# Synthesis of boron-containing tyrosine derivatives based on the *closo*-decaborate and *closo*-dodecaborate anions*

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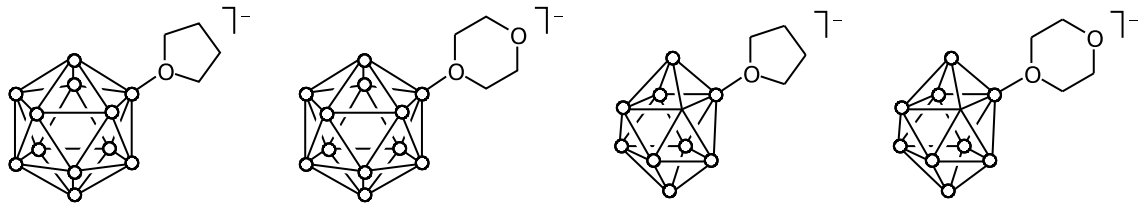
A series of new boron-containing tyrosine derivatives $[B_nH_{n-1}O(CH_2)_4O\text{-}4\text{-}C_6H_4CH_2CH(NH_3)COOH]^-$ and $[B_nH_{n-1}O(CH_2CH_2)_2O\text{-}4\text{-}C_6H_4CH_2CH(NH_3)COOH]^-$ ($n = 10, 12$) were prepared by ring opening of the cyclic oxonium derivatives of the decahydro-*closo*-decaborate and dodecahydro-*closo*-dodecaborate anions, respectively, with ethyl *N*-trifluoroacetyl-L-tyrosinate.

**Key words:** decahydro-*closo*-decaborate, dodecahydro-*closo*-dodecaborate, cyclic oxonium derivatives, amino acids, tyrosine, boron neutron capture therapy of cancer.

Despite the last achievements in surgery and radiation and chemotherapy of cancer, the prognosis for oncological patients with the brain tumors remains extremely disappointing.[1,2] Therefore, novel treament modes are being developed, for example, boron neutron capture therapy (BNCT) of cancer, which is based on selective accumulation of the non-radioactive $^{10}B$ isotope in cancer cells followed by their treatment with the thermal neutron flux. Irradiation results in the formation of high-energy fission products (α-particles and lithium nuclei) having a short particle range comparable with the cell size, which, in the ideal case, allows selective destruction of tumor cells without affecting the surrounding healthy tissue.[3—5] The selective boron accumulation in cancer cells can be achieved by linking *closo*-polyhedral boron hydrides to various bioactive molecules capable of being accumulated in tumor cells.

The principal difference between normal and cancer cells is their cellular metabolism. Cancer cell proliferation requires accelerated synthesis of such macromolecules as lipids, proteins, and nucleotides.[6] Since malignant transformation requires that the cells capture and use the material for the protein synthesis in a sufficient amount, the need for amino acids increases, which, in turn, increases the rate of amino-acid transport through blood-brain barrier. This property of cancer cells is currently used for tomographic diagnostics of brain tumors based on PET (Positron Emission Tomography) and SPECT (Single Photon Emission Computerized Tomography) using isotope-labeled amino acids.[7] In some cases, the use of labeled amino acids allows more distinct visualization of tumor borders as compared with the commonly used 2-fluoro-2-desoxy-D-glucose.[8] *O*-(2-[$^{18}$F]-Fluoroethyl)-L-tyrosine is an example of such amino acid, where the radioactive label is linked with the phenyl fragment of tyrosine through a flexible spacer.[9] We have used earlier[10] the analogous design in the synthesis of the boron-containing tyrosine derivative based on cobalt bis(dicarbollide). In the present work, we described the synthesis of boron-containing tyrosine derivative containing *closo*-decaborate and *closo*-dodecaborate fragments in the side chain of the amino acid.



**1** **2** **3** **4**

* Dedicated to the Academician of the Russian Academy of Sciences R. Z. Sagdeev on the occasion of his 70th birthday.

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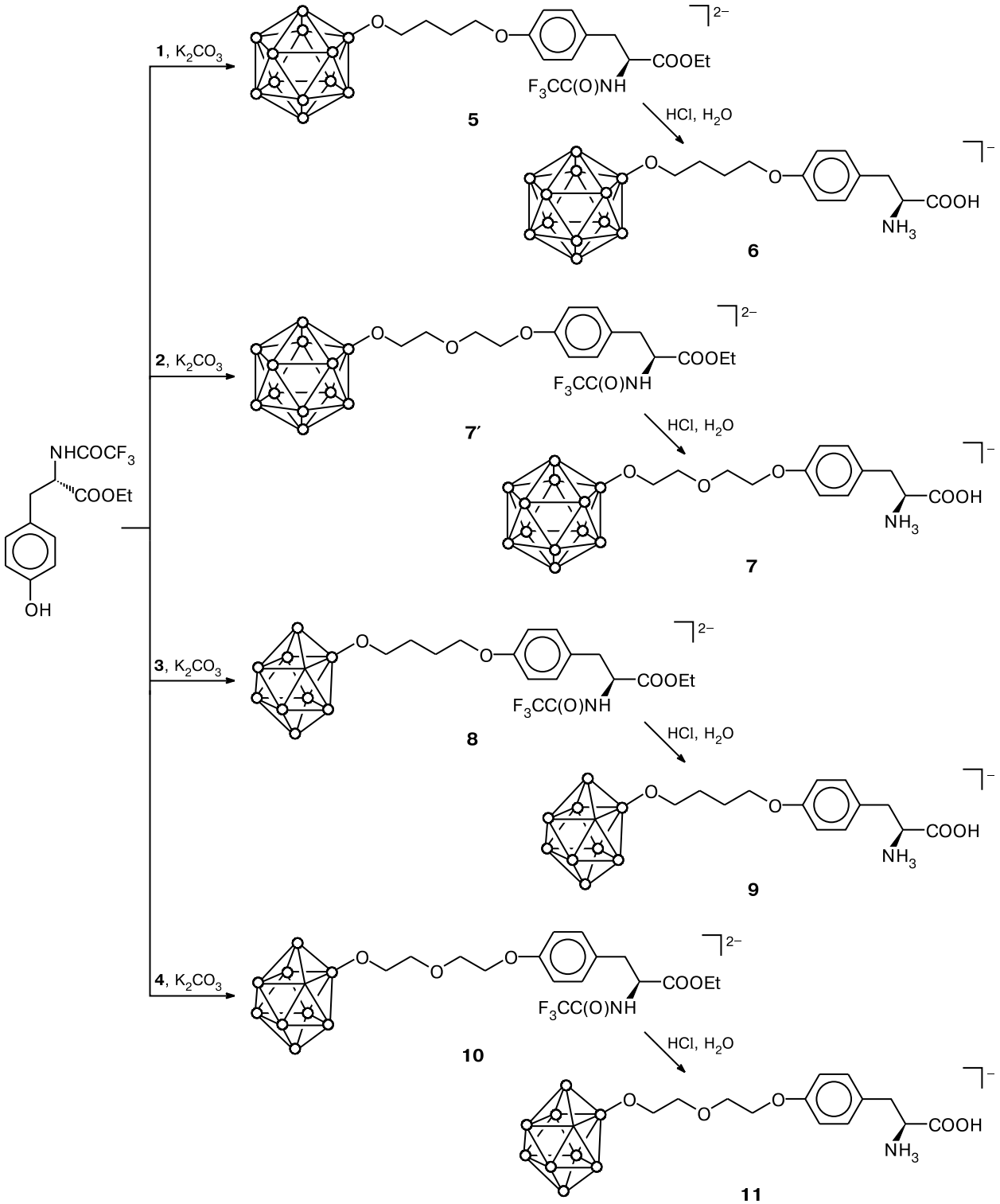
## Results and Discussion

Due to the combination of a high stability, low toxicity, and good water solubility (in the form of sodium and potassium salts), derivatives of *closo*-decaborate $[B_{10}H_{10}]^{2-}$ (see Ref. 11) and *closo*-dodecaborate $[B_{12}H_{12}]^{2-}$ anions (see Ref. 12) attract increasing attention for design of BNCT drugs. Earlier, we proposed the method for the

**Scheme 1**



functionalization of *closo*-dodecaborate anion by ring opening of cyclic oxonium derivatives,[13] which in recent years became a classic method for the preparation of its organic and bioorganic derivatives.[14] Ring opening of the cyclic oxonium derivatives of the *closo*-decaborate anion has been described later.[15]

Earlier,[13] we used this approach for the synthesis of the first amino acid based on the *closo*-dodecaborate anion by the ring opening of its tetrahydrofuran derivative with diethylacetamidomalonate followed by hydrolysis (according to the Sorenson method). In the present work, opening of the oxonium rings of the tetrahydrofuran and 1,4-dioxane derivatives of the *closo*-dodecaborate ($[B_{12}H_{11}O(CH_2)_4]^-$ (**1**) and $[B_{12}H_{11}O(CH_2CH_2)_2O]^-$ (**2**)) and *closo*-decaborate anions ($[2\text{-}B_{10}H_9O(CH_2)_4]^-$ (**3**) and $[2\text{-}B_{10}H_9O(CH_2CH_2)_2O]^-$ (**4**)) by the hydroxyl group of tyrosine was used for the synthesis of the corresponding boron-containing amino acids and their esters (**5**—**11**).

To avoid oxonium ring opening by the amine and carboxyl groups, we used ethyl *N*-(trifluoroacetyl)-L-tyrosinate as the reagent. The reaction was performed under the conditions used earlier for the preparation of various phenoxy derivatives of the *closo*-decaborate[16] and *closo*-dodecaborate[17] anions (Scheme 1).

The reactions of the cyclic oxonium derivative of the *closo*-dodecaborate (**1** and **2**) and *closo*-decaborate (**3** and **4**) anions (as $Bu_4N$ salts) with ethyl *N*-trifluoroacetyl-L-tyrosine in refluxing acetonitrile in the presence of $K_2CO_3$ afford the corresponding boron-containing ethyl esters of tyrosine isolated as cesium salts. The $^1H$ NMR spectra of compounds **5**, **8**, and **10** contain the signals for the aromatic protons in the region of δ 7.2—6.8, the $H_\alpha$ proton of tyrosine at δ ~4.5, the $H_\beta$ protons of tyrosine in the region of δ 3.10—2.95, and the ethyl group of ester at δ ~4.10 and 1.15, as well as the signals for the protons of the opened tetrahydrofuran and dioxane rings. The $^{13}C$ NMR spectra of these compounds exhibit the quartets typical of the carbon atoms of the trifluoroacetyl group at δ ~157 ($CF_3\underline{C}(O)N$) and 117 ($\underline{C}F_3C(O)N$). In the case of compound **5**, the presence of the trifluoroacetyl group was additionally confirmed by the $^{19}F$ NMR spectral data. The $^{11}B$ NMR spectra contain the set of signals typical of mono-substituted alkoxy derivatives of the *closo*-dodecaborate[18] and *closo*-decaborate[19] anions.

The acid hydrolysis of esters **5**, **8**, and **10** results in simultaneous removal of the *N*-trifluoroacetyl and *O*-ethyl protective groups to form the corresponding boron-containing tyrosine derivative **6**, **9**, and **11**. In the case of the 1,4-dioxane derivative of the *closo*-dodecaborate anion, no isolation of the protected form **7´** was performed and, after acid hydrolysis, the corresponding tyrosine derivative **7** was obtained. In the $^1H$ NMR spectra of the products of hydrolysis, the signals for the ethyl ester group disappear and the upfield shift of the signal for the $H_\alpha$ proton of tyrosin by 0.4 ppm was observed. The $^{13}C$ NMR spectra of the products of hydrolysis exhibit no signals for the trifluoroacetyl and ethyl protective groups. The absence of the trifluoroacetyl group was confirmed additionally by $^{19}F$ NMR spectroscopy. The isolation of the boron-containing tyrosines based on the *closo*-dodecaborate and *closo*-decaborate anions was performed by precipitation in the forms of water-insoluble tetrabutylammonium and tetraphenylphosphonium salts, respectively. It should be noted that the amino acids were isolated in the protonated form ($CH(N^+H_3)COOH$) upon precipitation as tetrabutylammonium salts and in the form of the classic zwitter-ion ($CH(N^+H_3)COO^-$) upon precipitation as tetraphenylphosphonium salts, which is apparently caused by a lower solubility of the salts of the double-charged anion and the equilibrium shift in favor of its formation.

Thus, in the present work four novel boron-containing amino acids based on L-tyrosine with different nature of the spacer between the boron skeleton and the amino-acid fragment were prepared by the ring opening of the oxonium derivatives of the *closo*-decaborate and *closo*-dodecaborate anions.

## Experimental

$^1H$, $^{13}C$, $^{11}B$, $^{11}B\{^1H\}$, and $^{19}F$ NMR spectra were recorded on Bruker Avance 400 and Bruker Avance 600 spectrometers. To determine the signal multiplicity for boron polyhedra, the $^{11}B$ NMR spectra were used (the spin-spin coupling constants $J_{B-H}$ are not given because of partial signal overlapping). The course of the reaction was monitored by thin-layer chromatography on Kieselgel 60 F245 plates (Merck) with visualization by a 0.5% $PdCl_2$ in MeOH—$H_2O$ (10 : 1) containing 1% HCl . Melting points were determined in an open capillary and were not corrected. Acetonitrile was dried by successive distillation over $P_2O_5$ and $CaH_2$. The compounds $(Bu_4N)[B_{12}H_{11}O(CH_2)_4]$ (**1**) (see Ref. 13), $(Bu_4N)[B_{12}H_{11}O(CH_2CH_2)_2O]$ (**2**) (see Ref. 20), $(Bu_4N)[2\text{-}B_{10}H_9O(CH_2)_4]$ (**3**) (see Ref. 21), $(Bu_4N)[2\text{-}B_{10}H_9O(CH_2CH_2)_2O]$ (**4**) (see Ref. 21), and ethyl *N*-(trifluoroacetyl)-L-tyrosinate[22] were obtained according to the previously described procedures.

**Cesium ethyl *N*-(trifluoroacetyl)-*O*-{4-[undecahydro-*closo*-dodecaboratooxy]butyl}-L-tyrosinate (5).** To a solution of ethyl *N*-(trifluoroacetyl)-L-tyrosinate (0.27 g, 0.88 mmol) in MeCN (80 mL), compound **1** (0.40 g, 0.88 mmol) and $K_2CO_3$ (0.61 g, 4.40 mmol) were added. The reaction mixture was refluxed for 8 h and cooled to room temperature. The excess of $K_2CO_3$ was filtered off and the solvent was removed on a rotary evaporator. The residue was dissolved in MeOH (10 mL) and a solution of CsF (0.27 g, 1.76 mmol) in MeOH (10 mL) was added. The precipitate was filtered off, washed with MeOH (30 mL), and dried in air. The yield was 0.46 g (67%). Found (%): C, 25.2; H, 4.14; N, 1.73. $C_{17}H_{32}B_{12}Cs_2F_3NO_5$. Calculated (%): C, 26.08; H, 4.12; N, 1.79. $^1H$ NMR (DMSO-$d_6$), δ: 9.95 (br.s, 1 H, NH); 7.17 (d, 2 H, $C_6H_4$, $J$ = 8.5 Hz); 6.87 (d, 2 H, $C_6H_4$, $J$ = 8.5 Hz); 4.54—4.49 (m, 1 H, $CH_\alpha$); 4.19—4.11 (m, 2 H, $CH_3C\underline{H}_2O$); 3.96—3.91 (m, 2 H, $C\underline{H}_2OC_6H_4$); 3.33—3.29 (m, 2 H, $CH_2OB_{12}H_{11}$); 3.15—2.92 (m, 2 H, $CH_\beta$); 1.70—1.65 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$); 1.49—1.45 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$);

1.18 (t, 3 H, $OCH_2C\underline{H}_3$, $J$ = 9.2 Hz). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.7 (C(O)OEt); 158.0 ($C_6H_4$); 157.0 (q, $CF_3\underline{C}(O)N$, $J$ = 38 Hz); 130.5 ($C_6H_4$); 128.6 ($C_6H_4$); 114.7 ($C_6H_4$); 116.1 (q, $CF_3$, $J$ = 290 Hz); 68.1 ($CH_2O$); 68.0 ($CH_2O$); 61.5 ($CH_2O$); 54.7 ($C_\alpha$); 35.1 ($C_\beta$); 28.7 ($CH_2CH_2$); 26.4 ($CH_2CH_2$); 14.4 ($\underline{C}H_3CH_2O$). $^{19}F$ NMR (DMSO-$d_6$), δ: −74.2 ($CF_3$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: 6.5 (s, 1 B); −16.8 (d, 5 B); −18.3 (d, 5 B); −22.8 (d, 1 B).

**Tetrabutylammonium 2-(4-[4-((*S*)-2-amino-2-carboxyethyl)-phenoxy]butoxy)undecahydro-*closo*-dodecaborate (6).** To a solution of compound **5** (0.46 g, 0.59 mmol) in water (40 mL), concentrated HCl (1 mL) was added and the mixture was refluxed for 16 h. After cooling, a solution $Bu_4NBr$ (0.19 g, 0.59 mmol) in water (5 mL) was added. The precipitated was filtered off, washed with water (10 mL), and dried *in vacuo*. The yield was 0.37 g (100%), m.p. 127 °C. Found (%): C, 53.92; H, 10.35; N, 4.38. $C_{29}H_{66}B_{12}N_2O_4$. Calculated (%): C, 54.72; H, 10.45; N, 4.40. $^1H$ NMR (DMSO-$d_6$), δ: 8.19 (br.s, 4 H, $NH_3$ and COOH); 7.12 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 6.86 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 4.15—4.10 (m, 1 H, $CH_\alpha$); 3.92 (t, 2 H, $C\underline{H}_2OC_6H_4$, $J$ = 6.7 Hz); 3.40 (t, 2 H, $CH_2OB_{12}H_{11}$, $J$ = 5.7 Hz); 3.15—3.11 (m, 8 H, $Bu_4N^+$); 3.03—2.95 (m, 2 H, $CH_\beta$); 1.65—1.61 (m, 4 H, $OCH_2(C\underline{H}_2)_2CH_2O$); 1.57—1.47 (m, 8 H, $Bu_4N^+$); 1.32—1.23 (m, 8 H, $Bu_4N^+$); 0.92 (t, 12 H, $Bu_4N^+$). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.9 (COOH); 158.5 ($C_6H_4$); 131.1 ($C_6H_4$); 126.5 ($C_6H_4$); 115.0 ($C_6H_4$); 68.6 ($CH_2O$); 67.9 ($CH_2O$); 58.0 ($Bu_4N^+$); 53.7 ($C_\alpha$); 35.4 ($C_\beta$); 27.8 ($CH_2CH_2$); 26.1 ($CH_2CH_2$); 23.5 ($Bu_4N^+$); 19.7 ($Bu_4N^+$); 14.0 ($Bu_4N^+$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$, δ, м.д.): 6.1 (s, 1 B); −16. 8 (d, 5 B); −18.0 (d, 5 B); −22.2 (d, 1 B).

**Tetrabutylammonium 2-(2-{2-[4-(*S*)-(2-amino-2-carboxyethyl)phenoxy]ethoxy}ethoxy)undecahydro-*closo*-dodecaborate (7).** To a solution of ethyl *N*-(trifluoroacetyl)-L-tyrosinate (0.20 g, 0.64 mmol) in MeCN (50 mL), compound **2** (0.30 g, 0.64 mmol) and $K_2CO_3$ (0.44 g, 3.20 mmol) were added, and the mixture was refluxed for 8 h. The excess of $K_2CO_3$ was filtered off and the solvent was removed on a rotary evaporator. The residue was dissolved in MeOH (10 mL) and a solution of CsF (0.20 g, 1.28 mmol) in MeOH (10 mL) was added. The precipitated was filtered off, washed with $CH_2Cl_2$, dried in air, and dissolved in water (10 mL), concentrated HCl (1 mL) was added to the solution and the mixture was refluxed for 16 h. After cooling, a solution of $Bu_4NBr$ (0.21 g, 0.64 mmol) in $H_2O$ (5 mL) was added. The precipitate was filtered off, washed with $H_2O$ (50 mL), and dried *in vacuo*. The yield was 0.27 g (65%), m.p. 198 °C. Found (%): C, 53.36; H, 10.19; N, 4.19. $C_{29}H_{66}B_{12}N_2O_5$. Calculated (%): C, 53.38; H, 10.19; N, 4.29. $^1H$ NMR (DMSO-$d_6$), δ: 8.14 (br.s, 4 H, $NH_3$ and COOH); 7.11 (d, 2 H, $C_6H_4$, $J$ = 6.7 Hz); 6.89 (d, 2 H, $C_6H_4$, $J$ = 6.7); 4.13—4.09 (м, 1 H, $CH_\alpha$); 4.05—3.95 (m, 2 H, $C\underline{H}_2OC_6H_4$); 3.70—3.62 (m, 2 H, $CH_2OB_{12}H_{11}$); 3.43—3.37 (m, 4 H, $CH_2O$); 3.18—3.12 (m, 8 H, $Bu_4N^+$); 3.03—2.97 (m, 2 H, $CH_\alpha$); 1.58—1.46 (m, 8 H, $Bu_4N^+$); 1.30—1.22 (m, 8 H, $Bu_4N^+$); 0.91 (t, 12 H, $Bu_4N^+$). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 171.0 (COOH); 158.3 ($C_6H_4$); 131.1 ($C_6H_4$); 126.8 ($C_6H_4$); 115.1 ($C_6H_4$); 72.6 ($CH_2O$); 69.2 ($CH_2O$); 67.8 ($CH_2O$); 67.7 ($CH_2O$); 58.0 ($Bu_4N^+$); 53.8 ($C_\alpha$); 35.4 ($C_\beta$); 23.5 ($Bu_4N^+$); 19.7 ($Bu_4N^+$); 14.0 ($Bu_4N^+$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: 6.5 (s, 1 B); −16.7 (d, 5 B); −18.2 (d, 5 B); −22.8 (d, 1 B).

**Cesium ethyl *N*-(trifluoroacetyl)-*O*-{4-[nonahydro-*closo*-decaborato-2-oxy]butyl}-L-tyrosinate (8).** To a solution of compound **3** (0.21 g, 0.5 mmol) in MeCN (20 mL), ethyl *N*-(trifluoroacetyl)-L-tyrosinate (0.15 g, 0.5 mmol) and $K_2CO_3$ (0.70 g, 5 mmol) were added. The reaction mixture was refluxed with vigorous stirring for 8 h, the excess of $K_2CO_3$ was filtered off, and the solvent was removed on a rotary evaporator. The residue was dissolved in EtOH and an excess of a solution of CsF in EtOH was added. The precipitate was washed with $CH_2Cl_2$ (20 mL) and dried over $P_2O_5$ to yield compound **8** (0.31 g, 81%) as a white powder. $^1H$ NMR (DMSO-$d_6$), δ: 9.74 (s, 1 H, NH); 7.10 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 6.80 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 4.48—4.45 (m, 1 H, $CH_\alpha$); 4.12—4.02 (m, 2 H, $CH_3C\underline{H}_2O$, $J$ = 7.2 Hz); 3.83 (t, 2 H, $C\underline{H}_2OC_6H_4$, $J$ = 6.4 Hz); 3.09—3.06 (m, 1 H, $CH_\beta$); 3.03 (t, 2 H, $CH_2OB_{10}H_9$, $J$ = 6.6 Hz); 2.97—2.93 (m, 1 H, $CH_\beta$); 1.55—1.51 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$); 1.33—1.29 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$); 1.14 (t, 3 H, $OCH_2C\underline{H}_3$, $J$ = 7.2 Hz). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.4 (C(O)OEt); 158.0 ($C_6H_4$); 156.9 (q, $CF_3\underline{C}(O)N$, $J_{C-F}$ = 37 Hz); 130.4 ($C_6H_4$); 128.6 ($C_6H_4$); 115.7 (q, $CF_3$, $J_{C-F}$ = 287 Hz); 114.7 ($C_6H_4$); 70.5 ($CH_2O$); 68.2 ($CH_2O$); 61.4 ($CH_3\underline{C}H_2O$); 54.8 ($C_\alpha$); 35.1 ($C_\beta$); 28.7 ($CH_2CH_2$); 26.3 ($CH_2CH_2$); 14.4 ($\underline{C}H_3CH_2O$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: −1.9 (s, 1 B); −3.1 (d, 1 B); −5.5 (d, 1 B); −23.7 (d, 4 B); −29.1 (d, 2 B); −34.1 (d, 1 B).

**Tetraphenylphosphonium 2-(4-[4-((*S*)-2-amino-2-carboxyethyl)phenoxy]butoxy)nonahydro-*closo*-decaborate (9).** To a solution of compound **8** (0.15 g, 0.2 mmol) in water (20 mL), concentrated HCl (2 mL) was added and the reaction mixture was refluxed for 4 h with continuous stirring and then cooled to room temperature. The solvent was removed on a rotary evaporator. The residue was dissolved in water (10 mL) and an excess of an aqueous solution of $Ph_4PCl$ was added. The precipitate was filtered off and dried in air. The yield was 0.16 g (76%). Found (%): C, 69.08; H, 6.51; N, 1.36; B, 10.34. $C_{61}H_{67}B_{10}NO_4P_2$. Calculated (%): C, 69.89; H, 6.44; N, 1.34; B, 10.31. $^1H$ NMR (DMSO-$d_6$), δ: 7.98—7.92 (m, 8 H, $Ph_4P^+$); 7.81—7.72 (m, 32 H, $Ph_4P^+$); 7.14 (d, 2 H, $C_6H_4$, $J$ = 8.5 Hz); 6.86 (d, 2 H, $C_6H_4$, $J$ = 8.5 Hz); 4.11—4.08 (m, 1 H, $CH_\alpha$); 3.88 (t, 2 H, $C\underline{H}_2OC_6H_4$, $J$ = 5.2 Hz); 3.03 (t, 2 H, $CH_2OB_{10}H_9$, $J$ = 6.7 Hz); 3.01—2.97 (m, 2 H, $CH_\beta$); 1.55—1.52 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$); 1.32—1.30 (m, 2 H, $OCH_2(C\underline{H}_2)_2CH_2O$). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.8 (COOH); 158.5 ($C_6H_4$); 135.8 ($Ph_4P^+$); 134.9 (d, $Ph_4P^+$, $J$ = 10 Hz); 130.9 (d, $Ph_4P^+$, $J$ = 12 Hz); 130.8 ($C_6H_4$); 128.4 ($C_6H_4$); 118.1 (d, $Ph_4P^+$, $J$ = 88 Hz); 115.1 ($C_6H_4$); 70.4 ($CH_2O$); 68.1 ($OCH_2$); 53.8 ($C_\alpha$); 35.4 ($C_\beta$); 28.6 ($CH_2CH_2$); 26.3 ($CH_2CH_2$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: −2.0 (s, 1 B); −3.3 (d, 1 B); −5.6 (d, 1 B); −23.7 (d, 4 B); −29.2 (d, 2 B); −34.1 (d, 1 B).

**Cesium ethyl *N*-(trifluoroacetyl)-*O*-{2-[2-(nonahydro-*closo*-decaborato-2-oxy)ethoxy]ethyl}-L-tyrosinate (10).** To a solution of compound **4** (0.22 g, 0.5 mmol) in MeCN (20 mL), ethyl *N*-(trifluoroacetyl)-L-tyrosinate (0.15 g, 0.5 mmol) and $K_2CO_3$ (0.70 g, 5 mmol) were added. The reaction mixture was refluxed with vigorous stirring for 8 h, the excess of $K_2CO_3$ was filtered off, and the solvent was removed on a rotary evaporator. The residue was dissolved in ethanol and an excess of CsF in EtOH was added. The precipitate was washed with $CH_2Cl_2$ (20 mL) and dried over $P_2O_5$ to yield compound **10** (0.29 g, 75%) as a white powder. $^1H$ NMR (DMSO-$d_6$), δ: 9.86 (s, 1 H, NH); 7.14 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 6.86 (d, 2 H, $C_6H_4$, $J$ = 8.6 Hz); 4.49—4.46 (m, 1 H, $CH_\alpha$); 4.12—4.01 (d, 2 H, $CH_3C\underline{H}_2O$, $J$ = 7.1 Hz); 4.00 (t, 2 H, $C\underline{H}_2OC_6H_4$, $J$ = 5.6 Hz); 3.60 (t, 2 H,

$CH_2O$, $J$ = 5.8 Hz); 3.28 (t, 2 H, $CH_2O$, $J$ = 5.5 Hz), 3.12 (t, 2 H, $CH_2OB_{10}H_9$, $J$ = 5.8 Hz); 3.11—3.08 (m, 1 H, $CH_\beta$); 2.98—2.95 (m, 1 H, $CH_\beta$); 1.15 (t, 3 H, $OCH_2C\underline{H}_3$, $J$ = 7.0 Hz). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.4 (C(O)OEt); 157.6 ($C_6H_4$); 157.0 (q, $CF_3\underline{C}(O)N$, $J_{C-F}$ = 36 Hz); 130.6 ($C_6H_4$); 129.1 ($C_6H_4$); 115.9 (q, $\underline{C}F_3$, $J_{C-F}$ = 288 Hz); 114.7 ($C_6H_4$); 72.8 ($CH_2O$); 69.8 ($CH_2O$); 68.9 ($CH_2O$); 67.4 ($CH_2O$); 61.5 ($CH_3\underline{C}H_2O$); 54.8 ($C_\alpha$); 35.1 ($C_\beta$); 14.3 ($\underline{C}H_3CH_2O$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: −2.1 (s, 1 B); −2.7 (d, 1 B); −5.6 (d, 1 B); −23.7 (d, 4 B); −29.3 (d, 2 B); −33.9 (d, 1 B).

**Tetraphenylphosphonium 2-(2-{2-[4-((*S*)-2-amino-2-carboxyethyl)phenoxy]ethoxy}ethoxy)nonahydro-*closo*-decaborate (11).** To a solution of compound **10** (0.15 g, 0.2 mmol) in water (20 mL), concentrated HCl (2 mL) was added and the reaction mixture was refluxed with continuous stirring for 4 h and then cooled to room temperature. The solvent was removed on a rotary evaporator. The residue was dissolved in water (10 mL) and an excess of an aqueous soltuion of $Ph_4PCl$ was added. The precipitate was filtered off and dried in air. The yield was 0.15 g (71%). Found (%): C, 68.23; H, 6.42; N, 1.38; B, 10.14. $C_{61}H_{67}B_{10}NO_5P_2$. Calculated (%): C, 68.84; H, 6.35; N, 1.32; B, 10.16. $^1H$ NMR (DMSO-$d_6$), δ: 7.96—7.90 (m, 8 H, $Ph_4P^+$); 7.82—7.72 (m, 32 H, $Ph_4P^+$); 7.16 (d, 2 H, $C_6H_4$, $J$ = 8.2 Hz); 6.86 (d, 2 H, $C_6H_4$, $J$ = 8.2 Hz); 4.12—4.08 (m, 1 H, $CH_\alpha$); 4.02 (t, 2 H, $C\underline{H}_2OC_6H_4$, $J$ = 5.2 Hz); 3.60 (t, 2 H, $CH_2O$, $J$ = 5.0 Hz); 3.28 (t, 2 H, $CH_2O$, $J$ = 5.0 Hz), 3.12 (t, 2 H, $CH_2OB_{10}H_9$, $J$ = 5.0 Hz); 3.11—3.05 (m, 1 H, $CH_\beta$); 2.85—2.79 (m, 1 H, $CH_\beta$). $^{13}C\{^1H\}$ NMR (DMSO-$d_6$), δ: 170.1 (COOH); 157.7 ($C_6H_4$); 135.8 ($Ph_4P^+$); 134.9 (d, $Ph_4P^+$, $J$ = 10 Hz); 130.9 (d, $Ph_4P^+$, $J$ = 12 Hz); 130.6 ($C_6H_4$); 129.4 ($C_6H_4$); 118.2 (d, $Ph_4P^+$, $J$ = 86 Hz); 114.9 ($C_6H_4$); 72.7 ($CH_2O$); 69.9 ($CH_2O$); 68.9 ($CH_2O$); 67.5 ($CH_2O$); 55.7 ($C_\alpha$); 36.3 ($C_\beta$). $^{11}B\{^1H\}$ NMR (DMSO-$d_6$), δ: −2.1 (s, 1 B); −2.8 (d, 1 B); −5.6 (d, 1 B); −23.6 (d, 4 B); −29.3 (d, 2 B); −33.8 (d, 1 B).

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