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Asymmetric Catalysis

# Enantioselective Cascade Reaction of α-Cyano Ketones and Isatylidene Malononitriles: Asymmetric Construction of Spiro[4*H*-pyran-oxindoles]

Jin Xie,[a] Wei-Long Xing,[a] Feng Sha,[a] and Xin-Yan Wu*[a]

**Abstract:** α-Cyano ketones have been employed for the first time as Michael donors in the construction of chiral spiro compounds. By using only 2 mol-% of a chiral multifunctional organocatalyst, chiral spiro[4*H*-pyran-oxindole] derivatives were prepared in yields of 97–99 % with enantioselectivities of 76–97 % *ee*. This method provides a new approach to the synthesis of chiral spirocyclic oxindoles.

## Introduction

The spirooxindole structure is commonly found in many alkaloids and pharmaceutical molecules.[1] Enormous effort has been made towards the synthesis of these spiro compounds because of their outstanding biological activity and wide range of biomedical applications.[2] Spiro[4*H*-pyran-oxindole] derivatives, which belong to the spirooxindole family of compounds, have various biological activities such as anticancer, antifungal, and antibacterial properties.[3] Because of the importance of such compounds, their construction has attracted great interest. However, the enantioselective synthesis of spiro[4*H*-pyran-oxindole] derivatives is rarely described. In 2010, Yuan first reported an enantioselective synthesis of spiro[4*H*-pyran-oxindoles] by using a domino Knoevenagel/Michael/cyclization reaction sequence between isatins, malononitrile, and 1,3-dicarbonyl compounds.[4] Several research groups[5–8] then developed asymmetric tandem reactions for the synthesis of spiro[4*H*-pyran-oxindole] compounds. In those reports, dicarbonyl or β-hydroxyl-α,β-unsaturated carbonyl compounds were used as the Michael donor, and the exploration of different Michael donors for use in an asymmetric tandem reaction to provide new chiral spiro[4*H*-pyran-oxindole] derivatives is still in demand.

α-Cyano ketones are good nucleophiles for the construction of chiral cyclic compounds. In recent years, α-cyano ketones have been widely employed as 1,3-bis(nucleophile)s to form chiral pyran derivatives.[9] Moreover, α-cyano ketones have been used as 1,1-bis(nucleophile)s in enantioselective [4+1] annulation reactions to produce five-membered ring compounds.[10] However, α-cyano ketones have never been employed in the construction of chiral spiro compounds. As there is continued interest in the enantioselective construction of chiral 3,3-disubstituted 2-oxindoles,[11] we sought to use α-cyano ketones as the Michael donor in an organocatalytic tandem reaction to provide chiral spirooxindoles. Herein, we report the first enantioselective cascade reaction of α-cyano ketones with isatylidene malononitriles to construct new spiro[4*H*-pyran-oxindole] derivatives.

## Results and Discussion

Initially, the enantioselective cascade reaction of α-cyanoacetophenone (**1a**) with *N*-benzyl isatylidene malononitrile (**2a**) was used as a model to screen chiral organocatalysts (Figure 1). The reactions were performed with 2 mol-% of the catalyst and 1 mol-% of piperidine in $CH_2Cl_2$ at 0 °C, and the results are summarized in Table 1. We began by using chiral bifunctional tertiary amine-thiourea organocatalysts **C1**–**C6**, and to our delight, the cascade reaction afforded spiro product **3aa** in excellent yields with moderate enantioselectivities (Table 1, Entries 1–6). Cinchona-derived thioureas gave similar results, and the absolute configuration of the product was controlled by the chiral backbone of these catalysts (Table 1, Entries 3–6). Quinidine-derived organocatalysts that contain different hydrogen-bonding donors were then examined. Surprisingly, squaramide **C7** and sulfamide **C8** afforded poor enantioselectivities of the product (Table 1, Entries 7 and 8). However, quinidine-derived organocatalysts that contain multiple hydrogen-bonding donors[12] provided improved enantioselectivities (Table 1, Entries 9–13 vs. 4). In particular, the preparation of spiro compound **3aa** was achieved in 99 % yield with 72 % *ee* in the presence of catalyst **C10**. To test the chirality match between a quinidine backbone and a 1,2-diphenylethanediamine, tertiary amine-thiourea-sulfamide **C14** was examined in the model reaction. However a lower enantioselectivity was the result (Table 1, Entry 14 vs. 9). The results also indicate that the absolute configuration of the product is better controlled by

[a] *Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai 200237, P. R. China*
*E-mail: xinyanwu@ecust.edu.cn*
*http://webmanage.ecust.edu.cn/s/230/t/262/a/57293/info.jspy*

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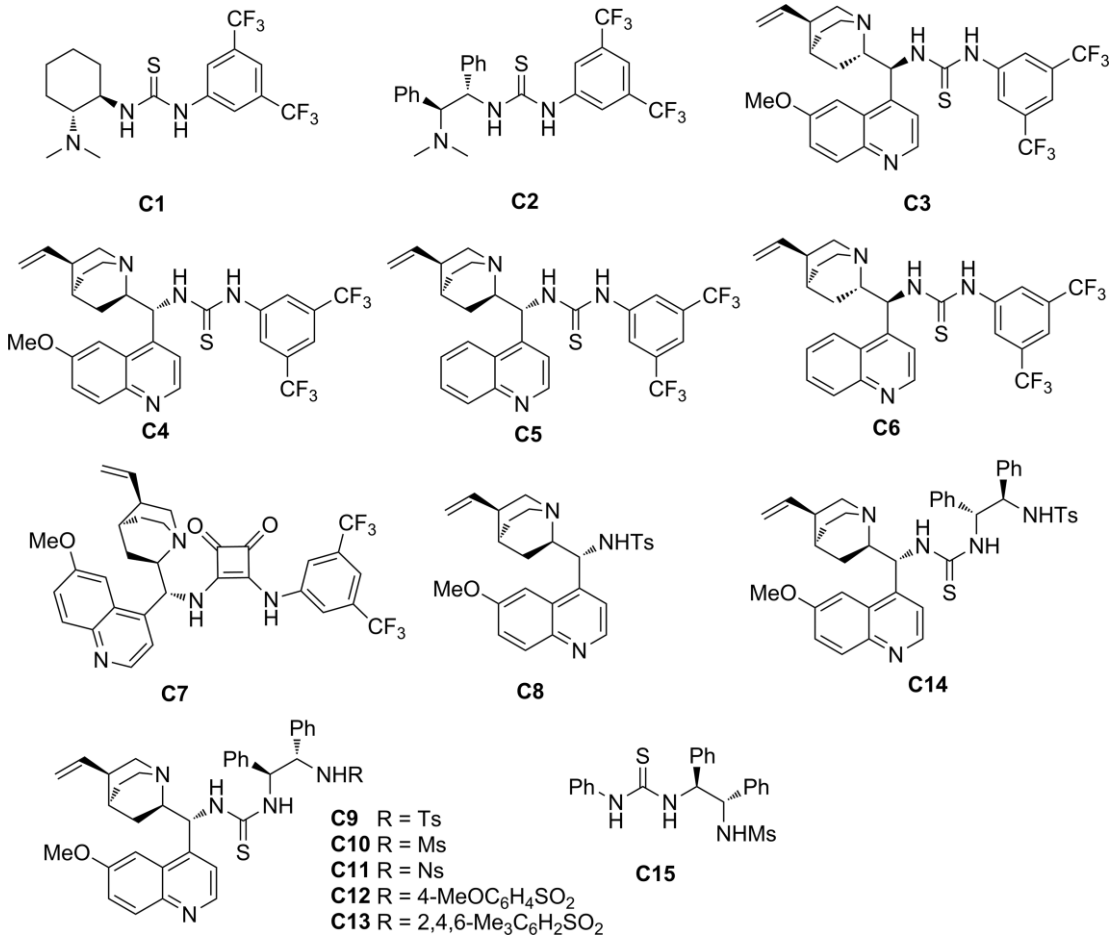
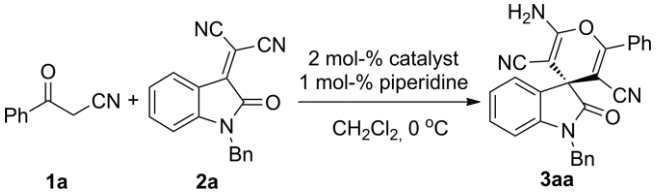



Figure 1. Structures of the chiral organocatalysts screened (Ts = *p*-tolylsulfonyl, Ms = methylsulfonyl, Ns = *p*-nitrophenylsulfonyl).

Table 1. Screening of the chiral organocatalysts for the cascade reaction.[a]




1a 2a 3aa

| Entry | Catalyst | Time [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|
| 1 | **C1** | 0.5 | 99 | 26 |
| 2 | **C2** | 0.5 | 99 | –45 |
| 3 | **C3** | 0.5 | 99 | –49 |
| 4 | **C4** | 0.5 | 99 | 48 |
| 5 | **C5** | 0.5 | 99 | 44 |
| 6 | **C6** | 0.5 | 99 | –47 |
| 7 | **C7** | 0.5 | 99 | –3 |
| 8 | **C8** | 0.5 | 99 | 3 |
| 9 | **C9** | 0.5 | 99 | 51 |
| 10 | **C10** | 0.5 | 99 | 72 |
| 11 | **C11** | 0.5 | 99 | 60 |
| 12 | **C12** | 0.5 | 99 | 63 |
| 13 | **C13** | 0.5 | 99 | 49 |
| 14 | **C14** | 0.5 | 99 | 34 |

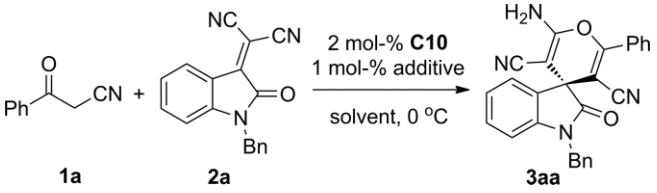
[a] The cascade reactions were performed with **1a** (0.11 mmol), **2a** (0.1 mmol), a catalyst (0.002 mmol), and piperidine (0.001 mmol) in $CH_2Cl_2$ (2 mL) at 0 °C. [b] Isolated yield of a mixture of enantiomers after column chromatography is reported. [c] The enantiomeric excess values of the product were determined by chiral HPLC analysis.

the quinidine backbone than the 1,2-diphenylethanediamine scaffold. Considering all of these results, we selected organocatalyst **C10** for use in our further investigations of the cascade reaction.

Next, the effects of additives were surveyed (Table 2, Entries 1–11). In the absence of a base, the cascade reaction provided low yield with a low enantioselectivity (Table 2, Entries 1 vs. 2). The addition of a primary amine such as benzylamine could promote the reaction rate as well as the chemical yield (Table 2, Entries 3 vs. 1). As expected, the existence of an achiral tertiary amine had a negative effect on the stereoselectivity (Table 2, Entry 4). These results indicate that a secondary amine is more suitable than a primary or tertiary amine (Table 2, Entries 5–11 and 2 vs. 3 and 4). Among all of the secondary amines that were screened, morpholine provided the best enantioselectivity (82 % *ee*, Table 2, Entry 6).

In the presence of catalyst **C10** and morpholine, the effect of the solvent was examined (Table 2, Entries 12–19). The cascade reaction in halogenated solvents such as dichloromethane, chloroform, and 1,2-dichloroethane provided better enantioselectivities than those obtained by carrying out the reaction in other solvents such as toluene, ethereal solvents, ethyl acetate, and $CH_3CN$ (Table 2, Entries 6, 12, and 13 vs. 14–19). From these results, $CH_2Cl_2$ was chosen as the solvent to optimize the other reaction conditions.

Table 2. Screening of the additives and solvents.[a]



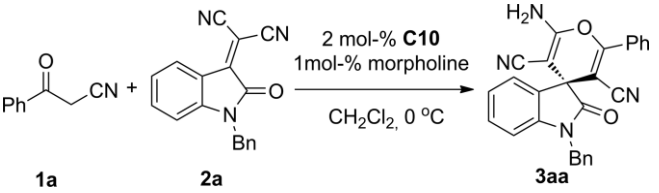

| Entry | Additive | Solvent | Time [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | – | $CH_2Cl_2$ | 2.0 | 79 | 49 |
| 2 | piperidine | $CH_2Cl_2$ | 0.5 | 99 | 72 |
| 3 | benzylamine | $CH_2Cl_2$ | 1.0 | 98 | 52 |
| 4 | DIPEA[d] | $CH_2Cl_2$ | 1.5 | 97 | 27 |
| 5 | pyrrolidine | $CH_2Cl_2$ | 0.5 | 98 | 57 |
| 6 | morpholine | $CH_2Cl_2$ | 1.0 | 99 | 82 |
| 7 | thiomorpholine | $CH_2Cl_2$ | 1.0 | 97 | 81 |
| 8 | piperazine | $CH_2Cl_2$ | 0.5 | 99 | 75 |
| 9 | 1-phenylpiperazine | $CH_2Cl_2$ | 1.0 | 99 | 78 |
| 10 | (3*S*)-*i*Pr-morpholine | $CH_2Cl_2$ | 3.0 | 99 | 54 |
| 11 | (3*R*)-*i*Pr-morpholine | $CH_2Cl_2$ | 2.0 | 99 | 51 |
| 12 | morpholine | $CHCl_3$ | 0.5 | 99 | 80 |
| 13 | morpholine | 1,2-DCE[d] | 0.5 | 99 | 80 |
| 14 | morpholine | toluene | 0.7 | 99 | 56 |
| 15 | morpholine | $Et_2O$ | 1.0 | 99 | 80 |
| 16 | morpholine | MTBE[d] | 1.5 | 99 | 73 |
| 17 | morpholine | THF[d] | 1.0 | 99 | 40 |
| 18 | morpholine | EtOAc | 1.5 | 99 | 58 |
| 19 | morpholine | $CH_3CN$ | 1.5 | 99 | 43 |

[a] The cascade reactions were performed with **1a** (0.11 mmol), **2a** (0.1 mmol), **C10** (0.002 mmol), and additive (0.001 mmol) in solvent (2 mL) at 0 °C. [b] Isolated yield of an enantiomeric mixture after column chromatography is reported. [c] The enantiomeric excess values of the product were determined by chiral HPLC analysis. [d] DIPEA = *N*,*N*-diisopropylethylamine, 1,2-DCE = 1,2-dichloroethane, MTBE = methyl *tert*-butyl ether, and THF = tetrahydrofuran.

Further reaction conditions, which include the ratio of substrate **1a** to **2a**, the concentration of the substrate, and the catalyst loading, were optimized (Table 3). These factors were determined to impact the reaction rate and enantioselectivities but not the chemical yields. The product could be produced in 99 % yield with 80 % *ee* by using only 1 mol-% of catalyst **C10** (Table 3, Entry 7).

Under the optimal reaction conditions (0.05 M isatylidene malononitrile **2** in $CH_2Cl_2$, 1.1 equiv. of α-cyano ketone **1**, 2 mol-% of **C10**, and 1 mol-% of morpholine at 0 °C), isatylidene malononitriles with different *N*-substituents were employed (Table 4). All of the substrates exhibited good reactivity and provided excellent yields, and the substituents on the nitrogen atom were found to have an impact on the stereoselectivity of the reaction. The low steric hindrance of an *N*-alkyl substituent increased the enantioselectivity of the product (Table 4, Entries 1–7). However, an *N*-acetyl-substituted substrate provided inferior enantioselectivity (Table 4, Entry 8). Notably, isatylidene malononitrile with a free NH group could smoothly undergo the cascade reaction, although the enantioselectivity of the reaction was 76 % *ee* (Table 4, Entry 9). When the reaction was carried out at –10 °C, the enantioselectivity improved to 90 % *ee* (Table 4, Entry 11).

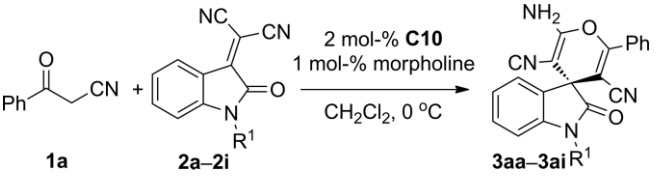
Table 3. Optimization of the reaction conditions.[a]




| Entry | **1a** [equiv.] | Conc. [M] | Time [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | 1.0 | 0.05 | 1.5 | 99 | 82 |
| 2 | 1.1 | 0.05 | 1.0 | 99 | 82 |
| 3 | 1.3 | 0.05 | 0.8 | 99 | 82 |
| 4 | 1.1 | 0.025 | 2.0 | 99 | 81 |
| 5 | 1.1 | 0.10 | 0.5 | 99 | 75 |
| 6[d] | 1.1 | 0.05 | 1.25 | 99 | 81 |
| 7[e] | 1.1 | 0.05 | 2.0 | 99 | 80 |

[a] Unless otherwise noted, the cascade reactions were performed with **1a**, **2a** (0.1 mmol), catalyst **C10** (0.002 mmol), and morpholine (0.001 mmol) in $CH_2Cl_2$ at 0 °C. [b] Isolated yield of an enantiomeric mixture after column chromatography is reported. [c] The enantiomeric excess values of the product were determined by chiral HPLC analysis. [d] Morpholine (0.5 mol-%) was used. [e] **C10** (1 mol-%) and morpholine (0.5 mol-%) were used.

Table 4. The effect of *N*-substituent of isatylidene malononitrile.[a]



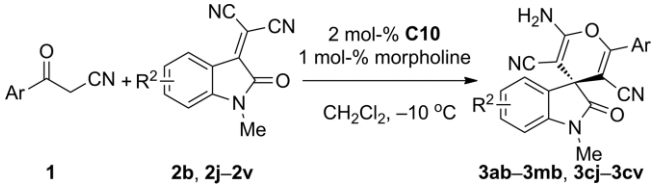

| Entry | $R^1$ | Time [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|
| 1 | Me | 1.0 | 99 (**3ab**) | 88 |
| 2 | Et | 1.0 | 98 (**3ac**) | 83 |
| 3 | allyl | 1.0 | 99 (**3ad**) | 83 |
| 4 | MOM[d] | 1.0 | 99 (**3ae**) | 82 |
| 5 | Bn | 1.0 | 99 (**3aa**) | 82 |
| 6 | PMB[d] | 1.0 | 99 (**3af**) | 79 |
| 7 | Tr[d] | 3.0 | 98 (**3ag**) | 11 |
| 8 | Ac | 1.0 | 99 (**3ah**) | 64 |
| 9 | H | 1.5 | 99 (**3ai**) | 76 |
| 10[e] | Me | 1.3 | 96 (**3ab**) | 70 |
| 11[f] | Me | 1.0 | 98 (**3ab**) | 90 |
| 12[g] | Me | 1.5 | 99 (**3ab**) | 88 |

[a] Unless otherwise noted, the cascade reactions were performed with **1a** (0.11 mmol), isatylidene malononitrile (0.1 mmol), catalyst **C10** (0.002 mmol), and morpholine (0.001 mmol) in $CH_2Cl_2$ (2 mL) at 0 °C. [b] Isolated yield of an enantiomeric mixture after column chromatography is reported. [c] The enantiomeric excess values were determined by chiral HPLC analysis. [d] MOM = methoxymethyl, PMB = *p*-methoxybenzyl, and Tr = triphenylmethyl. [e] The reaction was carried out at 25 °C. [f] The reaction was carried out at –10 °C. [g] The reaction was carried out at –25 °C.

Next, we investigated the scope of both substrates by using *N*-methyl isatylidene malononitriles as the electrophile in the reaction at –10 °C (Table 5). The results indicate that all of the examined substrates provided excellent chemical yields (97–99 %) with enantioselectivities that varied from 76 to 97 % *ee*. The α-cyano ketones that have an electron-rich substituent at the 4-position of its phenyl group provided better enantioselectivities than those obtained by α-cyano ketones that have

an electron-withdrawing group at the 4-position of the phenyl substituent (Table 5, Entries 2 and 3 vs. 6–8). Compared with a 4-methoxyphenyl-substituted compound, the corresponding 3- and 2-substituted substrates provided lower enantioselectivities, most likely the result of different stereoelectronic effects (Table 5, Entries 3–5). The enantioselectivity differences that result from different dimethoxy substrates are related to the positions of OMe (Table 5, Entries 9 and 10). Notably, heterocyclic and polycyclic α-cyano ketones provided excellent enantioselectivities (Table 5, Entries 11–13). The substituents at the 5-, 6-, and 7-position of the isatylidene malononitrile derivatives played a minimal role in the enantioselectivity results (91–97 % *ee*, Table 5, Entries 14–26). Although substrate **2o** exhibited low reactivity under the standard reaction conditions as well as low solubility in $CH_2Cl_2$, spirooxindole **3co** was prepared in 97 % yield with 92 % *ee* in 12 h (Table 5, Entry 19).

Table 5. Substrate scope of the enantioselective cascade reaction.[a]




**1** **2b**, **2j–2v** **3ab–3mb**, **3cj–3cv**

| Entry | Ar | $R^2$ | Time [h] | Yield [%][b] | *ee* [%][c] |
|---|---|---|---|---|---|
| 1 | $C_6H_5$ | H | 1.0 | 98 (**3ab**) | 90 |
| 2 | 4-$MeC_6H_4$ | H | 2.0 | 99 (**3bb**) | 91 |
| 3 | 4-$MeOC_6H_4$ | H | 2.0 | 99 (**3cb**) | 95 |
| 4 | 3-$MeOC_6H_4$ | H | 1.5 | 99 (**3db**) | 90 |
| 5 | 2-$MeOC_6H_4$ | H | 1.5 | 99 (**3eb**) | 76 |
| 6 | 4-$FC_6H_4$ | H | 1.0 | 99 (**3fb**) | 85 |
| 7 | 4-$ClC_6H_4$ | H | 2.0 | 98 (**3gb**) | 86 |
| 8 | 4-$BrC_6H_4$ | H | 1.0 | 99 (**3hb**) | 83 |
| 9 | 3,4-$(MeO)_2C_6H_3$ | H | 1.5 | 99 (**3ib**) | 94 |
| 10 | 3,5-$(MeO)_2C_6H_3$ | H | 1.5 | 99 (**3jb**) | 88 |
| 11 | 2-thienyl | H | 1.5 | 99 (**3kb**) | 90 |
| 12 | 2-furyl | H | 1.0 | 99 (**3lb**) | 93 |
| 13 | 2-naphthyl | H | 1.0 | 99 (**3mb**) | 92 |
| 14 | 4-$MeOC_6H_4$ | 5-Me | 1.0 | 99 (**3cj**) | 93 |
| 15 | 4-$MeOC_6H_4$ | 5-MeO | 1.5 | 98 (**3ck**) | 93 |
| 16 | 4-$MeOC_6H_4$ | 5-F | 1.0 | 99 (**3cl**) | 95 |
| 17 | 4-$MeOC_6H_4$ | 5-Cl | 1.0 | 99 (**3cm**) | 91 |
| 18 | 4-$MeOC_6H_4$ | 5-Br | 1.0 | 99 (**3cn**) | 94 |
| 19 | 4-$MeOC_6H_4$ | 6-Me | 12.0 | 97 (**3co**) | 92 |
| 20 | 4-$MeOC_6H_4$ | 6-Cl | 1.0 | 99 (**3cp**) | 96 |
| 21 | 4-$MeOC_6H_4$ | 6-Br | 1.0 | 99 (**3cq**) | 97 |
| 22 | 4-$MeOC_6H_4$ | 7-Me | 1.0 | 99 (**3cr**) | 94 |
| 23 | 4-$MeOC_6H_4$ | 7-F | 1.0 | 99 (**3cs**) | 94 |
| 24 | 4-$MeOC_6H_4$ | 7-Cl | 1.0 | 99 (**3ct**) | 94 |
| 25 | 4-$MeOC_6H_4$ | 7-Br | 1.0 | 99 (**3cu**) | 93 |
| 26 | 4-$MeOC_6H_4$ | 7-$CF_3$ | 0.75 | 99 (**3cv**) | 92 |

[a] The cascade reactions were performed with **1** (0.11 mmol), isatylidene malononitrile (0.1 mmol), catalyst **C10** (0.002 mmol), and morpholine (0.001 mmol) in $CH_2Cl_2$ (2 mL) at –10 °C. [b] Isolated yield of enantiomeric mixture after column chromatography is reported. [c] The enantiomeric excess values were determined by chiral HPLC analysis.

The absolute configuration of product **3cq** was determined as (*S*) by X-ray crystal structure analysis (Figure 2). The configurations of the other spiro[4*H*-pyran-oxindole] derivatives **3** were assigned by analogy.

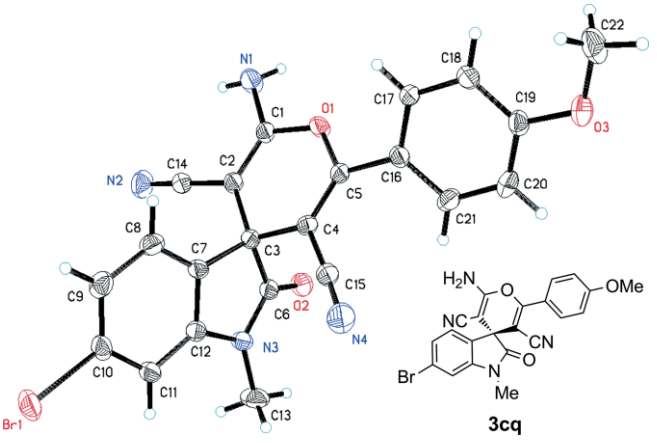
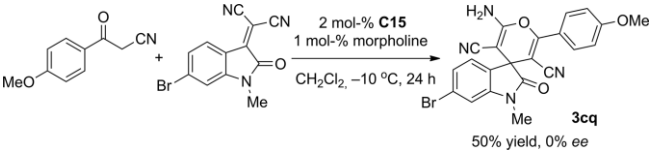


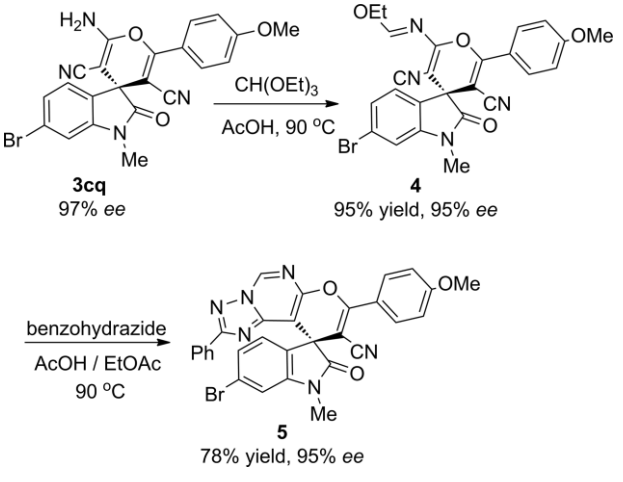

Figure 2. X-ray crystal structure of **3cq**.

To prove the importance of the chiral tertiary amine scaffold of the organocatalyst, chiral organocatalyst **C15**, which contains multiple hydrogen-bonding donors, was employed in the cascade reaction under the typical reaction condition. Because of the absence of the chiral tertiary amine scaffold, the racemic product was obtained in 50 % yield after 24 h (Scheme 1). This result suggests that the reaction rate and stereochemistry are mostly controlled by the tertiary amine moiety of the chiral organocatalyst.




Scheme 1. Control reaction catalyzed by chiral organocatalyst **C15** that has multiple hydrogen-bond donors.

It is known that pyranotriazolopyrimidine derivatives are found in many bioactive compounds such as antimicrobial,[13] antigenotoxic,[14] and antitumor substances.[15] Therefore, converting the cascade product into a pyranotriazolopyrimidine was investigated. As expected, spiro[4*H*-pyran-oxindole] **3cq** could be easily transformed into compound **4** in high yield with




Scheme 2. Transformation of spiro[4*H*-pyran-oxindole] **3cq**.

high enantioselectivity. Furthermore, compound **4** could undergo a reaction with benzohydrazide to afford chiral spiro-[indoline-3,10′-pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine] **5** in 78 % yield with 95 % *ee* (Scheme 2).

## Conclusions

In summary, we have developed the first organocatalytic enantioselective Michael/cyclization cascade reaction sequence between α-cyano ketones and isatylidene malononitriles. In the presence of 2 mol-% of tertiary amine catalyst **C10**, which contains multiple hydrogen-bonding donors, all of the corresponding spirooxindoles were obtained in excellent yields (97–99 %) with good-to-excellent enantioselectivities (76–97 % *ee*) within 2 h, with the exception of product **3co**. The method established herein represents a new protocol for the asymmetric construction of spiro[4*H*-pyran-oxindole] derivatives.

## Experimental Section

**General Methods:** The $^1$H and $^{13}$C NMR spectroscopic data were recorded with a Bruker 300 or Bruker 400 spectrometer. The chemical shifts of the $^1$H NMR spectra were referenced to tetramethylsilane ($\delta$ = 0.00 ppm) when $CDCl_3$ was used as the solvent. When [D$_6$]DMSO was used as the NMR solvent, the chemical shifts were referenced to the residual solvent signal [$\delta$ = 2.50 ppm for $(CD_3)(CHD_2)SO$]. The $^{13}$C NMR spectra were referenced to the carbon signals of the solvent ($\delta$ = 77.0 ppm for $CDCl_3$ and 39.52 ppm for [D$_6$]DMSO). IR spectra were recorded on a Nicolet Magna-I 550 spectrometer. High resolution mass spectrometry was carried out with an electrospray ionization time-of-flight (ESI-TOF) mass spectrometer. Optical rotations were measured on a WZZ-2A digital polarimeter at the wavelength of the sodium D line (589 nm). HPLC analysis was performed on equipment by Waters, which included a Daicel Chiralpak AD-H column and a Daicel Chiralpak AS-H column. Toluene, THF, ether, and MTBE were freshly distilled from sodium-benzophenone. Ethyl acetate, $CH_2Cl_2$, $CHCl_3$, $ClCH_2CH_2Cl$, and $CH_3CN$ were freshly distilled from $CaH_2$. Thin layer chromatography was performed on silica gel plates (10–40 μm). Column chromatography was performed on silica gel (300–400 mesh) and eluted with ethyl acetate and $CH_2Cl_2$. Catalysts **C1**,[16] **C2**,[17] **C3**–**C7**,[18] and **C8**[19] were prepared according to literature procedures. For the preparation and characterization of the chiral catalysts **C9**–**C15**,[20] see the Supporting Information.

**General Procedure for the Cascade Reaction of α-Cyano Ketones with Isatylidene Malononitriles:** To a solution of α-cyano ketone **1** (0.11 mmol), catalyst **C10** (1.3 mg, 0.002 mmol), and morpholine (0.08 μL, 0.001 mmol) in $CH_2Cl_2$ (2 mL) was added isatylidene malononitrile **2** (0.1 mmol) at –10 °C, and the resulting mixture was stirred at this temperature until the reaction reached completion (monitored by TLC). The solvent was removed under reduced pressure, and the residue was purified by column chromatography ($CH_2Cl_2$/EtOAc, 6:1) to give the desired product **3**.

**(*S*)-2′-Amino-1-benzyl-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3aa):** White solid (42.5 mg, 99 % yield, 82 % *ee*); m.p. 206.8–208.3 °C. $[\alpha]_D^{20}$ = +30.7 (*c* = 0.358, DMSO). $^1$H NMR (300 MHz, $CDCl_3$): $\delta$ = 7.77 (d, *J* = 8.1 Hz, 2 H), 7.52–7.25 (m, 10 H), 7.15 (t, *J* = 7.8 Hz, 1 H), 6.75 (d, *J* = 8.1 Hz, 1 H), 5.31 (s, 2 H), 5.01 (s, 2 H) ppm. $^{13}$C NMR (75 MHz, $CDCl_3$): $\delta$ = 175.3, 160.1, 159.4, 142.2, 134.5, 132.2, 130.6, 129.9, 129.2, 128.9, 128.7, 127.9, 127.8, 127.0, 125.0, 124.2, 116.1, 115.0, 110.3, 88.2, 57.9, 50.1, 44.6 ppm. IR (KBr): $\tilde{\nu}$ = 3455, 3321, 3178, 3061, 2205, 1714, 1670, 1611, 1487, 1468, 1406, 1357, 1321, 1312, 1265, 1191, 1148, 1102, 1080, 1032, 975, 910, 845, 738 cm$^{-1}$. HRMS (ESI): calcd. for $C_{27}H_{18}N_4NaO_2$ [M + Na]$^+$ 453.1327; found 453.1320. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30, flow rate: 0.9 mL min$^{-1}$): $t_R$ = 25.21 min (major), 27.99 min (minor).

**(*S*)-2′-Amino-1-methyl-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ab):** White solid (34.6 mg, 98 % yield, 90 % *ee*); m.p. 218.5–220.9 °C. $[\alpha]_D^{20}$ = +33.1 (*c* = 0.295, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.81 (d, *J* = 6.9 Hz, 2 H), 7.75 (s, 2 H), 7.64–7.512 (m, 4 H), 7.45 (t, *J* = 7.8 Hz, 1 H), 7.23–7.15 (m, 2 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 160.1, 159.9, 143.0, 132.3, 130.5, 130.4, 129.6, 128.9, 128.1, 125.2, 123.8, 117.0, 115.4, 109.4, 87.3, 53.6, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3432, 2245, 2193, 2125, 1663, 1496, 1470, 1370, 1309, 1263, 1152, 1052, 1026, 1003, 827, 762 cm$^{-1}$. HRMS (ESI): calcd. for $C_{21}H_{14}N_4NaO_2$ [M + Na]$^+$ 377.1014; found 377.1012. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 9.64 min (minor), 14.45 min (major).

**(*S*)-2′-Amino-1-ethyl-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ac):** White solid (36.2 mg, 98 % yield, 83 % *ee*); m.p. 213.2–215.3 °C. $[\alpha]_D^{20}$ = +52.5 (*c* = 0.305, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.81 (d, *J* = 7.2 Hz, 2 H), 7.74 (s, 2 H), 7.66–7.52 (m, 4 H), 7.43 (t, *J* = 7.8 Hz, 1 H), 7.23–7.16 (m, 2 H), 3.80 (q, *J* = 6.9 Hz, 2 H), 1.17 (t, *J* = 6.9 Hz, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 174.6, 160.0, 159.7, 141.9, 132.3, 130.9, 130.4, 129.6, 128.9, 128.0, 125.4, 123.6, 117.0, 115.3, 109.4, 87.3, 53.7, 49.7, 34.8, 12.5 ppm. IR (KBr): $\tilde{\nu}$ = 3400, 3190, 2636, 2256, 2122, 1655, 1052, 1027, 998, 825, 777 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{16}N_4NaO_2$ [M + Na]$^+$ 391.1171; found 391.1178; HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 8.77 min (minor), 13.96 min (major).

**(*S*)-1-Allyl-2′-amino-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ad):** White solid (38.0 mg, 99 % yield, 83 % *ee*); m.p. 203.9–204.3 °C. $[\alpha]_D^{20}$ = +24.2 (*c* = 0.317, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.84–7.76 (m, 4 H), 7.64–7.54 (m, 4 H), 7.41 (t, *J* = 7.5 Hz, 1 H), 7.20 (t, *J* = 7.5 Hz, 1 H), 7.06 (d, *J* = 7.5 Hz, 1 H), 5.90–5.80 (m, 1 H), 5.27–5.15 (m, 2 H), 4.41 (s, 2 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 174.8, 160.2, 159.8, 142.1, 132.3, 131.0, 130.5, 130.3, 129.6, 128.9, 128.1, 125.3, 123.8, 117.1, 116.5, 115.5, 110.0, 87.3, 53.7, 50.0, 42.0 ppm. IR (KBr): $\tilde{\nu}$ = 3421, 3008, 2261, 2193, 2123, 2003, 1717, 1669, 1607, 1489, 1464, 1410, 1355, 1308, 1237, 1199, 1148, 1053, 1026, 1006, 821, 777, 760 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{16}N_4NaO_2$ [M + Na]$^+$ 403.1171; found 403.1163. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.39 min (minor), 17.34 min (major).

**(*S*)-2′-Amino-1-(methoxymethyl)-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ae):** White solid (38.3 mg, 99 % yield, 82 % *ee*); m.p. 206.8–207.5 °C. $[\alpha]_D^{20}$ = +21.6 (*c* = 0.320, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.84–7.80 (m, 4 H), 7.67–7.58 (m, 4 H), 7.44 (t, *J* = 7.8 Hz, 1 H), 7.24 (t, *J* = 8.4 Hz, 2 H), 5.20 (s, 2 H), 3.27 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 175.7, 160.2, 159.8, 141.3, 132.4, 130.4, 130.1, 129.5, 129.0, 128.1, 125.5, 124.3, 117.1, 115.5, 110.4, 87.1, 71.2, 55.8, 53.7, 50.5 ppm. IR (KBr): $\tilde{\nu}$ = 3408, 3263, 2921, 2819, 2255, 2195, 2127, 1724, 1664, 1470, 1408, 1344, 1313, 1151, 1122, 1051, 1024, 1002 824, 775, 760 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{16}N_4NaO_3$ [M + Na]$^+$ 407.1120; found 407.1118. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 11.28 min (minor), 13.15 min (major).

**(*S*)-2′-Amino-1-(4-methoxybenzyl)-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3af):** White solid (45.8 mg,

99 % yield, 79 % *ee*), m.p. 209.2–211.1 °C. $[\alpha]_D^{20}$ = +19.1 (*c* = 0.383, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.86–7.79 (m, 4 H), 7.65–7.54 (m, 4 H), 7.33 (d, *J* = 8.1 Hz, 3 H), 7.17 (t, *J* = 7.5 Hz, 1 H), 6.98 (d, *J* = 7.8 Hz, 1 H), 6.86 (d, *J* = 7.5 Hz, 2 H), 4.95 (s, 2 H), 3.71 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 175.3, 160.3, 159.9, 158.7, 142.0, 132.3, 130.7, 130.2, 129.6, 129.0, 128.6, 128.1, 127.4, 125.4, 123.8, 117.1, 115.5, 114.0, 110.1, 87.3, 55.1, 53.8, 50.0, 42.9 ppm. IR (KBr): $\tilde{\nu}$ = 3394, 2255, 2128, 1660, 1513, 1309, 1250, 1181, 1151, 1052, 1029, 1000, 824, 763 cm$^{-1}$. HRMS (ESI): calcd. for $C_{28}H_{20}N_4NaO_3$ [M + Na]$^+$ 483.1433; found 483.1446. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 20.22 min (minor), 29.03 min (major).

**(*S*)-2′-Amino-2-oxo-6′-phenyl-1-tritylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ag):** White solid (57.2 mg, 98 % yield, 11 % *ee*); m.p. 239.6–240.7 °C. $[\alpha]_D^{20}$ = +6.2 (*c* = 0.485, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.82–7.76 (m, 4 H), 7.61–7.58 (m, 3 H), 7.52–7.44 (m, 7 H), 7.30–7.18 (m, 9 H), 7.10–7.00 (m, 2 H), 6.30 (d, *J* = 7.5 Hz, 1 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 176.3, 160.2, 159.7, 142.4, 141.5, 132.3, 130.9, 130.0, 129.6, 128.9, 128.6, 128.1, 127.8, 127.0, 125.1, 123.4, 117.5, 115.8, 115.8, 87.4, 74.4, 54.4, 50.4 ppm. IR (KBr): $\tilde{\nu}$ = 3426, 2253, 2126, 1657, 1052, 1023, 998, 827, 761 cm$^{-1}$. HRMS (ESI): calcd. for $C_{39}H_{26}N_4NaO_2$ [M + Na]$^+$ 605.1953; found 605.1940. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 90:10; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 13.42 min (minor), 16.07 min (major).

**(*S*)-1-Acetyl-2′-amino-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ah):** White solid (38.1 mg, 99 % yield, 64 % *ee*); m.p. 211.2–213.3 °C. $[\alpha]_D^{20}$ = +26.2 (*c* = 0.318, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 8.17 (d, *J* = 8.1 Hz, 1 H), 7.95 (s, 2 H), 7.85 (d, *J* = 6.3 Hz, 2 H), 7.70–7.59 (m, 4 H), 7.52 (t, *J* = 7.5 Hz, 1 H), 7.40 (t, *J* = 7.2 Hz, 1 H), 2.65 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 176.5, 170.4, 160.6, 160.0, 139.3, 132.6, 130.6, 129.4, 129.0, 128.2, 126.5, 125.7, 116.8, 116.1, 115.2, 108.8, 87.0, 53.9, 51.0, 26.3 ppm. IR (KBr): $\tilde{\nu}$ = 3422, 3012, 2988, 2262, 2120, 1653, 1047, 1025, 1001, 828, 776 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}N_4O_3$ [M + H]$^+$ 383.1144; found 383.1136. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 8.87 min (minor), 10.34 min (major).

**(*S*)-2′-Amino-2-oxo-6′-phenylspiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ai):** White solid (33.7 mg, 99 % yield, 76 % *ee*); m.p. 214.4–217.0 °C. $[\alpha]_D^{20}$ = +27.1 (*c* = 0.283, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 10.89 (s, 1 H), 7.80 (d, *J* = 7.2 Hz, 2 H), 7.69 (s, 2 H), 7.66–7.55 (m, 3 H), 7.46 (d, *J* = 7.5 Hz, 1 H), 7.33 (t, *J* = 7.5 Hz, 1 H), 7.11 (t, *J* = 7.5 Hz, 1 H), 6.94 (d, *J* = 7.8 Hz, 1 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 176.6, 159.9, 159.7, 141.6, 132.3, 131.4, 130.2, 129.6, 128.9, 128.0, 125.5, 123.1, 117.2, 115.5, 110.3, 87.6, 53.9, 50.3 ppm. IR (KBr): $\tilde{\nu}$ = 3415, 3005, 2919, 2597, 2134, 1970, 1902, 1657, 1439, 1407, 1317, 1243, 1022, 954, 901, 777, 709 cm$^{-1}$. HRMS (ESI): calcd. for $C_{20}H_{13}N_4O_2$ [M + H]$^+$ 341.1039; found 341.1034. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 8.78 min (minor), 10.78 min (major).

**(*S*)-2′-Amino-1-methyl-2-oxo-6′-(*p*-tolyl)spiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3bb):** White solid (36.4 mg, 99 % yield, 91 % *ee*); m.p. 219.7–223.1 °C. $[\alpha]_D^{20}$ = +51.2 (*c* = 0.307, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.72–7.69 (m, 4 H), 7.52–7.37 (m, 4 H), 7.22–7.15 (m, 2 H), 3.22 (s, 3 H), 2.38 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 175.0, 160.1, 159.9, 143.0, 142.6, 130.6, 130.3, 129.4, 127.9, 126.7, 125.1, 123.8, 117.1, 115.5, 109.4, 86.6, 53.6, 49.9, 26.7, 21.2 ppm. IR (KBr): $\tilde{\nu}$ = 3376, 2953, 2737, 2261, 2125, 1648, 1048, 1024, 995, 827, 781, 712 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{17}N_4O_2$ [M + H]$^+$ 369.1352; found 369.1345. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 14.07 min (minor), 16.48 min (major).

**(*S*)-2′-Amino-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cb):** White solid (37.9 mg, 99 % yield, 95 % *ee*); m.p. 217.7–220.5 °C. $[\alpha]_D^{20}$ = +40.9 (*c* = 0.320, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, *J* = 8.1 Hz, 2 H), 7.71 (s, 2 H), 7.51–7.40 (m, 2 H), 7.22–7.11 (m, 4 H), 3.84 (s, 3 H), 3.22 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 175.1, 162.2, 159.9, 159.7, 143.0, 130.6, 130.3, 129.9, 125.1, 123.7, 121.5, 117.1, 115.8, 114.3, 109.3, 85.4, 55.6, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3341, 3000, 2910, 2149, 1652, 1440, 1405, 1318, 1239, 1019, 952, 902, 777, 759, 708 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{16}N_4NaO_3$ [M + Na]$^+$ 407.1120; found 407.1119. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 14.89 min (minor), 18.95 min (major).

**(*S*)-2′-Amino-6′-(3-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3db):** White solid (37.9 mg, 99 % yield, 90 % *ee*); m.p. 247.6–248.6 °C. $[\alpha]_D^{20}$ = +71.2 (*c* = 0.32, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.73 (s, 2 H), 7.52–7.36 (m, 5 H), 7.22–7.15 (m, 3 H), 3.82 (s, 3 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 159.8, 159.7, 159.2, 143.0, 130.7, 130.5, 130.3, 130.2, 125.1, 123.7, 120.2, 118.0, 116.9, 115.3, 113.3, 109.3, 87.4, 55.5, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3348, 3297, 3180, 2920, 2205, 1701, 1666, 1597, 1461, 1413, 1368, 1310, 1268, 1239, 1151, 1128, 1089, 1034, 1019, 990, 937, 910, 852, 794, 772, 749 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{16}N_4NaO_3$ [M + Na]$^+$ 407.1120; found 407.1114. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 9.03 min (minor), 12.27 min (major).

**(*S*)-2′-Amino-6′-(2-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3eb):** White solid (38.1 mg, 99 % yield, 76 % *ee*); m.p. 227.5–230.2 °C. $[\alpha]_D^{20}$ = +41.4 (*c* = 0.320, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.62–7.54 (m, 3 H), 7.50–7.42 (m, 3 H), 7.24–7.14 (m, 3 H), 7.09 (t, *J* = 7.2 Hz, 1 H), 3.85 (s, 3 H), 3.22 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.7, 160.1, 159.0, 157.0, 142.9, 133.4, 130.7, 130.5, 130.3, 124.8, 123.7, 120.5, 119.0, 117.1, 114.6, 112.3, 109.3, 90.9, 56.0, 53.6, 49.7, 26.6 ppm. IR (KBr): $\tilde{\nu}$ = 3403, 3280, 3169, 2928, 2842, 2198, 1701, 1612, 1594, 1494, 1472, 1439, 1409, 1370, 1354, 1313, 1285, 1243, 1167, 1144, 1111, 1017, 936, 909, 799, 763 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{16}N_4NaO_3$ [M + Na]$^+$ 407.1120; found 407.1114. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 9.81 min (minor), 15.28 min (major).

**(*S*)-2′-Amino-6′-(4-fluorophenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3fb):** White solid (37.2 mg, 99 % yield, 85 % *ee*); m.p. 249.4–251.7 °C. $[\alpha]_D^{20}$ = +46.8 (*c* = 0.310, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.92–7.87 (m, 2 H), 7.73 (s, 2 H), 7.53 (d, *J* = 7.2 Hz, 1 H), 7.45 (t, *J* = 8.8 Hz, 3 H), 7.22–7.15 (m, 2 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 164.0 (d, $J_{C,F}$ = 249.4 Hz), 159.8, 159.1, 143.0, 130.9 (d, $J_{C,F}$ = 8.7 Hz), 130.4 (d, $J_{C,F}$ = 8.8 Hz), 126.1 (d, $J_{C,F}$ = 3.0 Hz), 125.2, 123.7, 116.9, 116.3, 116.0, 115.3, 109.3, 87.4, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3441, 3002, 2906, 2592, 2142, 1970, 1655, 1441, 1400, 1316, 1241, 1014, 952, 901, 784, 706 cm$^{-1}$. HRMS (ESI): calcd. for $C_{21}H_{13}FN_4NaO_2$ [M + Na]$^+$ 395.0920; found 395.0901. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.66 min (minor), 16.76 min (major).

**(*S*)-2′-Amino-6′-(4-chlorophenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3gb):** White solid (37.9 mg, 98 % yield, 86 % *ee*); m.p. 257.1–258.9 °C. $[\alpha]_D^{20}$ = +43.2 (*c* = 0.324, DMSO). $^1$H NMR (300 MHz, [D$_6$]DMSO): $\delta$ = 7.84 (d, *J* = 7.8 Hz, 2 H), 7.75 (s,

2 H), 7.68 (d, $J$ = 7.5 Hz, 2 H), 7.53 (d, $J$ = 6.0 Hz, 1 H), 7.44 (t, $J$ = 7.2 Hz, 1 H), 7.22–7.17 (m, 2 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (75 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 159.8, 159.0, 143.0, 137.0, 130.4, 130.0, 129.1, 128.4, 125.3, 123.8, 118.9, 117.0, 115.2, 109.4, 87.8, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3458, 2996, 2914, 2152, 1649, 1440, 1401, 1318, 1239, 1024, 951, 902, 784, 706 cm$^{-1}$. HRMS (ESI): calcd. for $C_{21}H_{13}{}^{35}ClN_4NaO_2$ [M + Na]$^+$ 411.0625; found 411.0630; calcd. for $C_{21}H_{13}{}^{37}ClN_4NaO_2$ [M + Na]$^+$ 413.0595; found 413.0598. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 13.21 min (minor), 22.12 min (major).

**(*S*)-2′-Amino-6′-(4-bromophenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3hb):** White solid (42.8 mg, 99 % yield, 83 % *ee*); m.p. 264.6–265.2 °C. $[\alpha]_D^{20}$ = +34.9 ($c$ = 0.361, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.83–7.74 (m, 6 H), 7.53 (d, $J$ = 7.6 Hz, 1 H), 7.44 (t, $J$ = 7.6 Hz, 1 H), 7.22–7.15 (m, 2 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.8, 159.8, 159.1, 143.0, 132.0, 130.4, 130.0, 128.7, 126.0, 125.2, 123.7, 116.9, 115.2, 109.3, 87.8, 62.8, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3401, 2258, 2127, 1651, 1066, 1032, 997, 827, 780, 717 cm$^{-1}$. HRMS (ESI): calcd. for $C_{21}H_{13}{}^{79}BrNaN_4O_2$ [M + Na]$^+$ 455.0120; found 455.0119; calcd. for $C_{21}H_{13}{}^{81}BrNaN_4O_2$ [M + Na]$^+$ 457.0100; found 457.0110. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 14.31 min (minor), 25.61 min (major).

**(*S*)-2′-Amino-6′-(3,4-dimethoxyphenyl)-1-methyl-2-oxospiro-[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ib):** White solid (41.0 mg, 99 % yield, 94 % *ee*); m.p. 253.3–254.1 °C. $[\alpha]_D^{20}$ = +87.5 ($c$ = 0.345, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.72 (s, 2 H), 7.49–7.41 (m, 3 H), 7.39 (s, 1 H), 7.22–7.12 (m, 3 H), 3.84 (s, 3 H), 3.81 (s, 3 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.1, 159.9, 159.6, 152.0, 148.5, 143.0, 130.6, 130.2, 125.1, 123.7, 121.7, 121.4, 117.0, 115.9, 111.4, 110.8, 109.3, 85.4, 55.8, 55.7, 53.7, 49.9, 26.6 ppm. IR (KBr): $\tilde{\nu}$ = 3429, 3167, 2903, 2194, 1704, 1662, 1599, 1473, 1410, 1347, 1311, 1242, 1206, 1163, 1143, 1060, 932, 859, 749, 671 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_4$ [M + Na]$^+$ 437.1226; found 437.1205. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 80:20; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 34.56 min (major), 39.70 min (minor).

**(*S*)-2′-Amino-6′-(3,5-dimethoxyphenyl)-1-methyl-2-oxospiro-[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3jb):** White solid (41.4 mg, 99 % yield, 88 % *ee*); m.p. 232.5–234.4 °C. $[\alpha]_D^{20}$ = +56.3 ($c$ = 0.340, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.73 (s, 2 H), 7.51 (d, $J$ = 7.2 Hz, 1 H), 7.44 (t, $J$ = 7.6 Hz, 1 H), 7.23–7.15 (m, 2 H), 6.97 (s, 2 H), 6.76 (s, 1 H), 3.80 (s, 6 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 160.5, 159.8, 159.5, 143.0, 131.1, 130.4, 130.3, 125.1, 123.7, 116.9, 115.2, 109.3, 106.0, 103.9, 87.5, 55.6, 53.7, 49.9, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3424, 3300, 3168, 2967, 2917, 2192, 1704, 1665, 1630, 1603, 1492, 1469, 1412, 1350, 1315, 1247, 1208, 1162, 1144, 1094, 1060, 1025, 927, 857, 817, 753, 703 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_4$ [M + Na]$^+$ 437.1226; found 437.1233. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 8.42 min (minor), 11.31 min (major).

**(*S*)-2′-Amino-1-methyl-2-oxo-6′-(thiophen-2-yl)spiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3kb):** White solid (35.6 mg, 99 % yield, 90 % *ee*); m.p. 233.8–234.2 °C. $[\alpha]_D^{20}$ = +50.3 ($c$ = 0.300, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 8.02 (d, $J$ = 4.8 Hz, 1 H), 7.95 (d, $J$ = 3.6 Hz, 1 H), 7.78 (s, 2 H), 7.50–7.42 (m, 2 H), 7.31 (t, $J$ = 4.0 Hz, 1 H), 7.21–7.15 (m, 2 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.0, 159.5, 153.9, 143.0, 132.8, 131.7, 131.1, 130.4, 130.3, 128.4, 125.1, 123.8, 116.9, 115.5, 109.4, 83.8, 53.6, 49.8, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3354, 3188, 2921, 2851, 2369, 1660, 1627, 1467, 1408, 1291, 1161, 1110, 1091, 1054, 937, 872, 780, 728 cm$^{-1}$. HRMS (ESI): calcd. for $C_{19}H_{12}N_4NaO_2S$ [M + Na]$^+$ 383.0579; found 383.0570. HPLC analysis (AS-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 17.04 min (minor), 21.85 min (major).

**(*S*)-2′-Amino-6′-(furan-2-yl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3lb):** White solid (34.0 mg, 99 % yield, 93 % *ee*) m.p. 245.3–248.2 °C. $[\alpha]_D^{20}$ = +182.0 ($c$ = 0.287, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 8.07 (s, 1 H), 7.73 (s, 2 H), 7.49–7.41 (m, 2 H), 7.23–7.15 (m, 3 H), 6.83 (s, 1 H), 3.22 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 159.4, 149.5, 147.4, 143.4, 143.1, 130.3, 130.3, 125.1, 123.7, 116.8, 115.9, 114.4, 112.9, 109.3, 83.4, 53.6, 49.5, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3358, 3184, 2917, 2846, 2371, 2200, 1710, 1666, 1598, 1467, 1366, 1329, 1225, 1190, 1125, 1097, 1015, 942, 902, 885, 833, 760, 730 cm$^{-1}$. HRMS (ESI): calcd. for $C_{19}H_{12}N_4NaO_3$ [M + Na]$^+$ 367.0807; found 367.0790. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.96 min (minor), 12.02 min (major).

**(*S*)-2′-Amino-1-methyl-6′-(naphthalen-2-yl)-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3mb):** White solid (39.9 mg, 99 % yield, 92 % *ee*); m.p. 260.3–261.7 °C. $[\alpha]_D^{20}$ = +42.8 ($c$ = 0.336, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 8.46 (s, 1 H), 8.11 (d, $J$ = 8.8 Hz, 1 H), 8.07 (d, $J$ = 7.6 Hz, 1 H), 8.03 (d, $J$ = 8.0 Hz, 1 H), 7.85 (dd, $J_1$ = 8.8 Hz, $J_2$ = 1.6 Hz, 1 H), 7.78 (s, 2 H), 7.70–7.61 (m, 2 H), 7.57 (d, $J$ = 7.2 Hz, 1 H), 7.46 (dt, $J_1$ = 8.0 Hz, $J_2$ = 0.8 Hz, 1 H), 7.24–7.17 (m, 2 H), 3.25 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.0, 160.2, 160.0, 143.0, 134.2, 131.9, 130.5, 130.3, 129.0, 128.9, 128.6, 128.6, 127.8, 127.4, 126.9, 125.2, 124.0, 123.8, 117.0, 115.5, 109.4, 87.8, 53.7, 50.0, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3346, 3168, 2920, 2201, 1707, 1663, 1625, 1492, 1468, 1413, 1370, 1302, 1238, 1151, 1126, 1019, 897, 869, 827, 768, 744, 680 cm$^{-1}$. HRMS (ESI): calcd. for $C_{25}H_{16}N_4NaO_2$ [M + Na]$^+$ 427.1171; found 427.1179. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 12.93 min (minor), 17.84 min (major).

**(*S*)-2′-Amino-6′-(4-methoxyphenyl)-1,5-dimethyl-2-oxospiro-[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cj):** White solid (39.7 mg, 99 % yield, 93 % *ee*); m.p. 259.3–259.7 °C. $[\alpha]_D^{20}$ = +75.7 ($c$ = 0.332, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, $J$ = 9.2 Hz, 2 H), 7.66 (s, 2 H), 7.31 (s, 1 H), 7.23 (d, $J$ = 8.0 Hz, 1 H), 7.12 (d, $J$ = 8.8 Hz, 2 H), 7.04 (d, $J$ = 8.0 Hz, 1 H), 3.84 (s, 3 H), 3.20 (s, 3 H), 2.33 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.0, 162.1, 159.8, 159.5, 140.6, 132.9, 130.8, 130.4, 129.8, 125.5, 121.5, 117.1, 115.8, 114.3, 109.0, 85.5, 55.6, 53.9, 50.0, 26.6, 20.6 ppm. IR (KBr): $\tilde{\nu}$ = 3305, 3184, 2926, 2840, 2205, 1708, 1674, 1629, 1605, 1515, 1452, 1417, 1358, 1327, 1312, 1258, 1182, 1156, 1116, 1067, 1026, 930, 845, 801, 777, 749, 700 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_3$ [M + Na]$^+$ 421.1277; found 421.1276. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.70 min (minor), 15.36 min (major).

**(*S*)-2′-Amino-5-methoxy-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ck):** White solid (40.4 mg, 98 % yield, 93 % *ee*); m.p. 237.8–237.9 °C. $[\alpha]_D^{20}$ = +136.2 ($c$ = 0.345, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, $J$ = 9.2 Hz, 2 H), 7.66 (s, 2 H), 7.17 (d, $J$ = 2.4 Hz, 1 H), 7.12 (d, $J$ = 8.8 Hz, 2 H), 7.07 (d, $J$ = 8.4 Hz, 1 H), 6.99 (dd, $J_1$ = 8.4 Hz, $J_2$ = 2.4 Hz, 1 H), 3.84 (s, 3 H), 3.77 (s, 3 H), 3.19 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.8, 162.1, 159.8, 159.6, 156.4, 136.3, 131.9, 129.8, 121.6, 117.1, 115.8, 114.8, 114.2, 111.9, 109.8, 85.4, 55.7, 55.6, 53.8, 50.3, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3349, 3299, 3170, 3013, 2917, 2849, 2197, 1697, 1664, 1626, 1605, 1513, 1495, 1452, 1410, 1358, 1299, 1288, 1264, 1176, 1153, 1031, 1012, 841, 810, 780, 724 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_4$ [M + Na]$^+$ 437.1226; found 437.1228.

HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 17.15 min (minor), 22.61 min (major).

**(*S*)-2′-Amino-5-fluoro-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cl):** White solid (39.8 mg, 99 % yield, 95 % *ee*); m.p. 262.2–262.8 °C. $[\alpha]_D^{20}$ = +33.6 (*c* = 0.335, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, *J* = 9.2 Hz, 2 H), 7.74 (s, 2 H), 7.57 (dd, $J_1$ = 7.6 Hz, $J_2$ = 2.4 Hz, 1 H), 7.29 (dt, $J_1$ = 8.8 Hz, $J_2$ = 2.8 Hz, 1 H), 7.18 (dd, $J_1$ = 8.8 Hz, $J_2$ = 4.4 Hz, 1 H), 7.13 (d, *J* = 9.2 Hz, 2 H), 3.84 (s, 3 H), 3.22 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.1, 162.2, 160.4, 159.9 (d, $J_{C,F}$ = 5.9 Hz), 158.1, 139.3 (d, $J_{C,F}$ = 1.4 Hz), 132.3 (d, $J_{C,F}$ = 8.0 Hz), 129.9, 121.5, 117.0, 116.7 (d, $J_{C,F}$ = 23.3 Hz), 115.8, 114.3, 113.3 (d, $J_{C,F}$ = 25.6 Hz), 110.4 (d, $J_{C,F}$ = 8.0 Hz), 84.8, 55.6, 53.3, 50.3, 26.8 ppm. IR (KBr): $\tilde{\nu}$ = 3295, 3166, 2208, 1704, 1667, 1603, 1509, 1494, 1462, 1414, 1357, 1317, 1300, 1268, 1258, 1176, 1149, 1118, 1032, 927, 883, 845, 819, 789, 768, 693 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}FN_4NaO_3$ [M + Na]$^+$ 425.1026; found 425.1022. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.90 min (minor), 15.43 min (major).

**(*S*)-2′-Amino-5-chloro-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cm):** White solid (41.6 mg, 99 % yield, 91 % *ee*); m.p. 249.4–250.7 °C. $[\alpha]_D^{20}$ = +95.1 (*c* = 0.341, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.81 (d, *J* = 8.4 Hz, 2 H), 7.74 (s, 3 H), 7.51 (d, *J* = 8.4 Hz, 1 H), 7.20 (d, *J* = 8.4 Hz, 1 H), 7.13 (d, *J* = 8.8 Hz, 2 H), 3.84 (s, 3 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.9, 162.2, 160.0, 159.9, 141.9, 132.5, 130.2, 129.9, 127.8, 125.5, 121.5, 117.0, 115.8, 114.2, 110.9, 84.6, 55.6, 53.1, 50.1, 26.8 ppm. IR (KBr): $\tilde{\nu}$ = 3341, 3291, 3166, 2195, 1706, 1664, 1607, 1513, 1478, 1409, 1347, 1298, 1258, 1180, 1156, 1028, 822, 737 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{35}ClN_4NaO_3$ [M + Na]$^+$ 441.0730; found 441.0729; calcd. for $C_{22}H_{15}{}^{37}ClN_4NaO_3$ [M + Na]$^+$ 443.0700; found 443.0698. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.29 min (minor), 15.57 min (major).

**(*S*)-2′-Amino-5-bromo-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cn):** White solid (45.7 mg, 99 % yield, 94 % *ee*); m.p. 237.9–239.0 °C. $[\alpha]_D^{20}$ = +56.2 (*c* = 0.380, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.84 (d, *J* = 2.0 Hz, 1 H), 7.81 (d, *J* = 8.8 Hz, 2 H), 7.75 (s, 2 H), 7.63 (dd, $J_1$ = 8.0 Hz, $J_2$ = 2.0 Hz, 1 H), 7.14 (t, *J* = 8.8 Hz, 3 H), 3.84 (s, 3 H), 3.22 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 174.8, 162.2, 160.0, 159.9, 142.3, 133.0, 132.9, 129.9, 128.2, 121.6, 117.0, 115.8, 115.5, 114.2, 111.4, 84.6, 55.6, 53.1, 50.1, 26.8 ppm. IR (KBr): $\tilde{\nu}$ = 3340, 3303, 3171, 2916, 2204, 1706, 1660, 1604, 1511, 1482, 1413, 1348, 1302, 1261, 1178, 1153, 1093, 1032, 832, 725 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{79}BrN_4NaO_3$ [M + Na]$^+$ 485.0225; found 485.0227; calcd. for $C_{22}H_{15}{}^{81}BrN_4NaO_3$ [M + Na]$^+$ 487.0205; found 487.0210. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 10.21 min (minor), 15.03 min (major).

**(*S*)-2′-Amino-6′-(4-methoxyphenyl)-1,6-dimethyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3co):** White solid (40.0 mg, 97 % yield, 92 % *ee*); m.p. 236.9–237.4 °C. $[\alpha]_D^{20}$ = +71.3 (*c* = 0.160, $CH_2Cl_2$). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.79 (d, *J* = 8.8 Hz, 2 H), 7.63 (s, 2 H), 7.37 (d, *J* = 8.0 Hz, 1 H), 7.12 (d, *J* = 9.2 Hz, 2 H), 6.79 (d, *J* = 2.4 Hz, 1 H), 6.71 (dd, $J_1$ = 8.4 Hz, $J_2$ = 2.4 Hz, 1 H), 3.84 (s, 3 H), 3.83 (s, 3 H), 3.21 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.7, 162.1, 161.2, 159.8, 159.4, 144.4, 129.8, 125.9, 122.3, 121.6, 117.1, 115.9, 114.3, 108.2, 96.6, 85.8, 55.6, 55.6, 54.1, 49.4, 26.7 ppm. IR (KBr): $\tilde{\nu}$ = 3334, 3298, 2928, 2834, 2312, 2208, 1668, 1631, 1598, 1510, 1458, 1413, 1373, 1295, 1258, 1181, 1151, 1121, 1088, 1025, 859, 844, 792, 696 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_4$ [M + Na]$^+$ 437.1226; found 437.1226. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 17.10 min (minor), 22.47 min (major).

**(*S*)-2′-Amino-6-chloro-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cp):** White solid (41.4 mg, 99 % yield, 96 % *ee*); m.p. 254.4–255.1 °C. $[\alpha]_D^{20}$ = +63.0 (*c* = 0.340, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, *J* = 8.4 Hz, 2 H), 7.75 (s, 2 H), 7.55 (d, *J* = 7.6 Hz, 1 H), 7.35 (s, 1 H), 7.24 (d, *J* = 8.0 Hz, 1 H), 7.13 (d, *J* = 8.8 Hz, 2 H), 3.84 (s, 3 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.2, 162.2, 159.9, 144.5, 134.8, 129.9, 129.3, 126.7, 123.4, 121.4, 116.9, 115.7, 114.3, 109.9, 84.8, 55.6, 53.2, 49.6, 26.9 ppm. IR (KBr): $\tilde{\nu}$ = 3304, 3173, 2919, 2204, 1704, 1663, 1601, 1513, 1489, 1415, 1371, 1296, 1259, 1181, 1148, 1114, 1073, 1029, 914, 868, 846, 806, 725 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{35}ClN_4NaO_3$ [M + Na]$^+$ 441.0730; found 441.0727; calcd. for $C_{22}H_{15}{}^{37}ClN_4NaO_3$ [M + Na]$^+$ 443.0700; found 443.0727. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 14.10 min (minor), 16.48 min (major).

**(*S*)-2′-Amino-6-bromo-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cq):** White solid (46.1 mg, 99 % yield, 97 % *ee*); m.p. 265.8–266.7 °C. $[\alpha]_D^{20}$ = +20.3 (*c* = 0.380, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.80 (d, *J* = 8.8 Hz, 2 H), 7.76 (s, 2 H), 7.50–7.37 (m, 3 H), 7.13 (d, *J* = 8.8 Hz, 2 H), 3.84 (s, 3 H), 3.23 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.1, 162.2, 159.9, 159.9, 144.6, 129.9, 129.7, 127.0, 126.3, 123.2, 121.4, 116.9, 115.7, 114.3, 112.6, 84.7, 55.6, 53.1, 49.7, 26.9 ppm. IR (KBr): $\tilde{\nu}$ = 3311, 3175, 2918, 2204, 1705, 1671, 1606, 1511, 1415, 1364, 1320, 1298, 1261, 1178, 1148, 1121, 1092, 1066, 1031, 945, 910, 870, 843, 802, 721 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{79}BrN_4NaO_3$ [M + Na]$^+$ 485.0225; found 485.0229; calcd. for $C_{22}H_{15}{}^{81}BrN_4NaO_3$ [M + Na]$^+$ 487.0205; found 487.0218. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 13.64 min (minor), 14.93 min (major).

**(*S*)-2′-Amino-6′-(4-methoxyphenyl)-1,7-dimethyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cr):** White solid (39.5 mg, 99 % yield, 94 % *ee*); m.p. 243.0–243.4 °C. $[\alpha]_D^{20}$ = +27.0 (*c* = 0.331, DMSO). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.72 (d, *J* = 8.8 Hz, 2 H), 7.16–7.03 (m, 3 H), 6.87 (d, *J* = 8.8 Hz, 2 H), 5.44 (d, *J* = 10.8 Hz, 2 H), 3.81 (s, 3 H), 3.56 (s, 3 H), 2.59 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 176.3, 162.6, 159.8, 159.7, 141.0, 134.5, 131.0, 129.9, 124.2, 123.2, 121.5, 121.0, 116.6, 115.7, 114.2, 86.6, 58.2, 55.6, 49.7, 30.7, 19.2 ppm. IR (KBr): $\tilde{\nu}$ = 3305, 3186, 2925, 2212, 2194, 1710, 1695, 1673, 1631, 1604, 1512, 1452, 1416, 1360, 1328, 1313, 1258, 1182, 1154, 1116, 1030, 929, 844, 800, 777, 748 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{18}N_4NaO_3$ [M + Na]$^+$ 421.1277; found 421.1273. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 13.33 min (minor), 16.35 min (major).

**(*S*)-2′-Amino-7-fluoro-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cs):** White solid (39.9 mg, 99 % yield, 94 % *ee*); m.p. 252.3–252.7 °C. $[\alpha]_D^{20}$ = +23.6 (*c* = 0.335, DMSO). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 7.72 (d, *J* = 8.8 Hz, 2 H), 7.14–7.12 (m, 3 H), 6.88 (d, *J* = 8.8 Hz, 2 H), 5.51 (s, 2 H), 3.82 (s, 3 H), 3.50 (d, *J* = 1.6 Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 175.4, 162.8, 160.0, 159.9, 148.0 (d, $J_{C,F}$ = 244.3 Hz), 132.9 (d, $J_{C,F}$ = 2.2 Hz), 130.1 (d, $J_{C,F}$ = 8.7 Hz), 129.9, 125.0 (d, $J_{C,F}$ = 5.8 Hz), 121.3, 121.1 (d, $J_{C,F}$ = 2.9 Hz), 118.8 (d, $J_{C,F}$ = 19.7 Hz), 116.3, 115.5, 114.3, 85.8, 57.4, 55.7, 50.5, 29.8 (d, $J_{C,F}$ = 5.1 Hz) ppm. IR (KBr): $\tilde{\nu}$ = 3307, 3184, 2923, 2190, 1722, 1704, 1673, 1626, 1604, 1512, 1462, 1413, 1363, 1325, 1310, 1254, 1178, 1150, 1121, 1025, 845, 781, 737 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}FN_4NaO_3$ [M + Na]$^+$ 425.1026; found 425.1026. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 12.12 min (minor), 15.86 min (major).

**(*S*)-2′-Amino-7-chloro-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3ct):** White solid (41.4 mg, 99 % yield, 94 % *ee*); m.p. 257.7–258.0 °C. $[\alpha]_D^{20}$ = +44.0 (*c* = 0.348, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.82–7.79 (m, 4 H), 7.53 (d, *J* = 6.4 Hz, 1 H), 7.45 (d, *J* = 7.6 Hz, 1 H), 7.23–7.11 (m, 3 H), 3.84 (s, 3 H), 3.54 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.6, 162.3, 159.9, 159.8, 138.6, 133.6, 132.3, 129.9, 125.1, 124.6, 121.4, 116.9, 115.6, 114.8, 114.3, 84.8, 55.6, 53.4, 49.8, 30.0 ppm. IR (KBr): $\tilde{\nu}$ = 3325, 3189, 2922, 2846, 2202, 1716, 1664, 1605, 1459, 1406, 1327, 1260, 1180, 1143, 1108, 1020, 837, 745 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{35}ClN_4NaO_3$ [M + Na]$^+$ 441.0730; found 441.0725; calcd. for $C_{22}H_{15}{}^{37}ClN_4NaO_3$ [M + Na]$^+$ 443.0700; found 443.0689. HPLC analysis (AD-H column; $\lambda$ = 254 nm; eluent: *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 12.07 min (minor), 14.34 min (major).

**(*S*)-2′-Amino-7-bromo-6′-(4-methoxyphenyl)-1-methyl-2-oxospiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cu):** White solid (46.1 mg, 99 % yield, 93 % *ee*); m.p. 246.2–247.4 °C. $[\alpha]_D^{20}$ = +21.7 (*c* = 0.380, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.82–7.78 (m, 4 H), 7.60 (d, *J* = 8.0 Hz, 1 H), 7.56 (d, *J* = 7.2 Hz, 1 H), 7.13 (d, *J* = 7.6 Hz, 3 H), 3.84 (s, 3 H), 3.55 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 175.8, 162.3, 159.9, 159.8, 140.0, 135.6, 133.9, 129.9, 126.7, 125.5, 125.1, 121.4, 116.9, 115.7, 114.3, 102.1, 84.8, 55.6, 53.4, 49.8, 30.2 ppm. IR (KBr): $\tilde{\nu}$ = 3315, 3173, 2920, 2850, 2373, 2210, 1707, 1664, 1601, 1409, 1299, 1256, 1180, 1153, 1100, 1020, 830, 781, 715 cm$^{-1}$. HRMS (ESI): calcd. for $C_{22}H_{15}{}^{79}BrN_4NaO_3$ [M + Na]$^+$ 485.0225; found 485.0227; calcd. for $C_{22}H_{15}{}^{81}BrN_4NaO_3$ [M + Na]$^+$ 487.0205; found 487.0205. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 11.66 min (minor), 14.53 min (major).

**(*S*)-2′-Amino-6′-(4-methoxyphenyl)-1-methyl-2-oxo-7-(trifluoromethyl)spiro[indoline-3,4′-pyran]-3′,5′-dicarbonitrile (3cv):** White solid (45.0 mg, 99 % yield, 92 % *ee*); m.p. 227.8–229.2 °C. $[\alpha]_D^{20}$ = +54.8 (*c* = 0.377, DMSO). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 7.92–7.80 (m, 6 H), 7.40 (t, *J* = 7.2 Hz, 1 H), 7.14 (d, *J* = 8.0 Hz, 2 H), 3.84 (s, 3 H), 3.38 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 176.3, 162.3, 160.2, 160.0, 140.6, 133.4, 129.9, 128.0 (q, $J_{C,F}$ = 5.1 Hz), 123.9, 123.4 (q, $J_{C,F}$ = 269.8 Hz), 121.3, 116.7, 115.5, 114.3, 111.4 (q, $J_{C,F}$ = 3.2 Hz), 84.5, 55.6, 53.1, 48.7, 29.3 (q, $J_{C,F}$ = 5.8 Hz) ppm. IR (KBr): $\tilde{\nu}$ = 3349, 3301, 3172, 2916, 2199, 1706, 1661, 1598, 1515, 1451, 1322, 1302, 1262, 1185, 1152, 1121, 1081, 1053, 1023, 827, 799, 752 cm$^{-1}$. HRMS (ESI): calcd. for $C_{23}H_{15}F_3N_4NaO_3$ [M + Na]$^+$ 475.0994; found 475.0999. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 9.02 min (minor), 10.80 min (major).

**Ethyl (*S*,*E*)-*N*-[6-Bromo-3′,5′-dicyano-2′-(4-methoxyphenyl)-1-methyl-2-oxospiro(indoline-3,4′-pyran)-6′-yl]formimidate (4):** A mixture of product **3cq** (46.3 mg, 0.1 mmol), triethyl orthoformate (0.75 mL), and acetic acid (0.25 mL) was heated at reflux for 2 h, whereupon the reaction reached completion (monitored by TLC). After the mixture was concentrated under reduced pressure, the residue was purified by column chromatography to give the desired product **4** (49.3 mg, 95 % yield, 95 % *ee*) as a colorless oil. $[\alpha]_D^{20}$ = +54.8 (*c* = 0.414, $CH_2Cl_2$). $^1$H NMR (400 MHz, $CDCl_3$): $\delta$ = 8.35 (s, 1 H), 7.75 (d, *J* = 8.0 Hz, 2 H), 7.34 (d, *J* = 7.6 Hz, 1 H), 7.23 (d, *J* = 8.0 Hz, 1 H), 7.11 (s, 1 H), 6.97 (d, *J* = 8.4 Hz, 2 H), 4.44 (t, *J* = 6.4 Hz, 2 H), 3.85 (s, 3 H), 3.30 (s, 3 H), 1.38 (t, *J* = 6.8 Hz, 3 H) ppm. $^{13}$C NMR (100 MHz, $CDCl_3$): $\delta$ = 173.8, 162.6, 160.5, 160.4, 158.1, 144.4, 129.7, 128.3, 126.9, 126.3, 124.7, 121.5, 115.1, 114.2, 114.1, 112.8, 85.0, 78.1, 65.0, 55.5, 51.2, 27.1, 13.7 ppm. IR (KBr): $\tilde{\nu}$ = 2955, 2921, 2851, 2307, 2215, 1725, 1659, 1601, 1513, 1460, 1367, 1261, 1207, 1181, 1022, 836, 725 cm$^{-1}$. HRMS (ESI): calcd. for $C_{25}H_{19}BrN_4NaO_4$ [M + Na]$^+$ 541.0487; found 541.0485. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 12.74 min (major), 15.70 min (minor).

**(*S*)-6-Bromo-8′-(4-methoxyphenyl)-1-methyl-2-oxo-2′-phenylspiro[indoline-3,10′-pyrano[3,2-*e*][1,2,4]triazolo[1,5-*c*]pyrimidine]-9′-carbonitrile (5):** To a solution of compound **4** (49.3 mg, 0.095 mmol) in anhydrous ethyl acetate (1 mL) were added benzohydrazide (19.4 mg, 0.143 mmol) and acetic acid (1 mL). The reaction mixture was heated at reflux for 5 h, whereupon the reaction reached completion (monitored by TLC). After the mixture was concentrated under reduced pressure, the residue was purified by column chromatography to give the desired product **5** (43.8 mg, 78 % yield, 95 % *ee*) as a white solid; m.p. 330.9–332.7 °C. $[\alpha]_D^{20}$ = –122.3 (*c* = 0.320, $CH_2Cl_2$). $^1$H NMR (400 MHz, [D$_6$]DMSO): $\delta$ = 9.80 (s, 1 H), 8.00–7.97 (m, 2 H), 7.88 (d, *J* = 9.2 Hz, 2 H), 7.63 (d, *J* = 1.6 Hz, 1 H), 7.54–7.47 (m, 4 H), 7.28 (dd, $J_1$ = 8.0 Hz, $J_2$ = 1.6 Hz, 1 H), 7.17 (d, *J* = 8.8 Hz, 2 H), 3.86 (s, 3 H), 3.43 (s, 3 H) ppm. $^{13}$C NMR (100 MHz, [D$_6$]DMSO): $\delta$ = 173.8, 165.8, 162.3, 161.5, 153.0, 150.9, 145.4, 142.0, 131.4, 130.1, 129.8, 129.2, 128.9, 127.2, 127.1, 126.1, 123.5, 121.8, 115.8, 114.4, 112.3, 97.3, 84.7, 55.6, 49.4, 27.2 ppm. IR (KBr): $\tilde{\nu}$ = 2953, 2920, 2840, 2349, 2313, 2213, 1725, 1634, 1603, 1504, 1455, 1409, 1364, 1324, 1265, 1234, 1175, 1125, 1086, 1062, 1022, 968, 936, 887, 837, 725, 684, 603 cm$^{-1}$. HRMS (ESI): calcd. for $C_{30}H_{20}BrN_6O_3$ [M + H]$^+$ 591.0780; found 591.0773. HPLC analysis (AD-H column; $\lambda$ = 254 nm; *n*-hexane/*i*PrOH, 70:30; flow rate: 0.9 mL min$^{-1}$): $t_R$ = 35.77 min (minor), 90.32 min (major).

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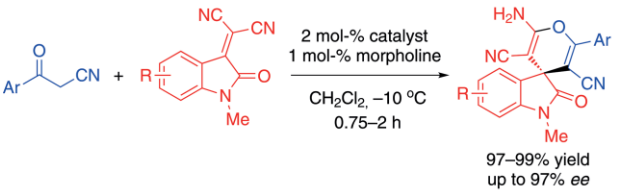
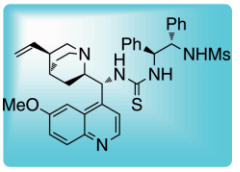
**Asymmetric Catalysis**





α-Cyano ketones have been used for the first time as Michael donors in the construction of chiral spiro compounds. In the presence of only 2 mol-% of a chiral multifunctional organocatalyst, chiral spiro[4*H*-pyran-oxindole] derivatives were prepared in excellent yields with good-to-excellent enantioselectivities. This method provides a new approach to the synthesis of chiral spirocyclic oxindoles.

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