Enantiomeric Resolution of Intramolecular Amine–Borane Complex with a Chiral Boron Center

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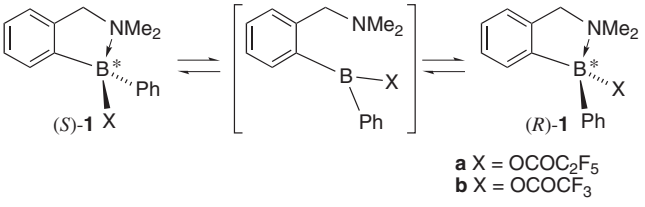
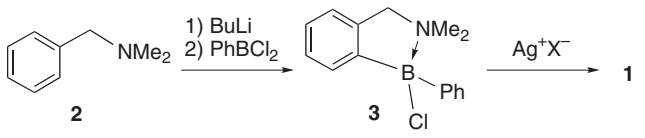
The enantiomers of [2-(dimethylaminomethyl)phenyl]-(pentafluoropropionyloxy)phenylborane were successfully resolved by chiral HPLC as a new type of intramolecular amine–borane complex with a chiral center at the tetrahedral boron atom. The X-ray structure, the barrier to racemization, and the chiroptical properties are reported.

We have been studying the molecular structures and dynamics of intramolecular amine–borane complexes with a 2-(dimethylaminomethyl)phenyl (DMP) ligand.[1,2] In most of these complexes, the boron atoms are configurationally labile in solution because of racemization via N–B bond dissociation, even though the tetrahedral boron atom is bonded to four different ligands. In general, several enantiopure borates and coordinated boranes are known,[3–8] some of which have been used in organic syntheses.[4,5] In most cases, however, the configuration at a boron atom is generated by other chiral elements in an identical molecule. Recently, enantiopure compounds with a chiral boron atom as the sole stereogenic center have been focused on, and complexes with phosphine[9] and amine[10] ligands have been used in stereochemical studies in relation to the isoelectronic species of tetrahedral carbons. We explored such compounds by using the DMP ligand and found that the introduction of a pentafluoropropionyloxy ($-OCOC_2F_5$) group at the boron atom enhances the configurational stability sufficiently to enable isolation of enantiomers at room temperature. We report herein the enantiomeric resolution and structure of **1a** as a novel optically active intramolecular amine–borane complex (Scheme 1).



Scheme 1.

(DMP)lithium prepared in a conventional manner was treated with dichlorophenylborane to give the chlorophenylborane complex **3** in 66% yield. The reaction of **3** with a silver carboxylate afforded the corresponding acyloxyborane (boric carboxylic anhydride) in good yield.[11] ^{11}B NMR signals of **1a** and **1b** were observed at ca. δ 10, typical of tetracoordinated boron atoms.[12]



Scheme 2.

The X-ray structure of *rac*-**1a** is shown in Figure 1.[13] The boron atom is tetrahedral because of intramolecular coordination of the amino nitrogen atom, where the N–B bond length is 1.668(4) Å. The tetrahedral character (THC) of the boron atom is 56% for **1a**, this value being smaller than those of the 9-BBN complex (9-DMP-9-borabicyclo[3.3.1]nonane **4**)[2c] and other intramolecular amine–diphenylborinate adducts (70–80%).[14]

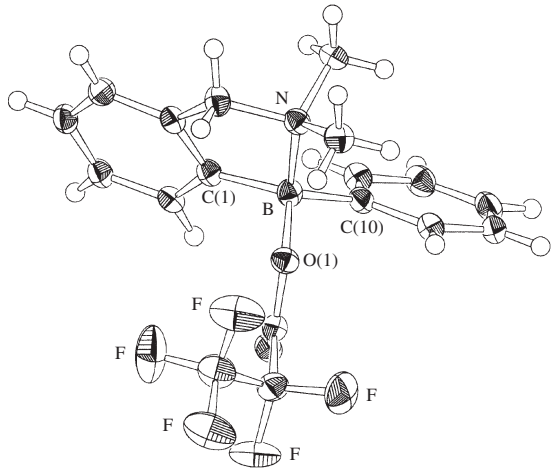


Figure 1. ORTEP diagram of *rac*-**1a** with thermal ellipsoids at 50% probability. B–N 1.668(4) Å, C(1)–B–O(1) 110.4(2), C(10)–B–O(1) 111.8(2), C(1)–B–C(10) 120.2(2)°.

The enantiomers of **1a** were resolved by chiral HPLC with a Daicel Chiralpak AD column (eluent: hexane/2-propanol, 50:1). Two fractions were eluted at 21.0 and 27.7 min with the baseline separation ($\alpha = 1.49$). This resolution was much higher than the case of **1b**, which showed only partial separation by chiral HPLC ($\alpha = 1.12$) and underwent significant decomposition during the separation. The specific rotations of the first and second eluted isomers were $[\alpha]_D^{27} + 169$ and -167 (*c* 0.10, acetone), respectively. As regards the CD spectra, the (+)-isomer showed a weak trough at 224 nm with a positive broad shoulder extending to the shorter wavelength region, whereas the spectrum of the (−)-isomer was practically its mirror image (Figure 2).

Complex **1a** slowly undergoes racemization in solution upon heating. The barrier to racemization was determined by classical kinetic measurement to be $\Delta G^{\neq}$ 116 kJ mol^{-1} (k 7.2 × 10^{-5} s^{-1}) in heptane at 83 °C, where the enantiomeric ratios were determined by chiral HPLC. The course of racemization was also monitored from the CD spectra (Figure 2). The racemization of **1b** is faster than that of **1a**, its barrier being 105 kJ mol^{-1} as estimated by saturation transfer experiments of the ^{1}H NMR sig-

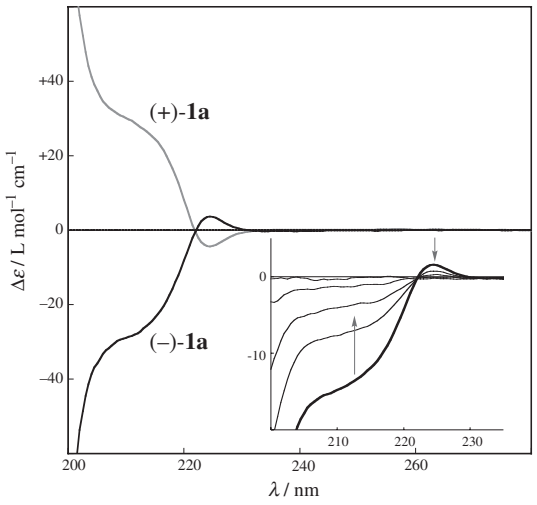


Figure 2. CD spectra of (+)- and (−)-**1a** in hexane. Inset spectra are changes during the racemization of (−)-**1a** upon heating for 0, 70, 300, 600, and 1080 min at 69 °C.

nals.

As proposed for other borane–amine complexes,[2a,b] the mechanism of racemization can be deduced from the dissociation of the N–B bond, the rotation about the C–B bond by 180°, and the recombination of the coordination bond, where the first step is rate-determining (Scheme 1). Thus, the rates of racemization mainly depend on the strength of the N–B coordination bonds. The above kinetic measurements revealed that the coordination bonds in **1** are stronger than those in **4** (ca. 75 kJ mol^{-1}), contrary to the small THC in the former; namely, perfluoroacyloxy groups as well as phenyl groups tend to enhance the Lewis acidity of boron atoms with a small structural change from trigonal to tetrahedral geometry. The difference in barrier heights between **1a** and **1b** is attributed to the inductive effect of extra fluorine atoms in the former, which increases the Lewis acidity of the boron atom.[15] The use of a $-OCOC_2F_5$ group not only enhances the barrier to racemization but also increases the chemical stability and the solubility, greatly facilitating the enantiomeric resolution.

In summary, we have successfully resolved enantiomers of the intramolecular amine–borane complexes with a chiral boron center by taking advantage of the DMP system with a $-OCOC_2F_5$ ligand. To the best of our knowledge, this compound is the first example of an enantiopure borane complex with four nonhydrogen ligands, and the racemization process is isoelectronically related to the S_N1 reaction at a tertiary carbon atom. Further studies on the effects of substituents at the boron atom on the barrier to racemization and the determination of absolute configuration are in progress.

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11 **1a**: Yield 66%; mp 140–142 °C; Found: C, 55.89; H, 4.78; N, 3.97% (Calcd for $C_{18}H_{17}BF_5NO_2$: C, 56.13; H, 4.45; N, 3.64%); ^{1}H NMR ($CDCl_3$) $\delta = 2.22$ (3H, s), 2.89 (3H, s), 3.95 and 4.46 (2H, ABq, $J_{AB} = 13.2$ Hz), 7.19 (1H, d, $J = 7.2$ Hz), 7.28–7.32 (5H, m), 7.41 (2H, m), 7.78 (1H, d, $J = 7.2$ Hz); ^{11}B NMR ($CDCl_3$) $\delta = 8.8$ (half-band width, 240 Hz). Enantiomers were resolved by chiral HPLC (Daicel, Chiralpak AD) with hexane:2-propanol (50:1) as eluent. Easily eluted isomer: mp 141–142 °C, $[\alpha]_D^{27} + 169$ (*c* 0.10, acetone), less easily eluted isomer: mp 141–143 °C, $[\alpha]_D^{27} - 167$ (*c* 0.10, acetone). **1b**: Yield 79%; mp 134–136 °C; Found: C, 60.57; H, 4.89; N, 4.42% (Calcd for $C_{17}H_{17}BF_3NO_2$: C, 60.93; H, 5.11; N, 4.18%); ^{1}H NMR ($CDCl_3$) $\delta = 2.23$ (3H, s), 2.90 (3H, s), 3.96 and 4.48 (2H, ABq, $J_{AB} = 13.5$ Hz), 7.20 (1H, m), 7.31–7.44 (7H, m), 7.80 (1H, m); ^{11}B NMR ($CDCl_3$) $\delta = 11.3$ (half-band width, 81 Hz).

12 ^{11}B NMR signals of similar borane complexes are observed at δ 4–12: for example, (*N–B*)-Bu(AcO)B$(CH_2)_3$NMe$_2$ δ 8.3. H. Nöth and B. Wrackmeyer, "Nuclear Magnetic Resonance Spectroscopy of Boron Compounds," Springer Verlag, Berlin (1978).

13 Crystal data for **1a**: $C_{18}H_{17}BF_5NO_2$, $M_r = 385.14$, orthorhombic, space group $P2_12_12_1$ (#19), $a = 7.7168(2)$, $b = 14.1933(5)$, $c = 17.0483(5)$ Å, $V = 1867.2(1)$ Å^3, $Z = 4$, $D_{calcd} = 1.370$ g cm^{-3}, μ(Mo Kα) = 1.21 cm^{-1}, $T = 93$ K, Rigaku RAXIS diffractometer, 2170 reflections, $R_1 = 0.049$, $R_w = 0.138$. CCDC deposition number: 227362.

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