reaction mixtures. The structures of the compounds were confirmed by GLC and GLC-MS spectrometric data for the individual heterocycles, as well as for reaction mixtures. The reaction conditions and yields of the main reaction products are given in Table 1.

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Synthesis of 1,7-bis(carboxyalkylcarbamoyl)-*m*-carboranes as precursors of possible water-soluble preparations for boron-neutron-capture treatment of cancer

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By the interaction of the corresponding amino acids with the dichloride of *m*-carboranedicarboxylic acid, 1,7-bis-(carboxyalkylcarbamoyl)-*m*-carboranes were prepared are characterized for the first time. These compounds are of interest as intermediates for the synthesis of water-soluble preparations for the boron-neutron-capture therapy of cancer.

Key words: bis(carboxyalkylcarbamoyl)-*m*-carboranes, *m*-carboranedicarboxylic acid, oligosalts.

One of the main challenges in the neutron-capture therapy of cancer is the development of water-soluble preparations that can act as boron carriers and are capable of being predominantly accumulated in the tissue of a tumor.

In recent years, studies aimed at the synthesis of boron-rich carborane-containing compounds have attracted considerable interest.[1—6] However, the compounds described in the literature are often poorly soluble in water and are obtained using complicated multistage procedures. Previously, a simple and accessible method for the preparation of oligosalts of *m*-carboranedicarboxylic acid, readily soluble in water, was proposed[7] and it was shown that these compounds can be used in the boron-neutron-capture therapy of cancer.

It would be expected that the introduction of organic and amide groups into these oligosalts would improve their biological properties.[8]

For this purpose, we synthesized the previously unknown 1,7-bis(carboxyalkylcarbamoyl)-*m*-carboranes (**1**) as intermediate compounds to be used for the preparation of water-soluble oligosalts.

These compounds were obtained by acylation of various amino acids with the dichloride of *m*-carborane-

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dicarboxylic acid by the Schotten—Bauman reaction:

$$2\ H_2NZCOOH + 4\ NaOH + ClOCCB_{10}H_{10}CCOCl \longrightarrow$$
$$\longrightarrow NaOOCZNHOCCB_{10}H_{10}CCONHZCOONa + 2\ NaCl \xrightarrow{HCl}$$
$$\xrightarrow{HCl} HOOCZNHOCCB_{10}H_{10}CCONHZCOOH,$$
$$\mathbf{1}$$

1	**a**	**b**	**c**	**d**	**e**	**f**
Z	$CH(CH_3)$	$(CH_2)_2$	$(CH_2)_6$	$(CH_2)_7$	$(CH_2)_9$	$CH(CH_2Ph)$

The resulting 1,7-bis-(carboxyalkylcarbamoyl)-*m*-carboranes are colorless powder-like or glassy substances or transparent resins, whose IR spectra exhibit typical absorption bands, due to the COOH (1730—1710 cm^{-1}), NHCO (1690—1680 cm^{-1}), and CH_2 (2940—2870 cm^{-1}) groups, and to the BH bond in the carborane moiety (2630—2620 cm^{-1}).

All of the compounds synthesized are readily soluble in acetone and ethanol; 1,7-bis-(1-carboxyethylcarbamoyl)-*m*-carborane and 1,7-bis-(2-carboxyethylcarbamoyl)-*m*-carborane are poorly soluble in water and the other compounds are insoluble in water.

The resulting 1,7-bis-(carboxyalkylcarbamoyl)-*m*-carboranes can be recommended for the synthesis of oligosalts with the aim of testing them in the radiation threatment of cancer by the method of neutron capture by boron atoms.

Experimental

m-Carboranedicarboxylic acid dichloride was synthesized by a procedure described in the literature.[9] The molecular weights of the compounds obtained were determined by the titration of the carboxylic groups with a 0.1 *N* aqueous solution of NaOH, and the melting points were found from the thermomechanical curves. IR spectra were recorded on a UR-20 spectrophotometer (pellets pressed with KBr) in the 400—4000 cm^{-1} region. The ^1H NMR spectra (in CD_3OD) were obtained on a Bruker WP-200-SV instrument (200.13 MHz) using tetramethylsilane as the internal standard. The protons of the amide and carboxyl groups in the compounds synthesized cannot be seen in the spectra, due to exchange reactions with the methanol hydroxyl group.

Synthesis of 1,7-bis(carboxyalkylcarbamoyl)-*m*-carboranes (1a—f) (general procedure). Sodium hydroxide (0.028 mol), amino acid (0.014 mol), and distilled water (20 mL) were placed in a two-neck flask equipped with a stirrer. *m*-Carboranedicarboxylic acid dichloride (0.07 mol) was added with stirring to the resulting solution, and stirring was continued for 2—3 h at 20—30 °C until a transparent or slightly turbid solution formed. After filtration and acidification with an aqueous solution of HCl, the corresponding dicarboxylic acid was isolated from this solution as a crystalline precipitate or as an oil. The resulting compounds were washed with distilled water to remove NaCl and dried in a vacuum gun at 80 °C to constant weight.

1,7-Bis(1-carboxyethylcarbamoyl)-*m*-carborane (1a). Yield 83%, m.p. 45 °C, mol. weight (found/calculated) 356/374. Found (%): C, 31.82; H, 5.95; B, 28.27; N, 6.62. $C_{10}H_{22}B_{10}O_6N_6$. Calculated (%): C, 32.08; H, 5.88; B, 28.89; N, 7.48. ^1H NMR, δ: 4.50 (q, 1 H, CH, J = 7.1 Hz); 1.58 (d, 3 H, CH_3, J = 7.1 Hz).

1,7-Bis(carboxyethylcarbamoyl)-*m*-carborane (1b). Yield 96%, m.p. 165 °C, mol. weight (found/calculated) 374/374. Found (%): C, 32.12; H, 5.95; B, 29.38; N, 7.48. $C_{10}H_{22}B_{10}N_2O_6$. Calculated (%): C, 32.08; H, 5.88; B, 28.89; N, 7.48. ^1H NMR, δ: 3.57 (t, 1 H, CH_2COOH, J = 6.8 Hz); 2.66 (t, 1 H, CH_2NH, J = 6.8 Hz).

1,7-Bis(6-carboxyhexylcarbamoyl)-*m*-carborane (1c). Yield 84%, m.p. 12 °C, mol. weight (found/calculated) 509/486. Found (%): C, 44.68; H, 8.05; B, 22.24; N, 5.55. $C_{18}H_{38}B_{10}N_2O_6$. Calculated (%): C, 44.44; H, 7.82; B, 22.22; N, 5.76. ^1H NMR, δ: 3.32 (t, 1 H, CH_2COOH, J = 6.8 Hz); 2.47 (t, 1 H, CH_2NH, J = 7.3 Hz); 1.78 (q, 1 H, CH_2CH_2COOH, J = 7.3 Hz); 1.66 (q, 1 H, CH_2CH_2NH, J = 7.0 Hz); 1.49 (m, 2 H, $(CH_2)_2$).

1,7-Bis(7-carboxyheptylcarbamoyl)-*m*-carborane (1d). Yield 90%, m.p. −5 °C, mol. weight (found/calculated) 490/514. Found (%): C, 46.73; H, 8.61; B, 19.48; N, 5.30. $C_{20}H_{42}B_{10}N_2O_6$. Calculated (%): C, 46.69; H, 8.17; B, 21.01; N, 5.45. ^1H NMR, δ: 3.32 (t, 1 H, CH_2COOH, J = 6.8 Hz); 2.47 (t, 1 H, CH_2NH, J = 7.3 Hz); 1.78 (q, 1 H, CH_2CH_2COOH, J = 6.3 Hz); 1.66 (q, 1 H, CH_2CH_2NH, J = 6.3 Hz); 1.50 (m, 3 H, $(CH_2)_3$).

1,7-Bis(9-carboxynonylcarbamoyl)-*m*-carborane (1e). Yield 94%, m.p. 102 °C, mol. weight (found/calculated) 583/570. Found (%): C, 50.28; H, 8.83; B, 18.73; N, 4.95. $C_{24}H_{50}B_{10}N_2O_6$. Calculated (%): C, 50.53; H, 8.77; B, 18.95; N, 4.91. ^1H NMR, δ: 3.32 (t, 1 H, CH_2COOH, J = 6.8 Hz); 2.46 (t, 1 H, CH_2NH, J = 7.3 Hz); 1.78 (q, 1 H, CH_2CH_2COOH, J = 6.5 Hz); 1.65 (q, 1 H, CH_2CH_2NH, J = 6.5 Hz); 1.49 (m, 5 H, $(CH_2)_5$).

1,7-Bis(1-carboxy-2-phenylethylcarbamoyl)-*m*-carborane (1f). Yield 98%, m.p. 82 °C, mol. weight (found/calculated) 501/526. Found (%): C, 50.09; H, 6.21; B, 20.38; N, 4.94. $C_{22}H_{30}B_{10}N_2O_6$. Calculated (%): C, 50.19; H, 5.70; B, 20.53; N, 5.32. ^1H NMR, δ: 7.26—7.55 (m, 5 H, Ph); 4.74 (q, 1 H, $CHCH_2Ph$, J = 4.6 Hz); 3.42 (dd, 1 H, $CH_aCH_bH_cPh$, J_{H_a,H_b} = 4.6 Hz, J_{H_c,H_b} = 4.9 Hz); 3.20 (dd, 1 H, $CH_aCH_bH_cPh$, J_{H_a,H_c} = 9.3 Hz, J_{H_b,H_c} = 9.6 Hz).

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