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Enantioselective synthesis of allylic boronates bearing a stereodefined (*E*)-alkenyl chloride by Cu-catalyzed borylation of allylic *gem*-dichlorides

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Chiral α,γ-substituted allyl boron reagents are valuable tools in organic synthesis. However, asymmetric catalytic strategies for synthesising this type of compound bearing a stereodefined alkenyl chloride are underdeveloped. Here we report a copper-catalyzed enantioselective borylation of allylic *gem*-dichlorides that provides optically active allylic boronates bearing an (*E*)-configured alkenyl chloride with high levels of enantioselectivity and *E*-selectivity. These enantioenriched allyl boronates serve as versatile building blocks for different stereospecific reactions, including their conversion into chiral propargyl alcohols and the diastereoselective addition to ketones to afford enantioenriched allylic chlorohydrins. DFT calculations provide mechanistic insight, revealing key noncovalent interactions that rationalize the observed stereocontrol. This study expands the synthetic utility of allylic boronates and offers a mechanistically informed approach to asymmetric catalysis involving *gem*-dichloride substrates.

Introduction

Chiral allyl boron reagents are versatile reagents in asymmetric synthesis, owing to their high stereospecificity in allylation reactions.[1,2] In particular, the stereodefined substitution at both the α-position and the double bond enables precise control over all stereochemical elements (enantioselectivity, *E*/*Z* geometry, and *syn*/*anti* diastereoselectivity) of the resulting homoallylic alcohols, *via* closed chair transition-state structures that minimize nonbonded steric interactions (Scheme 1a).[3] Since the pioneering work by Matteson[4,5] and Hoffman,[6–9] the stereoselecive synthesis of α-chiral allylboron compounds has undergone remarkable development. Notable advances include Aggarwal's lithiation–borylation strategy using Hoppe-type carbamates,[10,11] Morken's enantioselective cross-coupling of vinyl electrophiles and achiral geminal bisboronates[12] and platinum-catalyzed diboration of 1,3-dienes,[13,14] Szabó's asymmetric homologation of alkenylboronic acids with diazomethanes[15] and the nickel-catalysed asymmetric 1,1-difunctionalization of terminal alkenes, recently reported by Yin[16] (Scheme 1b). While these strategies enable efficient access to chiral allylboron compounds with carbon-based double bond substituents, methods for preparing chiral allylboron reagents bearing a stereodefined alkenyl chloride remain scarce. Burns reported a stepwise protocol for synthesizing a chiral (*Z*)-γ-chloroallylboronic ester *via* a chiral pool strategy has been reported (Scheme 1c).[17] However, catalytic asymmetric approaches to access chiral allylboron reagents incorporating a stereodefined alkenyl chloride remain largely unexplored. We reasoned that introducing this structural motif would be particularly valuable, as it would allow further functionalization while furnishing, upon carbonyl allylation, a synthetically versatile chiral allylic chlorohydrin with broad potential for downstream functionalization.

Copper-catalyzed enantioselective allylic borylation represents another efficient tool for the preparation of α-chiral allyl boron compounds (Scheme 1d). However, this powerful transformation has generally been applied to primary allylic substrates[18–20] and 1-trifluoromethyl alkenes,[21–23] where control over the geometry of the resulting double bond is not an issue. Ito and Hoveyda elegantly reported the *enantio*- and diastereoslective borylation of secondary allylic *gem*-difluorides that provides allylic boronates with a trisubstituted alkenyl fluoride with high enantioselectivity and *Z*-selectivity.[24] Importantly, the presence of a large R substituent at the allylic carbon was necessary to achieve high stereocontrol. Indeed, when a primary allylic *gem*-difluoride (R = H) was used, the corresponding product was obtained with high enantioselectivity but as a 1 : 1 mixture of *Z* : *E* isomers. This result already highlighted the difficulties associated with the concomitant control over both the enantioselectivity an olefin geometry when a 1,1-disubstituted allylic electrophile is used.[25]

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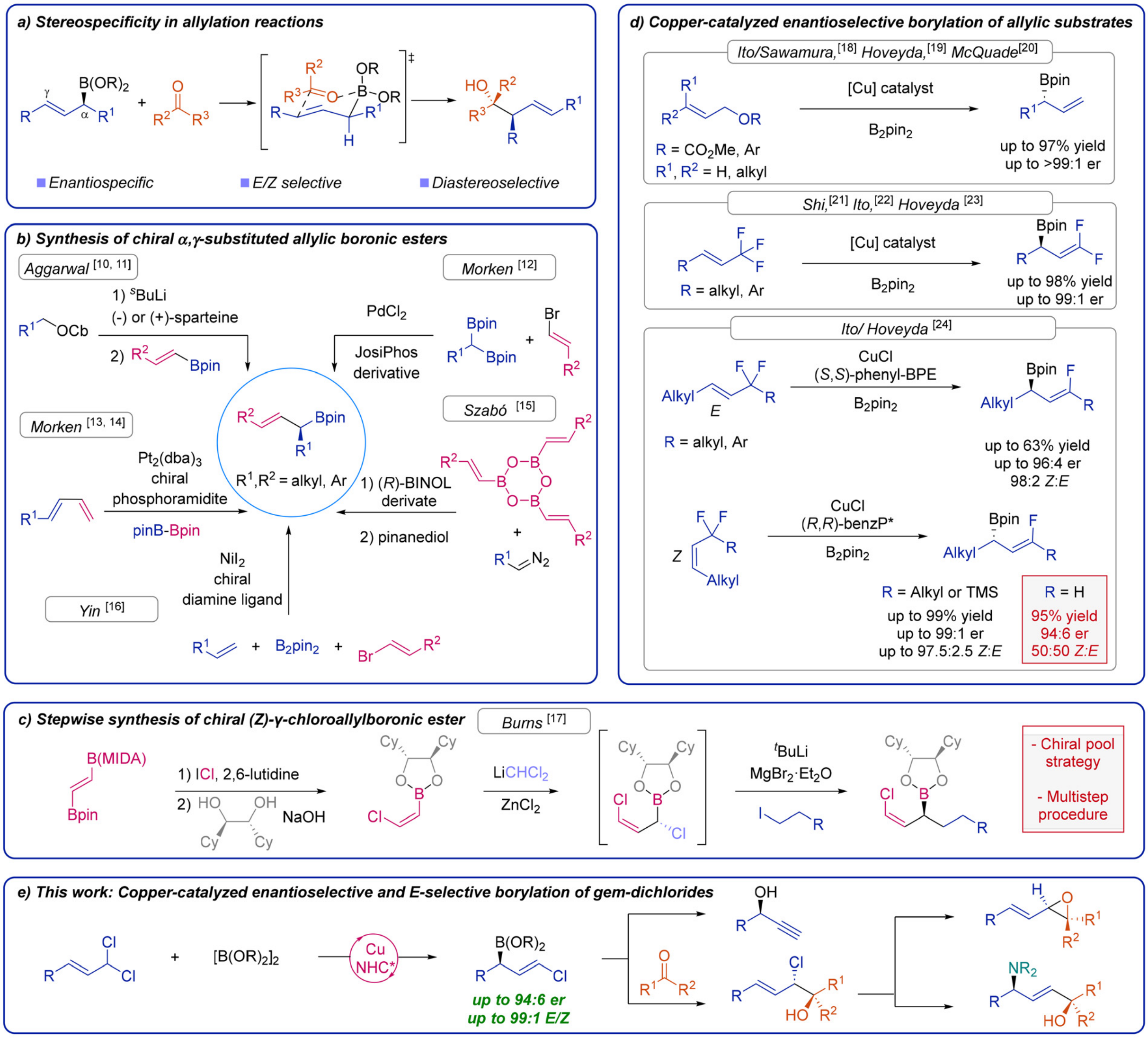


Scheme 1 Synthesis and applications of chiral α,γ-substituted allylic boronic esters. [a] Synthetic value in allylation reactions. [b] State of the art. [c] Synthesis of (*Z*)-γ-chloroallylboronic ester *via* chiral pool strategy. [d] Copper-catalyzed enantioselective allylic borylation. [e] Copper-catalyzed *enantio*- and *E*-selective borylation of *gem*-dichlorides.

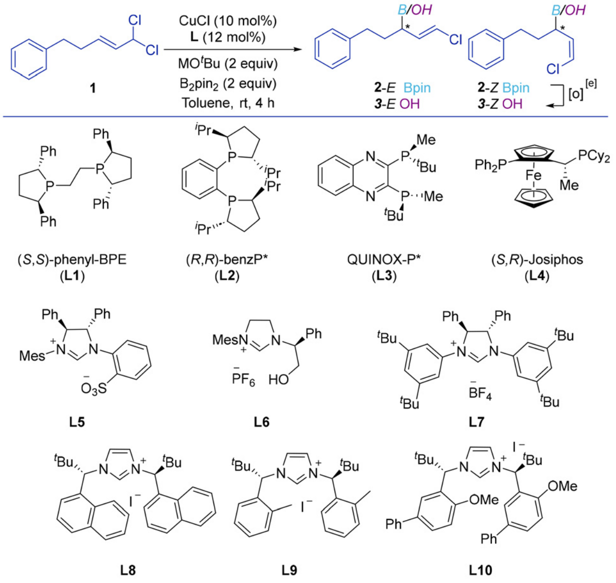
Considering the synthetic potential of α-chiral allylic boronates bearing a stereodefined disubstituted alkenyl chloride, we set out to explore the stereoselective borylation of allylic *gem*-dichlorides. Herein, we disclose a catalytic strategy that enables the efficient synthesis of γ-chloro-substituted α-chiral allylic boronates with high enantioselectivity and excellent *E*-selectivity. The transformation is mediated by a chiral NHC-Cu complex, and the products serve as versatile intermediates for the preparation of diverse non-racemic structures, including allylic chlorohydrins and their derivatives (Scheme 1e).

Results and discussion

Reaction optimization

We began our study by exploring the reaction between (*E*)-(5,5-dichloropent-3-en-1-yl)benzene (**1**) and B_2pin_2, using NaO^{t}Bu as the base and toluene as the solvent. To facilitate product analysis, borylation was coupled with an oxidation step to provide the corresponding allylic alcohol (Table 1). We first evaluated bisphosphine ligands since they proved to be optimal in previous studies on the borylation of other allylic substrates.[18,21,22,24] However, the use of ligands such as (*S*,*S*)-phenyl-BPE (**L1**) or (*R*,*R*)-benzP* (**L2**) resulted in no selectivity (Table 1, entries 1 and 2). QUINOX-P* (**L3**) provided some sort of *E* selectivity (79 : 21 *E* : *Z*), although both *E* and *Z* products were obtained as nearly racemic mixtures (Table 1, entry 3). Further studies with catalysts derived from (*S*,*R*)-Josiphos (**L4**) and related bisphosphine ligands (entry 4 and SI) further revealed the inefficacy of these systems in imparting any appreciable level of stereoselectivity. We next explored the use of sulfonate-bearing NHC ligands, which had proven highly efficient in our previous studies on the stereoselective allylboration of different unsaturated hydrocarbons with allylic

Table 1 Optimization studies



Entry[a]	L	M	**2*E*** : **2*Z*** ratio[b]	Yield (**3*E*** + **3*Z***)[c]	**3-*E*** er[d]
1	**L1**	Na	55 : 45	77	68 : 32
2	**L2**	Na	47 : 53	41	64 : 36
3	**L3**	Na	79 : 21	53	35 : 65
4	**L4**	Na	40 : 60	89	68 : 32
5	**L5**	Na	25 : 75	77	48 : 52
6	**L6**	Na	46 : 54	80	50 : 50
7	**L7**	Na	83 : 17	63	53 : 47
8	**L8**	Na	92 : 8	98	89 : 11
9	**L9**	Na	88 : 12	75	82 : 18
10	**L10**	Na	64 : 36	41	26 : 74
11	**L8**	Li	82 : 18	83	81 : 19
12	**L8**	K	97 : 3	80	89 : 11

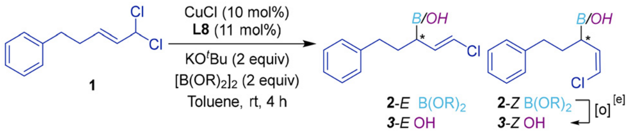
[a] Reaction conditions: **1** (0.2 mmol), B$_2$pin$_2$ (0.4 mmol), CuCl (10 mol%), ligand (12 mol%), base (0.4 mmol), toluene (1.5 mL) at rt. [b] Determined by GC analysis of reaction crude. [c] Yield of isolated product. [d] Enantiomeric ratio was determined by chiral SFC analysis of the alcohol **3** derived from the obtained boronate. [e] NaOH [2 M] (5 equiv.), H$_2$O$_2$ (8 equiv.), MeOH.

gem-dichlorides.[26–28] Some sort of selectivity towards the formation of the *Z* isomer (up to 25 : 75 *E* : *Z*) was observed when ligand **L5** and related systems were used, although products were obtained as nearly racemic mixtures (entry 5 and SI). Similarly, Mauduit-type ligand **L6** and C2-symmetric NHC ligands (*e.g.* **L7**) bearing a chiral backbone provided low levels of stereoselectivity (entries 6, 7 and SI). A significant improvement was observed when we tested Kündig's type NHC ligand **L8**, which selectively provided the *E*-isomer as the major product (92 : 8 *E* : *Z*) with a promising 89 : 11 er (entry 8). *ortho*-Tolyl (**L9**) and biphenyl (**L10**) derivatives were also tested, although poorer results were obtained in both cases (entries 9 and 10). Once having identified **L8** as the optimal ligand, we tested different metal *tert*-butoxide bases. When LiO^{t}Bu was used both the diastereo- and enantioselectivity decreased (entry 11). In contrast, the use of KO^{t}Bu delivered the product with the same enantioselectivity as NaO^{t}Bu, but with an increased 97 : 3 *E* : *Z* selectivity (entry 12).

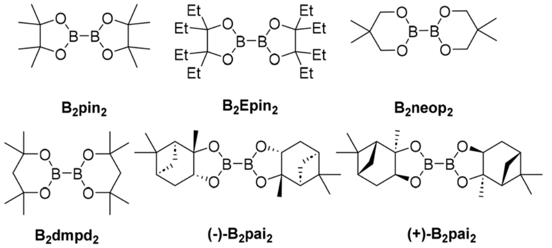
The influence of the diboron reagent on the reaction outcome was next investigated (Table 2). The use of B$_2$Epin$_2$ instead of B$_2$pin$_2$ did not lead to significant differences (Table 2, entries 1 and 2). Less sterically hindered six-membered boron reagents such as B$_2$neop$_2$ and B$_2$dmpd$_2$ resulted in diminished enantioselectivity and *E*-selectivity (Table 2, entries 3 and 4). In contrast, an improved outcome was observed when commercially available bicyclic B$_2$pai$_2$ compounds were used. While (−)-B$_2$pai$_2$ afforded the product with enantioselectivity similar to B$_2$pin$_2$ (Table 2, entry 5), the use of (+)-B$_2$pai$_2$ led to an increase in both enantioselectivity (91 : 9 er) and *E*-selectivity (98 : 2 *E* : *Z*) (Table 2, entry 6).

To assess whether the chirality of the B$_2$pai$_2$ reagent has an influence on the overall stereochemical outcome, we performed a series of control experiments (Table 3). In the absence of chiral ligand **L8**, the selectivity of the alkenyl chloride was reversed and enantioselectivity was lost (Table 3, entry 1). Likewise, the use of IMesCuCl as the catalyst using the chiral diboron compound led to a 1 : 2 mixture of *E* : *Z* isomers, with product **3-*E*** obtained as a racemate (Table 3, entry 2). Finally, no product was formed without the Cu catalyst (Table 3, entries 3 and 4). Taken together, these results indicate that *enantio*- and *E*-selectivity are governed by the chiral Cu-complex, while the structure of the diboron compound has just a minor effect, likely attributed to steric hindrance.

Table 2 Screening of diboron compounds

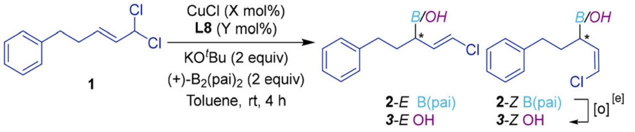


Entry[a]	[B(OR)$_2$]$_2$	**2*E*** : **2*Z*** ratio[b]	Yield (**3*E*** + **3*Z***)[c]	**3-*E*** er[d]
1	B$_2$pin$_2$	97 : 3	80	89 : 11
2	B$_2$Epin$_2$	96 : 4	80	88 : 12
3	B$_2$neop$_2$	75 : 25	40	71 : 29
4	B$_2$dmpd$_2$	70 : 30	44	66 : 34
5	(−)-B$_2$pai$_2$	92 : 8	69	89 : 11
6	(+)-B$_2$pai$_2$	98 : 2	97	91 : 9



[a] Reaction conditions: **1** (0.1 mmol), [B(OR)$_2$]$_2$ (0.2 mmol), CuCl (10 mol%), **L8** (11 mol%), KO^{t}Bu (0.2 mmol), toluene (0.75 mL) at rt. [b] Determined by GC analysis of reaction crude. [c] Yield of isolated product. [d] Enantiomeric ratio was determined by chiral SFC analysis of the alcohol **3** derived from the obtained boronate. [e] NaOH [2 M] (5 equiv.), H$_2$O$_2$ (8 equiv.), MeOH.

Table 3 Analysis of the effect of (+)-B_2pai_2 chirality on the stereochemical outcome of the reaction



Entry[a]	X	Y	2*E* : 2*Z* ratio[b]	1 recovered (%)	Yield (3*E* + 3*Z*)[c]	3-*E* er[d]
1	10	0	32 : 68	9	51	52 : 48
2	10[f]		33 : 67	—	80	52 : 48
3	0	10	—	80	—	—
4	0	0	—	78	—	—

[a] Reaction conditions: **1** (0.1 mmol), (+)-$B_2(pai)_2$ (0.2 mmol), CuCl (10 mol%), **L8** (11 mol%), KO^{t}Bu (0.2 mmol), toluene (0.75 mL) at rt. [b] Determined by GC analysis of reaction crude. [c] Yield of isolated product. [d] Enantiomeric ratio was determined by chiral SFC analysis of the alcohol **3** derived from the obtained boronate. [e] NaOH [2 M] (5 equiv.), H_2O_2 (8 equiv.), MeOH. [f] IMesCuCl was used.

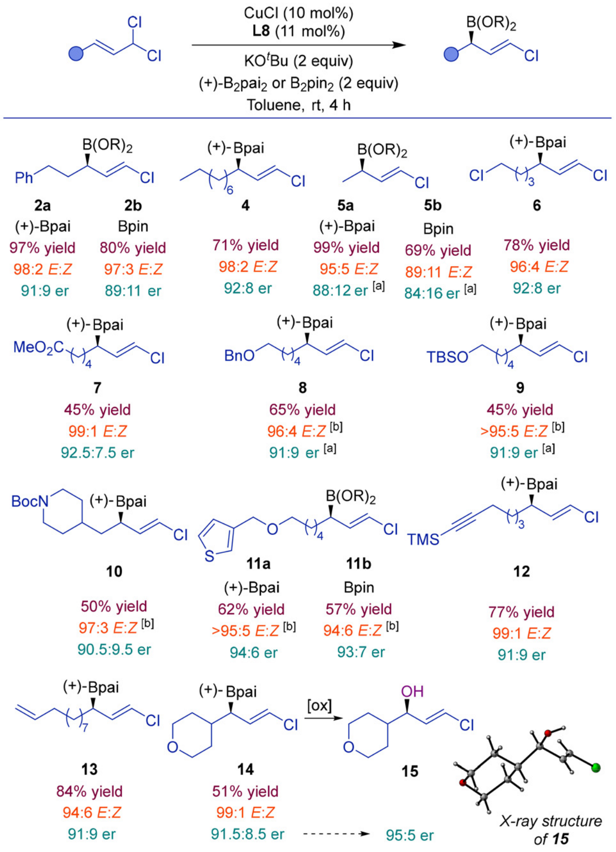
Substrate scope

With the optimal conditions for the asymmetric borylation of *gem*-dichlorides in hand, we set out to explore the scope of the reaction by using either B_2pin_2 or (+)-B_2pai_2 as the boron source (Scheme 2). The reaction proved to be efficient with allylic *gem*-dichlorides bearing long and short alkyl chains such as octyl (**4**) or methyl (**5**) groups. In both cases the corresponding product was obtained with excellent *E*-selectivity. The slightly lower enantioselectivity observed for the Me-substituted substrate is likely due to the reduced steric demand of the methyl group.[29] Notably, the reaction showed a remarkable functional group tolerance. Substrates featuring functionalities such as chlorine (**6**), ester (**7**), ether (**8**), silylether (**9**), carbamate (**10**), an heterocyclic ring (**11**), an alkyne (**12**) or even a terminal olefin (**13**) could be used providing the corresponding allylic boronates with total chemoselectivity, excellent *E*-selectivity and good enantioselectivity up to 94 : 6 er. Allylic *gem*-dichlorides featuring a secondary cyclic substituent were also compatible as demonstrated with the synthesis of tetrahydro-2*H*-pyran derivative **14**. Olefin stereochemistry and absolute configuration could be determined by X-ray diffraction analysis of oxidation product **15** (derived from **14**), which confirmed the *E*-configuration of the alkenyl chloride and revealed the (*R*) absolute configuration of the products.[30] Notably, the enantiomeric ratio was further improved to 95 : 5 er upon crystallization.

Unfortunately, allylic *gem*-dichlorides bearing aryl substituents were not compatible with this transformation, most likely due to the limited stability of the corresponding aryl-substituted allylic boronates under the reaction conditions.

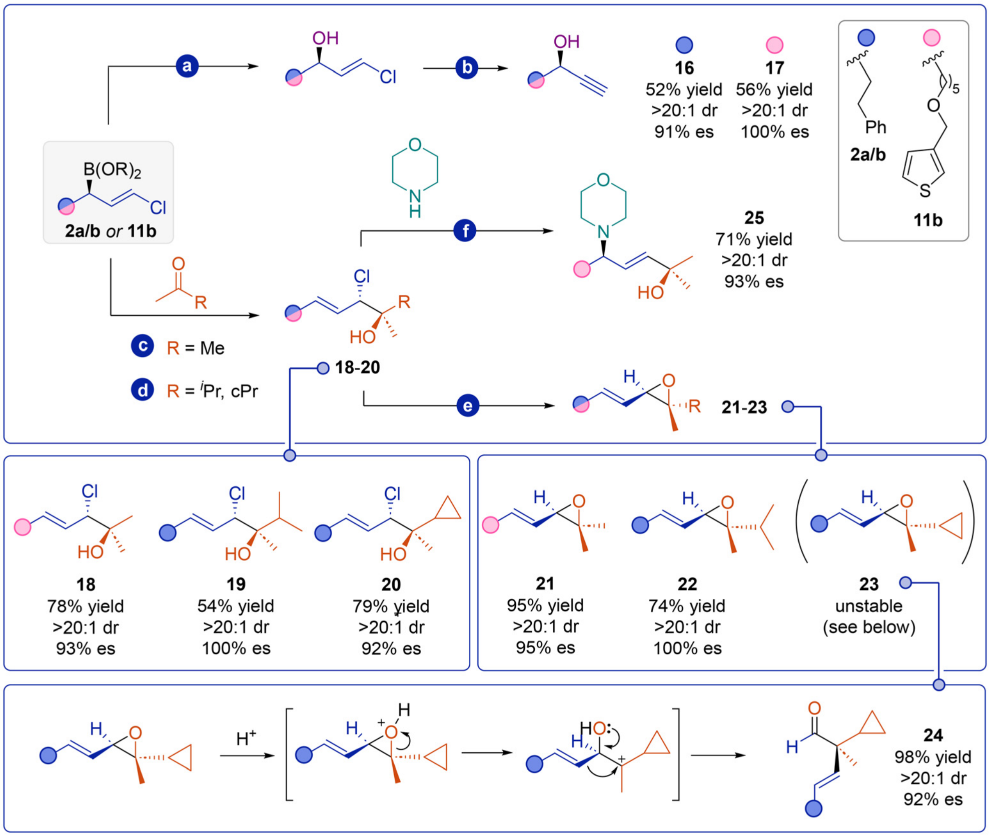
Synthetic modifications

The synthetic versatility of the products was demonstrated through several synthetic transformations (Scheme 3). The presence of an alkenyl chloride in the allyl alcohol structure makes these products excellent precursors for the synthesis of propargyl alcohols. By employing an LDA-mediated dehydrochlorination,[28] products **2a** and **11b** could be transformed into the corresponding chiral propargyl alcohols **16** and **17** without significant chiral erosion.



Scheme 2 Substrate scope. All reactions were performed on a 0.1 mmol scale under optimized conditions (Table 2, entry 6). Yield values refer to isolated products. Enantiomeric ratio was determined by chiral SFC analysis of the alcohol derived from the obtained boronate unless otherwise noted. [a] Enantiomeric ratio was determined by chiral SFC analysis of the benzoate-protected alcohol. [b] *E* : *Z* ratio was determined by ^{1}H NMR analysis of the corresponding alcohol.

This method can be also applied to the synthesis of homoallyl alcohols featuring a chloro-substituted allylic tertiary stereogenic carbon center, *i.e.* allylic chlorohydrins. The obtained allylic boronic esters did not react directly with carbonyl compounds. Nevertheless, by *in situ* hydrolysis to the corresponding allylic boronic acid using sodium periodate and ammonium acetate in a 2 : 1 acetone : water mixture,[31] allylic boronate **11** was converted into allylic chlorohydrin **18** in 78% yield as a single *E*-isomer. Notably, compound **18** was obtained with total enantiospecificity (es) despite the common configurational lability of secondary allylic halides.[32] The reaction is also amenable to the use of other carbonyl compounds different than acetone. By using THF instead of acetone, 3-methylbutan-2-one and 1-cyclopropylethan-1-one could be allylated with **2** affording products **19** and **20** with excellent diastereoselectivity and enantiospecificity.



Scheme 3 Synthetic modification of products. Conditions: (a) **2a** or **11b** (1 equiv.), NaOH [2 M] (5 equiv.), H_2O_2 (8 equiv.), MeOH, rt, 2 h. (b) ^{n}BuLi (3.5–10 equiv.), $^i Pr_2NH$ (3.7–10 equiv.), THF, −78 °C, 30 min. (c) **11b** (1 equiv.), $NaIO_4$ (3.1 equiv.), NH_4OAc (3.5 equiv.), acetone : H_2O 2 : 1, rt, 16 h. (d) **2b** (1 equiv.), $NaIO_4$ (3.1 equiv.), NH_4OAc (3.5 equiv.), 3-methylbutan-2-one (5 equiv.), THF : H_2O 2 : 1, rt, 16 h. (e) K_2CO_3 (3 equiv.), MeCN, 80 °C, 16 h. (f) Morpholine (5 equiv.), MeCN, 80 °C, 16 h.

The obtained chlorohydrins also represent valuable building blocks for accessing a range of different important chiral enantioenriched structures. Base-promoted intramolecular substitution provided chiral vinyl epoxides **21–23** in high yields and again with excellent enantiospecificity. Relative configuration could be determined by NOESY analysis of product **22**. Notably, attempts to purify compound **23** by silica gel chromatography resulted in the enantiospecific formation of aldehyde **24**, likely *via* a semipinacol-type rearrangement. This transformation is presumably facilitated by the stability of the cyclopropylcarbinyl cation intermediate.[33,34]

The presence of a stereodefined allylic chloride in the structure makes this compound also valuable for intermolecular allylic substitution reactions. Reaction of **18** with morpholine proceeded *via* an S_N2' process, affording 1,4-aminoalcohol **25** with excellent regioselectivity and enantiospecificity. This outcome likely results from a pathway that minimizes 1,3-allylic strain.[35]

DFT calculations

The use of a copper catalyst derived from Kündig's type NHC ligand **L8** was found to be crucial for achieving high levels of stereoselectivity in the borylation of allylic *gem*-dichlorides. To gather insight into the factors governing both enantioselectivity and *E*-selectivity, as well as to understand the unique role of this catalyst, density functional theory (DFT) calculations were performed using the coupling between (*E*)-1,1-dichlorobut-2-ene and B_2pin_2 as model reaction (Fig. 1). We first performed a conformational study to elucidate the most favorable structure for the association of the CuBpin complex **I** and the allylic *gem*-dichloride (see SI for details). Upon 362 possible structures, **II-*E*,*R*** proved to be the most favored species leading to the formation of the major enantiomer (black pathway) whereas **II-*E*, *S*** was associated with the formation of the minor enantiomer (blue pathway). Coordination of the allylic *gem*-dichloride to **II-*E*, *R*** produces intermediate **III-*E*,*R*** that upon olefin insertion through $\mathbf{TS_{III-IV}}$**-*E*,*R*** leads to the exergonic formation of σ-Cu(I) complex **IV-*E*,*R***. From this intermediate, barrierless β-Cl elimination *via* $\mathbf{TS_{IV-V}}$**-*E*,*R*** provides the chiral allylboron product π-coordinated to the NHC-Cu-Cl catalyst. Based on the computed energy profile, olefin insertion was identified as the enantiodetermining step, with transition state $\mathbf{TS_{III-IV}}$**-*E*,*R*** (black pathways) being favored by 3.4 kcal mol^{-1} over the competing enantiomeric transition state $\mathbf{TS_{III-IV-\mathit{E},\mathit{S}}}$ (blue pathway), in accordance with the experimentally observed absolute configuration of the major enantiomer.

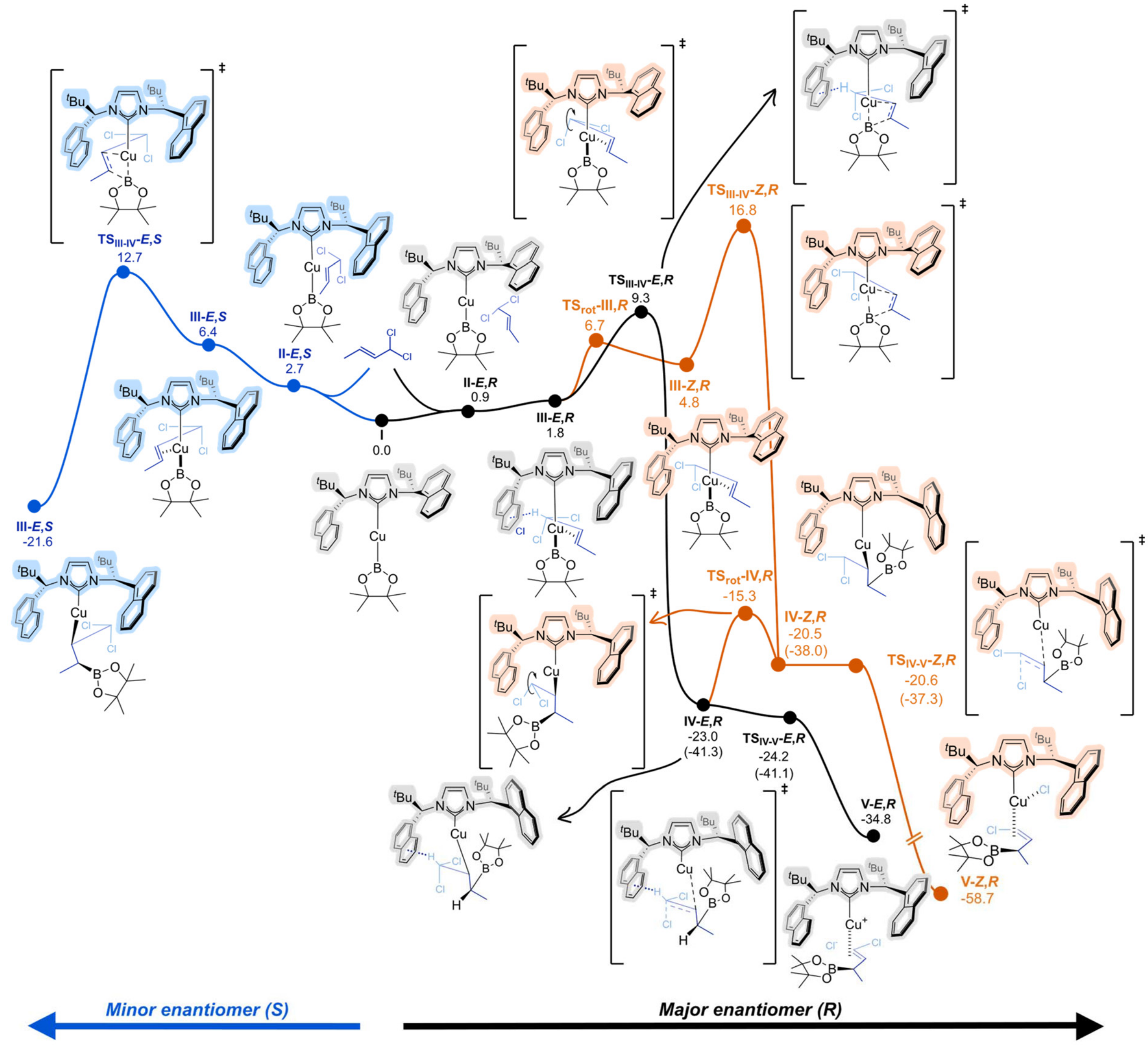


Fig. 1 Free energy profile computed at the ωB97XD/def2-TZVP/def2-QZVP (Cu) (scrf = smd, toluene)//ωB97XD/6-31G(d,p)/SDD+f (Cu) level for the pathways associated to the formation of **(*R*)-5b-*E*** (black pathway), **(*S*)-5b-*E*** (blue pathway) and **(*R*)-5b-*Z*** (orange pathway). The numbers are Gibbs energies in kcal mol^{-1} and are relative to complex **I** combined with those of the relevant substrates. Numbers in parentheses are enthalpy energies in kcal mol^{-1} and are relative to complex **I** combined with those of the relevant substrates.

Having identified olefin insertion as the enantiodetermining step, we next investigated the origin of *E*-selectivity. Since the geometry of the resulting alkenyl chloride is influenced by the conformation adopted by the C_α of the allylic *gem*-dichloride in key intermediates **III** and **IV**, we examined the rotation along the C_α–C_β bond in both intermediates (Fig. 2). Pro-*Z* intermediate **III-*Z*,*R*** is accesible *via* bond rotation in **III-*E*,*R*** with an affordable activation energy of 4.9 kcal mol^{-1} (orange pathway). However, olefin insertion from this pro-*Z* intermediate features a significantly higher energy barrier than the pro-*E* insertion ($\Delta G^{\ddagger}_{\mathbf{TSIII-IV-}Z,R} = 16.8\,\mathrm{kcal\,mol^{-1}}$ *vs.* $\Delta G^{\ddagger}_{\mathbf{TSIII-IV-}E,R} = 9.3\,\mathrm{kcal\,mol^{-1}}$). Similarly, pro-*Z* **IV-*Z*,*R*** conformation, obtained from C_α–C_β bond after olefin insertion, displays a higher energy pathway than intermediate **IV-*E*,*R***. These results perfectly match the observed experimental *E*-selectivity and point at the olefin insertion as the step which determines both the enantioselectivity and the *E*-selectivity.

To further validate our model and elucidate the key factors influencing stereoselectivity, we conducted a non-covalent interaction (NCI) analysis on the olefin insertion transition states (Fig. 2). We first examined the origin of enantioselectivity by analyzing the optimized structures for $\mathbf{TS_{III-IV}}$**-*E*,*R*** and $\mathbf{TS_{III-IV}}$**-*E*,*S*** (Fig. 2a and b). Notably, in $\mathbf{TS_{III-IV}}$**-*E*,*R*** (Fig. 2a), the allylic *gem*-dichloride's $C_\alpha(sp^3)$–H engages in attractive CH⋯π interactions[36–38] with the ligand's naphthyl ring. The acidic $C_\alpha(sp^3)$–H bond exhibits a strong affinity for the π-system of the naphthyl moiety, contributing significantly to stabilization. Additionally, the $C_\gamma(sp^2)$–H also participates in favorable CH⋯π interactions. Beyond these, the Bpin unit was found to engender weak attractive interactions by $C(sp^3)$–H⋯π

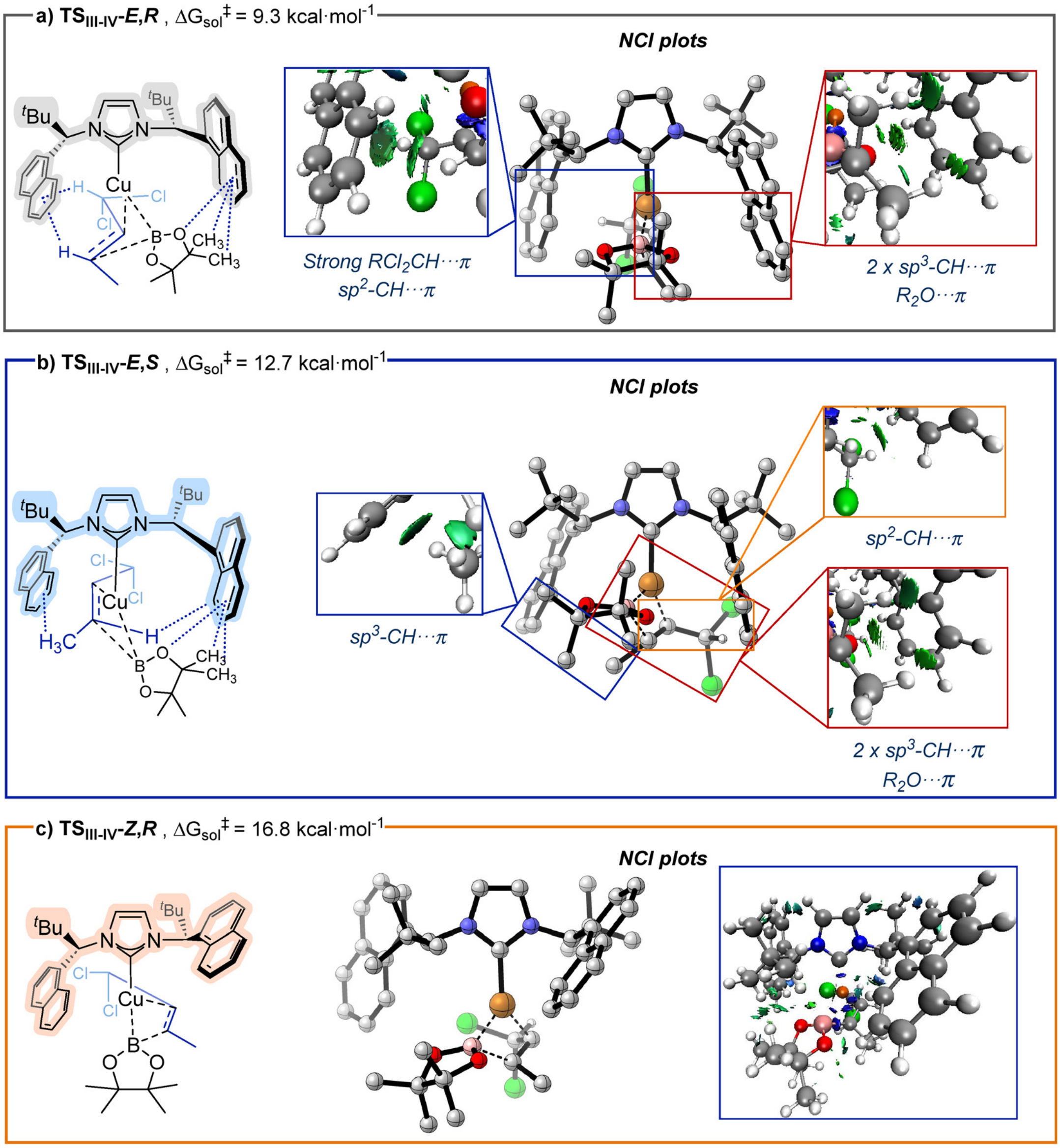


Fig. 2 Optimized structures and energies obtained from DFT calculations performed at the ωB97XD/def2-TZVP/def2-QZVP (Cu) (scrf = smd, toluene)//ωB97XD/6-31G(d,p)/SDD+f (Cu) level for the stereochemistry-determining oxidative-addition transition states associated with the most favored pathways leading to (***R***)-**5b**-***E***, (***S***)-**5b**-***E*** and (***R***)-**5b**-***Z***.

contacts between its methyl groups and the proximal naphthyl ring, as well as lone pair···π interactions[39–42] involving the oxygen atom and the naphthyl π-system. In contrast, **TS$_{\mathbf{III-IV}}$-*E*,*S*** (Fig. 2b), leading to the minor enantiomer, adopts a geometry that impedes the formation of the stronger $C_\alpha(sp^3)$–H···π interaction. Although isosurfaces between the Bpin unit and the naphthyl ring remain present, the allylic substrate's orientation favors only weaker $C_\gamma(sp^2)$–H···π and methyl C–H···π interactions. The absence of the more stabilizing $C_\alpha(sp^3)$–H···π interaction likely accounts for the higher energy of this transition state.

Regarding the origin of *E*-selectivity, analysis of transition state **TS$_{\mathbf{III-IV}}$-*Z*,*R*** revealed a geometry that precludes the establishment of significant stabilizing interactions (Fig. 2c). The spatial arrangement of the fragments in this transition state displaces them from regions where effective non-covalent contacts could otherwise form, resulting in a lack of notable interaction features.

Taken together, these results highlight the critical role of spatial arrangement and, in particular, the presence of the naphthyl substituent in ligand **L8** as key elements of stereocontrol in the copper-catalyzed asymmetric borylation of allylic *gem*-dichlorides.

Conclusion

In conclusion, we have developed an enantioselective borylation of allylic *gem*-dichlorides, enabling access to optically active allylic boronates bearing an (*E*)-configured alkenyl chloride. This transformation is distinguished by its high levels of enantioselectivity and *E*-selectivity, as well as the synthetic versatility of the resulting chiral products. These boronates serve as valuable intermediates for the stereospecific synthesis of diverse building blocks, including chiral propargyl alcohols and allylic chlorohydrins. Intrinsic mechanistic features were obtained through DFT calculations, which reveal key noncovalent interactions that underpin the observed stereocontrol, offering a rational basis for the reaction's selectivity and guiding future developments in asymmetric catalysis.

Author contributions

M. F. M. conceived and supervised the project. A. C.-P. and P. G.-R. performed the synthetic experiments and analysed the data. A. M. A. C. performed the DFT calculations. M. F. M. wrote the manuscript. All authors discussed the results and commented on the manuscript.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: list of starting materials, optimization studies, experimental procedures, compound characterization data, NMR spectra, HPLC traces, computational methods and cartesian coordinates. See DOI: **https://doi.org/10.1039/d6qo00061d**.

CCDC 2497816 (**15**) contains the supplementary crystallographic data for this paper.[30]

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This article is dedicated to Prof. Steven V. Ley on the occasion of his 80th birthday.

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