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Stereoselective chain extension of (*R*,*R*)- or (*S*,*S*)-1,2-dicyclohexylethane-1,2-diol trityloxymethylboronate to compounds having three stereogenic centers †

Donald S. Matteson * and Jing-Jing Yang

Contribution from the Department of Chemistry, Washington State University, Pullman, Washington 99164-4630, USA

Abstract: The highly diastereoselective chain extension of (*R*)- or (*S*)-(*R**,*R**)-1,2-dicyclohexylethane-1,2-diol ('DICHED') boronic esters has been applied to enantiomerically pure DICHED [(trityloxy)methyl]boronate to provide possible precursors of kainic acid. A five carbon chain has been assembled having the two critical stereogenic centers in the correct absolute configurations, with the third stereogenic center in a single absolute configuration potentially convertible to the correct amino acid diastereomer. However, peroxidic deboronation of the potential *sec*-kainic acid precursor took an unexpected course. © 1997 Published by Elsevier Science Ltd. All rights reserved.

Introduction

We have recently reported that [(trityloxy)methyl]boronic esters are easily prepared and are useful reagents for asymmetric synthesis.[1,2] Optimum chiral direction, exceeding 1000:1 in favorable cases, has been demonstrated with boronic esters of a diol of C_2 symmetry in a two step process involving treatment of the boronic ester with $LiCHCl_2$ followed by reaction of the resulting (α-chloroalkyl)boronic ester with a Grignard reagent to form a (*sec*-alkyl)boronic ester.[3]

With consideration of ease of preparation and recovery together with efficacy, (*R*)- or (*S*)-(*R**,*R**)-1,2-dicyclohexylethane-1,2-diol ('DICHED') boronic esters, first introduced by Hoffmann and coworkers,[4] are emerging as the reagents of choice for this type of synthesis. The preparation of DICHED via Sharpless dihydroxylation of *trans*-stilbene[5] and our recently improved hydrogenation of the phenyl groups[6] makes both pure enantiomers of DICHED readily accessible in >100 g quantities.

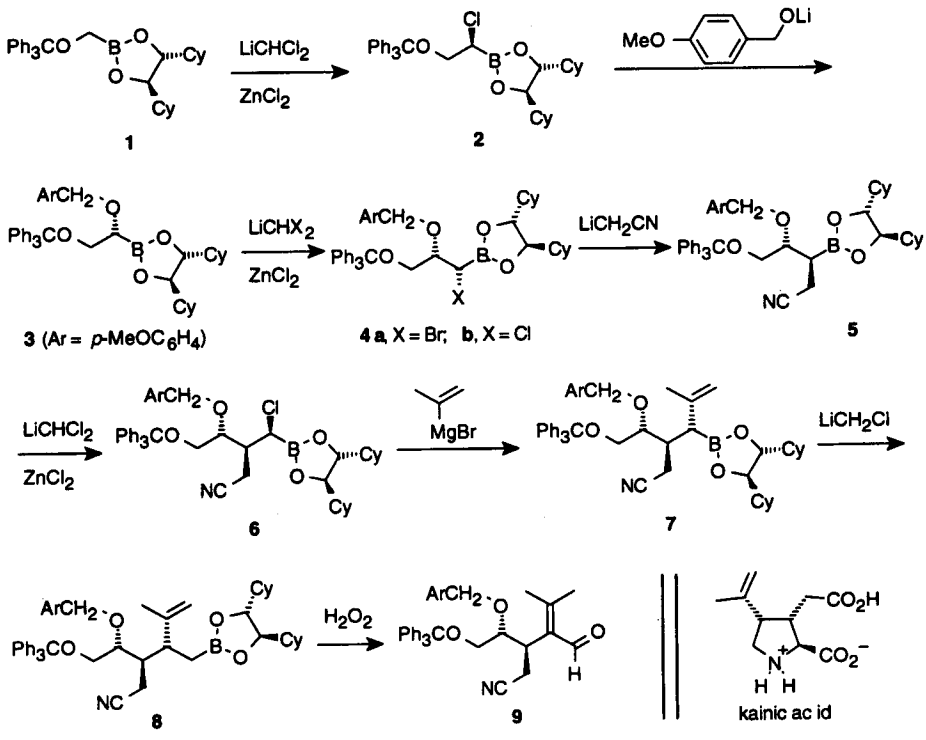
Results

The present work was undertaken as a model study for the synthesis of kainic acid and related compounds. (*R*)-DICHED [(trityloxy)methyl]boronate[1] **1** readily underwent a series of the usual types of chain extensions and substitutions as far as boronic ester **8**, which contains the complete carbon skeleton corresponding to the enantiomer of kainic acid (Scheme 1). The same series of reactions has been carried as far as the enantiomer of **8** with the (*S*)-DICHED isomers. Peroxidic deboronation of **8** did not yield the expected alcohol but an aldehyde tentatively assigned structure **9** on the basis of NMR and mass spectral evidence.

Reaction of (*R*)-DICHED [(trityloxy)methyl]boronate[1] **1** with (dichloromethyl)lithium to produce chloro boronic ester **2** followed by substitution with sodium *p*-methoxybenzyl oxide efficiently yielded (*R*)-DICHED (*R*)-[1-(*p*-methoxybenzyloxy)-2-(trityloxy)ethylboronate **3**. Although (dichloromethyl)lithium reacted readily enough with **3** to form the chain extended chloro boronic ester **4b**, attempted substitution with lithioacetonitrile was unsuccessful. (Dibromomethyl)lithium,

† Dedicated to Professor Herbert C. Brown on the occasion of his 85th birthday.

* Corresponding author.



Scheme 1.

generated *in situ* from dibromomethane and lithium diisopropylamide, converted **3** to bromo boronic ester **4a**, which did react efficiently with lithioacetonitrile to form the nitrile **5**.

Chain extension of **5** to chloro boronic ester **6** proceeded normally, as did reaction of **6** with 2-propenylmagnesium bromide to form boronic ester **7**. The enantiomer of **7** was also prepared via a similar sequence. Chain extension of **7** with chloromethyllithium (from chloroiodomethane and butyllithium *in situ*[7]) yielded **8**, which contains all of the carbon atoms and configuration corresponding to the enantiomer of kainic acid.

Oxidation of **8** with hydrogen peroxide and sodium hydroxide took an unexpected course. The only product was apparently the α,β-unsaturated aldehyde **9**, which was obtained in a mixture with DICHED. We know of no precedent for this particular reaction pathway, but other instances are known in which peroxidic oxidation of boronic acids leads to anomalous by-products.[8,9]

Discussion

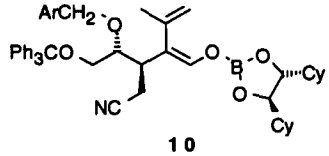
The multistep synthesis of boronic ester **8** has proved remarkably straightforward for a series of compounds with this much functionality. An earlier analogous synthesis of ribose had become inefficient as the number of benzyloxy substituents increased to three and four, and the insertion of the fifth carbon with (chloromethyl)lithium had proved difficult.[10] More recently, elaboration of [(trityloxy)methyl]boronic esters has proceeded as far as a (1-allyl-3-methyl-4-benzyloxy-5-trityloxy)pentylboronic ester,[2] in which the number of highly polar substituents is one less than in **8** and the methylene spacer at position 2 would appear less sterically demanding than the three adjacent asymmetric carbons of **8**.

The only minor delay in the entire sequence was the failure of chloro boronic ester **4b** to react with lithioacetonitrile, and the consequent necessity of using the more reactive bromo boronic ester **4a** as

the intermediate. This is not entirely surprising in view of the previous observation that ester enolates react inefficiently with chloro boronic esters, and bromo boronic esters have to be used.[11]

It should also be noted that sterically unhindered (α-bromoalkyl)boronic esters may epimerize very readily.[12] However, NMR data do not show any evidence of such epimerization of **4a**, consistent with earlier observations that benzyloxy substituted bromo boronic esters do not epimerize significantly under the usual reaction conditions.[10,12]

The anomalous oxidation of homoallylboronic ester **8** to what appears to be α,β-unsaturated aldehyde **9** can be rationalized by assuming that a free radical side reaction results in abstraction of an allylic hydrogen atom from **8** and subsequent formation of intermediate boron enolate **10** occurs. In view of the limited data obtained, further speculation about this reaction is not justified.



10

Although we know of no precedent for this particular reaction pathway, carbon–carbon bond cleavage is a general side reaction in the peroxidic deboronation of 1-alkenylboronic acids.[8] For example, 2-phenylpropeneboronic acid with hydrogen peroxide yielded as much as 40% acetophenone instead of the expected 2-phenylpropanal under weakly basic conditions.[8] Anomalous carbon–carbon bond formation was shown to occur during the oxidation step when 2-phenylethene-1,1-bis(1,3,2-dioxaborin) was treated with two equivalents of methyllithium followed by sodium perborate, which yielded phenylacetone (75%).[9]

It is unlikely that the problem with the peroxidic oxidation is insurmountable, but other synthetic routes to kainoids that may be more direct are being pursued first.

Summary

Several new asymmetric chain extensions of alkoxy and cyano substituted 1,2-dicyclohexyl-1,2-ethanediol boronic esters have been carried out and found to be highly efficient. An anomalous rearrangement and over-oxidation of a homoallylic boronic ester to an α,β-unsaturated aldehyde in the presence of hydrogen peroxide has been observed.

Experimental

THF (tetrahydrofuran) was freshly distilled from sodium benzophenone ketyl. Other commercial reagent grade chemicals were used without further purification. All operations involving carbanions or other air-sensitive intermediates were carried out under an argon atmosphere. Procedures for the preparation and use of (dichloromethyl)lithium have been described elsewhere.[1,13] The preparations of the series of compounds derived from (*R,R*)-DICHED are detailed below. The enantiomers of **1**, **2**, **3**, **4a**, **5**, **6**, and **7** were subsequently prepared from (*S,S*)-DICHED via the same procedures and yielded similar spectral data.

[4R-(2S,4α,5β)]-4,5-Dicyclohexyl-2-[1′-chloro-2′-(triphenylmethoxy)ethyl]-1,3,2-dioxaborolane* **2**

[*R*-(4α,5β)]-4,5-Dicyclohexyl-2-[(triphenylmethoxy)methyl]-1,3,2-dioxaborolane **1** was prepared according to the procedure previously reported.[1] (Dichloromethyl)lithium was prepared in the usual manner[1] by addition of butyllithium (23.6 mmol) via a cannula down the chilled wall of the reaction flask into a well stirred solution of dichloromethane (5 g, 59 mmol) in THF (70 mL) at −100°C. After 5 min., [*R*-(4α,5β)]-4,5-dicyclohexyl-2-[(triphenylmethoxy)methyl]-1,3,2-dioxaborolane **1** (10.0 g, 19.7 mmol) in THF (30 mL) was added to the cold solution via a cannula. After 10 min. zinc chloride (4.84 g, 35.5 mmol), which was fused before use, was added to the solution. The solution was allowed to warm to room temperature and kept for 18 h to form [4*R*-(2*S**,4α,5β)]-4,5-dicyclohexyl-2-[1′-chloro-2′-(triphenylmethoxy)ethyl]-1,3,2-dioxaborolane **2**. The mixture was worked up by addition

of saturated aqueous ammonium chloride (100 mL) and extraction with hexanes (3×100 mL). The organic solution was washed with water (3×100 mL) and brine (100 mL). Concentration in a rotary evaporator gave crude (*R,R*)-DICHED (1*S*)-[(1-chloro-2-triphenylmethoxy)ethyl]boronate **2**, which was recrystallized from pentane/diethyl ether, 10.96 g (95%); mp 105–106°C. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.80–1.33 and 1.56–1.72 (m, 22, C_6H_{11}), 3.38 (dd, *J*=5.8 Hz, 9.0 Hz, 1, C*H*Cl), 3.55 (m, 2, CH_2OCPh_3), 3.95 (d, *J*=4.5 Hz, 2, BOC*H*), 7.20–7.28 and 7.40–7.54 (m, 15, C_6H_5). ^{13}C NMR (75 MHz, $CDCl_3$); δ 25.8, 25.9, 26.3, 27.3, 28.1, 42.8, 65.9, 84.3, 86.9, 127.0, 127.7, 128.8, 143.9. HRMS: Calcd for $C_{35}H_{42}O_3BCl$, 556.2916. Found, 556.2909.

[4R-[2(R),4α,5β]]-4,5-Dicyclohexyl-2-[1′-(4-methoxybenzyl)oxy-2′-(triphenylmethoxy)ethyl]-1,3,2-dioxaborolane 3*

A solution of sodium *p*-methoxybenzyl oxide (21.7 mmol) was prepared by addition of sodium hydride (60% dispersion in mineral oil, 940 mg, 23.5 mmol) to *p*-methoxybenzyl alcohol (3.0 g, 21.7 mmol) in dimethyl sulfoxide (60 mL) and THF (30 mL) at room temperature and stirring overnight. This solution was cooled to 0°C and (*R,R*)-DICHED (1*S*)-[(1-chloro-2-triphenylmethoxy)ethyl]-boronate **2** (10.1 g, 18.1 mmol) in THF (10 mL) was added via a cannula. The solution was stirred for 24 h at room temperature. Saturated aqueous ammonium chloride (100 mL) was added, the phases were separated, and the aqueous phase was extracted with hexanes (3×150 mL). The organic solution was washed with water (3×150 mL) and brine (200 mL). Concentration in a rotary evaporator yielded crude **3**, which contained ~8% unchanged **2**. Flash chromatography on silica with 1:20 ethyl acetate:hexanes yielded **3**, 10.0 g, 85%; mp 109–111°C. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.88–1.40 and 1.58–1.84 (m, 22, C_6H_{11}), 3.34 (m, 2, CH_2OCPh_3), 3.48 (m, 1, BC*H*OR), 3.79 (s, 3, OCH_3), 3.90 (d, *J*=4.0 Hz, 2, BOC*H*), 4.47 (AB, *J*=12 Hz, 1, ArC*H*H′), 4.58 (AB, *J*=12 Hz, 1, ArCH*H*′), 6.83 (d, *J*=8.6 Hz, 2, $C_6H_4OCH_3$), 7.23–7.29 and 7.48–7.50 (m, 17, C_6H_5, C_6H_4). ^{13}C NMR (75 MHz, $CDCl_3$); δ 25.9, 26.0, 26.4, 27.4, 28.3, 42.8, 55.2, 64.4, 71.8, 83.8, 87.7, 113.5, 126.7, 127.6, 127.9, 128.8, 129.3, 144.2, 159.0. HRMS: Calcd for $C_{43}H_{51}O_5B$, 657.3751. Found, 657.3760.

[4R-[2(1S,2S*)4α,5β]]-4,5-Dicyclohexyl-2-[1′-bromo-2′-(4-methoxybenzyl)oxy-3′-(triphenyl methoxy)propyl]-1,3,2-dioxaborolane* ***4a***

A solution of **3** (2.5 g, 3.86 mmol) and dibromomethane (1.98 g, 11.4 mmol) in THF (40 mL) was stirred at −78°C during the dropwise addition of LDA (2.28 mL, 2.0 M, 4.55 mmol). Anhydrous (fused) zinc chloride (2.5 g, 19.0 mmol) was added. The solution was allowed to warm to 20–25°C and kept for 18 h, then poured into saturated ammonium chloride (50 mL) and ether:hexanes (1:1, 60 mL). The organic phase was dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude **4a** containing ~8% unchanged **3** was recrystallized from pentane and diethyl ether to yield **4a** (2.4 g, 85%); mp 120–122°C. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.88–1.23 and 1.50–1.72 (m, 22, C_6H_{11}), 3.27 (m, 2, CH_2OCPh_3), 3.62 (d, *J*=8.2 Hz, 1, C*H*Br), 3.80 (s, 3, OCH_3), 3.81 (s, 2, BOC*H*), 3.91 (m, 1, C*H*OCH$_2$Ar), 4.57 (AB, *J*=10.8 Hz, 1, C*H*H′C$_6$H$_4$OCH$_3$), 4.63 (AB, *J*=10.8 Hz, 1, CH*H*′C$_6$H$_4$OCH$_3$), 6.84 (dd, *J*=8.6 Hz, 2, $C_6H_4OCH_3$), 7.24–7.30 and 7.41–7.44 (m, 17, C_6H_5, C_6H_4). ^{13}C NMR (75 MHz, $CDCl_3$); δ 25.7, 25.9, 26.3, 27.5, 28.3, 42.7, 55.3, 64.7, 72.9, 79.5, 84.1, 87.1, 113.6, 127.0, 127.7, 128.9, 129.5, 130.5, 143.8, 158.1. HRMS: Calcd for $C_{44}H_{52}O_5BBr$, 750.3091. Found, 750.3088.

[4R-[2(1S,2S*)4α,5β]]-4,5-Dicyclohexyl-2-[1′-chloro-2′-(4-methoxybenzyl)oxy-3′-(triphenyl methoxy)propyl]-1,3,2-dioxaborolane* ***4b***

The procedure was similar to that used for the preparation of **2** (above). (Dichloromethyl)lithium from dichloromethane (0.723 g, 11.4 mmol), THF (10 mL), and butyllithium (4.80 mmol) were treated with **3** (2.5 g, 3.80 mmol) in THF (50 mL) followed by zinc chloride (2.0 g, 14.4 mmol). After 18 h at ~20–25°C the mixture was worked up in the usual manner, yielding **4b**; recystallized from pentane/diethyl ether, 2.42 g (90%); mp 115–116°C. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.88–1.23 and 1.45–1.69 (m, 22, C_6H_{11}), 3.28 (m, 2, CH_2OCPh_3), 3.75 (d, *J*=6.7 Hz, 1, C*H*ClBO), 3.80 (s, 3, OCH_3),

3.89 (d, J=5.0 Hz, 2, BOCH), 3.92 (m, 1, CHOCH$_2$Ar), 4.54 (AB, J=11 Hz, 1, CHH′C$_6$H$_4$OCH$_3$), 4.59 (AB, J=11 Hz, 1, CHH'C$_6$H$_4$OCH$_3$), 6.82 (d, J=8.6 Hz, 2, C$_6H_4$OCH$_3$), 7.24–7.27 and 7.40–7.41 (m, 17, C$_6H_5$, C$_6H_4$). ^{13}C NMR (75 MHz, CDCl$_3$); δ 25.7, 25.9, 26.3, 27.5, 28.3, 42.7, 55.3, 63.9, 72.8, 79.6, 84.3, 87.6, 113.6, 126.95, 126.97, 127.7, 128.7, 129.3, 143.1, 159.0. HRMS: Calcd for C$_{44}$H$_{51}$O$_5$^{10}BCl (M-1, ^{10}B isotope), 704.3554. Found, 704.3539.

[4R-[2(1S,2R*)4α,5β]]-4,5-Dicyclohexyl-2-[1′-cyanomethyl-2′-(4-methoxybenzyl)oxy-3′-(triphenylmethoxy)propyl]-1,3,2-dioxaborolane 5*

A solution of acetonitrile (0.28 mL, 5.37 mmol) in THF (5 mL) was added to LDA (2.933 mL, 2 M, 5.86 mmol) in THF (20 mL) stirred at −78°C. After 30 min, a solution of **4a** (4.0 g, 5.32 mmol) in THF (8 mL) was added at −78°C. The mixture was stirred at 20–25°C for 16 h and was worked up with saturated aqueous ammonium chloride and diethyl ether:hexanes (1:1). The organic phase was dried over anhydrous sodium sulfate, filtered, and concentrated to yield crude **5**; chromatographed on silica with 10:1 hexanes:ethyl acetate; 3.22 g (85%); mp 115–116°C. ^{1}H NMR (300 MHz, CDCl$_3$); δ 0.80–1.25 and 1.56–1.79 (m, 23, C$_6H_{11}$+BCH), 2.36 (d, 2, J=7.6 Hz, CH_2CN), 3.22 and 3.38 (m, 2, CH_2OCPh$_3$), 3.63 (s, 3, OCH_3), 3.6–3.8 (m, 3, CHOB+CHOCH$_2$Ar), 4.44 (AB, J=11.3 Hz, 1, CHH′C$_6$H$_4$OCH$_3$), 4.64 (AB, J=11.3 Hz, 1, CHH'C$_6$H$_4$OCH$_3$), 6.85 (d, J=8.6 Hz, 2, C$_6H_4$OCH$_3$), 7.23–7.29 and 7.43–7.46 (m, 17, C$_6H_5$, C$_6H_4$). ^{13}C NMR (75 MHz, CDCl$_3$); δ 15.5, 25.8, 25.9, 26.4, 27.4, 28.3, 42.7, 55.3, 65.1, 72.0, 78.8, 83.8, 87.7, 113.6, 120.3, 126.7, 127.6, 128.7, 128.8, 129.1, 144.0, 159.1. HRMS: Calcd for C$_{46}$H$_{54}$O$_5$BN (M, ^{10}B isotope), 710.4131. Found, 710.4134.

[4R-[2(1S,2S*,3R*)4α,5β]]-2-[1′-Chloro-2′-cyanomethyl-3′-(4-methoxybenzyl)oxy-4′-(triphenylmethoxy)butyl]-4,5-dicyclohexyl-1,3,2-dioxaborolane 6*

The procedure was similar to that described for the preparation of **2**. (Dichloromethyl)lithium from dichloromethane (0.62 mL, 9.7 mmol) in THF (20 mL) and butyllithium (3.88 mmol) at −100°C was treated with **5** (2.30 g, 3.23 mmol) in THF (5 mL) followed by zinc chloride (2.1 g, 15.5 mmol). After 18 h at 20–25°C the mixture was worked up with saturated aqueous ammonium chloride (50 mL) and 1:1 hexanes:diethyl ether (3×100 mL). The organic phase was washed with water (3×100 mL) and brine (100 mL) and concentrated under vacuum. Solid **6** was recystallized from pentane/diethyl ether; 2.0 g, 81%; mp 120–122°C. ^{1}H NMR (300 MHz, CDCl$_3$); δ 0.99–1.26 and 1.55–1.82 (m, 23, C$_6H_{11}$+CHCH$_2$CN), 2.37 (dd, J=5 Hz, 4.5 Hz, 1, CH_2CN), 2.56 (dd, J=5 Hz, 4.5 Hz, 1, CH_2CN), 2.70 (m, impurity), 3.12 and 3.39 (m, 2, CH_2OCPh$_3$), 3.60 (m, 1, CHOCH$_2$C$_6$H$_4$OCH$_3$), 3.75 (d, J=7.4 Hz, 1, CHClBO), 3.81 (s, 3, OCH_3), 3.87 (d, J=4.6 Hz, 1, BOCH), 4.45 (AB, J=11.55 Hz, 1, CHH′C$_6$H$_4$OCH$_3$), 4.59 (AB, J=11.55 Hz, 1, CHH'C$_6$H$_4$OCH$_3$), 6.88 (d, J=8.4 Hz, 2, C$_6H_4$OCH$_3$), 7.21–7.31 and 7.42–7.45 (m, 17, C$_6H_5$, C$_6H_4$). ^{13}C NMR (75 MHz, CDCl$_3$); δ 17.1, 25.8, 25.9, 26.4, 27.6, 28.6, 40.3, 42.7, 55.3, 62.8, 71.9, 77.4, 84.5, 87.7, 113.99, 119.7, 127.2, 127.9, 128.0, 128.6, 129.5, 143.6, 159.2. HRMS: Calcd for C$_{47}$H$_{55}$O$_5$BClN (M-1), 759.3862. Found, 759.3888.

[4R-[2(1R,2S*,3R*)4α,5β]]-2-[1′-(1-Methylethenyl)-2′-cyanomethyl-3′-(4-methoxybenzyl)oxy-4′-(triphenylmethoxy)butyl]-4,5-dicyclohexyl-1,3,2-dioxaborolane 7*

Isopropenylmagnesium bromide (2.1 mL, 0.88 M, 1.84 mmol) was added dropwise to a solution of **6** (1.0 g, 1.317 mmol) in THF (15 mL) stirred at −78°C. The solution was kept at 20–25°C for 18 h, then worked up with saturated aqueous ammonium chloride and diethyl ether:hexanes (1:1). The ether solution was dried over magnesium sulfate, then concentrated to yield crude **7**; crystallized from hexanes/diethyl ether; 1.15 g (90%); mp 117–118°C. ^{1}H NMR (300 MHz, CDCl$_3$); δ 0.90–1.25 and 1.43–1.71 (m, 26, C$_6H_{11}$+CHCH$_2$CN+CCH_3), 2.57 (m, 1, CHB), 2.69 and 2.71 (m, 2, CH_2CN), 3.18–3.29 (m, 2, CH_2OCPh$_3$), (m, 1, CHOCH$_2$C$_6$H$_4$OCH$_3$), 3.64 (m, 2, BOCH), 3.75 (impurity?), 3.80 (s, 3, OCH_3), 4.45 (AB, J=12 Hz, 1, CHH′C$_6$H$_4$OCH$_3$), 4.56 (AB, J=12 Hz, 1, CHH'C$_6$H$_4$OCH$_3$), 4.61 (s, 1, CHH′=C), 4.77 (s, 1, CHH'=C), 6.84 (d, J=8.6 Hz, 2, C$_6H_4$OCH$_3$), 7.21–7.31 and 7.40–7.45 (m, 17, C$_6H_5$, C$_6H_4$). ^{13}C NMR (75 MHz, CDCl$_3$); δ 17.6, 23.4, 25.76, 25.84, 26.4, 27.9, 28.7, 37.9,

42.7, 55.2, 62.9, 71.9, 77.9, 83.8, 87.0, 112.9, 113.7, 120.2, 127.0, 127.8, 127.9, 128.7, 129.2, 130.5, 143.7, 143.8, 159.1. HRMS: Calcd for $C_{50}H_{60}O_5BN$ (M-1), 764.4487. Found, 764.4500.

[4R-[2(2R,3R*,4R*)4α,5β]]-4,5-Dicyclohexyl-2-[2'-(1-methylethenyl)-3'-cyanomethyl-4'-(4-methoxybenzyl)oxy-5'-(triphenylmethoxy)pentyl]-1,3,2-dioxaborolane* **8**

A solution of **7** (1.412 g, 1.842 mmol) and chloroiodomethane (0.975 g, 5.53 mmol) in THF (20 mL) was stirred at −78°C during the dropwise addition of butyllithium (1.38 mL, 1.6 M, 2.21 mmol). At the end of the addition the mixture turned into a slurry. Stirring was continued for 24 h at room temperature. The mixture was worked up with saturated aqueous ammonium chloride and diethyl ether:hexanes (1:1). The organic phase was dried over magnesium sulfate, filtered, and concentrated under vacuum. The crude **8** contained ~8% unchanged **7**. Recystallization from pentane/diethyl ether yielded **8**, 2.0 g (76%); mp 115–116°C. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.80–1.37 and 1.43–1.71 (m, 28, C_6H_{11}, CH_2B, CH_3, $CHCH_2CN$), 2.15 and 2.42 (m, 3, CH_2CN and $CHC(=CH_2)(CH_3)$), 3.15+3.22 (AB m, 2, CH_2OCPh_3), 3.64 (d, J=4.5 Hz, 2, BOC*H*), 3.72 (s, 3, OCH_3), 3.5–3.7 (m, unresolved, C*H*OR), 4.38 (AB, J=11 Hz, $CHH'C_6H_4OCH_3$), 4.41 (s, 1, CHH'=CCH_3), 4.57 (AB, J=11 Hz, 1, $CHH'C_6H_4OCH_3$), 4.64 (s, 1, CHH=CCH_3), 6.81 (d, J=8.6 Hz, 2, $C_6H_4OCH_3$), 7.21–7.31 and 7.35–7.40 (m, 17, C_6H_5, C_6H_4). ^{13}C NMR (75 MHz, $CDCl_3$); δ 14.6, 20.8, 25.8, 26.0, 26.4, 27.5, 28.5, 39.7, 41.8, 43.0, 55.2, 62.9, 72.3, 77.8, 83.4, 86.9, 112.3, 113.7, 120.1, 127.0, 127.2, 127.9, 128.6, 143.7, 147.1, 159.2. HRMS: Calcd for $C_{51}H_{62}O_5BN$ (M-1), 778.4643. Found, 778.4634.

Impure (R)-(R,R*)-2-(1-methylethylidene)-3-(cyanomethyl)-[4-(4-methoxybenzyl)oxy]-5-(triphenylmethoxy)pentanal* **9**

A solution of (*R,R*)-DICHED (2*R*,3*R*,4*R*)-[3-cyanomethyl-2-isopropenyl-(4-(4-methoxy)benzyloxy)-5-triphenylmethoxy)pentanyl]boronate **8** (71.59 mg, 0.128 mmol) in THF (5 mL) was stirred in an ice bath. Aqueous sodium hydroxide (3 M, 0.05 mL, 0.14 mmol) was added. Hydrogen peroxide (30%, 0.02 mL, 0.166 mmol) was added dropwise. The mixture was stirred for an additional half hour at room temperature. It was worked up by treatment with water (5 mL) followed by saturated aqueous ammonium chloride and diethyl ether:hexanes (1:1). The organic phase was washed with water (3×20 mL), then dried over magnesium sulfate, filtered, and concentrated under vacuum to yield a mixture of **9**, DICHED, and the DICHED ester of boric acid. Attempted separation by chromatography was not successful, but the NMR peaks characteristic of the major product other than DICHED were deduced by comparison of several spectra of varying ratios of **9** to DICHED. ^{1}H NMR (300 MHz, $CDCl_3$); δ 0.8–2.0 (m, DICHED), 2.05 (s, 3, CH_3), 2.1–2.2 (partially obscured, C=C–$CHCH_2CN$), 2.18 (s, 3, CH_3), 2.77 (AB-dd, 2, CH_2CN), 3.29 (m, part of CH_2OCPh_3, usually+DICHED C*H*OH), 3.39 (m, 1, part of CH_2OCPh_3 AB pattern), 3.71 (m, 1, $CHOCH_2C_6H_4OCH_3$), 3.73 (s, 3, OCH_3), 4.05 (AB, J=11.31 Hz, 1, $CHH'C_6H_4OCH_3$), 4.43 (AB, J=11.31 Hz, 1, $CHH'C_6H_4OCH_3$), 6.76 (d, J=8.5 Hz, 2, $C_6H_4OCH_3$), 7.02 (d, J=8.5 Hz, 2, C_6H_4), 7.17–7.25 and 7.40–7.42 (m, 15, C_6H_5), 9.89 (s, 1, C*H*O). ^{13}C NMR (75 MHz, $CDCl_3$); δ 17.2, 20.7, 24.1, 38.0, 55.2, 62.1, 71.8, 77.6, 86.6, 113.5, 118.9, 127.1, 127.9, 128.5, 129.3, 130.3, 143.7, 159.1, 161.3, 191.2. HRMS: Calcd for $C_{37}H_{37}O_4N$ (M-1), 558.2645. Found, 558.2663.

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