Enantioselective Synthesis of L- and D-Carboranylalanine†

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The enantioselective synthesis of L- and D-carboranylalanine is reported. Imides **13** and **14** are treated with titanium tetrachloride, DIEA, and NBS to introduce a bromo functionality in 98:2 ratio at the α-center. Azide displacement with TMGA, displacement of the oxazolidinone template with titanium tetrabenzyloxide, and subsequent hydrogenolysis permits L- or D-carboranylalanine to be isolated in high stereoselectivity and 35−40% yields overall.

Introduction

We are interested in developing new boron-containing drugs for boron neutron capture therapy (BNCT), an alternative cancer therapy.[1,2] This experimental binary therapy is currently being investigated for treatment of malignant glioma and melanoma, in particular, and utilizes the large thermal neutron capture cross section of ^{10}B to bring about a ^{10}B (n,α) ^{7}Li reaction. The alpha particle and lithium ion dissipate their large kinetic energy before traveling one cell diameter (∼10 μm), affording the potential for precise cell killing. One stable, nontoxic, and synthetically amenable functionality that allows significant amounts of boron importation per group attachment is the 1,2 dicarbaclosododecaborane (*o*-carborane) cage. The C_2B_{10} cage has unique electronic and steric properties that also make it an intriguing moiety in drug design. Incorporation of an *o*-carboranyl group into the unnatural amino acid, carboranylalanine (**1**), yields a very hydrophobic phenylalanine isostere. Substitution of carboranylalanine for other amino acids in peptides may provide targeted delivery of boron-containing drugs to cancerous cells, securing another element of control and precision to this form of therapy.

A previously reported synthesis of L-carboranylalanine and an improvement thereof were published by Schwyzer *et al.*,[3] in 1976 and 1979, and proceeded in low yields (9% and 20% from propargylalanine). Racemic propargylalanine was resolved enzymatically, and the carborane functionality was constructed late in the sequence where purification was difficult. Sjöberg *et al.*[4] reported an asymmetric synthesis without experimental details, utilizing the chiral auxiliary developed by Seebach, and obtained the L-amino acid in 20% yield from the Seebach intermediate. Soloway *et al.*[5] published a racemic synthesis of D,L-carboranylalanine, procuring the amino acid via phase transfer alkylation of *N*-(diphenylmethylene)-aminoacetonitrile with propargyl bromide, boronation of the alkyne, and subsequent hydrolysis of the Schiff base and nitrile functions. More recently Moroder *et al.*[6] also developed a synthesis for L-carboranylalanine, using the method of Schollkopf, obtaining a 12:1 mixture at the α-center, which they were not able to resolve.

A higher yielding sequence is advantageous since the active isotope utilized in BNCT, ^{10}B, is only 20% naturally abundant and is relatively expensive in the form of >95% enriched borane precursors. We desire a high-yielding synthetic sequence that allows facile and complete purification. It is also of interest to develop an enantioselective approach that would allow the synthesis of L- or D-carboranylalanine at will, afford greater access to homologs, and provide practicable quantities of these amino acids.

Results and Discussion

In consideration of potential synthetic routes, the optimal approach would be to introduce the *o*-carboranyl functionality late in the sequence. A route (Scheme 1) was investigated that utilized Vederas' strategy in stereoselective ring opening at the β-carbon of a serine lactone.[7] This required the stoichiometric cuprate **3**, derived from the *o*-carboranyl Grignard reagent, to add as a good nucleophile regioselectively at the β-carbon of the lactone. However, no addition at that position was detected at reaction temperatures of −30 °C. When compound **3** was generated with catalytic amounts of copper bromide−dimethyl sulfide complex, a small amount of 1,2 addition to the serine lactone to yield compound **4** was noted only as the reaction was warmed to 0 °C. This little-explored copper species had previously been shown to act as a nucleophile only at room temperature.[8] The electronegative nature of the cage may reduce reactivity sufficiently to preclude addition at the lower temperatures required for the regioselective ring opening. Attempted ring openings with *m*-carboranyl copper species

† Dedicated to Clayton H. Heathcock on the occasion of his 60th birthday.

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(1) Abbreviations are as follows: boron neutron capture therapy (BNCT), diisopropylethylamine (DIEA), titanium tetrachloride ($TiCl_4$), tetramethylguanidinium azide (TMGA), *tert*-butyldimethylsilyl (*t*-BuDMSi), 9-borabicyclo[3.3.1]nonane (9-BBN), carbon tetrachloride (CCl_4), di-*n*-butylboron triflate (*n*-Bu_2B OTf), triisopropylbenzenesulfonyl azide (Tris azide), potassium hexamethyldisilazide (KHDMS), α-methoxy-α-(trifluoromethyl)phenylacetic acid (Mosher's acid or MTPA), *n*-butyllithium (*n*-BuLi), magnesium sulfate ($MgSO_4$), ethyl acetate (EtOAc), ether (Et_2O).

(2) Hatanaka, H.; Nakagawa, Y. *Int. Rad. Oncol.* **1994**, *28*, 1061−1066. Hawthorne, M. F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 950−984. Slatkin, D. N. *Brain* **1991**, *114*, 1609−1629. Fairchild, R. G.; Wheeler, F.; Slatkin, D. N.; Coderre, J.; Micca. P.; Laster, B.; Kahl, S. B.; Som, P.; Fand, I. *Strahlenther. Onkol.* ***1989***, *165*, 343−347.

(3) Leukart, O.; Caviezel, M.; Eberle, A.; Escher, E.; Tun-Kyi, A.; Schwyzer, R. *Helv. Chim. Acta* **1976**, *59* , 2184−2187. Fauchere, J.-L.; Leukart, O.; Eberle, A.; Schwyzer, R. *Helv. Chim. Acta* **1979,** *62*, 1382−1395.

(4) Sjöberg, S.; Carlsson, J.; Lindtrom, P.; Malmquist, J. *Current Topics In The Chemistry of Boron*; Kabalka, G. W., Ed.; Royal Society of Chemistry: Cambridge, U.K. **1994**; pp 172−176.

(5) Wyzlic, I. M.; Soloway, A. H. *Tetrahedron Lett.* **1992**, *33*, 7489−7490.

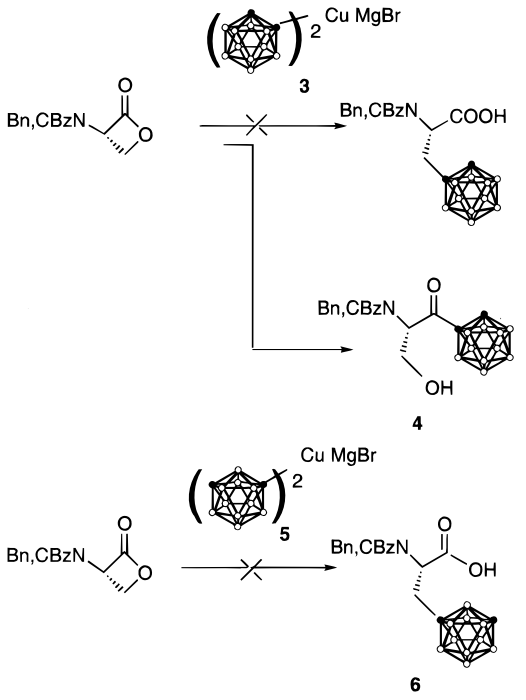
(6) Karnbrock, W.; Musiol, H.-J.; Moroder, L. *Tetrahedron* **1995**, *51*, 1187−1196.

(7) Arnold, L. D.; Drover, J. C. G.; Vederas, J. C. *J. Am. Chem. Soc.* **1987**, *109*, 4649−4659.

(8) Zakharkin, L. I.; Kovredov, A. I.; Shaugumbekova, Z. S.; Vinogradova, L. E.; Leites, L. A. *Zh. Obshch. Khim.* **1981**, *51*, 1582−1586.

S0022-3263(95)02271-7 CCC: $12.00

Scheme 1

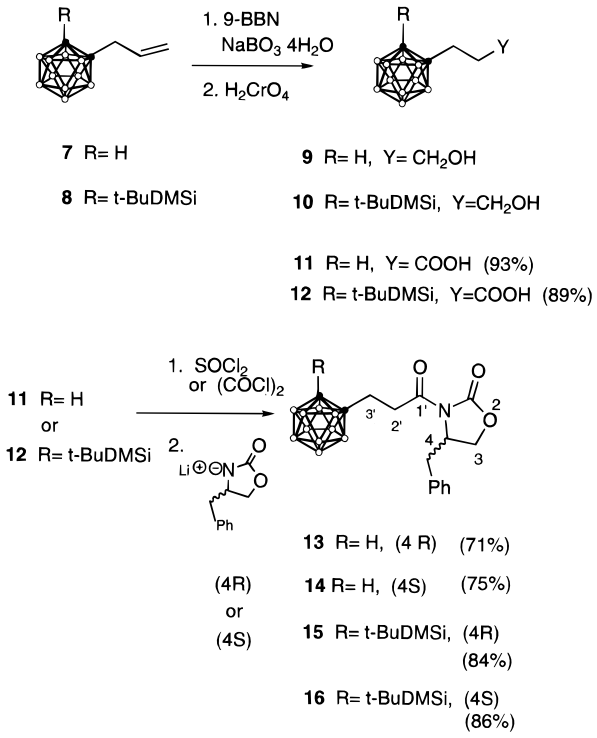


5,[9] which should be more reactive due to its decreased dipole-derived electron-withdrawing effect, also did not lead to the desired product **6**. The carboranyl cuprate may be too sterically hindered to add at the β-carbon, similar to the failure Vederas observed upon attempting addition of alkyl cuprate reagents to threonine-derived lactones. Only 1,2 addition was seen in those additions.[10]

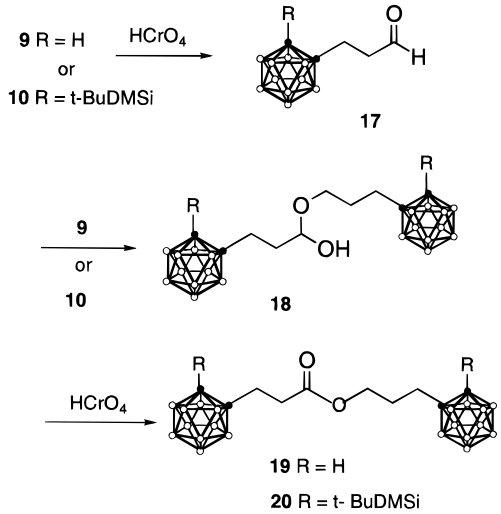
We then turned to a longer approach which incorporated the carborane cage functionality early, but which held the promise of high yields. Evans *et al.*[11] had developed a very selective, practical route for introduction of azide functions to imide systems, previously described for alkylations and aldol condensations. We wished to adapt this to our own target compound and felt that the carboranyl cage's steric bulk, roughly equivalent to a phenyl ring rotating on its 1,4 axis, would not interfere with the chemistry.

The desired imides **13** and **14** in Scheme 2 were synthesized from 3-carboranylpropionyl chloride and (*R*)- or (*S*)-4-benzyl-2-oxazolidinone. The acid chloride was synthesized in three steps from allyl carborane. 1-Allylcarborane (**7**) was hydroborated with a hindered borane, 9-BBN,[12] to yield only primary alcohol **9** after mild oxidative workup with sodium perborate,[13] as we have reported elsewhere,[14] in agreement with the findings of Kabalka *et al.*[15] The sensitivity of the carborane cage toward attack by alkaline peroxides did not permit the use of standard workup conditions, even if buffered, mildly alkaline hydrogen peroxide was used. The hydrophobic nature and electron-withdrawing dipole of the carboranyl cage of alcohol **9** complicated Jones oxidation to carboxylic acid **11**.[16] When the usual addition order of adding Jones reagent to a solution of alcohol **9** was carried out, a significant quantity of ester **19**, derived from a second oxidation of hemiacetal **18** (from alcohol acetalization of intermediate aldehyde **17**, Scheme 3) was found. Slow inverse addition of alcohol **9** (0.075 M in acetone) to a large excess (10 equiv) of Jones reagent allowed clean oxidation to acid **11** in 80−90% overall yield from allylcarborane. Formation of imides **13** and **14** proceeded in 71−75% yields, complicated by some competing deprotonation of the 2-methine carbon on the carboranyl cage.

Scheme 2



Scheme 3



(9) For many applications, the difference between incorporating a meta-carborane cage into the amino acid or incorporating an *o*-carborane functionality was not important.

(10) Pansare, S. V.; Vederas, J. C. *J. Org. Chem* **1989**, *54*, 2311−2316.

(11) Evans, D. A.; Britton, T. C.; Ellman, J. A.; Dorow, R. L. *J. Am. Chem. Soc.* **1990**, *112*, 4011−4030.

(12) Brown, H. C.; Zweifel, G. *J. Am. Chem. Soc.* **1960**, *82*, 4708−4712.

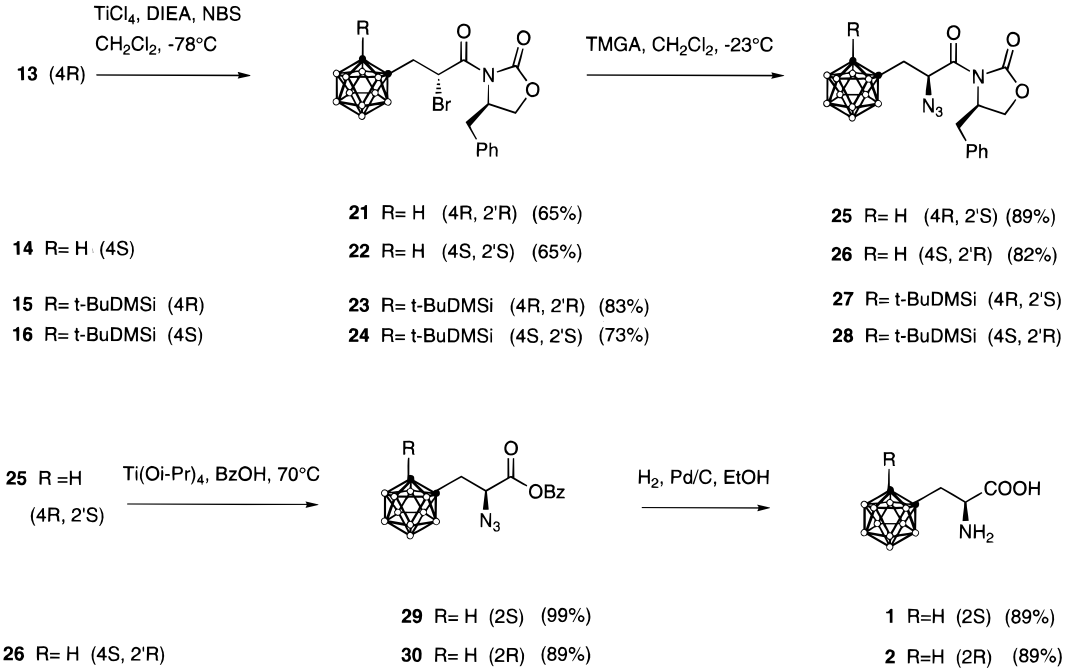
(13) Kabalka, W. G.; Shoup, T. M.; Goudgaon, N. M. *J. Org. Chem.* **1989**, *54*, 5930−5933.

(14) Kahl, S. B.; Radel, P. A. *Current Topics In The Chemistry of Boron*; Kabalka, G. W., Ed.; Royal Society of Chemistry: Cambridge, U.K. **1994**; pp 155−160.

(15) Hondrogiannis, G.; Kabalka, G. W. *Tetrahedron Lett.* **1995** *36*, 4365−4368.

(16) A one-pot sequence to obtain the carboxylic acid directly from allylcarborane by oxidation of the intermediate organoborane according to the method of Perisamy (Perisamy, M.; Narayana, C.; Anitha, N. *Indian J. Chem.* **1986**, *25B*, 844−846) was not successful.

Scheme 4



Synthesis of ^{10}B-enriched materials also needed to be addressed. ^{10}B-enriched allylcarborane is not available commercially, but the precursor, *o*-carborane, is. However, simple alkylation to 1-allyl-*o*-carborane is unavoidably accompanied by disproportionation of the anion of the carborane cage[17] and formation of the diallyl species. This severely complicates isolation of the desired species and reduces the yields intolerably. We proposed to solve both of these problems by using a protection strategy developed by Hawthorne *et al.*[18] Silyl protection of the remaining methine carbon on the cage permits these transformations to be effected in higher yields due to decreased competition from dianionic species in the case of alkylations or proton transfer in the case of imide formation. Deprotonation of *o*-carborane with *n*-butyllithium, followed by reaction with *t*-BuDMSiCl, proceeded to yield 1-(*tert*-butyldimethylsilyl)-*o*-carborane uncontaminated by disilylated products. The monosilyl *o*-carborane was then aklylated, by a modification[19] of Hawthorne's method to permit isolation of the 1-allyl-2-(*tert*-butyldimethylsilyl)carborane (**8**) in 91% yield.

Silyl-protected allylcarborane **8** was then treated in the same sequence of reactions as for the unprotected allyl carborane (Schemes 2 and 3). Some significant alterations had to be made to reaction conditions to ensure success. Hydroboration with a hindered borane led to isolation of only primary alcohol **10**, but the oxidative workup conditions had to be altered to slightly more forcing conditions (overnight at 30 °C). The increased hydrophobicity and steric hindrance due to the silyl protection of the carboranyl group was evident in the Jones oxidation of alcohol **10**. Applying the conditions to silyl alcohol **10** that cleanly oxidized **9** led to formation of hemiacetal oxidation product **20**, in 66% yield (Scheme 3). In order to obtain acid **12** in good yields, addition of alcohol **10** was made to Jones reagent over an even longer period, and the 1.25 M aqueous Jones reagent solution was diluted with acetone to 0.67 M. With these changes an 89% yield of acid **12** was obtained. The acid chloride was generated by reaction of acid **12** with oxalyl chloride in benzene. The crude product was reacted with the lithium anion of the (*R*)- or (*S*)-oxazolidinones to obtain (*R*)- and (*S*)-silyl imides **15** and **16** in improved yields of 84−86%.

Desilylation of the carborane cage of silyl imides **15** and **16** at this point yields imides **13** and **14** to converge with the original unprotected reaction manifold (Scheme 4). Deprotection was attempted by treating with tetrabutylammonium fluoride at low temperature, according to the procedure of Hawthorne *et al.*[18] We found that deprotection of these imides could not be carried out under such conditions; considerable decomposition was seen. The products were oxazolidinone, due to hydrolysis, and what appears to be the product of boron abstraction from the carborane cage by fluoride, resulting in an open cage (*nido*- carboranyl) imide. This type of attack on boron by fluoride had been reported previously by Onak *et al.*[20] Although no *nido* species were produced when imide **15** or **16** was treated with hydrogen fluoride/pyridine reagent, deprotection did not proceed either. Clean deprotection without cage attack was achieved by the initial addition of 1 equiv of trifluoroacetic acid, followed by addition of 1.2 equiv of TBAF at −78 °C. The desilylation to imides **13** and **14** was then realized in 88−92% yield.

Direct azidization of imide **14** (eq 1), with deprotonation by potassium hexamethyldisilazide and azide trans-

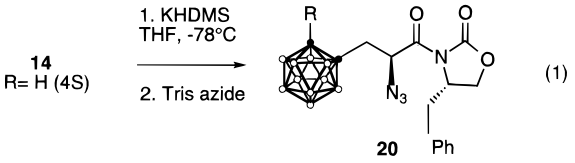
(17) Zaharkin L. I.; Grebennikov, A. V. Izv *Akad. Nauk. SSSR, Ser. Khim.* **1967**, 1376−1377.

(18) Gomez, F. A.; Hawthorne, M. F. *J. Org. Chem.* **1992**, *57*, 1384−1390.

(19) Changes made to the silylation and alkylation procedures of Gomez and Hawthorne included substitution of 1.6 M *n*-BuLi for 2.5 M material with additional Et_2O, giving final solvent proportions of 1:2 (Et_2O:benzene), to achieve a sufficiently polar mixture to permit reaction. The crude sublimed silyl-protected *o*-carborane was chromatographed on silica with hexane instead of final purification by distillation. Use of material purified in this manner, in the subsequent modified alkylation with allyl bromide, permitted 91% of the product 1-silyl 2-allyl *o*-carborane to be isolated, after chromatographic purification on silica gel.

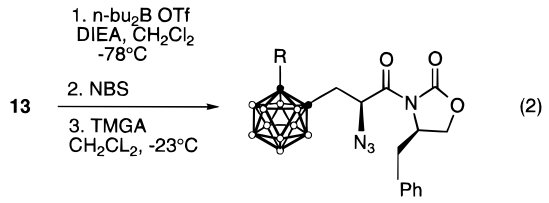
(20) Tomita, H.; Luu, H.; Onak, T. *Inorg. Chem.* **1991**, *30*, 812−815.

fer with triisopropylbenzenesulfonyl azide,[11] proved to be impossible. The cage was not stable to potassium amide



(1)

bases even at low temperatures and short time periods. A two-step introduction by diastereoselective bromination with subsequent azide displacement was then investigated (eq 2). Use of di-*n*-butylboron triflate to chelate and activate imide **13** for deprotonation by DIEA led to incomplete enolization. An alternative chelating agent,



(2)

$TiCl_4$, had been used in highly diastereoselective alkylations in these imide systems.[21] We decided to apply it here and observed much improved enolization (Scheme 4). Bromination proceeded cleanly to yield bromo imide **21**. The diastereoselectivity was excellent: 98:2 as determined by HPLC and ^{13}C NMR spectroscopy. Azide displacement using the bulky reagent TMGA[22] to give azide **25** proceeded without complication, in 65% yield overall,[23] from imide **13** and without incurring epimerization, as verified by analytical HPLC and ^{13}C NMR spectroscopy. Similarly, imide **14** was converted to azido imide **26** in equivalent yields and stereoselectivities.

We also examined the diastereoselective bromination of silyl imides **15** and **16**. These reactions proceeded in 73−83% yields and equivalent diastereoselectivities (97:3) to the unsilylated cases. While the yields of **23** and **24** are improved over that for the unprotected bromo imides **21** and **22**, desilylation at this point is not desirable as none of the bromo imide species are very stable. Conversion of **23** or **24** to silyl azido imides **27** and **28** was successful, but required extended reaction periods. Desilylation of the silyl azido imides was very sluggish, and decomposition was observed. The most convenient deprotection is the conversion of **15** and **16** to imides **13** and **14**.

The often used alkaline peroxidic hydrolysis of azido imides to an azido acid would likely damage the carborane cage in compounds **25** and **26**, as evidenced by our experience in hydroboration experiments. We therefore removed the oxazolidinone auxiliary by transesterification of azido imides **25** and **26** with titanium tetraisopropoxide and excess benzyl alcohol.[24] This proceeded smoothly, in 89−99% yield. Control of the temperature and reaction time allow this transformation to occur without racemization. Azido benzyl ester **29** was treated with hydrogen and palladium on carbon to yield L-amino acid **1.** D-Amino acid **2** was obtained in similar yields and diastereoselectivities from azido benzyl ester **30**.

Proof of the optical purity of the L- and D-amino acids was not straightforward. The reported rotation[3,25] was not reproducible, due to solubility problems. As an alternative, azido benzyl esters **29** and **30** were reduced to the free amino ester with triphenylphosphine.[26] The corresponding *N*-α Mosher amide was synthesized in order to carry out stereochemical analysis of the α-center.[27] Unfortunately, neither this benzyl ester, α-*N* amide or the methyl ester, α-*N* amide, available from stepwise esterification and amidation of the amino acid, could be resolved in the ^{19}F, ^{1}H, or ^{13}C NMR spectra sufficiently to quantify the ratio of isomers. Gas−liquid chromatography of the azido benzyl esters on a chiral cyclodextrin column was also unsuccessful. Chiral HPLC chromatography of the azido benzyl esters on a normal phase Chiralcel OJ column did permit base line separation and confirmation of a 98:2 ratio at the α-centers;[28] hydrogenolysis should not cause any loss of integrity at the stereocenter.

The yields in these sequences can be increased by deferring purification at several points. In the series R = H, the transformation from allylcarborane **7** to imide **13** or **14** was carried out in 67% yield overall, chromatographing only after isolating the imides. Conversion of imides **13** and **14** to azido imides **25** and **36** was completed in 65% overall yield if chromatography was deferred until the azide transfer reaction had been performed. This provides a 35−38% overall yield from allylcarborane **7** to amino acid **1** or **2**. In the silyl-protected series, the yield from allylcarborane **8** to imides **15** and **16** was 76% overall, thus giving an overall yield of 36−40% of the respective amino acid **1** or **2**.

This synthesis provides general, practical enantioselective access to L-carboranylalanine, its D-isomer, and a wide range of homologs in higher yields than the previously reported, more limited syntheses. The sequence utilized here is conducive to synthesis on a multigram scale, rendering this a practical route to carboranylalanine. The unique hydrophobic, space-filling, and electronic properties of this amino acid will make carboranylalanine a useful compound for drug development both within BNCT applications and in other general peptide structure/function work.

Experimental Section

General.[1] All reactions were performed under a dry argon atmosphere in oven-dried glassware, except those reactions utilizing water as a solvent, which were run under air. All dry solvents were distilled under argon from the appropriate drying agent before use. THF was freshly distilled from sodium/benzophenone. Anhydrous grades of CH_2Cl_2, oxalyl

(21) Evans, D. A.; Urpi, F.; Somers, T. C.; Clark, J. S.; Bilodeau, M. T. *J. Am. Chem. Soc.* **1990**, *112*, 8215−8216.

(22) Papa, A. J. *J. Org. Chem.* **1966**, *31*, 1426−1430.

(23) This improved overall yield differs from that in Scheme 4; it is the result of carrying crude bromo imide on to the azido imide intermediate. Scheme 4 reports stepwise yields, after chromatography. The bromo imide is susceptible to decomposition on silica gel.

(24) Evans, D. A.; Ellman, J. A.; Dorow, R. L. *Tetrahedron Lett.* **1987**, *28*, 1123−1126.

(25) The rotation had been reported using water as the solvent. Attempts to dissolve the stated amount of amino acid were not successful. Phenylalanine itself, a less hydrophobic amino acid, is only soluble to the extent of 2.96 g/100 mL of water. (*Handbook of Chemistry and Physics, 55th Ed.*; Weast, R. C., Ed.; CRC Press: Cleveland, OH, 1974; C-743). Attempts to improve the solubility by adding hydrochloric acid caused a change of sign of the rotation. This is also not unheard of for hydrophobic amino acids. Leucine is an example (*Ibid.*, p C-742).

(26) Vaultier, M.; Knouzi, N.; Carie, R. *Tetrahedron Lett.* **1983**, *24*, 763−764.

(27) Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543−2549.

(28) Several other columns and conditions were evaluated for their utility; neither Nucleosil-2 nor Chiralcel OT columns permitted separation of the isomers.

chloride (99%), 9-BBN, benzyl alcohol, titanium tetraisopropoxide, *n*-Bu_2BOTf (1.0 M in CH_2Cl_2), and $TiCl_4$ were purchased from Aldrich and used as such. Anhydrous ether was purchased from Fisher; a new bottle was opened for each use. Thionyl chloride was distilled prior to use. DIEA was distilled over CaH_2. (*R*)-(+)- and (*S*)-(−)-4-benzyl-2-oxazolidinones were purchased from Aldrich. *tert*-Butyldimethylsilyl chloride was purchased from Huls America Inc. and stored under argon. Allyl-*o*-carborane was purchased from Dexsil Corp. and distilled before use. *o*-Carborane and *m*-carborane were purchased from Dexsil Corp. and sublimed before use. NBS was recrystallized from water, dried under vacuum, and stored in the dark. For every use of NBS, TMGA, and oxazolidinones, the materials were first dried overnight under vacuum. Melting points are uncorrected. Infrared spectra were obtained as thin films. ^1H NMR and ^{13}C NMR spectra were recorded (300 MHz ^1H, 75.5 MHz ^{13}C) with either TMS (for ^1H, 0.0 ppm) or $DCCl_3$ (for ^{13}C, 77.0 ppm) as the internal reference. *J* values are in hertz. High-resolution mass spectral data is precise within ±5 ppm, as determined by routine standards evaluation. Bulb-to-bulb distillations were performed on a Kugelrohr distillation apparatus.

3-(1-(1′,2′-Dicarbaclosodecaboranyl))propionic Acid (11). Allylcarborane (**7**) (0.552 g, 3 mmol) and THF (3 mL) were cooled to −15 °C. A solution of 9-BBN in THF (9.0 mL, 4.5 mmol, 1.5 equiv, 0.5 M) was added in a dropwise fashion; the colorless solution was then warmed to room temperature and stirred for 2 h. Excess hydride reagent was quenched with the addition of water (2 mL). Sodium perborate (2.07 g, 13.5 mmol, 4.5 equiv) and water (10 mL) were added, and the cloudy mixture was stirred overnight at room temperature. The reaction was extracted with four 250 mL aliquots of ether. The combined organic layers were dried over magnesium sulfate and concentrated to an oil. This crude product was diluted in acetone (100 mL) and added in small portions to 48 mL of Jones reagent[29] (60 mmol, 20 equiv) over 2 h. The dark mixture was stirred overnight at room temperature, concentrated to remove all acetone, and extracted with four 300 mL portions of ether. The organic layers were washed exhaustively with water, dried over $MgSO_4$, and concentrated to a colorless oil. The crude product was dissolved in 10% ether/hexane (10 mL) and exhaustively extracted with 1 N potassium carbonate solution. The combined basic layers were acidified to a methyl orange endpoint with the dropwise addition of concentrated hydrochloric acid. The aqueous mixture was extracted with four 150 mL portions of ether. The combined organic layers were dried over $MgSO_4$ and concentrated to obtain 0.600 g of a white crystalline solid (93% yield): mp 147−149 °C;[30] IR 2593, 1707 cm^{-1}; ^1H NMR δ 1.20 −3.40 (bm, 10H), 2.59 (m, 4H), 3.68 (bs, 1H), 10.84 (bs, 1H); ^{13}C NMR 177.3, 76.6, 73.5, 61.6, 33.2, 32.3 ppm; HRMS EI calcd for M^+-($C_{12}H_{22}B_{10}O_2$, as the benzyl ester) = 306.2622, found 306.2602 (Δ = 6.5 ppm).

3-(1′-(2′-(*tert*-Butyldimethylsilyl)-1′,2′-dicarbaclosododecaboranyl))propionic Acid (12). 3-(1′-(2′-(*tert*-Butyldimethylsilyl)-1′,2′-dicarbaclosododecaboranyl))propan-1-ol (**10**) (1.65 g, 5.22 mmol) in 100 mL of acetone was added dropwise over 3 h to a mixture of acetone (40 mL) and an excess of Jones reagent (50.0 mmol, 9.6 equiv).[29] The mixture was stirred overnight at room temperature and worked up and purified as in the procedure for acid **11** to yield 1.53 g of silyl acid **12** (89% of theoretical yield): mp 139−142 °C; IR 3400−3000 (broad), 2586, 1715 cm^{-1}; ^1H NMR δ 0.35 (s, 6H); 1.04 (s, 9H); 3.4−1.20 (bm, 10H); 2.60 (m, 4H); 11.5−10.0 (bs, 1H); ^{13}C NMR 177.2, 79.3, 76.3, 34.0, 32.1, 27.5, 20.3, −2.6 ppm; HRMS EI calcd for M^+ ($C_{11}H_{30}B_{10}O_2Si$ − $C4H_9$) = 273.2314, found 273.2318 (Δ = 1.5 ppm).

(4R)-5-[3′-(1″-(1″,2″-Dicarbaclosododecaboranyl))propionyl]-4-benzyl-2-oxazolidinone (13). A. A solution of acid **11** (0.91 g, 4.21 mmol) in benzene (4 mL) was added dropwise over 60 min to thionyl chloride (3.07 mL, 5.00 g, 42 mmol, 10 equiv). The amber solution was heated at reflux overnight. The solution was cooled, and the solvent and thionyl chloride were removed with stirring under an argon stream. CCl_4 (5 mL) was added, and the solvent was removed as before. This was repeated twice. The crude acid chloride was concentrated under vacuum (0.4 Torr) for 1 h, dissolved in THF (5 mL), and cooled to −30 °C. In another flask, (*R*)-4-benzyl-2,5-oxazolidinone (1.34 g, 7.58 mmol, 1.80 equiv) and THF (20 mL) were cooled to −30 °C. A solution of *n*-butyllithium in hexane (4.60 mL, 7.37 mmol, 1.75 equiv, 1.6 M) was added slowly, and the reaction mixture was stirred with warming to 0 °C over 30 min. The cloudy mixture was recooled to −30 °C and added via cannula to the acid chloride solution. The solution was stirred for 30 min at −30 °C, the reaction was quenched with saturated aqueous ammonium chloride, and the solution was extracted with two portions of CH_2Cl_2. The combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated to a solid. Chromatography on silica gel with a gradient of ether/CH_2Cl_2/hexane (1:1:3) to ether/ CH_2Cl_2/ hexane (5:2:3) permitted 1.11 g of **13** (71% of the theoretical yield) to be isolated: mp 133−137 °C; $[\alpha]^{25}_D$ −50.55° (*c* = 4.2, CH_2Cl_2); IR 2586, 1778, 1700, 1384, 1208 cm^{-1}; ^1H NMR δ 3.3−1.05 (bm, 10H), 2.56 (m, 2H), 2.68 (dd, 1H, J_{H-H} = 13, 14), 3.06 (m, 2H), 3.21 (dd, 1H, J_{H-H} = 3, 14), 3.78 (s, 1H), 4.12 (m, 2H), 4.61 (m, 1H), 7.24 (m, 5H); ^{13}C NMR 170.5, 153.1, 134.7, 129.2, 128.8, 127.3, 74.1, 66.4, 61.4, 54.9, 37.5, 35.1, 31.6 ppm; HRMS EI calcd for M^+ ($C_{15}H_{25}B_{10}NO_3$) = 375.2837, found 375.2834 (Δ = 0.7 ppm).

B. Silyl imide **15** (0.80 g, 1.64 mmol) and THF (4 mL) were cooled to −78 °C, and trifluoroacetic acid (0.13 mL, 0.1187 g, 1.64 mmol, 1 equiv) was added. Tetrabutylammonium fluoride (1.97 mL, 1.97 mmol, 1 M, 1.2 equiv) in THF was added, and the colorless solution was warmed to room temperature over 30 min. The reaction was quenched with ammonium chloride, and the solution was extracted twice with EtOAc. The organic layers were washed with water and brine, then dried, and concentrated. The crude product was chromatographed on silica gel with an eluent gradient of CH_2Cl_2/hexane (1:4) to ether/CH_2Cl_2/hexane (5:2:3) to allow 0.532 g of imide **13** to be isolated (86% of theoretical).

(4*S*)-5-[3′-(1″-(1″,2″-Dicarbaclosododecaboranyl))propionyl]-4-benzyl-2-oxazolidinone (14). A. Acid **11** (0.600 g, 2.78 mmol, dried under vacuum) was treated with thionyl chloride as in procedure A for imide **13** to generate the acid chloride, which was isolated and used as the crude product. It was then treated with the lithium anion of (*S*)-(−)-4-benzyl-2,5-oxazolidinone (0.690 g, 3.90 mmol, 1.3 equiv), quenched, worked up, and purified to permit isolation of 0.790 g of imide **14** (75% yield): mp 133−136°C; $[\alpha]^{25}_D$ 52.84° (*c* = 6.1, CH_2Cl_2); IR 2586, 1778, 1700, 1384, 1208 cm^{-1}; ^1H NMR δ 3.30−1.05 (bm, 10H), 2.56 (m, 2H), 2.68 (dd, 1H, J_{H-H} = 13, 14), 3.08 (m, 2H), 3.23 (dd, 1H, J_{H-H} = 3, 14), 3.78 (s, 1H), 4.11 (m, 2H), 4.61 (m, 1H), 7.24 (m, 5H); ^{13}C NMR 170.5, 153.1, 134.7, 129.1, 128.8, 127.2, 74.1, 66.3, 61.4, 54.9, 37.5, 35.0, 31.6 ppm; HRMS EI calcd for M^+ ($C_{15}H_{25}B_{10}NO_3$) = 375.2837, found 375.2837 (Δ = 0.0 ppm).

B. Silyl imide **16** (0.613 g, 1.25 mmol) was treated with TFA and TBAF as in procedure B for imide **13** to yield 0.412g of imide **14** (88% of theoretical).

(4*R*)-5-[3′-(1″-(2″-(*tert*-Butyldimethylsilyl)-1",2"-dicarbaclosododecaboranyl))propionyl]-4-benzyl-2-oxazolidinone (15). Silyl acid **12** (0.343 g, 1.15 mmol) was dissolved in 5 mL of benzene and added dropwise over 1 h to a refluxing solution of oxalyl chloride (1.46 g, 1.00 mL, 11.5 mmol, 10 equiv) and 15 mL of benzene (15 mL), treated as in procedure A for imide **13** to generate the acid chloride, which was treated with the lithium anion of (*R*)-4-benzyl-2,5-oxazolidinone as in procedure A. Chromatography allowed 0.400 g of silyl imide **15** (86% yield) to be isolated; mp 106−108°C; $[\alpha]^{25}_D$ −44.4° (*c* = 2.0, CH_2Cl_2); IR 3050, 2576, 1775, 1690, 1386 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.4 (s, 6H), 1.1 (s, 9H), 3.4−1.4 (bs, 10H), 2.65 (m, 2H), 2.75 (dd, 1H, J_{H-H} = 9.5, 13.6), 3.17 (m, 2H), 3.25 (dd, 1H, J_{H-H} = 3.2, 13.6), 4.21 (m, 2H), 4.70 (m, 1H), 7.25 (m, 5H); ^{13}C NMR 170.5, 153.2, 134.9, 129.3, 128.9, 127.4,79.8, 76.2, 66.4, 55.0, 37.7, 35.1, 31.7,27.5, 20.4, −2.5 ppm; HRMS EI

(29) Meinwald, J.; Crandall, J.; Hymans, E. *Organic Synthesis*; Wiley: New York, 1973; Collect. Vol. 5, pp 866−868.

(30) Lit. mp 147−149 °C. Zaharkin, L. I.; Chapovsky, Y. A. *Tetrahedron Lett.* **1964**, *19*, 1147−1150.

calcd for $M^+(C_{21}H_{39}B_{10}BrNO_3Si - C_4H_9)$ = 432.2998, found 432.3019 (Δ = 4.8 ppm).

(4*S*)-5-[3′-(1″-(2″-(*tert*-Butyldimethylsilyl)-1″,2″-dicarbaclosododecaboranyl))propionyl]-4-benzyl-2-oxazolidinone (16). Silyl acid **12** (0.831 g, 2.51 mmol) was treated with oxalyl chloride as in the procedure for imide **15** to generate the acid chloride. The crude product was treated with the anion of (4*S*)-4-benzyl-2,5-oxazolidinone as in procedure A for imide **13** to allow 1.03 g (84% of theoretical) of imide **16** to be isolated after chromatographic purification: mp 106−108 °C; IR 2973, 2939, 2863, 2576, 1775, 1690, 1386 $cm^{-1;}$ $[\alpha]^{25}_D$ +43.04 (c = 2.3, CH_2Cl_2; ^1H NMR ($CDCl_3$) δ 0.4 (s, 6H), 1.1 (s., 9H), 3.4−1.4 (bs, 10H), 2.65 (m, 2H), 2.75 (dd, 1H, J_{H-H} = 9.5, 13.6), 3.17 (m, 2H), 3.25 (dd, 1H, J_{H-H} = 3.2, 13.6), 4.21 (m, 2H), 4.70 (m, 1H), 7.25 (m, 5H); ^{13}C NMR ($CDCl_3$) 170.4, 153.2, 134.9, 129.3, 128.9, 127.4, 79.8, 76.2, 66.4, 55.0, 37.7, 35.9, 31.7, 27.5, 20.4, −2.5 ppm; HRMS EI calcd for M^+ ($C_{21}H_{39}B_{10}BrNO_3Si - C_4H_9$) = 432.2998, found 432.3014 (Δ = 3.7 ppm).

(4*R*,2′*R*)-5-[3′-(1″-(1″, 2″-Dicarbaclosododecaboranyl))-2′-bromo propionyl]-4-benzyl-2-oxazolidinone (21). Imide **13** (0.177 g, 0.472 mmol) and 4 mL of anhydrous methylene chloride were cooled to −78 °C, and a slow dropwise addition of $TiCl_4$ (0.06 mL, 0.094 g, 0.496 mmol, 1.05 equiv) was carried out. The yellow solution was stirred at −78 °C for 5 min; a slow addition of DIEA (0.09 mL, 0.064 g, 0.496 mmol, 1.05 equiv) was then made. The burgundy solution was stirred at −78 °C for another 15 min, warmed to 0 °C for 1 h, recooled to −78 °C, and transferred via a Teflon cannula to a well-stirred mixture of NBS (0.093 g, 0.519 mmol, 1.1 equiv) and CH_2Cl_2 (1 mL) that had been cooled to −78 °C. The dark solution was stirred at −78 °C for 1.25 h, during which time the color discharged to an amber color, the reaction was then quenched by addition of 5% sodium bisulfate solution (saturated with sodium chloride), and the solution was extracted three times with ethyl acetate. The organic layers were washed well with a 5% sodium thiosulfate solution (saturated with sodium chloride), dried over sodium sulfate, and concentrated to a white solid. Analysis of the stereochemical ratio of products was made on this crude material. HPLC separation on a silica column and ^{13}C NMR spectroscopy both confirm a 98:2 ratio at the α-center. Chromatography on silica gel using a gradient of CH_2Cl_2/hexane (1:4) to ethyl ether/CH_2Cl_2/hexane (3:2:5) permitted 0.140 g of bromo imide **21** to be isolated (65% of theoretical): mp 149−150 °C; IR 3064, 2586, 1778, 1700, 1384, 1206 cm^{-1}; $[\alpha]^{25}_D$ −77.64° (c = 5.2, CH_2Cl_2); ^1H NMR δ 1.2−3.10 (bm, 10H), 2.69 (dd, 1H, J_{H-H} = 9.6, 13.6), 2.80 (dd, 1H, J_{H-H} = 3.5, 11.2), 3.18 (dd, 1H, J_{H-H} = 3.6, 13.5), 3.39 (dd, 1H, J_{H-H} = 10.5, 15.5), 3.76 (m, 1H), 4.23 (m, 2H), 4.74 (m, 1H), 5.73 (dd, 1H, J_{H-H} = 3.6, 10.5), 7.28 (m, 5H); ^{13}C NMR 167.8, 152.1, 134.4, 129.4, 129.1, 127.6, 71.9, 66.4, 60.7, 55.1, 40.5, 38.6, 36.8 ppm; HRMS EI calcd for M^+ ($C_{15}H_{24}B_{10}BrNO_3$) = 453.1943, found 453.1935 (Δ = 1.7 ppm).

(4*S*,2′*S*)-5-[3′-(1″-(1″,2″-Dicarbaclosododecaboranyl))-2′-bromo propionyl]-4-benzyl-2-oxazolidinone (22). Imide **14** (0.386 g, 1.03 mmol) was treated and worked up as in the procedure for bromo imide **21**. Chromatography allowed isolation of 0.306 g of bromo imide **22** (65% yield). HPLC analysis and ^{13}C NMR spectroscopy of the crude reaction product confirm a ratio of isomers of 98:2 at the α-center: mp 143−147 °C; $[\alpha]^{25}_D$ +72.77° (c = 1.3, CH_2Cl_2); IR 3064, 2593, 1778, 1700, 1392, 1208 cm^{-1}; ^1H NMR δ 1.2−3.10 (bm, 10H), 2.70(dd, 1H, J_{H-H} = 9.6, 13.6), 2.82 (dd, 1H, J_{H-H} = 3.5, 15.4), 3.20 (dd, 1H, J_{H-H} = 3.4, 13.5), 3.41 (dd, 1H, J_{H-H} = 10.5, 15.5), 3.71 (s, 1H), 4.16 (m, 2H), 4.66 (m, 1H), 5.65 (dd, 1H, J_{H-H} = 3.5, 10.4.), 7.23 (m, 5H); ^{13}C NMR 167.6, 152.0, 134.2, 129.3, 128.9, 127.5, 71.9, 66.4, 60.8, 55.1, 40.4, 38.6, 36.7 ppm; HRMS EI calcd for M^+($C_{15}H_{24}B_{10}BrNO_3$) = 453.1943, found 453.1935 (Δ = 1.7 ppm).

(4*R*,2′*R*)-5-[3′-(1″-(2″-(*tert*-Butyldimethylsilyl)-1″,2″-dicarbaclosododecaboranyl))-2′-bromopropionyl]-4-benzyl-2-oxazolidinone (23). Imide **15** (0.396 g, 0.809 mmol) was treated with $TiCl_4$, DIEA, and NBS as in the procedure for bromo imide **21**. Chromatography on silica gel yielded 0.381 g of bromo imide **23** (83% of theoretical): mp 51−54 °C; $[\alpha]^{25}_D$ −60.5° (c = 3.1, CH_2Cl_2); IR 2973, 2939, 2864, 2576, 1783, 1707 cm^{-1}; ^1H NMR δ 0.41 (s, 3H), 0.42 (s, 3H), 1.13 (s, 9H), 3.2−1.4 (bm, 10H), 2.79 (dd, 1H, J_{H-H} = 8.5, 14.1), 2.83 (dd, 1H, J_{H-H} = 10.4, 15), 3.27 (dd, 1H, J = 3.2, 14.1), 3.59 (dd, 1H, J = 10.5, 15), 4.24 (m, 2H), 4.77 (m, 1H), 5.80 (dd, 1H, J = 2.7, 10.4), 7.29 (m, 5H); ^{13}C NMR 166.9, 152.1, 134.4, 129.4, 128.9, 127.4, 77.7, 76.6, 66.2, 55.0, 40.2, 39.1, 36.6, 27.5, 20.3, −2.4, −2.7 ppm; HRMS EI calcd for M^+ ($C_{21}H_{38}B_{10}BrNO_3Si - C_4H_9$) = 510.2103, found 510.2170 (Δ = 12.3 ppm).

(4*S*,2′*S*)-5-[3′-(1″-(2″-(*tert*-Butyldimethylsilyl)-1″,2″-dicarbaclosododecaboranyl))-2′-bromopropionyl]-4-benzyl-2-oxazolidinone (24). Imide **16** (0.548 g, 1.12 mmol) was treated with TiCl4, DIEA, and NBS as in the procedure for bromo imide **21**. Chromatography on silica gel yielded 0.470 g of bromo imide **24** (73% of theoretical): mp 52−55 °C; $[\alpha]^{25}_D$ +65.0° (c = 2.0, CH_2Cl_2); IR 3025, 2860, 2580, 1766, 1702 $cm^{-1;}$ ^1H NMR ($CDCl_3$) δ 0.41 (s, 3H), 0.42 (s 3H), 1.12 (s, 9H), 3.20−1.40 (bm, 10H), 2.79 (dd, 1H, J_{H-H} = 8.5, 14.1), 2.84 (dd, 1H, J_{H-H} = 2.7, 15), 3.27 (dd, 1H, J_{H-H} = 3.2,14.1), 3.59 (dd, 1H, J_{H-H} = 10.5, 15), 4.24 (m, 2H), 4.77 (m, 1H), 5.80 (dd, 1H, J_{H-H} = 2.7, 10.5), 7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) 166.9, 152.1, 134.4, 129.4, 128.9, 127.4, 77.7, 76.6, 66.2, 55.0, 40.2, 39.1, 36.6, 27.5, 20.4, −2.4, −2.7 ppm; HRMS EI calcd for M^+($C_{21}H_{38}B_{10}BrNO_3Si - C_4H_9$) = 510.2103, found 510.2007 (Δ = 18.8 ppm).

(4*R*,2′*S*)-5-[3′-(1″-(2″-Dicarbaclosododecaboranyl))-2′-azidopropionyl]-4-benzyl-2-oxazolidinone (25). Bromo imide **21** (0.140 g, 0.308 mmol) and CH_2Cl_2 (1.0 mL) were cooled to −23 °C. A solution of TMGA (0.146 g, 0.924 mmol, 3 equiv) in CH_2Cl_2 (1 mL) was added dropwise over 2 min. Stirring was maintained for 3 h at −23 °C. The reaction was quenched with addition of saturated sodium bicarbonate solution, then the solution was extracted with two 100 mL portions of methylene chloride. The combined organic layers were washed successively with two portions of water and two portions of saturated brine, dried with sodium sulfate, concentrated, and chromatographed on silica gel with a gradient of CH_2Cl_2/hexane (1:4) to ethyl ether/CH_2Cl_2/hexane (3:2:5) as eluent, yielding 0.114 g of azido imide **25** (89% of theoretical yield). Analysis of the crude reaction product by HPLC separation on a normal phase silica column and by ^{13}C NMR spectroscopy confirmed a 98:2 ratio of diastereomers, indicating that these reaction conditions do not cause racemization. **25**: mp 98−99 °C; $[\alpha]^{25}_D$ −78.8 °C (c = 0.9, CH_2Cl_2); IR 3064, 2917, 2586, 2101, 1778, 1707, 1400, 1210 cm^{-1}; ^1H NMR δ 1.30−3.20 (bm, 10H), 2.49 (dd, 1H, J_{H-H} = 9.2, 15.6), 2.61 (dd, 1H, J_{H-H} = 3.7, 16), 2.80 (dd, 1H, J_{H-H} = 9.1, 13.4), 3.14 (dd, 1H, J_{H-H} = 3, 13.5), 3.88 (bs, 1H), 4.25 (m, 2H), 4.64 (m, 1H), 4.86 (dd, 1H, J_{H-H} = 3.6, 9.1), 7.20 (m, 5H); ^{13}C NMR 168.05, 152.89, 134.08, 129.30, 129.07, 127.80, 70.79, 67.46, 59.79, 59.78, 55.08, 38.16, 37.51 ppm; HRMS EI calcd for M^+ ($C_{15}H_{24}B_{10}N_4O_3$) = 416.2851, found 416.2817 (Δ = 8.1 ppm).

(4*S*,2′*R*)-5-[3′-(1″-(1″,2″-Dicarbaclosododecaboranyl))-2′-azidopropionyl]-4-benzyl-2-oxazolidinone (26). Bromo imide **22** (0.154 g, 0.339 mmol) was treated, worked up, and purified as in the procedure for azido imide **25** to give 0.093 g of azide **26** (82% yield): mp 97.5−99 °C; $[\alpha]^{25}_D$ +80.5° (c = 1.0, CH_2Cl_2); IR 3063, 2917, 2586, 2101, 1778, 1707, cm^{-1}; ^1H NMR δ 1.30−3.20 (bm, 10H), 2.50 (dd, 1H, J_{H-H} = 9, 15.8), 2.60 (dd, 1H, J_{H-H} = 3.6, 15.6), 2.81 (dd, 1H, J_{H-H} = 9.1,13.6), 3.14 (dd, 1H, J_{H-H} = 3, 13.4), 3.88 (bs, 1H), 4.24 (m, 2H), 4.64 (m, 1H), 4.86 (dd, 1H, J_{H-H} = 3.5, 9.1), 7.20 (m, 5H);^{13}C NMR 167.93, 152.85, 134.03, 129.23, 128.98, 127.71, 70.81 67.43, 59.82, 59.43, 54.48, 38.08, 37.41 ppm; HRMS EI calcd for M^+-($C_{15}H_{24}B_{10}N_4O_3$) = 416.2851, found 416.2838 (Δ = 3.1 ppm).

Benzyl (2*S*)-2-Azido-3-(1′-(1′,2′-dicarbaclosododecaboranyl))propionate (29). Titanium tetraisopropoxide (0.09 mL, 0.085 g, 0.299 mmol, 1.5 equiv) and benzyl alcohol (0.73 mL, 0.755 g, 6.98 mmol, 35 equiv) were stirred under vacuum for 1 h. The solution was transferred via syringe to a flask containing azido imide **25** (0.083 g, 0.20 mmol). The colorless solution was stirred at 75 °C for 5 h and then cooled to room temperature. The reaction was quenched by addition of 1 N HCl, and the solution was extracted with three portions of ethyl acetate. The combined organic layers were washed with brine, dried over sodium sulfate, and concentrated to a colorless oil. The benzyl alcohol was removed by bulb-to-bulb distillation at 0.025 Torr and 75 °C. The crude product was chromatographed on silica gel with hexane as eluent to yield

0.070 g of azido ester **29** (99% yield): mp 63−64 °C; IR 2586, 2115, 1743, 1265 cm^{-1}; $[\alpha]^{25}_D$ +80.5° (c = 1.0, CH_2Cl_2); ^1H NMR δ 1.20 −3.25 (bm, 10 H), 2.46 (dd, 1H, J_{H-H} = 12.3, 15.5), 2.80 (dd, 1H, J_{H-H} = 4, 15.5), 3.80 (bs, 1H), 4.06 (dd, 1H, J_{H-H} = 4, 9), 5.23 (s, 2H), 7.36 (s, 5H); ^{13}C NMR 168.12, 134.21, 128.98, 128.80, 128.64, 71.19, 68.45, 60.95, 60.20, 38.21 ppm; HRMS EI calcd for $M^+(C_{12}H_{21}B_{10}N_3O_2 - H)$ = 346.2559, found 346.2568 (Δ = 2.5 ppm).

Benzyl (2*R*)-2-Azido-3-(1′-(1′,2′-dicarbaclosododecaboranyl))propionate (30). Azido imide **26** (0.185 g, 0.445 mmol) was treated as for ester **29** to give 0.133 g of azido ester **30** (89%). HPLC chromatography on a Chiralcel -OJ column using hexane as eluent confirmed a 98:2 ratio of isomers: mp 63−64 °C; $[\alpha]^{25}_D$ −94.9 °C (c = 1.0, CH_2Cl_2); IR 2586, 2115, 1743, 1265 cm^{-1}; ^1H NMR δ 1.20 −3.25 (bm, 10 H), 2.46 (dd, 1H, J_{H-H} = 12.3, 15.5), 2.80 (dd, 1H, J_{H-H} = 4, 15.5), 3.80 (bs, 1H), 4.06 (dd, 1H, J_{H-H} = 4, 9), 5.23 (s, 2H), 7.36 (s, 5H); ^{13}C NMR 168.03, 134.17, 128.91 128.74, 128.56, 71.19, 68.45, 60.89, 60.23, 38.14 ppm: HRMS EI calcd for $M^+(C_{12}H_{21}B_{10}N_3O_2 - H)$ = 346.2559, found 346.2600 (Δ = 11.8 ppm).

(*S*)-*o*-Carboranylalanine (1). (*S*)-Azido benzyl ester **29** (0.116 g, 0.335 mmol), ethanol (35 mL), glacial acetic acid (5 mL), and 10% palladium on carbon (0.015 g) were placed under 20 psi of hydrogen and shaken for 18 h on a Parr apparatus. The suspension was filtered through Celite and rinsed with a total of 100 mL of ethanol. The combined filtrates were concentrated under water aspirator vacuum. The remaining acetic acid was removed by placing the crude product under vacuum (0.4 Torr) overnight. The resultant yellow oil was triturated with three 10 mL aliquots of hexane, removing the supernatant solution after each trituration. The white solid was dried under vacuum overnight to remove remaining traces of hexane, and 0.062 g of amino acid **1** was isolated (80% of theoretical yield): mp 166−167 °C, 203−206 °C dec; $[\alpha]^{25}_D$ +9° (c = 0.08, 1 N HCl), −5.7° (c = 0.052, H_20);[25, 31] IR 3062, 2586, 1647, 1400, 1320 cm^{-1}; ^1H NMR δ 1.10−3.12 (bm, 10H), 2.66 (d, J = 12, 1H), 3.10 (d, J = 12, 1H), 3.67 (bs, 1H), 4.86 (bs, 1H), 4.95 (s, 3H); ^{13}C NMR 172.6, 74.3, 63.3, 54.9, 39.7 ppm; FAB HRMS calcd for M + H ($C_5H_{18}B_{10}NO_2$) = 232.2341, found 232.2345.

(*R*)-*o*-Carboranylalanine (2). (*R*)-Azido benzyl ester **30** (0.083 g, 0.239 mmol) was treated as above to yield 0.048 g of amino acid **2** (89% of theoretical): mp 165−169 °C , 202−207 °C dec; $[\alpha]^{25}_D$ −9.5° (c = 0.08, 1 N HCl); IR 3062, 2586, 1647, 1400, 1320 cm^{-1}; ^1H NMR δ 1.12−3.10 (bm, 10H), 2.66 (d, J = 12, 1H), 3.10 (d, J = 12, 1H), 3.67 (bs, 1H), 4.86 (bs, 1H), 4.95 (s, 3H); ^{13}C NMR 172.2, 74.4, 63.5, 55.01, 39.9 ppm; FAB-HRMS calcd for M + H ($C_5H_{18}B_{10}NO_2$) = 232.2341, found 232.2343.

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Supporting Information Available: ^{13}C NMR data of compounds **1**, **2**, **11**−**16**, **21**−**26**, **29**, and **30** (16 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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(31) Moroder and co-workers also reported variability in the optical rotations for L-carboranylalanine. See ref 5. The value we report for the rotation in water is different than previously reported values due to the imprecision in the very small rotation actually observed at the low concentration that solubility permits.