

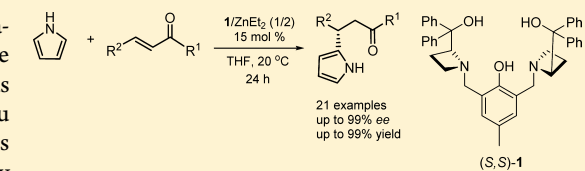
Enantioselective Friedel–Crafts Alkylation of Pyrrole with Chalcones Catalyzed by a Dinuclear Zinc Catalyst

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S Supporting Information

ABSTRACT: A highly enantioselective Friedel–Crafts (F–C) alkylation of pyrrole with a wide range of simple nonchelating chalcone derivatives catalyzed by a chiral $(\text{Zn}_2\text{EtL})_n$ ($L = (S,S)\text{-1}$) complex has been developed. The catalyst $(\text{Zn}_2\text{EtL})_n$ complex was prepared in situ by reacting the chiral ligand $(S,S)\text{-1}$ with 2 equiv of diethylzinc. A series of β -pyrrole-substituted dihydrochalcones were usually formed mostly in excellent yields (up to 99%) and excellent enantioselectivity [up to 99% enantiomeric excess (ee)] by using 15 mol % catalyst loading under mild conditions. The absolute stereochemistry of the products was determined to be the *S*-configuration by X-ray crystallographic analysis of **13g**. Meanwhile, a weak negative nonlinear effect was observed. On the basis of the experimental results and previous reports, a possible mechanism was proposed to explain the origin of the asymmetric induction.



INTRODUCTION

Since it was first reported in the year 1877,¹ the Friedel–Crafts reaction, one of the oldest organic synthetic methods, has proven its significance and been applied to substantial synthetic and industrial processes as one of the most powerful and employed tools to effect the construction of carbon–carbon bonds.²

Recently, the catalytic asymmetric Friedel–Crafts alkylation generating valuable classes of building blocks along with the creation of stereogenic carbon centers has been an appealing and demanding area of research.³ Among this transformation, the Michael-type catalytic asymmetric Friedel–Crafts alkylations of heteroaromatic compounds, which provide an efficient way to synthesize optically active heteroaromatics bearing chiral centers, plays a very important role.⁴ The first catalytic asymmetric example of this methodology by using indole/pyrrole and simple α,β -unsaturated aldehydes was reported by Paras and MacMillan in 2001.⁵ After this pioneering work, many groups have directed their efforts in developing new routes to devise efficient and adapted strategies for this purpose.⁴ Generally, an electron-rich heteroaromatic ring, an electron-poor alkene, and a suitably designed catalyst are three synergistic elements of a successful Michael-type catalytic asymmetric Friedel–Crafts alkylations of heteroaromatic compounds.⁶

As for the electron-rich heteroaromatic ring, indole/pyrroles are by far a privileged skeleton for the biologic relevance of these molecules. Pyrroles are abundant in natural products, medicinal agents, and a number of intermediates in multistep syntheses.⁷ However, there are far fewer reports about the use of pyrroles, especially unprotected pyrroles as an electron-rich heteroaromatic ring in Michael-type catalytic asymmetric Friedel–Crafts alkylations, than of indoles.⁴ Several reasons

could be responsible: (1) the regioselectivity issue caused by the similar nucleophilicity between the 2- and 3-positions of pyrroles;⁸ (2) the tendency of formation of 2,5-disubstituted pyrroles product; and (3) the relative instability of pyrroles toward acidic environments.⁹ Classical Friedel–Crafts conditions are unsuitable for this class of compounds. Instead, mild reaction conditions are required to implement a useful Friedel–Crafts protocol for pyrroles especially unprotected pyrrole.

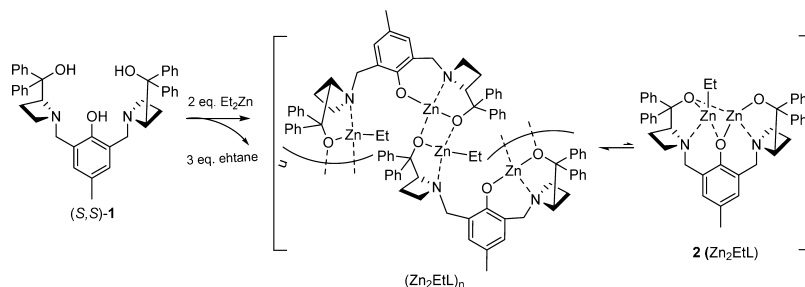
As for the electron-poor alkene, activated α,β -unsaturated carbonyl compounds are usually used when pyrroles act as an electron-rich heteroaromatic ring. A series of α,β -unsaturated carbonyl compounds, such as α,β -unsaturated aldehydes,¹⁰ β,γ -unsaturated α -ketoesters,¹¹ α,β -unsaturated 2-acyl imidazoles,¹² 2-enoylpyridine *N*-oxides,¹³ α' -hydroxy enones,¹⁴ ethane di- or tricarboxylate,¹⁵ α,β -unsaturated ketones,¹⁶ or a nitroalkene¹⁷ have been applied successfully as alkylation reagents to the catalytic asymmetric Friedel–Crafts alkylation of unprotected or protected pyrroles. However, there was only one example reported in moderate to excellent yields and up to 92% enantiomeric excess (ee) when simple chalcone derivatives were used in the asymmetric Friedel–Crafts alkylations of unprotected pyrroles.^{16b} The reason is probably owed to the low reactivity of nonchelating chalcone derivatives and the difficulty in enantiofacial differentiation. It would be highly desirable to conquer these problems.

As for the suitably designed catalyst, organocatalyst^{10,16c,17d,g} and metal catalyst based on a Lewis acid and a chiral ligand are often employed in the catalytic asymmetric Friedel–Crafts alkylation of unprotected or protected pyrroles. Among metal

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Scheme 1. Dinuclear Zinc Catalyst 2



catalysts, mononuclear metal complexes are by far preferred,^{10–17} whereas di- or trinuclear complexes are less frequently used.^{9,17f} It is necessary to develop new catalysts for guiding such enantioselective reactions.

Our previous work focused on exploring the use of chiral small-ring heterocycle ligands in catalytic asymmetric synthesis.¹⁸ We have found that among these chiral nitrogen heterocycles containing a β -amino alcohol moiety, the use of four-membered heterocycles as chiral ligands affords the best enantioselectivity in the catalytic asymmetric addition of diethylzinc to benzaldehyde.^{18a} In addition, we have recently reported a dinuclear zinc–AzePhenol catalyst **2** [Zn_2EtL ($L = (S,S)\text{-1}$)] prepared by reacting the chiral ligand $(S,S)\text{-1}$ with two equivalents of diethylzinc wherein 3 equiv of ethane evolved (Scheme 1). This catalyst catalyzed the asymmetric alternating copolymerization of carbon dioxide and cyclohexene oxide in quantitative yield and high enantioselectivity of up to 93.8% ee.¹⁹ This enantioselectivity was much better than that of Trost's dinuclear zinc–ProPhenol catalyst in the same reaction.²⁰ This activity is because of the relatively rigid ligand skeleton and appropriate chiral microenvironment provided by the four-membered heterocycle.

As part of our study on this chiral catalyst, herein we report the synthesis of chiral ligand $(S,S)\text{-1}$ and $(R,R)\text{-1}$ with a more rigid azetidine ring compared with that of pyrrolidine (Scheme 2) and the use of complex $(Zn_2EtL)_n$ prepared in situ as an

because of the electron-withdrawing character and the synthetic versatility of that functional group.²¹ To our knowledge, this study represents the first example of an enantioselective dinuclear zinc catalytic Friedel–Crafts reaction of unprotected pyrrole with chalcones. In this paper, we report our detailed studies on this subject.

RESULTS AND DISCUSSION

Synthesis of Chiral Ligands. The preparation of $(S,S)\text{-1}$ is shown in Scheme 2. Starting from the source of chirality L -(+)-methionine **3**, the synthetic route consisted of nine steps. Methyl L -2-amino-4-bromobutanoate **4** was prepared by our previously developed procedure.^{18a}

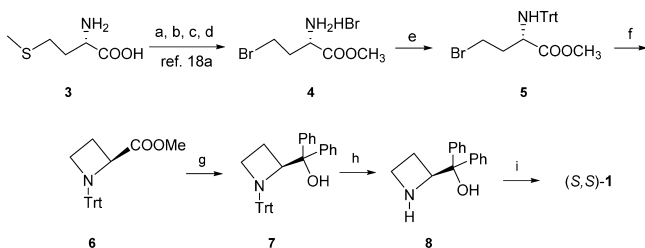
Construction of the four-membered ring heterocycle from an acyclic compound is a key step in this synthesis. We developed a simple protocol for the efficient conversion of methyl L -2-amino-4-bromobutanoate **4** to methyl (S) - N -tritylazetidide-2-carboxylate **6** involving two steps.^{18c} Triphenylmethyl (Trt or trityl) chloride first reacted with compound **4** in CH_3OH in the presence of Et_3N giving methyl (S) - N -trityl-2-amino-4-bromobutanoate **5** in 89% yield. The intramolecular cyclization of compound **5** was carried out in DMF with K_2CO_3 at 85 °C affording (S) - N -tritylazetidide-2-carboxylate **6** in 62% yield. The treatment of **6** with $PhMgBr$ afforded the corresponding chiral (S) - N -tritylazetidide-2-yl(diphenyl)-methanol **7** in 96% yield. The treatment of **7** with sulfuric acid in CH_3OH could deprotect the N -trityl group, and (S) -azetidide-2-yl(diphenyl)-methanol **8** was obtained in 95% yield. Finally, the chiral ligand $(S,S)\text{-1}$ was easily prepared from compound **8** and 2,6-bis(bromomethyl)- p -cresol.¹⁹

The chiral ligand $(R,R)\text{-1}$ was prepared by using a similar synthetic route from the starting source of chirality D -(-)-methionine, enantiomer of **3**.

The single-crystal growth of compound **8** was performed in a mixture of hexane/ethyl acetate (2:1) at room temperature, and colorless crystals were obtained. The absolute stereochemistry of **8** was confirmed to be the S -configuration by X-ray diffraction.

Optimization of Asymmetric Friedel–Crafts Alkylations of Pyrrole with Chalcones Reaction Conditions.

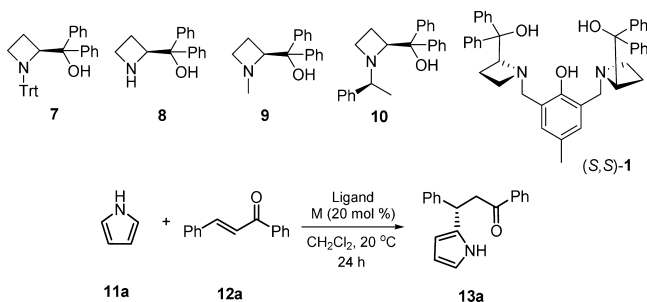
Our initial investigation began with screening several chiral ligands reacting with $ZnEt_2$ in situ to evaluate their ability to promote the addition of pyrrole **11a** to chalcone **12a** in CH_2Cl_2 . A series of ligands were examined, and the results were summarized in Table 1. Simple β -amino alcohol ligands were not efficient in enantioselectivity (Table 1, entries 1–4). Fortunately, the combination of ligand $(S,S)\text{-1}$ and $ZnEt_2$ gave the best results (Table 1, entry 5). As for the metal reagents, changing the metal reagents from $ZnEt_2$ to $Zn(CH_3)_2$ or $n\text{-Bu}_2Mg$ ^{20b,22} led to a significant reduction on both yields and

Scheme 2. Synthesis of Ligand $(S,S)\text{-1}$ ^a

^aConditions: (a) CH_3I , H_2O , CH_3OH , 30 °C, 24 h, 94%; (b) $NaHCO_3$, H_2O , reflux, 20 h, 68%; (c) HBr , CH_3COOH , 75–80 °C, 5 h, 85%; (d) dry CH_3OH , HCl , 35–40 °C, 2 h; (e) Et_3N , $TrtCl$, dry CH_2Cl_2 , 89%; (f) DMF , K_2CO_3 , 85 °C, 72 h, 62%; (g) dry THF , $PhMgBr$, 0 °C, 96%; (h) CH_3OH , H_2O , H_2SO_4 , rt, 48 h, 95%; (i) 2,6-bis(bromomethyl)- p -cresol, DMF , K_2CO_3 , rt, 24 h, 90%.

efficient catalyst to conduct catalytic asymmetric Friedel–Crafts alkylations of unprotected pyrrole **11a** with a broad range of chalcones **12**. The products of 2-substituted pyrroles **13** with an asymmetric carbon atom at the α -position are achieved in moderate to excellent yields (up to 99%) and excellent enantioselectivities (up to 99% ee) by using 15 mol % catalyst loading under mild conditions. The chalcones were chosen

Table 1. Effects of Ligand and Metal Reagent on Catalytic Asymmetric Friedel–Crafts Reaction of Pyrrole 11a and Chalcone 12a under the Indicated Conditions^a



entry	ligand (x mol %)	M	yield (%)	ee ^b (%)
1	7 (20)	ZnEt ₂	55	5
2	8 (20)	ZnEt ₂	61	4
3	9 (20)	ZnEt ₂	54	2
4	10 (20)	ZnEt ₂	50	5
5	(S,S)-1 (10)	ZnEt ₂	84	97
6	(S,S)-1 (10)	Zn(CH ₃) ₂	77	94
7	(S,S)-1 (10)	^t Bu ₂ Mg	68	23

^aUnless otherwise noted, all reactions were carried out with 11a (0.75 mmol) and 12a (0.25 mmol) in CH₂Cl₂ (1.0 mL) under nitrogen at 20 °C for 24 h. ^bDetermined by chiral HPLC.

ee values (Table 1, entries 6 and 7 compared with entry 5). Therefore, the (S,S)-1-ZnEt₂ (Zn₂EtL)_n system was chosen to assess other reaction parameters.

Encouraged by the initial results, various solvents were tested in the presence of the (Zn₂EtL)_n system (10 mol %) at 20 °C for 24 h. The results indicated that the reaction solvent plays an important role in governing the rate and enantioselectivity of the reaction. The reaction produced smoothly in CH₂Cl₂, CHCl₃, toluene, and THF, with high enantioselectivity (up to 98% ee in THF) (Table 2, entries 1–4). However, no reaction took place in CH₃CN and 1,4-dioxane (Table 2, entries 5 and 6). The reaction was carried out in THF in the presence of 40 mg 4 Å molecular sieves (MS), with a decreased ee value of 92% (Table 2, entry 7 compared with entry 4).

Subsequently, the reaction temperature and catalyst loading were examined also. Temperature proved to have a distinctive effect on the yields. Decreasing the reaction temperature led to lower reactivity, although the enantioselectivity was maintained (Table 2, entries 4, 8, and 9). When the temperature was increased from 20 to 30 °C, the enantioselectivity was somewhat reduced (Table 2, entry 10). The catalyst loading was then evaluated. Reducing the catalyst loading caused a notable drop in reactivity (Table 2, entry 11). Upon increasing the catalyst loading from 10 to 15 mol %, both the yield and the enantioselectivity were increased (Table 2, entry 12). Extensive screening showed that the optimal conditions were as follows: (Zn₂EtL)_n complexes (15 mol %), pyrrole 11a (0.75 mmol), and chalcone 12a (0.25 mmol) in THF (1 mL) at 20 °C. There was no 2,5-dialkylated product formed under these optimized reaction conditions.

Scope of Asymmetric Friedel–Crafts Alkylation Reaction. With these results in hand, various α,β -unsaturated ketones were then examined (Table 3). Excellent enantioselectivities were obtained, regardless of the electronic nature or positions of the substrates on the phenyl ring (R¹) (Table 3, entries 1–8). The electronic nature or positions of the substrates on the phenyl ring (R¹) affected the yields

Table 2. Effects of Solvent, Temperature, and Catalyst Loading on the Catalytic Asymmetric Friedel–Crafts Reaction of Pyrrole 11a and Chalcone 12a^a

entry	solvent	(S,S)-1 (mol %)	temp (°C)	time (h)	yield (%)	ee ^b (%)
1	CH ₂ Cl ₂	10	20	24	84	97
2	CHCl ₃	10	20	24	86	95
3	Toluene	10	20	24	87	96
4	THF	10	20	24	88	98
5	CH ₃ CN	10	20	24	NR ^c	
6	1,4-dioxane	10	20	24	NR ^c	
7 ^d	THF	10	20	24	89	92
8	THF	10	0	24	22	98
9	THF	10	10	24	67	98
10	THF	10	30	20	99	97
11	THF	5	20	24	54	97
12	THF	15	20	24	99	99

^aUnless otherwise noted, all reactions were carried out with 11a (0.75 mmol) and 12a (0.25 mmol) in solvent (1.0 mL) with (Zn₂EtL)_n (10 mol %) under nitrogen at 20 °C for 24 h. ^bDetermined by chiral HPLC. ^cNR: no reaction. ^d40 mg of 4 Å MS was added.

differently. The electron-donating group CH₃ at the *para* position and the electron-withdrawing group Cl at the *ortho* position of the phenyl ring (R¹) led to a decrease in yield (Table 3, entries 5 and 8).

The products were obtained in excellent yields and enantioselectivities wherever the electron-withdrawing group of the phenyl ring (R²) was present (Table 3, entries 9–13). The electron-donating group CH₃ of the phenyl ring (R²) did not affect the enantioselectivities; however, a decrease in yield was observed, especially when it occupied the *meta* position of the phenyl ring (R²) (Table 3, entries 14 and 15). 2-Naphthyl substrates reacted smoothly with pyrrole at the optical conditions giving the desired product with >99% ee (Table 3, entry 16).

The electron-withdrawing groups of R¹ or R² were beneficial for the reaction according to the results shown in Table 3. We synthesized a series of substrates with two electron-withdrawing groups occupying R¹ and R² separately. All of them reacted with pyrrole in excellent yields and enantioselectivities (Table 3, entries 17–21). Substrate 12u with a CH₃ group gave 99% ee but 70% yield.

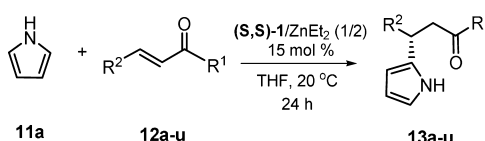
Substrates with a strongly electron-donating group CH₃O occupying the *para* position of the phenyl ring R¹ or R² led to more complex mixtures (Table 3, entries 22 and 23). No reaction occurred when alkyl-substituted α,β -unsaturated ketones, such as 12x, were used as a substrate (Table 3, entry 24).

(R,R)-1 was also used to catalyze this Friedel–Crafts reaction with the results of 99% yield and 99% ee (Table 3, entry 25, opposite optical activity compared with entry 1).

PROPOSED CATALYTIC MECHANISM

To gain insight into the reaction mechanism, a nonlinear effect and kinetic studies were also investigated to further elucidate the actual catalyst structure. The correlation between the ee

Table 3. Catalytic Asymmetric Friedel–Crafts Reaction of Pyrrole 11a and Chalcone Derivatives 12 under the Optimal Conditions^a



entry	substrate	R ¹	R ²	product	yield (%)	ee ^b (%)
1	12a	Ph	Ph	13a	99	99
2	12b	4-FC ₆ H ₄	Ph	13b	99	99
3	12c	4-ClC ₆ H ₄	Ph	13c	99	98
4	12d	4-BrC ₆ H ₄	Ph	13d	99	99
5	12e	4-CH ₃ C ₆ H ₄	Ph	13e	54	98
6	12f	3-ClC ₆ H ₄	Ph	13f	99	98
7	12g	3-BrC ₆ H ₄	Ph	13g	99	99 ^c
8	12h	2-ClC ₆ H ₄	Ph	13h	59	99
9	12i	Ph	4-ClC ₆ H ₄	13i	99	98
10	12j	Ph	4-BrC ₆ H ₄	13j	99	>99
11	12k	Ph	3-ClC ₆ H ₄	13k	99	99
12	12l	Ph	3-BrC ₆ H ₄	13l	99	98
13	12m	Ph	2-ClC ₆ H ₄	13m	99	98
14	12n	Ph	4-CH ₃ C ₆ H ₄	13n	94	98
15	12o	Ph	3-CH ₃ C ₆ H ₄	13o	67	98
16	12p	Ph	2-naphthyl	13p	94	>99
17	12q	4-ClC ₆ H ₄	2-ClC ₆ H ₄	13q	99	98
18	12r	4-FC ₆ H ₄	3-BrC ₆ H ₄	13r	99	99
19	12s	4-BrC ₆ H ₄	3-BrC ₆ H ₄	13s	99	99
20	12t	4-FC ₆ H ₄	4-ClC ₆ H ₄	13t	99	99
21	12u	4-CH ₃ C ₆ H ₄	4-ClC ₆ H ₄	13u	70	99
22 ^d	12v	4-CH ₃ OC ₆ H ₄	Ph			
23 ^d	12w	Ph	4-CH ₃ OC ₆ H ₄			
24	12x	Ph	ⁱ Pr		NR ^e	
25	12a	Ph	Ph	13a	99	99 ^f

^aUnless otherwise noted, all reactions were carried out with **11a** (0.75 mmol) and **12** (0.25 mmol) in THF (1.0 mL) with (Zn₂EtL)_n (15 mol %) under nitrogen at 20 °C for 24 h. ^bDetermined by chiral HPLC. ^cThe absolute configuration was *S* by X-ray crystallographic analysis. ^dMore complex mixture was obtained. ^eNR: no reaction. ^f(*R,R*)-**1** (15 mol %) was used.

values of ligand (*S,S*)-**1** and ee of the product **13a** was carefully examined, and the result showed that a weak negative nonlinear effect was observed in the Friedel–Crafts alkylation of unprotected pyrrole with nonsubstituted chalcone, as depicted in Figure 1 (a).²³ Kinetic studies revealed that the enantiopure catalyst afforded a slower reaction than the racemate catalyst,

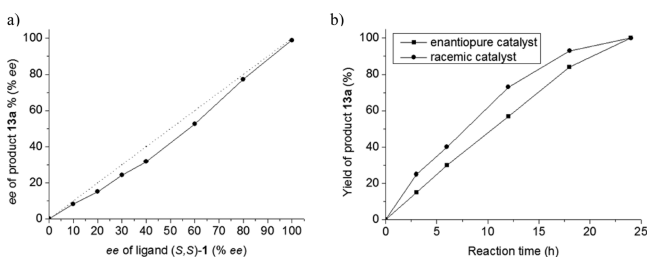
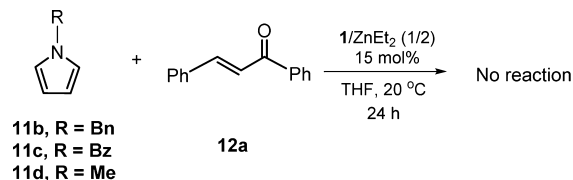


Figure 1. (a) Correlation between the ee values of the ligand (*S,S*)-**1** and the ee of product **13a**; (b) kinetic studies of the Friedel–Crafts alkylation of pyrrole with chalcone **12a** in THF.

although the racemate catalyst exhibited a little insolubility in THF (Figure 1 b). By using optically pure (*S,S*)-**1** as the chiral ligand, the catalyst complex prepared in situ in THF was soluble; however, when nonenantiopure **1** was used, a large amount of deposition was observed during the catalyst preparation (see a picture in the Supporting Information). As a result, we suggest that the catalytically inactive oligomeric aggregates (Zn₂EtL)_n containing two or more monomeric catalyst species are formed prior to monomeric Zn₂EtL when we put the ligand **1** and 2 equiv of ZnEt₂ together in THF (Scheme 1).²⁴ The reason is that the nonlinear effect should not exist in this reaction and there should not be deposition in preparing the racemate catalyst, if monomeric Zn₂EtL is the real complexation form of ligand **1** and ZnEt₂. In addition, the heterochiral oligomeric aggregates containing both (*S,S*) and (*R,R*) ligands are formed and decomposed in preference to those which are composed of the optically pure ligands under our reaction conditions, therefore generating a higher concentration of catalytically active monomeric species, which could further lead to the negative nonlinear effect and kinetic results. This phenomenon is quite different from most literature examples of dimeric metal complex catalysis.²⁵ Unfortunately, attempts to grow a single crystal of Zn₂EtL or (Zn₂EtL)_n were unsuccessful.

When *N*-benzylpyrrole (**11b**), *N*-benzoylpyrrole (**11c**), and *N*-methylpyrrole (**11d**) were prepared and treated with chalcone **12a**, respectively, no reaction was observed (Scheme 3), thereby demonstrating that the hydrogen atom on the *N*

Scheme 3. Oligomeric Aggregates (Zn₂EtL)_n Catalytic Asymmetric Friedel–Crafts Alkylation Reaction of Pyrrole **11b, **11c**, or **11d** and Chalcone **12a****

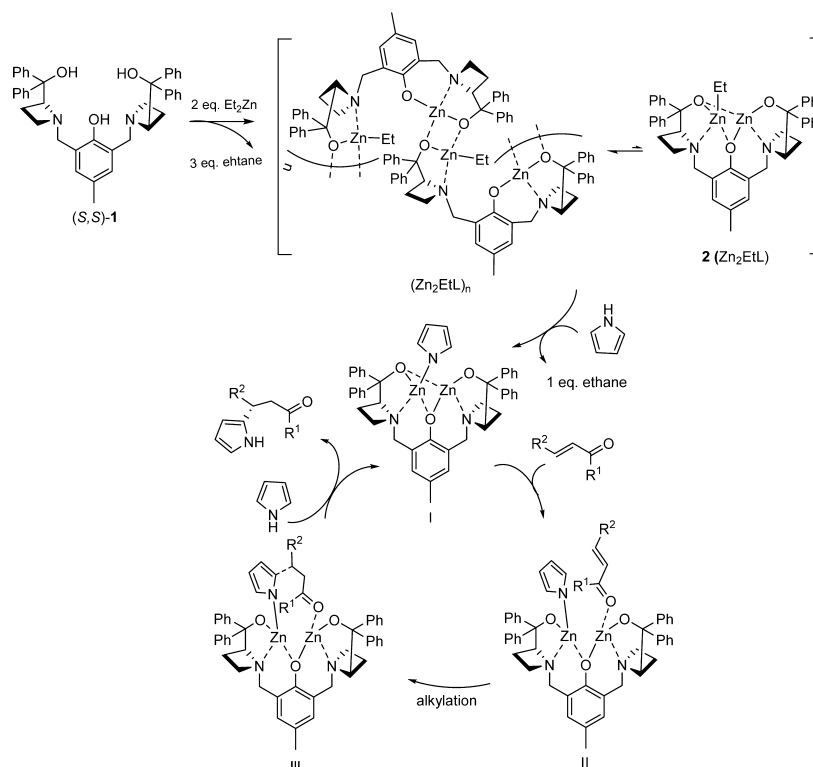


atom of the pyrrole is crucial for the activation of the reactants by oligomeric aggregates (Zn₂EtL)_n catalyst in this Friedel–Crafts reaction.

On the basis of these experimental results, a proposed mechanism that rationalizes the observed sense of asymmetric induction is provided in Scheme 4. Treatment of ligand (*S,S*)-**1** with 2 equiv of ZnEt₂ presumably affords catalytically inactive species (Zn₂EtL)_n. Then, the deprotonation of pyrrole is accomplished by (Zn₂EtL)_n accompanied by the formation of 1 equiv of ethane; meanwhile, the complex (Zn₂EtL)_n is decomposed to the catalytically active species **I**. Although direct structural evidence for complex **I** could not be ascertained by electrospray mass spectral analysis or X-ray crystallography, previously similar work by Ding and co-workers suggests the formation of a dinuclear zinc ProPhenol complex,²⁰ and a dinuclear zinc–AzePhenol complex **2** could be captured by benzoic acid molecules recently reported by us.¹⁹ Thus, we propose that the dinuclear zinc complex **I** is the real active catalyst species. The fact that *N*-benzylpyrrole (**11b**), *N*-benzoylpyrrole (**11c**), or *N*-methylpyrrole (**11d**) gives no reaction supports our guess.

Subsequently, the coordinating of chalcone to complexes **I** leads to the formation of complexes **II** with undergoing the

Scheme 4. Proposed Catalytic Cycle



alkylation reaction. Finally, the catalytic cycle is closed by a proton exchange with an incoming pyrrole to release the product and reform the active catalyst species I.

The absolute stereochemistry of the products was determined to be of the *S*-configuration by X-ray crystallographic analysis of **13g**. The catalytic cycle depicted in Scheme 4 also nicely accounts for this absolute configuration.

CONCLUSION

We have synthesized a pair of enantiomers of ligand **1** starting from enantiopure methionine **3**, respectively, and a catalytic asymmetric Friedel–Crafts alkylation of unprotected pyrrole with a variety of differently substituted chalcones promoted by a dinuclear zinc complex $(\text{Zn}_2\text{EtL})_n$ has been demonstrated. The $(\text{Zn}_2\text{EtL})_n$ system was prepared in situ by reacting the chiral ligand (S,S) -**1** with 2 equiv of diethylzinc. This type of electrophilic compound is challenging for F–C reactions on account of the nonchelating character of chalcones. A series of β -pyrrole-substituted dihydrochalcones were obtained with excellent enantioselectivities (up to 99% ee) and excellent yields (up to 99%) under mild conditions. A novel negative nonlinear effect was observed and discussed; meanwhile, according to kinetic studies and the other experimental results, a proposed mechanism was put forward to explain the origin of the asymmetric induction. Further work to determine the precise structure of the active species and applications of this $(\text{Zn}_2\text{EtL})_n$ system to other asymmetric reactions is currently underway in our group.

EXPERIMENTAL SECTION

General Methods. Solvents were dried with standard methods and freshly distilled prior to use if needed. All reactions sensitive to air or moisture were carried out under nitrogen using standard Schlenk and vacuum line techniques. Pyrrole was distilled prior to use.

Compounds **9**²⁶ and **10**^{18b} and chalcones **12**²⁷ were synthesized according to the literature. All other chemicals were used as purchased. NMR spectra were recorded on a 400 MHz NMR spectrometer with CDCl_3 as the solvent and TMS as an internal standard (400 MHz for ^1H and 100 MHz for ^{13}C). HRMS were determined on a Q-TOF Micro LC/MS System ESI spectrometer. Enantiomeric excesses values were determined with HPLC (chiral column; mobile phase hexane/*i*-PrOH).

Methyl (*S*)-*N*-Trityl-2-amino-4-bromobutanoate **5.** Methyl *L*-2-amino-4-bromobutanoate hydrochloride **4** (3.6 g, 13 mmol) was suspended in dry dichloromethane (30 mL), and the mixture was stirred and cooled to 0 °C. Triethylamine (39 mmol, 3.95 g) was added to the reaction mixture, and then trityl chloride (3.99 g, 14.3 mmol) in 20 mL dry dichloromethane was added dropwise. After being stirred for 48 h at 0 °C, the mixture was washed with 10% aqueous citric acid solution (3 × 20 mL) and water (3 × 20 mL). The organic phase was dried over Na_2SO_4 . After filtration, the solvent was removed under reduced pressure by using a rotary evaporator. The residue was purified by recrystallization (petroleum ether/ethyl acetate) to afford the methyl (*S*)-*N*-trityl-2-amino-4-bromobutanoate **5** as a slightly yellowish solid in 89% yield (5.07 g).^{18c} mp 115–116 °C; $[\alpha]_{\text{D}}^{20} = +47.4$ (*c* 1.0, in CHCl_3); ^1H NMR (400 MHz, CDCl_3) $\delta = 7.5$ – 7.2 (m, 15 H), 3.6–3.5 (m, 2 H), 3.7–3.4 (m, 1 H), 3.17 (s, 3 H), 2.73 (d, *J* = 10.3 Hz, 1 H), 2.3–2.1 (m, 2 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 174.5$, 145.6, 128.8, 127.9, 126.5, 71.1, 54.4, 51.8, 38.9, 28.6 ppm; IR (KBr pellet) 3343, 3057, 3028, 2952, 1722, 1596, 1489, 1447, 1263, 1029, 773, 712 cm^{-1} ; MS (EI) *m/z* = 460.10 $[\text{M} + \text{Na}]^+$.

(*S*)-*N*-Tritylazetidide-2-carboxylate **6.** To a stirred solution of (*S*)-*N*-tritylazetidide-2-carboxylate **5** (2.0 g, 4.56 mmol) in DMF (8 mL) was added K_2CO_3 (0.94 g, 6.8 mmol) portionwise at room temperature. The reaction mixture was stirred for 72 h at 80 °C. The mixture was quenched with water (8 mL) and ethyl acetate (10 mL), and the aqueous phase was extracted with ethyl acetate (3 × 10 mL). The combined organic layers were washed with brine twice and dried over magnesium sulfate. The solvent was removed under reduced pressure by using a rotary evaporator. The residue was purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford

the desired product (S)-*N*-tritylazetidino-2-carboxylate **6** as a white solid (62% yield, 1.01 g); ^{18}C mp 153–154 °C; $[\alpha]_{\text{D}}^{20} = -91$ (*c* 1.59, in CHCl_3); ^1H NMR (400 MHz, CDCl_3) $\delta = 7.53$ – 7.15 (m, 15 H), 3.58–3.54 (m, 1 H), 3.53–3.50 (m, 1 H), 3.48 (s, 3 H), 2.83–2.77 (m, 1 H), 2.40–2.31 (m, 2 H), 1.59–1.52 (m, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 173.8, 142.3, 129.5, 127.9, 127.8, 127.6, 127.3, 126.6, 75.7, 59.3, 51.5, 46.0, 20.1$ ppm; IR (KBr pellet) 3448, 3081, 3057, 3023, 2877, 1737, 1489, 1445, 1362, 1031, 749, 713 cm^{-1} ; MS (ESI) $m/z = 380.0$ $[\text{M} + \text{Na}]^+$.

(S)-*N*-Tritylazetidino-2-yl(diphenyl)methanol 7. A Grignard reagent was prepared in the usual way from 1.6 g (67 mmol) of magnesium and bromobenzene (10.52 g, 67 mmol) in dry THF (30 mL). The solution was cooled to 0 °C before addition of a solution of compound **6** (3.0 g, 8.4 mmol) in THF (10 mL). The reaction mixture was stirred for 3 h at 0 °C and then was allowed to warm room temperature for another 12 h. The reaction was quenched with saturated aqueous NH_4Cl (50 mL) at 0 °C. Et_2O (50 mL) was added, the organic phases were separated, and the aqueous phase was extracted with Et_2O (3×40 mL). The combined organic phases were washed with brine (40 mL) and dried over Na_2SO_4 . After filtration, the solvent was removed under reduced pressure by using a rotary evaporator. The resulting residue was purified by flash chromatography with petroleum ether/ethyl acetate (3:1) to afford the desired product (S)-*N*-tritylazetidino-2-yl(diphenyl)methanol **7** as a white solid (96% yield, 3.88 g); mp 148–149 °C; $[\alpha]_{\text{D}}^{20} = -90.7$ (*c* 1.13, in CHCl_3); ^1H NMR (400 MHz, CDCl_3) $\delta = 7.48$ – 6.87 (m, 25 H), 5.16 (s, 1 H), 4.44 (dd, *J* = 6.4, 2.8 Hz, 1 H), 3.68–63 (m, 1 H), 3.09–3.02 (m, 1 H), 1.71–1.64 (m, 1 H), 1.29–1.21 (m, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 147.0, 146.2, 142.8, 130.1, 129.5, 128.3, 128.0, 127.6, 127.4, 126.3, 126.1, 126.0, 125.6, 125.4, 77.9, 76.4, 67.2, 46.5, 19.3$ ppm; IR (KBr pellet) 3531, 3400, 3084, 3056, 3027, 2958, 2880, 1736, 1596, 1489, 1446, 1030, 743, 689 cm^{-1} ; MS (ESI) $m/z = 481.8$ $[\text{M} + \text{H}]^+$, 504.1 $[\text{M} + \text{Na}]^+$, 243.3 $[\text{CPh}_3]^+$; HRMS (ESI) m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{35}\text{H}_{31}\text{NNaO}$ 504.233, found 504.2305. Anal. Calcd for $\text{C}_{35}\text{H}_{31}\text{NO}$: C, 87.28; H, 6.49; N, 2.91. Found: C, 87.03; H, 6.55; N, 2.91.

(S)-Azetidino-2-yl(diphenyl)methanol 8. (S)-*N*-Tritylazetidino-2-yl(diphenyl)methanol **7** (3.05 g, 6.34 mmol) was dissolved in 37 mL mixture of CH_3OH , H_2O and H_2SO_4 in ratio of 60:8:3. The reaction mixture was stirred for 48 h at room temperature, and a white precipitate was produced. The solution was cooled to 0 °C before being quenched with 30 mL of H_2O . After filtration, NaOH 30% was added slowly to the aqueous phase until pH = 12–13. The solution was extracted with ethyl acetate (3×50 mL). The combined organic phases were washed with brine (60 mL) and dried over Na_2SO_4 . After filtration, the solvent was removed under reduced pressure by using a rotary evaporator. The resulting residue was purified by flash chromatography with dichloromethane/ethyl acetate (100:5) to afford the desired product (S)-azetidino-2-yl(diphenyl)methanol **8** as a white solid (95% yield, 1.44 g); mp 103.0–103.2 °C; $[\alpha]_{\text{D}}^{20} = -34.5$ (*c* 0.47, in CHCl_3) [lit.²⁸ mp 103.0–105 °C; $[\alpha]_{\text{D}}^{20} = -32.9$ (*c* 0.99, in CHCl_3)]; ^1H NMR (400 MHz, CDCl_3) $\delta = 7.45$ – 7.18 (m, 10 H), 4.91 (t, *J* = 8.0 Hz, 1 H), 3.66–3.60 (m, 1 H), 3.22–3.17 (m, 1 H), 2.41–2.36 (m, 1 H), 1.99–1.94 (m, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 146.5, 143.5, 128.1, 128.0, 126.7, 126.6, 126.2, 126.0, 77.4, 64.8, 42.4, 22.0$ ppm; IR (KBr pellet) 3323, 3057, 2953, 2878, 1489, 1446, 1384, 1328, 1173, 972, 867, 748, 699, 637 cm^{-1} ; MS (ESI) $m/z = 238.5$ $[\text{M} + \text{H}]^+$, 261.9 $[\text{M} + \text{Na}]^+$.

Ligand (S,S)-1. To a stirred and cooled solution of (S)-**8** (432 mg, 1.8 mmol) and K_2CO_3 (104 mg, 7.2 mmol) in dry DMF (3 mL) was added 2,6-bis(bromomethyl)-*p*-cresol (264.6 mg, 0.9 mmol) in one portion. The ice bath was removed after the addition, and the resulting solution was allowed to stir for 24 h at room temperature. The reaction mixture was diluted with water (10 mL) and ethyl acetate (10 mL). The phases were separated, and the aqueous phase was extracted with ethyl acetate (3×10 mL). The combined organic phases were washed with brine (10 mL) three times and dried over Na_2SO_4 , and after filtration the solvent was removed under reduced pressure. The resulting residue was purified by column chromatography on silica gel using petroleum ether/ethyl acetate (5:1) to give a white crusty foam

(S,S)-**1** (90% yield, 497 mg); mp 72.7–73.9 °C; $[\alpha]_{\text{D}}^{20} = +45$ (*c* 0.414, in CHCl_3); ^1H NMR (400 MHz, CDCl_3) $\delta = 7.58$ – 7.55 (d, *J* = 8.0 Hz, 4 H) 7.45–7.44 (d, *J* = 8.0 Hz, 4 H), 7.32–7.11 (m, 12 H), 6.56 (s, 2 H), 4.40–4.36 (m, 2 H), 3.26–3.19 (m, 4 H), 3.07–3.04 (d, *J* = 13.2 Hz, 2 H), 2.9–2.84 (m, 2 H), 2.29–2.18 (m, 2 H), 2.12 (s, 3 H), 2.07–2.02 (m, 2 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 152.5, 146.0, 144.1, 128.6, 128.3, 128.2, 127.4, 126.9, 126.8, 125.9, 125.9, 122.2, 77.3, 72.7, 57.8, 50.3, 20.4, 19.4$ ppm; IR (KBr pellet) 3432, 3057, 3025, 2960, 2857, 1733, 1599, 1475, 1447, 1168, 988, 866, 746, 700. MS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{41}\text{H}_{42}\text{N}_2\text{O}_3$ 611.7, found 611.4; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{41}\text{H}_{42}\text{N}_2\text{O}_3$ 611.3274, found 611.3270.

(R,R)-**1** was synthesized using the same procedures from the starting source of chirality D-(–)-methionine, enantiomer of **3**.

General Procedure for the Asymmetric Friedel–Crafts Alkylations of Pyrrole with Chalcones. In a flame-dried Schlenk tube, a solution of diethylzinc (0.075 mL, 1.0 mol L^{-1} in hexane, 0.075 mmol) was added to a solution of the chiral ligand (S,S)-**1** (22.9 mg, 0.0375 mmol) in dry THF (1.0 mL) under nitrogen. The mixture was stirred at room temperature for 30 min, and then the pyrrole substrate 52 μL (0.75 mmol) and the chalcone substrate (0.25 mmol) were added. Then the reaction mixture was stirred at 20 °C for 24 h. The mixture was quenched with water (1 mL), and the aqueous phase was extracted with diethyl ether (4×3 mL). The combined organic layers were washed with brine and dried over magnesium sulfate. The solvent was removed under reduced pressure by using a rotary evaporator. The residue was purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product **13**.

(S)-1,3-Diphenyl-3-(1*H*-pyrrol-2-yl)propan-1-one (13a). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: >99% yield (69 mg); 99% ee; $[\alpha]_{\text{D}}^{20} = -3.9$ (*c* 0.63, CHCl_3); the ee value was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 5/95, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 12.458 min, t_{R} (minor) = 14.300 min; ^1H NMR (400 MHz, CDCl_3) $\delta = 8.41$ (brs, 1 H), 8.12–7.96 (m, 2 H), 7.65 (t, *J* = 7.3 Hz, 1 H), 7.53 (t, *J* = 7.7 Hz, 2 H), 7.41 (d, *J* = 4.0 Hz, 4 H), 7.37–7.31 (m, 1 H), 6.73 (d, *J* = 1.3 Hz, 1 H), 6.19 (dd, *J* = 5.5, 2.7 Hz, 1 H), 5.97 (s, 1 H), 4.96–4.81 (m, 1 H), 3.90 (dd, *J* = 17.5, 8.0 Hz, 1 H), 3.69 (dd, *J* = 17.5, 5.7 Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 199.0, 143.0, 136.8, 134.5, 133.3, 128.6, 128.6, 128.1, 128.0, 126.8, 117.2, 107.8, 105.4, 45.2, 39.3$ ppm; IR (KBr pellet) 3379, 3360, 3327, 2893, 1681, 1596, 1579, 1493, 1449, 750, 700 cm^{-1} .

(S)-1-(4-Fluorophenyl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propan-1-one (13b). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil: >99% yield (74 mg); 99% ee; $[\alpha]_{\text{D}}^{20} = -1.5$ (*c* 0.73, CHCl_3); the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (minor) = 12.992 min, t_{R} (major) = 14.858 min; ^1H NMR (400 MHz, CDCl_3) $\delta = 8.27$ (bs, 1 H), 8.08–7.85 (m, 2 H), 7.35–7.26 (m, 4 H), 7.26–7.20 (m, 1 H), 7.09 (t, *J* = 8.6 Hz, 2 H), 6.63 (d, *J* = 1.4 Hz, 1 H), 6.08 (dd, *J* = 5.7, 2.8 Hz, 1 H), 5.86 (s, 1 H), 4.76 (dd, *J* = 7.5, 6.2 Hz, 1 H), 3.76 (dd, *J* = 17.4, 8.0 Hz, 1 H), 3.55 (dd, *J* = 17.4, 5.7 Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 197.5, 167.2/164.6$ (*J* = 253.5 Hz), 143.0, 134.4, 133.4/133.4 (*J* = 2.5 Hz), 130.9/130.8 (*J* = 9.3 Hz), 128.8, 128.1, 127.0, 117.3, 115.9/115.7 (*J* = 21.6 Hz), 108.0, 105.5, 45.2, 39.5 ppm; IR (KBr pellet) 3385, 3063, 3028, 2899, 1682, 1597, 1506, 1453, 838, 703 cm^{-1} .

(S)-1-(4-Chlorophenyl)-3-phenyl-3-(1*H*-pyrrol-2-yl)propan-1-one (13c). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil: >99% yield (78 mg); 98% ee; $[\alpha]_{\text{D}}^{20} = +1.1$ (*c* 0.70, CHCl_3); the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (minor) = 11.850 min, t_{R} (major) = 13.467 min; ^1H NMR (400 MHz, CDCl_3) $\delta = 8.28$ (brs, 1 H), 7.90 (d, *J* = 8.3 Hz, 2 H), 7.44 (d, *J* = 8.4 Hz, 2 H), 7.35 (q, *J* = 8.0 Hz, 4 H), 7.30–7.25 (m, 1 H), 6.67 (s, 1 H), 6.13 (d, *J* = 2.6 Hz, 1 H), 5.91 (s, 1 H), 4.89–4.70 (m, 1 H), 3.80 (dd, *J* = 17.5, 7.9 Hz, 1 H), 3.58 (dd, *J* = 17.4, 5.8 Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR

(100 MHz, CDCl₃) δ = 197.8, 142.9, 139.8, 135.2, 134.3, 129.6, 129.0, 128.8, 128.1, 127.0, 117.3, 108.0, 105.5, 45.3, 39.5 ppm; IR (KBr pellet) 3385, 3060, 3028, 2898, 1684, 1589, 1570, 1490, 1453, 703 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆ClNO 310.0993, found 310.0994.

(S)-1-(4-Bromophenyl)-3-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13d). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil: >99% yield (89 mg); 99% ee; [α]_D²⁰ = -4.2 (c 0.86, CHCl₃); the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (minor) = 12.817 min, t_R (major) = 14.567 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.29 (brs, 1 H), 7.90 (d, J = 8.5 Hz, 2 H), 7.44 (d, J = 8.5 Hz, 2 H), 7.40–7.31 (m, 4 H), 7.31–7.25 (m, 1 H), 6.67 (d, J = 1.3 Hz, 1 H), 6.14 (dd, J = 5.6, 2.8 Hz, 1 H), 5.92 (s, 1 H), 4.90–4.75 (m, 1 H), 3.80 (dd, J = 17.5, 7.9 Hz, 1 H), 3.59 (dd, J = 17.5, 5.8 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 197.8, 142.9, 139.8, 135.2, 134.3, 129.6, 129.0, 128.8, 128.1, 127.0, 117.4, 108.0, 105.5, 45.3, 39.4 ppm; IR (KBr pellet) 3387, 3095, 3060, 2898, 1685, 1586, 1491, 1453, 830, 719, 703 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆BrNO 354.0488, found 354.0492.

(S)-3-Phenyl-3-(1H-pyrrol-2-yl)-1-(*p*-tolyl)propan-1-one (13e). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 54% yield (39 mg); 98% ee; [α]_D²⁰ = -13.5 (c 0.55, CHCl₃); the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (minor) = 11.825 min, t_R (major) = 14.192 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.37 (brs, 1 H), 7.88 (d, J = 8.2 Hz, 2 H), 7.35–7.31 (m, 4 H), 7.29–7.24 (m, 3 H), 6.67 (dd, J = 4.0, 2.5 Hz, 1 H), 6.10 (dd, J = 5.8, 2.8 Hz, 1 H), 5.89–5.81 (m, 1 H), 4.80 (dd, J = 8.1, 5.4 Hz, 1 H), 3.81 (dd, J = 17.5, 8.2 Hz, 1 H), 3.59 (dd, J = 17.5, 5.4 Hz, 1 H), 2.41 (d, J = 10.4 Hz, 3 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 198.8, 144.2, 143.1, 134.8, 134.4, 129.4, 128.7, 128.3, 128.2, 126.9, 117.2, 107.8, 105.5, 45.2, 39.4, 21.7 ppm; IR (KBr pellet) 3380, 3060, 3028, 2921, 1678, 1606, 1493, 1453, 816, 702 cm⁻¹.

(S)-1-(3-Chlorophenyl)-3-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13f). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a white solid: mp 141–142 °C; >99% yield (78 mg); 98% ee; [α]_D²⁰ = +3.6 (c 0.52, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 14.592 min, t_R (minor) = 16.625 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.23 (s, 1 H), 7.93 (d, J = 1.5 Hz, 1 H), 7.83 (dd, J = 7.8, 0.8 Hz, 1 H), 7.59–7.50 (m, 1 H), 7.45–7.37 (m, 1 H), 7.37–7.29 (m, 4 H), 7.30–7.23 (m, 1 H), 6.67 (s, 1 H), 6.12 (s, 1 H), 5.91 (s, 1 H), 4.79 (t, J = 6.7 Hz, 1 H), 3.94–3.71 (m, 1 H), 3.68–3.44 (m, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 202.3, 147.3, 142.9, 139.6, 138.8, 137.8, 134.6, 133.4, 132.8, 132.7, 131.6, 130.8, 121.9, 112.6, 110.04, 49.9, 43.9 ppm; IR (KBr pellet) 3377, 3088, 3064, 2889, 1674, 1569, 1497, 1450, 774, 723, 706 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆ClNO 310.0993, found 310.1001.

(S)-1-(3-Bromophenyl)-3-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13g). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a white solid: mp 124–126 °C; >99% yield (89 mg); 99% ee; [α]_D²⁰ = +4.6 (c 0.83, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 15.258 min, t_R (minor) = 17.267 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.17 (brs, 1 H), 8.04 (s, 1 H), 7.83 (d, J = 7.8 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.34–7.25 (m, 5 H), 7.22 (t, J = 6.6 Hz, 1 H), 6.62 (s, 1 H), 6.08 (d, J = 2.7 Hz, 1 H), 5.86 (s, 1 H), 4.85–4.64 (m, 1 H), 3.74 (dd, J = 17.6, 7.9 Hz, 1 H), 3.53 (dd, J = 17.5, 5.8 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 202.2, 147.3, 143.1, 140.8, 138.8, 135.8, 134.9, 133.4, 132.7, 131.6, 131.2, 127.6, 121.9, 112.6, 110.0, 49.9, 43.9 ppm; IR (KBr pellet) 3379, 3086, 3061, 3028, 2890, 1676, 1566, 1496, 1449, 771, 722 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆BrNO 354.0488, found 354.0491.

(S)-1-(2-Chlorophenyl)-3-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13h). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 59% yield (46 mg); 99% ee; [α]_D²⁰ = +17.4 (c 0.68, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 11.658 min, t_R (minor) = 16.167 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.07 (brs, 1 H), 7.40–7.30 (m, 2 H), 7.30–7.16 (m, 7 H), 6.61 (s, 1 H), 6.08 (dd, J = 5.4, 2.6 Hz, 1 H), 5.89 (s, 1 H), 4.68 (t, J = 7.2 Hz, 1 H), 3.72 (dd, J = 17.3, 7.9 Hz, 1 H), 3.58 (dd, J = 17.3, 6.4 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 202.2, 142.5, 139.4, 133.9, 131.8, 130.8, 130.5, 129.1, 128.7, 128.1, 127.0, 126.9, 117.3, 108.0, 105.6, 49.5, 40.0 ppm; IR (KBr pellet) 3386, 3061, 3026, 2965, 2927, 1682, 1600, 1569, 1490, 1454, 755, 720 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆ClNO 310.0993, found 310.0997.

(S)-3-(4-Chlorophenyl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13i). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: >99% yield (78 mg); 98% ee; [α]_D²⁰ = -5.4 (c 0.74, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 12.825 min, t_R (minor) = 14.658 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.40 (brs, 1 H), 7.98 (d, J = 8.2 Hz, 2 H), 7.65–7.56 (m, 1 H), 7.49 (t, J = 7.1 Hz, 2 H), 7.37–7.22 (m, 4 H), 6.69 (s, 1 H), 6.14 (s, 1 H), 5.90 (s, 1 H), 4.80 (t, J = 6.7 Hz, 1 H), 3.82 (ddd, J = 17.5, 7.6, 1.1 Hz, 1 H), 3.61 (ddd, J = 17.6, 5.9, 1.1 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 198.7, 141.4, 136.6, 133.9, 133.4, 132.4, 129.4, 128.6, 128.6, 128.0, 117.3, 107.8, 105.4, 45.0, 38.6 ppm; IR (KBr pellet) 3383, 3098, 3061, 2899, 1682, 1596, 1579, 1490, 1448, 829, 758, 720, 690 cm⁻¹.

(S)-3-(4-Bromophenyl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13j). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: >99% yield (89 mg); >99% ee; [α]_D²⁰ = -7.3 (c 0.88, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 13.900 min, t_R (minor) = 15.817 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.39 (brs, 1 H), 7.98 (d, J = 7.5 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 7.48 (dd, J = 15.0, 8.0 Hz, 4 H), 7.21 (d, J = 8.3 Hz, 2 H), 6.69 (d, J = 1.3 Hz, 1 H), 6.14 (dd, J = 5.7, 2.8 Hz, 1 H), 5.90 (s, 1 H), 4.78 (t, J = 6.8 Hz, 1 H), 3.82 (dd, J = 17.6, 7.7 Hz, 1 H), 3.60 (dd, J = 17.6, 6.0 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 203.4, 146.7, 141.3, 138.5, 138.1, 136.3, 134.5, 133.3, 132.7, 125.3, 122.1, 112.6, 110.2, 49.6, 43.4 ppm; IR (KBr pellet) 3382, 3097, 3060, 2899, 1681, 1596, 1579, 1487, 1448, 818, 718, 689 cm⁻¹; HRMS (ESI) m/z [M + H]⁺ calcd for C₁₉H₁₆BrNO 354.0488, found 354.0487.

(S)-3-(3-Chlorophenyl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13k). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil; >99% yield (78 mg); 99% ee; [α]_D²⁰ = -8.8 (c 0.77, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 12.117 min, t_R (minor) = 14.758 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.41 (brs, 1 H), 7.99 (d, J = 7.3 Hz, 2 H), 7.60 (t, J = 7.4 Hz, 1 H), 7.49 (t, J = 7.7 Hz, 2 H), 7.34 (s, 1 H), 7.30–7.18 (m, 3 H), 6.69 (d, J = 1.2 Hz, 1 H), 6.25–6.07 (m, 1 H), 5.90 (s, 1 H), 4.87–4.73 (m, 1 H), 3.83 (dd, J = 17.7, 7.9 Hz, 1 H), 3.61 (dd, J = 17.7, 5.7 Hz, 1 H) ppm; ¹³C{¹H} NMR (100 MHz, CDCl₃) δ = 198.7, 145.2, 136.7, 134.5, 133.8, 133.5, 130.0, 128.8, 128.3, 128.2, 127.1, 126.4, 117.6, 108.0, 105.7, 45.1, 39.1 ppm; IR (KBr pellet) 3384, 3095, 3061, 2900, 1685, 1596, 1572, 1474, 1448, 788, 758, 719, 689 cm⁻¹.

(S)-3-(3-Bromophenyl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13l). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil: >99% yield (89 mg); 98% ee; [α]_D²⁰ = -5.3 (c 0.86, CHCl₃); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min⁻¹, λ = 254 nm), t_R (major) = 12.367 min, t_R (minor) = 15.483 min; ¹H NMR (400 MHz, CDCl₃) δ = 8.35 (brs, 1 H), 7.92 (d, J = 7.6 Hz, 2 H), 7.54 (t, J = 7.3 Hz, 1 H), 7.48–7.38 (m, 3 H), 7.33 (d, J = 7.8 Hz, 1 H), 7.21 (d, J =

7.8 Hz, 1 H), 7.14 (t, $J = 7.8$ Hz, 1 H), 6.62 (d, $J = 1.2$ Hz, 1 H), 6.07 (dd, $J = 5.6, 2.8$ Hz, 1 H), 5.83 (s, 1 H), 4.72 (dd, $J = 7.5, 6.0$ Hz, 1 H), 3.76 (dd, $J = 17.7, 8.0$ Hz, 1 H), 3.53 (dd, $J = 17.7, 5.6$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 45.5, 136.7, 133.8, 133.6, 131.2, 130.3, 130.1, 128.8, 128.2, 126.9, 122.8, 117.6, 108.0, 105.7, 45.1, 39.1 ppm; IR (KBr pellet) 3382, 3098, 3059, 2900, 1682, 1595, 1579, 1473, 1448, 787, 757, 719, 691 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{BrNO}$ 354.0488, found 354.0491.

(S)-3-(2-Chlorophenyl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13m). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as colorless oil: 99% yield (78 mg); 98% ee; $[\alpha]_{\text{D}}^{20} = +12.7$ (c 0.39, CHCl_3); the ee was determined by HPLC analysis using a chiral AD column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (minor) = 12.950 min, t_{R} (major) = 24.842 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.49 (brs, 1 H), 8.03 (d, $J = 7.5$ Hz, 2 H), 7.62 (t, $J = 7.4$ Hz, 1 H), 7.51 (t, $J = 7.7$ Hz, 2 H), 7.45 (dd, $J = 7.7, 1.0$ Hz, 1 H), 7.34 (dd, $J = 7.6, 1.5$ Hz, 1 H), 7.28 (d, $J = 6.6$ Hz, 1 H), 7.23 (td, $J = 7.5, 1.7$ Hz, 1 H), 6.71 (d, $J = 1.3$ Hz, 1 H), 6.14 (dd, $J = 5.6, 2.7$ Hz, 1 H), 5.92 (s, 1 H), 5.37 (dd, $J = 9.0, 4.7$ Hz, 1 H), 3.89 (dd, $J = 17.6, 9.0$ Hz, 1 H), 3.63 (dd, $J = 17.6, 4.7$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 203.0, 145.3, 141.3, 138.2, 138.0, 137.7, 134.5, 133.7, 133.3, 132.8, 132.6, 131.8, 121.9, 112.6, 110.2, 48.5, 40.4 ppm; IR (KBr pellet) 3382, 3098, 3062, 2900, 1674, 1595, 1571, 1448, 767, 760, 716, 687 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{16}\text{ClNO}$ 310.0993, found 310.0997.

(S)-1-Phenyl-3-(1H-pyrrol-2-yl)-3-(*p*-tolyl)propan-1-one (13n). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a white solid: mp 102–104 °C; 94% yield (68 mg); 98% ee; $[\alpha]_{\text{D}}^{20} = -6.3$ (c 0.60, CHCl_3); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 5/95, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 13.789 min, t_{R} (minor) = 15.933 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.35 (brs, 1 H), 8.01 (d, $J = 7.8$ Hz, 2 H), 7.61 (t, $J = 7.3$ Hz, 1 H), 7.50 (t, $J = 7.6$ Hz, 2 H), 7.26 (d, $J = 7.8$ Hz, 2 H), 7.19 (d, $J = 7.8$ Hz, 2 H), 6.69 (s, 1 H), 6.16 (d, $J = 2.7$ Hz, 1 H), 5.94 (s, 1 H), 4.81 (t, $J = 6.8$ Hz, 1 H), 3.85 (dd, $J = 17.5, 7.9$ Hz, 1 H), 3.64 (dd, $J = 17.5, 5.8$ Hz, 1 H), 2.39 (s, 3 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 199.2, 140.1, 137.0, 136.5, 134.9, 133.4, 129.5, 128.7, 128.2, 128.1, 117.2, 107.9, 105.4, 45.4, 39.0, 21.2 ppm; IR (KBr pellet) 3377, 3007, 2969, 2895, 1667, 1595, 1579, 1515, 1451, 819, 749, 713 cm^{-1} .

(S)-1-Phenyl-3-(1H-pyrrol-2-yl)-3-(*m*-tolyl)propan-1-one (13o). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 67% yield (48 mg); 98% ee; the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 9.925 min, t_{R} (minor) = 11.592 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.37 (brs, 1 H), 8.03 (d, $J = 7.5$ Hz, 2 H), 7.63 (t, $J = 7.4$ Hz, 1 H), 7.52 (t, $J = 7.7$ Hz, 2 H), 7.29 (t, $J = 7.4$ Hz, 1 H), 7.19 (d, $J = 7.6$ Hz, 2 H), 7.13 (d, $J = 7.3$ Hz, 1 H), 6.71 (d, $J = 1.4$ Hz, 1 H), 6.17 (d, $J = 2.7$ Hz, 1 H), 5.94 (s, 1 H), 4.83 (dd, $J = 7.5, 6.1$ Hz, 1 H), 3.88 (dd, $J = 17.5, 8.1$ Hz, 1 H), 3.66 (dd, $J = 17.5, 5.6$ Hz, 1 H), 2.40 (s, 3 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 3.0, 138.3, 137.0, 134.7, 133.3, 128.9, 128.7, 128.6, 128.2, 127.7, 125.1, 117.2, 107.9, 105.4, 45.3, 39.3, 21.6 ppm; IR (KBr pellet) 3385, 3099, 3057, 3025, 2919, 1682, 1597, 1580, 1489, 1448, 787, 762, 717, 691 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{20}\text{H}_{19}\text{NO}$ 290.1539, found 290.1543.

(S)-3-(Naphthalen-2-yl)-1-phenyl-3-(1H-pyrrol-2-yl)propan-1-one (13p). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 94% yield (76 mg); >99% ee; $[\alpha]_{\text{D}}^{20} = -5.4$ (c 0.73, CHCl_3); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 18.458 min, t_{R} (minor) = 20.933 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.19 (brs, 1 H), 8.16–8.09 (m, 1 H), 7.92 (d, $J = 8.0$ Hz, 2 H), 7.83 (dd, $J = 5.8, 3.5$ Hz, 1 H), 7.72 (d, $J = 7.7$ Hz, 1 H), 7.50 (t, $J = 7.3$ Hz, 1 H), 7.46–7.31 (m, 6 H), 6.54 (s, 1 H), 6.03 (d, $J = 2.5$ Hz, 1 H), 5.83 (s, 1 H), 5.61 (dd, $J = 9.0, 4.0$ Hz, 1 H), 3.95 (dd, $J = 17.7, 9.1$

Hz, 1 H), 3.60 (dd, $J = 17.7, 4.1$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 203.5, 143.6, 141.4, 138.7, 138.7, 138.0, 136.1, 133.6, 133.3, 132.8, 132.2, 131.1, 130.4, 130.1, 129.9, 128.1, 121.8, 112.5, 110.4, 49.5, 39.5 ppm; IR (KBr pellet) 3431, 3058, 2901, 1679, 1596, 1579, 1509, 1448, 760, 689 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{23}\text{H}_{19}\text{NO}$ 326.1539, found 326.1543.

(S)-3-(2-Chlorophenyl)-1-(4-chlorophenyl)-3-(1H-pyrrol-2-yl)propan-1-one (13q). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 99% yield (86 mg); 98% ee; $[\alpha]_{\text{D}}^{20} = +15.2$ (c 0.60, CHCl_3); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 12.950 min, t_{R} (minor) = 16.192 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.31 (brs, 1 H), 7.82 (d, $J = 8.5$ Hz, 2 H), 7.41–7.29 (m, 3 H), 7.14 (m, 3 H), 6.58 (d, $J = 1.3$ Hz, 1 H), 6.02 (dd, $J = 5.6, 2.8$ Hz, 1 H), 5.80 (s, 1 H), 5.21 (dd, $J = 9.0, 4.8$ Hz, 1 H), 3.72 (dd, $J = 17.5, 9.1$ Hz, 1 H), 3.45 (dd, $J = 17.5, 4.8$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 201.8, 145.1, 144.47, 139.6, 138.1, 137.4, 134.5, 134.2, 133.7, 133.6, 132.7, 131.8, 122.0, 112.6, 110.2, 48.4, 40.5 ppm; IR (KBr pellet) 3383, 3097, 3063, 2923, 1682, 1589, 1570, 1487, 1442, 830, 749, 722 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{15}\text{Cl}_2\text{NO}$ 344.0603, found 344.0602.

(S)-3-(3-Bromophenyl)-1-(4-fluorophenyl)-3-(1H-pyrrol-2-yl)propan-1-one (13r). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: >99% yield (93 mg); 99% ee; $[\alpha]_{\text{D}}^{20} = -3.4$ (c 0.92, CHCl_3); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 5/95, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 26.758 min, t_{R} (minor) = 32.117 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.34 (brs, 1 H), 8.00 (dd, $J = 8.7, 5.4$ Hz, 2 H), 7.47 (s, 1 H), 7.39 (d, $J = 7.8$ Hz, 1 H), 7.26 (d, $J = 8.9$ Hz, 1 H), 7.21 (d, $J = 7.7$ Hz, 1 H), 7.15 (dd, $J = 16.1, 7.6$ Hz, 2 H), 6.68 (d, $J = 1.1$ Hz, 1 H), 6.12 (dd, $J = 5.5, 2.7$ Hz, 1 H), 5.88 (s, 1 H), 4.76 (dd, $J = 7.3, 6.1$ Hz, 1 H), 3.78 (dd, $J = 17.6, 8.0$ Hz, 1 H), 3.55 (dd, $J = 17.6, 5.6$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 197.0, 167.2/164.7 ($J = 253.8$ Hz), 145.3, 133.6, 133.2/133.2 ($J = 2.8$ Hz), 131.1, 130.9/130.8 ($J = 9.3$ Hz), 130.3, 130.1, 126.8, 122.8, 117.6, 116.0/115.8 ($J = 21.7$ Hz), 115.8, 108.1, 105.8, 45.0, 39.1 ppm; IR (KBr pellet) 3385, 3066, 2900, 1681, 1595, 1567, 1506, 1473, 839, 787, 719 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{Na}]^+$ calcd for $\text{C}_{19}\text{H}_{13}\text{BrFNO}$ 394.0213, found 394.0219.

(S)-3-(3-Bromophenyl)-1-(4-bromophenyl)-3-(1H-pyrrol-2-yl)propan-1-one (13s). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a pale yellow oil: >99% yield (109 mg); 99% ee; $[\alpha]_{\text{D}}^{20} = -2.0$ (c 1.08, CHCl_3); the ee was determined by HPLC analysis using a chiral OD-H column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (major) = 19.275 min, t_{R} (minor) = 24.292 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.27 (brs, 1 H), 7.82–7.73 (m, 2 H), 7.61–7.51 (m, 2 H), 7.42 (s, 1 H), 7.34 (d, $J = 7.7$ Hz, 1 H), 7.23–7.18 (m, 1 H), 7.15 (t, $J = 7.6$ Hz, 1 H), 6.63 (s, 1 H), 6.07 (d, $J = 2.5$ Hz, 1 H), 5.84 (s, 1 H), 4.76–4.65 (m, 1 H), 3.72 (dd, $J = 17.6, 7.9$ Hz, 1 H), 3.48 (dd, $J = 17.6, 5.6$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 202.1, 149.9, 140.0, 138.0, 136.6, 135.7, 134.9, 134.7, 134.2, 133.3, 131.4, 127.4, 122.2, 112.7, 110.3, 49.5, 43.6 ppm; IR (KBr pellet) 3385, 3095, 3059, 2899, 1681, 1585, 1567, 1473, 1427, 827, 786, 719 cm^{-1} ; HRMS (ESI) m/z $[\text{M} + \text{H}]^+$ calcd for $\text{C}_{19}\text{H}_{15}\text{Br}_2\text{NO}$ 431.9593, found 431.9600.

(S)-3-(4-Chlorophenyl)-1-(4-fluorophenyl)-3-(1H-pyrrol-2-yl)propan-1-one (13t). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: >99% yield (82 mg); 99% ee; $[\alpha]_{\text{D}}^{20} = -1.5$ (c 0.81, CHCl_3); the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_{R} (minor) = 14.800 min, t_{R} (major) = 19.275 min; ^1H NMR (400 MHz, CDCl_3) δ = 8.27 (brs, 1 H), 8.02–7.84 (m, 2 H), 7.22 (dd, $J = 20.3, 8.3$ Hz, 4 H), 7.09 (t, $J = 8.4$ Hz, 2 H), 6.63 (s, 1 H), 6.07 (d, $J = 2.3$ Hz, 1 H), 5.83 (s, 1 H), 4.72 (t, $J = 6.7$ Hz, 1 H), 3.72 (dd, $J = 17.5, 7.7$ Hz, 1 H), 3.50 (dd, $J = 17.4, 5.8$ Hz, 1 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ = 197.1, 167.2/164.7 ($J = 254.1$ Hz),

141.4, 133.9, 133.2/133.2 ($J = 2.4$ Hz), 132.6, 130.9/130.8 ($J = 9.2$ Hz), 129.5, 128.9, 117.5, 116.0/115.8 ($J = 21.8$ Hz), 108.0, 105.6, 45.0, 38.8 ppm; IR (KBr pellet) 3384, 3100, 2900, 1682, 1597, 1489, 838, 721 cm^{-1} ; HRMS (ESI) m/z $[M + H]^+$ calcd for $\text{C}_{19}\text{H}_{15}\text{ClFNO}$ 328.0899, found 328.0901.

(S)-3-(4-Chlorophenyl)-3-(1H-pyrrol-2-yl)-1-(p-tolyl)propan-1-one (13u). Purified by flash chromatography with petroleum ether/ethyl acetate (5/1) to afford the desired product as a colorless oil: 70% yield (57 mg); 99% ee; the ee was determined by HPLC analysis using a chiral AS column (*i*-PrOH/hexane = 10/90, flow rate = 1.0 mL min^{-1} , $\lambda = 254$ nm), t_R (minor) = 12.275 min, t_R (major) = 17.767 min; ^1H NMR (400 MHz, CDCl_3) $\delta = 8.44$ (brs, 1 H), 7.88 (d, $J = 8.0$ Hz, 2 H), 7.28 (q, $J = 8.4$ Hz, 6 H), 6.69 (s, 1 H), 6.13 (d, $J = 2.6$ Hz, 1 H), 5.87 (s, 1 H), 4.79 (t, $J = 6.7$ Hz, 1 H), 3.79 (dd, $J = 17.5$, 7.8 Hz, 1 H), 3.58 (dd, $J = 17.5$, 5.8 Hz, 1 H), 2.44 (s, 3 H) ppm; $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) $\delta = 198.5$, 144.4, 141.7, 134.3, 134.2, 132.5, 129.6, 129.5, 128.8, 128.3, 117.5, 108.0, 105.6, 45.0, 38.8, 21.8 ppm; IR (KBr pellet) 3381, 3097, 3030, 2920, 1674, 1606, 1571, 1489, 814, 719 cm^{-1} ; HRMS (ESI) m/z $[M + H]^+$ calcd for $\text{C}_{20}\text{H}_{18}\text{ClNO}$ 324.1150, found 324.1153.

■ ASSOCIATED CONTENT

■ Supporting Information

^1H and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra of compounds **1**, **6**, **7**, and **13**; chiral HPLC spectra of compounds **13**, tables giving crystallographic details for compounds **8** and **13g**, crystallographic data for compounds **8** and **13g** (CIF). 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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