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# Synthesis of Carboranyl Derivatives of Alkynyl Glycosides as Potential BNCT Agents

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**Abstract**: A series of amphiphilic carbohydrate-carborane hybrids consisting of a lipophilic core (carborane cage) and a glycoside moiety for conferring high-affinity recognition by the cellular lectins have been prepared in a chemically accessible fashion. 

*Keywords*: Carboranes; glycosides; boron and compounds

Boron neutron capture therapy (BNCT) is a binary therapeutic strategy for cancer treatment utilising the selective irradiation by slow (thermal) neutrons of a $^{10}$B-containing drug (or biomolecule) in a tumour to elicit an efficient nuclear reaction.[1] This interaction produces an α particle and recoils a $^{7}$Li ion bearing 2.4 MeV (eq. 1).

$$^{10}_{5}\mathrm{B} + ^{1}_{0}n \rightarrow ^{7}_{3}\mathrm{Li} + ^{4}_{2}\mathrm{He} + 2.4\mathrm{MeV} \qquad \text{(eq.1)}$$

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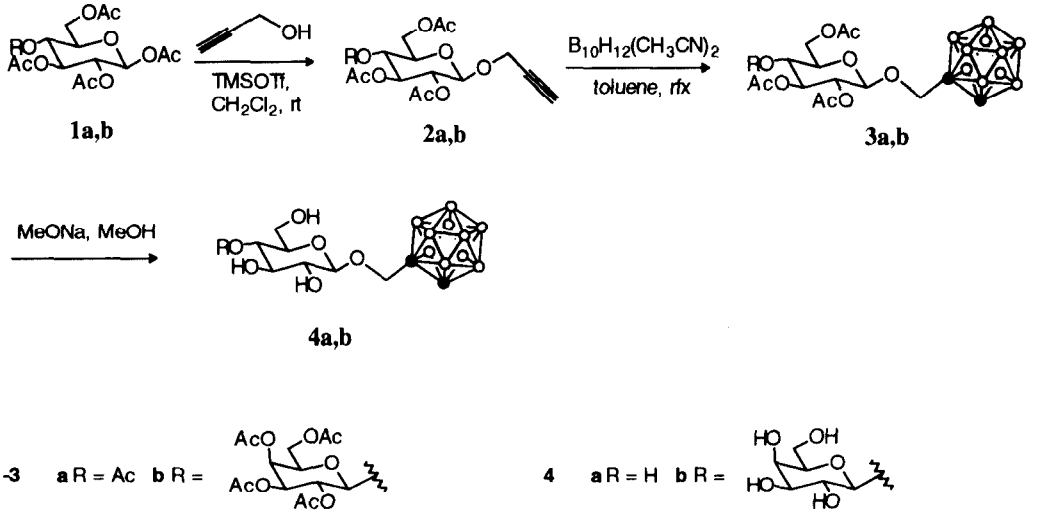
These dissipate their kinetic energy before travelling one cell diameter so that the destructive effect is highly localised to boron-loaded tissue. In order to be therapeutically useful, a boronated candidate must have a) high tumour-targeting selectivity; b) low cytotoxicity; c) high water solubility and d) high uptake by cancer cells. To meet these criteria several boron-containing molecules (*e.g.* amino acids, porphyrins, lipids, nucleosides, and carbohydrates) have been synthesised with a borane, cyanoborane, dihydroxyboryl and icosahedral carborane cluster embodied. However, most of these candidates suffer from one or more drawbacks. Therefore, the quest to develop new molecules for site directed delivery of boron based on molecular recognition processes has sparked recently. The significant role played by glycoconjugates in mediating critical biological events at the cellular level (*e.g.* adhesion, differentiation and metastasis) is well established.[2] Much effort has been directed to the search for the lactose-binding lectin (LBL) inhibitors in the response to the indication that LBLs are present on the tumour cell surface and are responsible for metastatic growth.[3] Accordingly, several β-lactosyl derivatives are known to be preferentially retained in tumours thereby inhibiting metastatic deposition of melanoma cells. This property makes glycosyl carboranes promising candidates for BNCT. The interest for a carborane cage as the boron source in BNCT is largely dictated by its intrinsic stability, versatility, structural array, electronic properties and, finally, a 10-fold increase of boron content compared to most of the above mentioned groups.[4] The design process of carbohydrate carborane hybrids requires a delicate balance between lipophilicity and hydrophilicity (*i.e.*, the amphiphilic character) of the molecule. It was reasoned that the lipophilic carborane cage would act as the "pharmacophore" and the hydrophilic carbohydrate would serve as an accessory appendage to escort the boronated moiety to the tumour cell surface.

Two general synthetic approaches leading to C-substituted 1,2-dicarba-*closo*-dodecaboranes (12) (*o*-carboranes) have been commonly used: a) reaction of substituted alkynes with commercially available decaborane $B_{10}H_{14}$ under appropriate conditions, ii) reaction of a metallo-*o*-carborane (*e.g.*, *o*-carboranyl lithium) with an electrophilic center.[5] We herein report the synthesis of new carbohydrate-*o*-carborane hybrids capitalising on the proclivity of an alkyne moiety (suitably anchored to the anomeric position) to react with complexes $B_{10}H_{12}L_2$ prepared from decaborane and Lewis bases (where L is MeCN, $R_3N$ or $R_2S$). Our initial efforts to prepare

the proposed boronated substrates (*e.g.*, alkynyl glycosides) focused on the Lewis acid-promoted glycosidation of pentaacetyl-D-glucose **1a** (and the respective lactose derivative **1b**) with 2-propyn-1-ol.

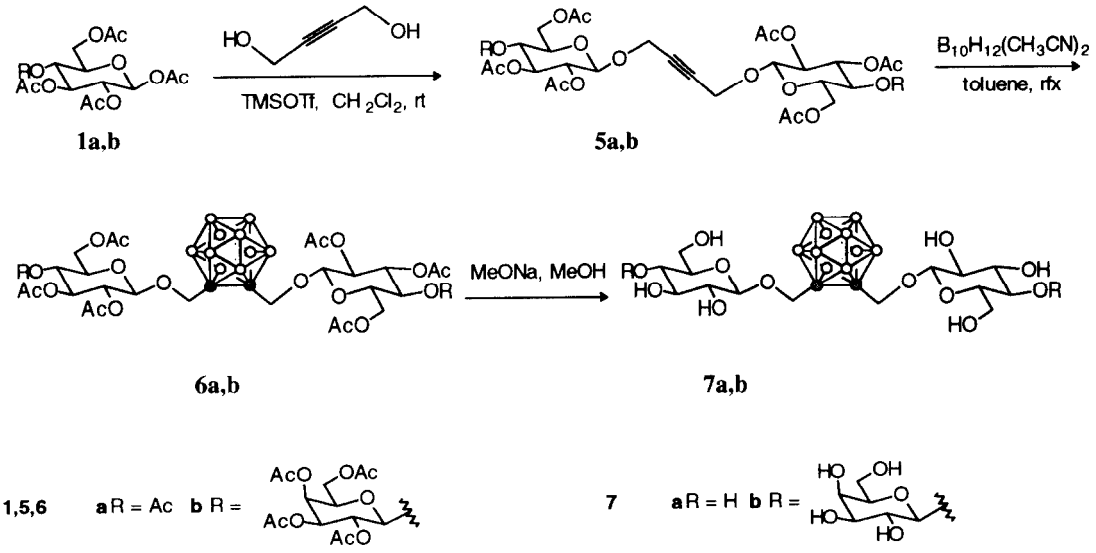
**Scheme I**




Best results were obtained by reaction of **1a** with 2.0 equiv of 2-propyn-1-ol in $CH_2Cl_2$ containing 2.0 equiv of TMSOTf (0°C, 1.5 h) (Scheme I) whereas glycosidation under other conditions (*i.e.*, with $BF_3{\cdot}Et_2O$[6]) did not lead to improved results. In order to enhance solubility of the final carboranes we also used 2-butyne-1,4-diol as precursor to 2-butyne-1,4-diyl glycosides in which the hydrophobic moiety is embedded within two hydrophilic ends (Scheme II). Such glycosides have been previously prepared albeit in modest yields using $SnCl_4$ as Lewis acid on bis(tri-*n*-butylstannyl)ether of 2-butyne-1,4-diol.[7] Under our optimised conditions, glycosides **2a,b** and **5a,b** were isolated in a yield varying from 18% to 57%. The $^1$H-NMR spectra of compounds **2a,b** showed the presence of a signal at 2.54 ppm (t, 4H, J = 2.4 Hz) attributable to the alkyne proton. The anomeric configuration of the glycosides **2a**, **5a** and lactosides **2b**, **5b** was confirmed by $^1$H-NMR spectra in which the corresponding H-1 protons appeared as a doublet (J = 7.7-8.2 Hz) at 4.65-4.75 ppm indicative of 1,2-*trans* glycosides. The

exclusive formation of β-derivatives is explained on the basis of neighbouring-group participation.

**Scheme II**

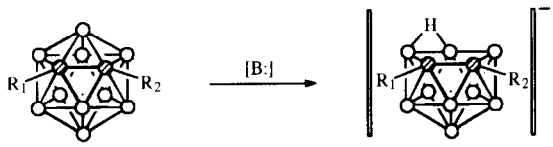



For the boronation of compounds **2a,b**-**5a,b**, solvent turned out to be a critical factor. Initial attempts with preformed 6,9-bis(acetonitrile)decaborane, $B_{10}H_{12}(MeCN)_2$[8] in refluxing toluene gave low yields, even after a prolonged reaction time. However, the use of MeCN as a cosolvent granted the corresponding glycosyl carboranes **3a,b**-**6a,b** in 60-75 % range yield, the disubstituted alkynes **5a,b** being less prone to boronation because of severe steric hindrance.

Positive electrospray ionisation (ESI) mass spectrometry was used to show that all the products had the expected molecular weight. The $^1$H-NMR spectra of compounds **3a,b** exhibited the presence of broadened signals between 1.4-3.0 ppm assigned to the B-H and a broad singlet at 3.9 ppm due to the proton linked to the carbon atom of the carborane cage. Moreover, the $\{^1H\}^{11}$B-NMR spectra showed the presence of three broad signals around -2, -7.5 and -11.7 ppm in a 1:2:2 ratio. Similarly, compounds **6a,b** showed the presence of broad signals at 1.2-3 ppm for B-H protons in the $^1$H-NMR spectra and, for compound **6b**, the $\{^1H\}^{11}$B-NMR spectrum showed the presence of two broad signals at -1.84 and -9.7 ppm in a 1:4 ratio. The

final deprotection of the acetyl protecting groups was first attempted on compound **3a** with $K_2CO_3$ in 9:1 EtOH-$H_2O$. However, compound **3a** reacted very slowly under these conditions. In fact, after 3 days at room temperature, a TLC revealed a complex mixture of partially deacetylated products. When the reaction mixture was warmed to 50° C, the deacetylation was complete but the formation of a mixture of two compounds was observed. In icosahedral carborane chemistry, base-induced degradation is understood to be the removal of one B vertex from the *closo*-1,2-$C_2B_{10}H_{11}$-cage to produce an hydrophilic [*nido*-7,8- $C_2B_9H_{11}$]$^-$-cage fragment which incorporates a negative charge (Scheme III).[4] Thus, on treatment of such mixture with pyrrolidine,[5d] which is known to promote this rearrangement, the less polar compound was converted into the more polar one, thereby suggesting that the two compounds were the *closo* and the *nido* derivatives, respectively. *Nido* structures have been used to prepare more soluble analogues, however their stability *in vivo* is not well documented and their ionic character suggests that interaction with reactive centers is highly probable.[9]

**Scheme III**




*Closo-* *Nido-*

Thus, the deacetylation was then attempted according to the Zemplén protocol[10] (MeONa, MeOH, r.t.) as it is known that under these conditions the above mentioned conversion can be avoided.[7] After careful optimisation of the reaction conditions, we found that the use of a 0.06-0.08 M solution of sodium methoxide in methanol deacetylated efficiently our compounds avoiding the formation of the corresponding *nido* derivative. The use of higher concentration of the base caused the formation of traces of a more polar compound, as previously described for the deacetylation with $K_2CO_3$ at 50° C, supposed to be the *nido* isomer. The final compounds were then isolated in good yield by neutralisation with Amberlite® IR-120 ($H^+$-form), filtration and evaporation of the solvent.

The $^1$H-NMR spectra of the final products showed the presence of the expected signals for the anomeric protons and the boron linked protons. The $\{^1H\}^{11}$B-NMR showed three signals

around -1.5, -6.6 and -10 ppm for compounds **4a,b** and two signals around -2.3 and -10 ppm for compounds **7a,b**. The ESI-MS (positive mode) of these compounds exhibited the respective cationised peaks $[M+Na]^+$. Expansion of these signals gave the expected isotope distribution and the molecular weight for **4a,b** and **7a,b** was further apparent from the corresponding negative ESI-MS which showed relevant peaks $[M+Cl]^-$.

In conclusion, we have synthesised several carbohydrate-carborane hybrids consisting of lipophilic and glycosidic moieties for conferring enhanced solubility and high-affinity recognition by the lectins. These advantageous properties open the way for the employment of these compounds as BNCT agents for the efficient targeting of amphiphilic or water-soluble carboranes to the tumour cell surface.

Pharmacological studies to determine the mode of action of these compounds have been initiated and their evaluation as BNCT agents against a panel of tumours is in progress.

## EXPERIMENTAL

### General Procedures and Materials

All reactions were performed under nitrogen atmosphere. Reagents and dry solvents were added *via* oven-dried syringes through septa. Dichloromethane and acetonitrile were distilled from calcium hydride. Toluene was distilled from sodium. Flash chromatography was performed as described in *J. Org. Chem.*, **1978**, *43*, 2923. Melting points were determined on a Büchi 510 apparatus and were uncorrected. Thin-layer chromatography (TLC) was performed on Merck silica gel 60 $F_{254}$ plates, and visualised by charring either with a 1:1 mixture of 20% sulphuric acid and $I_2$ (10 g) – KI (100 g) in $H_2O$ (500 ml) or with a solution of $(NH_4)_6Mo_7O_{24}$ (21 g), of $Ce(SO_4)_2$ (1 g) and conc. $H_2SO_4$ (31 mL) in $H_2O$ (500 mL) followed by heating or with $PdCl_2$-HCl[11] (for carborane-containing compounds). $^1$H-NMR and $^{13}$C-NMR spectra were recorded on a Bruker AC200 or AC300 instrument. $\{^1H\}^{11}$B-NMR spectra were recorded on a Jeol EX400 spectrometer and were referenced to $KBF_4$. IR spectra (KBr pellets) were performed on a Perkin-Elmer 237 instrument. Specific rotations ($[\alpha]_D$) were determined on a Perkin-Elmer 241 polarimeter at 20°C. Mass spectra (ESI/MS spectra) were recorded on a Finnigan MAT 700 spectrometer (MeCN as solvent) The mass value reported in each product characterisation refers

to the highest peak of the isotopic cluster. Decaborane(14) ($B_{10}H_{14}$) was purchased from Aldrich. **WARNING**: this highly toxic compound forms impact-sensitive mixtures with several materials, therefore the following experiments must be conducted with extreme caution. Elemental analyses for carbon and hydrogen were determined with a Perkin-Elmer 240 elemental analyser. Microanalyses of all non-crystalline compounds were performed after careful drying (0.15-0.30 kPa, 24-48h). In most cases the reported yields for the products were not optimised.

**Typical procedure for the preparation of propynyl glycosides 2a, 2b**

To a solution of pentaacetyl-D-glucose (2.73 g, 7 mmol) in dry $CH_2Cl_2$ (20 mL) were added oven-dried 4Å molecular sieves, 2-propyn-1-ol (0.83 mL, 14 mmol) and trimethylsilyl triflate [(2.53 mL, 14 mmol) except for the preparation of compound **2b** where 3.80 mL (21 mmol)] were used at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 1-1.5 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ and filtered through a Celite® pad. The organic layer was washed twice with water, dried over $Na_2SO_4$ and evaporated under reduced pressure. Flash-chromatography (hexane-EtOAc, 1:1) of the crude residue afforded the pure alkynyl glycosides.

***1-(2-Prop-1-ynyl)-2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside* (2a)**

(57%). Colourless solid, mp 115-117° C (MeOH-$H_2O$) (lit.[7] 114-116° C). $[\alpha]_D$ -36.8 (*c* 1.3, $CHCl_3$) (lit.[7] -37.4).

***1-(2-Prop-1-ynyl)-(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-gluco-pyranoside* (2b)**

(56%). Colourless solid, mp 153-155° C (MeOH). $[\alpha]_D$ -23.8 (*c* 1.0, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.32 (d, 1 H, $J_{3',4'}$ = 3.5 Hz, H-4'), 5.11 (t, 1 H, $J_{2,3} = J_{3,4}$ = 9.2 Hz, H-3), 4.98 (dd, 1 H, $J_{2',3'}$ = 10.1 Hz, $J_{1',2'}$ = 7.9 Hz, H-2'), 4.87 (dd, 1 H, $J_{2',3'}$ = 10.1 Hz, $J_{3',4'}$ = 3.5 Hz, H-3'), 4.80 (dd 1 H, $J_{1,2}$= 8.0 Hz, $J_{2,3}$ = 9.2 Hz, H-2), 4.64 (d, 1 H, $J_{1,2}$= 8.0 Hz, H-1), 4.48-4.32 (m, 2 H, H-1', H-6a), 4.22 (d, 1 H, J = 2.1 Hz, $OCH_2C$=), 4.12-3.92 (m, 3 H, H-6b, 2 H6'), 3.80 (br t, 1 H, $J_{5',6'}$ = 6.6 Hz, H-5'), 3.73 (t, 1 H, $J_{3,4} = J_{4,5}$ = 9.2 Hz, H-4), 3.55 (m, 1 H, H-5), 2.48 (m, 1 H, J = 2.1 Hz, C=CH) 1.9-2.3 (7 s, 21 H, $CH_3CO$). $^{13}$C-NMR (50.29 MHz, $CDCl_3$): δ 170.2-

168.7 (s, CO), 100.8, 97.8 (2d, C-1, C-1'), 78.0 (s, *C*=CH), 75.9 (d), 75.3 (d, C≡*C*H) 72.7 (d), 72.6 (d), 71.2 (d), 70.8 (d), 70.6 (d), 69.0 (d), 66.6 (d), 61.8, 60.8 (2t, C-6, C-6'), 55.7 ($CH_2C$=), 20.7-20.3 (q, $CH_3CO$). IR 3300, 2110, 1740 $cm^{-1}$. Calcd. for $C_{29}H_{38}O_{18}$: C 52.85, H 5.74; found: 52.68, H 5.85.

**Typical procedure for the preparation of alkynyl diglycosides 5a, 5b**

To a solution of pentaacetyl-D-glucose (2.73 g, 7 mmol) in dry $CH_2Cl_2$ (20 mL) were added oven-dried 4Å molecular sieves, 2-butyne-1,4-diol (301 mg, 3.5 mmol) and trimethylsilyl triflate [(2.53 mL, 14 mmol) except for the preparation of compound **5b** where 3.80 mL (21 mmol)] were used at 0°C. The reaction mixture was allowed to warm to room temperature and stirred for 1-1.5 h. The reaction was quenched by addition of a saturated solution of $NaHCO_3$ and filtered through a Celite® pad. The organic layer was washed twice with water, dried over $Na_2SO_4$ and evaporated under reduced pressure. Flash-chromatography (hexane-EtOAc, 1:1) of the crude residue afforded the pure alkynyl lactosides.

***1,4-Di-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)-2-butyne* (5a)**

(34%). Pale yellow solid, mp 118-120° C (EtOH-hexane) (lit.[7] 119-122° C). $[\alpha]_D$ -44.1 (*c* 1.2, $CHCl_3$) (lit.[7] -47.3).

***1,4-Di-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-gluco-pyranosyl-oxy]-2-butyne* (5b)**

(18%). Colourless glass. $[\alpha]_D$ -19.1 (*c* 1.2, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$, COSY) δ 5.31 (d, 1 H, $J_{3',4'}$ = 3.0 Hz, H-4'), 5.18 (t, 1 H, $J_{2,3}$ = $J_{3,4}$ = 9.2 Hz, H-3), 5.07 (dd, 1 H, $J_{2',3'}$ = 10.0 Hz, $J_{1',2'}$ = 7.7 Hz, H-2'), 4.93 (dd, 1 H, $J_{2',3'}$ = 10.0 Hz, $J_{3',4'}$ = 3.0 Hz, H-3'), 4.87 (dd 1 H, $J_{1,2}$= 8.1 Hz, $J_{2,3}$ = 9.2 Hz, H-2), 4.65 (d, 1 H, $J_{1',2'}$ = 7.7 Hz, H-1'), 4.60-4.40 (m, 2 H, H-1, H-6a), 4.34 (m, 2 H, $OCH_2C$=), 4.20-4.00 (m, 3 H, H-6b, 2 H6'), 3.90-3.70 (m, 2 H, H-4, H-5'), 3.62 (m, 1 H, H-5), 1.9-2.3 (7 s, 21 H, $CH_3CO$). $^{13}$C-NMR (75.46 MHz, $CDCl_3$): δ 170.2-168.9 (s, CO), 101.0, 98.1 (2d, C-1, C-1'), 81.7 (s, *C*, 76.0 (d), 72.7 (d, 2 C), 71.4 (d), 70.9 (d), 70.6 (d), 69.1 (d), 66.6 (d), 61.8, 60.8 (2t, C-6, C-6'), 56.0 (t, $CH_2C$=), 20.7-20.3 (q, $CH_3CO$). IR 3477, 2963, 1752 $cm^{-1}$. Calcd. for $C_{56}H_{74}O_{36}$: C 50.83, H 5.64; found: 50.69, H 5.70.

**General procedure for the preparation of the 1,2-dicarba-*closo*-carboranyl derivatives**

A flask containing $B_{10}H_{14}$ (73 mg, 0.60 mmol), $CH_3CN$ (3.1 mL, 60 mmol) and 8 mL of dry toluene was warmed at reflux for 1 h. After cooling, the appropriate alkynyl glycoside (0.30-0.50 mmol) was added and the mixture was warmed to 100°C and stirred at this temperature for 24-36 h. The mixture was cooled and filtered on paper, the filter was washed with toluene and the solvent evaporated under reduced pressure. The crude mixture was then purified by flash-chromatography (toluene-acetone, 85:15 or hexane-EtOAc, 1:1).

***[1,2-dicarba*-closo-*dodecaborane(12)-1-ylmethyl]2,3,4,6-tetra-O-acetyl-β-D-glucopyranoside* (3a)**

(56%). Colourless glass. $[\alpha]_D$ -24.6 (*c* 1.6, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.18 (t, 1 H, $J_{2,3} = J_{3,4} = 9.5$ Hz, H-3), 5.03 (t, 1 H, $J_{3,4} = J_{4,5} = 9.5$ Hz, H-4), 4.95 (dd, 1 H, $J_{2,3} = 9.5$ Hz, $J_{1,2} = 7.9$ Hz, H-2), 4.47 (d, 1 H, $J_{1,2} = 7.9$ Hz, H-1), 4.23 (d, 1 H, $^2J$ =10.9 Hz, OC*H*HC$_{cage}$), 4.21 (dd, 1H, $J_{5,6a} = 4.9$ Hz, $J_{6a,6b} = 12.5$ Hz, H-6a), 4.11 (dd, 1H, $J_{5,6b} = 2.3$ Hz, $J_{6a,6b} = 12.5$ Hz, H-6b), 3.94 (d, 1 H, $^2J$ =10.9 Hz, OCH*H*C$_{cage}$), 3.90 (br s, HC$_{cage}$), 3.65 (ddd, 1 H, $J_{4,5} = 9.5$ Hz, $J_{5,6a} = 4.9$ Hz, $J_{5,6b} = 2.3$ Hz, H-5), 1.9-2.2 (4s, 12 H, $CH_3CO$). $^{13}$C-NMR (50.29 MHz, $CDCl_3$): δ 169.2 (s, CO), 100.5 (d, C-1), 72.2 (d, 2 C), 71.6 (s, C$_{cage}$), 70.8 (d), 70.2 (t, *C*H$_2$C$_{cage}$), 68.1 (d), 61.5 (t, C-6), 20.4 (q, 4 *C*H$_3$CO). $^{11}$B-NMR ($CDCl_3$) δ -2.20 (2 B), -7.56 (4 B), -11.62 (4 B). IR 3450, 2920, 2590, 1754. ESI-MS: Calcd. for $C_{17}H_{32}B_{10}O_{10}$ 504 u.m.a.; found: 527 u.m.a. ($MNa^+$). [Found: C, 40.37; H, 6.53. $C_{17}H_{32}B_{10}O_{10}$ requires C, 40.47; H, 6.39%].

***[1,2-dicarba*-closo-*dodecaborane(12)-1-ylmethyl](2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-2,3,6-tri-O-acetyl-β-D-glucopyranoside* (3b)**

(60%). Colourless glass. $[\alpha]_D$ -12.9 (*c* 1.0, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$, COSY) δ 5.33 (d, 1 H, $J_{3',4'} = 3.3$ Hz, H-4'), 5.17 (t, 1 H, $J_{2,3} = J_{3,4} = 9.3$ Hz, H-3), 5.08 (dd, 1 H, $J_{2',3'} = 10.4$ Hz, $J_{1',2'} = 7.8$ Hz, H-2'), 4.94 (dd, 1 H, $J_{2',3'} = 10.4$ Hz, $J_{3',4'} = 3.3$ Hz, H-3'), 4.86 (dd 1 H, $J_{1,2}$= 8.0 Hz, $J_{2,3} = 9.3$ Hz, H-2), 4.55-4.40 (m, 3 H, H-1, H-1', H-6a), 4.18 (d, 1 H, $^2J$ = 10.9 Hz, OC*H*HC$_{cage}$), 4.17-4.00 (m, 3 H, H-6b, 2 H6'), 3.93 (d, 1 H, $^2J$ =10.9 Hz, OCH*H*C$_{cage}$), 3.90-3.80 (m, 2 H, HC$_{cage}$, H-5'), 3.76 (t, 1 H, $J_{3,4} = J_{4,5} = 9.3$ Hz, H-4), 3.57 (m, 1 H, H-5), 1.9-2.3 (7

s, 21 H, $CH_3CO$). $^{13}$C-NMR (75.46 MHz, $CDCl_3$): δ 170.2-168.7 (s, CO), 101.0, 100.4 (2d, C-1, C-1'), 75.8 (d), 73.1 (d), 72.1 (d), 71.6 (s, $C_{cage}$), 71.1 (d), 70.8 (d, 2 C), 70.3 (t, $CH_2C_{cage}$), 69.1 (d), 66.6 (d), 61.5, 60.8 (2t, C-6, C-6'), 20.7-20.3 (q, $CH_3CO$). $^{11}$B-NMR ($CDCl_3$) δ -2.0 (2 B), -7.49 (4 B), -11.77 (4 B). IR 3446, 2924, 2591, 1753 cm$^{-1}$. ESI-MS: Calcd. for $C_{29}H_{48}B_{10}O_{18}$ 793 u.m.a.; found: 816 u.m.a. ($MNa^+$). [Found: C, 43.80; H, 6.15. $C_{29}H_{48}B_{10}O_{18}$ requires C, 43.94; H, 6.10%].

***1,2-Di-(2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyloxy)methyl1,2-dicarba*-closo-*dodecaborane (12)* (6a)**

(43%). Colourless foam. $[\alpha]_D$ -12.1 (*c* 1.0, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$) δ 5.20 (t, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3), 5.05 (t, 1 H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 4.99 (dd, 1 H, $J_{2,3} = 9.4$ Hz, $J_{1,2} = 7.8$ Hz, H-2), 4.53 (d, 1 H, $J_{1,2} = 7.8$ Hz, H-1), 4.29 (d, 1 H, $^2J$ =12.7 Hz, OC*H*HC$_{cage}$), 4.25 (dd, 1 H, $J_{5,6a} = 4.8$ Hz, $J_{6a,6b} = 12.5$ Hz, H-6a), 4.12 (dd, 1 H, $J_{5,6b} = 2.3$ Hz, $J_{6a,6b} = 12.5$ Hz, H-6b), 3.98 (d, 1 H, $^2J$ =12.7 Hz, OCH*H*C$_{cage}$), 3.70 (ddd, 1 H, $J_{4,5} = 9.4$ Hz, $J_{5,6a} = 4.8$ Hz, $J_{5,6b} = 2.3$ Hz, H-5), 1.9-2.2 (m, 24 H, $CH_3CO$). $^{13}$C-NMR (50.29 MHz, $CDCl_3$): δ 171-169 (s, CO), 100.6 (d, C-1), 75.8 (s, $C_{cage}$), 72.3 (d), 72.0 (d), 70.8 (d), 68.7 (t, $CH_2C_{cage}$), 68.0 (d), 61.5 (t, C-6), 20.5 (q, $CH_3CO$). IR 3481, 1752 cm$^{-1}$. ESI-MS: Calcd. for $C_{32}H_{52}B_{10}O_{20}$ 865 u.m.a.; found: 888 u.m.a. ($MNa^+$). [Found: C, 44.41; H, 6.20. $C_{32}H_{52}B_{10}O_{20}$ requires C, 44.44; H, 6.06%].

***1,2-Di-[(2,3,4,6-tetra-O-acetyl-β-D-galactopyranosyl)-(1→4)-(2,3,6-tetra-O-acetyl-β-D-glucopyranosyloxy) methyl] 1,2-dicarba*-closo-*dodecaborane(12)* (6b)**

The title compound was obtained in 27% yield after careful silica gel chromatography using hexane-EtOAc-MeOH, 5:5:0.3 as the eluting solvent. Colourless foam. $[\alpha]_D$ -4.1 (*c* 1.0, $CHCl_3$). $^1$H-NMR (300 MHz, $CDCl_3$, COSY) δ 5.32 (d, 1 H, $J_{3',4'} = 3.1$ Hz, H-4'), 5.16 (t, 1 H, $J_{2,3} = J_{3,4} = 9.4$ Hz, H-3), 5.07 (dd, 1 H, $J_{2',3'} = 10.1$ Hz, $J_{1',2'} = 7.8$ Hz, H-2'), 4.95 (dd, 1 H, $J_{2',3'} = 10.1$ Hz, $J_{3',4'} = 3.1$ Hz, H-3'), 4.86 (dd 1 H, $J_{1,2} = 7.9$ Hz, $J_{2,3} = 9.4$ Hz, H-2), 4.60-4.40 (m, 3 H, H-1, H-1', H-6a), 4.22 (d, 1 H, $^2J = 12.8$ Hz, OC*H*HC$_{cage}$), 4.20-4.00 (m, 3 H, H-6b, 2 H6'), 3.93 (d, 1 H, $^2J$ =12.8 Hz, OCH*H*C$_{cage}$), 3.85 (br t, $J_{5',6'} = 6.9$ Hz, H-5'), 3.76 (t, 1 H, $J_{3,4} = J_{4,5} = 9.4$ Hz, H-4), 3.60 (m, 1 H, H-5), 1.9-2.3 (7 s, 21 H, $CH_3CO$). $^{13}$C-NMR (75.46 MHz, $CDCl_3$): δ 170.2-168.9

(s, CO), 101.0, 100.2 (2d, C-1, C-1'), 75.8 (d), 75.7 (s, $C_{cage}$), 73.0 (d), 72.3 (d), 71.2 (d), 70.9 (d), 70.7 (d), 69.1 (d), 68.6 (t, $CH_2C_{cage}$), 66.6 (d), 61.8, 60.8 (2t, C-6, C-6'), 20.7-20.3 (q, $CH_3CO$). $^{11}$B-NMR ($CDCl_3$) δ -1.84 (2 B), -9.70 (8 B). IR 3480, 1748 $cm^{-1}$. ESI-MS: Calcd. for $C_{56}H_{84}B_{10}O_{36}$ 1442 u.m.a.; found: 1465 u.m.a. ($MNa^+$). [Found: C, 46.49; H, 6.01. $C_{56}H_{84}B_{10}O_{36}$ requires C, 46.66; H, 5.87%].

**General procedure for the deacetylation reaction**

To a stirred 0.06-0.08 M solution of MeONa in dry MeOH (10 mL) under nitrogen was added the protected glycosyl carboranes (200 mg). After stirring for 4-6h (TLC, $CH_2Cl_2$-MeOH 9:1) at room temperature and subsequent neutralisation by addition of Amberlite® IR-120 ($H^+$-form) ion exchange resin (carefully washed with MeOH), filtration followed by concentration under reduced pressure afforded pure glycosyl carboranes.

***[1,2-dicarba*-closo-*dodecaborane(12)-1-ylmethyl] β-D-glucopyranoside* (4a)**

(95%). Colourless foam. $[\alpha]_D$ -24.7 (*c* 1.5, $CH_3OH$). $^1$H-NMR (300 MHz, $CD_3OD$) δ 4.33 (d, 1 H, $^2J$ =11.3 Hz, OC*H*HC$_{cage}$), 4.26 (d, 1 H, $J_{1,2}$ = 7.9 Hz, H-1), 4.10 (d, 1 H, $^2J$ =11.3 Hz, OCH*H*C$_{cage}$), 3.84 (br d, $J_{5,6a}$ = 11.7, H-6a), 3.62 (m, 1 H), 3.38-3.10 (m, 4 H), 2.9, 2.4, 1.8, 1.4, (4 br s, 10H, BH). $^{13}$C-NMR (50.29 MHz, $CD_3OD$):[12] δ 104.5 (d, C-1), 78.1 (d), 77.9 (d), 74.8 (d), 74.6 (s, $C_{cage}$), 71.7 (t, $CH_2C_{cage}$), 71.4 (d), 62.6 (t, C-6). $^{11}$B-NMR ($CD_3OD$) δ -1.44 (2 B), -6.65 (4 B), -9.50 (4 B). IR 3230, 2595. ESI-MS: Calcd. for $C_9H_{24}B_{10}O_6$ 336 u.m.a.; found: 359 u.m.a. ($MNa^+$). [Found: C, 31.99; H, 7.30. $C_9H_{24}B_{10}O_6$ requires C, 32.14; H, 7.19%].

***[1,2-dicarba*-closo-*dodecaborane(12)-1-ylmethyl](β-D-galactopyranosyl)-(1→4)-β-D-gluco-pyranoside* (4b)**

(95%). Colourless glass. $[\alpha]_D$ -11.7 (*c* 1.1, $CH_3OH$). $^1$H-NMR (300 MHz, $CD_3OD$) δ 4.34 (d, 1 H, $J_{1',2'}$ = 7.1 Hz, H-1'), 4.32 (d, 1 H, $^2J$ = 11.5 Hz, OC*H*HC$_{cage}$), 4.30 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H-1), 4.11 (d, 1 H, $^2J$ =11.5 Hz, OCH*H*C$_{cage}$), 3.95-3.65 (m, 5 H), 3.65-3.35 (m, 6 H), 3.25 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 8.4 Hz, H-4). $^{13}$C-NMR (75.46 MHz, $CD_3OD$) δ 105.1, 104.4 (2d, C-1, C-1'), 80.4 (d), 77.1 (d), 76.7 (d), 76.3 (d), 74.8 (d), 74.5 (d), 72.5 (d), 71.7 (t, $CH_2C_{cage}$), 70.3 (d), 62.5, 61.8 (2t, C-6, C-6'). $^{11}$B-NMR ($CD_3OD$)[12] δ -1.40 (2 B), -6.63 (4 B), -9.57 (4 B). IR 3222,

2592, 1633. ESI-MS: Calcd. for $C_{15}H_{34}B_{10}O_{11}$ 498 u.m.a.; found: 521 u.m.a. ($MNa^+$). [Found: C, 36.27; H, 6.95. $C_{15}H_{34}B_{10}O_{11}$ requires C, 36.14; H, 6.87%].

***1,2-Di-(β-D-glucopyranosyloxy)methyl-1,2-dicarba*-closo-*dodecaborane(12)* (7a)**

(95%). Colourless foam. $[\alpha]_D$ -14.0 (*c* 1.7, $CH_3OH$). $^1$H-NMR (300 MHz, $CD_3OD$) δ 4.49 (d, 1 H, $^2J$ =12.1 Hz, OC*H*HC$_{cage}$), 4.39 (d, 1 H, $J_{1,2}$ = 7.8 Hz, H-1), 4.28 (d, 1 H, $^2J$ =12.1 Hz, OCH*H*C$_{cage}$), 3.87 (m, 1 H, H-6a), 3.63 (m, 1 H, H-6b), 3.39-3.14 (m, 4 H). $^{13}$C-NMR (75.46 MHz, $CD_3OD$)[12] δ 103.9 (d, C-1), 78.2 (d, 2 C), 74.8 (d), 71.5 (d), 70.0 (t, *C*H$_2$C$_{cage}$), 62.7 (t, C-6). $^{11}$B-NMR ($CD_3OD$) δ -2.37 (2 B), -9.89 (8 B). IR 3050 ($\nu_{CHcage}$), 2590 ($\nu_{BH}$), 2920 and 2860 ($\nu_{CHalkyl}$); ESI-MS: Calcd. for $C_{16}H_{36}B_{10}O_{12}$ 528 u.m.a.; found: 551 u.m.a. ($MNa^+$). [Found: C, 36.12; H, 6.89. $C_{16}H_{36}B_{10}O_{12}$ requires C, 36.36; H, 6.86%].

***1,2-Di-[(β-D-galactopyranosyl)-(1→4)-β-D-glucopyranosyloxy)methyl]-1,2-dicarba*-closo-*dodecaborane* (7b)**

The title compound was obtained (83%) after repeated silica gel chromatography with MeOH-*i*PrOH-$H_2O$ 6:1.5:1.5 as the eluant. Colourless foam. $[\alpha]_D$ +3.78 (*c* 1.3, $CH_3OH$). $^1$H-NMR (300 MHz, $CD_3OD$) δ 4.46 (d, 1 H, $^2J$ = 12.5 Hz, OC*H*HC$_{cage}$), 4.45 (d, 1 H, $J_{1',2'}$ = 7.7 Hz, H-1' or H-1), 4.36 (d, 1 H, $J_{1,2}$ = 7.2 Hz, H-1 or H-1'), 4.29 (d, 1 H, $^2J$ =12.5 Hz, OCH*H*C$_{cage}$), 3.95-3.65 (m, 6 H), 3.65-3.37 (m, 5 H), 3.30 (t, 1 H, $J_{3,4}$ = $J_{4,5}$ = 8.2 Hz, H-4). $^{13}$C-NMR (75.46 MHz, $CDCl_3$): δ 105.0, 103.6 (2d, C-1, C-1'), 80.5 (d), 77.8 (s, C$_{cage}$), 77.0 (d), 76.6 (d), 76.4 (d), 74.7 (d), 74.4 (d), 72.5 (d), 70.3 (d), 70.0 (t, *C*H$_2$C$_{cage}$), 62.5, 61.9 (2t, C-6, C-6'), 20.7-20.3 (q, *C*H$_3$CO). $^{11}$B-NMR ($CD_3OD$) δ -2.21 (2 B), -10.27 (8 B). IR 3050 ($\nu_{CHcage}$), 2590 $cm^{-1}$ ($\nu_{BH}$). ESI-MS: Calcd. for $C_{28}H_{56}B_{10}O_{22}$ 853 u.m.a.; found: 876 u.m.a. ($MNa^+$). [Found: C, 39.15; H, 6.81. $C_{28}H_{56}B_{10}O_{22}$ requires C, 39.43; H, 6.62%].

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