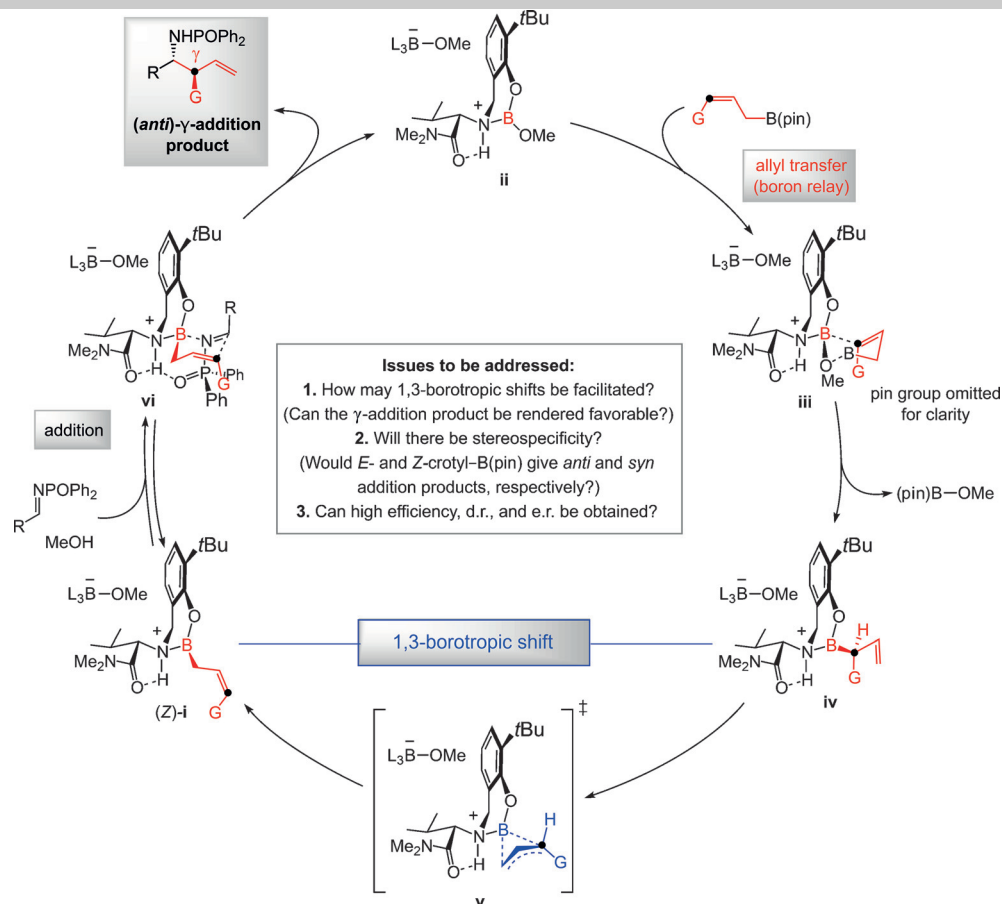
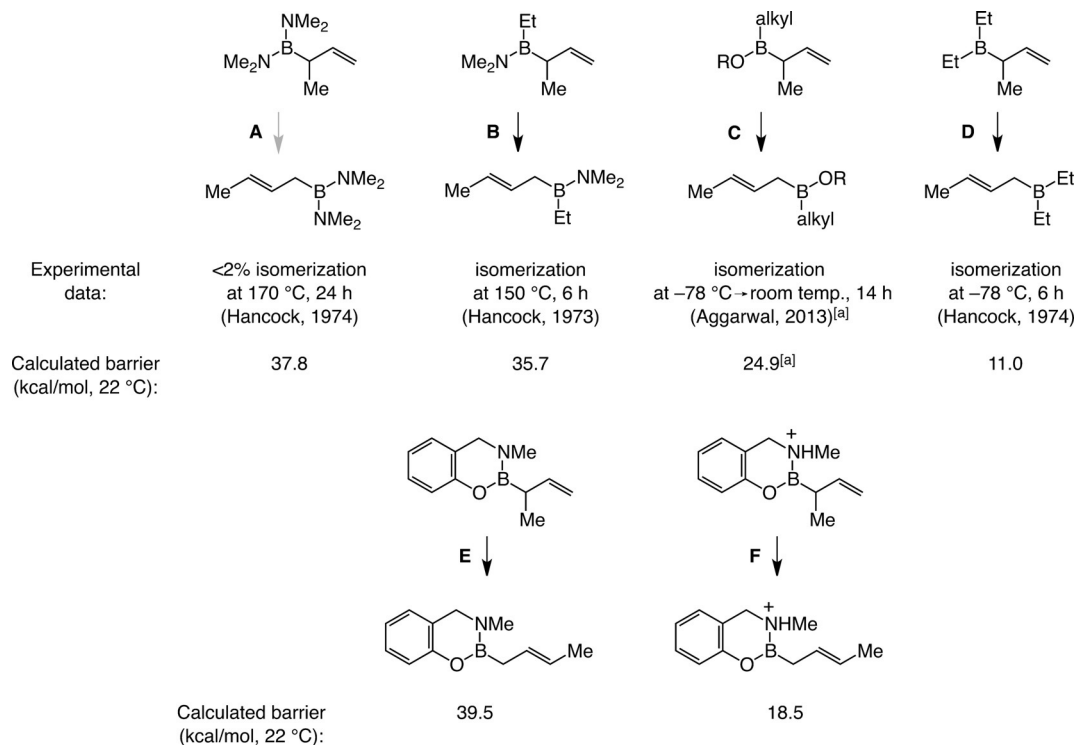




Scheme 2. A 1,3-borotropic shift ($\text{iv} \rightarrow \text{v} \rightarrow (\text{Z})\text{-i}$) might give rise to the preferential formation of γ -addition products.

place at -78°C (6 h). Cross-over experiments indicate that the rearrangements are intramolecular.^[6a,b] Congruent with Hancock's conclusions is the proposal by Aggarwal^[7a] and co-workers that an (alkoxy)-alkylboron species (**C**) rearranges at lower temperature ($-78 \rightarrow 22^\circ\text{C}$, 14 h); the energy barrier calculated by us for this transformation supports the suggested scenario (Scheme 3).^[8] In the systems more directly relevant to the studies below (**E** and **F**; Scheme 3), the ammonium salt derivative (i.e., **F**) should rearrange more readily. Still, the high α -selectivities in the original studies^[2] (see Scheme 1b) mean that the boron atom within a chiral complex (e.g., **iv**; Scheme 2) is not Lewis acidic enough for swift borotropic shifts.

The idea of deploying a Lewis acidic co-catalyst



Scheme 3. Previous observations and calculations performed in this study (with the $\omega\text{B97XD/Def2TZVPP}$ functional, solvation in toluene) point to a significant substituent influence on the rate of the borotropic shift (the more π -donating the substituent, the slower the rearrangement). [a] For the experimental observation: alkyl = *n*Bu, R = C(Me)₂C(Me)₂OLi. For the calculations: alkyl = Et, R = Me.

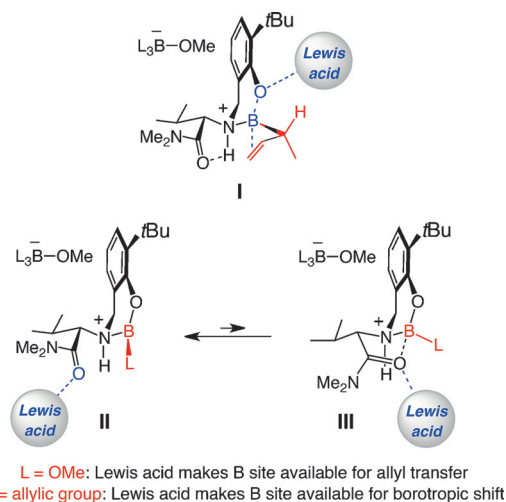
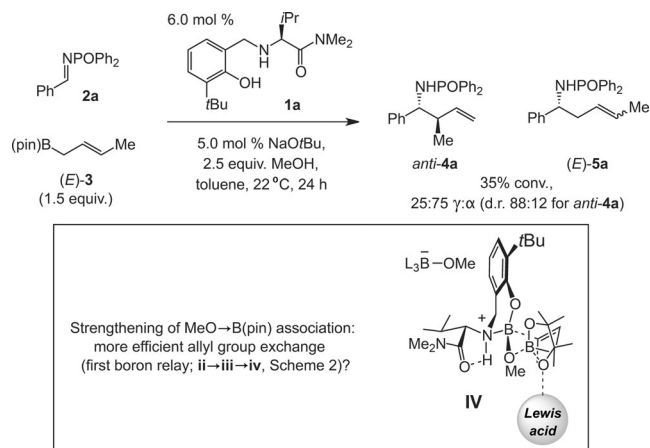


Figure 1. Possible ways through which a Lewis acid may facilitate borotropic shifts.

was based on the following reasoning: First, as illustrated in **I** (Figure 1), by coordination to the aryloxy arm of the chiral complex, the Lewis acidity of the boron center and thus the rate of isomerization could be enhanced (i.e., **iv** → **v** → (*Z*)-**i**; Scheme 2). Second, association of the amide carbonyl group with a Lewis acid (**II**, Figure 1) could disrupt its coordination with the boron atom (**III**), facilitating allyl exchange (L = OMe) and/or a 1,3-borotropic shift (L = allylic group). DFT calculations^[8] suggested that complex **III** (without the Lewis acid) is favored, although the reaction most probably proceeds via **II** (and/or the complex without a bound Lewis acid).

Our initial foray uncovered another problem (Scheme 4): Under the previous conditions,^[2] reaction of *E*-configured crotyl-B(pin) ((*E*)-**3**) with imine **2a** resulted in only 35 % conversion after 24 h [γ/α = 25:75; 88:12 diastereomeric ratio (d.r.) for the γ -product]. We surmised that the low rate might be due to the fact that the methyl substituent [vs. a terminal olefin in Scheme 1b or with allyl-B(pin)] causes the chiral allylboron intermediate to be generated inefficiently because of steric factors (i.e., **ii** → **iii** → **iv**; Scheme 2). We wondered if coordination of the same Lewis acidic co-catalyst to the B(pin) moiety^[9] might strengthen chelation of its boron center with the methoxy unit of the chiral complex to accelerate allyl transfer as well (Scheme 4).

Several Lewis acidic metal salts were screened,^[8] resulting in the discovery that with 2.5 mol % Zn(O*t*Bu)₂ (Scheme 5a) not only may efficiency be improved substantially (> 98 % vs. 35 % conv. with NaO*t*Bu; Scheme 4), but also the α -addition product was generated predominantly (γ/α = 25:75) in 89:11 d.r. and 95:5 enantiomeric ratio (e.r.). The catalyst's *tert*-butyl substituent meant that a diminutive co-catalyst could be better. Indeed, with the smaller Zn(OMe)₂, the γ/α ratio (90:10) and the dia-

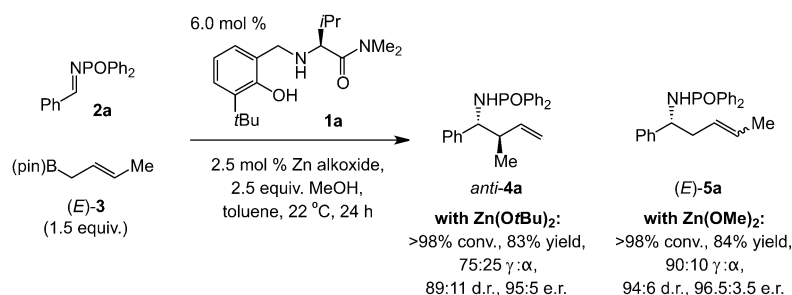


Scheme 4. Possible role of a Lewis acidic co-catalyst in facilitating the initial allyl transfer.

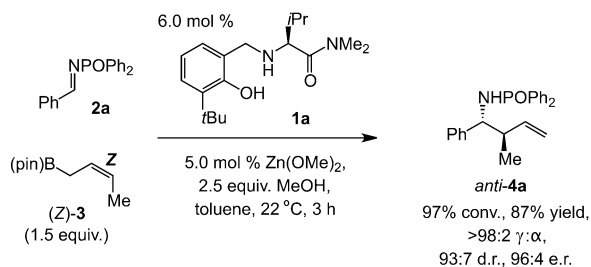
stereo- and enantioselectivity were higher still (94:6 d.r. and 96.5:3.5 e.r.).^[10] The transformation with the *Z*-configured organoboron reagent proceeded to 97 % conversion in three hours (vs. 24 h with (*E*)-**3**), furnishing the same diastereomer as with the *E* isomer in > 98 % γ -selectivity, 93:7 d.r., and 96:4 e.r. (Scheme 5b). Control experiments indicated that (*E*)- and (*Z*)-**3** do not undergo isomerization.

The data in Scheme 6 offer further insight.^[11] Reaction with deuterium-labeled allyl-B(pin) **6** led to high α -selectivity when NaO*t*Bu was present (96:4 [D₂]-**7a**/[D₂]-**7b**; Scheme 6a) but with Zn(OMe)₂, the γ -product was formed preferentially (γ/α = 70:30). The impact of the co-catalyst thus extends to the unsubstituted organoboron system. The γ/α ratio is lower (than with (*E*)- or (*Z*)-**3**; Scheme 5), likely because the less hindered chiral allylboron intermediate (see

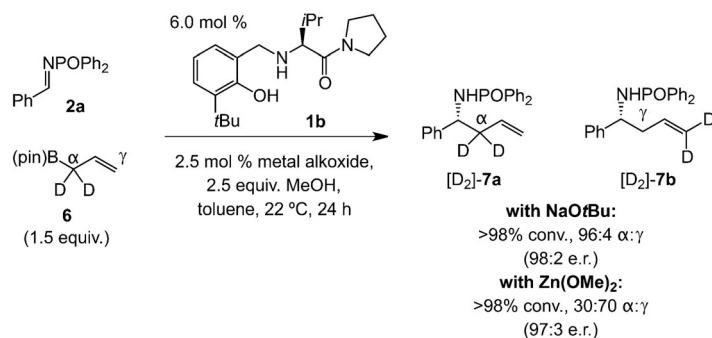
a. The effect of Zn alkoxides as co-catalysts:



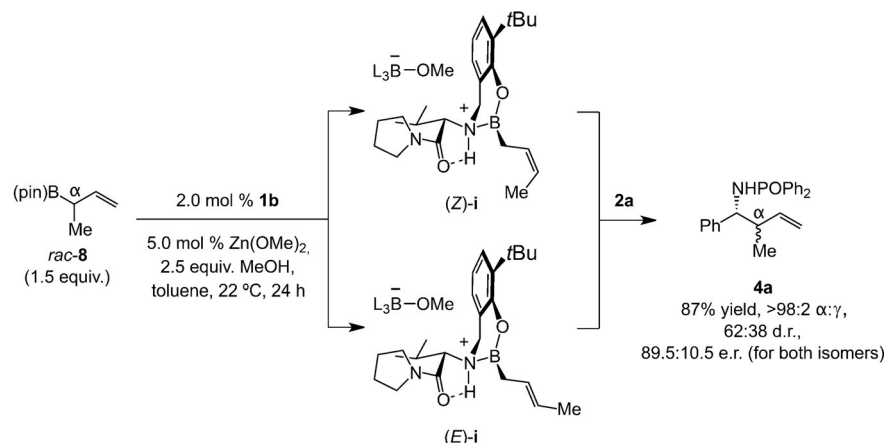
b. The influence of organoboron reagent stereochemistry:



Scheme 5. The influence of Zn(OMe)₂ and the crotyl-B(pin) stereochemistry on efficiency and selectivity.

a. $\text{Zn}(\text{OMe})_2$ promotes 1,3-boryl shift regardless of organoboron structure:

b. High diastereoselectivity is not due to higher activity of Z-allylboron:

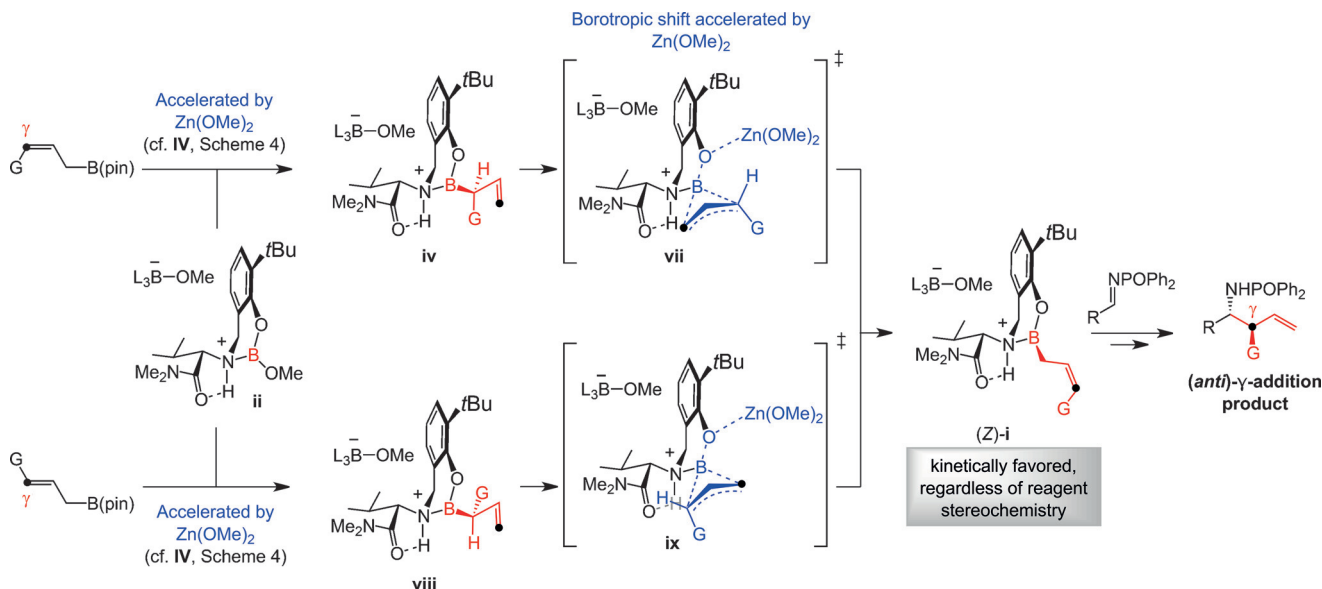


Z and E chiral organoboron intermediates afford *anti*- and *syn*-**4a**, respectively:
High *anti* selectivity with Z- or E-crotylboron reagents due to kinetically preferred formation of (Z)-i.

Scheme 6. Experiments indicating that a) $\text{Zn}(\text{OMe})_2$ promotes the borotropic shift and that b) formation of the *anti* diastereomer with the E and Z organoboron reagent is due to a kinetic preference for the formation of the chiral Z-crotylboron intermediate.

iv, G = H) reacts faster with the imine, competing more easily with a borotropic shift. There is no steric or electronic impetus for isomerization (see above). Furthermore, with *rac*-**8**, the

chemistry, product identity does not originate from the E and Z chiral allylboron isomers reacting via different transition structures to give the same stereoisomer.^[4f]



Scheme 7. Rationale for the preferential generation of the Z-configured crotylboryl intermediate ((Z)-i), irrespective of the reagent stereochemistry.

The catalytic protocol has considerable scope (Scheme 8).^[11] Reactions were often complete with 2.0 mol % aminophenol **1b** and 5.0 mol % $\text{Zn}(\text{OMe})_2$ within three hours at ambient temperature. Aryl-substituted imines with various electronic attributes were converted into the desired products efficiently and selectively (**4a–4l**). Similar results were obtained with heterocyclic moieties, including those containing an oxygen (**4m, 4n**), sulfur (**4o, 4p**), or nitrogen substituent (**4q**). Additions to α,β -unsaturated aldimines needed more forcing conditions (**4r**). Transformations with alkyl-substituted imines were equally efficient and considerably γ -selective but less diastereo- and enantioselective. This may be attributed to the diminished rates of addition to the more electron-rich aliphatic substrates, allowing for alternative (uncatalyzed) pathways with different

kinetic attributes (i.e., different turnover-limiting steps) to become competitive; related arguments may apply to the reaction leading to *para*-dimethylaminoaryl-substituted **4i**. Other than the processes with commercially available crotyl-B(pin) reagent (**Z**)-**3**, the synthesis of **9** and especially that of chloro-substituted **10**^[14] underscore the method's reach and versatility.

Reactions are scalable (see **4k**, Scheme 8), and the ligands and organoboron reagents are easy to access and manipulate. In most cases, the phosphinoyl group renders the substrates and products crystalline and isolable without chromatography, and it is removable under mild conditions at low cost.^[2a] These characteristics compare favorably to the alternative strategies.^[4] Homoallylic amines are precursors to an array of important enantiomerically enriched N-containing molecules,

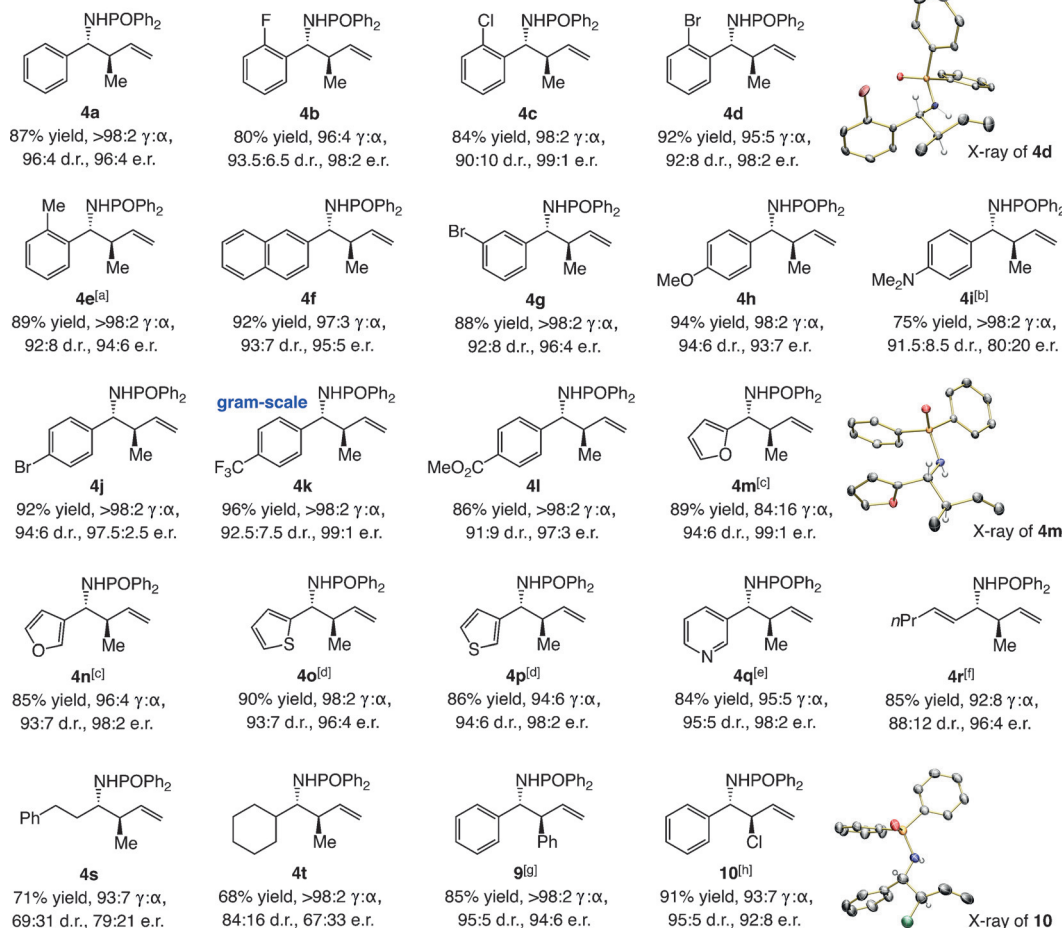
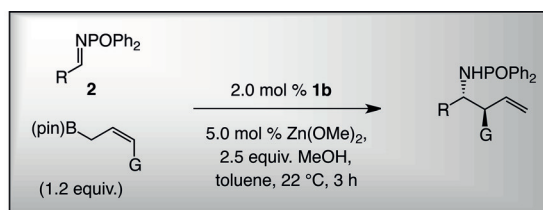
including β -amino acids.^[15,16]

The concepts elucidated here should find applications in the design of other efficient catalytic and stereoselective processes.

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Keywords: boron · borotropic shift · diastereoselective synthesis · enantioselective catalysis · homoallylic amines



Scheme 8. Products obtained from γ -, diastereo-, and enantioselective additions of different organoboron reagents (> 98% *E* for phenyl-substituted allylboronate and > 98% *Z* for the Cl-substituted reagent) to various aldimines. [a] **1b** (5.0 mol %). [b] Reaction time: 24 h. [c] 5 h. [d] 4 h. [e] With **1b** (10 mol %) and $\text{Zn}(\text{OMe})_2$ after 8 h. [f] With **1b** (12.5 mol %) and $\text{Zn}(\text{OMe})_2$ (7.5 mol %). [g] At 50 °C, 6 h. [h] **1b** (10 mol %) and $\text{Zn}(\text{OMe})_2$, 24 h. See the Supporting Information for details.

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- [11] Catalyst screening indicated that aminophenol **1b** generally delivers somewhat higher enantioselectivity than **1a**.
- [12] Initial isomerization of *rac*-**8** to (*E*)- and (*Z*)-**3** (prior to the first γ -addition to generate the chiral allylboron **iii**) is unlikely, as in that case, *anti*-**4a** would be formed with high diastereoselectivity. The stronger propensity of an aminophenol-based allylboron reagent to undergo a 1,3-borotropic shift is almost certainly due to its more Lewis acidic boron atom.
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