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# 1-Hydroxybenzotriazole-Assisted, N-Heterocyclic Carbene Catalyzed β-Functionalization of Saturated Carboxylic Esters: Access to Spirooxindole Lactones

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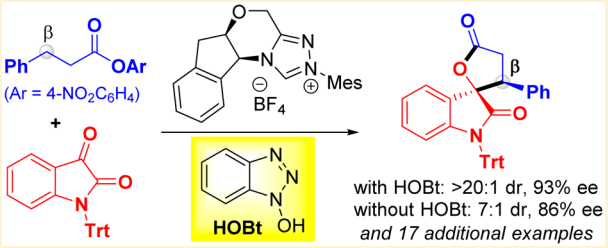
Supporting Information

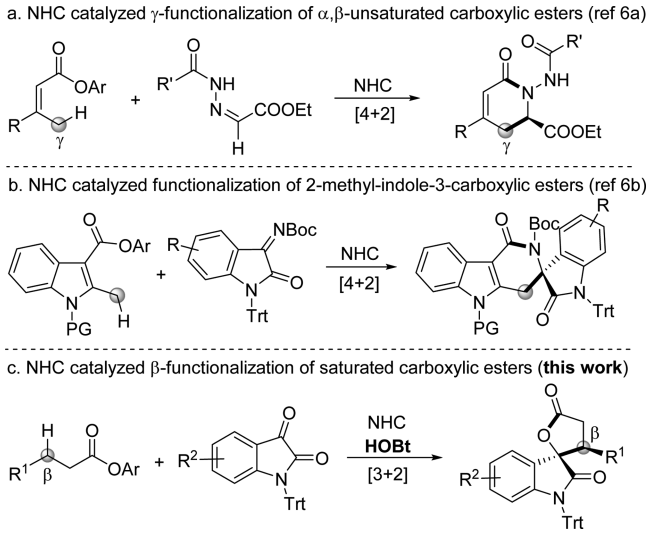
**ABSTRACT:** A 1-hydroxybenzotriazole-assisted, N-heterocyclic carbene catalyzed direct β-functionalization of saturated carboxylic esters is disclosed. This formal [3 + 2] annulation reaction of carboxylic esters with isatins affords optically pure spirooxindole lactones (on gram scale) bearing two vicinal stereogenic centers. A dual role of HOBt is proposed based on controlled experiments to rationalize the enhancement of diastereoselectivity and enantioselectivity.




Saturated carbonyl compounds such as esters and aldehydes are unambiguously vital building blocks for the preparation of pharmaceuticals, fine chemicals, and materials. Therefore, it is not surprising that considerable efforts have been devoted to the direct asymmetric functionalization of the carbonyl carbon and α-carbon of those compounds.[1] However, the direct catalytic incorporation of useful units on the saturated inert carbons remote from carbonyl group, such as the β-carbon, is more challenging.[2] Recently, several research groups have accomplished the direct enantioselective β-functionalization of saturated carbonyl compounds through organocatalysis.[3] In 2011, Wang[3b] and Hayashi[3c] independently turned the β-carbon of saturated aldehydes into an electrophilic reactive carbon via oxidative amine catalysis. In 2013, Chi and co-workers also formed an electrophilic β-carbon from saturated aldehydes mediated by an N-heterocyclic carbene (NHC) catalyst under oxidative condition.[3d] In 2013 and 2015, Chi's group and Yao's group further successfully converted the saturated β-carbon of esters,[3e,f] anhydrides,[3g,h] and acids[3i] into a nucleophilic reactive carbon via NHC catalysis. Despite the progress that has been achieved, the development of efficient strategies toward the direct introduction of functional groups at the β-position of saturated carbonyl compounds in a diastereo- and enantioselective manner is still in very high demand.

In the past several years, NHCs have been exploited as captivating organocatalysts for the activation of various substrates through many kinds of reaction modes to construct structurally complex and biologically active compounds.[4] Compared to oxygen-sensitive aldehydes and easily hydrolyzed anhydrides, carboxylic esters are bench-stable, readily available, and easy to handle substrates.[5] We are interested in the development of novel catalytic asymmetric reactions to synthesize enantiomerically enriched heterocycles from inexpensive 4-nitrophenol esters via NHC catalysis.[6] In 2013, we realized an NHC-catalyzed direct γ-functionalization of α,β-unsaturated carboxylic esters to prepare chiral δ-lactams, which could be further transformed to pipecolic acid derivatives (Scheme 1a).[6a] Very recently, we achieved an NHC-catalyzed formal [4 + 2] annulation reaction to furnish optically pure indole-fused δ-lactams by in situ generation of indole-2,3-quinodimethanes from 2-methylindole-3-carboxylic esters (Scheme 1b).[6b] Herein, we describe a HOBt-assisted, NHC-catalyzed formal [3 + 2] annulation reaction to afford spirooxindole lactones bearing two vicinal stereogenic centers

**Scheme 1. NHC-Catalyzed Synthesis of Heterocycles from Carboxylic Esters**

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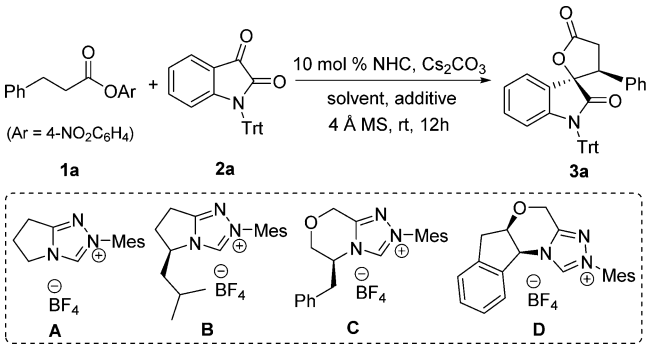
through direct $\beta$-functionalization of saturated carboxylic esters (Scheme 1c).[7] Notably, the employment of a catalytic amount of HOBt in our reaction could dramatically improve the diastereoselectivity and enantioselectivity, which is distinguished from other reactions in NHC catalysis where HOBt is simply used as a coupling reagent to form in situ generated activated benzotriazole esters.[8]

We started our investigation by using ester **1a** and isatin **2a** as the model substrates, and the key results are summarized in Table 1. As anticipated, when racemic NHC precatalyst **A**[9] was

**Table 1. Optimization of Reaction Conditions**[a]



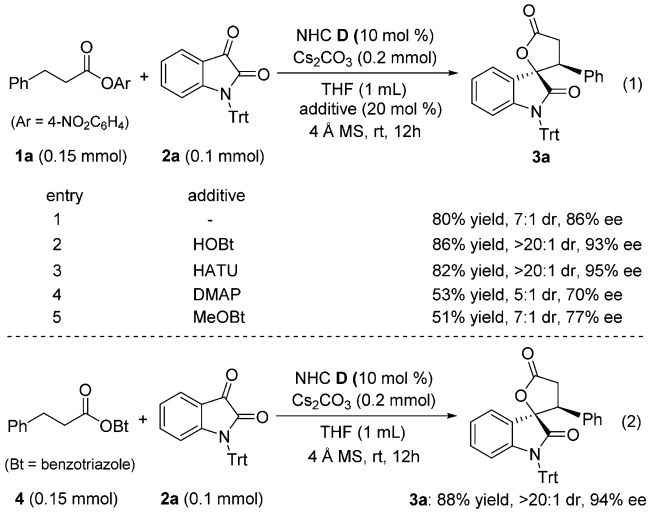

| entry | conditions | yield (%)[b] | dr[c] | ee (%)[d] |
|---|---|---|---|---|
| 1 | **A**, THF | 66 | 1:1 | |
| 2 | **B**, THF | 84 | 2:1 | 88 |
| 3 | **C**, THF | 72 | 3:1 | 64 |
| 4 | **D**, THF | 89 (80) | 7:1 | 86 |
| 5 | **D**, 1,4-dioxane | 82 | 8:1 | 82 |
| 6 | **D**, $CH_3CN$ | 79 | 3:1 | 78 |
| 7 | **D**, EtOAc | 68 | 3:1 | 80 |
| 8 | **D**, THF, $Sc(OTf)_3$ | 74 | 5:1 | 76 |
| 9 | **D**, THF, $Mg(OTf)_2$ | 73 | 5:1 | 82 |
| **10** | **D, THF, HOBt** | **91 (86)** | **>20:1** | **93** |

[a]Reaction conditions unless otherwise specified: **1a** (0.15 mmol), **2a** (0.1 mmol), NHC (10 mol %), $Cs_2CO_3$ (0.2 mmol), additive (20 mol %), solvent (1 mL), 4 Å MS (100 mg, powder) at room temperature for 12 h. [b]Yield estimated via $^1$H NMR analysis using 1,3,5-trimethoxybenzene as an internal standard; number in the parentheses is the isolated yield based on **2a**. [c]Diastereomeric ratio of **3a**, determined via $^1$H NMR analysis of crude reaction mixtures. [d]Enantiomeric excess of **3a**, determined via chiral phase HPLC analysis.

used, the [3 + 2] annulation product **3a** was successfully formed in 66% yield and 1:1 dr (Table 1, entry 1). L-Leucine-derived NHC precatalyst **B**[10] was the optimal precatalyst for our previous ester $\gamma$-functionalization,[6a] affording **3a** in 84% yield and 88% ee but only with 2:1 dr (entry 2). When L-phenylalanine-derived NHC precatalyst **C**[11] was employed, spirooxindole lactone **3a** was obtained in lower yield and enantioselectivity but slightly increased diastereoselectivity (entry 3). To our delight, when aminoindanol-derived NHC precatalyst **D**[12] was introduced, the desired product **3a** could be furnished with an encouraging 7:1 dr and similar yield and enantioselectivity (entry 4). With **D** as the optimal catalyst, we next set out to examine the solvent effect. 1,4-Dioxane helped this reaction to proceed smoothly, giving **3a** in 82% yield, 8:1 dr, and 82% ee (entry 5). $CH_3CN$ and EtOAc were less effective, as the diastereoselectivity value in both reactions dropped to 3:1 (entries 6 and 7). Lewis acids were previously proven to be able to improve diastereoselectivities and enantioselectivities in NHC catalysis,[13] so we tested $Sc(OTf)_3$ and $Mg(OTf)_2$ in our reaction, but unfortunately, only negative results were observed (entries 8 and 9). Finally, when 20 mol % of HOBt was exploited as an additive, we isolated **3a** in 86% yield, >20:1 dr, and 93% ee (entry 10).

To gain further insight into how HOBt functions in this reaction, we next set out to perform several additional experiments (Scheme 2). Similarly, when (1-[bis-

**Scheme 2. Controlled Experiments**




(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-*b*]-pyridinium 3-oxid hexafluorophosphate) (HATU) was used as an additive, the desired product **3a** was isolated in good yield with excellent diastereoselectivity and enantioselectivity (Scheme 2, eq 1, entry 3). However, 4-dimethylaminopyridine (DMAP), another commonly used coupling reagent in peptide synthesis, afforded a poor yield of **3a** (eq 1, entry 4). The use of methyl-substituted HOBt (MeOBt) also led to an unsatisfactory outcome, suggesting that hydrogen bonding may play a critical role in the current reaction (eq 1, entry 5). Finally, preformed benzotriazole ester **4** was employed as the ester substrate, and the corresponding product **3a** was obtained in 88% yield, >20:1 dr, and 94% ee (eq 2).

Based on the above observations, a plausible mechanism where HOBt plays a dual role is depicted in Scheme 3. HOBt (role no. 1: as an ester activating reagent) first replaces the 4-nitrophenol moiety of **1a** to afford activated benzotriazole ester **4**, which is next substituted by a chiral free NHC catalyst (formed by $Cs_2CO_3$-mediated deprotonation of NHC precatalyst **D**) to generate acyl azolium intermediate **I**. $\alpha$-Deprotonation of intermediate **I** furnishes enolate intermediate **II**, and subsequent proton transfer turns enolate intermediates **II** to homoenolate intermediate **III**.[3e,f,14] Due to the steric hindrance of the bulky indanol moiety on the NHC catalyst, isatin **2a** would prefer to approach intermediate **III** from the opposite face induced by hydrogen bonding from HOBt (role no. 2: as a hydrogen bonding donor); this reorganization of reactive species (transition state **TS**) may lead to the enhancement of diastereoselectivity and enantioselectivity. The anion on the $\beta$-carbon of intermediate **III** attacks isatin **2a** from the *si* face to furnish intermediate **IV**, and lactonization of intermediate **IV** finally releases spirooxindole lactone **3a** as the annulation product and regenerates free NHC catalyst.



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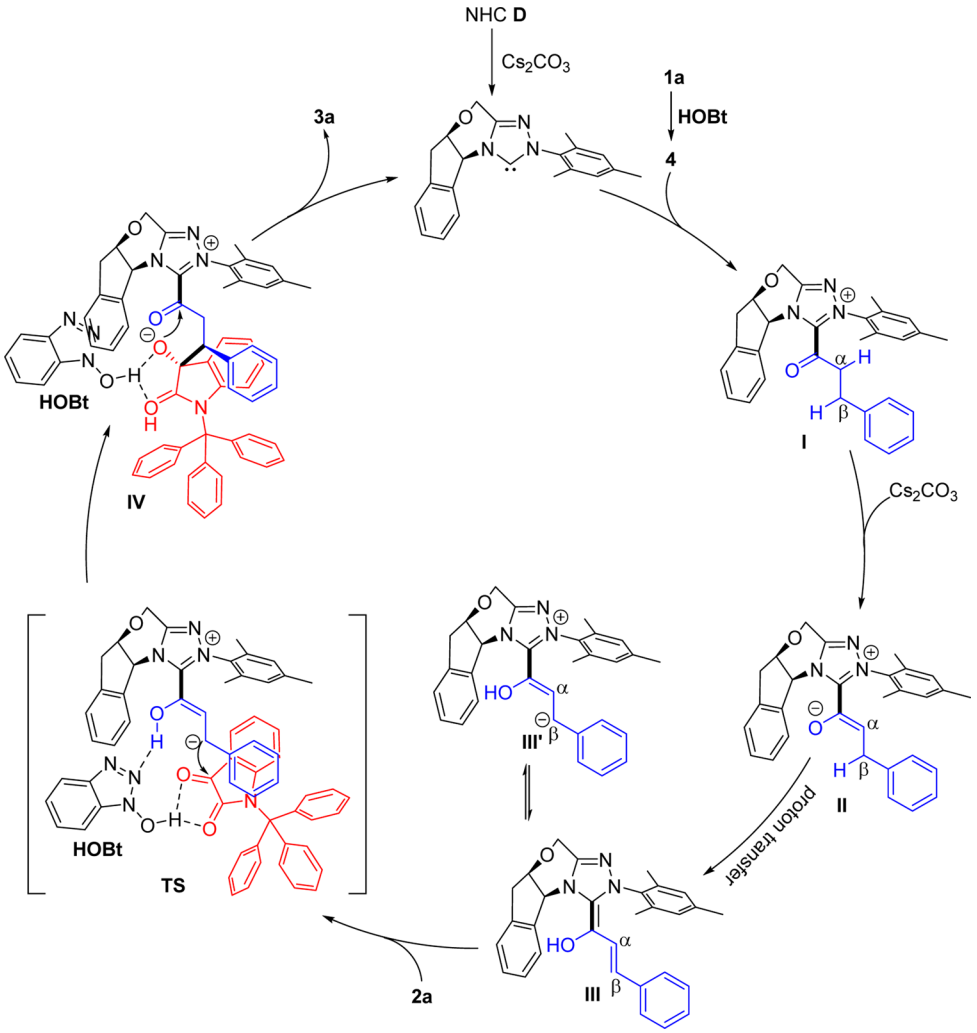
**Scheme 3. Proposed Catalytic Cycle**




With the optimized reaction conditions in hand (Table 1, entry 10), we then evaluated the scope of this formal [3 + 2] annulation reaction. As shown in Scheme 4, a broad range of carboxylic esters with diverse electronic and steric properties were first explored. The use of 4-nitrophenyl 3-phenylpropanoate (**1a**) provided the desired product **3a** in 86% yield with >20:1 dr and 93% ee. Esters with both electron-donating substituents (4-Me and 4-OMe) and electron-withdrawing substituents (4-F, 4-Cl, and 4-Br) on their $\beta$-phenyl ring were all well-tolerated, leading to the corresponding products **3b–f** in similar good yields, excellent diastereoselectivities, and enantioselectivities. The introduction of a sterically demanding substituent such as the 1-naphthyl group caused a decrease in both yield and enantioselectivity (**3g**). Heteroaryl-substituted carboxylic ester can be readily accommodated, thus affording the corresponding 2-furyl-substituted product **3h** in 80% yield, >20:1 dr, and 94% ee. It is worth noting that $\beta$-alkyl-substituted carboxylic ester was also compatible under the optimal conditions, furnishing product **3i** in lower 41% yield, >20:1 dr, and 98% ee. Modifications on the phenyl ring of the isatin substrates were feasible. The use of 5-Me- and 5-OMe-substituted isatins achieved the desired products **3j** and **3k** in good yields and excellent diastereoselectivities and enantioselectivities. However, when electron-withdrawing substituents (5-F, 5-Cl, 5-Br, and 5-I) were installed on the isatin phenyl ring, a slight drop in both yields and enantioselectivities were observed (**3l–o**), and the absolute configuration of the major enantiomer was assigned based on the X-ray structure of **3n**.[15] The substitution patterns on other positions of the isatin phenyl ring were also investigated, and the use of 7-Me-, 7-F-, and 5,7-dimethyl-substituted isatins gave the corresponding products **3p–r** in good yields and excellent diastereoselectivities and enantioselectivities, respectively.

Moreover, this reaction can be smoothly performed on a gram scale without loss of diastereoselectivity and enantioselectivity (Scheme 5, eq 1). The trityl protecting group on **3a** can be readily removed by trifluoroacetic acid (TFA) to form spirooxindole lactone **5**, which could be further transformed to 3-hydroxy oxindole **6** (Scheme 5, eq 2).[16] It is noteworthy that 3-hydroxy oxindoles are widely found as core skeletons in a variety of natural products and biologically active compounds.[17]

In summary, we have developed a HOBt-assisted, NHC-catalyzed direct $\beta$-functionalization reaction of saturated carboxylic esters that undergoes a formal [3 + 2] annulation with isatins in a highly efficient, diastereoselective, and enantioselective manner to afford chiral spirooxindole lactones. This reaction can be easily scaled up, and the trityl protecting group could be readily removed under mild conditions to give spirooxindole lactone which could be further converted to the biologically interesting 3-hydroxy oxindole. A dual role of



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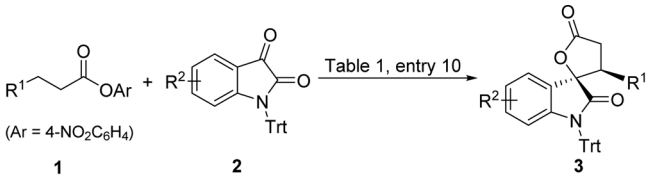
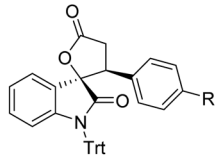
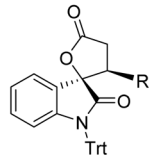
**Scheme 4. Scope of Reactions**[a]

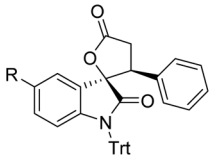


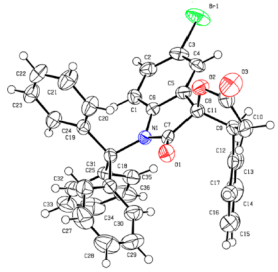
R = H, **3a**: 86% yield, >20:1 dr, 93% ee
Me, **3b**: 88% yield, >20:1 dr, 94% ee
OMe, **3c**: 86% yield, >20:1 dr, 94% ee
F, **3d**: 84% yield, >20:1 dr, 94% ee
Cl, **3e**: 87% yield, >20:1 dr, 92% ee
Br, **3f**: 85% yield, >20:1 dr, 93% ee



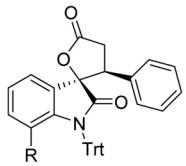
R = 1-Naphthyl, **3g**: 58% yield
>20:1 dr, 88% ee
2-Furyl, **3h**: 80% yield
>20:1 dr, 94% ee
n-Propyl, **3i**: 41% yield
>20:1 dr, 98% ee



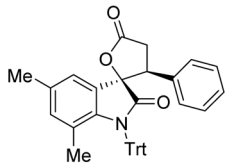
R = Me, **3j**: 92% yield, >20:1 dr, 94% ee
OMe, **3k**: 86% yield, >20:1 dr, 94% ee
F, **3l**: 77% yield, >20:1 dr, 88% ee
Cl, **3m**: 81% yield, >20:1 dr, 90% ee
Br, **3n**: 82% yield, >20:1 dr, 88% ee
I, **3o**: 76% yield, >20:1 dr, 84% ee



ORTEP diagram of **3n**



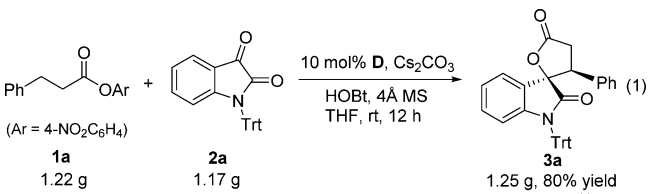
R = Me, **3p**: 90% yield, >20:1 dr, 94% ee
F, **3q**: 71% yield, >20:1 dr, 97% ee

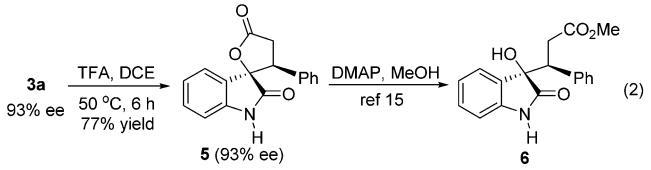


**3r**: 91% yield, >20:1 dr, 96% ee

[a]Reaction conditions: **1** (0.15 mmol), **2** (0.1 mmol), NHC **D** (10 mol %), $Cs_2CO_3$ (0.2 mmol), THF (1 mL), HOBt (20 mol %), 4 Å MS (100 mg, powder) at room temperature for 12 h. Isolated yields based on **2**. The diastereoselectivities were determined via $^1$H NMR analysis of crude reaction mixtures, and the enantioselectivities were determined via chiral phase HPLC analysis.

**Scheme 5. Gram-Scale Preparation and Synthetic Transformation of 3a**




HOBt is proposed to rationalize the enhancement of diastereoselectivity and enantioselectivity.

## EXPERIMENTAL SECTION

**General Information.** Commercially available materials were used as received. $^1$H and $^{13}$CNMR spectra were recorded at 400 and 100 MHz, respectively. Chemical shifts were recorded in parts per million (ppm, $\delta$) relative to tetramethylsilane ($\delta$ = 0.00) or chloroform ($\delta$ = 7.26). High-resolution mass spectra were obtained on a HRMS/LC-MS instrument using electrospray ionization (ESI) as the ionization method and an ion trap mass analyzer. The determination of enantioselectivity was performed via chiral HPLC analysis using IA and IC columns (25 × 0.46 cm) on an HPLC instrument. Optical rotations were measured using a 1 mL cell with a 1 dm path length and are reported as follows: $[\alpha]_D^{rt}$ ($c$ in g/100 mL solvent). All reactions were monitored by TLC with GF 254 silica-gel-coated plates. Flash column chromatography was carried out using 200−300 mesh silica gel, and melting points are uncorrected.

**General Procedure for the Catalytic Synthesis of Spirooxindole Lactones.** To a dry 10 mL Schlenk tube equipped with a magnetic stir bar were added **1** (0.15 mmol), **2** (0.1 mmol), $Cs_2CO_3$ (0.2 mmol), HOBt (0.02 mmol), 4 Å MS (100 mg), and chiral NHC precatalyst **D** (0.01 mmol). The tube was sealed with a septum, evacuated, and refilled with nitrogen (3 cycles). Freshly distilled anhydrous THF (1 mL) was added, and the reaction mixture was allowed to stir for 12 h at room temperature. After completion of the reaction, the reaction mixture was concentrated under reduced pressure and the residue was subjected to column chromatography using hexane/EtOAc = 5/1 as eluent to afford the desired spirooxindole lactones **3**. Note: The racemic catalyst that was used for the preparation of the corresponding racemic products for HPLC analysis was synthesized by mixing chiral precatalyst **D** and *ent*-**D** in a 1:1 ratio.

*(2R,3S)-3-Phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3a**):* 44.8 mg, 86% yield, >20:1 dr, white solid; mp 253−254 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47 (d, $J$ = 7.6 Hz, 1H), 7.41−7.39 (m, 3H), 7.16−7.11 (m, 11H), 7.05 (t, $J$ = 7.6 Hz, 1H), 6.94−6.92 (m, 7H), 6.13 (d, $J$ = 8.4 Hz, 1H), 4.14 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.0 Hz, 1H), 3.73 (dd, $J_1$ = 16.8 Hz, $J_2$ = 13.6 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.7, 174.3, 144.5, 140.9, 132.3, 129.6, 129.4, 128.9, 128.7, 128.3, 127.5, 127.0, 124.9, 123.4, 123.0, 116.7, 86.0, 74.8, 51.3, 31.7; HRMS (ESI, $m/z$) calcd for $C_{36}H_{27}NO_3Na^+$ 544.1889, found 544.1891; $[\alpha]_D^{21}$ = −90.1 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 93% ee [CHIRALPAK IA column; 1 mL/min; solvent system, *i*-PrOH/hexane = 5:95; retention times = 16.6 min (minor), 21.6 min (major)].

*(2R,3S)-3-(p-Tolyl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3b**):* 47.1 mg, 88% yield, >20:1 dr, pale yellow solid; mp 245−246 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.45 (d, $J$ = 7.2 Hz, 1H), 7.21−7.10 (m, 11H), 7.03−6.91 (m, 10H), 6.11 (d, $J$ = 8.0 Hz, 1H), 4.09 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.70 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.83 (dd, $J_1$ = 17.2 Hz, $J_2$ = 8.4 Hz, 1H), 2.34 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.8, 174.3, 144.4, 140.9, 138.7, 129.6, 129.4, 129.3, 129.2, 128.1, 127.4, 127.0, 124.9, 123.4, 122.9, 116.6, 86.1, 74.8, 51.2, 31.7, 21.2; HRMS (ESI, $m/z$) calcd for $C_{37}H_{29}NO_3Na^+$ 558.2045, found 558.2052; $[\alpha]_D^{21}$ = −100.7 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IA column; 1 mL/min; solvent system, *i*-PrOH/hexane = 5:95; retention times = 10.1 min (minor), 13.2 min (major)].

*(2R,3S)-3-(4-Methoxyphenyl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3c**):* 47.4 mg, 86% yield, >20:1 dr, pale yellow solid; mp 229−230 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44 (d, $J$ = 7.2 Hz, 1H), 7.16−7.11 (m, 9H), 7.05−6.89 (m, 12H), 6.12 (d, $J$ = 8.4 Hz, 1H), 4.08 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.77 (s, 3H), 3.67 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.82 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.8, 174.3, 160.0, 144.4, 140.9, 129.5, 129.4, 129.3, 127.4, 127.0, 124.8, 124.1, 123.4, 123.0, 116.6, 114.0, 86.1, 74.7, 55.3, 50.8, 31.9; HRMS (ESI, $m/z$) calcd for $C_{37}H_{29}NO_4Na^+$ 574.1994, found 574.1993; $[\alpha]_D^{21}$ = −105.9 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IA column; 1 mL/min; solvent system, *i*-PrOH/hexane = 5:95; retention times = 15.9 min (minor), 18.3 min (major)].



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*(2R,3S)-3-(4-Fluorophenyl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3d**):* 45.3 mg, 84% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.46 (d, $J$ = 6.8 Hz, 1H), 7.17−7.12 (m, 9H), 7.07−7.03 (m, 5H), 6.96−6.93 (m, 7H), 6.12 (d, $J$ = 8.4 Hz, 1H), 4.10 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.67 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.4, 174.0, 162.9 (d, $J_{C-F}$ = 247 Hz), 144.5, 140.8, 130.0 (d, $J_{C-F}$ = 8 Hz), 129.7, 129.4, 128.1 (d, $J_{C-F}$ = 2 Hz), 127.5, 127.1, 124.4, 123.4, 123.1, 116.8, 115.6 (d, $J_{C-F}$ = 21 Hz), 85.6, 74.8, 50.8, 32.0; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3FNa^+$ 562.1794, found 562.1790; $[\alpha]_D^{21}$ = −77.9 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 10.9 min (minor), 13.2 min (major)].

*(2R,3S)-3-(4-Chlorophenyl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3e**):* 48.3 mg, 87% yield, >20:1 dr, pale yellow solid; mp 209−211 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.46 (d, $J$ = 7.2 Hz, 1H), 7.32 (d, $J$ = 8.4 Hz, 2H), 7.18−7.13 (m, 9H), 7.07−6.91 (m, 10H), 6.11 (d, $J$ = 8.0 Hz, 1H), 4.08 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.67 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.85 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.3, 173.9, 144.6, 140.8, 134.9, 130.9, 129.8, 129.7, 129.4, 128.8, 127.5, 127.1, 124.3, 123.4, 123.1, 116.8, 85.8, 74.9, 50.8, 31.9; HRMS (ESI, $m/z$) calcd for $C_{36}H_{27}NO_3Cl^+$ 556.1679, found 556.1670; $[\alpha]_D^{21}$ = −97.5 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 92% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 11.1 min (minor), 14.0 min (major)].

*(2R,3S)-3-(4-Bromophenyl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3f**):* 51.0 mg, 85% yield, >20:1 dr, white solid; mp 224−225 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47 (d, $J$ = 8.0 Hz, 2H), 7.45 (d, $J$ = 8.4 Hz, 1H), 7.19−7.14 (m, 9H), 7.05 (t, $J$ = 7.2 Hz, 1H), 6.97−6.91 (m, 9H), 6.11 (d, $J$ = 8.0 Hz, 1H), 4.07 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.67 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.85 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.3, 173.9, 144.5, 140.8, 131.8, 130.4, 130.0, 129.8, 129.4, 127.5, 127.1, 124.3, 123.4, 123.1, 123.0, 116.8, 85.7, 74.9, 50.8, 31.9; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3{}^{81}BrNa^+$ 624.0973, found 624.0963; $[\alpha]_D^{21}$ = −96.7 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 93% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 11.7 min (minor), 15.1 min (major)].

*(2R,3S)-3-(Naphthalen-1-yl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3g**):* 33.1 mg, 58% yield, >20:1 dr, pale yellow solid; mp 262−263 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.95 (d, $J$ = 8.0 Hz, 1H), 7.88 (d, $J$ = 8.0 Hz, 1H), 7.71 (d, $J$ = 7.2 Hz, 1H), 7.58−7.64 (m, 2H), 7.52−7.45 (m, 2H), 7.18 (t, $J$ = 8.0 Hz, 1H), 7.11−7.05 (m, 4H), 7.02−6.98 (m, 6H), 6.80 (t, $J$ = 8.0 Hz, 1H), 6.59−6.57 (m, 6H), 5.85 (d, $J$ = 8.0 Hz, 1H), 5.04 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.4 Hz, 1H), 3.89 (dd, $J_1$ = 17.2 Hz, $J_2$ = 13.6 Hz, 1H), 3.00 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.8, 174.7, 144.1, 140.7, 134.2, 131.9, 129.4, 129.2, 129.0, 128.9, 128.3, 127.3, 126.8, 125.9, 125.8, 125.7, 125.6, 125.2, 123.3, 123.2, 122.8, 116.8, 86.2, 74.6, 45.7, 33.1; HRMS (ESI, $m/z$) calcd for $C_{40}H_{29}NO_3Na^+$ 594.2045, found 594.2039; $[\alpha]_D^{21}$ = +28.0 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 88% ee [CHIRALPAK ID column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 24.4 min (minor), 32.5 min (major)].

*(2R,3S)-3-(Furan-2-yl)-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3h**):* 40.9 mg, 80% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.39 (m, 2H), 7.20−7.11 (m, 15H), 7.03 (t, $J$ = 7.6 Hz, 1H), 6.97 (t, $J$ = 8.0 Hz, 1H), 6.44−6.42 (m, 1H), 6.28−6.26 (m, 1H), 6.24−6.22 (m, 1H), 4.18 (dd, $J_1$ = 13.2 Hz, $J_2$ = 8.4 Hz, 1H), 3.60 (dd, $J_1$ = 17.2 Hz, $J_2$ = 13.6 Hz, 1H), 2.92 (dd, $J_1$ = 17.2 Hz, $J_2$ = 8.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.0, 173.9, 148.2, 144.4, 142.8, 141.2, 129.6, 129.3, 127.5, 127.0, 125.0, 123.4, 123.0, 116.6, 110.8, 108.7, 84.5, 74.7, 44.8, 31.8; HRMS (ESI, $m/z$) calcd for $C_{34}H_{25}NO_4Na^+$ 534.1681, found 534.1683; $[\alpha]_D^{21}$ = −64.7 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK ID column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 19.0 min (minor), 20.6 min (major)].

*(2R,3R)-3-Propyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3i**):* 19.9 mg, 41% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42−7.40 (m, 6H), 7.30−7.20 (m, 11H), 7.02−6.96 (m, 2H), 6.31 (d, $J$ = 6.8 Hz, 1H), 2.90 (dd, $J_1$ = 15.6 Hz, $J_2$ = 12.0 Hz, 1H), 2.79−2.72 (m, 1H), 2.67 (dd, $J_1$ = 15.6 Hz, $J_2$ = 7.6 Hz, 1H), 1.43−1.36 (m, 1H), 1.26−1.15 (m, 2H), 1.07−1.00 (m, 1H), 0.79 (t, $J$ = 7.2 Hz, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 175.5, 174.3, 144.5, 141.4, 129.6, 129.3, 127.8, 127.1, 125.7, 123.8, 123.0, 116.4, 85.1, 75.0, 46.0, 33.9, 30.6, 21.4, 14.0; HRMS (ESI, $m/z$) calcd for $C_{33}H_{29}NO_3Na^+$ 510.2045, found 510.2053; $[\alpha]_D^{21}$ = +41.9 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 98% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 8.3 min (minor), 9.9 min (major)].

*(2R,3S)-5′-Methyl-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3j**):* 49.2 mg, 92% yield, >20:1 dr, pale yellow solid; mp 259−260 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.38 (m, 3H), 7.28 (s, 1H), 7.14−7.10 (m, 11H), 6.93−6.92 (m, 6H), 6.71 (d, $J$ = 8.4 Hz, 1H), 6.01 (d, $J$ = 8.4 Hz, 1H), 4.13 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.72 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.84 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H), 2.26 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.7, 174.3, 142.0, 141.0, 132.7, 132.4, 130.1, 129.4, 128.9, 128.7, 128.3, 127.4, 126.9, 124.8, 124.0, 116.4, 86.1, 74.7, 51.2, 31.7, 20.8; HRMS (ESI, $m/z$) calcd for $C_{37}H_{29}NO_3Na^+$ 558.2045, found 558.2039; $[\alpha]_D^{21}$ = −121.0 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 13.3 min (minor), 16.1 min (major)].

*(2R,3S)-5′-Methoxy-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3k**):* 47.4 mg, 86% yield, >20:1 dr, pale yellow solid; mp 241−242 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.42−7.39 (m, 3H), 7.15−7.10 (m, 11H), 7.03 (s, 1H), 6.94−6.91 (m, 6H), 6.47 (d, $J$ = 9.2 Hz, 1H), 6.03 (d, $J$ = 9.2 Hz, 1H), 4.12 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.77−3.70 (m, 4H), 2.85 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.7, 174.1, 155.8, 141.0, 137.5, 132.3, 129.4, 128.9, 128.7, 128.3, 127.4, 126.9, 126.0, 117.5, 115.0, 109.3, 86.2, 74.7, 55.6, 51.4, 31.7; HRMS (ESI, $m/z$) calcd for $C_{37}H_{29}NO_4Na^+$ 574.1994, found 574.1987; $[\alpha]_D^{21}$ = −128.5 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IC column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 46.2 min (major), 56.3 min (minor)].

*(2R,3S)-5′-Fluoro-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3l**):* 41.5 mg, 77% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.43−7.41 (m, 3H), 7.22−7.11 (m, 12H), 6.92−6.90 (m, 6H), 6.67−6.62 (m, 1H), 6.09−6.05 (m, 1H), 4.09 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.72 (dd, $J_1$ = 16.8 Hz, $J_2$ = 13.6 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.3, 174.1, 158.9 (d, $J_{C-F}$ = 243 Hz), 140.6, 140.3 (d, $J_{C-F}$ = 2 Hz), 131.9, 129.3, 129.1, 128.8, 128.3, 127.6, 127.1, 126.4 (d, $J_{C-F}$ = 8 Hz), 117.7 (d, $J_{C-F}$ = 7 Hz), 116.3 (d, $J_{C-F}$ = 22 Hz), 111.0 (d, $J_{C-F}$ = 25 Hz), 85.7, 74.9, 51.5, 31.6; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3FNa^+$ 562.1794, found 562.1791; $[\alpha]_D^{21}$ = −77.4 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 88% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 10.7 min (minor), 16.5 min (major)].

*(2R,3S)-5′-Chloro-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3m**):* 45.0 mg, 81% yield, >20:1 dr, white solid; mp 220−222 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.46−7.42 (m, 4H), 7.17−7.11 (m, 11H), 6.91−6.89 (m, 7H), 6.05 (d, $J$ = 8.8 Hz, 1H), 4.11 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.70 (dd, $J_1$ = 17.2 Hz, $J_2$ = 14.0 Hz, 1H), 2.86 (dd, $J_1$ = 17.2 Hz, $J_2$ = 8.4 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.2, 173.9, 143.0, 140.6, 131.9, 129.6, 129.3, 129.1, 128.8, 128.7, 128.3, 127.6, 127.2, 126.6, 123.7, 117.7, 85.6, 75.0, 51.4, 31.6; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3ClNa^+$ 578.1499, found 578.1503; $[\alpha]_D^{21}$ = −120.8 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 90% ee [CHIRALPAK ID column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 16.1 min (minor), 18.4 min (major)].

*(2R,3S)-5′-Bromo-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3n**):* 49.1 mg, 82% yield, >20:1 dr, white solid; mp 228−230 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.59 (s, 1H),



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7.43−7.42 (m, 3H), 7.17−7.11 (m, 11H), 7.04 (d, $J$ = 8.8 Hz, 1H), 6.91−6.88 (m, 6H), 6.00 (d, $J$ = 8.4 Hz, 1H), 4.11 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.4 Hz, 1H), 3.70 (dd, $J_1$ = 16.8 Hz, $J_2$ = 13.6 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.2, 173.8, 143.5, 140.5, 132.5, 131.9, 129.3, 129.1, 128.8, 127.9, 127.6, 127.2, 127.0, 126.6, 118.1, 116.0, 85.5, 75.0, 51.4, 31.6; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3BrNa^+$ 622.0994, found 622.0992; $[\alpha]_D^{21}$ = −122.4 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 88% ee [CHIRALPAK IC column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 25.4 min (major), 34.8 min (minor)].

*(2R,3S)-5′-Iodo-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3o**):* 49.2 mg, 76% yield, >20:1 dr, white solid; mp 262−264 °C; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.76 (s, 1H), 7.44−7.42 (m, 3H), 7.25−7.11 (m, 12H), 6.90−6.88 (m, 6H), 5.89 (d, $J$ = 8.4 Hz, 1H), 4.11 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.0 Hz, 1H), 3.70 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.2, 173.6, 144.3, 140.5, 138.4, 132.3, 131.9, 129.3, 129.1, 128.8, 128.3, 127.6, 127.2, 127.1, 118.5, 86.0, 85.4, 75.0, 51.3, 31.5; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3INa^+$ 670.0855, found 670.0834; $[\alpha]_D^{21}$ = −143.9 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 84% ee [CHIRALPAK IC column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 27.2 min (major), 37.4 min (minor)].

*(2R,3S)-7′-Methyl-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3p**):* 48.2 mg, 90% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.47 (d, $J$ = 6.4 Hz, 1H), 7.34−7.33 (m, 3H), 7.22−7.05 (m, 12H), 6.92−6.83 (m, 7H), 4.13 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.0 Hz, 1H), 3.66 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.81 (dd, $J_1$ = 16.4 Hz, $J_2$ = 8.0 Hz, 1H), 1.03 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.8, 174.4, 144.2, 143.3, 136.9, 132.1, 129.4, 128.9, 128.7, 128.6, 127.4, 127.1, 126.0, 124.4, 123.8, 110.0, 85.1, 74.9, 52.1, 32.4, 22.6; HRMS (ESI, $m/z$) calcd for $C_{37}H_{29}NO_3Na^+$ 558.2045, found 558.2043; $[\alpha]_D^{21}$ = −79.6 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 94% ee [CHIRALPAK IA column; 1 mL/min; solvent system, $i$-PrOH/hexane = 5:95; retention times = 11.3 min (minor), 17.7 min (major)].

*(2R,3S)-7′-Fluoro-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**3q**):* 38.3 mg, 71% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.41−7.36 (m, 4H), 7.18−7.09 (m, 12H), 6.90−6.88 (m, 6H), 6.77−6.72 (m, 1H), 4.13 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.4 Hz, 1H), 3.71 (dd, $J_1$ = 16.8 Hz, $J_2$ = 13.6 Hz, 1H), 2.86 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.3, 173.8, 146.5 (d, $J_{C-F}$ = 250 Hz), 142.4 (d, $J_{C-F}$ = 2 Hz), 131.9, 131.5 (d, $J_{C-F}$ = 8 Hz), 129.2, 129.0, 128.8, 128.3, 127.8, 127.3, 126.3, 125.1 (d, $J_{C-F}$ = 7 Hz), 120.2 (d, $J_{C-F}$ = 24 Hz), 119.8 (d, $J_{C-F}$ = 4 Hz), 85.6 (d, $J_{C-F}$ = 2 Hz), 75.6, 52.0, 31.9; HRMS (ESI, $m/z$) calcd for $C_{36}H_{26}NO_3FNa^+$ 562.1794, found 562.1807; $[\alpha]_D^{21}$ = −105.8 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 97% ee [CHIRALPAK ID column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 16.5 min (minor), 19.3 min (major)].

*(2R,3S)-5′,7′-Dimethyl-3-phenyl-1′-trityl-3,4-dihydro-5H-spiro-[furan-2,3′-indoline]-2′,5-dione (**3r**):* 49.9 mg, 91% yield, >20:1 dr, viscous solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.34−7.32 (m, 3H), 7.28 (s, 1H), 7.21−7.18 (m, 4H), 7.14−7.07 (m, 7H), 6.91−6.89 (m, 6H), 6.64 (s, 1H), 4.12 (dd, $J_1$ = 14.0 Hz, $J_2$ = 8.0 Hz, 1H), 3.64 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.80 (dd, $J_1$ = 16.8 Hz, $J_2$ = 8.4 Hz, 1H), 2.31 (s, 3H), 0.98 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.9, 174.5, 143.4, 141.7, 137.4, 133.4, 132.3, 129.5, 129.2, 128.8, 128.7, 127.3, 127.0, 126.0, 124.0, 122.7, 85.3, 74.7, 52.0, 32.5, 22.4, 20.4; HRMS (ESI, $m/z$) calcd for $C_{38}H_{31}NO_3Na^+$ 572.2202, found 572.2215; $[\alpha]_D^{21}$ = −82.7 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 96% ee [CHIRALPAK IC column; 1 mL/min; solvent system, $i$-PrOH/hexane = 10:90; retention times = 35.4 min (major), 41.6 min (minor)].

**Transformation of 3a to 5.** To a stirred solution of **3a** (104.2 mg, 0.2 mmol, 93% ee) in $ClCH_2CH_2Cl$ (2 mL) was carefully added TFA (154 μL, 2 mmol) at room temperature, and the reaction mixture was stirred at 50 °C for another 6 h. After completion of the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and quenched by saturated aqueous $NaHCO_3$ (4 mL). The aqueous phase was extracted with $CH_2Cl_2$, and the combined organic phase was washed with brine and dried over $Na_2SO_4$. Filtration and removal of solvent under reduced pressure gave a residue, which was purified by column chromatography using hexane/EtOAc = 4/1 as eluent to afford the desired product **5**.

*(2R,3S)-3-Phenyl-3,4-dihydro-5H-spiro[furan-2,3′-indoline]-2′,5-dione (**5**):* 42.9 mg, 77% yield, >20:1 dr, white solid; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.83 (br, 1H), 7.52 (d, $J$ = 7.6 Hz, 1H), 7.33 (t, $J$ = 7.6 Hz, 1H), 7.26−7.14 (m, 4H), 6.94 (d, $J$ = 7.6 Hz, 2H), 6.73 (d, $J$ = 7.6 Hz, 1H), 4.10 (dd, $J_1$ = 13.6 Hz, $J_2$ = 8.0 Hz, 1H), 3.76 (dd, $J_1$ = 16.8 Hz, $J_2$ = 14.0 Hz, 1H), 2.91 (dd, $J_1$ = 17.2 Hz, $J_2$ = 8.0 Hz, 1H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.9, 174.5, 141.4, 131.9, 131.3, 128.6, 128.3, 127.6, 124.9, 124.5, 123.5, 110.6, 86.5, 50.7, 32.1; HRMS (ESI, $m/z$) calcd for $C_{17}H_{13}NO_3Na^+$ 302.0793, found 302.0791; $[\alpha]_D^{21}$ = −60.1 ($c$ = 1.0 in $CHCl_3$); HPLC analysis 93% ee [CHIRALPAK IC column; 0.8 mL/min; solvent system, $i$-PrOH/hexane = 20:80; retention times = 32.8 min (major), 38.7 min (minor)].

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b02032.

$^1$H, $^{13}$C NMR, and HPLC spectra for all new compounds (PDF)

X-ray data for **3n** (CIF)

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### Notes

The authors declare no competing financial interest.

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