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Stereoselective Synthesis of Functionalized 1,3-Disubstituted Isoindolines via Rh(III)-Catalyzed Tandem Oxidative Olefination-Cyclization of 4-Aryl-cyclic Sulfamidate-5-Carboxylates

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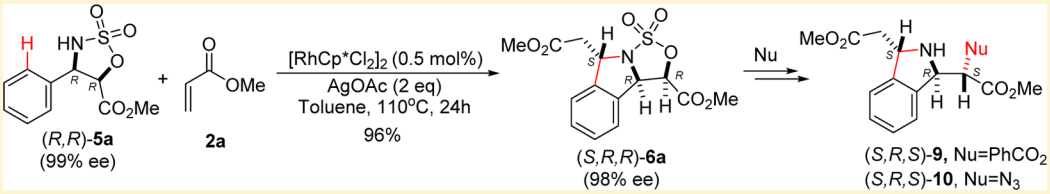
Supporting Information



ABSTRACT: A new method for the direct, stereoselective synthesis of highly functionalized 1,3-disubstituted isoindolines **6** from enantiomerically enriched cyclic 4-aryl-sulfamidate-5-carboxylates (**5**) is described. The process involves sulfamidate directed, Rh(III)-catalyzed tandem *ortho* C−H olefination of the 4-aryl-sulfamidate-5-carboxylates and subsequent cyclization by aza-Michael addition. In the reaction, which generates *trans*-1,3-disubstituted isoindolines exclusively, the configurational integrity of the stereogenic center in the starting cyclic sulfamidate is completely retained in the product. Examples are provided which show that the cyclic sulfamidate moiety not only serves as a chiral directing group but also as a versatile handle for further functionalization of the generated isoindoline ring system.

INTRODUCTION

The isoindoline substructure is present in a variety of natural and non-natural products that display interesting therapeutic activities.[1] However, only a limited number of approaches have been developed for the preparation of isoindolines and, in particular, 1,3-disubstituted isoindolines in either racemic and enantiomerically enriched forms.[1,2] Therefore, the development of strategies for the efficient enantioselective synthesis of 1,3-disubstituted isoindolines is of great interest in the field of synthetic organic chemistry.

Because of their step- and atom-economical nature, regioselective transition-metal-catalyzed C−H bond functionalization reactions of directing group bearing arenes serve as powerful and straightforward methods to prepare structurally diverse and complex substances.[3] Pd(II) complexes have been widely used to promote these processes.[3f,4] More recently, it was demonstrated that Ru(II)[5] and Rh(III)[6] complexes are active transition metal catalysts for highly selective *ortho*-olefination reactions of arenes. Processes promoted by these complexes require lower catalyst loading and they occur with higher efficiencies and broader functional group compatibilities than those induced by other transition metals.

Precoordination of the transition metal with a directing group followed by selective activation of an *ortho* C−H bond are fundamental steps in these catalytic C−H bond functionalization processes (Scheme 1).[3j] Consequently, a large effort has been given to the development of methods for site-selective reactions of arenes that rely on a variety of directing groups,[3j] such as ketones,[7] acids,[8] esters,[4i,6c] amides,[6b,i] anilides,[9] carbamates,[10] sulfonamides,[6g,h,11] and hydroxyls.[12] In addition to these monodentate groups, bidentate directing groups, such as 8-aminoquinoline amides[4h,13] and 2-aminomethylpyridine amides,[13,14] effectively promote activation of C−H bonds. These types of directing groups increase the activities of the transition metal catalysts and improve the regioselectivities of the reactions.

Despite the fact that significant advances in C−H activation chemistry have been made over the past decade, the ability to promote chirality transfer in these processes remains a great challenge.[15] As a result, the development of asymmetric versions of C−H activation reactions is clearly a significant undertaking. Diastereoselective transformations induced by C−H bond activation are typically achieved by incorporating a chiral auxiliary in the directing group[15b] or by employing transition metal catalysts that have chiral ligands.[15c−e] In this context, we recently described the use of an enantiomerically enriched 5-membered ring sulfamidate as a new chiral directing group. In that effort, we demonstrated that cyclic 4-aryl-sulfamidate (*R*)-**1** undergoes oxidative C−H olefination in the presence of Rh(III) as a catalyst and an alkene **2** to generate a styrene intermediate that spontaneously cyclizes to produce the 1,3-disubstituted

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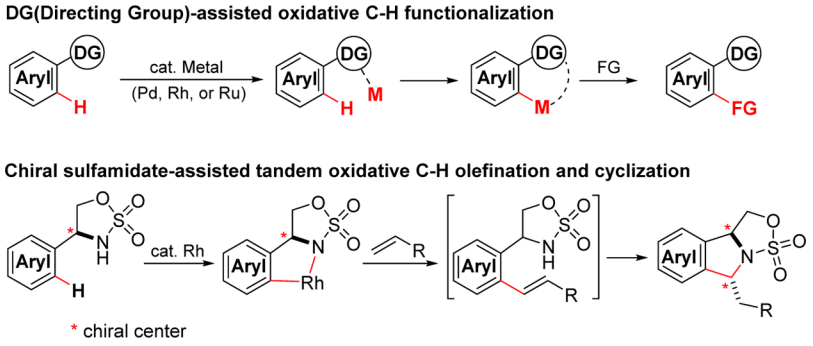
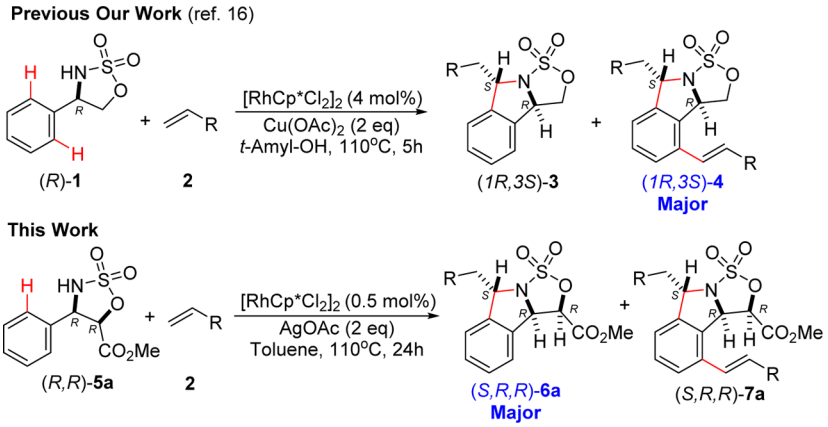
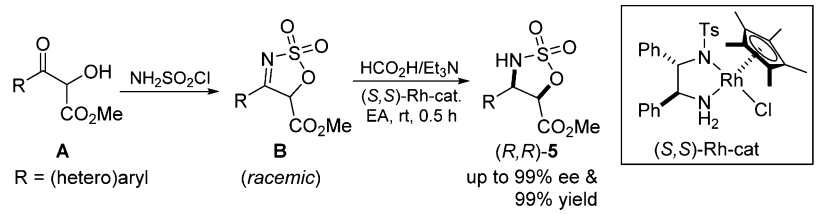
Scheme 1



Scheme 2



Scheme 3. Stereoselective Synthesis of Cyclic 4-Aryl-sulfamidate-5-carboxylates (5)



isoindoline (*R,S*)-**4**.[16] In this process, the configurational integrity of the stereogenic center in the starting cyclic sulfamidate is completely retained and *trans*-1,3-disubstituted isoindolines are formed exclusively (Scheme 2).

In the study described below, we further explored the utility of the chiral cyclic sulfamidate directing group by extending the scope of the tandem *ortho* C−H olefination reactions. Specifically, we demonstrated that Rh-catalyzed oxidative *ortho* C−H olefination reactions of 4-aryl-sulfamidate-5-carboxylates **5**, which contain a second stereogenic center, with olefins led to efficient and stereoselective formation of highly functionalized *trans*-1,3-disubstituted isoindolines **6** (Scheme 2).

RESULTS AND DISCUSSION

For the purpose of investigating in more detail the use of cyclic sulfamidates as chiral directing groups in tandem *ortho* C−H olefination-cyclization reactions, we prepared enantiomerically enriched cyclic 4-aryl-sulfamidates (*R,R*)-**5**, which have a carboxylate ester group at C-5 (Scheme 3)[17] and subjected them to oxidative olefination reactions promoted by the transition metal complex, [RhCp*Cl_2]$_2$. We anticipated that the chiral cyclic sulfamidate-5-carboxylates **5** would not only serve to enhance the stereochemical outcome of oxidative *ortho* C−H olefination reactions promoted by the transition metal complex, [RhCp*Cl_2]$_2$, but that it would also be a versatile synthetic handle for further functionalization of the formed isoindoline products.[18,19]

The requisite cyclic 4-aryl-sulfamidate-5-carboxylates **5** employed in this effort were prepared from the corresponding racemic imines **B** (Scheme 3) by using asymmetric transfer hydrogenation accompanied by dynamic kinetic resolution.[17] The reactions take place under both experimentally simple and mild conditions (rt, 30 min) and efficiently produce the target sulfamidates with high levels of stereoselectivity (up to >99% ee, dr >25:1) (Scheme 3 and see SI, Table S1).

(*R,R*)-4-Phenyl-sulfamidate-5-carboxylate **5a** and methyl acrylate **2a** were utilized as substrates in the initial studies aimed at optimizing the reaction conditions (Table 1). The results of extensive screening, using various transition metal catalysts, oxidants and solvents, showed that C−H olefination of (*R,R*)-**5a** with 3 eq. of **2a** takes place in the presence of 4 mol% [RhCp*Cl_2]$_2$ and 200 mol% of AgOAc in various solvents and this process is followed by spontaneous in situ cyclization to form a mixture of *trans*-1,3-disubstituted isoindolines (*S,R,R*)-**6a** and

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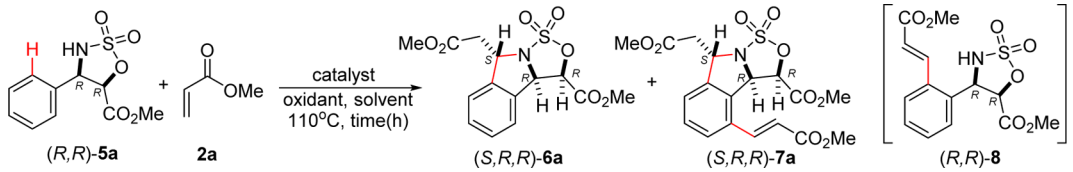
Table 1. Optimization of the Conditions for the Tandem Olefination-Cyclization Reactions[a]



entry	catalyst (mol%)	oxidant (mol%)	2a	solvent	time (h)	conversion (6a:7a)[b]	isolated yield
1	$[RhCp^*Cl_2]_2$ (4)	AgOAc (200)	3 eq	DCE	5	>99 (46:54)	
2	$[RhCp^*Cl_2]_2$ (4)	AgOAc (200)	3 eq	*t*-AmOH	5	>99 (70:30)	
3	$[RhCp^*Cl_2]_2$ (4)	AgOAc (200)	3 eq	1,4-dioxane	5	>99 (60:40)	
4	$[RhCp^*Cl_2]_2$ (4)	AgOAc (200)	3 eq	DMF	5	>99 (32:68)	
5	$[RhCp^*Cl_2]_2$ (4)	AgOAc (200)	3 eq	Acetone	5	>99 (31:69)	
6	**$[RhCp^*Cl_2]_2$ (4)**	**AgOAc (200)**	**3 eq**	**MeCN**	**5**	**>99 (23:77)**	
7	**$[RhCp^*Cl_2]_2$ (4)**	**AgOAc (200)**	**3 eq**	**toluene**	**8**	**>99 (88:12)**	
8	$[RhCp^*Cl_2]_2$ (4)	$Cu(OAc)_2$ (200)	3 eq	toluene	8	>99 (55:45)	
9	$[RhCp^*Cl_2]_2$ (1)	AgOAc (200)	2 eq	toluene	24	>99 (98:02)	91%
10	**$[RhCp^*Cl_2]_2$ (0.5)**	**AgOAc (200)**	**1.1 eq**	**toluene**	**24**	**>99 (100:0)**	**96%**
11	$[RhCp^*Cl_2]_2$ (0.5)	AgOAc (100)	1.1 eq	toluene	24	48 (100:0)[c]	
12	$[RhCp^*Cl_2]_2$ (0.5)	AgOAc (200)	1.1 eq	toluene[d]	24	80 (100:0)[e]	
13	$[RhCp^*Cl_2]_2$ (0.1)	AgOAc (200)	1.1 eq	toluene	24	>99 (94:06)	

[a]Conditions: **5a** (0.3 mmol), **2a** (0.9−0.33 mmol), $[RhCp^*Cl_2]_2$ (4−0.1 mol%), AgOAc (200 mol%), solvent 3 mL, 110 °C in a sealed tube. [b]Product ratio was determined by using ^1H NMR. [c]52% of starting material (**5a**) remained. [d]Reaction temperature = 80 °C. [e]**8** (4%) is also detected.

(*S,R,R*)-**7a** quantitatively. Moreover, the ratio of **6a** (mono-olefination) to **7a** (diolefination) was found to be highly dependent on solvent. Specifically, **7a** is the major product of the process carried out in acetonitrile (**6a**:**7a** = 23:77, Table 1 entry 6) whereas **6a** is predominates in the reaction in toluene (**6a**:**7a** = 88:12, Table 1 entry 7). The results showed that optimal conditions (96% isolated yield; **6a**:**7a** = 100:0, Table 1, entry 10) for the process involve the use of **5a** with 1.1 eq. of **2a**, 0.5 mol% of $[RhCp^*Cl_2]_2$ and 200 mol% of AgOAc in toluene. The structure and stereochemistry of (*S,R,R*)-**6a** were unambiguously determined by using X-ray crystallographic analysis (CCDC-1522721, see SI).

With optimized reaction conditions in hand, the scope and limitations of the tandem olefination-cyclization reaction were investigated using a variety of 4-aryl-sulfamidate-5-carboxylates **5** and methyl acrylate (**2a**). As the data in Table 2 show, the reactions proceed smoothly, irrespective of the electronic nature of aryl ring substituents in **5**, to afford the corresponding 1,3-disubstituted isoindolines **6** in high yields and with excellent levels of stereoselectivity. In addition, important functional groups, such as chloro, fluoro, and esters, which are known to be effective directing groups,[6c] are compatible with the process. It is also noteworthy that **5c** and **5e**, which possess *meta*-substituents, react to form products **6c** and **6e** arising by regioselective activation of the sterically less hindered *ortho* C−H position. The structures of the product were elucidated using 2D-NOESY spectroscopy for **6c** and X-ray crystallography for **6e** (see SI). Sulfamidate **5k**, having a 2-naphthyl moiety also undergoes regioselective C−H activation at the β- rather than α-position to form **6k** (CCDC-1522717) predominantly. Interestingly, the cyclic sulfamidate derivatives of thiophene, **5l**, and furan, **5m**, also generate oxidative-olefination products under the reaction conditions but, in these cases ensuing aza-Michael cyclization does not occur. As a result, the respective uncyclized products, **6l** and **6m**, are produced. Notably, the 4-furan substituted cyclic sulfamidate **5m** is unstable under the reaction conditions and, as a result, **6m** is formed in low yield (28%) even when an excess of methyl acrylate is employed.

The scope and limitations of process with (*R,R*)-**5a** was further probed utilizing various activated alkenes **2b**−**2j**. As the data in Table 3 show, not only methyl but also ethyl, benzyl, *tert*-butyl acrylates react with (*R,R*)-**5a** under the optimized conditions to produce the corresponding adducts **6ab**−**6ad**. Reactions of (*R,R*)-**5a** with other activated olefins, including phenyl vinyl sulfone (**2e**), methyl vinyl ketone (**2f**), and acrylonitrile (**2g**), also generate the corresponding products **6ae**, **6af**, and **6ag**. However, the reaction of *N,N*-dimethyl acrylamide (**2h**) with (*R,R*)-**5a** produces the corresponding adduct **6ah** in low yield (15%) even when **2h** is used in excess (3 equiv) along with 5 mol % of the Rh-catalyst. Finally, the branched acrylates **2i** and **2j** do not participate in an oxidative olefination reaction with (*R,R*)-**5a** even when increased amounts of these alkenes (3 equiv) and Rh-catalyst (5 mol%) are utilized.

A plausible mechanism for the reaction of (*R,R*)-**5a** forming (*S,R,R*)-**6a**, based on the one previously described for related C−H functionalization reactions, is outlined in Scheme 4.[6f,h,11,16] The pathway is likely initiated by coordination of the Rh(III) complex with the sulfamidate nitrogen followed by *ortho* C−H bond activation to form the Rh complex **I**. Olefination of **I** with methyl acrylate (**2a**) generates complex **II**. Subsequent elimination then generates olefination product (*R,R*)-**8** via complex **III**, which undergoes intramolecular aza-Michael addition of the sulfamide nitrogen to the β-carbon of acrylate moiety. Interestingly, the kinetic isotope effect (KIE) of the oxidative C−H olefination reaction is not high (KIE = 1.2) and the catalytic cleavage of *ortho* C−H bond of **5a** is not likely to be the rate-determining step in the olefination reaction (Scheme 5 and see, SI).

Importantly, the conversion of (*R,R*)-**5a** (99.4% ee) to (*S,R,R*)-**6a** (98.4% ee) takes place with complete retention of enantiomeric purity and the configuration of the newly generated stereogenic center in **6a** is (*S*), which corresponds to exclusive formation of the *trans*-1,3-disubstituted isoindoline (*S,R,R*)-**6a**.

The isoindolines **6**, produced in the process described above, contain cyclic sulfamidate moieties which are reactive with a variety of nuceophiles.[18] Consequently, this moiety can serve as a

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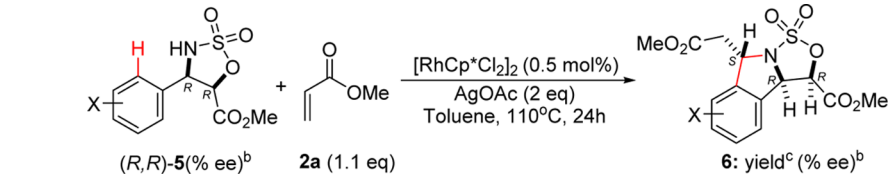
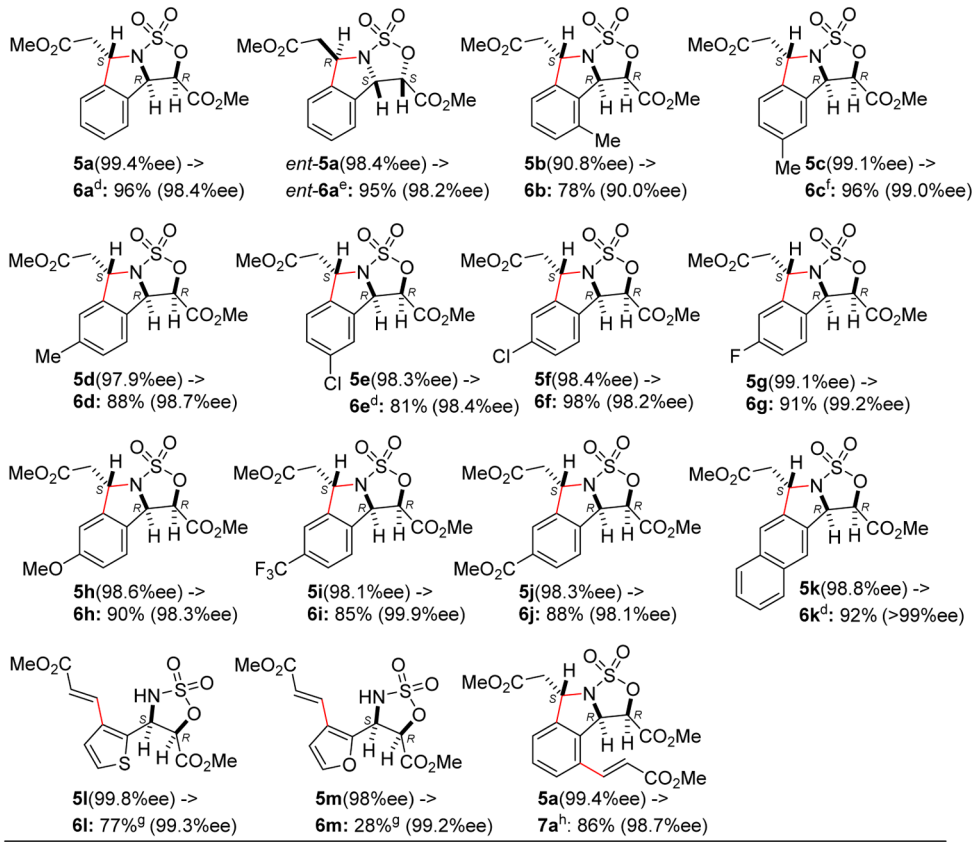
Table 2. Scope of Tandem Olefination-Cyclization Reaction of 4-Aryl-sulfamidate-5-carboxylates 5 with Methyl Acrylate (2a)[a]





[a]Reaction conditions: **5** (0.3 mmol), **2a** (0.33 mmol), $[RhCp^*Cl_2]_2$ (0.5 mol%), AgOAc (200 mol%), toluene 3 mL, 110 °C for 24 h in sealed tube. [b]ee was determined by using chiral HPLC. [c]Isolated yields after silica-gel chromatographic purification. [d]Structure was assigned by using X-ray crystallographic analysis. **6a**(CCDC-1522721), **6e**(CCDC-1522719), **6k**(CCDC-1522717) [e]*ent*-**5a** ((*S,S*)-**5a**) was used. [f]Regiochemistry was determined by using 2D-NOESY analysis (see, SI). [g]3 eq. of **2a** was used. [h]3 eq. of **2a** was used in CH_3CN.

versatile synthetic handle for further functionalization of the isoindoline ring system.[19,20] In a brief study aimed at demonstrating this potential, we observed that treatment of (*S,R,R*)-**6a** with ammonium benzoate and NaN_3 leads to generation of the respective 1-(benzoyl-methoxycarbonyl-methyl)-3-(methoxycarbonyl-methyl) substituted isoindoline **9** and 1-(azido-methoxycarbonyl-methyl)-3-(methoxycarbonyl-methyl) isoindoline **10**. Isoindoline **10** was further transformed to the tricyclic tetrahydropyrazinoisoindoline carboxylate **11** (Scheme 6).

CONCLUSION

In summary, in this effort we developed a Rh(III)-catalyzed tandem *ortho* C−H olefination-cyclization reaction of cyclic 4-aryl-sulfamidate-5-carboxylates (**5**) and activated olefins that produces highly functionalized 1,3-disubstituted isoindolines **6**. The process enables direct and stereoselective synthesis of highly functionalized 1,3-disubstituted isoindolines **6** from enantiomerically enriched 4-aryl-sulfamidate-5-carboxylates (**5**). A wide variety of aryl substituted sulfamidates and activated olefins participate in this process. In the two step one pot reaction, the configurational integrities of the two stereogenic centers in the starting cyclic sulfamidate are completely retained in the product and the process generates *trans*-1,3-disubstituted isoindoline exclusively. Finally, we have provided examples that show that the cyclic sulfamidate group not only serves as a chiral directing group in this process, but it also is a versatile synthetic handle for further functionalization of isoindoline ring system.

EXPERIMENTAL SECTION

General. All commercial reagents were used as obtained commercially unless otherwise noted. Reactions were performed using oven-dried glassware. Dichloromethane (DCM), ether, THF were dried and purified using a solvent purification system. Flash column chromatography was carried out on Fuji Chromatorex silica gel (38−75 μm). Analytical thin layer chromatography (TLC) was performed on Merck silica gel 60 F_{254} plates. Preparative thin layer chromatography (PLC) was performed on Merck silica gel 60 F_{254} 2 mm plates. Visualization of the developed chromatogram was accomplished with UV light and by staining with ethanolic phosphomolybdic acid (PMA) solution or ninhydrin solution followed by heating.

Nuclear magnetic resonance (NMR) spectra were recorded using Bruker 500 MHz NMR instrument (^{1}H NMR at 500 MHz and ^{13}C

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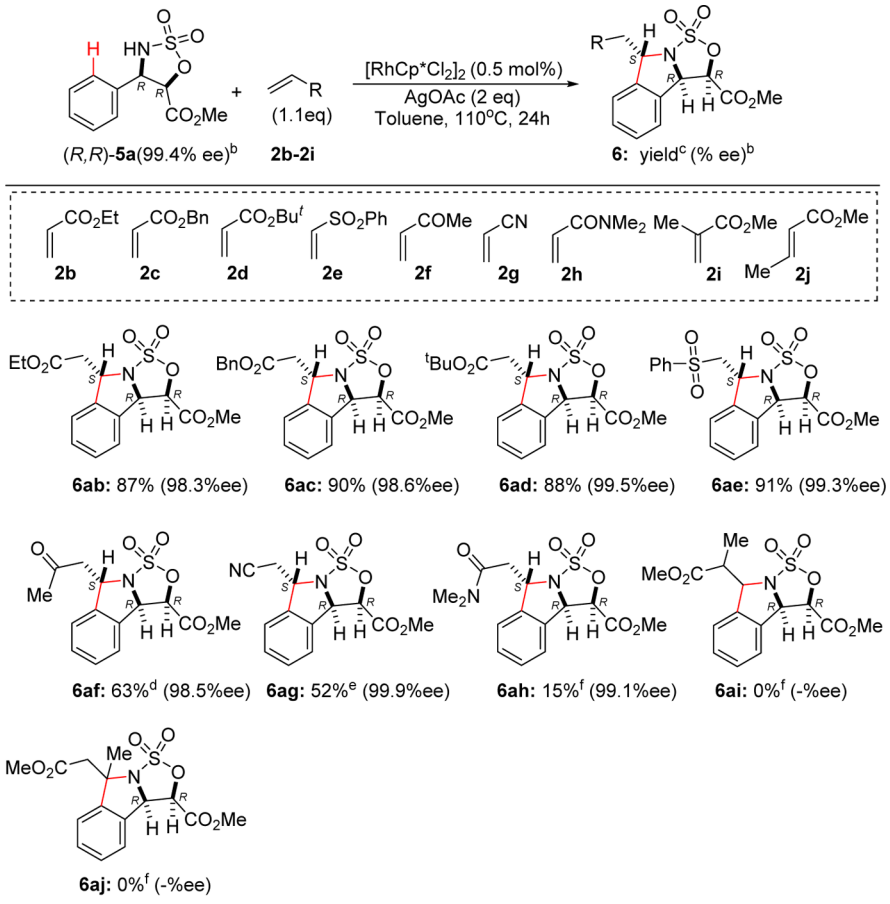
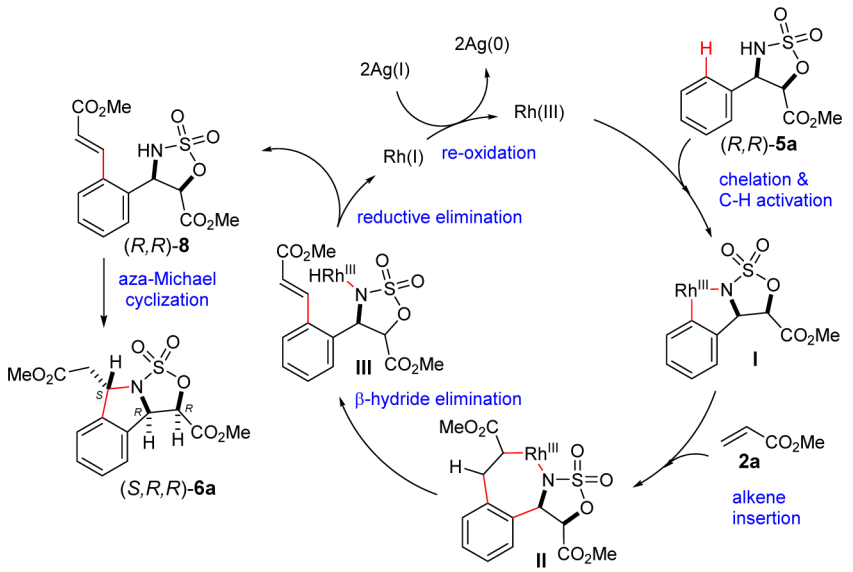
Table 3. Scope of Tandem Olefination-Cyclization Reaction of (*R,R*)-5a with Alkenes (2b−2j)[a]



[a]Reaction conditions: see Table 2. [b]ee was determined by using chiral HPLC. [c]Isolated yields after silica-gel chromatographic purification. [d]2 eq. of **2f** and 2.5 mol% of $[RhCp^*Cl_2]_2$ were used. [e]2 eq. of **2g** and 5 mol% of $[RhCp^*Cl_2]_2$ were used. [f]3 eq. of alkene and 5 mol% of $[RhCp^*Cl_2]_2$ were used.

Scheme 4. Proposed Mechanism for the Tandem Olefination-Cyclization Reaction



NMR at 125 MHz) or Bruker 300 MHz NMR instrument (^{1}H NMR at 300 MHz and ^{13}C NMR at 75 MHz). ^{1}H NMR data are reported as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), integration, coupling constants (Hz). Data for ^{13}C NMR are reported in terms of chemical shift (δ, ppm). High-performance liquid chromatography (HPLC) was carried out on a Young Lin HPLC system (7725i Injector, SDV 30 Plus Solvent Degassor & Valve Module (Helium Sparging), SP930D Solvent Delivery Pump, UV 730D Absorbance Detector) equipped with a Chiralpak IA, IB, IC, or Chiralpak AD-H column or an Aglient 1100

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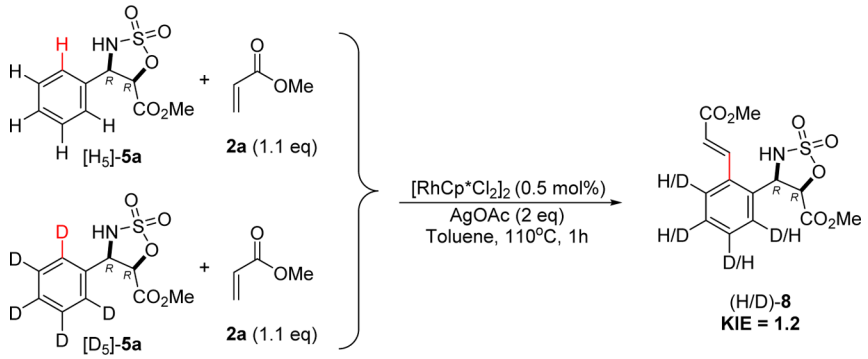
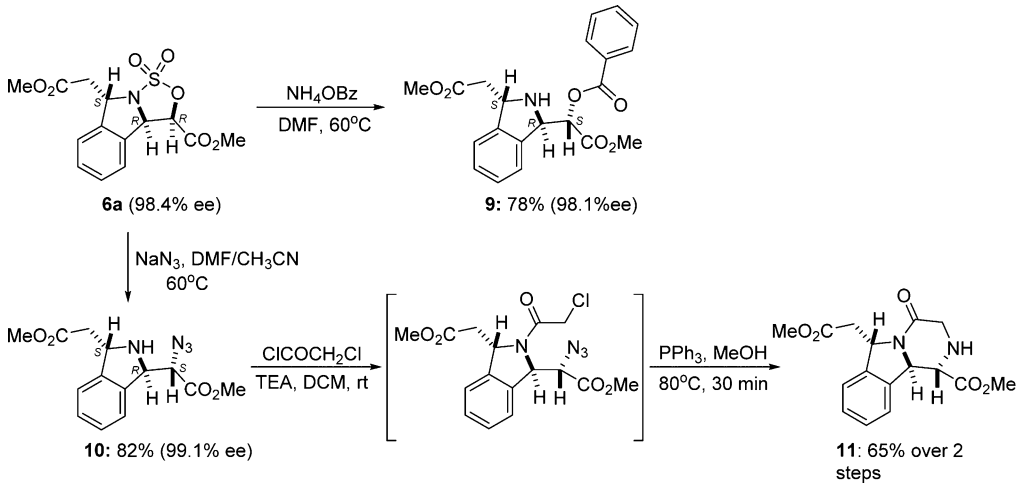
Scheme 5. KIE Experiments for Oxidative C−H Olefination of 5a



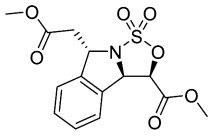
Scheme 6. Reactions of the Cyclic Sulfamidate Moieties in the Isoindoline 6



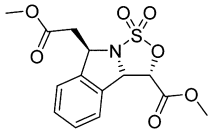
Series HPLC equipped with Chiralpak IB or Chiralpak IC column. Specific rotations were measured on a Rudolph Autopol IV (Automatic polarimeter). High-resolution mass spectra and elemental analysis were obtained from the Korea Research Institute of Chemical Technology (EI) or Korea Basic Science Institute (ESI). HR-MS were measured with electron impact (EI) ionization via double focusing mass analyzer (magnetic and electric fields) or electrospray ionization (ESI) via time-of-flight (TOF) analyzer. Enantiomerically enriched 4-aryl-cyclic sulfamidate-5-carboxylates (**5**) were prepared by employing our previous report.[17]

Typical Procedure for the Oxidative Olefination-Cyclization of 5 with 2. A 20 mL sealed tube equipped with a magnetic stirring bar was charged with (*R*,*R*)-**5a** (75 mg, 0.29 mmol), [Cp*RhCl2]2 (0.9 mg, 0.5 mol%), AgOAc (97 mg, 0.58 mmol), methyl acrylate **2a** (27 mg, 0.32 mmol) and 3 mL of anhydrous toluene. The reaction tube was capped and stirred at 110 °C (bath temperature). When the starting material was consumed completely (monitored by TLC), the tube was cooled to room temperature. The mixture was diluted with EtOAc and filtered through a pad of Celite. The evaporation of the solvent and volatiles under reduced pressure was followed by purification through flash column chromatography on silica gel (eluent EtOAc/hexane = 1/5 to 1/2, typically) to afford the title compound **6a** as a white solid.

***6a**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 96% (127 mg as a white solid); mp: 109.8−113.1 °C; 98.4% ee (Chiralpak IA, 30% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 18.2 min, t_R(minor) = 14.6 min); $[\alpha]_D^{21}$ = −19.79 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, *J* = 7.4 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.26 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 5.66−5.61 (m, 2H), 5.34 (d, *J* = 7.7 Hz, 1H), 3.76 (s, 3H), 3.42 (s, 3H), 2.99−2.89 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 165.3, 139.6, 132.9, 130.4, 128.5, 123.5, 122.8, 79.5, 67.4, 65.6, 52.5, 52.1, 41.4.; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{15}NO_7S$ 341.0569; Found 341.0571.



***ent-6a**: Methyl (3S,3aS,8R)-8-(2-Methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 95% (63 mg as a white solid); mp: 113.2−114.9 °C; 98.2% ee (Chiralpak IA, 30% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 20.8 min, t_R(minor) = 16.4 min); $[\alpha]_D^{21}$ = +14.14 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (t, *J* = 7.5 Hz, 1H), 7.37 (t, *J* = 7.5 Hz, 1H), 7.27 (d, *J* = 7.6 Hz, 1H), 7.22 (d, *J* = 7.6 Hz, 1H), 5.66−5.63 (m, 2H), 5.34 (d, *J* = 7.7 Hz, 1H), 3.76 (s, 3H), 3.43 (s, 3H), 2.99−2.90 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 165.3, 139.6, 132.9, 130.2, 128.5, 123.5, 122.8, 79.5, 67.4, 65.6, 52.5, 52.1, 41.4; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{15}NO_7S$ 341.0569; Found 341.0567.



***6b**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-4-methyl-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 78% (69 mg as a white solid); mp: 116.3−118.9 °C; 90.0% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 15.9 min, t_R(minor) = 11.1 min); $[\alpha]_D^{21}$ = −68.78 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.32 (t, *J* = 7.6 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 5.73 (d, *J* = 7.4 Hz, 1H), 5.60 (t, *J* = 6.0 Hz, 1H), 5.32 (d, *J* = 7.4 Hz, 1H), 3.76 (s, 3H), 3.25 (s,

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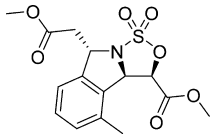
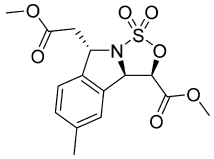
J. Org. Chem. 2017, 82, 7223−7233

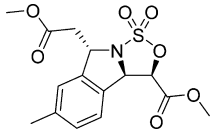
3H), 3.01−2.88 (m, 2H), 2.35 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 166.3, 139.6, 133.9, 131.8, 130.5, 129.8, 120.1, 80.9, 67.0, 65.6, 52.4, 52.1, 41.2, 19.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{17}NO_7S$ 355.0726; Found 355.0728.



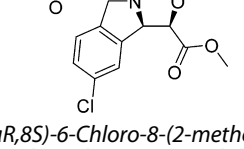
***6c**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-5-methyl-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 96% (94 mg as a white solid); mp: 98.4−101.1 °C; 99.0% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 11.7 min, t_R(minor) = 10.1 min); $[\alpha]_D^{21}$ = −46.77 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.22 (d, J = 7.9 Hz, 0H), 7.13 (d, J = 7.9 Hz, 0H), 7.01 (s, 1H), 5.61 (d, J = 7.7 Hz, 1H), 5.57 (t, J = 6.1 Hz, 1H), 5.31 (d, J = 7.7 Hz, 1H), 3.75 (s, 3H), 3.44 (s, 3H), 2.95−2.86 (m, 2H), 2.38 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 165.3, 138.7, 136.7, 133.0, 131.1, 123.9, 122.4, 79.5, 67.3, 65.5, 52.4, 52.0, 41.5, 21.2.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{17}NO_7S$ 355.0726; Found 355.0728.



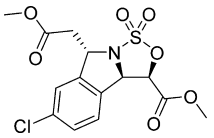
***6d**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-6-methyl-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 88% (78 mg as a slightly yellow solid); mp: 81.3−83.8 °C; 98.7% ee (Chiralpak IB, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 11.8 min, t_R(minor) = 9.5 min); $[\alpha]_D^{21}$ = −17.59 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.17 (d, J = 7.9 Hz, 1H), 7.08 (d, J = 7.9 Hz, 1H), 7.04 (s, 1H), 5.62 (d, J = 7.7 Hz, 1H), 5.58 (t, J = 6.2 Hz, 1H), 5.31 (d, J = 7.7 Hz, 1H), 3.77 (s, 3H), 3.46 (s, 3H), 2.92 (d, J = 6.1 Hz, 2H), 2.38 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.9, 165.4, 140.5, 139.8, 129.9, 129.4, 123.2, 79.5, 67.3, 65.5, 52.5, 52.1, 41.4, 21.5.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{17}NO_7S$ 355.0726; Found 355.0723.



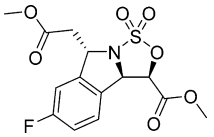
***6e**: Methyl (3R,3aR,8S)-5-Chloro-8-(2-methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 81% (72 mg as a white solid); mp: 110.1−112.4 °C; 98.4% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 9.7 min, t_R(minor) = 7.2 min); $[\alpha]_D^{21}$ = −50.76 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40 (dd, J = 1.5, 8.1 Hz, 1H), 7.22−7.20 (m, 2H), 5.61 (d, J = 7.5 Hz, 1H), 5.57−5.55 (m, 1H), 5.36−5.31 (m, 1H), 3.74 (s, 3H), 3.53 (s, 3H), 2.98−2.87 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 165.0, 138.2, 134.9, 134.6, 130.5, 124.1, 123.8, 79.1, 66.9, 65.2, 52.6, 52.1, 41.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{14}H_{14}ClNO_7S$ 375.0180; Found 375.0161.



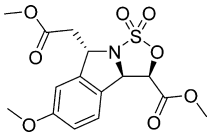
***6f**: Methyl (3R,3aR,8S)-6-Chloro-8-(2-methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 98% (88 mg as a white solid); mp: 111.2−113.1 °C; 98.2% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 9.1 min, t_R(minor) = 7.5 min); $[\alpha]_D^{21}$ = −11.60 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35 (d, J = 8.2 Hz, 1H), 7.28 (s, 1H), 7.15 (d, J = 8.2 Hz, 1H), 5.62 (d, J = 7.7 Hz, 1H), 5.58 (t, J = 5.8 Hz, 1H), 5.33 (d, J = 7.7 Hz, 1H), 3.76 (s, 3H), 3.50 (s, 3H), 2.99−2.89 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 165.1, 141.7, 136.4, 131.5, 128.9, 124.6, 123.3, 79.2, 66.9, 65.2, 52.7, 52.2, 40.9.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{14}H_{14}ClNO_7S$ 375.0180; Found 375.0150.



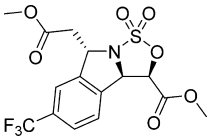
***6g**: Methyl (3R,3aR,8S)-6-Fluoro-8-(2-methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 91% (95 mg as a white solid); mp: 129.3−132.5 °C; 99.2% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.7 min, t_R(minor) = 7.2 min); $[\alpha]_D^{21}$ = −1.59 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19 (dd, J = 4.8, 8.5 Hz, 1H), 7.07 (td, J = 2.2, 8.5 Hz, 1H), 7.00 (dd, J = 1.7, 8.3 Hz, 1H), 5.62−5.58 (m, 2H), 5.32 (d, J = 7.6 Hz, 1H), 3.76 (s, 3H), 3.48 (s, 3H), 3.01−2.89 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 165.2, 163.9 (d, J_{CF} = 249.8 Hz), 142.2 (d, J_{CF} = 8.7 Hz), 128.5, 125.1 (d, J_{CF} = 9.2 Hz), 116.1 (d, J_{CF} = 23.3 Hz), 110.5 (d, J_{CF} = 24.5 Hz), 79.4, 66.8, 65.3, 52.6, 52.1, 40.9.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{14}H_{14}FNO_7S$ 359.0475; Found 359.0459.



***6h**: Methyl (3R,3aR,8S)-6-Methoxy-8-(2-methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 90% (81 mg as a white solid); mp: 72.2−73.8 °C; 98.3% ee (Chiralpak IC, 50% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 9.2 min, t_R(minor) = 8.0 min); $[\alpha]_D^{21}$ = −7.38 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.10 (d, J = 8.5 Hz, 1H), 6.88 (d, J = 8.5 Hz, 1H), 6.76 (s, 1H), 5.60−5.57 (m, 2H), 5.30 (d, J = 7.5 Hz, 1H), 3.82 (s, 3H), 3.76 (s, 3H), 3.48 (s, 3H), 2.96−2.88 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.1, 165.4, 161.4, 141.4, 124.5, 124.4, 114.9, 107.7, 79.6, 67.0, 65.5, 55.5, 52.6, 52.1, 41.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{17}NO_8S$ 371.0675; Found 371.0677.



***6i**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-6-(trifluoromethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 85% (78 mg as a slightly yellow solid); mp: 100.1−102.5 °C; 99.9% ee (Chiralpak IC, 20% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 10.9 min, t_R(minor) = 9.2 min); $[\alpha]_D^{21}$ = −3.58 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, J = 8.1 Hz, 1H), 7.56 (s, 1H), 7.36 (d, J = 8.1 Hz, 1H), 5.70 (d, J = 7.8 Hz, 1H), 5.66 (t, J = 5.8 Hz, 1H), 5.38 (d, J = 7.8 Hz, 1H), 3.76 (s, 3H), 3.48 (s, 3H), 3.04−2.95 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 164.9, 140.9, 136.9, 132.8 (q, J_{CF} = 32.9 Hz), 125.8, 124.1, 123.4 (q, J_{CF} = 271 Hz), 120.1 (d, J_{CF} = 7.4 Hz), 79.1, 67.1, 65.3, 52.7, 5227, 40.8.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{14}F_3NO_7S$ 409.0443; Found 409.0441.



***6j**: Dimethyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3,6-dicarboxylate 1,1-Dioxide.* Yield: 88% (73 mg as a white solid); mp: 80.1−82.9 °C; 98.1% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 15.0 min, t_R(minor) = 13.4 min); $[\alpha]_D^{21}$ = −35.38 (c

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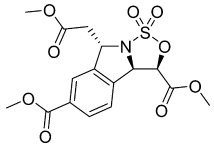
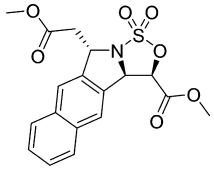
J. Org. Chem. 2017, 82, 7223−7233

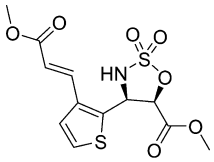
0.5, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, J = 8.1 Hz, 1H), 7.93 (s, 1H), 7.30 (d, J = 8.1 Hz, 1H), 5.69 (d, J = 7.8 Hz, 1H), 5.63 (t, J = 5.7 Hz, 1H), 5.37 (d, J = 7.8 Hz, 1H), 3.95 (s, 3H), 3.75 (s, 3H), 3.46 (s, 3H), 3.03−2.95 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.8, 165.9, 165.1, 140.3, 137.7, 132.3, 129.9, 123.9, 123.5, 79.1, 67.3, 65.3, 52.7, 52.6, 52.1, 40.7.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{17}NO_9S$ 399.0624; Found 399.0622.



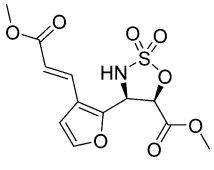
***6k**: Methyl (3R,3aR,10S)-10-(2-Methoxy-2-oxoethyl)-3a,10-dihydro-3H-benzo[f][1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 92% (94 mg as a white solid); mp: 158.7−161.6 °C; > 99% ee (Chiralpak IA, 40% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 12.1 min, t_R(minor) = 9.7 min); $[\alpha]_D^{21}$ = −126.54 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.86 (d, J = 7.4 Hz, 2H), 7.71 (d, J = 6.7 Hz, 2H), 7.57−7.52 (m, 2H), 5.81 (d, J = 7.9 Hz, 1H), 5.75 (t, J = 6.0 Hz, 1H), 5.41 (d, J = 7.9 Hz, 1H), 3.78 (s, 3H), 3.28 (s, 3H), 3.11−3.01 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.2, 165.4, 137.4, 134.0, 133.0, 131.5, 128.3, 128.0, 127.2, 126.9, 122.9, 121.8, 79.8, 66.8, 64.9, 52.5, 52.1, 41.5.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{18}H_{17}NO_7S$ 391.0726; Found 391.0725.



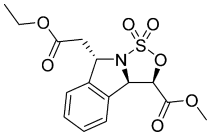
***6l**: Methyl (4S,5R)-4-(3-((E)-3-Methoxy-3-oxoprop-1-en-1-yl)-thiophen-2-yl)-1,2,3-oxathiazolidine-5-carboxylate 2,2-Dioxide.* Yield: 77% (41 mg as a white solid); mp: 144.2−147.1 °C; 99.3% ee (Chiralpak AD-H, 30% IPA/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.5 min, t_R(minor) = 10.1 min); $[\alpha]_D^{21}$ = −127.74 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.66 (d, J = 15.7 Hz, 1H), 7.41 (d, J = 5.4 Hz, 1H), 7.30−7.28 (m, 1H), 6.36 (d, J = 15.7 Hz, 1H), 5.88 (t, J = 7.05 Hz, 1H), 5.45 (d, J = 6.8 Hz, 1H), 5.39 (d, J = 7.2 Hz, 1H), 3.85 (s, 3H), 3.56 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 167.1, 164.7, 136.3, 135.7, 133.9, 127.2, 125.6, 120.4, 80.7, 55.7, 53.1, 52.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{12}H_{13}NO_7S_2$ 347.0133; Found 347.0132.



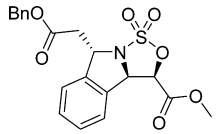
***6m**: Methyl (4S,5R)-4-(3-((E)-3-Methoxy-3-oxoprop-1-en-1-yl)-furan-2-yl)-1,2,3-oxathiazolidine-5-carboxylate 2,2-Dioxide.* Yield: 28% (11.2 mg as a yellow solid); mp: 78.1−80.2 °C; 99.2% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(major) = 12.1 min, t_R(minor) = 15.5 min); $[\alpha]_D^{21}$ = −57.47 (c 0.2, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 15.7 Hz, 1H), 7.47 (d, J = 1.6 Hz, 1H), 6.67 (d, J = 1.6 Hz, 1H), 6.29 (d, J = 15.7 Hz, 1H), 5.52 (dd, J = 7.1, 10.6 Hz, 1H), 5.26 (d, J = 7.1 Hz, 1H), 5.20 (d, J = 10.6 Hz, 1H), 3.84 (s, 3H), 3.67 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.6, 165.6, 144.8, 143.2, 131.6, 122.9, 120.9, 109.2, 79.9, 53.6, 53.5, 52.0.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{12}H_{13}NO_8S$ 331.0362; Found 331.0361.



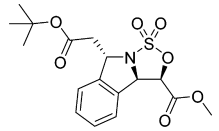
***6ab**: Methyl (3R,3aR,8S)-8-(2-Ethoxy-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 87% (84 mg as a white solid); mp: 53.9−55.4 °C; mp: 53.9−55.4 °C; 98.3% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 10.4 min, t_R(minor) = 8.8 min); $[\alpha]_D^{21}$ = +9.49 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, J = 7.5 Hz, 1H), 7.37 (t, J = 7.5 Hz, 1H), 7.28 (d, J = 7.6 Hz, 1H), 7.21 (d, J = 7.6 Hz, 1H), 5.66−5.62 (m, 2H), 5.34 (d, J = 7.6 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 3.43 (s, 3H), 2.97−2.88 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.7, 165.3, 139.7, 132.9, 130.2, 128.5, 123.5, 122.8, 79.5, 67.4, 65.7, 61.1, 52.5, 41.6, 14.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{15}H_{17}NO_7S$ 355.0726; Found 355.0723.



***6ac**: Methyl (3R,3aR,8S)-8-(2-(benzyloxy)-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-dioxide.* Yield: 90% (102 mg as a white solid); mp: 121.6−123.1 °C; 98.6% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(major) = 17.1 min, t_R(minor) = 12.1 min); $[\alpha]_D^{20}$ = −20.38 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39−7.34 (m, 7H), 7.19 (t, J = 7.3 Hz, 2H), 5.65 (t, J = 5.9 Hz, 1H), 5.59 (d, J = 7.8 Hz, 1H), 5.32 (d, J = 7.7 Hz, 1H), 5.18 (s, 2H), 3.42 (s, 3H), 3.04−2.95 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.4, 165.3, 139.5, 135.4, 132.9, 130.2, 128.6, 128.5, 128.4, 123.5, 122.8, 79.5, 67.4, 66.9, 65.6, 52.5, 41.4.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{20}H_{19}NO_7S$ 417.0882; Found 417.0882.



***6ad**: Methyl (3R,3aR,8S)-8-(2-(tert-Butoxy)-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 88% (91 mg as a yellow oil); 99.5% ee (Chiral Pak IC, 40% EtOH/*n*-hexanes, 0.9 mL/min, 215 nm, t_R(major) = 11.1 min, t_R(minor) = 8.8 min); $[\alpha]_D^{19}$ = +5.46 (c 1.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (t, J = 7.5 Hz, 1H), 7.36 (t, J = 7.5 Hz, 1H), 7.29 (d, J = 7.2 Hz, 1H), 7.20 (d, J = 7.6 Hz, 1H), 5.64−5.59 (m, 2H), 5.33 (d, J = 7.6 Hz, 1H), 3.44 (s, 3H), 2.91−2.80 (m, 2H), 1.45 (s, 9H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.8, 165.3, 140.0, 132.9, 130.1, 128.4, 123.4, 122.9, 81.6, 79.4, 67.4, 65.8, 52.5, 42.7, 27.9.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{17}H_{21}NO_7S$ 383.1039; Found 383.1041.



***6ae**: Methyl (3R,3aR,8R)-8-((Phenylsulfonyl)methyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 91% (75 mg as a yellow oil); mp: 150.1−152.2 °C; 99.3% ee (Chiralpak IC, 50% EtOH/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(major) = 11.1 min, t_R(minor) = 8.8 min); $[\alpha]_D^{22}$ = +10.59 (c 0.5, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.98 (d, J = 7.6 Hz, 1H), 7.72 (t, J = 7.5 Hz, 1H), 7.65−7.60 (m, 3H), 7.48 (t, J = 7.6 Hz, 1H), 7.40 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 7.7 Hz, 1H), 5.67 (t, J = 5.1 Hz, 1H), 5.54 (d, J = 7.7 Hz, 1H), 5.29 (d, J = 7.6 Hz, 1H), 3.78−3.69 (m, 2H), 3.44 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.0, 139.4, 137.9, 134.1, 132.8, 130.6, 129.5, 128.9, 128.2, 123.9, 123.3, 79.2, 67.3, 63.8, 61.8, 52.6.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{18}H_{17}NO_7S_2$ 423.0446; Found 423.0467.

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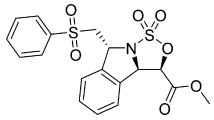
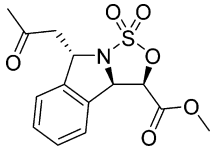
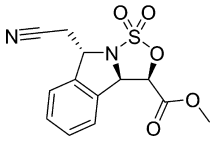
J. Org. Chem. 2017, 82, 7223−7233



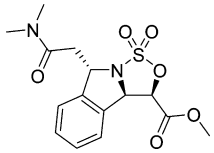
***6af**: Methyl (3R,3aR,8S)-8-(2-Oxopropyl)-3a,8-dihydro-3H-[1,2,3]-oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 63% (40 mg as a white solid); mp: 125.8−128.8 °C; 98.5% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 11.4 min, t_R(minor) = 9.9 min); $[\alpha]_D^{21}$ = +18.38 (c 0.6, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.39 (t, *J* = 7.3 Hz, 1H), 7.35 (t, *J* = 7.4 Hz, 1H), 7.24 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 5.67−5.61 (m, 2H), 5.32 (d, *J* = 7.7 Hz, 1H), 3.40 (s, 3H), 3.19 (dd, *J* = 17.5, 4.0 Hz, 1H), 3.06 (dd, *J* = 17.5, 8.0 Hz, 1H), 2.25 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1, 165.3, 140.2, 132.7, 130.3, 128.3, 123.5, 123.2, 79.7, 67.3, 65.0, 52.5, 50.3, 30.7.; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{15}NO_6S$ 325.0620; Found 325.0620.



***6ag**: Methyl (3R,3aR,8S)-8-(Cyanomethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 52% (31 mg as a pale yellow solid); mp: 160.3−162.5 °C; 99.9% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 9.05 min, t_R(minor) = 6.76 min); $[\alpha]_D^{21}$ = +45.76 (c 0.3, $CHCl_3$).; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.52 (t, *J* = 7.5 Hz, 1H), 7.46 (t, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.6 Hz, 1H), 7.29−7.27 (m, 1H), 5.73 (d, *J* = 7.7 Hz, 1H), 5.48 (t, *J* = 4.5 Hz, 1H), 5.36 (d, *J* = 7.7 Hz, 1H), 3.41 (s, 3H), 3.08 (d, *J* = 4.8 Hz, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 137.0, 133.2, 130.8, 129.5, 123.9, 122.6, 115.5, 79.9, 67.3, 64.6, 52.6, 25.3.; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{13}H_{12}N_2O_5S$ 308.0467; Found 308.0470.

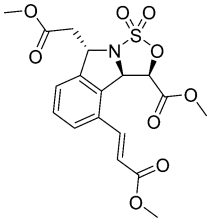


***6ah**: Methyl (3R,3aR,8S)-8-(2-(Dimethylamino)-2-oxoethyl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* Yield: 15% (10 mg as a pale yellow oil); 99.1% ee (Chiralpak IA, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 14.7 min, t_R(minor) = 10.6 min); $[\alpha]_D^{21}$ = +30.98 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, *J* = 7.6 Hz, 1H), 7.37 (t, *J* = 7.4 Hz, 1H), 7.32 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 5.72−5.70 (m, 1H), 5.61 (d, *J* = 7.8 Hz, 1H), 5.29 (d, *J* = 7.8 Hz, 1H), 3.35 (s, 3H), 3.10−3.04 (m, 1H), 3.03 (s, 3H), 2.99 (s, 3H), 2.86 (dd, *J* = 15.9, 8.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 168.9, 165.4, 140.5, 132.6, 130.2, 128.2, 123.9, 123.3, 79.8, 67.2, 66.4, 52.5, 41.0, 37.4, 35.5; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{15}H_{18}N_2O_6S$ 354.0886; Found 354.0885.

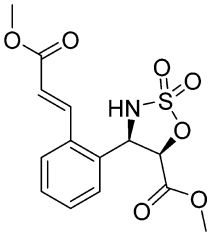


***7a**: Methyl (3R,3aR,8S)-8-(2-Methoxy-2-oxoethyl)-4-((E)-3-methoxy-3-oxoprop-1-en-1-yl)-3a,8-dihydro-3H-[1,2,3]oxathiazolo-[4,3-a]isoindole-3-carboxylate 1,1-Dioxide.* A 20 mL sealed tube equipped with a magnetic stirring bar was charged with (*R*,*R*)-**5a** (50 mg, 0.19 mmol), [Cp*RhCl2]2 (4.8 mg, 4.0 mol%), AgOAc (65 mg, 0.39 mmol), methyl acrylate (50 mg, 0.58 mmol), and 2 mL of anhydrous CH_3CN. The reaction tube was capped and stirred at 110 °C for 12 h. The resulting mixture was allowed to cool to room temperature, diluted with EtOAc, and filtered through a pad of Celite. The evaporation of the solvent and volatiles under reduced pressure was followed by purification through flash column chromatography on silica gel (eluent EtOAc/hexane = 1/5 to 1/2) to afford **7a** as a slightly yellow oil.

Yield: 86% (71 mg as a pale yellow oil); 98.7% ee (Chiralpak IC, 50% EtOH/*n*-hexanes, 1.1 mL/min, 215 nm, t_R(major) = 24.6 min, t_R(minor) = 10.2 min); $[\alpha]_D^{20}$ = −135.6 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.8 Hz, 1H), 7.57 (d, *J* = 15.9 Hz, 1H), 7.47 (t, *J* = 7.8 Hz, 1H), 7.30 (d, *J* = 7.8 Hz, 1H), 6.50 (d, *J* = 15.9 Hz, 1H), 5.90 (d, *J* = 8.8 Hz, 1H), 5.60 (t, *J* = 5.9 Hz, 1H), 5.39 (d, *J* = 7.6 Hz, 1H), 3.87 (s, 3H), 3.76 (s, 3H), 3.24 (s, 3H), 3.05 (dd, *J* = 16.0, 4.8 Hz, 1H), 2.95 (dd, *J* = 16.0, 7.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 169.9, 166.4, 165.8, 140.8, 139.3, 132.6, 130.9, 130.5, 125.9, 124.4, 120.9, 80.4, 66.5, 65.3, 52.3, 52.1, 40.7; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{18}H_{19}NO_9S$ 425.0781; Found 425.0781.

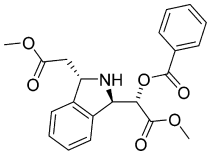


***8**: Methyl (4R,5R)-4-(2-((E)-3-Methoxy-3-oxoprop-1-en-1-yl)-phenyl)-1,2,3-oxathiazolidine-5-carboxylate 2,2-Dioxide.* White solid; mp: 112.9−115.0 °C; 99.0% ee (Chiralpak IC, 40% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.8 min, t_R(minor) = 14.4 min); $[\alpha]_D^{26}$ = −117.92 (c 0.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.95 (d, *J* = 15.6 Hz, 1H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.50−7.43 (m, 3H), 6.42 (d, *J* = 15.6 Hz, 1H), 5.72 (d, *J* = 7.1 Hz, 1H), 5.41 (d, *J* = 7.1 Hz, 1H), 5.38 (s, 1H), 3.87 (s, 3H), 3.33 (s, 3H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 166.5, 165.3, 139.8, 133.9, 130.8, 130.5, 129.9, 127.7, 125.5, 123.0, 80.8, 57.4, 52.6, 52.1.; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{14}H_{15}NO_7S$ 341.0569; Found 341.0570.



***9**: (S)-2-Methoxy-1-((1R,3S)-3-(2-methoxy-2-oxoethyl)isoindolin-1-yl)-2-oxoethyl Benzoate.* To a solution of **6a** (40 mg, 0.12 mmol) in DMF (2.0 mL) was added ammonium benzoate (33 mg, 0.23 mmol). The reaction mixture was heated to 60 °C for 12 h. The mixture was evaporated under vacuum to remove DMF, redissolved in dichloromethane (5.0 mL), and treated with 1 N HCl (aq). The mixture was stirred at rt for 6 h, diluted with $NaHCO_3$ (aq) and extracted with dichloromethane (2 × 25 mL). The combined organic layers were washed with H_2O and saturated NaCl (aq). The organic layer was evaporated under vacuum and the crude residue was purified on silica gel column chromatography using EtOAc/hexanes as an eluent to afford **9** as a colorless oil.

Yield: 78% (35 mg as a colorless oil); 98.1% ee (Chiralpak IC, 30% EtOH/*n*-hexanes, 0.8 mL/min, 215 nm, t_R(major) = 9.7 min, t_R(minor) = 11.1 min); $[\alpha]_D^{20}$ = +11.49 (c 0.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 7.6 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.8 Hz, 2H), 7.32−7.27 (m, 3H), 7.23 (d, *J* = 7.0 Hz, 1H), 5.48 (d, *J* = 3.0 Hz, 1H), 5.16−5.13 (m, 2H), 3.83 (s, 3H), 3.75 (s, 3H), 2.91 (dd, *J* = 15.8, 3.9 Hz, 1H), 2.62 (dd, *J* = 15.8, 8.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3, 169.1, 165.9, 143.1, 138.6, 133.4, 129.7, 129.0, 128.3, 127.8, 122.8, 122.1, 75.7, 63.7, 59.6, 52.6, 51.8, 42.1; HRMS (EI, double focusing) *m*/*z*: $[M]^+$ Calcd for $C_{21}H_{21}NO_6$ 383.1369; Found 383.1370.



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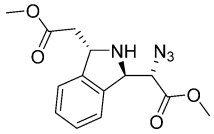
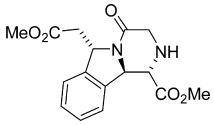
10: Methyl (S)-2-Azido-2-((1R,3S)-3-(2-methoxy-2-oxoethyl)-isoindolin-1-yl)acetate. NaN_3 (29 mg, 0.44 mmol) was added in a single portion to a solution of **6a** (30 mg, 0.08 mmol) in mixture of DMF and CH_3CN (3 mL, 1:1) at room temperature. The resulting mixture was warmed to 60 °C and stirred for 12 h. Upon completion, the reaction mixture was cooled to room temperature and the contents were diluted with Et_2O (3 mL), treated with 1*N* aqueous HCl (3 mL), and allowed to stir for an additional 2 h at room temperature. Once this operation was complete, the reaction mixture was poured into saturated $NaHCO_3$ (aq) and extracted with EtOAc (2 × 25 mL). The combined organic layers were then washed with water, dried ($MgSO_4$), and concentrated. The resulting brown solid was purified by flash column chromatography using EtOAc/hexanes as an eluent to afford **10**.

Yield: 82% (22 mg) as a brown solid; mp: 92.3−95.1 °C; 99.1% ee (Chiralpak IA, 30% EtOH/*n*-hexanes, 1.0 mL/min, 215 nm, t_R(major) = 8.8 min, t_R(minor) = 8.1 min); $[\alpha]_D^{23} = -65.5$ (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.33−7.28 (m, 2H), 7.22−7.18 (m, 2H), 5.07 (t, J = 3.0 Hz, 1H), 4.97−4.94 (m, 2H), 4.08 (d, J = 3.6 Hz, 1H), 3.85 (s, 3H), 3.69 (s, 3H), 2.81 (dd, J = 15.5, 4.1 Hz, 1H), 2.53 (dd, J = 15.5, 8.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.0, 169.6, 143.1, 138.8, 128.4, 127.9, 122.6, 122.5, 66.2, 64.1, 59.3, 52.8, 51.8, 41.9; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{14}H_{16}N_4O_4$ 304.1172; Found 304.1171.



11: Methyl (1S,6S,10bR)-6-(2-Methoxy-2-oxoethyl)-4-oxo-1,2,3,4,6,10b-hexahydropyrazino[2,1-a]isoindole-1-carboxylate. To a solution of (*S*,*R*,*S*)-**10** (30 mg, 0.099 mmol) in DCM (2.0 mL) was added chloroacetyl chloride (12 mg, 0.108 mmol) followed by TEA (20 mg, 0.198 mmol) at 0 °C. The reaction mixture was stirred at rt for 1 h, diluted with $NaHCO_3$ (aq), and extracted with DCM (2 × 25 mL). The combined organic layer was washed saturated NaCl (aq) and evaporated under reduced pressure. The crude mixture was dissolved in MeOH (2.0 mL) and PPh_3 (52 mg, 0.198 mmol)) was added to this mixture. The resulting mixture was heated to 80 °C for 30 min. The mixture was allowed to cool to rt and evaporated under reduced pressure. The crude mixture was purified on silica gel column chromatography using DCM/MeOH as an eluent (product is active in $KMnO_4$ stain) to afford title compound as a colorless viscous oil.

Yield: 65% (20 mg as a colorless viscous oil, over two steps); $[\alpha]_D^{26}$ = +100.04 (c 0.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.31 (m, 3H), 7.10 (d, J = 7.5 Hz, 1H), 5.73 (t, J = 5.7 Hz, 1H), 5.22 (d, J = 9.6 Hz, 1H), 3.95 (s, 3H), 3.78 (d, J = 18.0 Hz, 1H), 3.65 (s, 3H), 3.59 (d, J = 18.0 Hz, 1H), 3.51 (d, J = 9.6 Hz, 1H), 3.06−2.89 (m, 2H).; ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.0, 170.8, 166.8, 139.2, 136.8, 128.8, 128.3, 122.9, 122.4, 63.9, 60.3, 59.2, 52.7, 51.7, 48.3, 39.1.; HRMS (EI, double focusing) m/z: $[M]^+$ Calcd for $C_{16}H_{18}N_2O_5$ 318.1216; Found 318.1218.



■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00799.

Copies of ^{1}H and ^{13}C NMR, chiral HPLC chromatograms for all new compounds, and 2D-NOESY spectrum of **6c** (PDF)

X-ray crystallographic data for **6a**(CCDC-1522721) (CIF)

X-ray crystallographic data for **6e**(CCDC-1522719) (CIF)

X-ray crystallographic data for **6k**(CCDC-1522717) (CIF)

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Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) (a) Barrio, P.; Ibáñez, I.; Herrera, L.; Román, R.; Catalán, S.; Fustero, S. *Chem. - Eur. J.* **2015**, *21*, 11579. (b) Enders, D.; Narine, A. A.; Toulgoat, F.; Bisschops, T. *Angew. Chem., Int. Ed.* **2008**, *47*, 5661. (c) Pandey, G.; Varkhedkar, R.; Tiwari, D. *Org. Biomol. Chem.* **2015**, *13*, 4438.

(2) (a) Fustero, S.; Herrera, L.; Lázaro, R.; Rodríguez, E.; Maestro, M. A.; Mateu, N.; Barrio, P. *Chem. - Eur. J.* **2013**, *19*, 11776. (b) Takizawa, S.; Inoue, N.; Hirata, S.; Sasai, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 9725. (c) Xing, S.; Ren, J.; Wang, K.; Cui, H.; Yan, H.; Li, W. *Adv. Synth. Catal.* **2016**, *358*, 532. (d) He, Z.; Liu, T.; Tao, H.; Wang, C.-J. *Org. Lett.* **2012**, *14*, 6230. (e) Wang, C.; Chen, X.-H.; Zhou, S.-M.; Gong, L.-Z. *Chem. Commun.* **2010**, *46*, 1275.

(3) (a) Ackermann, L. *Chem. Rev.* **2011**, *111*, 1315. (b) Cho, S. H.; Kim, J. Y.; Kwak, J.; Chang, S. *Chem. Soc. Rev.* **2011**, *40*, 5068. (c) Wencel-Delord, J.; Droge, T.; Liu, F.; Glorius, F. *Chem. Soc. Rev.* **2011**, *40*, 4740. (d) Baudoin, O. *Chem. Soc. Rev.* **2011**, *40*, 4902. (e) McMurray, L.; O'Hara, F.; Gaunt, M. J. *Chem. Soc. Rev.* **2011**, *40*, 1885. (f) Le Bras, J.; Muzart, J. *Chem. Rev.* **2011**, *111*, 1170. (g) Engle, K. M.; Mei, T.-S.; Wasa, M.; Yu, J.-Q. *Acc. Chem. Res.* **2012**, *45*, 788. (h) Zhang, X.-S.; Chen, K.; Shi, Z.-J. *Chem. Sci.* **2014**, *5*, 2146. (i) Zhang, F.; Spring, D. R. *Chem. Soc. Rev.* **2014**, *43*, 6906. (j) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. *Org. Chem. Front.* **2015**, *2*, 1107.

(4) (a) Shi, B.-F.; Zhang, Y.-H.; Lam, J. K.; Wang, D.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 460. (b) Engle, K. M.; Wang, D.-H.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2010**, *49*, 6169. (c) Nishikata, T.; Lipshutz, B. H. *Org. Lett.* **2010**, *12*, 1972. (d) Wang, D.-H.; Engle, K. M.; Shi, B.-F.; Yu, J.-Q. *Science* **2010**, *327*, 315. (e) Lyons, T. W.; Sanford, M. S. *Chem. Rev.* **2010**, *110*, 1147. (f) Zhu, Y.-Q.; Qin, L.; Song, Q.; Su, F.; Xu, Y.-J.; Dong, L. *Org. Biomol. Chem.* **2016**, *14*, 9472. (g) Dai, H.-X.; Stepan, A. F.; Plummer, M. S.; Zhang, Y.-H.; Yu, J.-Q. *J. Am. Chem. Soc.* **2011**, *133*, 7222. (h) Deb, A.; Bag, S.; Kancherla, R.; Maiti, D. *J. Am. Chem. Soc.* **2014**, *136*, 13602. (i) Hu, J.; Guan, M.; Han, J.; Huang, Z.-B.; Shi, D.-Q.; Zhao, Y. *J. Org. Chem.* **2015**, *80*, 7896.

(5) (a) Arockiam, P. B.; Bruneau, C.; Dixneuf, P. H. *Chem. Rev.* **2012**, *112*, 5879. (b) Kozhushkov, S. I.; Ackermann, L. *Chem. Sci.* **2013**, *4*, 886. (c) Ackermann, L. *Acc. Chem. Res.* **2014**, *47*, 281.

(6) (a) Colby, D. A.; Bergman, R. G.; Ellman, J. A. *Chem. Rev.* **2010**, *110*, 624. (b) Wang, F.; Song, G.; Li, X. *Org. Lett.* **2010**, *12*, 5430. (c) Park, S. H.; Kim, J. Y.; Chang, S. *Org. Lett.* **2011**, *13*, 2372. (d) Song, G.; Wang, F.; Li, X. *Chem. Soc. Rev.* **2012**, *41*, 3651. (e) Patureau, F. W.; Wencel-Delord, J.; Glorius, F. *Aldrichchim. Acta* **2012**, *45*, 31. (f) Mishra, N. K.; Park, J.; Sharma, S.; Han, S.; Kim, M.; Shin, Y.; Jang, J.; Kwak, J. H.; Jung, Y. H.; Kim, I. S. *Chem. Commun.* **2014**, *50*, 2350. (g) Xie, W.; Yang, J.; Wang, B.; Li, B. *J. Org. Chem.* **2014**, *79*, 8278. (h) Ding, Q.; Liu, T.; Zheng, Q.; Zhang, Y.; Long, L.; Peng, Y. *RSC Adv.* **2014**, *4*, 51309. (i) Lu, Y.; Wang, H.-W.; Spangler, J. E.; Chen, K.; Cui, P.-P.; Zhao, Y.; Sun, W.-Y.; Yu, J.-Q. *Chem. Sci.* **2015**, *6*, 1923. (j) Song, G.; Li, X. *Acc. Chem. Res.* **2015**, *48*, 1007.

DOI: 10.1021/acs.joc.7b00799
J. Org. Chem. 2017, 82, 7223−7233

(7) Patureau, F. W.; Besset, T.; Glorius, F. *Angew. Chem., Int. Ed.* **2011**, *50*, 1064.
(8) (a) Ackermann, L.; Pospech, J. *Org. Lett.* **2011**, *13*, 4153. (b) Ma, S.; Villa, G.; Thuy-Boun, P. S.; Homs, A.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2014**, *53*, 734.
(9) Patureau, F. W.; Glorius, F. *J. Am. Chem. Soc.* **2010**, *132*, 9982.
(10) (a) Takahama, Y.; Shibata, Y.; Tanaka, K. *Chem. - Eur. J.* **2015**, *21*, 9053. (b) Gong, T.-J.; Xiao, B.; Liu, Z.-J.; Wan, J.; Xu, J.; Luo, D.-F.; Fu, Y.; Liu, L. *Org. Lett.* **2011**, *13*, 3235. (c) Feng, C.; Loh, T.-P. *Chem. Commun.* **2011**, *47*, 10458.
(11) Li, X.; Dong, Y.; Qu, F.; Liu, G. *J. Org. Chem.* **2015**, *80*, 790.
(12) (a) Lu, Y.; Wang, D.-H.; Engle, K. M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 5916. (b) Wang, X.; Lu, Y.; Dai, H.-X.; Yu, J.-Q. *J. Am. Chem. Soc.* **2010**, *132*, 12203.
(13) Zaitsev, V. G.; Shabashov, D.; Daugulis, O. *J. Am. Chem. Soc.* **2005**, *127*, 13154.
(14) Li, X.; Liu, Y.-H.; Gu, W.-J.; Li, B.; Chen, F.-J.; Shi, B.-F. *Org. Lett.* **2014**, *16*, 3904.
(15) (a) Wencel-Delord, J.; Colobert, F. *Chem. - Eur. J.* **2013**, *19*, 14010. (b) Wencel-Delord, J.; Colobert, F. *Synlett* **2015**, *26*, 2644. (c) Pedroni, J.; Cramer, N. *Chem. Commun.* **2015**, *51*, 17647. (d) Ye, B.; Cramer, N. *Acc. Chem. Res.* **2015**, *48*, 1308. (e) Laforteza, B. N.; Chan, K. S. L.; Yu, J.-Q. *Angew. Chem., Int. Ed.* **2015**, *54*, 11143. (f) Wangweerawong, A.; Bergman, R. G.; Ellman, J. A. *J. Am. Chem. Soc.* **2014**, *136*, 8520. (g) Kim, J.; Sim, M.; Kim, N.; Hong, S. *Chem. Sci.* **2015**, *6*, 3611.
(16) Son, S.-M.; Seo, Y. J.; Lee, H.-K. *Chem. Commun.* **2016**, *52*, 4286.
(17) Kim, J.-a.; Seo, Y. J.; Kang, S.; Han, J.; Lee, H.-K. *Chem. Commun.* **2014**, *50*, 13706.
(18) (a) Bower, J. F.; Rujirawanich, J.; Gallagher, T. *Org. Biomol. Chem.* **2010**, *8*, 1505. (b) Meléndez, R. E.; Lubell, W. D. *Tetrahedron* **2003**, *59*, 2581.
(19) (a) Seo, Y. J.; Kim, J.-a.; Lee, H.-K. *J. Org. Chem.* **2015**, *80*, 8887. (b) Lee, H.-K.; Kang, S.; Choi, E. B. *J. Org. Chem.* **2012**, *77*, 5454. (c) Han, J.; Kang, S.; Lee, H.-K. *Chem. Commun.* **2011**, *47*, 4004. (d) Kang, S.; Han, J.; Lee, E. S.; Choi, E. B.; Lee, H.-K. *Org. Lett.* **2010**, *12*, 4184.
(20) Nasir Baig, R. B.; Nadagouda, M. N.; Varma, R. S. *Aldrichchim. Acta* **2015**, *48*, 71.

DOI: 10.1021/acs.joc.7b00799
J. Org. Chem. 2017, 82, 7223−7233