ChemPubSoc Europe

DOI: 10.1002/ejoc.201501420

EurJOC European Journal of Organic Chemistry

Full Paper

All-Carbon Quaternary Stereocenters

Enantioselective Construction of Aryl-Substituted All-Carbon Quaternary Stereocenters by Using Tertiary Amine–Thiourea-Catalyzed Michael Additions

Peng Chen,[a] Xu Bao,[b] Le-Fen Zhang,[b] Guo-Jie Liu,[a] and Yi-Jun Jiang*[a]

Abstract: A catalytic enantioselective synthetic strategy for the aryl-substituted all-carbon quaternary stereocenters of bioactive hydrodibenzofuran alkaloids was achieved by the Michael addition reaction of α-cyano ketones and acrylates using a chiral tertiary amine–thiourea catalyst. This method can tolerate steric bulkiness and multiple functional groups, and 32 Michael adducts were prepared in good to excellent yields with moderate to good enantioselectivities. The enantiopurity of the products could also be enriched up to 99 % *ee* after one recrystallization. This enantioselective Michael addition features a low cost, metal-free, and easily operable procedure that can provide multifunctionalized enantiopure Michael adducts on a four-gram scale and supply sufficient amounts of potential precursors for a number of hydrodibenzofuran natural products.

Introduction

In modern organic synthesis, the catalytic enantioselective construction of quaternary centers is one of the most important areas of research. In particular, the catalytic enantioselective construction of all-carbon quaternary centers is one of the more challenging processes because of the substantial intrinsic steric bulkiness that arises from four carbon substituents bonded to a central carbon atom.[1] In recent years, a number of catalytic reactions that focus on the construction of chiral all-carbon quaternary centers have been reported. However, few of these can tolerate multiple functional groups, which limits their application for the enantioselective total synthesis of natural products.

Hydrodibenzofuran-type natural products belong to a series of structurally diverse alkaloids with a wide range of biological activities (Figure 1).[2] Their highly strained *cis*-hydrodibenzofuran core contains an aryl-substituted all-carbon quaternary chiral stereocenter, which poses a formidable challenge for synthetic chemists. Among these alkaloids, (–)-lycoramine and (–)-galanthamine have received much attention from medicinal and organic chemists because of their remarkable biological activity and pharmacological potential. The known strategies for the construction of the chiral aryl-substituted all-carbon quaternary centers in (–)-lycoramine and (–)-galanthamine can be divided into four categories (Scheme 1):[3] (1) a diastereoselective desymmetrized oxa-Michael addition induced by the chiral precursors that were obtained from a phenolic oxidative coupling reaction,[4] (2) diastereoselective [3,3] sigmatropic rearrangements from chiral precursors,[5] (3) diastereoselective Heck reactions of chiral precursors,[6] and (4) enantioselective catalytic Michael addition reactions from racemic substrates.[7] It should be mentioned that enantioenriched precursors were used in methods (1)–(3), which require extra steps because of the employment of the chiral auxiliaries or the careful operations needed to avoid the racemization of the chiral non-quaternary carbons in the late-stage steps. Therefore, directly introducing the chirality during the formation of the all-carbon quaternary center by using a catalytic enantioselective method is more attractive, as no chiral auxiliaries are needed, and it is difficult to racemize the all-carbon quaternary center once it has been fabricated. An elegant enantioselective synthesis of (–)-lycoramine and (–)-galanthamine was reported by Jia and co-workers using method (4), in which the all-carbon quaternary centers were constructed by a catalytic enantioselective

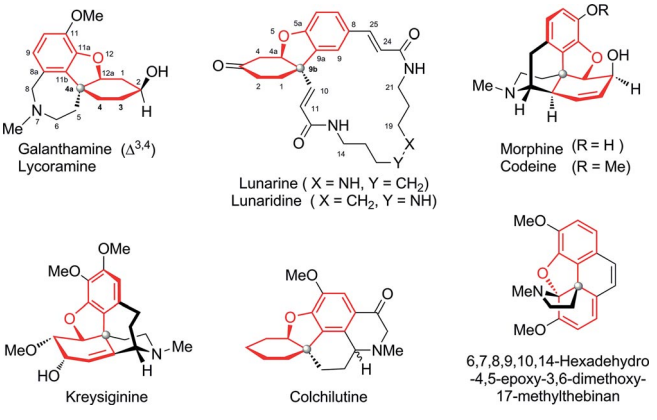
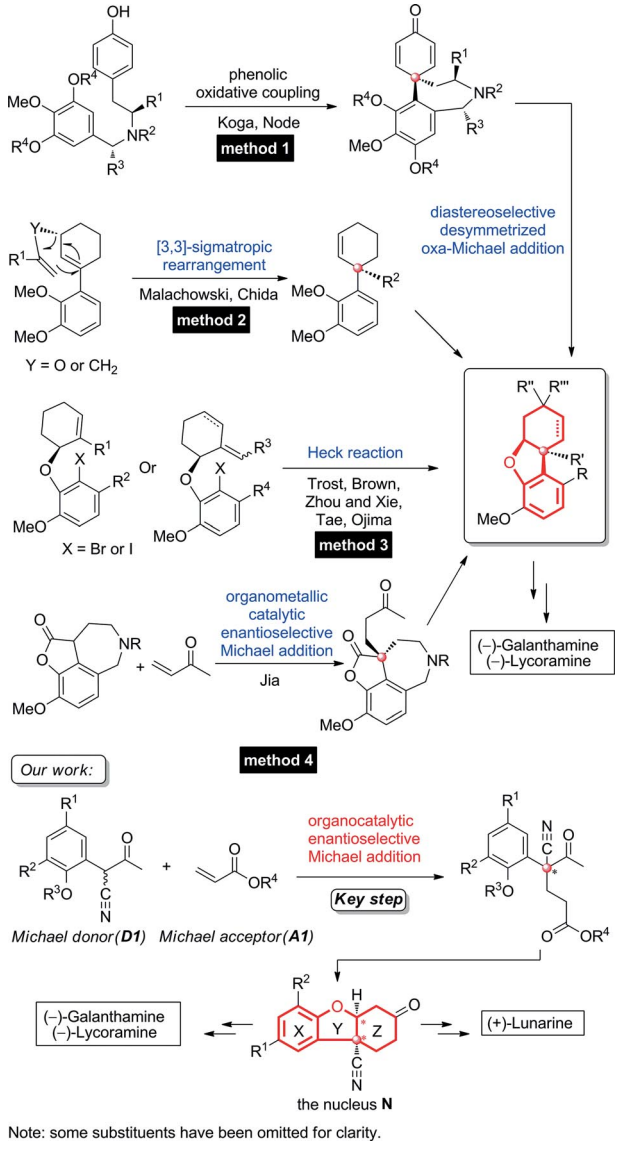


Figure 1. Representative members of hydrodibenzofuran alkaloids.

[a] *State Key Laboratory of Inorganic Synthesis and Preparative Chemistry, College of Chemistry, Jilin University, Changchun 130012, P. R. China*
E-mail: jiangyijun@jlu.edu.cn
http://supramol.jlu.edu.cn/people/sunjunqi/
[b] *College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, P. R. China*
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under http://dx.doi.org/10.1002/ejoc.201501420.

Michael addition reaction.[7a] However, metal catalysts and ligands as well as careful operations were needed for both the synthesis of the precursors and the key step, in which the chirality was introduced. Therefore, catalytic enantioselective strategies for the synthesis of (–)-lycoramine and (–)-galanthamine that feature lower costs, easier operations, and lower toxicity are still highly desirable.



Scheme 1. The known strategies to construct the chiral all-carbon quaternary centers in (–)-lycoramine and (–)-galanthamine.

Recently, we reported the enantioselective total synthesis of (–)-lycoramine and (–)-galanthamine, in which we also used an enantioselective Michael addition reaction to construct the key all-carbon quaternary stereocenters from entirely different substrates than those used by Jia and co-workers.[7b] By using the multifunctionalized Michael adducts that resulted from this key step, we could construct the nucleus **N** with a *cis*-hydrodibenzofuran core (Scheme 1). In our strategy, we used an inexpensive chiral amine–thiourea as the organocatalyst and easily performed the key step on a gram scale. Most importantly, our strategy was flexible, and by changing the substituents on the phenyl ring of the starting Michael donor **D1**, we could synthesize diversely substituted nuclei **N** for the total synthesis of hydrodibenzofuran-type natural products. Therefore, by using this new and divergent chiral amine–thiourea-catalyzed Michael addition between α-cyano ketones and acrylates, we accomplished not only the highly efficient catalytic enantioselective synthesis of the galanthamine-type alkaloids (–)-lycoramine and (–)-galanthamine but also the first enantioselective total synthesis of (+)-lunarine, the ring system of which is different from the galanthamine-type alkaloids.[7b]

During the last two decades, numerous efforts have been devoted to catalytic enantioselective Michael additions. However, catalytic enantioselective Michael additions that are capable of constructing all-carbon quaternary stereocenters have not been fully explored,[1,8–12] especially for processes that can tolerate multiple functional groups and be further applied to the asymmetric total synthesis of complex natural products. Although the abovementioned chiral amine–thiourea-catalyzed Michael addition reaction between α-cyano ketones and acrylates reported in our previous work[7b] were highly tolerant of multiple functional groups and showed great potential in the total synthesis of the hydrodibenzofuran alkaloids, the details and scope of its application have not been fully addressed. Herein, we detail the full account of this Michael addition approach. In addition, we have expanded this method to employ various substrates and provide a general way to synthesize highly functionalized building blocks that contain chiral aryl-substituted all-carbon quaternary stereocenters, which can later be used as crucial precursors for the total synthesis of related natural products.

Results and Discussion

By considering the features of the Michael addition reaction of **D1** and Michael acceptor **A1** (Figure 2), we envisaged that the enantioselective reaction could be realized by a mode of catalysis that involves the dual activation of donors and acceptors by using a chiral bifunctional catalyst that consists of a Brønsted acid and base (e.g., chiral amine-thiourea catalyst **4**,[13] Figure 2). On the basis of this dual mode of catalysis, α-aryl α-cyano ketone **1a** and 4-bromophenyl acrylate (**2a**) were selected as the model donor and acceptor and, along with Takemoto's catalyst **4a**,[13] were used to screen the reaction conditions of the Michael addition (Figure 3). Among the various

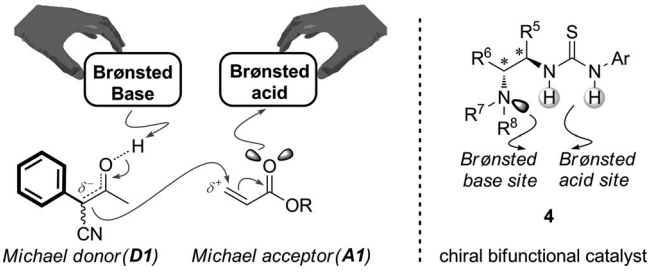


Figure 2. Dual activation of donors and acceptors by chiral bifunctional catalyst.

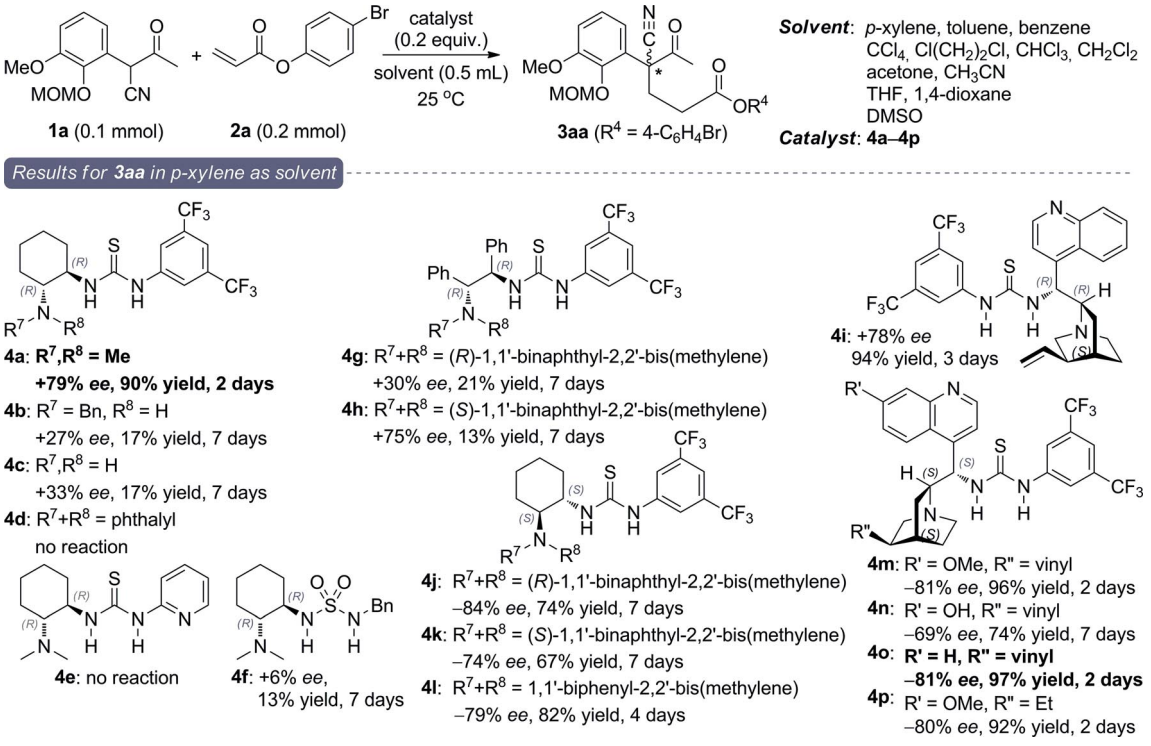


Figure 3. The model Michael addition catalyzed by chiral bifunctional amine-thiourea catalysts with (*R*,*R*)- and (*S*,*S*)-1,2-diamine scaffolds (MOM = methoxymethyl, THF = tetrahydrofuran, DMSO = dimethyl sulfoxide). ["+" or "–" before the *ee* values means that the major product has (*S*) absolute configuration or (*R*) absolute configuration, respectively.[15]]

screened solvents,[14] *p*-xylene gave the best results in terms of enantioselectivity and reactivity. Thus, in *p*-xylene as the solvent, a series of amine-thiourea catalysts **4b**–**4p**, structural variants of catalyst **4a** with the (*R*,*R*)-1,2-diamine skeleton, were then investigated (Figure 3).[14]

Upon comparing the enantioselectivity and catalytic reactivity of **4a** (90 % yield, 79 % *ee*) with the results obtained by **4b**–**4p** in the detailed screenings, several interesting features of the catalyst were revealed. First, one tertiary amine moiety as the Brønsted basic site was necessary for the efficiency of the Michael addition, and the catalysts with a secondary, primary, or deactivated tertiary amino group (i.e., **4b**–**4d**, Figure 3) were either less effective or ineffective. Notably, the bulky R^7 and R^8 substituents (Figure 2) on the tertiary amine group of **4g**, **4h**, and **4j**–**4l** reduced the reactivity but had little influence on the enantioselectivity in most cases, as the (*R*)-1,1′-binaphthyl-2,2′-bis(methylene) and (*S*,*S*)-diamine scaffolds, or vice versa, constitute a matched case in enantioselectivity. Second, the requisite catalytic activity of the Brønsted acidic site of the catalyst was influenced, to some extent, by the variation of *N*-substituted group or thiocarbonyl. Catalyst **4f** with a sulfonylurea moiety promoted this reaction very slowly, whereas **4e** was completely ineffective. Third, in addition to the catalysts **4a**–**4f** and **4j**–**4l**, which were derived from a chiral cyclic diamine (the R^5 and R^6 groups in **4** are linked, Figure 2), catalysts **4g**–**4i** and **4m**–**4p**, which stem from chiral acyclic diamines such as 1,2-diphenylethylenediamine and cinchona alkaloid derivatives[10b] (R^5 and R^6 groups in **4** are not linked, Figure 2) were also investigated. Interestingly, catalysts that contain the (*R*,*R*)-diamine moiety enantioselectively gave **3aa** with the (*S*) absolute configuration, and those that have the (*S*,*S*)-diamine moiety led to the reversed enantioselectivity and afforded the (*R*) absolute configuration of **3aa**.[15] As a result of the abovementioned experiments, the optimized reaction conditions for the designed enantioselective Michael addition of α-aryl α-cyano ketone **1a** and 4-bromophenyl acrylate (**2a**) were realized in *p*-xylene as the solvent at room temperature under the catalysis of tertiary amine-thiourea **4a** [**3aa**: 90 % yield, 79 % *ee*, (*S*) absolute configuration].[15] Importantly, the stereochemistry of **3aa** with the crucial quaternary stereogenic carbon center could be fine-tuned by using cinchonidine-derived bifunctional catalyst **4o** or **4m** [**3aa**: 97 % yield, 81 % *ee*, (*R*) absolute configuration],[15] which provided the possibility of access to the *cis*-hydrodibenzofuran nucleus **N** (Scheme 1) with the opposite absolute configuration.

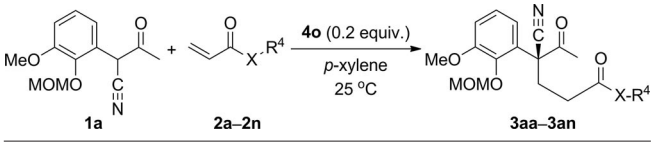
In terms of the catalytic efficiency as well as the availability of chiral diamines used for the preparations of amine-thiourea catalysts, **4a** and **4o** were eventually employed as the catalysts for the asymmetric control of both product enantiomers. Although the expected product **3aa** was only obtained with *ee* values of approximately 80 %, the present method proceeds under mild organocatalysis and constitutes the first example of this combination of substrates, that is, α-cyano ketones as Michael donors and acrylates as Michael acceptors. Strategically, this provides a new way for the direct catalytic enantioselective synthesis of chiral aryl-substituted all-carbon quaternary centers of multifunctionalized building blocks that contain cyano, ester, and ketone moieties.

To examine the generality of this asymmetric method for the catalytic enantioselective synthesis of aryl-substituted all-

carbon quaternary stereocenters, various Michael acceptors and donors were submitted to the reaction with **4o** as the catalyst. In Table 1, Entries 1–4, it can be seen that having an *ortho* or *meta* substituent on the phenyl ring of the aryl acrylates did not improve the yields or *ee* values. A series of aryl acrylates with electron-donating and electron-withdrawing *para* substituents were then examined (Table 1, Entries 5–10). Interestingly, the results obtained in Table 1, Entries 1–10 clearly demonstrate that electron-deficient aryl acrylates (i.e., **2a**–**2g**, **2i**, and **2j**) were better Michael acceptors. As a comparison, the Michael addition with phenyl acrylate **2k** as the acceptor proceeded very slowly (Table 1, Entry 11). As a structural comparison with **2k**, it is noteworthy that the halogen-substituted aryl acrylates (i.e., **2a**–**2c** and **2e**–**2g**) had an obvious accelerating effect on the reactivity, which may be a result of the electronic effect of the halogen atom. Although the reaction with 1-naphthyl acrylate (**2l**) as the acceptor proceeded readily, there was no observed improvement in the stereocontrol (Table 1, Entry 12). Surprisingly, alkyl acrylate **2m** was found to be totally ineffective in the current catalyzed reaction (Table 1, Entry 13). In addition, acrylic acid derivative **2n** as the Michael acceptor would be potentially useful in the synthesis of the *cis*-hydrodibenzofuran nucleus **N** (Scheme 1), but it would not provide any enantioselective improvement (Table 1, Entry 14).

Among the products formed, Michael adduct **3ag** (Table 1, Entry 7) was easily crystallized, mainly because of the presence

Table 1. Various Michael acceptors for the synthesis of aryl-substituted all-carbon quaternary stereocenters under the catalysis of **4o**.[a]



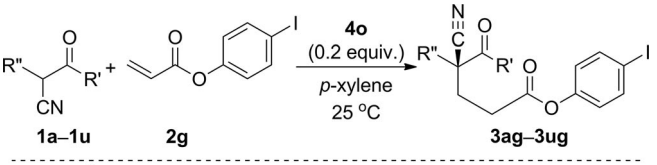
1a **2a–2n** **3aa–3an**

Entry	Acceptor (X–R^4)	Product	*t* [d]	Yield [%][b]	*ee* [%][c]
1	**2a** (O–4-C_6H_4Br)	3aa	2	97	81 (*R*)[d]
2	**2b** (O–3-C_6H_4Br)	3ab	1.5	92	80
3	**2c** (O–2-C_6H_4Br)	3ac	4.5	92	66
4	**2d** (O–2-$C_6H_4NO_2$)	3ad	2	89	78
5	**2e** (O–4-C_6H_4F)	3ae	4.5	96	80
6	**2f** (O–4-C_6H_4Cl)	3af	3	90	80
7	**2g** (O–4-C_6H_4I)	3ag	2	96 (76)[e]	81 [98 (*R*)][f]
8	**2h** (O–4-C_6H_4OMe)	3ah	7	10	–
9	**2i** (O–4-$C_6H_4CO_2Me$)	3ai	2	94	81
10	**2j** (O–4-$C_6H_4NO_2$)	3aj	1	99	81
11	**2k** (O–Ph)	3ak	7	82	80
12	**2l** (O–1-naphthyl)	3al	3.5	99	67
13	**2m** (O–Me)	3am	7	–	–
14	 **2n**	3an	1.5	92	77

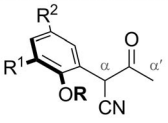
[a] To an oven-dried Schlenk tube were sequentially added catalyst **4o** (0.02 mmol), α-cyano ketone **1a** (0.1 mmol), *p*-xylene (0.5 mL), and Michael acceptor **2** (0.2 mmol) at 25 °C. The reaction mixture was stirred at this temperature until the donor had disappeared upon inspection by thin layer chromatography. [b] Yield of isolated product. [c] Determined by chiral HPLC analysis. [d] The absolute configuration was assigned by comparison to that reported in Table 1, Entry 7. [e] Yield of isolated crystallized product **3ag** after one recrystallization. [f] The *ee* value of enantioenriched product **3ag** after one recrystallization. The (*R*) absolute configuration was confirmed by X-ray crystallography[7b] (see Supporting Information).

of the iodine atom. After one recrystallization procedure, crystals of (*R*)-**3ag** were isolated from the mother liquor with >98 % *ee* (76 % isolated yield), and the absolute configuration

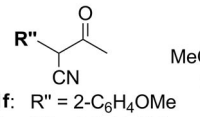
Table 2. Various Michael donors for the synthesis of aryl-substituted all-carbon quaternary stereocenters under the catalysis of **4o**.[a]



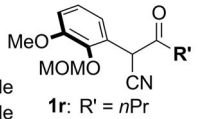
1a–1u **2g** **3ag–3ug**



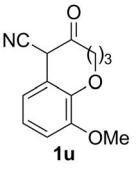
1a: R = MOM, R^1 = OMe, R^2 = H
1b: R = MOM, R^1 = H, R^2 = Br
1c: R = Allyl-OCH_2, R^1 = OMe, R^2 = H
1d: R = CH_2Ph, R^1 = OMe, R^2 = H
1e: R = Me, R^1 = OMe, R^2 = H



1f: R'' = 2-C_6H_4OMe
1g: R'' = 3-C_6H_4OMe
1h: R'' = 4-C_6H_4OMe
1i: R'' = 2-C_6H_4Br
1j: R'' = 3-C_6H_4Br
1k: R'' = 4-C_6H_4Br
1l: R'' = Ph
1m: R'' = 2-C_6H_4Me
1n: R'' = 2-C_6H_4F
1o: R'' = 2-C_6H_4Cl
1p: R'' = 1-naphthyl
1q: R''= CH_2Ph



1r: R' = *n*Pr
1s: R' = CH_2Ph
1t: R' = Ph



1u

Entry	Donor	Product	Yield [%][b]	*ee* [%][c]	Yield [%][d]	*ee* [%]
1	1a	3ag	96	81 (*R*)	76	99[e,f]
2	1b	3bg	93	77 (*R*)[g]	–	–
3	1c	3cg	86	80 (*R*)	–	–
4	1d	3dg	92	76 (*R*)	–	–
5	1e	3eg	95	73 (*R*)	42	90[e]
6	1f	3fg	96	72 (*R*)	64	91[h]
7	1g	3gg	95	64 (*R*)	60	90[h]
8	1h	3hg	95	71 (*R*)	73	87[h]
9	1i	3ig	63	59 (*R*)	41	95[h]
10	1j	3jg	90	58 (*R*)	–	–
11	1k	3kg	88	64 (*R*)	63	86[h]
12	1l	3lg	88	65 (*R*)	54	87[h]
13	1m	3mg	82	71 (*R*)	–	–
14	1n	3ng	85	68 (*R*)	57	88[h]
15	1o	3og	80	55 (*R*)	47	91[h]
16	1p	3pg	84	71 (*R*)	54	93[h]
17	1q	3qg	94	60 (*R*)	–	–
18	1r	3rg	89	76[i]	–	–
19	1s	3sg	52	54[i]	28	90[h]
20	1t	3tg	69	74[i]	–	–
21	1u	3ug	92	72 (*R*)	70	98[e]

[a] To an oven-dried Schlenk tube were sequentially added catalyst **4o** (0.04 mmol), α-cyano ketone **1a**–**1u** (0.2 mmol), *p*-xylene (1.0 mL), and Michael acceptor **2g** (0.4 mmol) at 25 °C. The reaction mixture was stirred at this temperature until the donor had disappeared upon inspection by thin layer chromatography. [b] Yield of isolated product. [c] All enantiomeric excess values were determined by chiral HPLC analysis. The (*R*) absolute configurations of **3ag**[7b] and **3ug** (see Figure 4) were established by X-ray crystallography, and accordingly the absolute stereochemistry for the major enantiomers of **3bg**–**3tg** were assigned provisionally as indicated in the parentheses. [d] Isolated yield of the enantioenriched product after one recrystallization. [e] The *ee* value of the isolated crystals after one recrystallization. [f] The reaction was carried out on a 2.5 g (10 mmol) scale of **1a**, and 4.0 g of almost enantiopure (*R*)-**3ag** could be obtained from one reaction. [g] In an earlier report, we further confirmed the (*R*) absolute configuration by a late-stage recrystallization of compound **7b**.[7b] [h] The *ee* value of the material collected from mother liquor after the crystallization of the racemate. [i] Unknown absolute configuration.

was further determined by X-ray crystallography.[7b,16] Considering that only good to moderate levels of enantioselectivity were observed in screening the potential Michael acceptors (66–81 % *ee*, Table 1), we believe that recrystallization may provide an alternative to increase the *ee* values of the Michael adducts, which could be significant, particularly in asymmetric total synthesis. Consequently, 4-iodophenyl acrylate **2g** was selected as the ideal acceptor to study this method.

Various Michael donors were then subjected to the current enantioselective Michael addition catalyzed by **4o** (Table 2). From the results obtained, it can be seen that most of the functionalized products (i.e., **3ag**–**3ug**) were afforded with good to moderate enantioselectivities in good to excellent yields, which indicates that challenges still remain in this current catalytic enantioselective Michael addition of α-cyano ketones and acrylates to install an aryl-substituted all-carbon quaternary center. Compared with the 65 % *ee* obtained by using α-phenyl α-cyano ketones **1l** (Table 2, Entry 12), most of the α-cyano ketones that have an *ortho*-substituted aryl ring at α-position (i.e., **1a**–**1f**, **1m**, and **1n**) gave an improved enantioselectivity that ranged from 68 to 81 % *ee*. Notably, to the best of our knowledge, there are few reports of the catalytic asymmetric construction of an *ortho*-substituted arylic all-carbon quaternary center through a Michael addition reaction[9a,9c,17] such as those products found in Table 2, Entries 1–6, 9, and 13–15. There are slight influences on the stereocontrol (58–71 % *ee*) of the reaction by employing Michael donors that have a *meta*- *or para*-substituted aryl ring at α-position (i.e., **1g**, **1h**, **1j**, and **1k**, Table 2, Entries 7, 8, 10, and 11). Despite the asymmetric control of only 60 % *ee*, one experiment that used an α-alkyl-substituted Michael donor, that is, α-cyano ketone **1q** (Table 2, Entry 17) was also conducted to investigate the construction of an alkyl-substituted all-carbon quaternary stereocenter. Furthermore, the influence of the group (R′) bonded to the carbonyl carbon was examined by using Michael donors **1r**–**1t** (Table 2, Entries 18–20), and in these cases, the observed enantioselectivity was lower than that observed with **1a**. In addition to the acyclic cyano ketones, cyclic substrate **1u** (Table 2, Entry 21) was investigated and afforded Michael adduct **3ug** in 92 % yield with 72 % *ee* (98 % *ee* after one recrystallization). Notably with the establishment of (*R*) absolute configuration of **3ug** by X-ray crystal structure analysis (Figure 4),[16] this example with a cyclic substrate is mechanistically interesting. During the tertiary amine–thiourea-catalyzed reaction, the configurationally

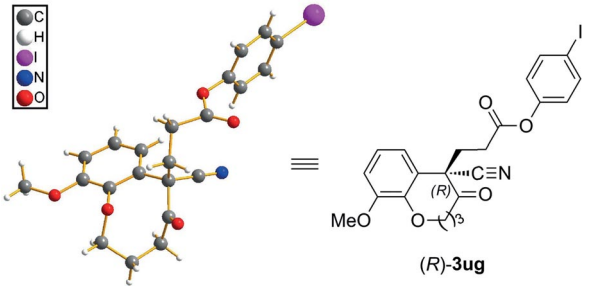


Figure 4. X-ray crystal structure of (*R*)-**3ug**.

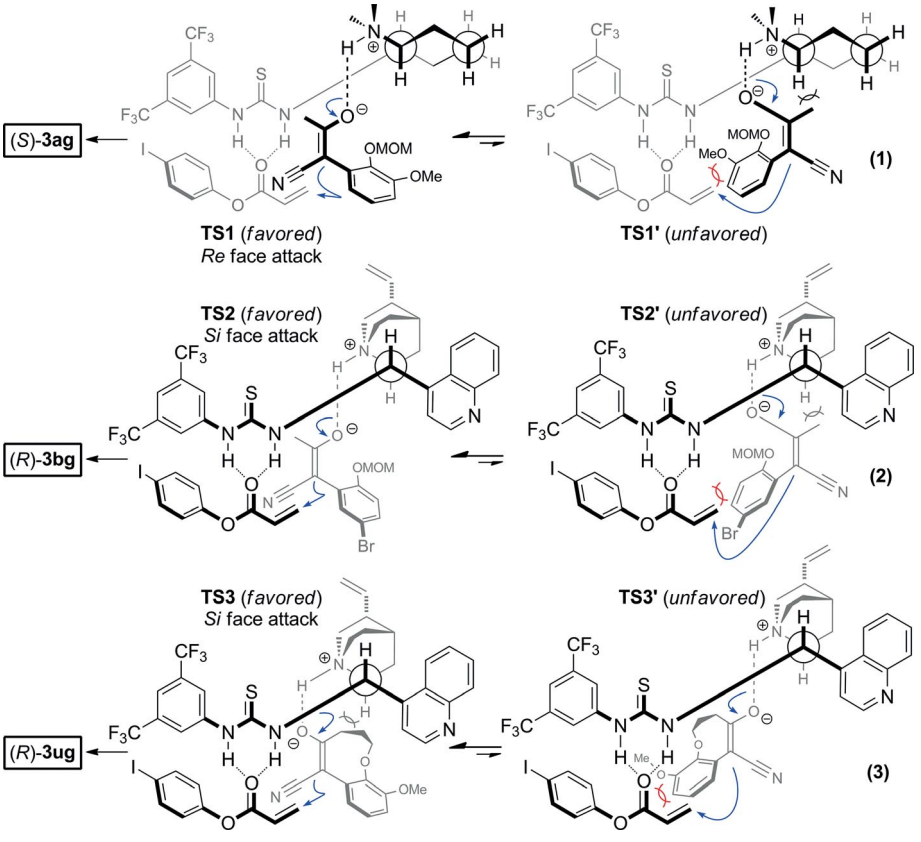


Figure 5. Proposed mechanistic rationale for tunable enantioselectivity under the catalysis of **4a** and **4o**.

defined (*Z*)-enolate will be unambiguously formed in situ by deprotonation of **1u**, which will help to gain more of an understanding about the stereoselectivity in the present enantioselective Michael addition.

To improve the optical purity of the Michael adducts containing the chiral quaternary carbon centers, a mixed solvent recrystallization was used. The enantiopurity for most of cases in Table 2 was enriched from 86 to 99 % *ee* after one recrystallization. Interestingly, a conglomerate crystallization with homochiral recognition ($f_{R,R}$, $f_{S,S} > f_{R,S}$) was observed for **3ag**, **3eg**, and **3ug** (Table 2, Entries 1, 5, and 21), which led to the isolation of crystals with high enantiomeric enrichment (up to 99 % *ee*). In most of the recrystallized samples (Table 2, Entries 6–9, 11, 12, 14–16, and 19), the racemate crystallized with preferential heterochiral interaction ($f_{R,S} > f_{R,R}$, $f_{S,S}$), which led to the successful enantiomeric enrichment of the mother liquors.

A mechanistic rationale was proposed for the enantioselectivity observed in the reactions to give **3ag**, **3bg**, and **3ug** (Figure 5), in which the synergistic noncovalent hydrogen-bonding activation of both the Michael donor and acceptor might be one of the crucial elements for the current stereocontrol. In contrast to the in situ generation of the configurationally defined (*Z*)-enolate in the Michael addition of cyclic cyano ketone **1u** [Figure 5, Equation (3); Table 2, Entry 21], the (*E*)-enolates of the acyclic cyano ketones would be preferentially formed [Figure 5, Equations (1) and (2)]. The present enantioselectivity observed in the products[16] may be supported by models **TS1**, **TS2**, and **TS3**, as an energetically unfavorable steric interaction exists between the donors and acceptors in models **TS1′**, **TS2′**, and **TS3′**, which is consistent with the fact that the planar aryl moiety of a Michael donor is usually bulkier than the linear cyano group.

Conclusions

We have described the details of the enantioselective Michael addition of α-cyano ketones and acrylates by using bifunctional tertiary amine-thiourea catalysts. By using this method, we synthesized 32 chiral all-carbon quaternary stereocentered Michael adducts with moderate to excellent enantioselectivities and yields. These multifunctionalized Michael adducts are potential precursors to a number of hydrodibenzofuran natural products. In addition, this metal-free, facile method can be increased to a four-gram scale, which can supply sufficient amounts of precursors for further transformations toward enantiopure hydrodibenzofuran-type natural products and their related derivatives for biological and medicinal purposes.

Experimental Section

General Methods: All reactions were carried out in oven- or heat-dried flasks. When necessary, the solvents used were purified by standard drying techniques. Reagents were purchased from commercial vendors and used without further purification. All reactions were monitored by thin layer chromatography on silica gel F_{254} plates by using UV light as the visualizing agent (if applicable) and a solution of ammonium molybdate tetrahydrate (50 g L^{-1}) in EtOH followed by heating as the developing agent. The products were purified by flash column chromatography on silica gel (200–300 mesh) from the Qingdao Marine Chemical Factory in China. The ^1H and ^{13}C NMR spectroscopic data were recorded in a $CDCl_3$ or [D_6]DMSO solution with a Bruker AM 400 MHz instrument. Chemical shifts (δ) were reported in ppm and calibrated by using the residual undeuterated solvent (for $CHCl_3$, δ = 7.27 ppm; for [D_5]DMSO, δ = 2.50 ppm) or tetramethylsilane (δ = 0.00 ppm) as the internal reference for ^1H NMR and the deuterated solvent (for $CDCl_3$, δ = 77.00 ppm; for [D_6]DMSO, δ = 39.51 ppm) or tetramethylsilane (δ = 0.00 ppm) as the internal standard for ^{13}C NMR spectroscopy. The coupling constants are reported in Hz. The following abbreviations were used to describe the multiplicities: s (singlet), d (doublet), t (triplet), q (quartet), br. (broad), td (triplet of doublets), dt (doublet of triplets), and m (multiplet). The MS data were obtained by using EI (70 eV) or ESI, and the relative intensity (%) is reported in brackets. High resolution mass spectrometry (HRMS) data were measured with a Bruker Apex II mass spectrometer by employing the ESI technique. IR spectra were recorded on a Nicolet Nexus 670 FTIR spectrometer. Optical rotations were measured by using a 1 mL cell with a 1 cm path length on a Perkin–Elmer 341 polarimeter or by using a 0.1 mL cell with a 1 cm path length on a Rudolph Autopol IV automatic polarimeter. The concentrations (*c*) were reported in g 100 mL^{-1}. The X-ray single-crystal structure analysis was performed with a Bruker APEX II X-ray single crystal diffractometer. Analytical HPLC was recorded on an HPLC instrument equipped with a Waters 1525 Binary HPLC Pump and Waters 2998 Photodiode Array Detector or an HPLC instrument equipped with an Agilent 1100 series quaternary pump and a UV diode array detector. The chiral stationary phase was a Daicel Chiracel OD (Ø = 0.46 cm, length = 25.0 cm), AD (Ø = 0.46 cm, length = 25.0 cm), IC (Ø = 0.46 cm, length = 25.0 cm), IA-3 (Ø = 0.46 cm, length = 25.0 cm), IC-3 (Ø = 0.46 cm, length = 25.0 cm), AD-H (Ø = 0.46 cm, length = 25.0 cm), or AY-H (Ø = 0.46 cm, length = 25.0 cm) column. For complete experimental procedures, copies of the NMR and HPLC spectra along with X-ray crystal structure analyses for (*R*)-**3ag** and (*R*)-**3ug**, see the Supporting Information.

General Experimental Procedure for Solvent and Catalyst Screenings: To an oven-dried 10 mL Schlenk tube were sequentially added the catalyst (0.02 mmol, 0.2 equiv.), α-cyano ketone **1a** (24.9 mg, 0.1 mmol), the solvent (0.5 mL), and 4-bromophenyl acrylate (**2a**, 45.4 mg, 0.2 mmol, 2.0 equiv.) at 25 °C. The resulting mixture was stirred at this temperature for the indicated time. Then, without further evaporation of the solvent, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to yield the desired Michael adduct **3aa**.

General Experimental Procedure Using Acceptors 2a–2n in the Catalytic Enantioselective Michael Addition Reaction: To an oven-dried 10 mL Schlenk tube were sequentially added catalyst **4o** (11.3 mg, 0.02 mmol, 0.2 equiv.), α-cyano ketone **1a** (24.9 mg, 0.1 mmol), *p*-xylene (0.5 mL), and Michael acceptor **2a**–**2n** (0.2 mmol, 2.0 equiv.) at 25 °C. The resulting mixture was stirred at this temperature for the indicated time. Then, without further evaporation of the solvent, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to yield the desired Michael adduct **3aa**–**3an**.

Analytical Data for Michael Adducts 3aa–3an

Compound 3aa: (Table 1, Entry 1). The general experimental procedure was followed to afford product **3aa** (46.0 mg, 0.097 mmol, 97 % yield); $[\alpha]_D^{17}$ = –35.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 81 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 32.5 min (major

enantiomer) and t_R = 23.5 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.49 (d, J = 8.8 Hz, 2 H), 7.23 (d, J = 7.6 Hz, 1 H), 7.16 (t, J = 7.6 Hz, 1 H), 7.01 (d, J = 7.6 Hz, 1 H), 6.93 (d, J = 8.8 Hz, 2 H), 5.21, 5.19 (ABq, J = 5.2 Hz, 2 H), 3.86 (s, 3 H), 3.54 (s, 3 H), 2.85–2.75 (m, 2 H), 2.72–2.64 (m, 1 H), 2.59–2.51 (m, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 170.2, 151.9, 149.5, 143.2, 132.4, 132.4, 127.3, 124.2, 123.2, 123.2, 120.5, 118.9, 118.5, 113.8, 99.1, 58.2, 56.5, 55.9, 30.3, 29.1, 26.0 ppm. MS (EI): m/z (%) = 435 (<1) [M(^{81}Br) – Ac + H]$^+$, 433 (<1) [M(^{79}Br) – Ac + H]$^+$, 403 (<1), 401 (<1), 304 (<1), 272 (1), 262 (<1), 261 (<1), 259 (<1), 245 (<1), 230 (11), 188 (3), 176 (3), 55 (8), 45 (100), 43 (28). HRMS (ESI): calcd. for $C_{22}H_{23}{}^{79}BrNO_6$ [M + H]$^+$ 476.0703; found 476.0701.

Compound 3ab: (Table 1, Entry 2). The general experimental procedure was followed to afford product **3ab** (44.0 mg, 0.092 mmol, 92 % yield); $[\alpha]_D^{17}$ = –36.0 (c = 1.0, $CHCl_3$)]. The enantiomeric excess value of 80 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 18.8 min (major enantiomer) and t_R = 15.2 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36–7.34 (m, 1 H), 7.25–7.22 (m, 2 H), 7.20–7.15 (m, 2 H), 7.04–6.97 (m, 2 H), 5.22, 5.19 (ABq, J = 4.8 Hz, 2 H), 3.86 (s, 3 H), 3.54 (s, 3 H), 2.85–2.66 (m, 3 H), 2.60–2.52 (m, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 170.2, 151.9, 150.9, 143.3, 130.4, 129.0, 127.2, 125.0, 124.2, 122.2, 120.6, 120.3, 118.5, 113.8, 99.1, 58.2, 56.6, 55.9, 30.3, 29.0, 26.0 ppm. MS (EI): m/z (%) = 435 (<1) [M(^{81}Br) – Ac + H]$^+$, 433 (<1) [M(^{79}Br) – Ac + H]$^+$, 403 (<1), 401 (<1), 304 (<1), 272 (1), 259 (2), 245 (<1), 230 (11), 217 (6), 202 (4), 188 (4), 175 (8), 55 (15), 45 (100), 43 (52). HRMS (ESI): calcd. for $C_{22}H_{23}{}^{79}BrNO_6$ [M + H]$^+$ 476.0703; found 476.0699.

Compound 3ac: (Table 1, Entry 3). The general experimental procedure was followed to afford product **3ac** (44.0 mg, 0.092 mmol, 92 % yield); $[\alpha]_D^{18}$ = –19.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 66 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 22.4 min (major enantiomer) and t_R = 17.3 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.60–7.57 (m, 1 H), 7.34–7.29 (m, 1 H), 7.25–7.23 (m, 1 H), 7.20–7.08 (m, 3 H), 7.04–7.01 (m, 1 H), 5.22, 5.20 (ABq, J = 4.8 Hz, 2 H), 3.87 (s, 3 H), 3.54 (s, 3 H), 2.92–2.80 (m, 2 H), 2.76–2.58 (m, 2 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 169.7, 151.9, 148.0, 143.1, 133.3, 128.4, 127.44, 127.38, 124.3, 123.6, 120.4, 118.6, 116.0, 113.8, 99.0, 58.2, 56.4, 55.9, 30.2, 29.2, 26.0 ppm. MS (EI): m/z (%) = 435 (<1) [M(^{81}Br) – Ac + H]$^+$, 433 (<1) [M(^{79}Br) – Ac + H]$^+$, 403 (<1), 401 (<1), 304 (<1), 272 (1), 259 (<1), 245 (<1), 230 (11), 188 (4), 176 (4), 55 (9), 45 (100), 43 (29). HRMS (ESI): calcd. for $C_{22}H_{23}{}^{79}BrNO_6$ [M + H]$^+$ 476.0703; found 476.0690.

Compound 3ad: (Table 1, Entry 4). The general experimental procedure was followed to afford product **3ad** (39.2 mg, 0.089 mmol, 89 % yield); $[\alpha]_D^{18}$ = –30.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 78 % was determine by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 65:35; flow rate: 1.0 mL min^{-1}): t_R = 13.8 min (major enantiomer) and t_R = 10.6 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.10–8.07 (m, 1 H), 7.68–7.63 (m, 1 H), 7.42–7.38 (m, 1 H), 7.24–7.15 (m, 3 H), 7.04–7.01 (m, 1 H), 5.23, 5.18 (ABq, J = 5.2 Hz, 2 H), 3.87 (s, 3 H), 3.54 (s, 3 H), 2.94–2.78 (m, 2 H), 2.76–2.61 (m, 2 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 169.9, 152.0, 143.9, 143.1, 141.5, 134.8, 127.4, 126.7, 125.8, 125.2, 124.3, 120.4, 118.5, 113.9, 99.0, 58.2, 56.4, 55.9, 30.2, 29.0, 26.0 ppm. MS (EI): m/z (%) = 400 (<1) [M – Ac + H]$^+$, 368 (2), 304 (<1), 272 (3), 245 (1), 230 (2), 217 (2), 202 (3), 188 (5), 175 (3), 156 (1), 128 (2), 55 (8), 45 (100), 43 (25). HRMS (ESI): calcd. for $C_{22}H_{23}N_2O_8$ [M + H]$^+$ 443.1449; found 443.1445.

Compound 3ae: (Table 1, Entry 5). The general experimental procedure was followed to afford product **3ae** (40.0 mg, 0.096 mmol, 96 % yield); $[\alpha]_D^{18}$ = –39.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 80 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 26.6 min (major enantiomer) and t_R = 19.8 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.23 (dd, J = 8.0, 1.0 Hz, 1 H), 7.17 (t, J = 8.0 Hz, 1 H), 7.08–6.98 (m, 5 H), 5.22, 5.19 (ABq, J = 5.2 Hz, 2 H), 3.86 (s, 3 H), 3.54 (s, 3 H), 2.84–2.75 (m, 2 H), 2.72–2.64 (m, 1 H), 2.62–2.50 (m, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 170.6, 161.4, 158.9, 151.9, 146.3, 146.2, 143.2, 127.4, 124.2, 122.84, 122.76, 120.4, 118.5, 116.1, 115.8, 113.8, 99.0, 58.1, 56.5, 55.9, 30.2, 29.1, 26.0 ppm. MS (EI): m/z (%) = 373 (<1) [M – Ac + H]$^+$, 341 (<1), 304 (<1), 272 (<1), 259 (<1), 245 (<1), 230 (7), 202 (2), 188 (3), 176 (3), 55 (8), 45 (100), 43 (31). HRMS (ESI): calcd. for $C_{22}H_{23}FNO_6$ [M + H]$^+$ 416.1504; found 416.1497.

Compound 3af: (Table 1, Entry 6). The general experimental procedure was followed to afford product **3af** (39.0 mg, 0.090 mmol, 90 % yield); $[\alpha]_D^{18}$ = –31.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 80 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 29.8 min (major enantiomer) and t_R = 21.8 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.33–7.30 (m, 2 H), 7.24–7.21 (m, 1 H), 7.18–7.14 (m, 1 H), 7.03–6.97 (m, 3 H), 5.22, 5.19 (ABq, J = 5.0 Hz, 2 H), 3.86 (s, 3 H), 3.54 (s, 3 H), 2.85–2.75 (m, 2 H), 2.72–2.64 (m, 1 H), 2.59–2.50 (m, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 170.3, 151.9, 148.9, 143.2, 131.2, 129.4, 129.4, 127.4, 124.2, 122.8, 122.8, 120.5, 118.5, 113.8, 99.1, 58.2, 56.5, 55.9, 30.3, 29.1, 26.0 ppm. MS (EI): m/z (%) = 391 (<1) [M(^{37}Cl) – Ac + H]$^+$, 389 (<1) [M(^{35}Cl) – Ac + H]$^+$, 359 (<1), 357 (<1), 304 (<1), 274 (<1), 272 (<1), 261 (<1), 245 (<1), 230 (10), 202 (2), 188 (2), 176 (3), 55 (9), 45 (100), 43 (32). HRMS (ESI): calcd. for $C_{22}H_{23}{}^{35}ClNO_6$ [M + H]$^+$ 432.1208; found 432.1209.

Compound 3ag: (Table 1, Entry 7). The general experimental procedure was followed to afford product **3ag** (50.0 mg, 0.096 mmol, 96 % yield). For the analytic data, recrystallization procedure, and X-ray crystal structure analysis of **3ag**, see below (Table 2, Entry 1).

Compound 3ai: (Table 1, Entry 9). The general experimental procedure was followed to afford product **3ai** (43.0 mg, 0.094 mmol, 94 % yield); $[\alpha]_D^{19}$ = –40.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 81 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 65:35; flow rate: 1.0 mL min^{-1}): t_R = 13.1 min (major enantiomer) and t_R = 11.4 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05–8.03 (m, 2 H), 7.24–7.22 (m, 1 H), 7.18–7.10 (m, 3 H), 7.02–7.00 (m, 1 H), 5.21, 5.19 (ABq, J = 5.2 Hz, 2 H), 3.90 (s, 3 H), 3.85 (s, 3 H), 3.53 (s, 3 H), 2.87–2.65 (m, 3 H), 2.61–2.52 (m, 1 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 170.0, 166.2, 154.1, 151.9, 143.2, 131.0, 131.0, 127.7, 127.3, 124.2, 121.4, 121.4, 120.5, 118.5, 113.8, 99.1, 58.1, 56.5, 55.9, 52.1, 30.4, 29.1, 26.0 ppm. MS (EI): m/z (%) = 413 (<1) [M – Ac + H]$^+$, 381 (1), 304 (<1), 281 (<1), 272 (1), 259 (<1), 245 (<1), 230 (9), 217 (3), 202 (4), 188 (3), 176 (4), 121(7), 55 (7), 45 (100), 43 (33). HRMS (ESI): calcd. for $C_{24}H_{26}NO_8$ [M + H]$^+$ 456.1653; found 456.1654.

Compound 3aj: (Table 1, Entry 10). The general experimental procedure was followed to afford product **3aj** (43.8 mg, 0.099 mmol, 99 % yield); $[\alpha]_D^{18}$ = –43.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 81 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 65:35; flow rate: 1.0 mL min^{-1}): t_R = 25.3 min (major enantiomer) and t_R = 15.9 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25–8.22 (m, 2 H), 7.25–7.21 (m, 3 H), 7.19–7.14 (m, 1 H), 7.03–7.01 (m, 1 H), 5.21, 5.19 (ABq, J = 5.2 Hz, 2 H), 3.86 (s, 3 H), 3.53 (s, 3 H), 2.89–2.77 (m, 2 H), 2.73–2.56 (m, 2 H), 2.24 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 169.7, 155.1, 151.9, 145.2, 143.2, 127.1, 125.1, 125.1, 124.2, 122.3, 122.3, 120.4,

118.4, 113.8, 99.1, 58.1, 56.5, 55.9, 30.4, 29.0, 26.0 ppm. MS (EI): *m/z* (%) = 400 (<1) [M – Ac + H]$^+$, 368 (2), 304 (<1), 272 (2), 259 (<1), 245 (<1), 230 (4), 217 (1), 202 (3), 188 (3), 176 (4), 55 (8), 45 (100), 43 (28). HRMS (ESI): calcd. for $C_{22}H_{23}N_2O_8$ [M + H]$^+$ 443.1449; found 443.1432.

Compound 3ak: (Table 1, Entry 11). The general experimental procedure was followed to afford product **3ak** (32.6 mg, 0.082 mmol, 82 % yield); $[\alpha]_D^{18}$ = –35.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 80 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 19.9 min (major enantiomer) and t_R = 16.5 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.36 (t, *J* = 8.0 Hz, 2 H), 7.25–7.15 (m, 3 H), 7.05–7.01 (m, 3 H), 5.22, 5.20 (ABq, *J* = 5.0 Hz, 2 H), 3.86 (s, 3 H), 3.55 (s, 3 H), 2.86–2.66 (m, 3 H), 2.61–2.53 (m, 1 H), 2.26 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 170.6, 152.0, 150.5, 143.2, 129.3, 129.3, 127.5, 125.8, 124.2, 121.4, 121.4, 120.5, 118.6, 113.8, 99.0, 58.2, 56.5, 55.9, 30.4, 29.2, 26.1 ppm. MS (EI): *m/z* (%) = 396 (<1) [M – H]$^+$, 355 (<1) [M – Ac + H]$^+$, 323 (<1), 272 (<1), 259 (2), 245 (<1), 230 (9), 217 (4), 202 (3), 188 (4), 175 (6), 94 (11), 77 (5), 55 (18), 45 (100), 43 (43). HRMS (ESI): calcd. for $C_{22}H_{24}NO_6$ [M + H]$^+$ 398.1598; found 398.1589.

Compound 3al: (Table 1, Entry 12). The general experimental procedure was followed to afford product **3al** (44.4 mg, 0.099 mmol, 99 % yield); $[\alpha]_D^{18}$ = –31.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 67 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 90:10; flow rate: 1.0 mL min^{-1}): t_R = 26.8 min (major enantiomer) and t_R = 20.7 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.83 (m, 2 H), 7.75–7.73 (m, 1 H), 7.54–7.49 (m, 2 H), 7.47–7.43 (m, 1 H), 7.30–7.27 (m, 1 H), 7.22–7.17 (m, 2 H), 7.04–7.02 (m, 1 H), 5.25, 5.23 (ABq, *J* = 5.2 Hz, 2 H), 3.87 (s, 3 H), 3.57 (s, 3 H), 3.07–2.99 (m, 1 H), 2.95–2.87 (m, 1 H), 2.84–2.72 (m, 2 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 170.6, 152.0, 146.4, 143.2, 134.6, 127.9, 127.5, 126.6, 126.41, 126.40, 126.0, 125.3, 124.3, 121.1, 120.5, 118.6, 117.9, 113.8, 99.1, 58.2, 56.6, 55.9, 30.3, 29.3, 26.1 ppm. MS (EI): *m/z* (%) = 386 (<1) [M – MOMO]$^+$, 372 (<1), 324 (<1), 304 (1), 272 (<1), 262 (<1), 245 (<1), 230 (10), 202 (3), 188 (5), 144 (6), 115 (9), 55 (7), 45 (100), 43 (28). HRMS (ESI): calcd. for $C_{26}H_{26}NO_6$ [M + H]$^+$ 448.1755; found 448.1738.

Compound 3an: (Table 1, Entry 14). The general experimental procedure was followed to afford product **3an** (35.8 mg, 0.092 mmol, 92 % yield); $[\alpha]_D^{18}$ = –42.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 77 % was measured by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 65:35; flow rate: 1.0 mL min^{-1}): t_R = 16.4 min (major enantiomer) and t_R = 18.1 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20 (dd, *J* = 8.0, 1.2 Hz, 1 H), 7.13 (t, *J* = 8.0 Hz, 1 H), 6.99 (dd, *J* = 8.0, 1.2 Hz, 1 H), 5.19, 5.15 (ABq, *J* = 5.2 Hz, 2 H), 4.42–4.33 (m, 2 H), 4.03–3.87 (m, 2 H), 3.85 (s, 3 H), 3.53 (s, 3 H), 3.13–3.05 (m, 1 H), 2.98–2.89 (m, 1 H), 2.73–2.58 (m, 2 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.8, 171.6, 153.2, 151.8, 143.1, 127.7, 124.1, 120.6, 118.7, 113.7, 99.0, 62.1, 58.1, 56.3, 55.9, 42.4, 31.2, 28.8, 26.2 ppm. MS (EI): *m/z* (%) = 348 (<1) [M – Ac + H]$^+$, 316 (4), 304 (<1), 272 (<1), 259 (1), 229 (10), 217 (5), 201 (5), 188 (9), 175 (6), 88 (7), 55 (17), 45 (100), 43 (70). HRMS (ESI): calcd. for $C_{19}H_{23}N_2O_7$ [M + H]$^+$ 391.1500; found 391.1492.

Gram-Scale Reaction for Preparation of 3ag: (Table 2, Entry 1). To an oven-dried round-bottom flask were sequentially added catalyst **4o** (1.13 g, 2.0 mmol, 0.2 equiv.), α-cyano ketone **1a** (2.48 g, 10.0 mmol), *p*-xylene (50 mL), and 4-iodophenyl acrylate (**2g**, 5.48 g, 20.0 mmol, 2.0 equiv.) at 25 °C. The resulting mixture was stirred at this temperature for 2.5 d. Then, without further evaporation of the solvent, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to yield the desired Michael adduct **3ag** (5.2 g, 9.9 mmol, 99 % yield). The enantiomeric excess value of 81 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 20.5 min (major enantiomer) and t_R = 15.1 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.0 Hz, 2 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.16 (t, *J* = 8.0 Hz, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.81 (d, *J* = 8.0 Hz, 2 H), 5.21, 5.19 (ABq, *J* = 5.2 Hz, 2 H), 3.86 (s, 3 H), 3.54 (s, 3 H), 2.84–2.64 (m, 3 H), 2.59–2.51 (m, 1 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 170.2, 151.9, 150.3, 143.2, 138.4, 138.4, 127.4, 124.2, 123.6, 123.6, 120.5, 118.5, 113.8, 99.1, 89.9, 58.2, 56.5, 55.9, 30.3, 29.1, 26.1 ppm. MS (EI): *m/z* (%) = 481 (<1) [M – Ac + H]$^+$, 449 (<1), 304 (1), 272 (<1), 264 (1), 245 (<1), 230 (28), 202 (5), 188 (5), 176 (6), 55 (9), 45 (100), 43 (32). IR: $\tilde{\nu}$ = 2240, 1479, 1199, 1165, 1140, 1097, 1077, 923 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{26}IN_2O_6$ [M + NH_4]$^+$ 541.0830; found 541.0837. The obtained product **3ag** (5.2 g, 9.9 mmol, 81 % *ee*) was dissolved in $CHCl_3$ (15 mL) followed by the sequential addition of 2-propanol (40 mL) and *n*-hexane (400 mL). The mixed solution was allowed to stand at room temperature for 7 d. The mixture was filtered, and the crystals were washed with *n*-hexane (4 × 5 mL) to give the enantioenriched crystal **3ag** (4.0 g, 7.6 mmol, 76 % yield, 99 % *ee*); m.p. 112–114 °C. $[\alpha]_D^{26}$ = –39.0 (*c* = 1.0, $CHCl_3$). A second recrystallization of crystal **3ag** (100 mg, 99 % *ee*) from a mixed solution of $CHCl_3$ (0.3 mL), 2-propanol (0.8 mL), and *n*-hexane (10 mL) gave the single crystal (99.5 % *ee*) that was used to determine the absolute configuration by X-ray crystal structure analysis.

General Experimental Procedure Using Donors 1b–1u in the Catalytic Enantioselective Michael Addition Reaction: To an oven-dried 10 mL Schlenk tube were sequentially added catalyst **4o** (22.6 mg, 0.04 mmol, 0.2 equiv.), α-cyano ketone **1b–1u** (0.2 mmol), *p*-xylene (1.0 mL), and 4-iodophenyl acrylate (**2g**, 109.6 mg, 0.4 mmol, 2.0 equiv.) at 25 °C. The resulitng mixture was stirred at this temperature until the donor had disappeared upon inspection by thin layer chromatography. Then, without further evaporation of solvent, the reaction mixture was directly subjected to purification by flash column chromatography on silica gel to yield the desired Michael adduct **3bg–3ug**.

Analytic Data for Michael Adducts 3bg–3ug

Compound 3bg: (Table 2, Entry 2). The general experimental procedure was followed to afford product **3bg** (106.8 mg, 0.187 mmol, 93 % yield); $[\alpha]_D^{24}$ = +6.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 77 % was determined by HPLC (Chiralcel OD; *n*-hexane/2-propanol, 85:15; flow rate: 1.0 mL min^{-1}): t_R = 15.6 min (major enantiomer) and t_R = 12.2 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.72 (d, *J* = 2.4 Hz, 1 H), 7.68–7.65 (m, 2 H), 7.50 (dd, *J* = 8.8, 2.4 Hz, 1 H), 7.08 (d, *J* = 8.8 Hz, 1 H), 6.83–6.79 (m, 2 H), 5.16, 5.14 (ABq, *J* = 6.8 Hz, 2 H), 3.44 (s, 3 H), 2.85–2.57 (m, 4 H), 2.22 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.2, 170.0, 153.1, 150.2, 138.4, 138.4, 133.8, 131.3, 125.0, 123.5, 123.5, 117.6, 116.2, 114.7, 94.5, 90.0, 56.8, 55.9, 30.1, 28.0, 25.9 ppm. IR: $\tilde{\nu}$ = 2240, 1759, 1734, 1482, 1200, 1164, 1137, 976 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{23}{}^{79}BrIN_2O_5$ [M + NH_4]$^+$ 588.9830; found 588.9819.

Compound 3cg: (Table 2, Entry 3). The general experimental procedure was followed to afford product **3cg** (94.5 mg, 0.172 mmol, 86 % yield); $[\alpha]_D^{24}$ = –34.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 80 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.5 min (major enantiomer) and t_R = 13.5 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 8.4 Hz, 2 H), 7.22 (d, *J* = 8.0 Hz, 1 H), 7.16 (t, *J* = 8.0 Hz, 1 H), 7.01 (d, *J* = 8.0 Hz, 1 H), 6.81 (d, *J* = 8.4 Hz, 2 H), 5.98–5.88 (m, 1 H), 5.37–5.20 (m, 4 H), 4.27, 4.19 (dABq, *J* = 5.6, 12.8 Hz, 2 H), 3.85 (s, 3 H), 2.83–2.50 (m, 4 H), 2.25 (s, 3

H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 170.1, 151.9, 150.3, 143.2, 138.3, 138.3, 133.7, 127.4, 124.2, 123.6, 123.6, 120.5, 118.5, 117.5, 113.8, 96.8, 89.8, 71.0, 56.5, 55.9, 30.3, 29.2, 26.1 ppm. IR: $\tilde{\nu}$ = 2237, 1761, 1479, 1270, 1201, 1167, 1144, 930 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{28}IN_2O_6$ $[M + NH_4]^+$ 567.0987; found 567.0990.

Compound 3dg: (Table 2, Entry 4). The general experimental procedure was followed to afford product **3dg** (104.7 mg, 0.184 mmol, 92 % yield); $[\alpha]_D^{24}$ = –21.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 76 % was determined by HPLC (Chiralcel IC; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 11.3 min (major enantiomer) and t_R = 13.8 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 8.6 Hz, 2 H), 7.49–7.33 (m, 5 H), 7.22–7.16 (m, 2 H), 7.09–7.04 (m, 1 H), 6.84 (d, *J* = 8.6 Hz, 2 H), 5.21, 5.15 (ABq, *J* = 10.8 Hz, 2 H), 3.91 (s, 3 H), 2.87–2.52 (m, 4 H), 2.20 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 170.1, 152.8, 150.2, 144.8, 138.3, 138.3, 136.6, 128.30, 128.30, 128.28, 128.28, 128.2, 128.0, 124.3, 123.6, 123.6, 119.8, 118.9, 113.8, 89.8, 74.1, 55.9, 55.8, 30.2, 29.4, 26.3 ppm. IR: $\tilde{\nu}$ = 2238, 1760, 1730, 1478, 1273, 1202, 1169, 1143 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{28}IN_2O_5$ $[M + NH_4]^+$ 587.1037; found 587.1043.

Compound 3eg: (Table 2, Entry 5). The general experimental procedure was followed to afford product **3eg** (93.5 mg, 0.190 mmol, 95 % yield). The enantiomeric excess value of 73 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.7 min (major enantiomer) and t_R = 14.0 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.66 (d, *J* = 8.8 Hz, 2 H), 7.17–7.12 (m, 2 H), 7.03–6.99 (m, 1 H), 6.82 (d, *J* = 8.8 Hz, 2 H), 3.89 (s, 3 H), 3.88 (s, 3 H), 2.84–2.50 (m, 4 H), 2.25 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.6, 170.1, 152.8, 150.3, 145.9, 138.4, 138.4, 127.9, 124.2, 123.6, 123.6, 119.6, 118.7, 113.9, 89.9, 60.3, 55.9, 55.8, 30.3, 29.3, 26.1 ppm. IR: $\tilde{\nu}$ = 2238, 1759, 1479, 1275, 1198, 1168, 1142, 1004 cm^{-1}. HRMS (ESI): calcd. for $C_{21}H_{24}IN_2O_5$ $[M + NH_4]^+$ 511.0724; found 511.0715. The obtained product **3eg** (93.5 mg, 0.190 mmol, 73 % *ee*) was dissolved in $CHCl_3$ (0.5 mL) followed by the sequential addition of 2-propanol (1.5 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 15 h. The mixture was filtered, and the crystals were washed with *n*-hexane (4 × 1 mL) to give the enantioenriched crystal **3eg** (41 mg, 0.0831 mmol, 42 % yield, 90 % *ee*); m.p. 110–115 °C. $[\alpha]_D^{29}$ = –2.0 (*c* = 1.0, $CHCl_3$).

Compound 3fg: (Table 2, Entry 6). The general experimental procedure was followed to afford product **3fg** (89.0 mg, 0.192 mmol, 96 % yield). The enantiomeric excess value of 72 % was determined by HPLC (Chiralcel IC; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 14.1 min (major enantiomer) and t_R = 12.6 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.61 (m, 3 H), 7.45–7.40 (m, 1 H), 7.13–7.08 (m, 1 H), 6.96–6.93 (m, 1 H), 6.82–6.78 (m, 2 H), 3.80 (s, 3 H), 2.82–2.70 (m, 2 H), 2.65–2.47 (m, 2 H), 2.17 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.0, 170.2, 155.9, 150.3, 138.4, 138.4, 130.9, 128.8, 123.6, 123.6, 122.6, 121.5, 118.2, 111.7, 89.8, 56.4, 55.3, 30.3, 28.0, 25.7 ppm. IR: $\tilde{\nu}$ = 2238, 1760, 1732, 1485, 1253, 1200, 1168, 1141 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{22}IN_2O_4$ $[M + NH_4]^+$ 481.0619; found 481.0626. The obtained product **3fg** (89.0 mg, 0.192 mmol, 72 % *ee*) was dissolved in $CHCl_3$ (0.5 mL) followed by the sequential addition of 2-propanol (1.2 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at 4 °C for 5 d. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3fg** (59.0 mg, 0.127 mmol, 64 % yield, 91 % *ee*); $[\alpha]_D^{24}$ = –21.0 (*c* = 1.0, $CHCl_3$).

Compound 3gg: (Table 2, Entry 7). The general experimental procedure was followed to afford product **3gg** (88.0 mg, 0.190 mmol, 95 % yield). The enantiomeric excess of 64 % value was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.5 min (major enantiomer) and t_R = 11.1 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69–7.65 (m, 2 H), 7.40–7.36 (m, 1 H), 7.04–6.93 (m, 3 H), 6.85–6.81 (m, 2 H), 3.84 (s, 3 H), 2.78–2.63 (m, 2 H), 2.55–2.45 (m, 2 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.5, 169.9, 160.5, 150.2, 138.4, 138.4, 134.2, 130.9, 123.6, 123.6, 118.5, 118.3, 114.5, 112.2, 89.9, 58.8, 55.4, 31.0, 30.3, 26.6 ppm. IR: $\tilde{\nu}$ = 2236, 1481, 1291, 1256, 1207, 1171, 1134, 1047 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{22}IN_2O_4$ $[M + NH_4]^+$ 481.0619; found 481.0624. The obtained product **3gg** (88.0 mg, 0.190 mmol, 64 % *ee*) was dissolved in $CHCl_3$ (0.3 mL) followed by the sequential addition of 2-propanol (0.5 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at 4 °C for 6 h. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3gg** (55.5 mg, 0.120 mmol, 60 % yield, 90 % *ee*); $[\alpha]_D^{24}$ = –38.0 (*c* = 1.0, $CHCl_3$).

Compound 3hg: (Table 2, Entry 8). The general experimental procedure was followed to afford product **3hg** (87.8 mg, 0.190 mmol, 95 % yield). The enantiomeric excess value of 71 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 20.4 min (major enantiomer) and t_R = 16.4 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, *J* = 8.8 Hz, 2 H), 7.37 (d, *J* = 8.8 Hz, 2 H), 6.97 (d, *J* = 8.8 Hz, 2 H), 6.83 (d, *J* = 8.8 Hz, 2 H), 3.84 (s, 3 H), 2.77–2.61 (m, 2 H), 2.54–2.45 (m, 2 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.9, 170.0, 160.3, 150.3, 138.4, 138.4, 127.6, 127.6, 124.4, 123.6, 123.6, 118.8, 115.1, 115.1, 90.0, 58.1, 55.4, 31.0, 30.3, 26.5 ppm. IR: $\tilde{\nu}$ = 2240, 1760, 1727, 1511, 1257, 1199, 1169, 1141 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{22}IN_2O_4$ $[M + NH_4]^+$ 481.0619; found 481.0626. The obtained product **3hg** (87.8 mg, 0.190 mmol, 71 % *ee*) was dissolved in Et_2O (1.5 mL) followed by addition of *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 5 d. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3hg** (67.8 mg, 0.146 mmol, 73 % yield, 87 % *ee*); $[\alpha]_D^{24}$ = –52.0 (*c* = 1.0, $CHCl_3$).

Compound 3ig: (Table 2, Entry 9). The general experimental procedure was followed to afford product **3ig** (64 mg, 0.125 mmol, 63 % yield). The enantiomeric excess value of 59 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 20.5 min (major enantiomer) and t_R = 14.1 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.78 (m, 1 H), 7.69–7.66 (m, 3 H), 7.53–7.49 (m, 1 H), 7.36–7.32 (m, 1 H), 6.85–6.81 (m, 2 H), 2.93–2.78 (m, 3 H), 2.59–2.49 (m, 1 H), 2.29 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.2, 169.9, 150.3, 138.5, 138.5, 135.6, 132.9, 131.0, 130.5, 128.6, 123.6, 123.6, 121.9, 117.4, 90.0, 60.0, 30.3, 28.4, 26.8 ppm. IR: $\tilde{\nu}$ = 2239, 1760, 1728, 1479, 1200, 1167, 1145, 1009 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}{}^{79}BrIN_2O_3$ $[M + NH_4]^+$ 528.9618; found 528.9627. The obtained product **3ig** (64 mg, 0.125 mmol, 59 % *ee*) was dissolved in $CHCl_3$ (0.4 mL) followed by the sequential addition of 2-propanol (1.0 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at 4 °C for 29 h. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3ig** (42 mg, 0.0820 mmol, 41 % yield, 95 % *ee*); $[\alpha]_D^{24}$ = +2.0 (*c* = 1.0, $CHCl_3$).

Compound 3jg: (Table 2, Entry 10). The general experimental procedure was followed to afford product **3jg** (91.7 mg, 0.179 mmol, 90 % yield); $[\alpha]_D^{24}$ = –19.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 58 % was determined by HPLC (Chiralcel AD; *n*-hexane/

2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 14.4 min (major enantiomer) and t_R = 10.7 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.4 Hz, 2 H), 7.63–7.56 (m, 2 H), 7.43–7.33 (m, 2 H), 6.84 (d, J = 8.4 Hz, 2 H), 2.79–2.67 (m, 2 H), 2.55–2.43 (m, 2 H), 2.33 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.1, 169.7, 150.2, 138.5, 138.5, 135.0, 132.7, 131.3, 129.3, 124.9, 124.0, 123.6, 123.6, 118.0, 90.0, 58.4, 31.1, 30.3, 26.8 ppm. IR: $\tilde{\nu}$ = 2241, 1762, 1730, 1477, 1200, 1166, 1139, 1009 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}{}^{79}BrIN_2O_3$ $[M + NH_4]^+$ 528.9618; found 528.9612.

Compound 3kg: (Table 2, Entry 11). The general experimental procedure was followed to afford product **3kg** (89.8 mg, 0.175 mmol, 88 % yield). The enantiomeric excess value of 64 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.9 min (major enantiomer) and t_R = 14.4 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.68 (d, J = 8.6 Hz, 2 H), 7.61 (d, J = 8.6 Hz, 2 H), 7.35 (d, J = 8.6 Hz, 2 H), 6.82 (d, J = 8.6 Hz, 2 H), 2.78–2.65 (m, 2 H), 2.54–2.44 (m, 2 H), 2.32 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.3, 169.8, 150.2, 138.5, 138.5, 133.0, 133.0, 131.8, 128.0, 128.0, 123.9, 123.6, 123.6, 118.2, 90.0, 58.4, 31.1, 30.2, 26.8 ppm. IR: $\tilde{\nu}$ = 2241, 1760, 1730, 1482, 1199, 1167, 1141, 1008 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}{}^{79}BrIN_2O_3$ $[M + NH_4]^+$ 528.9618; found 528.9622. The obtained product **3kg** (89.8 mg, 0.175 mmol, 64 % *ee*) was dissolved in Et_2O (1.5 mL) followed by the addition of *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 5 d. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3kg** (64.8 mg, 0.127 mmol, 63 % yield, 86 % *ee*); $[\alpha]_D^{24}$ = –32.0 (c = 1.0, $CHCl_3$).

Compound 3lg: (Table 2, Entry 12). The general experimental procedure was followed to afford product **3lg** (75.8 mg, 0.175 mmol, 88 % yield). The enantiomeric excess value of 65 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 14.6 min (major enantiomer) and t_R = 11.5 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.8 Hz, 2 H), 7.50–7.42 (m, 5 H), 6.83 (d, J = 8.8 Hz, 2 H), 2.79–2.67 (m, 2 H), 2.56–2.45 (m, 2 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.7, 169.9, 150.2, 138.4, 138.4, 132.8, 129.8, 129.8, 129.4, 126.2, 126.2, 123.6, 123.6, 118.5, 90.0, 58.8, 31.1, 30.3, 26.7 ppm. IR: $\tilde{\nu}$ = 2240, 1760, 1728, 1481, 1199, 1166, 1140, 1008 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{20}IN_2O_3$ $[M + NH_4]^+$ 451.0513; found 451.0518. The obtained product **3lg** (75.8 mg, 0.175 mmol, 65 % *ee*) was dissolved in $CHCl_3$ (0.2 mL) followed by sequential addition of 2-propanol (0.5 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at 4 °C for 30 h. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3lg** (46.8 mg, 0.108 mmol, 54 % yield, 87 % *ee*); $[\alpha]_D^{24}$ = –29.0 (c = 1.0, $CHCl_3$).

Compound 3mg: (Table 2, Entry 13). The general experimental procedure was followed to afford product **3mg** (73.2 mg, 0.164 mmol, 82 % yield); $[\alpha]_D^{24}$ = +12.0 (c = 1.0, $CHCl_3$). The enantiomeric excess value of 71 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 13.7 min (major enantiomer) and t_R = 11.7 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.67 (d, J = 8.8 Hz, 2 H), 7.61–7.57 (m, 1 H), 7.38–7.33 (m, 2 H), 7.28–7.24 (m, 1 H), 6.82 (d, J = 8.8 Hz, 2 H), 2.86–2.72 (m, 2 H), 2.70–2.61 (m, 2 H), 2.33 (s, 3 H), 2.18 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.2, 170.1, 150.2, 138.4, 138.4, 136.2, 133.3, 131.2, 129.4, 127.8, 127.3, 123.6, 123.6, 118.3, 90.0, 59.1, 30.2, 28.7, 26.1, 20.2 ppm. IR: $\tilde{\nu}$ = 2239, 1760, 1725, 1482, 1201, 1167, 1143, 1008 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{22}IN_2O_3$ $[M + NH_4]^+$ 465.0670; found 465.0675.

Compound 3ng: (Table 2, Entry 14). The general experimental procedure was followed to afford product **3ng** (76.5 mg, 0.170 mmol, 85 % yield). The enantiomeric excess value of 68 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 12.3 min (major enantiomer) and t_R = 10.6 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.70–7.65 (m, 3 H), 7.50–7.44 (m, 1 H), 7.35–7.30 (m, 1 H), 7.19–7.13 (m, 1 H), 6.84–6.80 (m, 2 H), 2.84–2.74 (m, 2 H), 2.61–2.50 (m, 2 H), 2.30 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 169.8, 160.8, 158.4, 150.2, 138.4, 138.4, 131.72, 131.64, 129.39, 129.36, 125.47, 125.44, 123.6, 123.6, 121.44, 121.32, 117.28, 117.15, 116.93, 90.0, 56.0, 30.3, 28.95, 28.93, 26.1 ppm. IR: $\tilde{\nu}$ = 2241, 1759, 1734, 1484, 1226, 1200, 1167, 1142 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}FIN_2O_3$ $[M + NH_4]^+$ 469.0419; found 469.0421. The obtained product **3ng** (76.5 mg, 0.170 mmol, 68 % *ee*) was dissolved in $CHCl_3$ (0.3 mL) followed by the sequential addition of 2-propanol (0.5 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at 4 °C for 2 d. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3ng** (51.5 mg, 0.114 mmol, 57 % yield, 88 % *ee*); $[\alpha]_D^{24}$ = –14.0 (c = 1.0, $CHCl_3$).

Compound 3og: (Table 2, Entry 15). The general experimental procedure was followed to afford product **3og** (74.8 mg, 0.160 mmol, 80 % yield). The enantiomeric excess value of 55 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 18.1 min (major enantiomer) and t_R = 12.9 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.80–7.77 (m, 1 H), 7.67 (d, J = 8.8 Hz, 2 H), 7.49–7.40 (m, 3 H), 6.82 (d, J = 8.8 Hz, 2 H), 2.90–2.72 (m, 3 H), 2.57–2.49 (m, 1 H), 2.27 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.0, 169.8, 150.2, 138.4, 138.4, 132.5, 131.9, 131.4, 130.9, 130.1, 128.1, 123.6, 123.6, 117.4, 90.0, 58.7, 30.3, 28.1, 26.4 ppm. IR: $\tilde{\nu}$ = 2239, 1759, 1730, 1479, 1200, 1166, 1143, 1008 cm^{-1}. HRMS (ESI): calcd. for $C_{19}H_{19}{}^{35}ClIN_2O_3$ $[M + NH_4]^+$ 485.0123; found 485.0122. The obtained product **3og** (74.8 mg, 0.160 mmol, 55 % *ee*) was dissolved in Et_2O (1.5 mL) followed by the addition of *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 3 d and then at 4 °C for 24 h. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3og** (43.8 mg, 0.0937 mmol, 47 % yield, 91 % *ee*); $[\alpha]_D^{24}$ = –1.0 (c = 1.0, $CHCl_3$).

Compound 3pg: (Table 2, Entry 16). The general experimental procedure was followed to afford product **3pg** (81.3 mg, 0.168 mmol, 84 % yield). The enantiomeric excess value of 71 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 95:5; flow rate: 1.0 mL min^{-1}): t_R = 35.3 min (major enantiomer) and t_R = 32.9 min (minor enantiomer). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.95 (m, 3 H), 7.85–7.82 (m, 1 H), 7.65 (d, J = 8.8 Hz, 2 H), 7.62–7.54 (m, 3 H), 6.77 (d, J = 8.8 Hz, 2 H), 3.06–2.82 (m, 3 H), 2.60–2.51 (m, 1 H), 2.12 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.3, 170.0, 150.2, 138.4, 138.4, 134.6, 130.9, 129.8, 129.6, 128.6, 127.8, 127.0, 126.6, 125.4, 123.5, 123.5, 122.5, 118.3, 89.9, 59.8, 30.4, 29.0, 26.1 ppm. IR: $\tilde{\nu}$ = 2238, 1759, 1722, 1480, 1200, 1168, 1143, 776 cm^{-1}. HRMS (ESI): calcd. for $C_{23}H_{22}IN_2O_3$ $[M + NH_4]^+$ 501.0670; found 501.0669. The obtained product **3pg** (81.3 mg, 0.168 mmol, 71 % *ee*) was dissolved in $CHCl_3$ (0.4 mL) followed by sequential addition of 2-propanol (1.0 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 38 h. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3pg** (52.4 mg, 0.108 mmol, 54 % yield, 93 % *ee*); $[\alpha]_D^{24}$ = –16.0 (c = 1.0, $CHCl_3$).

Compound 3qg: (Table 2, Entry 17). The general experimental procedure was followed to afford product **3qg** (84 mg, 0.188 mmol, 94 % yield); $[\alpha]_D^{24}$ = +3.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 60 % was determined by HPLC (Chiralcel IC; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 8.8 min (major enantiomer) and t_R = 9.7 min (minor enantiomer). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, *J* = 8.4 Hz, 2 H), 7.39–7.26 (m, 5 H), 6.87 (d, *J* = 8.4 Hz, 2 H), 3.16, 3.02 (ABq, *J* = 13.4 Hz, 2 H), 2.81–2.73 (m, 1 H), 2.67–2.59 (m, 1 H), 2.53–2.45 (m, 1 H), 2.23–2.14 (m, 1 H), 2.19 (s, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 202.2, 169.7, 150.2, 138.4, 138.4, 133.4, 129.9, 129.9, 128.8, 128.8, 128.0, 123.5, 123.5, 119.9, 90.0, 54.7, 43.2, 30.8, 30.2, 29.9 ppm. IR: $\tilde{\nu}$ = 2238, 1759, 1723, 1481, 1200, 1168, 1143, 1009 cm^{-1}. HRMS (ESI): calcd. for $C_{20}H_{22}IN_2O_3$ $[M + NH_4]^+$ 465.0670; found 465.0664.

Compound 3rg: (Table 2, Entry 18). The general experimental procedure was followed to afford product **3rg** (98.3 mg, 0.178 mmol, 89 % yield); $[\alpha]_D^{24}$ = –25.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 76 % was determined by HPLC (Chiralcel AD; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 14.8 min (major enantiomer) and t_R = 11.2 min (minor enantiomer). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.63 (m, 2 H), 7.24–7.21 (m, 1 H), 7.17–7.13 (m, 1 H), 7.02–6.99 (m, 1 H), 6.83–6.79 (m, 2 H), 5.21, 5.17 (ABq, *J* = 5.2 Hz, 2 H), 3.85 (s, 3 H), 3.53 (s, 3 H), 2.83–2.68 (m, 3 H), 2.61–2.41 (m, 3 H), 1.74–1.58 (m, 2 H), 0.89 (t, *J* = 7.4 Hz, 3 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 199.8, 170.2, 151.9, 150.3, 143.2, 138.3, 138.3, 127.4, 124.1, 123.6, 123.6, 120.6, 118.7, 113.7, 99.0, 89.8, 58.0, 56.4, 55.9, 40.4, 30.4, 29.2, 17.3, 13.3 ppm. IR: $\tilde{\nu}$ = 2236, 1761, 1479, 1271, 1200, 1168, 1142, 930 cm^{-1}. HRMS (ESI): calcd. for $C_{24}H_{30}IN_2O_6$ $[M + NH_4]^+$ 569.1143; found 569.1136.

Compound 3sg: (Table 2, Entry 19). The general experimental procedure was followed to afford product **3sg** (62.0 mg, 0.103 mmol, 52 % yield). The enantiomeric excess value of 54 % was determined by HPLC (Chiralcel IC; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.3 min (major enantiomer) and t_R = 24.5 min (minor enantiomer). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.63 (m, 2 H), 7.33–7.25 (m, 4 H), 7.23–7.16 (m, 3 H), 7.07–7.04 (m, 1 H), 6.80–6.77 (m, 2 H), 5.23, 5.20 (ABq, *J* = 5.2 Hz, 2 H), 3.93–3.75 (m, 5 H), 3.50 (s, 3 H), 2.87–2.69 (m, 3 H), 2.62–2.53 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 197.4, 170.2, 152.0, 150.3, 143.3, 138.4, 138.4, 133.3, 129.8, 129.8, 128.4, 128.4, 127.1, 124.3, 123.6, 123.6, 120.8, 118.5, 114.0, 99.1, 89.8, 58.2, 56.6, 56.0, 44.9, 30.3, 29.3 ppm. IR: $\tilde{\nu}$ = 2236, 1757, 1479, 1271, 1199, 1167, 1143, 929 cm^{-1}. HRMS (ESI): calcd. for $C_{28}H_{30}IN_2O_6$ $[M + NH_4]^+$ 617.1143; found 617.1134. The obtained product **3sg** (62.0 mg, 0.103 mmol, 54 % *ee*) was dissolved in Et_2O (1.0 mL) followed by addition of *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 8 d. The crystals with the lower *ee* value were separated from the solution by filtration, and the mother liquor was collected to afford the enantioenriched product **3sg** (34 mg, 0.0567 mmol, 28 % yield, 90 % *ee*); $[\alpha]_D^{24}$ = –19.0 (*c* = 1.0, $CHCl_3$).

Compound 3tg: (Table 2, Entry 20). The general experimental procedure was followed to afford product **3tg** (81.3 mg, 0.139 mmol, 69 % yield); $[\alpha]_D^{24}$ = –79.0 (*c* = 1.0, $CHCl_3$). The enantiomeric excess value of 74 % was determined by HPLC (Chiralcel IC; *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 15.9 min (major enantiomer) and t_R = 22.3 min (minor enantiomer). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.91–7.87 (m, 2 H), 7.66 (d, *J* = 8.4 Hz, 2 H), 7.48–7.39 (m, 2 H), 7.33–7.28 (m, 2 H), 7.21–7.16 (m, 1 H), 6.95–6.92 (m, 1 H), 6.83 (d, *J* = 8.4 Hz, 2 H), 5.08, 4.91 (ABq, *J* = 5.2 Hz, 2 H), 3.75 (s, 3 H), 3.52 (s, 3 H), 3.06–2.76 (m, 3 H), 2.65–2.57 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 189.2, 170.3, 152.1, 150.4, 143.0, 138.3, 138.3, 133.6, 133.3, 129.6, 129.6, 128.7, 128.2, 128.2, 124.3, 123.6, 123.6, 120.0, 118.9, 113.5, 98.7, 89.8, 58.0, 55.8, 53.8, 31.3, 30.4 ppm. IR: $\tilde{\nu}$ = 2235, 1700, 1479, 1270, 1227, 1200, 1168, 1140 cm^{-1}. HRMS (ESI): calcd. for $C_{27}H_{28}IN_2O_6$ $[M + NH_4]^+$ 603.0987; found 603.0983.

Compound 3ug: (Table 2, Entry 21). The general experimental procedure was followed to afford product **3ug** (92.2 mg, 0.182 mmol, 92 % yield). The enantiomeric excess value of 72 % was determined by HPLC (Chiralcel AD, *n*-hexane/2-propanol, 80:20; flow rate: 1.0 mL min^{-1}): t_R = 29.0 min (major enantiomer) and t_R = 35.5 min (minor enantiomer). ^1H NMR (400 MHz, $CDCl_3$): δ = 7.67–7.62 (m, 2 H), 7.26–7.16 (m, 2 H), 7.00–6.96 (m, 1 H), 6.82–6.76 (m, 2 H), 4.55–4.48 (m, 1 H), 3.89 (s, 3 H), 3.81–3.74 (m, 1 H), 2.89–2.80 (m, 1 H), 2.70–2.40 (m, 6 H), 2.04–1.94 (m, 1 H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 200.3, 170.3, 152.2, 150.4, 145.4, 138.4, 138.4, 129.8, 125.6, 123.6, 123.6, 120.4, 118.4, 113.1, 89.8, 74.2, 55.9, 54.1, 35.7, 32.3, 29.9, 29.6 ppm. IR: $\tilde{\nu}$ = 2235, 1759, 1723, 1480, 1281, 1201, 1168, 1134 cm^{-1}. HRMS (ESI): calcd. for $C_{22}H_{24}IN_2O_5$ $[M + NH_4]^+$ 523.0724; found 523.0715. The obtained product **3ug** (92.2 mg, 0.182 mmol, 72 % *ee*) was dissolved in $CHCl_3$ (0.5 mL) followed by sequential addition of 2-propanol (1.5 mL) and *n*-hexane (10 mL). The mixed solution was allowed to stand at room temperature for 14 h. The mixture was filtered, and the crystals were washed with *n*-hexane (3 × 1 mL) to give the enantioenriched crystal **3ug** (70.4 mg, 0.139 mmol, 70 % yield, 98 % *ee*); m.p. 123–125 °C. $[\alpha]_D^{19}$ = +43.0 (*c* = 1.0, $CHCl_3$). A second recrystallization of crystal **3ug** (30.0 mg, 98 % *ee*) from a mixed solution of $CHCl_3$ (0.2 mL), 2-propanol (1.0 mL), and *n*-hexane (8.0 mL) gave the single crystal (99.7 % *ee*), which was used to determine the absolute configuration by X-ray crystal structure analysis.

Acknowledgments

The authors are grateful for financial support from the National Natural Science Foundation of China (NSFC) (grant number 21302061), the Jilin Province Science & Technology Development Program (grant number 20140520084JH), the China Postdoctoral Science Foundation (grant numbers 2013T60318, 2012M510130), and the Specialized Research Fund for the Doctoral Program of Higher Education (grant number 20130061120016).

Keywords: Asymmetric catalysis · Organocatalysis · Michael addition · Enantioselectivity

[1] For recent excellent reviews on the catalytic asymmetric construction of all-carbon quaternary stereocenters, see: a) K. Fuji, *Chem. Rev.* **1993**, *93*, 2037–2066; b) E. J. Corey, A. Guzman-Perez, *Angew. Chem. Int. Ed.* **1998**, *37*, 388–401; *Angew. Chem.* **1998**, *110*, 2092; c) J. Christoffers, A. Mann, *Angew. Chem. Int. Ed.* **2001**, *40*, 4591–4597; *Angew. Chem.* **2001**, *113*, 4725; d) I. Denissova, L. Barriault, *Tetrahedron* **2003**, *59*, 10105–10146; e) J. Christoffers, A. Baro, *Angew. Chem. Int. Ed.* **2003**, *42*, 1688–1690; *Angew. Chem.* **2003**, *115*, 1726; f) C. J. Douglas, L. E. Overman, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5363–5367; g) J. Christoffers, A. Baro, *Adv. Synth. Catal.* **2005**, *347*, 1473–1482; h) B. M. Trost, C. H. Jiang, *Synthesis* **2006**, 369–396; i) P. G. Cozzi, R. Hilgraf, N. Zimmermann, *Eur. J. Org. Chem.* **2007**, 5969–5994; j) J. T. Mohr, B. M. Stoltz, *Chem. Asian J.* **2007**, *2*, 1476–1491; k) M. Bella, T. Gasperi, *Synthesis* **2009**, 1583–1614; l) C. Hawner, A. Alexakis, *Chem. Commun.* **2010**, *46*, 7295–7306; m) S. Jautze, R. Peters, *Synthesis* **2010**, 365–388; n) B. M. Trost, C. S. Brindle, *Chem. Soc. Rev.* **2010**, *39*, 1600–1632; o) J. P. Das, I. Marek, *Chem. Commun.* **2011**, *47*, 4593–4623; p) H. Kotsuki, N. Sasakura, in: *New and Future Developments*

in Catalysis (Ed.: S. L. Suib), Elsevier, Amsterdam, **2013**, p. 563–603; q) A. Y. Hong, B. M. Stoltz, *Eur. J. Org. Chem.* **2013**, 2745–2759.

[2] a) J. Buckingham, K. H. Baggaley, A. D. Roberts, L. F. Szabó (Eds.), *Dictionary of Alkaloids*, 2nd ed., CRC Press, **2010**; b) O. Hoshino, in: *The Alkaloids* (Ed.: G. A. Cordell), Academic Press, New York, **1998**, vol. 51, p. 323–424; c) S. F. Martin, in: *The Alkaloids* (Ed.: A. Brossi), Academic Press, New York, **1987**, vol. 30, p. 251–376.

[3] H. M. Wang, P. Chen, M. Tang, *Chin. J. Org. Chem.* **2014**, *34*, 852–864.

[4] a) K. Shimizu, K. Tomioka, S.-i. Yamada, K. Koga, *Heterocycles* **1977**, *8*, 277; b) S. Kodama, Y. Hamashima, K. Nishide, M. Node, *Angew. Chem. Int. Ed.* **2004**, *43*, 2659–2661; *Angew. Chem.* **2004**, *116*, 2713.

[5] a) W. P. Malachowski, T. Paul, S. Phounsavath, *J. Org. Chem.* **2007**, *72*, 6792–6796; b) T. Kato, H. Tanimoto, H. Yamada, N. Chida, *Heterocycles* **2010**, *82*, 563–579.

[6] a) B. M. Trost, F. D. Toste, *J. Am. Chem. Soc.* **2000**, *122*, 11262–11263; b) B. M. Trost, W. Tang, *Angew. Chem. Int. Ed.* **2002**, *41*, 2795–2797; *Angew. Chem.* **2002**, *114*, 2919; c) B. M. Trost, W. Tang, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 14785–14803; d) V. Satcharoen, N. J. McLean, S. C. Kemp, N. P. Camp, R. C. D. Brown, *Org. Lett.* **2007**, *9*, 1867–1869; e) J. Q. Chen, J. H. Xie, D. H. Bao, S. Liu, Q. L. Zhou, *Org. Lett.* **2012**, *14*, 2714–2717; f) Y. Zang, I. Ojima, *J. Org. Chem.* **2013**, *78*, 4013–4018; g) J. Choi, H. Kim, S. Park, J. Tae, *Synlett* **2013**, *24*, 379–382.

[7] a) L. Li, Q. Yang, Y. Wang, Y. Jia, *Angew. Chem. Int. Ed.* **2015**, *54*, 6255–6259; b) P. Chen, X. Bao, L. F. Zhang, M. Ding, X. J. Han, J. Li, G. B. Zhang, Y. Q. Tu, C. A. Fan, *Angew. Chem. Int. Ed.* **2011**, *50*, 8161–8166.

[8] For the Michael addition of α-aryl α-alkyl aldehydes and enones, see: a) M. Bella, D. M. Schietroma, P. P. Cusella, T. Gasperi, V. Visca, *Chem. Commun.* **2009**, 597–599; b) Y. Inokoishi, N. Sasakura, K. Nakano, Y. Ichikawa, H. Kotsuki, *Org. Lett.* **2010**, *12*, 1616–1619; c) H. Yang, R. G. Carter, *Tetrahedron* **2010**, *66*, 4854–4859; d) H. Yang, S. Banerjee, R. G. Carter, *Org. Biomol. Chem.* **2012**, *10*, 4851–4863; e) M. Yoshida, H. Ukigai, K. Shibatomi, S. Hara, *Tetrahedron Lett.* **2015**, *56*, 3890–3893.

[9] For the Michael addition of α-aryl α-cyano esters and enones, see: a) M. Sawamura, H. Hamashima, Y. Ito, *J. Am. Chem. Soc.* **1992**, *114*, 8295–8296; b) M. S. Taylor, D. N. Zalatan, A. M. Lerchner, E. N. Jacobsen, *J. Am. Chem. Soc.* **2005**, *127*, 1313–1317; c) T. Y. Liu, R. Li, Q. Chai, J. Long, B. J. Li, Y. Wu, L. S. Ding, Y. C. Chen, *Chem. Eur. J.* **2007**, *13*, 319–327; d) S. Jautze, R. Peters, *Angew. Chem. Int. Ed.* **2008**, *47*, 9284–9288; *Angew. Chem.* **2008**, *120*, 9424.

[10] For acyclic α-cyano ketones as donors in the enantioselective Michael addition reaction with highly active acrolein for the synthesis of aryl-substituted all-carbon quaternary centers, see: a) T. Morita, H. Yamada, A. Takehashi (Toa Eiyo), JP2002080444, **2002**; b) T. Marcelli, J. H. van Maarseveen, H. Hiemstra, *Angew. Chem. Int. Ed.* **2006**, *45*, 7496–7504; *Angew. Chem.* **2006**, *118*, 7658.

[11] For cyclic α-cyano ketones as donors in the catalytic enantioselective Michael addition reaction with highly active acrylonitrile derivatives for the synthesis of alkyl-substituted all-carbon quaternary centers, see: a) Y. Wang, X. Liu, L. Deng, *J. Am. Chem. Soc.* **2006**, *128*, 3928–3930; b) B. Wang, F. Wu, Y. Wang, X. Liu, L. Deng, *J. Am. Chem. Soc.* **2007**, *129*, 768–769.

[12] For acrylates as less active acceptors in the catalytic enantioselective Michael addition reaction with cyclic β-keto esters for the synthesis of alkyl-substituted all-carbon quaternary centers, see: a) C. L. Rigby, D. J. Dixon, *Chem. Commun.* **2008**, 3798–3800; b) S. Tarí, R. Chinchilla, C. Nájera, *Tetrahedron: Asymmetry* **2009**, *20*, 2651–2654.

[13] For recent reviews on chiral amine-thiourea catalysts, see: a) P. R. Schreiner, *Chem. Soc. Rev.* **2003**, *32*, 289–296; b) Y. Takemoto, *Org. Biomol. Chem.* **2005**, *3*, 4299–4306; c) M. S. Taylor, E. N. Jacobsen, *Angew. Chem. Int. Ed.* **2006**, *45*, 1520–1543; *Angew. Chem.* **2006**, *118*, 1550; d) S. J. Connon, *Chem. Eur. J.* **2006**, *12*, 5418–5427; e) T. Akiyama, J. Itoh, K. Fuchibe, *Adv. Synth. Catal.* **2006**, *348*, 999–1010; f) A. G. Doyle, E. N. Jacobsen, *Chem. Rev.* **2007**, *107*, 5713–5743; g) X. Yu, W. Wang, *Chem. Asian J.* **2008**, *3*, 516–532; h) S. Connon, *Synlett* **2009**, 354–376; i) Y. Takemoto, *Chem. Pharm. Bull.* **2010**, *58*, 593–601; j) M. Tsakos, C. G. Kokotos, *Tetrahedron* **2013**, *69*, 10199–10222; k) O. V. Serdyuk, C. M. Heckel, S. B. Tsogoeva, *Org. Biomol. Chem.* **2013**, *11*, 7051–7071; l) T. J. Auvil, A. G. Schafer, A. E. Mattson, *Eur. J. Org. Chem.* **2014**, 2633–2646.

[14] For details, see the Supporting Information.

[15] The stereochemical assignment of **3aa** in Figure 3 was determined by chiral HPLC analysis of the major enantiomer and by comparison with the absolute configuration of **3ag** (Table 1, Entry 7).

[16] CCDC 816143 [for (*R*)-**3ag**] and 1419107 [for (*R*)-**3ug**] contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

[17] J. Aleman, B. Richter, K. A. Jorgensen, *Angew. Chem. Int. Ed.* **2007**, *46*, 5515–5519; *Angew. Chem.* **2007**, *119*, 5611.

Received: November 9, 2015
Published Online: January 5, 2016