Chiral Carbanions, Part 4:[1] Borylation of (Trimethylsilyl)methyl *N*,*N*-Dialkylcarbamates – Diastereoselectivity and Structural Studies

Biljana Peric Simov,[a] Agnieszka Rohn,[a] Lothar Brecker,[a] Gerald Giester,[b] Friedrich Hammerschmidt*[a]

[a] Institut für Organische Chemie der Universität Wien, Währingerstraße 38, 1090 Wien, Austria
Fax +43(1)42779521; E-mail: friedrich.hammerschmidt@univie.ac.at

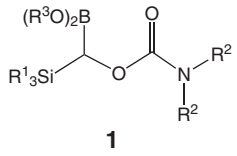
[b] Institut für Mineralogie und Kristallographie der Universität Wien, Geozentrum, Althanstrasse 14, 1090 Wien, Austria

Received 24 May 2004; revised 17 July 2004

Abstract: (Trimethylsilyl)methyl carbamates were prepared from (trimethylsilyl)methanol and *N*,*N*-dialkylcarbamoyl chlorides and were metalated by *s*-BuLi/TMEDA. The configurationally labile lithiated carbamates were reacted with borates derived from (+)-pinane-2,3-diol to give boronates diastereoselectively (yields up to 84%, dr up to 17:1). The absolute configurations at the boron-bearing carbon atoms of three boronates were assigned by single crystal X-ray structure analyses.

Key words: carbamates, carbanions, lithiation, nucleophilic substitution, diastereoselectivity

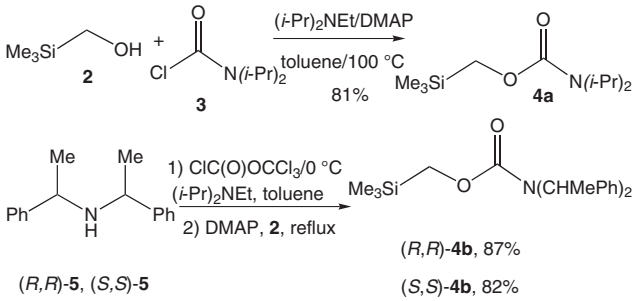
Boronic acids and their esters are versatile compounds in organic chemistry.[2] Their various applications range from the Suzuki–Miyaura coupling[3] and the use of allylboronates for the stereoselective allylation[4] of aldehydes to the asymmetric syntheses based on α-halo boronates[5] elegantly developed by Matteson et al. Borylation of lithium and magnesium organic compounds with trialkyl borates and hydroboration are very general approaches to their synthesis. In a project aiming at the direct chemical synthesis of chiral, nonracemic [$^2H_1$,^{3}H]methanol we got interested in the preparation of suitable precursors of type **1** (Figure 1). Here we report on their synthesis from metalated (trimethylsilyl)methyl carbamates and borates and the determination of their structures. Furthermore, we studied the influence of the solvent and the temperature on the diastereoselectivity of the reaction, which so far has not been addressed.



1

Figure 1

Three (trimethylsilyl)methyl carbamates, **4a** and (*R*,*R*)- and (*S*,*S*)-**4b** derived from C_2 symmetric amines[6] (*R*,*R*)- and (*S*,*S*)-**5** (>99% ee), were prepared to study the diastereoselectivity of borylation (Scheme 1). Carbamate **4a** was formed by esterification of trimethylsilylmethanol[7] (**2**) with commercially available carbamoyl chloride **3** in 81% yield.[8] The amines (*R*,*R*)- and (*S*,*S*)-**5** were first transformed into the intermediate carbamoyl chlorides using trichloromethyl chloroformate, which were converted in situ to the (trimethylsilyl)methyl esters (*R*,*R*)- and (*S*,*S*)-**4b** in 87% and 82% yield, respectively. The (trimethylsilyl)methanol was obtained by a modified literature procedure[7] in two steps from (chloromethyl)(trimethyl)silane. Nucleophilic substitution of chloride for acetate in dry DMF with NaOAc and a substoichiometric amount of NaI at 100 °C for 24 hours gave the (trimethylsilyl)methyl acetate in 76% yield (see experimental part), which was reduced with $LiAlH_4$.



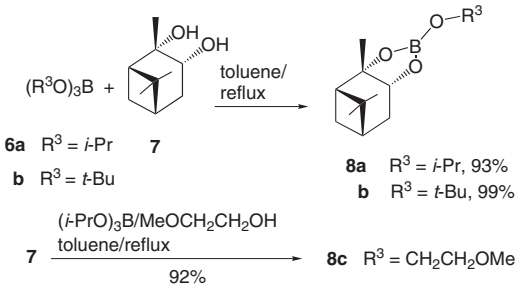
Scheme 1

To obtain hydrolytically stable boronates,[5] four mixed boric acid esters containing a 1,2-diol were used for borylation, isopropanol pinacol boric acid ester[9] and three borates **8** derived from (+)-pinane-2,3-diol (**7**, 99% ee) and trialkyl borates **6** by transesterification in high yields (>90%) (Scheme 2). The methoxyethyl borate **8c** was selected because of the additional ether oxygen atom in the leaving group. Matteson and Man found that boronic acid esters of pinane-2,3-diol are highly resistant to hydrolysis, which was desirable for our studies.[10]

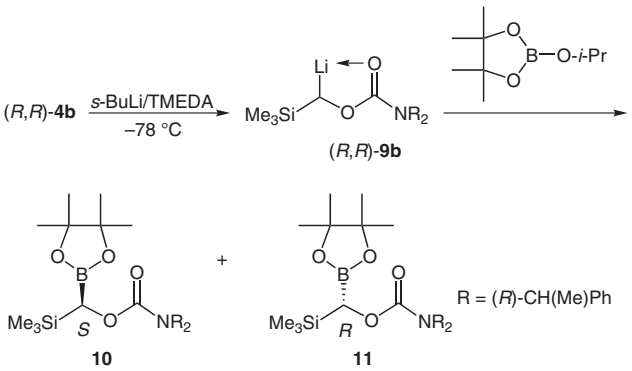
The first experiment was performed with carbamate (*R*,*R*)-**4b**. It was metalated with two equivalents of *s*-BuLi in THF at –78 °C for 15 minutes and then quenched with isopropanol pinacol boric acid ester (Scheme 3).

After allowing the reaction mixture to warm up to room temperature and work up, a crude product consisting of starting material and two new compounds of similar polarity was obtained. Flash chromatography with hexane–ethyl acetate furnished a mixture of the two new com-

SYNTHESIS 2004, No. 16, pp 2704–2710
Advanced online publication: 22.09.2004
DOI: 10.1055/s-2004-831237; Art ID: T05404SS



Scheme 2



Scheme 3

pounds in 35% yield, which were separated by flash chromatography using hexane–ethyl acetate (10:1).

The crystalline compounds turned out to be diastereomeric boronates (for nomenclature see ref.[11]) on the basis of their spectroscopic data. A single crystal X-ray structure analysis of the major diastereomer **10**, which is also the more polar one, revealed that the boron-bearing carbon atom has (*S*)-configuration (Figure 2).

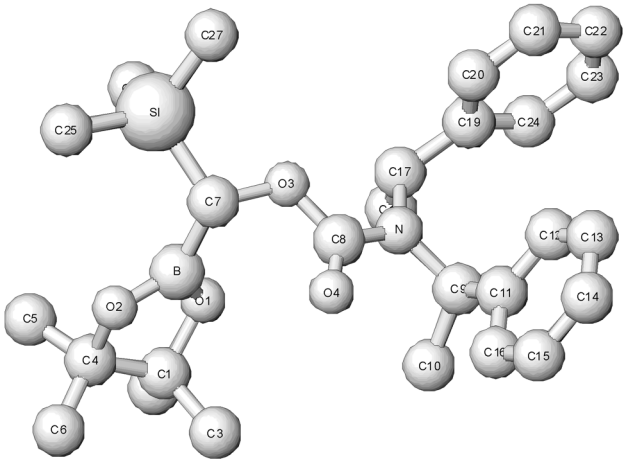
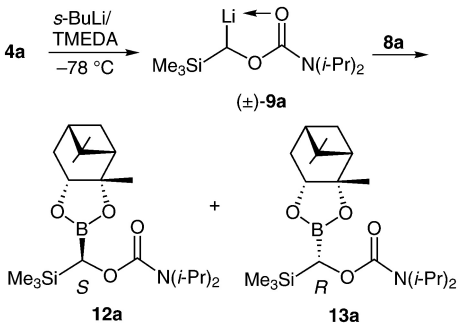


Figure 2 Crystal structure of boronate **10**; the hydrogen atoms were omitted for the sake of clarity

The ratio of boronates **10**:**11** in the crude product was 1.7:1. When the metalation was performed in hexane with two equivalents of *s*-BuLi/TMEDA for 30 minutes, the yield of the boronates increased to 77% and the ratio dropped to 1.5:1. This result demonstrates that the (trimethylsilyl)methyl carbamate can be deprotonated and borylated easily. The diastereomeric ratios of 1.5:1 and 1.7:1 are either the result of a combination of a diastereoselective metalation and a configurationally stable organolithium species or of the diastereoselectivity in the borylation of a configurationally labile organolithium.[12] As the stereogenic centers in the carbamoyl group are far away, their effect on both metalation and borylation are rather small. Metalated carbamates derived from aliphatic primary alcohols are configurationally stable as found by Hoppe and Hense.[13]

Next, we combined a racemic lithiated carbamate and a chiral boric acid ester (Scheme 4). Metalation of carbamate **4a** in hexane or THF as before with two equivalents of *s*-BuLi/TMEDA and borylation with **8a** produced mixtures of boronates **12a/13a** in yields of 86% and 90%, respectively.

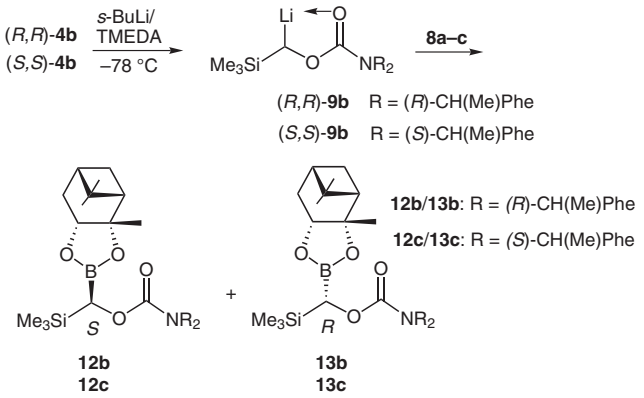


Scheme 4

The oily diastereomers could be separated by flash chromatography despite the small difference in their polarity (R_f 0.41 and 0.47 in hexane–ethyl acetate, 10:1). The diastereomeric ratios were 1.25:1 and 4:1, respectively, in favour of the major diastereomer **12a**. The assignment of the structure to the compounds is postponed and will be dealt with later. These two experiments prove that the lithiated carbamate is configurationally labile at the time scale of borylation. On the contrary, an enantiomerically enriched 1-lithio-1-(trimethylsilyl)ethyl carbamate was found to be configurationally stable (Hoppe et al.[14]).

At last, we combined chiral borates **8a**–**c** with C_2 symmetric carbamates (*R*,*R*)- and (*S*,*S*)-**4b** to produce mixtures of boronates **12b/13b** and **12c/13c**, **12b** and **12c** being the major diastereomers (Scheme 5). Lithiations were performed with 1.2 equivalent of *s*-BuLi/TMEDA, which evolved as the standard for the metalation of all (trimethylsilyl)methyl carbamates. *n*-BuLi was used as base in one exploratory experiment but was less efficient than *s*-BuLi. Single crystal X-ray structure analyses were necessary to determine the (*R*)-configuration of **13b** and the (*S*)-configuration of **12c** at the boron-bearing carbon atoms

(Figure 3). Therefore, the major diastereomers obtained in both cases have (*S*)-configuration at the newly formed asymmetric centres irrespective of the configuration of the 1-phenylethyl groups. The predominating formation of (*S*)-configuration is induced by the (+)-pinane-2,3-diol ligand of the boric acid ester.



Scheme 5

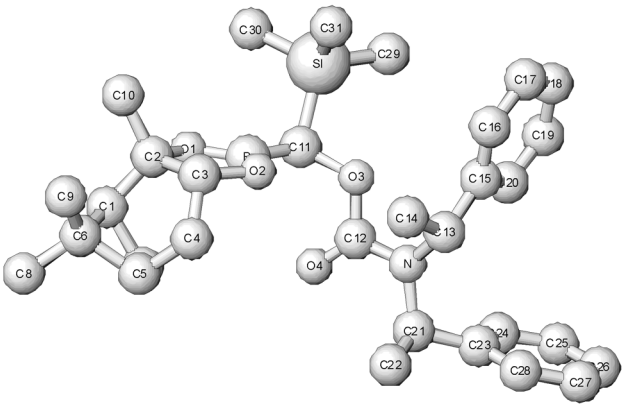


Figure 3 Crystal structure of boronate **13b**; the hydrogen atoms were omitted for the sake of clarity

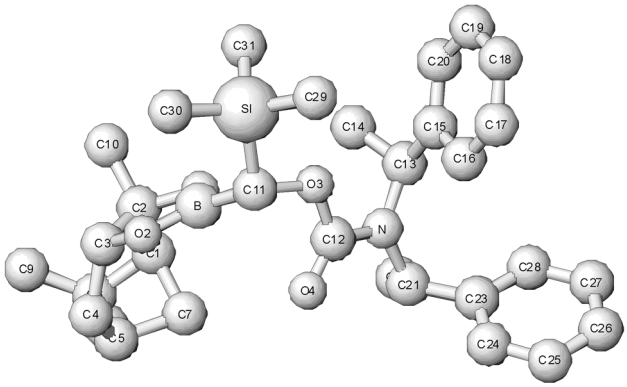


Figure 4 Crystal structure of boronate **12c**; the hydrogen atoms were omitted for the sake of clarity

The borylations were performed with three borates in either diethyl ether or THF at temperatures of –50 °C, –78 °C or –94 °C. The results are summarised in Table 1. The diastereoselectivity increased when carbamate (*R*,*R*)-**4b** and isopropyl borate **8a** were used, by lowering the reaction temperature from –78 °C (**12b**:**13b** = 4:1, Entry 1) to –94 °C (**12b**:**13b** = 7:1, Entry 2) in diethyl ether. When the isopropyl borate **8a** was replaced by *t*-butyl borate **8b** the diastereoselectivity reached was best (**12b**:**13b** = 17:1, Entry 3) but dropped when the reaction temperature was –94 °C (**12b**:**13b** = 9:1, Entry 4) or –50 °C (**12b**:**13b** = 6:1, Entry 5). The diastereoselectivity in THF at –78 °C (**12b**:**13b** = 8:1, Entry 6) was about half of that in diethyl ether under otherwise identical conditions. Surprisingly, the two diastereomers were formed in equal amounts when the methoxyethyl borate **8c** was used as electrophile (Entry 7). This may possibly be caused by the additional oxygen atom in the leaving group. The diastereoselectivity for carbamate (*S*,*S*)-**4b** was lower than that for carbamate (*R*,*R*)-**4b** under comparable conditions (Entries 8–10). The yields of the boronates were about 70%.

The diastereoselectivity did not change by going from *N*,*N*-diisopropylcarbamate **4a** to (*S*,*S*)-*N*,*N*-bis(1-phenyl-

Table 1 Preparation of Boronates **12/13b**,**c**

Entry	Carbamate	Borate	Solvent	Temperature (°C)	Boronates/Yield (%)/Ratio
1	(*R*,*R*)-**4b**	**8a**	Et_2O	–78	**12b** + **13b**/45/4:1
2	(*R*,*R*)-**4b**	**8a**	Et_2O	–94	**12b** + **13b**/65/7:1
3	(*R*,*R*)-**4b**	**8b**	Et_2O	–78	**12b** + **13b**/78/17:1
4	(*R*,*R*)-**4b**	**8b**	Et_2O	–94	**12b** + **13b**/54/9:1
5	(*R*,*R*)-**4b**	**8b**	Et_2O	–50	**12b** + **13b**/69/6:1
6	(*R*,*R*)-**4b**	**8b**	THF	–78	**12b** + **13b**/80/8:1
7	(*R*,*R*)-**4b**	**8c**	Et_2O	–78	**12b** + **13b**/73/1:1
8	(*S*,*S*)-**4b**	**8a**	THF	–78	**12c** + **13c**/84/4:1
9	(*S*,*S*)-**4b**	**8b**	THF	–78	**12c** + **13c**/66/4:1
10	(*S*,*S*)-**4b**	**8b**	Et_2O	–94	**12c** + **13c**/74/6:1

ethyl)carbamates **4b**, but increased significantly for (*R*,*R*)-*N*,*N*-bis(1-phenylethyl)carbamates **4b** in combination with *t*-butyl borate **8b**. The stereochemistry at the boron-bearing carbon atom is borate controlled. Borates **8a**,**b** derived from (+)-pinane-2,3-diol favour the formation of diastereomers with (*S*)-configuration at the boron-bearing carbon atom. The influence of the configuration of the carbamoyl group on the diastereoselectivity is of minor importance although (*S*)-configuration is formed preferentially from (*R*,*R*)-**4b** and an achiral borate. Combining carbamate (*R*,*R*)-**4b** with **8a**,**b** (matched case) gave higher diastereoselectivities than combining (*S*,*S*)-**4b** with **8a**,**8b** (mismatched case).[15] Consequently, we assume on the basis of analogy that boronate **12a**, the major diastereomer formed from *N*,*N*-diisopropylcarbamate **4a**, is also (*S*)-configured at the boron-bearing carbon atom.

We also tried to deduce the absolute configurations at the boron-bearing carbon atoms (C-1, which is C-11 in numbering used only for X-ray structures) of **12a** and **12b** by NMR spectroscopy. First, their proton and carbon signals (except that of NCH) were assigned. The shifts of respective atoms in the (+)-pinane-2,3-diol ligand varied insignificantly in $CDCl_3$ at 27 °C (see experimental part).[16] Surprisingly, only the chemical shift of H-7a was influenced markedly by the configuration at C-1 (δ 1.38 ppm for **12a** and δ 1.50 ppm for **13a**) which was also noticed by Matteson et al.[17] The same is true for **12b/13b** (δ 1.48 ppm and δ 1.40 ppm) and **12c/13c** (δ 1.31 ppm and δ 1.45 ppm). Unfortunately, the changes for H-7a and other signals with smaller shift differences are not consistent, so the configuration at C-1 cannot be deduced from the NMR spectra. All boronates are conformationally flexible in solution. NOESY spectra of **12a** and **13a** show NOEs between H-1 and H-7a indicating a spatial closeness between these two nuclei. Such vicinity is not present in any crystal structure [d(C=O···B) = 3.06 Å for **13b** and 2.89 Å for **12c**]. In solution, however, further conformations seem to allow a formation of a coordinative bond between the boron atom and the oxygen or nitrogen of the carbamoyloxy substituent. The dissociation rate constant of such coordinative bonds is in the same time scale as chemical shift differences of some respective atoms in the two different conformers. For that reason, ^{13}C atoms directly bound to the nitrogen of the carbamoyl group show broad signals with low intensity in NMR spectra. Namely the signal of the boron-bearing carbon atom was not directly detectable in ^{13}C spectra, but indirectly determined in HMQC and HMBC spectra.[18] In toluene-d_8 at 87 °C compared to $CDCl_3$ at 27 °C, however, the tendency of the boron atom to form a coordinative bond is much lower. For that reason the according dissociation rate constant is distinctly higher and all ^{13}C atoms (C-1 could not be detected) show sharp signals in the NMR spectra.

In summary, we have shown that (trimethylsilyl)methyl carbamates are deprotonated easily at –78 °C using *s*-BuLi/TMEDA to give configurationally labile organolithiums. These are borylated with borates derived from (+)-pinane-2,3-diol to give boronates in good yields diastereoselectively (dr up to 17:1). The observed stereoselection is the result of dynamic kinetic resolutions of chiral boron reagents on configurationally labile organolithiums.

^1H NMR spectra were measured in $CDCl_3$ at 300 K on a Bruker Avance DRX 400 or DRX 600 spectrometer at 400.13 MHz or 600.13 MHz, respectively. COSY, NOESY, HMQC, and HMBC spectra were recorded on a DRX 600 spectrometer under the same conditions using 1024 data points and 256 experiments for each spectrum. ^{13}C Frequency in the heteronuclear correlations was 150.86 MHz. Chemical shifts were referenced to residual $CHCl_3$ (δ_H = 7.24) and $CDCl_3$ (δ_C = 77.00). Additional ^{13}C spectra (*J* modulated) were measured at 360 K in toluene-d_8 on a DRX 400 spectrometer at 100.61 MHz and referenced to the CD_3 group (δ_C = 21.04). All chemical shift (δ) are given in ppm and coupling constants (*J*) in Hertz. IR spectra were run on a Perkin-Elmer 1600 FT-IR spectrometer; liquid samples were measured as films between NaCl plates or on a silicon disc.[19] Optical rotations were measured at 20 °C on a Perkin-Elmer 351 polarimeter in a 1 dm cell. TLC was carried out on 0.25 mm thick Merck plates, silica gel 60 F_{254}. Flash chromatography was performed with Merck silica gel 60 (230–240 mesh). Spots were visualised by UV and/or dipping the plate into a solution of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (23.0 g) and of $Ce(SO_4)_2\cdot 4H_2O$ (1.0 g) in 10% aq H_2SO_4 (500 mL), followed by heating with a hot gun. Melting points were determined on a Reichert Thermovar instrument and were uncorrected.

Single crystal X-ray diffraction data of boronates **10**, **12c** and **13b** were measured at –73 °C on a Nonius KappaCCD diffractometer (MoKα-radiation, $2\theta_{max}$ = 56.5°) equipped with a 0.3 mm monocapillary optics collimator. Several sets of ω scans were performed to complete the sphere. The extraction and correction of the intensity data, including a pseudoabsorption correction by frame scaling and the refinement of lattice parameters were performed with the program package DENZO-SMN.[20] For structure solutions by direct methods the program SHELXS-97[21] was used and the structure refinements based on full-matrix least squares techniques of F^2 were done with SHELXL-97.[22] The positions of all hydrogen atoms were located by final difference Fourier maps and refined.

(Trimethylsilyl)methyl Acetate

(Chloromethyl)(trimethyl)silane (24.5 g, 200 mmol), NaOAc (23.0 g, 280.4 mmol) and NaI (8.0 g, 53.4 mmol) in anhyd DMF (150 mL) were heated at 100 °C (bath temperature) for 24 h. The reaction mixture was cooled, diluted with H_2O (150 mL) and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with H_2O, 2 M HCl, H_2O, a sat. aq solution of $NaHCO_3$ (100 mL each), dried ($MgSO_4$) and concentrated under reduced pressure. The residue was purified by fractional distillation (70 °C/120 mbar) to give (trimethylsilyl)methyl acetate[7] (22.2 g, 76%) as a colourless liquid.

Preparation of Borates 6a–c

A mixture of (+)-pinane-2,3-diol (7.01 g, 41.2 mmol, ee 99%), triisopropyl borate (9.29 g, 11.4 mL, 49.4 mmol, 1.2 equiv) and anhyd toluene (60 mL) were refluxed for 30 min. After concentration of the reaction mixture under reduced pressure the residue was bulb-to-bulb distilled (97 °C/0.6 mbar) to give borate **6a** (9.85 g, 93%) as a colourless liquid.

Similarly, (+)-pinane-2,3-diol (5.40 g, 31.7 mmol) and tri-*t*-butyl borate (8.76 g, 10.8 mL, 38.04 mmol) in anhyd toluene (40 mL) were transformed into borate **6b** (7.94 g, 99%, 100 °C/0.8 mbar) as a colourless liquid.

Similarly, (+)-pinane-2,3-diol (3.41 g, 20.0 mmol), triisopropyl borate (4.51 g, 5.54 mL, 24.0 mmol) and 2-methoxyethanol (1.83 g, 1.89 mL, 24 mmol) in anhyd toluene (25 mL) were transformed into borate **6c** (4.68 g, 92%, 120 °C/0.3 mbar) as a colourless liquid.

(Trimethylsilyl)methyl *N*,*N*-Diisopropylcarbamate (4a)

A mixture of (trimethylsilyl)methanol (2.085 g, 20 mmol), *i*-$Pr_2NC(O)Cl$ (3.93 g, 24 mmol), *i*-Pr_2NEt (5.23 ml, 3.88 g, 30 mmol) and DMAP (0.20 g, 1.64 mmol) in anhyd toluene (20 mL) was heated at 100 °C for 16 h. H_2O (1 mL) was added and heating was continued for another h. After cooling, the mixture was concentrated and aq HCl (20 ml, 5%) and CH_2Cl_2 (30 mL) were added. The organic phase was separated and the aq phase was extracted with CH_2Cl_2 (30 mL). The combined organic layers were washed with H_2O, dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (hexane–EtOAc, 2:1; R_f 0.21) and then bulb-to-bulb distilled (100 °C/16 mbar) to give carbamate **4a** (3.75 g, 81%) as a colourless liquid.

IR (NaCl): 2967, 1694, 1441, 1328, 1310, 1250, 1053 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 4.00 (br s, 1 H, NCH), 3.75 (br s, 1 H, NCH), 3.70 (s, 2 H, CH_2O), 1.11 (d, *J* = 6.9 Hz, 12 H, Me_2CH), 0.06 (s, 9 H, $SiMe_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 157.4, 59.1, 47.6, 22.4, –1.6.

Anal. Calcd for $C_{11}H_{25}NO_2Si$: C, 57.09; H, 10.89; N, 6.05. Found: C, 57.32; H, 11.24; N, 6.08.

(*R*,*R*)-(+)- and (*S*,*S*)-(–)-(Trimethylsilyl)methyl *N*,*N*-Bis(1-phenylethyl)carbamate [(*R*,*R*)- and (*S*,*S*)-4b]

Trichloromethyl chloroformate (1.69 mL, 2.77 g, 14 mmol) was added dropwise at 0 °C to a stirred solution of (*R*,*R*)-*N*,*N*-bis(1-phenylethyl)amine (4.51 g, 20 mmol), *i*-Pr_2NEt (10.34 g, 13.94 mL, 80 mmol) in anhyd toluene (50 mL) under argon. After 30 min DMAP (0.611 g, 5 mmol) and (trimethylsilyl)methanol (3.79 mL, 3.13 g, 30 mmol) were added and the mixture was refluxed for 18 h and then cooled. Aq HCl (5 mL of concd aq HCl and 50 mL of H_2O) was added. The organic phase was separated and the aq phase was extracted with toluene (20 mL). The combined organic phases were washed with H_2O (30 mL), a sat. aq solution of $NaHCO_3$, dried ($MgSO_4$) and concentrated. The residue was purified by flash chromatography (hexane–EtOAc, 20:1; R_f 0.37, hexane–EtOAc, 10:1) to give carbamate (*R*,*R*)-**4b** (6.19 g, 87%) as a colourless oil; last traces of solvents were removed by heating at 100 °C/0.5 mbar; $[\alpha]_D^{20}$ +100.6 (*c* 2.31, acetone). Bulb-to-bulb distillation (140 °C/0.005 mbar) gave a product containing a decomposition product (4 mol%).

Similarly, (*S*,*S*)-*N*,*N*-bis(1-phenylethyl)amine (6.76 g, 30 mmol) was transformed into carbamate (*S*,*S*)-**4b** (8.74 g, 82%); $[\alpha]_D^{20}$ –105.7 (*c* 7.1, $CHCl_3$).

IR (NaCl): 2956, 1686, 1437, 1302, 1249, 1208 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.04–6.80 (m, 10 H, H_{arom}), 5.06 (br s, 2 H, NCH), 3.64 (AB system, *J* = 14.3 Hz, OCH_2), 1.68 (d, *J* = 7.4 Hz, 6 H, CH_3), –0.12 (s, 9 H, $SiMe_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 158.3, 143.9, 129.2, 129.0, 128.1, 59.7, 55.5, 19.9, –1.8.

Anal. Calcd for $C_{21}H_{29}NO_2Si$: C, 70.94; H, 8.22; N, 3.94. Found: C, 71.21; H, 8.41; N, 4.04.

Pinacol {(1*S*)- and (1*R*)-[(*R*,*R*)-*N*,*N*-Bis(1-phenylethyl)carbamoyloxy](trimethylsilyl)methyl}boronate (10 and 11)

A solution of (*R*,*R*)-**4a** (0.356 g, 1 mmol) in anhyd THF (10 mL) under argon was cooled at –78 °C. *s*-BuLi (1.54 mL, 2 mmol, 1.3 M solution in cyclohexane) was added dropwise. After stirring for 15 min, isopropanol pinacol boric acid ester (0.465 g, 2.5 mmol) dissolved in anhyd THF (5 mL) was added within 10 min. The reaction mixture was allowed to warm up to –40 °C within 3 h and then a sat. aq solution of NH_4Cl (25 mL) and hexane (30 mL) were added. The organic phase was separated and the aqueous one was extracted with hexane (2 × 15 mL). The combined organic layers were washed with HCl (5 mL, 1 M), H_2O (5 mL) and a sat. aq solution of $NaHCO_3$ (5 mL), dried (Na_2SO_4) and concentrated. The residue was purified by flash chromatography (hexane–EtOAc, 4:1, (*R*,*R*)-**4a**: R_f 0.59; **11**: R_f 0.43, **10**: R_f 0.36) to give a mixture of **10** and **11** (0.168 g, 35%, **10/11** 1.7:1, by ^1H NMR) which was separated by flash chromatography (hexane–EtOAc, 15:1).

Similarly, a solution of (*R*,*R*)-**4a** (1.067 g, 3 mmol), TMEDA (0.697 g, 0.91 mL, 6 mmol) in anhyd hexane (30 mL) under argon was cooled at –78 °C. *s*-BuLi (4.62 mL, 6 mmol, 1.3 M solution in cyclohexane) was added dropwise. After stirring for 30 min, isopropanol pinacol boric acid ester (1.116 g, 7 mmol) dissolved in anhyd hexane (5 mL) was added within 10 min. Following the above procedure with THF, a mixture of **10** and **11** (1.112 g, 77%, **10/11** 1.5:1, by ^1H NMR) was obtained.

10

Mp 115–116 °C (EtOH–H_2O, 15:1); $[\alpha]_D^{20}$ +81.6 (*c* 0.25, acetone).

IR (Si): 2976, 1678, 1600, 1330, 1248, 1146 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.20–7.00 (m, 10 H, H_{arom}), 5.03 (br s, 2 H, CHN), 3.65 (s, 1 H, BCHSi), 1.66 (d, *J* = 7.0 Hz, 6 H, $NCCH_3$), 1.220 (s, 6 H, CH_3), 1.217 (s, 6 H, CH_3), –0.11 (s, 9 H, $SiMe_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 160.0, 143.6, 129.2, 128.0, 84.2, 56.1, 26.6, 26.2, 20.1, –1.2.

Anal. Calcd for $C_{27}H_{40}BNO_4Si$: C, 67.35; H, 8.37; N, 2.91. Found: C, 67.17; H, 8.29; N, 3.11.

11

Crystalline solid which could not be crystallised from any solvent as it is too soluble; mp 85–87 °C; $[\alpha]_D^{20}$ +74.6 (*c* 0.94, acetone).

IR (Si): 2975, 2928, 1681, 1625, 1429, 1354, 1341, 1330, 1250, 1249, 1146 cm^{-1}.

^1H NMR (400.13 MHz, $CDCl_3$): δ = 7.40–6.90 (m, 10 H, H_{arom}), 5.02 (br s, 2 H, CHN), 3.71 (s, 1 H, BCHSi), 1.68 (d, *J* = 7.1 Hz, 6 H, $NCCH_3$), 1.24 (s, 6 H, CH_3), 1.21 (s, 6 H, CH_3), –0.08 (s, 9 H, $SiCH_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 159.6, 143.8, 129.2, 129.2, 128.0, 84.4, 56.0, 26.4, 26.2, 19.9, 1.3.

Anal. Calcd for $C_{27}H_{40}BNO_4Si$: C, 67.35; H, 8.37; N, 2.91. Found: C, 67.54; H, 8.57; N, 2.95.

(*S*)-Pinanediol {(1*S*)- and (1*R*)-[(*N*,*N*-Diisopropyl-carbamoyl)oxy](trimethylsilyl)methyl}boronate (12a and 13a)

Carbamate **4a** (0.694 g, 3 mmol) was metalated (30 min) in anhyd hexane (15 mL) using *s*-BuLi/TMEDA (6 mmol each), borylated with **8a** (1.67 g, 7 mmol, dissolved in 5 mL of anhyd hexane; 1 h at –78 °C) and worked up (extraction with Et_2O) as described for the preparation of **10/11**. The crude product (**12a/13a**, 1.25:1 by ^1H NMR) was flash-chromatographed (hexane–EtOAc, 10:1, **12a**: R_f 0.31; **13a**: R_f 0.36) to give a mixture of **12a/13a** (1.05 g, 86%) which was separated by flash chromatography (hexane–EtOAc, 20:1).

Similarly, carbamate **4a** (0.231 g, 1 mmol) gave a mixture of **12a/13a** (0.368 g, 90%; **12a/13a** 4:1 in crude product) in anhyd THF (5 mL).

12a

Oil; $[\alpha]_D^{20}$ +4.96 (*c* 2.60, acetone).

IR (Si): 2930, 1684, 1633, 1474, 1368, 1247, 1220, 1156, 1049, 1048 cm^{-1}.

^1H NMR (600.13 MHz, $CDCl_3$): δ = 4.16 (dd, *J* = 8.7, 2.2 Hz, 1 H, 3-H), 4.04 (br s, 1 H, CHN), 3.74 (br s, 1 H, CHN), 3.63 (s, 1 H, BCHSi), 2.29–2.23 (m, 1 H, 4-H_b), 2.09–2.03 (m, 1 H, 7-H_b), 1.93 (t, *J* = 5.9 Hz, 1 H, 1-H), 1.83–1.79 (m, 1 H, 5-H), 1.80 (td, *J* = 13.0,

2.6 Hz, 1 H, H-4$_a$), 1.38 (d, *J* = 10.5 Hz, 1 H, 7-H$_a$), 1.34 (s, 3 H, CH$_3$-10), 1.23 (s, 3 H, CH$_3$-8), 1.21 (d, *J* = 6.8 Hz, 6 H, NCCH$_3$), 1.19 (d, *J* = 6.8 Hz, 6 H, NCCH$_3$), 0.82 (s, 3 H, CH$_3$-9), 0.09 (s, 9 H, SiMe$_3$).

^{13}C NMR (150.90 MHz, CDCl$_3$): δ = 160.8, 83.0, 76.7, 66.9, 52.1, n.d. (NCH), 40.1, 38.1, 36.4, 29.1, 27.3, 26.4, 24.2, 20.7, –2.4.

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 159.8, 86.2, 79.3, 53.8, 48.0, 41.8, 39.6, 37.4, 30.4, 28.6, 27.9, 25.1, 22.3, 22.2, –1.1.

Anal. Calcd for C$_{21}$H$_{40}$BNO$_4$Si: C, 61.60; H, 9.85; N, 3.42. Found: C, 61.32; H, 10.07; N, 3.28.

13a

Oil, $[\alpha]_D^{20}$ +15.14 (*c* 2.45, acetone).

IR (Si): 2929, 1684, 1632, 1474, 1439, 1368, 1341, 1312, 1247, 1221, 1156, 1049, 1031 cm^{-1}.

^{1}H NMR (600.13 MHz, CDCl$_3$): δ = 4.21 (dd, *J* = 8.8, 2.4 Hz, 1 H, 3-H), 3.89 (br s, 2 H, NCH), 3.68 (s, 1 H, BCHSi), 2.29 (dddd, *J* = 14.3, 8.8, 2.7, 2.4 Hz, 1 H, 4-H$_b$), 2.14 (ddd, *J* = 10.7, 6.1, 2.3 Hz, 1 H, 7-H$_b$), 2.00 (dd, *J* = 6.1, 5.8 Hz, 1 H, 1-H), 1.84 (tdd, *J* = 5.8, 2.4, 2.3 Hz, 1 H, 5-H), 1.77 (ddd, *J* = 14.3, 2.4, 2.3 Hz, 1 H, 4-H$_a$), 1.50 (d, *J* = 10.7 Hz, 1 H, 7-H$_a$), 1.30 (s, 3 H, CH$_3$-10), 1.25 (s, 3 H, CH$_3$-8), 1.20 (d, *J* = 6.8 Hz, 6 H, NCCH$_3$), 1.19 (d, *J* = 6.8 Hz, 6 H, NCCH$_3$), 0.82 (s, 3 H, CH$_3$-9), 0.10 (s, 9 H, SiMe$_3$).

^{13}C NMR (150.90 MHz, CDCl$_3$): δ = 158.4, 84.6, 77.1, 62.8, 51.8, n.d. (NCH), 39.9, 38.3, 36.2, 28.9, 27.3, 26.5, 24.2, 20.6, –2.4.

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 159.5, 86.4, 79.2, 53.8, 48.0, 41.7, 39.6, 37.4, 30.2, 28.6, 28.0, 25.1, 22.3, 22.3, –1.0.

Anal. Calcd for C$_{21}$H$_{40}$BNO$_4$Si: C, 61.60; H, 9.85; N, 3.42. Found: C, 61.61; H, 10.06; N, 3.38.

Preparation of 12b/13b and 12c/13c; General Procedure

s-BuLi (1.2 mmol, 0.92 mL of a 1.3 M solution in cyclohexane) was added to a stirred solution of carbamate **4b** (0.356 g, 1 mmol) and TMEDA (0.116 g, 0.15 mL, 1.2 mmol) in anhyd solvent (see Table 1, 4 mL) under argon at –78 °C. After 30 min, borate **8** (see Table 1, 1.3 mmol) dissolved in the same solvent (2 mL) was added dropwise within 10 min (in some experiments a syringe pump was used) and stirring was continued for 1 h. The reaction mixture was diluted with a sat. solution of NH$_4$Cl or NaHCO$_3$ (20 mL) and extracted with Et$_2$O or CH$_2$Cl$_2$ (3 × 20 mL). The combined organic layers were washed with H$_2$O (20 mL), dried (MgSO$_4$ or Na$_2$SO$_4$) and concentrated. The residue was flash-chromatographed (hexane–EtOAc, 10:1) to furnish mixtures of **12b/13b** or **12c/13c** (for yields and ratios see Table 1), which were separated by flash chromatography (hexane–EtOAc, 20:1).

(*S*)-Pinanediol {(1*S*)- and (1*R*)-[(*R*,*R*)-*N*,*N*-Bis(1-phenylethyl)carbamoyloxy](trimethylsilyl)methyl}boronate (12b and 13b)

12b

Oil; TLC (hexane–EtOAc, 10:1): R_f 0.30; $[\alpha]_D^{20}$ +78.39 (*c* 1.80, acetone).

IR (Si): 2931, 1678, 1628, 1433, 1376, 1342, 1313, 1249, 1028 cm^{-1}.

^{1}H NMR (400.13 MHz, CDCl$_3$): δ = 7.23–6.98 (m, 10 H, H$_{arom}$), 5.02 (br s, 2 H, CHN), 4.24 (dd, *J* = 8.7, 1.9 Hz, 1 H, 3-H), 3.74 (s, 1 H, BCHSi), 2.35–2.26 (m, 1 H, 4-H$_b$), 2.19–2.12 (m, 1 H, 7-H$_b$), 2.01 (t, *J* = 5.6 Hz, 1 H, 1-H), 1.90–1.83 (m, 2 H, 4-H$_a$, 5-H), 1.67 (d, *J* = 7.1 Hz, 6 H, CH$_3$CN), 1.48 (d, *J* = 10.6 Hz, 1 H, 7-H$_a$), 1.33 (s, 3 H, CH$_3$), 1.28 (s, 3 H, CH$_3$), 0.84 (s, 3 H, CH$_3$), 0.09 (s, 9 H, SiMe$_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = n.d. (CO), 143.6, 129.2, 129.2, 128.0, 86.7, 79.6, 56.1, 53.8, 41.7, 39.6, 37.2, 30.4, 28.6, 28.0, 25.1, 20.1, –1.1.

Anal. Calcd for C$_{31}$H$_{44}$BNO$_4$Si: C, 69.78; H, 8.31; N, 2.63. Found: C, 69.49; H, 8.14; N, 2.61.

13b

TLC (hexane–EtOAc, 10:1): R_f 0.38; mp 115–117 °C (ethanol); $[\alpha]_D^{20}$ +61.20 (*c* 1.80, acetone).

IR (Si): 2931, 1680, 1428, 1359, 1315, 1249, 1122, 1078, 1029 cm^{-1}.

^{1}H NMR (400.13 MHz, CDCl$_3$): δ = 7.20–7.00 (m, 10 H, H$_{arom}$), 5.00 (br s, 2 H, NCH), 4.25 (dd, *J* = 8.8, 2.4 Hz, 1 H, 3-H), 3.81 (s, 1 H, BCHSi), 2.25 (tdd, *J* = 14.4, 8.8, 2.5 Hz, 1 H, 4-H$_b$), 2.17 (tdd, *J* = 10.9, 5.8, 2.3 Hz, 1 H, 7-H$_b$), 2.01 (t, *J* = 5.8 Hz, 1 H, 1-H), 1.88–1.81 (m, 1 H, 5-H), 1.68 (d, *J* = 7.1 Hz, 6 H, CH$_3$CN), 1.66 (td, *J* = 14.4, 2.4 Hz, 1 H, 4-H$_a$), 1.40 (d, *J* = 10.9 Hz, 1 H, 7-H$_a$), 1.27 (s, 3 H, CH$_3$), 1.267 (s, 3 H, CH$_3$), 0.81 (s, 3 H, CH$_3$), –0.09 (s, 9 H, SiMe$_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 159.3, 143.8, 129.2, 129.2, 128.0, 86.9, 79.5, 56.0, 53.7, 41.7, 39.6, 37.1, 30.2, 28.5, 27.9, 25.1, 19.9, –1.2.

Anal. Calcd for C$_{31}$H$_{44}$BNO$_4$Si: C, 69.78; H, 8.31; N, 2.63. Found: C, 70.27; H, 8.07; N, 2.51.

(*S*)-Pinanediol {(1*S*)- and (1*R*)-[(*S*,*S*)-*N*,*N*-Bis(1-phenylethyl)carbamoyloxy](trimethylsilyl)methyl}boronate (12c and 13c)

12c

Mp 87–88 °C (EtOH/10% H$_2$O); TLC (hexane–EtOAc, 10:1): R_f 0.31; $[\alpha]_D^{20}$ –48.10 (*c* 1.80, acetone).

IR (Si): 2927, 1679, 1429, 1376, 1358, 1314, 1249, 1208, 1028 cm^{-1}.

^{1}H NMR (400.13 MHz, CDCl$_3$): δ = 7.40–6.80 (m, 10 H, H$_{arom}$), 5.02 (br s, 2 H, NCH), 4.20 (dd, *J* = 8.7, 2.0 Hz, 1 H, 3-H), 3.79 (s, 1 H, BCHSi), 2.29 (dddd, *J* = 15.2, 8.7, 3.2, 2.1 Hz, 1 H, 4-H$_b$), 2.06 (tdd, *J* = 10.6, 5.8, 2.0 Hz, 1 H, 7-H$_b$), 1.96 (t, *J* = 5.8 Hz, 1 H, 1-H), 1.88–1.81 (m, 2 H, 4-H$_a$, 5-H), 1.68 (d, *J* = 7.1 Hz, 6 H, CH$_3$CN), 1.37 (s, 3 H, CH$_3$), 1.31 (d, *J* = 10.6 Hz, 1 H, 7-H$_a$), 1.26 (s, 3 H, CH$_3$), 0.82 (s, 3 H, CH$_3$), –0.07 (s, 9 H, SiMe$_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = 159.5, 143.8, 129.2, 129.1, 128.0, 86.8, 79.6, 56.0, 53.6, 41.6, 39.5, 37.2, 30.3, 28.5, 27.9, 25.0, 20.0, –1.2.

Anal. Calcd for C$_{31}$H$_{44}$BNO$_4$Si: C, 69.78; H, 8.31; N, 2.63. Found: C, 69.86; H, 8.03; N, 2.59.

13c

Oil, TLC (hexane–EtOAc, 10:1): R_f 0.27; $[\alpha]_D^{20}$ –70.64 (*c* 2.35, acetone).

IR (Si): 2930, 1677, 1433, 1376, 1358, 1340, 1314, 1249, 1208, 1029 cm^{-1}.

^{1}H NMR (400.13 MHz, CDCl$_3$): δ = 7.20–7.10 (m, 10 H, H$_{arom}$), 5.03 (br s, 2 H, CHN), 4.28 (dd, *J* = 8.8, 2.5 Hz, 1 H, 3-H), 3.74 (s, 1 H, BCHSi), 2.34 (tdd, *J* = 14.2, 8.8, 2.3 Hz, 1 H, 4-H$_b$), 2.18 (tdd, *J* = 10.6, 5.8. 2.0 Hz, 1 H, 7-H$_b$), 2.03 (t, *J* = 5.8 Hz, 1 H, 1-H), 1.91–1.86 (m, 1 H, 5-H), 1.83 (td, *J* = 14.2, 2.5 Hz, 1 H, 4-H$_a$), 1.66 (d, *J* = 7.1 Hz, 6 H, NCCH$_3$), 1.45 (d, *J* = 10.6 Hz, 1 H, 7-H$_a$), 1.37 (s, 3 H, CH$_3$), 1.28 (s, 3 H, CH$_3$), 0.83 (s, 3 H, CH$_3$), –0.08 (s, 9 H, SiMe$_3$).

^{13}C NMR (100.61 MHz, toluene-d_8, 360 K): δ = n.d. (CO), 143.6, 129.2, 129.2, 128.0, 86.7, 79.6, 56.1, 53.8, 41.7, 39.6, 37.2, 30.4, 28.6, 28.0, 25.1, 20.1, –1.1.

Anal. Calcd for $C_{31}H_{44}BNO_4Si$: C, 69.78; H, 8.31; N, 2.63. Found: C, 69.68; H, 8.37; N, 2.56.

X-ray Crystal Data[23] of Boronates 10, 12c and 13b

10

Formula $C_{27}H_{40}BNO_4Si$; space group $P2_1$; a = 12.559(2), b = 6.526(3), c = 17.214(3) Å; β = 101.59(1)°; V = 1382.1(4) Å^3; Z = 2; ρ_{calcd} = 1.16 cm^{-3}; μ(MoKα) = 1.2 cm^{-1}; crystal size: 0.17 × 0.20 × 0.40 mm^3. Single crystal data collection and refinement: Unique data set: 6598; F_o>4σ (F_o) = 5845; variables: 468; extinction coefficient: 0.020(2); flack × parameter: –0.06(10). $R1$ [for F_o>4σ(F_o)] [$R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$] = 0.038; $wR2$ [for all F_o^2] {$wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{1/2}$} = 0.098; $\rho_{min/max}$ = 0.21/–0.15 eÅ^{-3}.

12c

Formula $C_{31}H_{44}BNO_4Si$; space group $P2_12_12_1$; a = 6.614(1), b = 9.610(1), c = 48.711(10) Å; V = 3096.1(9) Å^3, Z = 4; ρ_{calcd} = 1.15 cm^{-3}; μ(MoKα) = 1.1 cm^{-1}; crystal size: 0.14 × 0.28 × 0.36 mm^3. Single crystal data collection and refinement: Unique data set: 7467; F_o>4σ (F_o) = 5225; variables: 520; extinction coefficient: 0.006(1); flack × parameter: –0.12(11). $R1$ [for F_o>4σ(F_o)] [$R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$] = 0.043; $wR2$ [for all F_o^2] {$wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{1/2}$} = 0.096; $\rho_{min/max}$ = 0.18/–0.17eÅ^{-3}.

13b

Formula $C_{31}H_{44}BNO_4Si$; space group $P2_12_12_1$; a = 6.182(1), b = 12.543(2), c = 39.209(6) Å; V = 3040.3(8) Å^3; Z = 4; ρ_{calcd} = 1.17 cm^{-3}; μ(MoKα) = 1.1 cm^{-1}; crystal size: 0.14 × 0.34 × 0.70 mm^3. Single crystal data collection and refinement: Unique data set: 7320; F_o>4σ (F_o) = 5992; variables: 520; extinction coefficient: 0.003(1); flack × parameter: –0.01(8). $R1$ [for F_o>4σ(F_o)] [$R1 = \Sigma||F_o|-|F_c||/\Sigma|F_o|$] = 0.035; $wR2$ [for all F_o^2] {$wR2 = [\Sigma w(F_o^2-F_c^2)^2/\Sigma wF_o^4]^{1/2}$}: 0.079; $\rho_{min/max}$ = 0.15/–0.14 eÅ^{-3}.

Acknowledgment

We thank the Fonds zur Förderung der wissenschaftlichen Forschung (Project No. P14985-N03) for financial support and S. Felsinger and C. Tyl for recording the NMR spectra.

References

(1) Part 3: Hammerschmidt, F.; Hanninger, A.; Peric Simov, B.; Völlenkle, H.; Werner, A. *Eur. J. Org. Chem.* **1999**, 3511.
(2) (a) Köster, R. In *Houben-Weyl Methods of Organic Chemistry*, 4th ed., Vol. 13, 3a; Köster, R., Ed.; Thieme: Stuttgart, **1982**, 616. (b) Matteson, D. S. *Tetrahedron* **1989**, *45*, 1859.
(3) (a) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.
(4) (a) Roush, W. R. In *Houben-Weyl Methods of Organic Chemistry*, 4th ed., Vol. E 21b; Helmchen, G.; Hoffmann, R. W.; Mulzer, J.; Schaumann, E., Eds.; Thieme: Stuttgart, **1995**, 1410. (b) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 555.
(5) Matteson, D. S. *Tetrahedron* **1998**, *54*, 10555.
(6) Cain, Ch. M.; Cousins, R. P. C.; Coumbarides, G.; Simpkins, N. S. *Tetrahedron* **1990**, *46*, 523.
(7) Ambasht, S.; Chiu, S. K.; Peterson, P. E.; Queen, J. *Synthesis* **1980**, 318.
(8) Carstens, A.; Hoppe, D. *Tetrahedron* **1994**, *50*, 6097.
(9) Andersen, M. W.; Hildebrandt, B.; Köster, G.; Hoffmann, R. W. *Chem. Ber.* **1989**, *122*, 1777.
(10) Matteson, D. S.; Man, H.-W. *J. Org. Chem.* **1996**, *61*, 6047.
(11) As the nomenclature of boronates is complex, the practical system of Matteson et al. is adopted: Matteson, D. S.; Kandil, A. A.; Soundararajan, R. *J. Am. Chem. Soc.* **1990**, *112*, 3964.
(12) Basu, A.; Thayumanavan, S. *Angew. Chem. Int. Ed.* **2002**, *41*, 716.
(13) Hoppe, D.; Hense, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2282.
(14) Hoppe, D.; Paetow, M.; Hintze, F. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 394.
(15) (a) Horeau, A.; Kagan, H.-B.; Vigneron, J.-P. *Bull. Soc. Chim. Fr.* **1968**, 3795. (b) Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(16) Lee, S.-G. *Magn. Reson. Chem.* **2002**, *40*, 311.
(17) Matteson, D. S.; Sadhu, K. M.; Peterson, M. L. *J. Am. Chem. Soc.* **1986**, *108*, 810.
(18) Wrackmeyer, B.; Köster, R. In *Houben-Weyl Methods of Organic Chemistry*, 4th ed., Vol. 13, 3c; Köster, R., Ed.; Thieme: Stuttgart, **1984**, 377.
(19) Mikenda, W. *Vib. Spectrosc.* **1992**, *3*, 327.
(20) DENZO-SMN program package, Nonius B. V., The Netherlands.
(21) Sheldrick, G. M. *SHELXS-97, A program for the solution of crystal structures*; Universität Göttingen: Germany, **1997**.
(22) Sheldrick, G. M. *SHELXS-97, A program for crystal structure refinement*; Universität Göttingen: Germany, **1997**.
(23) The structural data of compounds **10**, **12c** and **13b** have been deposited at the Cambridge Crystallographic Data Centre under the reference numbers CCDC 239224, 239226, 239225, respectively. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44 (1223)336033; e-mail: deposit@ccdc.cam.ac.uk].