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Factors Affecting Migration of Tertiary Alkyl Groups in Reactions of Alkylboronic Esters with Bromomethyllithium

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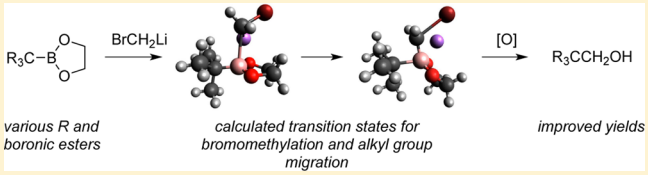
Supporting Information

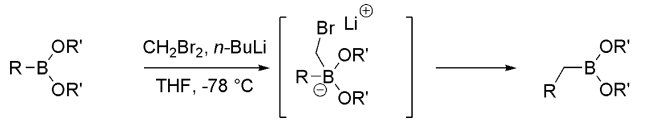
ABSTRACT: The reactions of bromomethyllithium with *tert*-alkylboronic esters could be of great potential for the formation of quaternary carbon centers but often give poor yields/conversions. Calculations and experimental evidence show that *tert*-alkyl groups migrate less effectively than other types of alkyl group in such reactions and that *O*-migration competes. Furthermore, slow/incomplete capture of the bromomethyl reagent by the boronic ester is a problem in more hindered systems, and an additional competing reaction, possibly Li−Br exchange on the bromomethylborate species, also leads to lower yields of migrated products. Based on this, experimental protocols have been devised in which the competing reactions are largely suppressed, leading to higher conversions to migrated product for several substrates.



INTRODUCTION

The migration of alkyl groups from boron to carbon is an important reaction for the formation of carbon−carbon bonds.[1] Although there are examples of migrations of *tert*-alkyl groups,[2] it is often found that *tert*-alkyl groups migrate less readily than other types of alkyl groups;[3] indeed thexyl is frequently used as a nonmigrating group.[4] This limitation restricts the applicability of such reactions for *tert*-alkyl migration and, therefore, their applicability to the construction of quaternary carbon centers. Addition of halomethyllithium[5] reagents to alkylboronic esters (Scheme 1 for $BrCH_2Li$), first reported by Matteson,[6] is a key reaction in this area, since it allows introduction of a functionalized one-carbon unit with considerable potential for further elaboration. Brown and colleagues reported homologation of a range of alkylboronic esters with halomethyllithium reagents but found that the *t*-Bu group migrated less well than other types of alkyl groups, at best a 66% (GC) yield of 2,2-dimethylpropanol being reported after oxidative work-up.[7] Aggarwal has recently reported homologation of chiral alkylboronic esters with halomethyllithium reagents and showed that steric hindrance plays a key role, with more hindered alkylboronic esters giving only modest yields of migrated products.[8,9] In both of these studies, ^{11}B NMR spectroscopic evidence suggested that migration of oxygen was a competing pathway, more so with $ClCH_2Li$ than with $BrCH_2Li$.

Scheme 1. Homologation of Alkylboronic Esters



1 (R = Me)
2 (R = Et)
3 (R = *i*-Pr)
4 (R = *t*-Bu)

5 (R = Me)
6 (R = Et)
7 (R = *i*-Pr)
8 (R = *t*-Bu)

9 (R = Me)
10 (R = Et)
11 (R = *i*-Pr)
12 (R = *t*-Bu)

a, R'R' = CH_3,CH_3; **b**, R'R' = CH_2CH_2; **c**, R'R' = $(CMe_2)_2$
d, R'R' = $(CH_2)_3$; **e**, R'R' = $CH_2CMe_2CH_2$

Clearly there is considerable scope for improvement of this reaction. The poor results for *tert*-alkyl group migration could be a result of a lower migratory aptitude or alternatively be the result of other processes being more favored. Since bromomethyllithium is highly unstable,[5] it is also possible that slow or incomplete capture of bromomethyllithium by the alkylboronic ester is the cause of the poor results for more hindered systems. Our goal in the present study was to gain a clearer understanding of how factors that influence organoboron rearrangements[1] would affect the outcome of these reactions. A combined experimental and computational study was therefore undertaken. Since it was likely that the nature of the boronic ester would affect the outcome, the study was planned to include a range of boronic esters of various alcohols, diols, and thiols.

COMPUTATIONAL STUDIES

Relative Migratory Aptitudes. A computational study published in 2003 by Bottoni et al.[10] suggested that, in the case of chloromethylborates analogous to structures **5b**−**8b** (Scheme 1), the barrier to migration of a tertiary alkyl group was lower than that for migration of other simple alkyl groups. In view of the experimental evidence that higher conversions are obtained with $BrCH_2Li$, we focused on homologation reactions with this reagent in this study. Minimum energy structures for the borates **5b**−**8b** were identified (Gaussian 03, B3LYP/6-31+G(d)), along with the transition states for

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subsequent *C*-and *O*-migration. The activation energies for these two processes are summarized in Table 1.

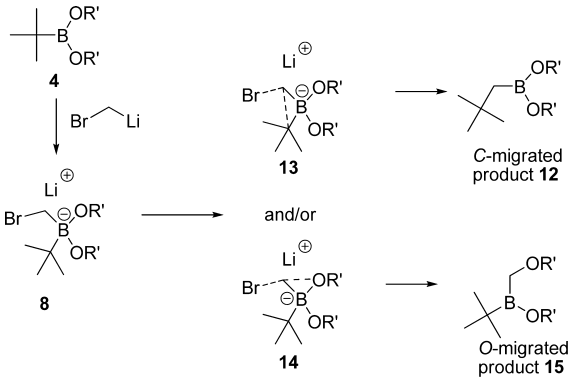
Table 1. $\Delta G^{\ddagger}$ for *C*- and *O*-Migration in 5b−8b

R	Me	Et	*i*-Pr	*t*-Bu
C-migration (kJ mol^{-1})	46.4	44.4	46.0	59.5
O-migration (kJ mol^{-1})	68.7	67.4	65.4	62.3
difference (kJ mol^{-1})	22.3	23.0	19.4	2.8

Our calculations suggest that the barrier to migration of the *t*-Bu group in this system is considerably higher than that for other types of alkyl group and, in particular, that *O*-migration is anticipated to be a significant competing reaction in this case. Furthermore, since there are two oxygen-bound groups, the effective activation barrier to *O*-migration is lowered further, by $RT \ln 2 = 1.7$ kJ mol^{-1} at 298 K, on entropic grounds. These results are consistent with experimental observations that lower yields of migrated products are obtained from tertiary alkyl boron compounds and with ^{11}B NMR data indicating that oxygen migration could be a competing pathway.

Effect of Different Boron-Bound Ligands. Since we were concerned particularly with the migration of tertiary alkyl groups, it was of interest to determine whether the bias for *C*- over *O*-migration could be modified by varying the ligands on boron. We therefore undertook a series of calculations to compare the two possible migration pathways, based on readily accessible *tert*-butylboronic esters **4a** to **4e** (Table 2). The lowest energy conformations for the

Table 2. $\Delta G^{\ddagger}$ for *C*- and *O*-Migration of 8



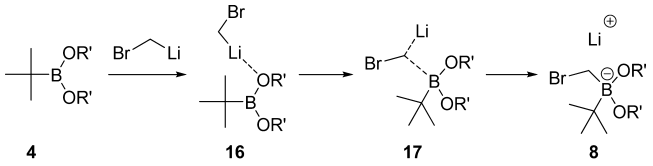
a, R'R' = CH_3,CH_3; **b**, R'R' = CH_2CH_2; **c**, R'R' = $(CMe_2)_2$; **d**, R'R' = $(CH_2)_3$; **e**, R'R' = $CH_2CMe_2CH_2$

$(R'O)_2$ series letter	$\Delta G^{\ddagger}$ for C migration/kJ mol^{-1}	$\Delta G^{\ddagger}$ for O migration/kJ mol^{-1}	difference/ kJ mol^{-1}
(a)	76.9	79.7	2.8
(b)	59.5	62.3	2.8
(c)	48.1	55.6	7.6
(d)	58.4	57.4	−1.0
(e)	54.3	62.5	8.2

bromomethylborates **8** were located, as were transition states **13** and **14** for *C*- (*t*-Bu) and *O*-migration, respectively. In the case of the six-membered ring borates, **8d** and **8e**, two conformers of the transition states for *C*- and *O*-migration were located in each case. Data for all conformers are presented in the Supporting Information.[11] The more hindered pinacol and 2,2-dimethyl-1,3-propanediol systems showed a significantly lower barrier to *C*-migration than to *O*-migration. Therefore, higher selectivity for *C*-migration should be achievable with borates **8c** and **8e** than with the other cases.

Formation of the Initial Halomethylborate. Both Aggarwal[8] and Brown[7] have suggested that incomplete capture of the carbenoid is partly responsible for the lower yields of products with more hindered alkylboronic esters. Therefore, we calculated the relative energy barriers for the complexation step. By systematic lengthening of the B−CH_2Br bond in the borates **8** (initially for series b at the PM3 semiempirical level, but then optimized (Gaussian 03, B3LYP/6-31+G(d)) for all alkoxy groups (series a−e)), plausible structures were identified for the transition states **17** for the addition of bromomethyllithium to the boron center and earlier intermediates **16**, in which bromomethyllithium was complexed to the alkylboronic esters **4** by a Li−O interaction (Table 3). Formation of the

Table 3. Free Energies (kJ mol^{-1}) of Reactions for 4 → 16 and 16 → 8 and Activation Barriers for 16 → 8



a, R'R' = CH_3,CH_3; **b**, R'R' = CH_2CH_2; **c**, R'R' = $(CMe_2)_2$ **d**, R'R' = $(CH_2)_3$; **e**, R'R' = $CH_2CMe_2CH_2$

$(R'O)_2$ series letter	ΔG_r for **4** + $BrCH_2Li$ → **16**	$\Delta G^{\ddagger}$ for **16** → **8**	ΔG_r for **16** → **8**
(a)	−30.0	35.5	−68.1
(b)	−32.5	28.0	−30.5
(c)	−49.0	39.4	−0.7
(d)	−36.7	31.4	−20.5
(e)	−41.3	34.5	−17.1

intermediates **16** was calculated to be essentially barrierless, based on a monomeric gas phase bromomethyllithium structure,[12] but in reality there would probably be a barrier, albeit small. Full thermodynamic and structural parameters are provided in the Supporting Information.

The calculations suggested that the free energies of activation for bromomethylation were higher for the dimethoxy case (transition state **17a**) and for the more hindered cyclic cases (**17c** and **17e**) than they were for the less hindered cyclic cases (**17b** and **17d**). Also, the free energies of reaction for bromomethylation of the more hindered compounds were much less favorable than those for the less hindered examples. Decomposition of bromomethyllithium would be expected to be particularly competitive in these cases, leading to lower yields of derived products.

Summary of Computational Findings. The calculations suggested that the reaction of bromomethyllithium with *tert*-butylboronic esters **4** could be yield-limited in two different ways.

1. With hindered alkylboronic esters (e.g., **4c** or **4e**) addition of bromomethyllithium to the ester would be less favorable, such that nonproductive decomposition of the bromomethyllithium could compete.
2. Potentially, *O*-migration competes with *C*-migration in the next step, with the predicted relative proportion of *C*-migration increasing for more hindered *tert*-butylboronic esters.

RESULTS AND DISCUSSION

Thexyl was chosen as a representative tertiary alkyl group, since thexylborane is easy to prepare and to derivatize. A range of thexylborane derivatives was prepared, including the simple dimethoxy compound, **18a**; several cyclic boronic esters with different ring sizes and different levels of steric hindrance; an electron-withdrawn dialkoxy compound, **18f**; and two compounds incorporating sulfur instead of oxygen (Figure 1). These were homologated according to **Method A** (see Experimental Section), involving use of a small excess each of dibromomethane and *n*-butyllithium. The ratio of thexylmethanol/thexanol produced is shown in parentheses in Figure 1.

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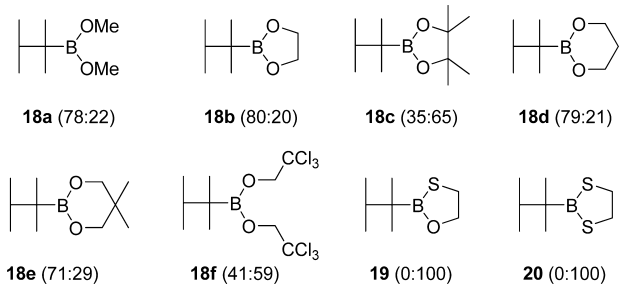
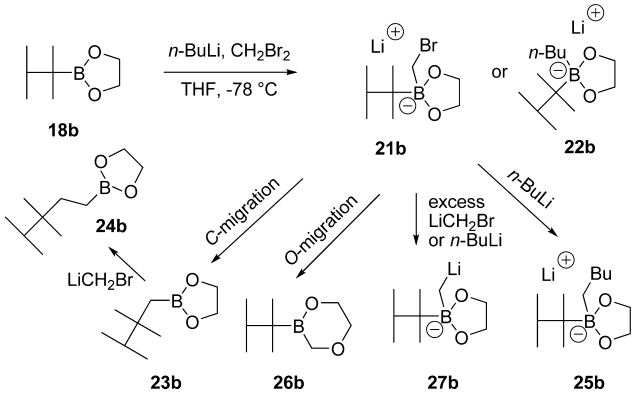


Figure 1. Thexylboron compounds used (and ratio of thexylmethanol/thexanol produced).

The compounds containing sulfur (**19**, **20**) gave no thexylmethanol at all, while the electron withdrawn boronic ester (**18f**) offered no advantages. In view of these observations, no further work was conducted with compounds **18f**, **19**, and **20**. There was essentially no difference between the results for the unhindered five- and six-membered cyclic boronic esters (**18b**, **18d**) and the dimethyl thexylboronic ester (**18a**). However, the more hindered boronic esters (**18c**, **18e**) gave consistently less of the migrated product than their less substituted counterparts.

While *ca.* 80% of the desired product was observed in three cases, it was of interest to determine what factors were limiting the yield to this level. Several possible explanations (Scheme 2) were considered to account for the 20% of thexanol produced in the reaction of **18b**:

Scheme 2. Possible Reactions of 18b with *n*-BuLi/CH_2Br_2



1. slow (and/or incomplete) rearrangement of the bromomethylborate **21b**;
2. direct addition of *n*-BuLi to the boronic ester, forming **22b**, which would then prevent the desired migration as well as reduce the amount of bromomethyllithium available;
3. incomplete capture of bromomethyllithium by the boronic ester, leading to decomposition of uncaptured bromomethyllithium and leaving unreacted boronic ester;
4. further reaction of the product **23b** with $BrCH_2Li$, leading to the (2-thexylethyl)boron compound **24b** and reducing the amount of $BrCH_2Li$ available, so that unreacted **18b** would remain;
5. nucleophilic substitution of the bromide in **21b** by *n*-BuLi to give the pentyl derivative **25b**;
6. *O*-migration (to give **26b**) competing with *C*-migration;
7. bromine–lithium exchange between *n*-BuLi (or bromomethyllithium) and the bromomethylborate **21b**, leading to the lithiated species **27b**.

In order to try to distinguish between some of these aspects, a series of experiments was undertaken with **18b**.

Incomplete Rearrangement of Borate 21b. When the reaction was quenched oxidatively at low temperature, the proportion of migration product was much reduced (thexylmethanol/thexanol 17:83), indicating that little rearrangement took place at −78 °C, so the migration step was clearly rate-limiting. Maintaining the reaction temperature at −78 °C for 30 min–4 h and then either rapid or slow (1 h) warming to room temperature followed by further stirring gave ratios in the range 74:26 to 80:20. Therefore, it seems unlikely that incomplete rearrangement was responsible for the unmigrated thexyl derivative.

Direct Addition of *n*-BuLi to 18b. There was no evidence from ^{11}B NMR spectroscopy for formation of butylborate **22b**, while GC of the product after oxidation showed levels of 1-butanol consistent only with butoxide impurities in the *n*-BuLi used. Use of larger excesses of CH_2Br_2 also did not improve the ratio of thexylmethanol/thexanol, and less nucleophilic lithium reagents (*sec*-BuLi, *t*-BuLi, and lithium 4,4′-di-*tert*-butylbiphenyl) all gave lower yields of migration products from their reactions with **18b** and CH_2Br_2. These experiments strongly argue against the formation of **22b** as a significant cause of the 20% of substrate not converted into thexylmethanol.

Incomplete Capture of $BrCH_2Li$ by 18b. If the problem was incomplete capture of the bromomethyllithium by **18b** (point 3 above), as a result of either a slow reaction between the two species or the formation of an equilibrium mixture in which a significant proportion of free **18b** was still present, use of excess reagent should improve the yield at least to some extent, but by use of boronic ester (1 equiv), dibromomethane (5 equiv), and *n*-BuLi (2 equiv) a similar yield of thexylmethanol was obtained as by use of the standard reactant proportions. Furthermore, carrying out the standard procedure as in **Method A**, but recooling the mixture to −78 °C after warming to room temperature, and then adding further dibromomethane (1.2 equiv) and *n*-BuLi (1.1 equiv) before warming again and carrying out the usual oxidative workup, gave a 26:51:23 ratio of thexylethanol/thexylmethanol/thexanol. If the nonmigrated product from **Method A** were a result of incomplete capture of the carbenoid, it would then react on the second addition. Since a similar amount of nonmigrated product was obtained in this case, even though further reaction of the major product to give thexylethanol had taken place, it is clear that the side products were no longer able to react with bromomethyllithium in the desired way. Therefore, incomplete capture of bromomethyllithium does not appear to be a significant factor, at least for this unhindered boronic ester (**18b**).

Formation of Compounds 24b/25b. Of the other processes considered as possibly responsible for limiting the yield of migrated product to 80%, two (points 4 and 5) should lead to the production of additional alcohols (2-thexylethanol for further reaction of product **23b** with $BrCH_2Li$ to give **24b** or 1-pentanol for nucleophilic substitution of bromide from **21b** to give **25b**). However, neither of these alcohols was identifiable in the standard product mixture. Therefore, these processes are unlikely to be significant reasons for the suppression of yield.

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Competing C/O-Migration and Li−Br Exchange on 21b. A typical reaction of *n*-BuLi/CH_2Br_2 with **18b** followed by rapid aqueous workup but *without oxidation* showed two coupled multiplets at 3.57 and 4.02 ppm in the ^{1}H NMR spectrum, tentatively attributed to the ethylenedioxy bridge of the oxygen migration product **26b**. This compound was estimated to account for no more than 2% of the crude product mixture. An identical experiment was carried out using $ClCH_2Br$. This gave a broadly similar result, although the amount of *O*-migration product **26b** was increased in line with previous reports.[7,8] However, the amount (approximately 5%) again did not account for a substantial proportion of the resultant thexanol (56:44 mixture of thexylmethanol:thexanol formed).

^{11}B NMR spectroscopy of the CH_2Br_2 reaction after washing showed major peaks at 31.8 and 33.3 ppm (typical for compounds of the type $RB(OR)_2$) and small peaks at 51.1 and 55.2 ppm (typical for R_2BOR). These observations support the formation of **26b** by oxygen migration, with hydrolysis products perhaps giving rise to one of the signals in each pair (this could mean that the amount of *O*-migration product reported has been underestimated somewhat). However, the amount of the product again seemed sufficient to account for only a fraction of the 20% of thexanol obtained on oxidation.

Furthermore, the ^{11}B NMR spectrum of the original reaction mixture prior to washing showed a small but significant peak at around 6 ppm and a very small peak around 9 ppm alongside the expected peak for **23b** at 33.5 ppm and two more small peaks at 51.2 and 55.5 ppm. The 6 ppm peak was not due to a simple adduct of the alkylboronic ester with *n*-BuLi; the borate **22b** derived by addition of *n*-BuLi to **18b** gave a very sharp peak at −15.8 ppm. The 6 ppm peak could be due to the Br−Li exchange product **27b**. Following a quick water wash, the peaks at 6 and 9 ppm disappeared and there was a noticeable increase in the size of the peak at 55 ppm. If **27b** is responsible for the peaks at 6/9 ppm, use of an excess of *n*-butyllithium should result in an increase in their intensity. Consistent with this expectation, such an experiment gave substantial increases in the peaks at 6 and 9 ppm and a corresponding decrease in the peak at 33 ppm, which was no longer bigger than the peak at 54 ppm. After a rapid water wash, only peaks at 30.9, 33.3, and 54.4 ppm remained, with the peak at 54.4 ppm (corresponding to a borinic species of the type R_2BOR) being considerably the largest. Furthermore, formation of the *O*-migrated product **26b** was completely suppressed (according to ^{1}H NMR spectroscopy), so the peak at 54 ppm was not due to **26b**. After oxidation, this reaction gave a 34:66 mixture of thexylmethanol/thexanol. The significant suppression of migration, increase in the ^{11}B NMR peak at 6 ppm, and diminution of the ^{11}B NMR peak at 33 ppm seem consistent with the formation of additional **27b** by reaction of **21b** with the excess *n*-BuLi. Furthermore, **27b** would give rise to *t*-Hx(Me)BOH on hydrolysis and this could be responsible for the enlarged peak at around 54 ppm in the ^{11}B NMR spectrum.

Similar experiments were undertaken using the 2,2-dimethyl-1,3-propanediol boronic ester **18e**. With 1.2 equiv of dibromomethane and 2.2 equiv of *n*-butyllithium, a 69:31 mixture of thexylmethanol/thexanol was obtained after oxidation, i.e. the same result as with 1.1 equiv of *n*-BuLi, so that in this case an excess of organolithium reagent did not suppress the desired migration. The ^{11}B NMR spectrum prior to an aqueous wash did not show peaks at 55, 9, or 6 ppm so that oxygen migration had been suppressed (in line with expectations based on the computational study), but the formation of **27e** by Br−Li exchange had also been suppressed. In the case of the pinacol boronic ester **18c**, NMR data suggested that the side reactions were also less prominent than in the case of the ethylene glycol boronic ester **18b**, but the suppression of these reactions was not as complete as for the 2,2-dimethyl-1,3-propanediol boronic ester **18e**.

Optimization of Reaction Conditions. We speculated that incomplete formation of the bromomethylborates in the hindered cases might be responsible for the lower yields. Therefore, we investigated a range of reaction stoichiometries and addition regimes in order to try to optimize the reactions. The standard procedure (1.0 equiv of substrate, 1.2 equiv of CH_2Br_2, 1.1 equiv of *n*-BuLi were added dropwise, and the mixture was stirred for 30 min at −78 °C; **Method A**) was used as a reference point. Increasing the amount of CH_2Br_2 (up to 5 equiv) and *n*-BuLi (up to 3 equiv) gave a small decrease in migration for **18b** and only a modest increase in migration for **18c**. However, sequential addition of three portions of CH_2Br_2 (1.2 equiv) and *n*-BuLi (1.1 equiv) in an alternating sequence (**Method B**) gave significantly improved yields for the more hindered boronic esters (Table 4, entries 3−6). With the 2,2-dimethyl-1,3-propanediol boronic ester **18e**, an analogous method involving five sequential additions of CH_2Br_2 and *n*-BuLi gave the highest proportion of migrated compound yet obtained (89:11; Table 4, entry 7). These observations confirmed that unreacted boronic ester remained after completion of the standard reaction (**Method A**) with the hindered cases, **18c** and **18e**, which supported the view that complexation of bromomethyllithium with such boronic esters was incomplete. The fact that yields of alkyl migration product could be increased to close to quantitative by sequential addition of CH_2Br_2 and *n*-BuLi showed that the side reactions that limited the yield for the ethylene glycol derivative to 80% could be suppressed by using the more hindered boronic esters.

With even more hindered *tert*-alkylboronic esters, the increases in yield were proportionately more significant. With triethylmethylboronic ester **28**, a good conversion to the migration product (72:28 ratio of Et_3CCH_2OH/Et_3COH) was achieved by use of **Method B**, compared with a 26:74 ratio using **Method A**. Even with trioctylmethylboronic esters **29** and **30** (which would have contained around 17% of 2-octylbis(1-octyl)methylboronic ester because the hydroboration of 1-octene is not totally regioselective[13]), around 20% of the homologated product was produced in each case by use of **Method A** (entries 10 and 12). While the application of **Method B** to **18b** had given a lower conversion to the homologated product (entry 2), with the more hindered alkyl group in compound **29**, **Method B** gave an increase to a 40:60 ratio of Oct_3CCH_2OH/Oct_3COH, marginally better than by application of **Method B** to the 2,2-dimethylpropane-1,3-diol ester **30** (37:63) (entries 11 and 13), so that the optimal method depends on a balance of steric properties, including those of the *tert*-alkyl group as well as the esterifying diol. While modest, this yield is still synthetically useful for a compound bearing such a high level of steric hindrance. However, the tricyclopentylmethylboronic esters **31** and **32** gave no homologation under any of the conditions investigated. It would appear that the extreme steric hindrance inherent in the tricyclopentylmethyl group has found the limitation to the method.

Aggarwal has developed an elegant approach to generation of stereodefined tertiary alkylboron compounds, but attempts to

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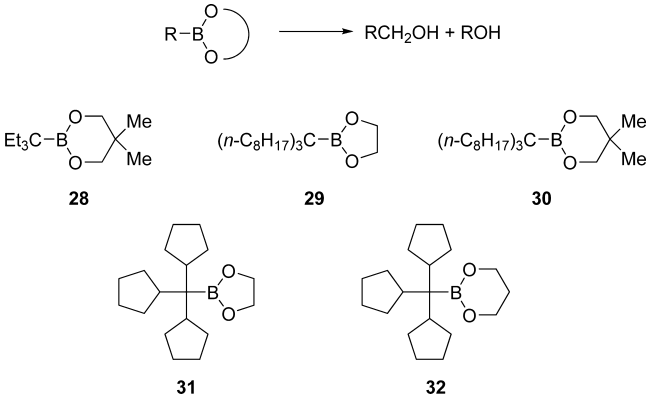
Table 4. Effect of Stoichiometry and Order of Addition on the Homologation Reactions



entry	substrate	overall proportions **substrate**/CH_2Br_2/*n*-BuLi	method[a]	RCH_2OH/ROH
1	**18b**	1:1.2:1.1	A	80:20
2	**18b**	1:3.6:3.3	B	70:30
3	**18c**	1:1.2:1.1	A	34:66
4	**18c**	1:3.6:3.3	B	59:41
5	**18e**	1:1.2:1.1	A	70:30
6	**18e**	1:3.6:3.3	B	85:15
7	**18e**	1:6.0:5.5	B[b]	89:11
8	**28**	1:1.2:1.1	A	26:74
9	**28**	1:3.6:3.3	B	72:28
10	**29**	1:1.2:1.1	A	20:80
11	**29**	1:3.6:3.3	B	40:60
12	**30**	1:1.2:1.1	A	18:82
13	**30**	1:3.6:3.3	B	37:63
14	**31**	1:1.2:1.1	A	0:100
15	**31**	1:3.6:3.3	B	0:100
16	**32**	1:3.6:3.3	B	0:100

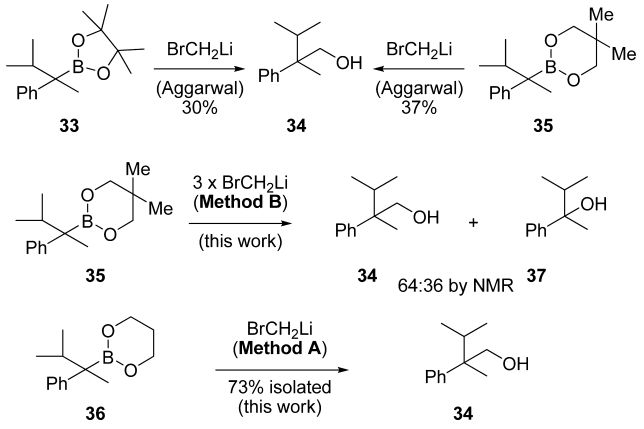
[a]**Method A**: 1 equiv of substrate, 1.2 equiv of CH_2Br_2, −78 °C, 1.1 equiv of *n*-BuLi, 30 min, then warm and oxidize. **Method B**: 1 equiv of substrate, 1.2 equiv of CH_2Br_2, −78 °C, 1.1 equiv of *n*-BuLi added over 30 min, 1.2 equiv of CH_2Br_2, 1.1 equiv of *n*-BuLi added over 30 min, 1.2 equiv of CH_2Br_2, 1.1 equiv of *n*-BuLi added over 30 min, then warm, and oxidize. [b]This experiment used a variation on **Method B** in which 5 additions of CH_2Br_2 and *n*-BuLi were carried out.

convert such compounds into the corresponding tertiary alkylmethanols often gave only low yields (30% of **34** from **33** and 37% from the less bulky 2,2-dimethyl-1,3-propanediol ester **35**, for example, Scheme 3).[8] Application of **Method B** to substrate **35** gave a 64:36 ratio of compounds **34**:**37** (compared to 50:50; 38% isolated yield using **Method A**). However, since the migrating group is particularly bulky, application of **Method A** to the less hindered diol derivative **36** proved superior, with a product ratio of 85:15 for **34**:**37** (73% isolated yield) being achieved. These results demonstrate the benefits of a greater understanding of the reaction for development of successful synthetic procedures and illustrate the potential for the formation of quaternary stereocenters.[14]

CONCLUSION

Following a thorough study by computational and experimental techniques it has been possible to identify three problems that inhibit success in generating *tert*-alkylmethanols in good yields by reactions of *tert*-alkylboronic esters with bromomethyllithium: (i) slow formation of the borate (e.g., **8**, **21**) from the boronic ester and bromomethyllithium (which is a particular problem with the most hindered boronic esters and leads to low yields because of competitive destruction of the bromomethyllithium by nonproductive processes); (ii) competition between migration of the *tert*-alkyl group and one of the oxygen groups (which has previously been discussed by others but accounts for only a small amount of the loss of yield of the *tert*-alkylmethanol in the case of 2-thexyl-1,3,2-dioxaborolane (**18b**)); and (iii) another reaction of the initial complex **21b** that we speculate may be Br−Li exchange, but in any case leads to a species that does not rearrange in the desired way. With more hindered *tert*-alkyl groups, boronic esters derived from less hindered diols give better results. However, with less hindered *tert*-alkyl groups, boronic esters derived from more hindered diols in conjunction with the use of a procedure (**Method B**) involving stepwise treatment three times with bromomethyllithium can be advantageous. With extremely hindered *tert*-alkyl groups, best results can be obtained from the combination of an unhindered diol and **Method B**. By use of these approaches we have shown that the reaction can provide higher yields for cases that have previously given only modest yields and have extended the level of steric hindrance of the *tert*-alkyl groups that can be accommodated by the reaction. Even with these improvements, however, the most hindered of *tert*-alkyl groups, such as the tricyclopentylmethyl group, fail to participate in the reaction. The homologation should now be applicable to a wider range of tertiary alkyl substrates. With this improved understanding of the factors affecting efficient bromomethylation/*tert*-alkyl migration in boronic ester systems, it should now be possible to apply this reaction to all but the most hindered boronic ester substrates.

Scheme 3. Optimization of Migration Reactions in Systems Related to Those Reported by Aggarwal[8]



EXPERIMENTAL SECTION

General Experimental Details. Melting point determinations were performed by the open capillary method and are reported uncorrected. ^1H and ^{13}C NMR chemical shifts δ are reported in parts per million (ppm) relative to TMS, and coupling constants J are reported to the nearest 0.1 Hz. C, CH, CH_2, or CH_3 ^{13}C signals are assigned from DEPT-90 and -135 spectra. In a number of cases, carbon atoms attached to boron gave very broad peaks in ^{13}C NMR spectra, and these could not always be distinguished. Hydrogen atoms attached to these carbons were not always observed in ^1H NMR spectra. Low- and high-resolution mass spectra were recorded on a time-of-flight mass spectrometer using electron impact (EI). High resolution mass spectra were recorded only for new compounds. IR spectra were recorded on an FT−IR spectrometer as a thin film (liquid samples) or applied as a solution in chloroform with the chloroform

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allowed to evaporate (solid samples). Column chromatography was carried out using 60A (35−70 μm) silica.

General Procedure for Preparation of Thexylboronic Esters and Related Compounds. A dry 50 mL round bottomed flask equipped with a magnetic stirrer bar and septum was assembled when hot and flushed with nitrogen for 10 min. Borane dimethyl sulfide complex (0.48 mL, 5.0 mmol) was added, and the flask was cooled using an ice bath. 2,3-Dimethyl-2-butene (0.59 mL, 5.4 mmol) was added dropwise with stirring over 5 min. The mixture was left to stir at 0 °C for 90 min. The appropriate alcohol (10 mmol) or diol/dithiol (5 mmol) was added dropwise with safe venting of the evolved hydrogen gas. The cooling bath was removed, and the mixture was left to stir for an additional 1 h. Excess dimethyl sulfide was removed under a fast stream of nitrogen to give the desired thexylborane derivative. Thexyldimethoxyborane[15] (**18a**), 2-thexyl-1,3,2-dioxaborolane[16] (**18b**), 2-thexyl-4,4,5,5-tetramethyl-1,3,2-dioxaborolane[16] (**18c**), 2-thexyl-1,3,2-dioxaborinane[17] (**18d**), and 2-thexyl-1,3,2-dithiaborolane[2c] (**20**) are known compounds.

*2-Thexyl-5,5-dimethyl-1,3,2-dioxaborinane (**18e**).* Using 2,2-dimethyl-1,3-propanediol (0.55 g, 5.25 mmol); colorless liquid (Found (TOF-EI): $[M - H]^+$, 197.1708. $C_{11}H_{22}BO_2$ requires 197.1713); δ_H (400 MHz; $CDCl_3$) 3.55 (4 H, s), 1.58 (1 H, septet, *J* 6.8), 0.91 (6 H, s), and 0.81−0.76 (12 H, m); δ_C (125 MHz; $CDCl_3$) 71.8 (2 × CH_2), 34.3 (CH), 31.4 (C), 21.9 (CH_3), 21.3 (CH_3) and 18.4 (CH_3); δ_B (96 MHz; $CDCl_3$) 30.1; $\nu_{max.}$ (neat) 2952, 2873, and 1476 cm^{-1}; *m*/*z* (EI) 197 ($[M - H]^+$, 6%), 183 (100%), 155.1 (100), 141 (43), 125 (15), 113 (90), 97 (97), 84 (89), 67 (100), and 55 (68).

*Thexylbis(2,2,2-trichloroethoxy)borane (**18f**).* Using 2,2,2-trichloroethanol (0.96 mL, 10.0 mmol); air-sensitive colorless liquid; δ_H (250 MHz; $CDCl_3$) 4.56 (4 H, s), 1.80 (1 H, septet, *J* 6.8), 0.99 (6 H, s), and 0.90 (6 H, d, *J* 6.8); δ_C (125 MHz; $CDCl_3$) 97.4 (C), 76.0 (CH_2), 33.8 (CH), 21.1 (CH_3), and 18.0 (CH_3); δ_B (96 MHz; $CDCl_3$) 29.8. The air sensitivity of this compound precluded the determination of HRMS data.

*2-Thexyl-1,3,2-oxathiaborolane (**19**).* Using 2-mercaptoethanol (0.35 mL, 5.0 mmol); slightly impure colorless liquid (Found (TOF-EI): M^+, 172.1097. $C_8H_{17}BOS$ requires 172.1093); δ_H (500 MHz; $CDCl_3$) 4.37 (2 H, t, *J* 7.4), 2.99 (2 H, t, *J* 7.4), 1.65 (1 H, septet, *J* 6.9), 0.92 (6 H, s), and 0.85 (6 H, d, *J* 6.9); δ_C (125 MHz; $CDCl_3$) 72.5 (CH_2), 35.4 (CH), 30.0 (CH_2), 22.2 (CH_3), and 18.5 (CH_3); δ_B (96 MHz; $CDCl_3$) 53.2; $\nu_{max.}$ (neat) 2956, 1567, 1393, 1180, 1131 cm^{-1}; *m*/*z* (EI) 172 (M^+, 8%), 153 (5), 130 (22), 113 (14), 85 (24), 84 (100), and 61 (78).

General Procedure for Tertiary Alkyl Group Migration by Method A. Dry THF (15 mL) was added to the boronic ester substrate (5.0 mmol). Dibromomethane (0.42 mL, 6.0 mmol) was added, and the solution was cooled using a dry ice−acetone bath. *n*-Butyllithium (2.2 mL of a 2.5 M solution in hexanes, 5.5 mmol) was added dropwise over 25−30 min with vigorous stirring. The mixture was left to stir for an additional 30 min, and the cooling bath was removed. The mixture was left to warm up for 1 h, before being cooled to 0 °C. A solution of sodium hydroxide (1.2 g, 30 mmol) in water (10 mL) was added dropwise, followed by excess aqueous hydrogen peroxide (30% by weight, 6 mL). Once the initial exothermic reaction had subsided, the cooling bath was removed and the mixture was stirred overnight. The aqueous layer was saturated with potassium carbonate, and the mixture was extracted with diethyl ether (3 × 25 mL). The organic extract was washed with brine (2 × 20 mL) and distilled water (2 × 20 mL), dried over magnesium sulfate, and filtered. The solvent was evaporated carefully under reduced pressure to around 120% of the maximum theoretical yield to give a mixture of migrated and nonmigrated products, the ratio of which was determined by ^1H NMR spectroscopy (see Supporting Information).

General Procedure for Tertiary Alkyl Group Migration by Triple Addition (Method B). The procedure was identical to that described in **Method A**, except that the addition of the dibromomethane and *n*-BuLi was repeated 3 times with no warming between additions.

Thexylmethanol (2,2,3-Trimethyl-1-butanol).[18] A sample of the migrated product was purified by column chromatography on silica (4:1 hexane/diethyl ether) to give pure thexylmethanol as a colorless liquid; δ_H (400 MHz; $CDCl_3$) 3.3 (2 H, s), 1.55 (1 H, septet, *J* 6.9), 1.54−1.47 (1 H, br), 0.80 (6 H, d, *J* 6.9), and 0.75 (6 H, s); δ_C (125 MHz; $CDCl_3$) 70.6 (CH_2), 37.2 (C), 32.5 (CH), 20.9 (CH_3), and 17.2 (CH_3); $\nu_{max.}$ (neat) 3367 and 2957 cm^{-1}; *m*/*z* (EI) 85 ($[M - CH_2OH]^+$, 100%), 73 (78), 69 (37), and 55 (72).

Thexyl Group Migration Using LiDBB. A 250 mL two-necked flask equipped with a stirrer bar was assembled while hot and flushed with nitrogen. 4,4′-di-*tert*-Butylbiphenyl (7.99 g, 30.0 mmol) was added to the flask when it was around 50 °C, the flask was flushed with nitrogen for a further 5 min, and dry THF (60 mL) was introduced *via* syringe. Lithium wire (0.174 g, 25.0 mmol, with 0.5−1% sodium) was cut into small pieces and pressed to increase surface area. The flask was cooled to 0 °C, and the lithium was introduced quickly *via* the side arm with vigorous stirring under a fast stream of nitrogen. The solution took the dark green/purple color of the radical anion within 2−5 min. The reaction was stirred vigorously for 5 h, by which time the Li was fully consumed. The solution was cooled to −78 °C and transferred dropwise over 45 min *via* cannula to a freshly prepared solution of 2-thexyl-1,3,2-dioxaborolane (**18b**) (0.78 g, 5.0 mmol) and dibromomethane (0.42 mL, 6.0 mmol) in dry THF (15 mL), also cooled to −78 °C. Additional THF (10 mL) was used to dissolve and transfer the thick residues at the bottom of the radical anion solution. The reaction was stirred for an additional 30 min at −78 °C, then the cooling bath was removed, and the solution was allowed to warm up over 1 h. The reaction mixture was oxidized as in **Method A**. The ratio of thexylmethanol to thexanol was determined to be 55:45 by GC analysis (Zebron ZB-5 column; 70−260 °C at 6 °C/min; hexadecane as internal standard).

*Lithium Butyl(thexyl)(ethylenedioxy)borate (**22b**).* THF (15 mL) was added to 2-thexyl-1,3,2-dioxaborolane (**18b**), and the mixture was cooled to −78 °C. *n*-BuLi (2.2 mL of a 2.5 M solution in hexanes, 5.5 mmol) was added dropwise over 10 min, and the cooling bath was removed. The mixture was concentrated under a fast stream of nitrogen, and the ^{11}B NMR spectrum was recorded; δ_B (96 MHz; $CDCl_3$) −15.8.

*5,5-Dimethyl-2-(3-ethylpent-2-yl)-1,3,2-dioxaborinane (**28**).* An oven-dried flask equipped with a stirrer bar and septum was flushed with nitrogen for 10 min. Triethylborane solution (15 mL, 1.0 M in THF, 15 mmol) was added, and the flask was placed in an ice bath. Once cooled, α,α-dichloromethyl methyl ether (1.5 mL, 15 mmol) was added dropwise via syringe, followed by the dropwise addition via cannula of a freshly prepared solution of lithium triethylcarboxide[19] (15 mmol) in dry THF (10 mL) over 15 min. The cooling bath was removed, and the mixture was stirred for a further 1 h. A solution of 2,2-dimethyl-1,3-propanediol (1.87 g, 18 mmol) in dry THF (5 mL) was added dropwise, and the solution stirred overnight at room temperature. The volatiles were evaporated under reduced pressure, and the crude product was purified by column chromatography on silica (petroleum ether, followed by 95:5 petroleum ether/ethyl acetate) to give the *title compound* (1.43 g, 45%) as a colorless liquid (Found (TOF-EI): M^+, 212.1954. $C_{12}H_{25}BO_2$ requires 212.1948); δ_H (400 MHz; $CDCl_3$) 3.58 (4 H, s), 1.32 (6 H, q, *J* 7.5), 0.95 (6 H, s), and 0.75 (9 H, t, *J* 7.5); δ_C (125 MHz; $CDCl_3$) 71.8 (CH_2), 31.4 (C), 25.6 (CH_2), 22.1 (CH_3), and 9.2 (CH_3); δ_B (96 MHz; $CDCl_3$) 30.3; $\nu_{max.}$ (neat) 2957, 2875, 1476, 1244, and 1157 cm^{-1}; *m*/*z* (EI) 212 (M^+, 2%), 183 (100), 182 (76), 141 (38), 98 (64), 97 (25), 87 (48), 83 (59), 69 (33), 57 (22), 55 (39).

*2-(9-Octylheptadecan-9-yl)-1,3,2-dioxaborolane (**29**).* An oven-dried flask equipped with a stirrer bar and septum was flushed with nitrogen for 10 min. Once immersed in an ice bath, a borane dimethyl sulfide complex (10.5 M, 0.86 mL, 10 mmol) was added via syringe, followed by the dropwise addition of 1-octene (4.7 mL, 30 mmol). The cooling bath was removed, and the solution was stirred for 3 h. The solution was cooled to 0 °C, and α,α-dichloromethyl methyl ether (1.0 mL, 11 mmol) was added dropwise via syringe, followed by the dropwise addition via cannula of a freshly prepared solution of lithium triethylcarboxide[19] (10 mmol) in dry THF (10 mL) over 15 min. The cooling bath was removed, and the mixture left to stir for a further 1 h. Ethylene glycol (0.56 mL, 10 mmol) was added dropwise, and the

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solution left to stir overnight at room temperature. The volatiles were evaporated under reduced pressure, hexane (30 mL) was added, and the mixture was filtered. The resulting clear hexane solution was washed with methanol (2 × 15 mL). The hexane layer was concentrated under reduced pressure to give the *title compound* (2.04 g, 48%) as a colorless viscous oil (Found (TOF-EI): M^+, 422.4297. $C_{27}H_{55}BO_2$ requires 422.4295); δ_H (400 MHz; $CDCl_3$) 4.15 (4 H, s), 1.37−1.05 (42 H, m), and 0.87 (9 H, t, *J* 6.6); δ_C (125 MHz; $CDCl_3$) 65.3 (CH_2), 34.6 (CH_2), 31.9 (CH_2), 30.6 (CH_2), 29.6 (CH_2), 29.4 (CH_2), 24.8 (CH_2), 22.7 (CH_2), and 14.1 (CH_3); δ_B (96 MHz; $CDCl_3$) 33.9; $\nu_{max.}$ (neat) 2924, 2853, 1466, 1389, and 1348 cm^{-1}; *m*/*z* (EI) 422 (M^+, 2%), 350 (5), 323 (22), 309 (100), 267 (7), 253 (14), 239 (18), 211 (17), 197 (38), 182 (11), 168 (15), 153 (17), and 139 (8).

*5,5-Dimethyl-2-(9-octylheptadecan-9-yl)-1,3,2-dioxaborinane (**30**).* The above procedure was repeated on a 15 mmol scale, but with a solution of 2,2-dimethyl-1,3-propanediol (1.87 g, 1.2 equiv, 18.0 mmol) in dry THF (5 mL) replacing ethylene glycol, to give the *title compound* (3.98 g, 57%) as a colorless oil (Found (TOF-EI): $[M - H]^+$, 463.4685. $C_{30}H_{60}BO_2$ requires 463.4686); δ_H (400 MHz; $CDCl_3$) 3.57 (4 H, s), 1.35−1.05 (42 H, m), 0.94 (6 H, s), and 0.88 (9 H, t, *J* 6.8); δ_C (100 MHz; $CDCl_3$) 71.8 (CH_2), 34.3 (CH_2), 32.0 (CH_2), 31.4 (C), 30.7 (CH_2), 29.7 (CH_2), 29.4 (CH_2), 24.8 (CH_2), 22.7 (CH_2), 22.1 (CH_3), and 14.1 (CH_3); δ_B (160.5 MHz; $CDCl_3$) 28.6; $\nu_{max.}$ (neat) 2923, 2952, 1476, 1467, and 1246 cm^{-1}; *m*/*z* (EI) 463 ($[M - H]^+$, 2%), 393 (10), 351 (98), 255 (98), 155 (100), and 71 (94).

*2-(Tricyclopentylmethyl)-1,3,2-dioxaborolane (**31**).* The procedure was the same as that for the preparation of **29**, except that cyclopentene (2.75 mL, 30 mmol) replaced octene and that the reaction was left to stir overnight after the ethylene glycol was added. The crude mixture was concentrated under reduced pressure, and methanol (40 mL) was added. The mixture was swirled vigorously until the oily substance at the bottom of the flask began to precipitate. The mixture was then cooled to 0 °C for 2 h, whereupon the *title compound* (1.53 g, 53%) precipitated as a white solid, mp 89−93 °C (Found (TOF-EI): M^+ − cyclopentyl, 221.1714. $C_{13}H_{22}BO_2$ requires 221.1713); δ_H (400 MHz; $CDCl_3$) 4.11 (4 H, s), 2.05−1.95 (3 H, m) and 1.72−1.36 (24 H, m); δ_C (125 MHz; $CDCl_3$) 64.8 (CH_2), 45.9 (CH), 30.0 (CH_2), and 25.1 (CH_2); δ_B (96 MHz; $CDCl_3$) 33.8; $\nu_{max.}$ (neat) 3019, 2952, 2869, 1389, and 1215 cm^{-1}; *m*/*z* (EI) 221 (M − cyclopentyl, 100%), 179 (50), 165 (91), 153 (82), 139 (83), 125 (28), 109 (62), 95 (77), 81 (66), 67 (78), and 55 (29).

*2-(Tricyclopentylmethyl)-1,3,2-dioxaborinane (**32**).* The procedure was the same as that for the preparation of **31**, except that 1,3-propanediol (1.25 g, 1.2 equiv, 12 mmol) replaced ethylene glycol, to give the *title compound* (1.72 g, 57%) as a white solid, mp 77−79 °C (Found (TOF-EI): M^+, 304.2577. $C_{19}H_{33}BO_2$ requires 304.2574); δ_H (400 MHz; $CDCl_3$) 3.94 (4 H, app. t, *J* 5.4), 1.99−1.84 (5 H, m), and 1.68−1.35 (24 H, m); δ_C (125 MHz; $CDCl_3$) 61.0 (CH_2), 46.4 (CH), 30.0 (CH_2), 27.6 (CH_2), and 25.3 (CH_2); δ_B (96 MHz; $CDCl_3$) 29.8; $\nu_{max.}$ (neat) 3019, 2951, 2868, 1480, 1413, 1267, and 1215 cm^{-1}; *m*/*z* (EI) 304 (M^+, 3%), 303 (12), 235 (100), 221 (20), 193 (56), 179 (98), 167 (85), 153 (96), 139 (32), 109 (90), 95 (95), 81 (97), and 67 (70).

Reaction of Boronic Ester 28 with Bromomethyllithium According to Method B. Method B was applied to boronic ester **28** (0.38 g, 1.81 mmol). ^1H NMR spectroscopy of the crude product after oxidation showed a mixture of 2,2-diethylbutanol and 3-ethyl-3-pentanol in a ratio of 72:28. A portion of the mixture was subjected to column chromatography on silica (petroleum ether, followed by 98:2 petroleum ether/ethyl acetate) to give 2,2-diethyl-1-butanol[20] as a colorless liquid; δ_H (400 MHz; $CDCl_3$) 3.36 (2 H, s), 1.35−1.25 (1 H, br s), 1.23 (6 H, q, *J* 7.5), and 0.79 (9 H, t, *J* 7.5); δ_C (125 MHz; $CDCl_3$) 65.9 (CH_2), 39.5 (C), 25.0 (CH_2), and 7.4 (CH_3); $\nu_{max.}$ (neat) 3365, 2965, 2927, 2880, 1465, 1379, and 1260 cm^{-1}; *m*/*z* (EI) 99 ($M^+ - CH_2OH$, 63%), 98 (65), 86 (100), 74 (100), 69 (60), and 59 (100).

Reaction of Boronic Ester 29 with Bromomethyllithium According to Method B. Method B was applied to 2-(9-octylheptadecan-9-yl)-1,3,2-dioxaborolane (**29**) (1.62 g, 3.84 mmol). ^1H NMR spectroscopy of the crude mixture after oxidation showed a mixture containing around 40% of 2,2-dioctyldecan-1-ol. Determination of the product ratio is discussed in the Supporting Information.

*(±)-2-(3-Methyl-2-phenylbutan-2-yl)-1,3,2-dioxaborinane (**36**).* A dry 100 mL flask equipped with a magnetic stirrer bar and stopcock was flushed with nitrogen for 10 min. (±)-1-Phenylethyl diisopropylcarbamate (1.18 g, 4.74 mmol), prepared by the literature procedure,[21] and dry diethyl ether (20 mL) were added, and the solution cooled to −78 °C using a dry ice acetone bath. *sec*-BuLi (1.3 M in 92:8 cyclohexane/hexane, 4.0 mL, 5.21 mmol) was added dropwise over 10 min, and the solution stirred for a further 20 min. To this was added a cold solution of 2-isopropyl-1,3,2-dioxaborinane[22] (0.92 g, 7.2 mmol) in diethyl ether (10 mL) dropwise over 10 min with vigorous stirring. The mixture was left to come to room temperature slowly as the dry ice/acetone bath gradually warmed. After stirring for 16 h, the mixture was cooled to 0 °C and saturated ammonium chloride solution (20 mL) was added. The aqueous layer was extracted with diethyl ether (3 × 15 mL), and the combined organic extracts were washed with water (15 mL) and brine (15 mL) and concentrated under reduced pressure. Methanol (20 mL) was added, and the mixture was left in the freezer for 1 h, whereupon some impurities precipitated out. After filtration of the impurities and evaporation of the methanol, diethyl ether (20 mL) was added. The supernatant layer was taken, and the diethyl ether evaporated under reduced pressure to give the essentially pure *title compound* (0.85 g, 77%) as a light yellow oil (Found (TOF-EI): M^+, 232.1634. $C_{14}H_{21}BO_2$ requires 232.1635); δ_H (400 MHz; $CDCl_3$) 7.39−7.35 (2 H, m), 7.27 (2 H, app. t, *J* 7.7), 7.12 (1 H, tt, *J* 7.2, 1.2), 4.00−3.94 (4 H, m), 2.40 (1 H, app. septet, *J* 6.8), 1.90−1.83 (2 H, m), 1.16 (3 H, s), 0.98 (3 H, d, *J* 6.8), and 0.54 (3 H, d, *J* 6.8); δ_C (125 MHz; $CDCl_3$) 147.8 (C), 127.8 (CH), 127.2 (CH), 124.5 (CH), 61.8 (CH_2), 33.8 (CH), 27.3 (CH_2), 20.5 (CH_3), 16.5 (CH_3), and 13.4 (CH_3); δ_B (96 MHz; $CDCl_3$) 29.5; $\nu_{max.}$ (neat) 2963, 1482, 1274, and 1159 cm^{-1}; *m*/*z* (EI) 232 (M^+, 69%), 189 (100), 117 (92), 105 (99), 84 (100).

*(±)-2,3-Dimethyl-2-phenylbutan-1-ol[8] (**34**) by Homologation of **36**.* The reaction was carried out using **Method A**, to give the crude product (85:15 ratio of migrated/nonmigrated product by ^1H NMR spectroscopy), which was purified by column chromatography on silica (95:5 petroleum ether/ethyl acetate (100 mL), followed by 90:10 petroleum ether/ethyl acetate (200 mL)) to give the *title compound* (0.44 g, 73%) as a colorless oil; δ_H (400 MHz; $CDCl_3$) 7.39−7.32 (4 H, m), 7.22 (1 H, app. tt, *J* 6.8, 1.8), 3.90 (1 H, d, *J* 10.9), 3.61 (1 H, d, *J* 10.9), 2.09 (1 H, app. septet, *J* 6.8), 1.28 (3 H, s), 1.16 (1 H, br), 0.98 (3 H, d, *J* 6.8), and 0.64 (3 H, d, *J* 6.8); δ_C (125 MHz; $CDCl_3$) 145.1 (C), 128.4 (CH), 127.0 (CH), 126.1 (CH), 70.8 (CH_2), 46.5 (C), 34.3 (CH), 18.0 (CH_3), 17.4 (CH_3), and 15.7 (CH_3); $\nu_{max.}$ (neat) 3399, 3089, 3058, 2971, 1600, 1498, 1467, 1444, and 1374 cm^{-1}; *m*/*z* (EI) 178 (M^+, 10%), 147 (100), 135 (100), 117 (100), 106 (100), 91 (100), 84 (100), 77 (88), 65 (34), and 57 (75).

*(±)-2,3-Dimethyl-2-phenylbutan-1-ol[8] (**34**) and (±)-3-Methyl-2-phenylbutan-2-ol[23] (**37**) by Homologation of **35**.* A dry 100 mL round bottomed flask equipped with a stopcock and magnetic stirrer was flushed with nitrogen for 10 min. The tertiary alkylboronic ester **35**[8] (0.73 g, 2.8 mmol), dry THF (15 mL), and dibromomethane (0.24 mL, 0.59 g, 3.4 mmol) were added, and the solution was cooled to −78 °C using a dry ice/acetone bath. *n*-BuLi in hexanes (2.1 mL, 1.5 M, 3.1 mmol) was added dropwise over 30 min with vigorous stirring. The solution was stirred for 30 min, the cooling bath was removed, and the mixture was stirred for 1 h more. The reaction mixture was cooled to 0 °C, and 3 M aqueous NaOH solution (10 mL) was added dropwise. Once the initial vigorous reaction had ceased, aqueous hydrogen peroxide solution (30% by weight, 6 mL) was added dropwise, and the solution was heated to 50 °C for 2 h. The aqueous layer was saturated with potassium carbonate, and the mixture was extracted with diethyl ether (3 × 25 mL). The organic extract was washed with brine (2 × 20 mL) and distilled water (2 × 20 mL), dried over magnesium sulfate, and filtered. The volatiles were evaporated under vacuum to give the crude product (50:50 ratio of **34**:**37** by ^1H

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NMR spectroscopy), which was purified by column chromatography on silica (95:5 petroleum ether/ethyl acetate (100 mL), followed by 90:10 petroleum ether/ethyl acetate (200 mL)) to give (±)-2,3-dimethyl-2-phenylbutan-1-ol (**34**) (0.19 g, 38%) and (±)-3-methyl-2-phenylbutan-2-ol (**37**) (0.11 g, 24%), both as colorless liquids. Data for (±)-**37** δ_H (400 MHz; $CDCl_3$) 7.44 (2 H, dd, *J* 8.2, 1.3), 7.35 (2 H, app. t, *J* 7.6), 7.25 (1 H, tt, *J* 7.3, 1.3), 2.04 (1 H, app. septet, *J* 7.3), 1.86 (1 H, br s), 1.55 (3 H, s), 0.92 (3 H, d, *J* 6.8), and 0.84 (3 H, d, *J* 6.9); δ_C (125 MHz; $CDCl_3$) 147.9 (C), 127.9 (CH), 126.4 (CH), 125.3 (CH), 76.8 (C), 38.6 (CH), 26.7 (CH_3), 17.5 (CH_3), and 17.2 (CH_3); $\nu_{max.}$ (neat) 3458, 2973, 1495, 1446, and 1373 cm^{-1}; *m*/*z* (EI) 164 (M^+, 4%), 147 (95), 131 (69), 122 (100), 105 (98), 91 (97), and 77 (96).

■ ASSOCIATED CONTENT

Supporting Information

Copies of ^1H, ^{13}C, and ^{11}B NMR spectra for all compounds. Calculated thermodynamic and structural parameters for all compounds discussed in the computational section of this work. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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