B-Decachloro-*o*-carborane Derivatives Suitable for the Preparation of Boron-Labeled Biological Macromolecules

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B-decachloro-*o*-carborane derivatives in which one of the carbon atoms was substituted by $-CH_2CH_2CO_2H$ (**I**), $-CH_2CHOHCH_2-O-CH_2CH=CH_2$ (**II**) and $-CH_2CHOHCH_2-O-p-C_6H_4NHCOOC(CH_3)_3$ (**III**) were prepared from decachloro-*o*-carborane and the corresponding bromo (**I**) or epoxi (**II** and **III**) derivatives under alkaline conditions. **II** could be epoxidized and bound to dextran, Concanavalin A, and human IgG, with a boron content of 4.3, 4.8, and 4.9% (w/w), respectively. **III** could be converted to the corresponding amine and further to the isothiocyanate. Such boron derivatives could be suitable compounds for neutron capture therapy of tumors, as they are well water soluble and could be attached to tumor specific antibodies.

For the specific destruction of tumor cells, the use of the boron neutron capture reaction ^{10}B (n, α) ^{7}Li has been suggested [1]. A prerequisite for a successful use of this reaction is the obtainment of a sufficient boron content in the target tissue [2]. Previous experiments to achieve this with tumor specific boron-labeled antibodies led to protein precipitation at boron contents above about 0.5 to 1% [3]. We have prepared here soluble biologically interesting macromolecules containing up to 7% boron, using C-substituted B-decachloro-*o*-carborane [4] as boron containing compounds.

B-Decachloro-*o*-carborane (**I**) is a weak acid [5] the anion has nucleophilic properties and is soluble in water without decomposition. Its reaction with methyl iodide, ethyl iodide, allyl bromide and benzyl bromide, leading to mono- and disubstituted compounds, have been described [6].

We found that reactions with other haloalkyl compounds took place only occasionally and under more drastic conditions. Thus, 3-bromopropionic acid reacted in refluxing dioxane or 1-propanol with the sodium salt of **I** to 3-decachloro-*o*-carboranyl propionic acid, but not in ethanol, where the reaction with the above mentioned alkyl halides proceeded well.

The reaction of the anion of **I** (generated by the action of butyl lithium or sterically hindered amines) with oxiranes in dioxane or diethyl ether was rapid. Typically, 2 mmol of butyllithium in 20 ml hexane was added to 2 mmol of **I** in 50 ml hexane at 0 ° under stirring. After 30 min, 2 mmol of the epoxide, dissolved in 5 ml hexane was added and stirred for 2 hours. The product was isolated after pouring the solution into water. Usually, the decachloro-*o*-carboranyl compound precipitated from the aqueous phase and was collected by filtration.

Thus, a great number of compounds, which are listed in Table I, could be obtained from the corresponding glycidyl ethers prepared according to Jahn [7]. The aromatic amine **V** could be obtained by the action of trifluoroacetic acid and could be converted [8] to the corresponding isothiocyanate **VI**. The compound was incorporated into poly-L-lysine (m.w. = 90 000) at pH 10 to a degree of 7.6% boron content. The alkene derivative **VII** could, after epoxidation with *p*-nitro peroxobenzoic acid, be bound

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Table I. New decachloro-*o*-carboranyl compounds.

Compound [a]		m.p. [°C]
Decloc-CH_2-CH_2-COOH [b]	(**II**)	> 360
Decloc-CH_2-CHOH-CH_2-O-pC_6H_4-$COCH_3$	(**III**)	95 – 100
Decloc-CH_2-CHOH-CH_2-O-pC_6H_4-NHCOOC$(CH_3)_3$	(**IV**)	160 [c]
Decloc-CH_2-CHOH-CH_2-O-pC_6H_4-$NH_2 \cdot CF_3COOH$	(**V**)	not crystalline
Decloc-CH_2-CHOH-CH_2-O-pC_6H_4-NCS	(**VII**)	oil
Decloc-CH_2-CHOH-CH_2-O-CH_2-CH=CH_2 [b]	(**VII**)	135
Decloc-CH_2-CHOH-CH_2-O-pC_6H_4-$NHCOCH_3$ [b]	(**VIII**)	> 360

[a] Decloc = $HB_{10}Cl_{10}C_2$-; all compounds were identified by their IR and NMR spectra.
[b] The composition was confirmed by elemental analysis (B, C, Cl, H, N).
[c] Decomposition.

to dextrane (m.w. = 40 000), concanavalin A, and human IgG, with a final boron content of 4.3, 4.8 and 4.9%, respectively. All products were well soluble in physiological buffer pH = 7.2.

The former compound should be useful to achieve local capillary damage in the blood system of animals [9], the latter two to determine the efectiveness of the ^{10}B (n, α) ^{7}Li reaction in damaging cells.

The derivatives described here and analogous compounds could also be used as the boron containing part of low molecular weight hormone derivatives [10], when an increased hydrophilicity is desired.

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