ARCHIVIO ISTITUZIONALE
DELLA RICERCA

Alma Mater Studiorum Università di Bologna
Archivio istituzionale della ricerca

Organocatalytic Asymmetric Electrophilic Amination of Allylic Boronates

This is the final peer-reviewed author's accepted manuscript (postprint) of the following publication:

Published Version:
Centonze, G., Grandi, A., Pellegrini, A., Righi, P., Portolani, C., Bencivenni, G. (2024). Organocatalytic Asymmetric Electrophilic Amination of Allylic Boronates. ACS CATALYSIS, 14(23), 17935-17944 [10.1021/acscatal.4c05237].

Availability:
This version is available at: https://hdl.handle.net/11585/1000573 since: 2025-01-07

Published:
DOI: http://doi.org/10.1021/acscatal.4c05237

Terms of use:

Some rights reserved. The terms and conditions for the reuse of this version of the manuscript are specified in the publishing policy. For all terms of use and more information see the publisher's website.

This item was downloaded from IRIS Università di Bologna (https://cris.unibo.it/).
When citing, please refer to the published version.

(Article begins on next page)

09 November 2026

Organocatalytic Asymmetric Electrophilic Amination of Allylic Boronates

Giovanni Centonze, Arianna Grandi, Andrea Pellegrini, Paolo Righi, Chiara Portolani and Giorgio Bencivenni*

Department of Industrial Chemistry "Toso Montanari", Alma Mater Studiorum University of Bologna, via Gobetti 85, 40129, Bologna -Italy

ABSTRACT: The asymmetric addition of allylic boronates to electrophiles is a powerful method for preparing chiral molecules bearing synthetically valuable allylic moieties. While effective catalytic methods exist, they have so far been limited to the enantioselective allyl- and crotyl-boration of carbonyl compounds and imines, thereby forming C-C bonds. Here, we present a strategy that expands the scope of this catalytic asymmetric platform to include the stereoselective formation of C-N bonds. We have identified an inexpensive and readily available chiral diol that catalyzes the addition of allylic boronates to azodicarboxylates, affording chiral allylic hydrazides with high stereocontrol. This electrophilic amination chemistry shows a broad substrate scope and requires mild conditions, proceeding at ambient temperature. Mechanistic studies reveal that the chiral diol catalyst facilitates the formation of a chiral allylic boronate through the reversible exchange of the boron's achiral alkoxy ligand. By coordinating with the electrophilic azodicarboxylate, the substrates mutually activate each other, allowing for the stereoselective transfer of the allyl group.

Keywords: *Electrophilic amination, chiral diol, allylic boronates, hydrazide, azodicarboxylate*

Introduction. Allylation reactions are fundamental chemical transformations largely employed to install the allyl functionality onto electrophilic species. As alternative to metal allylating agents, readily available boronic esters like (pinacolato)allylboron and (pinacolato)crotylboron represent a powerful toolbox[1] for the synthesis of homoallylic building blocks.[2] These reagents are characterized by high thermodynamic stability and consequently exhibit lower reactivity compared to metal-based analogues.[3] This results in greater ease of use, with numerous advantages in terms of reproducibility, cost, and sustainability. However, effective activation is required to achieve efficient catalytic transformations. This is generally realized through a ligand exchange process,[4] employing chiral alcohols to simultaneously achieve high reactivity and stereoselectivity. Fundamental examples have been reported by Schaus[5] and Hoveyda[6] for the allyboration of aldehydes, ketones and imines using chiral aromatic diols and a chiral amino alcohol derived from L-valine as catalysts, respectively (Figure 1a). The key aspect of these asymmetric catalytic protocols is the strong hydrogen bond coordination between the catalyst and the boron ligand. This interaction enhances the Lewis acidity of the boron centre, facilitating easier substrate binding and enabling the subsequent stereocontrolled allylic transfer via a well-structured closed transition state. Although these methodologies have significantly established boronic esters as substrates of choice for enantioselective allyl transfer reactions, they have so far been limited to additions to carbonyl substrates and imines and are thus restricted to C-C bond-forming processes. Here, we report a simple method to expand this strategy to asymmetric C-N bond-forming reactions (Figure 1b). Specifically, we used a simple chiral diol to activate the addition of allylic boronates **1** to azodicarboxylates **2**, resulting in the formation of allylic hydrazides **3**, a valuable class of key intermediates for the synthesis of bioactive compounds and amino derivatives[7] whose enantioselective synthesis is limited to few examples of Tsuji-Trost type allylic amination.[8] This process broadens the scope of allylic boronate in asymmetric catalysis and offers an unprecedented method for the synthesis of valuable chiral allylic amine compounds.

Results and Discussion. Our design plan for the catalytic asymmetric electrophilic amination of allylic boronates is detailed in Figure 2. From the outset, we recognized several challenges that likely precluded the use of electrophiles other than carbonyl compounds and imines for the activation of the boronic ester in previous studies. Firstly, we attributed the low reactivity between allylic boronic esters **1** and azodicarboxylates **2** to the steric hindrance surrounding the two reactants.[9,3]

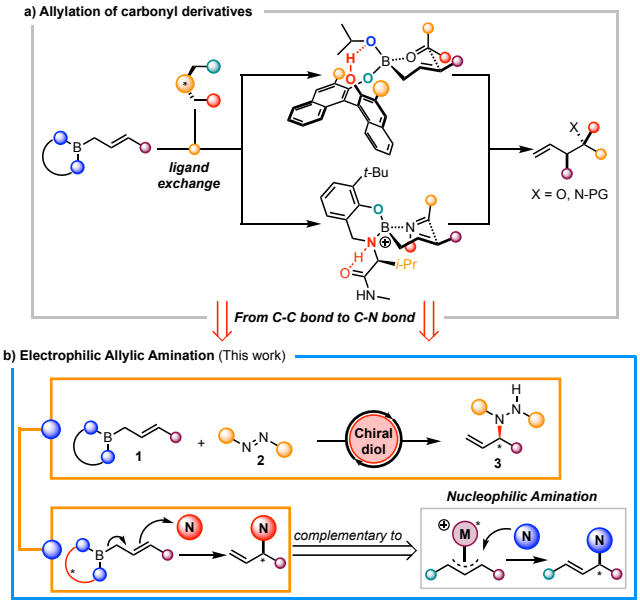


Figure 1. (a) Representative examples for the established reactivity of allyl and crotyl boronic esters with carbonyl compounds catalysed by chiral alcohols.[5-6] (b) The proposed electrophilic amination expands the scope of alkenylboronic esters to the enantioselective formation of C-N bonds.

The presence of alkoxycarbonyl groups on the nitrogen atoms in **2**, along with alkyl substituents close to the boron atom in **1**, hampered the coordination between the two species necessary for an effective reaction. We speculated that using a judiciously selected diol catalyst (**I**) with a small steric profile could facilitate, through a ligand exchange pathway, the formation of a less sterically demanding yet more reactive chiral boronic ester (**II**). The increased accessibility of the Lewis acid boron site in (**II**) could enable an n(N)-p(B) interaction between the nitrogen lone pair of the azodicarboxylate **2** and the empty p-orbital of the boron species.

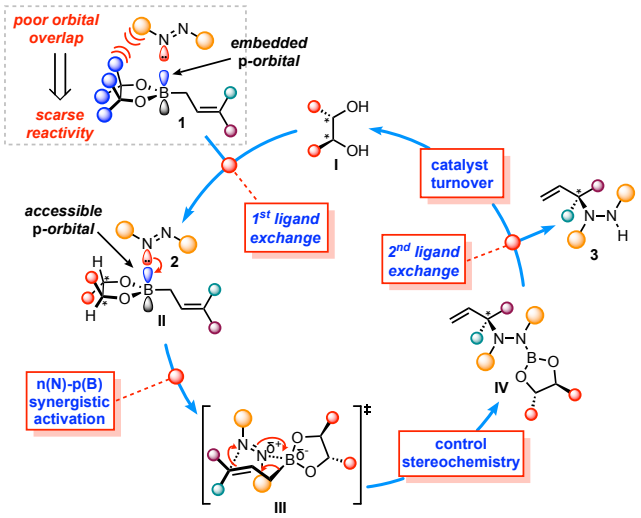
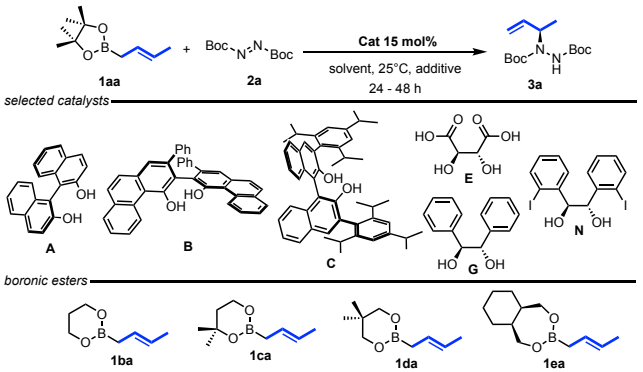


Figure 2. Design plan. A simple chiral diol (**I**) is proposed to enhance the Lewis acid reactivity of allylic boronates **1** by facilitating the n(N)-p(B) interaction which activates the two reactants for the subsequent allyl-transfer event in an enantioselective fashion.

This synergistic Lewis base-Lewis acid interaction could mutually activate both reagents, allowing them to react readily through a six-membered closed transition state (**III**). In addition to these reactivity problems, another challenge would be making the process enantioselective, which required identifying a suitable chiral diol that could effectively transfer its stereochemical information during the allyl transfer process. Achieving catalyst turnover was the final requirement we needed to address. This necessitated an efficient second ligand exchange pathway, transforming the aminoborylated species (**IV**) into allylic hydrazines (**3**) after hydrolysis of the B-N single bond. Here, we describe how this design plan was translated into experimental reality.

Optimization studies. The search for optimal reaction conditions began with the reaction between commercially available (*E*)-2-butenylboronic acid pinacol ester **1aa** and di-*tert*-butyl azodicarboxylate (DTBAD, **2a**) in toluene at 25°C (Table 1). The low yield of the racemic branched allylic hydrazide **3a** obtained after 48 hours (17%, entry 1) highlighted the intrinsic low reactivity of the boronic acid pinacol ester **1a** in the allylic amination. We then focused on the identification of a chiral diol catalyst that could enhance the reactivity while inferring enantiocontrol (for a comprehensive screening of the catalysts tested, see Supplementary Table S1). Chiral diols **A**, **B** and **C** (15 mol%), which proved effective in previous asymmetric allyl- and crotyl-boration of carbonyl compounds,[5a-c] led to racemic **3a** with a slight increase in reactivity (entries 2-4). In these initial studies, we observed that the addition of one equivalent of tert-butyl alcohol slightly enhanced the reactivity (entries 5-6). We therefore continued our studies using this additive and found that the commercially available (*R*,*R*)-tartaric acid **E** previously employed in allylation reaction of boronic esters[5d-e] revealed poor catalytic activity (entries 7). Surprisingly, (*S*,*S*)-(-)-hydrobenzoin **G** afforded product **3a** in 60% yield and 60% of enantiomeric ratio (e.r.) in 48 hours (entry 8). We then found that iodine-containing catalyst **N**, readily prepared from **G**, afforded **3a** with increased yield (70%) while maintaining the same e.r. (entry 9). A further round of optimization using catalyst **G** (see Supplementary Table S2-S6 for our extensive studies) identified mixture of 0.2 mL of isopropyl alcohol (IPA) and 0.2 mL of acetic acid (AcOH) as the optimal reaction medium, leading to improvements in both reactivity and enantioselectivity (entry 10).

Table 1. Optimization of the reaction conditions.[a]



entry	boronic ester	Catalyst	Solvent	Yield[b] (%)	e.r.[c]
1	1aa	/	Toluene	17	50:50
2	1aa	A	Toluene	17	50:50
3	1aa	B	Toluene	17	50:50
4	1aa	C	Toluene	22	50:50
5[d]	1aa	A	Toluene	21	50:50
6[d]	1aa	B	Toluene	23	50:50
7[d]	1aa	E	Toluene	27	52:48
8[d,e]	1aa	G	Toluene	60	80:20
9[d,e]	1aa	N	Toluene	70	80:20
10[f,g,h]	1aa	G	^{i}PrOH/AcOH	75	88:12
11[f,g]	1ba	G	^{i}PrOH/AcOH	84	78:22
12[f,g]	1ca	G	^{i}PrOH/AcOH	84	96:4
13[f,g]	1da	G	^{i}PrOH/AcOH	90	72:28
14[f,g]	1ea	G	^{i}PrOH/AcOH	95	60:40
15[g,h,i]	1ca	N	^{i}PrOH/AcOH	93	96:4

[a]Open-air reaction performed using 0.1 mmol of **1** and 0.1 mmol of **2a** without any precautions to exclude moisture and water in toluene (0.1 M) for 48 hours. [b]Yields refer to isolated product **3a** after flash column chromatography. [c]The enantiomeric ratio has been

determined using GC analysis on chiral stationary phase. [d]0.1 mmol of [t]BuOH were used. [e]0.2 mL of Toluene were used. [f]0.2 mL of [i]PrOH and 0.2 mL of AcOH were used. [g]Reaction time 24 hours. [h]10 mol% of **N** was used. [i]0.1 mL of [i]PrOH and 0.1 mL of AcOH were used.

We then tested the reactivity of (*E*)-crotylboronic esters with different alkoxy substituents (entries 11-14). The boronic ester **1ca** provided a significant increase in stereocontrol, affording product **3a** in 96:4 e.r. (entry 12). Lowering the catalyst loading (**N**, 10 mol%) yielded comparable results in terms of enantioinduction and catalytic activity, with **3a** isolated in 93% yield and 96:4 e.r. (entry 15).

Scope of the reaction. Using the optimized conditions in entry 14, we explored the scope of the amination reaction (Figure 3).

All reactions were performed by mixing the boronic ester **1** (0.3 mmol) and catalyst **N** (10 mol%) in IPA (0.3 mL) and AcOH (0.3 mL) and after 10 minutes **2** (0.3 mmol) was added. We reacted different azodicarboxylates (**2a-c**) with mono-, di-, and trisubstituted alkenylboronic esters (**1ca-cw**) obtaining the corresponding enantioenriched allylic hydrazide (**3a-3y**) in consistently high yields and enantioselectivities. We also performed the model reaction between **1ca** and **2a** using the opposite enantiomer of the catalyst (**ent-N**), which granted access to the antipode of product **ent-3a** with identical yield and enantiocontrol. The steric profile of the boronic ester substituent in **1** influenced both the reactivity and the enantioselectivity. When large substituents such as isopropyl, cyclohexyl and heptenyl were used, hydrazides **3d**, **3g** and **3h** were obtained in slightly lower yields and enantiomeric ratioes.

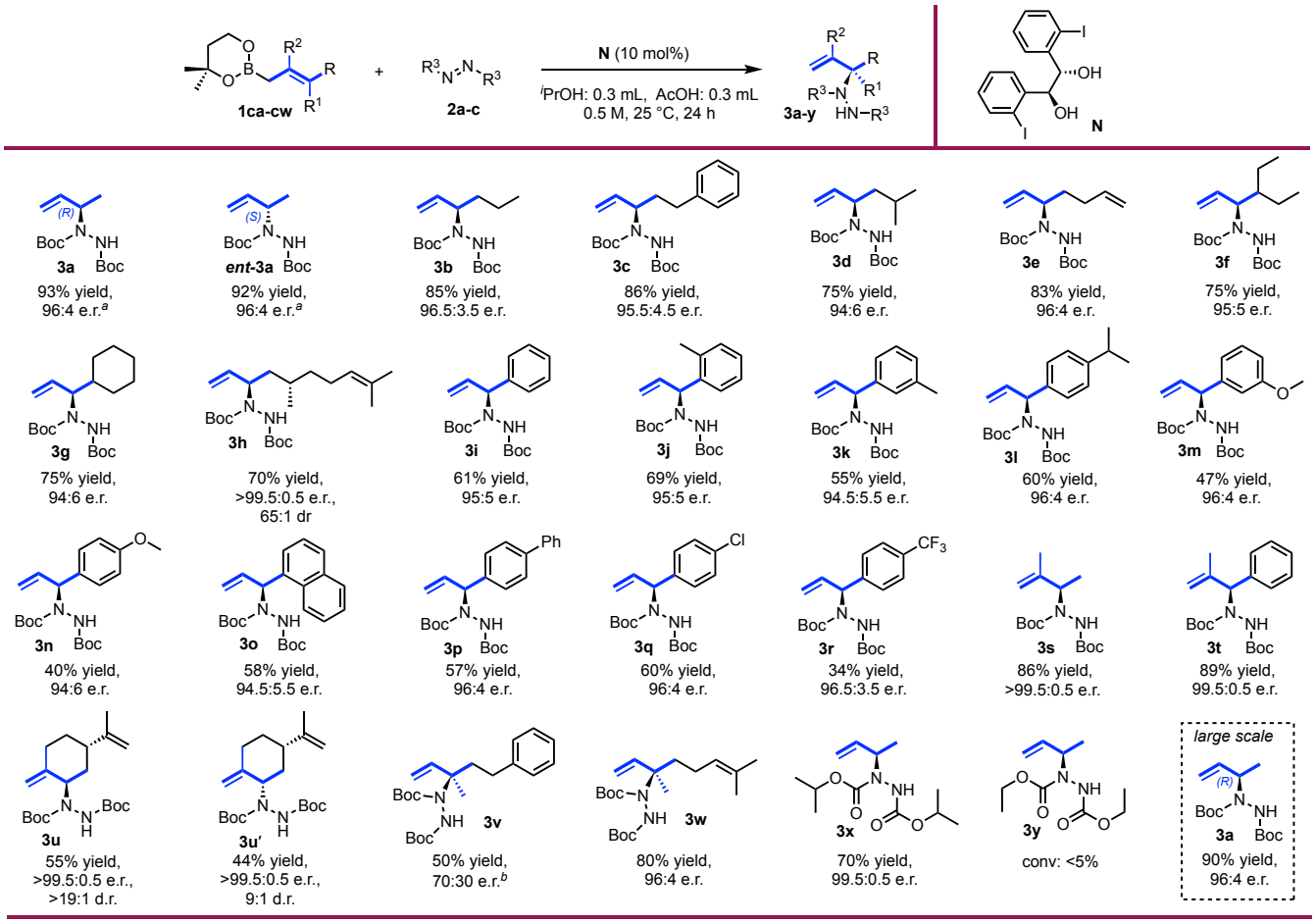


Figure 3. Reaction performed without any precaution to exclude moisture and water mixing 0.3 mmol of **1** and 10 mol% of **N** in 0.3 mL of IPA and 0.3 mL of AcOH. After 10 minutes 0.3 mmol of **2** is added. Yields refer to isolated products **3** after flesh column chromatography. Unless otherwise noted, the enantiomeric ratio has been determined using HPLC analysis on chiral stationary phase. Diastereoisomeric ratio (d.r.) was measured by ^{1}H NMR spectroscopy. [a]The enantiomeric ratio has been determined using GC analysis on chiral stationary phase. [b]The starting boronic ester was a 70:30 ratio of E:Z alkenes.

Boronic esters bearing aromatic substituents with electron-withdrawing and releasing groups could be successfully employed (**3i-3r**), albeit offering reduced reactivity. Interestingly, the electrophilic amination could be performed using boronic esters with substituents at either C2 and C3. In these cases, high yield and enantioselectivity were obtained with both alkyl and aryl group (**3s-3t**). When the cyclic framework from (*S*)-limonene was reacted, a high diastereoselectivity was obtained with both enantiomers of the catalyst, leading to the opposite diastereomers **3u** and **3u'**. This result confirmed that the process is completely under catalyst control. The protocol was also amenable to the formation of hydrazides containing a quaternary stereocenter obtained from the corresponding cinnamyl- and geranyl-boronic esters (**3v-3w**), highlighting the good reactivity of the system with sterically demanding reagents. Regarding the use of other electrophiles, only diisopropyl azodicarboxylate **2b** reacted with **1ca**, affording the corresponding hydrazide **3x** in 70% yield and 99.5:0.5 e.r.. In contrast, diethyl

azodicarboxylate **2c** showed poor reactivity and led to complicated reaction mixtures. Finally, the model reaction between **1ca** and **2a** could be performed on 1.5 mmol scale with almost identical results (386 mg of **3a** isolated in 90% yield, 96:4 e.r.).

Derivatization reactions. The presence of various functional groups makes the allylic hydrazide products suitable for further derivatizations (Figure 4). The double bond was readily converted in the corresponding primary alcohol **4a** in 70% yield and 96:4 e.r.by *anti*-Markovnikov hydroboration followed by oxidation with H_2O_2. A mixture of diastereoisomeric diols **5a** and **5a'** was obtained in 83% yield and 96:4 e.r. by reaction with $RuCl_3$ and $NaIO_4$. Cleavage of the C-C single bond with $NaIO_4$ gave the corresponding aldehyde **6a**, which was directly converted to the corresponding aminated (D)-alanine **7a** by Pinnick oxidation or reduced with $NaBH_4$ to primary alcohol **8a**. The enantiomer of alcohol **8a**, previously prepared was further alkylated to the diastereoisomeric N-N atropisomers **9a** and **9a'**.[10] The cleavage of the N-N single bond on the acetylated derivative of **3a** and **3j** with SmI_2 gave the *N*-Boc-protected allylamines **11a** and **11j** in good yield[11] and retained enantioselectivity. The (*R*)-absolute configuration of hydrazide **11a** was established by comparison of the optical rotation with the one previously reported.[12]

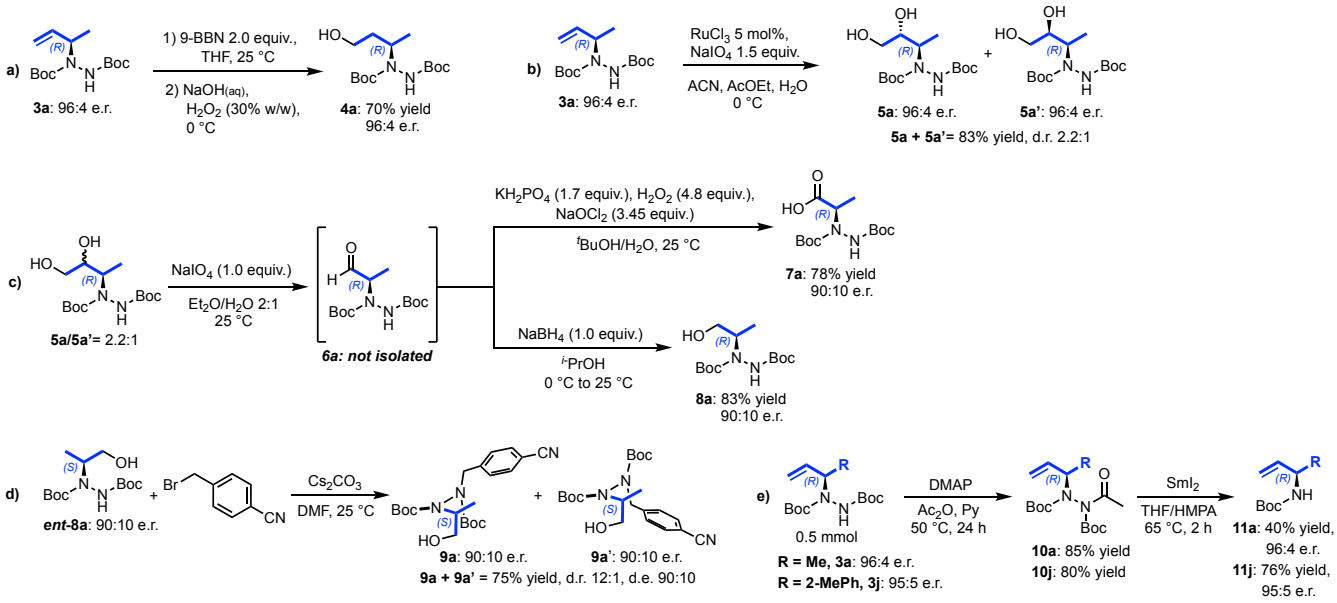
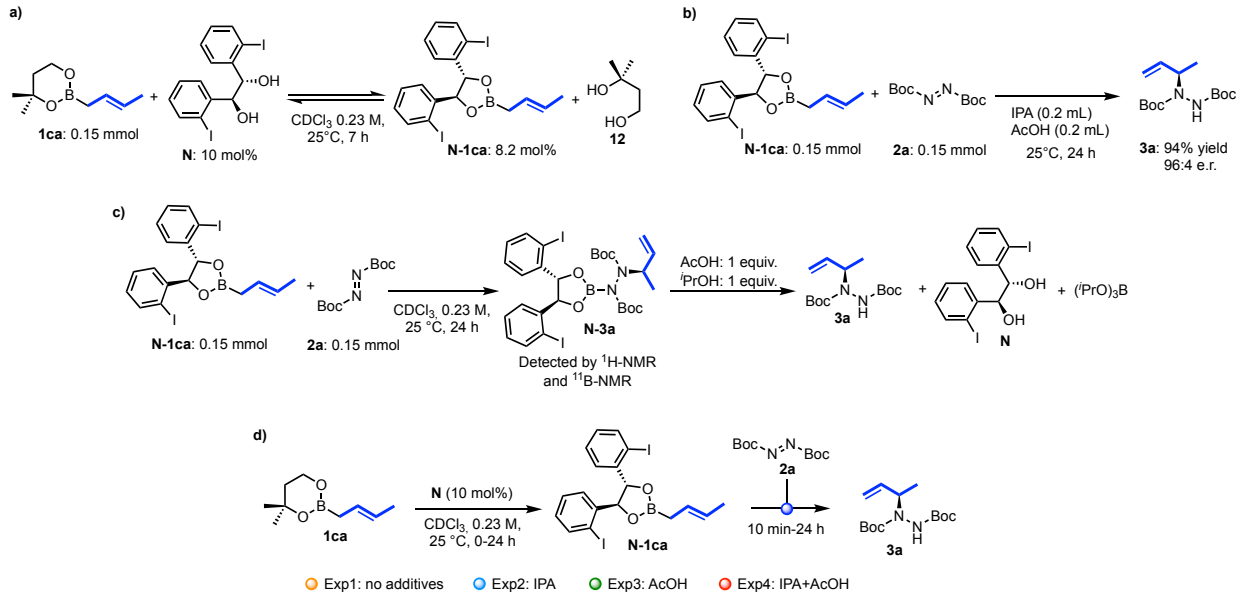


Figure 4. (a) Hydroboration followed by oxidation. (b) Dihydroxylation gives a mixture of inseparable diastereoisomers. (c) Oxidation of diol **5** to aldehyde **6a**. The crude aldehyde obtained was divided into two solutions and oxidized to aminated (D)-alanine **7a** or reduced to alcohol **8a**. Yields of **7a** and **8a** refer to the starting amount of diol **5a**. (d) Nitrogen alkylation to give atropisomeric tetrasubstituted hydrazide **9**. (e) Nitrogen acetylation followed by N-N cleavage using SmI_2 to prepare *N*-Boc protected chiral allylamines **11a** and **11j**.

Mechanistic studies. Our attention then turned to understanding the reaction mechanism through control experiments, kinetic studies, and density functional theory (DFT) calculations. As shown in Figure 5a, we monitored the reaction between **1ca** with 10 mol% of **N** in $CDCl_3$ by ^1H and ^{11}B NMR analysis and we observed a slow but consistent increase in the concentration of the chiral boronic ester intermediate **N-1ca**, generated by ligand exchange between the catalyst and substrate **1ca** (see Supporting Information for details). Then, we synthesized an authentic sample of **N-1ca** to test its reactivity under the reaction conditions. Upon mixing with an equimolar amount of **2a** in a mixture of IPA (0.3 mL) and AcOH (0.3 mL), the allylic hydrazide **3a** was isolated in 94% yield and 96:4 e.r., a result that perfectly matches those obtained under catalytic conditions (Figure 5b). This experiment indicates that **N-1ca** is responsible for the enantioselective allyl transfer. We then focused on establishing the rate-determining step (rds) of the process and the role of isopropanol and acetic acid in the mechanism. We repeated the reaction between **N-1ca** and **2a** in $CDCl_3$ and we observed the quantitative formation of hydrazido boronic ester **N-3a**. After the addition of IPA and AcOH to the crude mixture, **3a** and catalyst **N** were obtained quantitively. This experiment indicates that **N-3a** is a transient intermediate that under catalytic condition is rapidly transformed into the product **3a** for reaction with IPA and AcOH which enable also an efficient catalyst turnover (Figure 5c). We then tracked the concentration of the free catalyst **N** and intermediate [**N-1ca**], along with the conversion of **1c** into **3a** over time by ^1H and ^{11}B NMR analysis (Figure 5d). When mixing catalyst **N** (10 mol%) and **1c** in the absence of both isopropanol and acetic acid, only a very minor amount of intermediate **N-1ca** was generated over time. Upon the addition of azodicarboxylate **2a**, the concentration of **N-1ca** decreased during time and the conversion of the product was low, suggesting that catalyst turnover was not effective. Repeating the same experiment in the presence of 2.0 equiv. of isopropanol led to a faster formation of **N-1ca**. Importantly, intermediate **N-1ca** accumulated during the reaction with **2a**, as evidenced by its steadily increasing concentration. This indicates that catalyst turnover was more effective than the allyl group transfer process. Performing the same experiment in the presence of 2.0 equiv. of acetic acid but without IPA, intermediate **N-1ca** was fully formed after only 10 minutes. However, upon starting the reaction adding azodicarboxylate **2a**, the concentration of **N-1ca** decreased quickly, suggesting that catalyst turnover was not efficient. From these experiments, we inferred that isopropanol and acetic acid played different yet synergistic

roles in the catalysis: isopropanol assisted in fast catalyst turnover, while acetic acid triggered a quick ligand exchange, speeding up the formation of the chiral intermediate **N-1ca**.[13] The process conducted in the presence of both isopropanol and acetic acid showed faster kinetics, while the concentration of **N-1ca** remained steady during the process. This confirmed the synergistic action of the additives and established that, under the optimized conditions, the reaction between **N-1ca** and **2a**, which forms the C-N bond, is the rds of the process.



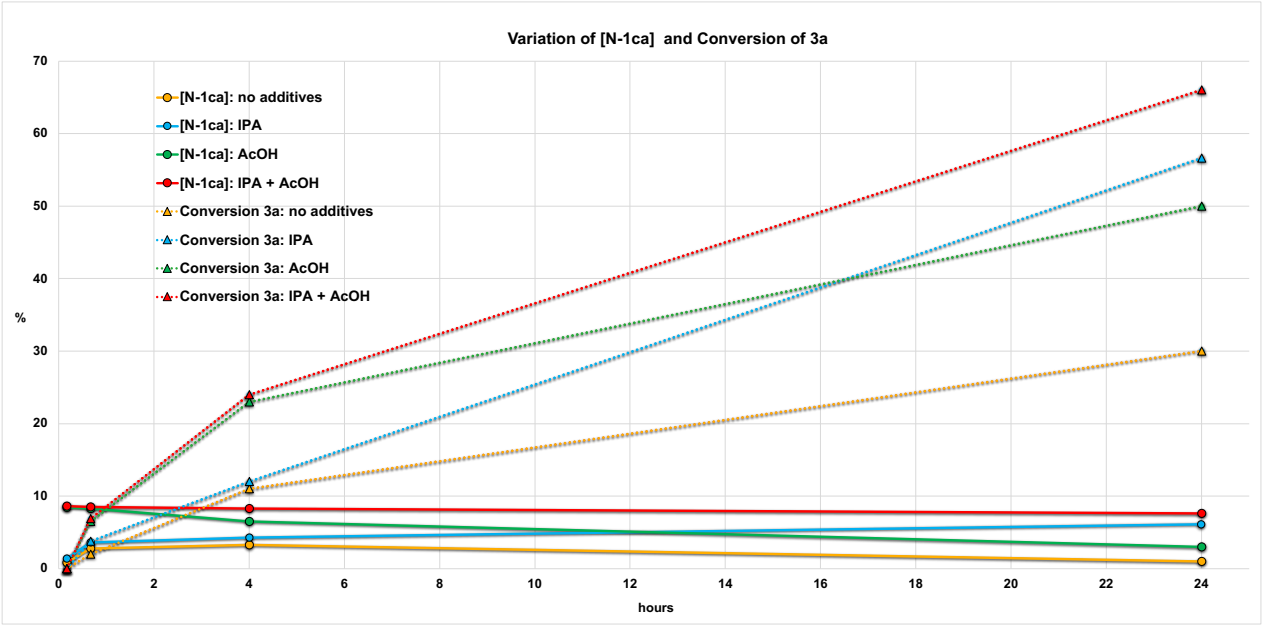


Figure 5. (a) Reaction between **1ca** and **N** in $CDCl_3$. The concentration of **N-1ca** reached the 82% of the total amount of **N** after 7 hours. Control experiment: (b) freshly prepared chiral crotylboronate **N-1ca** reacts with a stoichiometric amount of **2a** under optimized condition to give **3a**. Control experiment: (c) Reaction between **N-1ca** and **2a**. **N-3a** was detected by ^{1}H and ^{11}B NMR as the sole product of reaction after 24 hours. Allylic hydrazide **3a** and catalyst **N** have been obtained immediately after the addition of IPA and AcOH. (d) Effect of IPA and AcOH on the reaction. All the reactions have been performed by mixing **1ca** and **N** and after 10 minutes **2a** was added. The concentration of **N-1ca** (plain lines) and the conversion of **1ca** into **3a** (dashed lines) have been monitored during time.

We then performed a nonlinear effect[14] experiment and found a perfect linear correlation between the enantiopurity of catalyst **ent-N** and the enantiomeric ratio of **ent-3a** (see Supporting Information for details). This result suggests that a single molecule of **N** is involved in the enantiodetermining step.

Finally, we compared the reactivity of boronates **1aa** and **1da** with that of **1ca** by monitoring the formation of the catalytic species **N-1ca** and the conversion of **3a** during time by ^{1}H-NMR using $CDCl_3$ as solvent and IPA and AcOH as additives (Figure 6a). In analogy with the result obtained for **1ca**, by mixing catalyst **N** with boronates **1aa** and **1da** a rapid formation of **N-1ca** was measured. Upon the addition of azodicarboxylate **2a** the concentration of **N-1ca** remained steady during the process, but boronate **1da** showed a faster kinetic than **1aa** and **1ca** which gave similar results. Indeed, for the reaction with boronate **1da**, hydrazide **3a** was isolated with an enantiomeric ratio of 77:23

while with boronate **1aa** an enantiomeric ratio of 92.5:7.5 was measured. This results, suggest that the background uncatalyzed reaction operates with boronate **1aa** and **1da**. This hypothesis was confirmed when we repeated the previous experiments without catalyst **N** and followed the conversion of **3a** during time (Figure 6b). Boronates **1da** and **1aa** showed faster kinetics than **1ca**. The conversion after 24 hours of racemic **3a** was 70%, 24% and 9% respectively. This results clearly suggests that, despite the catalytic reaction is anyway highly faster than the racemic one, the latter operates in parallel to the formation of **3a** with boronate **1aa** and **1da** for which a lower enantiomeric ratio is obtained. Indeed, because the e.r. of the catalytic reaction with **1ca** matches the e.r. of the reaction with a stoichiometric amount of **N-1ca** (Figure 5b) we exclude that with this boronate the background reaction is operative.[15]

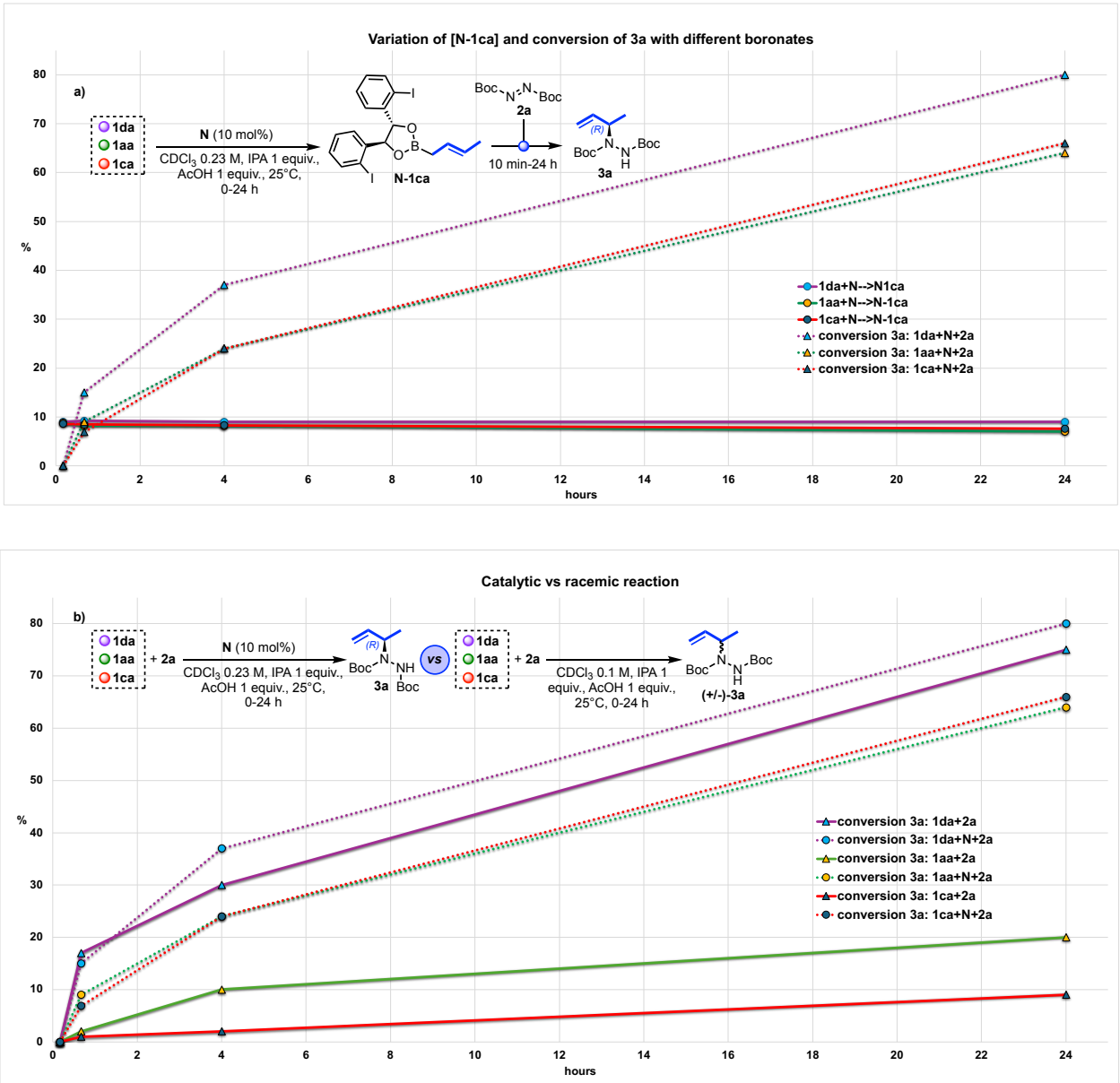


Figure 6. (a) All the reactions have been performed by mixing **1aa**, **1da**, **1ca** and **N** in a solution of $CDCl_3$ and 1 equiv. of IPA and AcOH. After 10 minutes **2a** was added. The concentration of **N-1ca** (plain lines) and the conversion of each boronate into **3a** (dashed lines) have been monitored during time. (b) Comparison between the catalytic (plain lines) and racemic (dashed lines) reactions of boronate **1aa**, **1da** and **1ca**.

We also performed DFT calculations to obtain the optimized transition state models for the allyl transfer reaction. These studies suggest that the steric profile of catalyst **N** controls the approach of **2a** on the less hindered *Re* face of the crotyl moiety through a concerted asynchronous six-membered chair-like transition state (**TS1-N-*Re***) leading to the (*R*) enantiomer of **3a** obtained experimentally (Figure 7a). The non-covalent interaction (NCI)[16] analyses of the **TSs** geometries evidenced three strong hydrogen bond and two London interactions which contribute to build up a tighter **TS1-N-*Re*** than **TS2-N-*Si***. In particular, one hydrogen bond interaction between the carbonyl group of **2a** and the H6 of the aromatic ring of the catalyst is crucial for stabilizing the TS geometry. This interaction, which is absent in the favored transition state for the reaction with catalyst **G** (**TS1-G-*Re***), highlights the key role of the iodine atom in catalyst **N**. In fact, it arises from the stable conformation of

two iodine atoms within the aromatic pocket, which directs H6 toward the oxygen of the carbonyl group of **2a**. **TS1-N-*Re*** results in fact more stable by 2.0 kcal/mol than the **TS1-G-*Re*** (Figure 7b). A plausible reaction mechanism is proposed in Figure 7c. Boronic ester **1ca** reacts with catalyst **N** forming **N-1ca** through an acetic acid promoted ligand exchange. The chiral intermediate coordinates with **2a** and readily transfer the allyl moiety in an enantioselective fashion through a closed six membered transition state. The resulting aminoborane **N-3a** releases **(*R*)-3a** and catalyst **N** after a rapid sequence of acid catalyzed ligand exchange and B-N alcoholysis (see Supporting Information for details)

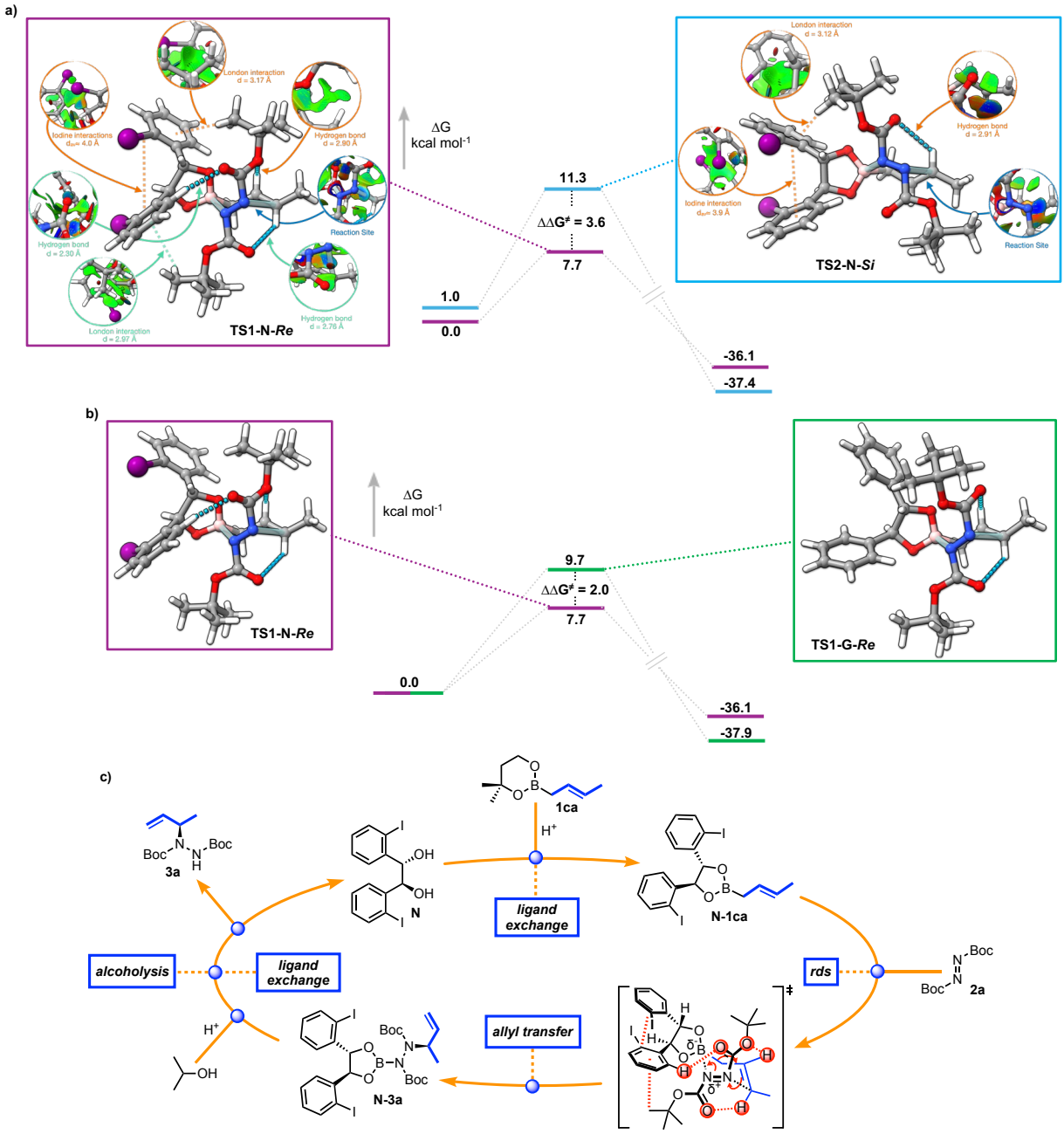


Figure 7. (a) Geometries of the transition states for the electrophilic amination. **TS1-N-*Re*** is more stable than **TS2-N-*Si*** as highlighted by the attractive H-bonding and London interactions between the **N-1ca** and **2a** resulting in a closer geometry. (b) Comparison between the two **TS** energies for the reaction with catalyst **N** (violet) and catalyst **G** (green) after setting arbitrarily to 0.0 kcal/mol the energy of both pre-reaction complexes. The conformation of the two iodine atoms inside the aromatic pocket stabilizes the **TS** geometry and allow a strong H-bond between H6 and the carbonyl of **2a**. (c) Proposed catalytic cycle. AcOH and IPA work in synergy to speed up the two ligand exchange processes and the alcoholysis. The reaction between **N-1ca** and **2a** is the rate determining step of the process.

Conclusions. In summary, we have developed the first example of enantioselective electrophilic amination of allylic boronic esters. The reaction, catalyzed by a simple chiral diol, provides an efficient, mild, and practical method for accessing chiral

allylic hydrazides in high yields and enantiocontrol using commercial and readily available starting materials. Mechanistic investigations revealed the efficiency of the catalyst to trigger the previously inaccessible enantioseletive reaction of allyl boronic esters with azodicarboxylate and clarified the role of isopropanol and acetic acid in ensuring efficient catalyst turnover. This methodology not only expands the reactivity of allylic boronic esters to include new electrophiles, but also enhances the asymmetric allylation platform by introducing a novel tool for asymmetric C-N bond-forming reactions.

ASSOCIATED CONTENT

AUTHOR INFORMATION

Corresponding Author

Giorgio Bencivenni – Department of Industrial Chemistry "Toso Montanari" - University of Bologna, via Piero Gobetti 85, 40129 Bologna. Email: giorgio.bencivenni2@unibo.it

Author Contributions

G.C., A.G. and C.P. performed the experiments. A.P. and P.R. performed the computational study. G.B. conceived and directed the project and wrote the manuscript.

Supporting Information

Experimental procedures, kinetic and control experiments, characterization data, NMR and HPLC spectra (PDF)

ACKNOWLEDGMENT

Financial support by the European Union, Next Generation EU, DM 737/2021, University of Bologna Project ALMArieCurie 2022, SUpER, and the "Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali" (INSTM). The authors thank Prof. Paolo Melchiorre for fruitful discussions.

REFERENCES

(1) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F.; Catalytic enantioselective allylation of carbonyl compounds and imines. *Chem. Rev.* **2011**, *111*, 7774–7854.

(2) Yus, M.; Gonzalez-Gomez, J. C.; Foubelo, F.; Diastereoselective allylation of carbonyl compounds and imines: application to the synthesis of natural products. *Chem. Rev.* **2013**, *113*, 5595–5698.

(3) Hall, D. G. Lewis and Brønsted acid catalyzed allylboration of carbonyl compounds: from discovery to mechanism and applications. *Synlett*, **2007**, *11*, 1644–1655.

(4) Roy, C. D.; Brown, H. C. Stability of boronic esters – structural effects on the relative rates of transesterification of 2-(phenyl)-1,3,2-dioxaborolane. *J. Organomet. Chem*. **2007**, *692*, 784–790.

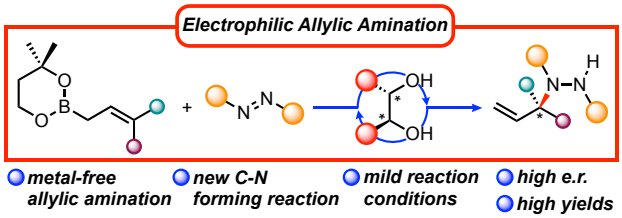
(5) (a) Lou, S.; Moquist, P. N.; Schaus, S. E. Asymmetric allyboration of ketones catalyzed by chiral diols. *J. Am. Chem. Soc*. **2006**, *128*, 12660–12661. (b) Lou, S.; Moquist, P. N.; Schaus, S. E. Asymmetric allyboration of acyl imines catalyzed by chiral diols. *J. Am. Chem. Soc*. **2007**, *129*, 15398–15404. (c) Barnett, D. S.; Moquist, P. N.; Schaus, S. E. The mechanism and an improved asymmetric allylboration of ketones catalyzed by chiral biphenols. *Angew. Chem. Int. Ed*. **2009**, *48*, 8679–8682. (d) Moquist, P. N.; Kodama, T.; Schaus, S. E. Enantioselective addition of boronates to Chromene acetals catalyzed by a chiral Bronsted acid /Lewis acid system. *Angew. Chem. Int. Ed*. **2010**, *49*, 7096–7100. (e) Kodama, T.; Moquist, P. N.; Schaus, S. E. Enantioselective boronates additions to *N*-acyl quinoliniums catalyzed by tartaric acid. *Org. Lett.*, **2011**, *13*, 6316–6319.

(6) (a) Silverio, D. L.; Torker, S.; Pilyugina, T.; Vieira, E. M.; Snapper, M. L.; Haeffner, F.; Hoveyda, A. H. Simple organic molecules as catalysts for enantioselective synthesis of amines and alcohols. *Nature*, **2013**, *494*, 216–221. (b) Wu H.; Haeffner F.; Hoveyda A. H. An efficient, practical, and enantioselective method for the synthesis of homoallenylamides catalyzed by an aminoalcohol-derived, boron-based catalyst. *J. Am. Chem. Soc.* **2014**, *136*, 3780–3783. For examples of allylation reaction using boronic acid derivatives see: (c) Alam, R.; Vollgraff, T.; Eriksson, L.; Szabó, K. J. Synthesis of adjacent quaternary stereocenters by catalytic asymmetric allylboration. *J. Am. Chem. Soc.* **2015**, *137*, 11262–11265. (d) Alam, R.; Diner, C.; Jonker, S.; Eriksson, L.; Szabó, K. J. Catalytic allylboration of indoles and dihydroisoquinolines with allylboronic acid: stereodivergent synthesis of up to three contiguous stereocenters. *Angew. Chem. Int. Ed*. **2016**, *55*, 14417–14421. (e) Huang, G.; Diner, C.; Szabó, K. J.; Himo, F. Mechanism and stereoselectivity of the BINOL-catalyzed allylboration of skatoles. *Org. Lett*., **2017**, *19*, 5904–5907.

(7) (a) Küçükgüzel, S ̧. G.; S ̧enkardes ̧ S. Recent advances in bioactive pyrazoles. *Eur. J. Med. Chem*. **2015**, 97, 786–815. (b) Blair, L. M.; Sperry, J. Natural products containing a nitrogen-nitrogen bond. *Nat. Prod.* **2013**, *76*, 794–812. (c) U. Ragnarsson, Synthetic methodology for alkyl substituted hydrazines. *Chem. Soc. Rev.* **2001**, *30*, 205–213. (d) Strick, B. F.; Mundal, D. A.; Thomson R. J. An oxidative [2,3]-sigmatropic rearrangement of allylic hydrazides. *J. Am. Chem. Soc.* **2011**, *133*, 14252–14255.

(8) (a) Yan, L.; Xu, J.-K.; Huang, C.-F.; He, Z.-Y.; Xu, Y.-N.; Tian, S.-K. Kinetic resolution of racemic allylic alcohols by catalytic asymmetric substitution of the OH group with monosubstituted hydrazines. *Chem. Eur. J*. **2016**, *22*, 13041–13045. (b) Rajkumar, S.; Clarkson, G. J.; Shipman, M. Regio- and stereocontrolled synthesis of 3-substituted 1,2-diazetidines by asymmetric allylic amination of vinyl epoxide. *Org. Lett.* **2017**, *19*, 2058–2061. (c) Jing-Kun, X.; Yonghong, G.; Shi-Kai T. Enantiospecific allylic alkylation of substituted hydrazines with allylic alcohols. *Chin. J. Org. Chem*. **2015**, *35*, 618–624. For a different approach to the synthesis of hydrazides using Lithium-boronates complexes see: García-Ruiz, C.; Chen, J. L.-Y.; Sandford, C.; Feeney, K.; Lorenzo, P.; Berionni, G.; Mayr, H.; Aggarwal V. K. Stereospecific allylic functionalization: the reactions of allylboronate complexes with electrophiles. *J. Am. Chem. Soc.* **2017**, *139*, 15324−15327.

(9) Kiyokawa, K.; Kainuma, S.; Minakata S. Electrophilic amination of allylic boranes with azodicarboxylates: synthesis of α,α-disubstituted allylic amines derivatives. *Chem. Lett*. **2019**, *48*, 1116–1118.

(10) (a) Portolani, C.; Centonze, G.; Luciani, S.; Pellegrini, A.; Righi, P.; Mazzanti, A.; Ciogli, A.; Sorato, A.; Bencivenni, G. Synthesis of atropisomeric hydrazides by one-pot sequential enantio- and diastereoselective catalysis *Angew. Chem. Int. Ed.* **2022**, *61*, e202209895. (b) Centonze, G.; Portolani, C.; Righi, P.; Bencivenni, G.

Enantioselective strategies for the synthesis of N-N atropisomers. *Angew. Chem. Int. Ed.* **2023**, *62*, e202303966.
(11) The low yield of isolated **11a** is likely related to a problem of high volatility. The reaction has been repeated several times with new SmI_2 and freshly distilled solvents with almost identical results revealing in any case a clean crude mixture without byproducts or residues of the starting material.
(12) Seehafer, K.; Malakar, C. C.; Bender, M.; Qu, J.; Liang, C.; Helmchen, G. Iridium-catalyzed asymmetric allylic substitutions with bulky amides/oxidative double bond cleavage-entry into the Reetz synthesis of amino alcohols. *Eur. J. Org. Chem*. **2016**, 493–501.
(13) Biosca, M.; Szabó, K. J.; Himo, F. Mechanism of asymmetric homologation of alkenylboronic acids with CF_3-diazomethane via borotropic rearrangement. *J. Org. Chem*., **2024**, *89*, 4538-4548.
(14) Girard, C.; Kagan, H. B. Nonlinear effects in asymmetric synthesis and stereoselective reactions: ten years of investigation. *Angew. Chem. Int. Ed.* **1998**, *37*, 2922–2959.
(15) During the reaction with a stoichiometric amount of **N-1ca** the presence of highly reactive boronates from a possible transesterification process with IPA has never been detected. This excludes the contribution of a racemic background from diisopropyl (*E*)-but-2-en-1-ylboronate reinforcing the hypothesis that the stereocontrol observed with **1ca** derives from a catalyst controlled reaction.
(16) Johnson, E. R.; Keinan, S.; Mori-Sánchez, P.; Contreras-García, J.; Cohen, A. J.; Yang, W. Revealing noncovalent interactions *J. Am. Chem. Soc.* **2010**, ***132***, 6498–6506.