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Enantioenriched Boron *C,N*-Chelates via Chirality Transfer

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Dedicated to Professor Andreas Pfaltz on the occasion of his 75th birthday.

Abstract: Molecules stereogenic only at tetrahedral boron atoms show great promise for applications, for example as chiroptical materials, but are scarcely investigated due to their synthetic challenge. Hence, this study reports a two-step synthesis of enantioenriched boron *C,N*-chelates. First, the diastereoselective complexation of alkyl/aryl borinates with chiral aminoalcohols furnished boron stereogenic heterocycles in up to 86% yield and d.r. > 98:2. Treatment of these *O,N*-complexes with chelate nucleophiles was surmised to transfer the stereoinformation via the ate-complex into the *C,N*-products. This chirality transfer succeeded by substitution of the *O,N*-chelates with lithiated phenyl pyridine to give boron stereogenic *C,N*-chelates in up to 84% yield and e.r. up to 97:3. The chiral aminoalcohol ligands could be recovered after isolation of the *C,N*-chelates. The chirality transfer tolerated alkyl, alkynyl and (hetero-)aryl moieties at boron and could be further extended by post-modification: transformations such as catalytic hydrogenations or sequential deprotonation/electrophilic trapping were feasible while maintaining the stereochemical integrity of the *C,N*-chelates. Structural aspects of the boron chelates were studied by variable temperature NMR and X-ray diffraction.

Introduction

Chiral tetrahedral elements are fundamental to modern synthetic chemistry and the asymmetric synthesis and catalysis of carbon-based molecules lies at the very heart of organic chemistry. Additionally, the enantioselective preparation and structure of other chiral (pseudo-)tetrahedral main group elements such as silicon,[1,2] phosphorus[3–5] or sulfur[6] is well explored. This led to applications of chiral phosphines in transition metal catalysis furnishing, for example, silicon-stereogenic compounds[7] or use of chiral sulfoxides as catalysts in organic synthesis.[6] On the other hand, chiral tetrahedral boron atoms originating from coordination of a donor atom D (e.g. D = N, P, NHC, …) to trivalent boron, remain scarcely investigated.[8–10] This is surprising, as numerous examples of (symmetrical) tetrahedral boron compounds have been applied in synthesis,[11] hydrogen storage,[12] luminescent materials,[13,14] OLEDs,[15,16] bioimaging[17] and stimuli-responsive materials.[18] The challenge encountered with chiral tetrahedral boron is often the labile B–D bond,[18,19] its dissociation and concomitant loss of stereochemical information. Yet, racemic mixtures such as *C,N*-chelate **1**[20] or NHC-borane **2**[21] with rather strongly bound chelate[20,22] or NHC-ligands[21,23,24] have been reported (Scheme 1a). Moreover, Toyota,[25–27] Nowak-Król[28] and others[29–32] showed that resolution of racemic mixtures of boron complexes via chiral HPLC is possible and give rise to, for example, **3**[25] or **4**[28] in enantiopure form (Schema 1b). Synthetic concepts towards enantioenriched boron atoms involve diastereoselective syntheses[30,33–36] as in case of NHC-borane **5**[8] (Scheme 1c) or intramolecular chirality transfer towards tridentate complex **6**[37] (Scheme 1d).

Most challenging is certainly the synthesis of compounds stereogenic only at boron and to the best of our knowledge only a handful of examples have been reported.[9,10,33,37] Among these, an efficient approach is the catalytic enantioselective desymmetrization via click-reaction or carbene insertion furnishing *N,N*- and *C,N*-chelates **8** and **10** (Scheme 1e).[9,10] Both methodologies use a Cu/BOX-ligand system and provide the enantioenriched boron-complexes **8** and **10** in high yields (up to 95%) and enantioselectivities (up to 99% *ee*). Notably, the *N,N*-chelates **8** exhibit circularly polarized luminescence (CPL)[9] useful for sensing applications.[38] Yet, these desymmetrization protocols are limited to triazole/alkyne or secondary carbons/hydrogen peripheral groups attached to boron, although the post-functionalization of these groups is feasible. A more recent protocol in terms of the peripheral substituents is a catalytic enantioselective C–H arylation giving rise to boron-stereogenic BODIPYs which have then been applied in chiral recognition.[39]

These peripheral substituents influence the configurational stability of the chelate systems[25] and can even tune the optical properties as illustrated for phenylpyridine chelates (Scheme 2). The phenylpyridine unit is a prominent ligand system for

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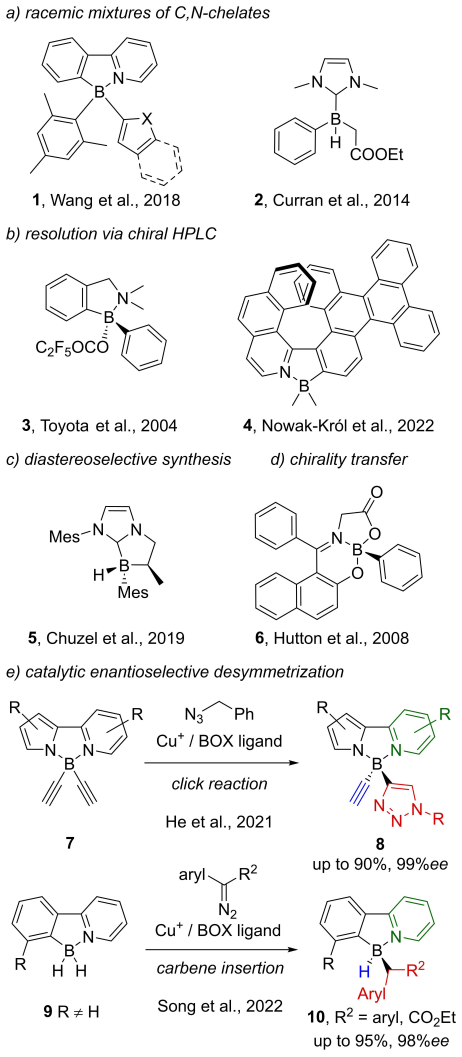
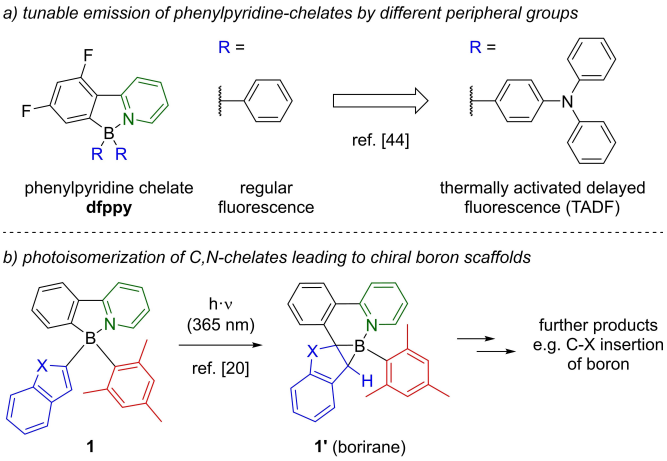


Scheme 1. Known chiral tetrahedral boron compounds and their preparation strategies a) racemic mixtures of *C,N*-chelate **1**[20] and NHC-borane **2**,[21] b) enantiopure boron complexes **3**[25] and **4**[28] by resolution of their racemic mixtures via chiral HPLC, c) enantioenriched boron complex **5**[8] via diastereoselective synthesis, d) enantioenriched boron complex **6**[37] via intramolecular chirality transfer, e) boron *N,N*- and *C,N*-chelates **8**[9] and **10**[10] via catalytic enantioselective desymmetrization.

boron-complexes due to its synthetic,[40,41] photoisomerization[20,42,43] and luminescent properties.[15,16,28,44]

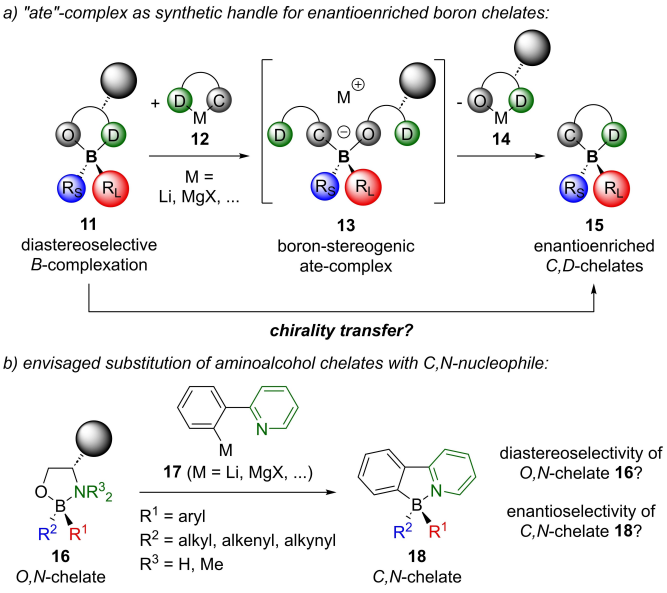
For phenylpyridine chelate **dfppy** (Scheme 2a), attaching triphenylamine moieties instead of phenyl groups to the boron atom lead to thermally activated delayed fluorescence (TADF), a property usually not observed for this type of *C,N*-chelates **dfppy**.[44] Introduction of this triphenylamine unit to a boron-stereogenic chelate might establish another way to CPL-active TADF materials.[45,46] Moreover, the photoisomerization of phenylpyridine-coordinated borons such as in **1** and related *C,N*-chelates has been extensively studied (Scheme 2 b).[20,42,43] Here, the peripheral groups play a crucial role for the photoreactivity and the tailor-made introduction of these groups to enantioenriched boron chelates would expand the potential of the photoisomerization even further. In order to control the



Scheme 2. Influence of peripheral boron groups on the emission (a) and reactivity (b) of phenylpyridine chelates **dfppy** and **1**.

reactivity pattern and optical properties of boron *C,N*-chelates, the variation of the peripheral substituents is highly desirable. Consequently, we devised our own strategy towards enantioenriched *C,N*-chelates **18** where boron is the single stereogenic center with a special emphasis on the peripheral groups.

For this endeavor, we drew inspiration from carbon-based stereoselective transformations using the boron ate-complex (such as **13**) as a synthetic handle (Scheme 3a).[47–49] We wondered if the versatility of the ate-complex could be expanded to the preparation of enantioenriched boron complexes **15**. A hypothetical boron chelate **11** carrying two substituents of different size (R_S, R_L) as well as a chiral *O,D*-



Scheme 3. a) Proposed strategy for the enantioselective synthesis of *C,D*-chelates **15** using the ate-complex **13** as chirality transferring intermediate, D = donor atom. b) substitution of chiral aminoalcohol borinates **16** with phenylpyridyl nucleophiles **17** towards enantioenriched boron *C,N*-chelates **18**.

alkoxide-ligand would serve as a starting point. The chiral backbone of **11** should control the boron stereogenic center by steric factors (i.e. diastereoselective synthesis). Although this concept is seemingly trivial, it is, to the best of our knowledge, rarely investigated for bidentate boron chelates.[8,50,51] Even more, chiral alkoxide chelate ligands such as aminoalcohols have been so far only coordinated to symmetrical boron units (e.g. RO-BPh_2, RO-BBN).[52–55] Our devised strategy would then commence by addition of a chelating organometallic nucleophile **12** to *O,D*-chelate **11** to form ate-complex **13**. This addition was surmised to proceed in a stereospecific manner, possibly by S_N2-type breaking of the B–D bond.[29,33,56–58]

Hence, the chiral information of starting chelate **11** would be maintained in the boron-stereogenic ate-complex **13**. If the alkoxide **14** would dissociate as a leaving group (LG) parallel to coordination of the donor atom D of the carbon nucleophile **12**, the stereoinformation should be transferred to the final *C,D*-chelate **15**. This proposed chirality transfer via the boron ate-complex **13** is, to the best of our knowledge, unprecedented and would give rise to enantioenriched chelates **15** stereogenic only at boron.

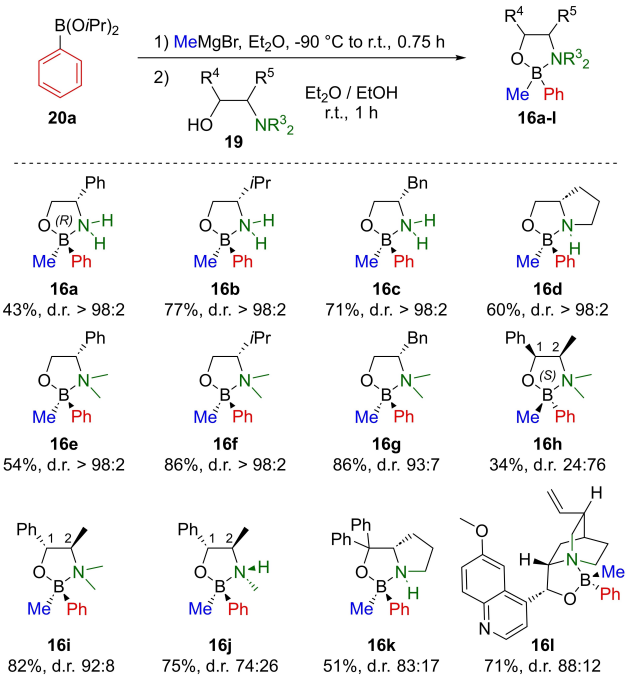
To realize this concept, two key challenges needed to be addressed, namely the diastereoselective complexation and subsequently the chirality transfer (Scheme 3b). The first task was to find a suitable ligand for the initial diastereoselective complexation. In this case, an alkyl (R^2)/aryl (R^1) substituted boron alkoxide should be coordinated to readily available chiral aminoalcohol ligands and the diastereoselectivity of these *O,N*-chelates **16** should be evaluated. For the second task, the chirality transfer from *O,N*-chelates **16** to enantioenriched *C,N*-chelates **18**, we chose the phenylpyridine unit **17** as a benchmark nucleophile due to its versatile applications discussed above. The envisaged chirality transfer via the ate-complex, its synthetic feasibility and the enantioselectivity of the *C,N*-chelates **18** are unexplored so far. In the current manuscript we disclose the realization of this novel approach towards boron-stereogenic chelates.

Results and Discussion

Diastereoselective borinate complexation with chiral aminoalcohol ligands

The synthesis of aminoalcohol chelates **16** started with treatment of diisopropylphenyl boronate **20a** with methylmagnesium bromide in Et_2O to generate an intermediate borinate PhMeBO*i*Pr (Scheme 4a), followed by in situ complexation with the respective aminoalcohol **19** in Et_2O/EtOH to provide the desired *O,N*-chelates **16** in >90% purity. The presence of a tetrahedral B–N boron was confirmed by ^{11}B NMR (δ(**16a–l**) = 7.0–11.1 ppm)[52] and the relative stereochemistry was elucidated using NOESY (for details see Supporting Information, chapter 1.5).

L-Phenylglycinol, valinol, phenylalaninol and prolinol furnished the *O,N*-chelates **16a–d** in 43–77% yield and d.r. >98:2 with boron in the $(R)_B$-configuration (Scheme 4, top). Additionally, we performed *N*-methylation[59] of the acyclic aminoalcohols and the respective chelates **16e–g** were obtained in 54–86% and d.r. 93:7 (**16g**) or up to >98:2 (**16e,f**) (Scheme 3, middle). The NOESY spectra of chelates **16e–g** proved inconclusive for stereochemical analysis (see Supporting Information, chapter 1.5), yet a solid-state structure of **16e** obtained from single crystal X-ray diffraction showed the absolute stereochemistry (for details see structural study below). The stereochemistry of **16f,g** was assigned in analogy. Furthermore, *cis*-disubstituted (1*S*,2*R*)-*N*-methylephedrine-based **16h** was prepared in 34% and d.r. 24:76. The *trans*-disubstituted (1*R*,2*R*)-*N*-methyl-pseudoephedrine **16i** could be isolated in 82% and d.r. 92:8 whereas the (1*R*,2*R*)-pseudoephedrine-ligand **16j** with NHMe-donor, isolated in 75%, showed a decreased diastereomeric purity (d.r. 74:26) (Scheme 3, bottom). The stereochemistry of the methylpseudoephedrine-chelate **16i** was supported by a solid-state structure as well (see structural study below). The chelates of more bulky ligands such as diphenylprolinol **16k** or even (−)-quinine **16l** were accessible in yields of 51% and 71%, respectively. These chelates possessed decreased diastereomeric ratios (**16k**, d.r. 83:17 and **16l**, d.r. 88:12) compared to mono-/disubstituted examples **16a–j** (up to d.r. > 98:2), indicating that additional bulk does not improve the diastereoselectivity. The major factor governing the boron stereo-chemistry of the *O,N*-chelates **16** is steric hindrance: the *B*-phenyl groups and the (more bulky) chiral substituent of the *O,N*-ligand **19** adapt a *trans*-relation on the oxazaborolidines **16**.

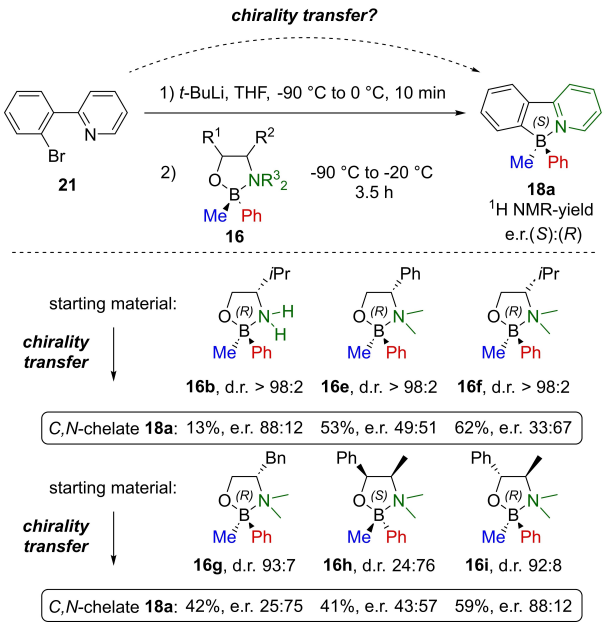


Scheme 4. Diastereoselective synthesis of aminoalcohol borinates **16a–l**. Diastereomeric ratios (d.r.) were determined by ^1H NMR. Stereochemistry at boron was elucidated by NOESY or solid-state structure (**16e–g**).

Screening of aminoalcohol complexes in the chirality transfer reaction

The obtained set of *O,N*-chelates **16a–l** was then treated with the lithiated phenylpyridine **21** to furnish the *C,N*-chelate **18a** and the results were evaluated regarding ^{1}H NMR yields and enantiomeric ratios (Scheme 5). The reaction conditions obtained after initial optimization (SI, Table S1) consisted of lithiation of 2-(2-bromophenyl)pyridine **21** with *t*-BuLi (2.0 equiv.) in THF, addition of the *O,N*-chelate **16** at −90 °C and warming to −20 °C. Chelates **16a,c,d,j,k** with free NH functionalities were supposed to be incompatible with the strongly basic aryllithium and together with quinine-compound **16l** only gave poor results (< 10% yield). Thus, these chelates are not discussed further with regards to the chirality transfer.

For NH_2-valinol complex **16b** the desired *C,N*-chelate **18a** was formed in 13% yield and e.r. 88:12. Albeit suffering from a low yield, the concept of chirality transfer could be successfully demonstrated: starting from a diastereomeric ratio > 98:2 the stereochemical information at boron was preserved, yet with a lower enantioselectivity (e.r. 88:12). An improved yield of 42–62% could be obtained for the monosubstituted dimethylaminoalcohol ligands **16e,f,g**. Unfortunately, the chirality transfer was less efficient for these monosubstituted NMe_2-ligands **16e,f,g** with e.r.'s ranging from virtually racemic (**16e**, e.r. 49:51) to moderate (**16f**, e.r. 33:67 and **16g**, e.r. 25:75). Notably, starting from the same $(R)_B$-configuration in **16e–g** as in **16b**, the opposite enantiomer of **18a** was obtained as major product in case of **16f,g**. The (1*S*,2*R*)-*N*-methylephedrine-based chelate **16h** (d.r. 24:76) provided **18a** in 41% and e.r. 43:57. The best result was obtained for (1*R*,2*R*)-*N*-methyl pseudoephedrine ligand **16i** combining 59% yield and e.r. 88:12. Here, the same enantioselectivity as for **16b** was observed and the enantiodivergent chirality transfer of **16b,h,i** and **16e–g** is part of ongoing investigation. An enantioenriched analytical sample of **18a** (e.r. 88:12) could be further recrystallized from toluene to e.r. > 99.5:0.5. Single crystals from this sample investigated by X-ray diffraction revealed the major enantiomer of **18a** to be (*S*)-configured at boron (for details see structural study below).



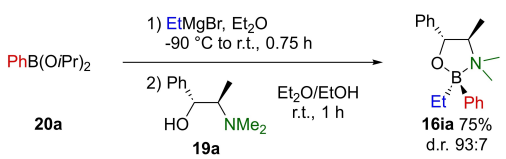
Scheme 5. Screening of *O,N*-chelates **16** in the chirality transfer reaction to *C,N*-chelate **18a**. Reactions were performed on 0.2 mmol scale. Results were examined by ^{1}H NMR yield using 1,3,5-trimethoxybenzene as internal standard and enantiomeric ratios (e.r.) were determined by chiral HPLC.

Substrate scope of pseudoephedrine borinates with alkyl/aryl substitution

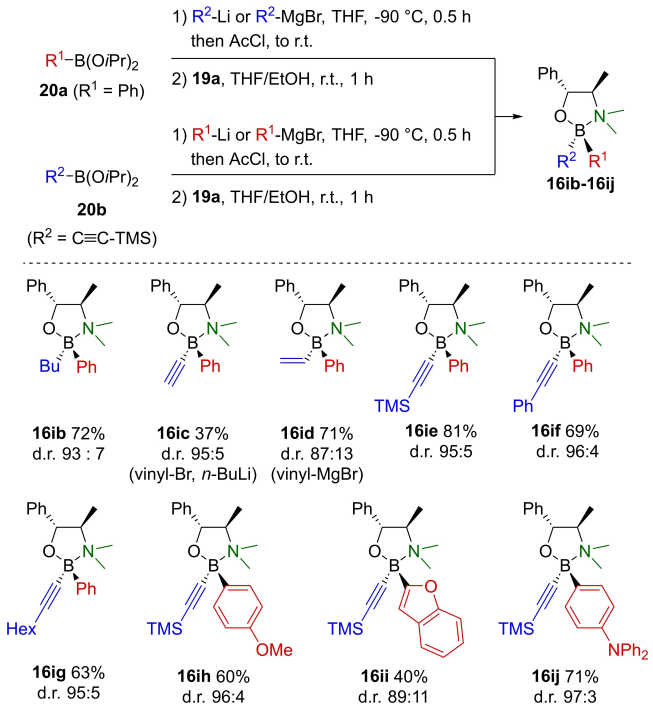
After proof of concept for the chirality transfer, we investigated the scope and limitations of the developed two-step sequence. First, *O,N*-chelates **16** based on the pseudoephedrine-ligand **19a** with peripheral boron-substituents (R^1 and R^2) other than methyl or phenyl were examined. By using the previously established Grignard method (see Scheme 3, **16i**) for the intermediate borinate generation (PhEtBO*i*Pr), the desired ethyl-substituted boron heterocycle **16ia** was formed in 75% yield and d.r. 93:7 (Scheme 6, method A).

However, the use of other Grignard reagents than MeMgBr or EtMgBr resulted in complex product mixtures und consequently, another protocol now employing organolithium reagents was developed. The respective lithium reagents R-Li were commercially available, or prepared by lithium-halogen exchange or deprotonation of alkynes (Scheme 7, method B). Phenyl **20a** or TMS-alkynyl boronates **20b** were then added to generate the intermediate ate-complexes, and the borinates were liberated by quenching with acetyl chloride.[60,61] The following in situ complexation with aminoalcohol **19a** proceeded smoothly in THF/EtOH mixtures. By this method B, butyl and ethynyl substituents were installed starting from diisopropylphenyl boronate **20a** in yields of 72% (**16ib**) and 37% (**16ic**) and d.r. 93:7 and 95:5 (Scheme 7). Notably, employing vinyl-MgBr under similar conditions provided **16id** in 71% and d.r. 87:13 thus expanding the scope of the developed protocol (method B) to Grignard reagents.

Moreover, TMS- (**16ie**), phenyl- (**16if**) and hexyl-capped (**16ig**) alkynes were introduced as alkyne lithium reagents in 63–81% and d.r. 95:5 or higher (Scheme 7). To further expand the scope TMS-alkynyl boronate **20b** was treated with different aryl- and heteroaryllithium compounds (R^1). The TMS-alkynyl-substituted chelates with *p*-MeO- (**16ih**) and *p*-NPh_2-phenyl-groups (**16ij**) were isolated in 60% (d.r. 96:4) and 71% (d.r. 97:3) while the benzofuryl-complex **16ii** gave a yield of 40% (d.r. 89:11).



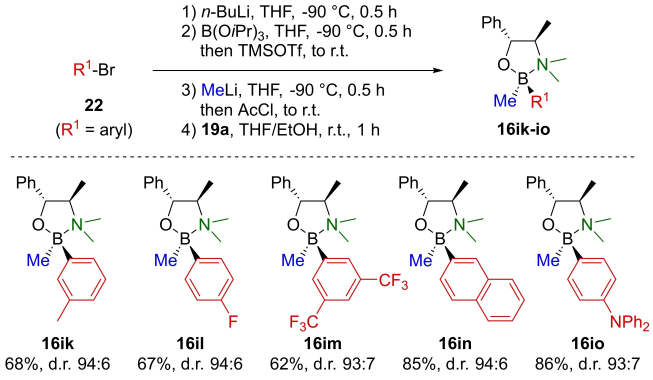
Scheme 6. Preparation of pseudoephedrine borinate **16ia** via method A. Diastereomeric ratios were determined by ^{1}H NMR.



Scheme 7. Preparation of pseudoephedrine borinates **16ib–ij** using different organolithium or Grignard reagents (method B). Diastereomeric ratios were determined by ^{1}H NMR.

Gratifyingly, the devised borinate complexation also allowed a one-pot preparation of the *O,N*-chelates **16** (Scheme 8, method C). For this, an aryllithium was mixed with B(O*i*Pr)$_3$ and treated with trimethylsilyl trifluoromethane sulfonate (TMSOTf)[62] to furnish a boronate R^{1}B(O*i*Pr)$_2$.

Subsequent addition of methyllithium followed by decomposition of the ate-complex with acetyl chloride furnished the intermediate borinates R^1(Me)BO*i*Pr which were then coordinated *in situ* to ligand **19a**. The protocol allowed the introduction of alkylated (**16ik**), fluorinated (**16il**), trifluoromethylated (**16im**) and π-extended or electron rich aryl moieties (**16in,o**). The yields ranging from 62–86% were reasonably high for a

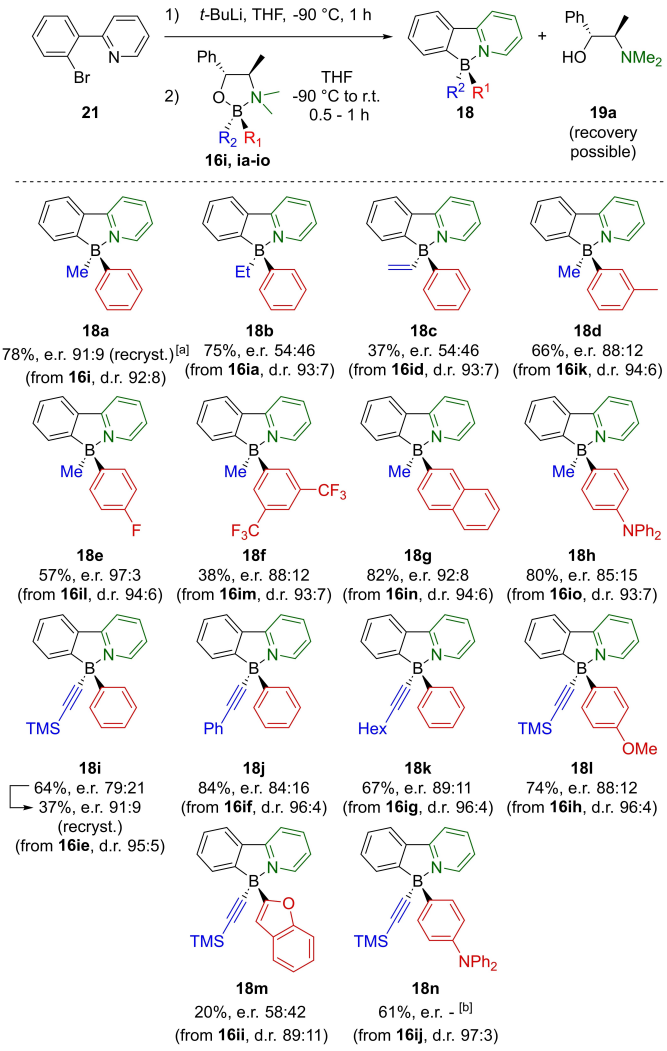


Scheme 8. Preparation of pseudoephedrine borinates **16ik–io** with different aryl-substituents at the boron atom via one-pot procedure (method C). Diastereomeric ratios were determined by ^{1}H NMR.

one-pot assembly and moreover, the diastereoselectivities were satisfying throughout (d.r. 92:8–94:6). The obtained set of aminoalcohol borinates was now to be probed in the substitution towards *C,N*-chelates.

Scope of chirality transfer to enantioenriched boron *C,N*-chelates

Exploring the devised chirality transfer required further synthetic optimization (for details see Supporting Information, Table S2) which included the lithiation of 2-(2-bromophenyl)pyridine **21** at −90 °C for 1 h instead warming up to 0 °C (Scheme 9). This finally enabled isolation of methyl/phenyl substituted **18a** in 78%. For **18a**, the crude e.r. of 87:13 (see Supporting Information, chapter 1.2) was improved by recrystallization to e.r. 91:9. Given the diastereomeric ratio of



Scheme 9. Scope of *C,N*-chelates **18a–n** prepared by the chirality transfer reaction from *O,N*-complexes **16ia,id–io** (including respective d.r.). Enantiomeric ratios (e.r.) were determined by chiral HPLC. [a] Enantiomeric ratio of the crude product was e.r. 87:13. [b] e.r. could not be determined by our means of chiral HPLC or NMR shift reagents. Instead, the e.r. of post-functionalized **18p** could be determined (e.r. 81:19).

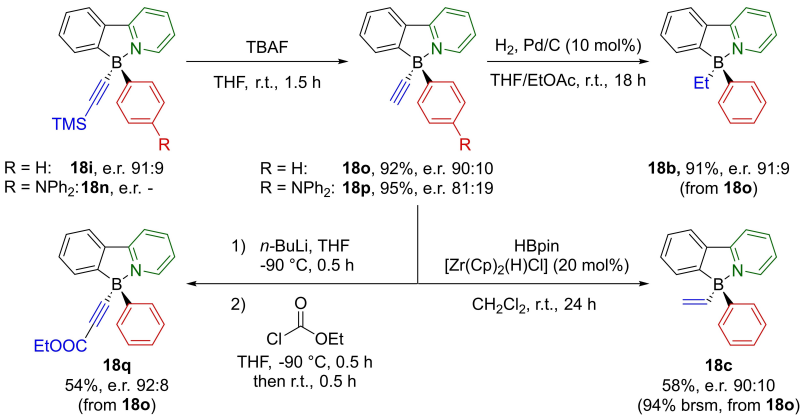
the *O,N*-chelated precursor **16i** (d.r. 92:8), the chiral information at the boron atom was transferred to the *C,N*-chelated **18a** (e.r. 91:9, crude e.r. 87:13) in a sufficient manner. It should be noted that the chiral aminoalcohol **19a** could be recovered by simple column chromatography (details see Supporting Information, chapter 1.2).

However, this conservation of stereochemical information did not succeed for substituents larger than a methyl group: ethyl- and vinyl-*C,N*-chelates **18b,c** could be isolated in 75% (**18b**) and 37% (**18c**) yield but gave virtually racemic mixtures (e.r. 54:46) in both cases. Thus, the chirality transfer seems quite sensitive to the size of the smaller peripheral substituent (R^2). On the other hand, by retaining the methyl-substituent and varying the aryl group we did not encounter such problems. For example, *m*-tolyl- and *p*-F-phenyl-substituted *C,N*-chelates **18d,e** could be isolated in 66% (**18d**) and 57% (**18e**) yield and enantioselectivities of e.r. 88:12 and 97:3. Additionally, a bistrifluoromethylated aryl group **18f** was tolerated in 38% yield and e.r. 88:12. Moreover, we were pleased to see that naphtyl-functionalized *C,N*-chelate **18g** or triphenylamine-equipped **18h** with bulky aromatic moieties could be obtained in high yields of 82% (**18g**) and 80% (**18h**) and selectivities (e.r. 92:8 (**18g**), 85:15 (**18h**)). Replacing the methyl-group with a TMS-protected alkyne provided the *C,N*-chelate **18i** in 64% and e.r. 79:21. Recrystallization improved the e.r. from 79:21 to 91:9 (37% yield). Other functionalized alkynes equipped with either a phenyl or hexyl group (**18j,k**) could be employed as well with yields of 67% and 81%. The e.r.'s of the TMS- (**18i**, e.r. 79:21 prior to recrystallization) and Ph-capped (**18j**, e.r. 84:16) examples were slightly lower than the hexyl-functionalized compound **18k** (e.r. 89:11). Interestingly, pairing the TMS-alkyne with a *p*-MeO-functionalized phenyl ring (**18l**) improved the yield to 74% and selectivity to e.r. 88:12. Finally, triphenylamine-functionalized **18n** was isolated in 61% but in contrast to methyl-chelate **18h**, the determination of the e.r. was not possible by our repertoire of chiral HPLC or NMR shift reagents. However, TMS-deprotection of **18n** to alkyne **18p** enabled chiral HPLC separation and indicated the e.r. of **18n** to be $\geq$81:19 (**18p**, Scheme 10). The major limitation for aromatic groups represented the benzofurane-complex **18m** which could be isolated only in 20% yield and e.r. 58:42.

The moderate enantiomeric ratios with larger groups than methyl or alkynyl could be tackled by post-functionalization of the obtained *C,N*-chelates (Scheme 10). First, the TBAF-mediated deprotection of TMS-alkynes **18i** and **18n** proceeded smoothly to give **18o** and **18p** in 92–95% and e.r. 90:10 (**18o**) and 81:19 (**18p**). Hydrogenation of **18o** with Pd/C provided ethyl-derivative **18b** in 91% yield. Gratifyingly, the enantiomeric ratio of the starting TMS-alkyne **18i** (e.r. 91:9) was completely retained over two steps (**18b** e.r. 91:9). Attempted hydroboration of alkyne **18o** with HBpin revealed a particular reactivity in form of concomitant deborylation which furnished the unsubstituted alkene **18c** in 58% yield (94% brsm) and e.r. 90:10 (for details of deborylation see Supporting Information, chapter 1.3). Finally, alkyne **18o** survived deprotonation with *n*-BuLi and electrophilic trapping gave rise to ester **18q** in 54% and e.r. 92:8. It should be emphasized, that neither hydroboration nor deprotonation/electrophilic trapping affected the boron stereocenter's integrity.

Structural study of boron *O,N*- and *C,N*-chelates by NMR and X-ray diffraction

The structural aspects of the *O,N*- and *C,N*-chelates were studied in solution and solid-state. NMR studies of the aminoalcohol complexes **16** revealed a dynamic behaviour illustrated by broadened/coalesced NMe_2-signals or exchange signals in the NOESY spectra (for ^{1}H NMR and exemplary NOESY spectra see Supporting Information, chapter 3 and 1.5). This phenomenon was observed for all *O,N*-chelates **16** besides the one with NH_2-donor **16a-c** or alkyne-substituents **16ie–ij**. The dynamic behavior was studied by variable temperature (VT) NMR (see Supporting Information, chapter 1.4) and will be discussed for dimethylvalinol-complex **16f** as representative example (Figure 1). The ^{1}H NMR spectrum of **16f** at 25 °C showed a single NMe_2-signal which was attributed to a rapid breaking of the B–N donor bond, rotation of acyclic isomer **23** and renewed formation of the B-N bond (Figure 1a and 1b). This type of



Scheme 10. TMS-deprotection of **18i** and **18n** and functionalization of alkyne **18o** to access *C,N*-chelate **18b**, **18c** and **18q**.

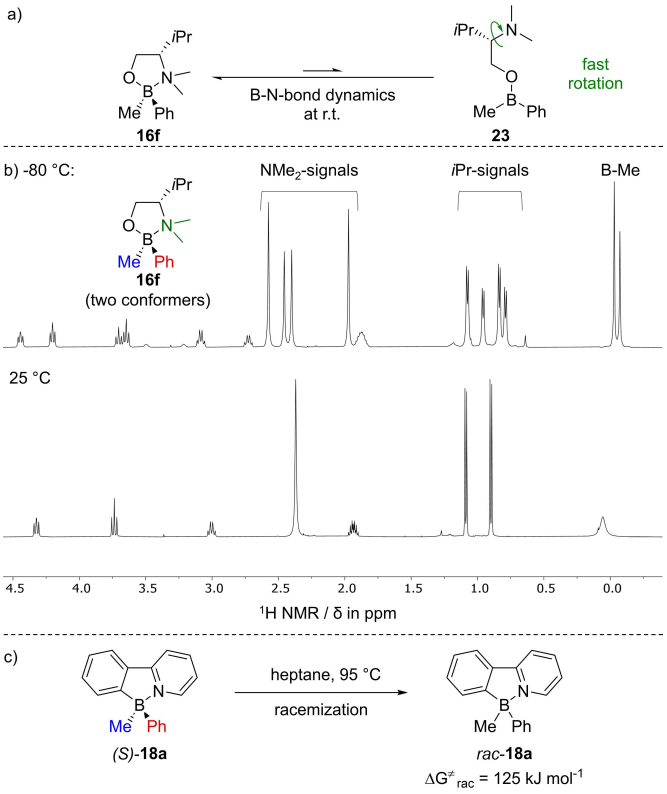


Figure 1. a) B–N bond dynamics of aminoalcohol complex **16f** at room temperature. b) ^{1}H NMR spectra of **16f** in CD_2Cl_2 (500 MHz) at 25 °C and −80 °C, c) racemization of *C,N*-chelate **18a** in heptane at 95 °C and racemization barrier $\Delta G^{\neq}_{rac}$.

dynamics has been described for comparable NMe_2-B-dative bonds and the barriers reported were in a range of 48–76 kJ mol^{-1}.[52,63,64] The acyclic isomer **23** could not be observed according to ^{11}B NMR with a single signal at δ(**16f**) = 11.1 ppm.

Cooling the sample to −80 °C resulted in splitting of the NMe_2-signal together with appearance of a second signal set in a ~55:45 ratio (^{1}H NMR, Figure 1b). The splitting of the NMe_2-signal is explained by freezing the B–N bond dynamics whereas the second signal set originates from another dynamic process.

Unfortunately, the overlapping signals of both processes prevented the exact barrier determination of the B-N bond strength by VT NMR (see Supporting Information, Figure S7). The second process is supposedly a conformational barrier resulting from a densely substituted oxaborolidine and such a conformational freeze of related six-membered boron-*O,N*-chelates has been reported.[53] The hypothesis of conformers was further supported as the *i*Pr-substituted NH_2-chelate **16b** with a stronger B–N bond[52] (and hence, a slower B–N bond dynamics) displayed similar doubling of signals at −80 °C (Figure S1, Supporting Information). On the other hand, the B–N bond for the enantioenriched *C,N*-chelate **18a** proved to be far more stable as illustrated by a racemization experiment in heptane at 95 °C (Figure 1 c, Supporting Information chapter 1.6). The racemization barrier $\Delta G^{\neq}_{rac}$ of **18a** was 125 kJ mol^{-1} and thus is higher than in comparable NMe_2-donor-complexes such as **3** (94–116 kJ mol^{-1})[25] but lower than respective *N,N*-chelates such as **8** (137–145 kJ mol^{-1}).[9]

In addition to solution studies, the solid-state structures of *O,N*-chelates **16e**, **16i** and of *C,N*-chelate **18a** were obtained from single crystal X-ray diffraction (Figure 2). For more details see Supporting Information, chapter 5. The single crystals were grown by slow evaporation of heptane/CH_2Cl_2 (**16e**), Et_2O (**16i**) or toluene (**18a**) solutions. These solid-state structures revealed the absolute stereochemistry of the respective compounds.

The monosubstituted *O,N*-chelate **16e** displayed a B–N bond length of 1.689(3) Å similar to the disubstituted **16i** (1.683(3) Å). The B–N length of **16i** is shorter than its corresponding BPh_2-derivative (1.74(1) Å),[52] likely due to steric reason (Figure 2 left). On the other hand, *C,N*-chelate **18a** has a comparable B–N-distance of 1.620(2) Å as its BPh_2- and B(biphenyl) pendants (1.618(3) Å and 1.617(5) Å).[41,43] The tetrahedral character (THC) according to Höpfl[65] is derived from all bond angles around the boron atom and, as a measure of the boron sp^3-hybridization, was 74% for *O,N*-**16e**, 76% for *O,N*-**16i** and 66% for *C,N*-**18a**.

Conclusion

The enantioselective synthesis of boron *C,N*-chelates **18** stereogenic only at the *B*-atom was realized by chirality transfer from *O,N*- to *C,N*-chelates. Initial borinate complexation with chiral aminoalcohols **19** provided *O,N*-chelates **16** in high diastereose-

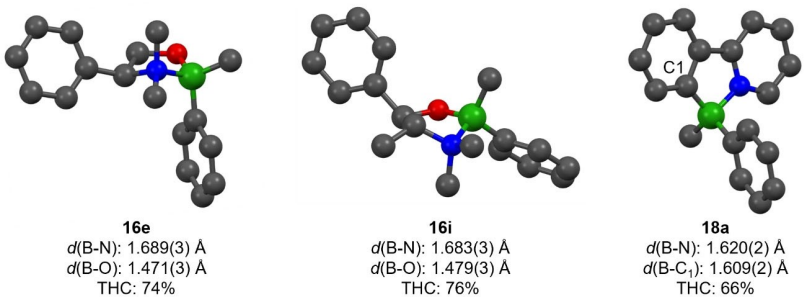


Figure 2. Solid-state structures of **16e**, **16i** and **18a** including selected bond lengths and their tetrahedral character (THC). Structures represent absolute configurations. H-atoms omitted for clarity. Grey: carbon, red: oxygen, blue: nitrogen, green: boron.

lectivity at the boron stereocenter. Among the tested aminoalcohols **19**, *N*-methylated pseudoephedrine **19a** was identified as the ligand of choice in the following chirality transfer reaction. The complexation of **19a** with a variety of alkyl/aryl borinates furnished a library of *O,N*-complexes (**16i**, **16ia**–**o**). This set of *O,N*-chelates **16** was subjected to the chirality transfer reaction and gave rise to the *C,N*-phenylpyridine-chelates **18a**–**o** in an enantioenriched fashion. A variety of peripheral groups such as methyl and alkynyl on the one side, and bulky and heteroatom-substituted aryl moieties on the other side could be introduced in yields up to 84% and up to e.r. 97:3. Notably, the aminoalcohol **19a** used for chirality transfer could be recovered by simple column chromatography. The post-functionalization enabled alkyne derivatization and introduction of larger alkyl and alkenyl substituents without affecting the boron stereocenter.

Gratifyingly, our devised concept of chirality transfer via the ate-complex for enantiocontrol at boron atoms succeeded and consequently expands the space of this synthetic handle from so far carbon-based stereoselective transformations. Further, the possibility to address the peripheral substitution complements the few hitherto known catalytic enantioselective approaches to *B*-stereogenic chelates, which predominantly focused on the boron chelate ligand. The tolerance of the presented chirality transfer regarding other types of chelate ligands and insights into the origin of stereoselectivity will be reported in due course.

Supporting Information

The Supporting Information contains the experimental procedures, NMR spectra, HPLC traces and supplementary experiments.

Additional references cited in the Supporting Information.[9,20,25,42,59,65–77]

Deposition Numbers 2249555 (for **16e**), 2235885 (for **16i**) and 2235887 (for **18a**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service.

Notes

The authors declare no competing financial interest.

Author Contributions

Y.S. conceived the project and prepared the boron *O,N*- and *C,N*-chelates. E.J.T. synthesized part of the *O,N*-complexes and racemic *C,N*-samples. W.F. performed X-ray diffraction measurements and evaluated the data. S.W. and B.C. measured the temperature dependent NMR spectra and analyzed the (dynamic) NMR data. A.Z. checked the data and Y.S. with help of A.Z. wrote the manuscript. S.L. supervised and coordinated the research. All authors proofread the manuscript and agreed to the final version.

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Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: boron · chelate · chirality transfer · enantioselective synthesis · stereogenic

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