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Phosphine-Catalyzed [3 + 2] Cycloaddition of Sulfamate-Derived Cyclic Imines with Allenoate: Synthesis of Sulfamate-Fused Dihydropyrroles

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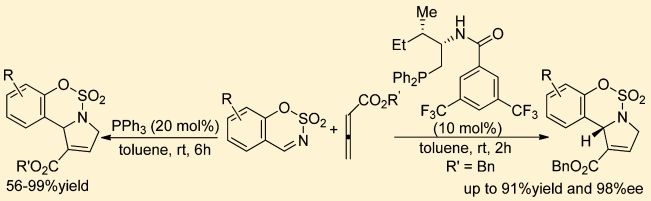
Supporting Information

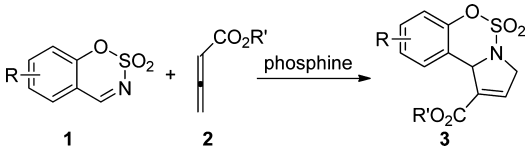
ABSTRACT: Ph_3P-catalyzed [3 + 2] cycloaddition reaction of sulfamate-derived cyclic imines with allenoate has been developed, affording sulfamate-fused dihydropyrroles under very mild conditions in high yields. Using amino acid-based bifunctional phosphine as chiral catalyst, its asymmetric variant provided the corresponding products in good yields with moderate to excellent enantiomeric excesses (up to 91% yield and up to 98% ee). Subsequent transformations of the heterocyclic products gave various pharmaceutically attractive compounds.



INTRODUCTION

In the past 20 years, nucleophilic phosphine-catalyzed cycloaddition reactions have been developed as a reliable and powerful tool for the synthesis of carbo- and heterocycles from readily available starting materials.[1] In the presence of phosphine, electrophilic-deficient imine is one of most often used electrophilic-coupling reagents since the pioneering contribution from Lu and co-workers.[2] In the presence of phosphine, imines could undergo [3 + 2],[2b,c,3] [4 + 2],[4] [4 + 1],[5] and [2 + 2 + 2][6] annulation with various activated substrates including allenes, allylic carbonates, alkynyl ketones, 3-alkylnoates, and conjugated dienes to give all kinds of nitrogen-containing heterocycles.[7] The enantioselective [3 + 2] and [4 + 2] cycloaddition reactions have also been achieved.[3c−e,h,j,m,o,4c,e] Certain reactions have successfully been applied to drug discovery[8] and total synthesis of natural products.[9] Although the imines have extensively been applied in the phosphine-catalyzed reactions, cyclic imines have received minimal attention. Only two examples described phosphine-catalyzed [2 + 2],[10a] [3 + 2],[10a] and [4 + 2][10b] cycloaddition reactions of cyclic ketimines with allenoates, which afforded sultam-fused azetidines, dihydropyrroles and tetrahydropyridine. To the best of our knowledge, the application of sulfamate-derived cyclic aldimines in phosphine-catalyzed cycloadditions remains unexplored. The sulfamate moiety could bring very appealing properties to the compounds incorporating it, leading to specific biological activities such as antibiotic, antiviral, antimetastatic, anticonvulsant, anticancer, antiobesity, antiarthritis, antiosteoporosis, inhibiting hyperlipidemia and atherosclerosis activity, and has widely been exploited in the drug design of various pharmacological agents.[11] Therefore, developing new reactions for the synthesis of sulfamate-fused molecules is highly desirable. The reactions employing the sulfamate-derived cyclic aldimines (**1** in Scheme 1) as the substrates, which are readily accessible and stable compounds,[12] can provide rapid and concise access to biologically active compounds containing sulfamate moiety, but received very limited attention. In 1987, Tripathi et al. reported the reaction of sulfamate-derived cyclic aldimines with 1,3-diphenylnitiolimine to synthesize heterocycles.[13] In 2009, Du Bois and co-workers studied C−H hydroxylation with cyclic aldimines like **1** as the catalyst.[14] Then Lam et al. presented enantioselective rhodium-catalyzed nucleophilic alkenylation of **1** with alkenylboron reagents[15a] and allylation of **1** with allylboron reagents in 2012.[15b] Most recently, Xu et al. reported Rh-catalyzed asymmetric arylations of **1** using new and simple sulfinamide-based branched olefin ligands.[16] Inspired by our continuing interest in exploring phosphine-catalyzed cycloaddition,[17] we anticipated to develop the cycloaddition of **1** with allenoates with phosphine as the catalyst (Scheme 1). Herein we disclose our results on phosphine-catalyzed [3 + 2] cycloaddition reaction of sulfamate-derived cyclic imines with allenoates and its asymmetric variant for the synthesis of sulfamate-fused dihydropyrroles.

Scheme 1. Phosphine-Catalyzed Annulation of Sulfamate-Derived Cyclic Imines with Allenoates



RESULTS AND DISCUSSION

In initial screening, the benzol[*e*][1,2,3]oxathiazine 2,2-dioxide (**1a**) was treated with ethyl buta-2,3-dienoate (**2a**) in

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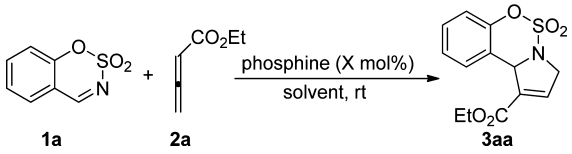
dichloromethane at room temperature in the presence of 20 mol % PPh_3. The reaction proceeded smoothly and could complete within 7 h. Gratifyingly, a new product **3a** was isolated in 97% yield. Its structure was established to be a [3 + 2] cycloaddition product by NMR spectra (Table 1, entry 1). A

Table 1. Optimization of the Reaction Conditions for Phosphine-Catalyzed [3 + 2] Cycloaddition of Cyclic Imine (1a) with Allenoate (2a)[a]



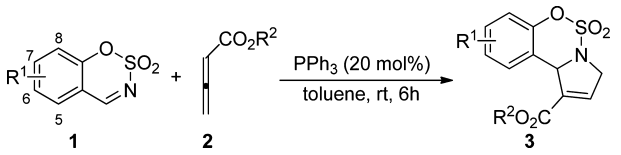
entry	phosphine	X	solvent	time (h)	yield (%)[b]
1	PPh_3	20	CH_2Cl_2	6	97
2	PPh_3	20	THF	6	78
3	PPh_3	20	toluene	6	99
4	PPh_3	20	CH_3OH	6	87
5	PPh_3	20	CH_3CN	6	64
6	PBu_3	20	toluene	6	trace
7	PMe_3	20	toluene	6	trace
8	$PMePh_2$	20	toluene	6	72
9	PPh_3	10	toluene	12	97
10	PPh_3	5	toluene	48	95

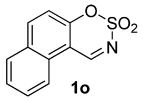
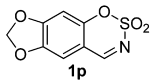
[a]All reactions were carried out with 0.125 mmol of **1a** and 0.15 mmol of **2a** in 2 mL of solvent, unless otherwise indicated. [b]Isolated yields, unless otherwise indicated.

subsequent screening of solvents indicated that a wide range of solvents such as THF, toluene, CH_3OH and CH_3CN are compatible for catalysis, providing the desired product in moderate to excellent yield (entries 2−5). In particular, when the reaction was carried out in toluene, the best 99% yield was obtained (Table 1, entry 3). Next, several typical phosphines such as PBu_3, PMe_3, and $PMePh_2$ were tested in the reaction of **1a** with ethyl buta-2,3-dienoate (**2a**) using toluene as the solvent at room temperature. The strong nucleophile PBu_3 and PMe_3 only led to trace of [3 + 2] cycloaddition product with most of the starting material **1a** left (entries 6−7). The relative weaker nucleophile $PMePh_2$ could give 72% yield (entry 8). When the catalyst loading of PPh_3 was decreased to 10 and 5 mol %, respectively, the cycloaddition reaction still proceeded efficiently nearly without deterioration of the yield, albeit in longer reaction time (entries 9−10).

With the optimized reaction conditions in hand, the substrate scope of the [3 + 2] cycloaddition reaction was examined (Table 2). With 20 mol % of PPh_3 as the catalyst, the [3 + 2] cycloadition reactions of various sulfamate-derived cyclic imines **1** with ethyl allenoate **2a** were performed in toluene at room temperature for 6 h to provide the sulfamate-fused 3,10b-dihydrobenzo[*e*]pyrrolo[1,2-*c*][1,2,3]oxathiazine-1-carboxylate 5,5-dioxide derivatives (**3aa**−**3pa**) in moderate to excellent yields (Table 2, entries 1−16)). The reactions were tolerant of a wide range of cyclic imines with electron-donating groups (Me, MeO, *t*-Bu) and electron-withdrawing groups (F, Cl, Br). Strangely, in contrast to other cyclic imines, the imine **1g** with 6-Br substituent only gave the product **3ga** in 56% yield (entry 7). Two special substrates **1o** and **1p** also worked very well to afford the corresponding product **3oa** and **3pa** in 88 and 77% yield, respectively (entries 15−16). The variation of allenoates was also tested. Tuning the ester moieties in allenoates had

Table 2. Substrate Scope for Phosphine-Catalyzed [3 + 2] Cycloaddition of Sulfamate-Derived Cyclic Imines (1) with Allenoates (2)[a]



entry	R^1 in **1**	R^2 in **2**	product	yield (%)[b]
1	H (**1a**)	Et (**2a**)	**3aa**	99
2	6-Me (**1b**)	Et (**2a**)	**3ba**	98
3	6-OMe (**1c**)	Et (**2a**)	**3ca**	95
4	6-*t*-Bu (**1d**)	Et (**2a**)	**3da**	98
5	6-F (**1e**)	Et (**2a**)	**3ea**	75
6	6-Cl (**1f**)	Et (**2a**)	**3fa**	88
7	6-Br (**1g**)	Et (**2a**)	**3ga**	56
8	7-MeO (**1h**)	Et (**2a**)	**3ha**	89
9	7-Cl (**1i**)	Et (**2a**)	**3ia**	92
10	7-Br (**1j**)	Et (**2a**)	**3ja**	79
11	8-Me (**1k**)	Et (**2a**)	**3ka**	92
12	8-OMe (**1l**)	Et (**2a**)	**3la**	98
13	8-*t*-Bu (**1m**)	Et (**2a**)	**3ma**	85
14	8-Cl (**1n**)	Et (**2a**)	**3na**	86
15		Et (**2a**)	**3oa**	88
16		Et (**2a**)	**3pa**	77
17	H (**1a**)	*i*-Pr (**2b**)	**3ab**	86
18	H (**1a**)	*t*-Bu (**2c**)	**3ac**	92
19	H (**1a**)	cyclohexyl (**2d**)	**3ad**	88
20	H (**1a**)	Ph (**2e**)	**3ae**	88
21	H (**1a**)	Bn (**2f**)	**3af**	92

[a]All reactions were carried out with 0.125 mmol of **1** and 0.15 mmol of **2** in 2 mL of toluene, unless otherwise indicated. [b]Isolated yields, unless otherwise indicated.

little influence on the reactivity of the reaction. Several allenoates with *i*-Pr, *t*-Bu, cyclohexyl, Ph and Bn group in ester moiety (**2b**−**2f**) smoothly underwent the [3 + 2] cycloaddition reaction to give the corresponding sulfamate-fused dihydropyrroles (**3ab**−**3af**) in 86−92% yield (entries 17−21).

Phosphine-catalyzed asymmetric annulations of allenoates with electron-deficient olefins and imines provide a concise and efficient access to enantiomerically enriched carbo- and heterocycles, which are useful building blocks for the synthesis

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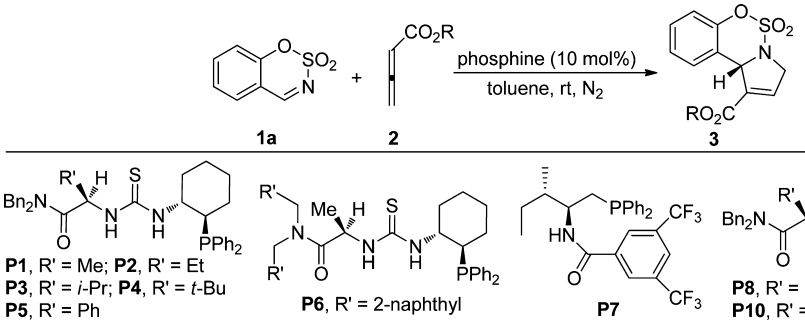
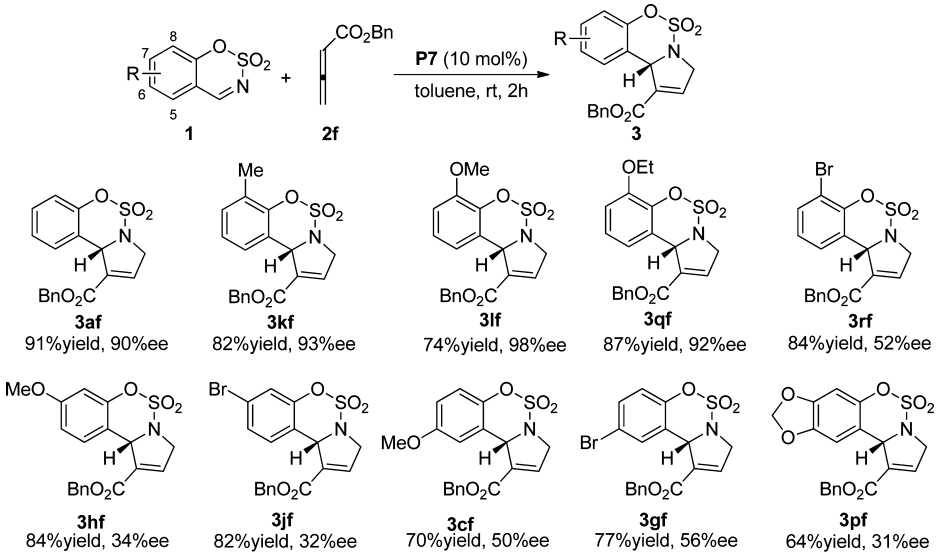
Table 3. Screening of Reaction Conditions of Asymmetric [3 + 2] Cycloaddition of Sulfamate-Derived Cyclic Imines (1a) with Allenoates (2)[a]



entry	phosphine	R	time (h)	product	yield (%)[b]	ee (%)[c]
1	**P1**	Et (**2a**)	12	**3aa**	86	38
2	**P2**	Et (**2a**)	12	**3aa**	93	27
3	**P3**	Et (**2a**)	48	**3aa**	74	4
4[d]	**P4**	Et (**2a**)	24	**3aa**	90	ND
5	**P5**	Et (**2a**)	12	**3aa**	94	ND
6	**P6**	Et (**2a**)	18	**3aa**	92	−8
7	**P7**	Et (**2a**)	2	**3aa**	70	45
8	**P8**	Et (**2a**)	12	**3aa**	74	24
9	**P9**	Et (**2a**)	12	**3aa**	86	22
10	**P10**	Et (**2a**)	36	**3aa**	96	26
11	**P7**	*i*-Pr (**2b**)	2	**3ab**	83	50
12	**P7**	*t*-Bu (**2c**)	12	**3ac**	85	83
13	**P7**	Cy (**2d**)	6	**3ad**	87	73
14	**P7**	Bn (**2f**)	2	**3af**	91	90

[a]Reaction conditions: **1a** (0.1 mmol), **2** (0.12 mmol), and the catalyst (0.01 mmol) in toluene (1.0 mL) at room temperature. [b]Yield of isolated product. [c]The ee values were determined by HPLC analysis using a chiral stationary phase. [d]20 mol % of phosphine was used.

Table 4. Asymmetric [3 + 2] Cycloaddition of Benzyl Allenoate (2f) with Cyclic Imines (1)[a,b,c]



[a]Reaction conditions: **1** (0.1 mmol), **2** (0.12 mmol), and the catalyst (0.01 mmol) in toluene (1.0 mL) at room temperature. [b]Isolated yield. [c]The ee values were determined by HPLC analysis using a chiral stationary phase.

of natural products and biologically active compounds. Therefore, phosphine-catalyzed enantioselective annulations have attracted much attention, and numerous reactions have successfully been accomplished in recent years.[11,m] In the research on enantioselective [3 + 2] cycloaddition of imine with allenoate, Jacobsen used thiourea-based chiral phosphine,[3h] and Lu employed the dipeptide-based chiral phosphine,[3o] respectively, accomplishing excellent enantioselectivity in the [3 + 2] cycloaddition of diphenylphosphinoyl imines with allenoates. However, chiral phosphine promoted asymmetric [3 + 2] cycloadditions of *N*-tosyl imines with allenes, generally affording functionalized 3-pyrrolines with moderate enantioselectivity.[3c−e,j] Particularly, the enantioselective annulations of cyclic imines with allenoates were still unexplored. In this

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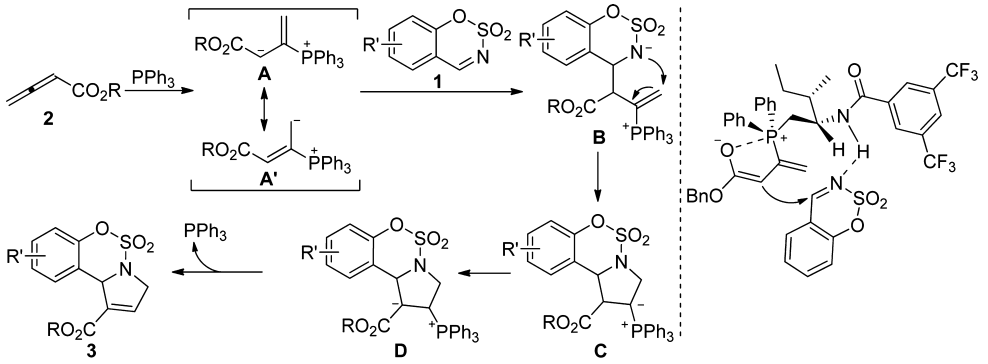
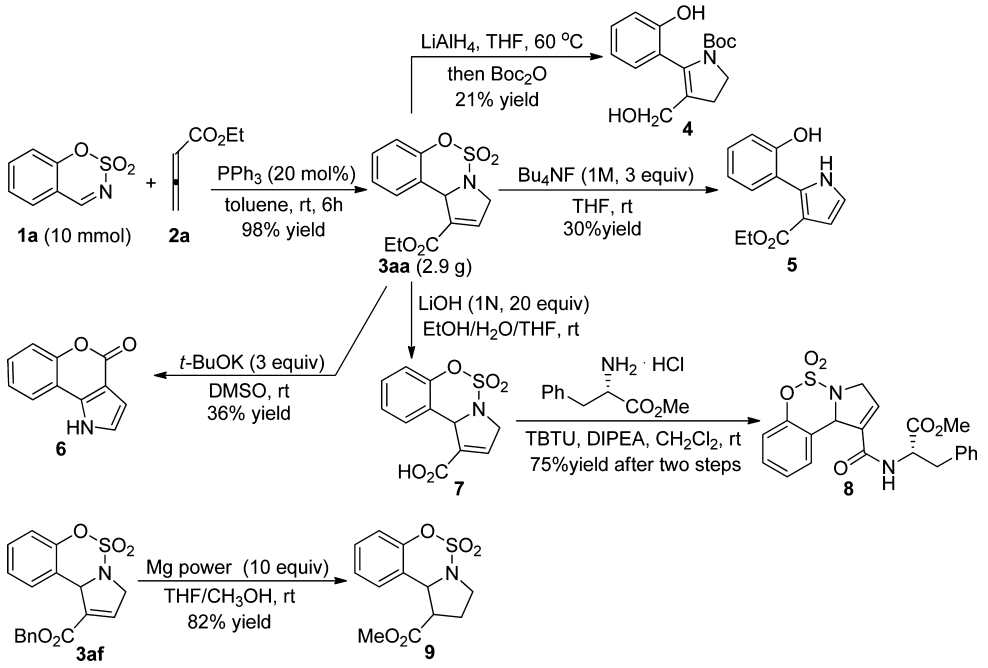
Scheme 2. Proposed Mechanism and Transition State Model



Scheme 3. Gram-Scale Synthesis of Dihydropyrrole Derivative and Further Transformations



context, we investigated asymmetric variant of phosphine-catalyzed [3 + 2] cycloaddition of sulfamate-derived cyclic imines with allenoate. Since amino acid and thiourea-based bifunctional chiral phosphines have demonstrated excellent enantioselective catalytic capability,[11] bifunctional chiral phosphines (**P1**−**P10**) were prepared and screened (Table 3). In the initial exploration, the [3 + 2] cycloaddition of the cyclic imine **1a** and ethyl allenoates **2** was selected as a model reaction (Table 3). To our delight, 10 mol % of the thiourea-based bifunctional chiral phosphine **P1** catalyzed the model reaction to produce the desired product in 86% yield with 38% ee (Table 3, entry 1). Subsequent examination of the phosphines **P2**−**P6**, which possess similar chiral backbone to **P1**, did not give better results (entries 2−6). Thus, the amino acid-based phosphine **P7** was tested,[3m] which displayed excellent enantioselectivity in [3 + 2] cycloaddition reaction of allenoates with dual activated olefins, and the encouraging result (70% yield and 45% ee) was obtained (entry 7). In the hope of getting more encouraging results, the catalysts **P8**−**P10** were designed by the combination of the major functional moieties of the catalysts **4** and **5** and prepared by reported procedure,[3h,m] but their catalytic results were disappointing (entries 8−10). In this situation, the amino acid-based phosphine **P7**, which afforded the highest 45% ee at present, was chosen to further optimize conditions by tuning the ester moieties in allenoates. The screening results indicated the benzyl ester proved to be superior to other esters in the allenoate structures, and the yield and ee of the cycloaddition product could be improved to 91 and 90%, respectively (entries 11−14). The absolute configuration was assigned as R by using X-ray crystallography of the homologous chiral sulfamate-fused dihydropyrrole **3kf** obtained from the [3 + 2] annulation of 8-methyl substituted cyclic imine (**1k**) with benzyl allenoate **2f**.

Under the optimized reaction conditions established, using the phosphine **P7** as the catalyst, the substrate scope of enantioselective [3 + 2] cycloaddition of benzyl allenoate (**2f**) with cyclic imines was examined (Table 4). A significant site effect and electronic effect of the substituent at Ar group was observed. The substrates with the electron-donating substituents at 8-position of cyclic imines carried out the reaction to give the corresponding products (**3kf**, **3lf**, **3qf**) in 92−98% ee, while the substrate with electron-withdrawing substituent at 8-position of cyclic imine afforded the product **3rf** in 52% ee. Those substrates with various substituents in other positions of cyclic imines, irrespective of the electronic nature of the substituents, were converted to the corresponding cyclo-

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addition products (**3hf**, **3jf**, **3cf**, **3gf**, **3pf**) with 31−53% ee in good yields. The exact reason of the poor enantioselectivities is still under exploration.

On the basis of Lu's proposal[2a] and recent mechanistic studies,[18] a plausible mechanism for [3 + 2] cycloaddition and transition state model for enantioselective catalysis are presented in Scheme 2. Upon conjugate addition of PPh_3 to the allenoate **2**, the zwitterion A is formed. It attacks cyclic imine **1** to give the intermediate **B**, which sequentially undergoes intramolecular addition reaction to give the intermediate **C**. The β-phosphonium ester **D** formed from **C** via a [1,2]-proton shift carries out a β-elimination to regenerate the catalyst, affording the final tricyclic product **3**. The imines **1** are highly active and might react with **A** quickly enough to prohibit the transformation of **A** to the delocalized structure **A′**, ensuring excellent regioselectivity to give the sole product **3**. As shown by the transition state model[3h,o] in Scheme 2, the hydrogen-bonding interaction and P−O interaction might adapt the flexible chiral bone of the catalyst to adopt a conformation favoring the Re-face attack of the imine, and the Si-face was blocked by the steric hindrance from the catalyst.

To evaluate the synthetic potential of this catalytic system, the gram-scale preparation of the cycloaddition adduct was investigated. The reaction of 10 mmol of the starting material (**1a**) proceeded smoothly, delivering the corresponding sulfamate-fused dihydropyrrole derivative **3aa** without any loss in reactivity (Scheme 3). The dihydropyrrole derivatives can be readily converted into various interesting compounds (Scheme 3). First, treatment of **3aa** with $LiAlH_4$ at reflux followed by Boc_2O afforded the Boc-protected dihydropyrrole **4**. Next, the sulfamate-fused dihydropyrrole **3aa** was treated with Bu_4NF in THF at room temperature, leading to desulfonylated aromatized product **5**.[19] This procedure provides a convenient and efficient access to pyrrole derivatives. More interestingly, a coumarin fused with pyrrole **6** was obtained by treatment of the cycloadduct **3aa** with *t*-BuOK in DMSO at room temperature.[20] The cycloadduct **3aa** could also be hydrolyzed using LiOH, providing the carboxylic acid **7**. Subsequent amidation of **7** with L-phenylalanine under TBTU/DIPEA conditions gave a L-phenylalanine amide derivative **8**, which could be potential inhibitor of protein prenyltransferases including GGTase I and RabGGTase.[21] Finally, the treatment of **3af** with Mg powder in THF and CH_3OH specifically reduced the double bond,[22] while concomitant transesterification resulted in displacement of benzyl with methyl group, thus affording sulfamate-fused tetrahydropyrrole **9**.

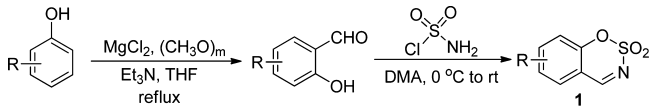
CONCLUSION

In summary, we have described a novel Ph_3P-catalyzed [3 + 2] cycloaddition of various sulfamate-derived cyclic imines with allenoates under mild reaction conditions to give the 3,10b-dihydrobenzo[*e*]pyrrolo[1,2-*c*][1,2,3]oxathiazine-1-carboxylate 5,5-dioxide derivatives in high yields. By using amino acid-based bifunctional phosphine as chiral catalyst, asymmetric variant of the [3 + 2] cycloaddition has also been developed, leading to chiral sulfamate-fused dihydropyrroles in good yields with moderate to excellent enantiomeric excesses. This reaction could be performed in gram scale and is a practical protocol. Subsequent transformations provided a concise access to various heterocycles and pharmaceutically attractive compounds.

EXPERIMENTAL SECTION

General Methods. Unless otherwise indicated, all compounds and reagents were purchased from commercial suppliers and purified by standard techniques. Reactions were monitored through thin-layer chromatography (TLC) on silica gel precoated glass plates. Chromatograms were visualized by fluorescence quenching under UV light at 254 nm. Flash column chromatography was performed using flash silica gel (200−300 mesh). IR spectra were recorded with an FT-IR spectrophotometer and are reported as cm^{-1}. ^1H and ^{13}C NMR spectra were recorded on a NMR instrument. HRMS analyses were carried out on an electrospray ionization (ESI) apparatus using time-of-flight (TOF) mass spectrometry. X-ray crystallographic data were collected using a diffractometer equipped with a low-temperature apparatus operated at 100 K.

General Procedures for Synthesis of Sulfamate-Derived Cyclic Imines 1. Some cyclic slufamate-derived cyclic imines were prepared from the corresponding substituted salicylaldehydes following reported procedures,[16] and others were prepared from corresponding substituted phenols by the following procedures.[16,23,24]



Typical Procedure for the Preparation of Salicylaldehyde Derivative.[23] Parafomaldehyde (2.1 g, 67.5 mmol) was added to a mixture of the phenolic derivative (10 mmol), anhydrous $MgCl_2$ (1.43 g, 15 mmol) and Et_3N (5.3 mL, 37.5 mmol) in THF (50 mL), and the mixture was heated to reflux for 24 h or until complete consumption of the starting material, as determined by TLC. After the reaction mixture was cooled to room temperature, the reaction was quenched with 1 M HCl, and the product was extracted with EtOAc (50 mL × 3). The organic layers were combined, washed with saturated brine, dried (Na_2SO_4) and filtered. All volatiles were removed under reduced pressure, and the product was isolated by flash chromatography (petroleum ether/EtOAc) on silica gel. The products were confirmed by NMR comparison to reported data.

Typical Procedure for the Preparation of Sulfamate-Derived Cyclic Imines.[16,23] Anhydrous formic acid (40.0 mmol, 1.85 g, 1.5 mL) was added dropwise to neat chlorosulfonyl isocyanate (40.0 mmol, 5.66 g, 3.5 mL) at 0 °C with rapid stirring. Vigorous gas evolution was observed during the addition process. The resulting viscous suspension was stirred at room temperature until gas evolution ceased (1−2 h). The resulting colorless solid was used in the following step immediately.

To a solution of salicylaldehyde (1.83 g, 15.0 mmol) in DMA (100 mL) at room temperature was carefully added freshly prepared $ClSO_2NH_2$ (4.62 g, 40.0 mmol) in small portions, and the resulting solution was stirred for 18 h. The reaction was quenched carefully with ice-cold H_2O (100 mL), and the mixture was transferred to a separating funnel containing CH_2Cl_2 (200 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (3 × 50 mL), and the combined organic layers were washed with saturated $NaHCO_3$ solution (100 mL), dried ($MgSO_4$), filtered through a short pad of silica using CH_2Cl_2 as eluent and concentrated in vacuo. The residue was heated to 180 °C under a vacuum to remove volatile impurities to leave **1**. The products were confirmed by NMR comparison to reported data.

General Procedure for the [3 + 2] Cycloaddition Reaction of Cyclic Imines with Allenoates. Under a nitrogen atmosphere, to a stirred solution of cyclic imines **1** (0.125 mmol, 1.0 equiv) and catalyst PPh_3 (0.025 mmol, 20 mol %) in toluene (2 mL) was added 2,3-butadienoate **2** (0.15 mmol, 1.2 equiv) via a syringe in one portion. Then the reaction solution was vigorously stirred at room temperature and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product.

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3aa. White solid (36.5 mg, 99% yield): mp 84−86 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.66 (d, J = 7.7 Hz, 1H), 7.35−7.27 (m, 1H), 7.17 (td, J = 1.2, 7.7 Hz, 1H), 7.03 (dd, J = 1.2, 7.7 Hz, 1H), 6.91−6.80 (m, 1H), 6.13 (d, J = 3.4 Hz, 1H), 4.52−4.39 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 149.8, 137.3, 135.4, 129.4, 127.3, 125.9, 120.8, 119.2, 66.6, 61.6, 55.9, 14.1; IR (film) ν_{max} 1738, 1722, 1404, 1373, 1230, 1208, 1175, 885, 763, 634, 570, 528 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{14}NO_5S^+$ $[M + H]^+$ 296.0587, found 296.0579.

3ba. White solid (37.8 mg, 98% yield): mp 86−89 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (s, 1H), 7.09 (d, J = 8.4 Hz, 1H), 6.91 (d, J = 8.4 Hz, 1H), 6.90−6.87 (m, 1H), 6.08 (d, J = 2.8 Hz, 1H), 4.54−4.23 (m, 4H), 2.29 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 147.7, 137.3, 135.8, 135.6, 130.0, 127.5, 120.3, 118.9, 66.6, 61.5, 55.9, 20.9, 14.1; IR (film) ν_{max} 1721, 1405, 1374, 1350, 1255, 1231, 1209, 1186, 1132, 1111, 842, 660, 626, 595 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{16}NO_5S^+$ $[M + H]^+$ 310.0744, found 310.0736.

3ca. White solid (38.5 mg, 95% yield): mp 159−161 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.55 (d, J = 8.8 Hz, 1H), 6.86−6.81 (m, 1H), 6.73 (dd, J = 2.6, 8.8 Hz, 1H), 6.55 (d, J = 2.6 Hz, 1H), 6.06 (d, J = 3.1 Hz, 1H), 4.50−4.38 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.78 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 160.2, 150.6, 136.9, 135.8, 128.1, 112.64, 112.60, 104.1, 66.3, 61.5, 55.9, 55.6, 14.1; IR (film) ν_{max} 1716, 1493, 1403, 1258, 1207, 1178, 1132, 842, 411 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{16}NO_6S^+$ $[M + H]^+$ 326.0693, found 326.0685.

3da. White solid (43.0 mg, 98% yield): mp 127−128 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.70 (d, J = 2.0 Hz, 1H), 7.30 (dd, J = 2.0, 8.7 Hz, 1H), 6.96 (d, J = 8.7 Hz, 1H), 6.86−6.81 (m, 1H), 6.13 (d, J = 3.1 Hz, 1H), 4.50−4.19 (m, 4H), 1.36 (t, J = 7.1 Hz, 3H), 1.26 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 149.1, 147.5, 137.1, 135.6, 126.4, 124.2, 119.9, 118.6, 66.9, 61.6, 55.9, 34.6, 31.2, 14.2; IR (film) ν_{max} 1719, 1406, 1254, 1195, 1179, 1122, 1100, 846, 779 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{22}NO_5S^+$ $[M + H]^+$ 352.1213, found 352.1206.

3ea. White solid (28.7 mg, 75% yield): mp 124−125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.51−7.44 (m, 1H), 7.06−6.97 (m, 2H), 6.91−6.88 (m, 1H), 6.09 (s, 1H), 4.50−4.40 (m, 2H), 4.40−4.29 (m, 2H), 1.37 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ162.2, 159.6 (d, J_{C-F} = 245.8 Hz), 145.8 (d, $^4J_{C-F}$ = 2.7 Hz), 137.8, 135.0, 122.4 (d, $^1J_{C-F}$ = 7.7 Hz), 120.7 (d, $^3J_{C-F}$ = 8.4 Hz), 116.5 (d, $^2J_{C-F}$ = 23.9 Hz), 114.2 (d, $^2J_{C-F}$ = 26.0 Hz), 66.6 (d, $^4J_{C-F}$ = 1.6 Hz), 61.8, 56.0, 14.1; IR (film) ν_{max} 1717, 1485, 1408, 1258, 1209, 1167, 1099, 843, 661, 421, 411 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}FNO_5S^+$ $[M + H]^+$ 314.0493, found 314.0483.

3fa. White solid (36.3 mg, 88% yield): mp 163−164 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 8.5 Hz, 1H), 7.15 (dd, J = 2.1, 8.5 Hz, 1H), 7.06 (d, J = 2.1 Hz, 1H), 6.92−6.80 (m, 1H), 6.10 (d, J = 1.2 Hz, 1H), 4.51−4.38 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 148.4, 137.8, 135.0, 131.2, 129.6, 127.5, 122.3, 120.6, 66.4, 61.8, 56.0, 14.1; IR (film) ν_{max} 1718, 1482, 1406, 1253, 1206, 1192, 1179, 1130, 1086, 922, 907, 774, 609, 568 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}ClNO_5S^+$ $[M + H]^+$ 330.0197, found 330.0197.

3ga. White solid (26.0 mg, 56% yield): mp 128−130 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 2.0 Hz, 1H), 7.42 (dd, J = 2.0, 8.7 Hz, 1H), 6.99−6.87 (m, 2H), 6.09 (s, 1H), 4.50−4.27 (m, 4H), 1.39 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.0, 137.9, 135.0, 132.5, 130.4, 122.7, 120.9, 118.6, 66.3, 61.8, 56.0, 14.1; IR (film) ν_{max} 1715, 1472, 1409, 1262, 1210, 1193, 1169, 1132, 1111, 879, 823, 774, 642, 588 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}BrNO_5S^+$ $[M + H]^+$ 373.9692, found 373.9683.

3ha. White solid (35.8 mg, 89% yield): mp 134−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26−7.22 (m, 1H), 6.96 (d, J = 9.0 Hz, 1H), 6.89−6.77 (m, 2H), 6.08 (d, J = 3.5 Hz, 1H), 4.50−4.38 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.75 (s, 3H), 1.36 (t, J = 7.1 Hz, 3H).^{13}C NMR (75 MHz, $CDCl_3$) δ 162.5, 157.1, 143.4, 137.5, 135.3, 121.5, 120.1, 115.5, 111.6, 66.8, 61.6, 56.0, 55.6, 14.1; IR (film) ν_{max} 1714, 1625, 1505, 1399, 1375, 1348, 1258, 1232, 1204, 1129, 1095, 1051, 956, 797, 784, 620 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{16}NO_6S^+$ $[M + H]^+$ 326.0693, found 326.0693.

3ia. White solid (38.0 mg, 92% yield): mp 170−173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.65 (d, J = 8.5 Hz, 1H), 7.15 (dd, J = 2.1, 8.5 Hz, 1H), 7.05 (d, J = 2.1 Hz, 1H), 6.89−6.83 (m, 1H), 6.12−6.06 (m, 1H), 4.51−4.39 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 150.3, 137.5, 135.2, 134.8, 128.6, 126.2, 119.5, 119.4, 66.4, 61.7, 56.0, 14.1; IR (film) ν_{max} 1715, 1408, 1251, 1210, 1195, 1170, 1113, 826, 777, 647, 612, 592, 552, 533, 498 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}ClNO_5S^+$ $[M + H]^+$ 330.0197, found 330.0193.

3ja. White solid (36.4 mg, 79% yield): mp 125−127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.5 Hz, 1H), 7.30 (dd, J = 2.0, 8.5 Hz, 1H), 7.21 (d, J = 2.0 Hz, 1H), 6.90−6.81 (m, 1H), 6.10−6.03 (m, 1H), 4.55−4.40 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 150.3, 137.5, 135.1, 129.2, 128.8, 122.39, 122.36, 119.9, 66.5, 61.7, 56.0, 14.1; IR (film) ν_{max} 1717, 1478, 1409, 1251, 1206, 1191, 1179, 1132, 1120, 1082, 897, 773, cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}BrNO_5S^+$ $[M + H]^+$ 373.9692, found 373.9685.

3ka. White solid (35.5 mg, 92% yield): mp 123−125 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 7.7 Hz, 1H), 7.15 (d, J = 7.7 Hz, 1H), 7.05 (t, J = 7.7 Hz, 1H), 6.86−6.79 (m, 1H), 6.12 (d, J = 3.6 Hz, 1H), 4.52−4.39 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 2.29 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 148.3, 137.1, 135.7, 130.9, 128.5, 125.2, 124.7, 120.5, 66.7, 61.5, 56.0, 15.6, 14.1; IR (film) ν_{max} 1719, 1404, 1374, 1252, 1232, 1205, 1159, 1131, 1079, 869, 768, 615, 587, 553 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{16}NO_5S^+$ $[M + H]^+$ 310.0744, found 310.0739.

3la. White solid (40.0 mg, 98% yield): mp 137−139 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20 (d, J = 7.7 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 6.95−6.76 (m, 2H), 6.13 (d, J = 2.3 Hz, 1H), 4.54−4.39 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.3, 149.0, 139.5, 137.3, 135.5, 125.6, 121.8, 118.2, 112.0, 66.7, 61.5, 56.2, 56.0, 14.1; IR (film) ν_{max} 1717, 1479, 1403, 1275, 1256, 1204, 1163, 1131, 1091, 1066, 867, 763, 605, 555 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{16}NO_6S^+$ $[M + H]^+$ 326.0693, found 326.0688.

3ma. White solid (37.1 mg, 85% yield): mp 132−135 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.57−7.49 (m, 1H), 7.31 (dd, J = 1.1, 7.9 Hz, 1H), 7.09 (t, J = 7.9 Hz, 1H), 6.88−6.81 (m, 1H), 6.13 (d, J = 4.2 Hz, 1H), 4.57−4.36 (m, 2H), 4.32 (q, J = 7.1 Hz, 2H), 1.41 (s, 9H), 1.34 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 149.2, 140.4, 137.2, 135.8, 127.0, 125.34, 125.30, 121.4, 67.0, 61.5, 56.3, 35.0, 30.0, 14.1; IR (film) ν_{max} 1719, 1405, 1199, 1128, 870, 775, 606, 420, 412, 405 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{22}NO_5S^+$ $[M + H]^+$ 352.1213, found 352.1207.

3na. White solid (35.6 mg, 86% yield): mp 169−170 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64−7.58 (m, 1H), 7.42−7.35 (m, 1H), 7.10 (t, J = 8.0 Hz, 1H), 6.90−6.84 (m, 1H), 6.14 (d, J = 3.9 Hz, 1H), 4.56−4.38 (m, 2H), 4.33 (q, J = 7.1 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 145.9, 137.5, 135.2, 130.2, 125.9, 125.7, 124.1, 122.7, 66.8, 61.7, 56.1, 14.1; IR (film) ν_{max} 1717, 1410, 1256, 1201, 1132, 858, 769, 671, 403 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}ClNO_5S^+$ $[M + H]^+$ 330.0197, found 330.0191.

3oa. White solid (38.0 mg, 88% yield): mp 153−155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27−8.17 (m, 1H), 7.84−7.76 (m, 2H), 7.54−7.43 (m, 2H), 7.15 (d, J = 8.9 Hz, 1H), 6.72 (d, J = 4.4 Hz, 1H), 6.59−6.51 (m, 1H), 4.70−4.56 (m, 1H), 4.46−4.34 (m, 1H), 4.11 (q, J = 7.1 Hz, 2H), 1.13 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.4, 147.9, 145.6, 144.3, 137.3, 135.6, 113.2, 106.0, 102.0, 100.7, 66.6, 61.6, 56.0, 14.1; IR (film) ν_{max} 1721, 1404, 1253, 1215, 1193, 1082, 871, 818, 650, 621 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{16}NO_5S^+$ $[M + H]^+$ 346.0744, found 346.0739.

3pa. White solid (32.8 mg, 77% yield): mp 176−178 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (s, 1H), 6.85 (s, 1H), 6.52 (s, 1H), 6.05−5.91 (m, 3H), 4.53−4.22 (m, 4H), 1.36 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 162.2, 145.9, 137.5, 135.2, 130.2, 125.9, 125.7, 124.1, 122.7, 66.8, 61.7, 56.1, 14.1; IR (film) νmax 1715, 1484, 1404,

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1249, 1205, 1141, 1087, 1037, 859, 820, 749, 620, 561 cm^{-1}; HRMS (ESI) calcd for C14H14NO7S$^+$ $[M + H]^+$ 340.0485, found 340.0481.

3ab. White solid (33.1 mg, 86% yield): mp 102−104 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 7.8 Hz, 1H), 7.35−7.27 (m, 1H), 7.23−7.11 (m, 1H), 7.07−7.00 (m, 1H), 6.83 (s, 1H), 6.13 (d, J = 2.8 Hz, 1H), 5.33−5.06 (m, 1H), 4.55−4.24 (m, 2H), 1.45−1.26 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 149.9, 137.0, 135.9, 129.4, 127.3, 125.9, 120.8, 119.2, 69.4, 66.6, 55.9, 21.8, 21.7; IR (film) ν_{max} 1713, 1405, 1374, 1257, 1208, 1193, 1175, 1133, 1103, 1074, 1057, 884, 862, 825, 770, 634, 570 cm^{-1}; HRMS (ESI) calcd for $C_{14}H_{15}NO_5SNa^+$ $[M + Na]^+$ 332.0563, found 332.0565.

3ac. White solid (37.1 mg, 92% yield): mp 120−122 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70−7.64 (m, 1H), 7.34−7.27 (m, 1H), 7.17 (td, J = 1.2, 8.0 Hz, 1H), 7.03 (dd, J = 1.2, 8.0 Hz, 1H), 6.75−6.72 (m, 1H), 6.09 (d, J = 3.2 Hz, 1H), 4.50−4.28 (m, 2H), 1.56 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.8, 149.9, 137.0, 136.0, 129.4, 127.3, 125.9, 120.8, 119.2, 74.3, 66.6, 55.9, 31.5, 31.5, 25.2, 23.7, 23.6, 0.97; IR (film) ν_{max} 1738, 1439, 1376, 1280, 1228, 1217, 1130, 749, 733, 694, 682, 623, 560, 528, 463, 436 cm^{-1}; HRMS (ESI) calcd for $C_{15}H_{17}NO_5SNa^+$ $[M + Na]^+$ 346.0720, found 346.0716.

3ad. White solid (38.3 mg, 88% yield): mp 122−125 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.67 (d, J = 7.7 Hz, 1H), 7.30 (t, J = 7.7 Hz, 1H), 7.16 (t, J = 7.7 Hz, 1H), 7.03 (d, J = 7.7 Hz, 1H), 6.84 (s, 1H), 6.14 (s, 1H), 5.06−4.84 (m, 1H), 4.52−4.28 (m, 2H), 2.04−1.19 (m, 11H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.7, 149.9, 137.0, 136.2, 129.4, 127.2, 125.9, 121.0, 119.2, 82.7, 66.6, 55.9, 28.1; IR (film) ν_{max} 1710, 1405, 1257, 1208, 1193, 1173, 1129, 1103, 884, 861, 772, 633, 569 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{19}NO_5SNa^+$ $[M + Na]^+$ 372.0876, found 372.0877.

3ae. White solid (37.7 mg, 88% yield): mp 153−156 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 8.0 Hz, 1H), 7.49−7.40 (m, 2H), 7.36−7.27 (m, 2H), 7.22−7.11 (m, 4H), 7.07 (dd, J = 1.2, 8.0 Hz, 1H), 6.23 (d, J = 3.7 Hz, 1H), 4.63−4.43 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 160.9, 150.1, 150.0, 139.6, 134.9, 129.7, 129.6, 127.4, 126.4, 126.1, 121.3, 120.7, 119.4, 66.7, 56.2; IR (film) ν_{max} 1736, 1488, 1404, 1356, 1235, 1208, 1192, 1175, 1118, 1102, 1050, 885, 772, 741, 635, 564 cm^{-1}; HRMS (ESI) calcd for $C_{17}H_{14}NO_5S^+$ $[M + H]^+$ 344.0587, found 344.0582.

3af. White solid (40.8 mg, 92% yield): mp 122−124 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62−7.56 (m, 1H), 7.37 (s, 5H), 7.30−7.22 (m, 1H), 7.13−7.05 (m, 1H), 7.00 (dd, J = 0.8, 8.2 Hz, 1H), 6.89−6.84 (m, 1H), 6.12 (d, J = 3.7 Hz, 1H), 5.30 (AB q, $\Delta\ \delta_{AB}$ = 0.10 ppm, J_{AB} = 12.0 Hz, 2H), 4.48−4.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.8, 137.9, 135.1, 135.0, 129.4, 128.7, 128.6, 128.39, 128.36, 127.3, 125.9, 120.6, 119.2, 67.2, 66.6, 55.9; IR (film) ν_{max} 1716, 1453, 1403, 1350, 1249, 1208, 1193, 1174, 1126, 1103, 1058, 884, 863, 763, 699, 635 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{15}NO_5SNa^+$ $[M + Na]^+$ 380.0563, found 380.0561.

Preparation of Bifunctional Chiral Phosphines. The chiral phosphines were prepared according to the procedure of Jacobsen[3h] and Zhao.[3m]

The NMR data of **P8**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.56−6.97 (m, 20H), 7.01 (br s, 1H), 6.58 (br s, 1H), 5.67 (s, 1H), 4.89−4.40 (m, 4H), 2.35−2.07 (m, 2H), 1.76 (s, 1H), 1.34 (d, J = 6.7 Hz,3H), 1.29−0.95 (m,1H), 0.84 (d, J = 6.5 Hz, 3H), 0.76 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.3, 162.3, 138.6, 138.4, 136.2, 135.8, 133.4, 133.1, 132.7, 132.4, 128.9, 128.7, 128.5, 128.45, 128.40, 128.36, 127.9, 127.8, 127.5, 127.2, 56.1, 55.9, 50.1, 48.2, 31.0, 30.8, 25.0, 19.2, 15.1, 11.6.

General Procedure for Asymmetric [3 + 2] Cycloaddition Reaction of Cyclic Imines with Benzyl 2, 3-Butadienoate. Under a nitrogen atmosphere, to a stirred solution of cyclic imines **1** (0.1 mmol, 1.0 equiv) and catalyst **P7** (0.01 mmol, 0.1 equiv) in toluene (1 mL) was added benzyl 2, 3-butadienoate **2f** (0.12 mmol, 1.2 equiv) via a syringe in one portion. Then the reaction solution was vigorously stirred at room temperature and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (petroleum ether/EtOAc as the eluent) to furnish the corresponding product.

3af. White solid (32.6 mg, 91% yield): $[\alpha]^{20}_D$ = +11.2 (c 0.44, $CHCl_3$); mp 122−124 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.62−7.56 (m, 1H), 7.37 (s, 5H), 7.30−7.22 (m, 1H), 7.13−7.05 (m, 1H), 7.00 (dd, J = 0.8, 8.2 Hz, 1H), 6.89−6.84 (m, 1H), 6.12 (d, J = 3.7 Hz, 1H), 5.30 (AB q, $\Delta\ \delta_{AB}$ = 0.10 ppm, J_{AB} = 12.0 Hz, 2H), 4.48−4.29 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.8, 137.9, 135.1, 135.0, 129.4, 128.7, 128.6, 128.39, 128.36, 127.3, 125.9, 120.6, 119.2, 67.2, 66.6, 55.9; IR (film) ν_{max} 1716, 1453, 1403, 1350, 1249, 1208, 1193, 1174, 1126, 1103, 1058, 884, 863, 763, 699, 635 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{15}NO_5SNa^+$ $[M + Na]^+$ 380.0563, found 380.0561; HPLC analysis 90% ee (Chiralcel AD-H 5:95 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 21.219 min, t_{R2} = 30.699 min.).

3kf. White solid (30.1 mg, 82% yield): $[\alpha]^{20}_D$ = +8.5 (c 0.52, $CHCl_3$); mp 134−136 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43−7.32 (m, 6H), 7.16−7.09 (m, 1H), 6.97 (t, J = 7.7 Hz, 1H), 6.89−6.80 (m, 1H), 6.12 (d, J = 3.9 Hz, 1H), 5.29 (AB q, $\Delta\ \delta_{AB}$ = 0.09 ppm, J_{AB} = 12.0 Hz, 2H), 4.51−4.30 (m, 2H), 2.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 148.2, 137.7, 135.3, 135.0, 130.8, 128.7, 128.6, 128.5, 128.4, 125.2, 124.6, 120.4, 67.2, 66.7, 56.0, 15.5; IR (film) ν_{max} 1719, 1463, 1404, 1350, 1250, 1205, 1159, 1128, 1077, 1056, 869, 765, 732, 699, 689, 664, 615, 582, 556 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}NO_5SNa^+$ $[M + Na]^+$ 394.0720, found 394.0717; HPLC analysis 93% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 9.911 min, t_{R2} = 12.521 min).

3lf. White solid (28.4 mg, 74% yield): $[\alpha]^{20}_D$ = +6.9 (c 1.32, $CHCl_3$); mp 177−179 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44−7.31 (m, 5H), 7.16−7.11 (m, 1H), 7.02 (t, J = 8.1 Hz, 1H), 6.89−6.84 (m, 2H), 6.13 (d, J = 4.0 Hz, 1H), 5.30 (AB q, $\Delta\ \delta_{AB}$ = 0.08 ppm, J_{AB} = 12.0 Hz, 2H), 4.56−4.27 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 149.0, 139.4, 137.8, 135.2, 135.0, 128.7, 128.6, 128.4, 125.6, 121.6, 118.2, 111.9, 67.2, 66.7, 56.2, 56.0; IR (film) ν_{max} 1719, 1478, 1403, 1276, 1259, 1205, 1163, 1128, 1091, 1064, 867, 761, 731, 700, 606, 555 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}NO_6NaS^+$ $[M + Na]^+$ 410.0669, found 410.0670; HPLC analysis 98% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 22.696 min, t_{R2} = 38.312 min).

3qf. White solid (36.8 mg, 87% yield): $[\alpha]^{20}_D$ = +5.6 (c 0.40, $CHCl_3$); mp 137−140 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.45−7.31 (m, 5H), 7.12 (m, 1H), 6.99 (t, J = 8.1 Hz, 1H), 6.89−6.81 (m, 1H), 6.12 (d, J = 4.1 Hz, 1H), 5.29 (AB q, $\Delta\ \delta_{AB}$ = 0.10 ppm, J_{AB} = 12.0 Hz, 2H), 4.50−4.29 (m, 1H), 4.05 (q, J = 7.1 Hz, 1H), 1.43 (t, J = 7.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 146.6, 138.1, 134.9, 134.8, 133.3, 128.7, 128.4, 126.44, 126.37, 122.6, 112.8, 67.3, 66.8, 56.1; IR (film) ν_{max} 1719, 1470, 1404, 1276, 1260, 1205, 1171, 1128, 1086, 1061, 867, 762, 732, 606, 557, cm^{-1}; HRMS (ESI) calcd for $C_{20}H_{19}NO_6SNa^+$ $[M + Na]^+$ 424.0825, found 424.0822; HPLC analysis 92% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 16.075 min, t_{R2} = 29.580 min).

3rf. White solid (36.3 mg, 84% yield): mp 123−126 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, J = 8.0 Hz, 1H), 7.51 (d, J = 8.0 Hz, 1H), 7.37 (s, 5H), 6.96 (t, J = 8.0 Hz, 1H), 6.90−6.87 (m, 1H), 6.12 (d, J = 3.8 Hz, 1H), 5.29 (AB q, $\Delta\ \delta_{AB}$ = 0.11 ppm, J_{AB} = 12.0 Hz, 2H), 4.52−4.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.9, 146.6, 138.1, 134.9, 134.8, 133.3, 128.7, 128.4, 126.44, 126.37, 122.6, 112.8, 67.3, 66.8, 56.1; IR (film) ν_{max} 1718, 1625, 1504, 1402, 1253, 1204, 1127, 1105, 1054, 955, 793, 744, 701, 619, 579 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}BrNO_5SNa^+$ $[M + Na]^+$ 457.9668, found 457.9671; HPLC analysis 52% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 15.989 min, t_{R2} = 21.563 min).

3hf. White solid (32.3 mg, 84% yield): mp 127−129 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51−7.44 (m, 1H), 7.41−7.33 (m, 5H), 6.89−6.81 (m, 1H), 6.65 (dd, J = 2.6, 8.8 Hz, 1H), 6.53 (d, J = 2.6 Hz, 1H), 6.06 (d, J = 3.5 Hz, 1H), 5.29 (AB q, $\Delta\delta_{AB}$ = 0.10 ppm, J_{AB} = 12.0 Hz, 2H), 4.47−4.31 (m, 2H), 3.76 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 160.2, 150.6, 137.5, 135.5, 135.0, 128.7, 128.6, 128.4, 128.0, 112.6, 112.4, 104.0, 67.2, 66.3, 55.9, 55.5; IR (film) ν_{max} 1718, 1625, 1504, 1402, 1253, 1204, 1127, 1105, 1054, 955, 862, 793, 744, 700, 619, 579 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}NO_6SNa^+$ $[M + Na]^+$ 410.0669, found 410.0672; HPLC analysis 34% ee (Chiralcel OD-H

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15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 20.814 min, t_{R2} = 25.570 min).

3cf. White solid (26.9 mg, 70% yield): mp 129−132 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42−7.32 (m, 1H), 7.20−7.15 (m, 5H), 6.94 (d, J = 9.0 Hz, 1H), 6.91−6.87 (m, 2H), 6.84−6.77 (m, 1H), 6.09 (d, J = 3.6 Hz, 1H), 5.36−5.26 (m, 2H), 4.52−4.30 (m, 2H), 3.62 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.2, 157.1, 143.3, 138.1, 135.0, 128.7, 128.6, 128.4, 121.3, 120.1, 115.7, 111.2, 67.3, 66.7, 55.9, 55.5; IR (film) ν_{max} 1718, 1625, 1504, 1403, 1253, 1204, 1127, 1105, 1055, 955, 862, 793, 745, 701, 619, 579 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{17}NO_6SNa^+$ $[M + Na]^+$ 410.0669, found 410.0667; HPLC analysis 50% ee (Chiralcel AD-H: 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1} = 20.324 min, t_{R2} = 25.743 min).

3jf. White solid (35.5 mg, 82% yield): mp 125−127 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 8.3 Hz, 1H), 7.38 (s, 5H), 7.24−7.16 (m,2H), 6.94−6.82 (m, 1H), 6.07 (s, 1H), 5.30 (AB q, $\Delta\ \delta_{AB}$ = 0.11 ppm, J_{AB} = 12.0 Hz, 2H), 4.53−4.33 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 150.2, 138.1, 134.85, 134.78, 129.1, 128.7, 128.4, 122.4, 122.3, 119.7, 67.4, 66.5, 56.0; IR (film) ν_{max} 1718, 1402, 1249, 1206, 1191, 1179, 1129, 1081, 899, 779, 768, 733, 699, 606, 556 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}BrNO_5SNa^+$ $[M + Na]^+$ 457.9668, found 457.9667; HPLC analysis 32% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 14.037 min, t_{R2} = 17.575 min).

3gf. White solid (33.5 mg, 77% yield): mp 152−154 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.46−7.34 (m, 6H), 7.03−6.97 (m, 1H), 6.93−6.90 (m, 1H), 6.12−6.06 (m, 1H), 5.31 (AB q, $\Delta\ \delta_{AB}$ = 0.08 ppm, J_{AB} = 12.0 Hz, 2H), 4.49−4.32 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.0, 161.2, 157.9, 145.74, 145.70, 138.3, 134.8, 134.7, 128.8, 128.5, 122.3, 122.2, 120.8, 120.7, 116.7, 116.3, 114.4, 114.0, 67.5, 66.6, 66.5, 56.0; IR (film) ν_{max} 1717, 1485, 1407, 1258, 1208, 1168, 1150, 1127, 1099, 1061, 913, 843, 801, 770, 749, 699, 661, 630, 601, 538 cm^{-1}; HRMS (ESI) calcd for $C_{18}H_{14}BrNO_5SNa^+$ $[M + Na]^+$ 457.9668, found 457.9666; HPLC analysis 56% ee (Chiralcel AD-H 15:85 isopropanol/hexane, 1 mL/min, 254 nm, t_{R1}= 17,143 min, t_{R2} = 25.250 min).

3pf. White solid (25.6 mg, 64% yield): mp 112−114 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (s, 5H), 7.09 (s, 1H), 6.87 (s, 1H), 6.50 (s, 1H), 5.99 (d, J = 3.6 Hz, 1H), 5.94 (s, 2H), 5.28 (AB q, $\Delta\ \delta_{AB}$ = 0.08 ppm, J_{AB} = 12.0 Hz, 2H), 4.46−4.28 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 147.9, 145.6, 144.2, 137.9, 135.2, 134.9, 128.7, 128.6, 128.4, 113.0, 105.9, 102.0, 100.6, 67.3, 66.6, 56.0; IR (film) ν_{max} 1717, 1504, 1483, 1404, 1249, 1205, 1140, 1087, 1037, 861, 814, 748, 702, 620, 560 cm^{-1}; HRMS (ESI) calcd for $C_{19}H_{15}NO_7SNa^+$ $[M + Na]^+$ 424.0461, found 424.0460; HPLC analysis 31% ee (Chiralcel AD-H 15:85 isopropanol:hexane, 1 mL/min, 254 nm, t_{R1}= 24.568 min, t_{R2} = 30.788 min).

General Procedure for the Scale-up Reaction. Under an N_2 atmosphere, to a stirred solution of cyclic imines **1a** (10 mmol, 1.0 equiv) and catalyst PPh_3 (2 mmol, 0.2 equiv) in toluene (100 mL) was added ethyl 2,3-butadienoate **2a** (12 mmol, 1.2 equiv) via a syringe in one portion. Then the reaction solution was vigorously stirred at room temperature and monitored by TLC. After the reaction was complete, the mixture was directly purified by column chromatography on silica gel (10:1 petroleum ether/EtOAc) to furnish the corresponding product **3a** (2.9 g) as a white solid (98% yield).

General Procedure for the Synthesis of 4. To a solution of **3aa** (75 mg, 0.26 mmol) in THF (0.5 mL) at room temperature was added $LiAlH_4$ (2.0 M in THF, 0.39 mL, 0.78 mmol) dropwise over 2 min. The mixture was heated at 60 °C for 2 h, cooled naturally to room temperature, and then to 0 °C with an ice bath. The reaction was quenched carefully with EtOAc (1 mL) followed by EtOH (1 mL) and H_2O (1 mL). To the resulting white turbid mixture was added Boc_2O (170 mg, 0.78 mmol) in one portion, and the mixture was stirred at room temperature for 1 h. The reaction was diluted with EtOAc (20 mL) and acidified with 2 M HCl until the aqueous layer became clear. The aqueous layer was separated and extracted with EtOAc (2 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (1:1 petroleum ether/EtOAc) gave **4** (15 mg, 21% yield) as a semisolid: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.20−6.83 (m, 4H), 6.58 (br s, 1H), 4.27 (s, 2H), 3.73 (br s, 1H), 3.20 (d, J = 6.6 Hz, 2H), 2.34 (t, J = 6.6 Hz, 2H), 1.40 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 156.6, 153.3, 129.6, 128.6, 123.9, 120.2, 115.9, 79.8, 66.4, 39.1, 29.8, 28.4; IR (film) ν_{max} 3450, 2956, 2919, 2851, 750 cm^{-1}; HRMS (ESI) calcd for $C_{16}H_{21}NO_4Na^+$ $[M + Na]^+$ 314.1363, found 314.1361.

General Procedure for the Synthesis of 5. To a solution of **3aa** (90 mg, 0.3 mmol) in THF (1 mL) was added a solution of Bu_4NF in THF (1M, 0.9 mL, 3 equiv). The mixture was then stirred at room temperature overnight. Methanol (2 mL) was added, and the mixture was concentrated under reduced pressure. The residue was diluted with ethyl acetate and washed with saturated $NaHCO_3$, and the aqueous layer was extracted twice with ethyl acetate. The combined organic phase was washed with brine, dried (Na_2SO_4), and concentrated. The residue was purified by column chromatography on silica gel (4:1 petroleum ether/EtOAc) to afford **5** (21 mg, 30% yield) as a white solid: mp 159−161 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 (br s, 1H), 8.38 (br s, 1H), 7.35−7.27 (m, 1H), 7.23 (dd, J = 1.4, 7.7 Hz, 1H), 7.13−7.07 (m, 1H), 6.97 (td, J = 1.4, 7.7 Hz, 1H), 6.82−6.77 (m, 1H), 6.74−6.70 (m, 1H), 4.30 (q, J = 7.1 Hz, 2H), 1.33 (t, J = 7.1 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 168.2, 154.8, 133.9, 130.4, 130.0, 121.8, 121.2, 120.0, 118.7, 113.4, 111.5, 61.0, 14.2; IR (film) ν_{max} 3302, 2956, 2919, 2851, 1658, 1463, 741 cm^{-1}; HRMS (ESI) calcd for $C_{13}H_{13}NO_3Na^+$ $[M + Na]^+$ 254.0788, found 254.0788.

General Procedure for the Synthesis of 6. *t*-BuOK (112 mg, 1.0 mmol) and **3aa** (90 mg, 0.3 mmol) were dissolved in DMSO (10 mL). The mixture was stirred at room temperature and monitored by TLC. After the starting material consumed, the reaction was quenched by addition of water, and the mixture was extracted with Et_2O. The combined organic extracts were evaporated, and the residue was purified through silica gel (1:1 petroleum ether/EtOAc with 0.5% Et_3N) to give the desired product **6** (20 mg, 36% yield) as a white solid: mp >250 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 12.63 (br s, 1H), 8.07−8.01 (m, 1H), 7.49−7.35 (m, 3H), 7.34−7.31 (m, 1H), 6.71−6.68 (m, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 158.7, 151.6, 135.5, 129.1, 124.5, 124.3, 121.7, 117.3, 114.3, 108.6, 107.3; IR (film) ν_{max} 3418, 1651, 1049, 1026, 1002, 826, 765, 631 cm^{-1}; HRMS (ESI) calcd for $C_{11}H_7NO_2Na^+$ $[M + Na]^+$ 208.0369, found 208.0357.

General Procedure for the Synthesis of 8. Six milliliters of 1 N LiOH in H_2O were added to the mixture of **3aa** (90 mg, 0.3 mmol) in THF (6 mL) and EtOH (6 mL). The mixture was stirred at room temperature for 1 h, acidified with 2 N HCl at 0 °C, and extracted with EtOAc. The combined organic extracts were dried (Na_2SO_4) and concentrated under reduced pressure to give crude product **7**, which was used in the following step without further purification.

To a mixture of carboxylic acid **7**, L-phenylalanine (85 mg, 0.45 mmol) and HBTU (210 mg, 0.6 mmol) in CH_2Cl_2 (5 mL) were added freshly distilled DIPEA (0.2 mL, 1.2 mmol). The resulting mixture was stirred under N_2 at room temperature for 24 h. The mixture was diluted with CH_2Cl_2 (5 mL), washed with aqueous solution of HCl (1 M, 3 × 5 mL), $NaHCO_3$ (5 mL), and dried over Na_2SO_4. After filtering Na_2SO_4 off, the solution was concentrated to give the crude product, which was further purified using flash chromatography (1:1 petroleum ether/EtOAc) to give **8** as a white solid (95.6 mg, 74.5% yield): mp 171−173 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.37−7.06 (m, 1H), 7.02−6.95 (m, 1H), 6.67−6.49 (m, 1H), 5.55 (d, J = 6.2 Hz, 1H), 4.11−3.98 (m, 1H), 3.96−3.87 (m, 1H), 3.79 (s, 1H), 3.22−3.17 (m, 1H), 3.15−3.07 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.7, 169.2, 149.4, 135.6, 129.3, 129.2, 129.0, 128.7, 127.2, 127.1, 126.2, 123.1, 118.8, 61.0, 58.51, 58.48, 53.0, 52.5, 37.8; IR (film) ν_{max} 1744, 1662, 1530, 1453, 1402, 1262, 1207, 1172, 1103, 1032, 824, 802, 761, 702, 561 cm^{-1}; HRMS (ESI) calcd for $C_{21}H_{20}N_2O_6SNa^+$ $[M + Na]^+$ 451.0934, found 451.0934.

General Procedure for the Synthesis of 9. A mixture of the cyclic imine **3af** (107 mg. 0.3 mmol) and Mg powder (10 equiv) in MeOH (5 mL) and THF (5 mL) was stirred for 12 h at room temperature. Then, the saturated NH_4Cl aqueous solution was added to the reaction mixture. The resulting mixture was extracted with CH_2Cl_2, and the combined organic extracts were dried (Na_2SO_4),

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filtered, and concentrated under reduced pressure. The residue was purified by silica gel chromatography (1:1 petroleum ether/EtOAc) to afford the product **9** as a white solid (70 mg, 82% yield): mp 78−80 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35−7.18 (m, 1H), 7.01 (d, J = 8.1 Hz, 1H), 5.50 (d, J = 3.6 Hz, 1H), 3.84 (s, 1H), 3.77−3.64 (m, 1H), 3.51−3.40 (m, 1H), 3.39−3.30 (m, 1H), 2.46−2.31 (m, 1H), 2.26−2.12 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.9, 150.3, 129.4, 126.8, 126.0, 121.7, 118.9, 64.6, 52.8, 52.2, 49.6, 27.1; IR (film) ν_{max} 1736, 1452, 1398, 1199, 1172, 1104, 878, 816, 761, 616, 554 cm^{-1}; HRMS (ESI) calcd for $C_{12}H_{13}NO_5SNa^+$ $[M + Na]^+$ 306.0407, found 306.0405.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra of all compounds, HPLC data of **3af**, **3kf**, **3lf**, **3qf**, **3rf**, **3hf**, **3jf**, **3cf**, **3gf**, and **3pf**, and crystallographic data (CIF) of **3kf**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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