Observation of Stereotopic Group Recognition in Chiral Borate Complexes in Solution

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The borate ester of **1a** and **2e** exhibits complete quaternization of the boron center. An equilibrium is observed between the two diastereomeric complexes **3** and **4** formed by coordination to the boron center of either amino group of **2e**. At –78°C, this equilibrium is slow on the NMR timescale and a diastereomeric ratio of about 3:1 is observed. At room temperature, a rapid equilibration is observed resulting in two NMR resonances (both ^{1}H and ^{13}C) for the dimethylamino groups of **2e** in **3/4**. Comparison with the NMR characteristics of the analogous borate complexes of **1h** and **1j** and of **2c** and **2d** shows that these resonances each correspond to both methyl groups of a single dimethylamino group. The chemical shift difference occurs solely from the difference between the time fractions that the dimethylamino groups are coordinated to the boron center, and forms, therefore, a direct measure of the ratio **3/4**. This ratio amounts to 63:37 at room temperature, which was confirmed by a protonation titration experiment. The elucidation of these NMR characteristics of B(**1a**)(**2e**) allowed the more rapid evaluation of the enantiotopic group recognition in many other borate complexes, which range from 57:43 to 67:33 at room temperature. The recognition of the (after complexation) diastereotopic dimethylamino groups of **2e** in the borate complex B(**1a**)(**2e**) was utilized in a consecutive methylation reaction, which yielded enantiomerically enriched ammonium salt **7**. The enantiomeric excess proved to be identical to the diastereomeric excess observed in the preceding recognition event. Strong evidence is presented that complex **3** is indeed the major diastereomer present in a solution of **3/4**, as expected from molecular models.

Introduction

Selective complexation of one of two enantiotopic groups present in a prochiral molecule by a chiral agent may be conceptually the simplest,[1] though both synthetically and analytically the hardest problem in the field of molecular recognition. Once the chiral compound becomes associated with the prochiral molecule, the initially enantiotopic groups of the latter become diastereotopic. It has been postulated that such a stereoselective recognition phenomenon occurs in the desymmetrization of prochiral or *meso*-compounds using enzymes,[2] chiral chemical reagents or catalysts.[3] Although examples of such reactions are amply found, and their importance for the preparation of asymmetric compounds is generally accepted, no spectroscopic evidence for the preceding enantiotopic group recognition events was ever presented.

The first direct evidence for enantiotopic group recognition in solution was described by our group.[1][4] In this study, one of two enantiotopic groups of a *meso*-diammonium guest molecule was found to be complexed selectively by a chiral crown ether host, as shown by NMR spectroscopy. At −78 °C for which slow exchange on the NMR timescale was observed, a ratio of 7:1 between the two diastereomeric complexes was found using the *cis*-1,2-cyclohexanediammonium guest, but the question which of the two enantio-conformers bound preferentially to the host remained unanswered. At room temperature, one set of six averaged signals was observed owing to the fast exchange between the two diastereomeric complexes and the uncomplexed guest. From the chemical shift differences between the resonances, a ratio of 5:1 was deduced for this system at room temperature. An analogous picture was observed for the *cis*-1,2-cyclopentane diammonium guest molecule. This system constitutes the first example ever for the direct observation of enantiotopic group recognition. However, visualization of this phenomenon by X-ray crystallography was not achieved. Furthermore, due to the low stability constant of the complex, it was not possible to utilize the host/guest complex in a synthetic reaction to convert the *meso*-compound into a chiral product. It was therefore not possible to correlate the recognition event with a stereoselective transformation.

In a short communication,[5] we recently reported the direct observation of enantiotopic group recognition induced by a chiral borate complex. This appeared to be a unique system, as one of the diastereomeric complexes crystallized out selectively in a quantitative fashion. Owing to the strong guest-complexing nature of the compounds, the recognition in solution was employed to produce an enantiomerically enriched product. This system constituted the first example for an enantioselective desymmetrization of a prochiral substrate shown to proceed via an intermediate enantiotopic group recognition event.

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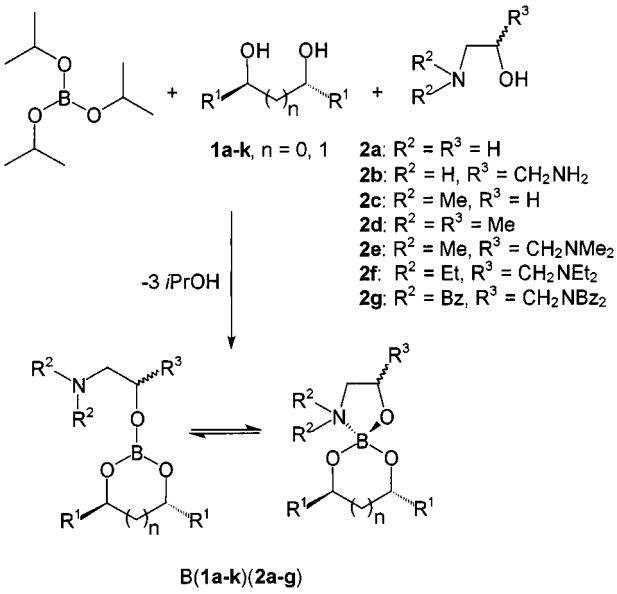
As mentioned above, not only finding systems exhibiting enantiotopic (or diastereotopic) group recognition is difficult, also analyzing and quantifying the degree of recognition remains a challenge. In the present paper we report the unique (NMR) spectroscopic properties of the borate complexes mentioned above which allowed us to quantify the ratio of the diastereomeric complexes in solution, even under fast exchange conditions. Attention is paid to the dynamic behavior of the complexes and the comparison with other model compounds revealing the boundary conditions for proper quantitative analysis. Furthermore, evidence is presented for the exact configuration of the major isomer in solution, confirming that this is the one selectively and quantitatively crystallizing out under equilibrium conditions.

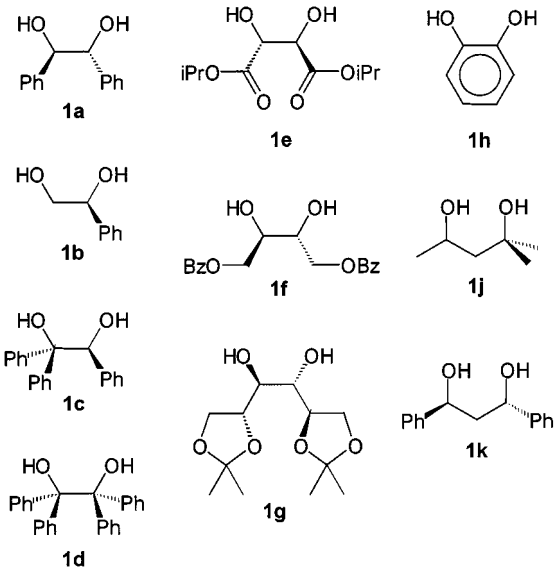
Results and Discussion

The borate esters discussed in this study were prepared by mixing equimolar amounts of $B(OiPr)_3$, a chiral diol (to induce the stereotopic selection), and a (di)amino alcohol (Scheme 1; diols used are depicted in Scheme 2). Coevaporating the evolving 2-propanol with toluene was necessary to drive the reaction to completion. It was envisaged that an equilibrium as shown in Scheme 1 would occur between tri- and tetracoordinated boron. An easy way to study this phenomenon appeared to be ^{11}B-NMR spectroscopy since the chemical shift of borate complexes is almost solely dependent on the atoms directly coordinated to the boron center and to the coordination geometry of the boron atom, especially the size of the chelate ring formed by the diol,[6] but not on residual groups further away. Typically, the ^{11}B shift (in $CDCl_3$) changed from $\delta = 23$ to 11 (while the resonances commonly had a width of a few ppm) upon complete coordination of an amine when a 1,2-diol was used, whereas for 1,3-diols these limiting shifts were $\delta = 18$ and 9, respectively. In general, borate complexes esterified with 1,2-diols gave complete formation of tetracoordinated boron when an additional amino alcohol was complexed. In contrast, borate-1,3-diol complexes gave only partial contributions of amino group coordination. The degree of participation depends in these cases on the basicity of the amino group. For example, an ^{11}B-NMR shift of $\delta = 15.3$ was observed for B(**1j**)(**2e**), leading to the conclusion that about 70% of the complex is present in the tricoordinated state and 30% in the tetracoordinated form (divided between both amino groups), while the ^{11}B-NMR shift of B(**1j**)(**2b**) ($\delta = 17.2$) indicates less than 10% participation of the latter coordination geometry. Similarly, B(**1k**)(**2e**) showed mainly tricoordinated boron. Probably, the five-membered chelate ring for boron-coordinated 1,2-diols provides a ring strain energy release upon formation of tetracoordinated boron, thus providing a driving force for amine coordination.

Apart from ^{11}B NMR, also ^1H NMR of the NH_2 protons of primary amino alcohols was indicative for coordination of NH_2 groups to the boron center. For example for B(**1e**)(**2a**), for which ^{11}B NMR ($\delta = 11.3$) showed complete



Scheme 1. Preparation of borate esters of diols and amino alcohols



Scheme 2. Diols employed in this study

quaternization of the boron center, the NH_2 proton resonance occurred at $\delta = 7.5$, while for uncomplexed aminoethanol (**2a**) $\delta = 1.5$ was observed. Similarly, the NH_2 ^1H-chemical shift for B(**1e**)(**2b**) (i.e. using a diamine) was $\delta = 4.5$, showing that half of the NH_2 groups are coordinated and the other half not, simply because only one group can be bound in the borate complex. It allows, however, no conclusion about possible stereotopic group recognition since the protons of the two NH_2 groups may interchange between the NH_2 groups.

In both complexes discussed here, two resonances were observed for the CHO−B carbon atoms of the tartrate unit. The de- and recoordination of amines, however, leading to the equilibrium shown in Scheme 1, is fast on the NMR timescale. Therefore, it was concluded that the dynamics of these complexes is as depicted in Figure 1: the de- and reco-

ordination of a single amino group is fast on the NMR timescale, but the rotation of the whole amino alcohol moiety in the tricoordinated state is slow most likely due to the low population degree of this coordination mode. For the monoamine complex B(**1e**)(**2a**), this implies that the fast de- and recoordination of the amino group takes place at the same side of the chelate ring formed by the chiral diol, whereas the rearrangement of the amine to the other side can occur only after the (slow) rotation around the B−O−C bond in the tricoordinated state. As a result, the two CHO−B carbons of the diol become diastereotopic. Analogously for B(**1e**)(**2b**), decoordination of an amino group and its recoordination or the coordination of the other amino group at the other side of the chelate ring (upper part of Figure 1) is rapid. This results, however, in the fact that the noncoordinated aminomethyl group is continuously at the same side of the chelate ring rendering the two CHO−B carbons of the diol diastereotopic.

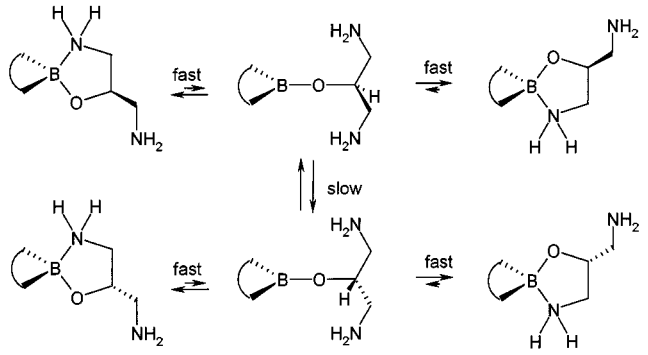
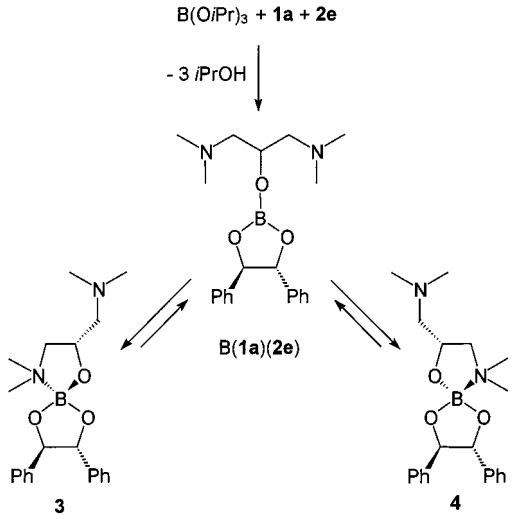


Figure 1. Dynamics of de- and recoordination equilibria relative to the NMR timescale (postulated)

For B(**1e**)(**2e**) and B(**1a**)(**2e**), however, only one CHO−B carbon signal is observed at room temperature. This cannot be attributed to a higher population degree of the tricoordinated state (i.e. a lower stability of the B−N coordination bond), since the methylated amino alcohols are more nucleophilic, leading to higher degrees of tetracoordinated boron complexes as confirmed by the ^{11}B-NMR shifts of B(**1j**)(**2b**) (δ = 17.2) and B(**1j**)(**2e**) (δ = 15.3). This dynamics suggests, therefore, an overall more rapid de- and recoordination and rotation kinetics for the methylated derivatives.

Due to the rapid exchange processes depicted in Figure 1, it was hard to quantify the stereotopic group recognition occurring for the primary diamino alcohols. We switched to tertiary amines such as **2e** in order to eliminate the possible interchanging of the amine protons. The borate ester B(**1a**)(**2e**) proved to be a fruitful model system, largely because the methyl resonances of the dimethylamino groups became additional NMR probes. As discussed above, this complex was expected to provide the tricoordinated intermediate, which should spontaneously form the two possible (diastereomeric) complexes **3** and **4** in a thermodynamically controlled process involving the complexation of the pro-(*S*) and pro-(*R*) amino groups, respectively (Scheme 3). Indeed, compounds **3** and **4** were obtained as the sole products as shown by ^{11}B-, ^{1}H-, and ^{13}C-NMR spectroscopy. The ^{11}B-NMR spectrum displays a signal at δ = 10.6, in the range expected for tetracoordinated boron, and leads to the conclusion that in each complex one of the amino groups is coordinated to boron while the other one remains noncoordinated (cf. **3** and **4**). The ^{1}H- and ^{13}C-NMR spectra are fully in accordance with this conclusion.



Scheme 3. Equilibration of **3** and **4** via the tricoordinated state

X-Ray structural analysis[5] showed the presence of a single diastereomer in the solid state, namely **3** in which the pro-(*S*) amino group is coordinated to the boron center. It appeared that this crystallization occurred in quantitative yield. A powder diffraction experiment[5] of the whole batch of crystals showed that **3** was the only isomer crystallizing out from solution. This leads to the conclusion that the crystallization of **3** occurs with concomitant re-equilibration of **3** and **4** in the remaining solution. A process in which a single compound crystallizes out quantitatively from an equilibrating mixture, such as the here observed crystallization of **3** from **3/4**, is called an "asymmetric transformation of the second kind".[7] In cases described so far equilibration is brought about by heating or by a catalyst, usually an acid or base. In the example described here, however, equilibration in solution occurs spontaneously. As a consequence, equilibration of **3/4** is resumed as soon as the solid is redissolved, in contrast to the systems described in the literature for which no re-equilibration occurs after redissolution.

At −78 °C, the exchange between the two tetracoordinated, diastereomeric complexes is slow on the NMR timescale, the ratio of diastereomers being roughly 3:1 (Figure 2, top; integration averaged 2.85:1). It was not possible to make unambiguous configurational assignments from these spectra alone. We assume, however, on the basis of molecular models that the major diastereomer is **3**, formed by the coordination of the pro-(*S*) amino group. These models show that for **3** the noncoordinated dimethylaminomethyl group occupies one of the two quadrants, formed by the planes through the spiro-configured five-membered rings, not occupied by a phenyl group of the chiral diol (Figure 3). This would mean that the isomer crystallizing out in the so-

called asymmetric transformation of the second kind is also the major one occurring in solution. This contrasts with most studies in this field in which it is usually observed that the minor isomer present in solution is the one crystallizing out preferentially (the so-called Van′t Hoff−Dimroth rule).[7] More evidence supporting the assumption for the exact configuration of **3** is presented below.

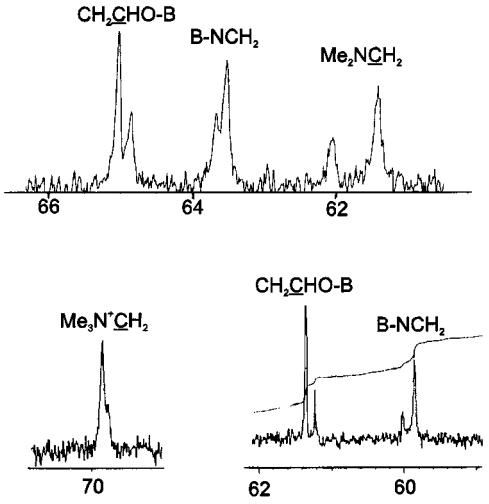


Figure 2. ^{13}C NMR spectra of the propane resonances of B(**1a**)(**2e**) (**3/4**) at −78 °C (top) and of B(**1a**)(**2e**); MeOTf (**5/6**) at room temperature (bottom)

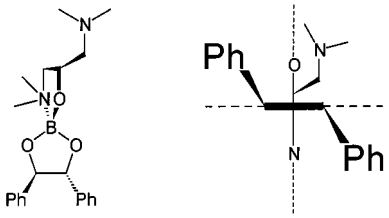


Figure 3. Schematical top (left) and side (right) views of **3**, with the planes through the two spiro-configured five-membered rings indicated by dashes

At room temperature, a rapid exchange process occurs. Two equally intense singlets for the dimethylamino groups were observed by both ^{1}H- (Figure 4) and ^{13}C-NMR spectroscopy. From these spectra alone it could not be concluded if such a singlet corresponds to (two) methyl groups from different or identical dimethylamino groups. Therefore, several model systems were prepared and the number of ^{13}C signals for the dimethylamino groups was determined (Table 1). For B(**1a**)(**2d**), two signals were observed. This shows that, in this case, *N*-inversion is slow on the NMR timescale due to (complete) coordination of the dimethylamino group to the boron center. The occurrence of two signals might be due to the chirality of the hydrobenzoin portion or to the stereocenter present in the amino alcohol. The latter appears to be true since B(**1a**)(**2c**) shows only one (slightly broadened) signal. This proves that the chirality in the latter system has little influence, and the two methyl resonances, although in principle diastereotopic, remain isochronous. This is confirmed by B(**1h**)(**2d**) and B(**1h**)(**2c**): the catechol portion is achiral but gives complete quaternization of the boron center (as does **1a**) and the occurrence of two signals for the former must therefore be due to the position of the *N*-methyl groups relative to the 2-methyl group.

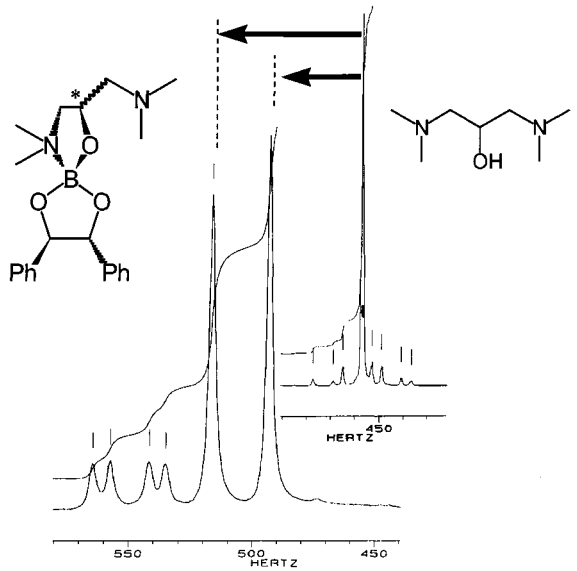


Figure 4. ^{1}H-NMR shifts (200 MHz) of the dimethylamino groups (singlets) of B(**1a**)(**2e**) relative to uncomplexed **2e**

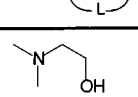
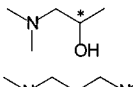
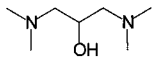
		1h	1j	1a
	**2c**	1	1	1[b]
	**2d**[a]	2	1	2
	**2e**	1	1	2

Table 1. Number of ^{13}C resonances of the dimethylamino groups of several borate model compounds, B(**1**)(**2**)
[a] No splitting of $N(CH_3)_2$ resonance(s) observed due to the occurrence of diastereomers (amino alcohol **2d** was applied as the racemate). − [b] Relatively broad (see text).

With 2-methyl-2,4-pentanediol (**1j**) as the (chiral) diol, a single resonance for the dimethylamino group was observed in all cases. This can be explained by the fact that only incomplete quaternization of the boron center occurs (as found commonly for 1,3-diols, see above) so that rapid *N*-inversion is possible whilst the amine is noncoordinated. For B(**1h**)(**2e**), only one resonance is observed also. In this case, no discrimination between the dimethylamino groups can occur since the diol is achiral, and therefore each group is coordinated for 50% of the time. When a group is not coordinated, rapid *N*-inversion occurs.

Returning to B(**1a**)(**2e**), it is concluded that no perfect recognition (i.e. 100% coordination) of one of the dimethylamino groups takes place since both resonances are

shifted relative to the free amino alcohol (Figure 4). Therefore, both groups are noncoordinated for substantial fractions of the time, during which rapid *N*-inversion can take place, while the sum of the time fractions that the groups are coordinated equals unity. Thus it is concluded that each of the two signals observed for this system can be ascribed to the two methyl groups of a single dimethylamino group. However, it was reasoned above that the chirality of **1a** does not cause a substantial chemical shift difference. Also, the emergence of a stereocenter on the CHO−B carbon of the **2e** moiety cannot explain the observed shift difference because the methyl groups on a single dimethylamino group are chemically equivalent, leading to a single methyl resonance B(**1j**)(**2e**). Therefore, the observed chemical shift difference is attributed solely to the difference between the time fractions that the two dimethylamino groups are coordinated to the boron center. Thus the chemical-shift difference is a direct measure for the stereotopic group recognition!

An analysis of the ^{1}H-NMR shifts corroborates this picture. The sum of the changes of the ^{1}H-chemical shifts (δ = 0.30 and 0.18, respectively; see Figure 4) of the dimethylamino groups in the diastereomeric mixture of B(**1a**)(**2e**) (**3** and **4**) relative to noncomplexed **2e** turned out to be equal to the analogous chemical shift change (δ = 0.48) of the singlet of B(**1a**)(**2c**) relative to **2c**. This supports the reasoning given above and, as a consequence, the observed ^{1}H-chemical shift changes of **3/4** can be quantitatively correlated with the relative amounts of coordination of each of the two dimethylamino groups to the boron center. This direct measure of the stereotopic group recognition in solution under fast exchange conditions at room temperature amounts to 62:38. From the equilibria of **3** and **4** at −78 and +25 °C, K values (= [**3**]/[**4**]) of 2.85 (by integration; slow exchange) and 1.63 (by shift analysis; fast exchange) were thus obtained, respectively. Assuming that the heat capacity is negligible over this temperature range, these data lead to $\Delta H° = -2.6$ kJ/mol and $\Delta S° = -4.8$ J/molK. The equilibrium is, therefore, enthalpy driven over this temperature range and these data suggest that a stronger B−N bond is formed for **3** compared to **4** but that **3** is less flexible.

In order to verify this ratio, a protonation titration was performed and monitored by ^{13}C NMR. Protonation occurs at a noncoordinated dimethylamino group and, therefore, the group which is least coordinated is more prone to protonation and concomitant chemical-shift change than the one coordinated to a larger degree. The ^{13}C resonances of the dimethylamino groups were chosen because the ^{1}H resonances showed smaller shifts and considerable line-broadening upon protonation. The titration experiment using trifluoromethanesulfonic acid (triflic acid, TfOH) as the proton source is shown in Figure 5. ^{11}B NMR confirmed that the boron center remained tetracoordinated as long as less than one equivalent of acid was used. Relative to **2e**, the ^{13}C resonances of the dimethylamino groups in nonprotonated B(**1a**)(**2e**) were shifted upfield, leading to the conclusion that the more shifted one is the one coordinated on average for a greater time. This was confirmed by the titration experiment where this resonance was less affected by protonation. The ratio of the slopes of the lines shown in Figure 5 equals the ratio between the diastereomers, more correctly the ratio between the protonated diastereomers. It was assumed that the protonation constants and the bound shifts were equal because the protonation sites are far away from the chiral center. The ratio of the slopes gave 62:38, which is equal to the ratio given above. A protonation experiment using *p*-toluenesulfonic acid as the proton source gave an identical ratio.

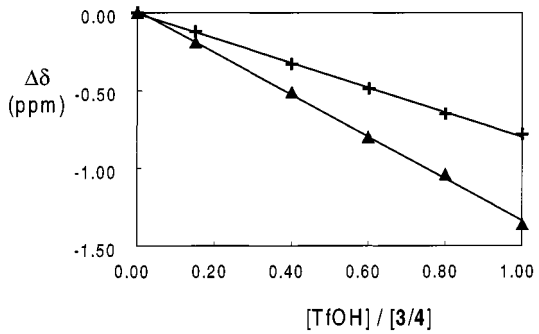
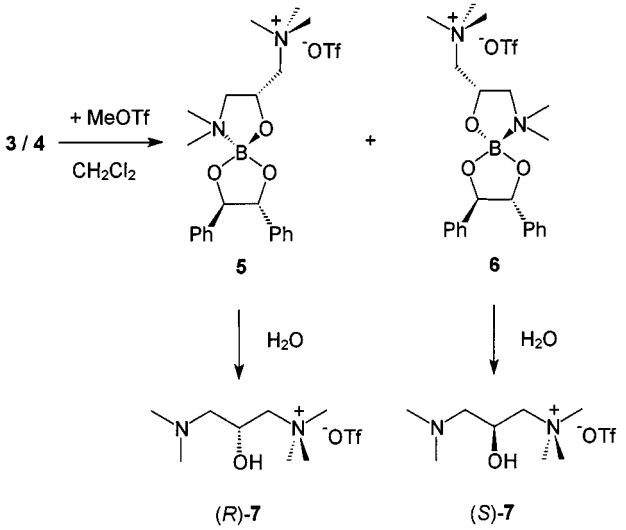


Figure 5. ^{13}C-NMR shift changes of the dimethylamino groups of B(**1a**)(**2e**) upon addition of triflic acid; more coordinated $N(CH_3)_2$ (+) and less coordinated $N(CH_3)_2$ (Δ) to boron

The dynamics of the B(**1a**)(**2e**) system shows the following picture. Exchange of the alkoxy group of the **2e** portion is slow on the NMR timescale at any temperature. The exchange of the dimethylamino groups between the coordinated and noncoordinated states, i.e. the **3/4** equilibrium, is rapid on the NMR timescale at room temperature, as also the rotation around the alkoxy bond in the boron-tricoordinated intermediate as discussed above. In a variable temperature NMR experiment, it appeared that the exchange of the dimethylamino groups becomes slow only below −60 °C (slow exchange was observed at −78 °C and very broad but coalesced resonances at −50 °C) which leads to an exchange rate of about 10−100 s^{-1} at this temperature. From this result can be deduced that at −78 °C the exchange is still chemically rapid, i.e. in the order of seconds. This was confirmed by an experiment in which a sample of crystalline **3** was dissolved in partly frozen CD_2Cl_2 (−95 °C) and measured (^{1}H NMR) within two minutes after bringing the sample into the magnet at −78 °C. Hereafter, a ^{13}C spectrum was taken (30 min) and another ^{1}H spectrum (after warming to room temperature and recooling to −78 °C). Both ^{1}H spectra were identical and equal to the spectrum of a sample prepared at room temperature. The latter was true for the ^{13}C spectrum also. Therefore, complete equilibration of **3** and **4** is reached within 1−2 min after dissolving **3** at −78 °C.

The B(**1a**)(**2e**) system constituted the first example for which stereotopic group recognition was observed and quantitatively assessed in both solution and the solid state. Selective functionalization of the noncoordinated amino group in the complexes **3/4** and consecutive release of the product from the boron moiety was attempted. To this end

a solution of **3/4** was treated with methyl trifluoromethanesulfonate (MeOTf) and subsequently with water (Scheme 4). Upon addition of one equivalent of MeOTf, complete chemoselectivity in favor of the monomethylated products **5/6** was observed. The ^{11}B spectrum showed still complete quaternization of the boron center. Only an excess of MeOTf led to the formation of the (undesired) dimethylated product. Therefore, it can be concluded that the noncoordinated dimethylamino group is methylated more rapidly, and that coordination of the remaining dimethylamino moiety to the boron center results in protection against further methylation. This was confirmed by the methylation of B(**1j**)(**2e**) for which the addition of one equivalent of MeOTf led to a mixture of mono- and dimethylated products. This is attributed to the fact that this complex is present in a tetracoordinated form for only 30% (see above) so that protection after monomethylation does not occur.



Scheme 4. Methylation of **3/4** and subsequent hydrolysis

Diastereomeric ratios **5/6** of 74:26 were observed by ^{13}C NMR when the methylation reaction was performed at −78 °C (see Figure 2, bottom), and 62:38 at 25 °C. These values were in agreement with the observed *ee* values of monomethylated **2e** (**7**) which were measured to be 48% at −78 °C and 26% at 25 °C. The *ee* determinations were performed by ^{1}H NMR using (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol as the (diamagnetic) chiral shift reagent.[8] The selectivity values found here are identical to the observed diastereomeric ratios **3/4** at the respective temperatures. Thus, the *ee* of **7** results from the thermodynamic process of enantiotopic group recognition of the dimethylamino groups of **2e** in the diastereomeric complexes **3/4**.

Three questions remained to be answered for this system: (i) what are the relative rates for the equilibration process of **3/4** versus methylation; (ii) is the noncoordinated dimethylamino group really the one being methylated; (iii) which diastereomer (**3** or **4**) forms preferentially in solution. The last question can, together with the answer to the second one, be reduced to determining the absolute stereochemistry of the major enantiomer of **7**.

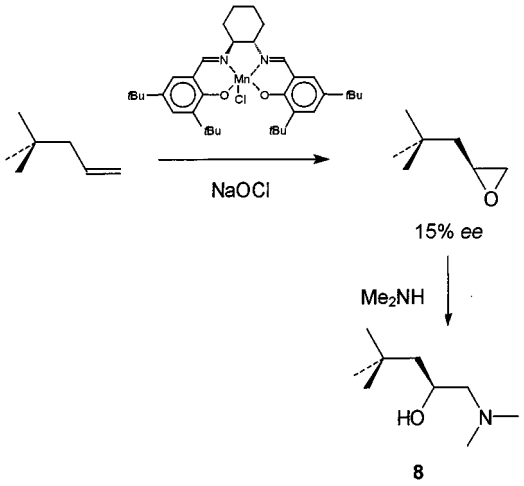
The methylation at −78 °C took several minutes to 1 h to reach completion, and it is therefore slower than the equilibration of **3/4**. This was confirmed by several experiments in which crystalline **3** was subjected to MeOTf before dissolution. None of these experiments gave other selectivities than those mentioned above. Therefore, methylation occurs only after dissolving **3**, and the equilibration to **3/4** is (at all temperatures) more rapid than the methylation. Because the methylation is slower than the equilibration and because the selectivities observed after methylation are identical to the degrees of stereotopic group recognition, this strongly suggests that the diastereomers **3/4** have identical reactivity towards methylation.

Whether the coordinated or the noncoordinated dimethylamino group is being methylated has been suggested by two pieces of evidence already. First is the observed protection effect of coordination to the boron center of the remaining dimethylamino group which proves the (much) lower methylation rate for boron-coordinated amino groups versus noncoordinated ones. Second are the identical methylation rates found for **3/4** which suggests that methylation takes place away from the chiral center. The third piece of evidence is found in Figure 2: the relative positions of the ^{13}C resonances of the alkoxy and the coordinated $B-NCH_2$ carbon atoms of the amino alcohol moieties are identical for the major and minor isomers of **3/4** and **5/6**. From these spectra is concluded that the noncoordinated group (either the dimethylamino group of **3/4** or the trimethylammonium group of **5/6**) assumes the same position with respect to the chelate ring of the boron-coordinated amino alcohol portion for both major isomers (and for both minor isomers also).

As discussed above, molecular models suggest the lower steric hindrance of **3** compared to **4**. Another way to answer the question of the major isomer **3** or **4** in solution is to try to elucidate the absolute stereochemistry of the major enantiomer of **7**. This proved to be a nontrivial problem, however. All attempts to eliminate trimethylamine from this compound to prepare (dimethylamino)methyloxirane failed. The other direction, i.e. to make the compound from optically pure epichlorohydrin and dimethylamine, also failed because the ring-opening reaction is not (completely) selective; probably reclosure under elimination of HCl occurs followed by reopening and addition of a second equivalent of dimethylamine. This impossibility to stop the reaction at the intermediate *N*,*N*-dimethyl-3-amino-1-chloro-2-propanol renders this approach useless. Attempts to crystallize **7** as a diastereomeric salt from the **5/6** mixture were also fruitless. No other chiral ligands were attempted to obtain selective crystallization.

The only other way was viewed to be to apply the ^{1}H-NMR methodology using the above described (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol shift reagent for identifying the absolute stereochemistry of **7**. In earlier papers,[8][9] it was shown that classes of compounds (e.g. lactones)[8] gave identical coordination behavior to this reagent so that definite conclusions about their stereochemistry could be made. Since it was not clear beforehand in which geometry an

analogous chelate ring would be formed by the shift reagent and **7**, the corresponding isoelectronic analog *N*,*N*-dimethyl-2-hydroxy-4,4-dimethyl-1-aminopentane **8** was prepared (Scheme 5). The first step, starting from 4,4-dimethyl-1-pentene was the enantioselective epoxidation using the Jacobsen procedure.[10] Although the epoxidation of primary aliphatic alkenes occurs slower and with less stereoselectivity, the (*S*)-epoxide was expected to be formed preferentially.[11] The goal of this study was not to reach a high *ee* for this reaction anyway, because both enantiomers had to be visible in the ^{1}H-NMR experiment. Therefore, the reaction was performed at room temperature to reach a comfortable reaction rate. After epoxide ring-opening with dimethylamine, the pure amino alcohol product **8** was obtained in an overall, isolated yield of 23%. The *ee* as determined by ^{1}H NMR proved to be about 15% (see below).



Scheme 5. Preparation of the isoelectronic analog **8** of **7**

Figure 6 shows parts of the ^{1}H-NMR spectra of **7** (left) and its isoelectronic analog **8** (right) in the presence of the chiral shift reagent. For **7** the best separation is observed for the $(CH_3)_3N^+$ resonance, whereas for **8** the corresponding $(CH_3)_3C$ signal shows only a poor resolution. It should be mentioned that the spectra for **7** were taken with 2.4 equivalents of chiral alcohol, whereas for **8** more than 13 equivalents were required to obtain this resolution, but this effect may be due to a smaller formation constant for the latter coordination complex. In favor of a similar binding mode for **7** and **8** coordinating to the chiral shift reagent, as is obligatory for analysis of the absolute stereochemistry, are the identical shift separations $(\Delta\delta_R - \Delta\delta_S)/(\Delta\delta_R + \Delta\delta_S)$ for the $N(CH_3)_2$ resonances and the fact that all shifts occur in the same direction (upfield) relative to the chemical shifts of **7** and **8** without the chiral shift reagent present. Figure 6 shows that for both **7** and **8** the major enantiomer gives the more upfield resonance. When a similar coordination mode is assumed, (*R*)-**7** is the major enantiomer [(*R*)-**7** is isoelectronic to (*S*)-**8** for (*R*/*S*)-configurational assignment reasons] formed during the methylation and subsequent hydrolysis of B(**1a**)(**2e**) so that **5** must be the major component of the diastereomeric mixture **5/6**. Combined with the fact that methylation occurs at the noncoordinated aminomethyl group so that **5** results from methylation of **3** and **6** of **4**, this suggests that **3** is indeed the major isomer present in the equilibrating diastereomeric mixture before methylation, in accordance with the reasoning given above depending on molecular models.

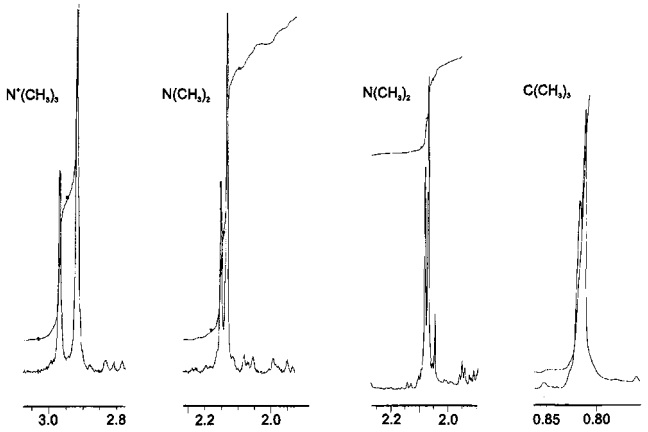


Figure 6. ^{1}H-NMR methyl singlets of **7** (left two parts) and **8** (right two parts) in the presence of (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol

It appeared that variation of the chiral 1,2-diol did not bring about substantial selectivity differences: B(**1g**)(**2e**) (62:38), B(**1e**)(**2e**) (63:37), and B(**1f**)(**2e**) (61:39) all gave similar values as determined by protonation titrations. Instructive is the lower value for B(**1b**)(**2e**) (57:43) because here only one face of the chelate ring formed by the diol is able to differentiate between the amino groups, leading to 50% less selectivity compared to B(**1a**)(**2e**). Using **1c**, it was attempted to get one phenyl group closer to the noncoordinated amino group, but it resulted in incomplete quaternization at the boron center (94%) resulting in a somewhat lower stereoselectivity for B(**1c**)(**2e**) (60:40). This steric hindrance was confirmed by B(**1d**)(**2e**), for which only 88% tetracoordinated boron was observed. As already mentioned above, 1,3-diols (**1j** and **1k**) did not give complete quaternization either so that these were not investigated further.

Changes were attempted at the substrate side, also, to see whether an increase of the bulkiness of the noncoordinating amino group would result in better recognition. **2g** appeared to be too bulky: the ^{11}B-NMR shift (δ = 23.1) observed for B(**1a**)(**2g**) indicated the complete lack of coordination of the amino groups. For B(**1a**)(**2f**), a slightly better selectivity compared to B(**1a**)(**2e**) was observed by protonation at room temperature (67:33), and clean monomethylation was observed after methylation at −78 °C.

Overall, these borate model systems provided valuable new information regarding the possibilities for studying stereotopic group recognition in solution. The B(**1a**)(**2e**) system showed three comfortable possibilities to study the (rapid) stereotopic group recognition events occurring in solution for such systems: (i) NMR shifts relative to the noncomplexed amines (as in Figure 4), (ii) NMR protonation titrations using the shift movements of easily observed resonances upon addition of acid (as in Figure 5),

and (iii) the methylation of tertiary to quaternary amines at any desired temperature so that the resulting, and nonequilibrating, product mixture (before or after hydrolysis) can be investigated by NMR at room temperature (as in Figure 2, bottom).

Conclusions

This study describes in detail the first example of enantiotopic group recognition observed in both solution and the solid state, implemented into an asymmetric reaction scheme in a consecutive methylation step. Thus, a product was obtained after hydrolysis of which the enantioselectivity was shown to result directly from the foregoing stereotopic group recognition event. Besides this phenomenon of enantiotopic group recognition, the spectroscopic properties observed in solution have provided more general tools for measuring the degree of stereotopic group recognition in solution. Hopefully, this will allow more systematic and detailed studies in this interesting part of the field of molecular recognition.

Experimental Section

General Remarks: All diols and (di)amino alcohols other than those described below were obtained from commercial sources and used without further purification. Triisopropyl borate was distilled and kept under argon. − Melting points were determined using apparatus from Gallenkamp Inc., UK. Values given are uncorrected. − Elemental analyses were determined by Mikroanalytisches Laboratorium Kolbe, Mülheim an der Ruhr, Germany.

NMR Measurements were performed at a Bruker AC200, AMX300, and DMX600. Samples measured at low temperature were filled under argon and sealed. Commercial $CDCl_3$ and D_2O were used; CD_2Cl_2 was distilled before use. No TMS was employed; for ^{1}H-NMR spectra, residual $CHCl_3$ (δ = 7.24) or $CHDCl_2$ (δ = 5.30) were used for internal reference. For ^{13}C-NMR spectra, $CDCl_3$ (δ = 77.0) or CD_2Cl_2 (δ = 53.8) were used. For spectra in D_2O, *tert*-butyl alcohol (CH_3: δ = 1.20 and 31.2 for ^{1}H and ^{13}C, respectively) was added. The ^{11}B spectra were recorded relative to external $BF_3 \times OEt_2$.

Several complexes were measured at both −78 °C and room temperature. For B(**1a**)(**2e**), series were measured from −78 to 22 °C at 20−30 °C intervals to investigate their dynamic behavior. This showed fast exchange at temperatures of −50 °C (very broad) or higher and slow exchange at −78 °C, with coalescence probably at about −60 °C. In another experiment, the crystalline form **3** was dissolved in CD_2Cl_2 at −95 °C and measured within two minutes (^{1}H) at −80 °C. After 30 min (^{13}C spectrum), the ^{1}H spectrum was remeasured. The ^{1}H spectra did not differ from each other and the ^{1}H and ^{13}C spectra were both identical to the spectra obtained for a sample which was prepared at room temperature.

The *ee* measurements described here employed commercial (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol as the (diamagnetic) chiral shift reagent. Samples generally contained 5−10 mg of the substance of which the *ee* was to be determined, dissolved in 0.75 mL $CDCl_3$. The shift reagent was added in portions of 5−10 mg until one or more ^{1}H-NMR resonances of the substance (usually an easily observed singlet) were completely resolved into their respective enantiomeric signals. The *ee* was determined by integration of these resolved signals.

For the determination of the stereotopic group recognition occurring in the borate complexes in solution under fast exchange conditions (usually > −50 °C), titrations with acid (trifluoromethanesulfonic acid, TfOH, or *p*-toluenesulfonic acid, TsOH) were employed. Generally 50−75 mg of a borate complex were dissolved in $CDCl_3$ and the acid was added in portions of 0.20−0.25 equivalents. Changes in ^{1}H- and ^{13}C-NMR chemical shifts were monitored, while ^{11}B spectra were recorded to verify the coordination number (3 or 4) at the boron center.

(*R*,*R*)-(+)-Hydrobenzoin (1a): 1a was prepared by enantioselective dihydroxylation of *trans*-stilbene according to a procedure by Sharpless.[12] − ^{1}H NMR (200 MHz, $CDCl_3/CD_3CN$ = 1:1): 7.05 (m, 10 H, Ph), 4.45 (dd, 2 H, CH, $^3J_{CHOH}$ = 2.0 Hz, $^4J_{CHOH}$ = 1.1 Hz), 3.45 (dd, 2 H, OH). ^{13}C NMR (50.3 MHz, $CDCl_3/CD_3CN$ = 1:1): 140.0 (*α*-Ph), 127.2, 126.5 (*o*/*m*-Ph), 126.9 (*p*-Ph), 78.1 (CHOH).

(±)-1,3-Diphenyl-1,3-propanediol (1k): The racemate of **1k** was prepared as reported[13] by reduction of dibenzoylmethane to give 19% of an off-white solid. Melting point: 130−132 °C (reported: 130°C).[13] − ^{1}H NMR (200 MHz, $CDCl_3$): 7.25−7.00 (m, 10 H, Ph), 4.77 (dt, 2 H, CH), 4.64 (d, 2 H, OH, $^3J_{CHOH}$ = 4.1 Hz), 1.89 (t, 2 H, CH_2, $^3J_{CHCH2}$ = 5.9 Hz). − ^{13}C NMR (50.3 MHz, $CDCl_3$): 144.8 (α-Ph), 127.7, 125.3 (*o*/*m*-Ph), 126.4 (*p*-Ph), 70.3 (CHOH), 47.0 (CH_2). MS (CI): 228 [M], 210 [M − H_2O].

***N*,*N*,*N*′,*N*′-Tetraethyl-1,3-diamino-2-propanol (2f):** 1,3-dibromo-2-propanol (436 mg, 2.00 mmol, purity: 95%) and diethyl amine (439 mg, 6.00 mmol) were dissolved in chloroform (5 mL). Potassium carbonate (829 mg, 6.00 mmol) was added and the mixture was heated at 50 °C overnight. After cooling and evaporation of the solvent, water (25 mL) was added and the pH of the water layer was adjusted to 1 using concentrated aqueous HCl. The water layer was washed with dichloromethane (3 × 25 mL). Hereafter, the pH was adjusted to 12 with 4 M NaOH (phase separation visible), and the water layer was extracted with dichloromethane (3 × 25 mL). The latter organic layers were combined and dried with $MgSO_4$. After filtration and evaporation in vacuo, **2f** was obtained (316 mg, 78%) as a clear liquid. The purity, according to NMR, was judged to be 94%. The contaminant was found to be *N*,*N*-diethyl-3-amino-1,2-propanediol and was attributed to the presence of 3-bromo-1,2-propanediol in the starting dibromide. Further purification was not attempted. − ^{1}H NMR (200 MHz, $CDCl_3$): 4.28 (br s, 1 H, OH), 3.63 (m, 1 H, CH), 2.48 (dq, 8 H, CH_2CH_3, $^3J_{CH2CH3}$ = 7.1 Hz), 2.34 (m, 4 H, CH_2CHOH), 0.92 (t, 12 H, CH_3). − ^{13}C NMR (50.3 MHz, $CDCl_3$): 65.2 (CHOH), 57.7 (CH_2CHOH), 47.2 (CH_2CH_3), 11.6 (CH_3).

***N*,*N*,*N*′,*N*′-Tetrabenzyl-1,3-diamino-2-propanol (2g):** Sodium carbonate (1.09 g, 10.3 mmol) and 1,3-diamino-2-propanol (201 mg, 2.23 mmol) were dissolved in water (10 mL) and heated to reflux. Benzyl bromide (1.57 g, 9.16 mmol) was added dropwise over 30 min. After additional refluxing for 1 h, the mixture was cooled to room temperature and extracted with diethyl ether (3 × 20 mL). The ether layers were washed with brine and dried with $MgSO_4$. After filtration and evaporation, **2g** (632 mg, 1.40 mmol, 63%) was obtained as a yellowish oil, contaminated with about 7 wt-% benzyl alcohol. This was used directly for the formation of B(**1a**)(**2g**) (see below). An acid/base extraction as described above for **2f** gave **2g** (218 mg, 0.484 mmol) with a purity > 97 w%. − ^{1}H NMR (200 MHz, $CDCl_3$): 7.40−7.25 (m, 20 H, Ph), 3.84 (qn, 1 H, CH, $^3J_{CHCH2}$ = 6.1 Hz), 3.59 (dd, 8 H, CH_2Ph, $^2J_{gem}$ = −13.5 Hz), 2.46 (d, 4 H, CH_2CH). − ^{13}C NMR (50.3 MHz, $CDCl_3$): 139.0 (α-Ph),

129.0, 128.2 (*o*/*m*-Ph), 127.0 (*p*-Ph), 65.7 (CHOH), 58.9 (CH_2Ph), 57.7 (CH_2CH).

(*S*)-*N*,*N*-Dimethyl-2-hydroxy-4,4-dimethyl-1-aminopentane (8): This amino alcohol derivative was prepared by Jacobsen-epoxidation[10] of 4,4-dimethyl-1-pentene, followed by ring-opening using Me_2NH, as follows. The catalyst (*S*,*S*)-(+)-*N*,*N*′-bis(3,5-di-*tert*-butylsalicylidene)-1,2-cyclohexanediaminomanganese(III) chloride, 68 mg, 0.107 mmol) and 4,4-dimethyl-1-pentene (196 mg, 2.00 mmol) were dissolved in dichloromethane (2 mL). A buffered sodium hypochlorite solution (2.5 mL, containing 1.43 M NaOCl and 14 mM phosphate buffer at pH 11.5) was added and the two-phase mixture was stirred vigorously at room temperature overnight. Hexane (20 mL) and water (20 mL) were added and the organic layer was washed with brine (2 × 20 mL). The combined water layers were extracted with dichloromethane (3 × 20 mL) and the combined organic layers were dried with $MgSO_4$. After filtration and evaporation of the solvent the crude epoxide was obtained as a brownish liquid, still containing manganese. In order to remove the catalyst remainder, the product was dissolved in dichloromethane (1 mL) and put through a small silica column (2 mL volume), eluted with dichloromethane. After evaporation of the solvent a (less-colored) liquid (160 mg, < 70%) was obtained, which still showed considerable line-broadening with ^{1}H NMR. This was used directly in the second step, the ring-opening with dimethylamine. After adding water (0.50 mL), 2-propanol (1.00 mL), and aqueous Me_2NH (0.50 mL 40%), the mixture was stirred at room temperature for 48 h. After evaporation of the solvent and the excess Me_2NH, the residue was taken up in water (20 mL) and acidified to pH 1 using concentrated aqueous HCl. The solution was washed with dichloromethane (3 × 20 mL), which was colored dark-brown. The pH of the water layer was raised to 12 using NaOH (300 mg), and extracted with dichloromethane (5 × 20 mL). The latter layers were combined, dried with $MgSO_4$, and the solvent was evaporated in vacuo resulting in > 90% pure *N*,*N*-dimethyl-2-hydroxy-4,4-dimethyl-1-aminopentane (**8**, 51 mg, 23%). An *ee* of 10−15% was determined by ^{1}H NMR using the diamagnetic chiral shift reagent (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol. − ^{1}H NMR (300 MHz, $CDCl_3$): 3.68 (m, 1 H, C*H*OH), 2.23 (s, 6 H, NCH_3), 2.21, 2.04 (m + dd, 2 H, NCH_2, for dd: $^3J_{CHCH2}$ = 3.3 Hz, $^2J_{gem}$ = −12.1 Hz), 1.29, 1.09 (2 dd, 2 H, C*H*$_2$tBu, $^3J_{CHCH2}$ = 7.9, 2.6 Hz, $^2J_{gem}$ = 14.4 Hz), 0.90 (s, 9 H, $C(CH_3)_3$). − ^{13}C NMR (75.5 MHz, $CDCl_3$): 66.8 (NCH_2), 64.2 (CHOH), 48.6 (*C*H_2tBu), 45.3 (NCH_3), 30.2 [*C*$(CH_3)_3$], 30.1 [C(*C*$H_3)_3$].

General Borate Esterification Procedure: Unless stated otherwise, each borate ester derivative described below was prepared as follows. Equimolar amounts of triisopropyl borate, diol, and amino alcohol were dissolved in toluene (1 mmol in 10 mL) and concentrated in vacuo at 50 °C. After twice repeated coevaporation of 2-propanol with toluene, the compound was dried in vacuo and used as such.

Borate Ester of (*R*,*R*)-Hydrobenzoin and (Dimethylamino)ethanol, B(1a)(2c): ^{1}H NMR (200 MHz, $CDCl_3$): 7.25 (m, 10 H, Ph), 4.76 (br s, 2 H, CH−Ph), 3.98 (m, 2 H, CH_2OB), 3.25−2.95 (m, 2 H, CH_2N), 2.74 (br s, 6 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.8. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 141.0 (α-Ph), 127.9, 126.3 (*o*/*m*-Ph), 127.2 (*p*-Ph), 85.0 (CH−Ph), 58.7, 57.9 (CH_2OB and CH_2N), 45.0 (NCH_3).

Borate Ester of (*R*,*R*)-Hydrobenzoin and (±)-*N*,*N*-Dimethyl-1-amino-2-propanol, B(1a)(2d) (1:1 mixture of diastereomers): ^{1}H NMR (200 MHz, $CDCl_3$): 7.26 (m, 10 H, Ph), 4.77 (m, 2 H, CH−Ph), 4.24 (m, 1 H, C*H*CH_3), 2.85−2.65 (m, 8 H, CH_2N and NCH_3), 1.33 (d, 3 H, CHC*H*$_3$, $^3J_{CHCH3}$ = 5.9 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.7. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 141.3, 141.0 (α-Ph), 128.0, 126.5 (*o*/*m*-Ph), 127.3 (*p*-Ph), 85.2 (CH−Ph), 65.9, 65.6 (CH_2N), 64.7, 64.4 (*C*HCH_3), 46.6, 45.4 (NCH_3), 21.7, 21.5 (CH*C*H_3).

Borate Ester of (*R*,*R*)-Hydrobenzoin and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol B(1a)(2e) (mixture of 3/4): Crystals suitable for single-crystal X-ray analysis were grown by slow evaporation of the solvent of a sample containing 720 mg of B(**1a**)(**2e**) in about 5 mL acetone under an argon stream. Crystals (**3**, 352 mg, 49%) were isolated while about half of the solvent was still present. These crystals were used for the X-ray and the elemental analyses. For a second batch, evaporation of all solvent was brought about resulting in quantitative crystallization. Washing of the crystals with ice-cold acetone resulted in pure B(**1a**)(**2e**) (**3**, > 85%) with the same melting point as found for the first batch. Melting point: 152 °C. − MS (EI): 369 [M + 1]. Elemental analysis calculated (found) for $C_{21}H_{29}BN_2O_3$: C 68.49 (68.36), H 7.94 (8.05), N 7.61 (7.51). − ^{1}H NMR (200 MHz, $CDCl_3$): 7.26 (m, 10 H, Ph), 4.74 (m, 2 H, CH−Ph), 4.26 (qn, 1 H, C*H*CH_2, $^3J_{CHCH2}$ = 6.9 Hz), 2.90−2.70 (m, 4 H, CH_2N), 2.61, 2.49 (2 s, 6 H+6 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.6. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 141.4 (α-Ph), 128.0, 126.4 (*o*/*m*-Ph), 127.3 (*p*-Ph), 85.2 (CH−Ph), 66.7 (*C*HCH_2), 64.4, 63.8 (CH_2N), 46.5, 45.7 (NCH_3). − ^{1}H NMR (300 MHz, CD_2Cl_2, −78°C): 7.34−7.00 (m, 10 H, Ph), 4.70−4.40 (m, 2 H, CH−Ph), 4.18 (br qn, 1 H, C*H*CH_2), 3.62−3.15 (m, 2 H, CH_2N−B), 2.90−2.40 [m, 2 H, CH_2N (uncoord.)], 2.82, 2.73, 2.70, 2.65 (4 s: about 1:3:3:1, 6 H, B−NCH_3), 2.20, 2.17 [2 s: about 3:1, 6 H, NCH_3 (uncoord.)]. − ^{13}C NMR (75.5 MHz, CD_2Cl_2, −78 °C): 140.3, 139.7, 139.5, 139.2 (about 3:3:1:1, α-Ph), 127.4−124.6 (> 10 resonances, *o*/*m*/*p*-Ph), 84.4, 84.2, 84.0, 83.5 (about 1:1:3:3, CH−Ph), 65.2, 65.0 (about 3:1, *C*HCH_2), 63.8, 63.7 (about 1:3, CH_2N−B), 62.2, 61.6 [about 1:3, CH_2N (uncoord.)], 46.2, 45.2 [about 1:3, NCH_3 (uncoord.)], 44.7, 44.0 (about 1:3, B−NCH_3). A sample prepared from (±)-hydrobenzoin gave identical NMR spectra.

Borate Ester of (*R*,*R*)-Hydrobenzoin and *N*,*N*,*N*′,*N*′-Tetraethyl-1,3-diamino-2-propanol, B(1a)(2f): ^{1}H NMR (200 MHz, $CDCl_3$): 7.37−7.08 (m, 10 H, Ph), 4.65 (m, 2 H, CH−Ph), 4.17 (m, 1 H, C*H*CH_2), 3.10−2.50 (m, 12 H, CHC*H*$_2$ and C*H*$_2$CH$_3$), 1.06 (br t, 12 H, CH_3, $^3J_{CH2CH3}$ = 6.8 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.0. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 141.3 (α-Ph), 127.9, 126.4 (*o*/*m*-Ph), 127.2 (*p*-Ph), 84.8 (CH−Ph), 66.0 (*C*HCH_2), 58.2, 57.6 (CH*C*H_2), 46.8 (*C*H_2CH_3), 9.8 (CH_3).

Borate Ester of (*R*,*R*)-Hydrobenzoin and *N*,*N*,*N*′,*N*′-Tetrabenzyl-1,3-diamino-2-propanol, B(**1a**)(**2g**)**:** ^{1}H NMR (200 MHz, $CDCl_3$): 7.46−7.20 (m, 30 H, Ph and Bz), 5.13 (s, 2 H, CH−Ph), 4.40 (m, 1 H, C*H*CH_2), 3.65 (m, 8 H, CH_2-Bz), 2.57 (m, 4 H, CHC*H*$_2$). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 23.1. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 140.1 (α-Ph), 139.2, 139.0 (α-Bz), 130.0−125.9 (*o*/*m*/*p*-Ph and -Bz), 85.5 (CH−Ph), 70.3 (br, *C*HCH_2), 58.9, 58.8 (CH_2-Bz), 57.7, 57.4 (CH*C*H_2).

Borate Ester of (*S*)-1-Phenyl-1,2-ethanediol and (±)-*N*,*N*-Dimethyl-1-amino-2-propanol: B(**1b**)(**2d**) (1:1 mixture of diastereomers): ^{1}H NMR (200 MHz, $CDCl_3$): 7.30−7.00 (m, 5 H, Ph), 5.03 (m, 1 H, CH−Ph), 4.20−4.00, 3.59 (2 m, 2H+1 H, C*H*CH_3 and CH_2OB), 2.90−2.60 (m, 2 H, CH_2N), 2.56 (s, 6 H, NCH_3), 1.22, 1.21 (2 d, 3 H, CHC*H*$_3$, $^3J_{CHCH3}$ = 6.1 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.0. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 142.7 (α-Ph), 128.1, 125.4 (*o*/*m*-Ph), 127.0 (*p*-Ph), 76.7 (CH−Ph), 71.5 (CH_2OB), 65.6, 65.4 (CH_2N), 64.6, 64.5 (*C*HCH_3), 45.9, 45.1 (NCH_3), 21.6, 21.5 (CH*C*H_3).

Borate Ester of (*S*)-1-Phenyl-1,2-ethanediol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1b)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 7.42−7.18 (m, 5 H, Ph), 5.02 (m, 1 H, CH−Ph), 4.28−4.04, 3.63 (2 m, 2H+1 H, CHOB and CH_2OB), 2.78−2.65 (m, 4 H, CH_2N), 2.55, 2.45 (2 s, 6 H + 6 H, NCH_3). ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.9. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 142.8 (α-Ph), 128.1, 125.7 (*o*/*m*-Ph), 127.0 (*p*-Ph), 76.4 (CH−Ph), 71.0 (CH_2OB), 66.4 (CHOB), 63.8, 63.3 (CH_2N), 45.8, 45.4 (NCH_3).

Borate Ester of (*S*)-1,1,2-Triphenyl-1,2-ethanediol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1c)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 7.84−6.98 (m, 15 H, Ph), 5.86 (s, 1 H, CH−Ph), 4.36 (m, 1 H, C*H*CH_2), 3.00−2.65 (m, 4 H, CH_2N), 2.42 (s, 12 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.4. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 148.3, 144.6, 141.3 (*α*-Ph), 128.8−125.0 (*o*/*m*/*p*-Ph), 87.6 (CPh_2), 86.0 (CH−Ph), 66.8 (*C*HCH_2), 64.0, 63.4 (CH_2N), 46.0, 45.3 (NCH_3).

Borate Ester of 1,1,2,2-Tetraphenyl-1,2-ethanediol and (±)-*N*,*N*-Dimethyl-1-amino-2-propanol, B(1d)(2d): ^{1}H NMR (200 MHz, $CDCl_3$): 7.28−7.00 (m, 20 H, Ph), 4.29 (m, 1 H, C*H*CH_3), 2.63 (m, 2 H, CH_2N), 2.14 (s, 6 H, NCH_3), 1.35 (d, 3 H, CHCH_3, $^3J_{CHCH3}$ = 5.6 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 14.0. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 145.9, 144.1 (α-Ph), 128.6−126.3 (*o*/*m*/*p*-Ph), 83.0 (Ph_2COB), 67.6 (CH_2N), 65.3 (br, *C*HCH_3), 46.0 (NCH_3).

Borate Ester of 1,1,2,2-Tetraphenyl-1,2-ethanediol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1d)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 7.37−6.98 (m, 20 H, Ph), 4.30 (m, 1 H, CHOB), 2.75 (m, 4 H, CH_2N), 2.23 (s, 12 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.9. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 146.8, 144.2 (α-Ph), 129.0−125.9 (*o*/*m*/*p*-Ph), 91.7, 82.9 (Ph_2COB), 67.2 (CHOB), 64.8 (CH_2N), 46.1 (NCH_3).

Borate Ester of (*R*,*R*)-Diisopropyltartrate and Aminoethanol, B(1e)(2a): Prepared by coevaporation with chloroform. ^{1}H NMR (200 MHz, CD_2Cl_2): 6.79 (br s, 2 H, NH_2), 4.93 (m, 2 H, C*H*CH_3), 4.23, 4.10 (2 s, 2 H, CHOB), 3.61 (br m, 2 H, CH_2OB), 2.93 (br m, 2 H, CH_2N), 1.13 (d, 12 H, CH_3, $^3J_{CHCH3}$ = 6.2 Hz). − ^{11}B NMR (64.2 MHz, CD_2Cl_2): 11.3. − ^{13}C NMR (50.3 MHz, CD_2Cl_2): 174.2 (COO), 76.2 (CHOB), 69.2 (*C*HCH_3), 58.8 (br, CH_2OB), 42.5 (br, CH_2N), 21.9 (CH_3).

Borate Ester of (*R*,*R*)-Diisopropyltartrate and 1,3-Diamino-2-propanol, B(1e)(2b): ^{1}H NMR (200 MHz, $CDCl_3$): 5.00 (m, 2 H, C*H*CH_3), 4.38, 4.25 (2 s, 2 H, CHOB **1e**), 4.20 (br s, 4 H, NH_2), 4.15 (m, 1 H, CHOB **2b**), 3.20−2.70 (m, 4 H, CH_2N), 1.23, 1.18 (2 d, 12 H, CH_3, $^3J_{CHCH3}$ = 6.2 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.1. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 173.5, 173.1 (COO), 76.5, 75.7 (CHOB **1e**), 73.0 (br, CHOB **2b**), 68.8, 68.5 (*C*HCH_3), 44.7, 44.6 (br, CH_2N), 21.7, 21.6 (CH_3).

Borate Ester of (*R*,*R*)-Diisopropyltartrate and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1e)(2e): ^{1}H NMR (200 MHz, CD_2Cl_2): 4.96 (sp, 2 H, C*H*CH_3, $^3J_{CHCH3}$ = 6.3 Hz), 4.28 (s, 2 H, CHCOO), 4.04 (m, 1 H, C*H*CH_2N), 2.80−2.40 (m, 4 H, CH_2N), 2.47, 2.31 (2 s, 6 H + 6 H, NCH_3), 1.17 (d, 12 H, CHCH_3). − ^{11}B NMR (64.2 MHz, CD_2Cl_2): 11.0. − ^{13}C NMR (50.3 MHz, CD_2Cl_2): 172.1 (br, COO), 76.9 (*C*HCOO), 68.5 (*C*HCH_3), 67.2 (*C*HCH_2N), 64.0, 63.8 (CH_2N), 46.3, 45.4 (NCH_3), 21.7 (CH*C*H_3).

Borate Ester of (*R*,*R*)-1,4-Dibenzylthreitol and (Dimethylamino)-ethanol, B(1f)(2c): ^{1}H NMR (200 MHz, $CDCl_3$): 7.21 (m, 10 H, Ph), 4.45 (s, 4 H, CH_2Ph), 3.98 (br, 2 H, CHOB), 3.77 (m, CH_2OB), 3.48 (br, 4 H, CH_2OBz), 3.02−2.67 (m, 2 H, CH_2N), 2.43 (s, 6 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.0. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 138.1 (α-Ph), 128.1, 127.5 (*o*/*m*-Ph), 127.3 (*p*-Ph), 76.4 (CHOB), 73.1 (CH_2Ph), 72.8 (CH_2OBz), 58.7, 58.0 (CH_2N and CH_2OB), 44.6 (NCH_3).

Borate Ester of (*R*,*R*)-1,4-Dibenzylthreitol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1f)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 7.20 (m, 10 H, Ph), 4.45, 4.44 (2 s, 2 H + 2 H, CH_2Ph), 4.02 (qn, 1 H, C*H*CH_2N), 3.92 (br, 2 H, CHOB), 3.48 (br, 4 H, CH_2OBz), 2.62−2.50 (m, 4 H, CH_2N), 2.31, 2.26 (2 s, 6 H + 6 H, NCH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.7. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 138.1 (α-Ph), 127.9, 127.3 (*o*/*m*-Ph), 127.1 (*p*-Ph), 76.0 (CHOB), 73.0 (CH_2Ph), 72.8 (CH_2OBz), 66.2 (*C*HCH_2N), 63.7, 63.5 (CH_2N), 45.8, 45.2 (NCH_3).

Borate Ester of 1,2:5,6-Diisopropylidene-D-mannitol and (Dimethylamino)ethanol, B(1g)(2c): ^{1}H NMR (200 MHz, $CDCl_3$): 4.11−3.75 (m, 10 H, CH_2OB and CH− and CH_2 **1g**), 3.05−2.76 (m, 2 H, CH_2N), 2.55 (s, 6 H, NCH_3), 1.35, 1.26 [2 s, 6 H + 6 H, $C(CH_3)_2$]. − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.8. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 108.9 [*C*$(CH_3)_2$], 78.0, 77.6 (CH **1g**), 66.4 (CH_2 **1g**), 59.4, 57.8 (CH_2N and CH_2OB), 45.1 (NCH_3), 26.3, 25.1 [C(*C*$H_3)_2$].

Borate Ester of 1,2:5,6-Diisopropylidene-D-mannitol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1g)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 4.07−3.65 (m, 9 H, C*H*CH_2N and CH− and CH_2 **1g**), 2.61 (m, 4 H, CH_2N), 2.45, 2.35 (2 s, 6 H + 6 H, NCH_3), 1.34, 1.27 [2 s, 6 H + 6 H, $C(CH_3)_2$]. − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.5. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 108.9 [*C*$(CH_3)_2$], 78.1, 77.6 (CH **1g**), 66.5 (*C*HCH_2N), 66.3 (CH_2 **1g**), 64.0, 63.4 (CH_2N), 46.0, 45.6 (NCH_3), 26.3, 25.2 [C(*C*$H_3)_2$].

Borate Ester of Catechol and (±)-*N*,*N*-Dimethyl-1-amino-2-propanol, B(1h)(2d): ^{1}H NMR (200 MHz, $CDCl_3$): 6.67−6.55 (m, 4 H, CH **1h**), 4.15 (m, 1 H, C*H*CH_3), 2.90, 2.71 (2 dd, 2 H, CH_2N, $^2J_{gem}$ = −11.3 Hz, $^3J_{CHCH2}$ = 5.1, 10.1 Hz), 2.52, 2.38 [2 s, 6 H, $N(CH_3)_2$], 1.20 (d, 3 H, CHCH_3, $^3J_{CHCH3}$ = 6.0 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.8. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 150.7, 150.6 (COB **1h**), 119.0, 118.5, 109.3, 108.7 (CH **1h**), 65.5, 65.3 (*C*HCH_2), 45.6, 44.5 [$N(CH_3)_2$], 21.2 (CH*C*H_3).

Borate Ester of Catechol and *N*,*N*,*N*′,*N*′-Tetramethyl-1,3-diamino-2-propanol, B(1h)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 6.69−6.47 (m, 4 H, CH **1h**), 4.17 (m, 1 H, CHOB), 2.65, (br, 4 H, CH_2N), 2.33 (br s, 12 H, CH_3). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 11.8. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 150.6, 150.5 (COB **1h**), 119.0, 118.8, 109.2, 108.4 (CH **1h**), 67.1 (CHOB), 62.9 (CH_2), 45.1 (CH_3).

Borate Ester of (±)-4-Methyl-2,4-pentanediol and 1,3-Diamino-2-propanol, B(1j)(2b): ^{1}H NMR (200 MHz, $CDCl_3$): 4.06 (m, 1 H, CH **1j**), 3.83 (m, 1 H, CH **2b**), 2.63, 2.51 (2 dd, 4 H, CH_2N, $^2J_{gem}$ = −12.9 Hz, $^3J_{CHCH2}$ = 4.4, 6.8 Hz), 1.58, 1.34 (2 dd, 2 H, CH_2 **1j**, $^2J_{gem}$ = −13.9 Hz, $^3J_{CHCH2}$ = 2.8, 11.6 Hz), 1.50 (br, 4 H, NH_2), 1.12 [s, 6 H, $C(CH_3)_2$], 1.08 (d, 3 H, CHCH_3, $^3J_{CHCH3}$ = 6.2 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 17.2. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 75.0 (br, CH **2b**), 71.4 [*C*$(CH_3)_2$], 65.3 (CH **1j**), 45.5 (CH_2 **1j**), 44.9 (CH_2N), 31.0, 27.5, 22.9 (CH_3).

Borate Ester of (±)-4-Methyl-2,4-pentanediol and (±)-*N*,*N*-Dimethyl-1-amino-2-propanol, B(1j)(2d) (1:1 mixture of diastereomers): ^{1}H NMR (200 MHz, $CDCl_3$): 4.32−4.02 (m, 2 H, CH **1j** and **2d**), 2.34−2.07 (m, 2 H, CH_2N), 2.18 (s, 6 H, NCH_3), 1.72−1.28 (m, 2 H, CH_2 **1j**), 1.20 [s, 6 H, $C(CH_3)_2$], 1.15 (d, 3 H, CHCH_3 **1j**, $^3J_{CHCH3}$ = 6.2 Hz), 1.08 (d, 3 H, CHCH_3 **2d**, $^3J_{CHCH3}$ = 6.2 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 17.3. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 71.3 [*C*$(CH_3)_2$], 66.7, 66.6 (CH_2N), 66.0, 65.9, 65.3, 65.2 (CH **1j** and **2d**), 46.0 (NCH_3), 45.8 (CH_2 **1j**), 31.2, 31.1, 27.8, 27.7, 23.1 (CH_3 **1j**), 20.9, 20.8 (CH_3 **2d**).

Borate Ester of (±)-4-Methyl-2,4-pentanediol and *N,N,N′,N′*-Tetramethyl-1,3-diamino-2-propanol, B(1j)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 4.11−3.89 (m, 2 H, CH **1j** and **2e**), 2.18 (d, 4 H, CH_2N, $^3J_{CHCH2}$ = 6.2 Hz), 2.08 (s, 12 H, NCH_3), 1.47, 1.22 (2 dd, 2 H, CH_2 **1j**), 1.06 [s, 6 H, $C(CH_3)_2$], 1.01 (d, 3 H, $CHCH_3$, $^3J_{CHCH3}$ = 6.1 Hz). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 15.3. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 70.5 [$C(CH_3)_2$], 67.3 (CH **2e**), 64.5 (CH **1j**), 63.6 (CH_2N), 45.7 (NCH_3 and CH_2 **1j**), 31.3, 27.7, 23.0 (CH_3 **1j**).

Borate Ester of (±)-1,3-Diphenyl-1,3-propanediol and (Dimethylamino)ethanol, B(1k)(2c): ^{1}H NMR (200 MHz, $CDCl_3$): 7.40−7.18 (m, 10 H, Ph), 5.13 (t, 2 H, CHPh, $^3J_{CHCH2}$ = 5.2 Hz), 4.06 (t, 2 H, CH_2OB, $^3J_{CH2CH2}$ = 6.0 Hz), 2.72 (t, 2 H, CH_2N), 2.42 (s, 6 H, NCH_3), 2.28 (t, 2 H, CH_2CHPh). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 17.2. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 142.5 (α-Ph), 128.2, 125.0 (*o*/*m*-Ph), 127.1 (*p*-Ph), 70.5 (CHPh), 60.1, 59.8 (CH_2OB and CH_2N), 45.4 (NCH_3), 41.4 (CH_2CHPh).

Borate Ester of (±)-1,3-Diphenyl-1,3-propanediol and *N,N,N′,N′*-Tetramethyl-1,3-diamino-2-propanol, B(1k)(2e): ^{1}H NMR (200 MHz, $CDCl_3$): 7.45−7.02 (m, 10 H, Ph), 5.06 (br t, 2 H, CHPh, $^3J_{CHCH2}$ = 5.3 Hz), 4.30 (m, 1 H, $CHCH_2N$), 2.68 (m, 4 H, CH_2N), 2.43 (s, 12 H, NCH_3), 2.28−2.15 (m, 2 H, CH_2CHPh). − ^{11}B NMR (64.2 MHz, $CDCl_3$): 19.1, 9.1. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 145.3, 141.7 (α-Ph), 128.2−124.8 (*o*/*m*/*p*-Ph), 71.6, 70.8 (CHPh), 66.6 ($CHCH_2N$), 64.3, 63.8 (CH_2N), 46.0, 45.7 (NCH_3), 42.4, 41.3 (CH_2CHPh).

General Methylation Procedure: Unless stated otherwise, each methylation described below was performed as follows. Freshly prepared borate ester was dissolved in dichloromethane (10 mL/mmol) and, when applicable, cooled to −78 °C. Methyl trifluoromethanesulfonate (MeOTf, 1.00 equivalents) was added, and the mixture was stirred for 1 h. After warming to room temperature, dichloromethane was evaporated in vacuo, water (5 mL) was added to bring about hydrolysis of the borate ester, and the pH was brought to 1 with concentrated aqueous HCl. After washing with diethyl ether, the solvent was removed in vacuo and boronic acid was removed as the trimethyl ester by coevaporation with MeOH. Water (5 mL) was added and the pH was brought to 12 with 4 M NaOH. The solvent was removed in vacuo and the residue was extracted with dichloromethane, which was dried with $MgSO_4$, filtered, and the solvent removed in vacuo.

Methylation of B(1a)(2e): (*R*,*R*)-Hydrobenzoin was used. The methylation was performed at −78 °C. Spectra for B(**1a**)(**2e**) · MeOTf (mix of diastereomers **5/6**, only product observed): ^{1}H NMR (200 MHz, $CDCl_3$): 7.26−7.06 (br m, 10 H, Ph), 4.75−4.50 (br m, 2 H, PhCHOB), 3.67, 3.61 (2 m: 1:3, CH_2CHOB), 3.26−3.07 [m, 11 H, $CH_2N(CH_3)_3$], 2.73−2.65 [m, 8 H, $CH_2N(CH_3)_2$]. − ^{11}B NMR (64.2 MHz, $CDCl_3$): 10.8. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 140.9, 140.5 (3:1, α-Ph), 128.6−125.8 (*o*/*m*/*p*-Ph), 85.3, 85.1 (PhCHOB), 69.9, 69.8 [3:1, $CH_2N(CH_3)_3$], 63.6, 63.3 (3:1, CH_2CHOB), 60.3, 59.9 [1:3, $CH_2N(CH_3)_2$], 54.6 [$N(CH_3)_3$], 45.1 [$N(CH_3)_2$]. After hydrolysis and consecutive purification, **2e** · MeOTf (**7**, 76%, contaminated with 6% **1a**) was obtained. After recrystallization from ethyl acetate, pure **7** (57%) was obtained as a white solid. An *ee* of 48% was determined by ^{1}H NMR using the diamagnetic chiral shift reagent (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol. Pure **1a** (84%) was recovered from the ether washings. MS (ESI^+): 161 (**7**). − Spectra for **7**: ^{1}H NMR (200 MHz, $CDCl_3$): 4.36 (br s, 1 H, OH), 4.10 (m, 1 H, CHOH), 3.47, 3.22 [2 dd, 2 H, $CH_2N(CH_3)_3$, $^3J_{CHCH2}$ = 1.5, 9.8 Hz, $^2J_{gem}$ = −13.3 Hz], 3.25 [s, 9 H, $N(CH_3)_3$], 2.30, 2.21 [2 dd, 2 H, $CH_2N(CH_3)_2$, $^3J_{CHCH2}$ = 5.9, 4.6 Hz, $^2J_{gem}$ = −12.3 Hz], 2.24 [s, 6 H, $N(CH_3)_2$]. ^{13}C NMR (50.3 MHz, $CDCl_3$): 120.5 (q, CF_3, $^1J_{CF}$ = 322 Hz), 70.0 [$CH_2N(CH_3)_3$], 62.5 (CHOH), 61.9 [$CH_2N(CH_3)_2$], 54.5 [$N(CH_3)_3$], 45.4 [$N(CH_3)_2$]. − Using (±)-hydrobenzoin, with methylation performed at −78 °C, a mixture of diastereomers **5/6** (63:37) was observed by ^{13}C NMR at room temperature. After hydrolysis, an *ee* of 0% was determined for **7** by ^{1}H NMR using the diamagnetic chiral shift reagent (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol. Using (*R*,*R*)-hydrobenzoin, with methylation performed at room temperature, a mixture of diastereomers **5/6** (63:37) was observed by ^{13}C NMR at room temperature. After hydrolysis, an *ee* of 26% was determined for **7** by ^{1}H NMR using the diamagnetic chiral shift reagent (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol.

Methylation of Solid B(1a)(2e): Crystallized B(**1a**)(**2e**) (**3**: a single diastereomer, see above) was used and ground in a mortar. (a) The solid was suspended in pentane, and MeOTf was added at −78 °C. The mixture was warmed to room temperature over 4 h, dichloromethane was added and the solvent was evaporated. A diastereomeric ratio (63:37) for **5/6** was observed by ^{13}C NMR. (b) MeOTf was added to the solid at room temperature without additional solvent, and kept overnight. After uptake in $CDCl_3$, a diastereomeric ratio (6:37) for **5/6** was observed by ^{13}C NMR. (c) MeOTf was added to dichloromethane (1 mL), and the mixture was cooled to freezing in N_2(l)/pentane. The borate (70 mg) was added and the sample was kept at freezing point for 1 h. After warming to room temperature and evaporation of the solvent, a diastereomeric ratio (3:1) for **5/6** was observed by ^{13}C NMR. (d) MeOTf was added to dichloromethane (0.35 mL), and the borate (65 mg) was added at room temperature under vigorous stirring. After evaporation of the solvent, a diastereomeric ratio (63:37) for **5/6** was observed by ^{13}C NMR. (e) The solid was suspended in pentane, and MeOTf was added at −78 °C. Small portions of precooled dichloromethane were added over 2 h until a clear mixture was obtained. After warming to room temperature and evaporation of the solvent, a diastereomeric ratio (3:1) for **5/6** was observed by ^{13}C NMR.

Methylation of B(1a)(2f): (*R*,*R*)-Hydrobenzoin was used. The methylation was performed at −78 °C. Selected resonances for B(**1a**)(**2f**) · MeOTf (mix of diastereomers, only product observed): ^{11}B NMR (64.2 MHz, $CDCl_3$): 6.2. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 84.6, 84.3 (2:1, PhCHOB), 56.2 (NCH_3). After hydrolysis and consecutive purification, **2f** · MeOTf (32%) was obtained. An *ee* of about 30% was determined by ^{1}H NMR using the diamagnetic chiral shift reagent (*S*)-1-(9-anthryl)-2,2,2-trifluoroethanol. Spectra for **2f** · MeOTf: ^{1}H NMR (200 MHz, $CDCl_3$): 4.02 (m, 1 H, CHOH), 3.50 (br q, 4 H, $NMeCH_2CH_3$), 3.21−2.93 (m, 2 H, CH_2NMeEt_2), 3.10 (s, 3 H, NCH_3), 2.60−2.24 (m, 2 H, CH_2NEt_2), 2.56 (q, 4 H, NCH_2CH_3), 1.35 (br t, 6 H, $NMeCH_2CH_3$, $^3J_{CH2CH3}$ = 7.1 Hz), 0.98 (t, 6 H, NCH_2CH_3, $^3J_{CH2CH3}$ = 7.1 Hz). − ^{13}C NMR (50.3 MHz, $CDCl_3$): 64.7 (CH_2NMeEt_2), 61.8 (CHOH), 57.8, 57.7 (CH_2NEt_2 and $NMeCH_2CH_3$), 56.5 (NCH_3), 47.0 (NCH_2CH_3), 11.9, 8.0 (CH_2CH_3).

Methylation of B(1j)(2c): Reaction performed at −78 °C. Selected resonances for B(**1j**)(**2c**) · MeOTf: ^{1}H NMR (200 MHz, $CDCl_3$): 3.13 [s, $N(CH_3)_3$]. − ^{11}B NMR (64.2 MHz, $CDCl_3$): 17.9. − ^{13}C NMR (50.3 MHz, $CDCl_3$): 53.8 [$N(CH_3)_3$]. Hydrolysis was performed without consecutive purification. − Spectra for **2c** · MeOTf: ^{1}H NMR (200 MHz, D_2O): 4.10 (t, 2 H, CH_2N), 3.56 (t, 2 H, CH_2OH), 3.26 [s, 9 H, $N(CH_3)_3$]. − ^{13}C NMR (50.3 MHz, D_2O): 68.9 (CH_2N), 57.0 (CH_2OH), 55.3 [$N(CH_3)_3$].

Methylation of B(1j)(2e): Reaction performed at −78 °C. Hydrolysis was performed without consecutive purification. A mixture of mono- and dimethylated product was obtained.

Double methylation of B(1j)(2e): Reaction performed at −78 °C. Hydrolysis was performed without consecutive purification. Spectra for **2e** · 2 MeOTf: ^{1}H NMR (200 MHz, D_2O): 3.25 [s, 18 H, $N(CH_3)_3$], 3.15 (m, 5 H, CH_2N and C*H*OH). − ^{13}C NMR (50.3 MHz, D_2O): 71.6 (CH_2N), 65.5 (CHOH), 55.6 [$N(CH_3)_3$].

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