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Control of Activation Mode To Achieve Diastereodivergence in Asymmetric Syntheses of Chiral Spiropiperidinone Derivatives

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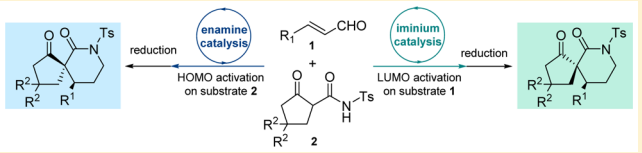
Supporting Information

ABSTRACT: An efficient organocatalytic cascade reaction has been developed involving a Michael−hemiaminalization relay for the asymmetric synthesis of spiropiperidinone derivatives bearing adjacent quaternary and tertiary chiral centers via LUMO or HOMO activation. Importantly, this methodology demonstrates that applying distinct activation modes to different substrates in the same reaction can diverge diastereoselectivity. To our knowledge, this is also one of the few published cases of primary amine catalytic [3 + 3] cycloaddition reactions involving α-branched β-ketoamides.



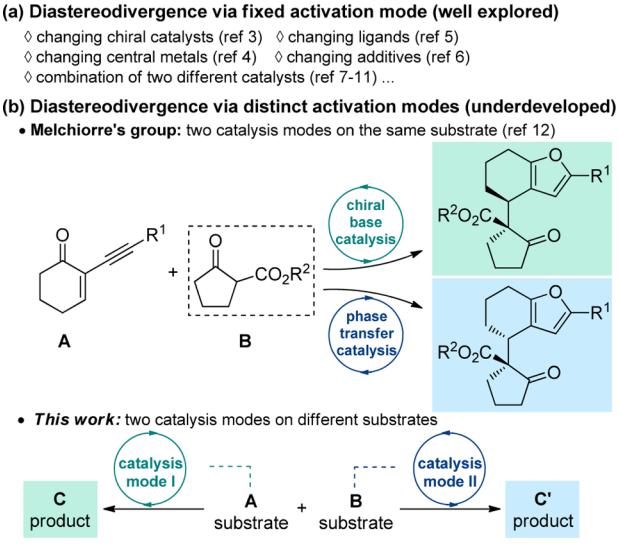
INTRODUCTION

Using enantioselective catalysis to synthesize complex molecules while controlling all stereocenters is crucial for the preparation of natural products and other synthetically important architectures.[1] In these reactions, usually only one of the product diastereomers and the corresponding enantiomer are preferred, and accessing the other complementary diastereomeric products is difficult, especially when multiple stereocenters are generated. This causes a problem in situations in which more than one diastereomer, or different diastereomers, is desired for different purposes.

To address this issue, researchers have recently developed methods to achieve "diastereodivergence", which implies the uncommon ability to selectively generate different possible diastereoisomer products from the same starting materials.[2] Such diastereochemical switching has been achieved in monocatalytic systems[3−6] through the use of different chiral catalysts,[3] central metals,[4] ligands,[5] or additives.[6] In dual catalytic systems,[7−11] different diastereoisomers can be selectively accessed by choosing the appropriate absolute configuration of each chiral catalyst, as demonstrated in work by the groups of MacMillan,[7] Dixon,[8] Carreira,[9] Zhao,[10] and others.[11] To date, it is worth noting that most strategies for diastereodivergence in the literature are based on a fixed activation mode (Scheme 1a). In 2015, Melchiorre exploited distinct catalysis modes of quinine on β-ketoesters, with the quinine derivatives acting as either general base or phase transfer catalyst, achieving a complete reversal of diastereoinduction in asymmetric Michael addition (Scheme 1b).[12] However, it is relatively rare for changing the totally different activation modes on different substrates to invert diastereoselectivity, and it is still a promising field to study.

Optically pure piperidine derivatives bearing multiple functional groups and stereocenters are found in many natural products and biologically active synthetic compounds.[13] Over the past decade, many ingenious organocatalytic approaches have been reported for asymmetrically constructing the chiral piperidine single heterocycle skeleton,[14] but fewer approaches have been published for stereoselective formation of spirocyclic piperidine frameworks.[15,16] Recently, the groups of Rodriguez and Constantieux presented the pioneering work of asymmetric synthesis of spiropiperidines through α-branched β-ketoamide-based [3 + 3] cycloaddition reactions catalyzed by a

Scheme 1. Strategies of Diastereodivergence in Asymmetric Synthesis



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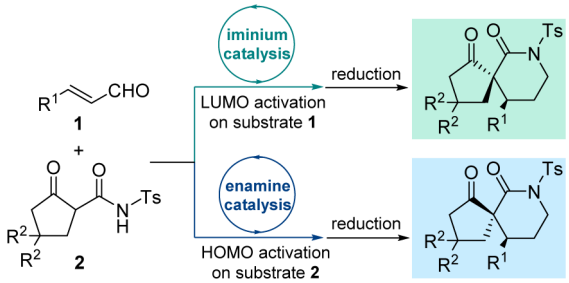
bifunctional thiourea tertiary amine.[16] Despite these advances, the development of efficient asymmetric reactions, especially utilizing other catalytic systems to assemble the synthetically important spiropiperidine scaffolds with high stereocontrol, is still desirable.

Combining our ongoing research on the synthesis of chiral spiroheterocycle compounds with our interest in catalytic diastereodivergence,[17] we report here the enantioselective, diastereocontrolled synthesis of spiropiperidinone scaffolds, in which α,β-unsaturated aldehydes **1** react with α-branched β-ketoamides **2** via two distinct activation modes on different substrates (Scheme 2).

Scheme 2. Activation-Mode-Controlled Diastereodivergence in the Synthesis of Chiral Spirocyclic Peridinones

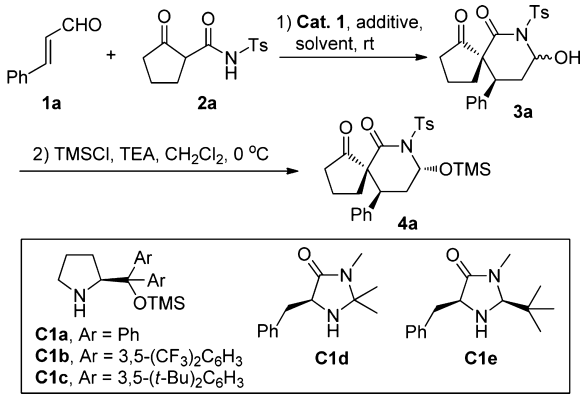


RESULTS AND DISCUSSION

Our preliminary investigations focused on the secondary amine-mediated iminium activation of α,β-unsaturated aldehyde **1**; this LUMO-lowering strategy has been widely employed in catalytic asymmetric synthesis.[18] Initially, the model reaction of cinnamaldehyde **1a** and cyclic β-ketoamide **2a** was explored using the Hayashi–Jørgensen catalyst **C1a**. This process involves the formation of an α,β-unsaturated iminium ion as a bis-electrophile, which participates in a Michael addition and an intramolecular hemiaminalization cascade involving a bis-nucleophilic β-ketoamide. We were gratified to find that the reaction led to the desired hemiaminal product **3a**. Direct protection of the hydroxyl with trimethylchlorosilane gave the corresponding product **4a** in 43% total yield, which is stabler and easier to analyze than **3a**, with good diastereoselectivity and moderate enantioselectivity (Table 1, entry 1). In efforts to enhance enantioselectivity, we did not obtain satisfying results when using other α,α-diphenylprolinol trimethylsilyl ether catalysts (entries 2 and 3), but we succeeded using MacMillan's imidazolidinone catalyst **C1e**[19] in the presence of 20 mol % of trifluoroacetic acid (entry 5). After screening various acidic additives and solvents in an attempt to improve yield (entries 6–10), we found that reaction efficiency was greatest in dichloromethane when benzoic acid was used (entry 10). The substituents on the benzoic acid were surveyed, as well, and benzoic acids with an electron-donating or electron-withdrawing group on the aromatic ring reduced the yields of the product, without obviously affecting stereoselectivities (entries 11 and 12).

Using these optimal conditions (Table 1, entry 10), we investigated the substrate scope and limitations of this [3 + 3] annulation reaction (Table 2). First, various β-aryl enals with diverse substitutions were explored in reactions with *N*-tosyl 2-oxocyclopentanecarboxamide **2a**. In general, reaction efficiency was slightly affected by the position and electronic properties of

Table 1. Optimization of the Secondary Amine-Catalyzed Asymmetric [3 + 3] Cycloaddition Reaction[a]



entry	cat. 1	additive	solvent	yield (%)[b]	dr[c]	ee (%)[d]
1	**C1a**	BzOH	MeCN	43	75:25	40
2	**C1b**	BzOH	MeCN	48	78:22	48
3	**C1c**	BzOH	MeCN	40	80:20	46
4	**C1d**	TFA	MeCN	63	80:20	70
5	**C1e**	TFA	MeCN	68	85:15	82
6	**C1e**	TsOH	MeCN	66	82:18	80
7	**C1e**	AcOH	MeCN	70	85:15	85
8	**C1e**	BzOH	MeCN	70	88:12	90
9	**C1e**	BzOH	THF	66	86:14	88
10	**C1e**	BzOH	CH_2Cl_2	73	88:12	92
11	**C1e**	3-NO_2PhCO$_2$H	CH_2Cl_2	67	88:12	92
12	**C1e**	4-MePhCO$_2$H	CH_2Cl_2	64	86:14	91

[a]Unless noted otherwise, reactions were performed with 0.12 mmol of **1a**, 0.1 mmol of **2a**, 0.02 mmol of catalyst **C1**, and 0.02 mmol of acidic additive in 2 mL of solvent at rt. For the absolute configuration of **4a**, see entry 13 in Table 2. [b]Yield of isolated major isomer **4a** over two steps. [c]Calculated based on ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis of the major diastereoisomer.

electron-deficient and -rich substituents at the *ortho*, *meta*, or *para* positions on the aromatic ring (entries 2–12). The heteroaromatic enal, such as 3-furanyl acrylaldehyde, was tolerated in the reaction, affording the desired product **4m** in 76% yield with good diastereoselectivity and excellent enantioselectivity (entry 13). The less reactive crotonaldehyde also participated in the cycloaddition reaction, giving the alkyl-functionalized product **4n**, albeit with poor stereoselectivity (entry 14). Next we explored the possibility of modifying the 2-oxocyclopentanecarboxamide **2**. Methyl substitutions on the cyclopentanone moiety were well-tolerated, and the desired spiro products bearing two quaternary carbon centers were obtained in good yields with high dr and ee values (entries 15–17). The cyclic β-ketoamide with benzenesulfonyl and methylsulfonyl protecting groups reacted well (entries 18 and 19). In terms of the alkyl protecting group, benzyl was also compatible with this reaction system, generating the product **4t** in good results (entry 20).[20] The hydroxy group of hemiaminal **3a** could be chemoselectively removed using Et_3SiH and $BF_3\cdot Et_2O$ at −10 °C, providing spiropiperidinone **5a** with adjacent quaternary and tertiary chiral centers (Scheme 3).

In the second stage, our explorations focused on the primary amine-mediated enamine activation of cyclic β-ketoamide **2** via a HOMO-raising activation mode. The α-branched β-ketocarbonyl compound in this reaction is considered one of

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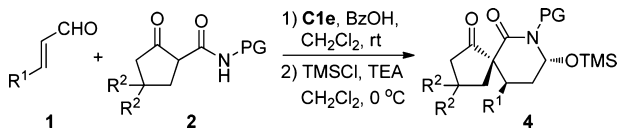
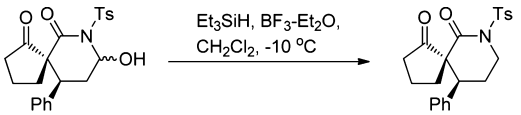
Table 2. Substrate Scope of the Secondary Amine-Catalyzed Asymmetric [3 + 3] Cycloaddition Reaction[a]



entry	R^1	R^2	PG	yield (%)[b]	dr[c]	ee (%)[d]
1	Ph	H	Ts	73 (**4a**)	88:12	92
2	2-FC_6H_4	H	Ts	68 (**4b**)	80:20	94
3	3-FC_6H_4	H	Ts	72 (**4c**)	83:17	94
4	4-FC_6H_4	H	Ts	75 (**4d**)	87:13	97
5	2-ClC_6H_4	H	Ts	66 (**4e**)	79:21	96
6	4-ClC_6H_4	H	Ts	76 (**4f**)	86:14	96
7	4-BrC_6H_4	H	Ts	77 (**4g**)	86:14	97
8	2-$NO_2C_6H_4$	H	Ts	71 (**4h**)	78:22	95
9	4-$NO_2C_6H_4$	H	Ts	78 (**4i**)	85:15	97
10	2-$MeOC_6H_4$	H	Ts	62 (**4j**)	80:20	93
11	4-MeC_6H_4	H	Ts	70 (**4k**)	82:18	93
12	4-$(Me)_2NC_6H_4$	H	Ts	61 (**4l**)	78:22	92
13[e]	2-furyl	H	Ts	76 (**4m**)	88:12	95
14	Me	H	Ts	51 (**4n**)	70:30	55
15	Ph	Me	Ts	69 (**4o**)	84:16	92
16	4-BrC_6H_4	Me	Ts	72 (**4p**)	88:12	93
17	2-furyl	Me	Ts	73 (**4q**)	88:12	93
18	Ph	H	$PhSO_2$	78 (**4r**)	85:15	95
19	Ph	H	$MeSO_2$	77 (**4s**)	90:10	97
20	Ph	H	Bn	72 (**4t**)	85:15	90

[a]See entry 10 and footnote a in Table 1. [b]Yield of isolated major isomer **4** over two steps. [c]Calculated based on ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis of the major diastereoisomer. [e]The absolute configuration of **4m** was determined by X-ray analysis,[21] and other products **4** and **5** were assigned by analogy.

Scheme 3. Reduction the Hydroxy Group of Hemiaminal 3a



74% yield (two steps),
88:12 dr, 95% ee

the most challenging carbonyl substrates in asymmetric aminocatalysis because of steric hindrance and difficulties with chemo- and stereocontrol.[22] Although some asymmetric reactions involving α-substituted β-ketoesters and primary aminocatalysis have been developed since the seminal work of Toste, Carter, Rodriguez, and Luo,[23] synthetic protocols of primary aminocatalysis involving α-branched β-ketoamides are still underdeveloped.[24] We wondered whether enamine activation of cyclic β-ketoamide could be achieved using a chiral primary amine to realize a [3 + 3] cycloaddition reaction[25] and whether this activation mode could be exploited jointly with the secondary amine-mediated iminium activation mode in the first stage of the research to modulate overall diastereoselectivity.

We first probed the feasibility of HOMO activation. ^{1}H NMR analysis of a 1:1 mixture of α-branched β-ketoamide substrate **2a** and chiral primary amine catalyst (*S*)-2-phenylglycine methyl ester **C2a** in deuterated chloroform clearly showed formation of the enaminone intermediate as a single regioisomer. In this intermediate, an intramolecular hydrogen bond may form between the carbonyl group and the secondary enamine N−H, thereby limiting the geometries possible (Figure 1).

In addition, we also needed to avoid competition between the two catalytic cycles in the overall reaction. Since both ketoamides and α,β-unsaturated aldehydes are amenable to aminocatalysis, competition between the two catalytic cycles would complicate stereocontrol. We found that slow addition of enal by syringe pump to the mixture of cyclic β-ketoamide substrate and primary amine catalyst ensured prior formation of enamine intermediate. This allowed the enamine activation mode to dominate in the reaction. The similar strategy has been employed by Luo's group to investigate the primary amine-catalyzed Robinson-type annulation of β-ketoesters with methyl vinyl ketone.[26]

Having confirmed that substrate **2** could be activated with a chiral primary amine, we examined this [3 + 3] cycloaddition reaction via enamine activation. The primary amine catalyst **C2a** at 20 mol % and TFA additive promoted the reaction smoothly (Table 3, entry 1). We were pleased to find that reducing the hydroxyl of the cyclohemiaminal yielded the spiropiperidinone **6a** as the major diastereoisomer, reversing product diastereoselectivity (entry 10 in Table 2 vs entry 1 in Table 3). To improve the somewhat low ee value of product **6a**, we screened primary amine catalysts **C2b**−**C2g** and optimized reaction parameters (Table 3). In the end, the model reaction in the presence of Luo's catalyst **C2g** (20 mol %) in dichloromethane and the additives TFA and 3-nitrobenzoic acid led to the final product **6a** in 70% yield with high enantioselectivity of 84% ee and a reversed diastereoselectivity of 85:15 dr (entry 10). These conditions were therefore chosen for further studies of diastereodivergence in our reaction.

We then evaluated in parallel the two activation modes in the reaction to optimize how to guide the reaction toward complementary diastereochemical outcomes. Cycloaddition between cyclic β-ketoamides and various aromatic enals proceeded well with both catalyst systems, giving the complementary diastereoisomers **5** and **6** in good yields and high or excellent ee values (Table 4). Generally, the enantioselectivity of products **5** controlled by the iminium catalysis is slightly higher than enantioselectivity of products **6** controlled by the enamine catalysis. Moreover, the equally good results were obtained when the cyclic moiety of the β-ketoamide was a six-membered ring instead of a five-membered ring (entry 7).

Next, we explored the possibility of using two opposite pairs of chiral amino catalysts to generate all four stereoisomers of cyclopentanone-fused spiropiperidinones (Scheme 4). From the same starting materials, we used MacMillan's imidazolidinone catalyst (*R*,*R*)-**C1e** for iminium activation of α,β-unsaturated aldehyde to generate product **5a**, while we used Luo's primary amine catalyst (*R*)-**C2g** for enamine activation of β-ketoamide **2a** to generate product **6a**. Changing the absolute configuration of these catalysts generated the other two stereoisomers.[28]

CONCLUSION

In summary, we have developed an efficient, highly stereoselective organocatalytic cascade reaction involving a Michael−hemiaminalization relay for the asymmetric assembly of α,β-unsaturated aldehydes and cyclic β-ketoamides into spiropiperidinone derivatives. These derivatives bear adjacent quaternary

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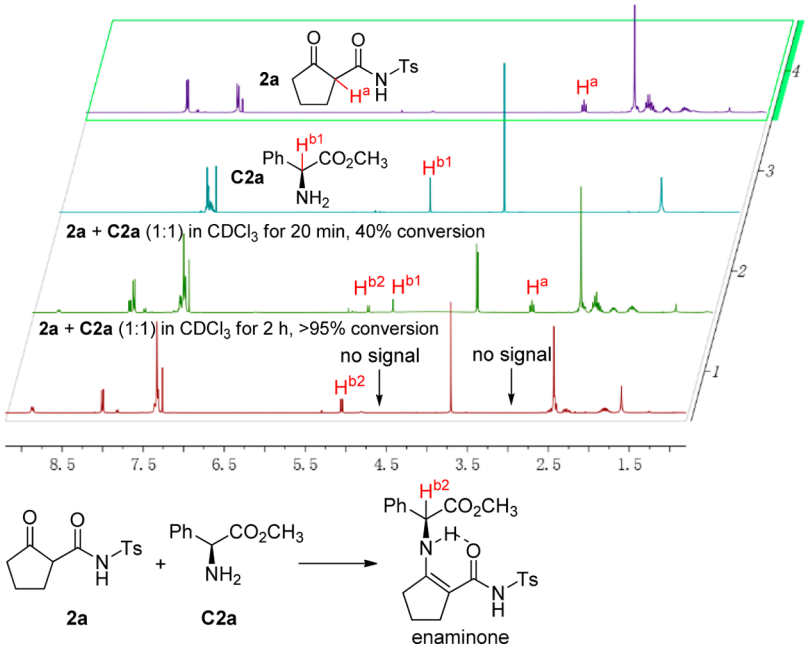
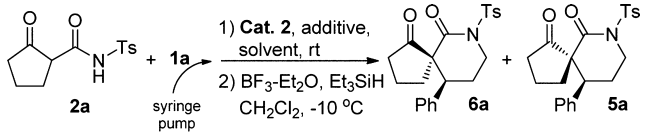
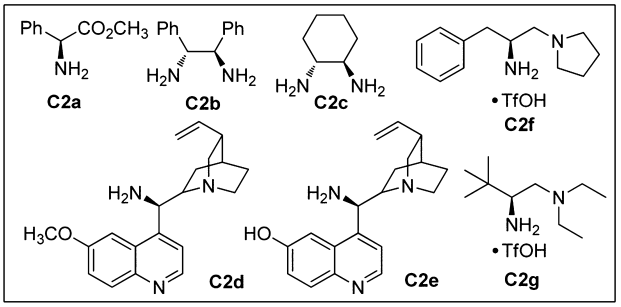


Figure 1. Formation of enaminone from α-branched β-ketoamide and chiral primary amine.

Table 3. Optimization of the Primary Amine-Catalyzed Asymmetric [3 + 3] Cycloaddition Reaction[a]





entry	cat. 2	additive	yield (%)[b]	dr (6a/5a)[c]	ee (%)[d]
1	C2a	TFA	62	75:25	42
2	C2b	TFA	38	60:40	40
3	C2c	TFA	35	55:45	35
4	C2d	TFA	43	30:70	27
5	C2e	TFA	40	30:70	33
6	C2f		58	72:28	67
7	C2g		63	75:25	72
8	C2g	2-FPhCO$_2$H	65	82:18	81
9	C2g	2-NO$_2$PhCO$_2$H	70	80:20	78
10	C2g	3-NO$_2$PhCO$_2$H	70	85:15	84

[a]Cinnamyl aldehyde **1a** (0.1 mmol) was dissolved in CH_2Cl_2 (0.2 mL) and slowly added to the mixture of **2a** (0.12 mmol), cat. **2** (0.02 mmol), acidic additive (0.02 mmol), and CH_2Cl_2 (0.4 mL) using a syringe pump for 24 h. [b]Yield of isolated major isomer **6a** over two steps. [c]Calculated based on ^{1}H NMR analysis of the crude reaction mixture. [d]Determined by chiral HPLC analysis of the major diastereoisomer.

and tertiary chiral centers. Importantly, this methodology demonstrates that applying distinct activation modes to different substrates in the same reaction can diverge diastereoselectivity. To our knowledge, this is also one of the few published cases of primary amine catalytic asymmetric [3 + 3] cycloaddition reactions involving α-branched β-ketoamides, considered a challenging goal in aminocatalysis. Further studies of activation-mode-controlled diastereodivergence are ongoing in our laboratory.

EXPERIMENTAL SECTION

General Methods. NMR data were obtained for ^{1}H at 400 MHz and for ^{13}C at 100 MHz. Chemical shifts are reported in parts per million from tetramethylsilane with the solvent resonance in $CDCl_3$ solution as the internal standard. Mass spectra were recorded using ESI as the ionization method. ESI-HRMS spectra were measured with a QTOF instrument. Enantiomeric ratios were determined by comparing HPLC analyses of products on chiral columns with results obtained using authentic racemates. UV detection was performed at 210, 220, or 254 nm. Optical rotation values were measured with instruments operating at λ = 589 nm, corresponding to the sodium D line at 20 °C. Column chromatography was performed on silica gel (200−300 mesh) using an eluent of ethyl acetate and petroleum ether. TLC was performed on glass-backed silica plates; products were visualized using UV light and I_2.

General Procedure for the Synthesis of Chiral Spirocyclic Piperidinones 4. To α,β-unsaturated aldehyde **1** (0.12 mmol), amine catalyst **Ie** (0.02 mmol, 4.9 mg), benzoic acid (0.02 mmol, 2.4 mg), and CH_2Cl_2 (1.5 mL) in a standard glass vial with stir bar was added β-ketoamide (0.10 mmol in 0.5 mL CH_2Cl_2). The reaction mixture was stirred at room temperature until the reaction completed (monitored by TLC). The reaction mixture was concentrated, and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give intermediate **3**. To a solution of intermediate **3** in CH_2Cl_2 (1.0 mL) was added TEA (0.3 mmol in 0.5 mL CH_2Cl_2) in an ice bath, after which TMSCl (0.2 mmol in 0.5 mL CH_2Cl_2) was added. The reaction mixture was stirred until the reaction completed (monitored by TLC). Then the reaction was quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 8:1) to give the

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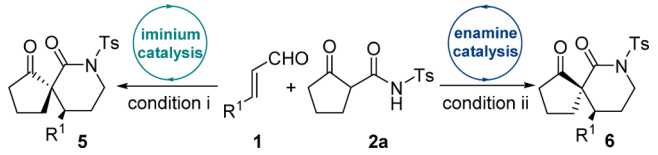
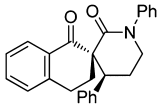
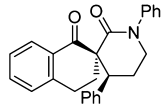
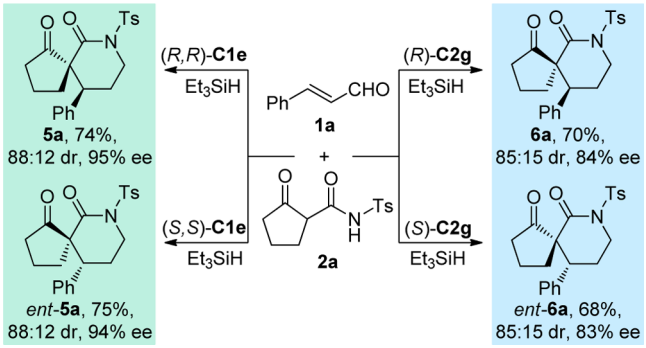
Table 4. Diastereodivergence in the Asymmetric Synthesis of Chiral Spirocyclic Piperidinones[a]



Entry	Product **5**	R^1	Product **6**
1	**5a**: 74% (88:12), 95% ee	Ph	**6a**: 70% (85:15), 84% ee
2	**5b**: 71% (82:18), 95% ee	3-Cl-C_6H_4	**6b**: 65% (80:20), 81% ee
3	**5c**: 76% (85:15), 95% ee	4-Br-C_6H_4	**6c**: 70% (78:22), 73% ee
4	**5d**: 78% (87:13), 97% ee	4-NO_2-C_6H_4	**6d**: 74% (85:15), 80% ee
5	**5e**: 69% (82:18), 93% ee	4-Me-C_6H_4	**6e**: 68% (80:20), 80% ee
6	**5f**: 75% (88:12), 96% ee	2-furyl	**6f**:[b] 72% (88:12), 86% ee
7	 **5g**: 70% (85:15), 91% ee	Ph	 **6g**: 66% (78:22), 72% ee

[a]Unless otherwise noted, the reactions were run on enals **1** and β-ketoamide **2a** under the standard conditions i (entry 10 in Table 1) and ii (entry 10 in Table 3). Yield of isolated major isomer over two steps. The dr (shown in parentheses) was determined by crude ^{1}H NMR analysis. The ee of the corresponding products was determined by chiral HPLC analysis. [b]The absolute configuration of **6f** was determined by X-ray analysis,[27] and other products **6** were assigned by analogy.

Scheme 4. Synthesis of All Four Stereoisomers Using Pairs of Chiral Amino Catalysts[29]



spirocyclic piperidinone which was dried under vacuum and further analyzed by ^{1}H NMR, ^{13}C NMR, HRMS, and chiral HPLC analysis.

(5R,8R,10S)-10-Phenyl-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro-[4.5]decane-1,6-dione ***4a:*** white solid, 35.4 mg, 73% yield, dr 88:12, ee 92%, $[\alpha]_D^{20}$ = −13.8 (CH_2Cl_2, *c* = 1.16); mp 193−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, *J* = 8.4 Hz, 2H), 7.31−7.28 (m, 5H), 7.11 (d, *J* = 7.2 Hz, 2H), 6.18 (br s, 1H), 4.19 (d, *J* = 13.6 Hz, 1H), 2.50 (t, *J* = 13.6 Hz, 1H), 2.43 (s, 3H), 2.34−2.56 (m, 1H), 2.17−2.08 (m, 3H), 1.85−1.64 (m, 2H), 1.05−0.95 (m, 1H), 0.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.1, 172.5, 144.5, 137.9, 136.2, 129.2 128.6, 128.6, 128.5, 127.6, 77.9, 77.3, 77.2, 77.0, 76.7, 63.0, 39.9, 36.52, 34.3, 30.8, 21.6, 19.2, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{31}NO_5SSiNa^+$ 508.1590, found 508.1588.

(5R,8R,10S)-10-(2-Fluorophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4b:*** white solid, 34.2 mg, 68% yield, dr 80:20, ee 94%, $[\alpha]_D^{20}$ = −14.6 (CH_2Cl_2, *c* = 0.98); mp 151−152 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 2H), 7.26−7.23 (m, 1H), 7.15−7.05 (m, 3H), 6.27 (t, *J* = 2.8 Hz, 1H), 4.17 (dd, *J* = 13.6, 2.4 Hz, 1H), 3.31 (td, *J* = 14.0, 1.2 Hz, 1H), 2.74−2.66 (m, 1H), 2.43 (s, 3H), 2.14−1.98 (m, 2H), 1.85−1.75 (m, 2H), 1.68−1.62 (m, 1H), 1.14−1.03 (m, 1H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.8, 170.2, 160.8 (d, J_{CF} = 244.0 Hz), 144.5, 136.5, 129.4 (d, J_{CF} = 9.2 Hz), 129.3 (d, J_{CF} = 3.4 Hz), 129.3, 128.7, 126.2 (d, J_{CF} = 13.7 Hz), 124.9 (d, J_{CF} = 3.6 Hz), 115.9 (d, J_{CF} = 23.3 Hz), 78.4, 62.1, 39.9, 34.1, 32.9, 32.6, 21.8, 20.0, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}FNO_5SSiNa^+$ 526.1496, found 526.1493.

(5R,8R,10S)-10-(3-Fluorophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4c:*** white solid, 36.2 mg, 72% yield, dr 83:17, ee 94%, $[\alpha]_D^{20}$ = −20.1 (CH_2Cl_2, *c* = 1.10); mp 190−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.4 Hz, 2H), 7.31−7.21 (m, 3H), 6.96 (td, *J* = 8.4, 2.4 Hz, 1H), 6.90−6.82 (m, 2H), 6.17 (t, *J* = 2.8 Hz, 1H), 4.20 (dd, *J* = 13.2, 1.6 Hz, 1H), 2.47 (dd, *J* = 13.6, 2.4 Hz, 1H), 2.43 (s, 3H), 2.38−2.20 (m, 1H), 2.19−2.04 (m, 3H), 1.90−1.68 (m, 2H), 1.14−1.04 (m, 1H), 0.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.7, 172.2, 162.9 (d, J_{CF} = 245.6 Hz), 144.6, 140.7 (d, J_{CF} = 6.8 Hz), 136.3, 130.3 (d, J_{CF} = 8.1 Hz), 129.3, 128.6, 124.5 (d, J_{CF} = 2.9 Hz), 115.7 (d, J_{CF} = 21.5 Hz), 114.7 (d, J_{CF} = 20.8 Hz), 77.8, 62.9, 39.9, 36.4, 34.41, 30.9, 21.7, 19.3, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}FNO_5SSiNa^+$ 526.1496, found 526.1496.

(5R,8R,10S)-10-(4-Fluorophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4d:*** white solid, 37.7 mg, 75% yield, dr 87:13, ee 97%, $[\alpha]_D^{20}$ = −10.2 (CH_2Cl_2, *c* = 1.01); mp 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.10−7.06 (m, 2H), 6.99 (t, *J* = 8.4 Hz, 2H), 6.17 (t, *J* = 2.8 Hz, 1H), 4.18 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.47 (dd, *J* = 13.6, 2.8 Hz, 1H), 2.43 (s, 3H), 2.37−2.28 (m, 1H), 2.19−2.03 (m, 3H), 1.90−1.78 (m, 1H), 1.73−1.65 (m, 1H), 1.13−1.03 (m, 1H), 0.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.9, 172.6, 162.2 (d, J_{CF} = 245.5 HZ), 144.6, 136.3, 133.8 (d, J_{CF} = 3.3 HZ), 130.3 (d, J_{CF} = 7.8 HZ), 129.3, 128.6, 115.7 (d, J_{CF} = 21.1 HZ), 77.9, 63.0, 39.9, 35.9, 34.6, 30.7, 21.7, 19.3, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}FNO_5SSiNa^+$ 526.1496, found 526.1498.

(5R,8R,10S)-10-(2-Chlorophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4e:*** white solid, 34.3 mg, 66% yield, dr

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79:21, ee 96%, $[\alpha]_D^{20}$ = −11.5 (CH_2Cl_2, *c* = 1.02); mp 139−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92 (d, *J* = 8.0 Hz, 2H), 7.42−7.40 (m, 1H), 7.31 (d, *J* = 8.0 Hz, 2H), 7.22−7.14 (m, 3H), 6.25 (br s, 1H), 4.49 (d, *J* = 12.8 Hz, 1H), 3.26 (t, *J* = 13.2 Hz, 1H), 2.70−2.63 (m, 1H), 2.43 (s, 3H), 2.15−2.07 (m, 2H), 1.85−1.64 (m, 3H), 1.10−1.00 (m, 1H), 0.25 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.1, 170.0, 144.3, 136.9, 136.4, 134.8, 130.2, 129.1, 129.1, 128.9, 128.6, 127.5, 78.3, 62.5, 39.9, 36.2, 34.7, 32.3, 21.7, 19.9, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}ClNO_5SSiNa^+$ 542.1200, found 542.1199.

(5R,8R,10S)-10-(4-Chlorophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4f:*** white solid, 39.5 mg, 76% yield, dr 86:14, ee 96%, $[\alpha]_D^{20}$ = −10.7 (CH_2Cl_2, *c* = 0.98); mp 189−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 6.8 Hz, 2H), 7.27−7.24 (m, 4H), 7.02 (d, *J* = 6.8 Hz, 2H), 6.14 (br s, 1H), 4.14 (d, *J* = 13.6 Hz, 1H), 2.46−2.43 (m, 1H), 2.39 (s, 3H), 2.32−2.24 (m, 1H), 2.11−2.04 (m, 3H), 1.87−1.76 (m, 1H), 1.71−1.63 (m, 1H), 1.10−1.08 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.8, 172.2, 144.7, 136.59, 136.3, 133.7, 130.1, 129.3, 129.0, 128.6, 77.9, 63.0, 39.9, 36.1, 34.5, 30.7, 21.8, 19.3, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}ClNO_5SSiNa^+$ 542.1200, found 542.1202.

(5R,8R,10S)-10-(4-Bromophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4g:*** white solid, 42.9 mg, 76% yield, dr 86:14, ee 97%, $[\alpha]_D^{20}$ = −8.9 (CH_2Cl_2, *c* = 1.04); mp 182−183 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.92(d, *J* = 8.0 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.29 (d, *J* = 8.4 Hz, 2H), 6.98 (d, *J* = 8.4 Hz, 2H), 6.17 (t, *J* = 2.4 Hz, 1H), 4.16 (d, *J* = 12.4 Hz, 1H), 2.47 (dd, *J* = 13.6, 2.4 Hz, 1H), 2.42 (s, 3H), 2.37−2.29 (m, 1H), 2.17−2.00 (m, 3H), 1.91−1.79 (m, 1H), 1.70 (dt, *J* = 18.0, 8.0 Hz, 1H), 1.18−1.08 (m, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.8, 172.2, 144.7, 137.1, 136.3, 131.9, 130.5, 129.3, 128.6, 121.8, 77.8, 62.9, 39.9, 36.1, 34.4, 30.7, 21.8, 19.3, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}BrNO_5SSiNa^+$ 586.0695, found 586.0692.

(5R,8R,10S)-10-(2-Nitrophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4h:*** white solid, 38.2 mg, 72% yield, dr 78:22, ee 95%, $[\alpha]_D^{20}$ = +8.7 (CH_2Cl_2, *c* = 0.97); mp 196−197 °C; ^{1}H NMR (400 MHz, CDCl3) δ (ppm) 7.90 (d, *J* = 8.4 Hz, 2H), 7.68 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.51 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.43 (dt, *J* = 7.6, 1.2 Hz, 1H), 7.35 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.30 (d, *J* = 8.4 Hz, 2H), 6.26 (t, *J* = 2.8 Hz, 1H), 4.35 (dd, *J* = 13.2, 2.4 Hz, 1H), 3.34 (td, *J* = 13.2, 2.4 Hz, 1H), 2.69−2.62 (m, 1H), 2.43 (s, 3H), 2.15 (dt, *J* = 18.4, 7.6 Hz, 1H), 1.91 (dt, *J* = 13.6, 2.8 Hz, 1H), 1.87−1.65 (m, 3H), 1.06−0.97 (m, 1H), 0.27 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.9, 169.4, 151.6, 144.5, 136.3, 132.4, 132.4, 129.4, 129.2, 128.7, 128.6, 124.2, 78.0, 62.0, 39.9, 34.7, 34.6, 33.1, 21.7, 19.8, 1.0, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}N_2O_7SSiNa^+$ 553.1441, found 553.1444.

(5R,8R,10S)-10-(4-Nitrophenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4i:*** white solid, 41.3 mg, 78% yield, dr 85:15, ee 97%, $[\alpha]_D^{20}$ = +9.2 (CH_2Cl_2, *c* = 0.97); mp 199−200 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.17 (d, *J* = 8.4 Hz, 2H), 7.92 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.4 Hz, 4H), 6.20 (t, *J* = 2.8 Hz, 1H), 4.34−4.30 (m, 1H), 2.53 (td, *J* = 13.6, 2.8 Hz, 1H), 2.43 (s, 3H), 2.40−2.34 (m, 1H), 2.24−2.18 (m, 1H), 2.13 (dt, *J* = 13.6, 2.8 Hz, 1H), 2.01−1.85 (m, 2H), 1.70 (dt, *J* = 18.4, 8.0 Hz, 1H), 1.19−1.09 (m, 1H), 0.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.1, 171.5, 147.4, 145.6, 144.7, 136.0, 129.8, 129.3, 128.6, 123.8, 77.6, 62.7, 39.6, 36.5, 34.3, 30.5, 21.7, 19.2, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{30}N_2O_7SSiNa^+$ 553.1441, found 553.1444.

(5R,8R,10S)-10-(2-Methoxyphenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4j:*** white solid, 31.9 mg, 62% yield, dr 80:20, ee 93%, $[\alpha]_D^{20}$ = +12.3 (CH_2Cl_2, *c* = 1.00); mp 191−192 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, *J* = 8.4 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 7.23 (td, *J* = 8.0, 1.6 Hz, 1H), 7.05 (dd, *J* = 8.0, 1.2 Hz, 1H), 6.89 (d, *J* = 8.0 Hz, 2H), 6.24 (t, *J* = 2.8 Hz, 1H), 4.38 (d, *J* = 12.0 Hz, 1H), 3.82 (s, 3H), 3.26 (td, *J* = 13.6, 2.4 Hz, 1H), 2.66−2.59 (m, 1H), 2.42 (s, 3H), 2.10−2.01 (m, 2H), 1.75−1.61(m, 3H), 1.06−0.96 (m, 1H), 0.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.4, 170.7, 157.4, 144.3, 136.7, 129.2, 128.7, 128.7, 127.8, 121.1, 111.6, 78.8, 62.6, 55.6, 39.9, 34.4, 32.5, 21.8, 19.9, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{33}NO_6SSiNa^+$ 538.1696, found 538.1694.

(5R,8R,10S)-10-(p-Tolyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4k:*** white solid, 34.9 mg, 70% yield, dr 82:18, ee 93%, $[\alpha]_D^{20}$ = −23.1 (CH_2Cl_2, *c* = 0.98); mp 150−151 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.17 (t, *J* = 2.8 Hz, 1H), 4.15 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.48 (dd, *J* = 13.6, 2.8 Hz, 1H), 2.42 (s, 3H), 2.31 (s, 3H), 2.30−2.25 (m, 1H), 2.14−2.08 (m, 3H), 1.85−1.64 (m, 2H), 1.09−0.99 (m, 1H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.1, 172.6, 144.4, 137.3, 136.4, 134.9, 129.3, 129.2, 128.5, 77.9, 63.1, 39.9, 36.2, 34.4, 30.9, 29.7, 21.7, 21.0, 19.3, 1.0, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{33}NO_5SSiNa^+$ 522.1746, found 522.1744.

(5R,8R,10S)-10-(4-(Dimethylamino)phenyl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4l:*** white solid, 32.2 mg, 61% yield, dr 78:22, ee 92%, $[\alpha]_D^{20}$ = −63.7 (CH_2Cl_2, *c* = 1.05); mp 186−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, *J* = 8.4 Hz, 2H), 7.28 (d, *J* = 8.4 Hz, 2H), 6.96 (d, *J* = 8.8 Hz, 2H), 6.63 (d, *J* = 8.8 Hz, 2H), 6.15 (t, *J* = 2.4 Hz, 1H), 4.09 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.92 (s, 6H), 2.45 (dd, *J* = 13.8, 2.4 Hz, 1H), 2.41 (s, 3H), 2.32−2.24 (m, 1H), 2.16−2.06 (m, 3H), 1.83−1.66 (m, 2H), 1.12−1.06 (m, 1H), 0.20 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.5, 172.9, 149.7, 144.3, 136.5, 129.3, 129.2, 128.5, 125.3, 112.32, 78.1, 63.3, 40.4, 39.9, 35.8, 34.6, 30.9, 21.6, 19.7, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{36}N_2O_5SSiNa^+$ 551.2012, found 551.2011.

(5R,8R,10S)-10-(Furan-2-yl)-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4m:*** white solid, 36.1 mg, 76% yield, dr 88:12, ee 95%, $[\alpha]_D^{20}$ = −62.9 (CH_2Cl_2, *c* = 1.12); mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.90 (d, *J* = 8.4 Hz, 2H), 7.29 (m, 3H), 6.29 (dd, *J* = 3.2, 1.6 Hz, 1H), 6.15 (t, *J* = 2.8 Hz, 1H), 6.04 (d, *J* = 3.2 Hz, 1H), 4.20 (dd, *J* = 13.2, 2.0 Hz, 1H), 2.42 (s, 3H), 2.34 (dd, *J* = 13.6, 2.4 Hz, 1H), 2.23−1.85 (m, 6H), 1.30−1.20 (m, 1H), 0.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.1, 171.8, 152.6, 144.5, 142.1, 136.3, 129.2, 128.5, 110.4, 107.5, 77.8, 61.7, 39.3, 32.7, 32.2, 31.8, 21.6, 19.0, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{29}NO_6SSiNa^+$ 498.1383, found 498.1381.

(5R,8R,10S)-10-Methyl-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4n:*** white solid, 21.6 mg, 51% yield, dr 70:30, ee 55%, $[\alpha]_D^{20}$ = −16.7 (CH_2Cl_2, *c* = 1.07); mp 146−147 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.4 Hz, 2H), 7.26 (d, *J* = 7.2 Hz, 2H), 6.00 (t, *J* = 2.8 Hz, 1H), 2.98−2.90 (m, 1H), 2.56−2.47 (m, 1H), 2.40 (s, 3H), 2.18−2.04 (m, 4H), 1.89−1.80 (m, 3H), 0.82 (d, *J* = 6.8 Hz, 3H), 0.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.8, 172.6, 144.4, 136.5, 129.1, 128.6, 78.5, 62.1, 39.8, 37.1, 29.4, 26.2, 21.6, 19.3, 15.7, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{29}NO_5SSiNa^+$ 446.1433, found 446.1430.

(5R,8R,10S)-3,3-Dimethyl-10-phenyl-7-tosyl-8-((trimethylsilyl)-oxy)-7-azaspiro[4.5]decane-1,6-dione ***4o:*** white solid, 32.2 mg, 69% yield, dr 84:16, ee 92%, $[\alpha]_D^{20}$ = −33.6 (CH_2Cl_2, *c* = 1.12); mp >210 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.94 (d, *J* = 8.4 Hz, 2H), 7.32−7.27 (m, 5H), 7.13−7.11 (m, 2H), 6.14 (t, *J* = 2.4 Hz, 1H), 4.18 (dd, *J* = 13.2, 2.0 Hz, 1H), 2.45−2.40 (m, 4H), 2.38−2.32 (m, 1H), 2.14−2.05 (m, 2H), 1.96 (d, *J* = 14.4 Hz, 1H), 1.51 (d, *J* = 18.4 Hz, 1H), 1.02 (s, 3H), 0.23 (s, 3H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.0, 172.9, 144.4, 138.3, 136.34, 129.3, 129.2, 128.7, 128.6, 127.8, 77.9, 65.4, 55.0, 43.5, 37.1, 34.5, 32.9, 30.5, 29.7, 21.6, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{35}NO_5SSiNa^+$ 536.1903, found 536.1907.

(5R,8R,10S)-10-(4-Bromophenyl)-3,3-dimethyl-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4p:*** white solid, 38.8 mg, 72% yield, dr 88:12, ee 93%, $[\alpha]_D^{20}$ = −17.6 (CH_2Cl_2, *c* = 0.98); mp 206−207 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.93 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.13 (t, *J* = 2.8 Hz, 1H), 4.14 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.44−2.39 (m, 4H), 2.40−2.33 (m, 1H), 2.05−2.00 (m, 3H), 1.04 (s, 3H), 0.90−0.82 (m, 1H), 0.28 (s, 3H), 0.19 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 214.6, 172.6, 144.52, 137.5, 136.2, 131.7, 131.0, 129.2, 128.7, 121.9, 77.8, 65.4, 55.0, 43.5, 36.4, 34.5, 32.9, 30.4, 29.9, 21.7, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{27}H_{34}BrNO_5SSiNa^+$ 614.1008, found 614.1005.

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(5R,8R,10S)-10-(Furan-2-yl)-3,3-dimethyl-7-tosyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4q:*** white solid, 33.4 mg, 73% yield, dr 88:12, ee 93%, $[\alpha]_D^{20}$ = −13.1 (CH_2Cl_2, *c* = 1.03); mp 108−109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.91 (d, *J* = 8.0 Hz, 2H), 7.32−7.26 (m, 3H), 6.29 (dd, *J* = 2.8, 2.0 Hz, 1H), 6.11 (t, *J* = 2.4 Hz, 1H), 6.08 (d, *J* = 2.8 Hz, 1H), 4.21 (dd, *J* = 13.2, 2.4 Hz, 1H), 2.50 (d, *J* = 18.0 Hz, 1H), 2.41 (s, 3H), 2.33 (td, *J* = 14.0, 2.8 Hz, 1H), 2.14−2.10 (m, 2H), 2.00−1.89 (m, 2H), 1.07 (s, 3H), 0.48 (s, 3H), 0.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 214.1, 172.3, 152.6, 144.5, 142.1, 136.3, 129.1, 128.6, 110.6, 108.5, 77.8, 64.0, 54.4, 44.8, 33.2, 33.0, 32.6, 30.61, 30.1, 21.6, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{33}NO_6SSiNa^+$ 526.1696, found 526.1698.

(5R,8R,10S)-10-Phenyl-7-(phenylsulfonyl)-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4r:*** white solid, 37.1 mg, 78% yield, dr 85:15, ee 95%, $[\alpha]_D^{20}$ = −13.8 (CH_2Cl_2, *c* = 0.97); mp 193−194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 8.08−8.04 (m, 2H), 7.62−7.58 (m, 1H), 7.53−7.48 (m, 2H), 7.31−7.27 (m, 3H), 7.12−7.10 (m, 2H), 6.19 (t, *J* = 2.8 Hz, 1H), 4.12 (dd, *J* = 13.6, 2.0 Hz, 1H), 2.51 (td, *J* = 13.6, 2.4 Hz, 1H), 2.29 (ddd, *J* = 18.0, 8.4, 6.8 Hz, 1H), 2.16−2.10 (m, 3H), 1.84−1.64 (m, 2H), 1.06−0.96 (m, 1H), 0.22 (s, 9H).^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 215.9, 172.6, 139.3, 137.9, 133.5, 128.7, 128.7, 128.6, 128.4, 127.6, 78.0, 63.1, 39.8, 36.6, 34.4, 30.9, 19.3, 0.2; HRMS (ESI) *m*/*z* calcd for $C_{24}H_{29}NO_5SSiNa^+$ 494.1433, found 494.1433.

(5R,8R,10S)-7-(Methylsulfonyl)-10-phenyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4s:*** white solid, 40.6 mg, 77% yield, dr 90:10, ee 97%, $[\alpha]_D^{20}$ = −32.7 (CH_2Cl_2, *c* = 0.96); mp 165−166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.34−7.28 (m, 3H), 7.14 (dd, *J* = 8.4, 2.0 Hz, 2H), 5.99 (t, *J* = 2.4 Hz, 1H), 4.24 (dd, *J* = 14.0, 2.4 Hz, 1H), 3.31 (s, 3H), 2.49 (td, *J* = 13.6, 2.4 Hz, 1H), 2.43−2.35 (m, 1H), 2.23−2.13 (m, 2H), 2.05 (dt, *J* = 14.0, 2.8 Hz, 1H), 1.92−1.70 (m, 2H), 1.20−1.10 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 216.3, 174.5, 138.0, 129.1, 129.0, 128.0, 79.1, 77.6, 77.3, 77.0, 63.4, 42.9, 40.1, 37.0, 34.3, 30.8, 19.5, 0.3; HRMS (ESI) *m*/*z* calcd for $C_{19}H_{27}NO_5SSiNa^+$ 432.1277, found 432.1277.

(5R,8R,10S)-7-Benzyl-10-phenyl-8-((trimethylsilyl)oxy)-7-azaspiro[4.5]decane-1,6-dione ***4t:*** white solid, 30.4 mg, 72% yield, dr 85:15, ee 90%, $[\alpha]_D^{20}$ = −20.4 (*c* = 1.02 in CH_2Cl_2); mp 164−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.37−7.23 (m, 8H), 7.16−7.14 (m, 2H), 5.16 (d, *J* = 15.2 Hz, 1H), 5.01 (dd, *J* = 7.6, 6.8 Hz, 1H), 4.30 (d, *J* = 14.4 Hz, 1H), 3.65−3.58 (m, 1H), 2.51−2.42 (m, 1H), 2.39−2.30 (m, 1H), 2.28−2.21 (m, 2H), 2.19−2.13 (m, 1H), 1.94−1.80 (m, 2H), 0.91−0.84 (m, 1H), 0.08 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 217.7, 171.9, 138.2, 136.3, 128.0, 128.1, 127.9, 127.1, 126.9, 126.6, 79.0, 60.6, 44.0, 39.5, 38.8, 34.6, 30.1, 19.3, −0.3; HRMS (ESI) *m*/*z* calcd for $C_{25}H_{31}NO_3SiNa^+$ 444.1971, found 444.1974.

General Procedure for the Synthesis of Chiral Spirocyclic Piperidinones 5. To *α*,*β*-unsaturated aldehyde **1** (0.12 mmol), amine catalyst **Ie** (0.02 mmol, 4.9 mg), benzoic acid (0.02 mmol, 2.4 mg), and CH_2Cl_2 (1.5 mL) in a standard glass vial with a stir bar was added *β*-ketoamide (0.10 mmol in 0.5 mL CH_2Cl_2). The reaction mixture was stirred at room temperature until the reaction completed (monitored by TLC). The reaction mixture was concentrated, and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give intermediate **3**. To a solution of intermediate **3** in CH_2Cl_2 (2 mL) was added BF_3/Et_2O (0.3 mmol) at −10 °C, after which Et_3SiH (0.3 mmol) was added. The reaction mixture was stirred until the reaction completed (monitored by TLC). Then the reaction was quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give the spirocyclic piperidinone, which was dried under vacuum and further analyzed by ^{1}H NMR, ^{13}C NMR, HRMS, and chiral HPLC analysis.

(5R,10S)-10-Phenyl-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5a:*** white solid, 29.4 mg, 74% yield, dr 88:12, ee 95%, $[\alpha]_D^{20}$ = +32.8 (CH_2Cl_2, *c* = 0.96); mp 140−141 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.89 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.30−7.27 (m, 3H), 7.14−7.12 (m, 2H), 4.46 (ddd, *J* = 12.0, 5.2, 2.0 Hz, 1H), 3.78 (td, *J* = 12.0, 4.4 Hz, 1H), 3.19−3.08 (m, 1H), 2.99 (dd, *J* = 13.6, 2.8 Hz, 1H), 2.74 (dt, *J* = 15.6, 8.0 Hz, 1H), 2.43 (s, 3H), 2.10−1.95 (m, 3H), 1.80−1.70 (m, 1H), 1.66−1.57 (m, 1H), 1.00−0.86 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 216.1, 170.4, 144.7, 139.1, 135.9, 129.4, 128.9, 128.5, 128.4, 127.9, 62.1, 48.9, 46.2, 40.0, 33.6, 25.5, 21.70, 19.7; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{23}NO_4SNa^+$ 420.1245, found 420.1246.

(5S,10R)-10-Phenyl-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ent- ***5a:*** white solid, 29.8 mg, 75% yield, dr 88:12, ee −94%, $[\alpha]_D^{20}$ = −32.8 (CH_2Cl_2, *c* = 1.03); mp 140−141 °C; The NMR data for the product *ent*-**5a** is consitent with the product **5a**; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{23}NO_4SNa^+$ 420.1245, found 420.1247.

(5R,10S)-10-(3-Chlorophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5b:*** white solid, 30.6 mg, 71% yield, dr 82:18, ee 95%, $[\alpha]_D^{20}$ = −3.7 (CH_2Cl_2, *c* = 0.98); mp 172−173 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.89 (d, *J* = 8.4 Hz, 2H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.26−7.19 (m, 2H), 7.05 (t, *J* = 1.6 Hz, 1H), 6.92 (dt, *J* = 7.2, 1.6 Hz, 1H), 4.24 (dt, *J* = 12.0, 4.8 Hz, 1H), 3.80 (ddd, *J* = 12.0, 10.4, 4.4 Hz, 1H), 3.50 (dd, *J* = 11.2, 2.8 Hz, 1H), 2.45 (s, 3H), 2.39−2.15 (m, 4H), 1.98−1.84 (m, 3H), 1.20−1.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 215.5, 171.3, 145.1, 140.6, 135.4, 134.7, 130.0, 129.5, 128.6, 128.4, 127.9, 126.6, 62.6, 45.3, 43.1, 39.2, 31.5, 25.9, 21.7, 19.4; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}ClNO_4SNa^+$ 454.0856, found 454.0855.

(5R,10S)-10-(4-Bromophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5c:*** white solid, 36.2 mg, 76% yield, dr 85:15, ee 95%, $[\alpha]_D^{20}$ = −38.8 (CH_2Cl_2, *c* = 1.01); mp 160−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.88 (d, *J* = 8.4 Hz, 2H), 7.41 (d, *J* = 8.8 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 4.25 (dt, *J* = 12.0, 4.8 Hz, 1H), 3.81−3.75 (m, 1H), 3.49 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.45 (s, 3H), 2.39−2.15 (m, 4H), 1.97−1.81 (m, 3H), 1.21−1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 215.7, 171.4, 145.1, 137.5, 135.4, 131.8, 130.0, 129.5, 128.6, 121.7, 45.4, 42.8, 39.3, 31.4, 25.7, 21.7, 19.4; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}BrNO_4SNa^+$ 498.0351, found 498.0348.

(5R,10S)-10-(4-Nitrophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5d:*** white solid, 34.5 mg, 78% yield, dr 87:13, ee 98%, $[\alpha]_D^{20}$ = −38.8 (CH_2Cl_2, *c* = 1.13); mp 186−187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 8.15 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.8 Hz, 2H), 4.28 (ddd, *J* = 12.0, 4.8, 4.0 Hz, 1H), 3.81 (ddd, *J* = 12.0, 10.8, 4.4 Hz, 1H), 3.66 (dd, *J* = 11.2, 3.2 Hz, 1H), 2.46 (s, 3H), 2.41−2.24 (m, 4H), 1.94−1.82 (m, 3H), 1.20−1.11 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 215.2, 170.8, 147.3, 146.0, 145.3, 135.2, 129.6, 129.4, 128.6, 123.8, 62.5, 45.2, 43.2, 39.2, 31.4, 25.8, 21.7, 19.4; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}N_2O_6SNa^+$ 465.1096, found 465.1097.

(5R,10S)-10-(p-Tolyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5e:*** white solid, 28.4 mg, 69% yield, dr 82:18, ee 93%, $[\alpha]_D^{20}$ = −35.6 (CH_2Cl_2, *c* = 1.12); mp 189−190 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.89 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 7.08 (d, *J* = 8.0 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 4.32 (dt, *J* = 12.0, 4.8 Hz, 1H), 3.79 (ddd, *J* = 11.6, 10.0, 4.4 Hz, 1H), 3.47 (dd, *J* = 10.8, 2.8 Hz, 1H), 2.44 (s, 3H), 2.35−2.32 (m, 1H), 2.30 (s, 3H), 2.28−2.15 (m, 3H), 2.04−1.96 (m, 1H), 1.92−1.78 (m, 2H), 1.15−1.04 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 216.1, 171.8, 144.9, 137.3, 135.6, 135.3, 129.5, 129.4, 128.5, 128.2, 62.9, 45.5, 43.0, 39.3, 31.6, 25.9, 21.7, 21.0, 19.4; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{25}NO_4SNa^+$ 434.1402, found 434.1401.

(5R,10S)-10-(Furan-2-yl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***5f:*** white solid, 29.0 mg, 75% yield, dr 88:12, ee 96%, $[\alpha]_D^{20}$ = −17.2 (CH_2Cl_2, *c* = 1.01); mp 156−157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ* (ppm) 7.87 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.27 (dd, *J* = 2.0, 0.8 Hz, 1H), 6.28 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.04 (d, *J* = 3.2 Hz, 1H), 4.25 (dt, *J* = 12.0, 4.8 Hz, 1H), 3.78 (ddd, *J* = 12.0, 10.8, 4.8 Hz, 1H), 3.57 (dd, *J* = 10.8, 3.2 Hz, 1H), 2.43 (s, 3H), 2.42−2.35 (m, 2H), 2.25−2.09 (m, 3H), 1.91−1.83 (m, 2H), 1.35−1.24 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ* (ppm) 215.2, 171.0, 152.4, 145.0, 142.1, 135.5, 129.5, 128.5, 110.4, 107.6, 77.4, 77.0, 76.8, 61.6, 45.5, 38.9, 38.0, 32.1, 24.0, 21.7, 19.2; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{21}NO_5SNa^+$ 410.1038, found 410.1040.

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(2R,4′S)-1′,4′-Diphenyl-3,4-dihydro-1H-spiro[naphthalene-2,3′-piperidine]-1,2′-dione ***5g:*** white solid, 26.3 mg, 70% yield, dr 85:15, ee 91%, $[\alpha]_D^{20}$ = +20.7 (CH_2Cl_2, *c* = 0.97); mp 160−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.78 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.35−7.31 (m, 2H), 7.23−7.17 (m, 4H), 7.12−7.01 (m, 6H), 6.87 (d, *J* = 7.6 Hz, 1H), 3.88 (td, *J* = 12.0, 4.4 Hz, 1H), 3.74 (ddd, *J* = 12.0, 5.2, 2.0 Hz, 1H), 3.28−3.18 (m, 2H), 3.13 (dd, *J* = 13.2, 2.4 Hz, 1H), 2.80 (ddd, *J* = 13.6, 7.2, 5.2 Hz, 1H), 2.46 (ddd, *J* = 16.4, 7.2, 5.2 Hz, 1H), 2.27 (ddd, *J* = 13.6, 8.4, 5.2 Hz, 1H), 1.88 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 197.3, 170.1, 143.0, 142.5, 139.0, 132.3, 128.2, 128.2, 127.1, 127.0, 126.5, 126.3, 125.9, 125.3, 76.3, 76.0, 75.7, 56.3, 50.8, 50.1, 31.2, 26.5, 25.4; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{23}NO_2Na^+$ 404.1626, found 404.1629.

General Procedure for the Synthesis of Chiral Spirocyclic Piperidinones 6. To β-ketoamide **2** (0.12 mmol), amine catalyst **IIg** (0.02 mmol, 3.5 mg), *m*-NO_2-BzOH (0.02 mmol, 3.3 mg), and CH_2Cl_2 (0.4 mL) in a standard glass vial with a stir bar was added α,β-unsaturated aldehyde **1** (0.10 mmol in 0.2 mL CH_2Cl_2) slowly using a syringe pump for 24 h. The reaction mixture was stirred at room temperature until the reaction completed (monitored by TLC). The reaction mixture was concentrated, and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give intermediate **3′**. To a solution of intermediate **3′** in CH_2Cl_2 (2 mL) was added BF_3/Et_2O (0.3 mmol) at −10 °C, after which Et_3SiH (0.3 mmol) was added. The reaction mixture was stirred until the reaction completed (monitored by TLC). Then the reaction was quenched with aqueous $NaHCO_3$ and extracted with CH_2Cl_2. The organic layer was dried over Na_2SO_4 and concentrated. The residue was purified by chromatography on silica gel (petroleum ether/ethyl acetate = 6:1) to give the spirocyclic piperidinone, which was dried under vacuum and further analyzed by ^{1}H NMR, ^{13}C NMR, HRMS, and chiral HPLC analysis.

(5S,10S)-10-Phenyl-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6a:*** white solid, 36.1 mg, 70% yield, dr 85:15, ee 84%, $[\alpha]_D^{20}$ = −29.2 (CH_2Cl_2, *c* = 1.03); mp 174−175 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.29−7.27 (m, 3H), 7.14−7.12 (m, 2H), 4.46 (ddd, *J* = 12.0, 5.6, 2.0 Hz, 1H), 3.78 (td, *J* = 12.4, 4.4 Hz, 1H), 3.19−3.08 (m, 1H), 2.99 (dd, *J* = 9.2, 2.8 Hz, 1H), 2.74 (dt, *J* = 13.6, 8.0 Hz, 2H), 2.43 (s, 3H), 2.10−1.95 (m, 3H), 1.80−1.69 (m, 1H), 1.65−1.57 (m, 1H), 1.00−0.89 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.1, 170.4, 144.7, 139.1, 135.9, 129.4, 128.8, 128.5, 128.4, 127.9, 62.1, 48.8, 46.2, 40.0, 33.5, 25.5, 21.7, 19.7; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{23}NO_4SNa^+$ 420.1245, found 420.1246.

(5R,10R)-10-Phenyl-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ent- ***6a:*** white solid, 28.4 mg, 66% yield, dr 78:22, ee −83%, $[\alpha]_D^{20}$ = +29.2 (CH_2Cl_2, *c* = 1.02); mp 174−175 °C; The NMR data for the product *ent*-**6a** is consistent with the product **6a**; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{23}NO_4SNa^+$ 420.1245, found 420.1248.

(5S,10S)-10-(3-Chlorophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6b:*** white solid, 38.4 mg, 65% yield, dr 80:20, ee 81%, $[\alpha]_D^{20}$ = +37.5 (CH_2Cl_2, *c* = 1.03); mp 158−159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.88 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.28−7.21 (m, 2H), 7.13 (t, *J* = 1.6 Hz, 1H), 7.03 (dt, *J* = 7.2, 1.6 Hz, 1H), 4.45 (ddd, *J* = 12.0, 5.2, 2.0 Hz, 1H), 3.77 (td, *J* = 12.0, 4.0 Hz, 1H), 3.16−3.04 (m, 1H), 2.97 (dd, *J* = 2.8 Hz, 1H), 2.74 (dt, *J* = 14.8, 7.6 Hz, 1H), 2.15−2.06 (m, 1H), 2.02−1.92 (m, 1H), 1.86−1.76 (m, 1H), 1.71−1.62 (m, 1H), 1.09−0.98 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.7, 170.0, 144.8, 141.2, 135.8, 134.8, 130.2, 129.4, 128.8, 128.4, 128.2, 126.6, 61.8, 48.4, 46.0, 40.0, 33.6, 25.4, 21.7, 19.8; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}ClNO_4SNa^+$ 454.0856, found 454.0855.

(5S,10S)-10-(4-Bromophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6c:*** white solid, 57.6 mg, 70% yield, dr78:22, ee 73%, $[\alpha]_D^{20}$ = +45.9 (CH_2Cl_2, *c* = 1.11); mp 166−167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.88 (d, *J* = 8.4 Hz, 2H), 7.42 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 4.45 (ddd, *J* = 12.0, 5.2, 2.0 Hz, 1H), 3.76 (td, *J* = 12.0, 4.0 Hz, 1H), 3.15−3.04 (m, 1H), 2.96 (dd, *J* = 13.2, 2.8 Hz, 1H), 2.73 (dt, *J* = 15.2, 8.0 Hz, 1H), 2.43 (s, 3H), 2.14−2.05 (m, 1H), 2.00−1.92 (m, 1H), 1.86−1.75 (m, 1H), 1.67−1.60 (m, 1H), 1.10−0.99 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.8, 170.0, 144.8, 138.1, 135.8, 132.0, 130.2, 129.4, 128.4, 121.9, 61.8, 48.2, 46.0, 40.0, 33.6, 25.5, 21.7, 19.8; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}BrNO_4SNa^+$ 498.0351, found 498.0353.

(5S,10S)-10-(4-Nitrophenyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6d:*** white solid, 47.5 mg, 74% yield, dr 85:15, ee 80%, $[\alpha]_D^{20}$ = +24.3 (CH_2Cl_2, *c* = 1.15); mp 175−176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.17 (d, *J* = 8.8 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H), 7.33 (d, *J* = 8.8 Hz, 4H), 4.50−4.44 (m, 1H), 3.84−3.77 (m, 1H), 3.19−3.13 (m, 2H), 2.81−2.73 (m, 1H), 2.44 (s, 3H), 2.15 (ddd, *J* = 18.4, 8.8, 7.2 Hz, 1H), 2.02−1.81 (m, 3H), 1.68−1.61 (m, 1H), 1.09−0.98 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 215.3, 169.5, 147.6, 146.5, 145.0, 135.6, 129.6, 129.5, 128.4, 124.0, 61.6, 48.4, 45.9, 40.0, 33.7, 25.4, 21.7, 19.8; HRMS (ESI) *m*/*z* calcd for $C_{22}H_{22}N_2O_6SNa^+$ 465.1096, found 465.1093.

(5S,10S)-10-(p-Tolyl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6e:*** white solid, 33.5 mg, 68% yield, dr 80:20, ee 80%, $[\alpha]_D^{20}$ = +37.5 (CH_2Cl_2, *c* = 1.10); mp 184−185 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.89 (d, *J* = 8.4 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.0 Hz, 2H), 7.01 (d, *J* = 8.0 Hz, 2H), 4.45 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.77 (td, *J* = 12.0, 4.4 Hz, 1H), 3.16−3.04 (m, 1H), 2.95 (dd, *J* = 13.2, 2.4 Hz, 1H), 2.72 (dt, *J* = 13.6, 7.6 Hz, 1H), 2.43 (s, 3H), 2.31 (s, 3H), 2.09−1.92 (m, 3H), 1.79−1.69 (m, 1H), 1.67−1.58 (m, 1H), 1.04−0.93 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 216.2, 170.5, 144.7, 137.6, 136.0, 136.0, 129.5, 129.4, 128.4, 128.3, 62.1, 48.5, 46.2, 40.0, 33.6, 25.6, 21.7, 21.0, 19.8; HRMS (ESI) *m*/*z* calcd for $C_{23}H_{25}NO_4SNa^+$ 434.1402, found 434.1404.

(5S,10S)-10-(Furan-2-yl)-7-tosyl-7-azaspiro[4.5]decane-1,6-dione ***6f:*** white solid, 27.9 mg, 72% yield, dr 88:12, ee 86%, $[\alpha]_D^{20}$ = −33.7 (CH_2Cl_2, *c* = 1.08); mp 161−162 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 7.87 (d, *J* = 8.4 Hz, 2H), 7.32−7.29 (m, 3H), 6.30 (dd, *J* = 3.2, 2.0 Hz, 1H), 6.07 (d, *J* = 3.2 Hz, 1H), 4.42 (ddd, *J* = 12.0, 5.6, 2.4 Hz, 1H), 3.76 (td, *J* = 12.0, 4.4 Hz, 1H), 3.17 (dd, *J* = 13.2, 2.8 Hz, 1H), 3.02−2.91 (m, 1H), 2.80−2.73 (m, 1H), 2.42 (s, 3H), 2.17−1.99 (m, 3H), 1.91−1.79 (m, 2H), 1.20−1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 214.6, 169.8, 152.8, 144.7, 141.7, 129.4, 128.4, 110.8, 107.5, 60.7, 45.7, 42.2, 39.3, 34.0, 24.6, 21.7, 19.5; HRMS (ESI) *m*/*z* calcd for $C_{20}H_{21}NO_5SNa^+$ 410.1038, found 410.1041.

(2S,4′S)-1′,4′-Diphenyl-3,4-dihydro-1H-spiro[naphthalene-2,3′-piperidine]-1,2′-dione ***6g:*** white solid, 32.8 mg, 66% yield, dr 78:22, ee 72%, $[\alpha]_D^{20}$ = +20.5 (CH_2Cl_2, *c* = 1.12); mp 171−172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 8.07 (d, *J* = 8.0 Hz, 1H), 7.44−7.25 (m, 12H), 7.13 (d, *J* = 7.6 Hz, 1H), 3.94 (dd, *J* = 7.6, 3.6 Hz, 1H), 3.79−3.68 (m, 2H), 2.96−2.89 (m, 1H), 2.83−2.66 (m, 2H), 2.41−2.33 (m, 1H), 2.18 (ddd, *J* = 14.0, 6.4, 4.4 Hz, 1H), 2.13−2.03 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 197.5, 170.2, 143.7, 143.2, 139.7, 133.4, 131.7, 129.2, 128.8, 128.7, 128.6, 128.3, 127.2, 127.0, 126.7, 126.3, 57.2, 48.6, 42.3, 27.4, 25.1, 25.1; HRMS (ESI) *m*/*z* calcd for $C_{26}H_{23}NO_2Na^+$ 404.1626, found 404.1628.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02489.

Crystal data for **4m** (CIF)
Crystal data for **6f** (CIF)
^{1}H and ^{13}C NMR spectra and HPLC chromatograms for products **4**, **5**, and **6** (PDF)

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Notes

The authors declare no competing financial interest.

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(29) When using pyrrolidine as achiral secondary amine catalyst, the inherent dr value of **5a**/**6a** is 64:36. When using benzylamine as achiral primary amine catalyst, the inherent dr value of **5a**/**6a** is 55:45.

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