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Absolute Configuration and Chiroptical Properties of an Enantiopure [5-Chloro-2-(dimethylaminomethyl)phenyl]-phenylborane Complex

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Enantiomers of the title intramolecular amine–borane complex with a *B*-pentafluoropropionyloxy ligand were resolved by chiral HPLC. X-ray analysis of the (+)-isomer revealed that the configuration of the chiral boron center was *S* by the Bijvoet method. Thus, the absolute configuration of this chiral borane compound was established as (*S*)-(+) or (*R*)-(−).

Optically active compounds with a chiral center at a tetrahedral boron atom are stereochemically interesting in relation to the chemistry of tetrahedral carbon atoms.[1] Actually, several types of borates and coordinated boranes have been enantiomerically resolved by the diastereomer method or chiral HPLC as stable entities at room temperature.[2–4] For example, enantiopure borane complexes with a phosphine or an amine ligand were applied to elucidate the S_N2 mechanism at the boron atoms.[5,6] The absolute configuration of the boron atoms has been established for some compounds by the X-ray analysis of their derivatives carrying an internal reference of known configuration.

We recently reported the structures and stereochemistry of the intramolecular amine–borane complexes with a 2-(dimethylaminomethyl)phenyl ligand.[7] When a pentafluoropropionyloxy (C_2F_5COO–) group was introduced at the boron atom, the configurational stability of the tetrahedral boron atom was enhanced enough to isolate the enantiomers of **1** at room temperature (Chart 1). The optical rotation and CD spectra of these enantiomers were measured, but the absolute configuration could not be determined yet because of the experimental restrictions. Therefore, we prepared complex **2** carrying a heavy atom for the application of the Bijvoet method by X-ray crystallography. This paper describes the absolute configuration and the chiroptical properties of **2** as an intramolecular amine–borane complex.

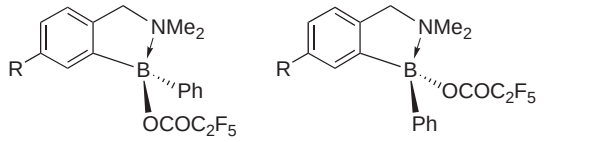
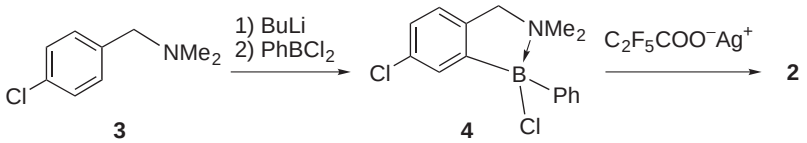


Chart 1.

Compound **2** was prepared in a similar manner to **1** (Scheme 1).[7] Reaction of 4-chloro-*N*,*N*-dimethylbenzylamine (**3**) with butyllithium gave the *o*-lithiated compound, which was then treated with dichlorophenylborane to form compound **4**. The reaction of this chloroborane with a silver acylate reagent gave the desired complex **2** in 88% yield. The ^{11}B NMR signal of **2** was observed at δ 8.6 as a very broad peak, this chemical shift being typical of tetracoordinated boron atoms.

A racemic sample of **2** was submitted to chiral HPLC with a Chiralpak AD column with hexane–2-propanol 50:1 eluent. The enantiomers were isolated with baseline separation. The specific rotations of the first and second fractions were $[\alpha]_D^{22}$ −158 and +157, respectively, in acetone. No racemization was observed as far as the sample solution was treated at room temperature. The CD spectra of (+)- and (−)-**2** were measured in hexane (Fig. 1). The less easily eluted (+)-isomer exhibits a small trough at 228 nm and small peaks in the range of 255–280 nm with a positive strong shoulder in the short wavelength region (<220 nm). The CD spectrum of the (−)-isomer was practically the mirror image of that of the (+)-isomer.

The X-ray analysis was carried out with a single crystal of the less easily eluted (+)-isomer of **2**. An ORTEP drawing is shown in Fig. 2. The B–N bond distance is 1.652(2) Å and the tetrahedral character (THC) of the boron atom is 56%.[8] These structural parameters are comparable to those of **1** (B–N 1.668(4) Å, THC 56%).[7] The carbonyl carbon atom is nearly *anti* relative to the nitrogen atom (torsion angle −163.7°), and the carbonyl oxygen atom and the pentafluoroethyl group are almost *syn* and *anti* relative to the boron atom, respectively. To determine the absolute configuration, structural refinements were carried out for the structure shown in Fig. 2 and



Scheme 1.

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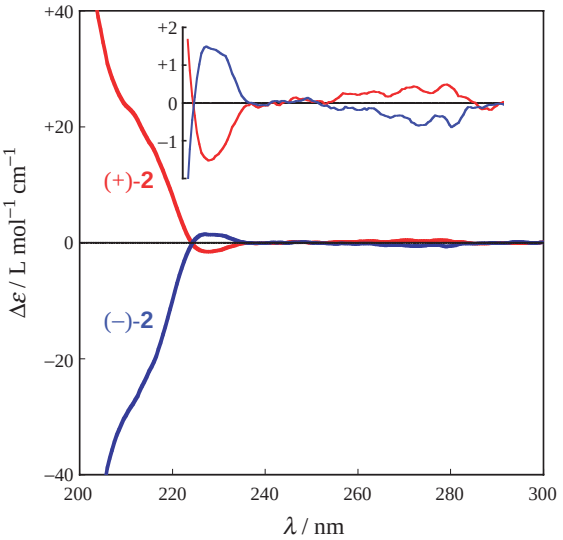

Fig. 1. CD spectra of enantiomers of **2** in hexane. The expanded spectra are inset.

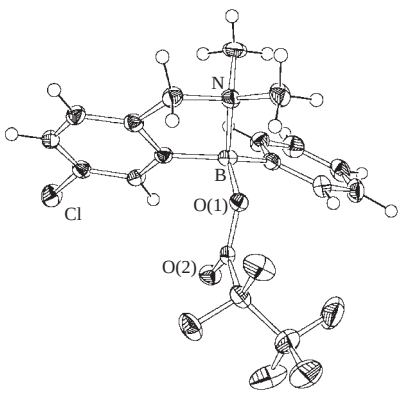

Fig. 2. ORTEP drawing of compound (*S*)-(+)-**2**.

its mirror image. While the residual factors *R* were the same down to the third decimal place for the two structures, the Flack parameters χ were 0.00(2) and 1.00(2) for the structures of the *S* and *R* configuration, respectively.[9] This result clearly indicates that the absolute configuration of the (+)-isomer should be *S*. Hence, the absolute configuration of **2** is established as (*S*)-(+) or (*R*)-(−).

To determine the stereochemical relationship between **2** and **1**, we attempted dechlorohydrogenation of **2** under various conditions, e.g., Pd-catalyzed hydrogenolysis.[10] However, reaction without affecting the boron moiety was unsuccessful. We also carried out the theoretical calculations of the CD spectra of these intramolecular amine–borane complexes by the time-dependent DFT (TDDFT) method.[11] The spectral pattern was sensitive to the conditions, so that we could not obtain a reliable conclusion of the correlation between the configuration and the CD spectra.[12] The specific rotation and the CD spectra of (+)-**2** and (−)-**2** are quite similar to those of (+)-**1** ($[\alpha]_D^{22}$ +169) and (−)-**1** ($[\alpha]_D^{22}$ −167), respectively.[7] If this similarity primarily depends on the configuration at the boron atom regardless of the presence of the chloro substituent, the absolute configuration of **1** can be assigned as (*S*)-(+) or (*R*)-(−).

Experimental

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. ^{11}B and ^{19}F NMR spectra were measured on a JEOL Lambda-300 spectrometer at 96 and 282 MHz, respectively. Optical rotations were measured on a JASCO DIP-1000 digital polarimeter with a 3.5ϕ × 100 mm cell. CD spectra were measured on a JASCO J-810 polarimeter with a 1 mm cell.

(*N–B*)-Chloro[5-chloro-2-(dimethylaminomethyl)phenyl]-phenylborane (4). To a solution of 4-chloro-*N*,*N*-dimethylbenzylamine[13] (230 mg, 1.36 mmol) in 10 mL of dry hexane was added a 1.0 mol L^{-1} butyllithium solution in hexane (0.90 mL, 1.5 mmol) at −78 °C under Ar. This reaction mixture was warmed to room temperature, and then refluxed for 24 h. This suspension was slowly added to a solution of dichlorophenylborane (0.20 mL, 1.5 mmol) in 10 mL of dry hexane in an ice bath from a dropping funnel. After the mixture had been stirred for 3 h at room temperature, the volatile materials were removed by evaporation. The residue was extracted with dichloromethane, and the organic solution was washed with aq $NaHCO_3$, dried over $MgSO_4$, and evaporated. The residue was recrystallized from hexane–dichloromethane to give 89 mg (22%) of the desired complex as colorless needles; mp 192–194 °C; ^{1}H NMR ($CDCl_3$) δ 2.27 (3H, s), 2.95 (3H, s), 3.92 and 4.49 (2H, ABq, J = 13.8 Hz), 7.18 (1H, d, J = 8.0 Hz), 7.24–7.38 (4H, m), 7.52 (1H, d, J = 2.0 Hz), 7.60–7.66 (2H, m); ^{13}C NMR ($CDCl_3$) δ 46.3, 48.5, 67.2, 123.7, 127.4, 127.5, 127.7, 130.7, 133.86, 133.89, 137.0, 140.8 (br), 150.9 (br); ^{11}B NMR ($CDCl_3$) δ 8.8 (half-band width 317 Hz); Anal. Found: C, 61.95; H, 5.64; N, 4.57%. Calcd for $C_{15}H_{16}BCl_2N$: C, 61.70; H, 5.52; N, 4.80%.

(±)-(*N–B*)-[5-Chloro-2-(dimethylaminomethyl)phenyl](pentafluoropropionyloxy)phenylborane (2). To a solution of the chloride **4** (50 mg, 0.19 mmol) in 4 mL of dry dichloromethane was added silver pentafluoropropionate (54 mg, 0.19 mmol). The reaction mixture was stirred for 3 h at room temperature and the formed precipitate was removed by filtration. The filtrate was evaporated and the residue was recrystallized from hexane–dichloromethane to give 119 mg (88%) of the desired compound as colorless crystals. mp 125–133 °C (dec); ^{1}H NMR ($CDCl_3$) δ 2.23 (3H, s), 2.88 (3H, s), 3.93 and 4.40 (2H, ABq, J = 13.5 Hz), 7.13 (1H, d, J = 7.9 Hz), 7.25–7.41 (6H, m), 7.74 (1H, d, J = 2.0 Hz); ^{13}C NMR ($CDCl_3$) δ 44.8, 48.2, 67.1, 105.8 (tq, J_{CF} = 261, 39 Hz), 118.1 (qt, J_{CF} = 285, 35 Hz), 123.6, 127.8, 128.0, 128.1, 132.5, 133.7, 138.0, 138.6 (br), 146.5 (br), 156.5 (t, J_{CF} = 28 Hz); ^{11}B NMR ($CDCl_3$) δ 8.6 (half-band width 259 Hz); ^{19}F NMR ($CDCl_3$) δ −79.1, −117.6; Found: C, 51.24; H, 3.98; N, 3.26%. Calcd for $C_{18}H_{16}BClF_5NO_2$: C, 51.53; H, 3.84; N, 3.34%.

Enantiomeric Resolution by Chiral HPLC. Chiral HPLC was carried out with a Daicel Chiralpak AD column (1 cmϕ × 25 cm) with hexane–2-propanol 50:1 as the eluent. About 10 mg of the racemic compound of **2** was dissolved in 20 mL of the eluent, and ca 1.5 mL of this solution was injected for each batch. The enantiomers were eluted at 16.1 and 19.4 min (α = 1.28) at a flow rate of 3.0 mL min^{-1}. Each enantiomer was recrystallized from hexane–dichloromethane to give colorless needles. The NMR spectra of these enantiomers are identical with that of the racemic compound. The first fraction (*R*)-(−)-**2**: mp 153–154 °C; $[\alpha]_D^{22}$ −158 (*c* 0.10, acetone); CD (hexane, 3.1 × 10^{-4} mol L^{-1}) $\lambda(\Delta\varepsilon)$ 212 (−28.1, sh), 227 (+1.5), 272 (−0.6), 279 (−0.6);

Found: C, 51.41; H, 3.89; N, 3.30%. Calcd for $C_{18}H_{16}BClF_5NO_2$: C, 51.53; H, 3.84; N, 3.34%. The second fraction (*S*)-(+)-**2**: mp 151–153 °C; $[\alpha]_D^{22}$ +157 (*c* 0.10, acetone); CD (hexane, 3.1×10^{-4} mol L^{-1}) $\lambda(\Delta\varepsilon)$ 211 (+22.9, sh), 227 (−1.5), 270 (+0.4), 278 (+0.5); Found: C, 51.29; H, 3.90; N, 3.28%. Calcd for $C_{18}H_{16}BClF_5NO_2$: C, 51.53; H, 3.84; N, 3.34%.

X-ray Analysis. A crystal of the (+)-isomer of **2** was obtained by crystallization from a hexane–dichloromethane solution. The diffraction data were collected on a Rigaku RAXIS RAPID imaging plate diffractometer with Mo Kα radiation ($\lambda = 0.71070$ Å) to a maximum 2θ value of 55.0° at −150 °C. The reflection data were corrected for the Lorentz-polarization effects. The structure was solved by the direct method (SIR97)[14] and refined by the full-matrix least-squares method. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included but not refined. (*S*)-**2**: Formula $C_{18}H_{16}BClF_5NO_2$, FW 419.58, Crystal size $0.33 \times 0.04 \times 0.03$ mm^3, Monoclinic, Space group $P2_1$ (No. 4), $a = 10.710(3)$, $b = 7.1467(16)$, $c = 12.542(3)$ Å, $\beta = 102.885(13)°$, $V = 935.8(4)$ Å^3, $Z = 2$, $D_{calcd} = 1.489$ g cm^{-3}, μ(Mo Kα) = 2.654 cm^{-1}, No. of data 13542, $R1$ ($I > 2.00\sigma(I)$) = 0.0275, $wR2 = 0.0816$, GOF = 0.968, $\chi = 0.00(2)$. Refinement data for the mirror image structure (*R* configuration): $R1$ ($I > 2.00\sigma(I)$) = 0.0275, $wR2 = 0.0816$, GOF = 0.968, $\chi = 1.00(2)$. Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (12, Union Road, Cambridge, CB2 1EZ, UK; fax: +44 1223 336033; deposit@ccdc.cam.ac.uk; http://www.ccdc.cam.ac.uk/conts/retrieving.html) and copies can be obtained on request, free of charge, by quoting the publication citation and the deposition number 294581.

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