fitting.

Registry No. 1 (R = $HOCH_2CH_2OCH_2CH_2$), 90343-24-1; 1 (R = $CH_3OCH_2CH_2OCH_2CH_2$), 40982-08-9; 1 (R = $HOCH_2CH(OCH_3)CH_2$), 90343-25-2; 1 (R = $CH_3OCH_2CH(OCH_3)CH_2$), 90343-26-3; 1 (R = $(CH_3OCH_2)_2CH$), 90367-59-2; 1 (R = $(CH_3)_2COHCH_2$), 90367-60-5; 1 (R = *cis*-$CH(OCH_3)CH_2CH_2CH_2CH_2CH$), 29863-11-4; 1 (R = $CH_3OCH_2CH_2$), 40982-05-6; 1 (R = $(C_2H_5O)_2CHCH_2$), 54195-50-5; 1 (R = $HOCH_2CH_2$), 15218-81-2; **2**, 37824-55-8; $CH_2{=}CHCH_2CH_2CH_2OH$, 821-09-0; $HOCH_2CH_2OH$, 107-21-1; $CH_2{=}CH_2$, 74-85-1; $CH_3OCH_2CH_2OH$, 109-86-4; $CH_2{=}CHCH_2OH$, 107-18-6; CH_3OH, 67-56-1; $CH_2{=}CHCH_2OCH_3$, 627-40-7; $CH_2{=}C(CH_3)_2$, 115-11-7; $CH{=}CHCH_2CH_2CH_2CH_2$, 110-83-8; $CH_2{=}CHOC_2H_5$, 109-92-2; C_2H_5OH, 64-17-5; cobalt chloride, 7646-79-9; dimethylglyoxime, 95-45-4; (2-bromomethyl)tetrahydrofuran, 1192-30-9; 2-(2-chloroethoxy)ethanol), 628-89-7; 1-(2-chloroethoxy)-2-methoxyethane, 52808-36-3; 1-bromo-2-methoxy-3-propanol, 90321-38-3; 1-chloro-2,3-dimethoxypropane, 34680-56-3; 3-methoxy-1-propene, 627-40-7; 2-bromo-1,3-dimethoxypropane, 90321-39-4; 1-bromo-2,3-dimethoxypropane, 90321-40-7.

Synthesis and Properties of Pinanediol α-Amido Boronic Esters

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The use of (+)-pinanediol as the chiral directing group for the synthesis of several α(*R*)-α-amido boronic esters and acids, which are boronic acid analogues of *N*-acyl-L-amino acids, has been explored. RBO_2Pin (Pin = *cis*-pinane-2,3-diyl) was homologated to (*S*)-$RCHClBO_2Pin$, which was converted to (*R*)-$RCH(NHAc)BO_2Pin$ and, for R = isopropyl, to (*R*)-$RCH(NHCOAc)B(OH)_2$ by previously reported methods. Where R = isobutyl, methyl, or (benzyloxy)methyl, zinc chloride catalysis was required for the homologation step. Two (*S*)-acetamido boronic esters (R = isopropyl, isobutyl) were made from (−)-pinanediol. Acylation of the unstable α-amino boronic ester intermediate with carbobenzyloxy chloride was accomplished in the synthesis of $PhCH_2CH(NHCOOCH_2Ph)BO_2Pin$, but attempted boron trichloride cleavage of the pinanediol boronic ester to the acid also cleaved the benzyloxy group. Hydroboration of allyl halides or allyl benzyl ether with (1,2-phenyldioxy)borane has yielded γ-substituted boronic esters. These were converted to (+)-pinanediol esters and converted by the general route outlined above to α-acetamido δ-substituted boronic esters. (Pinanediyldioxy)borane has been prepared and found to be a sluggish hydroborating agent.

Introduction

Homologation of boronic esters with (dichloromethyl)lithium to form α-chloro boronic esters has been shown to be highly efficient[1] and to result in exceptionally high chiral selectivity if pinanediol is used as the chiral directing group.[2,3] The conversion of (+)-pinanediol (*S*)-1-chloro-2-phenylethane-1-boronate to the corresponding α-acetamido boronic ester and acid has been described.[4,5] This boronic acid analogue of *N*-acetyl-L-phenylalanine has been shown to be a competitive inhibitor of chymotrypsin.[4] In the present study, the use of pinanediol boronic esters as intermediates for the synthesis of other chiral α-amido boronic esters has been explored.

Results

Homologation Conditions. The previously reported route to an α-amido boronic acid[4,5] proved directly applicable to the conversion of (+)-pinanediol 2-propaneboronate (**1a**) to (+)-pinanediol (*S*)-1-chloro-2-methylpropane-1-boronate (**2a**), which with *N*-lithiohexamethyldisilazane yielded the (*R*)-1-[bis(trimethylsilyl)amino]-2-methylpropane-1-boronate (**3a**). Acetic acid and acetic anhydride converted **3a** to (+)-pinanediol (*R*)-1-acetamido-2-methylpropane-1-boronate (**4a**), the first intermediate in the sequence that was isolated and characterized. The need for the silylated intermediate in order to circumvent the instability of α-amino boronic esters has been discussed previously.[5]

Cleavage of the pinanediol group with boron trichloride[2] completed the route synthesis of (*R*)-(−)-1-acetamido-2-methylpropane-1-boronic acid (**5a**), the boronic acid analogue of *N*-acetylvaline. Philipp and Maripuri have found that this compound is a moderately active inhibitor of elastase.[6] (−)-Pinanediol (*S*)-1-acetamido-2-methylpropane-1-boronate, the enantiomer of **4a**, was also prepared. Philipp and Maripuri have found that equilibration with aqueous boric acid removes the pinanediol satisfactorily for purposes of testing for enzyme inhibition and have found the resulting boronic acid to be a good inhibitor of penicillinase.[7]

In sharp contrast to the easy synthesis of **2a**, homologation of (+)-pinanediol 2-methylpropane-1-boronate (**1b**) with (dichloromethyl)lithium yielded only 15–33% of (+)-pinanediol (*S*)-1-chloro-3-methylpropane-1-boronate (**2b**), which was isolated by chromatography. Conversion

(1) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588–7590. (b) Matteson, D. S.; Majumdar, D. *Organometallics* **1983**, *2*, 1529–1535.
(2) (a) Matteson, D. S.; Ray, R. *J. Am. Chem. Soc.* **1980**, *102*, 7590–7591. (b) Matteson, D. S.; Ray, R.; Rocks, R. R.; Tsai, D. J. S. *Organometallics* **1983**, *2*, 1536–1543.
(3) (a) Matteson, D. S.; Sadhu, K. M. *J. Am. Chem. Soc.* **1983**, *105*, 2077–2078. (b) Matteson, D. S.; Sadhu, K. M., manuscript in preparation.
(4) Matteson, D. S.; Sadhu, K. M.; Lienhard, G. E. *J. Am. Chem. Soc.* **1981**, *103*, 5241–5242.
(5) Matteson, D. S.; Sadhu, K. M. *Organometallics* **1984**, *3*, 614–618.
(6) Philipp, M.; Maripuri, S., manuscript in preparation.
(7) Philipp, M.; Maripuri, S.; Matteson, D. S.; Jesthi, P. K.; Sadhu, K. M. *Biochemistry* **1983**, *22*, A13. (*S*)-1-Acetamido-3-methylbutane-1-boronic acid, the enantiomer of **5b**, has $K_i = 44 \times 10^{-6}$ M with *Bacillus cereus* β-lactamase at pH 7.

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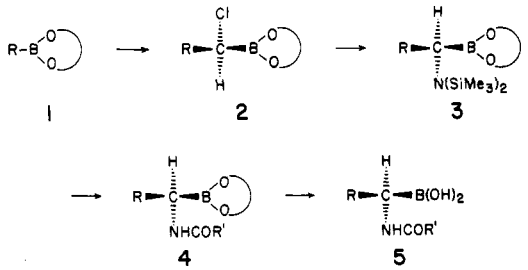
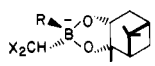


R: **a**, $(CH_3)_2CH$; **b**, $(CH_3)_2CHCH_2$; **c**, CH_3; **d**, $PhCH_2OCH_2$; **e**, $PhCH_2$

R': **a**, **b**, **c**, CH_3; **e**, OCH_2Ph

of this compound to the corresponding (*R*)-1-acetamido-3-methylbutane-1-boronic ester **4b** was straightforward. The enantiomer of **4b** proved to be a better inhibitor of penicillinase than that of **4a**.[7]

The difficulty with the homologation of **1b** promoted testing a variety of alternative conditions. One of these, starting from (+)-pinanediol dichloromethaneboronate and treating with isobutylmagnesium bromide, gave a good chemical yield with poor chiral selectivity for the opposite α-carbon configuration and has been reported previously.[8] Another approach was to isolate the intermediate borate salt **6b**-Cl and try a variety of conditions for its rearrangement. Alternatively, the corresponding bromo intermediate **6b**-Br was synthesized from (dibromomethyl)lithium, generated in situ from lithium dicyclohexylamide and dibromomethane.[9] However, attempts to purify either salt **6b** failed, and attempted rearrangements were accompanied by extensive decomposition, as found with the original conditions. Also explored briefly was the in situ generation of the (dihalomethyl)lithiums[9] in the presence of pinanediol benzylboronate (**1e**), which readily yielded 55–65% of the corresponding 1-chloro- and 1-bromo-2-phenylethaneboronates **2e** and **2e**-Br, based on 60-MHz NMR evidence.



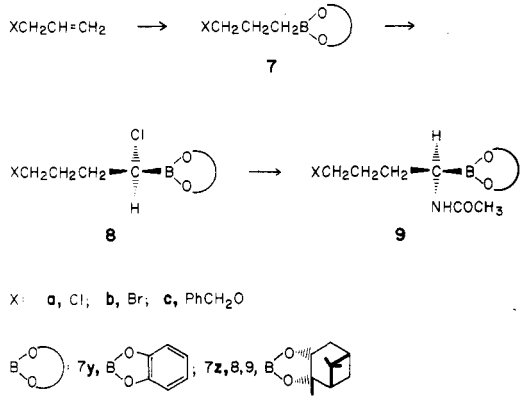
6

Mercuric chloride (1 equiv) was tested as a possible catalyst for the homologation but had essentially no effect on the yield of **2b**. Zinc chloride catalysis has dramatically improved the yield and diastereomeric purity of **2b** from this reaction.[3] Conversion of **2b** to (+)-pinanediol 1-acetamido-3-methylbutane-1-boronate (**4b**) was carried out in the usual manner.[4,5] The diastereomer content was 11% when zinc chloride catalysis was not used, as judged from the relative magnitudes of the well-separated NH peaks in the NMR.[8]

Failure of pinanediol (benzyloxy)methaneboronate (**1d**) to undergo homologation with (dichloromethyl)lithium has been reported[2b] and rechecked. With zinc chloride catalysis, this transformation to **2d** has been readily accomplished. NMR spectra of the chloro compound or its crude acetamido derivative have not provided any positive evidence for a second diastereomer, and the isomer ratio is therefore not established.

Acylation with an Acyl Halide. The synthesis of (+)-pinanediol (*R*)-1-[(carbobenzyloxy)amido]-2-phenylethane-1-boronate (**4e**) was accomplished in the same manner as that of the acetamido analogue **3** except that the desilyation of **3e** was carried out with a single equivalent of methanol and the (still half-silylated) amino boronic ester intermediate was acylated with carbobenzyloxy chloride (and no base).[10] An attempt to cleave the pinanediol group from **4e** with boron trichloride[2] resulted in debenzylation as well, and the resulting 1-amino-2-phenylethane-1-boronic acid decomposed as previously observed[4,5] to yield 2-phenylethylamine.

α-Amido δ-Substituted Boronic Esters. These were chosen as possible precursors to boronic acid analogues of arginine and proline. The synthetic route begins with hydroboration of an allyl halide[11] or allyl benzyl ether with catecholborane[12] to yield a γ-substituted boronic ester **7y**.



X: **a**, Cl; **b**, Br; **c**, $PhCH_2O$

This step proved straightforward and efficient, except that a substantial proportion of catechol 1-propaneboronate (10–15%) was formed as a byproduct of hydroboration of the allyl halides, as shown by the 200-MHz NMR spectrum of the bromo compound **7by**, and was not removed by simple distillation. It is not clear whether this byproduct is the result of lack of regioselectivity in the hydroboration,[11] followed by β elimination of boron and halide and rehydroboration of the propylene before it can escape or whether some other reduction mechanism is involved. In the exploratory work that was carried out, no attempt was made to remove this contaminant before proceeding with the subsequent steps of the synthesis.

Transesterification of the catechol esters **7y** with (+)-pinanediol to form the pinanediol esters **7z** has a favorable equilibrium constant and proceeds readily. Homologation of **7z** with (dichloromethyl)lithium and zinc chloride catalysis[3] yielded 68–80% of the α-chloro boronic esters **8**. Without zinc chloride catalysis, the yield of δ-benzyloxy product was ~35% and of δ-halo products zero. Conversion to the α-acetamido boronic esters by treatment with *N*-lithiohexamethyldisilazane followed by acetic acid and acetic anhydride yielded the α-acetamido boronic esters **9**.

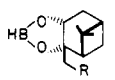
The purity of the crude δ-halo α-amido boronic esters (**9a** and **9b**) obtained at this point was generally ~90% as measured by the relative integrals of the larger and smaller of the two NH peaks in the NMR spectra. In view of the lack of regiospecificity in the hydroboration step, it appears likely that the second NH results from contamination by α-acetamidobutaneboronic ester. Similar impurity in the δ-benzyloxy compound could be regioi-

(8) Tsai, D. J. S.; Jesthi, P. K.; Matteson, D. S. *Organometallics* **1983**, *2*, 1543–1545.
(9) Taguchi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1974**, *96*, 3010–3011.
(10) Benzoyl chloride under similar conditions efficiently acylates a partially silylated aminoethaneboric ester: Lindquist, R. N.; Amiri, P.; Matteson, D. S.; Sadhu, K. M., manuscript in preparation.
(11) Hawthorne, M. F.; Dupont, J. A. *J. Am. Chem. Soc.* **1958**, *80*, 5830.
(12) Brown, H. C; Gupta, S. K. *J. Am. Chem. Soc.* **1971**, *93*, 1816–1818.

somer, though in view of our failure to achieve analytical purity, other contaminants might also be present. The expected ~1% or less of minor diastereomer,[3] which would also be likely to give rise to a separate NH peak,[8] was not detected. Distillation or crystallization of the δ-halo α-acetamido boronic esters (**9a,b**) provided pure samples.

In an attempt to cleave the pinanediol from the 4-(benzyloxy)-1-acetamidobutane-1-boronic ester **9c** with boron trichloride in the manner previously described,[2] it appeared that the benzyloxy group was also cleaved. Attempted purification of the resulting δ-hydroxy boronic acid was unsuccessful.

((+)-Pinanediyldioxy)borane (10a). In the hope that pinanediol 3-halo- or 3-(benzyloxy)propane-1-boronates (**7z**) could be made in one step, ((+)-pinanediyldioxy)borane (**10a**) was prepared from borane methyl sulfide and pinanediol. This compound was stable and easily handled, but it proved to be an inefficient hydroborating agent, requiring high temperatures and long reaction times to provide poor yields of 7z. We have also prepared {[2-(2-methoxyethyl)-6,6-dimethylbicyclo[3.1.1]heptane-2,3-diyl]dioxy}borane (**10b**), but in view of the poor results with **10a**, we have not tested it as a hydroborating agent.



a, R = H

b, enantiomer, R = CH_2OCH_3

Conclusions

This work establishes some generality as well as limitations in the use of (+)-pinanediol boronic esters in the directed chiral synthesis of (*R*)-α-amido boronic acids, which are boronic acid analogues of natural *N*-acyl-L-amino acids. The synthesis previously outlined for the *N*-acetylphenylalanine analogue[4,5] appears generally applicable, especially with the aid of zinc chloride catalysis for making the α-chloro boronic ester intermediates.[3] D-Amino acid analogues are readily available through the use of (−)-pinanediol. A good method for making a (carbobenzyloxy)amido boronic ester has been found, but unfortunately the benzyloxy group is cleaved by boron trichloride under the conditions needed to convert the pinanediol ester to the free boronic acid, and the need for a more readily hydrolyzable chiral directing group than pinanediol is indicated. γ-Halo or γ-alkoxy boronic esters can be made by hydroboration of appropriate allyl compounds with (1,2-phenyldioxy)borane, transesterified with pinanediol, and homologated to δ-halo or δ-alkoxy α-chloro boronic esters, from which the α-halide can be displaced selectively. (Pinanediyldioxy)borane has been synthesized but is not a useful hydroborating agent.

Experimental Section

General Data. The techniques for preparing (dichloromethyl)lithium and carrying out homologations of boronic esters have been described in detail elsewhere.[1-5] Proton NMR spectra were obtained at 200 MHz with a Nicolet NT-200 instrument or at 60 MHz with a Varian EM-360. Melting points were taken on a Fisher-Johns melting point block and are uncorrected. The (+)-pinanediol used was 92% enantiomeric excess except where 100% is specified. Microanalyses were by Galbraith Laboratories, Knoxville, TN.

(+)-Pinanediol 2-Propaneboronate (1a). This compound was prepared from 2-propaneboronic acid and optically pure potassium (+)-pinanediol borate in the manner previously described for analogous compounds:[2] bp 86 °C (0.25 torr); $[\alpha]^{26}_{546}$ +52.0° (*c* 3.2, toluene); 200-MHz NMR ($CDCl_3$) δ 0.84 (s, 3, CH_3), 0.95–1.21 (m, 8, isopropyl + pinanyl CH), 1.29 (s, 3, CH_3), 1.38 (s, 3, CH_3), 1.77–2.42 (m, 5, pinanyl), 4.25 (dd, 1, CHOB). Anal. Calcd for $C_{13}H_{23}BO_2$: C, 70.29; H, 10.44; B, 4.87. Found: C, 70.17; H, 10.41; B, 5.05.

(+)-Pinanediol (*R*)-1-Acetamido-2-methylpropane-1-boronate (4a). (+)-Propanediol 2-propaneboronate (100% ee) was treated with (dichloromethyl)lithium under the previously described conditions,[2] and the crude α-chloro boronic ester **2a** was treated first with lithiohexamethyldisilazane and then with 1 mol of acetic acid and 3 mol of acetic anhydride in the described manner.[4,5] The crude **4a** was chromatographed on silica gel, eluted with ether, 56%, and recrystallized twice from dichloromethane: mp 145–147 °C; $[\alpha]^{26}_{546}$ −20.5° (*c* 4.5, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.86 (s, 3, CH_3), 0.95 + 0.99 (d + d, 6, diastereotopic CH_3's), 1.27 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.42 (d, 1), 1.78–2.57 (m, 10), 4.22 (dd, 1, CHOB), 7.78 (br s, 1, NH). Anal. Calcd for $C_{16}H_{28}BNO_3$: C, 65.54; H, 9.62; B, 3.69; N, 4.78. Found: C, 65.13; H, 9.43; B, 3.48; N, 4.81.

(*R*)-1-Acetamido-2-methylpropane-1-boronic Acid (5a). Approximately 2 g of boron trichloride was condensed at −78 °C, and 0.924 g (3.1 mmol) of **4a** in 15 mL of dichloromethane was added dropwise from a syringe. The mixture was kept 25 min at ~20 °C (darkening occurred) and concentrated under vacuum. The solid residue was washed with ether (3 × 15 mL), dissolved in water (15 mL), washed with petroleum ether (4 × 5 mL), and treated with excess Dowex-8 ion-exchange resin bicarbonate until the solution was free of chloride as shown by silver nitrate. The solution was filtered and lyophilized. The solid was dissolved in methanol, and the methanol was distilled to remove methyl borate as the azeotrope. The residue was recrystallized from THF–water to yield 0.35 g (71%) of **5a**: mp 125–126 °C; $[\alpha]^{18.5}_{546}$ −93.6° (*c* 2.7, H_2O); 200-MHz NMR (CD_3OD) δ 0.93 (m, 6, diastereotopic CH_3's), 1.75 (m, 1, $CH(CH_3)_2$), 2.15 (s + m, 4, CH_3CO + NCHB), 4.9 (s, 2, OH). Anal. Calcd for $C_6H_{14}BNO_3$: C, 45.32; H, 8.87; B, 6.80; N, 8.81. Found: C, 45.20; H, 8.63; B, 6.95; N, 8.72.

(+)-Pinanediol 1-Chloro-3-methylbutane-1-boronate (2b). (+)-Pinanediol 2-methylpropane-1-boronate[13] (2.4 g, 10 mmol) in 5 mL of THF was added to 11 mmol of (dichloromethyl)lithium at −100 °C in 25 mL of THF, and the mixture was allowed to warm to 20–25 °C and stirred overnight. Direct distillation of the reaction mixture under vacuum[1] in a Kugelrohr at ~80–90 °C yielded 15–33% of **2b** together with 25–35% of unchanged 2-methylpropane-1-boronate and ~20% of unsaturated byproduct as judged from the 60-MHz NMR spectrum. Purification of **2b** was achieved by HPLC (5% ether/hexane, Waters Prep 500A instrument) (the zinc chloride catalyzed process[3] has subsequently given **2b** in high yields): 200-MHz NMR ($CDCl_3$) δ 0.79 (s, 3, CH_3), 0.83 + 0.87 (d's overlapping to appear as t, 6, diastereotopic $(CH_3)_2CH$), 1.12 (d, J = 11 Hz, 1, pinanyl), 1.18 (s, impurity), 1.23 (s, 3, CH_3), 1.34 (s, 3, CH_3), 1.5–1.8 (m, 3, $CHCH_2$), 1.8–2.3 (m, 5, pinanyl), 3.47 (m, 1, ClCHB), 4.29 (dd, 1, CHOB). Anal. Calcd for $C_{15}H_{26}BClO_2$: C, 63.30; H, 9.21; B, 3.80; Cl, 12.46. Found: C, 63.31; H, 9.16; B, 3.97; Cl, 12.49.

(+)-Pinanediol 1-Acetamido-3-methylbutane-1-boronate (4b). The preparation of **2b** was carried out as described in the preceding paragraph, but instead of distilling the product, the THF solution of **2b** was cooled to −78 °C and treated with an equivalent amount of *N*-lithiohexamethyldisilazane. The mixture was allowed to warm to 20–25 °C for 12 h, then cooled again to −78 °C, and treated with 3 equiv of acetic anhydride and 1 equiv of acetic acid. After overnight at 20–25 °C, the solution was concentrated and the product **4b** was isolated by chromatography on silica, 25–35%, and recrystallized from dichloromethane/hexane: mp 129–131 °C (low due to diastereomeric impurity, see enantiomer below); $[\alpha]^{23}_{546}$ −34.2° (low) (*c* 0.8, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.85 (s, 3, CH_3), 0.87 (m, 6, $(CH_3)_2CH$), 1.26 (s, 3, CH_3), 1.39 (s, 3, CH_3), 1.3–2.4 (m, pinanyl and CH_2CH), 2.05 (s, 3, $COCH_3$), 2.66 (t, 1, NCHB), 4.18 (dd, 1, CHOB), 7.68 + 8.38 (s + s, each 18–20 Hz wide at half-height, ratio 11.3/88.7 in crude sample, NH). The analysis for **4b** was reported previously.[8,14] The enantiomer of **4b** was prepared from enantiomerically purified (−)-pinanediol via the improved route with zinc chloride: mp 152–154 °C, $[\alpha]^{23}_{546}$ +53.9° (*c* 0.8, $CHCl_3$).

(*R*)-1-Acetamido-3-methylbutane-1-boronic Acid (5b). The procedure used for the preparation of **5a** was followed, starting from **4a**: 200-MHz NMR (D_2O) (methanol, δ 3.30 as internal

(13) Tsai, D. J. S.; Matteson, D. S. *Organometallics* **1983**, *2*, 236–241.

(14) Figures[8] were for the presently reported sample of **4b**, and the gross epimeric mixture[8] also yielded C, H, B, and N within 0.4%.

Table I. Properties of 3-Substituted Propaneboronic Esters

compd	bp, °C (torr)	yield,[a] %	NMR,[b] δ XCH_2	NMR,[b] δ CCH_2	NMR,[b] δ BCH_2	anal. calcd (found) C	H	B	Cl or Br
7ay	85–87 (0.4)	78	3.5	2.0	1.35	55.02 (55.29)	5.09 (5.20)	5.50 (5.57)	18.08 (16.98)
7by	110–112 (0.2)	84	3.5	2.25	1.5	44.85 (45.07)	4.15 (4.32)	4.48 (4.29)	33.23 (32.89)
7cy	150–160 (0.5)	83	3.6	2.05	1.35	71.69 (71.46)	6.35 (6.18)	4.03 (4.03)	
7az	110–115 (0.3)	73	3.6	2.0	1.0	60.87 (61.30)	8.58 (8.90)	4.21 (4.19)	13.85 (13.74)
7bz	135–139 (0.2)	73	3.35	2.0	1.0	51.86 (52.13)	7.31 (7.38)	3.59 (3.59)	26.60 (26.49)
7cz	160–165 (0.1)	68	3.5	2.0	1.1	73.22 (73.08)	8.85 (9.12)	3.29 (3.82)	

[a] For **7y**, by hydroboration; for **7z**, by transesterification. See text. [b] 60 MHz, carbon tetrachloride, external Me_4Si. Appropriate multiplicities were observed, as well as peaks corresponding to the catechol (**7y**) or pinanediol (**7z**) groups. For 200-MHz spectrum of **7by**, see text. The CCH_2C and BCH_2 of **7z** were partially obscured by the pinanyl peaks.

standard) δ 0.85 (m, 6, diastereotopic (CH_3)$_2$CH), 1.24 (m, 2, CHCH_2CH), 1.55 (m, 1, CCH(CH_3)$_2$), 1.96 (s, impurity), 2.09 (s, 3, COCH_3), 2.58 (t, 1, NCHB), 3.30 (s, ~4, CH_3OH) 4.80 (s, DOH). The analysis suggested the presence of some inert material. Anal. Calcd for $C_7H_{16}BNO_3$: C, 48.59; H, 9.32; B, 6.25; N, 8.10. Found: C, 45.49; H, 8.97; B, 5.10; N, 7.41.

Attempted Isolation of (Pinanediyldioxy)isobutyl(dibromomethyl)borate (6b-Br). Treatment of a solution of pinanediol 2-methylpropane-1-boronate (**2b**) and dibromomethane in THF with lithium diisopropylamide or dicyclohexylamide at −78 °C in accord with the previously described procedure[1,9] resulted in precipitation of a white solid, which did not dissolve at 20 °C. Analysis indicated the presence of C, H, B, Br, and Li, with the composition suggestive of a solvate or amine complex of **6b**-Br possibly mixed with B- but not Br-containing salt. Heating this material under vacuum yielded essentially no α-bromo boronic ester. The analogously prepared chloro compound (**6b**-Cl) appeared to be somewhat unstable at 20 °C and on destructive distillation under vacuum[1] yielded ~30% of **2b**.

(+)-Pinanediol (*R*)-1-Acetamidoethaneboronate (4c). (+)-Pinanediol (*S*)-1-chloroethaneboronate (**2c**) was prepared from (+)-pinanediol methaneboronate (92% ee) by the zinc chloride catalyzed process.[3] Treatment of 1.42 g (5.8 mmol) of **2c** with *N*-lithiohexamethyldisilazane followed by acetic acid/acetic anhydride according to the procedure described for **2a** yielded 1.46 g (95%) of **4c**. The 200-MHz NMR analysis of the crude product indicated that the content of *S* epimer was 4%, based on the integrals of the partially overlapping NH peaks. After recrystallization from dichloromethane: mp 197–198 °C; $[\alpha]^{121}_{546}$ −25.5° (*c* 2.9, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.83–2.6 (m, 16, pinanyl + BCHN), 1.10 (d, 3, CH_3), 2.03 (s, 3, CH_3CO), 4.16 (dd, 1, CHOB), 9.73 (br s, 1, NH). Anal. Calcd for $C_{14}H_{24}BNO_3$: C, 63.41; H, 9.12; B, 4.08; N, 5.28. Found: C, 63.25; H, 9.34; B, 4.17; N, 5.41.

(+)-Pinanediol 2-(Benzyloxy)-1-chloroethane-1-boronate (2d). This compound was obtained in 69% yield by application of the previously described procedure utilizing zinc chloride catalysis[3] to homologation of 2.5 mmol of (+)-pinanediol (benzyloxy)methaneboronate (**1d**). The analytical sample was obtained by chromatography on a silica gel plate with 10% ether/hexane: 200-MHz NMR ($CDCl_3$) δ 0.87 (s, 3, CH_3), 1.21 (d, 1, pinanyl), 1.31 (s, 3, CH_3), 1.43 (3, S, CH_3), 1.9–2.2 (m, 5, pinanyl), 3.66 (m, 1, ClCHB), 3.81 (m, 2, OCH_2CH), 4.36 (dd, 1, CHOB), 4.60 (s, 2, PhCH_2O), 7.34 (m, 5, C_6H_5). The crude material showed impurity peaks at δ 3.34 and 4.53. Anal. Calcd for $C_{19}H_{26}BClO_3$: C, 65.45; H, 7.52; B, 3.10; Cl, 10.17. Found: C, 65.74; H, 7.51; B, 3.06; Cl, 10.13.

(+)-Pinanediol 1-[(Carbobenzyloxy)amido]-2-phenylethane-1-boronate (4e). (+)-Pinanediol (*S*)-1-chloro-2-phenylethane-1-boronate (**2e**)[4,5] (7.98 g, 25 mmol) in THF (20 mL) at −78 °C was treated with 26 mmol of *N*-lithiohexamethyldisilazane in THF (15 mL). After being stirred overnight at 20 °C, the resulting solution of pinanediol 1-[bis(trimethylsilyl)amino]-2-phenylethane-1-boronate (**3e**)[15] was cooled to −78 °C, treated with 26 mmol of methanol, stirred 1.5 h at −78 °C, and treated with 3.9 mL (4.7 g, 27 mmol) of carbobenzyloxy chloride. After 14 h at 20 °C, the solution was concentrated to yield a 7.8-g residue of crude **4e** (72%). The material remained a gum even after purification by chromatography on silica gel with 20% ethyl acetate in hexane: $[\alpha]^{27}_{546}$ +15.6° (*c* 2, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.75 (s, 3, CH_3), 1.05 (d, *J* = 11 Hz, 1, pinanyl), 1.20 (s, 3, CH_3), 1.24 (s, 3, CH_3), impurity at 1.30 (s), 1.7-2.3 (m, 5, pinanyl), 2.80 (m, 1, CHCH*H*), 2.96 (m, 1, CHC*H*H), 3.37 (m, 1, C*H*CHH), impurity at 3.70 (s), 4.25 (dd, 1, C*H*OB), 4.85 (d, 1, N*H*), 5.00 + 5.02 with satellites (2, PhCH_2O), 7.1-7.25 (m, 10, C_6H_5). Anal. Calcd for $C_{26}H_{32}BNO_4$: C, 72.06; H, 7.44; B, 2.49; N, 3.23. Found: C, 72.14; H, 7.26; B, 2.38; N, 3.26.

(+)-Pinanediol 1-Halo-2-phenylethaneboronates (2e-Cl and -Br). Pinanediol benzylboronate (**1e**) and dichloromethane in dimethoxyethane at −78 °C were treated with lithium diisopropylamide according to the previously described "method B" for homologation of pinacol boronic esters.[1] After 2–3 h at 20 °C, the mixture was distilled to yield 55% of **2e**-Cl,[3-5] bp 120–140 °C (0.3 torr). A similar procedure with dibromomethane yielded 50% of **2e-Br**, bp 170–180 °C, or with dibromomethane and lithium dicyclohexylamide,[9] 65% of **2e**-Br. The 60-MHz NMR spectra of the chloro and bromo compounds were essentially the same except for differing details in the δ 3.0–3.5 region (CH_2C*H*X).

3-Substituted Propane-1-boronic Esters (7). Equivalent amounts of (phenyldioxy)borane and allyl chloride, allyl bromide, or allyl benzyl ether were heated under reflux 4 h with a bath at 100 °C for the halides or 120–130 °C for the ether. Distillation yielded the catechol esters **7y** with the properties summarized in Table I. For catechol 3-bromopropane-1-boronate (**7by**): 200-MHz NMR ($CDCl_3$) δ 1.43 (t, 2, BCH_2), 2.17 (m, 2, CCH_2), 3.49 (t, 2, BrCH_2), 7.05 + 7.17 (m, 4, C_6H_4), with the presence of 10 mol % of catechol 1-propaneboronate indicated by absorptions at δ 1.03 (t, 0.33, CH_3), 1.27 (broadened t, BCH_2), and 1.65 (m, CCH_2C).[16] Transesterification with (+)-pinanediol (92% ee) was accomplished by mixing equivalent amounts of the catechol ester **7y** and pinanediol in THF, concentration, chromatography on silica with ether/hexane to separate the catechol, and distillation. Properties of the pinanediol esters (**7z**) are also listed in Table I. Rotations: **7bz**, $[\alpha]^{27}_{546}$ +21.9° (*c* 3, $CHCl_3$); **7cz**, $[\alpha]^{26}$ +22.3° (*c* 2, $CHCl_3$); both are 92% ee. Direct synthesis of **7bz** from allyl bromide and (pinanediyldioxy)borane required 48-h reflux and only yielded 35% of **7bz**. Allyl benzyl ether and pinanediyldioxy)borane 24 h at 140–150 °C yielded 60% of **7cz**.

Pinanediol 4-Halo-1-acetamidobutane-1-boronates (9). Reaction of a 10-mmol sample of **7z** with 1 equiv of (dichloromethyl)lithium at −100 °C was carried out according to the previously published procedure,[1,2] and 5 mmol of zinc chloride was added before the solution was allowed to warm to room temperature overnight.[3] The mixture was concentrated and worked up with water and petroleum ether and the organic phase concentrated to yield crude **8**, which was then treated with *N*-lithiohexamethyldisilazane in THF at −78 °C.[4,5] The mixture was then warmed to 20 °C, cooled again to −78 °C, and treated with 3 equiv of acetic anhydride and 1 equiv of acetic acid, and the product was isolated in the manner described previously.[4] After partial concentration of the 20% ether/hexane used for chromatography the chloro compound **9a** crystallized: 68%; mp 56–58 °C, $[\alpha]^{29}_{546}$ −29.0° (*c* 0.4, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.8–2.5 (m, pinanediol + other), 3.55 (t, 2, ClCH_2), 4.2 (dd, 1, CHOB), 9.35 (br s, 1, NH). Anal. Calcd for $C_{16}H_{27}BClNO_3$: C, 58.65, H,

(15) Distillation of **3e**, bp 180–190 °C (0.3 torr), resulted in solidification, mp 193–195 °C, but no further characterization has been carried out.

(16) An authentic sample of catechol propaneboronate was not conveniently available, but an NMR spectrum of butaneboronic acid esterified with catechol was consistent with these assignments.

8.31; B, 3.30; Cl, 10.82; N, 4.27. Found: C, 58.52; H, 8.01; B, 3.35; Cl, 10.24; N, 4.09. Bromo compound **9b** (74%): mp 62–65 °C, $[\alpha]^{30}_{546}$ −37.1° (c 0.9, $CHCl_3$); 200-MHz NMR ($CDCl_3$) δ 0.75–2.5 (m, pinanediol + other), 3.45 (t, 2, $BrCH_2$), 4.2 (dd, 1, CHOB), 9.20 (br s, 1, NH). Anal. Calcd for $C_{16}H_{27}BBrNO_3$: C, 51.64; H, 7.31; B, 2.91; Br, 21.47; N, 3.76. Found: C, 51.76; H, 7.30; B, 2.98; Br, 21.32; N, 3.82.

Attempted Preparation of 1-Acetamido-4-hydroxybutane-1-boronic Acid. Homologation of (+)-pinanediol 3-(benzyloxy)propane-1-boronate (**7cz**) followed by conversion to the α-acetamido boronic ester **9c** was carried out as described for the halogen compounds in the preceding paragraph, but **9c** was not obtained analytically pure. Treatment with boron trichloride in dichloromethane[2] yielded a residue which was recrystallized from water. The 200-MHz NMR spectrum corresponded to 1-acetamido-2-phenylethane-1-boronic acid (D_2O, no internal ref): δ 1.35 (m, 2, CH_2CHB), 1.46 (m, 2, $CH_2CH_2CH_2$), 2.01 (s, 3, CH_3), 2.46 (t, 1, NCHB), 3.52 (m, 2, OCH_2), 4.724 (s, HOD), with small impurity peaks at δ 1.84 and 1.93. The analysis corresponded approximately to cocrystallization with 2 mol of boric acid. Anal. Calcd for $C_6H_{20}B_3NO_{10}$: C, 24.13; H, 6.75; B, 10.86; N, 4.69. Found: C, 23.42; H, 6.21; B, 10.46; N, 4.59.

((+)-Pinanediyldioxy)borane (10a). A solution of 17.0 g (10 mmol) of (+)-pinanediol in ~25 mL of THF was added dropwise to a solution of 7.6 g (10 mmol) of borane methyl sulfide in 25 mL of THF stirred under argon at 0 °C. The mixture was stirred at 20–25 °C for 2 h and then distilled to yield 78% of **10a**: bp 60–62 °C (0.2 torr); 200-MHz NMR ($CDCl_3$) δ 0.87 (s, 3, CH_3), 1.13 (d, J = 11 Hz, pinanyl CH), 1.30 (s, 3, CH_3), 1.40 (s, 3, CH_3), 1.8–2.4 (m, 5, pinanyl), 4.28 (dd, 1, CHOB), ~4–5 (very broad, visible only in integral, 1, B*H*). Anal. Calcd for $C_{10}H_{17}BO_2$: C, 66.71; H, 9.52; B, 6.00. Found: C, 67.09; H, 9.79; B, 6.17.

{[2-(2-Methoxyethyl)-6,6-dimethylbicyclo[3.1.1]heptane-2,3-diyl]dioxy}borane (10b). This compound was prepared from nopoldiol methyl ether[17] in the same manner as the pinanediol analogue **10a**, yield of **10b** 77%: bp 61–63 °C (0.2 torr); 200-MHz NMR ($CDCl_3$) δ 0.87 (s, 3, CH_3), 1.13 (d, J = 11 Hz, 1), 1.28 (s, 3, CH_3), 1.8–2.4 (m, 7), 3.32 (s, 3, OCH_3), 3.51 (t, 2, OCH_2CH_2), 4.46 (dd, 1, CHOB), ~4–5 (br, visible only in integral, 1, BH). Anal. Calcd for $C_{18}H_{21}BO_3$: C, 64.31; H, 9.45; B, 4.82. Found: C, 64.09; H, 9.46; B, 4.99.

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Registry No. **1a**, 90084-26-7; **1b**, 84110-34-9; **1c**, 84110-38-3; **1d**, 87190-25-8; **1e**, 78922-83-5; **2a**, 89618-77-9; **2b**, 85167-14-2; **2c**, 85167-12-0; **2d**, 90084-27-8; **2e**, 78902-03-1; **2e-Br**, 90084-28-9; **3e**, 78902-04-2; **4a**, 90084-29-0; **4b**, 87304-49-2; **4c**, 87249-62-5; **4e**, 90084-30-3; **5a**, 90084-31-4; **5b**, 90084-32-5; **6b** (X = Br), 90065-84-2; **6b** (X = Cl), 90191-39-2; **7ay**, 90084-33-6; **7az**, 90084-36-9; **7by**, 90084-34-7; **7bz**, 90084-37-0; **7cy**, 90084-35-8; **7cz**, 90084-38-1; **8a**, 90084-39-2; **8b**, 90084-40-5; **9a**, 90084-41-6; **9b**, 90084-42-7; **10a**, 90084-43-8; **10b**, 90084-44-9; $ClCH_2CH{=}CH_2$, 107-05-1; $BrCH_2CH{=}CH_2$, 106-95-6; $PhCH_2OCH_2CH{=}CH_2$, 14593-43-2; 2-propaneboronic acid, 80041-89-0; potassium (+)-pinanediol borate, 90130-50-0; lithiohexamethyldisilazane, 4039-32-1; (1,2-phenyldioxy)borane, 274-07-7; carbobenzyloxy chloride, 501-53-1.

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Molecular Structure and Chemical Properties of $[Et_4N][(Ph_3Sn)_3Cr(CO)_4]$, a Chromium Carbonyl Complex Containing Seven Unidentate Ligands

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The X-ray structure of $[Et_4N][(Ph_3Sn)_3Cr(CO)_4]$ shows the presence of seven-coordinate chromium bound to four terminal carbonyl groups and three triphenyltin units. The anion is of approximate C_{3v} symmetry; a triangular face of tin atoms is capped by a carbon monoxide unit. This is the first structurally characterized chromium carbonyl complex containing seven unidentate ligands and the initial example of a molecule of the general formula $X_3Cr(CO)_4^-$. The crystalline material is triclinic (space group $P\bar{1}$) with cell parameters a = 14.371 (4) Å, b = 20.560 (10) Å, c = 10.730 (5) Å, α = 99.21 (4)°, β = 105.07 (3)°, γ = 83.29 (3)°, V = 3012 (4) Å^3, and Z = 2. Reactions of $(Ph_3Sn)_3Cr(CO)_4^-$ with Ph_3SnLi, MeLi, Ph_3P, and hexamethylphophoramide result in the loss of one triphenyltin group and the formation of moderate to high yields of the six-coordinate anion $(Ph_3Sn)_2Cr(CO)_4^{2-}$.

Introduction

In 1978 we reported that the reaction of $Na_4[Cr(CO)_4]$[1] with excess Ph_3SnCl provided a compound that gave elemental analyses and IR and ^1H NMR spectra consistent with the formulation $[Et_4N][(Ph_3Sn)_3Cr(CO)_4]$.[2,3] At that time, trhe anion in this salt was proposed to be the sole example of a molecule containing a chromium atom attached to seven unidentate ligands. Subsequently, other similar seven-coordinate molecules, including $H_2Cr(P(OMe)_3)_5$,[4] $Cr(CN\text{-}t\text{-}Bu)_7^{2+}$,[5] $H(Ph_3Sn)_3Cr(CO)_3^-$,[6] and $H(Ph_3Sn)_2Cr(CO)_4^-$,[3] have been reported. To verify the seven-coordinate nature of the chromium atom in

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