Borabenzene Derivatives. 27. From (−)-α-Pinene to the First Chiral Boratabenzene Salt[1]

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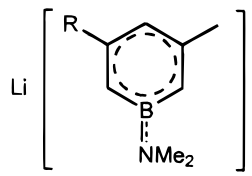
*Summary: Enantiomerically enriched (−)-α-pinene (**3**) is used to synthesize the β-pinene-derived alcohol **5** with a 3-exo-CMe_2OH group. Dehydration with $(CF_3SO_2)_2O$/pyridine produces a diene mixture **6** which, by means of double kaliation and subsequent ring closure with $BCl_2(NMe_2)$, is transformed into the tetrahydroborinine **7**. Metalation of **7** affords the enantiomerically pure lithium boratabenzene **8** in 80% yield (based on **6**).*

Chiral cyclopentadienylmetal complexes are of prime importance as mediators of enantioselective reactions.[3] The chiral derivatives of $TiCl_2Cp_2$ and $ZrCl_2Cp_2$, especially, play a key role in stereocontrolled olefin polymerization[4] and in enantioselective organic synthesis.[5]

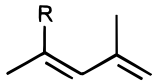
Boratabenzene ions are in some respects closely akin to the cyclopentadienide ion.[6−8] Hence, the synthesis of chiral boratabenzene salts is an important synthetic goal.

As we have shown recently, some lithium boratabenzenes **1** can be obtained from 2-methylpentadienes **2** in only three steps. Double kaliation of the diene, ring



1

a: R = H
b: R = Me
c: R = Bu^t



2

closure with $BCl_2(NMe_2)$, and subsequent metalation give boratabenzenes with a methyl group in the 3-position and a group R = H, Me, Bu^t in the 5-position of the ring.[7c]

We have now used (−)-α-pinene (**3**)[9] as the starting material for the construction of an annulated boratabenzene ion. In the first stage of this multi-step synthesis, it was necessary to transform **3** into a diene with a substructure of type **2** (Scheme 1). Kaliation[10] and subsequent borylation with $BClPr^i_2$ give the pinenylborane **4**.[11,12] Allyloboration of acetone with allylic borane **4** followed by hydrolysis yields alcohol **5**.[11,13] This reaction sequence directs the resulting Me_2COH group into the 3-position of the pinene skeleton where it occupies the less hindered exo-face; alternative regio- and diastereoisomers were not observed. Dehydration

(1) Part 26: See ref 2.

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(5) See, e.g.: (a) Hoveyda, A. H.; Morken, J. P. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 1262. (b) Pine, S. H. *Org. React.* **1993**, *43*, 1.

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(8) For leading refences to recent work on complexes, see: (a) Rogers, J. S.; Bazan, G. C.; Sperry, C. K. *J. Am. Chem. Soc.* **1997**, *119*, 9305. (b) Ashe, A. J., III.; Al-Ahmad, S.; Kampf, J. W.; Young, V. G., Jr. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2014. (c) Bazan, G. C.; Rodriguez, G.; Ashe, A. J., III.; Al-Ahmad, S.; Kampf, J. W. *Organometallics* **1997**, *16*, 2492. (d) Bazan, G. C.; Rodriguez, G.; Ashe, A. J., III.; Al-Ahmad, S.; Müller, C. *J. Am. Chem. Soc.* **1996**, *118*, 2291.

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(11) Preparation of **4** and **5**: Lochmann−Schlosser base was prepared from LiBu (300 mL, 1.6 M in hexane, 480 mmol) and KOBu^t (53.2 g, 474 mmol, suspended in hexane, 500 mL). Enantiomerically enriched (−)-α-pinene[9] (62.3 g, 457 mmol) was added with stirring at 0 °C, and stirring was continued at 25 °C for 12 h. The solid was collected by filtration and carefully washed with hot hexane. It was then suspended in hexane (800 mL), $BClPr^i_2$ (73.1 g, 552 mmol, in hexane (300 mL)) was added dropwise at 0 °C, and stirring was continued at 25 °C until the color of the reaction mixture turned white. Filtration (with the help of kieselguhr) and removal of the solvent under vacuum gave the borane **4** as a yellow oil. The oil was dissolved in ether (350 mL), excess acetone (120 mL, 1.63 mol) was added at 0 °C, and the reaction mixture was stirred at 25 °C for 2 h. Hydrolysis with aqueous NaOH (3M) while cooling with ice, workup with ether, and distillation (1 mbar, 94 °C) and crystallization from pentane at −30 °C afforded **5** (51.8 g, 58%) as colorless, analytically pure crystals (ee 98−99%, GC); $[\alpha]_D^{20}$ +23.3° (*c* 5.1%, EtOH); mp 32 °C. Anal. Calcd for $C_{13}H_{22}O$ (**5**): C, 80.35; H, 11.41. Found: C, 80.52; H, 11.27. Cf. borylation with $BClEt_2$: Zaidlewicz, M. *J. Organomet. Chem.* **1985**, *293*, 139. Cf. reaction with CH_2O: Zaidlewicz, M. *J. Organomet. Chem.* **1991**, *409*, 103.

(12) **4**: For the purpose of characterization, the crude borane **4** was distilled under vacuum. ^{1}H NMR (300 MHz, $CDCl_3$): δ 5.00 (m, CH=), 2.03 and 1.95 (m, 1H each, BCH_2), 1.61 (sept, J = 7.4 Hz, 2 BCH, BPr^i_2), 0.87 (d, J = 7.4 Hz, 4 Me, BPr^i_2). ^{13}C{^{1}H} NMR (76 MHz, $CDCl_3$): δ 146.5 (C-2), 116.0 (C-3), 33.8 (br, BCH2), 22.2 (br, BCH, BPr^i_2), 17.6 and 17.5 (BC*Me*, BPr^i_2). ^{11}B NMR (29 MHz, $CDCl_3$): δ 90.

(13) **5**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.04 and 4.76 (dd, J = 2.0, 2.0 Hz, 1H each, CH2=), 2.65 (dddd, J = 10.7, 4.6, 2.0, 2.0 Hz, 3-H), 2.38 (dd, J = 5.8, 5.8 Hz, 1-H), 2.23 (dddd, J = 10.1, 5.8, 5.8, 2.1 Hz, 7-H_{exo}), 2.01 (dddd, J = 13.7, 10.7, 2.9, 2.1 Hz, 4-H_{endo}), 1.93 (dddd, J = 5.8, 5.8, 2.9, 2.9 Hz, 5-H), 1.61 (ddd, J = 13.7, 4.6, 2.9 Hz, 4-H_{exo}), 1.30 (d, J = 10.1 Hz, 7-H_{endo}), 1.22 (s, 6-Me_{exo}), 0.74 (s, 6-Me_{endo}), 1.85 (s, OH, Me_2COH), 1.25 (s, Me, Me_2COH), 1.20 (s, Me, Me_2COH). ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ 152.0 (C-2), 111.2 (CH_2=), 45.5 (C-3) 73.7 (COH, Me_2COH), 29.1 and 26.6 (Me, Me_2COH). Assignments based on NOE difference sprectra: 4-H_{endo} is close to 6-Me_{endo} and 3-H, while 4-H_{exo} is close to Me of Me_2COH. This is consistent with $^3J_{3,4endo}$ = 10.7 (*cis* disposition) and $^3J_{3,4exo}$ = 4.6 Hz (*trans* disposition).

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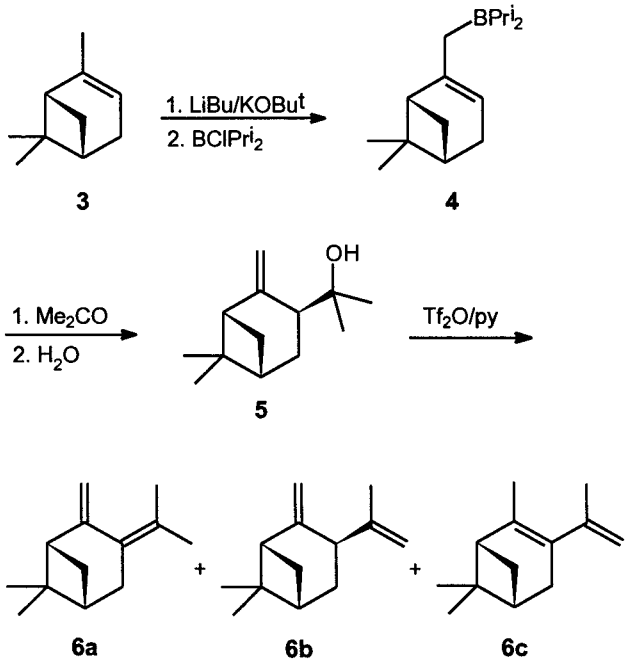
Scheme 1



of **5** with $(CF_3SO_2)_2O$ in pyridine as the solvent[14] at ambient temperature affords a diene mixture **6**[15,16] in good overall yield (50%, based on **3**).

The three dienes **6** give the same dipotassium derivative upon metalation with Lochmann−Schlosser base, and the subsequent ring-closure step with $BCl_2(NMe_2)$ produces the tetrahydroborinine **7** with a remarkably high yield (86%).[17,18] This result contrasts our previous work with the open-chain 2-methylpentadienes **2** where yields of only 17−47% were obtained.[7c] We note that in the dienes **6**, the substructure **2** is incorporated into a partly rigid framework. It is presumably this preorganization which causes the high efficiency of the ring-closure procedure observed here. Compound **7** in turn can be metalated with LDA in THF to give the salt **8** (93%);[19] addition of TMEDA and crystallization from THF/pentane afford the colorless microcrystalline sol-

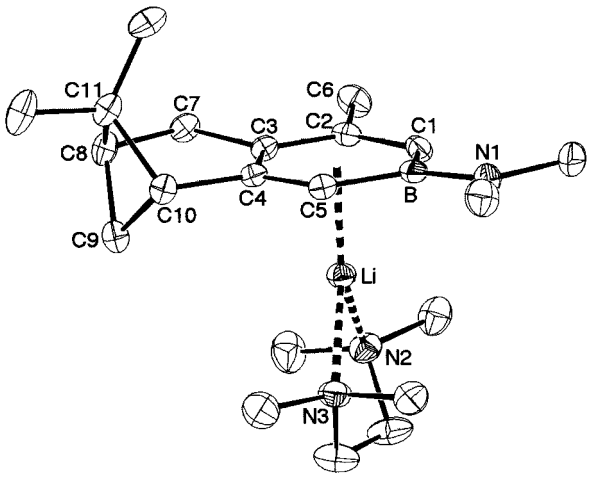
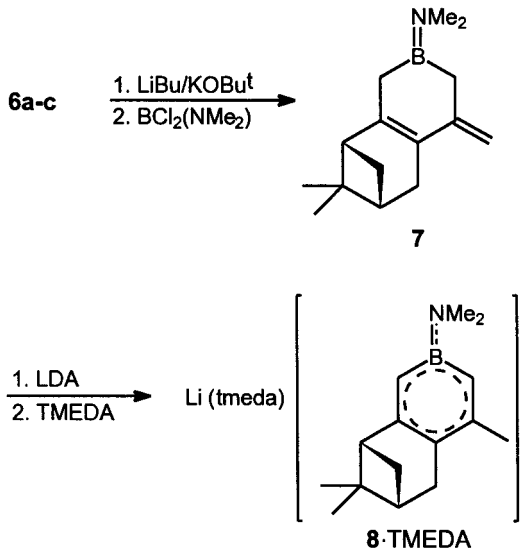


Figure 1. Platon plot of **8**·TMEDA (at the 30% probability level). Selected bond distances (pm): N1−B 145.3(4), C1−C2 139.7(4), C2−C3 140.6(3), C3−C4 142.9(3), C4−C5 138.7(3), C5−B 152.1(4), C1−B 151.9(4), C1−Li 234.0(5), C2−Li 236.0(5), C3−Li 235.5(5), C4−Li 235.7(5), C5−Li 240.4(5), B−Li 247.5(5).

Scheme 2



(14) Cf. Halterman, R. L.; Tretyakov, A. *Tetrahedron* **1995**, *51*, 4371.

(15) Preparation of the mixture **6**: Triflic acid anhydride $(CF_3SO_2)_2O$ (24.1 g, 85.4 mmol) was added dropwise to alcohol **5** (14.5 g, 74.6 mmol) in pyridine (75 mL) at 0 °C.; stirring was continued for 50 h at 25 °C. The mixture was separated with pentane/water. Filtration of the pentane phase through silica (6 cm layer) and removal of the pentane left the diene mixture **6** (11.5 g, 87%) as a colorless liquid; typical composition **6a**/**6b**/**6c** = 10/13/1. The nonconjugated isomer **6b** tends to rearrange.

(16) **6a**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.86 and 4.84 (d, J = 1.8 Hz, 1H each, CH2=), 1.97 and 1.75 (s, MeC=). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 150.6 (C-2), 131.6 and 127.2 (C-3 and Me_2C=), 110.4 (CH_2=), 23.7 (*Me*C=), 22.4 (*Me*C=). **6b**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.80 (m, 1H, CH_2=), 4.75 (m, CH_2=), 4.67 (m, 1H, CH_2=), 3.31 (ddm, ^3J = 10.7, 4.9 Hz, 3-H), 1.71 (dd, ^4J = 1.5, 1.2 Hz, 2-Me). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 152.8 (C-2), 149.9 (Me*C*=), 112.1 (CH_2=CMe), 109.1 (2-CH_2=), 19.4 (*Me*C=). **6c**: ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.92 (dq, J = 2.8, 1.5 Hz, 1H, CH_2=), 4.68 (dq, J = 2.8, 0.9 Hz, 1H, CH_2=), 1.81 (dd, J = 1.5, 0.9 Hz, *Me*CH_2=), 1.69 (s, 2-Me). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 145.1 (C-2), 137.5 (C-3), 129.2 (*C*=CH2), 112.4 (CH_2=), 22.4 (*Me*CH_2=), 20.6 (2-Me).

(17) Preparation of **7**: Lochmann−Schlosser base was prepared from LiBu (66 mL, 1.6 M in hexane, 106 mmol) and KOBu^t (11.8 g, 105 mmol, suspended in hexane, 150 mL). The diene mixture **6** (9.0 g, 51.0 mmol) was added at −50 °C. The mixture was allowed to warm to ambient temperature and was then stirred under reflux for 12 h. The solid was collected by filtration, washed with hot hexane, and then suspended in hexane (400 mL). The suspension was added dropwise to $BCl_2(NMe_2)$ (6.8 g, 54.1 mmol in hexane (200 mL)/THF (50 mL)) while the reaction mixture was stirred at 25 °C.; stirring was continued for 12 h. Filtration (with the help of kieselguhr), removal of the volatiles from the filtrate, and condensation of the raw product under high vacuum (∼120 °C/10^{-6} bar) gave 7 (10.1 g, 86%) as a yellow oil, contains a small admixture of C_{13} hydrocarbons and tends to isomerize to the corresponding dihydroborinine with the double bonds in the 2,6-positions.

(18) **7**: ^{1}H NMR (500 MHz, CDCl3) δ 4.77 and 4.61 (m, 1H each, CH_2=), 2.77 and 2.69 (s, NMe), 2.04 and 1.97 (dm, J = 17.1 Hz, 1H each, 5-H), 1.64 and 1.48 (dm, J = 21.4 Hz, 1H each, 3-H). $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ 146.5 (C-2), 146.5 (C-6), 126.2 (C-7), 104.6 (CH_2=), 38.8 and 38.7 (NMe), 25.9 (br, C-5), 25.0 (br, C-3). ^{11}B NMR (160 MHz, $CDCl_3$): δ 44.

(19) Preparation of **8**: LDA was prepared from $NHPr^i_2$ (2.50 g, 24.7 mmol in THF, 40 mL) and LiBu (13 mL, 1.6 M in hexane, 20.8 mmol). Compound **7** (3.20 g, 14.0 mmol, in THF, 15 mL) was added at −78 °C. The reaction mixture was allowed to warm to ambient temperature and was kept stirring for 50 h. After careful removal of the volatiles, the resulting residue was triturated with hexane. Filtration (with the help of kieselguhr), removal of the volatiles from the filtrate, and careful drying at 60 °C/10−6 bar left salt 8 as a yellowish powder which retains THF in small and varying quantities; typical yield: 93% (by NMR). Addition of TMEDA (2.1 mL, 14.1 mmol) and crystallization from THF/pentane at −30 °C gave **8**·TMEDA (3.35 g, 68%) as colorless, analytically pure crystals; $[\alpha]_D^{23}$ +26.4° (*c* 3.9%, THF). Anal. Calcd for $C_{21}H_{39}BLiN_3$ (**8**·TMEDA): C, 71.80; H, 11.19; N, 11.96. Found: C, 71.93; H, 10.95; N, 11.70.

vate **8**·TMEDA (68%) (Scheme 2).[19,20] The enantiomeric purity of **8**·TMEDA was not assessed experimentally. However, if it is accepted that an enantiomerization of the pinene skeleton is not a feasible process, the ee value for **8**·TMEDA can be related to that for the alcohol **5** (ee 98−99%). Since the salt **8**·TMEDA is isolated by crystallization, its enantiomeric purity should even be higher (ee > 98−99%) than that of **5**.

In the crystalline state, **8**·TMEDA (Figure 1)[21] shows an ion-pair structure with $Li(TMEDA)^+$ facially bound to the exo face of the anion;[22] admixtures of alternative structures, especially of the endo isomeric ion-pair structure, were shown to be absent by means of powder diffraction measurements.

The synthesis of boratabenzene derivatives with complex carbon skeletons seemed out of reach until now. With this work, we have obtained the first chiral and enantiomerically pure boratabenzene derivative. The salt **8** can be used to synthesize chirally modified borabenzene derivatives and boratabenzene complexes. Not surprisingly, complex formation reactions produce mixtures of diastereoisomers in many cases. These aspects are currently under investigation.

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Supporting Information Available: ^1H and ^{13}C NMR spectra of **4**, **6**, and **7** and tables of bond distances and angles, anisotropic thermal parameters, and hydrogen atom coordinates for **8**·TMEDA (13 pages). Ordering information is given on any current masthead page.

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(20) **8**·TMEDA: ^1H NMR (500 MHz, C6D6) δ 5.75 (d, J = 3.1 Hz, 5-H), 5.64 (d, J = 3.1 Hz, 3-H), 3.08 (s, NMe_2), 2.90 (dd, J = 15.0, 3.1 Hz, 8-H_{endo}), 2.82 (dd, J = 15.0, 3.1 Hz, 8-H_{exo}), 2.71 (dd, J = 5.8, 5.5 Hz, 1-H), 2.62 (dddd, J = 8.2, 5.8, 5.5, 0.6 Hz, 11-H_{exo}), 2.40 (dddd, J = 5.8, 5.8, 3.1, 3.1 Hz, 9-H), 2.31 (s, 6-Me), 1.45 (s, 10-Me_{exo}), 1.11 (d, J = 8.2 Hz, 11-H_{endo}), 0.96 (s, 10-Me_{endo}), 1.71 (s br, 4 Me, TMEDA), 1.55−1.30 (m, 2 CH_2, TMEDA). $^{13}C\{^1H\}$ NMR (126 MHz, C_6D_6): δ 151.9 (C-2), 141.8 (C-6), 109.3 (br, C-3), 107.4 (br, C-5), 101.2 (C-7), 53.2 (C-1), 42.1 (C-9), 39.7 (NMe_2), 39.6 (C-10), 33.7 (C-11), 32.3 (C-8), 27.0 (10-Me_{exo}), 24.2 (6-Me), 21.7 (10-Me_{endo}) 55.9 (CH_2, TMEDA), 45.2 (Me, TMEDA). ^{11}B NMR (160 MHz, C_6D_6): δ 31. ^7Li NMR (194 MHz, THF-d_8, 25 °C): δ −5.2.

(21) Crystal data for **8**·TMEDA: $C_{21}H_{39}BLiN_3$, colorless crystals, 0.65 × 0.65 × 0.40 mm, orthorhombic, space group $P2_12_12_1$ (No. 19), a = 825.8(3) pm, b = 1600.3(3) pm, c = 1721.8(8) pm, V = 2.275(2) nm^3, Z = 4, d_{calc} = 1.026 g cm^{-3}, μ = 4.10 cm^{-1}, $F(000)$ = 776. Data collection: Enraf-Nonius CAD4, Cu Kα radiation, graphite monochromator, $\omega-2\theta$ scans ($5° < \theta < 70°$) at 183 K.; correction for secondary extinction $E = 1.41 \times 10^{-6}$;[21a] 2614 reflections measured, 2356 unique reflections with $I > \sigma(I)$, no absorption correction applied. Solution[21b] and refinement:[21c] 328 parameters, R = 0.049, R_w = 0.058, $w^{-1} = \sigma^2(F_0)$, GOF = 1.810; non-hydrogen atoms were refined anisotropically; all hydrogen atoms of the anion were refined isotropically, those of the cation were treated as riding. Further details of the crystal structure determination are available on request from the Cambridge Crystallographic Data Centre, on quoting the depository number CCDC-100524. (a) Zachariasen, W. H. *Acta Crystallogr.* **1963**, *16*, 1139. (b) Sheldrick, G. M. *SHELXS-86, Program for Crystal Structure Solution*; University of Göttingen: Göttingen, Germany, 1986. (c) *MolEN, An Interactive Structure Solution Procedure*; Enraf-Nonius: Delft, The Netherlands, 1990.

(22) The first boratabenzene salt, $[Li(TMPDA)](C_5H_5BNMe_2)$, to be characterized structurally, is of the same type, see: Herberich, G. E.; Schmidt, B.; Englert, U.; Wagner, T. *Organometallics* **1993**, *12*, 2891. Cf. also ref 7c.