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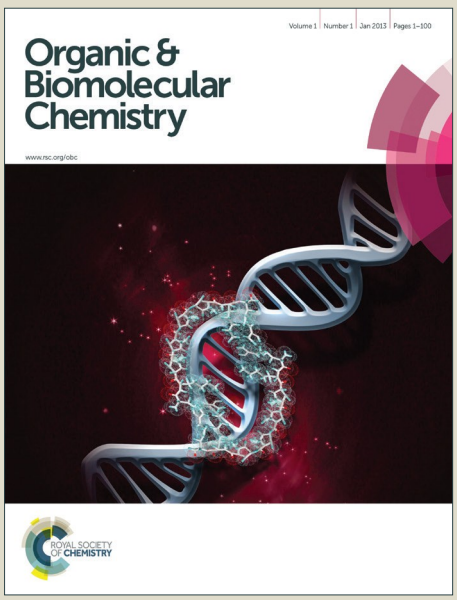





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# Enantioselective synthesis of $\alpha$-phenyl- and $\alpha$-(dimethylphenylsilyl)alkylboronic esters by ligand mediated stereoinductive reagent-controlled homologation using configurationally labile carbenoids

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Chain extension of boronic esters by the action of configurationally labile racemic lithium carbenoids in the presence of scalemic bisoxazoline ligands was explored for the enantioselective synthesis of the two title product classes. Enantioenriched 2° carbinols generated by oxidative work-up (NaOOH) of initial $\alpha$-phenylalkylboronate products were obtained in 35-83% yield and 70-96% ee by reaction of *B*-alkyl and *B*-aryl neopentyl glycol boronates with a combination of *O*-($\alpha$-lithiobenzyl)-*N*,*N*-diisopropylcarbamate and ligand 3,3-bis[(4*S*)-4,5-dihydro-4-isopropyloxazol-2-yl)pentane in toluene solvent (–78 °C to rt) with $MgBr_2$•$OEt_2$ additive. Enantioenriched $\alpha$-(dimethylsilylphenylsilyl)alkylboronates were obtained in 35-69% yield and 9-57% ee by reaction of *B*-alkyl pinacol boronates with a combination of lithio(dimethylphenylsilyl)methyl 2,4,6-triisopropylbenzoate and ligand 2,2-bis[(4*S*)-4,5-dihydro-4-isopropyloxazol-2-yl)propane in cumene solvent (–45°C to –95°C to rt). The stereochemical outcome of the second type of reaction depended on the temperature history of the organolithium•ligand complex indicating that the stereoinduction mechanism in this case involves some aspect of dynamic thermodynamic resolution.

## Introduction

The asymmetric chain extension of boronic esters provides a versatile and systematic approach to organic synthesis that complements more traditional methods for carbon-carbon bond formation.[1] Among the strategies that are conceivable for the stereoselective homologation of boronates,[2] only two have risen to prominence: the stereoinductive substrate-controlled process of Matteson et al.[3] and stereospecific reagent-controlled homologation (StReCH).[4] The first process leads to stereoregular arrays upon direct iteration while StReCH offers true stereochemical programming because the chain elongated adduct (**4**) arises via rearrangement of an intermediate ate-complex (**3**) formed via stereospecific trapping of a stereodefined carbenoid reagent (**2**) by a boronate substrate (**1**) (Figure 1). StReCH is a powerful technique but limited in scope to those carbenoid species that can be accessed in an enantioenriched form and which exhibit configurational stability on the time-scale of ate-complex formation. Carbenoids that have been successfully used in StReCH include $\alpha$-chloroalkyllithiums (generated by sulfoxide-lithium exchange),[5] and lithiated carbamates (typically generated by kinetic enantioselective lithiation),[6] among others.[7]

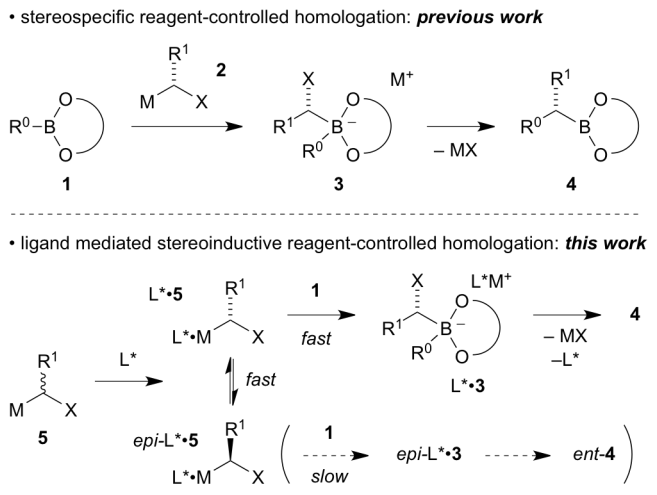



**Figure 1** Stereospecific reagent-controlled homologation (StReCH) of a boronic ester **1** requires a stereodefined, configurationally stable carbenoid **2** while ligand mediated stereoinductive reagent-controlled homologation (i-StReCH) relies on dynamic kinetic resolution (DKR, as illustrated above) or dynamic thermodynamic resolution (DTR, not illustrated above) of a configurationally labile racemic carbenoid **5** in the presence of a chiral ligand (L*); M = electrofugal substituent, X = nucleofugal substituent.

To broaden the scope of asymmetric chain extension, and taking our inspiration from the seminal work of Beak,[8] Hoppe,[9] and Toru,[10] a subtle but significant variation on the 'lithiation/borylation' StReCH strategy of Aggarwal and coworkers[6h] was envisioned involving chiral ligand mediated dynamic kinetic (or thermodynamic) resolution of a configurationally labile racemic carbenoid **5** (Figure 1). In this type of stereoinductive reagent-controlled homologation (i-StReCH) process, substituents $R^1$ may be introduced that would be prohibited in normal StReCH due to configurational instability issues; furthermore, since carbenoid generation is decoupled from the stereodetermining event, various lithiation tactics will be compatible with the technique (e.g., deprotonation, metal exchange phenomena, reductive lithiation etc.). Here we report successful realization of ligand mediated i-StReCH using two types of configurationally labile carbenoid, one a benzyllithium and the other an $\alpha$-silylmethyllithium, and so achieve the enantioselective synthesis of $\alpha$-phenyl- and $\alpha$-(dimethylphenylsilyl)alkylboronates.[11] During the course of our studies, Crudden and coworkers disclosed essentially identical independent results for the same benzylic carbenoid as applied to the i-StReCH of arylboronates (2014)[12] and, in an isolated example, a vinylboronate (late 2013).[13]

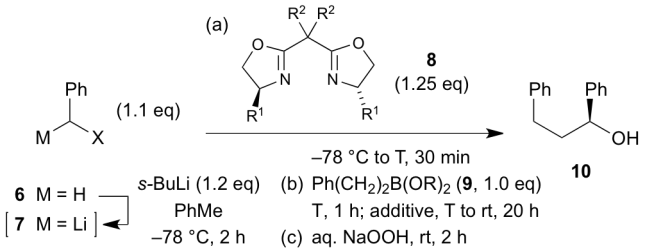
## Results and discussion

### Studies with benzyllithium based carbenoids: enantioselective synthesis of $\alpha$-phenylalkylboronates

Racemization of benzylic organolithiums **5** ($R^1$ = aryl, M = Li, X = heteroatom) is generally facile[9] making these species ideal candidates for the exploration of i-StReCH. Of note, Toru et al. reported highly enantioselective trapping of configurationally labile $\alpha$-phenyl-$\alpha$-(thioaryl)methyllithiums with simple probe electrophiles in the presence of scalemic bisoxazoline ligands (in PhMe or cumene, ≤–50 °C),[10] while Hoppe et al. achieved comparable results by applying similar reaction conditions to the lithiate of *O*-benzyl *N,N*-diisopropyl carbamate.[9] On the basis of this precedent, enantioselective synthesis of an $\alpha$-phenylalkylboronate from *B*-phenethylboronates **9** via chiral ligand mediated i-StReCH was evaluated using benzylic carbenoids generated from four potentially suitable precursors **6** (X = SPh, S-2-Py, OCb, and OTIB) under Toru/Hoppe reaction conditions (Table 1). The chain extended adduct was isolated as its carbinol derivative **10** following oxidative work-up with aq. NaOOH.

Carbenoids **7** possessing thiolate nucleofuges (X = SPh, S-2Py) were evaluated first; however, although these benzyllithiums could be generated efficiently from precursors **6** using either *t*-BuLi or *n*-BuLi (as established by quenching **7** with $CD_3OD$), they proved incapable of chain extending $BnCH_2Bpin$ either by thermolysis of the putative ate-complex or (as illustrated) by activation with a thiophile (Entries 1 and 2). The difficulty of homologating boronic esters with $\alpha$-(thioaryl)alkyllithiums has been previously documented,[14] although it is interesting to note that such reactions can be

**Table 1** Exploration of bisoxazoline (**8**) mediated stereoinductive reagent-controlled homologation of phenethylboronates **9** using four types of benzylic lithium carbenoids **7** (X = SPh, S-2Py, OCb, OTIB).




| Entry | X | $R^1/R^2$ | $B(OR)_2$ | T (°C) | Add. | Yield (%) | %Ee |
|---|---|---|---|---|---|---|---|
| 1[a] | SPh | *i*-Pr/Me | Bpin | –78 | $HgCl_2$ | 0 | na |
| 2[b] | S-2Py | *i*-Pr/Me | Bpin | –78 | $HgCl_2$ | 0 | na |
| 3 | OCb | *i*-Pr/Me | Bpin | –78 | none | 44 | 15 |
| 4 | OCb | *i*-Pr/Et | Bpin | –78 | none | 43 | 45 |
| 5 | OCb | *i*-Pr/Et | Bpin | –40 | none | 67 | 39 |
| 6 | OCb | *t*-Bu/Et | Bpin | –40 | none | 68 | –17 |
| 7[a] | OTIB | *i*-Pr/Et | Bpin | –78 | none | 74 | 33 |
| 8 | OCb | *i*-Pr/Et | Bneo | –78 | none | 54 | 74 |
| **9** | **OCb** | ***i*-Pr/Et** | **Bneo** | **–78** | **$MgBr_2$[d]** | **61** | **83** |
| 10[c] | OCb | *i*-Pr/Et | Bneo | –78 | $MgBr_2$[d] | 66 | 81 |

[a] Lithiation conducted with *t*-BuLi. [b] Lithiation conducted with *n*-BuLi. [c] $Et_2O$ as solvent (reaction conditions duplicated from Crudden et al. ref. 12). [d] $MgBr_2$•$OEt_2$ (3 eq) in $Et_2O$. 2Py = 2-pyridyl; Cb = *i*-$Pr_2NC(=O)$; TIB = 2,4,6-*i*-$Pr_3C_6H_2C(=O)$; Bpin = $B[O(CMe_2)_2O]$; Bneo = $B[OCH_2CMe_2CH_2O]$.

successfully accomplished with $\alpha$-alkoxy-$\alpha$-(thioaryl)-alkyllithiums (e.g., PhSCH(Li)OMe).[14b,15] Carbenoids **7** bearing carboxylate-type nucleofuges (X = OCb, OTIB) were studied next (Entries 3-10). Given the widespread use of lithiated carbamates[6] and TIB esters[7de] in conventional StReCH reactions, the fact that chain extension occurred with these benzyllithiums was not at all surprising; however, it was gratifying to realize meaningful enantioselectivity via i-StReCH upon evaluation of only a handful of standard bisoxazolines **8**. The ligand previously identified as optimal for asymmetric trapping of **7** (X = OCb) with electrophiles by Hoppe and coworkers (**8**, $R^1/R^2$ = *i*-Pr/Et),[9a] proved to be superior (cf. Entries 3, 4, and 6). The sense of stereoinduction was curiously dependent on the steric demand of the $R^1$ bisoxazoline substituent (Entry 5 vs. 6), and the lithiated carbamate **7** (X = OCb) offered higher enantioselectivity than the lithiated ester **7** (X = OTIB) (Entry 4 vs. 7). A signficant boost in %ee was realized by using a neopentyl glycol boronic ester starting material ($BnCH_2Bneo$) in place of the less reactive pinacol boronate employed earlier, and an additional gain in efficacy was obtained by using a Lewis acid additive ($MgBr_2$•$OEt_2$) to promote ate-complex rearrangement (cf. Entries 4, 8, and 9). We have previously taken advantage of both of these last two variable changes to optimize conventional StReCH reactions,[5a] and in their independent efforts, Crudden et al. likewise found that employment of neopentyl glycol boronates is essential for

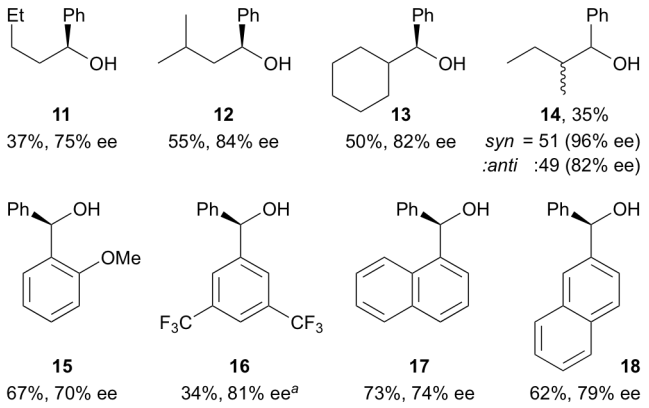
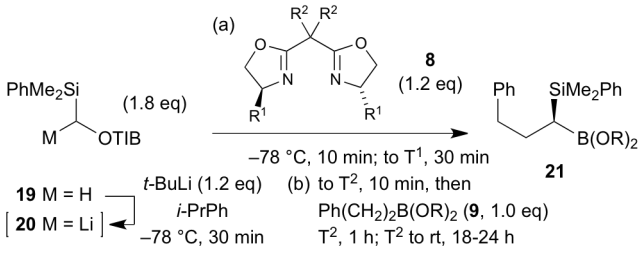



**Figure 2** Enantioenriched 2° alcohols RPhCHOH obtained by BOX ligand mediated i-StReCH of boronates RBneo by **7** (X = OCb) using reaction conditions as in Table 1, Entry 9. Chain extended adducts RCHPhBneo were oxidized to the illustrated carbinols **11**-**18** with aq. NaOOH prior to isolation and yield/%ee determination. Where indicated, absolute configuration determined by correlation to literature data. [a] Reaction mixture heated to 40°C for 16 h following addition of $MgBr_2 \bullet OEt_2$.

**Table 2** Exploration of bisoxazoline (**8**) mediated stereoinductive reagent-controlled homologation of phenethylboronates **9** using $\alpha$-lithio (dimethylphenylsilyl)methyl 2,4,6-triisopropylbenzoate **20**.




| Entry | $R^1/R^2$ | $B(OR)_2$ | $T^1$ (°C) | $T^2$ (°C) | Yield (%) | %Ee[a] |
|---|---|---|---|---|---|---|
| 1[b] | Ph/Me | Bpin | –78 | –78 | 0 | na |
| 2 | *t*-Bu/Me | Bpin | –78 | –78 | 92 | 14 |
| 3 | *i*-Pr/Me | Bpin | –78 | –78 | 78 | 21 |
| 4 | *i*-Pr/Me | Bpin | –95 | –95 | 75 | 41 |
| 5 | *i*-Pr/Me | Bpin | –45 | –45 | 68 | 23 |
| **6** | ***i*-Pr/Me** | **Bpin** | **–45** | **–95** | **69** | **57** |
| 7 | *i*-Pr/Et | Bpin | –45 | –95 | 66 | –47 |
| 8 | *i*-Pr/Me | Bneo | –45 | –95 | 58 | 54 |
| 9 | *i*-Pr/Et | Bneo | –45 | –95 | 13 | –42 |

[a] %Ee determined by CSP-HPLC analysis of the carbinol generated by aq. NaOOH oxidation of the boronate. [b] *s*-BuLi added to mixture of ester **19** and ligand **8**. TIB = 2,4,6-*i*-$Pr_3C_6H_2C(=O)$; Bpin = $B[O(CMe_2)_2O]$; Bneo = $B[OCH_2CMe_2CH_2O]$.

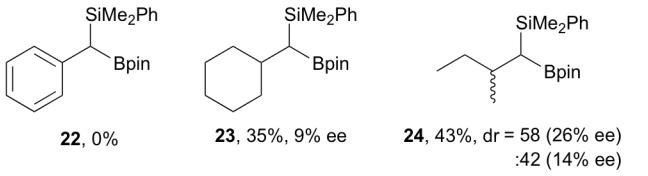
the obtainment of high ee when using benzylic carbenoid **7** (X = OCb).[12,13] Direct comparison of the near identical Crudden protocol (conducted in $Et_2O$ solvent and also using $MgBr_2$)[12] to our own (in PhMe sovent) revealed no significant difference for the homologation of a *B*-phenethyl substrate (Entry 9 vs. 10).

To evaluate scope, the optimized i-StReCH protocol (as in Table 1, Entry 9) was applied to a range of *B*-alkyl and *B*-aryl neopentyl glycol boronic esters and the homologated adducts were isolated as their carbinol derivatives following work-up with aq. NaOOH (Figure 2). Moderate yields of the expected alkyl/aryl 2° alcohols **11-14** were obtained from *B*-alkyl boronates possessing varying degrees of chain branching. Good enantioselectivity was observed throughout and both 1° and 2° *B*-alkyl boronates were successfully chain extended. Pleasingly, when (±)-*s*-BuBneo was used as substrate, the product (**14**) was obtained in low dr but with at least the usual level of ee for each diastereoisomer (n.b., a dr of 50:50 is the *desired* outcome from this experiment). This result is noteworthy because it reveals that preexisting stereochemistry in the substrate (albeit for a stereocenter bearing geminal Me & Et groups) did not influence stereoselectivity; i.e., reagent-control dominated and matching/mismatching effects are potentially of limited importance. The synthesis of diaryl 2° carbinols **15-18** from *B*-aryl boronates was consistent with the recently published findings of Crudden et al.[12] Gentle heating was required to obtain a reasonable yield of carbinol **16** from the corresponding boronic ester possessing an electron deficient 3,5-bis(trifluoromethyl)phenyl substituent.

### Studies with $\alpha$-silylmethyllithium based carbenoids: enantioselective synthesis of $\alpha$-silylalkylboronates

In common with most benzyllithiums, $\alpha$-silylmethyllithiums **5** ($R^1$ = $SiR_3$, M = Li, X = $OCb/O_2CR$) are configurationally labile and so their use in conventional StReCH is precluded. For example, Aggarwal et al. observed the formation of a racemic chain-extended boronate when the carbenoid generated by enantioselective lithiation of $TMSCH_2OCb$ with (–)-sparteine/*s*-BuLi was used as an homologation agent (at –78 °C).[16] A related silylmethyllithium ($PhMe_2SiCHLiO_2CTr$) was found to rapidly enantiomerize at –95 °C.[17] Given that low configurational stability is desired in ligand mediated i-StReCH, and considering that the direct introduction of heteroatom-bearing stereogenic centers via reagent-controlled homologation is a largely unsolved problem,[15,18] we elected to investigate boronic ester chain extension using the organolithium derived from silylmethyl benzoate **19** (Table 2). Ester **19** was obtained from methyl 2,4,6-triisopropylbenzoate (MeOTIB) by lithiation[19] followed by silylation (see ESI).

Evaluated reaction conditions paralleled those pioneered by Toru et al. for their work with lithiated benzylic thioethers,[10] and we found that carbenoid **20** (generated in racemic form from **19** by addition of *t*-BuLi at –78 °C) combined with ligand **8** ($R^1/R^2$ = *i*-Pr/Me) in cumene solvent gave the best results for the enantioselective generation of $\alpha$-silylalkylboronate **21** from *B*-phenethyl boronic ester precursors **9**. An alternate BOX ligand **8** with $R^1$ = Ph decomposed in the presence of *s*-BuLi (presumably via a ring-opening $\beta$-elimination pathway), while a bulky ligand **8** with $R^1$ = *t*-Bu gave the product **21** in superior yield but with low enantiomeric purity (Entries 1 and 2 vs. Entry 3). The effect of varying the temperature profile of the reaction was investigated using the initial ligand of choice (Entries 3-6). The operation of a purely DKR mechanism is revealed if product ee is independent of conversion and




**22**, 0% **23**, 35%, 9% ee **24**, 43%, dr = 58 (26% ee) :42 (14% ee)

**Figure 3** Enantioenriched $\alpha$-silylalkylboronates R($Me_2PhSi$)CHBpin obtained by BOX ligand mediated i-StReCH of boronates RBpin by **20** using reaction conditions as in Table 2, Entry 6. %Ee determined by CSP-HPLC analysis of the derived carbinols generated by aq. NaOOH oxidation of the illustrated boronates. Bpin = B[O($CMe_2$)$_2$O].

dependent on the temperature at which the electrophile is introduced ($T^2$) but not on the temperature history profile of the organolithium-ligand complex **20•8**.[8b] Sensitivity of product ee to conversion and to the temperature history profile (–78 °C to $T^1$ to $T^2$) of complex **20•8** indicates that DTR factors into the stereodetermining mechanism.[8b,10] In the event, for four reactions at comparable conversion, it was found that isothermal incubation of **20•8** at –95°C (following its generation at –78 °C) prior to the introduction of the boronate electophile gave a higher level of product ee than related reactions held at either –78 °C or –45°C (Entry 4 vs. Entries 3 and 5); however, initial warming of **20•8** to –45°C and an aging period of 30 minutes before cooling to –95 °C and then addition of the electrophile gave a better result still (Entry 6). Taken in sum, these data indicate that the origin of enantioselectivity cannot be solely DKR, nor solely a simple resolution, but that dynamic thermodynamic equilibration of diastereomeric organolithium-ligand complexes factors into the process in combination with kinetic effects influencing stereodetermination at the point of electrophile addition. Applying the optimal temperature history profile to the gem diethyl BOX ligand **8** ($R^1/R^2$ = *i*-Pr/Et) gave an inferior result to **8** ($R^1/R^2$ = *i*-Pr /Me), but interestingly the more elaborate ligand favored the opposite enantiomer of **21** (Entry 6 vs. Entry 7). Evaluation of a neopentyl glycol boronic ester substrate likewise did not result in a better outcome, but again gem dimethyl and gem diethyl type BOX ligands each favored a different major enantiomer of the chain-extension product (Entry 8 vs. Entry 9). The potential scope of the $\alpha$-silylalkylboronate synthesis was briefly examined by application of the optimized reaction conditions to three additional boronic ester substrates (Figure 3). An attempt to prepare $\alpha$-silylboronate **22** from *B*-phenyl pinnacol boronate failed but chain extension of two 2° alkyl pinacol boronates was successful, albeit with modest efficiency. Thus, *B*-cyclohexyl pinacol boronate afforded the sterically congested homologation adduct **23** in 35% yield and 9% ee, while racemic *B*-*sec*-butyl pinacol boronate gave as expected a pair of diastereomeric products **24** each in enantioenriched form. In this case, the preexisting stereocenter within the substrate had a bearing on stereochemical outcome since the diastereomers of **24** were not generated in equal quantity (cf. **14** above).

## Conclusions

In summary, it has been established that the enantioselective chain extension of various types of boronic esters can be effected with configurationally labile carbenoid species by employing the principle of ligand mediated stereoinductive reagent-controlled homologation (i-StReCH). This technique is potentially very versatile because it obviates the more stringent demands of conventional StReCH which requires both a configurationally stable carbenoid and a means to access it in an highly enantioenriched form. The method was successfully demonstrated for the synthesis of $\alpha$-phenylalkylboronates and $\alpha$-silylalkylboronates but the generation of other types of products previously inaccessible via reagent-controlled homologation is readily envisioned. Installation of heteroatom-bearing stereocenters is of particular value and in this regard the ability to control the configuration of a dimethylphenylsilyl substituted carbon atom within a growing chain is significant because this silane moiety is a surrogate for an oxygen atom via the Fleming oxidation.[20] Efforts to improve on the efficiency of ligand mediated i-StReCH and to widen its scope to encompass carbenoids bearing yet other types of useful substituents, including further heteroatoms, are in progress and will be reported in due course.

## Experimental section

All reactions requiring anhydrous/anaerobic conditions were conducted in flame-dried glassware under an atmosphere of Ar gas. Anhydrous THF and toluene were dispensed from a commercially available solvent purification system employing activated $Al_2O_3$ drying columns.[21] Anhydrous cumene (*i*-PrPh) was obtained by distillation from $CaH_2$ under Ar. Preparative chromatographic separations were performed on silica gel 60 (35-75 $\mu$m) and reactions followed by TLC analysis using silica gel 60 plates (2-25 $\mu$m) with fluorescent indicator (254 nm) and visualized with UV or phosphomolybdic acid. Commercially available reagents were used as received. Melting points were determined from open capillary tubes on a melting point apparatus and are uncorrected. Infra-red (IR) spectra were recorded in Fourier transform mode using KBr disks for solids, while oils were supported between NaCl plates ("neat"). $^1$H and $^{13}$C NMR spectra were recorded in Fourier transform mode at the field strength specified and from the indicated deuterated solvents in standard 5 mm diameter tubes. Chemical shift in ppm is quoted relative to residual solvent signals calibrated as follows: $CDCl_3$ $\delta_H$ ($CHCl_3$) = 7.26 ppm, $\delta_C$ = 77.2 ppm. Multiplicities in the $^1$H NMR spectra are described as: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Numbers in parentheses following carbon atom chemical shifts refer to the number of attached hydrogen atoms as revealed by the DEPT spectral editing technique. Low (MS) and high resolution (HRMS) mass spectra were obtained using either electron impact (EI) or electrospray (ES) ionization techniques. Ion mass/charge (*m/z*) ratios are reported as values in atomic mass units.



**Representative procedure for ligand mediated i-StReCH to α-phenylalkylboronates (Table 1, Entry 9)**

**(–)-(*S*)-1,3-Diphenyl-propan-1-ol (10).** A stirred solution of *O*-benzyl-*N,N*-diisopropylcarbamate (**6**, X = OCb, 26 mg, 0.110 mmol)[22] and (*S,S*)-bisoxazoline ligand **8** ($R^1/R^2$ = *i*-Pr/Et, 37 mg, 0.126 mmol)[23] in anhydrous toluene (0.8 mL) at –78 °C under Ar was treated with *s*-BuLi (0.10 mL, 1.20 M in cyclohexane, 0.12 mmol). After stirring at –78 °C for 2.5 h, a solution of neopentyl glycol boronate **9** (22 mg, 0.101 mmol) in anhydrous toluene (0.2 mL) was added dropwise during 3 min. The resulting mixture was stirred at –78 °C for 1 h and then a freshly prepared ethereal solution of $MgBr_2$•$OEt_2$ (0.30 mmol in ≤ 1.0 mL $Et_2O$, see ESI for details of preparation) was added dropwise during 3 min. The reaction mixture was allowed to stir for a further 30 min at –78 °C, allowed to warm to rt during 3 h, and then stirred for 16 h at rt. After this time, the reaction mixture was cooled to 0 °C and treated with 10 wt.% aq. NaOH (0.2 mL) followed by 30 wt.% aq. $H_2O_2$ (0.08 mL). The biphasic mixture was then allowed to warm to rt and stirred vigorously for 2 h. EtOAc (5 mL) and $H_2O$ (3 mL) were added and the layers shaken and separated. The aqueous phase was extracted with EtOAc (3x5 mL) and the combined organic phases washed with brine (5 mL), dried ($Na_2SO_4$), and concentrated *in vacuo*. The residue was purified by column chromatography ($SiO_2$, eluting with 6-12% EtOAc in hexanes) to afford (*S*)-**10** (13 mg, 0.061 mmol, 61%, 83% ee) as a colorless oil: $[\alpha]_D^{20}$ = –22.9 (c = 1.30, $CHCl_3$, at 83% ee); IR (neat) 3370, 3027, 2924, 1603, 1495, 1454, 1059, 1029, 914 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.37-7.35 (4H, m), 7.31-7.26 (3H, m), 7.22-7.18 (3H, m), 4.70 (1H, t, *J* = 6.0 Hz), 2.77 (1H, ddd, *J* = 14.0, 9.8, 5.9 Hz), 2.68 (1H, ddd, *J* = 13.9, 9.3, 6.6 Hz), 2.20-1.99 (2H, m), 1.88 (1H, br s) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$) δ = 144.7 (0), 142.0 (0), 128.7 (2C, 1), 128.62 (2C, 1), 128.57 (2C, 1), 127.8 (1), 126.1 (2C, 1), 126.0 (1), 74.1 (1), 40.6 (2), 32.2 (2) ppm. $^1H$ and $^{13}C$ NMR spectral data in agreement with those previously reported.[24] %Ee and absolute configuration determined by chiral stationary phase HPLC analysis following the method previously described by Liu and coworkers (see ESI for details).[24]

**Representative procedure for ligand mediated i-StReCH to α-(dimethylphenylsilyl)alkylboronates (Table 2, Entry 6)**

**(–)-(*S*)-2-[1-(Dimethylphenylsilyl)-3-phenylpropyl]-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (21):** A stirred solution of (dimethylphenylsilyl)methyl 2,4,6-triisopropylbenzoate (**19**, 179 mg, 0.451 mmol) in anhydrous cumene (1.3 mL) at –78 °C under Ar was treated dropwise with *t*-BuLi (0.190 mL, 1.57 M in pentane, 0.298 mmol) and allowed to stir for 30 min. The reaction mixture was then treated with (*S,S*)-bisoxazoline ligand **8** ($R^1/R^2$ = *i*-Pr/Me, 80 mg, 0.300 mmol)[25] in anhydrous cumene (0.40 mL) and the mixture incubated for 10 min at –78 °C. After this time, the reaction vessel was transferred to another cold bath held at –45 °C, stirred for 30 min, then transferred to a third cold bath held at –95 °C and stirred for an additional 10 min. A solution of *B*-phenethyl pinacol boronate **9** (58.0 mg, 0.250 mmol) in anhydrous cumene (0.40 mL) was then added dropwise during 3 min and the mixture allowed to stir for a further 1 h at –95 °C before the cold bath was removed and the vessel allowed to warm to rt during 24 h. Sat. aq. $NH_4Cl$ (4.0 mL) was added and the mixture partitioned between EtOAc (15 mL) and $H_2O$ (6 mL). The layers were separated and the aqueous phase was extracted with EtOAc (2x7 mL). The combined organic phases were washed with brine (2 mL), dried ($Na_2SO_4$), and concentrated *in vacuo*. The residue (396 mg) was purfied by column chromatography ($SiO_2$, eluting with 0-5% $Et_2O$ in hexanes) to afford (*S*)-**21** (65.8 mg, 0.173 mmol, 69%, 57% ee) as a colorless oil: $[\alpha]_D^{20}$ = –11.8 (c = 1.00, $CHCl_3$, at 57% ee) [lit.[16] for (*R*)-**21** $[\alpha]_D^{20}$ = +24 (c = 1.0, $CHCl_3$ at %ee ≥ 94%]; IR (neat) 2977, 1353, 1308, 1249, 1145, 1112, 995, 847, 815 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.52-7.48 (2H, m), 7.35-7.32 (3H, m), 7.28-7.25 (1H, m), 7.24 (1H, dm, *J* = 7.5 Hz), 7.16 (1H, tt, *J* = 7.4, 2.2 Hz), 7.12 (2H, dm, *J* = 6.9 Hz), 2.71 (1H, ddd, *J* = 13.8, 9.8, 4.9 Hz), 2.47 (1H, ddd, *J* = 13.4, 9.7, 6.8 Hz), 1.90 (1H, dddd, *J* = 13.6, 11.5, 9.8, 5.0), 1.65 (1H, dddd, *J* = 13.0, 9.9, 6.9, 3.1 Hz), 1.24 (6H, s), 1.21 (6H, s), 0.72 (1H, dd, *J* = 12.0, 3.0 Hz), 0.33 (3H, s), 0.31 (3H, s) ppm; $^{13}C$ NMR (100 MHz, $CDCl_3$) δ = 142.8 (0), 139.0 (0), 134.0 (2C, 1), 129.0 (1), 128.7 (2C, 1), 128.4 (2C, 1), 127.8 (2C, 1), 125.8 (1), 83.0 (2C, 0), 39.6 (2), 28.2 (2), 25.4 (2C, 3), 24.9 (2C, 3), 13.8 (1, br RCHBpin), –2.1 (3), –3.2 (3) ppm. $^1H$ and $^{13}C$ NMR spectral data in agreement with those previously reported by Aggarwal and coworkers.[16] %Ee determined by chiral stationary phase HPLC analysis of the derived NaOOH oxidation product (see ESI for details).

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## Notes and references

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† Electronic Supplementary Information (ESI) available: experimental procedures, characterization data, and $^1H$ and $^{13}C$ NMR spectra for all compounds; CSP HPLC chromatograms for %ee determinations. See DOI: 10.1039/b000000x/

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