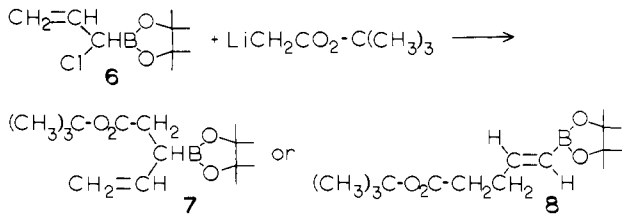
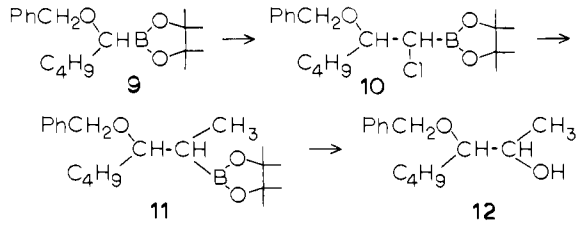


of **7** was confirmed by the vinyl pattern in the NMR at δ 5.1 (m, 2, $=CH_2$) and 5.9 (m, 1, =CH). When excess LDA was used in the prepartion of the lithioacetate, up to 65% of the product was **8**, perhaps produced by O-alkylation and Cope rearrangement. The two products were readily separable by distillation, and the structure of **8** was confirmed by the characteristic *trans*-alkeneboronic ester pattern[15] in the NMR at σ 5.55 (d, J = 19 Hz, =CHB) and 6.66 (m, HC=CB). Structures **7** and **8** were further confirmed by resolution with the shift reagent Eu(fod)$_3$.

Homologation of pinacol 1-(benzyloxy)pentane-1-boronate (**9**) (method A) followed by treatment of the crude α-chloro-β-(benzyloxy)alkaneboronic ester **10** with methylmagnesium bromide yielded the β-benzyloxy boronic ester **11**. Both **10** and **11** were unstable to distillation, partially decomposing by boron-oxygen β elimination, but oxidation of crude **11** with alkaline sodium perborate[16] yielded 3-(benzyloxy)-2-heptanol (**12**), 71% based on **9**.



The utility of these reactions in synthesis is limited by the formation of mixtures of diastereoisomers. Chiral control of the homologation process is described in the following communication.[17]

Acknowledgment. We thank the National Science Foundation for support (Grant No. CHE 77-11283).

(15) Matteson, D. S.; Jesthi, P. K. *J. Organomet. Chem.* **1976**, *110*, 25-37.
(16) Matteson, D. S.; Moody, R. J. *J. Org. Chem.* **1980**, *45*, 1091-5.
(17) Matteson, D. S.; Ray, R. *J. Am. Chem. Soc.*, following paper in this issue.

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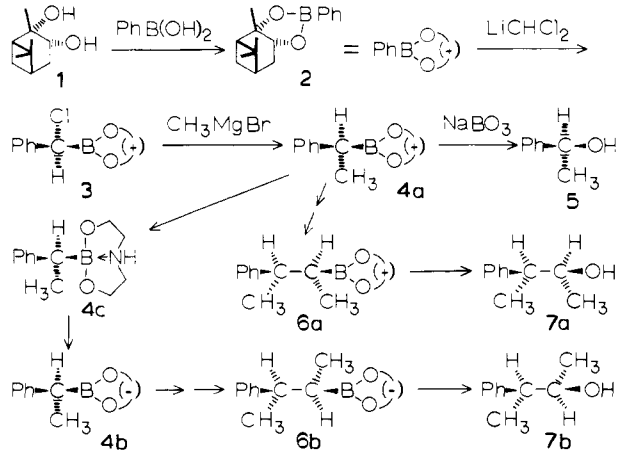
Directed Chiral Synthesis with Pinanediol Boronic Esters

Sir:

The efficient homologation of boronic esters to α-chloro boronic esters reported in the preceding communication[1] and the availability of (+)-pinanediol[2] (**1**) from (+)-α-pinene,[3] as well as the enantiomer from (-)-α-pinene, by our osmium tetraoxide catalyzed

Scheme I



hydroxylation[4] provide the basis for a promising new approach to directed chiral synthesis. To demonstrate, we have synthesized the known[5] (2*S*,3*S*)-3-phenyl-2-butanol (**7a**) (erythro isomer) and (2*R*,3*S*)-3-phenyl-2-butanol (**7b**) (threo isomer) from optically pure (+)-pinanediol benzeneboronate[6] (**2**) by double homologation and subsidiary transformations. Diastereoselectivities achieved were 97% (±1%) in the first homologation and 92-95% in the second homologations leading to **7a** and **7b**.

Semiquantitative exploratory experiments, summarized briefly in the final paragraph, established that homologation of boronic esters of (+)-pinanediol with (dichloromethyl)lithium yields αS α-chloro boronic esters but that prolonged exposure of these products to the chloride ion produced in the reaction may result in significant epimerization. Crystallization of the complex salt of (+)-pinanediol (**1**) with basic sodium borate was observed, which leads to enantiomerically pure **1** on regeneration with cold dilute acid.[7] On the basis of these results, the following efficient syntheses of **7a** and **7b** were designed directly.

(+)-Pinanediol benzeneboronate[6,8] (**2**) was added to (dichloromethyl)lithium[1] at -100 °C and the mixture was kept at 0 °C for 1 h, cooled to -78 °C, treated with methylmagnesium bromide, and kept at 20 °C overnight.[9] The resulting (+)-pinanediol (*S*)-1-phenylethaneboronate (**4a**) (94%) was found to contain 96.8% (±1%) *S* isomer, as estimated by oxidation with alkaline sodium perborate[10] to (*S*)-1-phenylethanol[11] (**5**) (100%), which was converted to the acetate ester for precise measurement of optical rotation,[12,13] enantiomeric excess (ee) 93.7%. The absolute configurations of the boronic esters **3** and **4a** are assigned

(4) Ray, R.; Matteson, D. S. *Tetrahedron Lett.* **1980**, *21*, 449-50.
(5) Cram, D. J. *J. Am. Chem. Soc.* **1949**, *71*, 3863-70, 3883-9.
(6) $[\alpha]^{23}_D$ +17.9° (8%, benzene).
(7) Crystallizes as $(C_{10}H_{16}O_2)_2B^-Na^+\cdot 2H_2O$ from THF/water, recrystallized from 95% ethanol/2-propanol. Treatment with 1 equiv of dilute hydrochloric acid, extraction with several portions of petroleum ether, and distillation regenerates **1**, contaminated with varying amounts of its boric acid ester, which does not interfere with synthetic use. Optical purity was determined on the derived benzeneboronate ester **2**.
(8) New compounds were characterized by ^{1}H NMR and satisfactory analyses (±0.4%) were obtained for all elements except oxygen, except for α-chloro boronic esters (**10**), of which only the homologation product from **4a** has been analyzed satisfactorily to date.
(9) Stoichiometric amounts of reactants were used, with 60 mL of THF solvent for 24 mmol. The product was worked up with aqueous acid, extraction with ether, and Kugelrohr distillation at 130-135 °C (0.1 torr): purity was confirmed by ^{1}H NMR.
(10) Matteson, D. S.; Moody, R. J. *J. Org. Chem.* **1980**, *45*, 1091-5. Sufficient conditions for these hindered boronic esters, 1 M in 1:1 THF/water, included 5-10% excess sodium perborate, 0.5 equiv of sodium hydroxide, and 15 h at 25 °C. Most samples were refluxed. On addition of petroleum ether, sodium pinanediol borate crystallized, and the other alcohol was purified by extraction and Kugelrohr distillation.
(11) Jacques, J.; Gros, C.; Bourcier, S. "Stereochemistry"; Kagan, H. B., Ed.; Georg Thieme: Stuttgart, 1977; Vol. 4.
(12) Obsd $[\alpha]^{23}_D$ -116.7° (3%, benzene) (lit.[13] $[\alpha]^{21}_D$ -124.5°).
(13) Huisgen, R.; Rüchardt, C. *Justus Liebigs Ann. Chem.* **1966**, *601*, 21-34.

(1) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.*, preceding paper in this issue.
(2) The rotation is low, $[\alpha]_D$ +3.3°: Schmidt, H. *Chem. Ber.* **1960**, *93*, 2485-90.
(3) Absolute configuration: Brewster, J. H. *J. Am. Chem. Soc.* **1959**, *81*, 5483-93. Commercial (+)-α-pinene, 92% ee, and (-)-α-pinene, 82% ee, were used.

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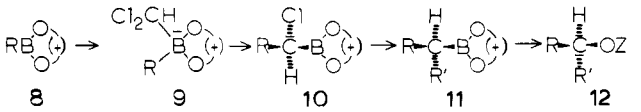
on the basis that nucleophilic displacement of chloride from **3** proceeds with inversion[14] and peroxidic deboronation of **4a** with retention.[15]

To prepare (2*S*,3*S*)-3-phenyl-2-butanol (**7a**), **4a** was homologated with (dichloromethyl)lithium in the same manner as described for **2**, except that the mixture was kept for 7 h at 25 °C before it was cooled and methylmagnesium bromide was added,[9] conditions which permitted completion of the reaction without significant epimerization in this case. The yield of (+)-pinanediol (2*S*,3*R*)-3-phenylbutane-2-boronate (**6a**) was 96%. Oxidation with sodium perborate[10] yielded 88% 3-phenyl-2-butanol, shown to contain 90% (±1%) erythro isomer (**7a**) and 10% threo isomer (**7b** and enantiomer) by ^{1}H NMR analysis with the aid of a shift reagent.[16] The overall yield of contained **7a** is 71%, based on **2**. As a result of the double-homologation sequence, the amount of enantiomer of **7a** present must be very small.[17]

To prepare (2*R*,3*S*)-3-phenyl-2-butanol (**7b**), the (+)-pinanediol ester **4a** was cleaved and the boronic acid was esterified with (−)-pinanediol to form **4b** before the second homologation. Conditions which would hydrolyze most boronic esters failed to affect **4a**, but destructive cleavage of the pinanediol was accomplished with boron trichloride, and the (*S*)-1-phenylethaneboronic acid was isolated as its crystalline diethanolamine ester[18,19] (**4c**) (75%), ee 100%.[20] Treatment of **4c** with 1 M hydrochloric acid regenerated the boronic acid, which was extracted with ether and esterified with (−)-pinanediol[21] to **4b** (79%).[22] Homologation of **4b** as described for **4a** yielded 91% (−)-pinanediol (2*R*,3*R*)-3-phenylbutane-2-boronate (**6b**),[23] which was oxidized[10] to 3-phenyl-2-butanol (93%) containing 94% (±1%) threo isomer (**7b**) and 6% erythro isomer (**7a**).[16,24]

The foregoing results confirm the expected retention of configuration of the migrating alkyl group. In view of the comparable specificities in the routes to **6a** and **6b**, any double-stereodifferentiation effect[25] is small compared to the directing influence of the pinanediol group.

Exploratory preliminary experiments had indicated that (+)-pinanediol boronic esters (**8**) yield dichloromethaneboronate complexes (**9**) which consistently rearrange to αS α-chloro boronic esters (**10**), as shown by reaction with lithium or Grignard reagents (inversion[14]) to form **11**, which were oxidized[10] (retention[15]) and esterified to known derivatives[11] (**12**). Thus, **8** (R = *n*-C_4H_9) homologated under the previously established conditions[1] yielded **10** with 89% diastereoselectivity, as indicated by the rotation of **12** (R′ = CH_3, Z = COPh),[26] or 91% based on an alternative **12** (R′ = Ph, Z = $COCH_3$).[27] An analogous treatment of **8** (R = cyclohexyl) indicated 83% diastereoselectivity, and **8** (R = CH_3) gave 74%. However, all these figures must be regarded as lower limits in view of the long exposure of **10** to chloride ion. The epimerization problem became apparent when **8** (R = Ph) yielded the "wrong" enantiomer of **12** (R′ = CH_3, Z = $COCH_3$) in 8% ee after 20-h exposure of the benzylic **10** (≡**3**) to lithium chloride at 25 °C, which was dramatically changed to 93.7% ee of the "right" isomer when the exposure was reduced to 1 h at 0 °C as outlined in the synthetic directions.



Acknowledgment. We thank the National Science Foundation for support (Grant No. CHE 77-11283).

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(16) Eu(fod)$_3$ shifts the most upfield CH_3 doublet of the threo isomer upfield from that of the erythro isomer. Integrals were evaluated at 60 and 90 MHz.
(17) Calculated enantiomer content is (0.03)(0.07) = 0.21%, too small to measure, if (+)-pinanediol was 100% ee. For our **7a**, obsd $[\alpha]_D$ −2.1° (neat) exceeds lit.[5] $[\alpha]^{25}_D$ −0.69° but is within experimental error of calcd $[\alpha]_D$ −1.9° for a mixture of 90% **7a**, 4% **7b** $[\alpha]^{25}_D$ −30.9°), and 6% racemate. Further confirmation of the predominant isomer as **7a** was provided by the 3-nitrophthalate, crystallized once: mp 138–139 °C; $[\alpha]^{20}_D$ +31.3° (4%, ethanol) (lit.[5] mp 144–145 °C; $[\alpha]^{25}_D$ +34.6°).
(18) Addition of 4 g of **4a** in 20 mL of dichloromethane to ~8 mL of boron trichloride at −78 °C was followed by 2 h at 25 °C, concentration, aqueous workup, and treatment of the crude boronic acid with 1 equiv of diethanolamine in 3 mL of 2-propanol and 10 mL of ether. The **4c** was recrystallized from chloroform/benzene, mp 200–201 °C [lit.[19] (racemate) mp 204 °C].
(19) Korcek, S.; Watts, G. B.; Ingold, K. U. *J. Chem. Soc., Perkin Trans. 2* **1972**, 242–8.
(20) Derived (*S*)-1-phenylethyl acetate, $[\alpha]^{25}_D$ −124.5° (lit.[13] identical).
(21) Benzeneboronate ester $[\alpha]^{19}_D$ −17.6°.
(22) Purified by chromatography on silica with 1:9 ether/petroleum ether.
(23) Simple distillation, bp 115–117 °C (0.03 torr).
(24) The 3-nitrophthalate, purified by way of aqueous extraction of the sodium salt, was obtained as an oil, $[\alpha]^{22}_D$ −30.0° (2%, ethanol); calcd $[\alpha]_D$ −30.1° for 94% **7b** nitrophthalate (lit.[5] $[\alpha]^{25}_D$ −34.2°) with 6% **7a** nitrophthalate (lit.[5] $[\alpha]^{25}_D$ +34.6°).
(25) Heathcock, C. H.; White, C. T. *J. Am. Chem. Soc.* **1979**, *101*, 7076–7.
(26) The starting material was 92% ee (+)-pinanediol boronic ester **12**, $[\alpha]^{21}_D$ +29.9° (lit. $[\alpha]_D$ +31.0°: Kenyon, J.; Pickard, R. H. *J. Chem. Soc.* **1915**, *107*, 115–32).
(27) From 92% ee (+)-pinanediol **12**, $[\alpha]^{20}_D$ +60.1° (lit. $[\alpha]_D$ +80.1°: Levine, P. A.; Marker, R. E. *J. Biol. Chem.* **1932**, *97*, 379–91).

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Superoxide-Ion Oxidation of Hydrophenazines, Reduced Flavins, Hydroxylamine, and Related Substrates via Hydrogen-Atom Transfer

Sir:

Numerous groups have cited evidence that superoxide ion ($O_2^{-}\cdot$) brings about a net oxidation of many substrates.[1-19] However, the direct transfer of an electron to $O_2^{-}\cdot$ is an unlikely process in aprotic media because of the extreme instability of the O_2^{2-} species. Recently, we have shown with acidic reducing substrates such as 3,5-di-*tert*-butylcatechol, α-tocopherol, and ascorbic acid that $O_2^{-}\cdot$ acts as a Brønsted base, and that the reported oxidations of these substrates by $O_2^{-}\cdot$ actually represent an initial proton abstraction to give substrate anion and dismutation species, HO_2^{-} and O_2; the latter oxidizes the substrate anion.[20] This mechanism appears

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