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Asymmetric Synthesis of *p*-Carboranylalanine (*p*-Car) and 2-Methyl-*o*-Carboranylalanine (Me-*o*-Car).

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Abstract: Two new α-amino acids containing the 1,2- and the 1,12-dicarba-*closo*-dodecaborane(12) cages, namely *p*-carboranylalanine (**1**), and 2-methyl-*o*-carboranylalanine (**2**), were prepared using Oppolzer's sultam methodologies. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

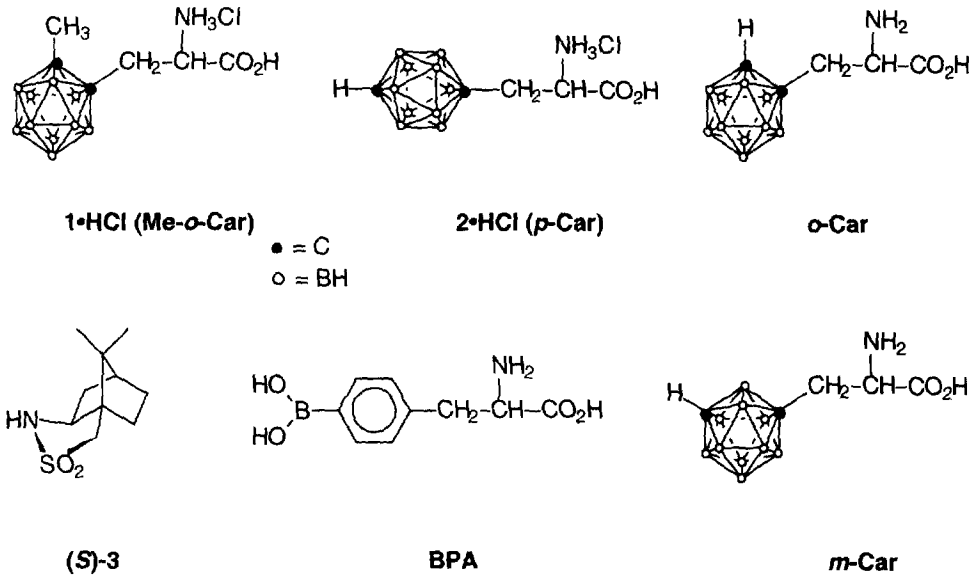
The amino acid *p*-boronophenylalanine (**BPA**), containing one boron atom, is presently of considerable clinical interest for use in Boron Neutron Capture Therapy (BNCT) of cancer. Amino acids substituted with polyhedral boron clusters are also of potential interest for BNCT due to their high boron content. The biological properties of a number of peptides in which L-phenylalanine was replaced with its highly lipophilic *o*-carboranyl analogue, L-*o*-carboranylalanine (**L-*o*-Car**) were extensively studied during the period 1976 – 1980. It was shown that for some cases enzyme and receptor binding was preserved when the phenyl group was substituted with the *o*-carborane cage. Earlier work on the synthesis and the evaluation of the biological properties of polyhedral borane-containing amino acids including the biological work on the *o*-carboranylalanine-contaning peptides has recently been reviewed.[1] Several groups are presently engaged in research concerning the use of ***o*-Car** or ***o*-Car**-containing peptides in BNCT.[1,2] We have recently published results from *in vitro* studies, for both L- and D-*o*-carboranylalanine, on penetration and binding in human melanoma spheroids [2,3] as well as the cellular binding and effect on BNCT using cultured Melanoma B 16 cells [2,4].

It has previously been shown in our laboratories that ***o*-Car** spontaneously undergoes self-degradation with a maximum rate at a pH around the isoelectric point[5]. The self-degradation was shown to be an intramolecular process were the *o*-carborane cage is transformed to the two corresponding diastereomeric *nido*-compounds, by action of both the carboxylate ion and the protonated amino function. This degradation process might complicate the use of the free amino acid *in vivo*.

To our knowledge no amino acid containing the *p*-carborane cage has been reported. *p*-Carborane was first synthesised by Papetti and Heying[6] via thermal rearrangement of *o*-carborane in 1964 and is known to be more stable towards degradation to *nido*-compounds than *o*-carborane.[7]

In this contribution we describe the asymmetric synthesis of the highly lipophilic amino acids 2-methyl-*o*-carboranylalanine (**1, Me-*o*-Car**), and *p*-carboranylalanine (**2, *p*-Car**) (Scheme 1).

Preclinical evaluation concerning binding and toxicity of **Me-*o*-Car** and ***p*-Car** to cultured human glioma and mouse melanoma cells will be published separately.



Scheme 1.

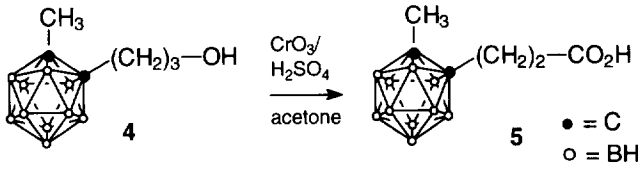
RESULTS AND DISCUSSION

The amino acids were synthesised using Oppolzer's sultam methodology for introducing the chirality. The carboranylalanines (*S*)-**1•HCl** and (*S*)-**2•HCl** were obtained via electrophilic hydroxyamination[8] of the corresponding *N*-carboranylpropanoyl derivatives of the bornanesultam (*S*)-**3**. The assignments of absolute configurations of amino acids **1** - **2** are based on the stereochemical outcome of previously reported hydroxyamination reactions of *N*-acyl derivatives of **3**[8].

Asymmetric synthesis of ***(S)-1•HCl*** *and* ***(S)-2•HCl*** *(Schemes 2-4).*

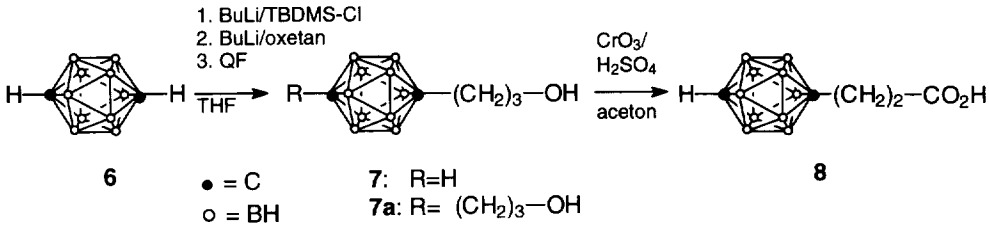
In the synthesis of the carboranylalanines (*S*)-2-methyl-*o*-carboranylalanine **[(*S*)-1•HCl]**, and (*S*)-*p*-carboranylalanine, **[(*S*)-2•HCl]**, the carboranylpropanoic acids **5** and **8** were required (Scheme 2 and Scheme 3 respectively). 3-(2-Methyl-*o*-carboranyl)propionic acid (**5**) was prepared by oxidation of 1-methyl-2-(3-hydroxypropyl)-*o*-carborane (**4**)[9] in acetone using CrO_3 and H_2SO_4 in 75% yield (Scheme 2).

Silylation of *p*-carborane (**6**) with TBDMS-Cl, followed by alkylation with oxetane and subsequent desilylation with Bu_4NF gave 1-(3-hydroxypropyl)-*p*-carborane (**7**) and 1,2-bis(3-hydroxypropyl)-*p*-carborane (**7a**) in 62% and 17% yield respectively. Unreacted *p*-carborane could be recovered by sublimation. When the



Scheme 2.

alcohol **7** was prepared from unprotected *p*-carborane the yield was ~27% of alcohol **7** and 49% of diol **7a**. The alcohol **7** was oxidised to the corresponding carboxylic acid **8** in acetone using CrO_3 and H_2SO_4 in a yield of 84% (Scheme 3).



Scheme 3.

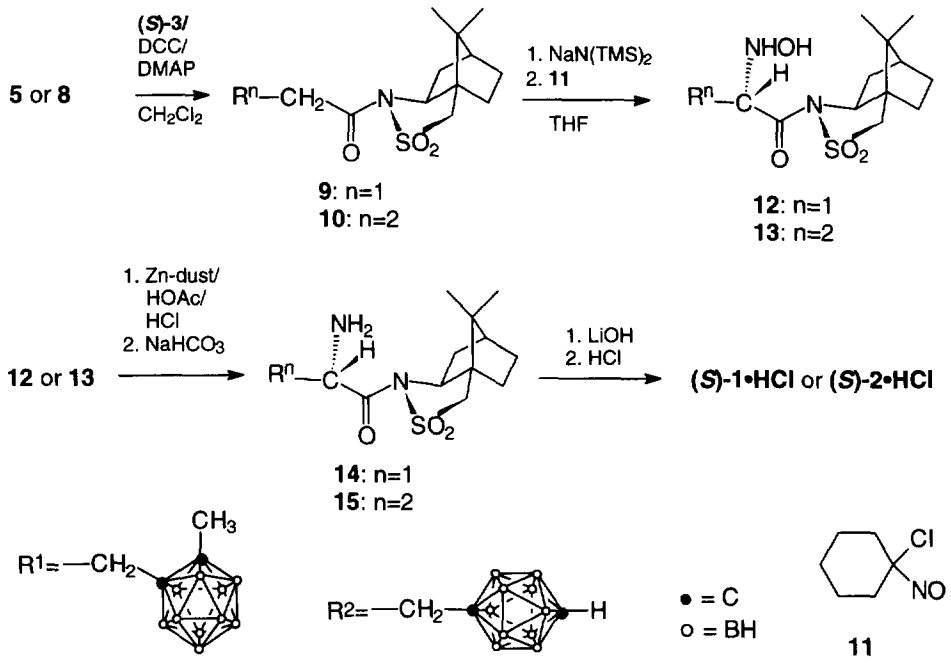
N-acylation of the sultam (*S*)-**3** with the carboranyl propanoic acids **5** and **8** was performed with DCC and DMAP[10] to give (*S*)-**9** and (*S*)-**10** in 88% and 84% yield respectively (Scheme 4).

Asymmetric hydroxyamination of the acyl sultams (*S*)-**9** and (*S*)-**10** was done by deprotonation with sodium hexamethyldisilazide at -78°C followed by the addition of the bright-blue compound 1-chloro-1-nitroso-cyclohexane (**11**) to afford, after workup, the hydroxyamino compounds (*S,S*)-**12** and (*S,S*)-**13** in a yield of 84% and 83% respectively. Hydrogenolysis of the oxim-sultams (*S,S*)-**12** and (*S,S*)-**13** with Zn-dust in AcOH/conc. HCl at 4 °C for a period of 3-6 days provided after basification the *N*-(α-amino-acyl)sultams (*S,S*)-**14** and (*S,S*)-**15** in 78 % and 77% yield after recrystallisation from methanol/water. (*S,S*)-**14** and (*S,S*)-**15** were diastereomerically pure according to ^{1}H-NMR. Hydrolysis of the amide groups with LiOH (THF/1M LiOH aq.) afforded, after acidification, with hydrochloric acid the amino acid hydrochlorides (*S*)-**1•HCl** and (*S*)-**2•HCl** in 71% and 75% yield respectively. The overall yield of amino acid (*S*)-**1•HCl** was 31% from acid **5** and that for amino acid **2** was 21% from *p*-carborane (34% from acid **8**) with enantiomeric purities of >99% for both (*S*)-**1•HCl** and (*S*)-**2•HCl**. The corresponding enantiomers (*R*)-**1•HCl** and (*R*)-**2•HCl** were prepared as described above for (*S*)-**1•HCl** and (*S*)-**2•HCl**.

In contrast to *p*-carboranylalanine, the amino acid 2-methyl-*o*-carboranylalanine was observed to self-degrade[11] in the same way as observed for *o*-carboranylalanine[5].

Determination of enantiomeric purity.

We have earlier shown that enantiomeric purities for *o*-carboranylalanine as well as 5-(1,2-dicarba-*closo*-dodecaborane(12)-1-yl)-2-aminopentanoic acid and 5-(2-methyl-1,2-dicarba-*closo*-dodecaborane(12)-1-yl)-2-aminopentanoic acid amino acid can be accurately determined via chromatographic separation (HPLC) of the diastereomeric derivatives formed with Marfey's reagent[12], *N*-α-(2,4-dinitro-5-fluoro-phenyl)-



Scheme 4.

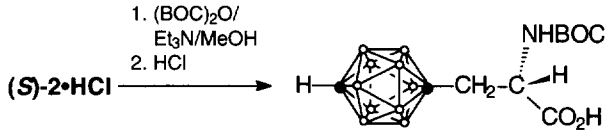
(*S*)-alanineamide.[5a,13] The accuracy of the method was verified by control determinations using the racemic amino acids and for *o*-carboranylalanine also by use of a chiral β-cyclodextrine based open tubular column SFC on the corresponding (*N*-trifluoroacetyl)propyl ester.[5a,14]

The enantiomeric purities of the enantiomers of **1** and **2** were found to be >99% by the method of Marfey. For (***R***)-**2** the enantiomeric purity was found to be 99.1%±0.2% using the chiral open tubular column SFC method,[5a,14] thus verifying the reliability of the method by Marfey. No method has yet been found for the determination of the enantiomeric purity of (*S*)-**1**.

Preparation of BOC-protected amino acid (**S**)-***16*** *(Scheme 5).*

In order to use *p*-carboranylalanine for peptide synthesis the BOC derivative was prepared using di(*tert*-butyl) dicarbonate and triethyl amine in methanol. Two rotamers were observed both in ^{1}H NMR and ^{13}C NMR. The amide-H and the α-H showed two signals, were those with the lower intensities disappeared upon heating to 50 °C. In ^{13}C NMR two signals were observed for the methyl groups of the BOC-group.

The steric demand of the cages in the three possible unsubstituted carboranylalanines (*ortho-*, *meta-* and *para-*) should be similar but the lipophilicities of the amino acids are expected to increase in the order $p > m > o$ due to the increase in dipole moments of the cages in going from the *p*-cage to the *o*-cage. The synthesis of *m*-carboranylalanine (***m*-Car**) is under progress in our laboratory. We plan to incorporate the carboranylalanines into small tumour seeking peptides in order to examine the effects of the differences in lipophilicities on receptor affinities.



(*S*)-16

Scheme 5.

EXPERIMENTAL SECTION

General Details. The ^{1}H, ^{13}C and ^{11}B NMR spectra were recorded in $CDCl_3$ (7.26 ppm, ^{1}H, 77.0 ppm ^{13}C) or CD_3OD (3.35 ppm, ^{1}H, 49.0 ppm ^{13}C) on a Varian Unity-400 spectrometer operating at 400, 100.6 and 128.3 MHz respectively. Boron trifluoride etherate was used as external standard for the boron spectra. IR spectra were obtained with a Perkin-Elmer 1600 FT-IR spectrometer and optical rotations were measured on a Perkin Elmer 241LC polarimeter. Elemental analyses were performed by Analytische Laboratorien, Gummersbach, GERMANY. For flash chromatography Merck Silica Gel 60 (230-400 mesh) was used. TLC was performed using Merck Silica 60 F_{254} gel. Melting points are uncorrected and were obtained using a Büchi capillary melting point apparatus. In the determination of enantiomeric purities of the amino acids according to the method by Marfey the separation of the diastereomeric derivatives were performed on a 250 mm × 4.6 mm Spherisorb ODS1 10μ column using a Waters HPLC system equipped with a Waters 991 Photodiode Array Detector (340 nm) and a Millennium 2010 Chromatographic Manager. Solvents A (0.01M potassium dihydrogen phosphate) and B (acetonitrile/water (50/7, v/v)) with the gradient system 25% B to 50% B were used as the eluting system. Mass spectra were recorded on a Finnigan Mat INCOS 50 instrument in the electron impact (EI) mode, a SX/SX 102A (JEOL) FAB mass spectrometer or on a Quattro single quadrupole mass spectrometer from VG Biotech with Electrospray (ESP+) ionisation (3.0 kV). The samples were in the EI case introduced via a direct inlet and for the ESP measurements via a RP18-column using solvent system C (5mM formic acid in acetonitrile) and D (5mM formic acid in water), 15% C to 98% C in 10 min. For preparation of analytical samples a 250 mm × 10 mm Spherisorb 10μ column on a Waters 501 HPLC Pump equipped with a Waters 441 Absorbance Detector and a Waters R401 Differential Refractometer detector using solvent system E (methanol) and F (water).Solvents were dried and distilled according to standard methods. "cb" is used for the carborane-cage.

3-(2-Methyl-o-carboranyl)propionic acid (5). 1-Methyl-2-(3-hydroxypropyl)-*o*-carborane (**4**) (4.95 g, 22.9 mmol) was dissolved in acetone (100 mL) and the solution was cooled to 0 °C. A solution of CrO_3 (9.16 g, 91.6 mmol) in 3M H_2SO_4 (50 mL) was added dropwise over a period of 0.5 h. The solution was stirred at RT for 3h and H_2O (100 mL) was added. The acetone was evaporated and the residue was extracted with diethyl ether (3 × 200 mL). The ether was stripped off and the solid residue was dissolved in 10% NaOH and filtered through celite. The acid was precipitated with conc. HCl, filtered and washed with water to give 75% acid **5** (3.95 g). The analytical sample was recrystallized from hexane. Mp. 170.5-172 °C. ^{1}H NMR ($CDCl_3$) δ 2.68 (m, 2H, CH_2-C=O), 2.54 (m, 2H, C-CH_2-), 2.05 (s, 3H, -CH_3); ^{13}C NMR ($CDCl_3$) δ 177.0 (C=O), 76.0

(cb *C*), 75.0 (cb *C*), 33.3 (*C*H_2-(C=O)-), 29.6 (C-*C*H_2-), 23.2 (-*C*H_3); ^{11}B NMR ($CDCl_3$) δ -4.1, -5.7, -9.4 (sh), -9.7 -10.4, -11.2; IR (KBr) ν 2590 (s), 1716 (s), 1427 (m), 1308 (m), 1223 (m) cm^{-1}; MS(EI) *m/z* calcd for M^+: 230, observed: 230 (100), 184 (27), 154 (22) (within the boron cluster envelopes); Anal. Calcd for $C_6H_{18}B_{10}O_2$: C, 31.29; H, 7.88; Found: C, 30.91; H, 7.72.

1-(3-Hydroxypropyl)-p-carborane (7). *p*-Carborane (**6**) (16.00 g, 111 mmol) was dissolved in anhydrous THF (200 mL) and cooled to 0 °C under N_2-atmosphere. A 1.6 M solution of n-butyllithium in hexane (69 mL, 111 mmol) was added and the mixture was stirred for 1h at 0 °C. *tert*-Butyl-dimethylsilyl chloride (16.68 g, 111 mmol), dissolved in THF (30 mL), was added and the reaction mixture was refluxed overnight. The reaction was cooled to RT and quenched with H_2O (100 mL). The THF was evaporated and the aqueous phase was extracted with diethyl ether (3 × 75 mL). The combined ether extracts was dried with Na_2SO_4, and filtered through silica. The diethyl ether was evaporated and the resulting crude silylated mixture (27.72 g) which was redissolved in THF (250 mL) and cooled to 0 °C under N_2-atmosphere. A solution of 1.6M n-butyllithium (69 mL, 111 mmol) in hexane was added and the resulting mixture was stirred for 1h and oxetane (6.6 mL, 97 mmol) was added. The reaction mixture was refluxed overnight, cooled to RT, and quenched with 1M HCl (100 mL). THF was evaporated and the water phase was extracted with diethyl ether (3 × 100 mL). The combined organic phases were dried with Na_2SO_4, filtered and evaporated to give a crude alkylated mixture (34.9 g). To this mixture dissolved in THF (250 mL) tetrabutylammonium fluoride (101 mL, 111 mmol, 1.1M solution in THF) was added dropwise at -78 °C under N_2-atmosphere. The reaction was stirred for 0.5 h and the temperature was raised to RT. The reaction was quenched with H_2O (300 mL) and the THF was evaporated. The water phase was extracted with diethyl ether (3 × 200 mL). The organic phase was dried with Na_2SO_4, filtered, and evaporated. Flash chromatography of the residue using diethyl ether:pentane 1:2 as the eluent to gave alcohol **7** (14.0g, 63%) (R_f = 0.40), *p*-carborane (0.47g, 3%) (R_f = 0.99) and diol **7a**[15] (4.9 g, 17%) (R_f = 0.14). An analytical sample of the alcohol **7** was obtained by recrystallization from hexane. Mp. 72.5-74.5 °C. ^{1}H NMR ($CDCl_3$) δ 3.46 (dt, 2H, C*H*$_2$-OH), 2.63 (s, 1H, *H*-C), 1.71 (m, 2H, C-C*H*$_2$-), 1.43 (t, 2H, -O*H*), 1.39 (m, 2H, CH$_2$-C*H*$_2$-CH$_2$); ^{13}C NMR ($CDCl_3$) δ 84.1 (cb *C*), 61.8 (*C*H$_2$-OH), 58.1 (H*C*), 35.3 (C-*C*H$_2$-CH$_2$), 32.2 (CH$_2$-*C*H$_2$-CH$_2$); ^{11}B NMR ($CDCl_3$) δ -12.8, -15.3; IR (KBr) ν 3318 (m, br), 2960 (w), 2934 (w), 2603 (s), 1450 (w), 1058 (s), 1006 (m), 728 (m) cm^{-1}; MS(EI) *m/z* calcd for $(M-H)^+$: 201, observed: 201 (34), 184 (100), 168 (33) (within the boron cluster envelopes); Anal. Calcd for $C_5H_{18}B_{10}O$: C, 29.69; H, 8.97; Found: C, 29.79; H, 9.01.

3-(p-Carboranyl)propionic acid (8). 1-(3-Hydroxypropyl)-*p*-carborane (**7**)[9] (1.00 g, 4.96 mmol) was dissolved in acetone (20 mL) and the solution was cooled to 0 °C. A solution of CrO_3 (2.00 g, 10 mmol) in 3M H_2SO_4 (10 mL) was added dropwise over a period of 0.5 h. The solution was stirred at ambient temperature for 3h, H_2O (20 mL) was added and the acetone was evaporated. The remaining residue was extracted with diethyl ether (3 × 20 mL) and evaporated. The solid was dissolved in 10% NaOH and filtered through celite. The acid was precipitated with conc. HCl, filtered and washed with water to give 84% acid **8** (903 mg). The analytical sample was obtained by recrystallization from hexane. Mp. 150.5-152 °C. ^{1}H NMR ($CDCl_3$) δ 2.65 (s, 1H, *H*-C), 2.23 (m, 2H, C*H*$_2$-C=O), 1.96 (m, 2H, C-C*H*$_2$-); ^{13}C NMR ($CDCl_3$) δ 177.4 (C=O), 82.4 (cb *C*), 58.4 (H*C*), 33.2 (-*C*H$_2$-(C=O)-), 32.9 (C-*C*H$_2$-); ^{11}B NMR ($CDCl_3$) δ -12.9, -15.2; IR (KBr) ν 3066 (w), 2609 (s), 1704 (s), 1435 (w), 1317 (w), 1227 (w) cm^{-1}; MS(EI) *m/z* calcd for M^+: 216, observed: 216 (100%).

(2S)-N-*[3'-(2"-Methyl-1",2"-dicarba*-closo-*dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(S)-9].* (*2S*)-Bornane-10,2-sultam [(*S*)-**3**], (1.04 g, 4.96 mmol) was acylated with 3-(2-Methyl-*o*-carboranyl)propionic acid (**5**) (1.11 g, 4.82 mmol) in the presence of DCC (1.11 g, 5.40 mmol) and of DMAP (30 mg) in dry CH_2Cl_2 (35 mL) under N_2-atmosphere at RT overnight. The precipitate was filtered and CH_2Cl_2 was evaporated. Flash column chromatography of the crude residue (2.28 g) with toluene:MeCN 97.5:2.5 as the eluent gave (*S*)-**9** (R_f = 0.21). Yield: 1.81 g (88%). The analytical sample was obtained by recrystallization from MeOH. Mp. 238.5-241 °C. $[\alpha]_{589}^{25.0}$ = +73.3°, $[\alpha]_{578}^{25.0}$ = +77.3°, $[\alpha]_{549}^{25.0}$ = +87.8°, $[\alpha]_{436}^{25.0}$ = +151.4°, $[\alpha]_{365}^{25.0}$ = +245.7° (c 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.84 (dd, *J* = 5, 8 Hz, 1H, -N-C*H*-), 3.48 (AB, *J* = 14 Hz, δ=22 Hz, 2H, -C*H*$_2$-SO_2-), 2.98 (m, 2H, (C=O)-C*H*$_2$-), 2.60 (m, 2H, (C=O)-CH_2-C*H*$_2$-), 2.07 (m, 2H, -CH-C*H*$_2$-CH-), 2.04 (s, 3H, cb-C*H*$_3$), 1.93 (m, 1H, C*H*$_2$-CH_2-CH-), 1.91 (m, 1H, CH_2-C*H*$_2$-CH-), 1.89 (m, 1H, CH_2-CH_2-C*H*-), 1.41 (m, 1H, C*H*$_2$-CH_2-CH), 1.36 (m, 1H, CH_2-C*H*$_2$-CH), 1.15 (s, 3H, C-C*H*$_3$), 0.98 (s, 3H, C-C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 169.1 (C=O), 76.4 (cb *C*), 75.1 (cb *C*), 65.2 (N-*C*H-), 52.8 (-*C*H$_2$-SO_2-), 48.7 (-CH_2-*C*-CH-), 47.8 (*C*-$(CH_3)_2$), 44.6 (-CH_2-CH_2-*C*H-), 38.3 (-CH-*C*H$_2$-CH-), 34.9 ((C=O)-*C*H$_2$-), 32.9 (-*C*H$_2$-CH_2-CH-), 29.5 (cb-*C*H$_2$-), 26.4 (-CH_2-*C*H$_2$-CH-), 23.2 (cb-*C*H$_3$), 20.8 (C-*C*H$_3$), 19.9 (C-*C*H$_3$); ^{11}B NMR ($CDCl_3$) δ -4.3, -5.8, -9.3 (sh), -9.8, -10.5; IR (KBr) ν 2962 (w), 2592 (s), 2360 (m), 2343 (w), 1694 (s), 1394 (m), 1328 (s), 1277 (m), 1238 (m), 1217 (m), 1166 (w), 1134 (m), 1117 (w), 535 (m) cm^{-1}; MS(EI) *m/z* calcd for M^+: 427, observed: 427 (0.21), 255 (1.6), 240 (1.2), 182 (11) (within the boron cluster envelopes); Anal. Calcd for $C_{16}H_{33}B_{10}NO_3S$: C, 44.94; H, 7.78; N, 3.28; Found: C, 44.69; H, 7.59; N, 3.25.

(2R)-N-*[3'-(2"-Methyl-1",2"-dicarba*-closo-*dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(R)-9].* (*2R*)-Bornane-10,2-sultam [(*R*)-**3**] was acylated with 3-(2-methyl-1,2-dicarba-*closo*-dodecaborane(12)-1-yl)propionic acid, **5**, as described for (*S*)-**9**. Mp. 238.5-241 °C. $[\alpha]_{589}^{25.0}$ = -73.5° (c 1.01, $CHCl_3$). Spectral data were in accordance with (*S*)-**9**.

(2S)-N-*[3'-(1",12"-Dicarba*-closo-*dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(S)-10].* (*2S*)-Bornane-10,2-sultam [(*S*)-**3**] (5.01g, 23.2 mmol) was acylated with 3-(*p*-carboranyl)propionic acid, **8**, (5.00 g, 23.1 mmol) in the presence of DCC (5.32 g, 25.8 mmol) and of DMAP (150 mg) in dry CH_2Cl_2 (120 mL) under N_2-atmosphere at RT overnight. The precipitate was filtered and CH_2Cl_2 was evaporated. Purification of the residue by flash chromatography with toluene:MeCN 97.5:2.5 gave (*S*)-**10** (R_f = 0.48). Yield 8.03 g (84%). An analytical sample was prepared by recrystallization from MeOH. Mp. 211.5-213.5 °C. $[\alpha]_{589}^{25.0}$ = +73.5°, $[\alpha]_{578}^{25.0}$ = +76.8°, $[\alpha]_{549}^{25.0}$ = +87.2°, $[\alpha]_{436}^{25.0}$ = +150.0°, $[\alpha]_{365}^{25.0}$ = +243.2° (c 1.04, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.78 (dd, *J* = 5, 8 Hz, 1H, -N-C*H*-), 3.44 (AB, *J* = 14 Hz, δ = 21 Hz, 2H, -C*H*$_2$-SO_2-), 2.63 (br s, 1H, cb C*H*), 2.59 (m, 2H, (C=O)-C*H*$_2$-), 2.04 (m, 2H, (C=O)-CH_2-C*H*$_2$-), 2.02 (m, 2H, -CH-C*H*$_2$-CH-), 1.90 (m, 1H, C*H*$_2$-CH_2-CH-), 1.88 (m, 1H, CH_2-C*H*$_2$-CH-), 1.86 (m, 1H, CH_2-CH_2-C*H*-), 1.37 (m, 1H, C*H*$_2$-CH_2-CH), 1.33 (m, 1H, CH_2-C*H*$_2$-CH), 1.12 (s, 3H, C-C*H*$_3$), 0.96 (s, 3H, C-C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 169.6 (C=O), 82.7 (cb *C*), 65.1 (N-*C*H-), 58.2 (cb *C*H), 52.8 (-*C*H$_2$-SO_2-), 48.5 (-CH_2-*C*-CH-), 47.8 (*C*-$(CH_3)_2$), 44.6 (-CH_2-CH_2-*C*H-), 38.3 (-CH-*C*H$_2$-CH-), 34.8 ((C=O)-*C*H$_2$-), 32.8 (-*C*H$_2$-CH_2-CH-), 32.6 (cb-*C*H$_2$-), 26.4 (-CH_2-*C*H$_2$-CH-), 20.8 (C-*C*H$_3$), 19.9 (C-*C*H$_3$); ^{11}B NMR ($CDCl_3$) δ -12.8, -15.2; IR (KBr) ν 2961 (w), 2606 (s), 1694 (s), 1391 (m), 1330 (s), 1266 (w), 1236 (m), 1218 (m), 1165 (w), 1135 (m), 1118 (m), 537 (m) cm^{-1}; MS(EI) *m/z* calcd for M^+: 414, observed: 414 (0.08), 349 (1.2), 306 (1), 199 (20), 169 (20) (within the boron cluster envelopes); Anal. Calcd for $C_{15}H_{31}B_{10}NO_3S$: C, 43.56; H, 7.56; N, 3.39; Found: C, 43.26; H, 7.35; N, 3.35.

(2R)-N-*[3'-(1",12"-Dicarba*-closo-*dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(**R**)-**10**].* (*2R*)-Bornane-10,2-sultam [(***R***)-**3**] was acylated with 3-(1,12-dicarba-*closo*-dodecaborane(12)-1-yl)propionic acid (**8**) as described for the synthesis (***S***)-**10**. Mp. 211.5-213.5 °C. $[\alpha]_{589}^{25.0}$ = -74.9° (c 1.01, $CHCl_3$). Spectral data were in accordance with (***S***)-**10**.

(2S,2'S)-N-*[3'-(2"-Methyl-1",2"-dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-(hydroxyamino)-propanoyl]bornane-10,2-sultam [(**S,S**)-**12**].* (*2S*)-*N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(***S***)-**9**] (1.71 g, 4.00 mmol) was dissolved in THF (50 mL) under N_2-atmosphere and cooled to -78 °C. A 1M solution of sodium *N*-bis(trimetylsilyl)amid in THF (4.8 mL, 4.8 mmol) was added dropwise. After stirring for 1h at -78°C, a 1.3 M solution of 1-chloro-1-nitrosocyclohexane, **11**, (5.7 mL, 4.4 mmol) was added. The mixture was stirred for 2 h and finally quenched with 1M HCl (15 mL). The reaction mixture was concentrated *in vacuo*, made basic with saturated $NaHCO_3$, and extraxted with CH_2Cl_2 (3 × 20 mL). The combined organic layers was dried with Na_2SO_4, filtered and concentrated. Purification of the residue (2.45g) by flash chromatography with the solvent system toluene:MeCN:Et_3N 95:5:1 as the eluent gave (***S,S***)-**12** (R_f = 0.20). Yield 1.53 g (84%). The analytical sample was obtained by washing with hexane and recrystallization of the residue from MeOH:H_2O. Mp. 212.5-214.5 °C dec. $[\alpha]_{589}^{25.0}$ = +63.1°, $[\alpha]_{578}^{25.0}$ = +64.4°, $[\alpha]_{549}^{25.0}$ = +73.0°, $[\alpha]_{436}^{25.0}$ = +120.6°, $[\alpha]_{365}^{25.0}$ = +180.8° (c 1.01, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 6.19 (br, 1H, N*H*OH), 4.52 (d, *J* = 2 Hz, 1H, NHO*H*), 4.31 (m, 1H, (C=O)-C*H*-), 3.94 (dd, *J* = 5, 8 Hz, 1H, -N-C*H*-CH_2-CH-), 3.52 (AB, *J* = 14 Hz, δ= 24 Hz, 2H, -C*H*$_2$-SO_2-), 2.91 (dd, *J* = 4, 15 Hz, 1H, (C=O)-CH-C*H*$_2$-), 2.46 (dd, *J* = 8, 15 Hz, 1H, (C=O)-CH-C*H*$_2$-), 2.10 (m, 2H, -CH-C*H*$_2$-CH-), 2.06 (s, 3H, cb C*H*$_3$), 1.95 (m, 1H, C*H*$_2$-CH_2-CH-), 1.93 (m, 1H, CH_2-C*H*$_2$-CH-), 1.89 (m, 1H, CH_2-CH_2-C*H*-), 1.44 (m, 1H, C*H*$_2$-CH_2-CH), 1.37 (m, 1H, CH_2-C*H*$_2$-CH), 1.19 (s, 3H, C-C*H*$_3$), 0.99 (s, 3H, C-C*H*$_3$); ^{13}C NMR ($CDCl_3$) δ 170.3 (C=O), 75.5 (cb *C*), 75.1 (cb *C*), 65.4 (N-*C*H-CH_2-CH-), 63.6 ((C=O)-*C*H), 53.0 (-*C*H$_2$-SO_2-), 49.1 (-CH_2-*C*-CH-), 47.9 (*C*-$(CH_3)_2$), 44.5 (-CH_2-CH_2-*C*H-), 38.0 (-CH-*C*H$_2$-CH-), 33.4 (cb-*C*H$_2$-), 32.7 (-*C*H$_2$-CH_2-CH-), 26.4 (-CH_2-*C*H$_2$-CH-), 23.4 (cb *C*H$_3$), 20.5 (C-*C*H$_3$), 19.9 (C-*C*H$_3$); ^{11}B NMR ($CDCl_3$) δ -4.0, -5.8, -9.3 (sh), -10.3; IR (KBr) ν 3511 (m, br), 2967 (m), 2590 (s), 1683 (s), 1320 (s), 1268 (w), 1237 (w), 1219 (m), 1165 (w), 1134 (s), 1117 (w), 1065 (w), 545 (m) cm^{-1}; MS(ESP+) *m/z* calcd for $(M+H)^+$: 460, observed: 460 (within the boron cluster envelope).

(2R,2'R)-N-*[3'-(2"-Methyl-1",2"-dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-(hydroxyamino)-propanoyl]bornane-10,2-sultam [(**R,R**)-**12**].* (*2R*)-*N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)propionyl]bornane-10,2-sultam [(***R***)-**9**] was transformed to (***R,R***)-**12** as described for (***S,S***)-**12**. Mp. 212.5-214.5 °C dec. $[\alpha]_{589}^{25.0}$ = -60.0° (c 1.01, $CHCl_3$). Spectral data were in accordance with (***S,S***)-**12**.

(2S,2'S)-N-*[3'-(1",12"-Dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-(hydroxyamino)propanoyl]-bornane-10,2-sultam [(**S,S**)-**13**].* (*2S*)-*N*-[3'-(1",12"-Dicarba-*closo*-dodecaborane(12)-1"-yl)propionyl]-bornane-10,2-sultam [(***S***)-**10**] (7.89 g, 19.1 mmol) was dissolved in THF (125 mL) under N_2-atmosphere and cooled to -78 °C. A 1M solution of sodium *N*-bis(trimetylsilyl)amid in THF (21.0 mL, 21.0 mmol) was added dropwise. After 1h a 1.3 M solution of 1-chloro-1-nitrosocyclohexane (**11**) (26.0 mL, 20.1 mmol) was added. The mixture was stirred for 2 h and finally quenched with 1M HCl (60 mL). Concentration *in vacuo*, basification with $NaHCO_3$, extraction with CH_2Cl_2 (3 × 20 mL), drying with Na_2SO_4, filtration and evaporation gave crude (***S,S***)-**13** (10.79 g). Purification by flash chromatography with the solvent system toluene:MeCN:Et_3N 95:5:1 as the eluent gave (***S,S***)-**13** (R_f = 0.31). Yield 7.05 g in (83%). The analytical

sample was obtained as described for **(*S,S*)-12.** Mp. 203.5-205.5 °C dec. $[\alpha]_{589}^{25.0}$ = +63.9°, $[\alpha]_{578}^{25.0}$ = +66.7°, $[\alpha]_{549}^{25.0}$ = +77.6°, $[\alpha]_{436}^{25.0}$ = +125.8°, $[\alpha]_{365}^{25.0}$ = +184.7° (c 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 5.93 (br, 1H, N*H*OH), 4.49 (br s, 1H, NHO*H*), 3.87 (dd, *J* = 5, 8 Hz, 1H, (C=O)-C*H*-), 3.87 (dd, *J* = 5, 8 Hz, 1H, -N-C*H*-CH_2-CH-), 3.49 (AB, *J* = 14 Hz, δ = 23 Hz, 2H, -CH_2-SO_2-), 2.64 (br s, 1H, cb C*H*), 2.32 (dd, *J* = 4, 15 Hz, 1H, (C=O)-CH-CH_2-), 2.08 (m, 2H, -CH-CH_2-CH-), 2.03 (dd, *J* = 8, 15 Hz, 1H, (C=O)-CH-CH_2-), 1.90 (m, 1H, CH_2-CH_2-CH-), 1.88 (m, 1H, CH_2-CH_2-CH-), 1.85 (m, 1H, CH_2-CH_2-C*H*-), 1.41 (m, 1H, CH_2-CH_2-CH), 1.34 (m, 1H, CH_2-CH_2-CH), 1.16 (s, 3H, C-CH_3), 0.97 (s, 3H, C-CH_3); ^{13}C NMR ($CDCl_3$) δ 170.7 (C=O), 81.1 (cb *C*), 65.3 (N-*C*H-CH_2-CH-), 63.5 ((C=O)-*C*H), 58.9 (cb *C*H), 53.0 (-*C*H$_2$-SO_2-), 49.0 (-CH_2-*C*-CH-), 47.9 (*C*-$(CH_3)_2$), 44.5 (-CH_2-CH_2-*C*H-), 38.0 (-CH-*C*H$_2$-CH-), 36.7 (cb-*C*H$_2$-), 32.8 (-*C*H$_2$-CH_2-CH-), 26.4 (-CH_2-*C*H$_2$-CH-), 20.5 (C-*C*H$_3$), 19.9 (C-*C*H$_3$); ^{11}B NMR ($CDCl_3$) δ -12.6, -15.3; IR (KBr) ν 3277 (w), 2960 (w), 2601 (s), 1716 (m), 1694 (s), 1321 (m), 1306 (s), 1286 (w), 1218 (m), 1166 (w), 1136 (m), 1117 (w), 1065 (m) 547 (m), 538 (m) cm^{-1}; MS(ESP+) *m/z* calcd for $(M+H)^+$: 445, observed: 445 (within the boron cluster envelope); Anal. Calcd for $C_{15}H_{32}B_{10}N_2O_4S$: C, 40.52; H, 7.25; N, 6.30; Found: C, 40.71; H, 7.04; N, 6.33.

*(2*R*,2'*R*)-*N*-[3'-(1",12"-Dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-(hydroxyamino)propanoyl]-bornane-10,2-sultam [(**R,R**)-13].* (*2R*)-*N*-[3'-(1",12"-Dicarba-*closo*-dodecaborane(12)-1"-yl)propionyl]-bornane-10,2-sultam **[(*R*)-10]**, was transformed to **(*R,R*)-13** as described for **(*S,S*)-13**. Mp. 203.5-205.5 °C dec. $[\alpha]_{589}^{25.0}$ = -63.1° (c 1.01, $CHCl_3$). Spectral data were in accordance with **(*S,S*)-13**.

*(2*S*,2'*S*)-*N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-aminopropanoyl]-bornane-10,2-sultam [(**S,S**)-14].* (*2S,2'S*)-*N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-(hydroxyamino)propanoyl]bornane-10,2-sultam **[(*S,S*)-12]** (1.14 g, 2.49 mmol) was dissolved in acetic acid:conc. HCl 11:1 (24 mL), cooled to 4 °C, mixed with Zn powder (3.01 g, 46.0 mmol) and stirred under N_2-atmosphere for 4 d. The mixture was filtered through glass wool and concentrated. The residue was partly dissolved in CH_2Cl_2 (40 mL), neutralized with aq. $NaHCO_3$ and filtered. Extraction with CH_2Cl_2 (4 × 30 mL), drying with Na_2SO_4, filtration and evaporation gave crude **(*S,S*)-14** (1.04 g). Recrystallization from methanol:water gave **(*S,S*)-14**. Yield 865 mg (78%). R_f = 0.39 in toluene:MeCN:Et_3N 80:20:2. Mp. 251.5 °C dec. $[\alpha]_{589}^{25.0}$ = +72.8°, $[\alpha]_{578}^{25.0}$ = +76.0°, $[\alpha]_{549}^{25.0}$ = +85.8°, $[\alpha]_{436}^{25.0}$ = +142.4°, $[\alpha]_{365}^{25.0}$ = +213.6° (c 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 4.17 (t, *J* = 6, 7 Hz, 1H, (C=O)-C*H*-), 3.90 (dd, *J* = 5, 7 Hz, 1H, -N-C*H*-CH_2-CH-), 3.52 (AB, *J* = 14 Hz, δ = 20 Hz, 2H, -CH_2-SO_2-), 2.87 (dd, *J* = 6, 16 Hz, 1H, (C=O)-CH-CH_2-), 2.33 (dd, *J* = 7, 16 Hz, 1H, (C=O)-CH-CH_2-), 2.09 (m, 2H, -CH-CH_2-CH-), 2.06 (s, 3H, cb CH_3), 1.94 (m, 1H, CH_2-CH_2-CH-), 1.92 (m, 1H, CH_2-CH_2-CH-), 1.90 (m, 1H, CH_2-CH_2-C*H*-), 1.7 (s, br, 2H, NH_2), 1.44 (m, 1H, CH_2-CH_2-CH), 1.36 (m, 1H, CH_2-CH_2-CH), 1.15 (s, 3H, C-CH_3), 0.99 (s, 3H, C-CH_3); ^{13}C NMR ($CDCl_3$) δ 172.3 (C=O), 75.5 (cb *C*), 75.2 (cb *C*), 65.2 (N-*C*H-CH_2-CH-), 53.9 ((C=O)-*C*H), 52.9 (-*C*H$_2$-SO_2-), 49.0 (-CH_2-*C*-CH-), 47.8 (*C*-$(CH_3)_2$), 44.5 (-CH_2-CH_2-*C*H-), 38.0 (-CH-*C*H$_2$-CH-), 37.9 (cb-*C*H$_2$-), 32.8 (-*C*H$_2$-CH_2-CH-), 26.4 (-CH_2-*C*H$_2$-CH-), 23.4 (cb *C*H$_3$), 20.9 (C-*C*H$_3$), 19.8 (C-*C*H$_3$); ^{11}B NMR ($CDCl_3$) δ -4.0, -5.8, -9.3 (sh), -10.4; IR (KBr) ν 3379 (w, br), 2962 (m), 2942 (m), 2576 (s), 1684 (s), 1328 (s), 1270 (w), 1236 (m), 1218 (m), 1166 (m), 1135 (s), 1118 (w), 1066 (m), 543 (m) cm^{-1}; MS(ESP+) *m/z* calcd for $(M+H)^+$: 444, observed: 444 (within the boron cluster envelope).

(2R,2'R)-N-*[3'-(2"-Methyl-1",2"-dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-aminopropanoyl]-bornane-10,2-sultam [(**R,R**)-**14**].* *(2R,2'R)-N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-(hydroxyamino)propanoyl]bornane-10,2-sultam [(***R,R***)-**12**] was transformed to (***R,R***)-**14** as described for (***S,S***)-**14**. Mp. 251.5 °C dec. $[\alpha]_{589}^{25.0}$ = -70.0° (c 1.01, $CHCl_3$). Spectral data were in accordance with (***S,S***)-**14**.

(2S,2'S)-N-*[3'-(1",12"-dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(**S,S**)-**15**].* *(2S,2'S)-N*-[3'-(1",12"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-(hydroxyamino)-propanoyl]bornane-10,2-sultam [(***S,S***)-**13**] (451 mg, 1.01 mmol) was dissolved in acetic acid:conc. HCl 11:1 (6 mL), cooled to 4 °C, mixed with Zn powder (756 mg, 11.6 mmol) and stirred under N_2 for 3 d. The mixture was filtered through glass wool and concentrated. The residue was partly dissolved in CH_2Cl_2 (10 mL), neutralized with aq. $NaHCO_3$ and filtered. Extraction of the residue with CH_2Cl_2 (4×10 mL), drying with Na_2SO_4, filtration and evaporation gave crude (***S,S***)-**15** (405 mg). Recrystallization from MeOH:H_2O gave (***S,S***)-**15**. Yield 333 mg (77%). R_f = 0.50 in toluene:MeCN:Et_3N 80:20:2. Mp. 231.5 °C dec. $[\alpha]_{589}^{25.0}$ = +75.5°, $[\alpha]_{578}^{25.0}$ = +78.5°, $[\alpha]_{549}^{25.0}$ = +88.7°, $[\alpha]_{436}^{25.0}$ = +145.1°, $[\alpha]_{365}^{25.0}$ = +176.7° (c 1.02, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 3.86 (dd, *J* = 6, 7 Hz, 1H, -N-C*H*-CH_2-CH-), 3.73 (t, *J* = 6 Hz, 1H, (C=O)-C*H*-), 3.49 (AB, *J* = 14 Hz, δ = 19 Hz, 2H, -CH_2-SO_2-), 2.64 (br s, 1H, cb C*H*), 2.33 (dd, *J* = 6, 15 Hz, 1H, (C=O)-CH-CH_2-), 2.06 (m, 2H, -CH-CH_2-CH-), 1.92 (m, 1H, CH_2-CH_2-CH-), 1.90 (m, 1H, CH_2-CH_2-CH-), 1.86 (m, 1H, CH_2-CH_2-C*H*-), 1.77 (dd, *J* = 7, 15 Hz, 1H, (C=O)-CH-CH_2-), 1.5 (s, br, 2H, NH_2), 1.42 (m, 1H, CH_2-CH_2-CH), 1.34 (m, 1H, CH_2-CH_2-CH), 1.12 (s, 3H, C-CH_3), 0.97 (s, 3H, C-CH_3); ^{13}C NMR ($CDCl_3$) δ 172.3 (C=O), 81.3 (cb *C*), 65.1 (N-*C*H-CH_2-CH-), 58.9 (cb *C*H), 53.8 ((C=O)-*C*H), 52.9 (-CH_2-SO_2-), 48.9 (-CH_2-*C*-CH-), 47.8 (*C*-$(CH_3)_2$), 44.5 (-CH_2-CH_2-*C*H-), 41.2 (cb-CH_2-), 38.0 (-CH-*C*H_2-CH-), 32.8 (-*C*H_2-CH_2-CH-), 26.4 (-CH_2-*C*H_2-CH-), 20.9 (C-*C*H_3), 19.8 (C-*C*H_3); ^{11}B NMR ($CDCl_3$) δ -12.6, -15.3; IR (KBr) ν 3396 (w, br), 2961 (w), 2607 (s), 1689 (s), 1327 (s), 1270 (w), 1236 (m), 1218 (m), 1166 (w), 1134 (m), 1117 (w), 1066 (m), 544 (m) cm^{-1}; MS(ESP+) *m/z* calcd for $(M+H)^+$: 430, observed: 430 (within the boron cluster envelope); Anal. Calcd for $C_{15}H_{32}B_{10}N_2O_3S$: C, 42.04; H, 7.53; N, 6.54; Found: C, 41.94; H, 7.19; N, 6.30.

(2R,2'R)-N-*[3'-(1",12"-dicarba*-closo-*dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(**R,R**)-**15**].* *(2R,2'R)-N*-[3'-(1",12"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-(hydroxyamino)-propanoyl]bornane-10,2-sultam [(***R,R***)-**13**] was transformed to (***R,R***)-**15** as described for (***S,S***)-**15**. Mp. 231.5 °C dec. $[\alpha]_{589}^{25.0}$ = -72.9° (c 1.02, $CHCl_3$). Spectral data were in accordance with (***S,S***)-**15**.

*(S)-2-Methyl-*o*-carboranylalanine hydrochloride [(**S**)-**1**•**HCl**].* *(2S,2'S)-N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(***S,S***)-**14**] (301 mg, 0.68 mmol) was dissolved in THF (6 mL), mixed with 1M LiOH (2 mL), and stirred at RT overnight. THF was evaporated, the water phase was acidified with 3M HCl (3 mL), mixed with CH_2Cl_2 (5 mL), and stirred for 0.5 h. The crystals formed were filtered, washed with CH_2Cl_2 and 3M HCl and dried in a dessicator over P_2O_5. The yield of amino acid (***S***)-**1**•**HCl** was 136 mg (71%). Mp. 252.5 °C dec (sublimation at 160 °C). E.P. > 99%. $[\alpha]_{589}^{25.0}$ = +6.70°, $[\alpha]_{578}^{25.0}$ = +7.10°, $[\alpha]_{549}^{25.0}$ = +8.28°, $[\alpha]_{436}^{25.0}$ = +16.6°, $[\alpha]_{365}^{25.0}$ = +31.2° (c 1.01, MeOH); ^{1}H NMR (CD_3OD) δ 4.27 (t, *J* = 6 Hz, 1H, -C*H*-CH_2-), 3.21 (dd, *J* = 6, 16 Hz, 1H, -CH-CH_2-), 2.80 (dd, *J* = 6, 16 Hz, 1H, -CH-CH_2-); ^{13}C NMR (CD_3OD) δ 169.9 (C=O), 78.2 (cb *C*), 75.9 (cb *C*), 53.4 (*C*H-CH_2-), 36.6 (CH-*C*H_2-), 23.6 (*C*H_3); ^{11}B NMR (CD_3OD) δ -3.0, -5.1, -8.8 (sh), -9.5; IR (KBr) ν 3447 (w, br), 2926 (m, br), 2590 (s), 1750 (m), 1507 (w), 1209 (m) cm^{-1}; Negative-ion FAB-MS *m/z* calcd for $[C_6H_{18}{}^{11}B_{10}NO_2$; M-H-HCl]$^-$: 246.2268, observed: 246.2300 (within the boron cluster envelope).

*(*R*)-2-Methyl-*o*-carboranylalanine hydrochloride [(**R**)-**1**•**HCl**].* (*2R,2'R*)-*N*-[3'-(2"-Methyl-1",2"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(***R,R*)-14**] was transformed to (***R*)-1•HCl** as described for (***S*)-1•HCl**. E.P. > 99%. Mp. 252.5 °C dec (sublimation at 160 °C). $[\alpha]_{589}^{25.0}$ = -6.67° (c 1.02, MeOH). Spectral data were in accordance with (***S*)-1•HCl**.

*(*S*)-p-Carboranylalanine hydrochloride [(**S**)-**2**•**HCl**].* (*2S,2'S*)-*N*-[3'-(1",12"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(***S,S*)-15**] (1.10 g, 2,56 mmol) was dissolved in THF (20 mL), mixed with 1M LiOH (7 mL) and stirred at RT overnight. THF was evaporated the water phase was acidified with 3M HCl (18 mL), mixed with CH_2Cl_2 (25 mL), and stirred for 0.5 h. The crystals formed were filtered, washed with CH_2Cl_2 and 3M HCl, and dried in a dessicator with P_2O_5. The yield of amino acid (***S*)-2•HCl** was 512 mg (75%). Mp. 238.5 °C dec (sublimation at 140 °C). E.P. > 99%. $[\alpha]_{589}^{25.0}$ = +7.98°, $[\alpha]_{578}^{25.0}$ = +8.47°, $[\alpha]_{549}^{25.0}$ = +9.85°, $[\alpha]_{436}^{25.0}$ = +19.2°, $[\alpha]_{365}^{25.0}$ = +36.3° (c 1.01, MeOH); ^{1}H NMR (CD_3OD) δ 3.79 (t, *J* = 6 Hz, 1H, -C*H*-CH_2-), 2.56 (dd, *J* = 6, 16 Hz, 1H, -CH-CH_2-), 2.12 (dd, *J* = 6, 16 Hz, 1H, -CH-CH_2-), The proton in 12 position is hidden under the OH-signal from the solvent (δ_H 3.35); ^{13}C NMR (CD_3OD) δ 170.3 (C=O), 81.2 (cb *C*), 61.2 (cb *C*H), 53.6 (*C*H-CH_2-), 40.1 (CH-*C*H_2-); ^{11}B NMR (CD_3OD) δ -12.1, -14.1; IR (KBr) ν 3420 (m, br), 2926 (m, br), 2610 (s), 1734 (w), 1497 (w) cm^{-1}; Negative-ion FAB-MS *m/z* calcd for [$C_5H_{16}{}^{11}B_{10}NO_2$; M-H-HCl]$^-$: 232.2111, observed: 232.2113 (within the boron cluster envelope).

*(*R*)-p-Carboranylalanine hydrochloride [(**R**)-**2**•**HCl**].* (*2R,2'R*)-*N*-[3'-(1",12"-dicarba-*closo*-dodecaborane(12)-1"-yl)-2'-aminopropanoyl]bornane-10,2-sultam [(***R,R*)-15**] was transformed to (***R*)-2•HCl** as described for (***S*)-2•HCl**. Mp. 238.5 °C dec (sublimation at 140 °C). E.P. > 99%. $[\alpha]_{589}^{25.0}$ = -7.94° (c 1.02, MeOH). Spectral data were in accordance with (***S*)-2•HCl**.

*(*S*)-N-[(tert-Butoxy)carbonyl]-p-carboranylalanine [(**S**)-**16**].* (*S*)-*p*-Carboranylalanine hydrochloride [(***S*)-2•HCl**] (200 mg, 0.75 mmol) was dissolved in MeOH (10 mL), mixed with triethyl amine (0.31 mL, 2.24 mmol) under N_2-atmosphere and cooled to 0 °C. Di(*tert*-butyl) dicarbonate (0.26 mL, 1.12 mmol) was added and the mixture was stirred at r.t. for 5.5 h. The solvent was evaporated and the solid residue was partioned between CH_2Cl_2 (25 mL) and 1M HCl (15 mL) at 0 °C and stirred for 0.5 h. The product that crystallized was filtered off to give (***S*)-16** (98 mg). The phases were separated and the water phase was extracted with CH_2Cl_2 (3 × 8 mL). The combined organic layers was dried with Na_2SO_4, filtered, and concentrated to crude (***S*)-16** (189 mg). The crude product was purified by flash chromatography using MeCN:MeOH 4:1 as the eluent (R_f = 0.33) to give (***S*)-16** (124 mg). The total yield of (***S*)-16** was 90%. Mp. 182.5-184.5 °C. $[\alpha]_{589}^{25.0}$ = -19.6°, $[\alpha]_{578}^{25.0}$ = -20.6°, $[\alpha]_{549}^{25.0}$ = -23.4°, $[\alpha]_{436}^{25.0}$ = -40.2°, $[\alpha]_{365}^{25.0}$ = -64.2° (c 1.00, MeOH); ^{1}H NMR (CD_3OD, major conformer) δ 6.84 (d, *J* = 8 Hz, 1H, N*H*), 3.87 (m, 1H, -C*H*-CH_2-), 3.20 (br s, 1H, cb C*H*), 2.30 (d, *J* = 14 Hz, 1H, -CH-CH_2-), 2.04 (dd, *J* = 11, 16 Hz, 1H, -CH-CH_2-), 1.40 (s, 9H, CH_3); ^{13}C NMR (CD_3OD, major conformer) δ 174.7 (C=O) 157.6 [(C=O)-NH], 83.1 (cb *C*), 80.6 (*C*-(CH_3)$_3$), 60.6 (cb *C*H), 54.8 (*C*H-CH_2-), 40.7 (CH-*C*H_2-), 28.8 (-CH_3); ^{11}B NMR (CD_3OD) δ -11.9, -14.5; IR (KBr) ν 3321 (w, br), 2981 (w), 2608 (s), 1729 (s, br), 1395 (m), 1369 (m), 1252 (w), 1164 (m) cm^{-1}; MS(ESP+) *m/z* calcd for [(M-BOC)+H]$^+$: 232, observed: 232 (within the boron cluster envelope); Anal. Calcd for $C_{10}H_{25}B_{10}NO_4$: C, 36.24; H, 7.60; N, 4.23; Found: C, 36.58; H, 7.31; N, 4.22.

Determination of enantiomeric purity.

To *ca.* 1 mg of amino acid hydrochloride, in a 1 mL glass vial was added Marfey's reagent[12] (0.200 mL 1% solution in acetone) followed by 1.0 M aqueous sodium hydrogencarbonate (0.040 mL). The vials were closed and then heated at 40 °C for *ca.* 1 hour. The reaction was quenched with 2 M hydrochloric acid (0.020 mL), diluted with DMSO (0.50 mL) and analysed.

The (*N*-trifluoroacetyl)propyl ester of the enantiomers of **1** and **2** was prepared and separated as described previously for ***o*-Car**[14] with the exception that the β-cyclodextrin methyloctylsiloxane CSP used in the SFC was methoxymethylated instead of methylated.

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