Copper(I)/guanidine catalyzed asymmetric allylic borylation reaction

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Asymmetric Allylic Borylation Reactions**

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SCHOOL OF PHYSICAL AND MATHEMATICAL SCIENCES
2018**

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ABSTRACT

Chiral organic boronates are versatile reaction intermediates as they could be readily converted into highly functionalized compounds with high regioselectivity and stereoselectivity. Although numerous reports arised in the enantioselective conjugated borylation and asymmetric hydroboration, limited attention was paid in the area of enantioselective allylic borylation. Additionally, allylboronates could further undergo nucleophilic addition to aldehydes, ketones or imines in which homoallylic alcohols or amines were obtained stereoselectively. However, stereoconvergent synthesis of such enantiopure allylboronates from racemic allylic substrates or the mixture of *E/Z* isomers, still remained challenging, especially for reactive allylic halides.

In the 1st Chapter of this thesis, a brief introduction will be presented involving the properties of organo boron compounds, utilization of diboron reagents, Miyaura borylation reaction and current achievement on allylic borylation as the background of our research.

In the following Chapter 2, our exploration on copper/guanidinium catalyzed allylic borylation reactions will be introduced. We managed to explore that in the presence of copper bicyclic guanidinium salt we were able to afford the desired allylic boronate with high enantioselectivity under optimized condition. Upon scope investigation, this novel system was found able to furnish a series of cyclic or linear secondary/tertiary boronates in a stereoconvergent manner. After that, the reaction mechanism was carefully probed with a variety of methods and techniques, including kinetic studies, ¹H and ¹¹B NMR, EPR

spectroscopy, X-ray crystallography, and radical clock and trapping experiments. With the results noted in Chapter 3, the reaction was proposed to undergo an enantioconvergent S_N2' substitution. Then the scaled-up reaction and further application of enantioenriched allylic boronates were investigated.

Finally, the synthetic routes and characterization data are listed in Chapter 4, and the soft copies of original spectra are attached in the Appendix.

PUBLICATIONS

1. He, T.; **Ge, Y.-C.**; Wu, L.-L.; Fu, H.-Y.; Chen, H.*; Li, X.-J. CuI/P(OCH₂CH₃)₃ Catalyzed Cross-Coupling Reaction of Aryl Iodides with Alkynes.
Chin. J. Catal. **2011**, *32*, 1376–1379.
2. Wu, L.-L.; **Ge, Y.-C.**; He, T.; Zhang, L.; Fu, X.-L.; Fu, H.-Y.; Chen, H.*; Li, R.-X. An Efficient One-Pot Synthesis of 3,5-disubstituted 1H-Pyrazols.
Synthesis. **2012**, *44*, 1577–1583.
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Chin. J. Catal. **2013**, *34*, 1667–1673.
4. He, W.; **Ge, Y.-C.**; Tan, C.-H.* Halogen Bonding Induced Hydrogen Transfer Reaction of C=N Bond with Hantzsch Ester.
Org. Lett. **2014**, *16*, 3244–3247.
5. **Ge, Y.-C.**; Cui, X.-Y.; Jiang, H.; Ren J.-Y.; Tan, C.-H.* Enantioconvergent Synthesis of Tertiary Cyclic Allylboronates via (Guanidine)copper-Catalyzed Allylic Borylation.
(Manuscript in preparation)
6. **Ge, Y.-C.**; He, W.; Tan, C.-H.* Halogen Bonding Induced Friedel-Craft-type Alkylation of Thiophenes with α,β -Unsaturated Carbonyl Compounds. (Manuscript in preparation)

ABBREVIATIONS

Ac	acetate
acac	acetylacetone
AIBN	2,2'-azo <i>bisisobutyronitrile</i>
Boc	<i>Tert</i> -butyloxycarbonyl
Bu	butyl
BHT	butylated hydroxytoluene
Bn	benzyl
Boc	<i>tert</i> -butyloxycarbonate
BPO	benzoyl peroxide
Bz	benzoyl
Cbz	benzyloxycarbonyl
COD	1,5-cyclooctadiene
CPME	cyclopentyl methyl ether
Cy	cyclohexyl
dba	dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCC	<i>N, N'</i> -dicyclohexylcarbodiimide
DCM	dichloromethane
DEC	diethyl carbonate
DECT	direct enantio-convergent transformation
DKR	dynamic kinetic resolution

DMA	<i>N, N</i> -dimethylacetamide
DMAP	4-dimethylaminopyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
Equiv.	equivalent
ESI	electrospray ionization
Et	ethyl
FC	flash chromatography
GC	gas chromatography
GCMS	gas chromatography-mass spectrometry
HRMS	high-resolution mass spectrometry
HPLC	high performance liquid chromatography
HWE	Horner-Wadsworth-Emmons
<i>i</i>	iso
IPA	isopropyl alcohol
KR	kinetic resolution
LDA	lithium diisopropylamide
<i>m</i>	meta
Me	methyl
Mes	mesityl
Ms	mesyl (methanesulfonyl)
<i>n</i>	normal
NBS	<i>N</i> -bromosuccinimide
NPs	nanoparticles

<i>o</i>	ortho
OAc	acetate
OTf	trifluoromethanesulfonate
<i>p</i>	para
Pin	pinacolate
Piv	pivaloyl
Ph	phenyl
Pr	propyl
r.d.s.	rate determining step
<i>s</i>	secondary
<i>t</i>	tertiary
TBAI	tetra-(<i>n</i> -butyl) ammonium iodide
TBAB	tetra-(<i>n</i> -butyl) ammonium bromide
TBS	<i>tert</i> -butyldimethylsilyl
TEA	triethyl amine
TEMPO	(2,2,6,6-tetramethylpiperidin-1-yl)oxyl
Tc	thiophene-2-carboxylate
Tf	triflate
TLC	thin layer chromatography
TMS	trimethylsilyl
Tol	toluene
Troc	2,2,2-trichloroethyl carbonate
Ts	4-toluenesulfonyl
TS	transition state
Xyl	xylene

α	alpha
β	beta
γ	gamma
μ	micro
π	pi
η	eta
ω	omega
σ	sigma

Chapter 1

Introduction

1.1 Introduction

Boron is an important chemical element in nature, which was symbolled as B with atomic number 5. It is a metalloid found in the period 2 under the group 13, p block of the periodic table (**Fig. 1.1.1**). As a low abundance element in nature, boron is rarely concentrated as its elemental form but more often found as borate minerals. Due to its metallic properties, elemental boron is rather active, which donates electrons and form compounds with electron negative elements with a valence of +3. In industry, boron and its derivatives, are largely used as additives in structural materials, such as fiberglass, polymers and ceramics. On the other hand, boron compounds are also employed as fertilizer in agriculture and insecticides in biology.

Boron		B Boron 5 10.81	
Group	13	Melting Point	2077 °C
Period	2	Boiling Point	4000 °C
Block	p	Density	2.34 g/cm ³
Atomic Number	5	Relative Atomic Mass	10.81
State(20°C)	Solid	Key Isotopes	¹¹ B
Electron Configuration	[He]2s ² 2p ¹	Atomic Radius	1.92 Å

Figure 1.1.1 Boron in periodic table.

In the area of organic chemistry, compounds bearing boron atoms are useful and versatile synthetic reagents or reaction intermediates as the boryl groups can be readily transformed to other functional groups regioselectively and stereoselectively under certain conditions ^[1–3]. The starting point of organic boron chemistry normally is considered as the addition of borane to olefins, the product of which can be further oxidized to the corresponding alcohol ^[4]. However, due to the unstable nature and high toxicity of boranes, researchers focus more on their environmental friendly alternatives which are expected to give similar or even better reactivity in organic transformation. Among them, boronic acids ^[5] and their derivatives are found to be more suitable because they are generally bench-stable which is ideal for long-term storage and non-toxic which requires minimal protection during reaction process.

In the ground state of boronic acid derivatives, the boron atoms are normally sp^2 -hybridized and triple covalently bonded with one carbon substituent and two hydroxyl or alkoxy groups. According to the octet rule, the central boron atom only owns six valence electrons in a trigonal planar geometry, which lacks two electrons to be saturated and thus exhibits somewhat Lewis acidity. Neutral but electron-deficient boron reagents (such as BF_3 and $B(C_6F_5)_3$) have been widely utilized as Lewis acid catalysts in a series of LUMO activation type organic transformations. More recently, a new catalytic concept was reported as the frustrated Lewis pair, and employed in hydrogen gas activation or C-H activation. Notably, such topic remained rather challenging in the area of organocatalysis, with boron-based Lewis acids.

However, comparably moderate stability can be observed with organic boronic acid and its derivatives. They are generally considered to be thermostable, air resistant and moisture insensitive, when looking at the electronegativity of boron (2.04) and their nucleophilic reactivity in cross-coupling reactions as organometallic compounds. These phenomena should

be mainly attributed to the specific oxophilicity (fluorophilicity in trifluoroborate salts) of boron. B–O bonds are short (around 1.30 Å) compared with C–O bonds (1.43 Å) and considerable stronger than the corresponding C–O bonds (130 kcal/mol vs 92 kcal/mol)^[5]. Due to the electron-deficiency of boron, the lone pairs of electrons on oxygen atoms tend to partially donate to boron, overlapped with its remaining empty p orbital. In such situation, the original B–O bond in the compounds no longer acts as a single bond but also exhibits partial double bond character, thus giving rise to those unique properties.

Although boronic acids exhibit high reactivity, it is often difficult to purify them after work-up procedure in a typical reaction. Besides, alkyl boronic acids are commonly considered thermally unstable, which are readily hydrolyzed or oxidized in the presence of moisture and air. In the past decades, a series of boronic acid derivatives have been discovered and employed in boron-mediated coupling reactions^[6], as illustrated in **Fig. 1.1.2**. Notably, they are typically less reactive as the original boronic acid in most cases, as the Lewis acidity of boron atom is neutralized in some extent by more electron-donating ligands or negative charges in a rigid ring. However, it is believed that, in the presence of water, these derivatives can gradually be hydrolyzed to boronic acids which are most commonly used in the organic synthesis. For the range of boronate or boronic ester in the literature, pinacol with its diol ligand in the BPin motif provides extra stability due to its high steric demand. Compared with boronic acids and other derivatives, the corresponding pinacol boronic esters **11.3** are much more soluble in non-polar solvents, accessible to be purified via silica column chromatography, and able to be stored long term, while a medium reactivity in the reaction was reserved. Boronic esters with less steric demanding or electron donating ligands, such as **11.5** and **11.7** only give fair stability

Neutral Boronic Acid: **I1.1****Neutral Boronate:** **I1.2** **I1.3 (RBPIn)** **I1.4 (RBeg)** **I1.5 (RBCat)** **I1.6 (RBHex)** **I1.7 (RBNeop)** **I1.8** **I1.9****Neutral Boronamide:** **I1.10 (RBDam)****Negatively Charged Borate:** **I1.11** **I1.12**

Figure 1.1.2 The structures of boronic acids and their derivatives

when bearing aromatic substituents, while **I1.2** and **I1.4** are commonly prepared *in situ* and used directly as solutions. On the contrary, boronamides, such as **I1.10**, sometimes are found rather reluctant in the reaction, thus normally serving as an inert surrogate of boryl group unless the strong acid was charged. Recently, Molander et al. also reported the utilization of potassium trifluoroborate salts **I1.12**, which gave similar behaviour to boronic acids in the presence of water when employed in Suzuki-type cross-coupling reactions ^[7].

Figure 1.1.3 The equilibrium of transesterification between boronic esters.

A more straightforward method to determine the stability of corresponding boronate or boronic ester is to conduct the analysis of transesterification equilibrium between ethylene glycol boronic ester **I1.13** and the free diol **I1.14** ^[8-9], as illustrated in **Fig. 1.1.3**.

Figure 1.1.4 The relative stability of boronic esters.

Upon the investigation of transesterification, the relative stabilities of a series of boronic esters were obtained, which was summarized in **Fig. 1.1.4**. Generally, six-membered cyclic diol as protecting group afforded the corresponding boronate in higher yields, which was attributed to a better overlap between the empty *p* orbital of boron and lone pair of electrons on oxygen atoms. Notably, **I1.16** (a *trans*-diol) was completely inactive, compared with its *cis* isomer.

Methyl substitution at the α -carbon enhanced stability as illustrated by **I1.17** to **I1.19** and **I1.20** to **I1.13**. Great stabilization effect was induced when pinacol was employed in **I1.21**, although due to steric hinderance the rate of ester exchange was also reduced. On the contray, catechol led to a substantial low conversion in the case of **I1.23**, as mentioned above, because of poor electron donation of the oxygen atoms due to the presence of a benzene ring next to them.

The reactivity of boronic acid and its derivatives normally arises as the activation of central boron atom by additional nucleophile or Lewis base. As shown in **Fig. 1.1.5**, medium Lewis acidic boronic acid derivative **I1.24** is able to accept one additional nucleophile to give a tetracoordinated boron with sp^3 hybridization ^[5]. The nucleophilicity of the corresponding adduct **I1.25** was found to acquire much enhanced reactivity in the model Suzuki-Miyaura cross-coupling reactions.

Figure 1.1.5 The activation mode of boronic acid and its derivatives.

Ligand exchange was observed, as **I1.26** might be obtained when original OR_1^- was removed. It was also the conventional method to synthesize boronic acids, as in the case that trimethyl borate was treated with Grignard reagents or organolithiums to afford the desired methyl ester or crude boronic acid after hydrolysis by strong acid.

1.2 Miyaura Borylation

The most practical synthesis of boronic acid and its derivatives is the nucleophilic attack of electrophilic boron reagents, followed by ligand exchange or protection. However, this method sometimes was limited to the reactivity of nucleophiles and functional group tolerance. In such situation, besides hydroboration, diboron reagent participated metal catalyzed direct borylation reaction has become more and more attractive.

Figure 1.2.1 The classic Pd catalyzed Miyaura borylation reaction.

The precedent successful utilization of diboron(4) compounds ^[10] to afford the versatile organoboronates is Miyaura borylation which is named after N. Miyaura from Hokkaido University for his pioneering investigation in 1995 ^[11]. Inspired by their initial work of platinum catalyzed diborylation of alkynes with diboron reagents ^[12], N. Miyaura first reported the substituted *sp*²-borylation reactions in 1995 when aryl halides and bis(pinacolato)diboron were found able to furnish the corresponding aryl boronates in the presence of palladium/phosphine complex as catalyst and KOAc as base ^[11]. The classic Miyaura borylation reaction is shown in **Figure 1.2.1**.

After decades of development, the substrates are now largely expanded but not limited to triflates ^[13], mesylate ^[14] and diazonium salts ^[15]. The reaction is no longer limited to stable aryl substrates but also vinyl, allyl or even alkyl, especially when cheap transition metals such as Ni ^[16], Cu ^[17–18], Zn ^[15, 19], Co ^[20] and Fe ^[21–24] are found to efficiently afford the corresponding

boronates. It is believed that these 1st row transition metals are weaker d orbital donors, and more likely to be involved in a single electron transfer (SET) mechanism^[16] with the formation of radical intermediates. Such characteristic inhibits the possibility of β -H elimination to give the corresponding olefin after oxidative addition, which is frequently observed in Pd catalyzed cross-coupling reactions with alkyl/allylic substrates bearing β -H atoms.

Figure 1.2.2 Reaction mechanism I for Miyaura borylation.

A proposed mechanism for Miyaura borylation was illustrated in Figure 1.2.2. Like most of palladium catalyzed coupling reactions, the catalytic cycle is believed to involve Pd(0) complexes as the true active catalytic species, which are normally initiated from the ligand dissociation from a stable tetra-coordinated Pd(0) complex or the degradation of Pd(II) precursors with some reducing agent, such as organic bases, ligands, organometallic reagents, or even solvents. Then such Pd(0) active species may act as the nucleophile to attack the aryl halide substrates, in this initial case, to give the corresponding aryl palladium halide complex

II.31. This step is attributed to oxidative addition, which may proceed in a concerted, S_NAr , S_N2 , or radical pathway. As a result, both of the coordination number and oxidation state are increased by 2. For a concerted oxidative addition, the reaction involves a 3-membered concerted transition state, so the geometry of the Ar and X in the corresponding product **II.31** is *cis*, which may further transform to the *trans*-complex to minimize the steric repulsion if mono-ligated phosphines are employed. For the transmetalation in the next step, with the help of base, diborons are activated and nucleophilic enough to transit to palladium center, generating the targeted aryl boryl palladium complex **II.32** and inactive boronates as by-product. The mechanism of transmetalation is still less known in details, compared with oxidative addition and reductive elimination. However, attempts to investigate this step have already showed some clues that both **Path A** and **B** shown in **Fig. 1.2.3** are responsible for the generation of four-membered concerted transition state **II.34** ^[25–27]. The aryl boryl palladium complex **II.32** is either *cis*- or *trans*- configuration in the reaction mixture, but will only afford the arylborate product from a *cis*-complex due to the geometric requirement of reductive elimination. After that, the initial active Pd(0) species is believed to be regenerated from the cycle.

Figure 1.2.3 The indistinguishable two pathways for transmetalation in palladium catalyzed reactions.

1.3 Achiral Allylic Borylation

Among numerous boron-containing compounds, allylic boronates have become highly valuable intermediates and versatile synthons in a wide-range of organic transformations. Besides multiple functionalizations performed with organic boronates, allyl boronates can be added to carbon-oxygen or carbon-nitrogen double bonds to afford the corresponding homoallylic alcohols or amines ^[28]. This reaction normally proceeds with the transition state bearing a chair-like six-membered ring ^[29–38], which exhibits high regio- and diastereoselectivity with almost quantitative yield, making it even more convenient and straightforward to give two or more chiral centre. Therefore, the development of a catalytic system that could provide boronates in an enantioselective fashion becomes highly desirable.

Conventionally ^[36, 39–42], the practical synthesis of allylic borane could be achieved by using organometallic reagents, such as organolithiums and Grignard reagents, with electrophilic boron like BCl₃ or B(OMe)₃. However, this approach normally suffered a limited substrate scope when the functional groups are sensitive to base or the allylic halide precursors are not available. In such situation, palladium catalyzed allylic substitution via an allylpalladium intermediate, alternatively, has become more favorable, as the allyl complexes derived from the corresponding carbonates or esters are able to readily undergo transmetallation with a series of organometallic compounds to give the desired coupling product after the upcoming reductive elimination ^[28].

The first example of achiral allylic borylation ^[43] was reported by N. Miyaura and his group members in 1996 after their previous foundational discovery of palladium catalyzed aryl borylation (**Fig. 1.3.2**) ^[11]. They found that in a similar condition allylboronates **13.2** can be

successfully generated with allyl carbonates **I3.1** as substrates in the presence of palladium(0) as catalyst, while bis(pinacolato)diboron was used as boron nucleophile. In this reaction, allylic dimerization was found to be a major side-reaction which may be derived from further cross-coupling of allylpalladium intermediate with furnished allyl boronates.

Figure 1.3.1 The first example of achiral allylic borylation with B₂Pin₂ reported by N. Miyaura.

During the investigation, the authors found that addition of extra ligand such as PPh₃ would slow down the reaction rate and the combination of Pd(dba)₂ with DMSO helped to prevent the formation of palladium black due to catalyst decomposition at early stage of the reaction. Among the carbonates they screened, acetates exhibited best results of furnishing desired boronate in high yields with minimum amount of dimerization. Interestingly, as shown in **Fig. 1.3.2**, it was observed that the regioselectivity was dramatically determined by the substituents. When branched allylic carbonate **I3.1a** was used, a less steric hindered linear product **I3.2a** was afforded after the allylic migration. However, when the double bond was conjugated to aromatic ring as it was in the case of linear substrate (*E*)-**I3.1b**, no migration was observed. Additionally, *Z*-configuration substrate **I3.1c** stereoselectively furnished the same *E*-type product **I3.2b**, which was also given by branched acetate **I3.1d** in high yield.

Figure 1.3.2 The regioselectivity of achiral allylic borylation reported by N. Miyaura.

In such situation, they proposed the preliminary reaction mechanism as illustrated in **Fig. 1.3.3** below, according to previous allylic nucleophilic substitution. In the mechanism they hypothesized that palladium(0) served as the true catalytic species and reacted with carbonate **I3.1** to give the corresponding allylpalladium intermediate **I3.4** after oxidative addition. In the presence of B_2Pin_2 , transmetallation occurred to give the boryl substituted palladium complex **I3.5**, which would give rise to product **I3.2** after reductive elimination. Meanwhile, if the transformation from **I3.4** to **I3.5** was sluggish, the possibility of dimer **I3.3** generation would largely be increased.

Figure 1.3.3 The proposed mechanism of palladium catalyzed allylic borylation reactions.

Later, they applied this system to a sequential reaction of allylborylation followed by intramolecular addition to carbonyl group (**Fig. 1.3.4**)^[44]. In this case, DMSO was found able to complex the boronate generated and thus inhibit the following cyclization (**I3.8**), so the solvent was change to less polar toluene with the help of $AsPh_3$ as ligand to increase the stability of Pd species. The 1H -NMR experiment investigation suggested that final product **I3.8** was given with a *cis*-cyclization in stereoselectivity.

In 1999, Tamaru et al. also reported the usage of trialkylborane, triethyl and tributyl in this case, as boron sources to react with allylic palladium complexes^[45]. As shown in **Fig. 1.3.5**, in the presence of Pd(0) catalyst, benzolate **I3.9** successfully reacted with triethylborane and attacked the aldehyde nucleophilically to give the desired homoallylic alcohol **I3.10** in an overall yield of 46%. During their investigation, they found that allylic halide wouldn't work and LiCl as additive would inhibit the reaction, which indicated that the counter-ions of the allyl complex were crucial for the process. Dimerization products were also observed in some

Figure 1.3.4 The sequential palladium catalyzed allylborylation/intramolecular cyclization reactions.

cases. Additionally, in their proposed mechanism, an ethyl-allyl exchange process occurred to afford the allylboronate intermediate, rather than transmetallation which was described by Prof. Miyaura.

Figure 1.3.5 The sequential palladium catalyzed allylborylation/homoallylation reactions with Et_3B .

However, Et_3B employed as the boron source generally led to a more rigid and complicated experimental protocol since it was highly toxic and sensitive to air. Meanwhile, the allylation products bearing BEt_2 substituent were also not stable enough to be isolated, which might result in poor regioselectivity in the following steps due to the interference by Lewis acidic palladium or other boron-containing species. Inspired by the pioneering studies, research

groups thus paid their attention to palladium-catalyzed allylic borylation reactions with diboron reagents instead.

Figure 1.3.6 One pot synthesis of homoallylic alcohol and amine by Prof. Szabó.

In 2003, Prof. Szabó's group reported their discovery of a concised one-pot synthesis of homoallylic alcohols and amines (**Fig. 1.3.6**)^[46]. Similar to the previous conditions established by Miyaura et al., they applied $\text{Pd}_2(\text{dba})_3$ as catalyst and DMSO as solvent. When allylic acetates **I3.11** was employed as substrates with bis(pinacolato)diboron, in the presence of aromatic aldehydes or imines, the corresponding nucleophilic addition products were furnished with excellent regioselectivity and remarkable stereoselectivity.

Interestingly, regardless of branched or linear allylic acetate **I3.11** was used, only branched C–C coupling products could be obtained. While homoallylic alcohol *anti*-**I3.13** was successfully generated in the absence of palladium upon their mechanistic investigation, the amine **I3.14** derived from sulfon-imines could be formed on the condition that palladium was present, but, with a configuration of *syn*- instead.

Figure 1.3.7 The regio- and stereo- selectivity in palladium catalyzed allylic borylation reactions.

Upon their mechanistic investigation, no allyl-allyl coupling was found to be taking place, as the conversion of allylic acetates **13.11** were faster when carbonyl electrophiles were present. It indicated that electrophiles helped to consume the accumulated allyl boronate **13.12**, and thus reactivated the catalytic borylation process and diminished the formation of bis-allylpalladium complexes which might lead to homocoupling products. As shown in **Fig. 1.3.7**, the high stereoselectivity was attributed to the selective formation of *trans*-allylpalladium complex **13.13** due to less steric hinderance. Meanwhile, after transborylation took place, in the absence of sterically demanding ligands, intermediate **13.15** was believed to give linear allylic boronate **13.16** as the major product. Detailed mechanistic studies were present in their follow-up publications ^[47]. In this work, Chiral diol derived diborons were also synthesized and employed as the boron source in the allylic borylation reaction, in order to give chiral auxillary based allylboronates. After the borylation products were further used in the addition to aldehyde, the enantioselective homoallylic alcohols could be obtained, as illustrated in **Fig. 1.3.8**. With chiral diboron **13.18**, final product **13.19** was isolated in a yield of 83% with 53% ee.

Figure 1.3.8 Chiral version of homoallylic alcohol synthesis by Prof. Szabó.

Further experiments were explored by the same group on the activation of more challenging substrates. Allylic alcohols were the most easily accessible substrates from which allyl carbonates and halides were normally derived. If the removal of reluctant hydroxyl groups were wanted, harsh reaction conditions and strong Lewis acids were usually required, but they are not suitable in the synthetic process of boronates ^[48].

Figure 1.3.9 SeCSe pincer complex mediated allylic borylation of allylic alcohol by Prof. Szabó.

In 2005, although diboronic acid, or tetra(hydroxyl)diborane, was employed in the palladium catalyzed allylic boronation with allylic acetates by Prof. Szabó, the reaction was found rather sluggish with an S_N2 or S_N2'-type routine depending on the substrate ^[49]. When the same protocol was applied to allylic alcohols **13.20**, with B₂(OH)₄ as boronation reagent, boryl substitution products **13.21** were successfully afforded in the presence of SeCSe pincer-type complex **13.19**. The reaction could proceed in mild conditions. Upon the product characterization, it clearly shown that the reaction underwent with a trans stereoselectivity and allylic rearrangement would occur to give the most stable and less steric hindered C=C double bonds. Besides, Brønsted acid *p*-toluene sulfonic acid (TsOH) was found able to

promote the reaction rate considerably. Armed with the above details, the author proposed a reaction mechanism involving activation of allylic alcohol as illustrated in **Fig. 1.3.10**.

Figure 1.3.10 Allylic alcohol activation mode proposed by Prof. Szabó.

It was believed that in the presence of diboronic acid, hydroxyl group on allylic alcohol was converted to good leaving group. Considering that methanol played an important role to maintain the reaction proceed smoothly, it was proposed that a six-membered ring transition state was involved in the activation of allylic alcohol. As shown in **Fig. 1.3.10**, substrate **I3.20** interacted with weak Lewis acidic diboronic acid to give a neutral adduct. With the aid of methanol, the allyloxy managed to replace hydroxy group, giving the corresponding boronic ester which could leave more easily. It was also mentioned that the water molecule generated during the esterification process would help to facilitate the B–B bond cleavage.

This methodology was further broadened to B_2Pin_2 as boryl source ^[50], while an acid like TsOH was needed as co-catalyst to transform B_2Pin_2 to $\text{B}_2(\text{OH})_4$ in order to activate allylic alcohol. One-pot synthesis of homoallylic alcohols were also attempted after combining the generation of allylic boronic acid or boronate with nucleophilic addition to aldehydes, the corresponding acetals, imine or even ketones ^[51–54].

In 2013, Prof. Szabó's group reported their detailed mechanistic investigation on this topic, together with a variation of allylic silylation reactions ^[55], in which case 5 mol% $[\text{Pd}(\text{MeCN})_4](\text{BF}_4)_2$ was employed as catalyst. After following the course of the reaction with

^1H , ^{11}B and ^{19}F -NMR spectroscopy, they found that Lewis acid BF_3 and decomposition product HOBPin was observed in the spectra as illustrated in **Fig. 1.3.11**. It indicated that the counter ion BF_4^- was decomposed in the presence of B_2Pin_2 to give BF_3 that could be further used in the activation of allylic alcohol.

Figure 1.3.11 ^{19}F and ^{11}B -NMR spectra of the crude reaction mixture after allylic borylation reported by Prof. Szabó^[55].

On the other hand, as shown in **Fig. 1.3.12**, allylpalladium complex **I3.23** with B_2Pin_2 gave the targeted boronate **I3.2b** in a clean and stoichiometrical way. It highly suggested that an alternative to precursor **I3.23**, marked as $[\text{AllylPdL}_2]\text{-X}$ here, was the true catalytic species in the reaction, which was also confirmed by the signal of a new allyl complex found in ^1H -NMR.

Figure 1.3.12 Stoichiometric control experiment between allyl palladium complex and B_2Pin_2 .

As for the stereoselectivity of this reaction, mechanism investigation was focused when *cis*-**13.24** was chosen as the borylation substrate. It was found that the borylation product **13.25** was isolated in 70% yield as a mixture with *trans*: *cis* ratio of 5:1.

When monitored with $^1\text{H-NMR}$, both *cis*- and *trans*-allyl palladium complex was detected to be generated during the reaction. The *trans* complex was shown to be the major stereoisomer via an inversed oxidation addition from substrate *cis*-**13.24**. It was also observed that the *trans*-complex underwent borylation process much faster than the *cis*-complex, which led to a selective formation of *trans*-**13.25** due to the stereo requirement of reductive elimination. Although in the stoichiometric reaction between isolated *trans* palladium complex **13.26** with B_2Pin_2 the stereoselectivity suffered a great loss, as shown in **Fig. 1.3.14**, the authors attributed this observation to stereoisomeric scrambling caused by $\text{Pd}(0)$ active species generated from reductive elimination in high catalyst loading. This conclusion was supported experimentally as the stereoselectivity was increased when lowering catalyst loading or charging reaction facilitator $\text{BF}_3 \cdot \text{Et}_2\text{O}$.

Based on their investigations of silylation reaction, they proposed a detailed reaction catalytic mechanism as illustrated in **Fig. 1.3.15**. The authors believed that when $\text{Pd}(\text{II})$ catalyst was charged in the reaction, in the presence of B_2Pin_2 , it was further reduced to $\text{Pd}(0)$ active species, giving BF_3 as well. The allylic alcohol **13.28**, after activated by generated BF_3 ,

underwent the oxidative addition with Pd(0) smoothly to give the corresponding allyl palladium complex **I3.30**. Further transmetalation with another equivalent of B₂Pin₂ afforded the allyl boryl palladium intermediate **I3.31**, which would give rise to final product **I3.32** after reductive elimination.

Figure 1.3.14 The stereoselectivity of the stoichiometric borylation with allyl palladium complex.

Besides the effort devoted by Prof. Szabó et al., in the area of palladium catalysis, Prof. Kabalka also contributed with their exploration on allylic borylation with Baylis-Hillman acetates ^[56–57]. Adduct **I3.33** readily reacted with B₂Pin₂ with Pd(OAc)₂ as catalyst, giving trifluoroborate **I3.34** in a total isolated yield of 70% after being treated with excess aqueous KHF₂ solution. Further application of the products was also evaluated ^[57].

Figure 1.3.15 The proposed mechanism of the palladium catalyzed allylic borylation with allyl alcohol as substrate

Figure 1.3.16 The palladium catalyzed allylic borylation with Baylis-Hillman adducts.

Another attempt to revise this borylation reaction was to utilize more accessible and naturally abundant metals as catalyst. In this direction, a series of cheap metals was tested in the borylation reaction involving allylic-type electrophiles, like Ni^[58–59], Fe^[22, 60] and Cu. Based on their investigation, except for palladium, copper was found to be very effective in this reaction. As early in 2000, Prof. Miyaura has already reported the employment of the combination of CuCl and KOAc in the conjugated addition and diborylation of unsaturated compounds^[61]. As shown in **Fig. 1.3.17**, they found such system was also able to afford the corresponding boronate **1.3.38** in a yield of 53% when allyl chloride was employed as electrophile. Although no evidence by spectroscopy, they proposed that a new Cu–B intermediate **1.3.35** was generated which acted as the nucleophile that dominated the following reaction after B₂Pin₂ activated by the Lewis base KOAc.

Figure 1.3.17 The first example of copper catalyzed borylation by Miyaura.

Baylis-Hillman adducts were also utilized in the copper catalyzed borylation system. Reported by Ramachandran in 2004 ^[62], which would give the allylic rearranged boronate **13.39** in an S_N2' addition pathway with a high *E/Z* stereoselectivity. When chiral diborons were employed as the boron source, allylic boronates generated were able to directly react with the aldehyde followed by the cyclization in the presence of acid, which would give the *cis*-favored lactone **13.41** with *ee* up to 27%.

Figure 1.3.18 The tandem reaction after copper catalyzed allylic borylation.

The significant feature of copper catalyzed borylation was discovered by Prof. Ito and Prof. Sawamura in 2005 ^[63]. They found that when pre-synthesized $\text{Cu-O}i\text{Bu}$ was used along with Xantphos (a phosphine ligand with the large bite angle) with allylic carbonate **13.42** as substrate, γ -selective boronate **13.44** was afforded stereospecifically in high yield after an S_N2' attack. On the contrary, when other phosphines such as dppe or PPh_3 were employed instead, low yield was obtained. However, preliminary reported CuCl-KOAc-LiCl catalytic system was found totally ineffective, and $\text{Pd}(\text{dba})_2$ as catalyst would suffer a poor regioselectivity (**13.43** : **13.44** = 43:57) although the yield was excellent.

Figure 1.3.19 The copper catalyzed regioselective and stereoselective allylic borylation of linear allylic carbonate reported by Ito and Sawamura.

Figure 1.3.20 The synthesis of optical active boronates from enantioenriched allylic carbonates.

More interestingly, it was also noted that when enantioenriched carbonates were employed, an expeditious and readily route to optical active allylic boronates resulted. As illustrated in **Fig. 1.3.20**, when enantioenriched (S)-(E)-**13.45** was used with their system, (S)-(E)-**13.46** was furnished in high yield with almost no erosion of enantioselectivity. With high stereoselectivity observed in the result, it was proposed that Cu–B active species attacked in an anti-S_N2' pathway. However, more importantly, when Z-formed carbonate **13.47** but with same configuration at the chiral center was used, a completely chirality inversion was found, which was also explained by avoiding allylic 1,3-strain. Notably, Prof. Ito and Sawamura also found that when conventional allylic carbonate was substituted with silyl group as shown as **13.49** in **Fig. 1.3.20**, almost no allylic borylation product **13.51** was obtained, but mostly a

borylation-cyclopropanation product **13.50** was formed with a high *trans/cis* selectivity ^[64]. Upon their further investigation, it was assumed that the silyl group activated the allylic carbonates in an unexpected way. As the weak Lewis acidic nature of silicon atoms, the addition of an active boryl-copper(I) intermediate to allylic substrates was proposed to be reversed in regioselectivity.

Figure 1.3.21 The boryl-cyclopropanation from silyl substituted allylic carbonates.

Moreover, a version of catalytic propargylic borylation reaction was also developed by Prof. Ito and Sawamura ^[65]. As shown in **Fig. 1.3.22**, propargylic carbonates **13.52** would be readily converted to multisubstituted allenylboronates **13.53** with their versatile copper-Xantphos system. Later in 2014 ^[66], Prof. Szabó's group managed to prepare the corresponding borylation product with terminal alkynes **13.54** as substrate with a Pd/Cu(Ag) bimetallic catalytic system, which failed when CuOtBu was employed. Delightfully, when CuCl was used instead of CuI as a co-catalyst, direct substitution at the propargylic position (**13.55**) occurred rather than the previous allenyl rearrangement. When replaced with Ag salts, the leaving group on **13.54** could even be broadened to acetates, which was considerably more difficult. After that, Prof. Szabó developed the one-pot synthesis of aryl allenes after aryl iodides were introduced into the system, as the Suzuki-type cross-coupling took place after borylation ^[67].

2008 Ito and Sawamura:

2014 Szabó:

Figure 1.3.22 The propargylic borylation reported by Prof. Ito, Sawamura and Szabó.

Transition-metal-free allylic borylation reaction was developed recently^[68]. Despite that the traditional two challenges were converged into one, Prof. Szabó and Prof. Fernández managed to carry out the borylation of allylic alcohols in the absence of any metallic compounds, only with diboron reagents, base and methanol. It was postulated that the success was due to the activation of one boryl unit by the direct quaternization with alkoxides, which led to the formation of Lewis acid-base adduct bearing an enhanced nucleophilic ability. The assumed catalytic cycle was demonstrated in **Fig. 1.3.23**.

In this proposed mechanism, the formation of the adduct **I3.56** was considered crucial for the borylation reaction. As borylated product **I3.59** was isolated after the reaction was completed, it seemed that the reaction underwent an S_N2' attack between adduct **I3.56** and allylic substrates. However, when allylic alcohol **I3.57** was replaced with benzyl protected ester **I3.58**, no desired product **I3.59** was found, which indicated that the hydroxyl group on **I3.57** played a significant role in the success of this transformation.

Figure 1.3.23 The proposed catalytic cycle for transition-metal-free allylic borylation.

1.4 Enantioselective Allylic Borylation

With the ability to be further functionalized with high stereoselectivity, optically active α -enantiogetic allylic boronates offered a great opportunity to afford versatile chiral building block and organic compounds ^[1, 5, 69–70]. Traditionally, chiral auxiliaries on boron atoms were utilized to induce enantioselectivity in stoichiometric reactions in order to obtain enantioenriched allylboronates ^[1, 35, 69–74]. Even though a series of catalytic enantioselective reaction, including hetero[4+2] reaction, 1,4-silaboration of 1,3-diene, diboration of allenes, alkylation of 3-halo- or 3-acetoxy-2-propenylboronates, and hydroboration, were reported which seemed much more attractive ^[75–80], there were only limited practical methods to perform direct substitutive allylic borylation with high enantioselectivity.

Precedential example in this area was reported by Ito and Sawamura^[70] in 2007 that with (*R,R*)-QuinoxP* employed as ligand a variety of (*Z*)- and (*E*)-type allylic carbonates were able to afford the corresponding allylic rearranged boronates in high yields and excellent enantiomeric purity. Compared with this privileged *P*-chiral phosphine ligand, commonly-used chiral ligands which exhibited excellent enantiocontrol in asymmetric hydrogenation reactions, such as DUPHOS, DIOP, SEGPBOS and BINAP, could not afford satisfied result in both activity and stereoselectivity. Notably, as (*E*)-**I4.1** could only lead to **I4.2** in 44% ee under the same reaction conditions, the enantioselectivity and absolute configuration of the product was found to be greatly influenced by *E/Z* configuration of the substrates.

Figure 1.4.1 The first example of catalytic asymmetric allylic borylation reported by Prof. Ito and Prof. Sawamura.

After a series of *Z*-type substrates were tested, the authors proposed a mechanism in which the regioselectivity and stereoselectivity were well-explained. According to their previous studies on copper catalyzed allylic borylation, copper alkoxide **I4.4** was proposed to undergo transmetallation to give the corresponding boryl-copper complex **I4.5**. After associated with the C=C double bond of allylic carbonates, intermediate **I4.6** went on boryl migratory insertion, affording γ -borylated intermediate **I4.7**. After reductive elimination and

decarboxylation, the desired boronate **14.8** was furnished with a methoxy substituted alternative of **14.4** regenerated.

Figure 1.4.2 The proposed reaction mechanism and enantiofacial discrimination of catalytic asymmetric allylic borylation reported by Prof. Ito and Prof. Sawamura. **a)** reaction intermediates and selectivity for (Z)-**14.3**; **b)** reaction intermediates and selectivity for (E)-**14.3**

With regard to regioselectivity, when (Z)-**14.3** was used, in the proposed four-membered ring transition state, **TS1** was more likely to be favoured to give **(S)-14.8**, compared with steric repulsion in **TS2**. However, in the case of (E)-**14.3**, due to both **TS3** and **TS4** suffering from steric issue, although the former might be favoured to furnish **(R)-14.8** as the major product,

the enantiodiscrimination between two conformation became less important, thus giving a poor enantiomeric excess.

In addition, this Cu/QuinoxP* system was later utilized by the same group in desymmetrization of *meso*-2-alkene-1,4-diol carbonate derivatives ^[81]. Because, in most of the substrates that they tested in this work, Z-configuration was locked due to the cyclic structure, the corresponding boronates were formed with high stereoselectivity. After nucleophilic attack with aldehyde, the enantiogenic boronates could afford homoallylic alcohol with three chiral centers in one pot with high enantioselectivity and diastereoselectivity.

In the area of asymmetric catalysis, how to convert racemic substrates into single enantiomeric product with a chiral catalytic system, is still underexplored. As shown in **Scheme A** in **Fig. 1.4.3**, conventional methods involved a kinetic resolution process. That is, when two enantiomers were treated with a catalyst, S_A reacted much faster than S_B , leading to the corresponding enantioenriched product P_A while S_B remained unreacted. However, the maximum yield of an ideal kinetic resolution process could only achieve 50%, and indeed this was not always the case. Another options were dynamic kinetic resolution (DKR) or dynamic kinetic asymmetric transformation (DYKAT) as shown, which indicated that a racemization process between substrates or a desymmetrization process to prochiral intermediate was involved. Unfortunately, most chiral starting materials were too stable to be racemized as DKR required. On the other hand, it was also difficult to find a way to convert substrates to prochiral or symmetric intermediate in the DYKAT process. Thus, when it met the situation that racemates were bearing robust chiral centers, deracemization to achieve enantiospecific product with suitable catalytic system remained unsolved.

Figure 1.4.3 Conceptual schemes for asymmetric reactions of racemic chiral substrates to produce enantioenrich products by Ito and Sawamura. **a)** Kinetic resolution (KR); **b)** Dynamic kinetic resolution (DKR); **c)** Dynamic kinetic asymmetric transformation; **d)** Direct enantioconvergent transformation.

In 2010, Prof. Ito and Prof. Sawamura developed a new method as direct enantioconvergent transformation to solve this challenging problem ^[82], which was to convert each enantiomer of a racemic mixture into the same enantiomeric product but with different pathway in excellent enantiocontrol (**Scheme d** in **Fig. 1.4.3**).

Figure 1.4.4 Direct enantioconvergent transformation for allylic borylation by Ito and Sawamura.

In their experiments, racemic cyclic ester **I4.8** was successfully converted to enantiopure boronate **I4.9** after the S_N2' attack and allylic migration. Up to 97% ee could be achieved

when their privileged ligand QuinoxP* was employed. Interestingly, when the single enantiomer of **14.8** was used in the catalytic system respectively, although the same enantiomeric boronate was obtained as the major product, different reaction rate and enantioselectivity were observed. When the reaction was not finished completely, unreacted **14.8** with enantiomeric excess was recovered.

Figure 1.4.5 Plausible schematic explanation on direct enantioconvergent transformation of allylic borylation by Ito and Sawamura.

Upon experimental studies, with deuterium labelled allylic ester as substrates, the author found that when using QuinoxP* as ligand both two enantiomers of starting material would afford the boronates with the same chirality on the α -carbon of the boryl group, with 99% and 88% diastereomeric excess respectively. Considering that the configuration of the chiral center bearing deuterium would not change during the reaction, that is to say, catalytic complex attacked the substrates in an $\text{S}_{\text{N}}2'$ pathway with both *anti*- and *syn*- facial selectivity. On the other hand, single enantiomer (S)-**14.8** was able to be converted to either (S)-**14.9** or (R)-**14.9** selectively, with varied enantioselectivity, depending on the achiral phosphine ligand employed. It was suggested that the borylation would not simply follow a specific

facial selectivity but chose the reaction pathway flexibly with regard to the structure of ligand. A more straightforward demonstration of such facial discrimination addition was illustrated in **Fig. 1.4.5**.

Recently, a sequential reaction of allylic borylation/nucleophilic addition was also reported with a similar system by Ito ^[83], in which allylic acetals were employed and α -chiral γ -alkoxy allyl boronates were obtained as the intermediates in the one-pot synthesis.

Except for Cu/QuinoxP* system, chiral N-heterocyclic carbenes (NHC) as ligands in asymmetric allylic borylation were also investigated. In the same year, Hoveyda's group reported their discovery ^[84] on copper catalyzed enantioselective allylic borylation reaction employing NHC as chiral ligand. With the help of bidentate ligand precursor **14.10**, allylboronates could be afforded with high regioselectivity (>98% S_N2') and enantioselectivity (>99:1 er). Complementary to previous achievements by Ito and Sawamura, Hoveyda's approach was able to be utilized on *E*-configuration linear allylic carbonates, with good tolerance of sterically hindered alkyl groups which led to synthetically attractive quaternary B-substituted stereogenic carbon.

Figure 1.4.6 NHC-Cu-Catalyzed allylic boryl substitution by Hoveyda.

Figure 1.4.7 The rationale of stereoconvergent synthesis of chiral allylboronates by McQuade.

Meanwhile, Prof. McQuade discovered a variation of stereoconvergent synthesis of chiral allylboronates from the *Z/E* mixture of terminal allylic aryl ethers^[85], in which a novel NHC-Cu complex **14.11** was used. During their investigation, they were gratified to find that both *E*- or *Z*- allylic esters were able to afford stereoconvergent boronate with almost same ee, in contrast to the discovery of Ito/Sawamura^[70] and Hoveyda^[84]. Although initially they expected that the reaction proceeded via a π -allyl-copper complex like what normally happened in palladium catalyzed allylic borylation, no isomerization of starting materials was found via ¹H-NMR analysis. None of the linear product from the direct substitution of substrates was observed. Based on their discovery, a plausible mechanism of stereoconvergent transformation was disclosed in **Fig. 1.4.7**. In addition, (*E*)-alkene was speculated to occur via a lower activation barrier than (*Z*)-configuration as the former reacted much faster when a 1:1 mixture of *E/Z* isomer were employed in the reaction.

After further investigation on kinetics, metholysis step was also considered to be rate-determining to help eliminate aryloxy group to give C=C bonds, which was added into catalytic cycle in their follow-up studies ^[86].

Very recently, Watson's group ^[87] disclosed that chiral allylic pivalates could be stereospecifically converted into chiral allylboronates in the presence of Ni(0) catalyst in both retention and inversion pathways, via the influence of solvents (**Fig. 1.4.8**). The enantioenriched pivalates could be readily prepared with high enantiomeric excess values from the allylic alcohol precursors via either Corey-Bakshi-Shibata reduction or kinetic resolution. After optimization, they found that toluene as the solvent, instead of MeCN, would remarkably switch the stereospecificity of the product. In such situation, products of both the absolute configuration inversion and retention could be acquired.

Upon further investigation, the authors believed that when non-polar solvents like toluene were employed nickel catalyst was not strongly coordinated by the solvent molecules but directed by the pivalate group. As the 7-membered-ring, chairlike structure was considered suitable for this closed transition state, the favored transition **14.17**, due to the absence of 1,3-pseudo-diaxial interaction, led to the formation of **14.19**. After the transmetallation of boryl group, it finally gave rise to the retention product **14.20**. On the contrary, if acetonitrile was used as the solvent, it would occupy the remaining coordination sites on the nickel atom.

Thus, it was highly possible that the pivalate no longer acted as a directing group and an open transition state would dominate the reaction process. Because of the 1,3-allylic strain presented in **I4.22**, the transition state **I4.21** was more favoured. Along with the cationic oxidative addition, **I4.23** was furnished. Since the nickel center had reached its maximum coordination number, boryl nucleophile was only able to attack from the back side with an outsphere mechanism, which would lead to the inversion product **I4.24** eventually.

Directed Oxidative Addition (Closed Transition State)

Undirected Oxidative Addition (Open Transition State)

Figure 1.4.9 The proposed mechanism of allylic borylation with retention and inversion by Watson.

1.5 Other Methods to Synthesize Chiral Allylic Boronates

Besides the classic substitutive borylation with allylic electrophiles, the methods to synthesize enantioenriched allylboronates were also well broadened in the past decade ^[88].

Figure 1.5.1 The lithiation-borylation approach to synthesis (allylic) boronates by Prof. Aggarwal.

In the area of non-catalytic synthesis, Prof. Aggarwal's group ^[89–95] first developed a lithiation-borylation approach which led chiral carbamates to organoboronates. As shown in **Fig. 1.5.1**, in the presence of *s*BuLi, chiral carbamate **15.1** could be deprotonated to give the corresponding α -lithiation intermediate **15.3**. Interestingly, when **15.3** was treated with the organic boronate, the transmetallation via concerted four-membered ring would lead to the formation of the retention adduct **15.4**. After the 1,2-metallate migration followed, **15.5** was furnished with high enantioselectivity. On the other hand, while **15.3** was treated with organoborane, the $\text{S}_{\text{N}}2'$ attack accompanied with the configuration inversion was preferred due to the absence of Lewis basic oxygen atoms for coordination and the enhanced Lewis acidity of the boron atom. In such situation, it finally resulted in the generation of borane **15.7** as the inversion product. Specifically, when the boronates employed bore the vinyl group or

its derivatives, the corresponding allylboronates were given in excellent yields and enantiomeric excess values.

Later, the Aggarwal group reported the synthesis of enantioenriched allylboronates with this approach and the subsequent *in situ* conversion to homoallylic alcohols and amines bearing quaternary stereogenic centers ^[96, 97].

With the traditional hydroboration process, chiral allylboronates could also be acquired when 1,3-dienes were employed as the substrates. However, it was still challenging to make the reaction selectively limited to 1,4-addition and avoid the formation of homoallylic boronates via 1,2-addition.

Figure 1.5.2 Asymmetric hydroboration of dienes to acquire homoallylic and allylic boronates.

In 2010, Ito disclosed that a variety of cyclic dienes could be converted into homoallylic and allylic boronates with high enantioselectivities with copper and (*R,R*)-Me-DuPhos as catalysts and methanol as the proton source ^[98]. Unfortunately, although the selective formation of allylboronates could be achieved by tuning the solvent and proton source, in most of the cases, homoallylic boronates were found as the major products as the result of 1,2-addition.

Such observation was explained by the same group as demonstrated in **Fig. 1.5.3**. The authors believed that when diene **15.11** reacted with the *in situ* generated boryl-copper intermediate

the *syn*-addition product **I5.12** was first acquired. If the reaction temperature was low and the protonation in an S_E2' fashion was fast, the intermediate would directly give rise to allylboronate **I5.13**. At higher temperature, **I5.12** would undergo allylic isomerization to form the thermodynamically stable **I5.14**, which resulted in the generation of homoallylic product **I5.15** after protonation by the alcohol additive.

Figure 1.5.3 Possible reaction mechanism with allylic shift and S_E2' protonation by Ito.

The selective formation of allylboronates via hydroboration could also be controlled by substrates. Lee and Yun^[99] found that when aryl-substituted diene **I5.16** was employed only **I5.17** was furnished with good enantioselectivity in the presence of copper and chiral phosphine catalyst. The observed selectivity was attributed to result from the conjugation effect presented in the reaction intermediates.

Figure 1.5.4 Substrate-controlled hydroboration of dienes to synthesis allylboronates.

Another way to acquire chiral allylboronates was diboration. In 2004, Morken's group first described an asymmetric diboration of allenes ^[100] which enabled the rapid construction of complex multifunctionalized structure. The success was based on the use of palladium and TADDOL-derived chiral phosphoramidite ligand (**Fig. 1.5.5**). When methyl-substituted prochiral allene **I5.18** was employed, the best enantioselectivity of 92% was achieved.

Figure 1.5.5 Palladium catalyzed diboration of prochiral allenes reported by Morken.

Soon, the same group reported the more detailed investigations on this diboration reaction ^[101]. As highlighted in **Fig. 1.5.6**, the more steric-demanding ligand **I5.23** would lead to improved yields and enantioselectivity.

Figure 1.5.6 Palladium catalyzed diboration of prochiral allenes with improved results.

Meanwhile, they also conducted a series of mechanistic experiments, such as isotopic labelling, *in situ* NMR and kinetic studies, which helped to reveal the true mechanism of this transformation as well as DFT calculations. Based on the experimental results, they postulated the catalytic cycle as followed in **Fig. 1.5.7**. The formation of diboryl palladium complex **I5.24** via the oxidative addition of B_2Pin_2 was believed to be the initial step. Subsequent insertion of allenes would finally give rise to the π -allyl palladium complex **I5.26**, which was found to go through the intermediate **I5.25**. After the *cis* reductive elimination, the diboration product **I5.19** was furnished with the regeneration of catalyst.

Figure 1.5.7 The proposed catalytic cycle of palladium catalyzed diboration by Morken.

The asymmetric diboration reaction could be applied to 1,3-dienes to acquire chiral allylboronates. Morken's group found that when TADDOL-derived chiral phosphoramidite ligand was combined with platinum as catalyst 1,3-conjugated dienes were able to be converted into the corresponding allylic bisboronates ^[102–103]. The reaction might undergo either 1,2-addition or 1,4-addition, depending on the substrate *Z/E* configuration, solvents and

variation of **15.33** was tested later ^[108], and the application of the corresponding product in the allylboration reaction was investigated.

Figure 1.5.10 The synthesis of chiral allylboronates via Kumada-type coupling.

Morken's group also reported an example of asymmetric Suzuki-type coupling reaction to furnish allylboronates ^[109]. As illustrated in **Fig. 1.5.11**, α,α -bis(boronate) **15.36** and vinyl bromide **15.37** were employed in this transformation. After the monosubstitution of the geminal bis(boronate), **15.38** was given in 95% yield and 86% ee when palladium acetate and chiral ligand **15.39** was used as the catalyst.

Figure 1.5.11 The synthesis of chiral allylboronates via Suzuki-type coupling.

Figure 1.5.13 The proposed mechanism for the borylative migration reaction.

Meanwhile, Prof. Kobayashi discovered that the enantioselective boryl conjugate additions to dienones and dienesters might acquire chiral allylic boronates as well ^[112]. With the ligand shown in **Fig. 1.5.14**, **I5.50** would be turned into **I5.51** when catalyzed by copper in water, with excellent enantiocontrol. Interestingly, for linear substrate, 1,4-addition was preferred. However, in the case of cyclic substrate, the selectivity between 1,4- or 1,6-addition depended on the copper(II) precursor employed. Only with copper(II) acetate as the catalyst, allylic boronates would be obtained as the product. While $\text{Cu}(\text{OH})_2$ was employed, 1,6-addition would dominate the reaction and thus gave rise to the corresponding boryl-substituted enone.

Figure 1.5.14 The synthesis of chiral allylboronates via 1,4-conjugated borylation.

Besides, chiral allylboronates were able to be synthesized via 1,6-conjugate addition of dienones and dienesters, reported by Lam et al ^[113]. After borylation, the prototation occurred at 2-position instead of 4-position in Kobayashi's work. Cyclopro substituent was preserved after the reaction, which indicated that the reaction was less likely to undergo a radical pathway.

Figure 1.5.15 The synthesis of chiral allylboronates via 1,6-conjugated borylation.

Last but not least, the enantioselective silicon-boron addition to 1,3-cyclohexadiene catalyzed by platinum was an interesting example of chiral allylboronate synthesis. Moberg's group ^[114] revealed this transformation in 2005 as shown in **Fig. 1.5.16**, although only moderate enantioselectivities were observed.

Figure 1.5.16 The synthesis of chiral allylboronates via silicon-boron addition.

1.6 Summary

In summary, organoboronic compounds are important reagents or reaction intermediates in the area of organic chemistry. In its ground state, sp^2 hybridized boron atom is Lewis acidic, as the empty p orbital was able to accept a pair of electrons from the donor. In this case, the afforded sp^3 hybridized quaternary boron exhibits nucleophilicity, as this character enables its further chemical transformation to a variety of functionalized chemicals, such as direct oxidation, amination, cross-coupling, homoligation, allylboration, and so on. Among the methods to synthesis organic boronates, Miyaura borylation reaction has become the most attractive way since the products could be afforded in satisfied yields with large substrate scope and high functional group tolerance in the presece of diboron reagents. As for the asymmetric catalysis, organic boronates with chiral α -borylated carbon are versatile reaction intermediates as they could be readily converted into highly functionalized compounds with high regioselectivity and stereoselectivity. Allylboronates could further undergo nucleophilic addition to aldehydes, ketones or imines in which homoallylic alcohols or amines stereospecifically. In the past decades, researchers have developed several catalytic borylation system involving palladium and copper as catalysts. Compared with numerous reports on the enantioselective conjugated borylation and asymmetric hydroboration, little attention was paid in the area of

enantioselective allylic borylation. Limited examples were only reported with allylic carbonates and esters as substrates while chiral phosphine or NHC ligands were employed. However, stereoconvergent synthesis of such enantiopure allylboronates from racemic allylic substrates or the mixture of *E/Z* isomers, still remained challenging. When it came to the case of allylic halides, due to the relative high reactivity, enantiomeric control became difficult, where a novel catalytic system to achieve excellent stereoselectivity was highly desired.

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Chapter 2

Copper/Guanidine Catalyzed Asymmetric Allylic Borylation of Allylic Halides with Diboron Reagents: Condition Optimization and Substrate Scope

2.1 Introduction

Chiral organic boronates are found to be useful synthetic intermediates for numerous optical active compounds. Among them, allylic boronates are crucial types due to its accessibility to synthesize homoallylic alcohol. Conventionally, chiral organoboranes are most commonly prepared by hydroboration^[1] or Micheal-type conjugated borylation^[2], which employed chiral phosphine or carbene ligands to induce enantioselectivity. Although much efforts have been put in those reactions, limited achievement is obtained in the area of asymmetric substituted borylation. As mentioned in Chapter 1, in 2005 Ito and Sawamura reported the first example of catalytic enantioselective synthesis of linear allylic boronates with enantiopure allylic carbonates as substrates, in which an S_N2' reaction pathway was proposed^[3]. A privileged *P*-chiral phosphine ligand QuinoxP* was discovered by the same group later on, which could afford the desired chiral allylboronates in high stereoselectivity in the presence of copper(I) salts^[4]. The catalytic system was further explored, and allylic esters were also able to be converted in the borylation reaction with NHC ligands. However, asymmetric allylic borylation of allylic halides was seldom reported. The reasons were as follow: 1) the transformation usually suffers from a series of side-reactions such as hydrolysis, dehaloprotonation, and homocoupling, due to high reactivity of allylic compounds; 2) the selectivity and enantiomeric control of the reaction proves to be difficult since the reaction exhibits some features of radical-based mechanism according to the results of achiral version of borylation^[5-6]; 3) in the case of the allylic borylation with racemic substrates, the reaction is usually found going through a stereospecific S_N2' pathway which leads to the enantiodivergent synthesis of allylboronates .

In this chapter, we will introduce our discovery on copper-guanidinium catalyzed enantioselective allylic borylation reaction. In the past decade, our group focused on asymmetric phase transfer catalysis employing a series of guanidinium salt, which enabled enantioselective nucleophilic attack via a HOMO activation mechanism ^[7–16]. Recently, we also found that guanidinium salts were able to carry anionic metal complex which could afford enantioenriched product induced by ion-pairing interaction ^[12, 14–15]. According to the preliminary studies on copper catalyzed allylic boration by Miyaura ^[17], bis(pinacolato)diboron in the presence of base would form formal boryl anion with enhanced nucleophilicity. On the other hand, copper was also able to accept anionic ligand to give cuprate ion bearing negative charges. Hence, there was a possibility that our guanidinium salts worked with cuprate anion to induce borylation process enantioselectively.

2.2 Investigation of Copper/Guanidine Catalyzed Asymmetric Allylic Borylation Reaction

Our initial work on the asymmetric allylic borylation reaction was inspired by the preliminary discovery of the promising enantioselective allylic alkynylation of racemic allylic bromide, as illustrated in **Fig 2.1**.

The commercially available six-membered ring allylic bromide **1-4a** reacts with phenylacetylene to give the corresponding alkynylation product **3** in a reasonable yield with a promising enantioselectivity (28% ee). The reaction involves cheap CuCl as catalyst, which promotes the cross-coupling reaction between allylic bromide and alkyne in the presence of a base. Interestingly, bisguanidinium **Gua 1**, which is conventionally treated as a phase-transfer catalyst (PTC), could furnish the product **3** with low enantioselectivity. Considering that **Gua 1**

generally exhibits good stability in basic condition and low catalyst loading is needed to achieve the enantiocontrol, it indicates that the chiral bisguanidinium/cuprate ion pairs may serve as the primary catalytic species.

Figure 2.1 The initial discovery of asymmetric allylic alkynylation (AAA) reaction using copper/guanidinium salt system under phase-transfer catalysis (PTC) condition.

Based on the above, we employed similar catalytic system to study the allylic asymmetric borylation reaction. As shown in **Fig. 2.2**, the model reaction used racemic cyclic allylic bromide **1-4a** as electrophile with 1.0 equivalent commercially available bis(pinacolato)diboron (B_2Pin_2) as the boron source. In the presence of 30 wt% sodium hydroxide aqueous solution, 20 mol% CuCl and 1.5 mol% **Gua 1** as catalyst in MTBE, the corresponding borylation product **4a** was formed in a reasonable 26% GC yield with 9% ee. However, a mixture of diastereomic bicyclic dienes **9** was also obtained as major by-product after the reaction was stopped, perhaps derived from the homocoupling of **1-4a** or further cross-coupling of **1-4a** with product **4a**, apparently.

Figure 2.2 The model reaction of asymmetric allylic borylation (**AAB**) using copper/guanidinium salt system under phase-transfer catalysis (PTC) condition.

With our preliminary results, we proceeded on to the optimization step. After obtaining irregular results based on numerous experiments and encountering the reproducibility issue for quite a while, we found that the air played a significant role for this reaction. So was the reagent addition sequence. As illustrated in **Fig 2.3**, the reaction with 1.5 equiv. B_2Pin_2 conducted in glovebox under Ar would furnish the corresponding allylic boronate quantitatively, but no enantioselectivity was obtained. However, if performed under air, 9% ee of the product was acquired consistently though low yield was observed due to the oxidation of the boryl group by oxygen during the process. It was indicated that oxygen actually played a crucial role to maintain an enantioselective borylation pathway. Further more, we tuned the sequence of the reagent addition in the reaction protocol which might slightly improve the selectivity to 13% ee if the base was charged first to the MTBE solution followed by the addition of allylic bromide **1-4a** eventually after 5 min stirring. Thus, it appears that the reaction catalytic species might also be changed in activity or concentration as the reaction protocol was revised.

Figure 2.3 The reaction condition setup for model reaction of asymmetric allylic borylation (**AAB**) using copper/guanidinium salt system.

After fixing the reaction protocol, we then start to optimize the reaction condition from the effect of base as the starting point. As shown in **Table 2.1**, the influence of base was carefully investigated. Considering that the initial sodium hydroxide solution was used with a fixed mass percent concentration (30 wt%), which may not be achieved for some inorganic base that has low solubility in water, such as LiOH and NaHCO₃, we decided to use the saturated solution of each base directly for screening to make this step fast and facile.

Table 2.1 The optimization of base in the model enantioselective allylic borylation reaction.

Rac-1-4a		4a	
Entry ^[a]	Base	Yield (%) ^[b]	ee (%) ^[c]
1	LiOH	Trace ^[d]	N.D.
2	NaOH	28	14
3	KOH	59	17
4	CsOH	31 ^[e]	15

5	Na ₂ CO ₃	30	10
6	NaHCO ₃	Trace	N.D.
7	NaOAc	Trace ^[f]	N.D.
8	KOAc	Trace ^[f]	N.D.
9	K ₂ CO ₃	92	18
10	K ₃ PO ₄	98	10
11	KF	Trace ^[e]	N.D.
12	CsF	23 ^[e]	15
13	Cs ₂ CO ₃	93	15
14	TEA ^[g]	N.R.	N.D.

[a]. Reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 20 mol% CuCl, 1.5 mol% **Gua 1**, 0.5 mL premixed saturated aqueous base solution, 1 mL MTBE, air atmosphere, stirred at room temperature for 6 h;

[b]. GCMS yields after normalization without further calibration;

[c]. Determined by chiral GC analysis;

[d]. **1-4a** was found mostly hydrolyzed to the corresponding alcohol;

[e]. The dimerization was found as the major side reaction;

[f]. The corresponding allylic acetate was found as the side product;

[g]. 2.0 equiv. of TEA was employed.

The results demonstrated that the strength of the base directly determined the success of the borylation reaction and product distribution. When racemic **1-4a** 3-bromocyclohex-1-ene was employed as model substrates, alkaline metal hydroxides as base would provide higher yields as the basicity increased (Entry 1–4, **Table 2.1**) except CsOH. When weak LiOH was employed, almost no product was detected, only **1-4a** found mostly decomposed to the corresponding allylic alcohol. Saturated NaOH solution would maintain the ee as 14%, while KOH solution was able to make a slight improvement. However, CsOH solution, as the strongest alkaline, could help to consume all the bromide but led to a low yield (31%) due to

the considerable dimerization of substrates. When OH^- was changed to other basic anions, such as carbonates (Entry 5, **Table 2.1**) gave a similar yield but lower ee, while bicarbonate (Entry 6, **Table 2.1**) was found too weak to activate the transformation and acetate (Entry 7 and 8, **Table 2.1**) was found too nucleophilic to give directly allylic acetate instead. Surprisingly, potassium carbonate, potassium phosphate, and cesium carbonate exhibited extraordinary reactivity for this reaction (Entry 9, 10 and 13, **Table 2.1**). All of them can provide full conversion to targeted allylic boronate with only trace amount of bicyclic dimer, with enantioselectivity achieving 18% ee, when saturated K_2CO_3 solution was used. Besides, fluorides (Entry 11 and 12, **Table 2.1**) that widely used in boron activation-type reaction, had no obvious effect. Organic base, triethylamine (Entry 14, **Table 2.1**), was also investigated, but no reaction did not proceed.

Next the solvent effect was investigated next. The selected representative results are listed in **Table 2.2**. Generally, ethers as solvents exhibited good efficiency for this reaction (Entry 1–7, **Table 2.2**). Among them, *n*Bu₂O and CPME showed better enantioselectivity but suffered low yields. When arenes were used as solvents (Entry 8–13, **Table 2.2**), mesitylene interestingly prevailed and offered a similar 25% ee to *n*Bu₂O. Normal non-polar alkane such as *n*Hexane (Entry 10, **Table 2.2**) could also provide excellent yield with 22% ee. To our surprise, halogenated alkane (Entry 11–13, **Table 2.2**), like DCM and chloroform, showed low reactivity and selectivity, on the contrary to other copper catalyzed allylic C–C bond forming reaction. Finally, we also tested pure aqueous condition, as additional 1 mL H₂O was charged into the reaction as solvents which might dilute the base as well. Delightly, the reaction still worked smoothly in a complete aqueous mixture, although diboron and product hydrolyzation were observed. Interestingly, the enantioselectivity got inversed, -6% ee obtained for the boronate product.

Table 2.2 The optimization of solvent in the model enantioselective allylic borylation reaction.

Entry ^[a]	Solvent	Yield (%) ^[b]	ee (%) ^[c]
1	Et ₂ O	98	12
2	<i>n</i> Bu ₂ O	57	26
3	DME	91	6
4	1,4-Dioxane	90	21
5	THF	N.R.	N.D.
6	CPME	79	20
7	<i>i</i> Pr ₂ O	97	10
8	Benzene	54	16
9	Toluene	99	18
10	<i>o</i> Xylene	63	17
11	Cumene	89	23
12	Mesitylene	74	25
13	PhCl	51	15
14	<i>n</i> Hexane	94	22
15	DCM	94	3
16	CHCl ₃	70	2

17	H ₂ O	60	-6
[a]. Reaction condition: 0.1 mmol <i>rac</i> - 1-4a , 0.15 mmol B ₂ Pin ₂ , 20 mol% CuCl, 1.5 mol% Gua 1 , 0.5 mL saturated K ₂ CO ₃ aqueous solution, 1 mL solvent, air atmosphere, stirred at room temperature for 24 h; [b]. GCMS yield after normalization without further calibration; [c]. Determined by chiral GC columns.			

Next the screening of conditions was moved on to the effect of copper precursors. After mesitylene was chosen as solvent, as listed in **Table 2.3**, a series of copper(I) and copper(II) salts were investigated. Different Cu(I) precursor offered varied characters due to the counter ion attached to Cu atom, if the reaction underwent an ion-pairing mode. Among them, CuPF₆(MeCN)₄ (Entry 1, **Table 2.3**) bearing a weak coordinating anion, led to a better ee of 21%, if CuCl was not taken into consideration. As air could be tolerated in the reaction, on the other side, it reflected that B₂Pin₂ might act as a strong and sufficient reducing agent in the mixture to consume O₂ to undermine its oxidizing function for Cu(I). Cu(II) salts could also furnish the product with guanidinium salt **Gua 1** under the same condition successfully (Entry 6–11, **Table 2.3**), sometime giving slightly higher enantioselectivity, which was believed Cu(II) being reduced to Cu(I) by B₂Pin₂ during the process but Cu(I) kept at low concentration under oxidative O₂ atmosphere. Generally speaking, salts bearing non-coordinating anions typically gave better results on enantiocontrol, perhaps resulting from the stronger ion-pairing interaction between phase transferring guanidinium cation and hydroxide attached cuprate anion. In such situation, to our delight, the cheap and readily available Cu(NO₃)₂•3H₂O was proven to be most effective, furnishing the targeted product in 47% yield and 26% ee, respectively. Then the optimization was continued based on Cu(NO₃)₂•3H₂O as metal catalyst.

Table 2.3 The optimization of copper salts in the model enantioselective allylic borylation reaction.

Entry ^[a]	Cu Precursor	Yield (%) ^[b]	ee (%) ^[c]
1	CuPF ₆ (MeCN) ₄	50	21
2	CuCN	26	13
3	CuBr	97	7
4	CuI	65	14
5	Cu ₂ O ^[d]	8	14
6	Cu(acac)	30	12
7	Cu(OAc) ₂ ^[e]	33	20
8	CuCl ₂	58	15
9	Cu(OTf) ₂	46	21
10	Cu(NO ₃) ₂ •3H ₂ O	47	26
11	CuSO ₄ •5H ₂ O	23	14

[a]. Reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 20 mol% Cu precursor, 1.5 mol% **Gua 1**, 0.5 mL saturated K₂CO₃ aqueous solution, 1 mL mesitylene, air atmosphere, stirred at room temperature for 24 h;
 [b]. GCMS yield after normalization without further calibration;
 [c]. Determined by chiral GC columns;
 [d]. 10 mol% Cu₂O was employed in the reaction;
 [e]. The corresponding allylic acetate was found as the side product.

To further understand the reaction profile, we looked back to solvents which was considered to influence the performance of borylation efficiency and selectivity. The results are shown in

Table 2.4. Basically, although most common solvents were tested in the second round of screening, no much improvement on enantioselectivity was obtained, only that high yields could be achieved in a shorted time (6h). Among the massive solvents rescreened, *n*Bu₂O stood out as excellent yield was achieved while 27% ee could also be obtained (Entry 2, **Table 2.4**). Surprisingly the result worsened when chloroalkanes were employed as solvents (Entry 19–21, **Table 2.4**), low yields and almost no enantioselectivity, especially comparing with the non-halogenated alkanes. To our surprise, carbonate-type solvent diethyl carbonate (DEC) could provide similar results although medium yield was obtained (Entry 22, **Table 2.4**).

Table 2.4 The 2nd optimization of solvent in the model enantioselective allylic borylation reaction.

<p><i>Rac</i>-1-4a 4a</p>			
Entry ^[a]	Solvent	Yield (%) ^[b]	ee (%) ^[c]
1	Et ₂ O	97	13
2	<i>n</i> Bu ₂ O	89	27
3	DME	91	6
4	THF	89	7
5	CPME	44	20
6	<i>i</i> Pr ₂ O	91	23
7	MTBE	92	15
8	Benzene	20	15
9	Toluene	23	19

10	<i>o</i> Xylene	42	23
11	<i>m</i> Xylene	27	18
12	<i>p</i> Xylene	56	2
13	Cumene	54	23
14	PhCl	31	9
15	Mesitylene	40	22
16	Ethylbenzene	20	14
17	<i>n</i> Hexane	61	20
18	CyH	84	26
19	DCM	22	3
20	DCE	22	1
21	CHCl ₃	Trace	N.D.
22	DEC	45	22

[a]. Reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 20 mol% Cu(NO₃)₂•3H₂O, 1.5 mol% **Gua 1**, 0.5 mL saturated K₂CO₃ aqueous solution, 1 mL solvent, air atmosphere, stirred at room temperature for 24 h;
[b]. GCMS yields after normalization without further calibration;
[c]. Determined by chiral GC columns.

Eventually, after gaining all the knowledge about the reaction, we started to investigate the influence of phase-transfer catalysts, which should be crucial for enantiocontrol. Considering that numerous type of chiral imidazolium, iminium, guanidinium, aminium and phosphonium salts had been employed in enantioselective phase-transfer catalysis, we divided our catalysts in hand and tested their performance with the optimized model allylic borylation reactions. As

illustrated in **Fig 2.4**, the first batch was established based on different bisguanidinium motifs. Compared with **Gua 1** as standard, other bisguanidinium salts with varied substituents didn't show much improvement on stereoselectivity. Bisguanidinium with electron-donating groups **Gua 2** and **Gua 6**, only offered a similar or worse yield and enantioselectivity. On the other hand, if the catalysts were substituted with electron-withdrawing group, saying **Gua 3** to **Gua 5**, from 2-position fluorinated to brominated respectively, comparable yields and enantioselectivity were also obtained. In such situation, electronic-effect on catalyst structure did not seem to affect this reaction much. Then, it was found that no matter what changes were made to the side-arm and linker, like **Gua 7** with less bulky *para-tert*-bulkyl group or **Gua 9** with a rigid bicyclic linkage, only similar results as **Gua 1** was observed. When side arm was changed to aliphatic long chain from aromatic ring, both yield and enantioselectivity deteriorated.

Viewing that pentanidium salts exhibited excellent selectivity on many enantioselective phase transfer reactions, we moved to this type of phase transfer catalysts we had. As illustrated in **Fig 2.5**, classic methyl substituted **Gua 11** was first investigated, with almost quantitative 96% yield and 28% ee for model borylation reaction. However, when methyl groups were changed to more bulky and rigid phenyl groups, the corresponding catalyst **Gua 12** failed. If benzyl groups as shown in **Gua 13** were presented in the structure, the efficiency and selectivity just retained. Long chain as side arm led to almost racemic product, as **Gua 14** did. More steric demanding (**Gua 15**) or more electron-deficient (**Gua 16**) substituents did no good to improve ee, which could be concluded that the results only depended on the core cationic backbone for this reaction.

Figure 2.4 The optimization of guanidinium salts in the model enantioselective allylic borylation reaction.

Figure 2.5 The optimization of pentanidium salts in the model enantioselective allylic borylation reaction.

With deeper understanding of the reaction profile, we checked other organic salts as phase transfer reagents. As shown in **Fig. 2.6**, when cinchona alkaloid derivatives were employed as catalysts, typical allylic bromide **1-4a** were unable to be converted to the wanted boronate in 6 h. With regards to enantioselectivity, benzyl salt **CA 17** furnished nearly no ee. After changing to the bulky anthracene substituents, **CA 18** improved yield slightly, retaining enantioselectivity. If the diastereomer **CA 19** was used, opposite enantioselectivity would be obtained. Moreover, electron-donating methoxyl group on quinoline block also didn't influence the outcome much as illustrated by **CA 20**. In summary, cinchona alkaloid derived aminium salts were not suitable catalysts for our copper catalyzed allylic borylation reaction.

Figure 2.6 The optimization of cinchona alkaloid derivatives in the model enantioselective allylic borylation reaction.

Eventually, we tested the bicyclic guanidinium salts which were exploited in numerous Brønsted base catalyzed reactions and found extraordinary stereocontrol. To our delight, *tert*-butyl substituted [5,5]-bicyclic guanidinium salts was found reactive in the borylation reaction, furnishing a nearly quantitative yield, while excellent ee was also achieved. As demonstrated in **Fig. 2.7**, 91% ee was obtained with either **Gua 21** or **Gua 22** as co-catalyst, regardless of different counter anion. The only difference was that iodide as anion might lead to the reduction of $\text{Cu}(\text{II})$ since the mixture soon became yellowish as they were mixed together. This did not affect the result much. Dimethylated guanidinium salt **Gua 23** only afforded the product in 12% yield and with 11% ee, which indicated that the protons significantly defined

the success of the reaction. If the chiral backbone was changed with other substituents, as shown in the case of **Gua 24** (iPr), **Gua 25** (Bn) and **Gua 26** ((*s*)-iBu), lower enantioselectivities were observed although the yields of **4a** were still satisfied. A benzyl-bridged dimer form of **Gua 22**, shown as **Gua 27**, was also synthesized and tested in the allylic borylation reaction. The enantiocontrol induced by **Gua 27** proved excellent, but the reaction was found sluggish.

Figure 2.7 The optimization of bicyclic guanidinium salts in the model enantioselective allylic borylation reaction.

Table 2.5 The further optimization of reaction condition for the model enantioselective allylic borylation reaction.

<div style="display: flex; align-items: center; justify-content: space-around;"> <div style="text-align: center;"> <p>Rac-1-4a</p> </div> <div style="text-align: center;"> $\xrightarrow[\text{K}_2\text{CO}_3 \text{ (satd. aq.)}, n\text{Bu}_2\text{O, RT, air, 6h}]{\text{B}_2\text{Pin}_2 \text{ (1.5 equiv.)}, \text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O} \text{ (20 mol\%)}, \text{Gua} \text{ (1.5 mol\%)}}$ </div> <div style="text-align: center;"> <p>4a</p> </div> </div>			
Entry ^[a]	Revised Condition	Yield (%) ^[b]	ee (%) ^[c]
1	Standard condition	91 (96) ^[d]	91
2	5 mol% Cu	>99	92
3	1 mol% Cu	>99	96
4	12 equiv. K ₂ CO ₃ ^[c]	96	91
5	<i>i</i> Pr ₂ O	99	87
6	MTBE	97	81
7	Mesitylene	>99	92
8	DCE	66	88
9	CyH	97	96
10	<i>n</i> Hexene	>99	95
11	CuPF ₆ (MeCN) ₄ ^[f]	>99	96
12	0 °C	97	95
13	0 °C ^[g]	>99	97
14	-20 °C ^[g]	Trace	N.D.

-
- [a]. Standard reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 20 mol% Cu(NO₃)₂•3H₂O, 1 mol% **Gua 22**, 0.5 mL saturated K₂CO₃ aqueous solution (about 30 equiv.), 1 mL *n*Bu₂O, air atmosphere, stirred at room temperature for 6 h;
[b]. GCMS yield after normalization without further calibration;
[c]. Determined by chiral GC columns;
[d]. Isolated yield was shown in the parentheses;
[e]. 0.2 mL saturated K₂CO₃ aqueous solution as base;
[f]. 1 mol% Cu, 0.2 mL saturated K₂CO₃ aqueous solution, 1 mL *n*Hexane;
[g]. 1 mol% Cu, 0.2 mL saturated K₂CO₃ aqueous solution, 1 mL *n*Hexane, 24h.
-

After achieving excellent reactivity and stereoselectivity, we further explored other factors for the reaction to see if the result could be further improved. As listed in **Table 2.5**, when the previous results were taken as standard (Entry 1, **Table 2.5**), eantioselectivity might reach 96% if the loading of copper was reduced to 1 mol%, maybe due to the suppression of achiral background reaction (Entry 2 and 3, **Table 2.5**). And less base would not affect the result significantly (Entry 4, **Table 2.5**). With further screening of solvents outstands non-polar cyclohexene and *n*Hexene (Entry 9 and 10, **Table 2.5**). Cu(I) salt (Entry 11, **Table 2.5**) as precursor was abandoned, although no change of outcome was found, with a facile and easy protocol taken into consideration. Finally, after lowering down the reaction temperature to 0 °C, highest ee of 97% so far was achieved (Entry 13, **Table 2.5**). Continuing decreasing temperature would completely kill the process as the aqueous basic solution was frozen at that moment (Entry 14, **Table 2.5**).

With optimized reaction condition in hand, we wanted to explore the scope of this copper-guanidinium catalyzed asymmetric allylic borylation reaction. So, first of all, we synthesized a variety of racemic symmetric cyclic allylic bromides. As shown in **Fig 2.8**, after increasing the loading of **Gua 22** a little bit, most of the cyclic allylic bromides were reactive in such catalytic system. The ring size could be well tolerated from five to eight, as demonstrated from **4a** to **4d**, with good to excellent yields and excellent ee. To our delight, the allylic chloride, which is normally considered much more unreactive, was also able to be employed in

Figure 2.8 Substrate scope for racemic symmetric cyclic allylic halides.

[a]. Standard reaction condition: 0.1 mmol *rac*-**1**, 0.15 mmol B₂Pin₂, 1 mol% Cu(NO₃)₂·3H₂O, 1.5 mol% **Gua 22**, 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 12~18 h. Yields were calculated via ¹H-NMR with CH₂Br₂ or 1,4-dimethoxybenzene as the internal standards. Isolated yields were presented in parentheses. Enantiomeric excess was determined by chiral GCMS or HPLC.

[b]. The corresponding allylic chloride was employed as substrate, 5 mol% Cu(NO₃)₂·3H₂O, 7.5 mol% **Gua 22**, with 3.0 equiv. B₂Pin₂ for 18 h.

[c]. GCMS yield after normalization without further calibration.

this protocol. Although more B₂Pin₂ and longer reaction time were required for this transformation, 62% NMR yield and 86% ee of **4a** was obtained after 18 h, with unreacted allylic chloride remained with 55% ee. However, unfortunately, when 2-position of the C=C double bond was occupied by any groups, such as **4h**, **4i**, **4j** and **4k**, a significant drop on enantioselectivity was observed. When methyl and phenyl group was at 2-position, as shown

for **4h** and **4i**, only medium enantioselectivity could be obtained. While electron-withdrawing ester group was taken, even lower ee was given with **1-4j** and **1-4k** as substrates. Notably, in the case of **1-4j** and **1-4k**, it was unknown whether substitution or conjugate addition initiated the borylation reaction, which might scramble the enantiocontrol on the other side. Additionally, when the substituents were far from the center of the reaction, just like in the case of **4e**, high yield was achieved, while excellent enantioselectivity of product was also obtained. And the efficiency of this catalytic borylation reaction was not much affected by changing to a heterocyclic substrate **1-4f**. Moreover, when the allylic system was conjugated with the aromatic ring, such as **1-4g**, the corresponding boronate could not be proceeded successfully, only leaving the bromide unreacted in the mixture.

Next the scope was expanded to unsymmetric cyclic allylic bromides. According to the previous reports, when allylic carbonate or ether as substrates, the S_N2' pathway would dominate the reaction with 1,3-shifted boronates as major products. In this case, we synthesized a series of 1-substituted allylic bromides *rac*-**1-5a** to *rac*-**1-5f** and employed them into our copper/guanidinium catalyzed borylation system to see how the products were distributed. Unfortunately, *rac*-**1-5a** failed to undergo boryl substitution. Only trace amount of product was detected by GCMS in the reaction residue after work-up. In such situation, the position of boryl group in the six-membered ring actually was difficult to be clarified. However, it was believed that the oxygen atom on the ring would strengthen the attached C=C double bond. Thus, the energy barrier that borylation needed to overcome was changed, leading to a deactivated allylic bromide or an unstable allylic intermediate. To our delight, it was found that 1-alkyl substituted allylic bromides were suitable substrates for this reaction, with almost no loss of enantioselectivity. For example, 3-bromo-1-methylcyclohex-1-ene **1-5b** will provide the corresponding allylic rearranged product **5b** with the regioselectivity of 94: 6, along with

Figure 2.9 Substrate scope for racemic unsymmetric cyclic allylic bromides.

[a]. Standard reaction condition: 0.1 mmol *rac*-**1**, 0.15 mmol B_2Pin_2 , 1 mol% $Cu(NO_3)_2 \cdot 3H_2O$, 1.5 mol% **Gua 22**, 0.2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 1 mL $nHex$, air atmosphere, stirred at 0 °C for 12~18 h. Yields were calculated via 1H -NMR with CH_2Br_2 or 1,4-dimethoxybenzene as the internal standards. Isolated yields were presented in parentheses. Enantiomeric excess was determined by chiral GCMS or HPLC after the boronated was oxidized to its corresponding allylic alcohol by $NaBO_3 \cdot 10H_2O$. Regioselectivities were determined by GCMS.

80% isolated yield and excellent 99% ee. Besides, ethyl and *n*butyl also worked well as **5c** and **5e** were formed in high enantiometric purity of 96%. *iso*-Propyl group suffered a loss but still could provide 78% ee for borylation product, probably due to its steric demanding on 1-position of olefin. Interestingly, 4-pentenyl substituted **1-5f** furnished the corresponding boronate **5f** in high efficiency with 94% ee and an excellent regioselectivity of 97:3. It was notable that the

cyclization, namely the “radical clock” reaction, was not observed during the borylation process. This exploration could be treated as the evidence that the reaction actually proceeded in a non-radical pathway. On the other hand, benzylic substrate **1-5g** was also proved suitable with such catalytic system. It was of interest as the phenyl ring could be easily modified and functionalized, as shown in the reaction affording **5h** and **5i** bearing electron-donating and electron-withdrawing groups, respectively. Eventually, homobenzylic substrate **5j** was also tested, and it was found that yield and stereoselectivity were not much affected.

Moreover, the reaction versatility was investigated on linear allylic bromides as starting materials (**Fig. 2.9**). First, simple and commercially available (*E*)-**1-6a** was tested as substrate under the same reaction condition. Fortunately, the corresponding allylic boronate was obtained in high yield with a 4:1 regioselectivity of allylic rearranged boronate **6a** as major product. However, the enantioselectivity was only acceptable at 65%. Then a series of linear terminal allylic bromides **1-6b** to **1-6i** were synthesized for investigation. As shown in **Fig. 2.9**, further functionalization of **1-6a** failed to give great improvement on enantioselectivity. Typically, good to excellent yields would be obtained, while olefin (**6c**) and ether (**6e**) could be well tolerated, with enantiomeric excess remained around 60%. When bulky *tert*-butyl group was introduced into the structure, without further improvement of ee. However, the regioselectivity to give the branched allylic boronate **6d** was found to increase to a ratio of 9:1. It was rather confusing as a steric hindered position was preferred in this reaction. Notably, when MTBE was used as solvents, substrates **1-6f** and **1-6g** could furnish the corresponding boronate product **6f** and **6g** with promoted 75% ee from 55% in *n*Hexane. Surprisingly, brominated **6h** was acquired with excellent 90% ee, compared with the others. Finally, when geranyl bromide was employed in such transformation, branched boronate **6i** was formed in 59% yield and 59% ee, with a very high branched vs. linear regioselectivity of 95:5. However,

Figure 2.10 Substrate scope for linear allylic bromides.

[a]. Standard reaction condition: 0.1 mmol **1**, 0.15 mmol B_2Pin_2 , 1 mol% $\text{Cu(NO}_3)_2 \cdot 3\text{H}_2\text{O}$, 1.5 mol% **Gua 22**, 0.2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h. Yields were calculated via $^1\text{H-NMR}$ with CH_2Br_2 or 1,4-dimethoxybenzene as the internal standards. Isolated yields were presented in parentheses. Enantiomeric excess was determined by chiral GCMS directly or after the boronated was oxidized to its corresponding allylic alcohol by $\text{NaBO}_3 \cdot 10\text{H}_2\text{O}$. Regioselectivity was determined by GCMS or $^1\text{H-NMR}$.

[b]. GCMS yield after normalization without further calibration.

[c]. The reactions were carried out in MTBE.

additional 13% radical cyclization product was found and isolated as the side product, if only 1 mol% **Gua 22** was employed in the reaction. Hence, it indicated that with the presence of insufficient amount of **Gua 22** a radical reaction pathway may occur.

In addition, we tested the potential of this system with various diboron reagents (**Fig. 2.11**). Although substrate bis(hexylene glycolato)diboron (B_2Hex_2) beared an additional chiral center and were employed as racemates, the corresponding borylation product **7a** was produced in 92% ee, with a d.r. of 1:1 deservedly. However, **7a** was not isolated successfully due to its instability to air, moisture and silica, so the yield was obtained as 73% after **7a** being oxidized to the alcohol. Unfortunately, B_2Neo_2 and B_2Cat_2 failed to furnish **7b** and **7c** successfully, since they were readily decomposed in the initial reaction mixture.

Figure 2.11 Substrate scope for diboron reagents.

[a]. Standard reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol $B_2(OR)_2$, 1 mol% $Cu(NO_3)_2 \cdot 3H_2O$, 1.5 mol% **Gua 22**, 0.2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h. Yields were calculated via 1H -NMR with 1,4-dimethoxybenzene as the internal standard. Isolated yields of the corresponding alcohol after oxidation were presented in parentheses. Enantiomeric excess was determined by GCMS.

[b]. Diborons were found rapidly decomposed under optimized conditions.

Finally, apart from allylic halides, other types of electrophiles were investigated as well. As illustrated in **Fig 2.12**, secondary bromide **1-8a** was chosen as substrates, but the boronate was only obtained in very low yield, less than 10% by GCMS. When the leaving group was changed to chloride, the reaction could not occur at all. To our disappointment, the benzyl type

Figure 2.11 Substrate scope for other types of electrophile bearing different leaving groups.

[a]. Standard reaction condition: 0.1 mmol *rac*-**1**, 0.15 mmol B₂(OR)₂, 1 mol% Cu(NO₃)₂•3H₂O, 1.5 mol% **Gua 22**, 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h. GCMS yield after normalization without further calibration;

[b]. Most of electrophile **1** was found unreacted.

[c]. **1** was found fully converted, dimerization as main product.

[d]. **1** was found fully converted, debromo-protonation as the main product.

compounds will not furnish the wanted boronates with this catalytic system successfully. Although substrate **1-8b** was fully consumed, only benzylic dimer was detected as the major product. Similarly, if the allylic system was conjugated with the aromatic ring, the corresponding dimerization dominated in the reaction. The only isomeric boronate was isolated from the mixture in low yield. As determined by ¹H-NMR, it was found to be the achiral linear borylation product rather than **8c** as the branched one. Thus, in this case, the generated branched boronate might decomposed in the reaction mixture due to its instability, with trace isomeric product remained. It was also possible that the reaction did not proceed in an S_N2'

mechanism with this kind of substrates. Besides, if the carbon to be borylated was bearing an electron-withdrawing group, the transformation also failed. In this case, no matter whether **1-8d** or **1-8e** was used, instead of simply forming dimers, debromo-protonation reaction prevailed as well. Lastly, when bromo atom on **1-a** was replaced by O-base leaving group, electrophiles would survive in this system. Almost no transformation was found. In such situation, it seemed that the conventional $\text{S}_{\text{N}}2$ type reaction had become less likely, since, for the trend of leaving ability, acetate and tosylate were normally considered much better than chloride, on the same level of bromide.

2.3 Conclusion

In conclusion, we have developed a new copper/guanidinium catalytic system which could be successfully employed in asymmetric allylic borylation reactions. Among the diverse type of guanidinium salt, bicyclic **Gua 22** exhibited great efficiency on reactivity and enantiocontrol. With only 1.5 mol% **Gua 22** in the presence of 1 mol% copper and excess amount of base, a series of symmetric and unsymmetric cyclic allylic halides and terminal allylic bromides could be transformed to the corresponding enantio-enriched allylic boronates in medium to high yields, along with good to excellent enantioselectivity. In general, for the unsymmetric allylic substrates, more substituted or branched boronates were preferred as the major products with regards to the product distribution, with γ/α regioselectivity larger than 90:10. Besides B_2Pin_2 , only B_2Hex_2 was successfully employed as the boron source, others decomposed rapidly in this catalytic system. We also found that non-allylic halides or allylic electrophiles bearing O-based leaving groups didn't work. The further application of this reaction and mechanism studies will be discussed in the next chapter.

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Chapter 3

Copper/Guanidine Catalyzed Asymmetric Allylic Borylation of Allylic Halides with Diboron Reagents: Mechanism Studies and Applications

3.1 Introduction

As illustrated earlier on, we have discovered a new copper/guanidinium catalytic system which could be successfully employed in asymmetric allylic borylation reactions. Among the various type of guanidinium salt, bicyclic **Gua 22** was able to provide great efficiency on reactivity and enantiocontrol. With only 1.5 mol% **Gua 22** in the presence of 1 mol% copper and excess amount of base, a series of symmetric and unsymmetric cyclic allylic halides and terminal allylic bromides could be transformed to the corresponding enantio-enriched allylic boronates in medium to high yields, along with good to excellent enantioselectivity. Generally, for the unsymmetric allylic substrates, more substituted or branched boronates were preferred with regard to product distribution, with regioselectivity higher than 5:1. However, besides B₂Pin₂, only B₂Hex₂ was successfully employed as the boron source. Others decomposed rapidly in this catalytic system. Nevertheless, non-allylic halides or allylic electrophiles bearing O-based leaving groups didn't work, only affording homo-coupling or hydrolyzed product in most cases.

In our preliminary condition optimization, it was found that this reaction relied on the presence of air and water in order to obtain satisfactory enantioselectivity, which was in agreement with previous reports by Szabó et al. ^[1–2]. Also, in the palladium catalyzed allylic borylation reaction, homocoupling occurred frequently, giving 1,5-dienes as by-product. This was a result of further Suzuki-type cross-coupling between allyl palladium complex with allylboronate product ^[3]. However, it was also reported that, in 1st row transition metal (Ni ^[4] and Cu ^[5]) catalyzed borylation of alkyl halide substrates, a SET initiated radical pathway was involved. Such dimerization was not observed in copper catalyzed allylic borylation with

allylic carbonates or ethers as substrates, which was detected in our system. Besides, the real catalytic species was still unclear. Meanwhile, questions remained unsolved on what was the driving force to give the required enantioselectivity and how racemic substrates were resolved to become enantioconvergent products. All of these issues urged us to make careful and detailed investigations on its reaction mechanism.

3.2 Control Experiment Investigation

To elucidate the mechanism of our present asymmetric allylic borylation reaction, we first ran a series of control experiments to see what truly determined the success of this transformation. The results are given in **Table 3.1**. Under the optimized standard condition, our copper/**Gua 22** system would provide allylic boronate in quantitative yield and excellent 97% ee (Entry 1, **Table 3.1**). However, if no copper was added into the reaction mixture, only trace amount of product could be detected by GCMS (Entry 2, **Table 3.1**), only **1-4a** found mostly hydrolyzed to the corresponding allylic alcohol in the presence of aqueous basic solution. It indicated that Cu had a great influence on bromide activation and boryl transfer. When pure water was employed instead of saturated K₂CO₃ solution, no product would be furnished (Entry 3, **Table 3.1**). In this case, the allylic bromide remained but diboron reagent was partially consumed by hydrolysis and oxidation, which showed that base activated B₂Pin₂ to form a stronger nucleophile. On the other hand, when no **Gua 22** was used, almost no reaction was observed (Entry 4, **Table 3.1**). Compared with the previous results, **Gua 22** may bind to copper species, not only providing enantiocontrol but also promoting the reactivity. From our preliminary observation, we found that the reaction under air would give higher ee compared with that under inert atmosphere, which was surprising as B₂Pin₂ and the formed boronates were considered to be less air and moisture stable in solution. Viewing this, we ran the reaction in Ar,

and this time it was found that only 49% **4a** in yield was obtained with a slightly decreased 89% ee (Entry 5, **Table 3.1**). Although **1-4a** was fully converted under Ar, dimerization product **9**, however, was determined as the major product. Considering that the enantioselectivity was not influenced much in this case, the non-guanidinium participated metallic Cu(0) catalysis pathway was excluded for the formation of the chiral allylic boronate. Conventionally, the S_N2' nucleophilic attack was believed the predominant mechanistic pathway in copper catalyzed allylic borylation with carbonates and ethers as substrates. Herein, radical-based dimerization was also taken into consideration. In addition, we also investigated the factor of water in this system. Based on the transformation, it seemed that no proton was needed for this reaction, different from the well-established conjugated borylation reaction to olefins bearing electron-withdrawing groups. To our surprise, the reaction could hardly work under water-free condition (Entry 6, **Table 3.1**). Typically, when a lesser amount of water than standard condition was used, a lower yield and decreased ee would be expected. According to the previous reports on borylation reactions, water or alcohol not only acted as the proton source, but also helped to activate B₂Pin₂ by exchanging pinacolate to methoxy or hydroxyl boronate which was less sterically demanding ^[6]. But, when water was replaced with 10 equivalent of MeOH (Entry 6, **Table 3.1**), we found that Cu(II) was readily reduced to copper black, leaving the reactants unreacted. It seemed that this biphasic system actually prevailed with excellent results, although there were still some details to be probed.

Table 3.1 The control experiment of copper/guanidinium catalyzed asymmetric allylic borylation.

Rac-1-4a	$\xrightarrow[\text{K}_2\text{CO}_3 \text{ (satd. aq.), } n\text{Hex, } 0^\circ\text{C, air, 24h}]{\text{B}_2\text{Pin}_2 \text{ (1.5 equiv.), Cu(NO}_3)_2 \cdot 3\text{H}_2\text{O (1 mol\%), Gua 22 (1.5 mol\%)}}$			4a
Entry ^[a]	Condition	Yield (%) ^[b]	ee (%) ^[c]	

1	Standard	99	97
2	No Cu	<5 ^[d]	N.A.
3	No K ₂ CO ₃	N.R. ^[e]	N.A.
4	No Gua 22	<5	N.A.
5	In Ar	49 ^[f]	89%
6	Solid K ₂ CO ₃	<5 ^[e]	N.A.
7	Solid K ₂ CO ₃ ^[g]	N.R. ^[e]	N.A.

[a]. Standard Reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 1 mol% Cu(NO₃)₂•3H₂O, 1.5 mol% **Gua 1**, 0.2 mL premixed saturated aqueous base solution, 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h;

[b]. GCMS yield after normalization without further calibration;

[c]. Determined by chiral GC columns;

[d]. **1-4a** was found mostly hydrolyzed to the corresponding alcohol;

[e]. **1-4a** was found remained in the reaction mixture;

[f]. The dimerization was found as the major side reaction;

[g]. 10 equiv. MeOH was added instead of water.

The control experiments showed that without copper, no reaction happened. To further understand the role of copper in this reaction, we went to test a series of metal salts that might be effective for borylation reaction. To ensure that the efficiency of metal catalyst was accurately examined, the loading was increased to at least 10 mol%. As shown in **Table 3.2**, among the metal investigated, only Pd as its acetate could afford the product in high yield (Entry 2, **Table 3.2**), however, almost no enantiocontrol was achieved. Iron salts, with +2 or +3 oxidation states or with different counter anions, proved to be ineffective (Entry 3–4, and 9 **Table 3.2**). Nickel was able to give high enantioselectivity, but offered low yield (Entry 5 and 6, **Table 3.2**). Similar results were obtained for cobalt (Entry 7, **Table 3.2**). Hardly any reaction was observed in the presence of zinc.

Table 3.2 The control experiment of metal catalyzed asymmetric allylic borylation.

Entry ^[a]	Metal (x mol%)	Yield (%) ^[b]	ee (%) ^[c]
1	Cu(NO ₃) ₂ ·3H ₂ O (1)	99	97
2	Pd(OAc) ₂ (10)	87 ^[d]	3
3	Fe(acac) ₂ (20)	<10 ^[e]	N.A.
4	Fe(acac) ₃ (20)	<10 ^[e]	N.A.
5	Ni(COD) ₂ (20)	39	83
6	NiF ₂ (20)	38	89
7	CoF ₂ (20)	14	92
8	Zn(OAc) ₂ ·2H ₂ O (20)	<10 ^[e]	N.A.
9	Fe(NO ₃) ₃ ·3H ₂ O (20)	<10 ^[e]	N.A.

[a]. Standard Reaction condition: 0.1 mmol *rac*-**1-4a**, 0.15 mmol B₂Pin₂, 10~20 mol% metal salts, 1 mol% **Gua 22**, 0.2 mL premixed saturated aqueous base solution, 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h;

[b]. GCMS yield after normalization without further calibration;

[c]. Determined by chiral GC columns;

[d]. Dimerization product was observed;

[e]. **1-4a** was found remained in the reaction mixture.

It seemed interesting that in this catalytic system, allylic dimerization occurred occasionally. In the previous reports, this dimerized product was normally formed when palladium was employed as metal catalyst. Due to its high reactivity, allyl palladium intermediate might continue to react with electrophile to give a bis-allyl complex, which led to diene after

reductive elimination. For copper catalytic borylation, generally benzyl type substrates were more eager to form diene. In this case, the formation of the diene was likely to result from oxidative coupling of the boronate, reductive coupling of the bromide, cross-coupling of the bromide and the boronate, or the dimerization of allylic radical intermediate. Thus, on the next series of experiments, we tested the corresponding potential coupling partners to see in which pathway the reaction really underwent. As illustrated in **Fig. 3.1**, first, allylic bromide **1-4a** and borylation product **4a** was mixed in the presence of our catalytic system and base. To our surprise, completely no dimerization was observed by GCMS, only **1-4a** and **4a** remained in the reaction mixture. When **1-4a** was employed in the absence of B_2Pin_2 , no reaction was detected. In the third experiment, to probe the chance of oxidative coupling, we added product **4a** into the system with 0.5 equivalent of B_2Pin_2 . However, even under air which could be treated as the oxidant, **4a** was found considerably stable without the observation of the formation of **9**. Hence, apart from cross-coupling and reductive coupling shown ahead, it seemed that the oxidative coupling mechanism could be excluded from the hypothesis. Nonetheless, we also tested the possibility of the hydroborylation process, as water was found crucial to provide excellent results. Since water was employed in the reaction and allylic bromide could transfer into diene after elimination in the presence of base, with the help of Cu, HBPIn or its alternative might be formed in the reaction mixture and added forward into the C=C double bond to give the same product but in a hydroboration approach. In this control experiment, we employed cyclohex-1,3-diene **10** as substrate, and 1.5 equivalent of B_2Pin_2 was added together with copper and guanidinium catalyst. As a result, targeted allylic boronate **4a** was not found anyway, which implied that hydroboration was not involved in this process.

Figure 3.1 The coupling experiment of copper/guanidinium catalyzed asymmetric allylic borylation.^[a]

[a]. Standard reaction condition: 0.1 mmol scale reaction, 5 mol% $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, 5 mol% **Gua 22**, 0.2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 1 mL $n\text{Hexane}$, air atmosphere, stirred at room temperature for 24 h.

[b]. Determined by GCMS.

The results of the control experiments suggested that the efficiency of our catalytic system relied on copper and the guanidinium salt. Only copper showed reactivity while fantastic enantiocontrol was also observed for the product. Guanidinium salt **Gua 22**, in this case, not only exhibited satisfactory ee, but also is likely to activate the copper species that facilitated the borylation process. Besides the well-documented fact that base will help to transfer diborons to more nucleophilic species, water and air were found to produce good results. In contrast, for the reaction under Ar, the dimerization seemed prohibited in the presence of air, oxygen as the oxidant or the radical trapper. Moreover, the former test has shown that the dimerization was not derived from the coupling between substrates and products. Therefore, it must appear

during the catalytic process as the intermediate. Further investigation on these issues will be discussed.

3.3 Kinetic Study: KIE with Deuterated Water

As we found that water played an important role in this borylation reaction, we decided to investigate how water was influencing this transformation. As we can imagine, water increased the apparent concentration of K_2CO_3 , which enhanced the reaction kinetically. Besides, water also helped K_2CO_3 to generate OH^- in aqueous solution, which may truly act as a base or pre-nucleophile to activate B_2Pin_2 . Among numerous techniques employed to probe the details of the reaction mechanism, kinetic isotope effect (KIE) was the most effective method as long as the targeted C–H bond was broken at the rate-limiting step. Although no deprotonation or protonation was involved in this reaction, according to the previous report on metal catalyzed borylation reaction, we still wanted to use kinetic isotope effect to check if KIE effect could be observed when H_2O was replaced with D_2O in the mixture. Since the presence of water determined the success of the reaction, the positive results of KIE experiment would indicate that there might be some unexplored steps beneath.

Two experiments were carried out, one with H_2O and another with D_2O completely in the saturated K_2CO_3 solutions employed. After the calibration curve was established with biphenyl employed as an internal standard, we chose the previous model reaction, and the GCMS yields were collected as the reaction proceeded. As illustrated in **Fig. 3.2**, the relationship between concentration and reaction time was plotted for reactions in H_2O and D_2O respectively. The trend lines for both graph are linear as their R^2 values were larger than 0.99. From the graph, we obtained the KIE value (k_H/k_D) as 0.95, which mean that no

obvious kinetic isotope effect was observed. In another word, despite water playing a crucial role in the reaction no H atom exchange was involved in any rate-determining or turnover-determining step. Even if water was employed in any step of the transformation, the process was too fast to influence the overall rate of the borylation.

Figure 3.2 The KIE experiments of copper/guanidinium catalyzed asymmetric allylic borylation.^[a]

[a]. Standard reaction condition: 2 mmol scale reaction, 3 mmol B₂Pin₂, 5 mol% Cu(NO₃)₂·3H₂O, 1 mol% **Gua 22**, 4 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 20 mL *n*Hexane, air atmosphere, stirred at room temperature for a certain time. Concentration determined by GCMS after dilution of sample and calibration with Biphenyl as internal standard.

3.4 ¹H-NMR Experiment: Guanidinium Phase Transfer Reagent or Guanidine Ligand

Next, we were going to investigate the role of guanidinium salt in the reaction. In previous studies, guanidinium salts have been employed as phase transfer catalysts ^[7-16]. From the discovery of our initial optimization work, it was also shown that positive charged bisguanidiniums and pentanidiums were able to afford low enantioselectivity in this reaction.

However, **Gua 22** was also utilized before as an organic guanidine base precursor after treated with inorganic base such as KOH solution. Considering that there were reports of carbenes or phosphines catalysis on conjugated borylation^[6, 17], the function of **Gua 22** was even more complicated. Generally, there are three possibilities. Firstly, it could act as a phase transfer agent which bound to anionic cuprate that completed the borylation process. Secondly, it might be deprotonated by base to give the corresponding free guanidine **Gua 22'**, which would then be employed as the ligand in the catalytic cycle. Thirdly, it was also possible that this free guanidine performed as Lewis base to activate B₂Pin₂, when Cu reacted with allylbromide to construct a metal-organic dual catalysis process. In such situation, at the beginning, it was necessary to figure out whether **Gua 22** salt was stable in saturated K₂CO₃ solution. The key question is: will it remain as the salt or be deprotonated to give the free guanidine?

To work on the above problem, the most effective and straight-forward method would be using ¹H-NMR experiment to check if there was any change on chemical shift of its proton peaks once treated with a base. As illustrated in **Fig. 3.3**, the ¹H-NMR spectrum of **Gua 22** in CDCl₃ was shown as **Exp. 1**. It was clear that two N–H protons (integrated as 1.78 H) were present at 8.32 ppm for **Gua 22**. When **Gua 22** was treated with K₂CO₃ solution in DCM overnight, the resulting organic solution would afford an off-white solid after drying and concentrating it. The yield achieved was 97% if free base **Gua 22'** was considered as the product. Such resulting compound, however, gave almost the same spectra as **Gua 22** when CDCl₃ was used as solvent. After consideration, we supposed that there might be considerable amount of DCl/HCl formed in CDCl₃ as it decomposed, which would cause acidification if the free base was obtained. To prevent the above complications, we repeated the test but using CD₂Cl₂ as solvent. This time, as shown as **Exp. 2**, all proton peaks migrated to upfield

Figure 3.3 The ^1H -NMR experiments of **Gua 22** after K_2CO_3 treatment and dilution.^[a]

[a]. Standard reaction condition: 1 mmol **Gua 22**, 5 mL DCM, 5 mL saturated K_2CO_3 aqueous solution (about 30 equiv.), air atmosphere, stirred at room temperature overnight. Isolated yield.

Experiment 1: ^1H -NMR spectrum of **Gua 22** in CDCl_3 .

Experiment 2: ^1H -NMR spectrum of **Gua 22'** in CD_2Cl_2 after treated by K_2CO_3 saturated solution.

Experiment 3: ^1H -NMR spectrum of **Gua 22'** in CD_2Cl_2 after 1st time dilution.

Experiment 4: ^1H -NMR spectrum of **Gua 22'** in CD_2Cl_2 after 2nd time dilution.

significantly, which indicated a much stronger shielding effect in the compound. We could then infer that the positive charge in **Gua 22**, might be removed. Interestingly, although in **Exp. 2** there was only one N–H proton left (integrated as 1.36 H), it always suffered a bad reproducing issue. It seemed that the number of active N–H protons was not constant, and the integration was not accurate. After a period of investigation, we found that, as the concentration of **Gua 22'** solution decreased, the proposed N-H proton peak would be shifted

upfield while the chemical shifts of all C–H protons remained the same. Meanwhile, the integration of proton numbers would also increase (**Exp. 3** and **Exp. 4**, from 1.36 to 2.04, to 4.76) as the solution was diluted, which might be attributed to the decomposition of **Gua 22'** oligomers and formation of new hydrogen bonding with trace water inside the solvent. Thus, with the help of ^1H -NMR experiments, we could conclude that, different from bisguanidiniums and pentanidiums, **Gua 22** would be deprotonated to give the corresponding free guanidine **Gua 22'** once treated with base. Thus, the possibility of guanidinium-cuprate ion-pairing catalysis was totally excluded. As for whether the generated **Gua 22'** was employed as a ligand, further studies were still required.

3.5 ^{11}B -NMR Experiment: B_2Pin_2 Activation Mode

The following investigation was focused on the activation of diboron reagent. As for this part, we placed our attention on how B_2Pin_2 was activated. Previous reports showed that B_2Pin_2 was attacked by a Lewis base such as alkoxyl anion, NHC or phosphine, due to its medium Lewis acidity derived from the unoccupied p orbital on boron atom. Thus, a desymmetrization process would be observed as one boron atom changed from sp^2 to sp^3 hybridization, while the other boron atom in this adduct became a formal “ BPin^- anion”. Another activation pathway was discussed in the **Chapter 1**. When B_2Pin_2 was attached to the base, transmetallation would occur if the geometry and energetic demand were met. After this four-membered ring concerted step, the newly generated metal-boryl complex would be taken into the following transformation as a superior boryl source.

After knowing that **Gua 22** would convert to the corresponding **Gua 22'** in the presence of base, we used ^{11}B -NMR technique this time to probe the transformation and generation of

Figure 3.4 The ^{11}B -NMR experiment investigation of B_2Pin_2 activation mode.^[a]

[a]. Standard reaction condition: 0.01 mmol scale reaction. B_2Pin_2 , **4a**, **Gua 22**, K_2CO_3 , and **1-4a** were all 1.0 equiv. to the reaction, if charged. 0.4 mL d^6 -benzene, 10 μL D_2O , air atmosphere, in NMR tube stood at room temperature for 3 h.

Experiment 1: ^{11}B -NMR spectrum of borylation product **4a** in d^6 -benzene.

Experiment 2: ^{11}B -NMR spectrum of B_2Pin_2 in d^6 -benzene.

Experiment 3: ^{11}B -NMR spectrum of the mixture of B_2Pin_2 and K_2CO_3 in d^6 -benzene.

Experiment 4: ^{11}B -NMR spectrum of the mixture of B_2Pin_2 , CuCl and K_2CO_3 in d^6 -benzene.

Experiment 5: ^{11}B -NMR spectrum of the mixture of B_2Pin_2 , **Gua 22** and K_2CO_3 in d^6 -benzene.

Experiment 6: ^{11}B -NMR spectrum of the mixture of B_2Pin_2 , CuCl , **Gua 22** and K_2CO_3 in d^6 -benzene.

Experiment 7: ^{11}B -NMR spectrum of the mixture of B_2Pin_2 , CuCl , **Gua 22**, **1-4a** and K_2CO_3 in d^6 -benzene.

boron species. The experimental results were demonstrated in **Fig. 3.4**. First, bis(pinacolato)diboron and borylation product **4a** were run with ^{11}B -NMR (**Exp. 1** and **Exp. 2**), giving their boron chemical shifts at 31.40 ppm and 33.54 ppm, respectively. If B_2Pin_2 was mixed with K_2CO_3 in the presence of D_2O for three hours, a small peak located at 4.77 ppm was

seen (**Exp. 3**), which indicated that a new sp^3 hybridized boron species was formed as B_2Pin_2 was decomposed. However, when CuCl (Cu^{2+} salts were unable to use due to their paramagnetic property) was added as well (**Exp. 4**), this peak was not significantly shown, but only trace was observed in the spectrum. It seemed that the presence of copper would not affect and facilitate the transformation of B_2Pin_2 . On the other hand, when **Gua 22** was used to replace CuCl, a new peak at around 8.03 ppm was observed from the spectrum (**Exp. 5**), which indicated that a new sp^3 boron, but different from the previous one, was formed. The same results could be obtained when CuCl and **Gua 22** were charged (**Exp. 6**). Eventually, when allylic bromide **1-4a** was employed, the peak of diboron was greatly diminished, while product **4a** was found generated, although in low yield (**Exp. 7**).

With the help of ^{11}B -NMR spectroscopy, we could conclude that copper did not directly help to activate B_2Pin_2 but **Gua 22** did. **Gua 22** was probably first neutralized to give **Gua 22'**, which was highly dissolved in organic phase than OH^- and thus more favored to activate B_2Pin_2 . This adduct might not be very stable in the presence of moisture and air, as no sp^2 hybridized boron was observed along with the sp^3 hybridized one, as it was soon decomposed and converted to tetra-coordinated boronate. Due to the limited dose of base, the actual basic anion in the solution would be different and also insufficient. As a result, the peak of sp^3 hybridized boron varied from 4.77 to 8.03. Once allylic bromides were added, with the aid of copper, the activated boryl group then was capable of completing the substitution. Similarly, due to the lack of base, neutral sp^2 hybridized boron, which was proposed to be HOBPin, was also observed in the spectrum.

3.6 EPR Experiment: Oxidation States of Real Copper Catalytic Species

Figure 3.5 The EPR spectrometry investigation on oxidation state of copper species in asymmetric allylic borylation.^[a]

[a]. Experiments were carried out in CHCl_3 under air at room temperature.

Exp. 1 for black line: CuCl_2 aqueous solution;

Exp. 2 for red line: CuCl_2 and basified **Gua 22** (the solution of compound **11**);

Exp. 3 for blue line: B_2Pin_2 was added for 5 min;

Exp. 4 for pink line: B_2Pin_2 was added for one week

Although Cu(I) salts were more reactive in this reaction that could furnish the product in a shorter time, Cu(II) salts, however, showed higher enantioselectivity and yield generally. Based on previous investigation on this topic, Cu(I) catalysts were more commonly involved in allylic borylation, with only one example using $\text{Cu}(\text{OTf})_2$ by Hoveyda^[18]. In their paper, the author proposed that the Cu(II) salt was reduced by B_2Pin_2 *in situ* to give the catalytically active Cu(I) complex. However, no further investigation was made regarding this issue. Recently, catalytic reactions involving Cu(III) were also published, which made this exploration attractive. Thus, we put our attention on determining the oxidation state of the

active catalytic copper species. Considering the unique paramagnetic property of Cu(II) bearing unpaired electrons, we tried to use electron paramagnetic resonance (EPR) spectroscopy to see how the initial Cu(II) got involved in the reaction mixture.

The experimental results are overlaid and shown in **Fig. 3.5**. In this investigation, anhydrous CuCl₂ was employed as model since the performance of ERP instrument was sensitive to water content. All tests were carried out in CHCl₃. First, since solid CuCl₂ failed to give a clear and precise spectrum, we obtained the EPR spectrum of CuCl₂ with minimum amount of water, as a singlet peak was detected with g-factor of 2.19. After comparing with other Cu(II) salts bearing combined water, it could be confirmed that the signal should be attributed to hydrated ion Cu²⁺(H₂O)_n. There was no significant change except that the counter anion was oxidized to I₂, when CuCl₂ was mixed with **Gua 22**. Interestingly, when anhydrous CuCl₂ was treated with free base **Gua 22'** in DCM, a deep brown solution was formed. After concentration, the solution might give a brown solid, which was later defined as compound **11**. When the corresponding solid was dissolved in chloroform and got tested by EPR, a new peak with g-factor of 2.15 was found. To our surprise, when B₂Pin₂ was introduced into the brown solution, the colour faded rapidly to pale-yellow, which indicated that some transformation occurred in the mixture. If the mixture was tested immediately, the previous signal (g-factor: 2.15) was found almost fully disappeared. However, without **Gua 22'**, due to low solubility of CuCl₂, no signal loss of Cu²⁺ would be observed. Meanwhile, a new small triplet signal (g-factor: 1.99, 2.00, 2.01) could be observed in the spectrum which was normally attributed to organic radicals. Similar triple peaks were also observed when a mixture of B₂Pin₂ and **Gua 22'** were tested. When the sample was allowed to stand at room temperature for a long time, one week in our case, only blank with noises would be shown. But, when it was exposed in the air, the peak of g-factor 2.15 will be regenerated again, with

colour back to brown at the same time. It was indicated that air atmosphere initially in the reaction could help to maintain the Cu(I) species in a low concentration and slow down the reduction process which might further deactivate the reaction by over-reduction to metallic copper or cause any achiral pathway. Herein, as a conclusion of EPR experiments, it was shown that: 1) Free base **Gua 22'** interacted with Cu(II) salt to generate a new paramagnetic compound; 2) Paramagnetic Cu(II) species would be reduced to a diamagnetic species, most likely to be Cu(I), with the help of **Gua 22'**; 3) the furnished Cu(I) could also be further oxidized to the former Cu(II) species in the presence of air; 4) **Gua 22'** was able to interact with B₂Pin₂ to give a small amount of unknown radicals, which were not stable in the presence of air.

Figure 3.6 The crystal structure of (Gua 22)₂CuCl₄ complex **11**. Most of the hydrogen atoms have been omitted for clarity.

The single crystal of compound **11** derived from experiment two was grown in chloroform with ether, and analyzed using X-ray crystallography. As shown in **Fig. 3.6**, the brown compound was the cuprate salt with bicyclic guanidinium as counter ions, which could be presented as (Gua 22)₂CuCl₄ in convenience. In the molecule of complex **11**, copper atom

with oxidation state +2 was coordinated with four chlorides, thus bearing two bicyclic guanidinium motifs as counter ions. N–H protons on guanidinium ions formed hydrogen bonds with chlorides on cuprate ion. Notably, complex **11** was generated when CuCl₂ was mixed with **Gua 22'** even with the molar ratio 1:1. In this situation, it seemed that Cu²⁺ ions could not form stable complex with Lewis base **Gua 22'** as they facilitated the hydrolysis of each other rapidly. It was believed that guanidine **Gua 22'** was acidified by the HCl released from the hydrolysis of Cu(II) salts in the presence of trace amount of water, although Cu(OH)₂ as the evidence might be precipitated in the process and was not observed in the crystal. Compound **11** was generally stable in the absence of moisture, otherwise it would go on hydrolyzing to give copper hydroxide until completely.

3.7 Catalyst Precursor and the Crystal Structure

Having confirmed that Cu(I) was the real catalytic specie in this reaction, we tried to discover the structure of catalyst precursor one step further. We mixed CuCl and **Gua 22'** in DCM under argon, upon which a white solid was obtained after concentration. After growing in DCE and Et₂O in the absence of moisture and air, the crystal of such compound was obtained and disclosed the real structure of CuCl/**Gua 22** adduct. As shown below in **Fig. 3.7**, it was actually a complex of Cu(**Gua 22'**)Cl **12** that bore two coordination pattern. One form **A** is that the guanidine was mono-coordinated to CuCl with a weak Cu–Cu interaction between two metal cores, while the other **B** is the dichlorocuprate salt form with di-coordinated Cu(I) cation as the counter ion. These two structures were present as 1:1 molar ratio in the crystal cell, which implied that in reality they would transform to each other in solution, although the distribution might vary depending on the solvent.

Figure 3.7 The crystal structure of Cu(**Gua 22'**)Cl complex **12** and its ORTEP representation. Most of the hydrogen atoms have been omitted for clarity.^[a]

The compound **12** was re-employed in the reaction directly at the loading of 1 mol% under air. Without the presence of additional copper and guanidinium, almost the same result was obtained with 99% GC yield and 97% ee. This discovery confirmed that **12** somehow participated the reaction catalytic cycle, at least as the catalyst precursor. The question now is, which structure is the dominant one in the reaction. Notably, in the salt form **B** of **12**, because Cu atom in the cationic part was fully coordinated with two guanidine, which was almost steric shielded, it should be less likely to be responsible for boryl group transfer. The counter anionic part thus became more active and was able to establish enantioselectivity on allylic product under the cover of chiral copper cation, with ion-pairing interaction. If the negative charge was always preserved on this copper center during the process, this might give rise to

enantioselectivity observed in the case of pentanidiums and bisguanidiniums as catalysts. Otherwise, this would be the reason of losing ee when reaction condition, such as solvent, was changed. Besides, regardless of the weak Cu–Cu bond, once the chiral cation was replaced with an achiral one, the enantiometric introduction would be also terminated. Without the protection of guanidine ligand, Cu(I) species was also suffering from over-reduction to Cu(0) particles, even copper black in the end.

Figure 3.8 The crystal structure of $\text{Cu}_2(\text{Gua } \mathbf{22'})_2$ complex **13** and its ORTEP representation. Most of the hydrogen atoms have been omitted for clarity.^[a]

Other possibilities were also explored. Compound **12** was treated with strong base like KO^tBu, in order to exchange the chloride with ^tBuO[−], as reported in NHC catalyzed reaction to pursue Copper–Boryl intermediate later. However, only a new complex **13** as $\text{Cu}_2(\text{Gua } \mathbf{22'})_2$ was disclosed with the structure shown in **Fig. 3.8** below by its single crystal. It seemed that **13** was generated due to the deprotonation of guanidine **Gua 22'** attached to copper in

complex **12** followed by dimerization. Still, a Cu–Cu bond was present in the crystal structure, with average bond length of 2.73 Å, shorter than the sum of Van der waal’s radius of 2.80 Å. Complex **13** was grown a colorless crystal, with much higher stability to air and moisture than expected.

Later, we enrolled the complex **13** into the borylation reaction. Surprisingly, when NaOMe was employed as base, almost no reaction was observed as **1-4a** was used as allylic electrophile. Anhydrous K₂CO₃ gave almost same result. However, when saturated K₂CO₃ solution was employed, previous excellent results were once again repeated, which implied that acidic protons were needed to degrade this dimer complex to monomers as true catalytic species. It was also demonstrated that complex **13** was inactive for borylation reaction. And the reason why **Gua 22** could not be employed alone in the presence of strong organic base was due to the importance of water as proton source.

Figure 3.9 The control experiments of complex **13** catalyzed asymmetric allylic borylation.^[a]

Condition A: NaOMe, N.R.

Condition B: anhydrous K₂CO₃, N.R.

Condition C: saturated K₂CO₃ solution, > 99% GC Yield, 97% ee

[a]. Reaction condition: 0.1 mmol scale reaction, 0.15 mmol B₂Pin₂, 0.5 mol% Cu₂(**Gua 22'**)₂, 1 mL *n*Hexane, Ar, stirred at 0 °C for 24 h. Yields determined by GCMS after calibration with Biphenyl as internal standard. ee determined by chiral GC columns.

Condition A: 2.0 equiv. NaOMe was employed.

Condition B: 12 equiv. anhydrous K₂CO₃ was employed.

Condition C: 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.) was employed.

3.8 Non-linear Effect Investigation

Considering that two kinds of structures in complex **12** might transfer to each other in the real reaction mixture as an equilibrium, which might give different reactivity and selectivity, we checked if there was any non-linear effect in the catalytic reaction to figure out which type of complex was the true catalytic active species. A series of experiments employing **Gua 22** with varied ee was carried out. As shown in the **Table 3.3** below, almost no obvious non-linear effect could be observed from the reaction of racemic allylic bromide **1-4a** and B_2Pin_2 , in the presence of $Cu(NO_3)_2 \cdot 3H_2O$ and enantio-impure **Gua 22**. The ee of product **4a** decreased gradually as the ee of **Gua 22** employed decreased. All plots could be assumed to be linear with $R^2=0.99$. In the crystal of complex **12**, the complex form **A** depicted similar catalyst structure presented in the NHC assisted copper catalyzed borylation reaction. However, in form **B**, the borylation process should be induced by two chiral guanidine motif at the same time. As there was no positive non-linear effect observed, hence, it could be concluded that true catalytic active species were more likely to be the monomeric mono-coordinated $Cu(\text{Gua 22})Cl$ complex **A** on the left.

Table 3.3 The investigation of non-linear effect in the model enantioselective allylic borylation reaction.

Entry ^[a]	ee of Gua 22	Yield (%) ^[b]	ee of 4a (%) ^[c]
1	100	96	97
2	80	98	71
3	60	95	56
4	40	94	44
5	20	92	23
6	0	89	1

[a]. Reaction condition: 0.1 mmol scale reaction, 0.15 mmol B_2Pin_2 , 1 mol% $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$, 1 mol% **Gua 22**, 0.2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 12 h.

[b]. GCMS yield after calibration with biphenyl as internal standard.

[c]. Determined by chiral GC columns.

3.9 Radical Trapping Experiments

Another issue of the mechanism investigation is how chiral but racemic substrates were able to be transferred into enantioenriched boronates. In the palladium catalyzed allylic borylation reactions, normally an allylic palladium complex was generated. However, according to the previous studies, copper in borylation reaction preferred to interact with the boron species to give copper-boryl complexes as the first step. In this situation, three plausible reaction pathways, which were demonstrated in **Fig. 3.10**, were brought forward: 1) After borylation, Cu–B species reacted with allylic bromide to give allyl boryl complex, then reductive elimination occurred to give chiral boronates under the control of guanidine ligands; 2) the

copper-boryl intermediate coordinated to the C=C double bond followed by the boryl S_N2' nucleophilic attack, and the bromide was removed as the leaving group; 3) the electron-rich copper-boryl complex transferred one electron to allylbromide to give allylic radical, with the product obtained after redox radical-boryl coupling. It was noteworthy that both the cleavage of C–Br bond and the formation of C–B bond could undergo either the intersphere or outersphere pathway.

Figure 3.10 The plausible reaction pathway of copper/guanidinium catalyzed asymmetric allylic borylation.

The detailed mechanism of allylic radical generation was proposed as illustrated in **Fig. 3.11**. If the activation of the allylic bromide underwent a radical pathway, it was believed that the process involved either inner-sphere redox mechanism or outer-sphere redox mechanism.

In the inner-sphere mechanism, the covalent bonding interaction existed between the copper core and the radical intermediate. It was believed that allylic bromide first attached to the Cu(I)-boryl complex, followed by the intramolecular electron transfer. The redox process gave rise to the radical-anionic allylic bromide, while the oxidation state of copper was increased to +2. After the bromine anion dissociated from the allylic motif, the allylic radical was given in the copper complex. It was noteworthy that the radical generated might soon give η^3 -allyl copper complex and might not be treated as a free radical.

Figure 3.11 Innersphere and outersphere mechanism of allylic radical generation.

Innersphere Mechanism of Allylic Radical Generation:

Outersphere Mechanism of Allylic Radical Generation:

Another possibility was that the radical was generated with the outer-sphere mechanism. In this case, the reductive Cu(I)-boryl complex interacted with the bromine atom directly without the initial coordination. After the electron transfer, the allylic radical was formed, giving the corresponding copper(II) bromide at the same time.

For the reaction between allylic radical and boryl group, not only inner-/outer-sphere mechanism, but also in-/out-of-cage mechanism should be considered. As demonstrated in **Fig. 3.12**, once the allylic radical was generated, it could direct react with the original copper-boryl complex in the cage constructed by solvent molecules. This happened especially when the radical was very reactive with a short lifetime or the cage effect of the solvents was strong.

that the racemates might react with copper catalyst independently in different rates. However, as the reaction could be completed with products in high ee, it seemed less likely that the borylation proceeded through kinetic resolution. Considering that in our previous investigations considerable amount of dimerization product was observed under certain conditions, along with the intramolecular cyclization found in the production of **6i**, it was possible that the reaction involved a radical pathway, via the “pathway C” shown in **Fig. 3.10**. However, it was still unclear how the radical was generated and whether such radical intermediate was responsible for the formation of enantioenriched allylboronates. In addition, different from the previously reported allylic S_N2' boryl nucleophilic substitution, allylic electrophiles with oxygen-based leaving groups were found not working with the present system. Thus, the exploration begun with radical trapping experiments to see if the reaction was influenced by radical scavengers.

The results of trapping experiments were listed in **Table 3.4** below.

Table 3.4 The radical trapping experiments of the asymmetric allylic borylation reaction.^[a]

<p><i>Rac-1-4a</i> $\xrightarrow[\text{Radical Scavenger (2.0 eq.), } n\text{Hex, K}_2\text{CO}_3 \text{ (satd), RT, air}]{\text{B}_2\text{Pin}_2 \text{ (1.0 equiv.), Cu(NO}_3)_2 \cdot 3\text{H}_2\text{O (1 mol\%), Gua 22 (1 mol\%)}}$ 4a + 9</p>			
Entry ^[a]	Radical Scavenger	Product	Yield (%) ^[b]
1	None	4a	70
2	TEMPO	4a	58
3	BHT	4a	42

Entry ^[a]	Radical Scavenger	Product	Yield (%) ^[b]
4	None	9'	>99
5	TEMPO	None	N.A.
6	BHT	9'	33

[a]. Reaction condition: 0.1 mmol scale reaction, 0.1 mmol B₂Pin₂, 1 mol% Cu(NO₃)₂·3H₂O, 1 mol% **Gua 22**, 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at room temperature for 6 h.

[b]. GCMS yield after calibration with biphenyl as internal standard.

As

shown, when **1-4a** was employed, as 1.0 equiv. B₂Pin₂ was charged, 70% GC yield of product **4a** would be obtained, without the formation of dimer **9** (Entry 1, **Table 3.4**). After 6 hours, B₂Pin₂ was fully consumed, and there was still some unreacted **1-4a** remaining. However, in the presence of 2 equiv. TEMPO, the yield was decreased to 58% (Entry 2, **Table 3.4**), with TEMPO partially reduced to the corresponding amine. This could be possibly attributed to the oxidizing ability of TEMPO, which consumed B₂Pin₂ or the reductive Cu intermediate. While the reductive radical scavenger BHT was employed, an obvious drop in yield was also detected (Entry 3, **Table 3.4**). Both radical scavengers failed to influence the enantiomeric excess values of **4a** obtained. It was also notably that no trapping product was isolated from the reaction mixture or detected by GCMS. So, it was highly possible that the radical scavengers were unable to capture the targeted organic radical intermediates. Meanwhile, the process to give chiral boronate **4a** was not much influenced by the radical trappers, which indicated that the enantioselective allylic borylation might not involve any allylic radical intermediate.

Different from **1-4a**, when benzylic bromide **1-8b** was chosen as the substrate with the standard reaction conditions, it almost completely furnished dimer **9'**. In this case, radical scavengers

TEMPO and BHT prevented the homocoupling drastically (Entry 5–6, **Table 3.4**). All **1-8b** remained unreacted in the system. It seemed that the catalyst was deactivated before it interacted with the benzyl bromide, as there was no radical trapping product being detected. It showed great consistency with the results of the reactions employing **1-4a**. Herein, we suspected that such dimerization product was derived from the combination of benzylic radicals but radical scavengers were able to diminish the catalytic species responsible for radical process. Since TEMPO and BHT also affected the yield of **4a**, such catalytic species might also lead to the generation of allylic boronates in the reaction process.

3.10 Radical Clock Experiments

With preliminary knowledge that the reaction might involve a radical process, we went on to discover the mechanism with radical clock experiments. Radical clock experiments were valuable tools as the evidence of a radical-based reaction pathway. As illustrated in **Fig 3.13**, two kinds of primary bromides, **14a** and **14b**, were tested in the optimized borylation reaction conditions. Due to low reactivity of primary bromide, initially, no reaction was observed in *n*Hexane with 1 mol% of catalyst loading. However, when the solvent was changed to more polar MTBE, the reaction began to give the desired boronate in low yields with 5 mol% catalyst loading. In the case of **14a**, no direct substitution occurred, but in an isolated yield of 9%, cyclized boronate **15a** was obtained as a single isomer, with most of **14a** unreacted. While in the case of **14b**, only ring-opening product **15b** was detected, and successfully isolated in medium yield, followed by characterization with $^1\text{H-NMR}$.

Figure 3.13 The radical clock experiments of copper/guanidinium catalyzed borylation.^[a]

[a]. Standard reaction condition: 1 mmol scale reaction, 5 mol% $\text{Cu(NO}_3)_2 \cdot 3\text{H}_2\text{O}$, 5 mol% **Gua 22**, 2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 10 mL MTBE, air atmosphere, stirred at room temperature for 12 h. Isolated Yields. Selectivity was confirmed by GCMS and $^1\text{H-NMR}$.

In radical clock experiments, the reaction was found to cease after 30 minutes. Initially, Cu(II) was rapidly reduced to Cu(I) as the blue colour faded to give a white suspension. However, because of the low reactivity of substrates, the suspension soon turned grey which indicated the formation of Cu(0) particles, as all oxygen was consumed. No further improvement was achieved when the suspension with Cu(0) black was allowed to move on reacting. Thus it was shown that Cu(0) species, especially the copper black, could not compete with our Cu(I) catalyst.

However, in the case of **5f** and **6i**, there was no evidence that the formation of allylic boronates resulted from the allylic radical. Only when insufficient guanidinium salt was used in the reaction of **6i**, the cyclization product would be observed in small amount.

After considering all the results of radical-related experiments, we postulated the transformation of catalytic species. As demonstrated in **Fig. 3.14**, when the copper(II) salt was introduced into the reaction mixture, it would be reduced and form the Cu(I)-boryl

complex in the presence of B₂Pin₂, base and the guanidinium salt. The Cu(I)-boryl complex would react with allylic bromide to give the corresponding boronates. If all oxygen was consumed and the substrate was not so reactive, the complex was believed to be further reduced to Cu(0) complexes or Cu(0) metallic nanoparticles. Such copper(0) intermediates might initiate the generation of allylic radicals. When TEMPO was added to the reaction, it would oxidize the copper-boryl complex and copper(0) species, which influenced the rate of allylic borylation and terminated the generation of radicals. While BHT was used, it would reduce the Cu(I)-boryl complex and copper(0) species, giving rise to the unreactive copper black.

Figure 3.14 The proposed transformation of copper species.

3.11 Investigations on the Product Distribution with Allylic Isomeric Substrates

To further explore the reaction mechanism, experiments with allylic isomeric substrates were conducted. *Rac*-**16a** and **16b** were employed respectively as the substrates (Fig. 3.15). When pure **16a** was used, S_N2' substitution product **4a'** was found as the only product after 5 hours under the optimized conditions, with a GC yield of 78% and the *Z/E* ratio of 1:3. While **16b**

was employed (the commercially available **16b** contained about 10 mol% **16a**), the corresponding S_N2' product **4a** was found with the yield of 26% after 5 hours (**4a'** existed was attributed to the product of 10 mol% **16a** inside), with some of **16b** remained in the system.

Figure 3.15 The allylic borylation reactions with allylic isomeric substrates ^[a].

[a]. Standard reaction condition: 0.1 mmol scale reaction, 1 mol% Cu(NO₃)₂·3H₂O, 1.5 mol% **Gua 22**, 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C for 5 h. GC Yields without calibration. The ratio of *Z/E*-configuration was confirmed by ¹H-NMR.

The results clearly show that the reaction proceeded in a manner of S_N2' substitution. Linear allylic chloride **16b** reacted much slower than the branched **16a** under the standard allylic borylation conditions. Previously, all allylic boronates **5** and **6** were furnished as the branched products, while in the case of **16a** only less steric hindered **4a'** was achieved. Taking into account the results of the reaction with **16b** as the substrate, it seemed that the mechanism involving the π-allyl copper complex was unlikely.

3.12 Investigations on the Enantiomeric Excess of the Unreacted Allylic Bromide

Next, we conducted the model reaction of allylic borylation, with checking the ee of the unreacted allylic bromide as the reaction proceeded. The results are shown in **Table 3.5**.

Table 3.5 The investigation of the enantiomeric excess of the unreacted allylic bromide.^[a]

<i>Rac</i> - 1-4a				4a
Entry ^[a]	Reaction Time (h)	Yield of 4a (%) ^[b]	ee of unreacted 1-4a (%) ^[c]	ee of 4a (%) ^[c]
1	0.5	16	2	95
2	1	25	5	96
3	3	76	32	96
4	6	94	39	96

[a]. Reaction condition: 0.1 mmol scale reaction, 0.1 mmol B₂Pin₂, 1 mol% Cu(NO₃)₂·3H₂O, 1.5 mol% **Gua 22**, 0.2 mL saturated K₂CO₃ aqueous solution (about 12 equiv.), 1 mL *n*Hexane, air atmosphere, stirred at 0 °C.

[b]. GCMS yield after calibration with biphenyl as internal standard.

[c]. Determined by chiral GC columns.

work of asymmetric allylic alkynylation^[19], we found that two enantiomers of allylic bromide **1-4a** interconverted very fast when the (guanidine)copper complex was present. As the enantioenriched allylic bromide **1-4a** would turn racemic and no ee of **1-4a** was observed during the alkynylation reaction, it was believed that the reaction led to a dynamic kinetic resolution (DKR) mechanism. However, in the case of such allylic borylation, we found that the ee of the allyl bromide increased as the reaction proceeded. We speculated that reaction

rate of the borylation reaction (full conversion with 95% ee in 0.5~3 hours at room temperature depending on the catalyst loading) was comparable with the rate of bromide racemization process. Thus, non-racemic allylic bromides could be observed due to the dynamic kinetic resolution of two allylic bromide enantiomers.

Notably, we could not fully exclude the possibility that the reaction underwent the direct enantio-convergent transformation (DECT) mechanism. Different reaction rates of the two enantiomers could also give the non-racemic **1-4a**, although Ito pointed out that allylic halides with such labile leaving groups favored to undergo DKR mechanism ^[20].

Figure 3.16 The possible mechanism of the enantioconvergent borylation process.

Kinetic Resolution: $k_2 \gg k_4 \gg k_1 \approx k_{-1}$

Dynamic Kinetic Resolution (Alkynylation): $k_1 \approx k_{-1} \gg k_2 > k_4$

Dynamic Kinetic Resolution (Borylation): $k_2 > k_1 \approx k_{-1} > k_4$

Direct Enantio-convergent Transformation (Borylation): $k_2 > k_3 > k_4, k_3 \gg k_1 \approx k_{-1}$

An overview of the proposed mechanism of the enantioconvergent borylation process is illustrated in **Fig. 3.16**. Either DKR process or DECT process might be responsible for the

resolution of racemic allylic bromide. Both of them will lead to the increase of enantiomeric excess value of **1-4a** during the reaction. Whether the reaction undergoes a DKR or DECT mechanism is depending on the reaction rates of the transformation shown in **Fig. 3.16**.

3.13 Proposed Reaction Mechanism

Based on the previous investigations, we proposed a dynamic kinetic resolution mechanism as illustrated in **Fig. 3.17**.

Figure 3.17 The proposed DKR reaction mechanism of copper/guanidinium catalyzed asymmetric allylic borylation.

As illustrated, initially, Cu(II) salt was reduced to Cu(I) hydroxide complex **II** with the help of B_2Pin_2 , base and neutralized guanidine. As transmetalation occurred, copper-boryl complex **III** was generated, with HOBPIn as by-product. Then the complex **III** reacted with (*R*)-**1-4a** much faster than its enantiomer (*S*)-**1-4a** in a manner of *anti*- $\text{S}_{\text{N}}2'$ substitution, giving the desired product (*R*)-**4a** and the complex **I**. (*S*)-**1-4a** was mostly converted into

(*R*)-**1-4a** via the fast racemization. After anionic ligand exchange, complex **I** regenerated active specie **II** once again with catalytic cycle continuing.

Figure 3.18 The proposed DECT reaction mechanism of copper/guanidinium catalyzed asymmetric allylic borylation.

Although it is less likely due to the rapid racemization of allylic bromides, the direct enantio-convergent transformation is still not fully excluded. Similar to the DKR process, the complex **III** was believed to be generated in the reaction mixture. However, if the borylation process was fast enough, both allylic bromide enantiomers would react with **III** together. While (*R*)-**1-4a** underwent borylation in an *anti*-S_N2' pathway, (*S*)-**1-4a** chose the *syn*-S_N2' version due to the steric effect of the guanidine ligand. Both two pathways gave rise to the formation of (*R*)-**4a**.

3.14 Scaled-up Reaction and Product Applications

To further explore the practicability of this catalytic system, a 10 mmol scaled-up reaction was conducted with the model substrate **1-4a**. To our pleasure, the corresponding allylic boronate **4a** was produced in grams with 80% isolated yield, without any erosion of enantioselectivity (**Fig. 3.13**).

Figure 3.19 The scaled-up experiments of model copper/guanidinium catalyzed asymmetric allylic borylation reaction.^[a]

[a]. Standard reaction condition: 10 mmol scale reaction, 15 mmol B_2Pin_2 , 1 mol% $\text{Cu(NO}_3)_2\cdot 3\text{H}_2\text{O}$, 1.5 mol% **Gua 22**, 2 mL saturated K_2CO_3 aqueous solution (about 12 equiv.), 10 mL *n*Hexane, air atmosphere, stirred at 0 °C for 24 h. Isolated yield. The ee was determined by chiral GC column.

The chiral boronates obtained could also be stereospecifically converted to a variety of useful compounds which new functionalities can be introduced to the chiral allylic motif (**Fig 3.14**). With enantioenriched boronate **4a** as building block, homoallylation of aldehyde was successfully achieved with high yield and high stereoselectivity to give **16a**. After oxidized to the corresponding alcohol **16b**, it could be further transformed to chiral allylic ester **16c**. Meanwhile, in the presence of a strong base or a nucleophilic activator, **4a** was able to undergo allylic heteroarylation, homologation and amination in certain conditions almost without any loss of ee to give the corresponding pyridine **16d**, boronate **16e** and Boc-protected amine **16f**. Finally, we also investigated the efficiency of asymmetric Suzuki-type coupling with chiral boronates obtained. In the presence of $\text{Pd}_2(\text{dba})_3$ and XPhos, **4a** reacted with arylbromide to furnish the corresponding coupling product **16g** quantitatively with 73% ee. The erosion in enantiomeric purity might be attributed to the formation of allylpalladium intermediate after transmetallation.

Figure 3.20 Diverse allylic functionalization via stereospecific conversion of the enantiopure allylic boronate.

3.15 Conclusion

In conclusion, we have employed a series of methods, including kinetic studies, NMR, EPR, crystallography, radical trapping and clock experiments, to probe the real mechanism of this borylation reaction. The presence of air and water was found to be crucial for the allylic borylation reaction if excellent results were wanted. Copper-guanidine complex **12** was likely to be the true catalytic precursor for the reaction, while two structure of it was determined as only complex form was proven effective. As for the substrate resolution process, three possible pathways were proposed. After the evaluation using radical scavengers and radical clock experiments, it was concluded that a dynamic kinetic resolution process was occurred during the borylation. The copper/guanidinium catalytic allylic borylation reaction was also shown to be useful for the gram-scale synthesis. Finally, the obtained boronate was utilized in a series of

stereospecific functional group transformation, with good yield and excellent enantioselectivity.

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Chapter 4

Experimental

4.1 General Methods

A. Commercially available reagents and solvents

Commercially available chemicals were obtained from Acros, Alfa Aesar, Merck, Sigma-Aldrich, and used without further purified once delivered unless otherwise noted. Solvents are directly used as A.R. grade, or simply distilled once for P.G. grade. If an oxygen- and moisture-free system is required, they are distilled in the presence of NaH or Na under N₂ atmosphere, or taken from MBraun (MB SPS-800) solvent drying equipment. Or the solvents are bought from the supplier as anhydrous and oxygen-free ones, stored in the glovebox under Ar atmosphere once arrived.

B. Instrumentals and materials

For reactions employing oxygen- or moisture-sensitive reagents, glassware was dried at 110 °C in the oven overnight, or dried under high vacuum using oil pump. The reactions are carried out with Schlenk equipments, or in the normal 4mL vial but under an argon atmosphere in the glovebox. Reagents are injected with microsyringe or peppitte via a rubber septum or added into the Schlenk reaction tube under argon counter-flow. For light-sensitive reagents, they are used and stored in the container covered with aluminum foil in the dark.

Thin layer chromatography (TLC) was performed on silica TLC plates bought from Merck (silica gel 60, F₂₅₄). Detection was carried out by fluorescence under UV light (wavelength, λ = 254 nm) or KMnO₄ dip. The corresponding R_f values and eluting solvents used are listed in the experimental section. Flash column chromatography was performed with silica gel (grain

size 0.04-0.063 cm, *Merck, Si60*) under the pressure of approximately 1.5 atm (hand air pump). The eluting ratio are listed with experiments respectively.

Nuclear magnetic resonance (NMR) spectra were acquired on Bruker AV300, AV400, BBFO 400 and AV500 MHz for ^1H NMR spectrometer. Chemical shifts (δ) are reported in parts per million (ppm) related to residual solvent signals (CHCl_3 , 7.26 ppm, CH_2Cl_2 , 5.32 ppm, C_6H_6 , 7.16 ppm for ^1H NMR; CDCl_3 , 77.0 ppm, C_6H_6 , 128.1 ppm for ^{13}C NMR; 85% $\text{BF}_3 \cdot \text{Et}_2\text{O}$, 0.0 ppm for ^{11}B NMR). Deuterated solvents were used (CDCl_3 , C_6D_6 and CD_2Cl_2). The following abbreviations were used to indicate the assignment of the signals and their multiplicities in NMR spectra: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; bs, broad signal; app, apparent. The given coupling constants J are listed as an average. ^{13}C NMR were acquired on a broad band decoupled mode.

Gas chromatography yield (GC yield) was calculated in the total ion chromatogram (TIC) mode on the Shimadzu QP2010SE Standard Gas Chromatograph-Mass Spectrometer equipped with achiral Restek Rxi-5ms fused silica capillary column, followed by the calibration with biphenyl as internal standard.

Low resolution mass spectra (LRMS) were obtained on the ThermoFinnigan PolarisQ MS (ESI^+) and ThermoFinnigan LCQ Fleet MS (ESI^+). High resolution mass spectra (HRMS) were obtained on the Q-ToF Premier mass spectrometer (Waters Corporation). LRMS and HRMS were reported in units of mass of charge ratio (m/z).

X-ray crystallography analysis was performed on Bruker X8 APEX X-ray diffractometer.

Optical rotations were measured as a DCM solution through a 10mm quartz cell on a JASCO P-1030 polarimeter.

EPR spectra were obtained on Bruker ELEXSYS E 500 Electronic Paramagnetic Resonance spectrometer at room temperature with Wilmad[®] quartz (CFQ) EPR tubes (O.D., 4 mm; length, 250 mm).

The enantiometric excess (ee) of the products were determined by chiral stationary phase HPLC (Daicel Chiralpak AD-H and Daicel Chiralcel OD-H/OB-H columns) or by GCMS using chiral fused silica capillary columns (Restek Rt- β DEXse, Astec CHIRALDEX G-TA/B-DM/B-DA, length, 30 m; I.D., 0.25 mm; film, 0.25 μ m).

4.2 The Synthesis of Chiral Guanidinium Salts

4.2.1 The Synthesis of Chiral Bisguanidinium Salt Gua 1

The synthesis of bisguanidinium **Gua 1** was chosen as the standard for all other bisguanidinium salts as listed below in **Fig. 4.1**. All other bisguanidinium salts could be prepared with varied side arms and linkers.

The synthesis of 4-2:

To the suspension of 3.3 g (5 mol%) AlCl_3 in 53 mL (0.5 mol) toluene, 120 mL (1.1 mol) *t*BuCl was charged slowly at 0 °C. Then the yellow suspension was allowed to warm up and keep stirred overnight. After that, the suspension was carefully quenched with 100 mL H_2O . The organic phase was collected, washed with 30 mL H_2O and 50 mL saturated brine. After

dried over Na₂SO₄ anhydrous and filtered, the filtrate was concentrated *in vacuo* to afford a yellow liquid. The crude product was further purified via silica column chromatography to give 12.2g colorless liquid. The product was **4-2** as majority with trace isomeric impurity, which was directly used in the next step without further purification. Yield: 60%.

Figure 4.1 The synthetic route of bisguanidinium salt **Gua 1**.

The synthesis of 4-3:

To a dry 250 mL RBF, 6.1 g (30 mmol) **4-2** was charged together with 5.9 g (33 mmol) NBS and 36 mg (0.5 mol%) BPO, followed by the addition of 80 mL cyclohexane. The resulting mixture was heated to reflux at 80 °C overnight. After that, the suspension was filtered while the filter cake was washed with hexane. The combined filtrate was concentrated under vacuum to give a pale-orange oil. The crude product was further purified via silica column chromatography to give 4.1g colorless liquid as **4-3**. Yield: 49%.

The synthesis of 4-4:

To a suspension of 1.5 g (7.1 mmol) (*S,S*)-DPEN in 25 mL MeCN along with 2.2 g (2.2 equiv.) K₂CO₃, 4.1 g (14.5 mmol) **4-3** dissolved in 25 mL MeCN was added dropwise in 2 h. Then the suspension was stirred at room temperature overnight until the reaction was completed. After that the reaction was quenched with 20 mL brine. The aqueous phase was extracted with 50 mL DCM trice. Then the combined organic phase was dried over Na₂SO₄

anhydrous, filtered and concentrated to give a pale-yellow oil. The crude product was further purified via silica column chromatography to give 1.3 g pale-yellow foam-like solid as **4-4** after dried under vacuum. Yield: 28%.

The synthesis of 4-5:

To a 25 mL RBF, 0.62 g (1 mmol) **4-4** was charged together with 0.35 g (2.5 equiv.) K_2CO_3 , followed by the addition of 5 mL DCM and 5 mL H_2O . The yellow emulsion was vigorously stirred at 0 °C and charged with 92 μ L (1.2 mmol) $CSCl_2$ dropwise. After finished, the mixture was allowed to warm up and kept stirred at room temperature overnight. After that, the resulting mixture was separated, and aqueous phase was extracted with 5 mL DCM thrice. Then the combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated to give a pale-yellow foam. The crude product was further purified via silica column chromatography to give 0.49 g white foam-like solid as **4-5** after dried under vacuum. Yield: 74%.

The synthesis of 4-6:

To an oven-dried 25 mL Schlenk tube, 0.33 g (0.5 mmol) **4-5** was charged. After the tube purged with N_2 , 2 mL freshly distilled toluene was added, followed by the addition of 860 μ L (20 equiv.) $(COCl)_2$. Then the mixture was heated to reflux under N_2 flow overnight. After that, the resulting mixture was cooled to room temperature, dried *in vacuo* to give a white foam as **4-6**. Due to its sensitivity towards moisture, the product was directly used in the next step without further treatment.

The synthesis of 4-7:

Under N_2 protection, 17 mg (0.2 mmol, 0.4 equiv.) piperazine was charged to the tube with **4-6** inside in one portion, followed by the addition of 2 mL dry MeCN and 210 μ L (3.0 equiv.) TEA. Then the mixture was heated to reflux under N_2 flow overnight. After that, the resulting

mixture was concentrated under vacuum to give a brown foam, which was further purified via silica column chromatography to give 219 mg pale-brown powder as **4-7**. Yield: 78%.

4.2.2 The Synthesis of Chiral Pentanidium Salt Gua 13

The synthesis of pentanidium **Gua 13** was chosen as the standard for all other pentanidium salts as listed below in **Fig. 4.2**. All other pentanidium salts could be prepared with varied side arms and linkers.

Figure 4.2 The synthetic route of pentanidium salt **Gua 13**.

The synthesis of 4-10:

To a mixture of 1.1 g (5 mmol) (*S,S*)-DPEN and 1.7 mL (2.5 equiv.) TEA in 10 mL DCM, 1.3 mL (11 mmol) PhCOCl dissolved in 10 mL DCM was added dropwise at $0\text{ }^{\circ}\text{C}$ in 5 min. The mixture was stirred vigorously for 2 h to become a white suspension. After that, the resulting suspension was filtered, and the precipitates was washed with 20 mL DCM trice and 10 mL acetone. Due to its low solubility, the remained 1.9 g white solid was directly used in the next step without further purification as **4-10** after dried under vacuum. Yield: 90%.

The synthesis of 4-11:

To a dry 25 mL Schlenk tube, 2.0 g (4.8 mmol) **4-10** was charged, followed by the addition of 100 mL THF. Then 12 mL (12 mmol) $\text{BH}_3 \cdot \text{Me}_2\text{S}$ was added dropwise at 0 °C. After the addition finished, the resulting mixture was heated to reflux for 3 h, before cooled down to room temperature and stirred overnight. After that, it was quenched with 50 mL MeOH at 0 °C for 15 min, until the gas was fully released. Then the residual was acidified with 30 mL 1 M HCl and refluxed for 1 h to give a colorless transparent solution. After that, the solution was basified with 1 M NaOH solution to pH =14. Then it was extracted with 50 mL DCM trice. The combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated to give a white powder. The crude product was further purified via silica column chromatography to give 1.3 g colorless grease as **4-11** after dried under vacuum. Yield: 75%.

The synthesis of 4-12:

To a 25 mL RBF, 0.51 g (1.3 mmol) **4-11** was charged together with 0.45 g (2.5 equiv.) K_2CO_3 , followed by the addition of 5 mL DCM and 5 mL H_2O . The yellow emulsion was vigorously stirred at 0 °C and charged with 120 μL (1.6 mmol) CSCl_2 dropwise. After finished, the mixture was allowed to warm up and kept stirred at room temperature overnight. After that, the resulting mixture was separated, and aqueous phase was extracted with 5 mL DCM trice. Then the combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated to give a yellow oil. The crude product was further purified via silica column chromatography to give 0.60 g white needle crystalline solid as **4-12**. Yield: 86%.

The synthesis of 4-13:

To an oven-dried 25 mL Schlenk tube, 0.44 g (1 mmol) **4-12** was charged. After the tube purged with N_2 , 10 mL freshly distilled toluene was added, followed by the addition of 1.7 mL (20 equiv.) $(\text{COCl})_2$. Then the mixture was heated to reflux under N_2 flow overnight.

After that, the resulting mixture was cooled to room temperature, dried *in vacuo* to give a white foam as **4-13**. Due to its sensitivity towards moisture, the product was directly used in the next step without further treatment.

The synthesis of 4-14:

To an oven-dried 25 mL Schlenk tube, 0.47 g (1.2 mmol) **4-11** was charged. After the tube purged with N₂, 3 mL freshly distilled MeCN was added. Then 128 mg (1.2 mmol) BrCN in 3 mL MeCN was added in one portion. Then the mixture was heated to reflux under N₂ flow for 24h. After that, the resulting mixture was cooled to room temperature, concentrated *in vacuo* to give a yellow foam. The crude product was further purified via silica column chromatography to give 0.67 g pale-yellow foam-like solid as **4-14**. Yield: 99%.

The synthesis of 4-15:

Under N₂ protection, 455 mg (0.91 mmol, 0.9 equiv.) **4-14** was charged to the tube with **4-13** inside in one portion, followed by the addition of 5 mL dry MeCN and 420 μ L (3.0 equiv.) TEA. Then the mixture was heated to reflux under N₂ flow overnight. After that, the resulting mixture was concentrated and treated with a 1:1 mixture of DCM and Et₂O. After filtration, the filtrate was concentrated under vacuum to give a pale-brown foam. The crude product was further purified via silica column chromatography to give 0.35 g off-white solid as **4-15**. Yield: 41%.

4.2.3 The Synthesis of Chiral Bicyclic Guanidinium Salt Gua 22

The synthesis of bicyclic guanidinium **Gua 22** was chosen as the standard for all other bicyclic guanidinium salts as listed below in **Fig. 4.3**. All other bisguanidinium salts could be prepared with varied commercially available amino acids.

Figure 4.3 The synthetic route of bicyclic guanidinium salt **Gua 22**.

The synthesis of **4-17**:

To a dry 250 mL three-necked RBF, 10 g (76 mmol) *L*-Leucine was added. After purged with N₂, 100 mL THF was added. The suspension was cooled to 0 °C and 7.0 g (185 mmol) NaBH₄ was charged under the protection of N₂ in portions. Then 19 g (75 mmol) I₂ in 50 mL THF was added dropwise in 30 min at 0 °C, before the mixture was heated to 80 °C for 18 h. After cooled to room temperature, the white suspension was carefully quenched with 50 mL MeOH to give a clear solution. Then it was concentrated to give a slurry followed by treatment of 75 mL 20w% KOH solution for additional 5 h. After extracted with 60 mL DCM for six times, the crude product was obtained as a 7.6 g colorless liquid in full conversion after being dried over Na₂SO₄ anhydrous, filtered and concentrated. The product **4-17** was directly used in the next step without further purification. Yield: > 99%.

The synthesis of **4-18**:

To a 100 mL RBF, 3.6 g (35 mmol) **4-17** was charged followed by the addition of 25 mL pyridine. Then 14.7 g (77 mmol) TsCl was carefully added portionwise at 0 °C. The resulting dark red solution was stirred at room temperature overnight to give a dark brown suspension,

which was later concentrated *in vacuo* to give an orange oil. Upon dissolved in 100 mL benzene, it was further treated with 30 mL 20w% KOH solution at room temperature for 2 h. Then water was added to separate the organic phase. The aqueous phase was extracted with 50 mL EA three times. The combined organic phase was dried over Na₂SO₄ anhydrous, filtered and concentrated to give a red oil. The crude product was further purified via silica column chromatography to give 3.9 g white crystalline solid as **4-18**. Yield: 41%.

The synthesis of 4-19:

To a 250 mL RBF, 2.4 g (10 mmol) **4-18** was charged followed by the addition of 100 mL MeOH. Then the solution was bubbled with NH₃ at 0 °C until saturated. The resulting yellow solution was stirred at room temperature for three days until **4-18** inside was fully converted which was determined by LRMS. Then the solution was carefully concentrated to give a yellow liq. The product **4-17** was directly used in the next step without further purification. Yield: >99%.

The synthesis of 4-20:

2.4 g (10 mmol) **4-18** was charged into a 50 mL seal tube together with **4-19**, followed by the addition of 30 mL MeCN. Then the suspension was heated to 100 °C for three days until **4-18** inside was fully converted which was determined by LRMS. Then the solution was concentrated to give a yellow solid. The crude product was further purified via silica column chromatography to give 2.2 g white powder as **4-20**. Yield: 44%.

The synthesis of 4-21:

To a dry 250 mL three-necked RBF, 2.0 g (4 mmol) **4-20** was added. After purged with N₂, 10 mL THF was added to give a suspension. Then it was cooled to -78 °C and 200 mL liquid NH₃ was charged to give a colorless solution. At -78 °C, 9.2 g (400 mmol) Na in small blocks was added portionwise till the mixture turned dark blue. Then it was kept vigorously stirred for at least 18 h. Upon fully converted, the blue suspension was allowed to warm up. 100 mL

DCM was carefully added before it was quenched with 50 g NH_4Cl to give white slurry. After filtration, the resulting yellow solution was concentrated to give a 0.5 g yellow liq as **4-21**. The crude product was directly used in the next step without further purification. Yield: 67%.

The synthesis of **4-22**:

To a 25 mL RBF, 0.5 g (2.7 mmol) **4-21** was charged followed by the addition of 15 mL MeNO_2 . Then 370 μL (3.3 mmol) $\text{C}_3\text{H}_6\text{S}_3$ was added in one portion before the mixture was refluxed for 4 h. The resulting orange-brown solution was charged with 0.6 mL pure HOAc and 2.5 mL MeI in the absence of light and air. Later the mixture was heated to reflux overnight with fine cooling system. After that the residual was concentrated *in vacuo* to give a brown solid. The crude product was further carefully purified via silica column chromatography to give 0.66 g white solid as **4-22**. Yield: 47%.

4.3 The Synthesis of Allylic Substrates

4.3.1 General Method I: The Synthesis of Allylic Halides via Direct Bromination with NBS.

Figure 4.4 The Synthesis of allylic bromide via direct bromination with NBS.

The synthesis of **4-24**:

To a 50 mL RBF, 10 mmol **4-23** was charged together with 10.5 mmol NBS and 5 mol% AIBN. After 20 mL CCl₄ was added, the mixture was heated to reflux for 2 h. Then the solution was concentrated. Pure product **4-24** was obtained via vacuum distillation.

The allylic bromide synthesized via the general method I was summarized in **Fig. 4.5**.

Figure 4.5 The scope of allylic bromide via direct bromination with NBS.

4.3.2 General Method II: The Synthesis of Allylic Halides via Bromination of Alcohols.

Figure 4.6 The Synthesis of allylic bromide via bromination of alcohol.

The synthesis of **4-27**:

In a 250 mL RBF, 10 mmol **4-25** was added dropwise into a suspension of 20 mmol (2.0 equiv.) Grignard reagent and 3.5 g (2 equiv.) LiBr in 100 mL THF at $0\text{ }^{\circ}\text{C}$. Then the suspension was stirred for 30 min before it was allowed to warm up and stir for additional 2 h. After that, the reaction was quenched with saturated NH_4Cl solution and the aqueous phase was extracted

with 20 mL Et₂O trice. The combined organic phase was dried with Na₂SO₄ anhydrous, filtered and concentrated to give a colorless liquid. The crude product was further purified via silica column chromatography to give the corresponding allylic alcohol **4-26**.

In a 4 mL vial, 1.5 mL hydrobromic acid was charged. Upon stirring, at 0 °C 0.4 mL **4-26** was added dropwise. After 5 min, the mixture was extracted with 1.5 mL DCM trice. The combined DCM solution was passed through a short Celite column and dried with Na₂SO₄ anhydrous. After filtration, the filtrate was concentrated to give a yellow liquid. Then 1 mL *n*Hexane was added, and the resulted solution was rapidly passed through a short silica column to remove the unreacted alcohol. Allylic bromide **4-27** was obtained as colorless liquid after concentration and was directly used without further purification.

The allylic alcohols synthesized via the general method **II** was summarized in **Fig. 4.7**.

Figure 4.7 The scope of allylic alcohols via 1,2-addition of ketone **4-25** with the corresponding lithium/Grignard reagents.

The allylic bromides synthesized via the general method **II** was summarized in **Fig. 4.8**.

Figure 4.8 The scope of allylic bromides via bromination of alcohols.

4.3.3 The Synthesis of Other Specific Allylic Bromides.

Other allylic bromides were synthesized according to the previous reports.

4.4 Experimental Procedures for Asymmetric Allylic Borylation Reactions

Typical procedure of asymmetric allylic borylation with allylic bromide 1-4a and B₂Pin₂ as substrates:

To a 4 mL vial, 38 mg (0.15 mmol) B₂Pin₂ and 0.5 mg (1.5 mol%) **Gua 22** were charged, followed by the addition of 1 mL *n*Hexane. The solution was stirred at 0 °C for 5 min before 0.2 mL saturated K₂CO₃ aqueous solution and 5 μL (0.2 M, 1 mol%) Cu(NO₃)₂·3H₂O solution were added to give a pale-blue suspension at 0 °C. After stirred for another 5 min, 12 μL (0.1 mmol) allylic bromide **1-4a** was added. Then the mixture was allowed to be stirred vigorously for 24 h at 0 °C. The progress was monitored by TLC and GC-MS. When the reaction was finished, the reaction was quenched with 1 mL H₂O and the aqueous phase was extracted with 2 mL Et₂O trice. The combined organic phase was passed through a short Celite

column and dried with Na₂SO₄ anhydrous. After filtration, the filtrate was concentrated to give a colorless liquid. The crude product was further purified via silica column chromatography as fast as possible to afford 17.8 mg the desired allylic boronate **4a** in a yield of 86% with 97% ee.

4.5 Instrumental Setting for EPR Experiments

4.5.1 General Information

The EPR spectra were recorded on Bruke ELEXSYS E 500 Electronic Paramagnetic Resonance spectrometer at room temperature. The samples were charged into Wilmad[®] quartz (CFQ) EPR tubes (O.D., 4 mm; length, 250 mm) under air, mixed with shaking and then run through EPR spectrometer with indicated parameters.

4.5.2 The Procedure for EPR Experiments

To an oven-dried Wilmad[®] quartz (CFQ) EPR tube was added CuCl₂ (0.1 mmol) and CHCl₃ (0.5 mL). Minimum amount of water was added to make CuCl₂ dissolved. Then the sample was analyzed by EPR at room temperature which gave the result as the **Black Line** in **Fig. 3.5**. The EPR spectra were recorded at 298 K on EPR spectrometer operated at 9.4158 GHz. Typical spectrometer parameters are shown as follows: scan range: 8000.0 G; center field set: 4000.0 G; time constant: 163.84 ms; scan time: 30.72 s; modulation amplitude: 1.0 G; modulation frequency: 100 kHz; receiver gain: 30; microwave power: 0.6325 mW.

To an oven-dried Wilmad[®] quartz (CFQ) EPR tube was added CuCl₂ (0.1 mmol) and CHCl₃ (0.5 mL). Later, **Gua 22'** (0.1 mmol) was added to make CuCl₂ dissolved and give a transparent yellow solution. Then the sample was analyzed by EPR at room temperature

which gave the result as the **Red Line** in **Fig. 3.5**. The EPR spectra were recorded at 298 K on EPR spectrometer operated at 9.4158 GHz. Typical spectrometer parameters are shown as follows: scan range: 8000.0 G; center field set: 4000.0 G; time constant: 163.84 ms; scan time: 30.72 s; modulation amplitude: 1.0 G; modulation frequency: 100 kHz; receiver gain: 30; microwave power: 0.6325 mW.

To the remaining mixture, B₂Pin₂ (0.2 mmol) was added. After shaken to make B₂Pin₂ fully dissolved, the solution turned into pale-yellow. Then the sample was analyzed by EPR at room temperature which gave the result as the **Blue Line** in **Fig. 3.5**. The EPR spectra were recorded at 298 K on EPR spectrometer operated at 9.4158 GHz. Typical spectrometer parameters are shown as follows: scan range: 8000.0 G; center field set: 4000.0 G; time constant: 163.84 ms; scan time: 30.72 s; modulation amplitude: 1.0 G; modulation frequency: 100 kHz; receiver gain: 30; microwave power: 0.6325 mW.

After stood for 1 week to give an almost colorless solution, the sample was analyzed by EPR at room temperature which gave the result as the **Pink Line** in **Fig. 3.5**. The EPR spectra were recorded at 298 K on EPR spectrometer operated at 9.4158 GHz. Typical spectrometer parameters are shown as follows: scan range: 8000.0 G; center field set: 4000.0 G; time constant: 163.84 ms; scan time: 30.72 s; modulation amplitude: 1.0 G; modulation frequency: 100 kHz; receiver gain: 30; microwave power: 0.6325 mW.

4.6 Experimental Procedures for Scaled-up Reactions and Applications

4.6.1 Procedure of Scale-up Asymmetric Allylic Borylation with Allylic Bromide 1-4a and B₂Pin₂ as Substrates

To a 50 mL RBF, 380 mg (1.5 mmol) B_2Pin_2 , 2.4 mg $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ and 5 mg (1.5 mol%) **Gua 22** were charged, followed by the addition of 10 mL *n*Hexane. The solution was stirred at 0 °C for 10 min before 2 mL saturated K_2CO_3 aqueous solution was added to give a pale-blue suspension at 0 °C. After stirred for another 10 min, 115 μL (1 mmol) allylic bromide **1-4a** was added. Then the mixture was allowed to be stirred vigorously for 24 h at 0 °C. The progress was monitored by TLC and GC-MS. When the reaction was finished, the reaction was quenched with 10 mL H_2O and the aqueous phase was extracted with 20 mL Et_2O trice. The combined organic phase was dried with Na_2SO_4 anhydrous. After filtration, the filtrate was concentrated to give a colorless liquid. The crude product was further purified via silica column chromatography as fast as possible to afford 165 mg the desired allylic boronate **4a** in a yield of 80% with 97% ee.

4.6.2 The Experimental Procedure of Further Functionalization of Allylic Boronate **4a** (97% ee)

The synthesis of **17a**:

To a dry Schlenk tube purged with N_2 , 1 mL DCM was charged at -78 °C, followed by the addition of 42 μL (0.2 mmol) **4a**, 22 μL (1.05 equiv.) PhCHO and 28 μL (1.1 equiv.) $\text{BF}_3 \cdot \text{Et}_2\text{O}$ in sequence. Then the reaction was stirred at -78 °C under N_2 for 18 h. After that, 1 mL saturated aqueous NaHCO_3 solution was added and the reaction was allowed to warm to room temperature. The mixture was extracted with 5 mL ether trice. The combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17a** as a colorless liquid. (34.1 mg, 91% yield, 89% ee, d.r. > 20 :1)

Figure 4.9 Diverse allylic functionalization via stereospecific conversion of enantiopure allylic boronate.

The synthesis of **17b**:

To a 25 mL RBF, 308 mg $\text{NaBO}_3 \cdot 4\text{H}_2\text{O}$ (10 equiv.) was charged, followed by the addition of 2.4 mL THF and 1.6 mL H_2O to give a white suspension. Then 42 μL (0.2 mmol) **4a** was introduced and the reaction was allowed to stir vigorously at room temperature for 1.5 h. The mixture was extracted with 5 mL ether trice. The combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17b** as a colorless liquid after concentration under vacuum with care. (17.4 mg, 89% yield, 97% ee)

The synthesis of **17c**:

To a dry 25 mL RBF, 98 mg **17b** (1 mmol) was charged, followed by the addition of 2 mL freshly distilled DCM. Then 372 mg 2-iodobenzoic acid (1.5 equiv.) was introduced in one portion. To the mixture, 350 mg DCC (1.7 equiv.) and 183 mg DMAP (1.5 equiv.) was charged portionwise successfully. Then the reaction mixture was allowed to stir vigorously at

room temperature overnight. After the reaction was finished, the mixture was diluted with ether to give a white suspension. The suspension was filtered through a cotton pad and the resulting solution was washed with brine, dried over Na₂SO₄ anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17c** as a pale-yellow liquid after concentration under vacuum with care. (276 mg, 84% yield, 96% ee)

The synthesis of 17d:

To a dry Schlenk tube in the glovebox, 2.5 mL THF was charged and sealed with a rubber septum before the setup was taken outside. After 62 μ L (2.2 equiv.) iPr₂NH was introduced, the reaction setup was cooled to -78 °C, followed by the addition of 0.22 mL (2.2 equiv., 2.0 M in CyH) *n*BuLi solution in one portion. The mixture was allowed to warm to room temperature and stirred for 15 min, before it was cooled to -78 °C again. After that, 35 μ L (2.0 equiv.) 3-fluoropyridine was charged in one portion and the reaction was stirred at -78 °C for additional 30 min. Then 42 μ L (0.2 mmol) **4a** was added, followed by keeping it reacted for 2 h. After that, 61 μ L TrocCl was introduced to the mixture, and the reaction mixture was allowed to warm to room temperature and stir vigorously overnight. After the reaction was finished, it was quenched by water and extracted with 5 mL EA six times. The combined organic phase was dried over Na₂SO₄ anhydrous, filtered and concentrated *in vacuo*. The crude product was dissolved in 2 mL THF. At 0 °C, a premixed solution of NaOH (2 M aq.) and 30 w% H₂O₂ (aq.) was added dropwise. The resulting solution was warmed to room temperature and stirred for additional 3 hours before it was quenched by 10 mL water. Then the reaction mixture was extracted with 5 mL EA six times. The combined organic phase was dried over Na₂SO₄ anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17d** as a white solid. (20.9 mg, 59% yield, 97% ee)

The synthesis of 17e:

To a dry Schlenk tube in the glovebox, 2 mL THF was charged, followed by the addition of 42 μ L (0.2 mmol) **4a** and 27 μ L CH₂BrCl (2.0 equiv). Then the tube was sealed with a rubber septum before it was taken outside. At -78 °C, a solution of *n*BuLi (150 μ L, 2.0 M in hexanes, 1.5 equiv) was added dropwise. The resulting mixture was allowed to stir for 10 min, warmed to rt and stirred for additional 4 h. After the reaction was finished, it was carefully quenched with water and extracted with DCM (5 mL) twice. The organic layers were combined, dried over Na₂SO₄, and concentrated. The residual was further purified via silica column chromatography to give **17e** as a colorless oil. (40.0 mg, 90% yield, 98% ee)

The synthesis of 17f:

To a 25 mL dry Schlenk tube in the glovebox, 58.5 mg (3.0 equiv) MeONHMe·HCl was charged, followed by the addition of 1 mL THF to give a suspension. The tube was then sealed with a rubber septum before it was taken outside. The mixture was cooled to -78 °C, followed by the addition of 0.65 mL (6.5 equiv., 2.0 M in CyH) *n*BuLi solution. The mixture was stirred at -78 °C for 30 min, before 42 μ L (0.2 mmol) **4a** was introduced. Then the reaction was allowed to warm to room temperature and heated at 60 °C for 12 h. After that, it was cooled to room temperature, and 150 μ L (3.3 equiv) Boc₂O was added before the reaction was stirred overnight. After the reaction was finished, it was quenched by 5 mL water and extracted with 5 mL EA three times. The combined organic phase was dried over Na₂SO₄ anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17f** as a colorless oil. (28.2 mg, 67% yield, 98% ee)

The synthesis of 17g:

To a 25 mL dry Schlenk tube in the glovebox, 9.5 mg (5 mol%) Pd₂(dba)₃, 11.4 mg (12 mol%) XPhos and 97 mg (5.0 equiv.) NaOtBu were charged, followed by the addition of 1 mL toluene. After 140 μ L (5.0 equiv.) 1-bromo-4-(trifluoromethyl)benzene was added, the

mixture was stirred for 5 min until a yellow solution was formed. Then 42 μL (0.2 mmol) **4a** was introduced. The tube was sealed and taken outside, and the reaction was stirred at room temperature for 48 h. After that, was quenched by 5 mL water and extracted with 5 mL EA three times. The combined organic phase was dried over Na_2SO_4 anhydrous, filtered and concentrated. The residual was further purified via silica column chromatography to give **17g** as a colorless oil. (38.2 mg, 85% yield, 77% ee)

4.7 The Identification of the Absolute Configuration

The absolute configuration of **4a** was determined by oxidizing it to **17b**. By comparing its optical rotation power with the literature reports, the absolute configuration of **17b** should be *R*.

17b

Measured optical rotation power: $[\alpha]^{23}_{\text{D}} (589 \text{ nm}) = +90.2$ ($c=1.0$ in CH_2Cl_2 , 97% ee)

Reported optical rotation power in the literature: $[\alpha]^{20}_{\text{D}} (589 \text{ nm}) = +110.8$ ($c=1.2$ in CH_2Cl_2)

The absolute configuration of other allylboronates were postulated from the case of **4a**. The absolute configuration of the functionalization products was postulated according to the previous reports.

4.8 Analytical Data

4.8.1 Analytical data of allylic borylation products

(*R*)-2-(cyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4a**

The ^1H NMR spectrum of the crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 91%. Purification by FC (*n*hexane/ethyl acetate=100:0~2, column size 5 x 0.5 cm) within 5 min yielded a total of 17.9 mg (0.086 mmol, 86%) of product as a colorless/pale yellow liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.68 (m, 2H), 1.98 (m, 2H), 1.84 – 1.71 (m, 2H), 1.69 – 1.62 (m, 2H), 1.58 (m, 1H), 1.24 (s, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 127.6, 126.0, 83.1, 25.0, 24.8, 24.7, 24.1, 22.5;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.4;

IR (thin film) ν_{max} (cm^{-1}): 3019, 2976, 2857, 2835, 1643, 1449, 1360, 1314, 1280, 1250, 1163, 1146, 1109, 968, 860, 656;

HRMS (ESI+) calcd for $\text{C}_{12}\text{H}_{22}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 209.1713; found: 209.1699;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +94.0 ($c=1.0$ in CH_2Cl_2 , 97% ee)

GC analysis of **4a** indicated an enantiomeric excess of 97% (Restek Rt- β DEXse, 50 °C for 1 min, 50–115 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_{R} = 61.3min; minor enantiomer t_{R} = 60.6 min.

(*R*)-2-(cyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4a'**

The ^1H NMR spectrum of the crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 62%.

GC analysis of **4a'** indicated an enantiomeric excess of 86% (Restek Rt- β DEXse, 50 °C for 1 min, 50–115 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 60.8min; minor enantiomer t_R = 60.3 min.

(*R*)-2-(cyclopent-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4b**

The GCMS detection of the crude reaction mixture without further calibration indicated a GC yield of 90%. Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a small amount of product as a pale yellow liquid which was used directly for characterization.

^1H NMR (CDCl₃, 400 MHz) δ_{H} (ppm): 5.71 (m, 2H), 2.34 (m, 2H), 2.15 (m, 1H), 2.02 (m, 1H), 1.86 (m, 1H), 1.24 (s, 12H);

^{13}C NMR (CDCl₃, 100 MHz) δ_{C} (ppm): 135.4, 129.7, 83.1, 32.9, 25.5, 24.7 (Due to quadrupolar relaxation, the carbon attached to the boron atom was not detected.);

^{11}B NMR (CDCl₃, 128 MHz) δ_{B} (ppm): 33.6;

HRMS (ESI+) calcd for C₁₁H₂₀O₂B⁺ [M + H⁺]: 195.1556; found: 195.1563;

(*R*)-2-(cyclohept-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4c**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 98%. Purification by FC (*n*hexane/ethyl acetate=100:0~2, column size 5 x 0.5 cm) within 5 min yielded a total of 17.8 mg (0.080mmol, 80%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.83 (qd, $J_1 = 11.2$ Hz, $J_2 = 5.8$ Hz, 2H), 2.13 (m, 2H), 1.99 (m, 1H), 1.80 (m, 1H), 1.74 (m, 1H), 1.68 (m, 2H), 1.59 – 1.45 (m, 2H), 1.27 (s, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 133.1, 131.6, 83.2, 31.3, 28.9, 28.8, 27.4, 24.8, 24.7;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.8;

IR (thin film) ν_{max} (cm^{-1}): 3013, 2976, 2918, 2851, 1651, 1445, 1369, 1344, 1317, 1211, 1143, 976, 860, 691;

HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 223.1869; found: 223.1873;

(*R,Z*)-2-(cyclooct-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4d**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 93%. Purification by FC (*n*hexane/ethyl acetate=100:0~2, column size 5 x 0.5 cm) within 5 min yielded a total of 17.7 mg (0.075 mmol, 75%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.78 – 5.62 (m, 1H), 5.56 (td, $J_1 = 10.0$ Hz, $J_2 = 1.3$ Hz, 1H), 2.33 – 2.19 (m, 1H), 2.13 (m, 1H), 2.07 – 1.96 (m, 1H), 1.72 – 1.59 (m, 3H), 1.52 (m, 2H), 1.47 – 1.27 (m, 3H), 1.25 (s, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 130.5, 130.1, 83.1, 31.0, 29.5, 26.6, 26.2, 24.8, 24.7 (Due to quadrapolar relaxation, the carbon attached to the boron atom was not detected.);

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 34.1;

IR (thin film) ν_{max} (cm^{-1}): 2976, 2924, 2851, 1643, 1456, 1445, 1404, 1363, 1319, 1146, 968, 851, 760;

HRMS (ESI+) calcd for $\text{C}_{14}\text{H}_{26}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 237.2026; found: 237.2019;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = -60.1 ($c=1.0$ in CH_2Cl_2 , 92% ee)

GC analysis of **4d** indicated an enantiomeric excess of 92% (Restek Rt- β DEXse, 50 °C for 1 min, 50–140 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_{R} = 86.3min; minor enantiomer t_{R} = 87.0 min.

(*R*)-2-(5,5-dimethylcyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4e**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 98%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 15.3 mg (0.065mmol, 65%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.68 (d, $J = 10.0$ Hz, 1H), 5.58 (m, 1H), 1.89 – 1.78 (m, 2H), 1.75 – 1.65 (m, 1H), 1.49 – 1.36 (m, 2H), 1.24 (s, 12H), 0.92 (s, 3H), 0.87 (s, 3H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 126.2, 125.0, 83.2, 38.8, 36.7, 30.7, 28.4, 26.0, 24.8, 24.7;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.8;

IR (thin film) ν_{max} (cm^{-1}): 3020, 2976, 2949, 2928, 2901, 2868, 2830, 1645, 1470, 1460, 1431, 1371, 1360, 1342, 1315, 1283, 1273, 1213, 1146, 1107, 1018, 972, 901, 866, 854, 731, 658;

HRMS (ESI+) calcd for $\text{C}_{14}\text{H}_{26}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 237.2026; found: 237.2034;

$[\alpha]_D^{23}$ (589 nm) = +57.3 (c=1.0 in CH₂Cl₂, 97% ee)

GC analysis of **4e** indicated an enantiomeric excess of 97% (Restek Rt-βDEXse, 50 °C for 1 min, 50–140 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 70.9 min; minor enantiomer t_R = 70.4 min.

(*S*)-2-(3,6-dihydro-2H-pyran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **4f**

The ¹H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 99%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 16.8 mg (0.080mmol, 80%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.94 – 5.83 (m, 1H), 5.68 (dq, J_1 = 10.2 Hz, J_2 = 2.7 Hz, 1H), 4.12 (dt, J_1 = 3.4 Hz, J_2 = 2.4 Hz, 2H), 3.94 (dd, J_1 = 11.1 Hz, J_2 = 5.3 Hz, 1H), 3.75 (dd, J_1 = 11.1 Hz, J_2 = 7.9 Hz, 1H), 2.05 (m, 1H), 1.24 (s, 12H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 125.3, 125.2, 83.5, 65.7, 65.4, 24.8, 24.7;

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 32.6;

IR (thin film) ν_{max} (cm⁻¹): 3032, 2976, 2930, 2884, 2853, 2746, 1645, 1514, 1470, 1462, 1454, 1381, 1371, 1354, 1327, 1271, 1225, 1215, 1167, 1144, 1107, 1047, 968, 872, 852, 656;

HRMS (ESI+) calcd for C₁₁H₂₀O₂B⁺ [M + H⁺]: 211.1506; found: 211.1503;

$[\alpha]_D^{23}$ (589 nm) = +31.5 (c=1.0 in CH₂Cl₂, 78% ee)

GC analysis of **4f** indicated an enantiomeric excess of 97% (Restek Rt-βDEXse, 50 °C for 1 min, 50–100 °C at 1 °C /min, 100 °C for 40 min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 82.6 min; minor enantiomer t_R = 81.2 min.

(*R*)-4,4,5,5-tetramethyl-2-(2-methylcyclohex-2-en-1-yl)-1,3,2-dioxaborolane **4h**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 70%. Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a total of 15.3 mg (0.069mmol, 69%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.41 (m, 1H), 2.02 – 1.94 (m, 2H), 1.75 – 1.71 (m, 1H), 1.69 (m, 4H), 1.64 – 1.49 (m, 3H), 1.24 (d, $J = 3.2$ Hz, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 134.5, 120.4, 83.1, 25.3, 25.0, 24.8, 24.5, 24.3, 21.7;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.6;

IR (thin film) ν_{max} (cm^{-1}): 2976, 2930, 2857, 2835, 1664, 1449, 1333, 1321, 1275, 1252, 1215, 1196, 1165, 1144, 1109, 1032, 980, 885, 839, 797;

HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 223.1869; found: 223.1885;

GC analysis of **4h** indicated an enantiomeric excess of 45% (Restek Rt- β DEXse, 50 °C for 1 min, 50–110 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_{R} = 64.4 min; minor enantiomer t_{R} = 63.8 min.

(*R*)-4,4,5,5-tetramethyl-2-(2,3,4,5-tetrahydro-[1,1'-biphenyl]-2-yl)-1,3,2-dioxaborolane **4i**

The GCMS detection of the crude reaction mixture without further calibration indicated a GC yield of 99%.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 7.44 – 7.37 (m, 2H), 7.31 – 7.26 (m, 2H), 7.23 – 7.15 (m, 1H), 6.12 (td, *J*₁ = 4.0 Hz, *J*₂ = 1.9 Hz, 1H), 2.43 (m, 1H), 2.26 (tq, *J*₁ = 6.4 Hz, *J*₂ = 3.4 Hz, 2H), 1.93 (m, 1H), 1.79 (m, 2H), 1.66 (m, 1H), 1.12 (s, 6H), 1.04 (s, 6H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 143.3, 137.8, 128.0, 126.3, 125.4, 123.9, 83.1, 25.7, 24.9, 24.5, 24.3, 21.5;

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.7;

IR (thin film) ν_{max} (cm⁻¹): 3101, 3080, 3055, 3020, 2978, 2930, 2857, 2832, 1638, 1600, 1491, 1443, 1364, 1323, 1273, 1240, 1213, 1188, 1165, 1143, 1107, 1043, 968, 889, 853, 758, 696;

HRMS (ESI+) calcd for C₁₈H₂₆O₂B⁺ [M + H⁺]: 285.2026; found: 285.2035;

Methyl (*R*)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)cyclohex-1-ene-1-carboxylate **4j**

The ¹H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 84%.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 6.97 (td, *J*₁ = 4.1 Hz, *J*₂ = 2.1 Hz, 1H), 3.69 (s, 3H), 2.19 (m, 2H), 2.03 (m, 1H), 1.87 – 1.75 (m, 1H), 1.64 (m, 2H), 1.53 (m, 1H), 1.25 (s, 6H), 1.21 (s, 6H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 168.3, 138.3, 131.5, 83.2, 51.4, 25.7, 24.7, 24.4, 23.93, 21.2;

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.2;

IR (thin film) ν_{max} (cm⁻¹): 3032, 2976, 2930, 2884, 2853, 2746, 1645, 1514, 1470, 1462, 1454, 1381, 1371, 1354, 1327, 1271, 1225, 1215, 1167, 1144, 1107, 1047, 968, 872, 852, 656;

HRMS (ESI+) calcd for $C_{14}H_{24}O_4B^+$ [$M + H^+$]: 267.1768; found: 267.1772;

GC analysis of **4j** indicated an enantiomeric excess of 4% (Restek Rt- β DEXse, 50 °C for 1 min, 50–120 °C at 1 °C /min, 120 °C for 120 min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 158.7 min; minor enantiomer t_R = 156.3 min.

(*S*)-4,4,5,5-tetramethyl-2-(1-methylcyclohex-2-en-1-yl)-1,3,2-dioxaborolane **5b**

The 1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 81%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 17.8 mg (0.080mmol, 80%) of product as a colorless liquid.

1H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.62 (dt, $J_1 = 10.0$ Hz, $J_2 = 3.3$ Hz, 1H), 5.56 (d, $J = 10.2$ Hz, 1H), 1.94 (m, 2H), 1.91 – 1.84 (m, 1H), 1.75 – 1.60 (m, 2H), 1.52 (m, 1H), 1.22 (d, $J = 2.9$ Hz, 12H), 1.01 (s, 3H);

^{13}C NMR (CDCl₃, 100 MHz) δ_C (ppm): 134.5, 124.8, 83.0, 33.1, 25.0, 24.7, 24.5, 20.9 (Due to quadrupolar relaxation, the carbon attached to the boron atom was not detected.);

^{11}B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.8;

IR (thin film) ν_{max} (cm⁻¹): 2976, 2926, 2857, 1643, 1514, 1479, 1470, 1462, 1454, 1447, 1377, 1371, 1348, 1308, 1279, 1125, 1144, 1105, 968, 851;

HRMS (ESI+) calcd for $C_{13}H_{24}O_2B^+$ [$M + H^+$]: 223.1869; found: 223.1872;

$[\alpha]^{23}_D$ (589 nm) = +44.1 ($c=1.0$ in CH₂Cl₂, 99% ee)

After **5b** being oxidized to its corresponding alcohol, GC analysis of the alcohol indicated an enantiomeric excess of 99% (Astec CHIRALDEX B-DM, 50 °C for 1 min, 50–100 °C at

1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 25.6 min; minor enantiomer t_R = 24.5 min.

(*S*)-2-(1-ethylcyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5c**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 85%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 17.5 mg (0.074mmol, 74%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.65 (dt, J_1 = 10.2 Hz, J_2 = 3.1 Hz, 1H), 5.60 (dq, J_1 = 10.0 Hz, J_2 = 1.4 Hz, 1H), 1.97 – 1.85 (m, 3H), 1.70 (m, 2H), 1.56 (m, 1H), 1.51 – 1.43 (m, 1H), 1.41 – 1.32 (m, 1H), 1.23 (d, J = 3.3 Hz, 12H), 0.88 (t, J = 7.5 Hz, 3H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 133.3, 125.3, 83.0, 31.5, 30.4, 25.3, 24.8, 24.6, 21.1, 10.2;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.8;

IR (thin film) ν_{max} (cm^{-1}): 2976, 2930, 2874, 2835, 1638, 1458, 1445, 1369, 1307, 1260, 1213, 1144, 1111, 858;

HRMS (ESI+) calcd for $\text{C}_{14}\text{H}_{26}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 237.2026; found: 237.2023;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +47.3 (c =1.0 in CH_2Cl_2 , 96% ee)

After **5c** being oxidized to its corresponding alcohol, GC analysis of the alcohol indicated an enantiomeric excess of 96% (Astec CHIRALDEX B-DM, 70 °C for 20 min, 70–100 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_R = 30.7 min; minor enantiomer t_R = 30.1 min.

(*R*)-2-(1-isopropylcyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5d**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 87%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 19.3 mg (0.077mmol, 77%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.67 (dt, $J_1 = 10.2$ Hz, $J_2 = 3.6$ Hz, 1H), 5.55 (dd, $J_1 = 10.2$ Hz, $J_2 = 1.9$ Hz, 1H), 1.97 – 1.84 (m, 2H), 1.76 (m, 3H), 1.55 (m, 1H), 1.30 (td, $J_1 = 12.5$ Hz, $J_2 = 2.7$ Hz, 2H), 1.23 (d, $J = 4.2$ Hz, 12H), 0.87 (dd, $J_1 = 13.3$ Hz, $J_2 = 6.9$ Hz, 6H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 132.8, 125.7, 82.9, 33.9, 26.0, 25.2, 24.9, 24.5, 21.7, 19.1, 18.0;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.7;

IR (thin film) ν_{max} (cm^{-1}): 3011, 2974, 2955, 2930, 2870, 2835, 1641, 1462, 1447, 1385, 1371, 1352, 1331, 1304, 1271, 1254, 1213, 1165, 1144, 972, 862;

HRMS (ESI+) calcd for $\text{C}_{15}\text{H}_{28}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 251.2182; found: 251.2189;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +51.2 ($c=1.0$ in CH_2Cl_2 , 78% ee)

After **5d** being oxidized to its corresponding alcohol, GC analysis of the alcohol indicated an enantiomeric excess of 78% (Astec CHIRALDEX B-DM, 50 °C for 1 min, 50–110 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer $t_{\text{R}} = 54.9$ min; minor enantiomer $t_{\text{R}} = 54.2$ min.

(*S*)-2-(1-butylcyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5e**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 95%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 16.1 mg (0.061mmol, 61%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.72 – 5.52 (m, 2H), 1.98 – 1.84 (m, 3H), 1.70 (m, 1H), 1.59 – 1.49 (m, 1H), 1.49 – 1.39 (m, 1H), 1.39 – 1.32 (m, 1H), 1.32 – 1.24 (m, 5H), 1.23 (d, $J = 3.8$ Hz, 12H), 0.91 – 0.85 (m, 3H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 133.6, 125.1, 83.0, 38.8, 30.9, 28.1, 25.2, 24.8, 24.5, 23.56, 21.2, 14.1;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.8;

IR (thin film) ν_{max} (cm^{-1}): 3013, 2974, 2953, 2928, 2857, 1641, 1466, 1454, 1447, 1387, 1371, 1334, 1308, 1273, 1252, 1217, 1165, 1144, 1130, 1111, 976, 735, 658;

HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{30}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 265.2339; found: 265.2349;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +24.4 ($c=1.0$ in CH_2Cl_2 , 95% ee)

After **5e** being oxidized to its corresponding alcohol, GC analysis of the alcohol indicated an enantiomeric excess of 95% (Astec CHIRALDEX B-DM, 70 °C for 20 min, 70–110 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer $t_{\text{R}} = 52.7$ min; minor enantiomer $t_{\text{R}} = 51.8$ min.

(*S*)-4,4,5,5-tetramethyl-2-(1-(pent-4-en-1-yl)cyclohex-2-en-1-yl)-1,3,2-dioxaborolane **5f**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 88%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 15.2 mg (0.055mmol, 55%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.80 (ddt, $J_1 = 16.9$ Hz, $J_2 = 10.2$ Hz, $J_3 = 6.6$ Hz, 1H), 5.71 – 5.51 (m, 2H), 5.06 – 4.85 (m, 2H), 2.02 (q, $J = 6.8$ Hz, 2H), 1.94 (m, 2H), 1.88 (m, 1H), 1.74 – 1.65 (m, 1H), 1.60 – 1.45 (m, 2H), 1.44 – 1.27 (m, 4H), 1.22 (d, $J = 3.6$ Hz, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 139.0, 133.3, 125.3, 114.2, 83.1, 38.6, 34.6, 30.8, 25.2, 24.8, 24.5, 21.1 (Due to quadrapolar relaxation, the carbon attached to the boron atom was not detected.);

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.7;

IR (thin film) ν_{max} (cm^{-1}): 3074, 3011, 2976, 2930, 2855, 2841, 1639, 1510, 1468, 1458, 1447, 1389, 1371, 1334, 1308, 1252, 1213, 1165, 1144, 1111, 989, 970, 910, 860, 733;

HRMS (ESI+) calcd for $\text{C}_{11}\text{H}_{20}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 277.2339; found: 277.2346;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +24.9 ($c=1.0$ in CH_2Cl_2 , 94% ee)

After **5f** being oxidized to its corresponding alcohol, GC analysis of the alcohol indicated an enantiomeric excess of 94% (Astec CHIRALDEX B-DM, 70 °C for 20 min, 70–150 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer $t_{\text{R}} = 65.0$ min; minor enantiomer $t_{\text{R}} = 64.6$ min.

(*R*)-2-(1-benzylcyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5g**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 82%. Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a total of 19.4 mg (0.065mmol, 65%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 7.23 (d, $J = 4.4$ Hz, 4H), 7.19 – 7.15 (m, 1H), 5.75 – 5.61 (m, 2H), 2.84 – 2.66 (m, 2H), 1.97 – 1.90 (m, 2H), 1.85 (ddd, $J_1 = 12.8$ Hz, $J_2 = 6.5$ Hz, $J_3 = 3.0$ Hz, 1H), 1.74 – 1.65 (m, 1H), 1.65 – 1.58 (m, 1H), 1.37 (ddd, $J_1 = 12.7$ Hz, $J_2 = 10.8$ Hz, $J_3 = 3.2$ Hz, 1H), 1.21 (d, $J = 2.6$ Hz, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 139.9, 132.9, 130.2, 127.7, 126.0, 125.8, 83.2, 44.59, 30.8, 25.1, 24.8, 24.7, 20.5;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.5;

IR (thin film) ν_{max} (cm^{-1}): 3082, 3061, 3024, 3014, 2953, 2924, 2853, 1603, 1495, 1454, 1389, 1369, 1344, 1331, 1317, 1254, 1223, 1211, 1186, 1165, 1142, 1113, 1089, 1030, 989, 927, 856, 839, 737, 706, 669;

HRMS (ESI+) calcd for $\text{C}_{19}\text{H}_{28}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 299.2182; found: 299.2178;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +29.3 ($c=1.0$ in CH_2Cl_2 , 96% ee)

After **5g** being oxidized to its corresponding alcohol, HPLC analysis of the alcohol indicated an enantiomeric excess of 96% (Daicel Chiralpak AD-H, *n*Hexane : IPA= 100 : 5, column flow rate: 1 mL/min, 210 nm); major enantiomer t_{R} = 12.8 min; minor enantiomer t_{R} = 11.7 min.

(*R*)-2-(1-(4-methoxybenzyl)cyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5h**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 82%. Purification by FC (*n*hexane/ethyl acetate=100:0.5~100:5, column size 5 x 0.5 cm) within 5 min yielded a total of 25.3 mg (0.077mmol, 77%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 7.14 (d, J = 8.6 Hz, 2H), 6.78 (d, J = 8.6 Hz, 2H), 5.74 – 5.61 (m, 2H), 3.77 (s, 3H), 2.77 – 2.60 (m, 2H), 1.99 – 1.90 (m, 2H), 1.83 (ddd, J_1 = 12.8 Hz, J_2 = 6.5 Hz, J_3 = 2.9 Hz, 1H), 1.68 (m, 1H), 1.64 – 1.54 (m, 1H), 1.40 – 1.29 (m, 1H), 1.20 (d, J = 2.0 Hz, 12H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 157.8, 132.9, 132.0, 131.1, 125.9, 113.1, 83.2, 55.2, 43.6, 30.7, 25.1, 24.9, 24.7, 20.5.;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.6;

IR (thin film) ν_{max} (cm^{-1}): 3001, 2955, 2932, 2862, 2832, 1612, 1512, 1450, 1366, 1327, 1296, 1256, 1250, 1173, 1103, 1034, 972, 872, 748;

HRMS (ESI+) calcd for $\text{C}_{20}\text{H}_{30}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 329.2288; found: 329.2290;

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +18.9 (c =1.0 in CH_2Cl_2 , 96% ee)

After **5h** being oxidized to its corresponding alcohol, HPLC analysis of the alcohol indicated an enantiomeric excess of 96% (Daicel Chiralpak AD-H, *n*Hexane : IPA= 100 : 5, column flow rate: 1 mL/min, 230 nm); major enantiomer t_{R} = 12.8 min; minor enantiomer t_{R} = 11.4 min.

(*R*)-2-(1-(4-chlorobenzyl)cyclohex-2-en-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **5i**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 70%. Purification by FC (*n*hexane/ethyl acetate=100:0.5,

column size 5 x 0.5 cm) within 5 min yielded a total of 12.7 mg (0.038mmol, 49%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 7.25 – 7.12 (m, 4H), 5.69 (dt, *J*₁ = 10.0 Hz, *J*₂ = 3.5 Hz, 1H), 5.60 (d, *J* = 10.2 Hz, 1H), 2.79 – 2.58 (m, 2H), 1.92 (m, 2H), 1.81 (m, 1H), 1.71 – 1.57 (m, 2H), 1.32 (m, 1H), 1.20 (d, *J* = 1.5 Hz, 12H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 138.3, 132.4, 131.6, 131.5, 127.8, 126.4, 83.3, 43.8, 30.6, 25.0, 24.8, 24.7, 20.4;

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.6;

IR (thin film) ν_{max} (cm⁻¹): 3013, 2978, 2932, 2857, 1639, 1597, 1489, 1450, 1381, 1371, 1312, 1273, 1203, 1144, 1094, 1016, 837, 734;

HRMS (ESI+) calcd for C₁₉H₂₇O₂ClB⁺ [*M* + H⁺]: 333.1793; found: 333.1797;

[α]_D²³ (589 nm) = +17.4 (c=1.0 in CH₂Cl₂, 93% ee)

After **5i** being oxidized to its corresponding alcohol, HPLC analysis of the alcohol indicated an enantiomeric excess of 93% (Daicel Chiralpak AD-H, *n*Hexane : IPA= 100 : 5, column flow rate: 1 mL/min, 210 nm); major enantiomer *t*_R = 10.6 min; minor enantiomer *t*_R = 9.3 min.

(*R*)-4,4,5,5-tetramethyl-2-(1-phenethylcyclohex-2-en-1-yl)-1,3,2-dioxaborolane **5j**

The ¹H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 95%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 16.8 mg (0.095mmol, 95%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 7.31 – 7.24 (m, 2H), 7.23 – 7.15 (m, 3H), 5.76 – 5.64 (m, 2H), 2.61 (dd, *J*₁ = 9.9 Hz, *J*₂ = 7.7 Hz, 2H), 2.04 – 1.94 (m, 3H), 1.82 – 1.73 (m, 2H), 1.70 – 1.59 (m, 2H), 1.38 (ddd, *J*₁ = 12.7 Hz, *J*₂ = 11.4 Hz, *J*₃ = 2.9 Hz, 1H), 1.27 (d, *J* = 2.8 Hz, 12H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 143.4, 132.9, 128.4, 128.3, 125.7, 125.6, 83.2, 41.27, 32.5, 30.7, 25.2, 24.9, 24.6, 21.1;

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.8;

IR (thin film) ν_{max} (cm⁻¹): 3086, 3063, 3017, 2924, 2855, 2754, 1643, 1497, 1389, 1366, 1258, 1211, 1142, 964, 856, 694;

HRMS (ESI+) calcd for C₂₀H₃₀O₂B⁺ [M + H⁺]: 313.2339; found: 313.2343;

[α]_D²³ (589 nm) = -4.3 (c=1.0 in CH₂Cl₂, 96% ee)

After **5j** being oxidized to its corresponding alcohol, HPLC analysis of the alcohol indicated an enantiomeric excess of 96% (Daicel Chiralpak AD-H, *n*Hexane : IPA= 100 : 5, column flow rate: 0.5 mL/min, 190 nm); major enantiomer *t*_R = 19.4 min; minor enantiomer *t*_R = 17.9 min.

(*S*)-2-(1-cyclopentylallyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **6f**

Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a total of 16.0 mg (0.068mmol, 68%) of product as a colorless liquid.

¹H NMR (CDCl₃, 500 MHz) δ_H (ppm): 5.76 (dt, *J*₁ = 17.1 Hz, *J*₂ = 9.8 Hz, 1H), 4.96 (dd, *J*₁ = 17.1 Hz, *J*₂ = 2.1 Hz, 1H), 4.90 (dd, *J*₁ = 10.1 Hz, *J*₂ = 2.1 Hz, 1H), 2.00 (m, 1H), 1.79 – 1.65 (m, 4H), 1.61 (m, 1H), 1.60 – 1.53 (m, 2H), 1.53 – 1.46 (m, 2H), 1.24 – 1.22 (s, 12H), 1.12 (m, 2H);

¹³C NMR (CDCl₃, 125MHz) δ_C (ppm): 139.2, 122.7, 113.8, 83.0, 40.8, 33.3, 32.0, 32.0, 25.3, 25.0, 24.7, 24.7, 24.6 (Due to the existence of allylic isomer, the number of carbon atoms is more than eight.);

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 32.9;

IR (thin film) ν_{max} (cm⁻¹): 3075, 2978, 2951, 2868, 2746, 1630, 1477, 1468, 1458, 1449, 1379, 1371, 1358, 1321, 1271, 1144, 1110, 1047, 995, 970, 901, 849, 735;

HRMS (ESI+) calcd for C₁₄H₂₆O₂B⁺ [M + H⁺]: 237.2026; found: 237.2031;

(*S*)-2-(1-cyclohexylallyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **6g**

Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a total of 16.5 mg (0.066mmol, 66%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.73 (dt, *J*₁ = 17.1 Hz, *J*₂ = 10.0 Hz, 1H), 4.99 – 4.88 (m, 2H), 1.76 (m, 1H), 1.73 – 1.56 (m, 6H), 1.50 (m, 1H), 1.23 (s, 12H), 1.19 – 1.06 (m, 2H), 1.06 – 0.94 (m, 1H), 0.91 – 0.79 (m, 1H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 138.6, 114.4, 83.0, 38.29, 33.2, 32.4, 26.6, 26.5, 26.45, 24.7, 24.7, 24.7 (Due to the existence of allylic isomer, the number of carbon atoms is more than nine.);

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.0;

IR (thin film) ν_{max} (cm⁻¹): 3073, 2978, 2924, 2851, 1628, 1462, 1387, 1379, 1371, 1348, 1319, 1279, 1215, 1144, 1105, 997;

HRMS (ESI+) calcd for C₁₅H₂₈O₂B⁺ [M + H⁺]: 251.2182; found: 251.2167.

(*R*)-2-(6-bromohex-1-en-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **6h**

Purification by FC (*n*hexane/ethyl acetate=100:2, column size 5 x 0.5 cm) within 5 min yielded a total of 16.8 mg (0.060mmol, 60%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.76 (ddd, *J*₁ = 17.1 Hz, *J*₂ = 10.2 Hz, *J*₃ = 8.7 Hz, 1H), 5.03 – 4.93 (m, 2H), 3.40 (m, 3H), 2.22 – 2.09 (m, 1H), 1.98 – 1.87 (m, 2H), 1.87 – 1.77 (m, 2H), 1.74 – 1.62 (m, 2H), 1.56 (m, 2H), 1.24 (s, 6H), 1.24 (s, 12H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 138.8, 114.2, 83.3, 33.8, 32.2, 28.7, 24.8, 24.7, 24.6 (Due to the existence of allylic isomer, the number of carbon atoms is more than eight.);

¹¹B NMR (CDCl₃, 128 MHz) δ_B (ppm): 33.0;

IR (thin film) ν_{max} (cm⁻¹): 3075, 2959, 2930, 2870, 2860, 1632, 1600, 1460, 1379, 1371, 1360, 1325, 1277, 1269, 1213, 1165, 1142, 1107, 1126, 1072, 966, 849, 743;

HRMS (ESI+) calcd for C₁₂H₂₃BrO₂B⁺ [M + H⁺]: 289.0974; found: 289.0967.

(*R*)-4,4,5,5-tetramethyl-2-(7-methylocta-1,6-dien-3-yl)-1,3,2-dioxaborolane **6i**

The ¹H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 99%. Purification by FC (*n*hexane/ethyl acetate=100:0.5, column size 5 x 0.5 cm) within 5 min yielded a total of 16.8 mg (0.080mmol, 80%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.91 (dd, *J*₁ = 17.4 Hz, *J*₂ = 10.8 Hz, 1H), 5.12 (m, 1H), 4.98 – 4.95 (m, 1H), 4.95 – 4.90 (m, 1H), 1.93 (m, 2H), 1.67 (s, 3H), 1.59 (s, 3H), 1.52 (m, 1H), 1.38 (m, 1H), 1.22 (s, 12H), 1.07 (s, 3H), 0.07 (s, 3H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 145.4, 131.0, 125.0, 111.0, 83.3, 38.3, 25.7, 24.7, 24.6, 24.4, 19.5, 17.6;

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.6;

IR (thin film) ν_{max} (cm^{-1}): 3082, 2995, 2982, 2936, 1628, 1456, 1348, 1312, 1260, 1215, 1192, 1165, 1146, 1111, 1003, 966, 901, 853;

HRMS (ESI+) calcd for $\text{C}_{16}\text{H}_{30}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 265.2339; found: 265.2347.

2-((*R*)-cyclohex-2-en-1-yl)-4,4,6-trimethyl-1,3,2-dioxaborinane **7a**

The ^1H NMR spectrum of crude reaction mixture with 1,4-dimethoxybenzene as the internal standard indicated a NMR yield of 86%. After extraction, the crude product was directly oxidized by $\text{NaBO}_3 \cdot 10\text{H}_2\text{O}$ in $\text{THF}/\text{H}_2\text{O}$. The corresponding allylic alcohol was further purified by FC (*n*hexane/ethyl acetate=100:2~100:5, column size 5 x 0.5 cm) and concentrated under 200 Torr at 25 °C to yield a total of 7.2 mg (0.073mmol, 73%) colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.74 (m, 1H), 5.60 (m, 1H), 4.15 (m, 1H), 1.96 (m, 2H), 1.75 (dd, $J_1 = 13.9$ Hz, $J_2 = 3.0$ Hz, 1H), 1.72 – 1.48 (m, 5H), 1.43 (dd, $J_1 = 13.9$ Hz, $J_2 = 11.7$ Hz, 1H), 1.26 (s, 6H), 1.23 (d, $J = 6.2$ Hz, 3H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 129.4, 129.4, 124.9, 124.9, 70.4, 70.4, 64.6, 64.6, 46.0, 46.0, 31.2, 28.1, 28.0, 25.2, 25.1, 24.2, 23.2, 22.7, 22.6 (Due to the existence of diastereomer, the number of carbon atoms is more than twelve.);

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 29.5;

IR (thin film) ν_{max} (cm^{-1}): 3019, 2972, 2930, 2855, 2835, 1643, 1442, 1412, 1389, 1319, 1302, 1246, 1225, 1192, 1169, 878, 652;

HRMS (ESI+) calcd for $\text{C}_{12}\text{H}_{22}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 209.1713; found: 209.1724;

$[\alpha]_D^{23} (589 \text{ nm}) = +7.7$ ($c=1.0$ in CH_2Cl_2 , 92% ee)

GC analysis of **4f** indicated an enantiomeric excess of 97% (Restek Rt- β DEXse, 50 °C for 1 min, 50–110 °C at 1 °C /min, 110 °C for 10 min, Helium, column flow rate: 1 mL/min); major enantiomer $t_R = 65.1$ min; minor enantiomer $t_R = 64.5$ min.

4.8.2 Analytical data of application products

(*R*)-((*S*)-cyclohex-2-en-1-yl)(phenyl)methanol **17a**

Purification by FC (*n*hexane/ethyl acetate=100:2) yielded a total of 34.1 mg (0.182 mmol, 91%) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 7.35 (d, $J = 4.3$ Hz, 4H), 7.28 (m, 1H), 5.82 (dq, $J_1 = 9.9$ Hz, $J_2 = 3.5$ Hz, 1H), 5.39 (dd, $J_1 = 10.2$ Hz, $J_2 = 2.0$ Hz, 1H), 4.59 (d, $J = 6.5$ Hz, 1H), 2.50 (m, 1H), 1.99 (m, 2H), 1.85 (s, 1H), 1.81 – 1.68 (m, 2H), 1.59 – 1.46 (m, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 142.9, 130.4, 128.2, 128.0, 127.4, 126.5, 77.4, 43.0, 25.2, 23.87, 21.1;

IR (thin film) ν_{max} (cm^{-1}): 3383, 3065, 3026, 2924, 2860, 2837, 1651, 1603, 1494, 1454, 1393, 1346, 1310, 1234, 1219, 1200, 1182, 1138, 1088, 1067, 1018, 983, 914, 885;

HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{27}\text{O}^+$ [$\text{M} + \text{H}^+$]: 189.1279; found: 189.1278;

$[\alpha]_D^{23} (589 \text{ nm}) = -5.7$ ($c=1.0$ in CH_2Cl_2 , 89% ee, d.r. > 20 :1)

HPLC analysis of **17a** indicated an enantiomeric excess of 89% (Daicel Chiralcel OB-H + OB-H, *n*Hexane : IPA= 100 : 0.3, column flow rate: 0.6 mL/min, 210 nm); major enantiomer $t_R = 66.5$ min; minor enantiomer $t_R = 38.4$ min.

(*R*)-cyclohex-2-en-1-ol **17b**

Purification by FC (*n*hexane/ethyl acetate=100:5) yielded a total of 17.4 mg (0.178 mmol, 89%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.83 (d, *J* = 10.1 Hz, 1H), 5.75 (d, *J* = 11.5 Hz, 1H), 4.20 (s, 1H), 1.99 (m, 2H), 1.88 (m, 1H), 1.72 (m, 1H), 1.63 – 1.53 (m, 2H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 130.6, 129.8, 65.5, 32.0, 25.1, 18.9;

IR (thin film) ν_{max} (cm⁻¹): 3336, 3022, 2933, 2860, 2835, 1651, 1450, 1435, 1418, 1385, 1337, 1315, 1281, 1252, 1159, 1049, 1003, 959;

HRMS (ESI+) calcd for C₆H₁₁O⁺ [*M* + H⁺]: 99.0810; found: 99.0808.

[α]_D²³ (589 nm) = +90.2 (c=1.0 in CH₂Cl₂, 97% ee)

GC analysis of **17b** indicated an enantiomeric excess of 97% (Restek Rt-βDEXse, 70 °C for 1 min, 70–90 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer t_R= 19.2 min; minor enantiomer t_R = 18.6 min.

(*R*)-cyclohex-2-en-1-yl 2-iodobenzoate **17c**

Purification by FC (*n*hexane/ethyl acetate=100:2) yielded a total of 276 mg (0.84 mmol, 84%) of product as a pale-yellow liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 7.97 (d, *J* = 7.9 Hz, 1H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.39 (t, *J* = 7.6 Hz, 1H), 7.13 (t, *J* = 7.7 Hz, 1H), 6.02 (dt, *J*₁ = 7.1 Hz, *J*₂ = 3.2 Hz, 1H), 5.87

(d, $J = 10.0$ Hz, 1H), 5.53 (s, 1H), 2.18 – 2.00 (m, 2H), 1.96 (m, 2H), 1.85 (m, 1H), 1.71 (m, 1H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 166.4, 141.2, 135.8, 133.2, 132.4, 130.9, 127.9, 125.3, 93.9, 69.7, 28.2, 24.9, 18.9;

IR (thin film) ν_{max} (cm^{-1}): 3065, 3030, 2934, 2864, 2833, 2116, 1713, 1651, 1582, 1558, 1464, 1427, 1395, 1335, 1323, 1285, 1246, 1163, 1126, 1099, 1042, 1015, 910, 835;

HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{14}\text{O}_2\text{I}^+$ [$\text{M} + \text{H}^+$]: 329.0039; found: 329.0040.

(*R*)-2-(cyclohex-2-en-1-ylmethyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane **17e**

Purification by FC (*n*hexane/ethyl acetate=100:0.5) yielded a total of 40.0 mg (0.180mmol, 90 %) of product as a colorless liquid.

^1H NMR (CDCl_3 , 400 MHz) δ_{H} (ppm): 5.66 – 5.52 (m, 2H), 2.30 (m, 1H), 2.01 – 1.89 (m, 2H), 1.82 (m, 1H), 1.70 (m, 1H), 1.57 – 1.45 (m, 1H), 1.25 (s, 12H), 0.82 (h, $J = 7.6$ Hz, 2H);

^{13}C NMR (CDCl_3 , 100 MHz) δ_{C} (ppm): 133.9, 126.2, 83.0, 31.8, 316, 25.1, 24.8, 21.6 (Due to quadrapolar relaxation, the carbon attached to the boron atom was not detected.);

^{11}B NMR (CDCl_3 , 128 MHz) δ_{B} (ppm): 33.9;

IR (thin film) ν_{max} (cm^{-1}): 3013, 2978, 2924, 2857, 1647, 1369, 1319, 1310, 1273, 1256, 1146, 1107, 970, 883, 847, 721;

HRMS (ESI+) calcd for $\text{C}_{13}\text{H}_{24}\text{O}_2\text{B}^+$ [$\text{M} + \text{H}^+$]: 223.1869; found: 223.1874.

$[\alpha]_{\text{D}}^{23}$ (589 nm) = +48.7 ($c=1.0$ in CH_2Cl_2 , 98% ee)

GC analysis of **17e** indicated an enantiomeric excess of 98% (Astec CHIRALDEX B-DM, 50 °C for 1 min, 50–100 °C at 1 °C /min, 100 °C for 40 min, Helium, column flow rate: 1 mL/min); major enantiomer t_{R} = 82.8 min; minor enantiomer t_{R} = 82.4 min.

tert-Butyl (*R*)-cyclohex-2-en-1-yl(methyl)carbamate **17f**

Purification by FC (*n*hexane/ethyl acetate=100:2) yielded a total of 28.2 mg (0.134mmol, 67%) of product as a colorless liquid. (28.2 mg, 67% yield, 98% ee)

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 5.84 (dq, *J*₁ = 9.5 Hz, *J*₂ = 3.1 Hz, 1H), 5.45 (d, *J* = 10.2 Hz, 1H), 4.65 (s, 1H), 2.68 (s, 3H), 2.02 – 1.94 (m, 2H), 1.83 – 1.73 (m, 2H), 1.68 – 1.57 (m, 1H), 1.57 – 1.49 (m, 1H), 1.45 (s, 9H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 155.9, 130.7, 128.9, 79.2, 52.2, 29.1, 28.5, 26.7, 24.6, 21.4;

IR (thin film) ν_{max} (cm⁻¹): 3022, 3005, 2972, 2932, 2862, 2839, 1695, 1477, 1458, 1449, 1396, 1381, 1366, 1348, 1314, 1246, 1177, 1148, 1130, 1030, 804;

HRMS (ESI+) calcd for C₁₂H₂₂NO₂⁺ [*M* + H⁺]: 212.1651; found: 212.1648.

[α]_D²³ (589 nm) = +29.7 (c=1.0 in CH₂Cl₂, 98% ee)

GC analysis of **17f** indicated an enantiomeric excess of 98% (Restek Rt-βDEXse, 50 °C for 1 min, 50–140 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer *t*_R = 77.7 min; minor enantiomer *t*_R = 79.1 min.

(*S*)-4'-(trifluoromethyl)-1,2,3,4-tetrahydro-1,1'-biphenyl **17g**

Purification by FC (*n*hexane) yielded a total of 38.2 mg (0.170mmol, 85%) of product as a colorless liquid.

¹H NMR (CDCl₃, 400 MHz) δ_H (ppm): 7.55 (d, *J* = 7.8 Hz, 2H), 7.33 (d, *J* = 7.8 Hz, 2H), 5.94 (d, *J* = 9.5 Hz, 1H), 5.69 (d, *J* = 9.9 Hz, 1H), 3.47 (s, 1H), 2.20 – 1.95 (m, 3H), 1.81 – 1.48 (m, 3H);

¹³C NMR (CDCl₃, 100 MHz) δ_C (ppm): 150.7, 129.2, 129.1, 128.1, 125.2, 125.2, 41.7, 32.4, 24.9, 21.0;

¹⁹F NMR (CDCl₃, 376 MHz) δ_F (ppm): -62.3;

IR (thin film) ν_{max} (cm⁻¹): 3065, 3022, 2936, 2860, 2841, 1651, 1618, 1446, 1418, 1325, 1263, 1246, 1163, 1126, 1109, 1069, 1043, 1018, 986, 901, 883, 835;

HRMS (ESI+) calcd for C₁₃H₁₄F₃⁺ [*M* + H⁺]: 227.1048; found: 227.1040;

[α]²³_D (589 nm) = -2.5 (c=1.0 in CH₂Cl₂, 77% ee)

GC analysis of **17g** indicated an enantiomeric excess of 77% (Restek Rt-βDEXse, 50 °C for 1 min, 50–130 °C at 1 °C /min, Helium, column flow rate: 1 mL/min); major enantiomer *t*_R = 73.6 min; minor enantiomer *t*_R = 75.1 min.

Appendix

I. NMR Spectra

I.1 The NMR spectra of isolated allylic boronates.

4a:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

¹¹B-NMR (128 MHz, CDCl₃):

BPIn

1H NMR spectrum of compound 10. The x-axis is chemical shift (ppm) from 0 to 10. The spectrum shows a broad peak at ~7.2 ppm (1H), a multiplet at ~5.7 ppm (1H), a multiplet at ~5.2 ppm (1H), a multiplet at ~2.0 ppm (1H), and a sharp peak at ~1.2 ppm (12H). Integration values are shown below the peaks: 1.00, 1.00, 1.00, 1.00, and 12.00.

¹¹B-NMR (128 MHz, CDCl₃):

4c:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

4d:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

4e:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

4f:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

¹¹B-NMR (128 MHz, CDCl₃):

4h:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

4i:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

4j:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

^{11}B -NMR (128 MHz, CDCl_3):

5b:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

5c:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

5d:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

¹¹B-NMR (128 MHz, CDCl₃):

5e:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

¹H NMR spectrum (CDCl₃) of compound 10a. The x-axis represents the chemical shift in ppm, ranging from 0.0 to 10.0. The spectrum shows several peaks corresponding to the protons in the molecule. Integration values are provided below the baseline for specific peak regions.

Chemical Shift (ppm)	Integration
~1.2	12.13
~1.4	12.11
~3.3	3.00
~4.8	1.98
~5.6	1.98

¹¹B-NMR (128 MHz, CDCl₃):

Chemical shifts (ppm): 7.2602, 7.2380, 7.2271, 7.2164, 7.1860, 7.1775, 7.1745, 7.1642, 7.1570, 7.1525, 5.6923, 5.6845, 5.6779, 5.6741, 5.6712, 5.6679, 2.8014, 2.7688, 2.7193, 2.6869, 1.9568, 1.9523, 1.9484, 1.9438, 1.9390, 1.9356, 1.9306, 1.9226, 1.9192, 1.9167, 1.8383, 1.8296, 1.8220, 1.6821, 1.6741, 1.6699, 1.6660, 1.6180, 1.6006, 1.5923, 1.5739, 1.4046, 1.3965, 1.3777, 1.3727, 1.3695, 1.3649, 1.2111, 1.2046.

^{11}B -NMR (128 MHz, CDCl_3):

5h:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

5i:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

5j:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

6f:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

GYC11277 B11 (BBF01) dissolved in CDCl₃ at 10:47 on Jun 01

— 32.86

```

NAME      GYC11277 B11
EXPNO     1
PROCNO    1
Date_     20170601
Time      10.53
INSTRUM   spect
PROBHD    5 mm PABBO BB-
PULPROG   zg
TD         65536
SOLVENT   CDCl3
NS         128
DS         4
SWH        25510.203 Hz
FIDRES     0.389255 Hz
AQ         1.2845586 sec
RG         203
DW         19.600 usec
DE         6.50 usec
TE         296.9 K
D1         1.00000000 sec
TDO        1
===== CHANNEL f1 =====
NUC1      11B
P1         11.00 usec
PL1        0.00 dB
PL1W       31.90095711 W
SF01      128.3776052 MHz
SI         32768
SF         128.3776050 MHz
WDW        EM
SSB        0
LB         1.00 Hz
GB         0
PC         1.40
  
```

6g:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

6h:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

¹¹B-NMR (128 MHz, CDCl₃):

6i:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

7a:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

¹¹B-NMR (128 MHz, CDCl₃):

I.2 The NMR spectra of isolated allylic halides.

1-4a':

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4c:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4d:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4e:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4f:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4h:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4i:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-4j:

¹H-NMR (300 MHz, CDCl₃):

¹³C-NMR (75 MHz, CDCl₃):

1-5a:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-5b:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-5c:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-5e:

^1H -NMR (400 MHz, CDCl_3):

¹³C-NMR (100 MHz, CDCl₃):

1-5f:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

$^{13}\text{C-NMR}$ (100 MHz, CDCl_3):

1-5g:

¹H-NMR (400 MHz, CDCl₃):

^{13}C -NMR (100 MHz, CDCl_3):

1-5h:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

1-5j:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-6e:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-6f:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-6g:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

1-6h:

¹H-NMR (400 MHz, CDCl₃):

^{13}C -NMR (100 MHz, CDCl_3):

18-5c:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

18-5d:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

18-5e:

¹H-NMR (400 MHz, CDCl₃):

^{13}C -NMR (100 MHz, CDCl_3):

18-5f:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

18-5g:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

18-5h:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

18-5i:

$^1\text{H-NMR}$ (400 MHz, CDCl_3):

¹³C-NMR (100 MHz, CDCl₃):

18-5j:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

I.4 The NMR spectra of functionalization products.

17a:

^1H -NMR (400 MHz, CDCl_3):

¹³C-NMR (100 MHz, CDCl₃):

17b:

^1H -NMR (400 MHz, CDCl_3):

¹³C-NMR (100 MHz, CDCl₃):

17c:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

17e:

^1H -NMR (400 MHz, CDCl_3):

^{13}C -NMR (100 MHz, CDCl_3):

^{11}B -NMR (128 MHz, CDCl_3):

17f:

^1H -NMR (400 MHz, CDCl_3):

¹³C-NMR (100 MHz, CDCl₃):

17g:

¹H-NMR (400 MHz, CDCl₃):

¹³C-NMR (100 MHz, CDCl₃):

¹⁹F-NMR (376 MHz, CDCl₃):

II. GCMS/HPLC Resolution Chromatographic Spectra for Chiral Compounds

Compound **4a**:

Racemic:

Chiral: 96.6% ee

Compound **4a'**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	61.180	60.925	61.520	MIC1	12853192	49.88	1189368	50.78	10.81	MI
2	61.776	61.520	62.505	MIC1	12914904	50.12	1152776	49.22	11.20	MI

Chiral: 86.0% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	60.266	60.070	60.575	TIC	2325462	7.02	229863	7.56	10.12	MI
2	60.836	60.595	61.550	TIC	30821152	92.98	2808911	92.44	10.97	MI

Compound **4d**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	87.069	86.835	87.460	MIC1	678859	49.77	66823	50.58	10.16	MI
2	87.895	87.650	88.355	MIC1	685103	50.23	65291	49.42	10.49	MI

Chiral: 91.4 % ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	86.271	85.740	86.725	TIC	52775045	95.69	3579352	95.75	14.74	MI
2	86.965	86.725	87.280	TIC	2377017	4.31	158811	4.25	14.97	MI

Compound **4e**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	70.407	70.125	70.640	TIC	20850258	48.95	1944996	50.81	10.72	MI
2	70.876	70.640	71.890	TIC	21743479	51.05	1882993	49.19	11.55	MI

Chiral: 96.6% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	70.409	70.250	70.605	TIC	823294	1.70	77447	1.88	10.63	MI
2	70.928	70.605	71.565	TIC	47509615	98.30	4046765	98.12	11.74	MI

Compound **4f**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	81.160	80.635	82.055	TIC	24439795	49.67	978595	52.32	24.97	MI
2	82.601	82.055	84.000	TIC	24762983	50.33	891786	47.68	27.77	MI

Chiral: 78.2% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	81.174	80.740	81.940	MIC1	2228170	10.91	96511	12.83	23.09	MI
2	82.570	81.940	84.265	MIC1	18191643	89.09	655629	87.17	27.75	MI

Compound **4h**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	66.835	66.605	67.280	MIC1	2211582	48.96	218011	49.50	10.14	MI
2	68.408	68.165	68.880	MIC1	2305253	51.04	222406	50.50	10.37	MI

Chiral: 45.3% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	63.848	63.735	64.135	MIC1	13352277	27.35	3096025	27.19	4.31	MI
2	64.369	64.245	65.115	MIC1	35473231	72.65	8290151	72.81	4.28	MI

Compound **4j**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	159.614	157.660	160.510	TIC	58160135	49.82	929806	49.19	62.55	MI
2	162.235	160.510	163.260	TIC	58584692	50.18	960586	50.81	60.99	MI

Chiral: 4.5% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	156.279	154.345	157.120	TIC	67066886	47.76	1098978	47.44	61.03	MI
2	158.668	157.120	160.710	TIC	73366415	52.24	1217457	52.56	60.26	MI

Compound **5b**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	24.489	24.360	25.360	TIC	5466889	50.31	301150	51.62	18.15	MI
2	26.060	25.940	26.950	TIC	5398920	49.69	282301	48.38	19.12	MI

Chiral: 98.8% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	24.524	24.395	24.825	MIC1	66791	0.61	5668	1.44	11.78	MI
2	25.631	25.500	27.175	MIC1	10835205	99.39	389185	98.56	27.84	MI

Compound **5c**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	29.871	29.640	31.100	TIC	10964259	50.52	416510	51.18	26.32	MI
2	31.350	31.175	32.730	TIC	10738433	49.48	397242	48.82	27.03	MI

Chiral: 94.8% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	30.076	29.945	30.605	TIC	1598518	2.62	118178	9.27	13.53	MI
2	30.753	30.620	33.265	TIC	59511381	97.38	1156873	90.73	51.44	MI

Compound **5d**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	54.315	53.800	55.055	MIC1	2787493	47.87	76573	53.43	36.40	MI
2	55.528	55.055	57.390	MIC1	3035322	52.13	66733	46.57	45.48	MI

Chiral: 77.7% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	54.156	53.800	54.645	MIC1	647786	11.17	24000	19.51	26.99	MI
2	54.949	54.645	58.165	MIC1	5153391	88.83	98999	80.49	52.05	MI

Compound **5e**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	51.515	51.250	52.495	TIC	10229306	49.84	409855	50.18	24.96	MI
2	52.875	52.665	54.275	TIC	10293992	50.16	406876	49.82	25.30	MI

Chiral: 94.9% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	51.783	51.540	52.280	TIC	855985	2.56	47419	4.51	18.05	MI
2	52.731	52.570	54.680	TIC	32550657	97.44	1004593	95.49	32.40	MI

Compound **5f**:

Racemic:

Chiral: 93.7% ee

Compound **5g**:

Racemic:

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.950	16259	539511	0.000	49.841
2	13.057	16363	498402	0.000	50.159
Total		32622	1037913	0.000	100.000

Chiral: 96.1% ee

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.673	28518	11329	0.000	1.958
2	12.757	14283	459210	0.000	98.042
Total		14568	470539	0.000	100.000

Compound **5h**:

Racemic:

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.398	48680	1671157	0.000	48.621
2	12.954	51442	1416881	0.000	51.379
Total		10012	3088038	0.000	100.000

Chiral: 96.4% ee

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	11.413	32726	16679	0.000	1.776
2	12.802	18098	563205	0.000	98.224
Total		18425	579884	0.000	100.000

Compound **5i**:

Racemic:

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.606	81785	373509	0.000	49.413
2	10.968	83728	334479	0.000	50.587
Total		16551	707989	0.000	100.000

Chiral: 93.1% ee

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	9.325	23434	99149	0.000	3.432
2	10.642	65938	2890285	0.000	96.568
Total		68282	2989435	0.000	100.000

Compound **5j**:

Racemic:

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	18.214	25141	633508	47.645	47.645
2	19.780	27627	591747	52.355	52.355
Total		52768	1225255	100.000	100.000

Chiral: 96.4% ee

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	17.880	68037	23667	1.776	1.776
2	19.381	37638	1017159	98.224	98.224
Total		38319	1040826	100.000	100.000

Compound 7a:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	63.729	63.255	64.055	TIC	10708869	48.89	447308	42.49	23.94	MI
2	64.331	64.055	65.035	TIC	11196023	51.11	605546	57.51	18.49	MI

Chiral: 91.8% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	64.473	64.110	64.635	TIC	1058518	4.80	57348	4.09	18.46	MI
2	65.095	64.760	65.895	TIC	21013046	95.20	1346180	95.91	15.61	MI

Compound **17a**:

Racemic:

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	39.434	30374	65176	0.000	25.358
2	40.811	29062	59048	0.000	24.263
3	42.768	29823	54620	0.000	24.898
4	67.885	30520	28412	0.000	25.481
Total		11978	207255	0.000	100.000

Chiral: 88.7% ee, d.r.>99:1

Peak#	Ret. Time	Area	Height	Conc.	Area%
1	38.440	44389	83284	0.000	5.576
2	41.575	50636	9502	0.000	0.636
3	43.039	20841	4262	0.000	0.262
4	66.472	74455	662758	0.000	93.526
Total		79608	759807	0.000	100.000

Compound 17b:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	18.976	18.820	19.850	MIC1	5492160	49.93	387346	52.68	14.18	MI
2	20.264	20.115	21.315	MIC1	5506619	50.07	347907	47.32	15.83	MI

Chiral: 96.9% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	18.580	18.480	18.920	MIC1	668498	1.57	88814	8.09	7.53	MI
2	19.188	19.115	22.245	MIC1	41819588	98.43	1009185	91.91	41.44	MI

Compound **17d**:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	71.227	71.065	71.705	TIC	5223780	50.20	387402	50.61	13.48	MI
2	73.084	72.960	73.620	TIC	5181365	49.80	378065	49.39	13.70	MI

Chiral: 96.6% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	71.120	71.000	71.875	TIC	17086329	98.29	962701	97.24	17.75	MI
2	73.360	73.230	73.620	TIC	297740	1.71	27344	2.76	10.89	MI

Compound 17e:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	82.475	82.115	82.930	TIC	3898819	49.27	162866	53.30	23.94	MI
2	83.285	82.930	83.960	TIC	4013865	50.73	142718	46.70	28.12	MI

Chiral: 98.1% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	82.429	82.200	82.545	TIC	399461	0.96	31315	3.11	12.76	MI
2	82.783	82.545	85.235	TIC	41412546	99.04	976864	96.89	42.39	MI

Compound 17f:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	77.160	76.905	77.995	MIC1	14771270	49.95	1430253	51.50	10.33	MI
2	78.470	78.235	79.420	MIC1	14803132	50.05	1346685	48.50	10.99	MI

Chiral: 97.8% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	77.678	77.420	78.470	TIC	27746186	98.89	2655704	98.76	10.45	MI
2	79.056	78.940	79.245	TIC	312660	1.11	33215	1.24	9.41	MI

Compound 17g:

Racemic:

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	73.430	73.230	74.040	MIC1	4122294	50.30	320781	51.31	12.85	MI
2	74.768	74.555	75.360	MIC1	4073281	49.70	304380	48.69	13.38	MI

Chiral: 77.3% ee

Peak#	Ret. Time	Start Tm	End Tm	m/z	Area	Area%	Height	Height%	A/H	Mark
1	73.557	73.415	74.380	TIC	17313700	88.63	1364164	84.61	12.69	MI
2	75.079	74.920	75.345	TIC	2221690	11.37	248050	15.39	8.96	MI

III. X-Ray Crystallographic Structures and Information

III.1 The X-ray analysis of complex 11:

A yellow needle-like specimen of $\text{C}_{26}\text{H}_{48}\text{Cl}_4\text{CuN}_6$, approximate dimensions 0.020 mm x 0.060 mm x 0.280 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 0.88 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a tetragonal unit cell yielded a total of 15647 reflections to a maximum θ angle of 66.40° ($0.84 \text{ \AA}$ resolution), of which 2877 were independent (average redundancy 5.439, completeness = 99.9%, $R_{\text{int}} = 8.09\%$, $R_{\text{sig}} = 6.00\%$) and 2709 (94.16%) were greater than $2\sigma(F_2)$. The final cell constants of $a = 13.4859(13) \text{ \AA}$, $b = 13.4859(13) \text{ \AA}$, $c = 9.1493(10) \text{ \AA}$, volume = $1664.0(4) \text{ \AA}^3$, are based upon the refinement of the XYZ-centroids of 7972 reflections above $20 \sigma(I)$ with $6.554^\circ < 2\theta < 132.4^\circ$. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.370. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.3960 and 0.9230.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P 4_2$, with $Z = 2$ for the formula unit, $\text{C}_{26}\text{H}_{48}\text{Cl}_4\text{CuN}_6$. The final anisotropic full-matrix least-squares refinement on F_2 with 175 variables converged at $R_1 = 5.02\%$, for the observed data and $wR_2 = 13.81\%$ for all data. The goodness-of-fit was 1.047. The largest peak in the final difference electron density synthesis was $0.925 \text{ e}/\text{\AA}^3$ and the largest hole was $-0.530 \text{ e}/\text{\AA}^3$ with an RMS deviation of $0.088 \text{ e}/\text{\AA}^3$. On the basis of the final model, the calculated density was 1.297 g/cm^3 and $F(000)$, 686 e-.

Figure SIII.1 ORTEP drawing of complex **11** with thermal ellipsoids at 50% probability levels.

Table SIII.1 Sample and crystal data for complex **11**.

Identification code	tch95s	
Chemical formula	$\text{C}_{26}\text{H}_{48}\text{Cl}_4\text{CuN}_6$	
Formula weight	650.04 g/mol	
Temperature	103(2) K	
Wavelength	1.54178 Å	
Crystal size	0.020 x 0.060 x 0.280 mm	
Crystal habit	yellow needle	
Crystal system	tetragonal	
Space group	P 42	
Unit cell dimensions	$a = 13.4859(13)$ Å	$\alpha = 90^\circ$
	$b = 13.4859(13)$ Å	$\beta = 90^\circ$
	$c = 9.1493(10)$ Å	$\gamma = 90^\circ$
Volume	$1664.0(4)$ Å ³	
Z	2	

Density (calculated)	1.297 g/cm ³
Absorption coefficient	4.067 mm ⁻¹
F(000)	686

Table SIII.2 Data collection and structure refinement for complex **11**.

Theta range for data collection	3.28 to 66.40°
Index ranges	-16≤h≤16, -16≤k≤14, -10≤l≤10
Reflections collected	15647
Independent reflections	2877 [R(int) = 0.0809]
Coverage of independent reflections	99.9%
Absorption correction	Multi-Scan
Max. and min. transmission	0.9230 and 0.3960
Structure solution technique	direct methods
Structure solution program	XS, VERSION 2013/1
Refinement method	Full-matrix least-squares on F ²
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	Σ w(F _o ² - F _c ²) ²
Data / restraints / parameters	2877 / 1 / 175
Goodness-of-fit on F ²	1.047
Final R indices	2709 data; I>2σ(I) R1 = 0.0502, wR2 = 0.1357 all data R1 = 0.0522, wR2 = 0.1381
Weighting scheme	w=1/[σ ² (F _o ²)+(0.0970P) ² +0.3537P] where P=(F _o ² +2F _c ²)/3
Absolute structure parameter	0.05(3)
Largest diff. peak and hole	0.925 and -0.530 eÅ ⁻³
R.M.S. deviation from mean	0.088 eÅ ⁻³

Table SIII.3 Atomic coordinates and equivalent isotropic atomic displacement parameters (Å²) for complex **11**.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.2630(4)	0.8368(4)	0.7283(6)	0.0258(10)

	x/a	y/b	z/c	U(eq)
C2	0.2387(4)	0.7250(4)	0.7065(6)	0.0258(11)
C3	0.2077(4)	0.0089(4)	0.7841(7)	0.0339(12)
C4	0.1757(4)	0.9003(4)	0.7810(6)	0.0284(11)
C5	0.1491(5)	0.8695(4)	0.9369(7)	0.0424(16)
C6	0.0867(5)	0.8872(5)	0.6809(10)	0.0499(18)
C7	0.2554(4)	0.6804(4)	0.3011(7)	0.0291(10)
C8	0.3341(4)	0.6226(4)	0.2133(6)	0.0279(11)
C9	0.2281(5)	0.6331(4)	0.4514(6)	0.0319(12)
C10	0.2970(4)	0.5170(4)	0.1914(7)	0.0340(12)
C11	0.3457(5)	0.6726(4)	0.0633(6)	0.0358(12)
C12	0.4344(4)	0.6234(5)	0.2907(8)	0.0418(13)
C13	0.2736(4)	0.7942(4)	0.4854(6)	0.0286(11)
Cl1	0.60099(9)	0.93095(9)	0.47260(17)	0.0354(4)
Cl2	0.38406(13)	0.95295(13)	0.14316(17)	0.0530(5)
Cu1	0.5	0.0	0.30506(14)	0.0288(3)
N1	0.2267(3)	0.7187(3)	0.5484(5)	0.0270(9)
N2	0.2977(4)	0.8645(3)	0.5793(6)	0.0334(10)
N3	0.2887(4)	0.7811(3)	0.3445(5)	0.0356(12)

Table SIII.4 Bond lengths (Å) for complex **11**.

C1-N2	1.488(7)	C1-C4	1.533(7)
C1-C2	1.556(7)	C2-N1	1.458(7)
C3-C4	1.527(7)	C4-C6	1.521(8)
C4-C5	1.529(8)	C7-N3	1.485(7)
C7-C8	1.543(7)	C7-C9	1.560(8)
C8-C10	1.522(8)	C8-C12	1.526(8)
C8-C11	1.537(8)	C9-N1	1.456(7)
C13-N3	1.317(8)	C13-N2	1.320(8)
C13-N1	1.330(7)	Cl1-Cu1	2.2520(16)
Cl2-Cu1	2.2453(17)	Cu1-Cl2	2.2453(17)
Cu1-Cl1	2.2519(16)		

Table SIII.5 Bond angles (°) for complex **11**.

N2-C1-C4	112.9(4)	N2-C1-C2	101.1(4)
C4-C1-C2	114.8(4)	N1-C2-C1	101.9(4)
C6-C4-C3	110.2(5)	C6-C4-C5	110.2(5)
C3-C4-C5	108.0(5)	C6-C4-C1	110.6(5)

C3-C4-C1	109.0(5)	C5-C4-C1	108.8(5)
N3-C7-C8	113.2(4)	N3-C7-C9	102.1(4)
C8-C7-C9	114.6(4)	C10-C8-C12	111.0(5)
C10-C8-C11	109.0(5)	C12-C8-C11	108.7(5)
C10-C8-C7	108.4(4)	C12-C8-C7	111.3(5)
C11-C8-C7	108.3(4)	N1-C9-C7	102.5(4)
N3-C13-N2	134.1(5)	N3-C13-N1	113.3(5)
N2-C13-N1	112.6(5)	Cl2-Cu1-Cl2	97.44(10)
Cl2-Cu1-Cl1	98.33(6)	Cl2-Cu1-Cl1	138.88(5)
Cl2-Cu1-Cl1	138.88(5)	Cl2-Cu1-Cl1	98.32(6)
Cl1-Cu1-Cl1	94.21(8)	C13-N1-C9	109.7(4)
C13-N1-C2	109.5(5)	C9-N1-C2	130.5(5)
C13-N2-C1	109.8(4)	C13-N3-C7	109.7(5)

Table SIII.6 Anisotropic atomic displacement parameters ($\text{\AA}^2$) for complex **11**.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.032(3)	0.026(3)	0.020(2)	-0.001(2)	-0.001(2)	0.003(2)
C2	0.031(3)	0.025(2)	0.022(3)	0.0000(19)	0.0049(19)	0.0051(19)
C3	0.047(3)	0.026(2)	0.029(3)	-0.003(2)	-0.004(2)	0.002(2)
C4	0.029(2)	0.025(2)	0.031(3)	-0.006(2)	-0.002(2)	0.0018(19)
C5	0.053(4)	0.031(3)	0.043(4)	-0.013(3)	0.026(3)	-0.009(3)
C6	0.035(3)	0.038(3)	0.076(5)	-0.027(3)	-0.022(3)	0.012(2)
C7	0.041(3)	0.027(2)	0.019(2)	0.002(2)	-0.003(2)	0.003(2)
C8	0.030(3)	0.033(3)	0.021(3)	-0.001(2)	-0.002(2)	0.007(2)
C9	0.048(3)	0.026(2)	0.022(3)	-0.002(2)	0.007(2)	0.003(2)
C10	0.042(3)	0.034(3)	0.025(3)	-0.003(2)	0.001(2)	0.010(2)
C11	0.042(3)	0.044(3)	0.022(3)	-0.001(2)	0.007(2)	0.001(2)
C12	0.037(3)	0.054(3)	0.035(3)	-0.006(3)	-0.006(3)	0.005(2)
C13	0.034(3)	0.029(2)	0.022(3)	0.000(2)	0.005(2)	0.007(2)
Cl1	0.0319(6)	0.0317(6)	0.0425(8)	-0.0032(6)	-0.0051(5)	0.0047(5)
Cl2	0.0728(11)	0.0544(9)	0.0319(8)	0.0125(7)	-0.0198(7)	-0.0325(8)
Cu1	0.0347(6)	0.0290(5)	0.0228(6)	0	0	-0.0065(4)
N1	0.034(2)	0.026(2)	0.021(2)	0.0009(16)	0.0031(17)	-0.0013(17)
N2	0.041(3)	0.030(2)	0.028(2)	-0.0022(18)	0.009(2)	-0.0018(19)
N3	0.053(3)	0.028(2)	0.026(3)	0.0021(17)	0.0074(19)	0.001(2)

Table SIII.7 Hydrogen atomic coordinates and isotropic atomic displacement parameters ($\text{\AA}^2$) for complex **11**.

	x/a	y/b	z/c	U(eq)
H1	0.3193	0.8435	0.7987	0.031
H2A	0.2937	0.6823	0.7409	0.031
H2B	0.1769	0.7062	0.7580	0.031
H3A	0.1532	1.0497	0.8215	0.051
H3B	0.2248	1.0304	0.6849	0.051
H3C	0.2656	1.0162	0.8478	0.051
H5A	0.1295	0.7995	0.9379	0.064
H5B	0.0940	0.9104	0.9723	0.064
H5C	0.2068	0.8789	1.0006	0.064
H6A	0.0630	0.8186	0.6870	0.075
H6B	0.1060	0.9020	0.5800	0.075
H6C	0.0337	0.9324	0.7112	0.075
H7	0.1939	0.6864	0.2408	0.035
H9A	0.1624	0.6005	0.4477	0.038
H9B	0.2786	0.5842	0.4825	0.038
H10A	0.3451	0.4799	0.1327	0.051
H10B	0.2330	0.5185	0.1406	0.051
H10C	0.2890	0.4848	0.2867	0.051
H11A	0.3697	0.7406	0.0766	0.054
H11B	0.2814	0.6739	0.0134	0.054
H11C	0.3934	0.6352	0.0042	0.054
H12A	0.4294	0.5860	0.3822	0.063
H12B	0.4536	0.6919	0.3120	0.063
H12C	0.4844	0.5927	0.2275	0.063

III.2 The X-ray analysis of complex **12**:

A yellow needle-like specimen of $\text{C}_{52}\text{H}_{100}\text{Cl}_4\text{Cu}_4\text{N}_{12}$, approximate dimensions 0.060 mm x 0.080 mm x 0.340 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 0.32 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 12359 reflections to a maximum θ angle of 66.63° ($0.84 \text{ \AA}$ resolution), of which 5201 were independent (average redundancy 2.376,

completeness = 98.2%, R_{int} = 3.61%, R_{sig} = 4.63%) and 5046 (97.02%) were greater than $2\sigma(F_2)$. The final cell constants of $a = 22.1473(2)$ Å, $b = 6.19645(6)$ Å, $c = 22.9433(2)$ Å, $\beta = 92.9914(5)^\circ$, volume = $3144.33(5)$ Å³, are based upon the refinement of the XYZ-centroids of 9976 reflections above $20\sigma(I)$ with $8.695^\circ < 2\theta < 133.2^\circ$. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.572. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.3900 and 0.8210.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $C 1 2 1$, with $Z = 2$ for the formula unit, $C_{52}H_{100}Cl_4Cu_4N_{12}$. The final anisotropic full-matrix least-squares refinement on F_2 with 338 variables converged at $R_1 = 2.95\%$, for the observed data and $wR_2 = 7.73\%$ for all data. The goodness-of-fit was 1.034. The largest peak in the final difference electron density synthesis was 0.552 e-/Å³ and the largest hole was -0.536 e-/Å³ with an RMS deviation of 0.060 e-/Å³. On the basis of the final model, the calculated density was 1.362 g/cm³ and $F(000)$, 1360 e-.

Figure SIII.2 ORTEP drawing of complex **12** with thermal ellipsoids at 50% probability levels.

Table SIII.8 Sample and crystal data for complex **12**.

Identification code	tch91s	
Chemical formula	C ₅₂ H ₁₀₀ Cl ₄ Cu ₄ N ₁₂	
Formula weight	1289.39 g/mol	
Temperature	133(2) K	
Wavelength	1.54178 Å	
Crystal size	0.060 x 0.080 x 0.340 mm	
Crystal habit	yellow needle	
Crystal system	monoclinic	
Space group	C 1 2 1	
Unit cell dimensions	a = 22.1473(2) Å	$\alpha = 90^\circ$
	b = 6.19645(6) Å	$\beta = 92.9914(5)^\circ$
	c = 22.9433(2) Å	$\gamma = 90^\circ$
Volume	3144.33(5) Å ³	
Z	2	
Density (calculated)	1.362 g/cm ³	
Absorption coefficient	3.413 mm ⁻¹	
F(000)	1360	

Table SIII.9 Data collection and structure refinement for complex **12**.

Theta range for data collection	4.35 to 66.63°
Index ranges	-25 ≤ h ≤ 26, -7 ≤ k ≤ 6, -21 ≤ l ≤ 27
Reflections collected	12359
Independent reflections	5201 [R(int) = 0.0361]
Coverage of independent reflections	98.2%
Absorption correction	Multi-Scan
Max. and min. transmission	0.8210 and 0.3900
Structure solution technique	direct methods
Structure solution program	XT, VERSION 2014/5
Refinement method	Full-matrix least-squares on F ²
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)
Function minimized	$\sum w(F_o^2 - F_c^2)^2$
Data / restraints / parameters	5201 / 1 / 338
Goodness-of-fit on F²	1.034

$\Delta/\sigma_{\max}$	0.001
Final R indices	5046 data; $I > 2\sigma(I)$ $R1 = 0.0295$, $wR2 = 0.0766$ all data $R1 = 0.0305$, $wR2 = 0.0773$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0444P)^2 + 0.3773P]$ where $P = (F_o^2 + 2F_c^2)/3$
Absolute structure parameter	0.012(9)
Largest diff. peak and hole	0.552 and -0.536 $e\text{\AA}^{-3}$
R.M.S. deviation from mean	0.060 $e\text{\AA}^{-3}$

Table SIII.10 Atomic coordinates and equivalent isotropic atomic displacement parameters ($\text{\AA}^2$) for complex **12**.

U(eq) is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.67374(15)	0.5559(6)	0.08986(15)	0.0209(7)
C2	0.69476(17)	0.7064(7)	0.04244(18)	0.0328(9)
C3	0.71094(17)	0.3483(7)	0.08723(18)	0.0325(10)
C4	0.68432(16)	0.6645(7)	0.14928(16)	0.0318(9)
C5	0.60636(15)	0.4970(6)	0.07691(14)	0.0179(7)
C6	0.57887(16)	0.3429(5)	0.12164(15)	0.0199(7)
C7	0.53228(14)	0.6664(6)	0.12177(13)	0.0167(7)
C8	0.48955(14)	0.4393(6)	0.18701(15)	0.0211(8)
C9	0.45995(14)	0.6650(6)	0.19038(14)	0.0182(7)
C10	0.39031(15)	0.6673(6)	0.18950(14)	0.0201(7)
C11	0.36168(16)	0.5716(7)	0.13356(18)	0.0300(9)
C12	0.36915(16)	0.9012(7)	0.19612(15)	0.0273(7)
C13	0.37170(17)	0.5365(7)	0.24225(17)	0.0310(9)
C14	0.36288(14)	0.1032(6)	0.40154(14)	0.0195(7)
C15	0.42205(15)	0.1042(7)	0.36955(14)	0.0251(8)
C16	0.31246(17)	0.1938(7)	0.36000(15)	0.0288(9)
C17	0.34717(16)	0.8732(7)	0.41916(15)	0.0263(8)
C18	0.37081(14)	0.2523(6)	0.45571(14)	0.0173(7)
C19	0.31350(15)	0.2867(6)	0.49125(15)	0.0219(7)
C20	0.38584(14)	0.1097(6)	0.54517(14)	0.0171(7)
C21	0.30192(14)	0.1495(6)	0.59805(14)	0.0210(7)
C22	0.35018(15)	0.0199(6)	0.63447(14)	0.0188(7)
C23	0.36242(15)	0.0982(6)	0.69722(14)	0.0203(7)
C24	0.38146(18)	0.3355(6)	0.69993(16)	0.0279(9)
C25	0.41237(17)	0.9606(6)	0.72654(16)	0.0268(8)

	x/a	y/b	z/c	U(eq)
C26	0.30386(17)	0.0687(7)	0.72931(16)	0.0305(9)
Cl1	0.57253(4)	0.12638(15)	0.95095(3)	0.0286(2)
Cl2	0.51232(5)	0.61647(16)	0.40921(5)	0.0398(2)
Cu1	0.56107(2)	0.89815(8)	0.01817(2)	0.02102(14)
Cu2	0.5	0.16645(11)	0.5	0.01876(18)
Cu3	0.5	0.62473(13)	0.5	0.0341(2)
N1	0.56512(12)	0.6890(5)	0.07689(12)	0.0189(6)
N2	0.54497(12)	0.4913(5)	0.15682(12)	0.0170(6)
N3	0.48570(13)	0.7787(5)	0.14113(12)	0.0205(6)
N4	0.41575(12)	0.1641(5)	0.50004(11)	0.0172(6)
N5	0.32467(11)	0.1383(5)	0.53954(11)	0.0187(6)
N6	0.40360(12)	0.0414(5)	0.59885(12)	0.0202(6)

Table SIII.11 Bond lengths (Å) for complex **12**.

C1-C2	1.524(5)	C1-C4	1.527(5)
C1-C3	1.530(5)	C1-C5	1.550(5)
C2-H2A	0.98	C2-H2B	0.98
C2-H2C	0.98	C3-H3A	0.98
C3-H3B	0.98	C3-H3C	0.98
C4-H4A	0.98	C4-H4B	0.98
C4-H4C	0.98	C5-N1	1.500(4)
C5-C6	1.549(5)	C5-H5	1.0
C6-N2	1.457(4)	C6-H6A	0.99
C6-H6B	0.99	C7-N1	1.299(4)
C7-N3	1.339(4)	C7-N2	1.371(4)
C8-N2	1.476(4)	C8-C9	1.548(5)
C8-H8A	0.99	C8-H8B	0.99
C9-N3	1.471(4)	C9-C10	1.542(4)
C9-H9	1.0	C10-C11	1.522(5)
C10-C13	1.531(5)	C10-C12	1.533(6)
C11-H11A	0.98	C11-H11B	0.98
C11-H11C	0.98	C12-H12A	0.98
C12-H12B	0.98	C12-H12C	0.98
C13-H13A	0.98	C13-H13B	0.98
C13-H13C	0.98	C14-C17	1.526(6)
C14-C15	1.535(5)	C14-C16	1.536(5)
C14-C18	1.551(5)	C15-H15A	0.98

C15-H15B	0.98	C15-H15C	0.98
C16-H16A	0.98	C16-H16B	0.98
C16-H16C	0.98	C17-H17A	0.98
C17-H17B	0.98	C17-H17C	0.98
C18-N4	1.490(4)	C18-C19	1.559(5)
C18-H18	1.0	C19-N5	1.451(5)
C19-H19A	0.99	C19-H19B	0.99
C20-N4	1.302(4)	C20-N6	1.342(4)
C20-N5	1.366(4)	C21-N5	1.460(4)
C21-C22	1.547(5)	C21-H21A	0.99
C21-H21B	0.99	C22-N6	1.479(4)
C22-C23	1.530(5)	C22-H22	1.0
C23-C25	1.525(5)	C23-C24	1.530(5)
C23-C26	1.535(5)	C24-H24A	0.98
C24-H24B	0.98	C24-H24C	0.98
C25-H25A	0.98	C25-H25B	0.98
C25-H25C	0.98	C26-H26A	0.98
C26-H26B	0.98	C26-H26C	0.98
Cl1-Cu1	2.1174(9)	Cl2-Cu3	2.1156(11)
Cu1-N1	1.868(3)	Cu1-Cu1	2.7889(9)
Cu2-N4	1.866(3)	Cu2-N4	1.866(3)
Cu2-Cu3	2.8397(10)	Cu3-Cl2	2.1155(11)
N3-H3	0.88	N6-H6	0.88

Table SIII.12 Bond angles (°) for complex **12**.

C2-C1-C4	109.2(3)	C2-C1-C3	107.5(3)
C4-C1-C3	110.3(3)	C2-C1-C5	109.5(3)
C4-C1-C5	112.1(3)	C3-C1-C5	108.0(3)
C1-C2-H2A	109.5	C1-C2-H2B	109.5
H2A-C2-H2B	109.5	C1-C2-H2C	109.5
H2A-C2-H2C	109.5	H2B-C2-H2C	109.5
C1-C3-H3A	109.5	C1-C3-H3B	109.5
H3A-C3-H3B	109.5	C1-C3-H3C	109.5
H3A-C3-H3C	109.5	H3B-C3-H3C	109.5
C1-C4-H4A	109.5	C1-C4-H4B	109.5
H4A-C4-H4B	109.5	C1-C4-H4C	109.5
H4A-C4-H4C	109.5	H4B-C4-H4C	109.5
N1-C5-C6	103.2(2)	N1-C5-C1	113.2(3)

C6-C5-C1	115.2(3)	N1-C5-H5	108.3
C6-C5-H5	108.3	C1-C5-H5	108.3
N2-C6-C5	102.1(2)	N2-C6-H6A	111.3
C5-C6-H6A	111.3	N2-C6-H6B	111.3
C5-C6-H6B	111.3	H6A-C6-H6B	109.2
N1-C7-N3	132.8(3)	N1-C7-N2	116.4(3)
N3-C7-N2	110.8(3)	N2-C8-C9	101.0(3)
N2-C8-H8A	111.6	C9-C8-H8A	111.6
N2-C8-H8B	111.6	C9-C8-H8B	111.6
H8A-C8-H8B	109.4	N3-C9-C10	114.4(3)
N3-C9-C8	102.2(2)	C10-C9-C8	115.7(3)
N3-C9-H9	108.0	C10-C9-H9	108.0
C8-C9-H9	108.0	C11-C10-C13	110.0(3)
C11-C10-C12	109.6(3)	C13-C10-C12	109.0(3)
C11-C10-C9	112.3(3)	C13-C10-C9	107.2(3)
C12-C10-C9	108.6(3)	C10-C11-H11A	109.5
C10-C11-H11B	109.5	H11A-C11-H11B	109.5
C10-C11-H11C	109.5	H11A-C11-H11C	109.5
H11B-C11-H11C	109.5	C10-C12-H12A	109.5
C10-C12-H12B	109.5	H12A-C12-H12B	109.5
C10-C12-H12C	109.5	H12A-C12-H12C	109.5
H12B-C12-H12C	109.5	C10-C13-H13A	109.5
C10-C13-H13B	109.5	H13A-C13-H13B	109.5
C10-C13-H13C	109.5	H13A-C13-H13C	109.5
H13B-C13-H13C	109.5	C17-C14-C15	110.0(3)
C17-C14-C16	109.7(3)	C15-C14-C16	108.2(3)
C17-C14-C18	111.2(3)	C15-C14-C18	108.5(3)
C16-C14-C18	109.1(3)	C14-C15-H15A	109.5
C14-C15-H15B	109.5	H15A-C15-H15B	109.5
C14-C15-H15C	109.5	H15A-C15-H15C	109.5
H15B-C15-H15C	109.5	C14-C16-H16A	109.5
C14-C16-H16B	109.5	H16A-C16-H16B	109.5
C14-C16-H16C	109.5	H16A-C16-H16C	109.5
H16B-C16-H16C	109.5	C14-C17-H17A	109.5
C14-C17-H17B	109.5	H17A-C17-H17B	109.5
C14-C17-H17C	109.5	H17A-C17-H17C	109.5
H17B-C17-H17C	109.5	N4-C18-C14	111.8(3)
N4-C18-C19	103.1(2)	C14-C18-C19	116.1(3)
N4-C18-H18	108.5	C14-C18-H18	108.5
C19-C18-H18	108.5	N5-C19-C18	101.7(3)
N5-C19-H19A	111.4	C18-C19-H19A	111.4

N5-C19-H19B	111.4	C18-C19-H19B	111.4
H19A-C19-H19B	109.3	N4-C20-N6	132.4(3)
N4-C20-N5	115.8(3)	N6-C20-N5	111.7(3)
N5-C21-C22	102.1(2)	N5-C21-H21A	111.3
C22-C21-H21A	111.3	N5-C21-H21B	111.3
C22-C21-H21B	111.3	H21A-C21-H21B	109.2
N6-C22-C23	112.6(3)	N6-C22-C21	101.8(3)
C23-C22-C21	115.3(3)	N6-C22-H22	108.9
C23-C22-H22	108.9	C21-C22-H22	108.9
C25-C23-C22	109.1(3)	C25-C23-C24	109.1(3)
C22-C23-C24	112.2(3)	C25-C23-C26	109.5(3)
C22-C23-C26	107.5(3)	C24-C23-C26	109.5(3)
C23-C24-H24A	109.5	C23-C24-H24B	109.5
H24A-C24-H24B	109.5	C23-C24-H24C	109.5
H24A-C24-H24C	109.5	H24B-C24-H24C	109.5
C23-C25-H25A	109.5	C23-C25-H25B	109.5
H25A-C25-H25B	109.5	C23-C25-H25C	109.5
H25A-C25-H25C	109.5	H25B-C25-H25C	109.5
C23-C26-H26A	109.5	C23-C26-H26B	109.5
H26A-C26-H26B	109.5	C23-C26-H26C	109.5
H26A-C26-H26C	109.5	H26B-C26-H26C	109.5
N1-Cu1-Cl1	170.23(9)	N1-Cu1-Cu1	103.00(9)
Cl1-Cu1-Cu1	86.18(3)	N4-Cu2-N4	179.09(19)
N4-Cu2-Cu3	90.46(9)	N4-Cu2-Cu3	90.46(9)
Cl2-Cu3-Cl2	177.23(7)	Cl2-Cu3-Cu2	88.61(4)
Cl2-Cu3-Cu2	88.61(4)	C7-N1-C5	106.3(3)
C7-N1-Cu1	129.7(2)	C5-N1-Cu1	123.8(2)
C7-N2-C6	105.7(3)	C7-N2-C8	107.3(3)
C6-N2-C8	126.0(3)	C7-N3-C9	110.0(3)
C7-N3-H3	125.0	C9-N3-H3	125.0
C20-N4-C18	106.8(2)	C20-N4-Cu2	123.6(2)
C18-N4-Cu2	129.0(2)	C20-N5-C19	106.4(3)
C20-N5-C21	107.9(2)	C19-N5-C21	128.2(3)
C20-N6-C22	109.3(3)	C20-N6-H6	125.3
C22-N6-H6	125.3		

Table SIII.13 Anisotropic atomic displacement parameters (Å²) for complex **12**.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0172(16)	0.028(2)	0.0181(16)	-0.0003(13)	0.0045(13)	0.0031(14)
C2	0.0230(19)	0.041(3)	0.035(2)	0.0047(18)	0.0080(16)	-0.0028(16)
C3	0.0238(19)	0.039(3)	0.035(2)	0.0033(17)	0.0093(16)	0.0100(16)
C4	0.0225(18)	0.044(3)	0.0292(19)	-0.0091(18)	0.0010(15)	-0.0048(17)
C5	0.0193(17)	0.0182(17)	0.0165(16)	-0.0014(13)	0.0032(13)	0.0009(13)
C6	0.0223(17)	0.013(2)	0.0249(17)	0.0024(12)	0.0025(14)	0.0022(12)
C7	0.0144(15)	0.0185(18)	0.0168(15)	0.0015(12)	-0.0025(12)	-0.0011(13)
C8	0.0148(15)	0.023(2)	0.0255(17)	0.0104(13)	0.0050(13)	0.0023(13)
C9	0.0181(16)	0.0216(19)	0.0150(15)	0.0029(13)	0.0027(12)	-0.0008(13)
C10	0.0192(16)	0.0192(19)	0.0224(16)	-0.0004(13)	0.0067(13)	0.0025(13)
C11	0.0197(18)	0.030(2)	0.040(2)	-0.0088(16)	-0.0024(16)	0.0040(14)
C12	0.0301(18)	0.0238(19)	0.0286(17)	-0.0018(17)	0.0081(14)	0.0073(18)
C13	0.029(2)	0.029(2)	0.037(2)	0.0108(17)	0.0167(17)	0.0074(16)
C14	0.0195(16)	0.0215(19)	0.0175(15)	-0.0013(14)	0.0010(13)	-0.0003(13)
C15	0.0210(17)	0.034(2)	0.0208(17)	-0.0042(15)	0.0030(14)	-0.0007(15)
C16	0.0248(19)	0.042(3)	0.0196(17)	0.0013(15)	-0.0024(14)	0.0053(16)
C17	0.0258(17)	0.023(2)	0.0296(17)	-0.0035(16)	-0.0006(14)	-0.0067(16)
C18	0.0146(16)	0.0183(19)	0.0191(16)	0.0024(13)	0.0016(13)	-0.0009(13)
C19	0.0175(17)	0.027(2)	0.0211(17)	0.0026(14)	0.0007(13)	0.0074(14)
C20	0.0140(15)	0.0177(18)	0.0195(15)	-0.0038(13)	0.0008(12)	0.0021(13)
C21	0.0167(16)	0.028(2)	0.0184(16)	0.0000(14)	0.0046(12)	0.0021(14)
C22	0.0155(15)	0.0206(19)	0.0205(17)	-0.0003(14)	0.0016(13)	-0.0013(13)
C23	0.0194(16)	0.0236(19)	0.0180(16)	0.0019(14)	0.0031(13)	-0.0011(14)
C24	0.034(2)	0.025(2)	0.0240(18)	-0.0018(14)	-0.0010(15)	-0.0010(15)
C25	0.0275(19)	0.030(2)	0.0226(17)	0.0027(13)	-0.0039(15)	0.0018(14)
C26	0.0252(19)	0.046(3)	0.0205(18)	0.0023(15)	0.0068(15)	-0.0017(16)
Cl1	0.0474(5)	0.0219(5)	0.0164(4)	0.0021(3)	0.0001(3)	-0.0117(4)
Cl2	0.0425(5)	0.0219(5)	0.0562(6)	-0.0020(4)	0.0135(4)	-0.0053(4)
Cu1	0.0260(3)	0.0209(3)	0.0163(2)	0.0041(2)	0.00210(18)	-0.0023(2)
Cu2	0.0119(3)	0.0252(4)	0.0193(3)	0	0.0020(3)	0
Cu3	0.0253(4)	0.0230(5)	0.0545(5)	0	0.0074(4)	0
N1	0.0187(14)	0.0205(16)	0.0178(14)	0.0009(11)	0.0026(11)	0.0017(11)
N2	0.0144(13)	0.0180(15)	0.0189(14)	0.0057(11)	0.0039(11)	0.0008(11)
N3	0.0238(15)	0.0149(15)	0.0232(14)	0.0086(11)	0.0069(12)	0.0074(12)
N4	0.0135(12)	0.0204(16)	0.0178(13)	0.0006(11)	0.0016(10)	0.0004(11)
N5	0.0121(13)	0.0252(17)	0.0191(13)	0.0024(12)	0.0038(10)	0.0028(11)
N6	0.0128(13)	0.0285(18)	0.0194(14)	0.0009(11)	0.0012(11)	0.0030(11)

Table SIII.14 Hydrogen atomic coordinates and isotropic atomic displacement parameters ($\text{\AA}^2$) for complex **12**.

	x/a	y/b	z/c	U(eq)
H2A	0.7383	0.7320	0.0484	0.049
H2B	0.6731	0.8440	0.0443	0.049
H2C	0.6864	0.6401	0.0041	0.049
H3A	0.7031	0.2790	0.0492	0.049
H3B	0.6994	0.2500	0.1182	0.049
H3C	0.7540	0.3830	0.0926	0.049
H4A	0.6726	0.5655	0.1800	0.048
H4B	0.6599	0.7961	0.1505	0.048
H4C	0.7272	0.7016	0.1554	0.048
H5	0.6023	0.4277	0.0375	0.022
H6A	0.5519	0.2347	0.1020	0.024
H6B	0.6108	0.2676	0.1456	0.024
H8A	0.4991	0.3787	0.2264	0.025
H8B	0.4634	0.3370	0.1641	0.025
H9	0.4756	0.7358	0.2273	0.022
H11A	0.3736	0.6569	0.1001	0.045
H11B	0.3176	0.5740	0.1352	0.045
H11C	0.3754	0.4223	0.1293	0.045
H12A	0.3896	0.9654	0.2308	0.041
H12B	0.3253	0.9036	0.2003	0.041
H12C	0.3790	0.9841	0.1615	0.041
H13A	0.3834	0.3852	0.2374	0.046
H13B	0.3278	0.5458	0.2453	0.046
H13C	0.3920	0.5946	0.2778	0.046
H15A	0.4550	0.0495	0.3957	0.038
H15B	0.4313	0.2520	0.3577	0.038
H15C	0.4176	0.0119	0.3349	0.038
H16A	0.3105	0.1103	0.3237	0.043
H16B	0.3210	0.3452	0.3513	0.043
H16C	0.2737	0.1836	0.3785	0.043
H17A	0.3427	-0.2175	0.3842	0.039
H17B	0.3091	-0.1261	0.4392	0.039
H17C	0.3796	-0.1844	0.4454	0.039
H18	0.3853	0.3964	0.4427	0.021
H19A	0.3105	0.4375	0.5050	0.026
H19B	0.2761	0.2486	0.4680	0.026
H21A	0.2615	0.0819	0.5994	0.025

	x/a	y/b	z/c	U(eq)
H21B	0.2996	0.3006	0.6118	0.025
H22	0.3377	-0.1352	0.6352	0.023
H24A	0.3940	0.3735	0.7402	0.042
H24B	0.3473	0.4264	0.6865	0.042
H24C	0.4153	0.3584	0.6748	0.042
H25A	0.4183	0.0027	0.7676	0.04
H25B	0.4500	-0.0174	0.7068	0.04
H25C	0.4008	-0.1920	0.7241	0.04
H26A	0.2917	-0.0833	0.7276	0.046
H26B	0.2718	0.1578	0.7106	0.046
H26C	0.3107	0.1127	0.7701	0.046
H3	0.4724	0.9023	0.1265	0.025
H6	0.4412	0.0138	0.6110	0.024

III.3 The X-ray analysis of complex 13:

A colorless block-like specimen of $C_{26}H_{48}Cu_2N_6$, approximate dimensions 0.200 mm x 0.260 mm x 0.380 mm, was used for the X-ray crystallographic analysis. The X-ray intensity data were measured.

The total exposure time was 0.65 hours. The frames were integrated with the Bruker SAINT software package using a narrow-frame algorithm. The integration of the data using a monoclinic unit cell yielded a total of 54460 reflections to a maximum θ angle of 31.16° (0.69 Å resolution), of which 18507 were independent (average redundancy 2.943, completeness = 99.8%, $R_{int} = 2.99\%$, $R_{sig} = 4.73\%$) and 16847 (91.03%) were greater than $2\sigma(F_2)$. The final cell constants of $a = 10.6771(4)$ Å, $b = 24.0871(10)$ Å, $c = 11.9844(5)$ Å, $\beta = 111.4299(9)^\circ$, volume = $2869.1(2)$ Å³, are based upon the refinement of the XYZ-centroids of 9845 reflections above $20 \sigma(I)$ with $4.433^\circ < 2\theta < 61.11^\circ$. Data were corrected for absorption effects using the Multi-Scan method (SADABS). The ratio of minimum to maximum apparent transmission was 0.778. The calculated minimum and maximum transmission coefficients (based on crystal size) are 0.5980 and 0.7530.

The structure was solved and refined using the Bruker SHELXTL Software Package, using the space group $P 1 2_1 1$, with $Z = 4$ for the formula unit, $C_{26}H_{48}Cu_2N_6$. The final anisotropic full-matrix least-squares refinement on F_2 with 637 variables converged at $R_1 = 2.59\%$, for the observed data and $wR_2 = 5.08\%$ for all data. The goodness-of-fit was 0.991.

The largest peak in the final difference electron density synthesis was 0.381 e-/Å³ and the largest hole was -0.289 e-/Å³ with an RMS deviation of 0.054 e-/Å³. On the basis of the final model, the calculated density was 1.324 g/cm³ and F(000), 1216 e-.

Figure SIII.3 ORTEP drawing of complex **13** with thermal ellipsoids at 50% probability levels.

Table SIII.15 Sample and crystal data for complex **13**.

Identification code	tch104	
Chemical formula	C ₂₆ H ₄₈ Cu ₂ N ₆	
Formula weight	571.78 g/mol	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal size	0.200 x 0.260 x 0.380 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 2 1	
Unit cell dimensions	a = 10.6771(4) Å	α = 90°

	$b = 24.0871(10) \text{ \AA}$	$\beta = 111.4299(9)^\circ$
	$c = 11.9844(5) \text{ \AA}$	$\gamma = 90^\circ$
Volume	$2869.1(2) \text{ \AA}^3$	
Z	4	
Density (calculated)	1.324 g/cm^3	
Absorption coefficient	1.507 mm^{-1}	
F(000)	1216	

Table SIII.16 Data collection and structure refinement for complex **13**.

Theta range for data collection	1.69 to 31.16°	
Index ranges	$-12 \leq h \leq 15$, $-35 \leq k \leq 35$, $-17 \leq l \leq 16$	
Reflections collected	54460	
Independent reflections	18507 [$R(\text{int}) = 0.0299$]	
Coverage of independent reflections	99.8%	
Absorption correction	Multi-Scan	
Max. and min. transmission	0.7530 and 0.5980	
Structure solution technique	direct methods	
Structure solution program	XS, VERSION 2013/1	
Refinement method	Full-matrix least-squares on F^2	
Refinement program	SHELXL-2014/7 (Sheldrick, 2014)	
Function minimized	$\Sigma w(F_o^2 - F_c^2)^2$	
Data / restraints / parameters	18507 / 1 / 637	
Goodness-of-fit on F^2	0.991	
$\Delta/\sigma_{\text{max}}$	0.003	
Final R indices	16847 data; $I > 2\sigma(I)$	$R1 = 0.0259$, $wR2 = 0.0495$
	all data	$R1 = 0.0315$, $wR2 = 0.0508$
Weighting scheme	$w = 1/[\sigma^2(F_o^2) + (0.0141P)^2]$ where $P = (F_o^2 + 2F_c^2)/3$	
Absolute structure parameter	0.002(3)	
Largest diff. peak and hole	0.381 and $-0.289 \text{ e\AA}^{-3}$	
R.M.S. deviation from mean	$0.054 \text{ e\AA}^{-3}$	

Table SIII.17 Atomic coordinates and equivalent isotropic atomic displacement parameters ($\text{\AA}^2$) for complex **13**.

$U(\text{eq})$ is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	x/a	y/b	z/c	U(eq)
C1	0.0210(2)	0.30361(8)	0.3565(2)	0.0126(4)
C2	0.9058(2)	0.29812(9)	0.15810(19)	0.0147(4)

	x/a	y/b	z/c	U(eq)
C3	0.9095(2)	0.24045(9)	0.2161(2)	0.0164(4)
C4	0.9988(2)	0.22265(8)	0.4469(2)	0.0140(4)
C5	0.0833(2)	0.26575(8)	0.5417(2)	0.0126(4)
C6	0.9269(2)	0.29874(9)	0.0381(2)	0.0170(5)
C7	0.0666(2)	0.27812(11)	0.0498(2)	0.0226(5)
C8	0.9081(3)	0.35864(10)	0.9897(2)	0.0259(6)
C9	0.8172(3)	0.26248(11)	0.9496(2)	0.0271(6)
C10	0.0198(2)	0.28411(9)	0.6335(2)	0.0138(4)
C11	0.0057(3)	0.23276(9)	0.7042(2)	0.0197(5)
C12	0.8836(2)	0.31126(10)	0.5714(2)	0.0196(5)
C13	0.1147(2)	0.32552(9)	0.7211(2)	0.0180(5)
C14	0.2547(2)	0.47669(9)	0.4145(2)	0.0131(4)
C15	0.1789(2)	0.51854(9)	0.2333(2)	0.0153(4)
C16	0.2989(2)	0.55204(9)	0.3212(2)	0.0180(5)
C17	0.4307(2)	0.52421(9)	0.5437(2)	0.0185(5)
C18	0.3937(2)	0.47409(9)	0.6069(2)	0.0141(4)
C19	0.0442(2)	0.55102(9)	0.1830(2)	0.0175(5)
C20	0.0000(3)	0.57083(10)	0.2844(2)	0.0245(5)
C21	0.9353(3)	0.51328(10)	0.0979(2)	0.0241(5)
C22	0.0637(3)	0.60095(10)	0.1114(2)	0.0230(5)
C23	0.5132(2)	0.43941(9)	0.68786(19)	0.0146(4)
C24	0.5904(2)	0.41187(10)	0.6172(2)	0.0205(5)
C25	0.6076(2)	0.47856(10)	0.7834(2)	0.0204(5)
C26	0.4610(2)	0.39421(10)	0.7504(2)	0.0195(5)
C28	0.5569(2)	0.55773(9)	0.14724(18)	0.0110(4)
C29	0.5886(2)	0.46583(8)	0.14874(18)	0.0130(4)
C30	0.4716(2)	0.48271(9)	0.03301(19)	0.0170(5)
C31	0.4043(2)	0.58445(9)	0.9677(2)	0.0166(5)
C32	0.4647(2)	0.63572(9)	0.04657(18)	0.0127(4)
C33	0.5657(2)	0.41286(8)	0.20921(19)	0.0146(4)
C34	0.6968(2)	0.39703(10)	0.3110(2)	0.0208(5)
C35	0.4538(2)	0.41994(10)	0.2596(2)	0.0203(5)
C36	0.5270(3)	0.36604(9)	0.1161(2)	0.0208(5)
C37	0.5528(2)	0.67441(9)	0.00168(19)	0.0138(4)
C38	0.6714(2)	0.64306(11)	0.9904(2)	0.0235(5)
C39	0.6048(3)	0.72200(10)	0.0907(2)	0.0237(5)
C40	0.4668(3)	0.69954(10)	0.8811(2)	0.0227(5)
C41	0.7473(2)	0.61460(9)	0.55715(18)	0.0105(4)
C42	0.8621(2)	0.54020(9)	0.65925(18)	0.0117(4)
C43	0.8542(2)	0.58547(9)	0.74940(19)	0.0140(4)

	x/a	y/b	z/c	U(eq)
C44	0.7202(2)	0.67815(9)	0.68576(19)	0.0141(4)
C45	0.6622(2)	0.70028(9)	0.55589(19)	0.0126(4)
C46	0.0059(2)	0.52413(9)	0.66820(19)	0.0139(4)
C47	0.9949(2)	0.48034(9)	0.5729(2)	0.0188(5)
C48	0.0797(2)	0.49801(10)	0.7916(2)	0.0223(5)
C49	0.0831(2)	0.57477(9)	0.6497(2)	0.0219(5)
C50	0.5224(2)	0.72756(9)	0.5182(2)	0.0147(4)
C51	0.4147(2)	0.68739(9)	0.5242(2)	0.0209(5)
C52	0.4829(3)	0.74944(10)	0.3901(2)	0.0230(5)
C53	0.5342(3)	0.77699(9)	0.6016(2)	0.0192(5)
Cu1	0.08354(3)	0.40032(2)	0.26458(2)	0.01277(6)
Cu2	0.20864(3)	0.37552(2)	0.50122(2)	0.01153(6)
Cu3	0.70213(3)	0.53314(2)	0.38544(2)	0.01114(5)
Cu4	0.59971(3)	0.63739(2)	0.32036(2)	0.01203(5)
N1	0.00728(19)	0.32998(7)	0.25558(16)	0.0136(4)
N2	0.10209(19)	0.31223(7)	0.46841(16)	0.0127(4)
N3	0.94022(19)	0.25706(7)	0.34016(16)	0.0142(4)
N4	0.29628(18)	0.44260(7)	0.50777(16)	0.0128(4)
N5	0.17254(18)	0.46807(7)	0.30256(16)	0.0138(4)
N6	0.30960(19)	0.52874(8)	0.43730(16)	0.0154(4)
N7	0.61093(19)	0.51694(7)	0.22317(16)	0.0123(4)
N8	0.54108(19)	0.61113(7)	0.16505(15)	0.0126(4)
N9	0.50090(19)	0.54149(7)	0.02821(15)	0.0139(4)
N10	0.77659(18)	0.56249(7)	0.54027(15)	0.0112(3)
N11	0.66597(18)	0.65114(7)	0.48296(15)	0.0124(4)
N12	0.80783(18)	0.63377(7)	0.67297(15)	0.0115(3)

Table SIII.18 Bond lengths (Å) for complex **13**.

C1-N2	1.320(3)	C1-N1	1.326(3)
C1-N3	1.384(3)	C2-N1	1.484(3)
C2-C6	1.535(3)	C2-C3	1.548(3)
C3-N3	1.456(3)	C4-N3	1.459(3)
C4-C5	1.560(3)	C5-N2	1.481(3)
C5-C10	1.553(3)	C6-C7	1.529(3)
C6-C9	1.533(3)	C6-C8	1.541(3)
C10-C12	1.519(3)	C10-C13	1.532(3)
C10-C11	1.538(3)	C14-N5	1.324(3)
C14-N4	1.326(3)	C14-N6	1.369(3)

C15-N5	1.487(3)	C15-C19	1.553(3)
C15-C16	1.554(3)	C16-N6	1.466(3)
C17-N6	1.450(3)	C17-C18	1.551(3)
C18-N4	1.472(3)	C18-C23	1.538(3)
C19-C20	1.532(3)	C19-C21	1.533(3)
C19-C22	1.535(3)	C23-C24	1.531(3)
C23-C26	1.538(3)	C23-C25	1.540(3)
C28-N7	1.320(3)	C28-N8	1.325(3)
C28-N9	1.386(3)	C29-N7	1.487(3)
C29-C33	1.530(3)	C29-C30	1.544(3)
C30-N9	1.456(3)	C31-N9	1.454(3)
C31-C32	1.546(3)	C32-N8	1.478(3)
C32-C37	1.554(3)	C33-C34	1.531(3)
C33-C35	1.532(3)	C33-C36	1.533(3)
C37-C38	1.521(3)	C37-C39	1.526(3)
C37-C40	1.526(3)	C41-N11	1.325(3)
C41-N10	1.327(3)	C41-N12	1.379(3)
C42-N10	1.484(3)	C42-C46	1.549(3)
C42-C43	1.559(3)	C43-N12	1.451(3)
C44-N12	1.465(3)	C44-C45	1.545(3)
C45-N11	1.480(3)	C45-C50	1.541(3)
C46-C47	1.528(3)	C46-C49	1.533(3)
C46-C48	1.533(3)	C50-C51	1.525(3)
C50-C52	1.529(3)	C50-C53	1.530(3)
Cu1-N5	1.8594(18)	Cu1-N1	1.8658(18)
Cu1-Cu2	2.7232(4)	Cu2-N4	1.8544(17)
Cu2-N2	1.8563(17)	Cu3-N10	1.8699(17)
Cu3-N7	1.8706(18)	Cu3-Cu4	2.7361(4)
Cu4-N11	1.8440(17)	Cu4-N8	1.8452(17)

Table SIII.19 Bond angles (°) for complex **13**.

N2-C1-N1	131.6(2)	N2-C1-N3	114.51(19)
N1-C1-N3	113.76(19)	N1-C2-C6	114.73(18)
N1-C2-C3	102.65(17)	C6-C2-C3	116.20(18)
N3-C3-C2	99.87(17)	N3-C4-C5	102.05(16)
N2-C5-C10	113.18(17)	N2-C5-C4	103.83(17)
C10-C5-C4	114.81(18)	C7-C6-C9	110.6(2)
C7-C6-C2	112.49(19)	C9-C6-C2	107.8(2)
C7-C6-C8	109.1(2)	C9-C6-C8	108.2(2)

C2-C6-C8	108.54(19)	C12-C10-C13	109.29(18)
C12-C10-C11	110.29(19)	C13-C10-C11	108.65(18)
C12-C10-C5	111.31(18)	C13-C10-C5	108.72(18)
C11-C10-C5	108.52(17)	N5-C14-N4	130.6(2)
N5-C14-N6	115.02(19)	N4-C14-N6	114.31(19)
N5-C15-C19	113.82(18)	N5-C15-C16	103.95(17)
C19-C15-C16	114.77(18)	N6-C16-C15	101.73(17)
N6-C17-C18	100.58(17)	N4-C18-C23	114.09(17)
N4-C18-C17	103.74(17)	C23-C18-C17	115.46(18)
C20-C19-C21	109.5(2)	C20-C19-C22	110.09(19)
C21-C19-C22	108.5(2)	C20-C19-C15	111.01(19)
C21-C19-C15	109.23(18)	C22-C19-C15	108.44(19)
C24-C23-C18	112.16(18)	C24-C23-C26	109.10(19)
C18-C23-C26	109.07(18)	C24-C23-C25	109.75(19)
C18-C23-C25	107.65(18)	C26-C23-C25	109.06(18)
N7-C28-N8	131.38(19)	N7-C28-N9	114.50(18)
N8-C28-N9	114.03(18)	N7-C29-C33	115.13(17)
N7-C29-C30	102.75(17)	C33-C29-C30	115.37(18)
N9-C30-C29	100.17(17)	N9-C31-C32	101.68(17)
N8-C32-C31	103.17(17)	N8-C32-C37	112.40(17)
C31-C32-C37	115.94(18)	C29-C33-C34	109.12(18)
C29-C33-C35	112.08(18)	C34-C33-C35	109.33(19)
C29-C33-C36	108.41(18)	C34-C33-C36	108.78(18)
C35-C33-C36	109.07(19)	C38-C37-C39	109.45(19)
C38-C37-C40	110.19(19)	C39-C37-C40	107.67(19)
C38-C37-C32	111.22(18)	C39-C37-C32	108.68(19)
C40-C37-C32	109.54(18)	N11-C41-N10	131.26(19)
N11-C41-N12	113.82(18)	N10-C41-N12	114.87(18)
N10-C42-C46	113.76(17)	N10-C42-C43	104.06(16)
C46-C42-C43	115.48(18)	N12-C43-C42	102.45(16)
N12-C44-C45	100.51(16)	N11-C45-C50	113.57(18)
N11-C45-C44	103.40(16)	C50-C45-C44	115.56(18)
C47-C46-C49	109.83(19)	C47-C46-C48	108.04(18)
C49-C46-C48	110.60(19)	C47-C46-C42	108.53(18)
C49-C46-C42	111.29(18)	C48-C46-C42	108.46(18)
C51-C50-C52	109.30(19)	C51-C50-C53	110.27(19)
C52-C50-C53	108.35(18)	C51-C50-C45	112.49(18)
C52-C50-C45	108.88(19)	C53-C50-C45	107.46(18)
N5-Cu1-N1	169.85(8)	N5-Cu1-Cu2	85.71(6)
N1-Cu1-Cu2	84.18(6)	N4-Cu2-N2	170.14(8)
N4-Cu2-Cu1	84.31(6)	N2-Cu2-Cu1	85.99(6)

N10-Cu3-N7	169.00(8)	N10-Cu3-Cu4	85.22(5)
N7-Cu3-Cu4	83.86(5)	N11-Cu4-N8	170.18(8)
N11-Cu4-Cu3	84.52(5)	N8-Cu4-Cu3	85.76(5)
C1-N1-C2	106.04(17)	C1-N1-Cu1	118.79(14)
C2-N1-Cu1	133.83(14)	C1-N2-C5	107.62(17)
C1-N2-Cu2	117.90(14)	C5-N2-Cu2	134.48(14)
C1-N3-C3	105.28(17)	C1-N3-C4	106.89(17)
C3-N3-C4	127.09(18)	C14-N4-C18	106.37(17)
C14-N4-Cu2	119.69(15)	C18-N4-Cu2	132.85(14)
C14-N5-C15	106.78(17)	C14-N5-Cu1	118.41(15)
C15-N5-Cu1	134.78(15)	C14-N6-C17	106.61(18)
C14-N6-C16	106.39(17)	C17-N6-C16	126.75(19)
C28-N7-C29	105.59(17)	C28-N7-Cu3	119.45(14)
C29-N7-Cu3	134.80(14)	C28-N8-C32	107.00(17)
C28-N8-Cu4	118.62(14)	C32-N8-Cu4	134.13(14)
C28-N9-C31	105.84(17)	C28-N9-C30	104.58(16)
C31-N9-C30	126.03(19)	C41-N10-C42	106.98(16)
C41-N10-Cu3	118.07(14)	C42-N10-Cu3	134.89(13)
C41-N11-C45	106.71(17)	C41-N11-Cu4	119.61(14)
C45-N11-Cu4	133.22(14)	C41-N12-C43	107.04(16)
C41-N12-C44	105.52(16)	C43-N12-C44	127.04(17)

Table SIII.20 Anisotropic atomic displacement parameters ($\text{\AA}^2$) for complex **13**.

The anisotropic atomic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U_{11} + \dots + 2 h k a^* b^* U_{12}]$

	U_{11}	U_{22}	U_{33}	U_{23}	U_{13}	U_{12}
C1	0.0125(11)	0.0099(9)	0.0178(10)	-0.0016(8)	0.0085(9)	0.0003(8)
C2	0.0108(11)	0.0162(10)	0.0151(10)	-0.0029(8)	0.0023(8)	-0.0006(8)
C3	0.0155(12)	0.0153(10)	0.0180(11)	-0.0044(8)	0.0057(9)	-0.0037(8)
C4	0.0165(11)	0.0103(9)	0.0180(11)	0.0006(8)	0.0095(9)	-0.0013(8)
C5	0.0119(11)	0.0104(9)	0.0170(10)	0.0022(8)	0.0068(9)	-0.0007(8)
C6	0.0162(12)	0.0190(11)	0.0148(10)	-0.0026(9)	0.0044(9)	0.0007(9)
C7	0.0188(13)	0.0332(13)	0.0162(11)	-0.0010(10)	0.0067(10)	0.0028(10)
C8	0.0314(15)	0.0267(13)	0.0182(12)	0.0045(10)	0.0072(11)	0.0051(11)
C9	0.0230(14)	0.0360(14)	0.0176(12)	-0.0069(11)	0.0019(10)	-0.0034(11)
C10	0.0156(11)	0.0126(10)	0.0155(10)	0.0024(8)	0.0084(9)	-0.0005(8)
C11	0.0224(13)	0.0187(11)	0.0208(12)	0.0035(9)	0.0114(10)	-0.0015(9)
C12	0.0181(12)	0.0184(11)	0.0254(12)	0.0003(9)	0.0115(10)	0.0019(9)
C13	0.0219(13)	0.0169(10)	0.0167(11)	0.0002(9)	0.0089(10)	-0.0016(9)
C14	0.0104(10)	0.0119(9)	0.0199(11)	0.0010(8)	0.0091(9)	0.0014(8)

	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
C15	0.0152(11)	0.0136(9)	0.0192(11)	0.0037(8)	0.0089(9)	0.0001(8)
C16	0.0195(12)	0.0114(10)	0.0242(12)	0.0044(9)	0.0094(10)	-0.0023(9)
C17	0.0194(12)	0.0120(10)	0.0230(11)	-0.0010(8)	0.0064(9)	-0.0039(9)
C18	0.0154(11)	0.0115(9)	0.0176(10)	-0.0020(8)	0.0085(9)	-0.0028(8)
C19	0.0198(12)	0.0145(10)	0.0204(11)	0.0051(9)	0.0098(10)	0.0033(9)
C20	0.0277(14)	0.0216(12)	0.0285(13)	0.0080(10)	0.0151(11)	0.0105(10)
C21	0.0192(13)	0.0228(12)	0.0271(13)	0.0062(10)	0.0045(10)	0.0027(10)
C22	0.0294(14)	0.0180(11)	0.0248(12)	0.0068(10)	0.0135(11)	0.0040(10)
C23	0.0145(11)	0.0161(10)	0.0142(10)	-0.0034(8)	0.0065(9)	-0.0027(8)
C24	0.0173(12)	0.0215(12)	0.0233(12)	-0.0060(9)	0.0081(10)	0.0021(9)
C25	0.0198(12)	0.0213(11)	0.0195(11)	-0.0054(9)	0.0064(10)	-0.0074(10)
C26	0.0221(12)	0.0177(11)	0.0156(10)	-0.0010(9)	0.0030(9)	-0.0043(9)
C28	0.0124(11)	0.0123(9)	0.0098(9)	-0.0015(8)	0.0059(8)	-0.0032(8)
C29	0.0172(11)	0.0119(9)	0.0118(10)	-0.0035(8)	0.0076(9)	-0.0015(8)
C30	0.0253(13)	0.0131(10)	0.0114(10)	-0.0020(8)	0.0053(9)	-0.0057(9)
C31	0.0187(12)	0.0162(10)	0.0112(10)	0.0013(8)	0.0013(9)	-0.0028(9)
C32	0.0128(10)	0.0136(9)	0.0106(9)	0.0013(8)	0.0031(8)	0.0012(9)
C33	0.0176(11)	0.0112(9)	0.0155(10)	0.0004(8)	0.0069(9)	0.0008(8)
C34	0.0223(12)	0.0144(10)	0.0224(12)	0.0001(10)	0.0045(10)	0.0020(10)
C35	0.0247(13)	0.0171(11)	0.0242(12)	0.0043(9)	0.0150(11)	0.0000(9)
C36	0.0255(13)	0.0114(10)	0.0254(12)	-0.0042(9)	0.0091(10)	-0.0025(9)
C37	0.0143(11)	0.0141(10)	0.0125(10)	0.0018(8)	0.0041(8)	0.0003(8)
C38	0.0211(12)	0.0232(12)	0.0318(13)	0.0088(11)	0.0164(11)	0.0050(10)
C39	0.0255(14)	0.0175(11)	0.0247(13)	0.0016(10)	0.0052(11)	-0.0057(10)
C40	0.0252(13)	0.0217(12)	0.0184(12)	0.0079(9)	0.0045(10)	-0.0020(10)
C41	0.0099(10)	0.0133(9)	0.0096(9)	-0.0018(8)	0.0051(8)	-0.0015(8)
C42	0.0126(10)	0.0123(10)	0.0108(9)	-0.0006(8)	0.0051(8)	-0.0010(8)
C43	0.0157(11)	0.0139(9)	0.0126(10)	-0.0011(8)	0.0053(8)	-0.0003(8)
C44	0.0170(11)	0.0138(10)	0.0121(10)	-0.0046(8)	0.0058(9)	0.0013(8)
C45	0.0153(11)	0.0110(9)	0.0127(10)	-0.0043(8)	0.0065(9)	0.0001(8)
C46	0.0107(10)	0.0135(10)	0.0162(10)	0.0007(8)	0.0036(8)	0.0010(8)
C47	0.0195(12)	0.0169(10)	0.0210(12)	-0.0004(9)	0.0086(10)	0.0046(9)
C48	0.0192(13)	0.0210(11)	0.0218(12)	0.0022(9)	0.0017(10)	0.0043(10)
C49	0.0151(12)	0.0183(11)	0.0348(14)	0.0001(10)	0.0120(10)	-0.0002(9)
C50	0.0165(11)	0.0116(9)	0.0163(11)	-0.0013(8)	0.0065(9)	0.0030(8)
C51	0.0158(12)	0.0170(11)	0.0287(13)	-0.0021(10)	0.0065(10)	0.0009(9)
C52	0.0314(15)	0.0171(11)	0.0197(12)	0.0017(9)	0.0084(11)	0.0092(10)
C53	0.0228(13)	0.0132(10)	0.0254(12)	-0.0045(9)	0.0132(10)	0.0012(9)
Cu1	0.01420(13)	0.01070(12)	0.01398(13)	0.00066(10)	0.00583(10)	-0.00142(10)
Cu2	0.01242(13)	0.00943(11)	0.01358(12)	-0.00017(10)	0.00572(10)	-0.00243(10)

	U ₁₁	U ₂₂	U ₃₃	U ₂₃	U ₁₃	U ₁₂
Cu3	0.01407(13)	0.01000(11)	0.00923(11)	-0.00158(9)	0.00411(10)	0.00071(10)
Cu4	0.01598(13)	0.01032(11)	0.00948(11)	-0.00140(10)	0.00428(10)	0.00155(10)
N1	0.0150(10)	0.0122(8)	0.0133(9)	-0.0014(7)	0.0050(7)	-0.0025(7)
N2	0.0149(9)	0.0098(8)	0.0154(9)	0.0006(7)	0.0077(7)	-0.0037(7)
N3	0.0137(9)	0.0123(8)	0.0164(9)	-0.0013(7)	0.0054(8)	-0.0041(7)
N4	0.0122(9)	0.0099(8)	0.0153(9)	0.0003(7)	0.0041(7)	-0.0027(7)
N5	0.0150(10)	0.0104(8)	0.0166(9)	0.0034(7)	0.0065(8)	-0.0005(7)
N6	0.0166(10)	0.0107(8)	0.0185(9)	0.0011(7)	0.0060(7)	-0.0026(7)
N7	0.0190(10)	0.0089(8)	0.0104(8)	-0.0018(6)	0.0069(7)	-0.0011(7)
N8	0.0163(10)	0.0122(8)	0.0085(8)	0.0019(7)	0.0035(7)	0.0006(7)
N9	0.0211(10)	0.0115(8)	0.0082(8)	-0.0005(7)	0.0042(7)	-0.0033(7)
N10	0.0123(9)	0.0108(8)	0.0097(8)	-0.0017(7)	0.0031(7)	0.0013(7)
N11	0.0166(9)	0.0095(8)	0.0113(8)	-0.0036(6)	0.0053(7)	0.0035(7)
N12	0.0135(9)	0.0106(8)	0.0095(8)	-0.0023(7)	0.0033(7)	0.0004(7)

Table SIII.21 Hydrogen atomic coordinates and isotropic atomic displacement parameters (Å²) for complex **13**.

	x/a	y/b	z/c	U(eq)
H2	-0.1842	0.3149	0.1443	0.018
H3A	-0.1784	0.2213	0.1824	0.02
H3B	-0.0193	0.2165	0.2075	0.02
H4A	0.0565	0.1931	0.4340	0.017
H4B	-0.0718	0.2055	0.4710	0.017
H5	0.1734	0.2491	0.5869	0.015
H7A	0.1352	0.2980	0.1152	0.034
H7B	0.0807	0.2849	-0.0254	0.034
H7C	0.0735	0.2382	0.0671	0.034
H8A	-0.0190	0.3820	0.0422	0.039
H8B	-0.1785	0.3731	-0.0123	0.039
H8C	-0.0901	0.3590	-0.0915	0.039
H9A	-0.1784	0.2657	-0.1304	0.041
H9B	-0.2713	0.2749	-0.0531	0.041
H9C	-0.1688	0.2237	-0.0242	0.041
H11A	-0.0214	0.2444	0.7704	0.029
H11B	0.0921	0.2133	0.7363	0.029
H11C	-0.0627	0.2079	0.6509	0.029
H12A	-0.1759	0.2855	0.5123	0.029
H12B	-0.1053	0.3452	0.5309	0.029

	x/a	y/b	z/c	U(eq)
H12C	-0.1561	0.3206	0.6310	0.029
H13A	0.0783	0.3357	0.7824	0.027
H13B	0.1230	0.3588	0.6774	0.027
H13C	0.2035	0.3085	0.7595	0.027
H15	0.2036	0.5067	0.1641	0.018
H16A	0.3823	0.5458	0.3049	0.022
H16B	0.2791	0.5923	0.3169	0.022
H17A	0.4467	0.5582	0.5933	0.022
H17B	0.5107	0.5163	0.5232	0.022
H18	0.3450	0.4888	0.6579	0.017
H20A	0.0683	0.5959	0.3373	0.037
H20B	-0.0105	0.5387	0.3305	0.037
H20C	-0.0859	0.5905	0.2504	0.037
H21A	-0.0797	0.4816	0.1428	0.036
H21B	-0.0354	0.4999	0.0342	0.036
H21C	-0.1486	0.5343	0.0625	0.036
H22A	-0.0229	0.6195	0.0715	0.035
H22B	0.0992	0.5881	0.0511	0.035
H22C	0.1273	0.6271	0.1659	0.035
H24A	0.6270	0.4406	0.5797	0.031
H24B	0.5293	0.3879	0.5550	0.031
H24C	0.6642	0.3896	0.6717	0.031
H25A	0.6824	0.4571	0.8392	0.031
H25B	0.5575	0.4965	0.8275	0.031
H25C	0.6431	0.5069	0.7442	0.031
H26A	0.5374	0.3756	0.8111	0.029
H26B	0.4085	0.3670	0.6911	0.029
H26C	0.4039	0.4112	0.7891	0.029
H29	0.6701	0.4599	0.1278	0.016
H30A	0.4747	0.4625	-0.0378	0.02
H30B	0.3830	0.4768	0.0400	0.02
H31A	0.3135	0.5756	-0.0330	0.02
H31B	0.3994	0.5900	-0.1156	0.02
H32	0.3891	0.6582	0.0536	0.015
H34A	0.6843	0.3619	0.3469	0.031
H34B	0.7213	0.4262	0.3721	0.031
H34C	0.7687	0.3928	0.2791	0.031
H35A	0.4407	0.3849	0.2954	0.03
H35B	0.3700	0.4304	0.1947	0.03
H35C	0.4792	0.4491	0.3209	0.03

	x/a	y/b	z/c	U(eq)
H36A	0.5945	0.3634	0.0787	0.031
H36B	0.4388	0.3740	0.0545	0.031
H36C	0.5229	0.3308	0.1555	0.031
H38A	0.7258	0.6685	-0.0370	0.035
H38B	0.6380	0.6128	-0.0677	0.035
H38C	0.7267	0.6276	0.0686	0.035
H39A	0.6631	0.7072	0.1685	0.036
H39B	0.5286	0.7415	0.0998	0.036
H39C	0.6562	0.7479	0.0609	0.036
H40A	0.5228	0.7234	-0.1478	0.034
H40B	0.3942	0.7216	-0.1094	0.034
H40C	0.4280	0.6697	-0.1769	0.034
H42	0.8176	0.5059	0.6741	0.014
H43A	0.7895	0.5749	0.7875	0.017
H43B	0.9434	0.5922	0.8125	0.017
H44A	0.7718	0.7071	0.7427	0.017
H44B	0.6486	0.6635	0.7118	0.017
H45	0.7265	0.7285	0.5465	0.015
H47A	0.9455	0.4958	0.4932	0.028
H47B	0.9470	0.4478	0.5861	0.028
H47C	1.0853	0.4694	0.5782	0.028
H48A	1.0268	0.4669	0.8034	0.033
H48B	1.0914	0.5259	0.8541	0.033
H48C	1.1680	0.4846	0.7960	0.033
H49A	1.1738	0.5634	0.6567	0.033
H49B	1.0892	0.6028	0.7107	0.033
H49C	1.0356	0.5904	0.5698	0.033
H51A	0.4352	0.6761	0.6076	0.031
H51B	0.4129	0.6546	0.4753	0.031
H51C	0.3267	0.7057	0.4937	0.031
H52A	0.4688	0.7181	0.3346	0.034
H52B	0.5550	0.7732	0.3846	0.034
H52C	0.3997	0.7710	0.3690	0.034
H53A	0.4483	0.7969	0.5763	0.029
H53B	0.6049	0.8021	0.5982	0.029
H53C	0.5571	0.7636	0.6840	0.029