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Synthesis and application of dual chiral [2.2]paracyclophane-based N-heterocyclic carbene in enantioselective β-boration of acyclic enones

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Enantioselective conjugate addition of boron to α, β-unsaturated ketones catalysed by either a N-heterocycle carbene or a copper–carbene complex generated in situ from a new chiral bicyclic triazolium based on [2.2]paracyclophane is presented. The dual chiral carbene-copper catalyst has significant advantange than its carbene counterpart as an organocatalyst in asymmetric β-boration of acyclic enones, giving a variety of chiral β-boryl ketones in good yields and enantioselectivities. This is a successful example of employing the same N-heterocyclic carbene in one catalytic reaction as both an organocatalyst and a ligand for transition metal catalysis.

Introduction

The asymmetric conjugate addition of diboron reagents to α, β-unsaturated compounds is one of the most powerful and efficient methods for the formation of chiral C–B bonds. In pioneering work Suzuki and Miyaura disclosed that efficient addition of diborons to α, β-unsaturated compounds can be promoted by Pt catalysts.[1] The first attempt to catalyze the asymmetric β-boration of α,β-unsaturated nitriles and esters by copper/chiral phosphine catalysts in the presence of alcohol additives was made by Yun and co-workers.[2] In 2009, Fernández and co-workers reported the first asymmetric β-boration of α,β-unsaturated compounds using chiral N-heterocyclic carbene–copper catalysts.[3] Asymmetric conjugate borylation reactions catalyzed by both chiral phosphine and chiral carbene complexes of copper, palladium and nickel have been reported.[4] NHC–metal complexes have emerged as a powerful tool for asymmetric catalysis[5] due to significant advantages over phosphines.[6] However, one challenge still remains to be overcome: the development of a metal-free asymmetric boron-addition reaction with achiral boron reagents.

In 2000, Hosomi and co-workers reported that PBu_3 could induce slight conversion of benzylideneacetophenone into the β-borated ketone in the absence of the catalyst precursor CuOTf.[7] Fernández and co-workers demonstrated that asymmetric β-boration of α,β-unsaturated esters and ketones can be efficiently carried out by organocatalysis, with tertiary phosphorus compounds as chiral auxiliaries.[8] And these results represent the first example of enantioselection in organoboron synthesis without the application of transition-metal catalysts or chiral boron reagents. Since Hoveyda reported that N-heterocyclic carbenes catalyze the β-position of α,β-unsaturated molecules interest in this reaction has blossomed.[9a] The NHC-catalyzed enantioselective boron conjugate additions were shown to be mechanistically unique, allowing them to be complementary to the more extensively examined copper-catalyzed variants.[9] Until now, to the best of our knowledge, there is little reported work on the use of the same N-heterocyclic carbene in one catalytic reaction as both an organocatalyst and a ligand for transition metal catalysis. Despite the fact that our group synthesized a series of new [2.2]paracyclophane-based carbene precursors which induced exceptional enantioselectivities in the copper(I)-meditated β-boration of α,β-unsaturated compounds,[10] the design and synthesis of new efficient chiral N-heterocyclic carbenes to meet the needs of the metal-free enantioselective boron conjugate addition to α,β-unsaturated ketones is still a challenge. Herein, the application of a new carbene precursor as both an organocatalyst and a ligand for transition-metal catalysis in asymmetric boration reaction is reported.

Results and discussion

According to previously reported procedure for the metal-free asymmetric boration of α,β-unsaturated compounds,[9] we first probed a number of easily accessible chiral carbenes that might be used to catalyze the formation of **2a** efficiently and enantioselectively (Table 1). When chiral triazolium salts **3a-d**[11] derived from L-pyroglutamic acid were used as carbene precursors, in the presence of 20 mol% of DBU and 60 equiv of MeOH, the desired boration reaction proceeded smoothly at 22 °C in THF affording product **2a** in high yields (76–96%) and low to moderate enantioselectivities (8–51% ee) (Table 1, entries 1–4). It was found that amino-indanol derived triazolium

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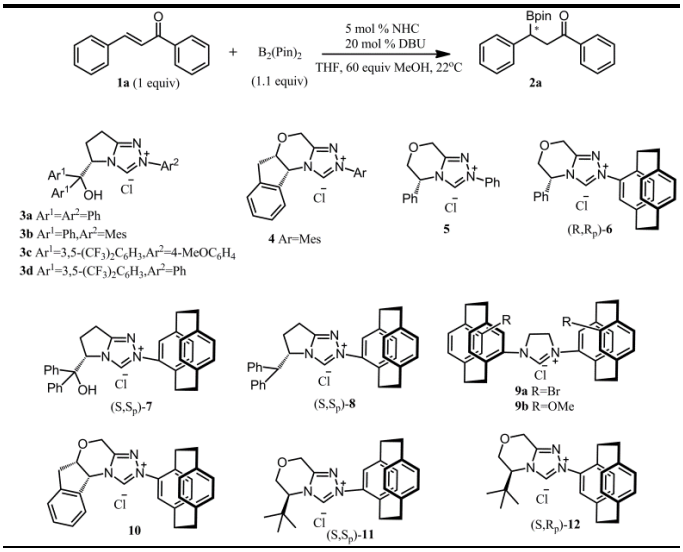
Table 1 Initial Examination of Chiral NHC Catalysts[a]



entry	NHC	time	yield(%)	ee(%)[b]
1	3a	7 h	91%	36% (*R*)
2	3b	7 h	76%	8% (*S*)
3	3c	7 h	83%	51% (*R*)
4	3d	1.5 h	96%	34% (*R*)
5	4	22 h	81%	46% (*R*)
6	5	22 h	15%	92% (*R*)
7	(*R*,R_p)-6	22 h	< 5%	nd
8	(*S*,S_p)-7	2 h	89%	18% (*R*)
9	(*S*,S_p)-8	7 h	72%	26% (*R*)
10	9a	22 h	< 5%	nd
11	9b	22 h	< 5%	nd
12	10	22 h	< 5%	nd
13	(*S*,S_p)-11	22 h	76%	80% (*S*)
14	(*S*,R_p)-12	22 h	49%	57% (*S*)

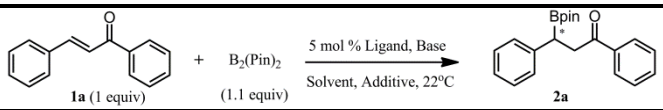
[a]The reaction was carried out with NHC (5 mol %), DBU (20 mol%), B_2Pin_2 (0.11 mmol), **1a** (0.1 mmol), and MeOH (6 mmol) in THF (0.15 ml) at 22 ℃ under N_2 atmosphere.
[b]Determined by HPLC analysis using a chiral stationary phase (Chiralpak IA column).

salt **4**[12] and phenylglycinol derived triazolium salt **5**[13] also catalyzed the reaction under the above conditions. The reaction with carbene precursor **5** afforded high enantioselectivity (92% ee), but low yield (15%) (Table 1, entry 6). Improved yield was obtained with ligand **4** (Table 1, entry 5), whilst the selectivity was still not satisfactory. As shown in previous reports, planar chiral [2.2]paracyclophane-based ligands play an important role in asymmetric catalysis.[14] We were interested to see if introduction of a planar chiral [2.2]paracyclophane into bicyclic triazolium backbone could enhance the enantioselectivity and catalytic activity in the asymmetric conjugate boration. Then we synthesized a series of triazolium salts based on [2.2]paracyclophane and tested them in the β-boration of chalcone. Unfortunately, the chiral triazolium salts **6** and **10** derived from [2.2]paracyclophane were less efficient (Table 1, entries 7 and 12). And the reaction with the [2.2]paracyclophane-based triazolium salt **7** or **8** achieved high yield but low enantioselectivity (Table 1, entries 8 and 9). It is known that many exciting results have been obtained by Hoveyda's imidazolinium salts in the metal-free β-boration of α,β-unsaturated compounds.[9] However, almost no product was detected when [2.2]paracyclophane-based imidazolinium salt **9a** and **9b** were used as catalyst precursors. (Table 1, entries 10 and 11).[15] To our delight, the reaction afforded improved enantioselectivity (80% ee) and yield (76%) by using chiral triazolium salt (*S*,S_p)-**11** (Table 1, entry 13). Then, we tested its diastereomer (*S*,R_p)-**12** as the catalyst under the same reaction conditions. The enantioselectivity and yield dropped severely, but the absolute configuration of the product was not changed (Table 1, entry 14). This result indicated that the diastereomer (*S*,R_p)-**12** showed mismatched planar and central chirality while diastereomer (*S*,S_p)-**11** was matched. In addition, the absolute configuration was determined by the central chirality of the triazolium salts.

To obtained a better yield and enantioselectivity, we then explored the factors affecting the catalytic activities of the carbene precursors **5** and (*S*,S_p)-**11** by using chalcone **1a** as a model substrate. Since using alcohol additives for rate acceleration in this transformation was unavoidable, a number of reaction conditions with different additives were used to enhance catalytic activity of the carbene precursor **5**. Unfortunately, trifluoroethanol, hexafluoroisopropanol and phenol additives were not as effective as MeOH in this reaction (Table 2, entries 1-5). Although the conversion could be increased by increasing reaction temperature from 22 to 60 ℃, lower level of enantioselectivity was obtained (Table 2, entry 6). In addition, the enantioselectivity was obviously dropped by using Cs_2CO_3 instead of DBU (Table 2, entry 7). Disappointed with these results, we therefore turned our attention to another ligand (*S*,S_p)-**11**. The impact of the amounts of MeOH on the boration reaction was investigated first. When the amount of 120 equiv MeOH was used, the carbene catalyst displayed the highest catalytic activity within the range of experimental conditions (Table 2, entries 8-11). The influence of the solvent on the asymmetric induction was studied next. Among the solvents screened (Table 2, entries 9, 12−15), THF gave the best enantioselectivity (80% ee) and a good yield (80%), so it was chosen as the optimal solvent (Table 2, entry 9). Moreover, the effect of the base was also evaluated: *t*-BuOK, DIPEA (N, N-Diisopropylethylamine) and AcOK were much less active than DBU (Table 2, entries 9, 16-18). Increasing the amount of DBU from 20 to 30 mol% caused a slightly increase in the reaction rate and enantioselectivity (Table 2, entries 9 and 20), while decreasing the amount of DBU resulted in lower enantioselectivity and yield (Table 2, entry 19).

As catalytic activity of the carbene precursor (*S*,S_p)-**11** reached an acceptable level, the substrate scope of α,β-unsaturated ketones was surveyed under the optimized reaction conditions (Table 3). It appears that substituents on the aromatic rings of the unsaturated enones have little effect on the reactivity and enantioselectivity (Table 3, entries 1-12). Moreover, a heteroaromatic thiophene-substituted substrate was also tolerated and gave the corresponding compound **2m** in moderate yield and stereoselectivity (Table 3, entry 13). The scope was also extended to β-alkyl-substituted unsaturated enones. When a methyl group was introduced at the β-position of α,β-unsaturated ketone, the desired product **2n** was obtained in good yield (87%) and moderate enantioselectivity (72% ee) (Table 3, entry 14). However, the reactions did not proceed at all or proceeded very sluggishly when a methyl group or *tert*-butyl group was introduced at the carbonyl carbon of the enone (Table 3, entries 15 and 16).

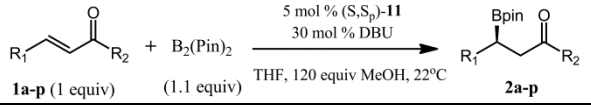
Table 2 Screening of the Reaction Conditions[a]



entry	Ligand	Base	additive	solvent	yield	ee(%)[b]
1	5	20 mol% DBU	60 equiv CF_3CH_2OH	THF	trace	nd
2	5	20 mol% DBU	60 equiv $(CF_3)_2CHOH$	THF	trace	nd
3	5	20 mol% DBU	60 equiv MeOH, 10 mol% phenol	THF	trace	nd
4	5	20 mol% DBU	50 equiv MeOH, 10 eq CF_3CH_2OH	THF	trace	nd
5	5	20 mol% DBU	120 equiv MeOH	THF	18%	91%
6[c]	5	20 mol% DBU	60 equiv MeOH	THF	65%	74%
7	5	20 mol% Cs_2CO_3	60 equiv MeOH	THF	19%	86%
8	(S,S_p)-11	20 mol% DBU	60 equiv MeOH	THF	76%	80%
9	(S,S_p)-11	20 mol% DBU	120 equiv MeOH	THF	80%	80%
10	(S,S_p)-11	20 mol% DBU	150 equiv MeOH	THF	59%	74%
11	(S,S_p)-11	20 mol% DBU	180 equiv MeOH	THF	43%	75%
12	(S,S_p)-11	20 mol% DBU	120 equiv MeOH	toluene	41%	72%
13	(S,S_p)-11	20 mol% DBU	120 equiv MeOH	DME	67%	81%
14	(S,S_p)-11	20 mol% DBU	120 equiv MeOH	dioxane	56%	83%
15[d]	(S,S_p)-11	20 mol% DBU	120 equiv MeOH	DME-H_2O	37%	68%
16	(S,S_p)-11	20 mol% AcOK	120 equiv MeOH	THF	trace	nd
17	(S,S_p)-11	20 mol% DIPEA	120 equiv MeOH	THF	32%	80%
18	(S,S_p)-11	20 mol% *t*-BuOK	120 equiv MeOH	THF	59%	42%
19	(S,S_p)-11	10 mol% DBU	120 equiv MeOH	THF	33%	75%
20	(S,S_p)-11	30 mol% DBU	120 equiv MeOH	THF	81%	83%

[a]Reactions were performed under N_2 atmosphere. [b]Determined by HPLC analysis using a chiral stationary phase (Chiralpak IA column).
[c]reaction was performed at 60 ℃. [d] DME : H_2O = 10 : 1.

Table 3 Investigating the Substrate Scope of the Reaction[a]

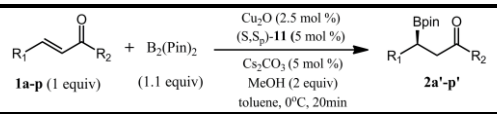


entry	R_1	R_2	yield(%)	ee(%)[b]
1	Ph	Ph	81%	83%(**2a**)
2	2-ClC_6H_4	Ph	76%	84%(**2b**)
3	3-ClC_6H_4	Ph	43%	77%(**2c**)
4	4-ClC_6H_4	Ph	42%	81%(**2d**)
5	2-$MeOC_6H_4$	Ph	41%	76%(**2e**)
6	3-$MeOC_6H_4$	Ph	90%	75%(**2f**)
7	4-$MeOC_6H_4$	Ph	91%	74%(**2g**)
8	4-MeC_6H_4	Ph	92%	76%(**2h**)
9	1-Naphthyl	Ph	42%	78%(**2i**)
10	Ph	4-FC_6H_4	93%	76%(**2j**)
11	Ph	4-$MeOC_6H_4$	83%	82%(**2k**)
12	Ph	4-MeC_6H_4	89%	82%(**2l**)
13	2-Thienyl	Ph	32%	65%(**2m**)
14	Me	Ph	87%	72%(**2n**)
15	Ph	Me	nr	nd
16	Ph	*t*-Bu	nr	nd

[a]Reactions were performed under N_2 atmosphere.
[b]Determined by HPLC analysis using a chiral stationary phase (Chiralpak IA column).

The goal of this study was utilization of a carbene precursor as both an organocatalyst and a ligand for transition-metal catalysis in asymmetric boration reaction. Having identified the appropriate organocatalyst, we then explored the copper-catalyzed β-boration of α,β-unsaturated ketones by using carbene precursor (S,S_p)-**11** as the ligand. According to our previously reported procedure for the copper-catalyzed asymmetric boration of α,β-unsaturated ketones,[10a] a range of α,β-unsaturated ketones were screened for the reaction (Table 4). To our delight, when chalcone **1a** was used as substrate, the boration reaction was completed within 20 min at 0 ℃ and the desired product was obtained in excellent yield (97%) and enantioselectivity (98% ee) (Table 4, entry 1). The markedly different catalytic performance of carbene precursor (S,S_p)-**11** in the presence or absence of transition metal indicates that the mechanisms of the transition-metal catalysis and organocatalysis must be entirely different.[9] It is worth to noting that the electronic properties of the chalcone derivatives have an important effect on both reactivity and enantioselectivity. The substrates bearing an electron-withdrawing group such as Cl and F at the 2- or 4-position in the phenyl ring provided the products with high enantiomeric excesses (84-92% ee) (Table 4, entries3-4 and 10), while 2-position substitution at the aromatic ring afforded exceptional enantioselectivity (99% ee) (Table 4, entry 2). When the chalcone derivatives having an electron-donating group in the phenyl ring were subjected to the boration reaction, good yields (86-96%) and excellent enantiopurities (94-99% ee) were observed (Table 4, entries 5-8 and 11-12). Moreover, 1-Naphthyl

Table 4 Copper(I)-catalyzed enantioselective β-boration of acyclic enones[a]



entry	R_1	R_2	yield(%)	ee(%)[b]
1	Ph	Ph	97%	98%(**2a'**)
2	2-ClC_6H_4	Ph	88%	99%(**2b'**)
3	3-ClC_6H_4	Ph	81%	84%(**2c'**)
4	4-ClC_6H_4	Ph	83%	86%(**2d'**)
5	2-MeOC_6H_4	Ph	93%	99%(**2e'**)
6	3-MeOC_6H_4	Ph	90%	99%(**2f'**)
7	4-MeOC_6H_4	Ph	86%	99%(**2g'**)
8	4-MeC_6H_4	Ph	90%	94%(**2h'**)
9	1-Naphthyl	Ph	83%	96%(**2i'**)
10	Ph	4-FC_6H_4	95%	92%(**2j'**)
11	Ph	4-MeOC_6H_4	96%	95%(**2k'**)
12	Ph	4-MeC_6H_4	92%	95%(**2l'**)
13	2-Thienyl	Ph	90%	99%(**2m'**)
14	Me	Ph	85%	89%(**2n'**)
15	Ph	Me	90%	58%(**2o'**)
16	Ph	*t*-Bu	97%	94%(**2p'**)

[a]Reactions were performed under N_2 atmosphere.
[b]Determined by HPLC analysis using a chiral stationary phase (Chiralpak IA column or IB column).

and heteroaromatic thiophene-substituted substrates were also tolerated and the corresponding products were isolated in 83% and 90% yields with 96% and 99% ee, respectively (Table 4, entries 9, 13). In addition, for the methyl-substituted at the β-position of the α,β-unsaturated enone, the β-boryl ketone was obtained with enantioselectivity of 89% ee (Table 4, entry 14). In contrast to the carbene-catalyzed reaction, which did not proceed at all when a methyl group or *tert*-butyl group was introduced at the carbonyl carbon of the enone (Table 3, entries 15 and 16), the Cu-catalyzed variants gave the desired products in high yields (Table 4, entries 15 and 16). It is worth noting that the steric hindrance of the alkyl group at the carbonyl carbon can significantly affect the enantioselectivity of the reaction (Table 4, entries 15-16).

Conclusions

A series of new chiral bicyclic triazolium salts based on [2.2]paracyclophane backbone were synthesized and successfully applied to carbene-catalyzed and Cu-catalyzed asymmetric β-boration of acyclic enones. The present account puts forth the first application of a carbene precursor as both an organocatalyst and a ligand for transition-metal catalysis in asymmetric boration reaction. The dual chiral carbene-copper catalyst has significant advantange than its carbene counterpart as an organocatalyst with regard to both reactivity and enantioselectivity and affords the desired products with high yields and excellent enantiomeric excesses. The design and development of other carbene-catalyzed and copper-catalyzed processes and applications to asymmetric synthesis of complex molecules are additional goals of future investigations.

Experimental section

General remarks

Commercially available reagents were used without further purification unless otherwise noted. Solvents were reagent grade and purified by standard techniques. Purification of the reaction products was carried out by chromatography on silica gel (200-400 mesh). Melting points were recorded on a melting point apparatus and are uncorrected. Optical rotations were taken on a polarimeter with a wavelength of 589 nm. ^{1}H NMR and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker AVANCE-300 spectrometer at 298 K. Chemical shifts are reported in parts per million (ppm) downfield from tetramethylsilane (TMS) with reference to the internal solvent for ^{1}H NMR and ^{13}C NMR spectra. Mass spectra were recorded on an Agilent Technologies 6510 Q-Tof LC/MS. The concentration "*c*" had units of g/100 mL (or 10 mg/mL). Enantiomeric excess was determined using HPLC on a Chiralpak IA chiral column.

Preparation of ligands 6-9

Triazolium salts (R,R_p)-**6**, (S,S_p)-**7** and (S,S_p)-**8** were synthesised according to the literature procedures.[10] Imidazolinium salts **9a-b** were prepared according to the literature procedure.[15]

General procedure for the synthesis of ligands 10

To a solution of iminoether[13a] (223 mg, 1.1 mmol) in MeOH (3 mL), was added (R_p)-4-formohydrazine[2.2]paracyclophane hydrochloride[10] (303 mg, 1 mmol) at room temperature. The mixture was warmed to 50 ℃ and stirred for 2 h. Then solvent was evaporated under reduced pressure, trimethyl orthoformate (4 mL) and anhydrous 4 M EtOH/HCl (0.05 ml, 0.2 mmol) were added to the residue. The reaction mixture was stirred for 3 hours at 120 ℃. After completion (monitored by TLC), the solvent was removed in vacuo and the residue was purified by flash chromatography (CH_2Cl_2/Methanol = 20:1) to afford **10** as a white solid (416 mg, 91% yield, two steps). MP: 192–194 ℃; $[\alpha]_D^{20}$ = -341.0 (*c* 1.0, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.4 (s, 1H), 7.82–7.80 (d, J = 7.5 Hz, 1H), 7.28–7.07 (m, 3H), 6.98 (s, 1H), 6.78 (m, 3H), 6.64–6.47 (m, 4H), 5.30–5.21 (m, 2H), 5.02–4.97 (m, 1H), 3.49–3.45 (m, 1H), 3.18–2.83 (m, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.8, 142.7, 142.3, 140.1, 139.1, 139.0, 137.3, 135.8, 135.7, 134.4, 133.9, 132.6, 132.0, 130.1, 129.0, 127.4, 126.7, 125.0, 77.9, 77.4, 77.2, 62.4, 60.4, 37.4, 35.0, 34.8, 34.6, 32.5; HRMS (ESI-TOF) calcd. for $C_{28}H_{26}N_3O$ (M-Cl)$^+$: 420.2076, Found: 420.2100.

General procedure for the synthesis of ligands (S,S_p)-11 and (S,R_p)-12

To a solution of iminoether[16] (188 mg, 1.1 mmol) in MeOH (3 mL), was added 4-formohydrazine[2.2]paracyclophane hydrochloride[11] (303 mg, 1 mmol) at room temperature. The mixture was warmed to 50 ℃ and stirred for 2 h. Then solvent was evaporated under reduced pressure, trimethyl orthoformate (4 mL) and anhydrous 4 M EtOH/HCl (0.05 ml, 0.2 mmol) were added to the residue. The reaction mixture was stirred for 4 h at 110 ℃. After completion (monitored by TLC), the solvent was removed in vacuo and the residue was purified by flash column

chromatography (CH_2Cl_2/MeOH = 20/1) to afford the product as a white solid.

Triazolium Salt **(S,S_p)-11.** White solid: 361 mg, 85% yield; MP: 243–245 ℃,$[\alpha]_D^{20}$ = +222 (*c* 0.5, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.46 (s, 1H), 6.90 (s, 1H), 6.76–6.57 (m, 6H), 5.27–5.22 (m, 2H), 5.03 (d, *J* = 16.5 Hz, 1H), 4.50–4.44 (m, 1H), 4.16 (d, *J* = 13.5 Hz, 1H), 3.39-3.33 (m, 1H), 3.30–2.99 (m, 6H), 2.94–2.88 (m, 1H), 1.20 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.9, 143.0, 142.7, 139.4, 138.9, 137.5, 135.9, 134.0, 133.5, 133.4, 132.8, 132.7, 130.9, 127.3, 64.4, 63.1, 61.4, 35.1, 35.0, 34.8, 34.7, 32.8, 27.3; HRMS (ESI-TOF) calcd for $C_{25}H_{30}N_3O$ $(M\text{-}Cl)^+$: 388.2389, found: 388.2390.

Triazolium Salt **(S,R_p)-12.** Whit solid: 382 mg, 90% yield; M.P: 235–237 ℃; $[\alpha]_D^{20}$ = +56 (*c* 0.1, CH_2Cl_2); ^{1}H NMR (300 MHz, $CDCl_3$): δ 12.03 (s, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.66 (d, 8.1 Hz, 1H), 6.55 (t, *J* = 7.8 Hz, 2H), 5.25 (d, *J* = 16.8 Hz, 1H), 5.28–5.20 (m, 2H), 4.98 (d, *J* = 16.8 Hz, 1H), 4.57 (d, *J* = 12.9 Hz, 1H), 4.09–4.03 (m, 1H), 3.62–3.58 (m, 1H), 3.41–3.20 (m, 2H), 3.19–2.95 (m, 4H), 2.73–2.69 (m, 1H), 2.05 (s, 1H), 1.29 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 150.0, 143.9, 143.3, 140.1, 138.8, 137.2, 135.8, 134.3, 133.4, 133.3, 133.2, 132.8, 128.2, 127.3 64.6, 63.3, 61.5, 35.3, 35.1, 34.9, 34.7, 32.6, 27.4; HRMS(ESI) calcd for $C_{25}H_{30}N_3O$ $(M\text{-}Cl)^+$: 388.2389, found: 388.3171.

General procedure for the metal-free catalytic enantioselective β-boration of α, β-unsaturated enones

Under an N_2 atmosphere, triazolium salt (S,S_p)-**11** (2.12 mg, 5×10^{-3} mmol) and DBU (4.56 mg, 3×10^{-2} mmol) were added to 0.25 mL of anhydrous THF in an oven-dried vial equipped with a stir bar. The mixture was stirred at 22 ℃ for 30 min. Bis(pinacolato)diboron (27.9 mg, 0.11 mmol), α, β-unsaturated enones (0.1 mmol) and MeOH (0.48 ml, 12 mmol) were added simultaneously to the vial. After the mixture was stirred for 22 h at 22 ℃, the solvent was removed in vacuum and the crude product was purified by flash column chromatography (ethyl acetate/hexane = 1:20) to afford the corresponding product **2.**

(*S*)-1,3-Diphenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2a). Colorless oil: 27.2 mg, 81% yield, 83% ee; $[\alpha]_D^{20}$ = +14.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 12.7 min (*S*, major), t_R = 16.9 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-3-(2-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2b) Colorless oil: 28.1 mg, 76% yield, 84% ee; $[\alpha]_D^{20}$ = +39.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (200 : 1), flow rate = 0.5 mL/min; t_R = 19.1 min (*S*, major), t_R = 21.5 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(3-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2c). Colorless oil: 15.9 mg, 43% yield, 77% ee; $[\alpha]_D^{20}$ = +125 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 14.2 min (*S*, major), t_R = 18.0 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(4-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2d). Colorless oil: 15.5 mg, 42% yield, 81% ee; $[\alpha]_D^{20}$ = +20.5 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 17.1 min (*S*, major), t_R = 26.7 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[17]

(*S*)-3-(2-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2e) Colorless oil: 15.0 mg, 41% yield, 76% ee; $[\alpha]_D^{20}$ = +30.5 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (200 : 1), flow rate = 0.5 mL/min; t_R = 34.1 min (*S*, major), t_R = 35.9 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(3-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2f) Colorless oil: 32.8 mg, 90% yield, 75% ee; $[\alpha]_D^{20}$ = +21.0 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 19.0 min (*S*, major), t_R = 25.8 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(4-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2g) Colorless oil: 33.3 mg, 91% yield, 74% ee; $[\alpha]_D^{20}$ = +11.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 20.2 min (*S*, major), t_R = 28.8 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[17]

(*S*)-1-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-p-tolylpropan-1-one (2h) Colorless oil; 32.2 mg, 92% yield, 76% ee; $[\alpha]_D^{20}$ = +12.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 14.2 min (*S*, major), t_R = 19.2 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-3-(Naphthalen-1-yl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one(2i). Colorless oil; 16.2 mg, 42% yield, 78% ee; $[\alpha]_D^{20}$ = +82 (*c* 0.15, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak

IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 16.2 min (*S*, major), t_R = 17.4 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-1-(4-Fluorophenyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2j). Colorless oil; 32.8 mg, 93% yield, 76% ee; $[\alpha]_D^{20}$ = +13.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 15.0 min (*S*, major), t_R = 19.9 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-1-(4-Methoxyphenyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2k) Colorless oil; 30.3 mg, 83% yield, 82% ee; $[\alpha]_D^{20}$ = +13.9 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 27.7 min (*S*, major), t_R = 42.9 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-p-tolylpropan-1-one (2l). Colorless oil; 31.0 mg, 89% yield, 82% ee; $[\alpha]_D^{20}$ = +17.0 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 17.0 min (*S*, major), t_R = 29.2 min (*R*, minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(Thienyl-2-yl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2m). Colorless oil; 11.0 mg, 32% yield, 65% ee; $[\alpha]_D^{20}$ = +21.0 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 15.0 min (*S*, major), t_R = 19.9 min (*R*, minor); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.60–7.51 (m, 1H), 7.50–7.41 (m, 2H), 7.11 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.97–6.86 (m, 2H), 3.61–3.48 (m, 2H), 3.09 (dd, *J* = 8.9, 6.4 Hz, 1H), 1.27 (d, *J* = 6.6 Hz, 7H), 1.21 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.2, 144.7, 136.6, 133.1, 128.5, 128.1, 126.9, 124.2, 122.9, 44.0, 29.7, 24.6, 24.6.

(*R*)-1-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-1-one (2n) Colorless oil; 23.8 mg, 87% yield, 72% ee; $[\alpha]_D^{20}$ = -70.5 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 10.3 min (*R*, major), t_R = 12.9 min (*S*, minor); Other spectra and properties data matched those reported in the literature.[5d]

General procedure for the Cu-NHC-catalazed enantio-selective β-boration of α, β-unsaturated enones

Under an argon atmosphere, triazolium salt (*S*,S_p)-**11** (2.12 mg, 5×10^{-3} mmol) and Cu_2O (0.35 mg, 2.5×10^{-3} mmol) were added to 1 mL of anhydrous Dichloroethane in an oven-dried Schlenk flask. The mixture was stirred at 80 ℃ overnight to give a colorless solution of the Cu complex.Then the solvent was evaporated under argon at 90 ℃, and 1.0 mL of anhydrous toluene was added at room temperature. Cs_2CO_3 (1.6 mg, 5×10^{-3} mmol) and bis(pinacolato)diboron (27.9 mg, 0.11 mmol) were added consecutively. The mixture was stirred at room temperature for 5 min and cooled to 0 ℃. Then α, β -unsaturated enones (0.1 mmol) and MeOH (8 μL, 0.2 mmol) were added simultaneously to the stirred mixture. After the mixture was stirred for 20 min at 0 ℃, the solvent was removed in vacuum and the crude product was purified by flash column chromatography (ethyl acetate/hexane = 1 : 20) to afford the corresponding product.

(*S*)-1,3-Diphenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2a'). Colorless oil: 32.6 mg, 97% yield, 98% ee; $[\alpha]_D^{20}$ = +19.2 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (200 : 1), flow rate = 0.5 mL/min; t_R = 42.3 min (*S*, minor), t_R = 44.4min (*R*, major); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-3-(2-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2b') Colorless oil: 32.5 mg, 88% yield, 99% ee; $[\alpha]_D^{20}$ = +44.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (200 : 1), flow rate = 0.5 mL/min; t_R = 16.0 min (major), t_R = 17.2 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(3-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2c'). Colorless oil: 29.9 mg, 81% yield, 84% ee; $[\alpha]_D^{20}$ = +59.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 13.2 min (major), t_R = 18.0 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(4-Chlorophenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2d'). Colorless oil: 30.6 mg, 83% yield, 86% ee; $[\alpha]_D^{20}$ = +24.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 15.8 min (major), t_R = 22.4 min (minor); Other spectra and properties data matched those reported in the literature.[17]

(*S*)-3-(2-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2e') Colorless oil: 34.0 mg, 93% yield, 99% ee; $[\alpha]_D^{20}$ = +40.4 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (200 : 1), flow rate = 0.5 mL/min; t_R = 48.2 min (major), t_R = 51.3min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(3-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2f') Colorless oil: 32.8

mg, 90% yield, 99% ee; $[\alpha]_D^{20}$ = +28.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 18.4 min (major), t_R = 23.9 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(4-Methoxyphenyl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2g') Colorless oil: 31.5 mg, 86% yield, 99% ee; $[\alpha]_D^{20}$ = +16.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 20.2 min (major), t_R = 28.8 min (minor); Other spectra and properties data matched those reported in the literature.[17]

(*S*)-1-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-p-tolylpropan-1-one (2h') Colorless oil; 31.5 mg, 90% yield, 94% ee; $[\alpha]_D^{20}$ = +14.0 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 13.6 min (major), t_R = 18.2 min (minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-3-(Naphthalen-1-yl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2i'). Colorless oil; 32.1 mg, 83% yield, 96% ee; $[\alpha]_D^{20}$ = +28.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 14.4 min (major), t_R = 15.8 min (minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-1-(4-Fluorophenyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2j'). Colorless oil; 33.7 mg, 95% yield, 92% ee; $[\alpha]_D^{20}$ = +11.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 14.7 min (major), t_R = 19.3 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-1-(4-Methoxyphenyl)-3-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2k') Colorless oil; 35.1 mg, 96% yield, 95% ee; $[\alpha]_D^{20}$ = +58.3 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 27.4 min (major), t_R = 41.0 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1-tolylpropan-1-one (2l'). Colorless oil; 32.2 mg, 92% yield, 95% ee; $[\alpha]_D^{20}$ = +37.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 16.3 min (major), t_R = 26.9 min (minor); Other spectra and properties data matched those reported in the literature.[10]

(*S*)-3-(Thienyl-2-yl)-1-phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)propan-1-one (2m'). Colorless oil; 30.9 mg, 90% yield, 99% ee; $[\alpha]_D^{20}$ = +45.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 14.9 min (major), t_R = 17.6 min (minor); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (dd, *J* = 5.2, 3.3 Hz, 2H), 7.60 – 7.51 (m, 1H), 7.50 – 7.41 (m, 2H), 7.11 (dd, *J* = 5.1, 1.2 Hz, 1H), 6.97 – 6.86 (m, 2H), 3.61 – 3.48 (m, 2H), 3.09 (dd, *J* = 8.9, 6.4 Hz, 1H), 1.27 (d, *J* = 6.6 Hz, 7H), 1.21 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 199.2, 144.7, 136.6, 133.1, 128.5, 128.1, 126.9, 124.2, 122.9, 44.0, 29.7, 24.6, 24.6.

(*R*)-1-Phenyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) butan-1-one (2n'). Colorless oil; 23.3 mg, 85% yield, 89% ee; $[\alpha]_D^{20}$ = -57.5 (*c* 0.1, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm, eluent: hexane/*i*-PrOH (50 : 1), flow rate = 0.5 mL/min; t_R = 10.2 min (major), t_R = 12.4min (minor); Other spectra and properties data matched those reported in the literature.[5d]

(*S*)-4-Phenyl-4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)butan-2-one. (2o'). Colorless oil: 24.7 mg, 90% yield, 58% ee; $[\alpha]_D^{20}$ = +15.5 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC witha Chiralpak IB column: λ = 254 nm; eluent, hexane/i-PrOH (100 : 1); flow rate = 0.5 mL/min; t_R= 76.9 min (S, major); t_R= 79.0 min (R ,minor). Other spectra and properties data matched those reported in the literature[5d]

(*S*)-4,4-Dimethyl-1-phenyl-1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl) pentan-3-one (2p'). Colorless oil: 30.6 mg, 97%yield, 94% ee; $[\alpha]_D^{20}$ = +32.7 (*c* 0.2, $CHCl_3$); The enantiomeric excess was determined by HPLC with a Chiralpak IA column: λ = 254 nm;eluent, hexane/ i-PrOH (200 : 1); flow rate = 0.5 mL/min; t_R= 17.0min (major); t_R= 19.6 min (minor). Other spectra and properties data matched those reported in the literature[2b]

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