87190-38-3; 7(BuPhAc), 87190-35-0; 7(c-HxMeH), 3113-98-2; 7-(c-HxMe)(hydrogen phthalate), 87190-40-7; 7(MePhH), 1517-69-7; 7(MePhAc), 16197-92-5; 7(ViBuH), 87247-44-7; 8(BuMeCOPh), 87190-41-8; 8(BuPhAc), 87190-42-9; 8(c-HxMeH), 3113-99-3; 8-(ViBuH), 87247-56-1; 9, 76110-81-1; 10, 74365-65-4; 10 (3-nitrophthalate), 87190-37-2; 11, 76101-96-7; 12, 76155-63-0; 13, 76155-64-1; 14, 76155-51-6; 14(3-nitrophthalate), 87247-45-8; $LiCHCl_2$, 2146-67-0; BCl_3, 10294-34-5; MeBr, 74-83-9; MeLi, 917-54-4; PhBr, 108-86-1; BuBr, 109-65-9; butaneboronic acid, 4426-47-5; benzeneboronic acid, 98-80-6; (+)-pinanediol, 18680-27-8; (−)-pinanediol, 22422-34-0; cyclohexaneboronic acid, 4441-56-9; methaneboronic anhydride, 823-96-1; *anti*-(+)/(+)-sodium bis[(+)-pinanediol] borate, 87248-20-2; *syn*-(+)/(+)-sodium bis-[(+)-pinanediol] borate, 87247-42-5; *anti*-(−)/(−)-sodium bis-[(−)-pinanediol] borate, 87190-20-3; *syn*-(−)/(−)-sodium bis-[(−)-pinanediol borate, 87247-43-6; sodium borate, 14312-40-4; benzoyl chloride, 98-88-4; dibutyl iodomethaneboronate, 13251-29-1; lithium benzyloxide, 15082-42-5; diacetone mannitol, 1707-77-3; (+)-dimethyl L-tartrate, 608-68-4; diethyl L-tartrate, 87-91-2.

Diastereoselection in Reactions of Pinanediol Dichloromethaneboronate

David J. S. Tsai, Pradipta K. Jesthi, and Donald S. Matteson*

Department of Chemistry, Washington State University, Pullman, Washington 99164

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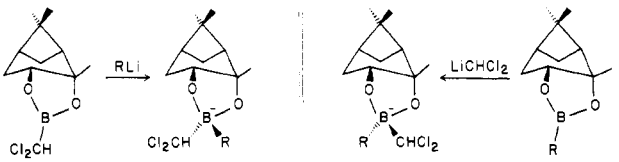
Dichloromethaneboronic acid was converted to its (+)-pinanediol ester (**1**) (92% ee), which was treated with lithium or Grignard reagents to form the corresponding intermediate borate complexes (**2**), diastereomeric with the borates **3** obtained by adding (dichloromethyl)lithium to the corresponding (+)-pinanediol boronic esters. Rearrangement of the lithium *n*-butylborate complex **2a** to the 1-chloropentane-1-boronic esters (**4a** and **5a**) followed by treatment with phenyllithium to form the 1-phenylpentane-1-boronic esters (**6a** and **1a**) and finally oxidation with alkaline hydrogen peroxide yielded predominantly (*R*)-(+)-1-phenyl-1-pentanol (**8r**) (0.92 × 31% ee). This low enantiomeric excess contrasts with the 80% ee obtained previously in a similar sequence from the oppositely assembled borate complex **3a**. Starting with the phenylborate complex **2b**, rearranging, treating with butyllithium, and oxidizing yielded (*S*)-(−)-1-phenyl-1-pentanol (**8s**) (0.92 × 37% ee). The magnesium isobutylborate complex **2c** was rearranged and converted to the 1-acetamido-3-methylbutane-1-boronic esters (**9c** and **10c**), which showed separate NH peaks in the ^1H NMR, ratio 34/66, opposite the stereoselectivity for **2a** and **2b**. Similarly, the methyl complex **2d** yielded a 22/78 ratio of **9d** and **10d**. Zinc chloride catalysis of the rearrangements of **2c** and **2d** yielded **9/10** ratios of 92/8 and 51/49, respectively.

Dichloromethaneboronic esters, $Cl_2CHB(OR')_2$ and alkyllithiums, RLi, have been found by Rathke and coworkers to yield α-chloro boronic esters, $RCHClB(OR')_2$.[1] The reaction must proceed by way of a borate complex, $Cl_2CHB(R)(OR')_2^-$, for which the components R and Cl_2CH can just as well be assembled in the reverse order, from (dichloromethyl)lithium and a boronic ester.[2] We have extended this reaction to pinanediol boronic esters and discovered a new and broadly useful method of directed chiral synthesis.[3-5] Two diastereomeric (+)-pinanediol borate complexes (**2** and **3**) are possible and may give different stereochemical results. In the present work, we have explored the possibility of starting the chiral synthesis from (+)-pinanediol dichloromethaneboronate (**1**). The results have proved disappointing from a practical point of view but do confirm that the diastereomers **2** and **3** behave very differently and that there is a very high degree of kinetic control in the formation of the useful isomer **3** from (dichloromethyl)lithium and (+)-pinanediol alkaneboronates.



1 2 3

Results

Dichloromethaneboronic acid[1] was esterified with (+)-pinanediol (92% ee) to yield **1**. Reaction of **1** with butyllithium to form **2a**, followed by the usual spontaneous rearrangement,[3] yielded a mixture of diastereomeric (+)-pinanediol 1-chloropentane-1-boronates (**4a** and **5a**). For an estimate of the **4a/5a** isomer ratio, the mixture was treated with phenyllithium and the resulting mixture of (+)-pinanediol 1-phenylpentane-1-boronates (**6a** and **7a**) was oxidized to (*R*)- and (*S*)-1-phenyl-1-pentanol (**8r** and **8s**), for which the absolute configuration and rotation have been established.[6] The *R* isomer **8r** was predominant, but

(1) Rathke, M. W.; Chao, E.; Wu, G. *J. Organomet. Chem.* **1976**, *122*, 145–149.
(2) (a) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588–7590. (b) Matteson, D. S.; Majumdar, D. *Organometallics*, preceding paper in this issue.
(3) (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*, preceding paper in this issue.
(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. *J. Am. Chem. Soc.* **1983**, *105*, 2077–2078.
(6) Levene, P. A.; Marker, R. E. *J. Biol. Chem.* **1932**, *97*, 379–391.
(7) Tsai, D. J. S.; Matteson, D. S. *Organometallics* **1983**, *2*, 236–241.

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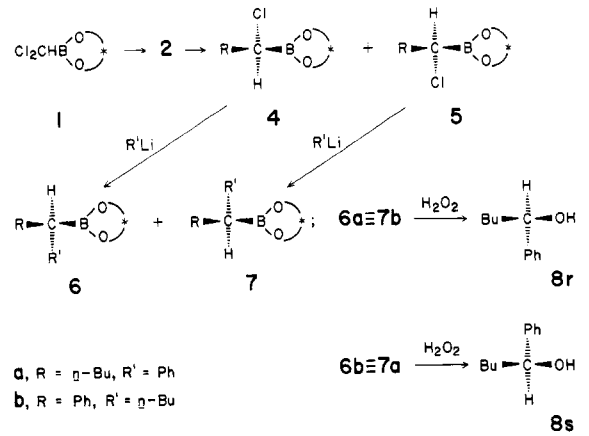
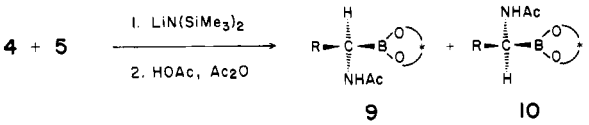
the induced enantiomeric excess (ee) after correcting for the ee of the pinanediol was only 31%.



To check the generality of the result, phenyllithium was added to 1 to form intermediate borate **2b** and then (+)-pinanediol α-chlorobenzylboronate (**4b** and **5b**). Treatment with butyllithium yielded the 1-phenylpentane-1-boronates (**6b** and **7b**), the same products as the first sequence but with R and R′ interchanged. The same ~2:1 diastereoselection was observed, in this case yielding (*S*)-1-phenyl-1-pentanol (**8s**), 37% ee (corrected for pinanediol ee).

Discouraging as these results were, this approach was tried once again when it was found that the yield of (+)-pinanediol (*R*)-1-acetamido-3-methylbutane-1-boronate (**9c**) that could be obtained by the usual route[3] from borate complex **3c** by way of the α-chloro boronic ester **4c** was only 25–35%.[8] The yield of α-chloro boronic esters (**4c** and **5c**) immediately rose to 79% when the route from the



c, R = $(CH_3)_2CHCH_2$; d, R = CH_3

dichloromethaneboronic ester **1** and isobutylmagnesium chloride was tested. The NMR spectra of the acetamido derivatives **9d** and **10c** prepared by either route were similar, except that the two well-separated NH peaks of the crude mixture of **9c** and **10c** typically showed an integral ratio of 89/11 (downfield/upfield) when the material was prepared by way of **3c** but showed a ratio of 34/66 when it was prepared from dichloromethaneboronic ester **1** by way of **2c**. The NH peak positions between δ 7 and 10 were concentration dependent, each moving downfield semiindependently of the other with increasing concentration, but the separation remained substantial (δ 0.5–1) in all cases examined, and mixing samples of different composition yielded the expected pattern. The optical rotations were grossly different: for **9c** and **10c** prepared from **3c**, $[\alpha]^{23}_{546}$ −34°; prepared from **1** via **2c**, $[\alpha]^{17}_{546}$ +31° ($CHCl_3$). Correct elemental analyses were obtained for both mixtures, and the melting point of the 34/66 mixture was 60 degrees lower than that of the 89/11 mixture.

The **9d/10d** ratio was an almost useful 22/78 when methylmagnesium bromide was used to convert **1** to **4d** and **5d**, and these were converted to the acetamido derivatives **9d** and **10d** in the usual manner. The NH peaks of **9d** and **10d** were not separated quite as cleanly as the previous example, but **9d** remained downfield of **10d**. The relationship to these NH peaks has been independently confirmed by the usual determination of the rotation of a derived alcohol from a 96/4 mixture of **4d** and **5d**, the same sample of which was also converted to **9d** and **10d**.[5]

The effect of zinc chloride catalysis[5] on the rearrangement of **2c** and **2d** was then tested. The isobutyl compounds **9c** and **10c** showed a 92/8 diastereomer ratio based on the NH peak integrals. The methyl compounds **9d** and **10d** came out 51/49.

Discussion

Two positive and one negative conclusion can be drawn from the foregoing results. The kinetic selectivity must be high for attack of (dichloromethyl)lithium at the less hindered side of the boron atom in pinanediol boronic esters to yield borate complexes **3** rather than **2**. Structures **2** and **3** are postulated, the exo side of the boron atom obviously being less hindered. If all of the (+)-pinanediol (αR)-α-chlorobenzylboronate (**5b**) byproduct contaminating the αS isomer **4b** were derived from endo (dichloromethyl)borate (**2**) byproduct in the reaction of pinanediol phenylboronate with (dichloromethyl)lithium to form **3**, then the previously observed 97–98% diastereoselectivity in favor of **4b** over **5b**[3] allows no more than ~6–9% formation of **2** as an intermediate. Similarly, the 99.5% diastereoselectivity in the formation of **9c** from **3c** in the zinc chloride catalyzed rearrangement[5] and the 8% formation of **10c** from **2c** under similar conditions are consistent with no more than 6% formation of **2c** from (dichloromethyl)lithium and pinanediol isobutylboronate. Since it is unlikely that the rearrangement of **3** is stereospecific and since rates of epimerization of **4** to **5** are sufficient to account qualitatively for the observed deviations from stereospecificity,[9] the actual amounts of **2** formed from pinanediol boronic esters and (dichloromethyl)lithium are perhaps vanishingly small.

The second positive conclusion is that the NH peaks in the NMR spectra of the respective diastereomers **9** and **10** are, at least in some cases, a convenient means for quantitative estimation of the diastereomer ratio in mixtures of α-chloro boronic esters (**4** and **5**).

The bad news is that pinanediol dichloromethaneboronate (**1**) is not a useful starting material for chiral synthesis. However, it may be noted that boronic ester groups having a C_2 symmetry axis would yield a single borate complex and the order of adding the dichloromethyl and alkyl groups to the boron would not matter. We are searching for suitable chiral boronic ester groups having C_2 symmetry.

Experimental Section

General Data. Previously described techniques for drying tetrahydrofuran (THF), preparing boronic esters, and working under an inert atmosphere were followed.[2,3] Proton NMR spectra were determined at 60 MHz on a Varian EM360 or at 200 MHz on a Nicolet NT 200 instrument. Rotations were determined with a JASCO DIP-181 digital polarimeter. Microanalyses were by Galbraith Laboratories, Knoxville, TN.

(+)-Pinanediol Dichloromethaneboronate (1). Dichloromethaneboronic acid[1] was esterified with (+)-pinanediol (92% enantiomeric excess) in ether according to the usual method:[3] yield of 1, 84%; bp 95–96 °C (0.6 torr); ^{1}H NMR (60 MHz, $CDCl_3$) δ 0.7–2.8 (m, 15), 4.58 (dd, 1, CHOB), 5.50 (s, 1, $CHCl_2$). Anal. Calcd for $C_{11}H_{17}BCl_2O_2$: C, 50.24; H, 6.52; B, 4.11; Cl, 26.96. Found: C, 50.50; H, 6.67; B, 4.28; Cl, 27.04.

(+)-Pinanediol 1-Chloropentane-1-boronate (4a and 5a). *n*-Butyllithium (9.3 mmol) (1.6 M in hexane) was added dropwise to a stirred solution of 9.3 mmol of (+)-pinanediol dichloro-

(8) Matteson, D. S.; Sadhu, K. M.; Jesthi, P. K., manuscript in preparation.

(9) Matteson, D. S.; Erdik, E. *Organometallics* **1983**, *2*, 1083–1088.

methaneboronate (1) in 50 mL of THF at −78 °C. The solution was allowed to reach room temperature overnight and then treated with concentrated aqueous ammonium chloride and ether. Distillation of the ether extracts yielded **4a** and **5a**: 79%; bp 120 °C (0.6 torr) (lit.[3b] for **4a** 100 °C (0.1 torr)).

(+)-Pinanediol 1-Phenylpentane-1-boronate (6a and 7a). The reported procedure[3] was followed: 85% yield, bp 145–150 °C (0.7 torr) (lit.[3] 125–128 °C (0.1 torr)).

1-Phenylpentanol (8). Oxidation of 1.74 mmol of **4a** and **5a** with 1.5 mL of 30% hydrogen peroxide and 5 mL of 3 M aqueous sodium hydroxide in 10 mL of THF at 0 °C yielded 85% 1-phenylpentanol: $[\alpha]^{21}_{589}$ +8.33° (*c* 3.3, benzene) (lit.[6] 31.3° (*c* 3.3, benzene)).

(+)-Pinanediol 1-Phenylpentane-1-boronate (6b and 7b). Treatment of (+)-pinanediol dichloromethaneboronate (1) with phenyllithium in THF at −78 °C, warming to 0 °C for 1 h, cooling again to −78 °C, and treating with an equivalent amount of *n*-butyllithium, and the usual workup yielded 80% of **6a** and **7b**. Hydrogen peroxide oxidation of this batch according to the procedure in the preceding paragraph yielded 1-phenyl-1-pentanol: $[\alpha]^{21}_{589}$ −10.5° (*c* 2.7, benzene).

(+)-Pinanediol 1-Chloro-3-methylbutane-1-boronate (4c and 5c). Isobutylmagnesium chloride was added to an equivalent amount of (+)-pinanediol dichloromethaneboronate (1) in THF at −78 °C and allowed to warm to 25 °C overnight. The magnesium chloride that separated was filtered, and the product **4c** and **5c**[8] was chromatographed on silica with ether/petroleum ether: yield 79%.

(+)-Pinanediol 1-Acetamido-3-methylbutane-1-boronate (9c and 10c). The mixture of **4c** and **5c** from the preceding paragraph was treated with lithiohexamethyldisilazane followed by acetic acid and acetic anhydride under the conditions described previously[4] to yield a mixture of **9c** and **10c**, which was chromatographed: mp 68–70 °C; $[\alpha]^{17}_{546}$ +31.0° (*c* 13, $CHCl_3$). The 200 MHz NMR spectrum was similar to that of purer **9c**: $[\alpha]^{23}_{546}$ −34.2° (*c* 8, $CHCl_3$), prepared from (+)-pinanediol isobutaneboronate,[8] though with some extra peaks in multiplets, with the major difference being that the NH peaks at δ 9.36 (**9c**) and 8.94 (**10c**) appeared in the ratio 34:66. Anal. Calcd for $C_{17}H_{30}BNO_3$: C, 66.46; H, 9.84; B, 3.52; N, 4.56. Found: C, 66.55; H, 10.01; B, 3.59; N, 4.38.

(+)-Pinanediol 1-Acetamidoethane-1-boronate (9d and 10d). Methylmagnesium bromide was added to 1 and the same general procedure described for preparation of **4c** and **5c** was used to prepare **4d** and **5d**, which was then converted in the usual manner[4,8] to **9d** and **10d**, ratio 22/78 from the respective NMR NH peaks at δ 9.39 and 9.24. Anal. Calcd for $C_{14}H_{24}BNO_3$: C, 63.42; H, 9.12; N, 5.28. Found: C, 64.02; H, 9.30; N, 4.83.

Zinc Chloride Catalysis. A. (+)-Pinanediol 1-Acetamido-3-methylbutane-1-boronate (9c and 10c). The same procedure described in a preceding paragraph was used to prepare **4c** and **5c**, except that 0.5 equiv of anhydrous zinc chloride was added after mixing the Grignard reagent and 1 at −78 °C.[5] The **4c** and **5c** was converted by the usual procedure to **9c** and **10c**, ratio 92/8 from the NH peaks: $[\alpha]^{27}_{546}$ −36.9° (*c* 13, $CHCl_3$); recrystallized from dichloromethane/hexane, mp 143–145 °C: $[\alpha]^{27}_{546}$ −36.9° ($CHCl_3$). Anal. ($C_{17}H_{30}BNO_3$) C, H, B, N.

B. (+)-Pinanediol 1-Acetamidoethane-1-boronate (9d and 10d). By similar procedures to the foregoing, a mixture of **9d** and **10d** was prepared, ratio 51/49 from the NH peaks at δ 9.86 and 9.71: $[\alpha]^{24}_{546}$ +11.9° (*c* 5, $CHCl_3$), mp 139–141 °C.

Acknowledgment. We thank the National Science Foundation for support, Grant No. CHE-8025229, and the Boeing Corp. for a gift in support of the departmental Nicolet 200-MHz NMR instrument.

Registry No. 1, 87249-60-3; **4a**, 85167-13-1; **4c**, 85167-14-2; **4d**, 85167-12-0; **5a**, 87247-48-1; **5c**, 87304-47-0; **5d**, 87247-50-5; **6a**, 87190-31-6; **7a**, 87247-53-8; **8r**, 19641-53-3; **8s**, 33652-83-4; **9c**, 87304-49-2; **9d**, 87249-62-5; **10c**, 87249-61-4; **10d**, 87304-48-1; $Cl_2CHB(OH)_2$, 62260-98-4; *n*-BuLi, 109-72-8; PhLi, 591-51-5; $LiN(SiMe_3)_2$, 4039-32-1; (+)-pinanediol, 22422-34-0; isobutyl chloride, 513-36-0; methyl bromide, 74-83-9.

Stereochemistry of Titanium-Assisted Additions of Organoaluminum Compounds to Hydroxybicyclo[2.2.1]hept-2-enes[1]

Herman G. Richey, Jr.,* L. Meredith Moses, and Jon J. Hangeland

Department of Chemistry, The Pennsylvania State University, University Park, Pennsylvania 16802

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In the presence of a titanium(IV) compound, dimethylaluminum chloride and diethylaluminum chloride add to *syn*-bicyclo[2.2.1]hept-2-en-7-ol to produce 2-*exo*-methyl- and 2-*exo*-ethyl-*syn*-bicyclo[2.2.1]heptan-7-ol and to *endo*-bicyclo[2.2.1]hept-5-en-2-ol to produce 5-*endo*-methyl- and 5-*endo*-ethyl-*endo*-bicyclo-[2.2.1]heptan-2-ol. These results indicate a preference in such titanium-assisted additions of alkylaluminum compounds to alkenols for attachment of the alkyl group to the side of the double bond nearer the hydroxyl group.

Thompson and co-workers have reported a variety of titanium-assisted additions of organoaluminum compounds to the multiple bonds of alkenols and alkynols.[2-8] In some instances, the reactions were carried out by treating the alcohol with Cp_2TiCl_2, $Ti(acac)_2Cl_2$, or $TiCl_4$ to form an alkoxychlorotitanium(IV) compound (1) which then was allowed to react with an organoaluminum compound. In other reactions, an excess of the organoaluminum com-

(1) Much of this work is taken from: Moses, L. M. M.S. Dissertation, The Pennsylvani State University, University Park, PA, 1981.
(2) Harris, T. V.; Coleman, R. A.; Dickson, R. B.; Thompson, D. W. *J. Organomet. Chem.* **1974**, *69*, C27.
(3) Coleman, R. A.; O'Doherty, C. M.; Tweedy, H. E.; Harris, T. V.; Thompson, D. W. *J. Organomet. Chem.* **1976**, *107*, C15.
(4) Tweedy, H. E.; Hahn, P. E.; Smedley, L. C.; Youngblood, A. V.; Coleman, R. A.; Thompson, D. W. *J. Mol. Catal.* **1977**, *3*, 239.
(5) Tweedy, H. E.; Coleman, R. A.; Thompson, D. W. *J. Organomet. Chem.* **1977**, *129*, 69.
(6) Smedley, L. C.; Tweedy, H. E.; Coleman, R. A.; Thompson, D. W. *J. Org. Chem.* **1977**, *42*, 4147.
(7) Youngblood, A.V.; Nichols, S. A.; Coleman, R. A.; Thompson, D. W. *J. Organomet. Chem.* **1978**, *146*, 221.
(8) Brown, D. C.; Nichols, S. A.; Gilpin, A. B.; Thompson, D. W. *J. Org. Chem.* **1979**, *44*, 3457. Schiavelli, M. D.; Plunkett, J. J.; Thompson, D. W. *J. Org. Chem.* **1981**, *46*, 807.

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