöslich und zeigen eine nur sehr geringe Cytotoxizität, was sie zu vielversprechenden Kandidaten für den Einsatz in der Bor-Neutroneneinfang-Tumortherapie macht.*

Abstract in Italian: *Viene descritta la sintesi di una nuova serie di carboranil C-glicosidi deprotetti **2** e **20**–**24** a partire dagli etinil C-glicosidi **1, 5**–**8, 10** e **13**. I nuovi composti oltre ad essere molto solubili in acqua mostrano una bassa citossicità così che si presentano come promettenti candidati nella terapia del cancro basata sulla cattura di neutroni da parte del boro.*

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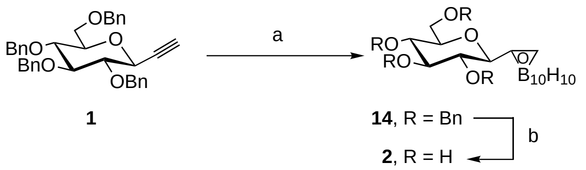
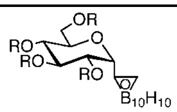
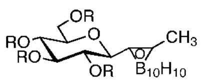
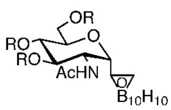
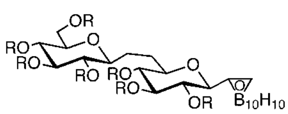
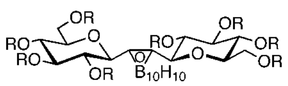
yields depending on the substituents in the vicinity of the triple bond. Thus, starting from the β-ethynyl *C*-glucoside **1**, the yield of the corresponding carborane **14** was 92% (Scheme 3), whereas the C_2-symmetric carborane **19** was obtained in only 13% yield from ethynyl bisglucoside **10** due to the steric demand of the two sugar moieties. Ethynyl *C*-glycosides with terminal triple bonds such as **1**, **5**, **6**, and **13** gave consistently higher yields (64–92%) as compared to the acetylenes **8** and **10** with internal triple bonds (13–31%). Astoundingly, in the case of the acetyl amide **6**, protection of the acidic amide NH, as reported in our previous work,[3e] was not necessary and the corresponding carborane **17** was obtained in 73% yield. In contrast, starting from azide **7**, no carborane was obtained, presumably due to the thermal instability of the azido group (Table 1).



Scheme 3. Synthesis of **2**. a) $B_{10}H_{14}$, CH_3CN, reflux 30–60 min; then **1** in toluene, reflux, 16–18 h, 92%; b) $Pd(OH)_2/C$, H_2 (2–3 bar), MeOH/EtOAc, RT, 5–8 h, 81%.

Debenzylation was carried out by hydrogenation under elevated H_2 pressure (2–3 bar) in the presence of Pearlman's catalyst[11] ($Pd(OH)_2$ on activated charcoal). The deprotected carboranyl *C*-glycosides **2**, **20**–**24** were obtained in good yields in every case (Table 1). The novel compounds **2**, **20**–**24** could not be purified by column chromatography due to partial degradation under the conditions employed. This decomposition also occurred on standing for several days in MeOH. Therefore, the crude products obtained by removal of the catalyst and evaporation of the solvents were merely washed with Et_2O to give satisfactory purities.

Table 1. Structures and yields of the carboranyl *C*-glycosides and -bisglycosides. Reaction conditions for carborane formation and debenzylation were similar to those given in Scheme 3.

Starting	Structures of the carboranes obtained	Yield [%] after carborane formation (R = Bn)	Yield [%] after hydrogenation (R = H)
5		**15**, 68	**20**, 82
8		**16**, 31	**21**, 61
7	decomp		
6		**17**, 73	**22**, 75
13		**18**, 64	**23**, 69
10		**19**, 13	**24**, quant.

Structure determination of the carboranyl *C*-glycosides: The structures of the new compounds were determined by means of ^{1}H and ^{13}C NMR spectroscopy (1D and 2D experiments) and mass spectrometry. As is typical for carboranes, a broad signal due to the ten protons attached to boron atoms is seen at $\delta = 0.5–4.0$ ppm in the ^{1}H NMR spectra. Furthermore, the IR spectra of the novel carboranes feature the typical strong B–H stretching signal at approximately 2590 cm^{-1}. The prepared boron compounds contain the natural isotopic distribution of boron. In the mass spectra of the new compounds, a broad assembly of peaks is therefore detected, together with the peak of highest intensity, which correlates to the most abundant $^{10}B/^{11}B$ ratio. As proven by NMR experiments on the compounds obtained, upon addition of $B_{10}H_{14}$ to the triple bond of the ethynyl *C*-glycosides and subsequent deprotection, the configuration at the pseudoanomeric center is not affected. The β-linkage at the anomeric centers of the carboranyl *C*-glycosides **2**, **14**, **16**, **18**, **19**, **21**, **23**, and **24** was also confirmed by the large values (9.0–10.0 Hz) of the vicinal coupling constant of the doublets attributable to the anomeric protons, as is typical for a *trans*-diaxial arrangement. In contrast, the α-linkage at the pseudoanomeric centers of compounds **15**, **17**, **20**, and **22** was indicated by the low *J* values (1.0–2.0 Hz) observed for the signals of the anomeric protons due to an equatorial–axial arrangement. The C–*H* of the carborane moiety of *C*-glycosides with monosubstituted carboranes gives rise to a characteristic broad singlet at around $\delta = 4.0$ in the ^{1}H NMR spectra. In the case of the C_2 symmetric bisglucosides **10**, **19**, and **24**, with an internal triple bond or carborane moiety, two equivalent carbons give rise to just one signal in the ^{13}C NMR spectra.

In vitro cytotoxicity tests: The cytotoxicities of the novel carboranyl *C*-glycosides **2** and **20**–**23** were determined using the MTT test.[12] This test is based on the irreversible reduction of the yellow tetrazolium salt 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) into a dark blue, water-insoluble but alcohol-soluble formazane derivative by mitochondrial dehydrogenases of viable cells. MTT is taken up by viable cells and then reduced. The concentration of the resulting blue formazane derivative is measured with a photometer after cell lysis. The optical density of the blue formazane derivative is proportional to the fraction of the living, metabolically active cells.[12]

In vitro studies with the new compounds were carried out on four different cell lines: on human bronchial carcinoma cells of line A 549,[13] on murine melanoma cells of line B-16, on human pancreas carcinoma cells of line PancTu 1,[14] and on colonrectal human adeno carcinoma cells of line LoVo.[15]

The results of these in vitro studies are presented in Table 2 and Figure 1. The β- and α-carboranyl *C*-glucosides **2** and **20**, with ED_{50} values in the range 227–482 µM (ED_{50} = drug concentration required for 50% effect on target cells), show only a low cytotoxicity. The ED_{50} values for the methylcarborane **21** and acetamide **22** are slightly lower, falling in the

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Table 2. Cytotoxicities of carboranyl *C*-glycosides **2** and **20**–**23** as well as hydroxymethylcarborane **25**.

	R^1	R^2	R^3	ED_{50} Values [μM]			
				A 549	B-16	PancTu 1	Lovo
2	*β*-carboranyl	OH	OH	379	472	355	410
20	*α*-carboranyl	OH	OH	482	–[b]	236	227
21	*β*-carboranylmethyl	OH	OH	178	203	198	199
22	*α*-carboranyl	NHAc	OH	291	> 124	278	222
23	*β*-carboranyl	OH	X[a]	> 1100	> 1100	> 1100	> 1100
25[16]	–	–	–	78	–[b]	–[b]	–[b]

[a] X = methylene-*β*-D-*C*-glucosyl. [b] Not determined.

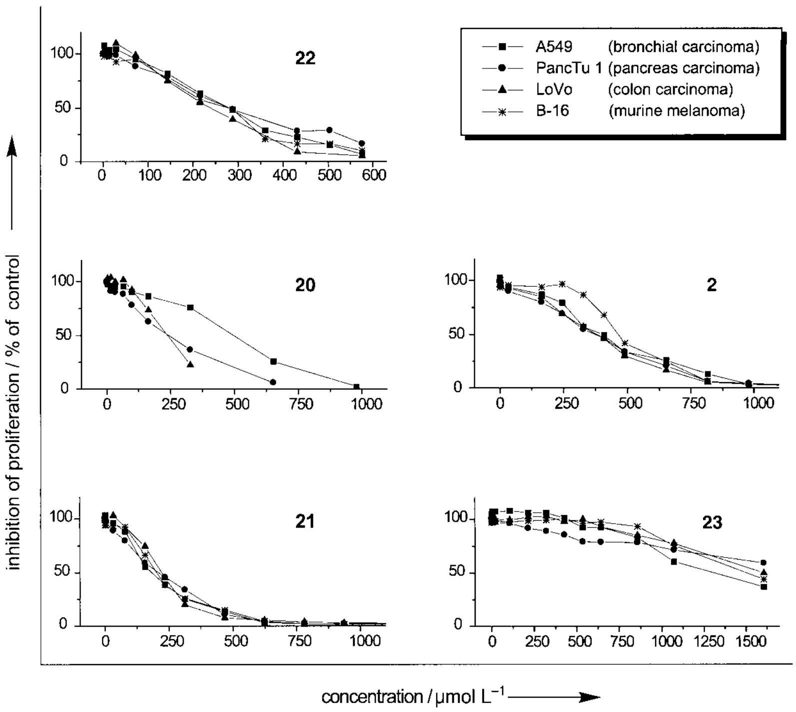
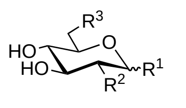
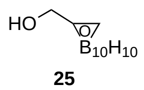


Figure 1. Inhibition of proliferation on different cell lines by the novel carboranyl *C*-glycosides **2** and **20**–**23**.

range > 124–293 μM. With ED_{50} values greater than 1.1 mM with all four cell lines, carboranyl *C*-gentiobiose **23** displays the lowest cytotoxicity among the carboranes investigated. In comparison, hydroxymethylcarboranes such as **25**, which we have investigated in our previous work,[3] have a significantly higher toxicity. For example, an ED_{50} value of 78 μM was measured in the case of **25**[3c, 16] (Table 2, Figure 1).





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In conclusion, we have prepared several novel *C*-glycosidic carboranes by way of a short and convenient synthesis from the corresponding alkynes. As shown by an MTT cytotoxicity assay, this new class of compounds displays lower cytotoxicities and an increased water solubility compared to simple carborane derivatives such as hydroxymethylcarborane **25**. The biological properties of the carboranyl *C*-glycosides make them promising candidates for use in boron neutron capture therapy for the treatment of cancer.

Experimental Section

Synthesis of the *C*-glycosides: general: All moisture-sensitive reactions were performed under a nitrogen or argon atmosphere using oven-dried glassware. Anhydrous solvents were dried over standard drying agents[17] and were freshly distilled prior to use. Commercially available powdered 4 Å molecular sieves (average particle size 5 mm) was used without further activation. Reactions were monitored by TLC on silica gel 60 F_{254} with detection using sulfuric acid alone or in conjunction with vanillin. Flash column chromatography[18] was performed on silica gel 60 (230–400 mesh). The sugar lactone **9**[19] was prepared by oxidation of the corresponding hemiacetal with pyridinium chlorochromate.[20]

Melting points were determined with a capillary apparatus and are uncorrected. Optical rotations were measured at 20 ± 2 °C in the stated solvent; $[\alpha]_D^{20}$ values are given in 10^{-1} deg cm² g⁻¹. IR spectra were recorded on a Bruker Vector 22 spectrometer. ^1H and ^{13}C NMR spectra were recorded on Varian XL-200, Unity 300, Inova 500, Unity Inova 600, and Bruker AMX 300 spectrometers, at room temperature unless otherwise specified; chemical shifts are quoted in ppm (*δ*) from $SiMe_4$ (TMS) as an internal standard; assignments were aided by homo- and heteronuclear two-dimensional experiments. Signals marked with an asterisk (*) could not be assigned with certainty. In the ^1H NMR data listed below, the *n* and *m* values quoted for geminal or vicinal proton-proton coupling constants $J_{n,m}$ denote the number of corresponding sugar protons, where applicable. Mass spectra were measured on a Finnigan MAT 95 spectrometer. MALDI-TOF mass spectra were acquired using *α*-cyano-4-hydroxycinnamic acid as the matrix. Elemental analysis was carried out in the analytical laboratories of the universities of Göttingen and Ferrara.

4,8-Anhydro-5,6,7,9-tetra-*O*-benzyl-1,2,3-trideoxy-D-*glycero*-L-*manno*-non-2-ynitol (8): A stirred solution of **1** (549 mg, 1.00 mmol) in anhydrous THF (10 mL) was cooled to −50 °C, whereupon butyllithium (1.25 mL, 2.00 mmol, 1.6 M solution in hexane) was added dropwise. Stirring was continued at −50 °C for 10 min, and then methyl trifluoromethanesulfonate (340 μL, 3.00 mmol) was added. After an additional 30 min at −50 °C, the reaction mixture was diluted with 1 M phosphate buffer at pH 7 (20 mL), allowed to warm to room temperature, and extracted with Et_2O (2 × 100 mL). The combined organic phases were dried (Na_2SO_4) and concentrated. The residue was chromatographed on a column of silica gel eluting with cyclohexane/EtOAc (9:1) to give **8** (506 mg, 90 %) as a syrup. $[\alpha]_D^{20}$ = +1.5° (*c* = 1.2, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6): *δ* = 1.42 (d, 3 H; 1-H), 3.24 (ddd, 1 H; 8-H), 3.64 (dd, $J_{8,9b}$ = 2.0 Hz, 1 H; 9b-H), 3.66 (dd, $J_{5,6}$ = 9.0 Hz, 1 H; 5-H), 3.68 (dd, $J_{8,9a}$ = 3.5, $J_{9a,9b}$ = 10.8 Hz, 1 H; 9a-H), 3.78 (dd, $J_{7,8}$ = 9.7, $J_{6,7}$ = 8.9 Hz, 1 H; 7-H), 4.06 (dq, $J_{4,5}$ = 9.5, $J_{1,4}$ = 2.0 Hz, 1 H; 4-H), 4.34 and 4.47 (2 d, *J* = 12.0 Hz, 2 H; PhCH_2), 4.60 and 4.86 (2 d, *J* = 11.1 Hz, 2 H; PhCH_2), 4.80 and 4.91 (2 d, *J* = 11.5 Hz, 2 H; PhCH_2), 4.82 and 5.05 (2 d, *J* = 11.0 Hz, 2 H; PhCH_2), 7.02–7.40 ppm (m, 20 H; 4 Ph); ^{13}C NMR (75 MHz, C_6D_6): *δ* = 3.2 (C-1), 69.4 (C-9), 70.7 (C-4), 73.6, 74.9, 75.3, and 75.5 (4 PhCH_2), 78.2 (C-7), 79.4 (C-8), 77.8 and 82.0 (C-2, C-3), 83.2 (C-5), 86.4 (C-6), 127.6–128.4, 138.9, 139.2, 139.3, and 139.5 ppm (Ph); elemental

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analysis (%) calcd for $C_{37}H_{38}O_5$ (562.7): C 76.98, H 6.81; found: C 77.20, H 6.71.

1,2-Bis(2′,3′,4′,6′-tetra-*O*-benzyl-*β*-D-glucopyranosyl)ethyne (10): A stirred solution of **1** (200 mg, 0.36 mmol) in anhydrous THF (3.6 mL) was cooled to −70 °C, whereupon butyllithium (0.25 mL, 0.40 mmol, 1.6 M solution in hexane) was added dropwise. Stirring was continued at −70 °C for 15 min, and then a solution of lactone **9** (194 mg, 0.36 mmol) in anhydrous THF (3.6 mL) was added. After a further 1.5 h at −70 °C, the reaction mixture was diluted with 1 M phosphate buffer at pH 7 (20 mL), allowed to warm to room temperature, and extracted with CH_2Cl_2 (2 × 100 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to afford the hemiacetal as a mixture of anomers. A stirred mixture of the crude hemiacetal, activated 4 Å powdered molecular sieves (0.36 g), and triethylsilane (240 mL, 1.49 mmol) in anhydrous CH_3CN (6.5 mL) and CH_2Cl_2 (2.5 mL) was cooled to −10 °C, and then freshly distilled $BF_3 \cdot Et_2O$ (180 µL, 1.40 mmol) was added dropwise. Stirring was continued at −10 °C for 1 h, and then the mixture was diluted with Et_3N (0.6 mL) and CH_2Cl_2 (50 mL), filtered through a pad of Celite, and concentrated. The residue was chromatographed on a column of silica gel eluting with cyclohexane/EtOAc (12:1 → 5:1) to give **10** (200 mg, 52%) as a white solid; m.p. 89–90 °C (cyclohexane/pentane); $[\alpha]_D^{20} = -20.5°$ ($c = 1.3$, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6): $\delta = 3.21$ (ddd, 2H; 2 5′-H), 3.50 (dd, 2H; 2 3′-H), 3.60 (dd, $J_{5',6'b} = 1.8$ Hz, 2H; 2 6′b-H), 3.65 (dd, $J_{6'a,6'b} = 11.2$, $J_{5',6'a} = 3.6$ Hz, 2H; 2 6′a-H), 3.68 (dd, $J_{2',3'} = 9.1$ Hz, 2H; 2 2′-H), 3.74 (dd, $J_{4',5'} = 9.8$, $J_{3',4'} = 8.7$ Hz, 2H; 2 4′-H), 4.08 (d, $J_{1',2'} = 9.2$ Hz, 2H; 2 1′-H), 4.30 and 4.42 (2d, J = 12.1 Hz, 4H; 2 PhCH_2), 4.56 and 4.82 (2d, J = 11.4 Hz, 4H; 2 PhCH_2), 4.78 and 4.90 (2d, J = 11.5 Hz, 4H; 2 PhCH_2), 4.84 and 5.19 (2d, J = 11.0 Hz, 4H; 2 PhCH_2), 7.03–7.32 and 7.47–7.53 ppm (2m, 40H; 8 Ph); ^{13}C NMR (75 MHz, C_6D_6): $\delta = 69.3$ (2 C-6′), 70.4 (2 C-1′), 74.9, 75.4, and 77.9 (8 PhCH_2), 79.6 (2 C-5′), 82.5 (2 C-2′), 84.0 (C-1, C-2), 86.3 (2 C-3′), 127.7–128.7, 138.8, 138.9, 139.2, and 139.5 ppm (Ph); MS (MALDI-TOF): m/z: 1095.6 [M+H+Na], 1111.8 [M+H+K]; elemental analysis (%) calcd for $C_{70}H_{70}O_{10}$ (1071.3): C 76.48, H 6.59; found: C 76.31, H 6.74.

8,12-Anhydro-2,3,4,9,10,11,13-hepta-*O*-benzyl-6,7-dideoxy-D-*glycero*-D-*gulo*-D-*gluco*-tridecopyranolactone (12): A stirred solution of **11** (450 mg, 0.46 mmol) in acetic acid (18 mL) was heated to 100 °C, and then 1 M aqueous H_2SO_4 (1.8 mL) was added dropwise. The solution was stirred at 100 °C for a further 75 min, and then cooled to room temperature, diluted with CH_2Cl_2 (100 mL), and washed with saturated aqueous Na_2CO_3 solution (5 × 20 mL). The organic phase was dried (Na_2SO_4) and concentrated. The residue was chromatographed on a column of silica gel eluting with cyclohexane/EtOAc (8:1 → 4:1) to give the disaccharidic hemiacetal as an approximately 1:1 mixture of anomers (370 mg). A mixture of this product, activated 4 Å powdered molecular sieves (0.38 g), and anhydrous CH_2Cl_2 (3.8 mL) was stirred at room temperature for 15 min, and then pyridinium chlorochromate (410 mg, 1.90 mmol) was added in one portion. The mixture was vigorously stirred at room temperature for 60 min until the starting material had been consumed (TLC analysis), and then diluted with cyclohexane (3.8 mL) and Et_2O (7.6 mL) to precipitate the chromium salts. Stirring was continued for a further 10 min, and then the brown suspension was filtered through a pad of silica gel (5 × 4 cm). Further elution with Et_2O/cyclohexane (2:1; ca. 100 mL) gave **12** as a white solid (363 mg, 82%); m.p. 117–119 °C (cyclohexane); $[\alpha]_D^{20} = +36.3°$ ($c = 0.9$, $CHCl_3$); ^1H NMR (300 MHz, C_6D_6): $\delta = 1.52$–1.62 (m, 1H; 7b-H), 1.65–1.75 (m, 1H; 6b-H), 2.12–2.23 (m, 2H; 6a-H, 7a-H), 3.20–3.27 (m, 2H), 3.38 (dd, $J_{4,5} = 8.4$ Hz, 1H; 4-H), 3.34–3.40 (m, 1H), 3.65–3.79 (m, 4H), 3.83 (dd, $J_{3,4} = 5.3$ Hz, 1H; 3-H), 4.10 (d, $J_{2,3} = 5.4$ Hz, 1H; 2-H), 4.38 and 4.46 (2d, J = 12.1 Hz, 2H; PhCH_2), 4.39–4.45 (m, 1H; 5-H), 4.28 and 4.47 (2d, J = 11.5 Hz, 2H; PhCH_2), 4.32 and 4.51 (2d, J = 11.5 Hz, 2H; PhCH_2), 4.50 and 4.84 (2d, J = 11.3 Hz, 2H; PhCH_2), 4.54 and 4.93 (2d, J = 11.8 Hz, 2H; PhCH_2), 4.65 and 4.90 (2d, J = 11.4 Hz, 2H; PhCH_2), 4.90 (s, 2H; PhCH_2), 7.02–7.36 ppm (m, 35H; 7 Ph); elemental analysis (%) calcd for $C_{62}H_{64}O_{10}$ (969.2): C 76.84, H 6.66; found: C 76.60, H 6.92.

3,7:10,14-Dianhydro-4,5,6,11,12,13,15-hepta-*O*-benzyl-1,2,8,9-tetradeoxy-D-*erythro*-L-*talo*-D-*gulo*-pentadec-1-ynitol (13): Commercially available $CeCl_3 \cdot 7H_2O$ (261 mg, 0.70 mmol) was heated in a reaction flask at 120 °C/0.1 mbar for 1 h and at 140 °C/0.1 mbar for 1 h, and then cooled to 0 °C under an argon atmosphere. It was taken up in anhydrous THF (2.8 mL), the suspension was stirred at room temperature for 2 h, and then cooled to −78 °C. Meanwhile, a stirred solution of commercially available trimethylsilylacetylene (122 µL, 0.88 mmol) in anhydrous THF (1 mL) was cooled to −78 °C, and then butyllithium (0.55 mL, 0.88 mmol, 1.6 M solution in hexane) was slowly added. The resulting solution was stirred at −78 °C for 45 min, and then transferred via a cannula into the stirred suspension of $CeCl_3$ in THF, prepared immediately prior to use as described above. The yellow mixture obtained was stirred at −78 °C for 30 min, and then a solution of lactone **12** (336 mg, 0.35 mmol) in anhydrous THF (2.5 mL) was added dropwise. The mixture was stirred at −78 °C for an additional 2 h, then diluted with 0.1 M HCl (4 mL), allowed to warm to room temperature, and extracted with Et_2O (3 × 50 mL). The combined organic layers were dried (Na_2SO_4) and concentrated to give the disaccharidic hemiacetal as an approximately 1:1 mixture of anomers. A stirred mixture of the hemiacetal, activated 4 Å powdered molecular sieves (0.35 g), and triethylsilane (232 µL, 1.45 mmol) in anhydrous CH_3CN (6 mL) and CH_2Cl_2 (2 mL) was cooled to −10 °C, and then freshly distilled $BF_3 \cdot Et_2O$ (174 µL, 1.37 mmol) was added dropwise. Stirring was continued at −10 °C for a further 1 h, and then the mixture was diluted with Et_3N (0.6 mL) and CH_2Cl_2 (50 mL), filtered through a pad of Celite, and concentrated. A solution of the residue in CH_2Cl_2 (100 mL) was washed with H_2O, dried (Na_2SO_4), and concentrated. A solution of the crude silylated *C*-disaccharide in CH_3OH/THF (1:1; 12 mL) was treated with 1 M NaOH (0.7 mL) for 1 h at room temperature, then neutralized with 1 M HCl, and concentrated to remove the organic solvents. The residue was diluted with CH_2Cl_2 (100 mL), and this solution was washed with H_2O, dried (Na_2SO_4), and concentrated. The residue was chromatographed on a column of silica gel eluting with CH_2Cl_2/Et_2O (40:1 → 30:1) to afford **13** (213 mg, 63%) as a white solid; m.p. 178–180 °C (EtOAc/cyclohexane); $[\alpha]_D^{20} = +7.4°$ ($c = 1.0$, $CHCl_3$); selected ^1H NMR data (300 MHz, C_6D_6): $\delta = 1.99$ (d, 1H; 1-H), 1.63–1.69 and 2.25–2.29 (2m, 4H; 2 8-H, 2 9-H), 3.18–3.29 (m, 4H), 3.34–3.40 (m, 1H), 3.45–3.51 (m, 3H), 3.66–3.72 (m, 3H), 3.76 (dd, $J_{4,5} = 8.8$, $J_{5,6} = 9.7$ Hz, 1H; 5-H), 3.96 ppm (dd, 1H, $J_{1,3} = 2.2$, $J_{3,4} = 9.7$ Hz; 3-H); elemental analysis (%) calcd for $C_{64}H_{66}O_9$ (979.2): C 78.50, H 6.79; found: C 78.72, H 6.61.

Synthesis of the perbenzylated carboranyl *C*-glycosides: general procedure: Decaborane(14) ($B_{10}H_{14}$, 1.3–1.4 equivalents with respect to the alkyne as the starting material) was heated in refluxing CH_3CN (2 mL per mmol of the alkyne) for 30 min, in the course of which the solution turned yellow, indicating the formation of the adduct $B_{10}H_{12} \cdot 2CH_3CN$. A solution of the alkyne in toluene (2 mL per mmol) was then added and heating was continued for 16–18 h. For work-up, MeOH (1 mL) was added, the mixture was heated to reflux for 30 min, cooled to room temperature, and concentrated in vacuo. Baseline impurities were removed by filtration through a short plug of silica with EtOAc as eluent. The pure products were obtained by column chromatography using *n*-pentane/EtOAc (15:1) as the eluent.

(2*R*,3*R*,4*R*,5*S*,6*S*)-3,4,5-Tris(benzyloxy)-2-benzyloxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylethyl)tetrahydropyran (14): 92% from **1**, colorless solid; R_f (*n*-pentane/EtOAc, 15:1) = 0.52; $[\alpha]_D^{20} = +32.0°$ ($c = 0.2$, $CHCl_3$); IR (KBr): $\tilde{\nu}$ = 2866, 2584 (B–H), 1362, 1098 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 205.0 (4.462), 257.5 nm (2.930); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.00$–3.20 (brs, 10H; BH), 3.42 (ddd, J = 9.3, 3.7, 3.2 Hz, 1H; 2-H), 3.54 (dd, J = 9.2, 8.0 Hz, 1H; 4-H), 3.59–3.69 (m, 3H; 5-H, CH_2OBn), 3.72 (dd, J = 9.3, 8.0 Hz, 1H; 3-H), 3.79 (d, J = 9.4 Hz, 1H; 6-H), 4.09 (brs, 1H; carborane-CH), 4.52 (s, 2H; PhCH_2OCH_2), 4.62 and 4.76 (2d, J = 10.8 Hz, 2H; PhCH_2), 4.72 and 5.02 (2d, J = 11.0 Hz, 2H; PhCH_2), 4.77 and 4.98 (2d, J = 11.4 Hz, 2H; PhCH_2), 7.16–7.39 ppm (m, 20H; 4 Ph); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 59.42$ (carborane-*C*H), 68.14 (CH_2OBn), 73.09 (PhCH_2OCH_2), 73.61 (PhCH_2), 74.76 (carborane-C-1′), 74.94 (PhCH_2), 75.26 (PhCH_2), 77.64 (C-5), 77.88 (C-6), 79.01 (C-2), 79.97 (C-4), 87.31 (C-3), 127.3–128.5, 137.4, 137.6, 137.8, 137.9 (Ph); MS (DCI): m/z (%): 685 (100) [M+NH_4]$^+$; elemental analysis (%) calcd for $C_{36}H_{46}B_{10}O_5$ (666.9): C 64.84, H 6.95; found: C 64.72, H 6.82.

(2*R*,3*R*,4*R*,5*S*,6*R*)-3,4,5-Tris(benzyloxy)-2-benzyloxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)yl-ethyl)tetrahydropyran (15): 68% from **5**, colorless oil; R_f (*n*-pentane/EtOAc, 15:1) = 0.35; $[\alpha]_D^{20} = +24.2°$ ($c = 0.6$, $CHCl_3$); IR (film): $\tilde{\nu}$ = 3031 (C–H), 2865, 2582 (B–H), 1497, 1454, 1362, 1095 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 191.0 (5.124), 205.5 (4.477), 257.5 nm (2.914); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.00$–3.20 (brs, 10H; BH), 3.58 (dd, J = 10.6, 4.0 Hz, 1H; CH_aH_bOBn), 3.61–3.73 (m, 3H; 3-H, 5-H, CH_aH_bOBn), 3.85 (dd, J = 3.8, 2.7 Hz, 1H; 4-H), 4.08–4.17 (m, 2H; carborane-C*H*, 2-H), 4.35 (d, J = 1.8 Hz, 1H; 6-H), 4.36 and 4.54 (2d, J = 10.8 Hz, 2H; PhCH_2), 4.46–4.53 (m, 6H; 3 PhCH_2), 7.19–7.41 ppm (m, 20H; 4 Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 58.10$ (carborane-*C*H), 68.50 (*C*H$_2$OBn), 71.37 (C-6), 71.76, 72.05, 72.69, 73.16 (4 Ph*C*H$_2$), 74.45 (C-5*), 74.97 (carborane-C-1′), 75.28, 76.08, 76.31 (C-2, C-3, C-4*), 127.4 – 128.7, 136.6, 137.1, 137.8, 138.0 ppm (Ph); MS (DCI): *m*/*z* (%): 685 (100) $[M+NH_4]^+$, 594 (20) $[M-Bn+NH_4]^+$; $C_{36}H_{46}B_{10}O_5$ (666.9).

(2*R*,3*R*,4*R*,5*S*,6*S*)-3,4,5-Tris(benzyloxy)-2-benzyloxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylpropyl)tetrahydropyran (16): 31% from **8**, colorless solid; R_f (*n*-pentane/EtOAc, 12:1) = 0.29; $[\alpha]^{20}_D = +23.9°$ (*c* = 0.6, $CHCl_3$); IR (film): $\tilde{\nu} = 3031$, 2868, 2582 (B – H), 1736, 1497, 1362, 1097 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 191.0 (4.958), 251.5 (2.768), 257.0 nm (2.785); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.00 - 3.20$ (brs, 10H; BH), 1.96 (s, 3H; CH_3), 3.42 (ddd, *J* = 9.3, 4.1, 3.1 Hz, 1H; 2-H), 3.65 – 3.71 (m, 5H; C*H*$_2$OBn, 3-H, 5*-H, 6-H), 3.72 (ddd, *J* = 9.0, 5.8, 1.5 Hz, 1H; 4*-H), 4.46 and 4.57 (2d, *J* = 12.2 Hz, 2H; PhC*H*$_2$OCH$_2$), 4.62 and 4.77 (2d, *J* = 11.0 Hz, 2H; PhC*H*$_2$), 4.74 and 5.01 (d, *J* = 10.9 Hz, 1H; PhC*H*$_2$), 4.76 and 4.98 (2d, *J* = 11.0 Hz, 2H; PhC*H*$_2$), 7.18 – 7.38 ppm (m, 20H; 4 Ph); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 23.27$ (CH_3), 68.63 (*C*H$_2$OBn), 73.31 (Ph*C*H$_2$OCH$_2$), 73.43, 74.73 (2 Ph*C*H$_2$), 74.79 and 78.15 (carborane-C), 75.05 (Ph*C*H$_2$), 76.86 (C-5), 77.54 (C-6), 79.26 (C-2), 79.62 (C-4), 87.37 (C-3), 127.3 – 128.5, 137.6, 137.7, 137.9, 138.0 ppm (Ph); MS (DCI): *m*/*z* (%): 699 (100) $[M+NH_4]^+$; elemental analysis (%) calcd for $C_{37}H_{48}B_{10}O_5$ (680.9): C 65.27, H 7.11; found: C 65.42, H 7.01.

(2*R*,3*S*,4*R*,5*R*,6*R*)-*N*-[4,5-Bis(benzyloxy)-6-benzyloxymethyl-2-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)yl-ethyl)tetrahydropyran-3-yl]acetamide (17): 73% from **6**, colorless oil; R_f (toluene/acetone, 10:1) = 0.37; $[\alpha]^{20}_D = -19.0°$ (*c* = 0.5, $CHCl_3$); IR (film): $\tilde{\nu} = 3424$ (N – H), 3032, 2920 (C – H), 2579 (B – H), 1660 (C=O), 1454, 1030 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 192.5 nm (5.079), 251.5 (3.176), 257.0 (3.206); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.00 - 3.20$ (brs, 10H; BH), 1.83 (s, 3H; CH_3 of NAc), 3.33 (brs, 1H; 5-H*), 3.49 (dd, *J* = 10.4, 6.2 Hz, 1H; C*H*$_a$H$_b$OBn), 3.73 (brs, 1H; 4-H*), 3.83 (dd, *J* = 10.4, 8.2 Hz, 1H; CH$_a$*H*$_b$OBn), 4.01 (brs, 1H; carborane-C*H*), 4.28 – 4.23 (m, 3H; 2-H, 3-H, PhC*H*), 4.39 – 4.53 (m, 5H; 6-H, PhC*H*$_2$OCH$_2$, 2 PhC*H*), 4.64 (d, *J* = 11.9 Hz, 1H; PhC*H*), 6.26 (d, *J* = 10.1 Hz, 1H; NH), 7.14 – 7.40 ppm (m, 15H; 3 Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 23.25$ (*C*H$_3$ of NAc), 46.82 (C-3), 58.16 (carborane-CH), 66.35 (*C*H$_2$OBn), 67.67 (C-2), 71.69 (Ph*C*H$_2$), 72.42 (Ph*C*H$_2$), 72.64 (C-4*), 73.31 (Ph*C*H$_2$OCH$_2$), 73.46 (carborane-C-1′), 73.92 (C-5*), 77.83 (C-6), 127.7 – 128.6, 136.7, 136.9, 137.8, 137.4 (Ph), 169.8 ppm (C=O); MS (DCI): *m*/*z* (%): 636 (100) $[M+NH_4]^+$, 619 (25) $[M+H]^+$, 547 (25) $[M-Bn+NH_4]^+$, 529 (5) $[M-Bn+H]^+$; $C_{31}H_{43}B_{10}NO_5$ (617.8).

(2a*S*,3a*S*,4a*R*,5a*R*,6a*R*,2b*S*,3b*S*,4b*R*,5b*R*,6b*R*)-2a-(1*C*,2*C*-Dicarba-*closo*-dodecaboran(12)yl-ethyl)-3a,4a,5a-tris(benzyloxy)-6a-{2-[3b,4b,5b-tris(benzyloxy)-6b-benzyloxymethyl-tetrahydropyran-2b-yl]-ethyl}tetrahydropyran (18): 64% from **13**, colorless foam; R_f (*n*-pentane/EtOAc, 5:1) = 0.74; $[\alpha]^{20}_D = +19.4°$ (*c* = 0.5, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3030$ (C – H), 2862, 2577 (B – H), 1454, 1361, 1095 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 191.5 nm (5.331); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.20 - 2.80$ (brs, 10H; BH), 1.45 (m$_c$, 2H; 2″-H$_2$), 1.97 (dt, *J* = 9.0, 2.3 Hz, 1H; 1″-H$_a$), 2.06 – 2.14 (m, 1H; 1″-H$_b$), 3.15 – 3.25 (m, 3H; 5a-H, 6a-H, 3b-H), 3.33 (td, *J* = 9.0, 3.0 Hz, 1H; 2b-H), 3.39 (ddd, *J* = 9.0, 4.4, 2.3 Hz, 1H; 6b-H), 3.49 (dd, *J* = 9.3, 8.4 Hz, 1H; 4a-H), 3.58 (dd, *J* = 9.3, 9.3 Hz, 1H; 3a-H), 3.62 (dd, *J* = 8.8, 8.4 Hz, 1H; 4b-H), 3.64 (m, 1H; C*H*$_a$H$_b$OBn), 3.66 (dd, *J* = 10.8, 2.3 Hz, 1H; CH$_a$*H*$_b$OBn), 3.67 (dd, *J* = 9.0, 8.8 Hz, 1H; 5b-H), 3.75 (d, *J* = 9.3 Hz, 1H; 2a-H), 4.09 (brs, 1H; carborane-CH), 4.48 and 4.54 (2d, *J* = 12.2 Hz, 2H; PhC*H*$_2$), 4.55 and 4.70 (2d, *J* = 10.9 Hz, 2H; PhC*H*$_2$), 4.59 and 4.74 (2d, *J* = 10.9 Hz, 2H; PhC*H*$_2$), 4.60 and 4.81 (2d, *J* = 10.9 Hz, 2H; PhC*H*$_2$), 4.68 and 4.87 (2d, *J* = 10.6 Hz, 2H; PhC*H*$_2$), 4.90 – 4.93 (m, 3H; PhCH$_2$OC*H*$_2$, PhC*H*), 5.01 (d, *J* = 10.9 Hz, 1H; PhC*H*), 7.10 – 7.34 ppm (m, 35H; 7 Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 27.64$, 28.10 (C-1″, C-2″), 59.20 (carborane-*C*H), 69.29 (*C*H$_2$OBn), 73.41, 73.52, 75.02, 75.20, 75.49, 75.57, 76.88 (7 Ph*C*H$_2$), 77.29 (carborane-C-1′), 77.74, 78.64, 78.74, 79.49, 79.74, 80.26, 81.94, 82.20, 87.23, 87.27 (C-2a, C-2b, C-3a, C-3b, C-4a, C-4b, C-5a, C-5b, C-6a, C-6b), 127.3 – 128.6, 137.5, 137.6, 137.8, 137.9, 138.0, 138.1, 138.5 ppm (Ph); MS (ESI): *m*/*z* (%): 1120 (100) $[M+Na]^+$; elemental analysis (%) calcd for $C_{64}H_{76}B_{10}O_9$ (1097.4): C 70.05, H 6.98; found: C 70.36, H 6.75.

(2a*R*,3a*R*,4a*R*,5a*S*,6a*S*,2b*R*,3b*R*,4b*R*,5b*S*,6b*S*)-1,2-Bis[3,4,5-tris(benzyloxy)-2-benzyloxymethyltetrahydropyran-6-yl]-1*C*,2*C*-dicarba-*closo*-dodecaborane(12) (19): 13% from **10**, yellowish wax-like solid; R_f (*n*-pentane/EtOAc, 6:1) = 0.78; $[\alpha]^{20}_D = +33.3°$ (*c* = 0.5, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3031$ (C – H), 2866, 2574 (B – H), 1497, 1454, 1362, 1101 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 191.5 (5.388), 257.0 nm (2.850); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 1.00 - 3.20$ (brs, 10H; BH), 3.48 – 3.67 (m, 10H; 2 C*H*$_2$OBn, 2a-H, 2b-H, 3a-H, 3b-H, 4a-H, 4b-H, 5a-H, 5b-H), 4.14 (d, *J* = 9.0 Hz, 2H; 6a-H, 6b-H), 4.46 (d, *J* = 12.2 Hz, 2H; PhC*H*), 4.53 (d, *J* = 12.2 Hz, 2H; PhC*H*), 4.53 (d, *J* = 11.2 Hz, 2H; PhC*H*), 4.60 (d, *J* = 11.2 Hz, 2H; PhC*H*), 4.61 (d, *J* = 10.9 Hz, 2H; PhC*H*), 4.69 (d, *J* = 10.9 Hz, 2H; PhC*H*), 4.80 (d, *J* = 11.2 Hz, 2H; PhC*H*), 4.90 (d, *J* = 11.2 Hz, 2H; PhC*H*), 7.13 – 7.40 ppm (m, 40H; 8 Ph); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 69.01$ (2 *C*H$_2$OBn), 72.66 (2 Ph*C*H$_2$OCH$_2$), 73.46 (2 Ph*C*H$_2$), 74.34 (2 Ph*C*H$_2$), 74.86 (2 Ph*C*H$_2$), 76.67 (C-5a, C-5b), 77.57 (C-6a, C-6b), 78.98 (C-2a, C-2b), 79.82 (C-4a, C-4b), 80.27 (2 carborane-C), 86.92 (C-3a, C-3b), 127.3 – 128.5, 137.7, 137.8, 137.9, 138.0 ppm (Ph); MS (ESI): *m*/*z* (%): 1212 (100) $[M+Na]^+$; $C_{70}H_{80}B_{10}O_{10}$ (1189.5).

Deprotection of the perbenzylated carboranyl *C*-glycosides: general procedure: The benzylated sugar derivative was dissolved in EtOAc/MeOH (1:5; 1 mL/25 µmol of the *C*-glycoside), $Pd(OH)_2$/C (10%, 1 mg/µmol of the *C*-glycoside) was added, and the resulting mixture shaken under H_2 atmosphere (up to 3 bar) in a Parr apparatus for 5 – 8 h. The progress of the reaction was monitored by TLC. The catalyst was carefully filtered off (*danger of spontaneous combustion when dry!*), the solvents were removed, and the residue was washed with Et_2O to obtain the deprotected compound.

(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-Tris(hydroxy)-2-hydroxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylethyl)tetrahydropyran (2): 81% from **14**, colorless solid; R_f (EtOAc/MeOH, 4:1) = 0.29; $[\alpha]^{20}_D = +11.6°$ (*c* = 0.5, MeOH); IR (KBr): $\tilde{\nu} = 3396$ (O – H), 2916 (C – H), 2581 (B – H), 1339, 1094 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 275.0 nm (1.929); ^{1}H NMR (300 MHz, CD_3OD): $\delta = 1.00 - 3.00$ (brs, 10H; BH), 3.16 (dd, *J* = 9.2, 9.2 Hz, 1H; 5-H), 3.18 – 3.15 (m, 3H; 2-H, 3-H, 4-H), 3.57 (dd, *J* = 12.4, 6.3 Hz, 1H; C*H*$_a$H$_b$OH), 3.71 (d, *J* = 9.2 Hz, 1H; 6-H), 3.84 (dd, *J* = 12.4, 2.0 Hz, 1H; CH$_a$*H*$_b$OH), 4.60 ppm (brs, 1H; carborane-CH); ^{13}C NMR (50 MHz, CD_3OD): $\delta = 61.56$ (carborane-CH), 62.72 (*C*H$_2$OH), 70.83 (C-5), 74.66 (C-3), 76.73 (carborane-C-1′), 79.39 (C-6), 82.02 (C-4), 82.44 ppm (C-2); MS (ESI$^-$): *m*/*z* (%): 612 (10) $[2M-H]^-$, 305 (100) $[M-H]^-$; $C_8H_{22}B_{10}O_5$ (306.4).

(2*R*,3*S*,4*R*,5*R*,6*R*)-3,4,5-Tris(hydroxy)-2-hydroxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylethyl)tetrahydropyran (20): 82% from **15**, colorless solid; R_f (EtOAc/MeOH, 4:1) = 0.10; $[\alpha]^{20}_D = +7.7°$ (*c* = 0.1, MeOH); IR (KBr): $\tilde{\nu} = 3417$ (O – H), 2928 (C – H), 2583 (B – H), 2361, 1384, 1038 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 195.0 nm (3.267); ^{1}H NMR (500 MHz, CD_3OD): $\delta = 1.20 - 3.00$ (brs, 10H; BH), 3.52 (m$_c$, 1H; 3-H*), 3.63 (dd, *J* = 12.0, 4.0 Hz, 1H; C*H*$_a$H$_b$OH), 3.69 (m$_c$, 1H; 5-H), 3.85 (m$_c$, 1H; 4-H*), 3.92 (dd, *J* = 12.0, 8.3 Hz, 1H; C*H*$_a$H$_b$OH), 3.98 – 4.06 (m, 1H; 2-H), 4.34 (d, *J* = 0.9 Hz, 1H; 6-H), 4.70 ppm (brs, 1H; carborane-CH); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 60.32$ (carborane-CH), 60.64 (*C*H$_2$OH), 69.54, 70.43, 71.17, 71.44 (C-3, C-4, C-5, C-6), 76.97 (carborane-C-1′), 82.63 ppm (C-2); MS (ESI$^-$): *m*/*z* (%): 612 (10) $[2M-H]^-$, 351 (100) $[M+EtOH-H]^-$, 306 (80) $[M-H]^-$; $C_8H_{22}B_{10}O_5$ (306.4).

(2*R*,3*S*,4*R*,5*R*,6*S*)-3,4,5-Tris(hydroxy)-2-hydroxymethyl-6-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylpropyl)tetrahydropyran (21): 61% from **16**, colorless solid. R_f (EtOAc/MeOH, 4:1) = 0.16; $[\alpha]^{20}_D = +2.0°$ (*c* = 0.3, MeOH); IR (KBr): $\tilde{\nu} = 3417$ (O – H), 2936 (C – H), 2581 (B – H), 1385, 1092 cm^{-1}; ^{1}H NMR (300 MHz, CD_3OD): $\delta = 1.20 - 3.00$ (brs, 10H; BH), 2.05 (s, 3H; CH_3), 3.17 – 3.15 (m, 4H; 2-H, 3-H, 4-H, 5-H), 3.59 (dd, *J* = 12.0, 6.0 Hz, 1H; C*H*$_a$H$_b$OH), 3.65 (d, *J* = 10.0 Hz, 1H; 6-H), 3.84 ppm (dd, *J* = 12.0, 2.0 Hz, 1H; CH$_a$*H*$_b$OH); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 23.63$ (CH_3), 62.80 (*C*H$_2$OH), 70.91 (C-5), 74.31 (C-3), 76.39 (carborane-C-1′*), 77.89 (C-6), 80.05 (carborane-C-2′*), 80.39, 82.06 (C-2, C-4); MS (ESI$^-$): *m*/*z* (%): 639 (100) $[2M-H]^-$, 319 (20) $[M-H]^-$; $C_9H_{24}B_{10}O_5$ (320.4).

(2*R*,3*R*,4*R*,5*S*,6*R*)-*N*-[4,5-Bis(hydroxy)-6-hydroxymethyl-2-(1*C*,2*C*-dicarba-*closo*-dodecaboran(12)ylethyl)tetrahydropyran-3-yl]acetamide (22): 75% from **17**, colorless solid; R_f (EtOAc/MeOH, 4:1) = 0.09; $[\alpha]^{20}_D = +28.2°$ (*c* = 0.5, MeOH); IR (KBr): $\tilde{\nu} = 3407$ (N – H, O – H), 2925 (C – H), 2584 (B – H), 1656 (C=O), 1384, 1054 cm^{-1}; UV (CH_3CN): λ_{max} (lgε) = 254.0 nm (2.373); ^{1}H NMR (500 MHz, CD_3OD): $\delta = 1.00 - 3.20$ (brs, 10H; BH), 1.99 (s, 3H; CH_3 of NAc), 3.52 (ddd, *J* = 2.6, 1.3, 1.3 Hz, 1H; 4-H*), 3.60 (dd, *J* = 11.9, 4.5 Hz, 1H; C*H*$_a$H$_b$OH), 3.73 (dd, *J* = 2.6, 2.6 Hz, 1H; 5-H*), 3.98 (dd, *J* = 11.9, 9.0 Hz, 1H; CH$_a$*H*$_b$OH), 4.02 – 4.07 (m, 2H; 3-H, 6-H), 4.58 (d, *J* = 1.1 Hz, 1H; 2-H), 4.66 (brs, 1H; carborane-C*H*), 7.47 ppm (d, *J* = 9.9 Hz, 1H; NH); ^{13}C NMR (150 MHz, CD_3OD): $\delta = 23.02$ (*C*H$_3$ of NAc), 51.81

(C-3), 60.11 (CH_2OH), 60.63 (carborane-CH), 68.50, 68.68, 70.94 (C-2, C-4, C-5), 75.98 (carborane-C-1′), 83.88 (C-6), 172.7 ppm (C=O); MS (ESI^-): m/z (%): 694 (50) $[2M-H]^-$, 384 (70) $[M+H_2O+H_2O-H]^-$, 346 (100) $[M-H]^-$; $C_{10}H_{25}B_{10}NO_5$ (347.4).

(2a*S*,3a*R*,4a*S*,5a*S*,6a*R*,2b*S*,3b*S*,4b*R*,5b*S*,6b*R*)-2a-(1*C*,2*C*-Dicarba-*closo*-dodecaboran(12)yl-ethyl)-3a,4a,5a-tris(hydroxy)-6a-{2-[3b,4b,5b-tris(hydroxy)-6b-hydroxymethyltetrahydropyran-2b-yl]ethyl}tetrahydropyran (23): 69% from **18**, colorless solid containing traces of impurities; R_f (EtOAc/MeOH, 4:1) = 0.09; $[\alpha]_D^{20} = +16.5°$ ($c = 0.6$, MeOH); IR (KBr): $\tilde{\nu} = 3406$ (O–H), 2920 (C–H), 2590 (B–H), 1384, 1087 cm^{-1}; ^1H NMR (500 MHz, CD_3OD): $\delta = 1.00-3.00$ (brs, 10H; BH), 1.32–1.48, 2.05–2.20 (2m, 2 × 2H; 1″-H_2, 2″-H_2), 3.00–3.40 (m, 9H; 2b-H, 3a-H, 3b-H, 4a-H, 4b-H, 5a-H, 5b-H, 6a-H), 3.60 (dd, $J = 12.1$, 5.8 Hz, 1H; CH_aH_bOH), 3.69 (d, $J = 9.0$ Hz, 1H; 2a-H), 3.83 (dd, $J = 12.1$, 2.4 Hz, 1H; CH_aH_bOH), 3.84 (m, 1H; 6b-H), 4.62 ppm (brs, 1H; carborane-CH); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 28.80$, 28.81 (C-1″, C-2″), 61.11 (carborane-CH), 63.10 (CH_2OH), 71.94 (C-3a), 74.43, 74.74 (C-2b, C-6a), 75.33 (C-4a*), 76.93 (carborane-C-1′), 79.24 (C-4b*), 79.50 (C-2a), 79.72, 81.02 (C-5a, C-3b), 81.39 (C-5b*), 81.47 ppm (C-6b); MS (ESI^-): m/z (%): 465 (100) $[M-H]^-$; $C_{15}H_{34}B_{10}O_9$ (466.5).

(2a*R*,3a*S*,4a*R*,5a*R*,6a*S*,2b*R*,3b*S*,4b*R*,5b*R*,6b*S*)-1,2-Bis[3,4,5-tris(hydroxy)-2-hydroxymethyltetrahydropyran-6-yl]-1*C*,2*C*-dicarba-*closo*-dodecaborane(12) (24): Quantitative from **19**, colorless solid; R_f (EtOAc/MeOH, 4:1) = 0.06; $[\alpha]_D^{20} = +7.5°$ ($c = 0.1$, MeOH); IR (KBr): $\tilde{\nu} = 3385$ (O–H), 2925 (C–H), 2574 (B–H), 1339, 1094 cm^{-1}; UV (CH_3CN): λ_{max} ($\lg\varepsilon$) = 191.0 (3.847), 248.5 (3.376), 280.0 (2.965), 326.0 nm (3.278); ^1H NMR (500 MHz, CD_3OD): $\delta = 1.50-3.00$ (brs, 10H; BH), 3.14 (dd, $J = 9.2$, 9.2 Hz, 2H; 5a-H, 5b-H), 3.26 (ddd, $J = 9.5$, 7.3, 2.2 Hz, 2H; 2a-H, 2b-H), 3.33–3.39 (m, 4H; 3a-H, 3b-H, 4a-H, 4b-H), 3.58 (dd, $J = 12.1$, 7.3 Hz, 2H; 2 CH_aH_bOH), 3.67 (d, $J = 9.1$ Hz, 2H; 6a-H, 6b-H), 3.89 ppm (dd, $J = 12.1$, 2.2 Hz, 2H; 2 CH_aH_bOH); ^{13}C NMR (125 MHz, CD_3OD): $\delta = 63.15$ (2 CH_2OH), 71.17 (C-5a, C-5b), 74.61 (C-3a, C-3b), 77.49 (C-6a, C-6b), 80.49 (C-4a, C-4b), 81.75 (2 carborane-C), 82.47 ppm (C-2a, C-2b); MS (ESI): m/z (%): 960 (100) $[2M+Na]^+$, 492 (45) $[M+Na]^+$; $C_{14}H_{32}B_{10}O_{10}$ (468.5).

Cytotoxicity tests: Adherent cells of the human bronchial carcinoma cell line A549, of the murine melanoma cell line B-16, of the human pancreas carcinoma cell line PancTu 1, and of the colorectal human adeno carcinoma cell line LoVo were seeded in 96-well plates (TC Microwell 96F, Nunc) and cultivated at 37 °C under air with a CO_2 content enriched to 7.5% in Dulbecco's modified Eagle's medium (DMEM, Biochrom) supplemented with L-glutamine (4 mM, Gibco), $NaHCO_3$ (44 mM, Biochrom), and 10% fetal calf serum (FCS, heat-inactivated for 30 min at 56 °C, Gibco). The cells were incubated with compounds **2** and **20**–**23** at various concentrations for 24 h in a serum-free medium (Ultra Culture, Cambrex) containing 1% DMSO. After five days of cultivation, the cells were treated with MTT (final concentration 0.5 mg mL^{-1}) for 4 h, and with a solubilizing solution (10% SDS in 0.1 M HCl) overnight. The optical density of the resulting blue formazane derivative was measured with a photometer (thermo max microplate reader, Molecular Devices) after cell lysis. The measured optical density is proportional to the fraction of the living, metabolically active cells. The experiments were performed in duplicate.

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