Ortho-Carboranyl Glycosides of Glucose, Mannose, Maltose and Lactose for Cancer Treatment by Boron Neutron-Capture Therapy

Lutz F. Tietze* and Ulrich Bothe

Abstract: Glycosidation of alkynols using the trichloroacetimidate method led to the alkynyl glycosides **2a**,**b**, **6**, **10** and **14** in 53–68% yield, which by reaction with decaborane(14) afforded the protected peracetylated *o*-carboranyl glycosides **3a**,**b**, **7**, **11** and **15** in 43–61% yield. Base-catalyzed solvolysis gave the unprotected glycosides **4a**,**b**, **8**, **12** and **16** in 71–97% yield.

Keywords: antitumor agents · carboranes · drug research · glycosides

Introduction

The selective treatment of cancer remains one of the unsolved problems in medicine. A new development in this field, of growing importance, is boron neutron-capture therapy.[1] However, successful utilization of this method, which is based on the cytotoxic boron neutron-capture reaction [^{10}B(^{1}n,^{4}He)^{7}Li] depends on the selective deposition of large quantities (20–30 μg boron per g tumor tissue) in the malignant cells. For selective targeting, conjugates of carboranes with antibodies that bind to tumor-associated antigens were used;[2] however, a loss of immunoactivity was frequently observed owing to the hydrophobicity of the carborane unit. Additionally, it has been shown that antibody conjugates bind only to a very small portion of the cancer cells. This approach seems to be less suitable, since the cytotoxic effect of the lithium formed from the boron neutron-capture reaction depends strongly on the proximity to the DNA in the cell.[3]

Our approach was to improve the selectivity of cancer treatment in the utilisation of phenotypic and genetic differences of normal and cancer cells.[4] The first approach is based upon the increased rate of glycolysis in cancer cells under hyperglycemic conditions. The second approach was based upon the use of conjugates of enzymes and monoclonal antibodies which bind to tumor-associated antigens in order to enzymatically cleave nontoxic prodrugs selectively at cancer cells with the liberation of a cytotoxic compound.[5] This approach has the advantage that the monoclonal antibody enzyme conjugate is used in a catalytic way and that the usually lipophilic toxin formed can be distributed to all cancer cell nuclei. For boron neutron-capture therapy our approach looks for the use of glycosides of *ortho*-carborane (1,2-dicarba-*closo*-dodecaborane) which do not penetrate the cell membrane due to their polarity. However, after selective removal of the sugar moiety by enzymatic hydrolysis by the antibody enzyme conjugate the lipophilic carboranyl alcohol should penetrate the cell membrane.

In this paper we describe the stereoselective synthesis of novel water-soluble glycosidic carboranes.[6] It should be noted that the glycosidation of hydroxyalkylcarboranes by addition to 3,4,6-tri-*O*-acetyl-D-glucal has already been described;[7] however, the glycosides thus obtained are not suitable for our approach since they are formed as mixtures of anomers and their water solubility is quite low. Since carboranes are usually prepared by reaction of alkynes and decaborane(14),[8] we first prepared alkynyl glycosides which were then transformed into the glycosidic carboranes. The necessary alkynyl glycosides are easily accessible using the known trichloroimidate glycosidation procedure.[9]

Results and Discussion

Reaction of glucose trichloroimidate (**1**) and 3-butyn-1-ol in the presence of $BF_3 \cdot Et_2O$ afforded butynyl β-glucoside (**2a**) in 55% yield stereoselectively. In a similar way hexynyl β-glucoside (**2b**) could be prepared by reaction of **1** and 5-hexyn-1-ol in 54% yield. For the formation of carboranyl glucoside **3a** decaborane(14) was heated in acetonitrile under reflux for 1 h to give the $B_{10}H_{12} \cdot 2CH_3CN$ adduct,[10] which was treated with **2a** in toluene to give the protected carboranyl glucoside **3a** in 61% yield (Scheme 1). Similarly, reaction of **2b** with the $B_{10}H_{12} \cdot 2CH_3CN$ adduct afforded the carboranyl glucoside **3b** in 51% yield. Solvolysis with catalytic amounts of sodium methoxide in methanol gave the desired carboranyl glucosides **4a** and **4b** in 97% and 74%

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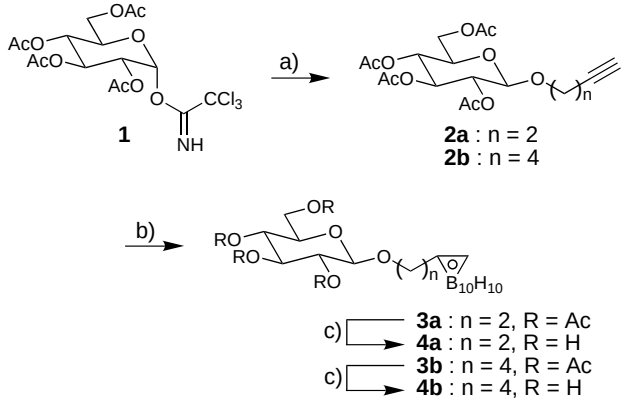
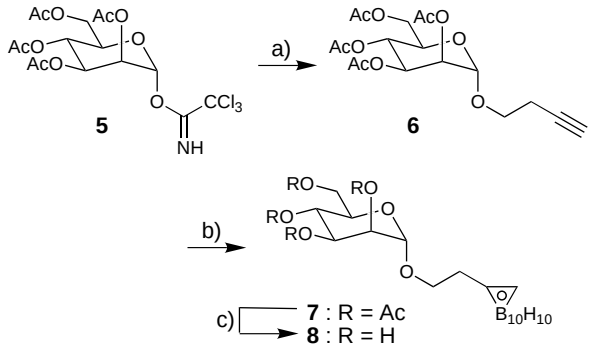
yield, respectively. It is well known that *ortho*-carboranes (*closo* form) can readily be converted into the *nido* form upon treatment with a base. However, this was not observed during solvolysis of the peracetylated *ortho*-carboranyl glycosides under the described conditions as confirmed by mass spectroscopy of the deprotected products.



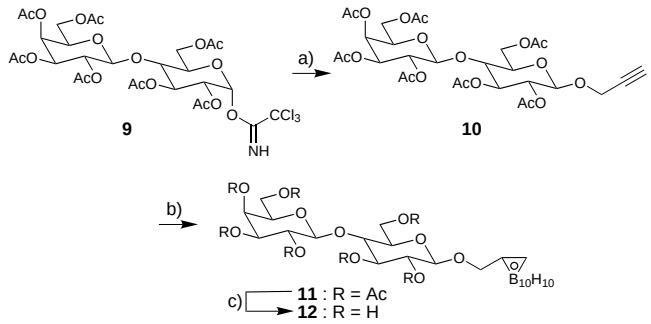
Scheme 1. Preparation of carboranyl glucosides **4a** and **4b**. Reagents: a) **2a**: 3-butyn-1-ol, CH_2Cl_2, $BF_3 \cdot Et_2O$, 0 °C to RT, 55 %; **2b**: 5-hexyn-1-ol, CH_2Cl_2, $BF_3 \cdot Et_2O$, 0 °C to RT, 54 %; b) **3a**: $B_{10}H_{14}$, CH_3CN, reflux, then **2a** in toluene, reflux, 61 %; **3b**: $B_{10}H_{14}$, CH_3CN, reflux, then **2b** in toluene, reflux, 51 %; c) **4a**: NaOMe, MeOH, RT, 97 %; **4b**: NaOMe, MeOH, RT, 74 %.

For the preparation of carboranyl mannoside **6**, mannose trichloroimidate (**5**) was treated with 3-butyn-1-ol to afford **6** as the α-anomer in 68 % yield (Scheme 2). Reaction with decaborane(14) gave **7** in 59 % yield; this was deprotected to afford the desired carboranyl mannoside **8** nearly quantitatively.



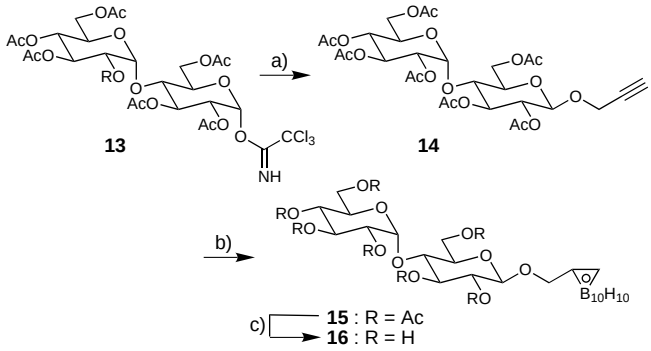
Scheme 2. Preparation of carboranyl mannoside **8**. Reagents: a) 3-butyn-1-ol, CH_2Cl_2, $BF_3 \cdot Et_2O$, 0 °C to RT, 68 %; b) $B_{10}H_{14}$, CH_3CN, reflux; then **6** in toluene, reflux, 59 %; c) NaOMe, MeOH, RT, 91 %.

As already mentioned, the carboranyl glycosides of monosaccharides are less suitable since their water solubility is not sufficient; we therefore also prepared carboranes linked to disaccharides such as lactose and maltose. Reaction of lactose trichloroimidate (**9**, Scheme 3) with propargyl alcohol catalyzed by $BF_3 \cdot Et_2O$ afforded propargyl lactoside (**10**) in 66 % yield, which was then converted into the carboranyl lactoside **11** in 43 % yield. Solvolysis of **11** in the usual way afforded **12** in 71 % yield.



Scheme 3. Preparation of carboranyl lactoside **12**. Reagents: a) propargyl alcohol, CH_2Cl_2, $BF_3 \cdot Et_2O$, RT, 66 %; b) $B_{10}H_{14}$, CH_3CN, reflux; then **10** in toluene, reflux, 43 %; c) NaOMe, MeOH, RT, 71 %.

For the preparation of carboranyl maltoside **16** the maltose imidate **13** was treated with propargyl alcohol in the presence of TMSOTf to afford **14** in 53 % yield. Reaction with decaborane(14) gave carboranyl maltoside **15** in 49 % yield, which was then deprotected to afford the water-soluble carboranyl maltoside **16** in 83 % yield (Scheme 4).



Scheme 4. Preparation of carboranyl maltoside **16**. Reagents: a) propargyl alcohol, CH_2Cl_2, TMSOTf, 0 °C, 53 %; b) $B_{10}H_{14}$, CH_3CN, reflux; then **14** in toluene, reflux, 49 %; c) NaOMe, MeOH, RT, 83 %.

In toxicity tests[11] on human bronchial carcinoma cells of line A549[12] we found that **12** and **16** display almost no cytotoxicity up to concentrations of 0.40 μM.

The structures of the new compounds have been mainly determined by ^1H and ^{13}C NMR spectroscopy. 1-H at the anomeric centre of the alkynyl glucosides **2a** and **2b** as well as of propargyl lactoside (**10**) and propargyl maltoside (**14**), respectively, resonate at $\delta = 4.5 - 4.9$ as doublets with $J =$ 7.9 Hz indicating the existence of β-glycosides. In contrast, 1-H of butynyl mannoside (**6**) resonates at $\delta = 4.87$ as doublet with $J = 1.7$ Hz, confirming the α-configuration at the anomeric centre. Interestingly, only one doublet at $\delta = 4.34$ with $J =$ 2.4 Hz was found for the diastereotopic protons of the alkynyl moiety in the lactoside **10** and at $\delta = 4.35$ with $J = 2.5$ Hz in the maltoside **14**, whereas as expected for the monosaccharides **2a**, **2b** and **6** separated triplets of doublets are observed. Thus, for example, in the spectrum of **2b** signals appear at $\delta = 3.47$ with $J = 10.0/5.9$ Hz and at $\delta = 3.87$ with $J = 9.8/5.4$ Hz. The ^1H NMR spectra of the carboranyl glycosides all show a very broad signal at $\delta = 0.7 - 3.5$, which is typical for the carborane moiety and counts for the hydrogens at the boron atoms. The

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proton attached to the carbon of the carborane moiety of the acetylated carboranyl glycosides **3a**, **3b**, **7**, **11**, **15** resonates as a broad singlet at $\delta = 3.6-3.9$ whereas for the deprotected carboranyl glycosides **4a**, **4b**, **8**, **12** and **16** a downfield shift is observed with signals at $\delta = 4.3-4.8$. In contrast to the spectra of **10** and **14,** the diastereotopic protons of the CH_2 group of the carboranyl lactosides **11** and **12** as well as of the carboranyl maltosides **15** and **16** now resonate as separated doublets with a large coupling constant of $J = 10.5-12.0$ Hz.

Conclusions

To summarize, we prepared several novel glycosidic carboranes which show increased water solubility, especially in the case of the disaccharides. These are suitable for an antibody-directed enzymatic prodrug boron neutron-capture therapy, which is a new approach in the selective treatment of cancer. The new compounds described will now be tested in animal treatment studies in cooperation with Prof. Dr. Yoshinori Yamamoto in Sendai (Japan).

Experimental Section

General: ^{1}H NMR and ^{13}C NMR: Varian XL-500 and VXR-200, Bruker AM-300; multiplicities were determined with an APT pulse sequence. MS: Varian MAT 311A. IR: Bruker IFS25. Melting points: Mettler FP61. Elemental analyses were carried out in the analytical laboratory of the University of Göttingen. All solvents were distilled prior to use. Reagents and materials were obtained from commercial suppliers and were used without further purification. All reactions were carried out under positive argon pressure and monitored by TLC (Machery–Nagel, Polygram SIL G/UV_{254}). Products were isolated by column chromatography on silica gel (ICN Silica 63–200, 60 A, ICN Biomedicals). The solvent systems used for chromatography were A) petroleum ether PE/EtOAc (2:1), B) PE/EtOAc (1:1), C) EtOAc/MeOH 6:1, D) EtOAc/MeOH 5:1 and E) EtOAc/MeOH 3:1.

General procedure I: Synthesis of alkynyl glycosides: A solution of the glycosyl trichloroimidate and the alkynol in CH_2Cl_2 containing molecular sieves (4 Å) was stirred in the presence of $BF_3 \cdot Et_2O$ or TMSOTf at 0 °C. After addition of water the organic layer was separated and washed with saturated aqueous sodium bicarbonate solution, water, and brine and dried with Na_2SO_4. Then the solvent was evaporated in vacuo and the residue was purified by chromatography on silica gel (solvent system A for alkynyl glucosides and mannoside, solvent system B for alkynyl maltoside and lactoside) to afford the alkynyl glycosides as white foams.

3-Butynyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**2a**): Reaction of glucose trichloroimidate (**1**, 1.46 g, 2.96 mmol) and 3-butyn-1-ol (270 mg, 3.85 mmol) according to general procedure I in CH_2Cl_2 (50 mL) with $BF_3 \cdot Et_20$ (0.10 mL, 0.81 mmol) for 75 min at 0 °C and 105 min at 20 °C gave **2a** after crystallization from Et_2O and purification by column chromatography (651 mg, 1.63 mmol, 55%), m.p. 135–136 °C; $R_f = 0.24$ (solvent A); $[\alpha]_D^{20} = -18.2$ ($c = 1.0$, MeOH); IR (KBr): $\tilde{\nu} = 3272$ cm^{-1} (C≡C-*H*), 2968, 2946, 2926, 2904, 2890, 2840 (C–H), 2124 (C≡C), 1740 (C=O), 1380 ($OCOCH_3$), 1224 (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.96$ (t, $J = 2.7$ Hz, 1H; 4′-H), 2.01, 2.03, 2.06, 2.09 (4s, 12H; $4CH_3$), 2.47 (td, $J = 6.8$, 2.6 Hz, 2H; 2′-H), 3.61–3.75 (m, 2H; 1′-H_a, 5-H), 3.95 (dt, $J = 9.8$, 6.6 Hz, 1H; 1′-H_b), 4.12 (dd, $J = 12.0$, 2.3 Hz, 1H; 6-H_a), 4.27 (dd, $J = 12.3$, 4.7 Hz, 1H; 6-H_b), 4.57 (d, $J = 7.9$ Hz, 1H; 1-H), 4.99 (dd, $J = 9.3$, 7.9 Hz, 1H; 2-H), 5.08 (t, $J = 9.4$ Hz, 1H; 4-H), 5.22 (t, $J = 9.3$ Hz, 1H; 3-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 19.79$, 20.55, 20.66, 20.70, 61.83, 67.87, 68.29, 69.50, 71.04, 71.75, 72.65, 80.50, 100.7, 169.3, 169.3, 170.2, 170.6; MS (200 eV, DCI/NH_3): m/z (%) = 418 (100) $[M+NH_4]^+$; $C_{18}H_{24}O_{10}$ (400.4): calcd C 54.00, H 6.04; found C 54.29, H 5.78.

5-Hexynyl 2,3,4,6-tetra-*O*-acetyl-β-D-glucopyranoside (**2b**): Reaction of glucose trichloroimidate (**1**, 3.80 g, 7.71 mmol) and 5-hexyn-1-ol (834 mg, 8.50 mmol) according to general procedure I with $BF_3 \cdot Et_2O$ (0.10 mL, 0.81 mmol) in CH_2Cl_2 (50 mL) for 30 min at 0 °C and 1 h at 20 °C gave **2b** (1.77 g, 4.13 mmol, 54%), m.p. 64 °C; $R_f = 0.27$ (solvent A); $[\alpha]_D^{20} = -19.6$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3252$ cm^{-1} (C≡C-*H*), 2992, 2940, 2916, 2884, 2866, 2798 (C–H), 2126 (C≡C), 1746 (C=O), 1384 ($OCOCH_3$), 1226 (C-O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 1.48-1.74$ (m, 4H; 2′-H, 3′-H), 1.91 (t, $J = 2.4$ Hz, 1H; 6′-H), 1.97, 1.99, 2.01, 2.05 (4s, 12H; $4CH_3$), 2.16 (td, $J = 6.6$, 2.4 Hz, 2H; 4′-H), 3.47 (dt, $J = 10.0$, 5.9 Hz, 1H; 1′-H_a), 3.66 (ddd, $J = 9.6$, 4.7, 2.4 Hz, 1H; 5-H), 3.87 (dt, $J = 9.8$, 5.4 Hz, 1H; 1′-H_b), 4.09 (dd, $J = 12.2$, 2.3 Hz, 1H; 6-H_a),4.23 (dd, $J = 12.4$, 4.5 Hz, 1H; 6-H_b), 4.46 (d, $J = 7.8$ Hz, 1H; 1-H), 4.95 (t, $J = 8.9$ Hz, 1H; 2-H), 5.04 (t, $J = 9.9$ Hz, 1H; 4-H), 5.17 (t, $J = 9.2$ Hz, 1H; 3-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 17.95$, 20.55, 20.58, 20.60, 20.70, 24.72, 28.28, 61.89, 68.37, 69.35, 68.53, 71.22, 71.69, 72.76, 83.98, 100.7, 169.2, 169.3, 170.2, 170.6; MS (200 eV, DCI/NH_3): m/z (%) = 446 (100) $[M+NH_4]^+$; $C_{20}H_{28}O_{10}$ (428.4): calcd C 56.07, H 6.59; found C 55.84, H 6.29.

3-Butynyl 2,3,4,6-tetra-*O*-acetyl-α-D-mannopyranoside (**6**): Reaction of mannose trichloroimidate (**5**, 1.88 g, 3.82 mmol) and 3-butyn-1-ol (283 mg, 4.04 mmol) according to general procedure I with $BF_3 \cdot Et_2O$ (0.10 mL, 0.81 mmol) in CH_2Cl_2 (30 mL) for 3 h at 0 °C and 14 h at 20 °C gave **6** (1.04 g, 2.60 mmol, 68%), m.p. 62–63 °C; $R_f = 0.29$ (solvent A), m.p. 73 °C; $[\alpha]_D^{20} = +48.7$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3312$ cm^{-1} (C≡C-*H*), 2998, 2956, 2936, 2896 (C–H), 2124 (C≡C), 1746 (C=O), 1380 ($OCOCH_3$), 1240 (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.02-2.03$ (m, 1H; 4′-H), 2.00, 2.05, 2.11, 2.16 (4s, 12H; $4CH_3$), 2.53 (td, $J = 6.7$, 2.6 Hz, 2H; 2′-H), 3.65 (dt, $J = 9.8$, 6.6 Hz, 1H; 1′-H_a), 3.81 (dt, $J = 9.7$, 7.0 Hz, 1H; 1′-H_b), 4.07–4.16 (m, 2H; 5-H, 6-H_a), 4.29 (dd, $J = 12.5$, 5.4 Hz, 1H; 6-H_b), 4.87 (d, $J = 1.7$ Hz, 1H; 1-H), 5.23–5.39 (m, 3H; 2-H, 3-H, 4,-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 19.65$, 20.64, 20.85, 62.32, 65.99, 66.40, 68.65, 68.95, 69.44, 69.85, 80.50, 97.56, 169.7, 169.8, 169.9, 170.6; MS (200 eV, DCI/NH_3): m/z (%) = 418 (100) $[M+NH_4]^+$; $C_{18}H_{24}O_{10}$ (400.4): calcd C 54.00, H 6.04; found C 54.24, H 6.04.

2-Propynyl 2,3,4,6,2′,3′,6′-hepta-*O*-acetyl-β-D-lactopyranoside (**10**): Reaction of lactose trichloroimidate (**9,** 7.68 g, 9.83 mmol) and propargyl alcohol (947 mg, 16.9 mmol) according to general procedure I with $BF_3 \cdot Et_2O$ (0.10 mL, 0.81 mmol) in CH_2Cl_2 (100 mL) for 23 h at 20 °C gave **10** (4.40 g, 6.52 mmol, 66%), m.p. 74–75 °C; $R_f = 0.17$ (solvent A); $[\alpha]_D^{20} = -15.0$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3280$ cm^{-1} (C≡C-*H*), 2966, 2946, 2886 (C–H), 2122 (C≡C), 1754 (C=O), 1372 ($OCOCH_3$), 1234 (C–O); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta = 1.97$, 2.05, 2.05, 2.06, 2.07, 2.13, 2.16 (7s, 21H; 7 CH_3), 2.46 (t, $J = 2.5$, 1H; 3″-H), 3.64 (ddd, $J = 9.8$, 4.8, 2.0 Hz, 1H; 5′-H), 3.82 (t, $J = 9.8$, 1H; 4′-H), 3.87 (ddd, $J = 7.5$, 6.4, 1.2 Hz, 5-H), 4.06–4.13 (m, 2H; 6-H or 6′-H), 4.14 (dd, $J = 6.4$, 4.8 Hz, 1H; 6-H or 6′-H), 4.34 (d, $J = 2.4$ Hz, 2H; 1″-H), 4.48 (d, $J = 7.9$ Hz, 1H; 1-H), 4.51 (dd, $J = 12.0$, 2.2 Hz, 1H; 6-H or 6′-H), 4.75 (d, $J = 7.9$ Hz, 1′-H), 4.92 (dd, $J = 9.5$, 8.0 Hz, 1H; 2′-H), 4.96 (dd, $J = 10.4$, 3.6 Hz, 1H; 3-H), 5.11 (dd, $J = 10.6$, 7.9 Hz, 1H; 2-H), 5.23 (t, $J = 9.3$ Hz, 1H; 3′-H), 5.35 (dd, $J = 3.5$, 1.1 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.47$, 20.60, 20.68, 20.75, 20.82, 55.81, 60.76, 61.75, 66.53, 69.00, 70.61, 70.91, 71.22, 72.60, 72.66, 76.05, 75.43, 78.01, 97.78, 100.9, 169.0, 169.7, 170.0, 170.1, 170.3; MS (200 eV, DCI/NH_3): m/z (%) = 366 (100), 692 (84) $[M+NH_4]^+$; $C_{29}H_{38}O_{18}$ (674.6): calcd C 51.63, H 5.68; found C 51.36, H 5.76.

2-Propynyl 2,3,4,6,2′,3′,6′-hepta-*O*-acetyl-β-D-maltopyranoside (**14**): Reaction of maltose trichloroimidate (**13**, 378 mg, 0.48 mmol) and propargyl alcohol (340 mg, 6.06 mmol) according to general procedure I with TMSOTf (0.10 mL, 0.55 mmol) in CH_2Cl_2 for 4 h at 0 °C gave **14** (173 g, 0.26 mmol, 53%), m.p. 63 °C; $R_f = 0.43$ (solvent B); $[\alpha]_D^{20} = +39.0$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3278$ cm^{-1} (C≡C–*H*), 2962 (C–H), 2122 (C≡C), 1754 (C=O), 1372 ($OCOCH_3$), 1236 (C–O); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 2.03-2.17$ (m, 21H; 7 CH_3), 2.46–2.48 (m, 1H; 3″-H), 3.70–3.76 (m, 1H; 5-H), 3.92–4.00 (m, 1H; 5′-H), 3.98–4.14 (m, 2H; 4′-H, 6-H or 6′-H), 4.23 (dd, $J = 12.1$, 4.7 Hz, 1H; 6-H or 6′-H), 4.25 (dd, $J = 12.2$, 3.9 Hz, 1H; 6-H or 6′-H), 4.35 (d, $J = 2.5$ Hz, 2H; 1″-H), 4.49 (dd, $J = 12.0$, 2.2 Hz, 1H; 6-H or 6′-H), 4.77–4.90 (m, 3H; 1′-H, 2-H, 2′-H), 5.05 (t, $J = 9.7$ Hz, 1H; 4-H), 5.28 (t, $J = 8.4$ Hz, 1H; 3′-H), 5.36 (t, $J = 9.9$ Hz, 1H; 3-H), 5.41 (d, $J = 3.4$ Hz, 1H; 1-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.55$, 20.58, 20.64, 20.66, 20.81, 20.87, 55.85, 61.43, 62.58, 67.94, 68.45, 69.26, 69.96, 71.73, 72.20, 72.49, 75.29, 75.51, 78.01, 95.47, 97.56, 170.5, 170.4, 170.2, 169.9, 169.7, 169.4;

MS (200 eV, DCI/NH_3): m/z (%) = 692 (100) $[M+NH_4]^+ - 1$; $C_{29}H_{38}O_{18}$ (674.6): calcd C 51.63, H 5.68; found C 51.48, H 5.61.

General procedure II: Synthesis of carboranyl glycosides: A mixture of decaborane(14) in acetonitrile containing molecular sieves (4 Å) was refluxed for 1 h to give the $B_{10}H_{12}\cdot 2CH_3CN$ adduct. Then the alkynyl glycoside dissolved in toluene was added and the solution was heated under reflux for 18 h. Methanol (5 mL) was added and the mixture was heated under reflux for 30 min. After evaporation of the solvents in vacuo the residue was purified by chromatography on silica gel to afford the carboranyl glycoside as a white foam (**3a** and **4**: solvent system A; **11** and **15**: solvent system B; **3b** was purified by crystallization from methanol).

1-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)ethyl]-1,2-dicarba-*closo*-dodecaborane (**3a**): Reaction of decaborane(14) (118 mg, 0.97 mmol), acetonitrile (10 mL) and butynyl glucoside **2a** (259 mg, 0.65 mmol) according to general procedure II in toluene (10 mL) gave the carboranyl glucoside **3a** (203 mg, 0.39 mmol, 61%), m.p. 123-124 °C; $R_f = 0.20$ (solvent A); $[\alpha]_D^{20} = +10.3$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3072\ cm^{-1}$ (carborane C–H), 2962 (C–H), 2592 (B–H), 1754 (C=O), 1372 ($OCOCH_3$), 1234 (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 2.01$, 2.03, 2.08, 2.10 (4s, 12H; 4 CH_3), 2.51–2.58 (m, 2H; 2′-H), 3.55–3.74 (m, 2H; 1′-H_a, 5-H), 3.84–3.88 (brs, 1H; carborane C-H), 3.94 (dt, $J = 10.2$, 5.6 Hz, 1H; 1′-H_b), 4.15 (dd, $J = 12.3$, 2.5 Hz, 1H; 6-H_a), 4.24 (dd, $J = 12.5$, 4.6 Hz, 1H; 6-H_b), 4.48 (d, $J = 7.9$ Hz, 1H; 1-H), 4.96 (dd, $J = 9.4$, 7.9 Hz, 1H; 2-H), 5.07 (t, $J = 9.4$ Hz, 1H; 4-H), 5.21 (t, $J = 9.2$ Hz, 1H; 3-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.56$, 20.71, 20.84, 37.45, 60.11, 61.62, 66.70, 68.12, 70.98, 71.90, 72.46, 72.7, 100.1, 169.3, 169.3, 170.1, 170.5; MS (200 eV, DCI/NH_3): m/z (%) = 536 (100) $[M+NH_4]^+$; $C_{18}H_{34}O_{10}B_{10}$ (518.6).

1-[(2,3,4,6-Tetra-*O*-acetyl-*β*-D-glucopyranosyl)butyl]-1,2-dicarba-*closo*-dodecaborane (**3b**): Reaction of decaborane(14) (485 mg, 3.97 mmol), acetonitrile (20 mL) and hexynyl glucoside (**2b**, 1.27 g, 2.96 mmol) in toluene (20 mL) according to general procedure II for 15 h gave carboranyl glucoside **3b** (834 mg, 1.53 mmol, 51%) after crystallization from methanol and washing of the crude product with cold methanol and pentane. M.p. 142–143 °C; $R_f = 0.44$ (solvent A); $[\alpha]_D^{20} = -18.0$ ($c = 0.4$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3054\ cm^{-1}$ (carborane C–H), 2964 (C–H), 2596 (B–H), 1758, 1748 (C=O), 1372 ($OCOCH_3$), 1230 (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.49$–1.55 (m, 4H; 2′-H, 3′-H), 1.99, 2.01, 2.03, 2.07 (4s, 12H; 4 CH_3), 2.17 (m, 2H; 4′-H_2), 3.45 (m, 1H; 1′-H_a), 3.66 (ddd, $J = 9.8$, 4.5, 2.7 Hz, 1H; 5-H), 3.59–3.62 (brs, 1H; carborane C-H), 3.83 (m, 1H; 1′-H_b), 4.12 (dd, $J = 12.2$, 2.4 Hz, 1H; 6-H_a), 4.24 (dd, $J = 12.2$, 4.7 Hz, 1H; 6-H_b), 4.45 (d, $J = 7.9$ Hz, 1H; 1-H), 4.94 (dd, $J = 9.6$, 8.1 Hz, 1H; 2-H), 5.06 (t, $J = 9.6$ Hz, 1H; 4-H), 5.18 (t, $J = 9.4$ Hz, 1H; 3-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta =$ 20.59, 20.70, 20.74, 25.99, 28.62, 37.67, 61.22, 61.83, 68.97, 68.34, 71.25, 71.82, 72.71, 75.14, 100.6, 169.3, 169.4, 170.3, 170.6; MS (200 eV, DCI/NH_3): m/z (%) = 564 (100) $[M+NH_4]^+$; $C_{20}H_{38}O_{10}B_{10}$ (546.6): calcd C 43.95, H 7.01; found C 43.85, H 7.11.

1-[(2,3,4,6-Tetra-*O*-acetyl-*α*-D-mannopyranosyl)ethyl]-1,2-dicarba-*closo*-dodecaborane (**7**): Reaction of decaborane (352 mg, 2.88 mmol), acetonitrile (20 mL) and butynyl mannoside (**6**, 917 mg, 2.29 mmol) according to general procedure II in toluene (20 mL) for 19 h gave carboranyl mannoside **7** (698 mg, 1.35 mmol, 59%), m.p. 129 °C; $R_f = 0.28$ (solvent A); $[\alpha]_D^{20} = +40.3$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3064\ cm^{-1}$ (carborane C–H), 3000, 2962, 2936, 2898, 2810 (C–H), 2596 (B-H), 1746 (C=O), 1372 ($OCOCH_3$), 1244, 1222 (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 2.01$, 2.06, 2.11, 2.16 (4s, 12H; 4 CH_3), 2.56 (t, $J = 6.6$ Hz, 2H; 2′-H), 3.57 (dt, $J =$ 10.3, 6.8 Hz, 1H; 1′-H_a), 3.71–3.72 (brs, 1H; carborane C-H), 3.82 (dt, $J =$ 10.2, 6.4 Hz, 1H; 1′-H_b), 3.92 (ddd, $J = 9.0$, 5.8, 2.5 Hz, 1H; 5-H), 4.12 (dd, $J = 12.2$, 2.5 Hz, 1H; 6-H_a), 4.26 (dd, $J = 12.2$, 5.8 Hz, 1H; 6-H_b), 4.80 (d, $J = 1.8$ Hz, 1H; 1-H), 5.18 (dd, $J = 2.9$, 1.8 Hz, 1H; 2-H), 5.25 (dd, $J = 9.5$, 2.5 Hz, 1H; 3-H), 5.27 (dd, $J = 10.0$, 8.9 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.63$, 20.66, 20.70, 20.82, 37.15, 60.92, 62.49, 65.86, 68.71, 69.16, 69.16, 65.93, 71.90, 97.53, 169.6, 169.9, 169.9, 170.5; MS (200 eV, DCI/NH_3): m/z (%) = 537 (100) $[M+NH_4]^+$; $C_{18}H_{34}O_{10}B_{10}$ (518.6): calcd C 41.69, H 6.61; found C 41.39, H 6.57.

1-[(2,3,4,6,2′,3′,6′-Hepta-*O*-acetyl-*β*-D-lactopyranosyl)methyl]-1,2-dicarba-*closo*-dodecaborane (**11**): Reaction of decaborane(14) (1.19 g, 9.71 mmol), acetonitrile (11 mL) and propargyl lactoside **10** (4.01 g, 5.94 mmol) in toluene (12 mL) for 21.5 h gave carboranyl lactoside **11** (2.02 g, 2.55 mmol, 43%), m.p. 110 °C; $R_f = 0.33$ (solvent B); $[\alpha]_D^{20} = -14.7$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3070\ cm^{-1}$ (carborane C–H), 2964, 2940 (C–H), 2592 (B–H), 1754 (C=O), 1372 ($OCOCH_3$), 1230 (C–O); ^1H NMR (500 MHz, $CDCl_3$): $\delta = 1.97$, 2.04, 2.05, 2.06, 2.07, 2.14, 2.15 (7s, 21H; CH_3), 3.59 (ddd, $J = 9.9$, 4.8, 2.1 Hz, 1H; 5′-H), 3.78 (t, $J = 9.5$ Hz, 1H; 4′-H), 3.86–3.90 (m, 2H; 5-H, carborane C-H), 3.96 (d, $J = 11.0$ Hz, 1H; 1″-H_a), 4.05–4.09 (m, 2H; 6-H or 6′-H), 4.13 (dd, $J = 11.2$, 6.2 Hz, 1H; 6-H or 6′-H), 4.20 (d, $J = 11.0$ Hz, 1H; 1″-H_b), 4.45 (d, $J = 8.0$ Hz, 1H; 1-H or 1′-H), 4.48 (d, $J = 8.0$ Hz, 1H; 1-H or 1′-H), 4.50 (dd, $J = 7.2$, 2.1 Hz, 1H; 6-H or 6′-H), 4.88 (dd, $J = 9.6$, 7.8 Hz, 1H; 2′-H), 4.96 (dd, $J = 10.3$, 3.4 Hz, 1H; 3-H), 5.10 (dd, $J = 10.5$, 8.0 Hz, 1H; 2-H), 5.20 (t, $J = 9.3$ Hz, 1H; 3′-H), 5.35 (dd, $J = 3.4$, 1.2 Hz, 1H; 4-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 20.46$, 20.58, 20.70, 20.76, 58.01, 60.69, 61.40, 70.25, 71.54, 66.49, 68.99, 70.68, 70.81, 70.97, 71.91, 72.93, 75.71, 100.3, 101.0 (C-1), 169.0, 169.5, 169.5, 169.9, 170.0, 170.1, 170.2; MS (200 eV, DCI/NH_3): m/z (%) = 812 (100) $[M+NH_4]^+$; $C_{29}H_{48}O_{18}B_{10}$ (792.8).

1-[(2,3,4,6,2′,3′,6′-Hepta-*O*-acetyl-*β*-D-maltopyranosyl)methyl]-1,2-dicarba-*closo*-dodecaborane (**15**): Reaction of decaborane (1.71 g, 14.0 mmol), acetonitrile (16 mL) and propargyl maltoside (**14**, 6.37 g, 9.44 mmol) according to general procedure II in toluene (16 mL) gave carboranyl maltoside **15** (3.66 g, 4.62 mmol, 49%), m.p. 91–92 °C; $R_f = 0.26$ (solvent A); $[\alpha]_D^{20} = +37.0$ ($c = 1.0$, $CHCl_3$); IR (KBr): $\tilde{\nu} = 3076\ cm^{-1}$ (carborane C–H), 3026, 2956, 2896, 2824 (C–H), 2608, 2584 (B–H), 1756 (C=O), 1370 ($OCOCH_3$), 1234 (C–O); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 1.97$, 1.99, 2.00, 2.01, 2.02, 2.07, 2.12 (7s, 21H; 7 CH_3), 3.63 (ddd, $J = 9.8$, 4.1, 2.7 Hz, 1H; 5-H), 3.84–3.87 (brs, carborane C-H), 3.89 (m, 1H; 5′-H), 3.93 (d, $J =$ 10.9 Hz, 1H; 1″-H_a), 3.94 (t, $J = 8.6$ Hz, 1H; 4′-H), 4.02 (dd, $J = 12.4$, 2.3 Hz, 1H; 6-H or 6′-H), 4.15 (dd, $J = 12.0$, 4.6 Hz, 1H; 6-H or 6′-H), 4.19 (d, $J = 10.5$ Hz, 1H; 1″-H_b), 4.22 (dd, $J = 11.3$, 4.0 Hz, 1H; 6-H or 6′-H), 4.47 (d, $J = 8.0$ Hz, 1H; 1′-H), 4.45–4.49 (m, 1H; 6-H or 6′-H), 4.78 (dd, $J =$ 9.6, 7.8 Hz, 1H; 2′-H), 4.82 (dd, $J = 10.5$, 4.1 Hz, 1H; 2-H), 5.02 (t, $J =$ 10.0 Hz, 1H; 4-H), 5.21 (t, $J = 9.2$ Hz, 1H; 3′-H), 5.31 (t, $J = 10.2$ Hz, 1H; 3-H), 5.36 (d, $J = 4.1$ Hz, 1H; 1-H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 20.51$, 20.58, 20.63, 20.67, 20.75, 20.78, 20.83, 58.00, 61.39, 62.64, 67.89, 68.56, 69.17, 69.96, 70.33, 71.47, 71.52, 72.29, 72.52, 74.47, 95.57, 100.1, 169.4, 169.6, 169.9, 170.0, 170.3, 170.5; MS (200 eV, DCI/NH_3): m/z (%) = 811 (100) $[M+NH_4]^+$; $C_{29}H_{48}O_{18}B_{10}$ (792.8): calcd C 43.94, H 6.10; found C 43.76, H 6.31.

General procedure III: Deprotection of the acetylated carboranyl glycosides: Sodium methoxide (5M solution in methanol) was added to the acetylated carboranyl glycoside in methanol. The mixture was stirred for 1 h at 20 °C, neutralized by addition of ion-exchange resin (Duolite) and the solvent evaporated in vacuo. Purification by chromatography on silica gel afforded the free carboranyl glycosides as a white foam.

1-[(*β*-D-Glucopyranosyl)ethyl]-1,2-dicarba-*closo*-dodecaborane (**4a**): Reaction of **3a** (49 mg, 0.094 mmol) and NaOMe (0.10 mL) in methanol (5 mL) according to general procedure III gave carboranyl glucoside **4a** (32 mg, 0.091 mmol, 97%), solvent system C, m.p. 169 °C; $R_f = 0.44$ (solvent D); $[\alpha]_D^{20} = -17.8$ ($c = 1.0$, MeOH); IR (KBr): $\tilde{\nu} = 3508\ cm^{-1}$ (OH), 3088 (carborane C–H), 2966, 2942, 2914, 2880 (C–H), 2592 (B–H), 1070 (C–O); ^1H NMR (200 MHz, CD_3OD): $\delta = 2.53$ (t, $J = 6.2$ Hz, 2H; 2′-H), 3.03 (dd, $J = 9.0$, 7.9 Hz, 1H; 2-H), 3.15–3.19 (m, 1H), 3.52–3.62 (m, 3H), 3.78 (dd, $J = 11.7$, 1.9 Hz, 1H; 6-H), 3.90 (dt, $J = 11.0$, J′ = 5.9 Hz, 1H; 1′-H_b), 4.14 (d, $J = 7.9$ Hz, 1H; 1-H), 4.62–4.64 (brs, 1H; carborane C-H); ^{13}C NMR (CD_3OD, 75 MHz): $\delta = 38.31$, 62.50, 62.68, 68.23, 74.92, 71.52, 74.87, 77.99, 78.02, 104.1; MS (200 eV, DCI/NH_3): m/z (%) = 368 (100) $[M+NH_4]^+$; $C_{10}H_{26}O_6B_{10}$ (350.4): calcd C 34.28, H 7.48; found C 34.54, H 7.51.

1-[(*β*-D-Glucopyranosyl)butyl]-1,2-dicarba-*closo*-dodecaborane (**4b**): Reaction of **3b** (445 mg, 0.81 mmol) and sodium methoxide (0.20 mL) in methanol (20 mL) according to general procedure III gave carboranyl glucoside **4b** (228 mg, 0.60 mmol, 74%), solvent system C, m.p. 142–143 °C; $R_f = 0.42$ (solvent C); $[\alpha]_D^{20} = -15.8$ ($c = 0.5$, MeOH); IR (KBr): $\tilde{\nu} = 3374\ cm^{-1}$ (O–H), 3048 (carborane C–H), 2976, 2934, 2878 (C–H), 2582 (B–H), 1078, 1038 (C–O); ^1H NMR (200 MHz, $CDCl_3$): $\delta = 1.42$–1.57 (m, 4H; 2′-H, 3′-H), 2.17–2.26 (m, 2H; 4′-H), 3.07 (dd, $J = 8.7$, 7.8 Hz, 1H; 2-H), 3.15–3.26 (m, 3H), 3.42–3.61 (m, 2H), 3.75–3.82 (m, 2H), 4.14 (d, $J = 7.5$ Hz, 1H; 1-H), 4.40–4.50 (brs, 1H; carborane C-H); ^{13}C NMR (50 MHz, CD_3OD): $\delta = 27.16$, 29.91, 38.19, 62.72, 63.52, 69.88, 71.61, 75.03, 78.07, 78.07, 77.87, 101.2; MS (200 eV, DCI/NH_3): m/z (%) = 396 (100) $[M+NH_4]^+$; $C_{12}H_{30}O_6B_{10}$ (378.5).

1-[(*α*-D-Mannopyranosyl)ethyl]-1,2-dicarba-*closo*-dodecaborane (**8**): Reaction of **7** (335 mg, 0.65 mmol) and sodium methoxide (0.10 mL) in

0947-6539/98/0407-1182 $ 17.50+.50/0 *Chem. Eur. J.* **1998**, *4*, No. 7

methanol (10 mL) according to general procedure III gave carboranyl mannoside **8** (207 mg, 0.59 mmol, 91 %), solvent system D, m.p. 197 °C; $R_f = 0.24$ (solvent C); $[\alpha]_D^{20} = +51.8$ ($c = 1.0$, MeOH); IR (KBr): $\tilde{\nu} =$ 3404 cm^{-1} (O–H), 3064 (carborane C–H), 2928 (C–H), 2586 (B–H); ^1H NMR (200 MHz, CD_3OD): $\delta = 2.50$ (t, $J = 6.1$ Hz, 2H; 2′-H), 3.39–3.80 (m, 8H), 4.28–4.43 (br s, 1H; carborane C-H) 4.66 (d, $J = 1.7$ Hz, 1H; 1-H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 38.37$, 62.61, 63.31, 66.39, 68.30, 71.88, 72.41, 75.02, 74.72, 101.7; MS (200 eV, DCI/NH_3): m/z (%) = 368 $[M+NH_4]^+$; $C_{10}H_{26}O_6B_{10}$ (350.4): calcd C 34.28, H 7.48; found C 34.31, H 7.41.

1-[(β-D-Lactopyranosyl)methyl]-1,2-dicarba-*closo*-dodecaborane (**12**): Reaction of **11** (49 mg, 0.062 mmol) and sodium methoxide (50 μL) in methanol (5 mL) according to general procedure III gave carboranyl lactoside **12** (22 mg, 0.044 mmol, 71 %), solvent system E; $R_f = 0.24$ (EtOAc/MeOH 4:1); $[\alpha]_D^{20} = -14.0$ ($c = 0.5$, MeOH); IR (KBr): $\tilde{\nu} =$ 3384 cm^{-1} (O–H), 3074 (carborane C–H), 2928, 2890 (C–H), 2590 (B–H), 1068 (C–O); ^1H NMR (300 MHz, CD_3OD): $\delta = 3.25$ (t, $J = 8.4$ Hz, 1H; 4′-H), 3.40 (ddd, $J = 9.3$, 3.9, 2.4 Hz, 1H; 5-H), 3.45–3.60 (m, 5H), 3.68 (dd, $J = 11.3$, 4.5 Hz, 1H; 6-H), 3.75 (d, $J = 7.5$ Hz, 1H; 1-H or 1′-H), 3.78–3.80 (m, 1H; 6-H), 3.83 (dd, $J = 9.4$, 4.2 Hz, 1H; 6′-H), 3.89 (dd, $J = 12.1$, 2.3 Hz, 1H; 6-H), 4.12 (d, $J = 11.7$ Hz, 1H; 1″-H_a), 4.31–4.34 (m, 2H), 4.33 (d, $J =$ 11.7 Hz, 1H; 1″-H_b), 4.74–4.80 (br s, 1H; carborane C-H); ^{13}C NMR (75 MHz, CD_3OD): $\delta = 60.41$, 61.67, 62.47, 71.65, 74.52, 70.25, 72.47, 74.40, 74.75, 76.17, 76.63, 77.04, 80.22, 104.3, 105.0; MS (200 eV, DCI/NH_3): m/z (%) = 516 (100) $[M+NH_4]^+$; $C_{15}H_{34}O_{11}B_{10}$ (498.5).

1-[(β-D-Maltopyranosyl)methyl]-1,2-dicarba-*closo*-dodecaborane (**16**): Reaction of **15** (52 mg, 0.066 mmol) and sodium methoxide (0.10 mL) in methanol (5 mL) according to general procedure III gave carboranyl maltoside **16** (27 mg, 0.054 mmol, 83 %) as a white solid, solvent system E, m.p. 134 °C; $R_f = 0.34$ (solvent E); $[\alpha]_D^{20} = +51.3$ ($c = 1.0$, MeOH); IR (KBr): $\tilde{\nu} = 3384$ cm^{-1} (O–H), 3070 (carborane C–H), 2930, 2896 (C–H), 2590 (B–H); ^1H NMR (300 MHz, CD_3OD): $\delta = 3.18$ (t, $J = 8.6$ Hz, 1H), 3.26 (t, $J = 9.2$ Hz, 1H), 3.38–3.76 (m, 10H), 4.02 (d, $J = 12.0$ Hz, 1H; 1″-H_a), 4.20 (d, $J = 11.6$ Hz, 1H; 1″-H_b), 4.22–4.28 (m, 1H), 4.34–4.39 (br s, 1H; carborane C-H), 5.19 (d, $J = 3.8$ Hz, 1H; 1-H); ^{13}C NMR (50 MHz, CD_3OD): $\delta = 60.41$, 61.96, 62.66, 71.63, 74.50, 71.39, 74.02, 74.30, 74.73, 74.97, 76.70, 77.51, 80.81, 102.8, 104.4; MS (200 eV, DCI/NH_3): m/z (%) = 516 (87) $[M+NH_4]^+$, 534 (100) $[M+NH_4+NH_3]^+$; $C_{15}H_{34}O_{11}B_{10}$ (498.5).

Toxicity tests: Adherent cells of a human tumor cell line were sown in triplicate in 6 multiwell plates at concentrations of 10^2, 10^3, 10^4, 10^5 cells per cavity, and were incubated with freshly prepared solutions of the compound to be tested at various concentrations. DMSO was used as solubilizing agent (final concentration 0.2 %). After cultivation (11 d for **12**; 12 d for **16**) at 37 °C and 7.5 % CO_2 in air, the medium was removed; the clones were dried, stained with Löffler's methylene blue, and counted under a microscope. The relative clone-forming rate was determined according to the following formula: relative clone-forming rate [%] = (number of clones counted after exposure)/(number of clones counted in the control) × 100.

Cells for the toxicity tests were cultivated at 37 °C and 7.5 % CO_2 in air in 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). During exposure of the cells to the test substances the medium did not contain any FCS to prevent enzymatic hydrolysis by glycohydrolases.[5b]

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[1] a) M. F. Hawthorne, *Angew. Chem.* **1993**, *105*, 997–1033; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 950–984; b) C. Mooren, *Tetrahedron* **1994**, *50*, 12521–12569; c) R. F. Barth, A. H. Soloway, R. G. Fairchild, R. M. Brugger, *Cancer* **1992**, *70*, 2995–3007; d) D. Gabel, *Chem. Unserer Zeit* **1997**, *31*, 235–240.

[2] R. F. Barth, A. H. Soloway, R. G. Fairchild, *Cancer Res.* **1990**, *50*, 1061–1070 and references therein.

[3] D. Gabel, S. Foster, R. G. Fairchild, *Radiat. Res.* **1987**, *111*, 14–25.

[4] a) L. F. Tietze, R. Fischer, R. Lögers, M. Beller, *Carbohydr. Res.* **1989**, *194*, 155–162; b) L. F. Tietze, M. Neumann, R. Fischer, T. Möllers, K. H. Glüsenkamp, M. F. Rajewsky, E. Jähde, *Cancer Res.* **1989**, *49*, 4179–4184; c) L. F. Tietze, M. Beller, R. Fischer, M. Lögers, E. Jähde, K. H. Glüsenkamp, R. F. Rajewsky, *Angew. Chem.* **1990**, *102*, 812–813; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 782–783; d) L. F. Tietze, A. Fischer-Beller, *Carbohydr. Res.* **1994**, *254*, 169–182; e) L. F. Tietze, H. Keim, *Angew. Chem.* **1997**, *109*, 1704–1706; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 1615–1617.

[5] a) L. N. Jungheim, T. A. Shepherd, *Chem. Rev.* **1994**, *94*, 1553–1566; b) L. F. Tietze, R. Hannemann, W. Buhr, M. Lögers, P. Menningen, M. Lieb, D. Starck, T. Grote, A. Döring, I. Schubert, *Angew. Chem.* **1996**, *108*, 2840–2842; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2674–2677.

[6] Synthesis of carboranes linked to sugars: a) W. V. Dahlhoff, J. Bruckmann, K. Angermund, C. Krüger, *Liebigs Ann. Chem.* **1993**, 831–835; b) W. Tjarks, A. K. M. Anisuzzaman, L. Liu, A. H. Soloway, R. F. Barth, D. J. Perkins, D. M. Adams, *J. Med. Chem.* **1992**, *35*, 1628–1633; c) J. L. Maurer, F. Berchier, A. J. Serino, C. B. Knobler, M. F. Hawthorne, *J. Org. Chem.* **1990**, *55*, 838–843.

[7] J. L. Maurer, A. J. Serino, M. F. Hawthorne, *Organometallics* **1988**, *7*, 2519–2524.

[8] It is known that reaction of alkynes with decaborane gives 1,2-dicarba-*closo*-dodecaborane: a) T. L. Heying, J. W. Ager, S. L. Clark, D. J. Mangold, H. L. Goldstein, M. Hillman, R. J. Polak, J. W. Szymanski, *Inorg. Chem.* **1963**, *2*, 1089–1092; b) M. M. Flein, D. Grafstein, J. E. Paustian, J. Bobinski, B. M. Lichstein, N. Mayes, N. N. Schwartz, M. S. Cohen, *Inorg. Chem.* **1963**, *2*, 1115–1119.

[9] Glycosidation by imidates: R. R. Schmidt, *Angew. Chem.* **1986**, *98*, 213–236; *Angew. Chem. Int. Ed. Engl.* **1986**, *25*, 212–235.

[10] R. Schaeffer, *J. Am. Chem. Soc.* **1957**, *79*, 1006–1007.

[11] The in vitro toxicity tests were carried out by Dr. I. Schubert and A. Döring in the cell culture laboratory of the Institut für Organische Chemie.

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