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Crown Ether-Derived Chiral BINOL: Enantioselective Michael Addition of Alkenyl Boronic Acids to α,β-Unsaturated Ketones

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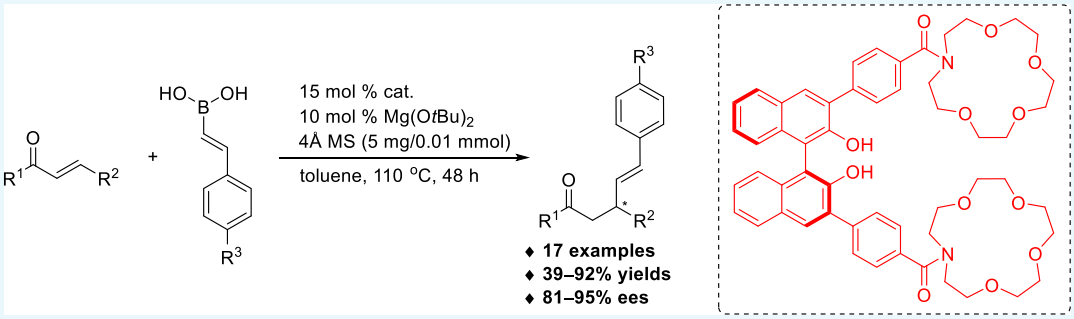

ABSTRACT: A new class of aza-crown ether-derived chiral BINOL catalysts were designed, synthesized, and applied in the asymmetric Michael addition of alkenylboronic acids to α,β-unsaturated ketones. It was found that introducing aza-crown ethers to the BINOL catalyst could achieve apparently higher enantioselectivity than a similar BINOL catalyst without aza-crown ethers did, although the host−guest complexation of alkali ions by the aza-crown ethers could not further improve the catalysis effectiveness. Under mediation of the aza-crown ether-derived chiral BINOL and in the presence of a magnesium salt, an array of chiral γ,δ-unsaturated ketones were furnished in good enantioselectivities (81−95% ees).

INTRODUCTION

Asymmetric Michael addition is a class of highly effective carbon−carbon bond formation reactions for the construction of stereocenters.[1] In the past few decades, asymmetric Michael addition of saturated carbanion nucleophiles to α,β-unsaturated carbonyl compounds has achieved great success.[2] Although the methods with unsaturated carbons as nucleophiles have also been developed, the Michael addition of using unsaturated nucleophiles mainly focused on the metal-mediated systems.[3] The studies on organometallic reagents' asymmetric conjugate additions of α,β-unsaturated carbonyl compounds have engendered a few reliable catalytic methods.[3] The most outstanding approach among them is the Rh-catalyzed asymmetric conjugate addition of organoboronic acid to α,β-unsaturated carbonyl substrates.[4,5] Palladium[6] and copper[7] complexes are also effective catalysts. To avoid the use of precious chiral metal catalysts, endeavors on employing organocatalysts, such as binaphthol (BINOL) derivatives, led to the advent of non-metal catalytic methods. The Chong group first reported the asymmetric conjugate addition of enones with alkynylboronates and alkenylboronates catalyzed by chiral 3,3′-disubstituted BINOLs without using metal catalysts in 2005 and 2007, respectively.[8] The conjugate addition performed in uniformly high yields and good enantioselectivities for most substituted enones and boronates. In 2011, they extended this catalytic system to the enantioselective conjugate addition of arylboronates to enones with 3,3′-dichloro-BINOL as the best catalyst.[9] The catalytic mechanisms were proposed to undergo transesterification of the boronates with BINOLs. The BINOL-catalyzed reactions of boronic esters were also applied in the asymmetric 1,2-addition of ketones, imines, or iminiums (Petasis reactions).[10] However, the use of boronic esters is problematic owing to their hydrolytic instability and loss of purity during storage.[11,12] Therefore, organoboronic acid compounds, such as alkenylboronic acids, were investigated for the asymmetric conjugate additions due to their easier access, low toxicity, high stability, and operational simplicity.[12] It was found that the BINOL derivatives,[11] hydroxyl carboxylic acids,[13] hydroxyl thioureas,[14] and secondary amines[15] were capable of activating alkenylboronic acids in conjugate addition of enones or enals. Nonetheless, the use of alkenylboronic acids in these reactions usually led to lower enantioselectivities. May and co-workers

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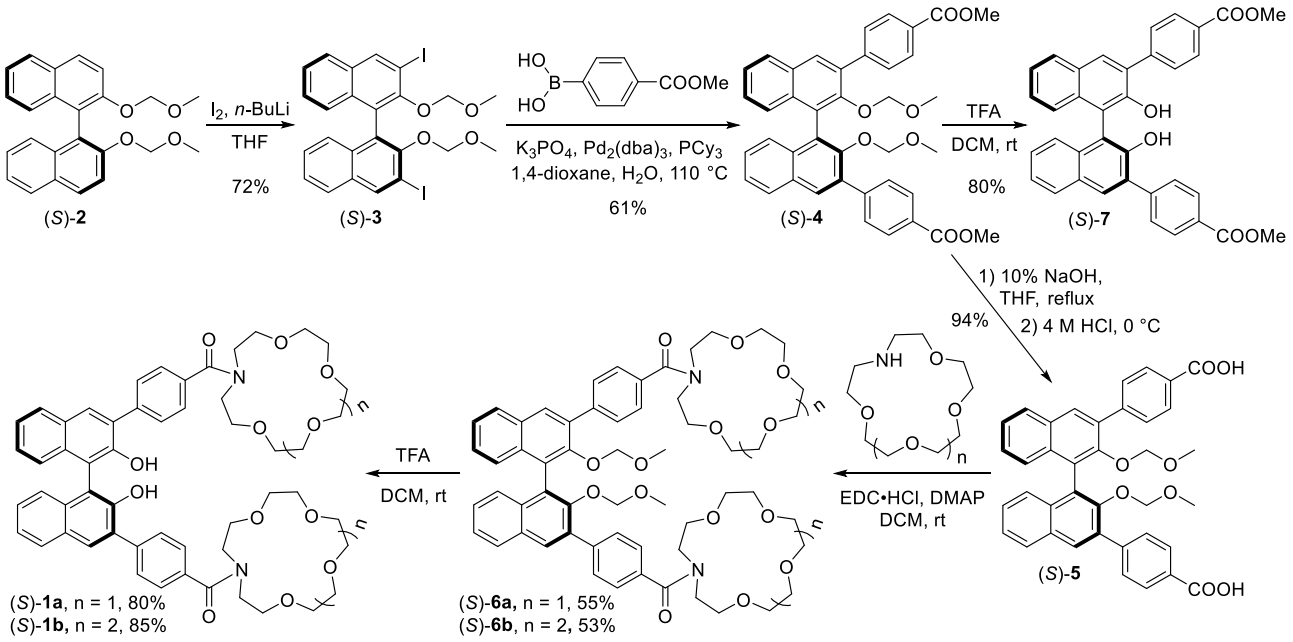
Scheme 1. Synthesis of the Crown Ether-Derived BINOL Catalysts (*S*)-1



reported that the conjugate addition of alkenylboronic acids to heteroaryl enones could achieve relatively high enantioselectivities under the catalysis of a highly electron-deficient chiral BINOL, 3,3′-bisperfluorophenyl-substituted BINOL,[11] but the conjugate addition of non-heteroaryl and alkyl enones by alkenylboronic acids still remains a challenge.

Crown ethers and their derivatives have been widely utilized in host−guest recognition for metallic or organic cations, chemical sensors, the preparation of mechanically interlocked molecules, and supramolecular polymers.[16] The specific host−guest recognition properties of crown ethers also enable them to be used as supramolecular catalysts or as regulation factors to tune the asymmetric catalytic reactions.[17,18] Fan and coworkers[18a] synthesized a BINOL-based phosphoramidite ligand bearing an aza-crown ether on the phosphor atom and found its application as a switchable catalysis prototype in rhodium-catalyzed asymmetric hydrogenation reactions, triggered by host−guest interactions of aza-crown ether with metal cations. In 2016, our group[18b] reported another example of supramolecularly tunable chiral catalysts by decorating two pyridyl-containing crown ethers onto a chiral dipyridylphosphine skeleton to be applied in Rh or Ir-mediated asymmetric hydrogenation of α-dehydroamino acid esters and quinoline derivatives. Obviously enhanced enantioselectivities (up to 22% ee increased) were obtained after the complexation of pyridylaza-crown ethers with alkali ions. Here, we wish to extend this supramolecularly tuned strategy to a chiral BINOL-based catalytic system. A kind of new crown ether-attached BINOL catalysts were designed, synthesized, and applied in the asymmetric alkenylation of α,β-unsaturated ketones. Although it was found that the addition of alkali ions could not improve the catalysis in this case, these BINOL catalysts appended with two aza-crown ethers could effectively catalyze the conjugate addition of alkenylboronic acids to aryl or alkyl-substituted enones in higher enantioselectivity than a similar BINOL catalyst without crown ethers did.

RESULTS AND DISCUSSION

Synthesis of the Crown Ether-Derived BINOL Catalysts. It is worthy of being mentioned that the first achiral 3,3′-bis(aza-crown ether)-substituted BINOL was synthesized by Roithová *et al. via* Cu(II)-catalyzed cross-coupling of naphthol derivatives.[19] Here, we first synthesized the chiral 3,3′-bis(aza-crown ether)-derived BINOL catalysts (*S*)-**1a** and (*S*)-**1b** in five steps, respectively, from 2,2′-bis(methoxymethoxy)-1,1′-binaphthalene (*S*)-**2** (Scheme 1). After iodination of (*S*)-**2**, the resulting BINOL (*S*)-**3** underwent the palladium-catalyzed Suzuki−Miyaura coupling reaction with (4-(methoxycarbonyl)phenyl)boronic acid to produce (*S*)-**4** in 61% yield. Hydrolysis of (*S*)-**4** and then amidation of dicarboxylic acid (*S*)-**5** with aza-15-crown-5 or aza-18-crown-6 furnished the intermediates (*S*)-**6a** and (*S*)-**6b**, respectively. Finally, the aza-15-crown-5-derived BINOL (*S*)-**1a** and aza-18-crown-6-derived BINOL (*S*)-**1b** were prepared by deprotection of (*S*)-**6a** and (*S*)-**6b** under the catalysis of trifluoroacetic acid (TFA) in 80 and 85% yields, respectively.

Optimization of Reaction Conditions. The catalysis performance of (*S*)-**1a** was investigated initially by using the addition reaction between 4-phenylbut-3-en-2-one **8a** and (*E*)-styrylboronic acid **9a** in toluene at 70 °C to afford the desired product **10a** in 37% conversion with 89% ee (Table 1, entry 1). On the basis of this study, we subsequently screened various reaction conditions including additives, solvents, temperature, and the ratio of reactants to optimize the reaction activity and enantioselectivity. As the previous reports demonstrated that the presence of metal salts could improve the catalytic effectiveness of BINOLs in the addition reactions,[11,12] a variety of metal salts were examined as the additives under a given set of reaction conditions (Table 1, entries 2−11). Among several selected *tert*-butoxide salts, the addition of 0.1 equivalent of $Mg(OtBu)_2$ increased the conversion from 37 to 42% (entry 2 *vs* entry 1) with no change of enantioselectivity, while the other *tert*-butoxide salts led to lower reactivity or even lower enantioselectivity (entries 3−6). It was found that the addition of Cs_2CO_3 greatly inhibited the reaction (entry

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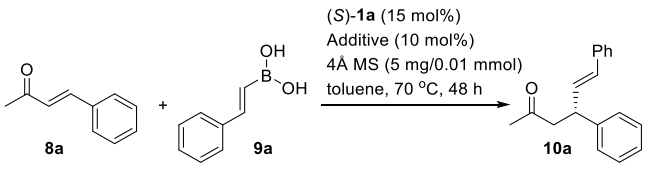
Table 1. Effect of Metal Salt Additives on the Asymmetric Addition[a]



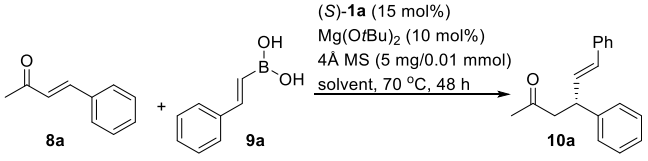
entry	additive	conversion (%)[b]	ee (%)[c]
1		37	89
2	$Mg(OtBu)_2$	42	89
3	$LiOtBu$	30	88
4	$NaOtBu$	27	85
5	$KOtBu$	32	81
6	$Al(OtBu)_3$	31	89
7	Cs_2CO_3	trace	n.d.[d]
8	$MgSO_4$	35	88
9	$MgCl_2$	40	89
10	$MgBr_2$	32	88
11	$Mg(OEt)_2$	40	89
12	$Mg(SO_3CF_3)_2$	35	86
13[e]	$Mg(OtBu)_2$	21	n.d.[d]
14[f]	$Mg(OtBu)_2$, *t*BuOH	26	n.d.[d]
15	$NaBAr_F$	15	32

[a]Reaction conditions: 0.04 mmol **8a**, concentration of **8a** = 0.05 M. [b]Determined by integration of the product in ^{1}H NMR spectra. [c]Determined by HPLC analysis. [d]Not determined. [e]1 equiv $Mg(OtBu)_2$ used. [f]0.1 equiv $Mg(OtBu)_2$ and 2 equiv *t*BuOH used.

7). The use of $Mg(OtBu)_2$ and $Al(OtBu)_3$ provided the adducts with relatively higher enantioselectivity (entries 2 and 6 *vs* entries 3−5). Comparatively, Mg salt was preferable, possibly due to its better solubility and higher activity. Further studies demonstrated that use of the other Mg salts resulted in slightly lower conversions than $Mg(OtBu)_2$ did, but with no significant change of enantioselectivity (entries 8−12). When the dosage of $Mg(OtBu)_2$ was increased to 1 equivalent, only 21% conversion was achieved (entry 13). Addition of 2 equivalent of *t*-BuOH accompanied with 0.1 equivalent of $Mg(OtBu)_2$ as the additives also led to obviously decreased catalytic activity, in 26% conversion (entry 14). As our previous work revealed that the crown ether-based host−guest chemistry could act as supramolecular regulation sites to improve the asymmetric catalytic efficiency,[18b] we further examined the effect of host−guest complexation between the aza-crown ethers of **1a** and NaBArF [BAr_F^- = ((3,5-$(CF_3)_2C_6H_3)_4B^-$)], a strong binding guest for crown ethers, on the catalysis. Unfortunately, the addition of NaBArF induced significantly depressed reactivity and much lower enantioselectivity in this case (entry 15), which was probably because the complexation between the aza-crown ethers and NaBArF disturbed the catalysis process.

The influence of the reaction solvent on the asymmetric conjugate addition under the catalysis of (*S*)-**1a** was subsequently studied (Table 2). A brief screen of solvents revealed that the polar solvents, such as 1,4-dioxane, *N*,*N*-dimethylformamide (DMF), THF, and acetonitrile, were detrimental to the reaction (Table 2, entries 1−4). The use of dichloroethane was also unfavorable for the reaction, probably attributing to its low boiling point (Table 2, entry 5), while the less polar solvents with higher boiling points, such as toluene (Table 1, entry 2), dichloroethane (Table 2, entry 6),

Table 2. Optimization of the Reaction Solvent[a]



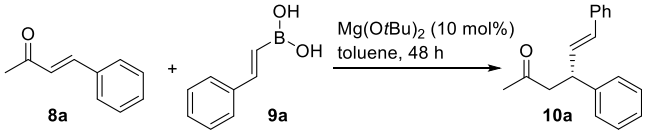
entry	solvent	conversion (%)[b]	ee (%)[c]
1	1,4-dioxane	trace	n.d.[d]
2	DMF	trace	n.d.
3	THF	trace	n.d.
4	CH_3CN	20	n.d.
5[e]	dichloromethane	15	n.d.
6	dichloroethane	35	78
7	xylene	38	87

[a]Reaction conditions: 0.04 mmol **8a**, concentration of **8a** = 0.05 M. [b]Determined by integration of the product in ^{1}H NMR spectra. [c]Determined by HPLC analysis. [d]Not determined. [e]Reacted at reflux (40 °C).

and xylene (Table 2, entry 7), were propitious to the catalytic reaction. It is reasonably inferred that the non-polar solvents favored the formation of catalytically competent boronates from styrylboronic acid and the BINOL catalyst. Among the selected solvents, toluene offered the highest conversion and enantioselectivity (Table 1, entry 2).

We then investigated the influence of the other reaction conditions, including the temperature, substrate concentration, dosage of the molecular sieve, and catalysts. As the reaction temperature increased to 110 °C, at a substrate concentration of 0.05 M, the conversion was slightly increased with unchanged enantioselectivity (Table 3, entry 1 *vs* Table 1, entry 2). The impact of the substrate concentration was further investigated. Both the activity and stereoselectivity of the reaction reduced somewhat when the substrate concentration

Table 3. Optimization of the Other Reaction Conditions[a]



entry	catalyst	temp. (°C)	conc. (M)	4Å MS (mg)	Cat. (mol %)	conversion (%)[b]	ee (%)[c]
1	(S)-**1a**	110	0.05	20	15	48	89
2	(S)-**1a**	70	0.08	20	15	39	83
3	(S)-**1a**	70	0.03	20	15	31	83
4	(S)-**1a**	110	0.03	20	15	41	88
5	(S)-**1a**	70	0.05	0	15	29	78
6	(S)-**1a**	70	0.05	40	15	37	86
7	(S)-**1a**	110	0.05	20	10	45	85
8	(S)-**1a**	110	0.05	20	20	53	89
9	(S)-**1b**	110	0.05	20	15	37	80
10	(S)-7	110	0.05	20	15	35	75
11[d]	(S)-7	110	0.05	20	15	32	23
12[e]	(S)-7	110	0.05	20	15	30	27
13[f]	(S)-**1a**	110	0.05	20	15	42[g]	88

[a]Reaction conditions: 0.04 mmol **8a**. [b]Determined by integration of the product in ^{1}H NMR spectra. [c]Determined by HPLC analysis. [d]No $Mg(OtBu)_2$ added. [e]$NaBAr_F$ used instead of $Mg(OtBu)_2$. [f]1 mmol **8a** used. [g]Isolated yield.

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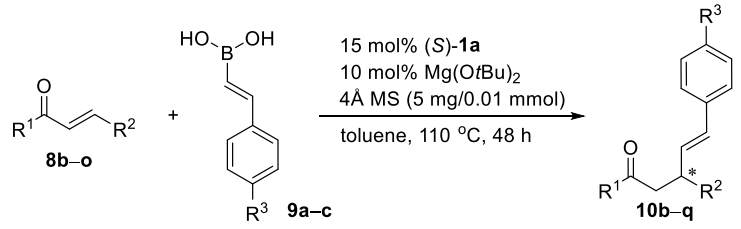
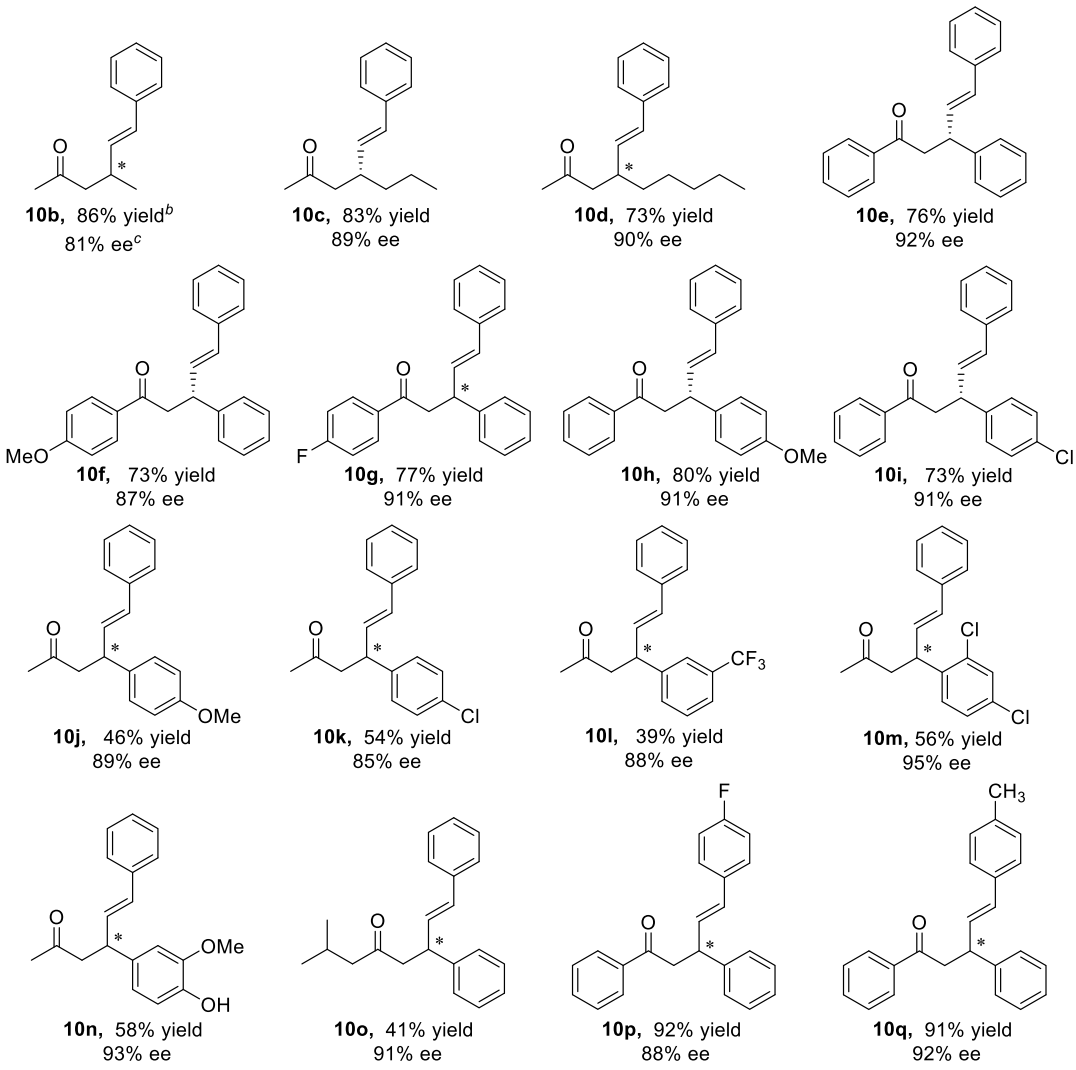
Scheme 2. Substrate Scope of α,β-Unsaturated Ketones and Styrylboronic Acids[a]





[a]Reaction conditions: 0.04 mmol α,β-unsaturated carbonyl substrate, substrate concentration = 0.05 M. [b]Isolated yield. [c]Determined by HPLC analysis.

decreased to 0.03 M or increased to 0.08 M from 0.05 M (Table 3, entries 2 and 3 *vs* entry 1). There were slight improvements in the reaction conversion and enantioselectivity when the temperature increased to 110 °C at the substrate concentration of 0.03 M (Table 3, entry 4 *vs* entry 3). Furthermore, it was found that both the absence of 4 Å MS and increasing 4 Å MS to 40 mg led to the abatement of conversion (Table 3, entries 5 and 6). Decreasing the catalyst loading to 10 mol % afforded the desired product in a slightly lower enantioselectivity (Table 3, entry 7 *vs* entry 1), while increasing the catalyst loading to 20 mol % achieved a higher conversion but the same enantioselectivity (Table 3, entry 8 *vs* entry 1). Comparatively, when the aza-18-crown-6-derived BINOL (*S*)-**1b** was employed, both reactivity and enantioselectivity decreased slightly (Table 3, entry 9 *vs* entry 1), implying that larger aza-crown ether is unfavorable to this reaction. Moreover, the use of a similar BINOL catalyst (*S*)-**7** without aza-crown ethers attached gave an obviously diminished conversion and enantioselectivity under the same conditions (Table 3, entry 10 *vs* entry 1). When no $Mg(OtBu)_2$ additive was added (entry 11) or NaBArF was used instead of $Mg(OtBu)_2$ (entry 12), the catalyst (*S*)-**7** without crown ethers provided much lower enantioselectivities, indicative of that the aza-crown ethers are really advantageous to this addition reaction. As we compared the results of using catalysts **1a** and **7**, it could be concluded that **7** was more

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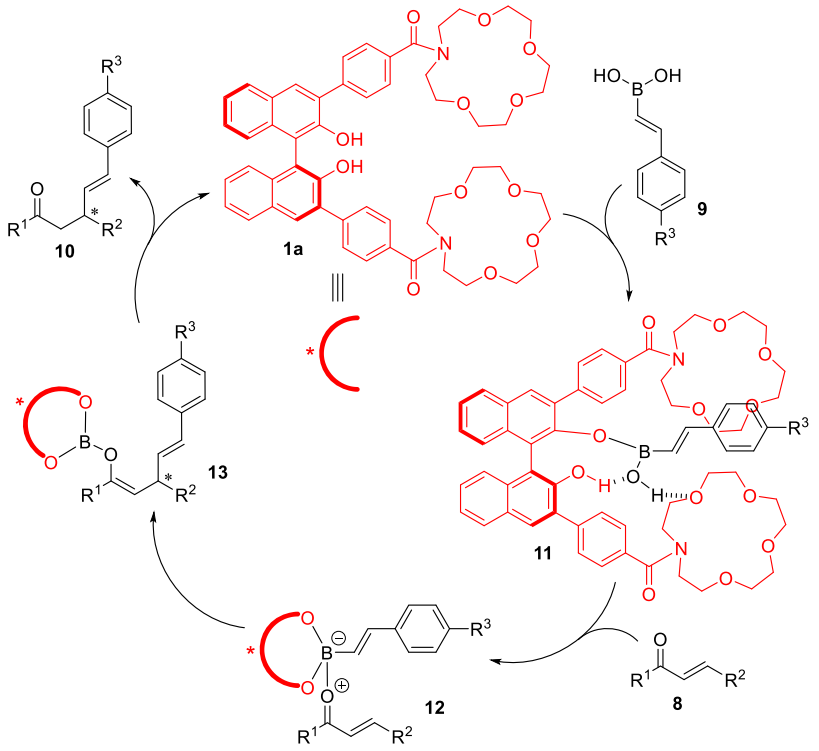

Figure 1. Proposed Catalytic Mechanism.

sensitive to the addition of $Mg(OtBu)_2$ (ee improved from 23 to 75%, entry 10 *vs* entry 11), while the addition of $Mg(OtBu)_2$ had no obvious effect on the ee of the product but only slightly increased the reactivity. These results imply that the bulky steric hindrance of crown ethers plays an important role for the improvement of enantioselectivity and the introduction of crown ethers is beneficial to increase the catalytic activity. In brief, the optimal reaction conditions were determined to be a 0.05 M substrate concentration, 15 mol % catalyst **1a**, 5 mg/0.01 mmol 4 Å MS, and 0.1 equivalent $Mg(OtBu)_2$ in dry toluene at 110 °C. To further demonstrate the practicability of this protocol, 1 mmol scale-up reaction catalyzed by **1a** was carried out, in which the product was obtained in 42% isolated yield with an almost unchanged enantioselectivity (Table 3, entry 13).

Substrate Scope. After the optimization of reaction conditions, the substrate scope of *α,β*-unsaturated ketones and styrylboronic acids was expanded (Scheme 2). The substituents at R^1, R^2, and R^3 positions were all tolerated under the standard reaction conditions to furnish the adducts (**10b−q**) with 39−92% yields and 81−95% ees. Alkyl substituents of both R^1 and R^2 afforded good yields (73−86%) and enantioselectivities (81−90% ees). Once R^2 was changed with an increasing bulky alkyl group from methyl to *n*-propyl and *n*-butyl, the yields slightly decreased and the enantioselectivity enhanced gradually (**10b−d**). The employment of various chalcone substrates provided the corresponding products in good yields (73−92%) and high enantioselectivities (87−92% ees, **10e−i**, **10p**, and **10q**), regardless of the presence of electron-donating or electron-withdrawing groups on the phenyl. When *α,β*-unsaturated ketones with an alkyl R^1 and an aryl R^2 were employed, the adducts were released with relatively lower yields (39−58%) but still good enantioselectivities (85−95% ees, **10j−o**). The presence of bulky aromatic groups, such as 2,4-dichlorophenyl and 4-hydroxy-3-methoxyphenyl, at the R^2 position were especially beneficial to the achievement of high enantioselectivities (95% ee for **10m** and 93% ee for **10n**). Either an electron-withdrawing or electron-donating substituent of R^3 promoted the improvement of reactivity but had no obvious influence on the enantioselectivity (**10p** and **10q**).

Proposed Catalytic Mechanism. As demonstrated by the previous reports,[8,10,11a,12] it was conjectured that the BINOL-catalyzed conjugate addition of boronates or boronic acids went through a boronate-catalyst complex. Both theoretical[20] and experimental[21] mechanistic studies supported this hypothesis. The reaction presented here should also similarly undergo the process *via* a boronate-catalyst complex. The difference is that the aza-crown ethers on catalyst **1a** may participate in the interaction with the alkenylboronic acids. As illustrated by the compared ^1H NMR spectra of **1a**, a mixture of **1a** and 4-methylstyrylboronic acid **9c**, and **9c** (Figure S76 and S77), an apparent change of the crown ether peaks and obvious upfield shifts of the protons on **9c** were observed, which evidenced the existence of hydrogen bonding between the aza-crown ethers and boronic acid. Therefore, it is reasonable to propose the reaction mechanism going through a boronate-catalyst intermediate **11**, in which hydrogen bonding is presented between the aza-crown ether and boronic acid (Figure 1). Intermediate **11** reacts with the enone to form a zwitterion complex **12**, and the subsequent intramolecular addition allows the transformation of **12** to boron enolate **13**. Lysis of **13** releases the product and the recovered catalyst. This proposed mechanism is in agreement with the results that the addition of a strong alkali cation guest $NaBAr_F$ seriously inhibited the reaction and caused a much lower enantioselectivity of the adduct (Table 1, entry 15). $Mg(OtBu)_2$ and other tight ion pairs usually are weak guests for the crown ethers.[22] Therefore, these salts could relatively tolerate the formation of hydrogen bonding between the catalyst and

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substrates. Nonetheless, the presence of much excessive $Mg(OtBu)_2$ or *t*BuOH would impede the hydrogen bonding between the catalyst and substrates, thus obviously inhibiting the reaction (Table 1, entries 13 and 14, respectively). These results suggest that the hydrogen bonding between the crown ethers and substrates may play an important role to promote this catalytic reaction, which could also interpret why the catalyst (*S*)-**7** without appended aza-crown ethers gave relatively lower reactivity and enantioselectivity (Table 3, entry 10 *vs* entry 1).

CONCLUSIONS

In summary, we synthesized a new kind of crown ether-appended chiral BINOL catalyst and applied it in the asymmetric Michael addition of alkenylboronic acids to α,β-unsaturated ketones. The introduction of the bulky crown ethers to the BINOL catalyst could increase the steric hindrance of the catalyst, thus improving the reaction enantioselectivity. However, the host−guest complexation between the aza-crown ethers and alkali ions was found to be not conducive to further improve the catalysis effectiveness, which is probably because the introduction of alkali cations interferes the binding of the catalyst with the reactants. Under the catalysis of crown ether-derived chiral BINOL, a series of chiral γ,δ-unsaturated ketones were obtained with medium-to-good yields (39−92%) and good enantioselectivities (81−95% ees), with the advantages including no use of precious metals and unstable borates as well as operational simplicity. Further investigations to expand the crown ether-derived chiral catalyst in other asymmetric reactions are underway in our laboratories.

EXPERIMENTAL SECTION

General Information. Tetrahydrofuran (THF), toluene, and xylene were dried over sodium metal and freshly distilled under a nitrogen atmosphere prior to use. Dichloromethane and 1,2-dichloroethane were dried over calcium hydride and freshly distilled before use. Ultra-dry 1,4-dioxane and DMF were purchased and directly used. (*S*)-2,2′-Bis-(methoxymethoxy)-1,1′-binaphthalene ((*S*)-**2**) was synthesized according to the literature method.[23] The other solvents and reagents were of commercial reagent grade and used as purchased without further purification unless otherwise stated. The racemates of addition products were prepared according to the literature methods.[24] Column chromatography was performed using a silica gel packing column with low pressure or atmospheric pressure operation. NMR spectra were recorded using a Bruker Avance 500 MHz NMR spectrometer at room temperature. All NMR data are reported in ppm and relative to the residual peak of the deuterated solvent or internal standard TMS. Mass (MS) spectra were recorded on an Agilent 1290-6530 UPLC-Q-TOF spectrometer using electrospray ionization (ESI). HPLC was carried out on an Agilent 1200 liquid chromatography system equipped with a UV detector. Chiral products were separated on a Daicel Chiralpak AD-H, OD-H, or Chiralpak IC column. Optical rotation analyses were performed on an MCP 500 optical instrument.

Synthesis of (*S*)-3,3′-Diiodo-2,2′-bis-(methoxymethoxy)-1,1′-binaphthalene (3). To a solution of (*S*)-**2** (6.5 g, 17.4 mmol) in 100 mL of dried THF, *n*-butyllithium (20.8 mL, 2.5 M in hexanes, 52.0 mmol) was added dropwise at −78 °C.[23] The reaction mixture was stirred at the same temperature for 30 min, followed by 3 h at room temperature. After the solution was cooled to −78 °C, a solution of iodine (13.0 g, 52.0 mmol) in 30 mL of THF was added dropwise. The mixture was slowly warmed up to room temperature and was further stirred at room temperature for 2 h. The reaction was then quenched with methanol and washed with saturated sodium thiosulfate solution to remove unreacted iodine. After the solution was extracted three times with ethyl acetate, the organic phases were combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The resulting residue was purified by column chromatography over silica gel (petroleum ether/ethyl acetate = 200:1) to afford (*S*)-**3** as a white solid (7.85 g, 72% yield). mp 115−116 °C. $[\alpha]_D^{20}$ = +34.6 (*c* = 0.05 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.54 (s, 2H), 7.77 (d, *J* = 8.2 Hz, 2H), 7.42 (ddd, *J* = 8.1, 6.8, 1.1 Hz, 2H), 7.29 (ddd, *J* = 8.2, 6.8, 1.3 Hz, 2H), 7.17 (dd, *J* = 8.2, 0.5 Hz, 2H), 4.81 (d, *J* = 5.7 Hz, 2H), 4.69 (d, *J* = 5.7 Hz, 2H), 2.60 (s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 152.2, 140.1, 133.9, 132.3, 127.2, 126.8, 126.6, 126.3, 125.9, 99.4, 92.5, 56.6 ppm. HRMS (ESI/Q-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{24}H_{20}I_2NaO_4^+$, 648.9343; found, 648.9374, error: −4.7 ppm.

Synthesis of (*S*)-3,3′-Bis(4-(Methoxycarbonyl)-phenyl)-2,2′-bis(methoxymethoxy)- 1,1′-binaphthalene (4). After (*S*)-**3** (2.00 g, 3.19 mmol), 4-(methoxycarbonyl)-phenylboronic acid (1.18 g, 6.54 mmol), tripotassium phosphate (4.07 mg, 19.2 mmol), tris(dibenzylideneacetone)-dipalladium (58.4 mg, 0.064 mmol), and tricyclohexylphosphine (42.0 mg, 0.146 mmol) were added to a three-necked round-bottom flask, a mixture of 1,4-dioxane and H_2O (4:1, *v*/*v*, 50 mL) was added under a nitrogen atmosphere. The reaction mixture was stirred at reflux for 18 h. After complete consumption of the starting material, the mixture was cooled down to room temperature and quenched with saturated ethylenediaminetetraacetic acid (EDTA) solution. The mixture was extracted three times with dichloromethane, and the organic phases were combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography over silica gel (petroleum ether/ethyl acetate = 10:1) to afford (*S*)-**4** as a white solid (1.25 g, 61% yield). mp 207−208 °C. $[\alpha]_D^{20}$ = +146.8 (*c* = 0.05 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.20 (d, *J* = 8.2 Hz, 4H), 8.03 (s, 2H), 7.96 (d, *J* = 8.2 Hz, 2H), 7.90 (d, *J* = 8.2 Hz, 4H), 7.49 (dd, *J* = 10.6, 4.0 Hz, 2H), 7.35 (q, *J* = 8.8 Hz, 4H), 4.42 (dd, *J* = 15.2, 5.9 Hz, 4H), 4.01 (s, 6H), 2.40 (s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 167.1, 151.3, 143.9, 134.6, 134.0, 130.9, 130.9, 129.8, 129.7, 129.1, 128.2, 126.9, 126.6, 126.5, 125.6, 98.9, 56.1, 52.3 ppm. HRMS (ESI/Q-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{40}H_{34}NaO_8^+$, 665.2146; found, 665.2123, error: 3.4 ppm.

Synthesis of (*S*)-4,4′-(2,2′-Bis(Methoxymethoxy)-[1,1′-binaphthalene]-3,3′-diyl) Dibenzoic Acid (5). A solution of (*S*)-**4** (2.00 g, 1.55 mmol) in 30 mL of THF and 5 mL of 10% sodium hydroxide aqueous solution was heated at reflux for 12 h. After complete consumption of the starting material, the mixture was cooled down to 0 °C and 4 M aqueous HCl solution was added dropwise to adjust the pH of the solution to 3−4. The mixture was extracted three times with ethyl acetate, and the organic phases were combined, washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography over silica gel (petroleum ether/ethyl acetate = 10:1) to afford (*S*)-**5** as a white solid (1.79 g, 94% yield). mp

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245−247 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 13.07 (s, 2H), 8.19 (s, 2H), 8.10−8.06 (m, 6H), 7.86 (d, J = 8.3 Hz, 4H), 7.50 (t, J = 7.5 Hz, 2H), 7.41−7.33 (m, 2H), 7.16 (d, J = 8.5 Hz, 2H), 4.33 (dd, J = 38.1, 5.7 Hz, 4H), 2.30 (s, 6H) ppm. ^{13}C NMR (126 MHz, DMSO-d_6): δ 167.3, 150.5, 142.9, 134.1, 133.2, 130.8, 130.5, 129.7, 129.5, 129.5, 128.4, 127.0, 125.9, 125.7, 125.4, 98.0, 55.3 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{38}H_{30}NaO_8^+$, 637.1833; found, 637.1829, error: 0.6 ppm.

Synthesis of (*S*)-((2,2′-Bis(Methoxymethoxy)-[1,1′-binaphthalene]-3,3′-diyl) bis(4,1-phenylene))bis-((1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)-methanone) (6a). A mixture of (*S*)-**5** (500 mg, 0.813 mmol), 1-aza-15-crown-5 (375 mg, 1.71 mmol), 4-dimethylaminopyridine (DMAP, 229 mg, 1.87 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 343 mg, 1.79 mmol) were added to a three-necked round-bottom flask. Under protection of a nitrogen atmosphere, 25 mL of dichloromethane was added and the reaction mixture was stirred for 24 h at room temperature. After complete consumption of the starting material, 10 mL of water was added and the solution was extracted with dichloromethane three times. The organic phases were combined, washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography over silica gel (pure ethyl acetate to dichloromethane/methanol = 60:1) to afford (*S*)-**6a** as a white solid (458 mg, 55% yield). mp 176−178 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.96 (s, 2H), 7.90 (d, J = 8.1 Hz, 2H), 7.84−7.77 (m, 4H), 7.59−7.50 (m, 4H), 7.43 (ddd, J = 8.1, 5.9, 2.0 Hz, 2H), 7.35−7.27 (m, 4H), 4.40−4.37 (m, 4H), 3.99−3.43 (m, 40H), 2.35 (s, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.2, 151.3, 140.2, 135.6, 134.6, 133.7, 130.8, 130.7, 129.7, 128.0, 126.8, 126.6, 126.5, 126.4, 125.4, 98.7, 71.5, 70.8, 70.3, 69.8, 69.3, 55.9 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{58}H_{68}N_2NaO_{14}^+$, 1039.4563; found, 1039.4607, error: 4.2 ppm.

Synthesis of (*S*)-((2,2′-Dihydroxy-[1,1′-binaphthalene]-3,3′-diyl)bis (4,1-phenylene))bis((1,4,7,10-tetraoxa-13-azacyclopentadecan-13-yl)methanone) (1a). To a solution of (*S*)-**6a** (200 mg, 0.197 mmol) in 20 mL of dried dichloromethane, TFA (0.1 mL) was added dropwise and the mixture was stirred for 12 h at room temperature. After complete consumption of the starting material, 50 mL of water was added and the mixture was extracted with dichloromethane three times. The organic phases were combined, washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The reside was purified by column chromatography over silica gel (dichloromethane/methanol = 50:1) to afford (*S*)-**1a** as a white solid (146 mg, 80% yield). mp 170−171 °C. $[\alpha]_D^{20}$ = −2.38 (c = 1.0 in $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.00 (s, 2H), 7.91 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 7.8 Hz, 4H), 7.50 (d, J = 7.8 Hz, 4H), 7.39 (t, J = 7.5 Hz, 2H), 7.33 (d, J = 7.9 Hz, 2H), 7.20 (d, J = 8.5 Hz, 2H), 3.90−3.43 (m, 40H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 172.3, 150.2, 138.8, 135.6, 133.1, 131.6, 129.9, 129.7, 129.4, 128.5, 127.6, 126.8, 124.4, 124.2, 112.4, 71.3, 70.7, 70.2, 70.31, 69.8 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{54}H_{60}N_2NaO_{12}^+$, 951.4038; found, 951.4031, error: −0.7 ppm.

Synthesis of (*S*)-((2,2′-Bis(Methoxymethoxy)-[1,1′-binaphthalene]-3,3′-diyl)bis(4,1-phenylene))bis-((1,4,7,10,13-pentaoxa-16-azacyclooctadecan-16-yl)-methanone) (6b). A mixture of (*S*)-**5** (500 mg, 0.813 mmol), 1-aza-18-crown-6 (450 mg, 1.71 mmol), 4-dimethylaminopyridine (DMAP, 229 mg, 1.87 mmol), and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 343 mg, 1.79 mmol) were added to a three-necked round-bottom flask. Under protection of a nitrogen atmosphere, 25 mL of dichloromethane was added and the reaction mixture was stirred for 24 h at room temperature. After complete consumption of the starting material, 10 mL of water was added and the solution was extracted with dichloromethane three times. The organic phases were combined, washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by column chromatography over silica gel (pure ethyl acetate to dichloromethane/methanol = 60:1) to afford (*S*)-**6b** as a white solid (477 mg, 53% yield). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (s, 2H), 7.89 (d, J = 8.2 Hz, 2H), 7.79 (d, J = 8.1 Hz, 4H), 7.53 (d, J = 8.1 Hz, 4H), 7.46−7.37 (m, 2H), 7.33−7.27 (m, 4H), 4.38 (dd, J = 14.7, 6.0 Hz, 4H), 3.86−3.55 (m, 48H), 2.34 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.1, 151.3, 140.1, 135.7, 134.6, 133.7, 130.8, 130.7, 129.6, 128.0, 126.9, 126.6, 126.4, 125.4, 98.7, 70.7, 70.6, 70.4, 69.8, 69.5, 55.9 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{62}H_{76}N_2NaO_{16}^+$, 1127.5087; found, 1127.5088, error: 0.1 ppm.

Synthesis of (*S*)-((2,2′-Dihydroxy-[1,1′-binaphthalene]-3,3′-diyl)bis(4,1-phenylene))bis((1,4,7,10,13-pentaoxa-16-azacyclooctadecan-16-yl)methanone) (1b). To a solution of (*S*)-**6b** (200 mg, 0.181 mmol) in 20 mL of dried dichloromethane, TFA (0.1 mL) was added dropwise and the mixture was stirred for 12 h at room temperature. After complete consumption of the starting material, 50 mL of water was added and the mixture was extracted with dichloromethane three times. The organic phases were combined, washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The reside was purified by column chromatography over silica gel (dichloromethane/methanol = 50:1) to afford (*S*)-**1b** as a white solid (156 mg, 85% yield). $[\alpha]_D^{20}$ = −4.00 (c = 0.05 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.01 (s, 2H), 7.93 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.2 Hz, 4H), 7.51 (d, J = 8.2 Hz, 4H), 7.40 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.6 Hz, 2H), 7.21 (d, J = 8.4 Hz, 2H), 3.84−3.56 (m, 48H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 172.1, 150.2, 138.6, 136.0, 133.1, 131.6, 130.0, 129.7, 129.4, 128.5, 127.6, 126.9, 124.5, 124.2, 112.4, 70.7, 70.6, 70.4, 69.8, 69.7, 69.5 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{58}H_{68}N_2NaO_{14}^+$, 1039.4563; found, 1039.4560, error: −0.3 ppm.

Synthesis of Dimethyl 4,4′-(2,2′-Bis-(Methoxymethoxy)-[1,1′-binaphthalene]-3,3′-diyl) (*S*)-dibenzoate (7). To a solution of (*S*)-**4** (200 mg, 0.311 mmol) in 20 mL of dried dichloromethane, TFA (0.1 mL) was added dropwise and the mixture was stirred for 12 h at room temperature. After complete consumption of the starting material, 50 mL of water was added and the mixture was extracted with dichloromethane three times. The organic phases were combined, washed with water and saturated brine, dried over Na_2SO_4, and concentrated in vacuo. The reside was purified by column chromatography over silica gel (dichloromethane/methanol = 50:1) to afford (*S*)-**7** as a white solid (138 mg, 80% yield). $[\alpha]_D^{20}$ = −6.75 (c = 0.05 in $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.15 (d, J = 7.7 Hz, 4H), 8.07 (s, 2H), 7.95 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 7.7 Hz, 4H), 7.43 (t,

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J = 7.4 Hz, 2H), 7.36 (t, J = 7.6 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 5.39 (s, 4H), 3.95 (s, 6H) ppm. ^{13}C NMR (101 MHz, $CDCl_3$): δ 167.0, 150.1, 142.2, 131.9, 129.7, 129.6, 128.7, 124.1, 112.1, 52.2 ppm. HRMS (ESI/Q-TOF) m/z: $[M - H]^-$ calcd for $C_{36}H_{25}O_6^-$, 553.1657; found, 553.1659, error: −0.4 ppm.

Typical Procedure of the Asymmetric Addition Reaction Catalyzed by (*S*)-1a (with 10a as an Example, Table 1, Entry 2). To a dry Schlenk reaction tube, 4-phenyl-3-buten-2-one (5.92 mg, 0.04 mmol), *trans*-2-phenylvinylboronic acid (7.19 mg, 0.048 mmol), magnesium *t*-butoxide (0.69 mg, 0.004 mmol), (*S*)-**1a** (5.65 mg, 0.006 mmol), and 4Å molecular sieves (20 mg) were added. Under a nitrogen atmosphere, dried toluene was added. After it was stirred at 110 °C for 48 h, the reaction mixture was cooled down to room temperature and then quenched with methanol. After suction filtration, the solvent was removed in vacuo and the residue was re-dissolved in $CDCl_3$ to directly determine the conversion by using ^{1}H NMR. The crude product was purified by column chromatography over silica gel (petroleum ether/dichloromethane = 2:1−1:1), and enantioselectivity was measured by HPLC analysis using a chiral stationary phase column.

(*R*,*E*)-4,6-Diphenylhex-5-en-2-one (10a). 42% yield, 89% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40−7.27 (m, 7H), 7.25−7.14 (m, 2H), 6.47−6.21 (m, 2H), 4.09 (q, J = 7.1 Hz, 1H), 3.09−2.81 (m, 2H), 2.12 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.9, 143.0, 137.1, 132.4, 130.0, 128.7, 128.5, 127.7, 127.4, 126.7, 126.3, 49.5, 44.0, 30.8 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{18}NaO^+$, 273.1250; found, 273.1254. $[\alpha]_D^{20}$ = +15.0 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(*R*, major) = 11.670 min, t_R(*S*, minor) = 12.812 min.

(*E*)-4-Methyl-6-phenylhex-5-en-2-one (10b). 86% yield, 81% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.37−7.32 (m, 2H), 7.29 (dd, J = 10.4, 4.9 Hz, 2H), 7.20 (t, J = 7.2 Hz, 1H), 6.39 (d, J = 15.9 Hz, 1H), 6.14 (dd, J = 15.9, 7.4 Hz, 1H), 2.90 (dt, J = 13.6, 6.8 Hz, 1H), 2.57 (dd, J = 16.1, 6.8 Hz, 1H), 2.47 (dd, J = 16.1, 7.2 Hz, 1H), 2.15 (s, 3H), 1.37−1.26 (m, 4H), 0.90 (d, J = 6.8 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.9, 137.4, 134.6, 128.7, 128.5, 127.2, 126.1, 50.7, 30.9, 30.6, 20.3 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_{17}O^+$, 189.1274; found, 189.1279. $[\alpha]_D^{20}$ = −5.14 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(minor) = 7.678 min, t_R(major) = 9.689 min.

(*R*,*E*)-4-Styrylheptan-2-one (10c). 83% yield, 89% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 8.1, 1.0 Hz, 2H), 7.29 (dd, J = 10.4, 4.9 Hz, 2H), 7.23−7.17 (m, 1H), 6.39 (d, J = 15.8 Hz, 1H), 5.99 (dd, J = 15.8, 8.8 Hz, 1H), 2.74 (dd, J = 12.6, 7.5 Hz, 1H), 2.52 (d, J = 7.0 Hz, 2H), 2.13 (s, 3H), 1.41−1.20 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.1, 137.4, 133.2, 130.2, 128.5, 127.1, 126.1, 49.5, 38.8, 37.3, 30.7, 20.4, 14.0 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{15}H_{21}O^+$, 217.1587; found, 217.1594. $[\alpha]_D^{20}$ = −8.50 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(*S*, minor) = 11.727 min, t_R(*R*, major) = 12.786 min.

(*E*)-4-Styrylnonan-2-one (10d). 73% yield, 90% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.32 (ddd, J = 27.1, 11.0, 4.7 Hz, 4H), 7.23−7.17 (m, 1H), 6.38 (d, J = 15.8 Hz, 1H), 6.00 (dd, J = 15.8, 8.8 Hz, 1H), 2.82−2.67 (m, 1H), 2.53 (t, J = 8.0 Hz, 2H), 2.13 (s, 3H), 1.40−1.15 (m, 8H), 0.96−0.76 (m, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.2, 137.4, 133.3, 130.2, 128.5, 127.1, 126.1, 49.6, 39.0, 35.1, 31.8, 30.7, 26.9, 22.6, 14.1 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{17}H_{25}O^+$, 245.1900; found, 245.1898. $[\alpha]_D^{20}$ = −15.62 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(minor) = 8.712 min, t_R(major) = 9.885 min.

(*R*,*E*)-1,3,5-Triphenylpent-4-en-1-one (10e)[12]. 76% yield, 92% ee. H NMR (500 MHz, CD_2Cl_2): δ 7.97 (d, J = 7.8 Hz, 2H), 7.58 (dd, J = 10.6, 4.1 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.43−7.12 (m, 10H), 6.51−6.32 (m, 2H), 4.40−4.22 (m, 1H), 3.54 (d, J = 7.1 Hz, 2H) ppm. ^{13}C NMR (126 MHz, CD_2Cl_2): δ 197.9, 143.5, 137.3, 137.2, 133.1, 132.9, 129.8, 128.6, 128.5, 128.0, 127.8, 127.3, 126.6, 126.1, 44.3, 44.1 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{21}O^+$, 313.1587; found, 313.1580. $[\alpha]_D^{20}$ = +7.92 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(*R*, major) = 10.536 min, t_R(*S*, minor) = 11.650 min.

(*R*,*E*)-1-(4-Methoxyphenyl)-3,5-diphenylpent-4-en-1-one (10f). 73% yield, 87% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.99−7.87 (m, 2H), 7.31 (dd, J = 17.7, 9.0 Hz, 7H), 7.26−7.11 (m, 3H), 6.92 (dd, J = 9.3, 2.3 Hz, 2H), 6.51−6.26 (m, 2H), 4.30 (dd, J = 13.5, 6.8 Hz, 1H), 3.86 (s, 3H), 3.57−3.22 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.7, 163.5, 143.5, 137.3, 132.8, 130.4, 130.2, 130.0, 128.7, 128.5, 127.8, 127.2, 126.6, 126.3, 113.8, 55.5, 44.1, 44.1 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{23}O_2^+$, 343.1693; found, 343.1697. $[\alpha]_D^{20}$ = +7.25 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(*R*, major) = 30.042 min, t_R(*S*, minor) = 44.807 min.

(*E*)-1-(4-Fluorophenyl)-3,5-diphenylpent-4-en-1-one (10g). 77% yield, 91% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.09−7.88 (m, 2H), 7.35−7.28 (m, 6H), 7.27−7.15 (m, 4H), 7.10 (dd, J = 14.2, 5.7 Hz, 2H), 6.51−6.30 (m, 2H), 4.28 (dd, J = 11.9, 7.0 Hz, 1H), 3.56−3.32 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 196.6, 166.8, 164.8, 143.2, 137.2, 133.6, 132.5, 130.8, 130.7, 130.2, 128.7, 128.5, 127.8, 127.3, 126.7, 126.3, 115.8, 115.7, 44.5, 44.0 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}FO^+$, 331.1493; found, 331.1500. $[\alpha]_D^{20}$ = +6.21 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak IC (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(minor) = 7.038 min, t_R(major) = 7.450 min.

(*R*,*E*)-3-(4-Methoxyphenyl)-1,5-diphenylpent-4-en-1-one (10h). 80% yield, 91% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.94 (dd, J = 5.2, 3.3 Hz, 2H), 7.69−7.52 (m, 1H), 7.45 (dd, J = 10.6, 4.8 Hz, 2H), 7.36−7.27 (m, 3H), 7.23 (dd, J = 6.8, 4.8 Hz, 2H), 7.21−7.14 (m, 1H), 6.95−6.79 (m, 2H), 6.52−6.23 (m, 2H), 4.26 (dd, J = 13.2, 6.9 Hz, 1H), 3.79 (s, 3H), 3.55−3.28 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.4, 158.4, 137.4, 137.3, 135.4, 133.2, 133.1, 129.9, 128.8, 128.7, 128.6, 128.2, 127.3, 126.3, 114.2, 55.4, 44.8, 43.2 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{24}H_{23}O_2^+$, 343.1693; found, 343.1691. $[\alpha]_D^{20}$ = +10.9 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/*i*-PrOH, flow rate 1.0 mL/min, λ= 254 nm), t_R(*R*, major) = 19.426 min, t_R(*S*, minor) = 25.214 min.

(*R*,*E*)-3-(4-Chlorophenyl)-1,5-diphenylpent-4-en-1-one (10i). 73% yield, 91% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34 (dd, J = 8.1, 1.0 Hz, 2H), 7.29 (dd, J = 10.4, 4.9 Hz,

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2H), 7.23−7.17 (m, 1H), 6.39 (d, J = 15.8 Hz, 1H), 5.99 (dd, J = 15.8, 8.8 Hz, 1H), 2.74 (dd, J = 12.6, 7.5 Hz, 1H), 2.52 (d, J = 7.0 Hz, 2H), 2.13 (s, 3H), 1.41−1.20 (m, 4H), 0.90 (t, J = 7.0 Hz, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 197.8, 141.8, 137.0, 137.0, 133.3, 132.4, 132.1, 130.4, 129.2, 128.8, 128.7, 128.6, 128.1, 127.5, 126.3, 44.3, 44.3 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{20}ClO^+$, 347.1197; found, 347.1201. $[\alpha]_D^{20}$ = +20.8 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak IC (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(S, minor) = 7.283 min, t_R(R, major) = 7.740 min.

(*E*)-4-(4-Methoxyphenyl)-6-phenylhex-5-en-2-one (10j). 46% yield, 89% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.35−7.26 (m, 4H), 7.26−7.10 (m, 4H), 6.90−6.82 (m, 2H), 6.40−6.25 (m, 2H), 4.03 (dd, J = 13.6, 7.2 Hz, 1H), 3.84−3.72 (m, 3H), 3.01−2.80 (m, 2H), 2.10 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.2, 158.3, 137.2, 135.0, 132.7, 129.7, 128.7, 128.5, 127.3, 126.3, 114.1, 55.3, 49.6, 43.2, 30.8 ppm. HRMS (ESI/Q-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{21}O_2^+$, 281.1536; found, 281.1541. $[\alpha]_D^{20}$ = +22.9 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 19.683 min, t_R(minor) = 22.043 min.

(*E*)-4-(4-Chlorophenyl)-6-phenylhex-5-en-2-one (10k). 54% yield, 85% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.26 (m, 6H), 7.23−7.16 (m, 3H), 6.30 (dt, J = 15.9, 11.4 Hz, 2H), 4.07 (q, J = 7.1 Hz, 1H), 2.93 (qd, J = 16.6, 7.3 Hz, 2H), 2.12 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.5, 141.5, 136.9, 132.4, 131.8, 130.4, 129.1, 128.8, 128.6, 127.2, 126.3, 49.2, 43.2, 30.8 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{17}ClNaO^+$, 307.0860; found, 307.0861. $[\alpha]_D^{20}$ = +14.6 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 11.862 min, t_R(minor) = 12.653 min.

(*E*)-6-Phenyl-4-(3-(trifluoromethyl)phenyl)hex-5-en-2-one (10l). 39% yield, 88% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.54−7.39 (m, 4H), 7.36−7.27 (m, 4H), 7.24−7.18 (m, 1H), 6.50−6.22 (m, 2H), 4.17 (q, J = 7.2 Hz, 1H), 2.98 (qd, J = 16.8, 7.2 Hz, 2H), 2.14 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.2, 144.1, 136.8, 131.4, 131.3, 130.8, 129.2, 128.6, 127.6, 126.3, 124.3, 124.3, 123.7, 123.6, 49.1, 43.6, 30.8 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{17}F_3NaO^+$, 341.1129; found, 341.1041. $[\alpha]_D^{20}$ = +18.3 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(minor) = 6.821 min, t_R(major) = 7.663 min.

(*E*)-4-(2,4-Dichlorophenyl)-6-phenylhex-5-en-2-one (10m). 56% yield, 95% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40 (d, J = 1.5 Hz, 1H), 7.30 (ddd, J = 15.1, 10.7, 4.6 Hz, 4H), 7.24−7.16 (m, 3H), 6.44−6.16 (m, 2H), 4.55 (q, J = 7.2 Hz, 1H), 2.95 (qd, J = 16.7, 7.2 Hz, 2H), 2.17 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 206.0, 139.0, 136.8, 134.4, 132.9, 131.2, 129.9, 129.8, 129.5, 128.6, 127.6, 127.4, 126.3, 48.3, 39.7, 30.3 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{18}H_{16}Cl_2NaO^+$, 341.0470; found, 341.0494. $[\alpha]_D^{20}$ = −5.30 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 9.065 min, t_R(minor) = 14.171 min.

(*E*)-4-(4-Hydroxy-3-methoxyphenyl)-6-phenylhex-5-en-2-one (10n). 58% yield, 93% ee.[23] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.31 (dd, J = 19.0, 7.4 Hz, 4H), 7.20 (t, J = 7.2 Hz, 1H), 6.87 (d, J = 8.7 Hz, 1H), 6.79−6.70 (m, 2H), 6.44−6.24 (m, 2H), 5.54 (s, 1H), 4.09−3.96 (m, 1H), 3.91 (d, J = 27.1 Hz, 3H), 3.02−2.82 (m, 2H), 2.11 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 207.2, 146.6, 144.3, 137.1, 134.9, 132.6, 129.7, 128.5, 127.3, 126.3, 120.0, 114.5, 110.5, 56.0, 49.6, 43.7, 30.9 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{20}NaO^+$, 319.1305; found, 319.1310. $[\alpha]_D^{20}$ = +7.40 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 65.768 min, t_R(minor) = 74.504 min.

(*E*)-2-Methyl-6,8-diphenyloct-7-en-4-one (10o). 41% yield, 91% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.34−7.26 (m, 7H), 7.25−7.14 (m, 3H), 6.45−6.18 (m, 2H), 4.10 (q, J = 7.1 Hz, 1H), 2.97−2.81 (m, 2H), 2.23 (qd, J = 16.0, 6.9 Hz, 2H), 2.16−1.97 (m, 1H), 0.83 (dd, J = 6.6, 2.3 Hz, 6H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 208.8, 143.1, 137.2, 132.6, 130.0, 128.7, 128.5, 127.7, 127.3, 126.7, 126.3, 52.8, 49.0, 43.9, 24.4, 22.5 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{21}H_{24}NaO^+$, 315.1719; found, 315.1729. $[\alpha]_D^{20}$ = +4.09 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak AD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 9.849 min, t_R(minor) = 11.266 min.

(*E*)-5-(4-Fluorophenyl)-1,3-diphenylpent-4-en-1-one (10p). 92% yield, 88% ee. ^{1}H NM (500 MHz, $CDCl_3$): δ 7.98−7.78 (m, 2H), 7.54−7.46 (m, 1H), 7.39 (dd, J = 10.6, 4.8 Hz, 2H), 7.37−7.23 (m, 4H), 7.22−7.16 (m, 3H), 7.01−6.78 (m, 2H), 6.36−6.17 (m, 2H), 4.23 (dd, J = 13.0, 6.7 Hz, 1H), 3.54−3.35 (m, 2H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.1, 163.1, 161.2, 143.3, 137.1, 133.4, 133.2, 132.4, 129.0, 128.8, 128.7, 128.1, 127.8, 126.7, 115.4, 115.3, 44.5, 43.9 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{23}H_{19}FNaO^+$, 353.1318; found, 353.1304. $[\alpha]_D^{20}$ = −4.43 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak OD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(major) = 12.635 min, t_R(minor) = 15.017 min.

(*E*)-5-(*p*-Tolyl)-1,3-diphenylpent-4-en-1-one (10q). 91% yield, 92% ee. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.98−7.90 (m, 2H), 7.58−7.53 (m, 1H), 7.45 (t, J = 7.7 Hz, 2H), 7.36−7.28 (m, 4H), 7.24−7.17 (m, 3H), 7.07 (d, J = 7.9 Hz, 2H), 6.36 (d, J = 3.1 Hz, 2H), 4.29 (ddd, J = 10.0, 6.9, 2.9 Hz, 1H), 3.56−3.44 (m, 2H), 2.30 (s, 3H) ppm. ^{13}C NMR (126 MHz, $CDCl_3$): δ 198.3, 143.5, 137.2, 137.0, 134.4, 133.1, 131.6, 130.0, 129.2, 128.7, 128.6, 128.1, 127.8, 126.6, 126.2, 44.6, 44.0, 21.2 ppm. HRMS (ESI/Q-TOF) m/z: $[M + Na]^+$ calcd for $C_{25}H_{24}NaO_2^+$, 379.1669; found, 379.1676. $[\alpha]_D^{20}$ = −5.72 (c = 0.05 in $CHCl_3$). HPLC: Chiralpak OD-H (hexane/i-PrOH, flow rate 1.0 mL/min, λ = 254 nm), t_R(minor) = 12.476 min, t_R(major) = 13.369 min.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsomega.1c05875.

Characterization of the crown ether-derived BINOLs, intermediates, and asymmetric addition products (PDF)

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Notes

The authors declare no competing financial interest.

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