Letters to the Editor

Conjugates of polyhedral boron compounds with carbohydrates
3.* The first synthesis of a conjugate of the dodecaborate anion with a disaccharide lactose as a potential agent for boron neutron capture therapy of cancer**

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Polyhedral boron compounds are potential agents for boron neutron capture therapy of cancer.[2,3] Conjugates of polyhedral boron compounds with carbohydrates can be used for targeted delivery of polyhedral boron compounds to lectins exposed on the surface of tumor cells.[4] Of polyhedral boron compounds, the *closo*-dodecaborate anion and *ortho*-carborane are of most practical interest.

Several syntheses of conjugates of the dodecaborate anion with carbohydrates were documented.[5—8] However, these compounds contain only monosaccharides as the carbohydrate fragment. These conjugates were prepared by the reactions of bromo- or iodo-substituted monosaccharide derivatives with sodium mercaptoundecahydro-*closo*-dodecaborate or cesium hydroxyundecahydro-*closo*-dodecaborate.

In the present study, we developed an approach to the synthesis of conjugates of the dodecaborate anion with oligosaccharides. The method of conjugation is based on the use of a carboxy derivative of the dodecaborate anion, a simple preparation of which has been described recently.[9] The conjugaiton is exemplified by a reaction with a derivative of a readily accessible disaccharide lactose, which serves as a ligand of lectins expressed on the surface of melanoma cells (Scheme 1).

The conjugate was synthesized starting from *N*-glycyl-β-lactosylamine.[10] Condensation of the latter with $[B_{12}H_{11}O(CH_2)_4CO_2]^{3-} \cdot 3Bu_4N^+$ in a 2 : 1 methanol—water mixture in the presence of *N*-(4,6-dimethoxy-1,3,5-triazin-2-yl)-*N*-methylmorpholinium chloride (DMT-MM)[11] as a condensing agent (this reagent proved

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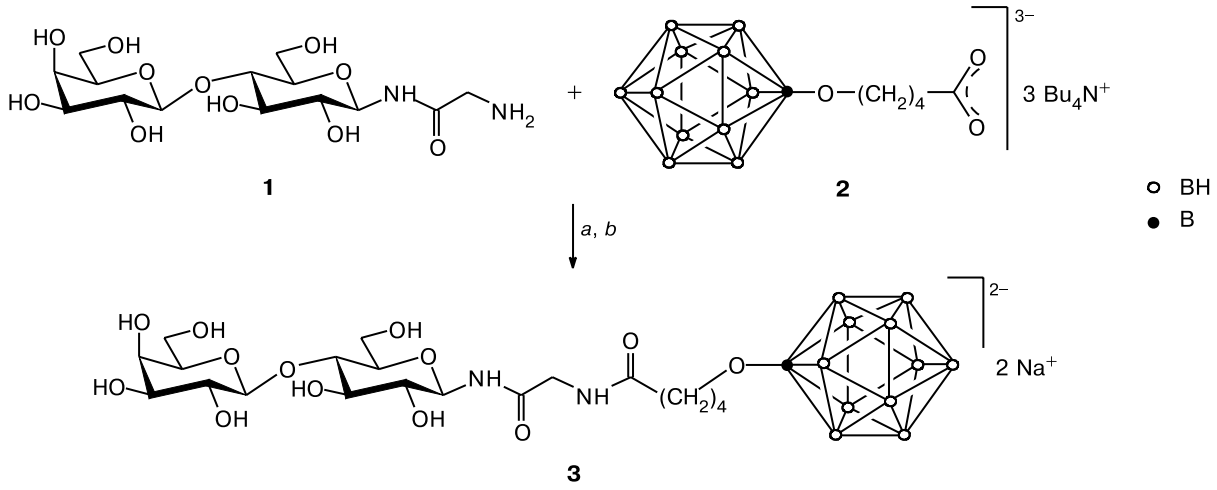
Scheme 1



Reagents and conditions: *a*. DMT-MM, MeOH—H_2O (2 : 1); *b*. Dowex 50Wx8 (Na^+ form).

to be efficient in the synthesis of a conjugate of lactose with *ortho*-carborane[1]) afforded conjugate **3** isolated in 57% yield.

^{1}H NMR (characteristic signals; Bruker AC-200, 200 MHz, D_2O, δ): 4.46 (d, 1 H, H(1), Gal, J = 7.7 Hz); 5.02 (d, 1 H, H(1), Glc, J = 9.1 Hz). ^{13}C NMR (50.32 MHz, D_2O, δ, a 1,4-dioxane solution in D_2O as the external standard (δ_C 67.4)): 22.7 ($COCH_2\underline{C}H_2$); 30.8 ($OCH_2\underline{C}H_2$); 36.2 ($CO\underline{C}H_2(CH_2)_3$); 43.5 ($CO\underline{C}H_2NH$); 60.8 (C(6), Glc); 61.9 (C(6), Gal); 69.5 (C(4) Gal); 69.8 ($O\underline{C}H_2(CH_2)_3$); 71.8 (C(2), Gal); 72.3 (C(3), Gal); 73.3 (C(2), Glc); 75.9 (C(3), Glc); 76.2 (C(5), Glc); 77.3 (C(5), Gal); 78.7 (C(4), Glc); 80.0 (C(1), Glc); 103.8 (C(1), Gal); 173.7, 178.7 (NHC(O)). ^{11}B{^{1}H} NMR (64.21 MHz, D_2O, δ, $BF_3 \cdot Et_2O$ as the external standard (δ_B 0.0)): −23.5 (1 B); −18.6 (5 B); −16.6 (5 B); 6.2 (1 B).

ESI MS (Finnigan LCQ, $2 \cdot 10^{-5}$ M solution in MeOH), for the monoisotopic ion, m/z 663.5 [M − Na]. $C_{19}H_{44}B_{12}N_2NaO_{13}^-$. Calculated: m/z 663.4 [M − Na].

The procedure developed in the present study can be used for conjugation of the dodecaborate anion with amino-containing oligosaccharide derivatives of virtually any complexity.

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