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L-Amino Acid Based Urea−Tertiary Amine-Catalyzed Chemoselective and Asymmetric Stereoablative Carboxylation of 3-Bromooxindoles with Malonic Acid Half Thioesters

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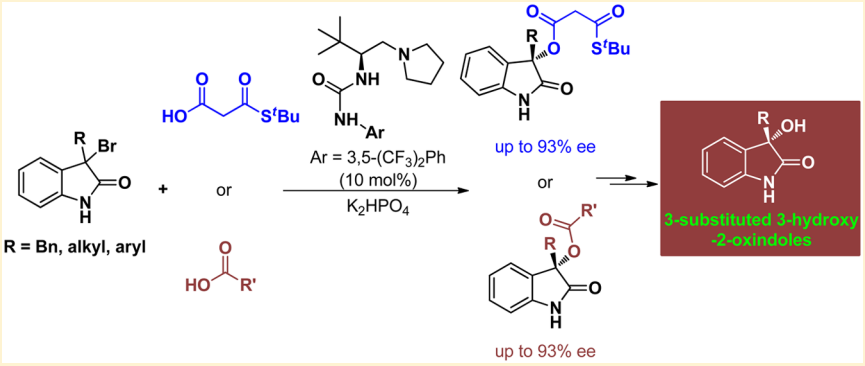
Supporting Information



ABSTRACT: An L-amino acid based urea−tertiary amine-catalyzed enantioselective stereoablative carboxylation of 3-bromooxindoles with malonic acid half thioesters (MAHTs) and diverse commercially available carboxylic acids has been developed. A series of valuable 3-substituted 3-hydroxy-2-oxindoles were obtained in high enantioselectivities (up to 93% ee). This chemoselective reaction represents the first example of MAHTs as carboxylating agents.

3-Substituted 3-hydroxy-2-oxindoles and their derivatives, which structurally feature a heteroquaternary stereogenic center at the C3 position, are a class of active and important natural and medicinal agents.[1] In the past decades, the development of an efficient method for enantioselective installation of these entities has attracted considerable attention of chemists.[2−7] Great advances have been made in two asymmetric synthetic strategies that are the aldol reaction[3] of nucleophiles to isatins and the direct hydroxylation[4] of 3-monosubstituted oxindoles. In order to expand upon the building block of valuable enantiopure 3-substituted 3-hydroxy-2-oxindole derivatives, development of efficient methods to realize that is highly desirable.[5−7] Yuan and co-workers[7] introduced an organocatalytic asymmetric stereoablative hydroxylation of 3-halooxindoles using aromatic oximes as hydroxylating agents, thus providing diverse hydroxylated 3-benzyl and alkyl-substituted oxindoles with high enantioselectivities (Figure 1a). We attempt to use 3-aryl-substituted 3-halooxindoles, not reported in Yuan's work, as a significant extension to asymmetric stereoablative transformation of 3-halooxindoles[8] to build 3,3-disubstituted oxindoles.

Carboxylation by utilizing commercially available or conveniently accessible carboxylic acids is an alternative to produce chiral alcohols through hydrolysis. Rare examples of catalytic asymmetric carboxylation[9] have yet been reported to date probably due to the weak nucleophilicity of carboxylic acids and elusive stereocontrol especially for H-bonding catalysis. As an extension of our recent contributions toward organocatalytic asymmetric synthesis of chiral tertiary alcohols[3d,4f,10] and asymmetric decarboxylative[11] reactions, we report herein the first enantioselective stereoablative carboxylation of various 3-bromooxindoles with MAHTs by employing an L-amino acid based bifunctional urea−tertiary amine catalyst (Figure 1b). More importantly, readily commercially available carboxylic acids could be used.

Inspired by the biosynthesis of polyketides,[12] MAHTs have been successfully applied in many enantioselective decarboxylative reactions over the past few years.[11,13] MAHTs contain two possible nucleophilic positions (β-methylene and carboxylate), and mechanistic studies have shown that the β-methylene nucleophilic addition of MAHTs to electrophiles is followed by decarboxylation. To the best of our knowledge, direct carboxylation of MAHTs has yet to be reported.

We initiated our study with the model reaction between 3-benzyl-3-bromooxindole **1a** and *tert*-butyl-substituted MAHT

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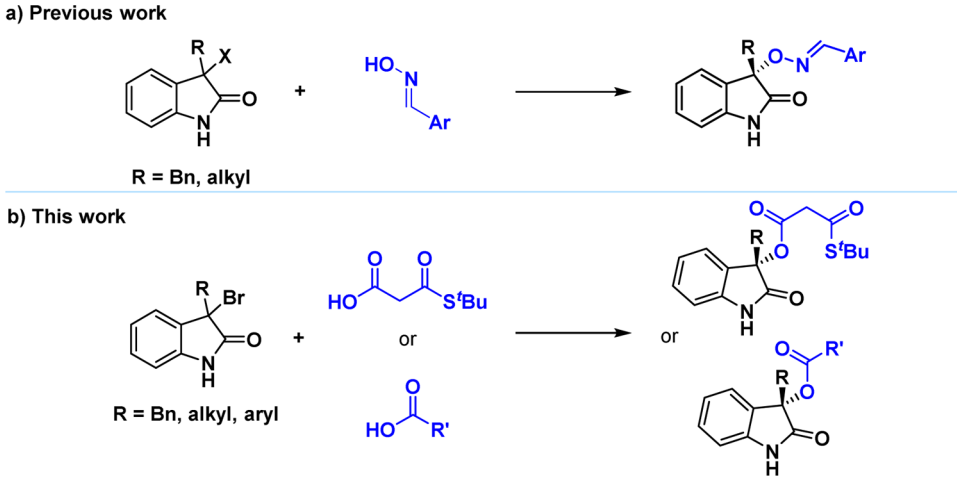
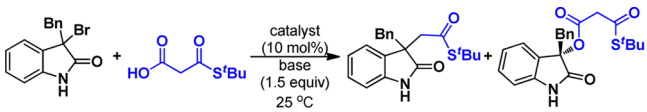
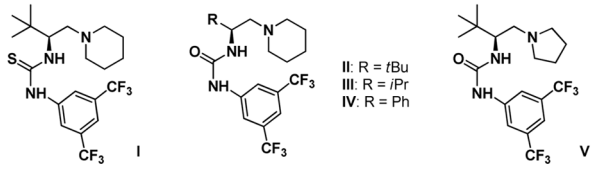


Figure 1. Stereoablative hydroxylation and carboxylation.

Table 1. Optimization of the Reaction Conditions[a]





entry	catalyst	base	solvent	t (h)	yield[b] (%)	ee[c] (%)
1[d]	I	K_2CO_3	CH_2Cl_2	24	34	0
2	II	K_2CO_3	CH_2Cl_2	24	68	79
3	III	K_2CO_3	CH_2Cl_2	24	76	57
4	IV	K_2CO_3	CH_2Cl_2	24	74	51
5	V	K_2CO_3	CH_2Cl_2	24	51	71
6	II	K_3PO_4	CH_2Cl_2	12	70	71
7	II	Na_2CO_3	CH_2Cl_2	96	62	77
8	II	K_2HPO_4	CH_2Cl_2	12	83	81
9	II	K_2HPO_4	toluene	12	70	87
10	II	K_2HPO_4	THF	12	68	72
11	II	K_2HPO_4	Et_2O	48	58	90
12	II	K_2HPO_4	MTBE	68	81	92

[a]The reaction was carried out with 0.05 mmol of **1a**, 0.065 mmol of **2a**, and 0.005 mmol of catalyst in 0.5 mL of solvent. [b]Isolated yield of **4a**. [c]ee value of **4a** determined by HPLC methods. [d]64% conversion was determined by crude ^{1}H NMR.

2a (Table 1). The reaction was first performed in CH_2Cl_2 at 25 °C with K_2CO_3 as base and 10 mol % of a highly efficient L-*tert*-leucine-derived thiourea–tertiary amine catalyst (**I**, entry 1).[3d,10a,c,14] It was found that the reaction was slightly sluggish and only 64% conversion was observed after 24 h. To our surprise, the yield of decarboxylated product **3a** was low while the major product was determined to be carboxylate **4a** with 34% yield (no enantioselectivity). This challenged us to attempt various catalysts in order to fine-tune the reaction to provide only **4a**, the carboxylate product. When we repeated the reaction using urea–tertiary amine **II** as the catalyst (entry 2), product **4a** was selectively obtained in 68% yield with 79% ee after 24 h, indicating that urea as the H-bond donor is crucial. Next, urea–tertiary amines **III**–**IV** derived from L-valine (**III**) and L-phenylglycine (**IV**) were tested. There was slightly improved yields but lower ee (entries 3–4). Similarly catalyst **V** with pyrrolidine as the tertiary amine moiety gave modest results (entry 5). A screening of inorganic bases (entries 6–8) revealed that K_2HPO_4 was the most optimal base by improving yield and ee value (entry 8). Next, we screened different solvents (entries 9–12) and found that MTBE (methyl *tert*-butyl ether) was the most suitable, in which **4a** was obtained in 81% yield with 92% ee (entry 12). Two other MAHTs **1b–c** with a bulkier or a less hindered ester group did not give better ee values (see the Supporting Information for details).

With the optimized conditions in hand, we expanded the substrate scope investigation, and the results are summarized in Table 2. Initially, we attempted enantioselective stereoablative carboxylation of **2a** with a wide range of 3-benzyl-substituted 3-bromooxindoles in the presence of 10 mol % of catalyst **II** at 25 °C and MTBE as the solvent (Table 2, entries 1–16). The corresponding carboxylated products **4a–p** were obtained in 58–99% yield with 89–92% ee within 24–96 h. 3-Allyl- and 3-methyl-substituted 3-bromooxindoles were also suitable, affording adducts **4q–r** with excellent enantioselectivities (entries 17–18). 3-Aryl-substituted 3-bromooxindoles with phenyl (**4s**) and 4-fluorophenyl (**4t**) as the representative aryl groups were subjected to carboxylation with MAHT **2a** to expand the feasibility of the protocol (entries 19–20). It was observed that adducts **4s–t** could be achieved with similar enantioselectivities and in moderate yields.

A series of commercially available carboxylic acids **5a–g** were further evaluated for synthetic utility (10 mol % of catalyst **II**, 1.5 equiv of K_2HPO_4, toluene as solvent, and at 10 °C). To our delight, all the reactions worked smoothly, providing the corresponding adducts **6a–g** in 81–96% yield with 69–91% ee within 20–84 h (Table 3). It is worth mentioning that aromatic carboxylic acids (**5e–g**) gave higher enantioselectivity (entries 5–7), and the best result was attained with benzoic acid **5g** as the nucleophile (entry 7), which could also be obtained in gram-scale. Next, the reaction of benzoic acid **5g** with various 3-bromooxindoles was tested. As shown in Table 4, a variety of carboxylated products **6h–q** could be achieved in moderate to good yields with excellent enantioselectivites.

On account of the totally different enantioselectivity compared with the thiourea–tertiary amine catalyst,[10c] the urea–tertiary amine catalyst should have a distinct transition-state model (Figure 2). The tertiary amine of the catalyst deprotonates the MAHT to yield a carboxylic ion, which should bind to the R_3NH^+ arm of the catalyst through hydrogen bonding. Because of the

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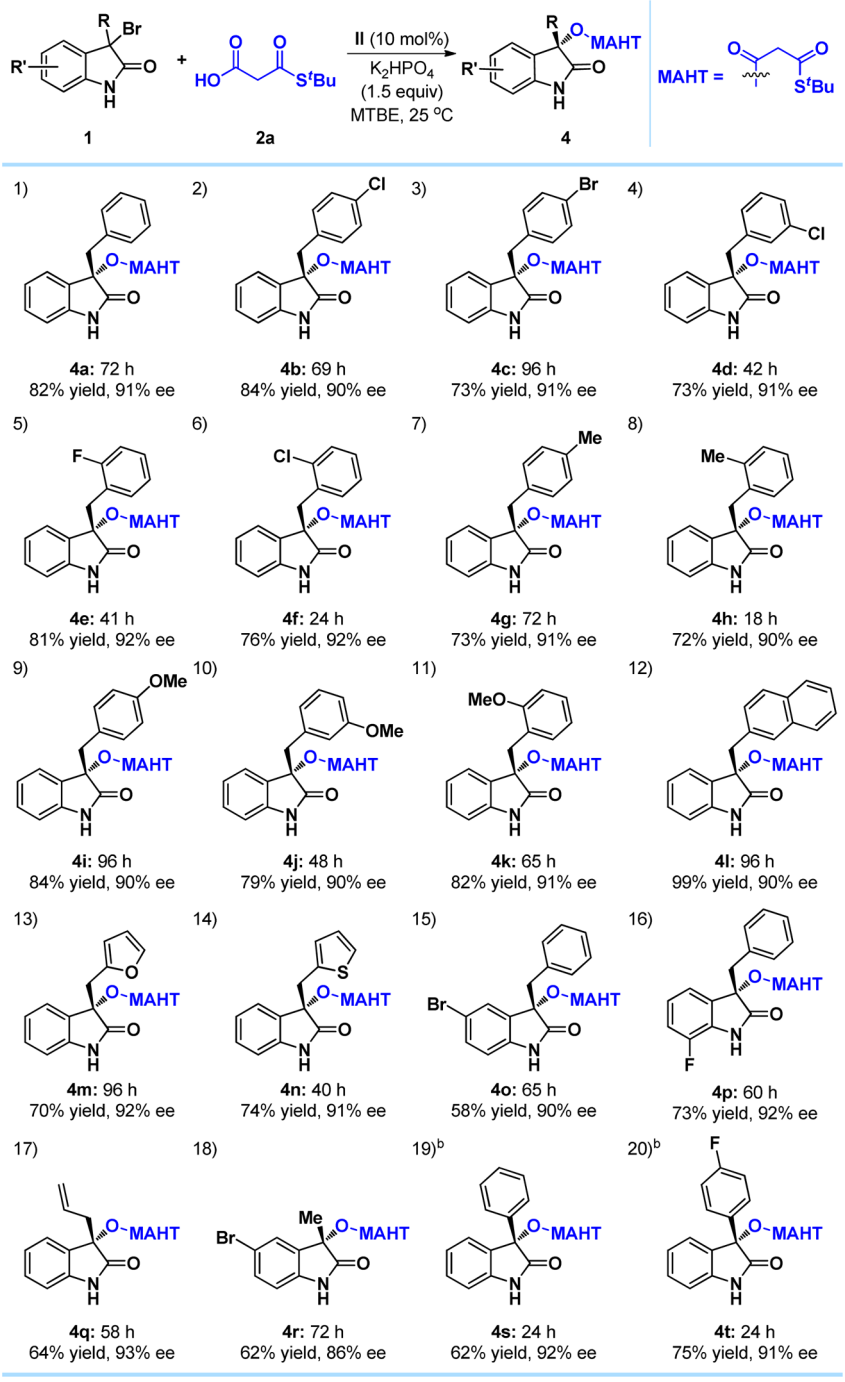
Table 2. Variation of 3-Substituted 3-Bromo-2-oxindoles 1[a]



[a]The reaction was carried out with 0.1 mmol of **1**, 0.13 mmol of **2**, 0.15 mmol of K_2HPO_4, and 0.01 mmol of catalyst **II** in 1.0 mL of MTBE at 25 °C. Isolated yield. ee values were determined by HPLC methods. [b]0.3 mmol of K_2HPO_4, 0 °C.

lower acidity of urea than thiourea, its N−H bond is shorter and would be more suitable to contribute another H-bonding interaction with the formed carboxylate ion.[10f] The dual H-bonding mode can strongly stabilize the carboxylic ion and benefit the enantioselectivity. Meanwhile, the generated indol-2-one interacts with another N−H bond of urea through H-bonding. After nucleophilic addition, the carboxylated adducts were obtained with the observed enantioselective results.

All established protocols using MAHTs aforementioned undergo decarboxylation. In this context, we propose a plausible mechanism whereby the sterically bulky *tert*-butyl group of MAHT **2a** retards the nucleophilic addition, leading to the observed chemoselectivity. If we attempted the reaction of 3-halooxindoles with less hindered aryl mercaptan-substituted MAHTs, it is reasonable that decarboxylative stereoablation should proceed. As shown in eq 1, the reaction between 3-bromooxindole **1a** and *para*-methylphenyl-substituted MAHT **7** with the presence of catalyst **II** in toluene and at 25 °C produced the stereoablative decarboxylation product **8** in 57% yield, but no enantioselectivity. Furthermore, the ee value of product **8** could be improved to 63% by using a quinidine catalyst.

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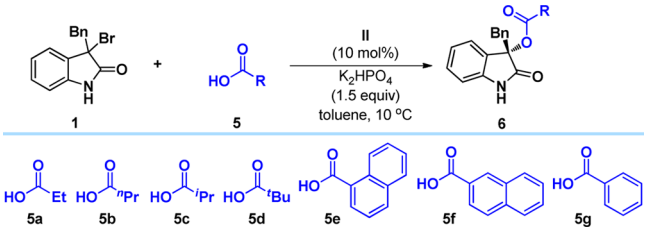
Table 3. Reactions of 3-Substituted 3-Bromo-2-oxindoles 1 with Various Carboxylic Acids 5[a]



entry	5	t (h)	6	yield[b] (%)	ee[c] (%)
1	**5a**	20	**6a**	95	90
2	**5b**	42	**6b**	83	85
3	**5c**	64	**6c**	91	79
4	**5d**	64	**6d**	92	69
5	**5e**	60	**6e**	95	80
6	**5f**	65	**6f**	96	89
7[d]	**5g**	84	**6g**	81	91

[a]The reaction was carried out with 0.1 mmol of **1**, 0.15 mmol of **5**, 0.15 mmol of K_2HPO_4, and 0.01 mmol of catalyst **II** in 1.0 mL of toluene at 10 °C. [b]Isolated yield. [c]ee values were determined by HPLC methods. [d]1 mmol scale, 92 h, 76% yield, 91% ee.

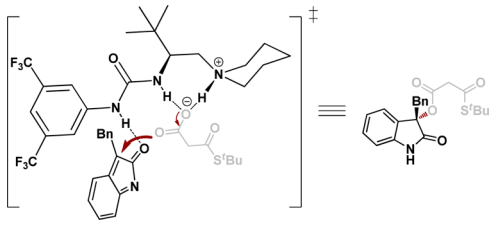


Figure 2. Proposed transition state.

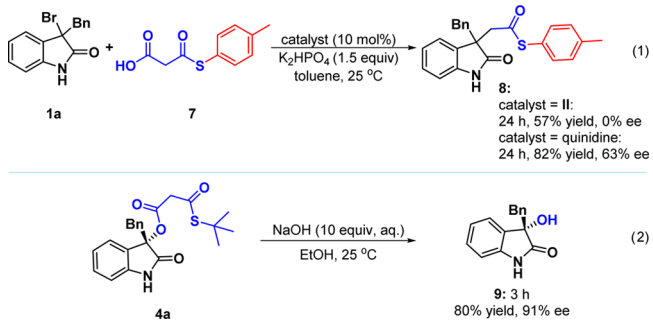
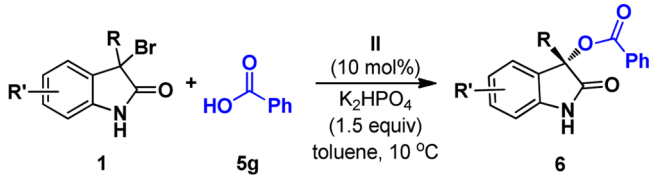
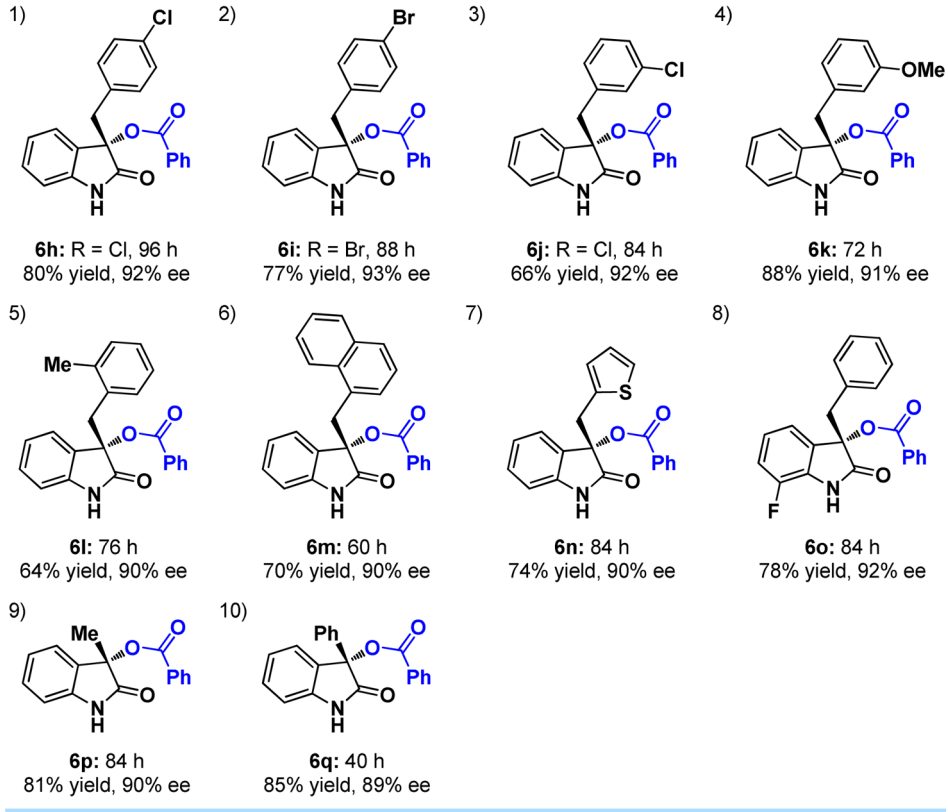


Table 4. Variation of 1 in the Reaction with Carboxylic Acids 5g[a]





[a]The reaction was carried out with 0.1 mmol of **1**, 0.15 mmol of **5g**, 0.15 mmol of K_2HPO_4, and 0.01 mmol of catalyst **II** in 1.0 mL of toluene at 10 °C. Isolated yield. ee values were determined by HPLC methods.

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Finally, we demonstrate the synthetic viability by transformation of carboxylated adducts (eq 2). It was found that the adduct **4a** could be conveniently hydrolyzed by NaOH at 25 °C to provide 3-benzyl-substituted 3-hydroxy-2-oxindole **9** without compromising the ee value.[15]

In summary, we have developed a novel enantioselective stereoablative carboxylation of 3-bromooxindoles with MAHTs and a series of commercially available carboxylic acids by employing an L-tertiary amine based urea−tertiary amine bifunctional catalyst. The current method provides an efficient and practical strategy to synthesize a broad scope of chiral 3-substituted 3-hydroxy-2-oxindoles with excellent enantioselectivities. This chemoselective reaction represents the first example of MAHTs as carboxylative nucleophiles.

EXPERIMENTAL SECTION

General Information. *General Procedures and Methods.* Experiments involving moisture- and/or air-sensitive components were performed under a positive pressure of nitrogen in oven-dried glassware equipped with a rubber septum inlet. Dried solvents and liquid reagents were transferred by oven-dried syringes or hypodermic syringe cooled to ambient temperature in a desiccator. Reaction mixtures were stirred in a 10 mL sample vial with Teflon-coated magnetic stirring bars unless otherwise stated. Moisture in nonvolatile reagents/compounds was removed in high vacuo by means of an oil pump and subsequent purging with nitrogen. Solvents were removed in vacuo under ∼30 mmHg and heated with a water bath at 30−35 °C using a rotary evaporator with aspirator. The condenser was cooled with running water at 0 °C.

All experiments were monitored by analytical thin-layer chromatography (TLC). TLC was performed on precoated plates, 60 F_{254}. After elution, the plate was visualized under UV illumination at 254 nm for UV active material. Further visualization was achieved by staining $KMnO_4$, ceric molybdate, or anisaldehyde solution. For those using the aqueous stains, the TLC plates were heated on a hot plate.

Columns for flash chromatography (FC) contained silica gel 200−300 mesh. Columns were packed as a slurry of *silica gel* in petroleum ether and equilibrated solution using the appropriate solvent system. The elution was assisted by applying pressure of about 2 atm with an air pump.

Instrumentation. Proton nuclear magnetic resonance (^{1}H NMR) and carbon NMR (^{13}C NMR) spectra were recorded in $CDCl_3$ unless otherwise stated. ^{1}H (400/300 MHz) and ^{13}C (100/75 MHz) were performed on 400/300 MHz spectrometers. Chemical shifts are reported in parts per million (ppm), using the residual solvent signal as an internal standard: $CDCl_3$ (^{1}H NMR: δ 7.26, singlet; ^{13}C NMR: δ 77.0, triplet). Multiplicities were given as s (singlet), d (doublet), t (triplet), q (quartet), *quintet*, m (multiplets), dd (doublet of doublets), dt (doublet of triplets), and br (broad). Coupling constants (J) were recorded in hertz (Hz). The number of proton atoms (n) for a given resonance was indicated by nH. The number of carbon atoms (n) for a given resonance was indicated by nC. HRMS was reported in units of mass of charge ratio (m/z). HRMS (Analyzer: TOF) were reported in units of mass of charge ratio (m/z). Mass samples were dissolved in DCM and MeOH (HPLC grade) unless otherwise stated. Optical rotations were recorded on a polarimeter with a sodium lamp of wavelength 589 nm and reported as follows: $[\alpha]_\lambda^{T\,^\circ C}$ (c = g/100 mL, solvent). Melting points were determined on a microscopic melting point apparatus.

Enantiomeric excesses were determined by chiral high performance liquid chromatography (HPLC) analysis. UV detection was monitored at 254, 230, and 210 nm at the same time. HPLC samples were dissolved in HPLC grade isopropanol (IPA) unless otherwise stated.

Materials. All commercial reagents were purchased with the highest purity grade. They were used without further purification unless specified. All solvents used, mainly petroleum ether (PE) and ethyl acetate (EtOAc), were distilled. Anhydrous DCM and MeCN were freshly distilled from CaH_2 and stored under a N_2 atmosphere. THF, Et_2O, MTBE, and toluene were freshly distilled from sodium/benzophenone before use. Anhydrous methanol and etanol were distilled from Mg. All compounds synthesized were stored in a −20 °C freezer, and light-sensitive compounds were protected with aluminum foil.

General Procedure 1. (MAHTs as nucleophiles): A solution of 3-benzyl-3-bromooxindole **1a** (0.1 mmol, 1.0 equiv), catalyst **II** (0.01 mmol, 0.1 equiv), and K_2HPO_4 (0.15 mmol, 1.5 equiv) in MTBE (1.0 mL) was stirred at 25 °C for 20 min. Then, *tert*-butyl-substituted MAHT **2a** (0.13 mmol, 1.3 equiv) was added. TLC was monitored during the whole process, until the reaction was complete. The solvent was concentrated under reduced pressure, and the residue was purified by flash column chromatography on *silica gel* (petroleum ether/ethyl acetate) to furnish the corresponding products **4**.

General Procedure 2. (Carboxylic acids as nucleophiles): A solution of 3-benzyl-3-bromooxindole **1a** (0.1 mmol, 1.0 equiv), catalyst **II** (0.01 mmol, 0.1 equiv), and K_2HPO_4 (0.15 mmol, 1.5 equiv) in toluene (1.0 mL) was stirred at 10 °C for 20 min. Then, carboxylic acids **5a−g** (0.15 mmol, 1.5 equiv) was added. TLC was monitored during the whole process, until the reaction was complete. Then, the reaction mixture was subjected to flash column chromatography on *silica gel* (petroleum ether/ethyl acetate) to furnish the corresponding products **6**.

General Procedure 3. (Synthesis of products **8**): A solution of 3-benzyl-3-bromooxindole **1a** (0.1 mmol, 1.0 equiv), quinidine (0.01 mmol, 0.1 equiv), and K_2HPO_4 (0.15 mmol, 1.5 equiv) in toluene (1.0 mL) was stirred at 10 °C for 20 min. Then, *para*-methylphenyl-substituted MAHT **7** (0.15 mmol, 1.5 equiv) was added. TLC was monitored during the whole process, until the reaction was complete. Then, the reaction mixture was subjected to flash column chromatography on *silica gel* (petroleum ether/ethyl acetate) to furnish the corresponding products **8**.

General Procedure 4. (Synthesis of products **9**): A mixture of **4a** (0.1 mmol, 1 equiv) and NaOH (1 mmol, 10 equiv) in H_2O (300 μL) and EtOH (1 mL) was stirred vigorously at 25 °C for 3 h. TLC was monitored during the whole process, until the reaction was complete. Then, the reaction mixture was extracted with EtOAc (3 mL × 3) and the combined organic phase was dried over anhydrous sodium sulfate and evaporated in vacuo. Flash column chromatography on *silica gel* (petroleum ether/ethyl acetate) furnished 3-benzyl-substituted 3-hydroxy-2-oxindole **9**.

*(S)-3-Benzyl-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4a**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.4 (petroleum ether/ethyl acetate = 3/1); yellow oil; 28.6 mg (0.1 mmol); 82% yield; 91% ee; $[\alpha]_D^{26}$ + 11.92 (c 1.86, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.87 (d, J = 13.8 Hz, 1H), 7.21−7.12 (m, 4H), 7.00−6.91 (m, 3H), 6.86 (d, J = 7.1 Hz, 1H), 6.70 (d, J = 7.7 Hz, 1H), 3.60 (d, J = 15.0 Hz, 1H), 3.49−3.40 (m, 2H), 3.08 (d, J = 13.2 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 175.0 (−CONH−), 164.0 (−COO−), 140.5 (−C−), 132.5 (−C−), 130.8 (−2 × CH−), 129.9 (−CH−), 127.8 (−2 × CH−), 127.2 (−CH−), 126.3 (−C−), 124.2 (−CH−), 122.4 (−CH−), 109.9 (−CH−), 81.1 (−C-O−), 49.8 (−CH_2−), 49.2 (−C−), 42.3 (−CH_2−), 29.6 (−$(CH_3)_3$); HRMS (ESI) m/z 398.1423 (M + H^+), calc. for $C_{22}H_{24}NO_4S$ 398.1426. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 9.6 min (minor) and 14.4 min (major).

*(S)-3-(4-Chlorobenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4b**).* Reagents: 3-(4-chlorobenzyl)-3-bromooxindole **1b** (33.7 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 36.3 mg (0.1 mmol); 84% yield; 91% ee; $[\alpha]_D^{26}$ + 50.17 (c 1.71, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.20 (t, J = 7.1 Hz, 1H), 7.13 (d, J = 8.3 Hz, 2H), 6.99−6.88 (m, 4H), 6.71 (d, J = 7.7 Hz, 1H), 3.59 (d, J = 15.0 Hz, 1H), 3.46 (d, J = 15.0 Hz, 1H), 3.37 (d, J = 13.3 Hz, 1H), 3.06 (d, J = 13.3 Hz, 1H), 1.46 (s, 9 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 174.9 (−CONH−), 163.9 (−COO−), 140.6 (−C−), 133.3 (−C−), 132.1 (−2 × CH−), 131.0 (−CH−), 130.0 (−CH−), 128.0 (−2 × CH−), 126.0 (−C−), 124.1 (−CH−), 122.5 (−CH−),

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J. Org. Chem. 2015, 80, 12686−12696

110.2 (−CH−), 80.9 (−C-O−), 49.8 ($-CH_2-$), 49.2 (−C−), 41.6 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 432.1042 (M + H^+), calc. for $C_{22}H_{23}ClNO_4S$ 432.1036. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.1 min (minor) and 24.6 min (major).

*(S)-3-(4-Bromobenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4c**).* Reagents: 3-(4-bromobenzyl)-3-bromooxindole **1c** (38.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 34.8 mg (0.1 mmol); 73% yield; 91% ee; $[\alpha]_D^{26}$ + 33.93 (*c* 0.92, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54 (s, 1H), 7.28 (d, *J* = 8.4 Hz, 2H), 7.21 (td, *J* = 7.6, 1.4 Hz, 1H), 7.00−6.84 (m, 4H), 6.71 (d, *J* = 7.8 Hz, 1H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.46 (d, *J* = 15.0 Hz, 1H), 3.35 (d, *J* = 13.2 Hz, 1H), 3.04 (d, *J* = 13.2 Hz, 1H), 1.46(s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 174.8 (−CONH−), 163.8 (−COO−), 140.6 (−C−), 132.5 (2 × −CH−), 131.5 (−C−), 131.0 (2 × −CH−), 130.1 (−CH−), 126.1 (−C−), 124.1 (−CH−), 122.5 (−CH−), 121.5 (−C−), 110.1 (−CH−), 80.8 (−C-O−), 49.8 ($-CH_2-$), 49.2 (−C−), 41.7 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 476.0537 (M + H^+), calc. for $C_{22}H_{23}BrNO_4S$ 476.0531. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.8 min (minor) and 25.0 min (major).

*(S)-3-(3-Chlorobenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4d**).* Reagents: 3-(3-chlorobenzyl)-3-bromooxindole **1d** (33.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 31.5 mg (0.1 mmol); 73% yield; 91% ee; $[\alpha]_D^{26}$ + 36.34 (*c* 0.93, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.24−7.17 (m, 2H), 7.09 (t, *J* = 7.8 Hz, 1H), 7.00−6.95 (m, 2H), 6.90−6.87 (m, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 3.60 (d, *J* = 15.0 Hz, 1H), 3.47 (d, *J* = 15.0 Hz, 1H), 3.38 (d, *J* = 13.2 Hz, 1H), 3.05 (d, *J* = 13.3 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 174.7 (−CONH−), 163.8 (−COO−), 140.5 (−C−), 134.6 (−C−), 133.6 (−C−), 130.8 (−CH−), 130.1 (−CH−), 129.1 (−CH−), 129.0 (−CH−), 127.5 (−CH−), 126.0 (−C−), 124.1 (−CH−), 122.5 (−CH−), 110.1 (−CH−), 80.7 (−C-O−), 49.8 ($-CH_2-$), 49.2 (−C−), 41.9 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 432.1039 (M + H^+), calc. for $C_{22}H_{23}ClNO_4S$ 432.1036. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.3 min (minor) and 24.0 min (major).

*(S)-3-(2-Fluorobenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4e**).* Reagents: 3-(2-fluorobenzyl)-3-bromooxindole **1e** (31.9 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 33.6 mg (0.1 mmol); 81% yield, 92% ee; $[\alpha]_D^{26}$ + 50.32 (*c* 1.22, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J* = 6.2 Hz, 1H), 7.25−7.16 (m, 3H), 7.02 (td, *J* = 7.5, 1.0 Hz, 1H), 6.94−6.84 (m, 3H), 6.73 (d, *J* = 7.8 Hz, 1H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.46 (d, *J* = 14.9 Hz, 2H), 3.17 (d, *J* = 13.7 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 175.1 (−CONH−), 163.9 (−COO−), 162.6 (−CF−), 160.1 (−CF−), 140.5 (−C−), 132.8 (two peaks, −CH−), 129.9 (−CH−), 129.2 (−CH−), 129.1 (−CH−), 126.1 (−C−), 124.1 (two peaks, −CH−), 123.6 (two peaks, −CH−), 122.4 (−CH−), 120.2 (−C−), 120.1 (−C−), 115.2 (−CH−), 114.9 (−CH−), 110.0 (−CH−), 80.6 (−C−), 49.8 ($-CH_2-$), 49.1 (−C−), 34.6 (two peaks, $-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 416.1337 (M + H^+), calc. for $C_{22}H_{23}FNO_4S$ 416.1332. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 16.4 min (minor) and 25.2 min (major).

*(S)-3-(2-Chlorobenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4f**).* Reagents: 3-(2-chlorobenzyl)-3-bromooxindole **1f** (33.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 32.8 mg (0.1 mmol); 76% yield; 92% ee; $[\alpha]_D^{26}$ + 8.25 (*c* 1.29, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.42−7.40 (m, 1H), 7.24−7.18 (m, 4H), 6.87 (td, *J* = 7.6, 0.5 Hz, 1H), 6.78 (d, *J* = 7.8 Hz, 1H), 6.65 (d, *J* = 7.4 Hz, 1H), 3.61 (d, *J* = 15.0 Hz, 1H), 3.55 (d, *J* = 14.0 Hz, 1H), 3.46 (d, *J* = 15.0 Hz, 1H), 3.32 (d, *J* = 14.0 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 175.3 (−CONH−), 163.8 (−COO−), 140.4 (−C−), 135.6 (−C−), 132.8 (−CH−), 131.4 (−C−), 129.9 (−CH−), 129.3 (−CH−), 128.7 (−CH−), 126.4 (−CH−), 126.0 (−C−), 124.3 (−CH−), 122.4 (−CH−), 110.0 (−CH−), 80.6 (−C−), 49.9 ($-CH_2-$), 49.1 (−C−), 38.3 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 432.1035 (M + H^+), calc. for $C_{22}H_{23}ClNO_4S$ 432.1036. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 22.9 min (minor) and 15.4 min (major).

*(S)-3-(4-Methylbenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4g**).* Reagents: 3-(4-methylbenzyl)-3-bromooxindole **1g** (31.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 30.0 mg (0.1 mmol); 73% yield; 91% ee; $[\alpha]_D^{26}$ + 52.57 (*c* 1.01, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.19 (td, *J* = 7.6, 1.7 Hz, 1H), 6.98−6.89(m, 4H), 6.86 (d, *J* = 8.0 Hz, 2H), 6.69 (d, *J* = 7.8 Hz, 1H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.46 (d, *J* = 15.0 Hz, 1H), 3.37 (d, *J* = 13.2 Hz, 1H), 3.06 (d, *J* = 13.2 Hz, 1H), 2.26 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 175.1 (−CONH−), 163.9 (−COO−), 140.7 (−C−), 136.7 (-C−), 130.7 (2 × −CH−), 129.8 (−CH−), 129.4 (−CH−), 128.5 (−2 × CH−), 126.5 (−C−), 124.2 (−CH−), 122.3 (−CH−), 110.0 (−CH−), 81.2 (−C−), 49.8 ($-CH_2-$), 49.1 (−C−), 41.9 ($-CH_2-$), 29.6 ($-(CH_3)_3$), 21.0 ($-CH_3$); HRMS (ESI) *m*/*z* 412.1580 (M + H^+), calc. for $C_{23}H_{26}NO_4S$ 412.1583. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.3 min (minor) and 21.0 min (major).

*(S)-3-(2-Methylbenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4h**).* Reagents: 3-(2-methylbenzyl)-3-bromooxindole **1g** (31.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil, 29.6 mg (0.1 mmol); 72% yield; 90% ee; $[\alpha]_D^{26}$ + 41.83 (*c* 0.95, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (s, 1H), 7.22−7.13 (m, 3H), 7.11−7.06 (m, 2H), 6.86−6.79 (m, 2H), 6.52 (d, *J* = 7.4, 1H), 3.60 (d, *J* = 15.0 Hz, 1H), 3.48−3.41 (m, 2H), 3.04 (d, *J* = 14.1 Hz, 1H), 1.92 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 175.8 (−CONH−), 163.9 (−COO−), 140.4 (−C−), 137.9 (−C−), 131.8 (−CH−), 131.7 (−C−), 130.2 (−CH−), 129.8 (−CH−), 127.3 (−CH−), 126.4 (−C−), 125.4 (−CH−), 124.4 (−CH−), 122.2 (−CH−), 110.0 (−CH−), 81.1 (−C−), 49.9 ($-CH_2-$), 49.1 (−C−), 38.3 ($-CH_2-$), 29.6 ($-(CH_3)_3$), 19.7 ($-CH_3$); HRMS (ESI) *m*/*z* 412.1585 (M + H^+), calc. for $C_{23}H_{26}NO_4S$ 412.1583. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 15.1 min (minor) and 22.1 min (major).

*(S)-3-(4-Methoxybenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4i**).* Reagents: 3-(4-methoxybenzyl)-3-bromooxindole **1i** (33.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 35.9 mg (0.1 mmol); 84% yield; 90% ee; $[\alpha]_D^{26}$ + 58.48 (*c* 1.97, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.18 (td, *J* = 7.6, 1.5 Hz, 1H), 6.97−6.87 (m, 4H), 6.72−6.67 (m, 3H), 3.74 (s, 3H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.46 (d, *J* = 15.0 Hz, 1H), 3.35 (d, *J* = 13.4 Hz, 1H), 3.04 (d, *J* = 13.4 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 175.2 (−CONH−), 163.9 (−COO−), 158.7 (−C−), 140.7 (−C−), 131.8 (−2 × CH−), 129.8 (−CH−), 126.5 (−C−), 124.5 (−C−), 124.1 (−CH−), 122.3 (−CH−), 113.2 (2 × −CH−), 110.0 (−CH−), 81.3 (−C−), 55.1 ($-OCH_3$), 49.8 ($-CH_2-$), 49.1 (−C−), 41.5 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 428.1533 (M + H^+), calc. for $C_{23}H_{26}NO_5S$ 428.1532. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20;

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J. Org. Chem. 2015, 80, 12686−12696

flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.5 min (minor) and 25.4 min (major).

*(S)-3-(3-Methoxybenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4j**).* Reagents: 3-(3-methoxybenzyl)-3-bromooxindole **1j** (33.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 33.8 mg (0.1 mmol); 79% yield; 90% ee; $[\alpha]_D^{26}$ + 46.41 (*c* 1.07, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.21−7.17 (m, 1H), 7.06 (t, *J* = 7.9 Hz, 1H), 6.99−6.94 (m, 2H), 6.75−6.68 (m, 2H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.48−6.47 (m, 1H), 3.65 (s, 3H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.47 (d, *J* = 15.0 Hz, 1H), 3.39 (d, *J* = 13.1 Hz, 1H), 3.08 (d, *J* = 13.1 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 175.0 (−CONH−), 163.9 (−COO−), 158.9 (−C−), 140.7 (−C−), 133.9 (−C−), 129.9 (−CH−), 128.8 (−CH−), 126.3 (−C−), 124.2 (−CH−), 123.3 (−CH−), 122.3 (−CH−), 115.8 (−CH−), 113.3 (−CH−), 110.0 (−CH−), 81.1 (−C−), 55.0 ($-OCH_3$), 49.8 ($-CH_2-$), 49.1 (−C−), 42.4 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 428.1536 (M + H^+), calc. for $C_{23}H_{26}NO_5S$ 428.1532. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 17.1 min (minor) and 26.2 min (major).

*(S)-3-(2-Methoxybenzyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4k**).* Reagents: 3-(2-methoxybenzyl)-3-bromooxindole **1k** (33.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 35.0 mg (0.1 mmol); 82% yield; 91% ee; $[\alpha]_D^{26}$ + 28.96 (*c* 2.22, $CHCl_3$). ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 (s, 1H), 7.25−7.11 (m, 3H), 6.85 (qd, *J* = 7.3, 0.8 Hz, 2H), 6.78 (d, *J* = 7.2 Hz, 1H), 6.71−6.65 (m, 2H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.49−3.43 (m, 5H), 3.24 (d, *J* = 13.4 Hz, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5 (−CO-S−), 175.7 (−CONH−), 164.0 (−COO−), 157.8 (−C−), 140.4 (−C−), 132.2 (−CH−), 129.4 (−CH−), 128.6 (−CH−), 126.8 (−C−), 124.2 (−CH−), 121.7 (−CH−), 121.5 (−C−), 120.0 (−CH−), 110.0 (−CH−), 109.6 (−CH−), 81.2 (−C−), 54.7, 49.9 ($-CH_3$), 49.1 (−C−), 34.9 (−CH−), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 428.1534 (M + H^+), calc. for $C_{23}H_{26}NO_5S$ 428.1532. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 30.8 min (major) and 18.5 min (minor).

*(S)-3-(Naphthalen-2-ylmethyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4l**).* Reagents: 3-(naphthalen-2-ylmethyl)-3-bromooxindole **1l** (35.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 44.3 mg (0.1 mmol); 99% yield; 90% ee; $[\alpha]_D^{26}$ + 52.17 (*c* 1.32, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.77−7.74 (m, 1H), 7.67−7.61 (m, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.54 (s, 1H), 7.46 (s, 1H), 7.44−7.39 (m, 2H), 7.18−7.15 (m, 1H), 7.08 (dd, *J* = 8.4, 1.7 Hz, 1H), 6.97−6.92 (m, 2H), 6.64 (d, *J* = 7.8 Hz, 1H), 3.64−3.47 (m, 3H), 3.26 (d, *J* = 9.9 Hz 1H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 175.1 (−CONH−), 163.9 (−COO−), 140.6 (−C−), 133.0 (−C−), 132.4 (−C−), 130.1 (−C−), 129.9 (2 × −CH−), 128.7 (−CH−), 127.8 (−CH−), 127.3 (−CH−), 127.3 (−CH−), 126.3 (−C−), 125.8 (two peaks, −CH− and −CH−), 124.2 (−CH−), 122.4 (−CH−), 110.1 (−CH−), 81.2 (−C−), 49.9 ($-CH_2-$), 49.1 (−C−), 42.4 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 448.1586 (M + H^+), calc. for $C_{26}H_{26}NO_4S$ 448.1583. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 17.6 min (minor) and 25.4 min (major).

*(S)-3-(Furan-2-ylmethyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4m**).* Reagents: 3-(furan-2-ylmethyl)-3-bromooxindole **1m** (29.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 27.1 mg (0.1 mmol); 70% yield; 92% ee; $[\alpha]_D^{26}$ + 37.91 (*c* 0.59, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.25−7.19 (m, 2H), 7.00−6.91 (m, 2H), 6.77 (d, *J* = 7.8 Hz, 1H), 6.24−6.22 (m, 1H), 6.06 (d, *J* = 3.1 Hz, 1H), 3.36−3.43 (m, 3H), 3.19 (d, *J* = 14.7 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 174.8 (−CONH−), 163.9 (−COO−), 147.6 (−C−), 141.9 (−CH−), 140.7 (−C−), 130.0 (−CH−), 126.3 (−C−), 123.9 (−CH−), 122.6 (−CH−), 110.4 (−CH−), 110.1 (−CH−), 109.5 (−CH−), 79.8 (−C−), 49.8 ($-CH_2-$), 49.2 (−C−), 35.1 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 388.1217 (M + H^+), calc. for $C_{20}H_{22}NO_5S$ 388.1219. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 17.6 min (minor) and 27.0 min (major).

*(S)-2-Oxo-3-(thiophen-2-ylmethyl)indolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4n**).* Reagents: 3-(thiophen-2-ylmethyl)-3-bromooxindole **1n** (30.7 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 29.8 mg (0.1 mmol); 74% yield; 91% ee; $[\alpha]_D^{26}$ + 29.41 (*c* 1.17, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.22 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.12 (dd, *J* = 5.1, 0.8 Hz, 1H), 7.00−6.91 (m, 2H), 6.87−6.84 (m, 1H) 6.77−6.71 (m, 2H), 3.64−3.58(m, 2H), 3.49 (d, *J* = 15.1 Hz, 1H), 3.35 (d, *J* = 14.4 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 174.7 (−CONH−), 163.9 (−COO−), 140.9 (−C−), 134.0 (−C−), 130.1 (−CH−), 128.5 (−CH−), 126.4 (−CH−), 126.1 (−CH−), 125.4 (−C−), 124.2 (−CH−), 122.6 (−CH−), 110.1 (−CH−), 80.4 (−C−), 49.8 ($-CH_2-$), 49.2 (−C−), 36.7 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 404.0986 (M + H^+), calc. for $C_{20}H_{22}NO_4S_2$ 404.0990. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 17.2 min (minor) and 27.3 min (major).

*(S)-3-Benzyl-5-bromo-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4o**).* Reagents: 3-benzyl-5-bromo-3-bromooxindole **1o** (38.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 27.6 mg (0.1 mmol); 58% yield; 90% ee; $[\alpha]_D^{26}$ + 80.60 (*c* 0.97, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.62 (s, 1H), 7.31 (dd, *J* = 8.3, 2.0 Hz, 1H), 7.23−7.14 (m, 3H), 7.00−6.97 (m, 3H), 6.58 (d, *J* = 8.3 Hz, 1H), 3.60 (d, *J* = 14.8 Hz, 1H), 3.48 (d, *J* = 14.8 Hz, 1H), 3.39 (d, *J* = 13.2 Hz, 1H), 3.08 (d, *J* = 13.2 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.1 (−CO-S−), 174.9 (−CONH−), 164.0 (−COO−), 139.6 (−C−), 132.7 (−CH−), 131.9 (−C−), 130.8 (2 × −CH−), 128.2 (−C−), 128.0 (2 × −CH−), 127.4 (−CH−), 114.8 (−CH−), 111.6 (−CH−), 80.8 (−C−), 49.9 ($-CH_2-$), 49.3 (−C−), 42.2 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 476.0529 (M + H^+), calc. for $C_{22}H_{23}BrNO_4S$ 476.0531. The ee was determined by HPLC analysis. CHIRALPAK IB (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 14.5 min (minor) and 28.7 min (major).

*(S)-3-Benzyl-7-fluoro-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4p**).* Reagents: 3-benzyl-7-fluoro-3-bromooxindole **1p** (31.9 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.5 (petroleum ether/ethyl acetate = 3/1); yellow oil; 30.3 mg (0.1 mmol); 73% yield; 92% ee; $[\alpha]_D^{26}$ + 44.49 (*c* 1.37, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.57 (s, 1H), 7.21−7.13 (m, 3H), 7.01−6.87 (m, 4H), 6.69 (d, *J* = 7.2 Hz, 1H), 3.61 (d, *J* = 15.1 Hz, 1H), 3.50−3.40 (m, 2H), 3.10 (d, *J* = 13.2 Hz, 1H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 174.2 (−CONH−), 164.0 (−COO−), 148.0 (−CF−), 145.6 (−CF−), 132.1 (−C−), 130.7 (2 × −CH−), 128.9 (two peaks, −C−), 127.9 (2 × −CH−), 127.4 (−CH−), 123.0 (two peaks, −C−), 119.9 (two peack, −CH−), 117.0 (−CH−), 116.9 (−CH−), 81.0 (−C−), 49.7 ($-CH_2-$), 49.2 (−C−), 42.3 ($-CH_2-$), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 416.1337 (M + H^+), calc. for $C_{22}H_{23}FNO_4S$ 416.1332. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.2 min (major) and 16.3 min (minor).

*(S)-3-Allyl-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4q**).* Reagents: 3-allyl-3-bromooxindole **1q** (25.1 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 22.2 mg (0.1 mmol);

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J. Org. Chem. 2015, 80, 12686−12696

64% yield; 93% ee; $[\alpha]_D^{26}$ + 40.99 (*c* 0.74, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.28−7.23 (m, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 6.84 (d, *J* = 7.7 Hz, 1H), 5.70−5.56 (m, 1H), 5.12−5.06 (m, 2H), 3.56 (d, *J* = 15.1 Hz, 1H), 3.44 (d, *J* = 15.1 Hz, 1H), 2.87−2.81 (m, 1H), 2.64−2.57 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.5 (−CO-S−), 175.0 (−CONH−), 164.1 (−COO−), 140.5 (−C−), 129.9 (−CH−), 129.0 (−CH−), 126.8 (−C−), 123.8 (−CH−), 122.6 (−CH−), 120.9 ($-CH_2-$), 110.1 (−C−), 80.2 (−C−), 49.7 ($-CH_2-$), 49.1 ($-CH_2-$), 40.8 (−C−), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 348.1271 (M + H^+), calc. for $C_{18}H_{22}NO_4S$ 348.1270. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 13.8 min (major) and 21.6 min (minor).

*(S)-5-Bromo-3-methyl-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4r**).* Reagents: 5-bromo-3-methyl-3-bromooxindole **1r** (30.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 24.8 mg (0.1 mmol); 62% yield; 86% ee; $[\alpha]_D^{26}$ + 8.93 (*c* 1.91, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (s, 1H), 7.37−7.35 (m, 2H), 6.75 (d, *J* = 8.8 Hz, 1H), 3.56 (d, *J* = 14.9 Hz, 1H), 3.46 (d, *J* = 14.9 Hz, 1H), 1.64 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.3 (−CO-S−), 175.5 (−CONH−), 164.2 (−COO−), 139.2 (−C−), 132.7 (−CH−), 130.7 (−C−), 126.1 (−CH−), 115.4 (−C−), 111.9 (−CH−), 78.0 (−C−), 49.8 ($-CH_2-$), 49.3 (−C−), 29.6 ($-(CH_3)_3$), 23.0 ($-CH_3$); HRMS (ESI) *m*/*z* 400.0216 (M + H^+), calc. for $C_{16}H_{19}BrNO_4S$ 400.0218. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.1 min (minor) and 28.4 min (major).

*(S)-2-Oxo-3-phenylindolin-3-yl-3-(tert-butylthio)-3-oxopropanoate (**4s**).* Reagents: 3-phenyl-3-bromooxindole **1r** (28.7 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 23.8 mg (0.1 mmol); 62% yield; 92% ee; $[\alpha]_D^{26}$ + 72.03 (*c* 0.66, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.77 (s, 1H), 7.39−7.30 (m, 6H), 7.24 (s, 1H), 7.09 (dt, *J* = 7.6, 0.7 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 3.66 (d, *J* = 15.1 Hz, 1H), 3.56 (d, *J* = 15.1 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.5 (−CO-S−), 175.1 (−CONH−), 164.3 (−COO−), 141.5 (−C−), 135.8 (−C−), 130.3 (−CH−), 129.0 (−CH−), 128.6 (2 × −CH−), 127.9 (−C−), 126.2 (2 × −CH−), 124.8 (−CH−), 123.1 (−CH−), 110.5 (−CH−), 82.2 (−C−), 49.9 ($-CH_2-$), 49.2 (−C−), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 384.1272 (M + H^+), calc. for $C_{21}H_{22}NO_4S$ 384.1270. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 55/45; flow rate 10 mL/min; 25 °C; 254 nm; retention time: 10.6 min (minor) and 33.2 min (major).

*(S)-3-(4-Fluorophenyl)-2-oxoindolin-3-yl 3-(tert-Butylthio)-3-oxopropanoate (**4t**).* Reagents: 3-(4-fluorophenyl)-3-bromooxindole **1r** (30.5 mg, 0.1 mmol), *tert*-butyl-substituted MAHT **2a** (23 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 30.1 mg (0.1 mmol); 75% yield, 91% ee; $[\alpha]_D^{26}$ + 22.27 (*c* 1.20, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.30−7.21 (m, 2H), 7.16 (s, 1H), 7.10−6.93 (m, 4H), 6.86 (d, *J* = 7.8 Hz, 1H), 3.59 (d, *J* = 15.1 Hz, 1H), 3.48 (d, *J* = 15.1 Hz, 1H), 1.41 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 190.4 (−CO-S−), 174.8 (−CONH−), 164.8 (−CF−), 164.2 (−COO−), 161.5 (−CF−), 141.4 (−C−), 131.7 (−C−), 131.6 (−C−), 130.5 (−CH−), 128.5 (2 × −CH−), 128.4 (2 × −CH−), 127.6 (−C−), 124.9 (−CH−), 123.3 (−CH−), 115.7 (2 × −CH−), 115.4 (2 × −CH−), 110.6 (−CH−), 81.6 (−C−), 49.9 ($-CH_2-$), 49.3 (−C−), 29.6 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 402.1174 (M + H^+), calc. for $C_{21}H_{21}FNO_4S$ 402.1175. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 70/30; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.3 min (major) and 18.7 min (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl 3-(Isopropylthio)-3-oxopropanoate (**4u**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), *i*-pr-substituted MAHT **2b** (21 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 32.6 mg (0.1 mmol); 85% yield; 91% ee; $[\alpha]_D^{26}$ + 59.2 (c 1.47, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.22−7.12 (m, 4H), 6.99−6.92 (m, 3H), 6.87 (d, *J* = 7.2 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 3.73−3.63 (m, 2H), 3.53 (d, *J* = 15.3 Hz, 1H), 3.42 (d, *J* = 13.2 Hz, 1H), 3.08 (d, *J* = 13.2 Hz, 1H), 1.31 (t, *J* = 7.3 Hz, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.2 (−CO-S−), 175.3 (−CONH−), 163.9 (−COO−), 140.6 (−C−), 132.5 (−C−), 130.8 (2 × −CH−), 129.9 (−CH−), 127.8 (2 × −CH−), 126.2 (−C−), 124.2 (−CH−), 122.3 (−CH−), 110.0 (−CH−), 81.2 (−C−), 49.2 ($-CH_2-$), 42.3 ($-CH_2-$), 35.6 (−CH−), 22.7 (two peaks, 2 × $-CH_3$); HRMS (ESI) *m*/*z* 384.1263 (M + H^+), calc. for $C_{21}H_{22}NO_4S$ 384.1270. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 25.3 min (minor) and 16.8 min (major).

*(S)-3-Benzyl-2-oxoindolin-3-yl 3-Oxo-3-((2,4,4-trimethylpentan-2-yl)thio)propanoate (**4v**).* Reagent: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), 2,4,4-trimethylpentan-substituted MAHT **2c** (23.2 mg, 0.13 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), MTBE (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 45 mg (0.1 mmol); 99% yield; 87% ee; $[\alpha]_D^{26}$ + 0.38(c 1.32, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 7.58 (s, 1H), 7.21−7.13 (m, 4H), 6.99−6.88 (m, 4H), 6.68 (d, *J* = 7.8 Hz, 1H), 3.59 (d, *J* = 15.0 Hz, 1H), 3.48−3.39 (m, 2H), 3.10 (d, *J* = 13.1 Hz, 1H), 1.80 (s, 2H), 1.56 (d, *J* = 2.1 Hz, 6H), 1.01 (s, 9H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 190.2 (−CO-S−), 175.2 (−CONH−), 163.9 (−COO−), 140.6 (−C−), 132.5 (−C−), 130.8 (2 × −CH−), 129.8 (−CH−), 127.8 (2 × −CH−), 127.2 (−CH−), 126.3 (−C−), 124.2 (−CH−), 122.3 (−CH−), 110.0 (−CH−), 81.2 (−C−), 54.3 (−C−), 53.5 ($-CH_2-$), 49.9 ($-CH_2-$), 42.3 ($-CH_2-$), 32.6 (−C−), 31.6 ($-(CH_3)_3$), 29.3 (two peaks, 2 × $-CH_3$); HRMS (ESI) *m*/*z* 454.2043 (M + H^+), calc. for $C_{26}H_{32}NO_4S$ 454.2052. The ee was determined by HPLC analysis. CHIRALPAK IA (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 27.3 min (minor) and 17.2 min (major).

*(S)-3-Benzyl-2-oxoindolin-3-yl Propionate (**6a**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), propionic acid **5a** (11.1 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 28.0 mg (0.1 mmol); 95% yield, 90% ee; $[\alpha]_D^{26}$ + 28.64 (*c* 2.10, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.20−7.13 (m, 4H), 7.01 (dd, *J* = 7.6, 1.6 Hz, 2H), 6.92 (td, *J* = 7.6, 0.8 Hz, 1H), 6.79 (d, *J* = 7.4 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 3.41 (d, *J* = 13.2 Hz, 1H), 3.05 (d, *J* = 13.2 Hz, 1H), 2.52−2.30 (m, 2H), 1.10 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (−CONH−), 172.3 (−COO−), 140.8 (−C−), 132.9 (−C−), 130.8 (2 × −CH−), 129.6 (−C−), 127.7 (2 × −CH−), 127.1 (−CH−), 123.6 (−CH−), 122.1 (−CH−), 110.1 (−CH−), 80.2 (−C−), 42.4 ($-CH_2-$), 27.2 ($-CH_2-$), 8.7 ($-CH_3$); HRMS (ESI) *m*/*z* 296.1295 (M + H^+), calc. for $C_{18}H_{18}NO_3$ 296.1287. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.4 min (major) and 8.9 (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl Butyrate (**6b**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), butyric acid **5b** (13.2 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 25.7 mg (0.1 mmol); 83% yield; 85% ee; $[\alpha]_D^{26}$ + 25.99 (*c* 2.46, $CHCl_3$); ^1H NMR (300 MHz, $(CD_3)_2CO$) δ 9.38 (s, 1H), 7.24−7.09 (m, 4H), 7.01−6.87 (m, 4H), 6.71 (d, *J* = 7.8 Hz, 1H), 3.38 (d, *J* = 12.9 Hz, 1H), 3.06 (d, *J* = 12.9 Hz, 1H), 2.33 (t, *J* = 7.2 Hz, 2H), 1.63−1.51 (m, 2H), 0.89 (t, *J* = 7.4 Hz, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ 175.9 (−CONH−), 171.5 (−COO−), 143.2 (−C−), 134.2 (−C−), 131.6 (2 × −CH−), 130.2 (−CH−), 128.4 (2 × −CH−), 128.3 (−C−), 127.7 (−CH−), 124.4 (−CH−), 122.1 (−CH−), 110.4 (−CH−), 81.0 (−C−), 43.1 ($-CH_2-$), 36.1 ($-CH_2-$), 19.0 ($-CH_2-$), 13.7 ($-CH_3$); HRMS (ESI) *m*/*z* 310.1445 (M + H^+), calc. for $C_{19}H_{20}NO_3$ 310.1443. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 min (major) and 9.8 (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl Isobutyrate (**6c**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), isobutyric acid **5c** (13.2 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol),

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toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; 90.7−92.4 °C; 28.2 mg (0.1 mmol); 91% yield; 79% ee; $[\alpha]_D^{26}$ + 15.52 (*c* 2.21, $CHCl_3$); ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 9.38 (s, 1H), 7.22−7.12 (m, 4H), 7.03−7.00 (dd, *J* = 7.4, 2.0 Hz, 2H), 6.89 (d, *J* = 4.3 Hz, 2H), 6.72 (d, *J* = 7.8 Hz, 1H), 3.39 (d, *J* = 13.0 Hz, 1H), 3.04 (d, *J* = 13.0 Hz, 1H), 2.68−2.54 (m, 1H), 1.11 (d, *J* = 2.2 Hz, 3H), 1.09 (d, *J* = 2.2 Hz, 3H); ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ 175.9 (−CONH−), 174.8 (−COO−) 143.2 (−C−), 134.3 (−C−), 131.7 (2 × −CH−), 130.2 (−CH−), 128.4 (2 × −CH−), 128.3 (−C−), 127.7 (−CH−), 124.3 (−CH−), 122.1 (−CH−), 110.4 (−CH−), 80.7 (−C−), 43.0 ($-CH_2-$), 34.1 (−CH−), 19.0 ($-(CH_3)_2$), 18.8; HRMS (ESI) *m*/*z* 310.1446 (M + H$^+$), calc. for $C_{19}H_{20}NO_3$ 310.1443. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 4.7 (major) and 8.1 (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl Pivalate (**6d**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), pivalic acid **5d** (15.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 109.7−111.0 °C; 29.8 mg (0.1 mmol); 92% yield; 69% ee; $[\alpha]_D^{26}$ + 10.75 (*c* 2.71, $CHCl_3$); ^{1}H NMR (300 MHz, $(CD_3)_2CO$) δ 9.41 (s, 1H), 7.20−7.15 (m, 4H), 7.06−7.03 (m, 2H), 6.88 (td, *J* = 7.5, 0.9 Hz, 1H), 6.81−6.75 (m, 2H), 3.40 (d, *J* = 13.1 Hz, 1H), 3.01 (d, *J* = 13.1 Hz, 1H), 1.17 (s, 9H); ^{13}C NMR (75 MHz, $(CD_3)_2CO$) δ 176.1 (two peaks, −CONH− and −COO−), 143.2 (−C−), 134.4 (−C−), 131.9 (2 × −CH−), 130.1 (−CH−), 128.42 (2 × −CH−), 128.3 (−C−), 127.8 (−CH−), 124.2 (−CH−), 122.1 (−CH−), 110.4 (−CH−), 80.6 (−C−), 43.0 ($-CH_2-$), 38.9 (−C−), 27.2 ($-(CH_3)_3$); HRMS (ESI) *m*/*z* 324.1605 (M + H$^+$), calc. for $C_{20}H_{22}NO_3$ 324.1600. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 4.1 min (major) and 6.3 min (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl 1-Naphthoate (**6e**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), 1-naphthoic acid **5e** (25.8 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 146.9−148.4 °C; 37.4 mg (0.1 mmol); 95% yield; 80% ee; $[\alpha]_D^{26}$ + 28.46 (*c* 3.19, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80−8.76 (m, 1H), 8.40 (s, 1H), 8.33 (dd, *J* = 7.3, 1.2 Hz, 1H), 8.05 (d, *J* = 8.2 Hz, 1H), 7.89−7.86 (m, 1H), 7.58−7.48 (m, 3H), 7.31−7.28 (m, 1H), 7.25−7.13 (m, 5H), 6.97−6.88 (m, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 3.65 (d, *J* = 13.2 Hz, 1H), 3.24 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.4 (−CONH−), 165.3 (−COO−), 140.9 (−C−), 133.9, 133.7 (−C−), 133.0 (−C−), 131.3 (−C−), 131.1 (2 × −CH−), 130.7 (−CH−), 129.7 (−CH−), 128.4 (−CH−), 127.9 (−CH−), 127.8 (2 × −CH−), 127.2 (−CH−), 127.1 (−C−), 126.3 (−CH−), 125.8 (two peaks, −C− and −CH−), 124.4 (−CH−), 123.9 (−CH−), 122.2 (−CH−), 110.3 (−CH−), 80.9 (−C−), 42.6 ($-CH_2-$); HRMS (ESI) *m*/*z* 394.1451 (M + H$^+$), calc. for $C_{26}H_{20}NO_3$ 394.1443. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 6.8 min (major) and 14.4 min (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl 2-Naphthoate (**6f**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), 2-naphthoic acid **5e** (25.8 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 78.3−79.1 °C; 37.8 mg (0.1 mmol); 96% yield; 89% ee; $[\alpha]_D^{26}$ + 138.19 (*c* 3.52, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.64 (s, 1H), 8.24 (s, 1H), 8.05 (dd, *J* = 8.6, 1.6 Hz, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.88 (d, *J* = 8.6 Hz, 2H), 7.64−7.54 (m, 2H), 7.28 (d, *J* = 3.2 Hz, 2H), 7.23−7.16 (m, 3H), 6.96−6.88 (m, 2H), 6.80 (d, *J* = 7.8 Hz, 1H), 3.67 (d, *J* = 13.2 Hz, 1H), 3.27 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (−CONH−), 164.7 (−COO−), 140.9 (−C−), 135.7 (−C−), 133.0 (−C−), 132.3 (-C−), 131.8 (−CH−), 131.1 (2 × −CH−), 129.8 (−CH−), 129.4 (−CH−), 128.5 (−CH−), 128.2 (−CH−), 127.9 (2 × −CH−), 127.8 (−CH−), 127.3 (−CH−), 127.1 (−C−), 126.7 (−CH−), 126.3 (−C−), 125.2 (−CH−), 124.0 (−CH−), 122.2 (−CH−), 110.2 (−CH−), 80.7 (−C−), 42.6 ($-CH_2-$); HRMS (ESI) *m*/*z* 394.1454 (M + H$^+$), calc. for $C_{26}H_{20}NO_3$ 394.1443. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 12.7 min (major) and 18.2 min (minor).

*(S)-3-Benzyl-2-oxoindolin-3-yl Benzoate (**6g**).* Reagents: 3-benzyl-3-bromooxindole **1a** (30.2 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 27.8 mg (0.1 mmol); 81% yield; 91% ee; $[\alpha]_D^{26}$ + 67.41 (*c* 0.97, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99−7.93 (m, 2H), 7.69 (s, 1H), 7.51 (t, *J* = 7.4, 1H), 7.38 (t, *J* = 7.6, 2H), 7.17−7.11 (m, 4H), 7.05−7.02 (m, 2H), 6.86 (t, *J* = 7.3 Hz, 1H), 6.79 (d, *J* = 7.1 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 3.52 (d, *J* = 13.1 Hz, 1H), 3.14 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3 (−CONH−), 164.5 (−COO−), 140.8 (−C−), 133.5 (−CH−), 132.9 (−C−), 131.0 (2 × −CH−), 129.8 (2 × −CH−), 129.7 (−CH−), 129.1 (−C−), 128.4 (2 × −CH−), 127.8 (2 × −CH−), 127.2 (−CH−), 127.0 (−C−), 124.0 (−CH−), 122.2 (−CH−), 110.2 (−CH−), 80.6 (−C−), 42.5 ($-CH_2-$); HRMS (ESI) *m*/*z* 344.1294 (M + H$^+$), calc. for $C_{22}H_{18}NO_3$ 344.1287. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.2 min (major) and 26.5 min (minor).

*(S)-3-(4-Chlorobenzyl)-2-oxoindolin-3-yl Benzoate (**6h**).* Reagents: 3-(4-chlorobenzyl)-3-bromooxindole **1b** (33.5 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 75.2−76.8 °C; 30.2 mg (0.1 mmol); 80% yield; 92% ee; $[\alpha]_D^{26}$ + 72.79 (*c* 2.41, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03−8.00 (m, 2H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.52 (s, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.23−7.17 (m, 3H), 7.02−6.91 (m, 4H), 6.78 (d, *J* = 7.8 Hz, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.21 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1 (−CONH−), 164.5 (−COO−), 140.9 (−C−), 133.6 (−CH−), 133.4 (−C−), 132.3 (2 × −CH−), 131.4 (−CH−), 130.0 (two peaks, −CH− and 2 × −CH−), 129.0 (−C−), 128.5 (2 × −CH−), 128.1 (2 × −CH−), 126.8 (−C−), 123.9 (−CH−), 122.4 (−CH−), 110.4 (−CH−), 80.5 (−C−), 41.9 ($-CH_2-$); HRMS (ESI) *m*/*z* 400.0710 (M + Na$^+$), calc. for $C_{22}H_{16}ClNO_3Na$ 400.0716. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.0 min (major) and 25.0 min (minor).

*(S)-3-(4-Bromobenzyl)-2-oxoindolin-3-yl Benzoate (**6i**).* Reagents: 3-(4-bromobenzyl)-3-bromooxindole **1c** (38.1 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 84.2−85.7 °C; 32.5 mg (0.1 mmol); 77% yield, 93% ee; $[\alpha]_D^{26}$ + 89.72 (*c* 0.64, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.03−8.01 (m, 2H), 7.67 (s, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.34 (d, *J* = 8.3 Hz, 2H), 7.22 (dd, *J* = 7.6, 1.7 Hz, 1H), 6.98−6.90 (m, 4H), 6.78 (d, *J* = 7.8 Hz, 1H), 3.52 (d, *J* = 13.2 Hz, 1H), 3.19 (d, *J* = 13.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.1 (−CONH−), 164.4 (−COO−), 140.8 (−C−), 133.6 (−CH−), 132.6 (2 × −CH−), 131.9 (−C−), 131.0 (2 × −CH−), 129.9 (two peaks, −CH− and 2 × −CH−), 128.8 (−C−), 128.4 (2 × −CH−), 126.6 (−C−), 123.8 (−CH−), 122.3 (−CH−), 121.5 (−C−), 110.4 (−CH−), 80.3 (−C−), 41.9 ($-CH_2-$); HRMS (ESI) *m*/*z* 422.0403 (M + H$^+$), calc. for $C_{22}H_{17}BrNO_3$ 422.0392. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.5 min (major) and 26.5 min (minor).

*(S)-3-(3-Chlorobenzyl)-2-oxoindolin-3-yl Benzoate (**6j**).* Reagents: 3-(3-chlorobenzyl)-3-bromooxindole **1d** (33.5 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); Yellow solid; mp 122.4−124.3 °C; 24.9 mg (0.1 mmol); 66% yield; 92% ee; $[\alpha]_D^{26}$ + 84.12 (*c* 2.46, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05−8.02 (m, 2H), 7.97 (s, 1H), 7.59 (t, *J* = 7.4 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.23−7.14 (m, 3H), 7.00−6.92 (m, 2H), 6.82 (t, *J* = 7.7 Hz, 2H), 3.55 (d, *J* = 13.2 Hz, 1H), 3.15 (d, *J* = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0 (−CONH−), 164.4 (−COO−), 140.7 (−C−),

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135.0 (−C−), 133.6 (two peaks, −C− and −CH−), 131.1 (−CH−), 130.0 (−CH−), 129.9 (2 × −CH−), 129.2 (−CH−), 129.1 (−CH−), 128.9 (−C−), 128.5 (2 × −CH−), 127.5 (−CH−), 126.6 (−C−), 123.9 (−CH−), 122.3 (−CH−), 110.4 (−CH−), 80.2 (−C−), 42.1 ($-CH_2-$); HRMS (ESI) m/z 378.0899 ($M + H^+$), calc. for $C_{22}H_{17}ClNO_3$ 378.0897. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 0.8 mL/min; 25 °C; 254 nm; retention time: 6.7 min (major) and 19.2 min (minor).

*(S)-3-(3-Methoxybenzyl)-2-oxoindolin-3-yl Benzoate (**6k**).* Reagents: 3-(3-methoxybenzyl)-3-bromooxindole **1j** (33.1 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; mp 142.9−143.3 °C; 32.9 mg (0.1 mmol); 88% yield; 91% ee; $[\alpha]_D^{26}$ + 88.53 (c 3.07, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05 (d, J = 7.3 Hz, 2H), 7.72 (s, 1H), 7.58 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 7.24−7.17 (m, 1H), 7.14 (t, J = 7.9 Hz, 1H), 6.97−6.90 (m, 2H), 6.80−6.76 (m, 2H), 6.71 (d, J = 7.6 Hz, 1H), 6.60 (s, 1H), 3.69 (s, 3H), 3.57 (d, J = 13.1 Hz, 1H), 3.19 (d, J = 13.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (−CONH−), 164.5 (−COO−), 158.9 (−C−), 140.9 (−C−), 134.4 (−C−), 133.4 (−CH−), 129.9 (2 × −CH−), 129.8 (−CH−), 129.0 (−C−), 128.8 (−CH−), 128.4 (2 × −CH−), 126.9 (−C−), 124.0 (−CH−), 123.4 (−CH−), 122.1 (−CH−), 116.0 (−CH−), 113.3 (−CH−), 110.3 (−CH−), 80.6 (−C−), 55.0 ($-OCH_3$), 42.5 ($-CH_2-$); HRMS (ESI) m/z 374.1393 ($M + H^+$), calc. for $C_{23}H_{20}NO_4$ 374.1392. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.8 min (major) and 27.9 min (minor).

*(S)-3-(2-Methylbenzyl)-2-oxoindolin-3-yl Benzoate (**6l**).* Reagents: 3-(2-methylbenzyl)-3-bromooxindole **1h** (31.5 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 22.9 mg (0.1 mmol); 64% yield; 90% ee; $[\alpha]_D^{26}$ + 101.65 (c 1.66, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.98−7.95 (m, 2H), 7.50 (t, J = 7.4, 1H), 7.37 (t, J = 7.8 Hz, 2H), 7.33−7.30 (m, 1H), 7.16−7.10 (m, 3H), 7.07−7.02 (m, 1H), 6.82−6.72 (m, 2H), 6.44 (d, J = 7.4 Hz, 1H), 3.52 (d, J = 14.1 Hz, 1H), 3.10 (d, J = 14.1 Hz, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.8 (−CONH−), 164.7 (−COO−), 140.7 (−C−), 138.1 (−C−), 133.5 (−CH−), 132.2 (−C−), 131.8 (−CH−), 130.3 (−CH−), 130.0 (2 × −CH−), 129.7 (−C−), 129.2 (−CH−), 128.5 (2 × −CH−), 127.5 (−CH−), 127.2 (−C−), 125.5 (−CH−), 124.1 (−CH−), 122.2 (−CH−), 110.2 (−CH−), 80.6 (−C−), 38.5 ($-CH_2-$), 19.7 ($-CH_3$); HRMS (ESI) m/z 358.1445 ($M + H^+$), calc. for $C_{23}H_{20}NO_3$ 358.1443. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.6 (major) and 21.8 (minor).

*(S)-3-(Naphthalen-1-ylmethyl)-2-oxoindolin-3-yl Benzoate (**6m**).* Reagents: 3-(naphthalen-1-ylmethyl)-3-bromooxindole **1l** (35.1 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid, 75.8−77.0 °C; 27.5 mg (0.1 mmol); 70% yield; 90% ee; $[\alpha]_D^{26}$ + 105.61 (c 0.94, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.16−8.13 (m, 1H), 8.06 (s, 1H), 7.89−7.80 (m, 4H), 7.54−7.39 (m, 4H), 7.35−7.28 (m, 3H), 7.18 (td, J = 7.8, 1.1 Hz, 1H), 6.86 (d, J = 7.7 Hz, 1H), 6.74 (td, J = 7.6, 0.7 Hz, 1H), 6.52 (d, J = 7.4 Hz, 1H), 4.15 (d, J = 14.2 Hz, 1H), 3.51 (d, J = 14.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.9 (−CONH−), 164.7 (−COO−), 140.6 (−C−), 133.7 (−C−), 133.4 (−CH−), 133.2 (−C−), 130.1 (−CH− and 2 × −CH−), 129.9 (−C−), 129.6 (−CH−), 128.8 (−C−), 128.5 (−CH−), 128.3 (−CH−), 128.2 (2 × −CH−), 127.1 (−C−), 125.7 (−CH−), 125.5 (−CH−), 125.0 (−CH−), 124.7 (−CH−), 124.6 (−CH−), 122.0 (−CH−), 110.3 (−CH−), 80.7 (−C−), 38.3 ($-CH_2-$); HRMS (ESI) m/z 416.1267 ($M + Na^+$), calc. for $C_{26}H_{19}NO_3$ 416.1263. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35 flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 8.0 (major) and 17.8 (minor).

*(S)-2-Oxo-3-(thiophen-2-ylmethyl)indolin-3-yl Benzoate (**6n**).* Reagents: 3-(thiophen-2-ylmethyl)-3-bromooxindole **1n** (30.7 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; 138.4−140.1 °C; 25.9 mg (0.1 mmol); 74% yield; 90% ee; $[\alpha]_D^{26}$ + 64.71 (c 2.63, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.13−8.10 (m, 2H), 7.79 (s, 1H), 7.62−7.56 (m, 1H), 7.46 (t, J = 7.8 Hz, 2H), 7.28−7.24 (m, 1H), 7.22−7.20 (m, 1H), 6.96−6.90 (m, 2H), 6.85−6.82 (m, 2H), 6.77 (d, J = 3.2 Hz, 1H), 3.78 (d, J = 14.5 Hz, 1H), 3.42 (d, J = 14.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.9 (two peaks, −CONH−), 164.5 (−COO−), 141.0 (−C−), 134.5 (−C−), 133.5 (−CH−), 130.1 (2 × −CH−), 130.0 (−CH−), 128.8 (−C−), 128.7 (−CH−),128.4 (2 × −CH−), 126.6 (−C−), 126.4 (−CH−), 125.6 (−CH−), 123.9 (−CH−), 122.4 (−CH−), 110.3 (−CH−), 79.9 (−C−), 36.9 ($-CH_2-$); HRMS (ESI) m/z 350.0847 ($M + H^+$), calc. for $C_{20}H_{16}NO_3S$ 350.0851. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/15; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.3 (major) and 30.1 (minor).

*(S)-3-Benzyl-7-fluoro-2-oxoindolin-3-yl Benzoate (**6o**).* Reagents: 3-benzyl-7-fluoro-3-bromooxindole **1p** (31.9 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow solid; 118.7−120.2 °C; 28.2 mg (0.1 mmol); 78% yield; 92% ee; $[\alpha]_D^{26}$ + 119.62 (c 2.81, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.05−8.02 (m, 2H), 7.62−7.57 (m, 2H), 7.45 (t, J = 7.6 Hz, 2H), 7.25−7.20 (m, 3H), 7.10−7.07 (m, 2H), 7.04−6.97 (m, 1H), 6.92−6.86 (m, 1H), 6.67 (d, J = 7.4 Hz, 1H), 3.59 (d, J = 13.2 Hz, 1H), 3.22 (d, J = 13.2 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.2 (−CONH−), 164.5 (−COO−), 148.5 (−CF−), 145.2 (−CF−), 133.6 (−CH−), 132.5 (−C−), 130.9 (2 × −CH−), 129.9 (2 × −CH−), 129.6 (two peaks, −C−), 128.7 (−C−), 128.4 (2 × −CH−), 128.2 (−C−), 128.0 (−C−), 127.9 (2 × −CH−), 127.4 (−CH−), 122.9 (−CH−), 122.8 (−CH−), 119.7 (−CH−), 119.6 (−CH−), 117.0 (−CH−), 116.8 (−CH−), 80.4 (two peaks, −C−), 42.4 ($-CH_2-$); HRMS (ESI) m/z 362.1184 ($M + H^+$), calc. for $C_{22}H_{17}FNO_3$ 362.1192. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.3 (major) and 21.0 (minor).

*(S)-3-Methyl-2-oxoindolin-3-yl Benzoate (**6p**).* Reagents: 3-methyl-3-bromooxindole **1w** (22.5 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); white solid; 73.1−74.5 °C; 21.6 mg (0.1 mmol); 81% yield; 90% ee; $[\alpha]_D^{26}$ + 76.68 (c 1.91, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (s, 1H), 8.12−8.09 (m, 2H), 7.62 (t, J = 7.4 Hz, 1H), 7.48 (t, J = 7.6 Hz, 2H), 7.30 (d, J = 7.5 Hz, 2H), 7.08−7.02 (m, 1H), 6.97 (d, J = 7.6 Hz, 1H), 1.85 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.2 (−CONH−), 164.6 (−COO−), 140.5 (−C−), 133.4 (−CH−), 129.9 (2 × −CH−), 129.7 (−CH−), 129.4 (−C−), 129.0 (−C−), 128.3 (2 × −CH−), 122.7 (−CH−), 122.4 (−CH−), 110.6 (−CH−), 77.9 (−C−), 23.3 ($-CH_3$); HRMS (ESI) m/z 268.0971 ($M + H^+$), calc. for $C_{16}H_{14}NO_3$ 268.0974. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.1 min (major) and 24.3 min (minor).

*(S)-2-Oxo-3-phenylindolin-3-yl Benzoate (**6q**).* Reagents: 3-phenyl-3-bromooxindole **1s** (28.7 mg, 0.1 mmol), benzoic acid **5e** (18.3 mg, 0.15 mmol), catalyst **II** (4.4 mg, 0.01 mmol), K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); white solid; 63.4−65.1 °C; 28.0 mg (0.1 mmol); 85% yield; 89% ee; $[\alpha]_D^{26}$ + 91.15 (c 3.37, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (s, 1H), 8.13−8.08 (m, 2H), 7.60 (t, J = 7.4 Hz, 1H), 7.51−7.37 (m, 7H), 7.33 (td, J = 7.7, 1.2 Hz, 1H), 7.24 (s, 1H), 7.06 (td, J = 7.6, 0.8 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5 (−CONH−), 164.8 (−COO−), 141.7 (−C−), 136.5 (−C−), 133.6 (−CH−), 130.2 (−CH−), 130.0 (2 × −CH−), 129.1 (−C−), 129.0 (−CH−), 128.7 (2 × −CH−), 128.5 (two peaks, −C− and 2 × −CH−), 126.3 (2 × −CH−), 124.6 (−CH−), 123.1 (−CH−), 110.5 (−CH−), 81.6 (−C−); HRMS (ESI) m/z 330.1136 ($M + H^+$), calc. for $C_{21}H_{16}NO_3$ 330.1130. The ee was determined by HPLC analysis. CHIRALPAK IC (4.6 mm i.d. × 250 mm); hexane/2-propanol = 65/35; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 7.4 (major) and 17.1 (minor).

*(S)-p-Tolyl 2-(3-Benzyl-2-oxoindolin-3-yl)ethanethioate (**8**).* Reagents: 3-benzyl-3-bromooxindole (30.2 mg, 0.1 mmol), 3-oxo-3-(*p*-tolylthio)-propanoic acid **7** (31.5 mg, 0.15 mmol), quinidine (3.2 mg, 0.01 mmol),

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J. Org. Chem. 2015, 80, 12686−12696

K_2HPO_4 (26.1 mg, 0.15 mmol), toluene (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 3/1); yellow oil; 31.8 mg (0.1 mmol); 82% yield; 63% ee; $[\alpha]_D^{26}$ + 7.63 (*c* 0.53, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43 (s, 1H), 7.17−6.98 (m, 10H), 6.87−6.84 (m, 2H), 6.61 (d, *J* = 7.7 Hz, 1H), 3.42 (d, *J* = 16.1 Hz, 1H), 3.31 (d, *J* = 16.1 Hz, 1H), 3.11 (d, *J* = 12.9 Hz, 1H), 3.05 (d, *J* = 12.9 Hz, 1H), 2.30 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 194.1 (−CO-S−), 179.6 (−CONH−), 140.9 (−C−), 139.8 (−C−), 134.6 (−C−), 134.3 (2 × −CH−), 130.2 (2 × −CH−), 130.0 (2 × −CH−), 129.9 (−C−), 128.2 (−CH−), 127.7 (2 × −CH−), 126.8 (−CH−), 124.1 (−CH−), 123.6 (−C−), 121.9 (−CH−), 109.7 (−CH−), 52.0 (−C−), 48.8 ($-CH_2-$), 43.6 ($-CH_2-$), 21.3 ($-CH_3$); HRMS (ESI) *m*/*z* 388.1382 (M + H^+), calc. for $C_{24}H_{22}NO_2S$ 388.1371. The ee was determined by HPLC analysis. LUX 5U CELLULOSE-4 (4.6 mm i.d. × 250 mm); hexane/2-propanol = 80/20; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 18.2 (minor) and 22.4 (major).

*(S)-3-Benzyl-3-hydroxyindolin-2-one (**9**).* Reagents: (*S*)-3-benzyl-2-oxoindolin-3-yl 3-(*tert*-butylthio)-3-oxopropanoate **4a** (39.7 mg, 0.1 mmol), NaOH (40 mg, 1 mmol), H_2O (300 μL), EtOH (1.0 mL); R_f = 0.3 (petroleum ether/ethyl acetate = 2/1); white solid; 167.6−168.9 °C; 19.2 mg (0.1 mmol); 80% yield; 91% ee; ^{1}H NMR (300 MHz, CD_3OD) δ 7.22 (d, *J* = 7.4 Hz, 1H), 7.15 (td, *J* = 7.7, 1.2 Hz, 1H), 7.09−6.97 (m, 4H), 6.93−6.92 (m, 2H), 6.65 (d, *J* = 7.7 Hz, 1H), 3.25 (d, *J* = 12.6 Hz, 1H), 3.14 (d, *J* = 12.6 Hz, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ 181.7 (−CONH−), 142.8 (−C−), 135.8 (−C−), 132.0 (−C−), 131.4 (2 × −CH−), 130.4 (−CH−), 128.6 (2 × −CH−), 127.6 (−CH−), 125.8 (−CH−), 123.3 (−CH−), 110.9 (−CH−), 78.9 (−C−), 45.0 ($-CH_2-$); HRMS (ESI) *m*/*z* 240.1027 (M + H^+), calc. for $C_{15}H_{14}NO_2$ 240.1025; The ee was determined by HPLC analysis. CHIRALPAK AD-H (4.6 mm i.d. × 250 mm); hexane/2-propanol = 90/10; flow rate 1.0 mL/min; 25 °C; 254 nm; retention time: 5.7 (major) and 6.4 (minor).

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.5b02286.

General information, copies of HPLC spectra, and copies of NMR spectra (PDF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Peddibhotla, S. *Curr. Bioact. Compd.* **2009**, *5*, 20−38. (b) Tokunaga, T.; Hume, W. E.; Umezome, T.; Okazaki, K.; Ueki, Y.; Kumagai, K.; Hourai, S.; Nagamine, J.; Seki, H.; Taiji, M.; Noguchi, H.; Nagata, R. *J. Med. Chem.* **2001**, *44*, 4641−4649. (c) Hewawasam, P.; Erway, M.; Moon, S. L.; Knipe, J.; Weiner, H.; Boissard, C. G.; Post-Munson, D. J.; Gao, Q.; Huang, S.; Gribkoff, V. K.; Meanwell, N. A. *J. Med. Chem.* **2002**, *45*, 1487−1499. (d) Tokunaga, T.; Hume, W. E.; Nagamine, J.; Kawamura, T.; Taiji, M.; Nagata, R. *Bioorg. Med. Chem. Lett.* **2005**, *15*, 1789−1792. (e) Marqués-López, E.; Herrera, R. P.; Christmann, M. *Nat. Prod. Rep.* **2010**, *27*, 1138−1167.

(2) For selected reviews, see: (a) Zhou, F.; Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (b) Dalpozzo, R.; Bartoli, G.; Bencivenni, G. *Chem. Soc. Rev.* **2012**, *41*, 7247.

(3) For selected examples, see: (a) Itoh, T.; Ishikawa, H.; Hayashi, Y. *Org. Lett.* **2009**, *11*, 3854. (b) Chen, W.-B.; Du, X.-L.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Tetrahedron* **2010**, *66*, 1441. (c) Hara, N.; Nakamura, S.; Funahashi, Y.; Shibata, N. *Adv. Synth. Catal.* **2011**, *353*, 2976. (d) Zhang, W.; Tan, D.; Lee, R.; Tong, G.; Chen, W.; Qi, B.; Huang, K.-W.; Tan, C.-H.; Jiang, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 10069.

(4) For selected examples, see: (a) Ishimaru, T.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *J. Am. Chem. Soc.* **2006**, *128*, 16488. (b) Sano, D.; Nagata, K.; Itoh, T. *Org. Lett.* **2008**, *10*, 1593. (c) Bui, T.; Candeias, N. R.; Barbas, C. F., III *J. Am. Chem. Soc.* **2010**, *132*, 5574. (d) Zhang, Z.; Zheng, W.; Antilla, J. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 1135. (e) Shen, K.; Liu, X.; Wang, G.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 4684. (f) Yang, Y.; Moinodeen, F.; Chin, W.; Ma, T.; Jiang, Z.; Tan, C.-H. *Org. Lett.* **2012**, *14*, 4762.

(5) Jayakumar, S.; Kumarswamyreddy, N.; Prakash, M.; Kesavan, V. *Org. Lett.* **2015**, *17*, 1066.

(6) (a) Jia, Y.-X.; Hillgren, J. M.; Watson, E. L.; Marsden, S. P.; Kündig, E. P. *Chem. Commun.* **2008**, 4040. (b) Yin, L.; Kanai, M.; Shibasaki, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 7620.

(7) Liao, Y.-H.; Wu, Z.-J.; Han, W.-Y.; Zhang, X.-M.; Yuan, W.-C. *Chem. - Eur. J.* **2012**, *18*, 8916.

(8) For selected examples, see: (a) Fuchs, J. R.; Funk, R. L. *J. Am. Chem. Soc.* **2004**, *126*, 5068. (b) Ma, S.; Han, X.; Krishnan, S.; Virgil, S. C.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2009**, *48*, 8037. (c) Zuo, J.; Liao, Y.-H.; Zhang, X.-M.; Yuan, W.-C. *J. Org. Chem.* **2012**, *77*, 11325. (d) Zhang, H.; Hong, L.; Kang, H.; Wang, R. *J. Am. Chem. Soc.* **2013**, *135*, 14098. (e) Dou, X.; Yao, W.; Zhou, B.; Lu, Y. *Chem. Commun.* **2013**, *49*, 9224. (f) Wu, C.; Li, G.; Sun, W.; Zhang, M.; Hong, L.; Wang, R. *Org. Lett.* **2014**, *16*, 1960.

(9) For selected examples, see: (a) Zhang, W.; Liu, N.; Schienebeck, C. M.; Zhou, X.; Izhar, I. I.; Guzei, I. A.; Tang, W. *Chem. Sci.* **2013**, *4*, 2652. (b) Li, L.; Su, C.; Liu, X.; Tian, H.; Shi, Y. *Org. Lett.* **2014**, *16*, 3728. (c) Xia, Y.; Lin, L.; Chang, F.; Fu, X.; Liu, X.; Feng, X. *Angew. Chem., Int. Ed.* **2015**, *54*, 13748.

(10) (a) Zhang, W.; Tan, D.; Lee, R.; Tong, G.; Chen, W.; Qi, B.; Huang, K.-W.; Tan, C.-H.; Jiang, Z. *Angew. Chem., Int. Ed.* **2012**, *51*, 10069. (b) Han, Z.; Yang, W.; Tan, C.-H.; Jiang, Z. *Adv. Synth. Catal.* **2013**, *355*, 1505. (c) Qiao, B.; An, Y.; Liu, Q.; Yang, W.; Liu, H.; Shen, J.; Yan, L.; Jiang, Z. *Org. Lett.* **2013**, *15*, 2358. (d) Liu, Q.; Qiao, B.; Chin, K. F.; Tan, C.-H.; Jiang, Z. *Adv. Synth. Catal.* **2014**, *356*, 3777. (e) Xu, M.; Qiao, B.; Duan, S.; Liu, H.; Jiang, Z. *Tetrahedron* **2014**, *70*, 8696. (f) Duan, S.; Li, S.; Ye, X.; Du, N.-N.; Tan, C.-H.; Jiang, Z. *J. Org. Chem.* **2015**, *80*, 7770.

(11) (a) Pan, Y.; Kee, C. W.; Jiang, Z.; Ma, T.; Zhao, Y.; Yang, Y.; Xue, H.; Tan, C.-H. *Chem.—Eur. J.* **2011**, *17*, 8363. (b) Qiao, B.; Liu, Q.; Liu, H.; Yan, L.; Jiang, Z. *Chem.—Asian J.* **2014**, *9*, 1252.

(12) Austin, M. B.; Izumikawa, M.; Bowman, M. E.; Udwary, D. W.; Ferrer, J.-L.; Moore, B. S.; Noel, J. P. *J. Biol. Chem.* **2004**, *279*, 45162.

(13) For selected organocatalytic asymmetric decarboxylic reactions, see: (a) Ricci, A.; Pettersen, D.; Bernardi, L.; Fini, F.; Fochi, M.; Herrera, R. P.; Sgarzani, V. *Adv. Synth. Catal.* **2007**, *349*, 1037. (b) Lubkoll, J.; Wennemers, H. *Angew. Chem., Int. Ed.* **2007**, *46*, 6841. (c) Bae, H. Y.; Some, S. J.; Lee, H.; Kim, J.-Y.; Song, M. J.; Lee, S.; Zhang, Y. J.; Song, C. E. *Adv. Synth. Catal.* **2011**, *353*, 3196. (d) Hara, N.; Nakamura, S.; Funahashi, Y.; Shibata, N. *Adv. Synth. Catal.* **2011**, *353*, 2976. (e) Hara, N.; Nakamura, S.; Sano, M.; Tamura, R.; Funahashi, Y.; Shibata, N. *Chem.—Eur. J.* **2012**, *18*, 9276. (f) Pan, Y.; Kee, C. W.; Jiang, Z.; Ma, T.; Zhao, Y.; Yang, Y.; Xue, H.; Tan, C.-H. *Chem.—Eur. J.* **2011**, *17*, 8363. (g) Bae, H. Y.; Sim, J. H.; Lee, J.-W.; List, B.; Song, C. E. *Angew. Chem., Int. Ed.* **2013**, *52*, 12143.

(14) For selected reviews, see: (a) Chai, Z.; Zhao, G. *Catal. Sci. Technol.* **2012**, *2*, 29. (b) Serdyuk, O. V.; Heckel, C. M.; Tsogoeva, S. B. *Org. Biomol. Chem.* **2013**, *11*, 7051. (c) Zhao, X.; Zhu, B.; Jiang, Z. *Synlett* **2015**, *26*, 2216.

(15) According to the comparison of HPLC results of **9** with ref 7, the absolute configurations of stereoablative carboxylated products **4** and **6** were determined as *S*.

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