Organic & Biomolecular Chemistry

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 5245

www.rsc.org/obc

PAPER

Enantioselective synthesis of 3,3′-dihydropyrryl-spirooxindoles *via* an organocatalytic three-component reaction†

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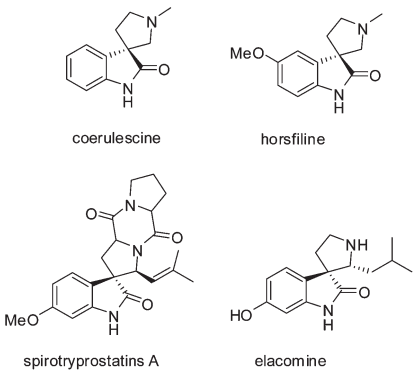
Received 27th March 2012, Accepted 17th May 2012
DOI: 10.1039/c2ob25629k

An organocatalytic three-component reaction of isatins, malononitrile and isocyanoacetates provided 3,3′-dihydropyrryl-spirooxindoles in excellent yields and enantioselectivities. The products could be readily converted to valuable 3,3′-pyrrolidinyl-spirooxindoles.

Introduction

The 3,3′-pyrrolidinyl-spirooxindole scaffold is the common core of a large family of alkaloids and medicinally relevant compounds.[1] Many chiral 3,3′-pyrrolidinyl-spirooxindoles, such as coerulescine, horsfiline, spirotryprostatins A and elacomine show interesting biological activities (Scheme 1). Extensive efforts have been made to develop efficient synthetic methods for these compounds.[2] In recent years, organocatalytic cascade reactions have proven to be extremely useful for the synthesis of chiral cyclic compounds.[3] A number of excellent examples have been reported for the preparation of chiral spirooxindoles *via* organocatalytic cascade reactions.[4] Wang and co-workers reported the organocatalytic double Michael addition of α,β-unsaturated ketones to isatylidene malononitriles. 3,3′-Cyclohexanyl-spirooxindoles were obtained in excellent yields and enantioselectivities.[4e] Lu and co-workers developed an highly enantioselective [3 + 2] annulation of Morita–Baylis–Hillman adducts and isatylidene malononitriles catalyzed by threonine-derived chiral phosphines. The reaction provided chiral 3,3′-cyclopentenyl-spirooxindoles efficiently.[4i] Yuan and co-workers reported the organocatalytic three-component reactions of isatins, malononitrile and 1,3-dicarbonyl compounds. A range of 3,3′-(4*H*-pyranyl)-spirooxindoles were obtained in good yields and enantioselectivities.[4j] Recently we also found that the cascade Michael–Michael–oxa-Michael reaction of curcumins and isatylidene malononitriles provided multicyclic spirooxindoles in excellent yields.[4k] Isocyanoacetates are highly attractive nucleophilic reagents for a number of cascade reactions and multi-component reactions.[5] Their α-protons are readily removed by bases to generate nucleophilic anions. The resulting reaction intermediates are subsequently trapped by the isocyano groups to provide cyclic products. Asymmetric organocatalytic cascade reaction of isocyanoacetates with aldehydes,[6] imines,[7] α,β-unsaturated ketones,[8] nitroolefins[9] and azodicarboxylates[10] have been developed. A variety of chiral nitrogen-containing heterocyclic compounds were obtained in good yields and enantioselectivities. In this paper, we report an organocatalytic three-component reaction of isatins, malononitrile and isocyanoacetates. Dihydropyrryl-spirooxindoles could be prepared in excellent yields and enantioselectivities.



Scheme 1 Representative examples of bioactive 3,3′-pyrrolidinyl-spirooxindole natural products.

Results and discussion

Initially we examined the reaction of isatylidene malononitrile and methyl isocyanoacetate **3a** in the presence of Takemoto's catalyst **4c** (Scheme 2, eqn (1)). The reaction gave 3,3′-dihydropyrryl-spirooxindoles **5a** and **5a′** in excellent yields and enantioselectivities. Since isatylidene malononitriles are readily generated from isatin and malononitrile, we further investigated the three-component reaction of isatin **1a**, malononitrile **2a** and isocyanoacetate **3a**. To our delight, similar yield,

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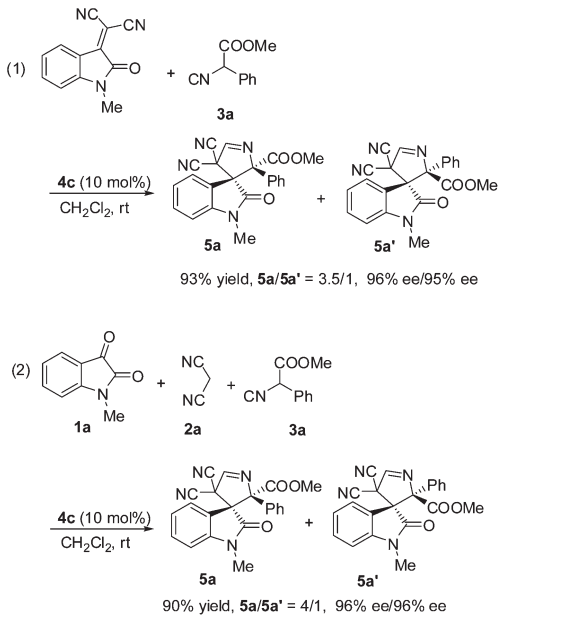
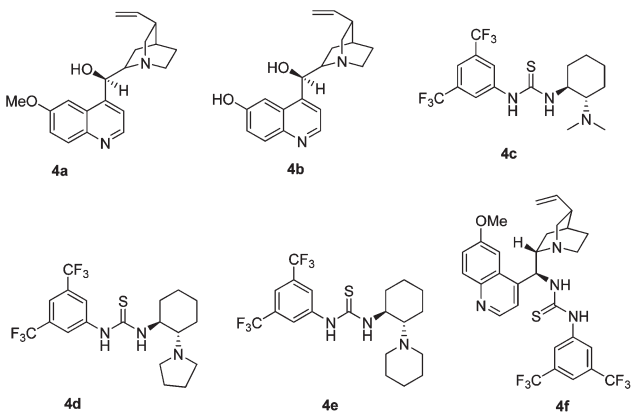
†Electronic supplementary information (ESI) available: Including the characterization data of the products and HPLC chromatograms. CCDC 859158. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob25629k



Scheme 2 Organocatalytic reactions of isocyanoacetate **3a** with isatylidene malononitrile.



Scheme 3 Organocatalysts examined in the reaction.

enantioselectivities and diastereoselectivities were observed (Scheme 2, eqn (2)). The result suggests that the formation of isatylidene malononitrile is fast enough and the reaction can be carried out in one pot.

Cinchona alkaloids **4a–4b** and chiral tertiary amine-thioureas **4c–4f** were examined as the organocatalysts in the three-component reaction of isatin **1a**, malononitrile **2a** and isocyanoacetate **3a** (Scheme 3). The results are summarized in Table 1. Quinine **4a** provided the products **5a**/**5a′** in good yield and moderate enantioselectivities (Table 1, entry 1). The 6′-demethyl quinine **4b** gave similar yield, but with lower enantioselectivities (Table 1, entry 2). Takemoto's catalyst **4c** provided excellent yield and enantioselectivities (Table 1, entry 3). More sterically demanding catalysts **4d** and **4e** led to lower enantioselectivities (Table 1, entries 4–5). Tertiary amine-thiourea **4f** derived from quinine was found to give the product **5a** with the best enantioselectivity (Table 1, entry 6).

Furthermore, the effect of the reaction solvents was examined. Slightly better yields were observed for the reactions in toluene, ethyl acetate, acetonitrile and methanol; however, lower enantioselectivities were obtained (Table 1, entries 7–10). The reactions in several other solvents also provided inferior results (Table 1, entries 11–14). Decreasing the reaction temperature is slightly beneficial to the enantioselectivity, but an extended reaction time was required (Table 1, entries 15–17). The enantioselectivity and diastereoselectivity remained almost unchanged while the catalyst loading was reduced from 10 to 1 mol%; however, longer reaction time was necessary (Table 1, entries 18–20). The 2 mol % catalyst loading was preferred in terms of good yield and reasonable reaction time (Table 1, entry 19).

With the optimized reaction conditions in hand, the three-component reaction of isatins **1a–1k**, malononitrile **2a** and isocyanoacetate **3a** were investigated. The results are summarized in Table 2. The influence of the *N*-substitution of isatins was firstly studied. The *N*-benzyl substituted isatin **1b** gave a similar yield and enantioselectivities to *N*-methyl substituted isatin **1a**, but better diastereoselectivity was obtained (Table 2, entry 2). When the *N*-unsubstituted isatin **1c** was used, a slight loss of enantioselectivity was observed (Table 2, entry 3). The introduction of electron-withdrawing groups such as *tert*-butoxylcarbonyl and acetyl completely inhibited the reaction (Table 2, entries 4 and 5). A variety of isatins with substitutions at the benzene ring were also examined (Table 2, entries 6–11). The 4-halogen substitutions led to lower yields and enantioselectivities (Table 2, entries 6 and 7). The substitutions of halogen and methoxyl at 5, 6 or 7-position increased the diastereoselectivities, but slightly decreased the yields and enantioselectivities (Table 2, entries 8–11).

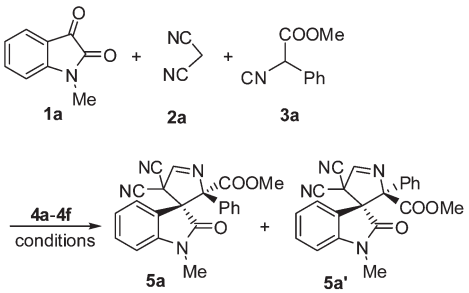
The relative and absolute configurations of the product **5g** were determined by X-ray diffraction analysis (Fig. 1).† The configurations of other products were assigned analogously.[11]

The effect of α-substituents on the isocyanoacetates was also studied (Scheme 4). α-Unsubstituted isocyanoacetate **3b** provided the spirooxindole **5l** in good yield, but with poor enantioselectivity. In addition, the 1,5-double bond of the dihydropyrrole ring migrated to the 1,2-position. The *p*-methoxyl-phenyl and *p*-chloro-phenyl substituted isocyanoacetates **3c** and **3d** gave the products with good yields and excellent enantioselectivities. The *o*-chloro-phenyl substituted isocyanoacetate **3e** is unreactive, probably due to the streric hindrance. The α-isopropyl isocyanoacetate **3f** and α-benzyl isocyanoacetate **3g** are also unreactive in the transformation. The results confirm that the α-aryl substitution is crucial for achieving good reactivity and enantioselectivity.

Several analogous nucleophiles of malononitrile including methyl cyanoacetate, diethyl malonate, and ethyl nitroacetate were examined in the one pot reaction with isatin **1a** and isocyanoacetate **3a**, but no expected 3,3′-dihydropyrryl-spirooxindole was obtained.

A plausible reaction mechanism is proposed (Scheme 5).[4j] Initially the fast Knoevenagel condensation of isatin **1a** and malononitrile **2a** affords isatylidene malononitrile. The deprotonation of methyl α-phenyl-isocyanoacetate **3a** in the presence of organocatalyst **4f** generates the nucleophilic anion, which is expected to form an ion pair with protonated **4f**. In addition, the H-bond interaction of **4f** with isatylidene malononitrile increases

Table 1 Catalyst screening and the optimization of reaction conditions[a]



En	Cat. (mol%)	Solvent	T (°C)	Time (h)	Yield[b] (%)	**5a** : **5a′**[c]	ee[d] (%)
1	**4a** (10)	CH_2Cl_2	RT	2	80	84 : 16	56/35
2	**4b** (10)	CH_2Cl_2	RT	5	82	75 : 25	0/12
3	**4c** (10)	CH_2Cl_2	RT	3	90	80 : 20	95/96
4	**4d** (10)	CH_2Cl_2	RT	1	85	80 : 20	88/90
5	**4e** (10)	CH_2Cl_2	RT	3	83	67 : 33	92/95
6	**4f** (10)	CH_2Cl_2	RT	2	89	80 : 20	97/94
7	**4f** (10)	Toluene	RT	1	93	78 : 22	93/95
8	**4f** (10)	AcOEt	RT	2	94	80 : 20	93/93
9	**4f** (10)	CH_3CN	RT	8	95	73 : 27	78/72
10	**4f** (10)	CH_3OH	RT	1	93	80 : 20	0/13
11	**4f** (10)	1,4-Dioxane	RT	4	90	78 : 22	92/94
12	**4f** (10)	$(CH_2Cl)_2$	RT	20	90	78 : 22	95/95
13	**4f** (10)	THF	RT	20	73	86 : 14	93/92
14	**4f** (10)	$CHCl_3$	RT	1	84	75 : 15	96/92
15	**4f** (10)	CH_2Cl_2	0	4	92	78 : 22	97/95
16	**4f** (10)	CH_2Cl_2	−20	12	88	78 : 22	98/95
17	**4f** (10)	CH_2Cl_2	−40	20	83	80 : 20	99/96
18	**4f** (5)	CH_2Cl_2	RT	3	92	78 : 22	97/94
19	**4f** (2)	CH_2Cl_2	RT	8	92	78 : 22	97/94
20	**4f** (1)	CH_2Cl_2	RT	30	85	80 : 20	97/94

[a] The reactions were carried out with **1a** (0.050 mmol), **2a** (0.050 mmol) and **3a** (0.055 mmol). [b] Combined yields of **5a** and **5a′** after column chromatography. [c] Determined by ^{1}H NMR analysis of the crude reaction mixture. [d] Determined by chiral HPLC.

its electrophilic reactivity and also directs the attack of the isocyanoacetate anion from the *si*-face of the double bond. The resulting intermediate **B** undergoes the intramolecular cycloaddition to give the products **5a**/**5a′**. The π–π interaction of isatylidene malononitrile with α-phenyl-isocyanoacetate anion accounts for the preferential formation of **5a**.

The product **5a** was further treated with $NaBH_3CN$. Selective reduction of the imine group was achieved to give 3,3′-pyrrolidinyl-spirooxindole **6a** in excellent yield and enantioselectivity (Scheme 6).

Conclusion

In conclusion, we have developed an organocatalytic three-component reaction of isatins, malononitrile and α-aryl-isocyanoacetates. The thiourea derived from quinine was identified as the most efficient catalyst. A number of 3,3′-dihydropyrryl-spirooxindoles were prepared in excellent yields and enantioselectivities. The products can be readily converted to valuable 3,3′-pyrrolidinyl-spirooxindoles *via* a selective reduction. This new method is highly attractive for the synthesis of spirooxindole derivatives in terms of the convenience and efficiency.

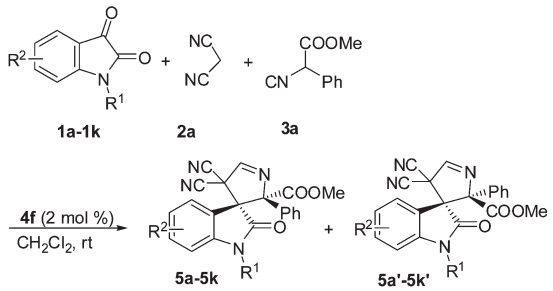
Experimental

General

1a (32.2 mg, 0.200 mmol), **2a** (13.2 mg, 0.200 mmol), **3a** (38.8 mg, 0.220 mmol), **4f** (2.3 mg, 0.004 mmol) and dichloromethane (2 mL) in a flask were stirred at room temperature for 8 h. After evaporation of the solvent under vacuum, the residue was separated by flash chromatography over silica gel to give **5a** and **5a′** (70.6 g, 92% yield) as white solids.

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5a). The product was obtained following the general procedure. White solid. Mp 239–241 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 7.46–7.41 (m, 2H), 7.38–7.34 (m, 2H), 7.04 (d, J = 7.2 Hz, 2H), 6.97 (d, J = 7.9 Hz, 1H), 6.83 (t, J = 7.7 Hz, 1H), 5.92 (d, J = 7.7 Hz, 1H), 3.76 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.48, 169.84, 152.75, 145.18, 131.19, 130.63, 130.18, 128.67, 127.98, 127.28, 122.47, 119.52, 109.77, 109.04, 108.79, 91.74, 64.31, 53.85, 51.23, 26.97; IR (KBr, thin film) ν/cm^{-1}: 2920, 2851, 1732, 1710, 1611, 1599, 1564, 1473, 1297, 1101, 1074, 577; HRMS (ESI) calcd for $C_{22}H_{16}N_4NaO_3$ $(M + Na)^+$: 407.1115, found: 407.1114; $[\alpha]_D^{20}$ = 25.6 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC

Table 2 Organocatalytic three-component reaction of isatins **1a–1k**, malononitrile **2a** and isocyanoacetate **3a**[a]



En	1	R^1	R^2	Time (h)	Yield[b] (%)	5 : 5′[c]	ee[d] (%)
1	**1a**	Me	H	8	92, **5a**/**5a′**	78 : 22	97/94
2	**1b**	$PhCH_2$	H	8	95, **5b**/**5b′**	86 : 14	96/94
3	**1c**	H	H	14	94, **5c**/**5c′**	83 : 17	92/82
4[e]	**1d**	CH_3CO	H	240	—	—	—
5[e]	**1e**	Boc	H	240	—	—	—
6	**1f**	Me	4-Cl	20	81, **5f**/**5f′**	94 : 6	92/—
7	**1g**	Me	4-Br	17	83, **5g**/**5g′**	93 : 7	82/—
8	**1h**	Me	5-Cl	8	85, **5h**/**5h′**	88 : 12	96/92
9	**1i**	Me	7-Br	12	88, **5i**/**5i′**	86 : 14	89/97
10	**1j**	Me	5-OCH_3	13	92, **5j**/**5j′**	83 : 17	80/94
11	**1k**	Me	6-OCH_3	48	86, **5k**/**5k′**	83 : 17	96/92

[a] The reactions were carried out with **1a–1k** (0.200 mmol), **2a** (0.200 mmol), **3a** (0.220 mmol) and **4f** (0.004 mmol) in dichloromethane (2 mL) at room temperature. [b] Combined yields of **5**/**5′** after column chromatography. [c] Determined by ^{1}H NMR analysis of the crude reaction mixture. [d] Determined by chiral HPLC. [e] No reaction.

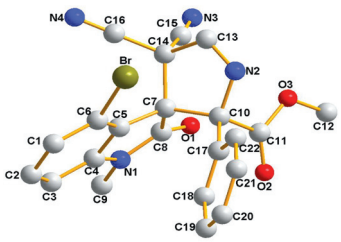
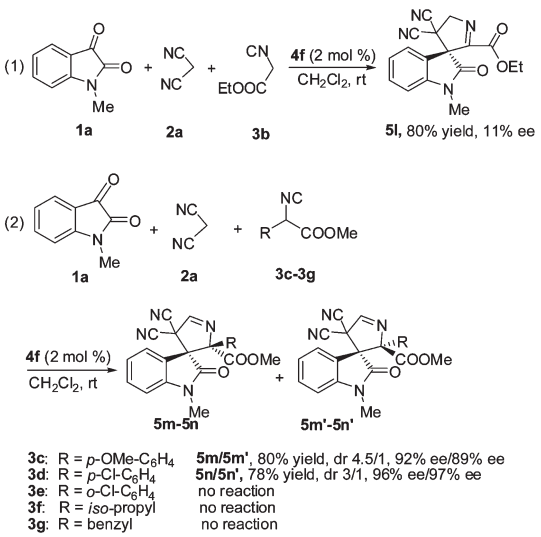
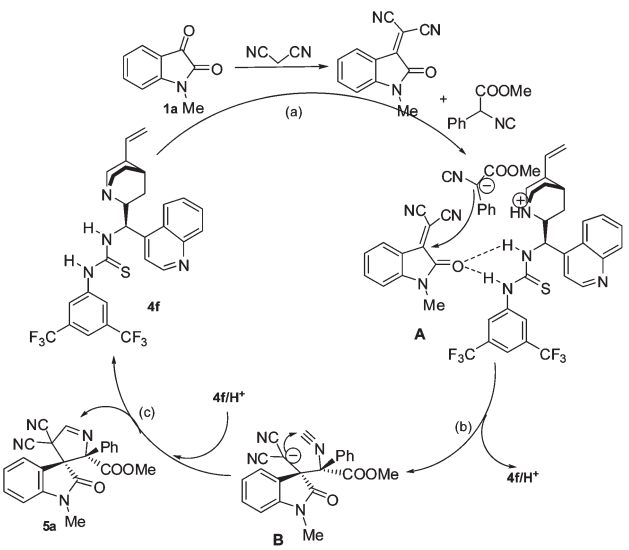


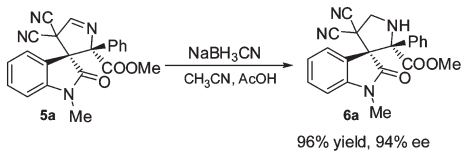
Fig. 1 X-ray structure of **5g**.



Scheme 4 Reaction of α-substituted isocyanoacetates with isatin **1a** and malononitrile **2a**.



Scheme 5 Proposed reaction mechanism.



Scheme 6 Preparation of 3,3′-pyrrolidinyl-spirooxindole **6a**.

with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 208 nm), t_R (major) = 34.4 min, t_R (minor) = 55.7 min, 97% ee).

(2′*R*,3*R*)-Methyl-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5a′). The product was obtained following the general procedure. White solid. Mp 225–227 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.10 (s, 1H), 7.56 (t, J = 8.2 Hz, 2H), 7.28 (d, J = 7.0 Hz, 2H), 7.21 (t, J = 7.6 Hz, 2H), 7.12 (d, J = 7.9 Hz, 2H), 6.93 (d, J = 7.7 Hz, 1H), 3.81 (s, 3H), 2.83 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.17, 166.86, 154.18, 145.16, 135.02, 131.85, 128.89, 127.85, 126.64, 126.39, 123.74, 119.54, 110.49, 109.54, 109.27, 90.09, 53.46, 51.58, 29.68, 26.29; IR (KBr, thin film) ν/cm^{-1}: 2925, 2030, 1728, 1613, 1461, 1386, 1243, 1157, 1082, 577; HRMS (ESI) calcd for $C_{22}H_{16}N_4NaO_3$ $(M + Na)^+$: 407.1115, found: 407.1115; $[\alpha]_D^{20}$ = 28.3 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 208 nm), t_R (major) = 27.2 min, t_R (minor) = 36.6 min, 94% ee).

(2′*S*,3*R*)-Methyl-1-benzyl-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5b). The product was obtained following the general procedure. White solid. Mp 196–198 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 (s, 1H), 7.45 (t, J = 8.2 Hz, 3H), 7.40–7.33 (m, 4H), 7.28 (dd, J = 8.9, 7.8 Hz, 2H), 7.08 (d, J = 7.3 Hz, 2H), 6.83–6.76 (m, 2H), 5.91 (d, J = 7.7 Hz, 1H), 5.04 (d, J = 15.7 Hz, 1H), 4.93 (d, J = 15.7 Hz, 1H), 3.76 (s, 3H), 3.58 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.67, 169.76, 152.75, 144.44, 134.64, 131.02, 130.51, 130.19, 128.87, 128.65, 128.00, 127.96, 127.71, 127.34, 122.41, 119.50, 110.22, 109.92, 108.73, 91.72, 64.29, 53.85, 51.37, 44.90; IR (KBr, thin film) ν/cm^{-1}: 3063, 2955, 1737, 1706, 1610, 1564, 1131, 1077, 576; HRMS (ESI) calcd for $C_{28}H_{20}N_4NaO_3$ $(M + Na)^+$: 483.1428, found: 483.1430; $[\alpha]_D^{20}$ = 38.5 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 230 nm), t_R (major) = 18.9 min, t_R (minor) = 62.8 min, 96% ee).

(2′*R*,3*R*)-Methyl-1-benzyl-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5b′). The product was obtained following the general procedure. White solid. Mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.14 (s, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.46–7.40 (m, 1H), 7.31–7.27 (m, 1H), 7.25–7.21 (m, 4H), 7.21–7.15 (m, 4H), 7.00 (dd, J = 6.5, 2.9 Hz, 2H), 6.83 (d, J = 7.9 Hz, 1H), 4.51 (s, 2H), 3.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.49, 166.94, 154.16, 144.41, 134.90, 134.15, 131.74, 128.82, 128.64, 128.13, 127.95, 127.70, 126.81, 126.54, 123.73, 119.47, 110.60, 110.35, 109.48, 89.66, 65.96, 53.51, 52.08, 44.47; IR (KBr, thin film) ν/cm^{-1}: 3057, 2928, 2032, 1728, 1612, 1456, 1386, 1259, 1163, 1076, 577; HRMS (ESI) calcd for $C_{28}H_{20}N_4NaO_3$ $(M + Na)^+$: 483.1428, found: 483.1422; $[\alpha]_D^{20}$ = 40.0 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 230 nm), t_R (major) = 27.5 min, t_R (minor) = 63.3 min, 94% ee).

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5c). The product was obtained following the general procedure. White solid. Mp 109–111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.17 (s, 1H), 8.03 (s, 1H), 7.45 (d, J = 6.3 Hz, 1H), 7.40–7.30 (m, 3H), 7.08 (d, J = 7.3 Hz, 2H), 6.99 (d, J = 7.8 Hz, 1H), 6.81 (t, J = 7.7 Hz, 1H), 5.91 (d, J = 7.8 Hz, 1H), 3.78 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 175.46, 169.80, 153.04, 142.39, 131.17, 130.49, 130.23, 128.71, 128.18, 127.29, 122.39, 120.01, 110.95, 109.79, 108.62, 91.67, 64.84, 53.91, 51.37; IR (KBr, thin film) ν/cm^{-1}: 2957, 2925, 2852, 1780, 1735, 1620, 1599, 1472, 1398, 1297, 1197, 1077, 603; HRMS (ESI) calcd for $C_{21}H_{14}N_4NaO_3$ $(M + Na)^+$: 393.0958, found: 393.0952; $[\alpha]_D^{20}$ = 61.7 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 230 nm), t_R (major) = 23.0 min, t_R (minor) = 56.3 min, 92% ee).

(2′*R*,3*R*)-Methyl-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5c′). The product was obtained following the general procedure. White solid. Mp 185–187 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (s, 1H), 7.56 (d, J = 7.8 Hz, 1H), 7.51 (d, J = 7.8 Hz, 1H), 7.47 (d, J = 6.7 Hz, 1H), 7.28–7.23 (m, 5H), 6.95 (d, J = 7.8 Hz, 1H), 3.82 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 172.16, 166.83, 153.94, 142.01, 135.01, 131.74, 128.95, 128.17, 126.73, 126.57, 123.74, 120.11, 111.29, 110.40, 109.32, 89.98, 66.19, 53.50, 51.97; IR (KBr, thin film) ν/cm^{-1}: 2923, 2852, 1793, 1601, 1564, 1435, 1325, 1269, 1230, 1022, 577; HRMS (ESI) calcd for $C_{21}H_{14}NaN_4O_3$ $(M + Na)^+$: 393.0958, found: 393.0958; $[\alpha]_D^{20}$ = 22.5 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak OD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 208 nm), t_R (major) = 16.5 min, t_R (minor) = 14.5 min, 82% ee).

(2′*S*,3*S*)-Methyl-4-chloro-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5f). The product was obtained following the general procedure. White solid. Mp 245–248 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.06 (s, 1H), 7.18 (t, J = 8.1 Hz, 2H), 7.11 (d, J = 7.2 Hz, 2H), 7.04 (s, 2H), 6.81 (d, J = 7.9 Hz, 1H), 6.71 (d, J = 8.2 Hz, 1H), 3.87 (s, 3H), 3.42 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.99, 166.14, 153.26, 145.03, 134.04, 132.65, 132.00, 128.58, 127.30, 126.99, 125.39, 122.60, 109.81, 107.83, 107.48, 93.28, 66.28, 53.64, 52.63, 27.73; IR (KBr, thin film) ν/cm^{-1}: 3063, 2957, 1742, 1720, 1659, 1604, 1564, 1428, 1128, 1010, 596; HRMS (ESI) calcd for $C_{22}H_{15}N_4NaO_3Cl$ $(M + Na)^+$: 441.0725, found: 441.0726; $[\alpha]_D^{20}$ = −155.5 (c 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 40.1 min, t_R (minor) = 29.1 min, 92% ee).

(2′*S*,3*S*)-Methyl-4-bromo-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5g). The product was obtained following the general procedure. White solid. Mp 250–253 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (s, 1H), 7.39–7.30 (m, 1H), 7.14–7.08 (m, 3H), 7.04 (s, 2H), 6.92 (d, J = 8.0 Hz, 1H), 6.86 (d, J = 7.8 Hz, 1H), 3.86 (s, 3H), 3.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.95, 166.38, 153.66, 145.41, 133.94, 131.95, 129.10, 128.58, 127.58, 126.95, 124.39, 121.66, 109.88, 108.04, 107.82, 93.45, 66.60, 53.67, 52.65, 27.70; IR (KBr, thin film) ν/cm^{-1}: 3086, 2957, 1742,

1721, 1659, 1601, 1564, 1459, 1243, 1008, 595; HRMS (ESI) calcd for $C_{22}H_{15}N_4NaO_3Br$ (M + Na)$^+$: 485.0220, found: 485.0221; $[\alpha]_D^{20}$ = −203.8 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 46.3 min, t_R (minor) = 30.9 min, 82% ee).

(2′*S*,3*R*)-Methyl-5-chloro-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5h). The product was obtained following the general procedure. White solid. Mp 245–248 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.16 (s, 1H), 7.50 (d, *J* = 7.3 Hz, 1H), 7.43–7.38 (m, 3H), 7.03 (d, *J* = 6.9 Hz, 2H), 6.90 (d, *J* = 8.4 Hz, 1H), 5.76 (d, *J* = 1.8 Hz, 1H), 3.77 (s, 3H), 3.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 173.01, 169.71, 152.56, 143.69, 131.05, 130.53, 130.07, 128.80, 128.39, 127.98, 127.11, 121.07, 109.86, 109.51, 108.46, 92.08, 64.07, 53.96, 50.89, 27.08; IR (KBr, thin film) *ν*/cm^{-1}: 2921, 2851, 1716, 1603, 1564, 1489, 1356, 1148, 579; HRMS (ESI) calcd for $C_{22}H_{15}N_4NaO_3Cl$ (M + Na)$^+$: 441.0725, found: 441.0725; $[\alpha]_D^{20}$ = 76.6 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 230 nm), t_R (major) = 46.2 min, t_R (minor) = 58.8 min, 96% ee).

(2′*R*,3*R*)-Methyl-5-chloro-4′,4′-dicyano-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5h′). The product was obtained following the general procedure. White solid. Mp 129–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.08 (s, 1H), 7.59 (s, 1H), 7.54 (dd, *J* = 8.4, 1.9 Hz, 1H), 7.28 (s, 1H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.11 (d, *J* = 7.2 Hz, 2H), 6.85 (d, *J* = 8.4 Hz, 1H), 3.82 (s, 3H), 2.81 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.78, 166.85, 154.06, 143.72, 134.69, 131.81, 129.28, 129.04, 127.94, 127.16, 126.58, 121.25, 110.21, 110.06, 109.21, 90.38, 65.55, 53.65, 51.44, 26.40; IR (KBr, thin film) *ν*/cm^{-1}: 2919, 2850, 1729, 1602, 1564, 1491, 1144, 577; HRMS (ESI) calcd for $C_{22}H_{15}N_4NaO_3Cl$ (M + Na)$^+$: 441.0725, found: 441.0722; $[\alpha]_D^{20}$ = 23.3 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 26.2 min, t_R (minor) = 37.0 min, 92% ee).

(2′*S*,3*R*)-Methyl-7-bromo-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5i). The product was obtained following the general procedure. White solid. Mp 249–251 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.16 (s, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.43 (d, *J* = 7.2 Hz, 1H), 7.40–7.30 (m, 2H), 7.03 (d, *J* = 4.8 Hz, 2H), 6.65 (t, *J* = 7.9 Hz, 1H), 5.80 (d, *J* = 7.5 Hz, 1H), 3.77 (s, 3H), 3.68 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.15, 169.66, 152.58, 142.59, 136.91, 130.33, 130.30, 128.75, 127.27, 126.99, 123.27, 122.41, 109.52, 108.57, 103.09, 92.28, 63.55, 53.91, 51.37, 30.93; IR (KBr, thin film) *ν*/cm^{-1}: 2925, 2030, 1720, 1605, 1451, 1373, 1270, 1160, 1086, 577; HRMS (ESI) calcd for $C_{22}H_{15}N_4NaO_3Br$ (M + Na)$^+$: 485.0220, found: 485.0221; $[\alpha]_D^{20}$ = 36.7 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 23.8 min, t_R (minor) = 34.4 min, 89% ee).

(2′*R*,3*R*)-Methyl-7-bromo-4′,4′-dicyano-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5i′). The product was obtained following the general procedure. White solid. Mp 165–167 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.09 (s, 1H), 7.67 (d, *J* = 8.3 Hz, 1H), 7.52 (d, *J* = 7.7 Hz, 1H), 7.32–7.24 (m, 3H), 7.14–7.09 (m, 3H), 3.79 (s, 3H), 3.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 170.77, 166.68, 154.08, 142.58, 137.56, 134.55, 129.08, 127.98, 126.68, 125.32, 124.53, 122.54, 110.21, 109.34, 103.38, 90.48, 65.29, 53.52, 51.63, 30.28; IR (KBr, thin film) *ν*/cm^{-1}: 2921, 2851, 2361, 2025, 1729, 1601, 1459, 1361, 1162, 1076, 578; HRMS (ESI) calcd for $C_{22}H_{15}N_4O_3NaBr$ (M + Na)$^+$: 485.0220, found: 485.0217; $[\alpha]_D^{20}$ = 15.2 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 90/10, 0.8 mL min^{-1}, 230 nm, t_R (major) = 22.8 min, t_R (minor) = 15.4 min, 97% ee).

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-5-methoxy-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5j). The product was obtained following the general procedure. White solid. Mp 240–242 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.18 (s, 1H), 7.45 (d, *J* = 7.2 Hz, 1H), 7.39 (t, *J* = 7.4 Hz, 2H), 7.08 (d, *J* = 7.0 Hz, 2H), 6.94 (dd, *J* = 8.6, 2.5 Hz, 1H), 6.87 (d, *J* = 8.6 Hz, 1H), 5.50 (d, *J* = 2.4 Hz, 1H), 3.77 (s, 3H), 3.43 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 173.18, 169.75, 155.22, 152.75, 138.39, 130.59, 130.09, 128.71, 127.39, 120.32, 117.12, 113.90, 109.70, 109.56, 108.80, 91.69, 64.37, 55.45, 53.83, 51.29, 27.00; IR (KBr, thin film) *ν*/cm^{-1}: 2920, 2851, 1717, 1602, 1564, 1500, 1386, 1206, 1076, 577; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1216; $[\alpha]_D^{20}$ = 69.0 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 41.2 min, t_R (minor) = 64.6 min, 80% ee).

(2′*R*,3*R*)-Methyl-4′,4′-dicyano-5-methoxy-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5j′). The product was obtained following the general procedure. White solid. Mp 192–194 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.08 (s, 1H), 7.23–7.19 (m, 4H), 7.12 (d, *J* = 7.4 Hz, 2H), 7.06 (dd, *J* = 8.6, 2.4 Hz, 1H), 6.82 (d, *J* = 8.6 Hz, 1H), 3.86 (s, 3H), 3.82 (s, 3H), 2.80 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 169.95, 166.91, 156.52, 154.25, 138.42, 135.13, 128.87, 127.83, 126.69, 120.66, 116.37, 113.87, 110.54, 109.64, 109.61, 90.32, 65.83, 55.94, 53.43, 51.73, 26.36; IR (KBr, thin film) *ν*/cm^{-1}: 2921, 2850, 2025, 1722, 1600, 1497, 1468, 1364, 1293, 1169, 1076, 577; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1215; $[\alpha]_D^{20}$ = 21.3 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm), t_R (major) = 31.6 min, t_R (minor) = 44.6 min, 94% ee).

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-6-methoxy-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5k). The product was obtained following the general procedure. Red solid. Mp 95–97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.15 (s, 1H), 7.43 (d, *J* = 7.3 Hz, 1H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.06 (d, *J* = 7.7 Hz, 2H), 6.52 (d, *J* = 2.0 Hz, 1H), 6.31 (dd, *J* = 8.6, 2.2 Hz, 1H), 5.82 (d, *J* = 8.5 Hz, 1H), 3.82 (s, 3H), 3.75 (s, 3H), 3.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 174.08, 169.85,

162.40, 152.86, 146.55, 130.71, 130.06, 128.91, 128.59, 127.24, 110.84, 109.88, 108.89, 106.43, 96.97, 91.22, 64.36, 55.57, 53.78, 51.18, 26.94; IR (KBr, thin film) ν/cm^{-1}: 2957, 2919, 2850, 1763, 1720, 1627, 1598, 1510, 1378, 1146, 1098, 1039, 583; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1221; $[\alpha]_D^{20}$ = 49.3 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 208 nm), t_R (major) = 20.5 min, t_R (minor) = 40.8 min, 96% ee).

(2′*R*,3*R*)-Methyl-4′,4′-dicyano-6-methoxy-1-methyl-2-oxo-2′-phenyl-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5k′). The product was obtained following the general procedure. White solid. Mp 90–92 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.08 (s, 1H), 7.48 (d, *J* = 8.6 Hz, 1H), 7.28 (d, *J* = 7.2 Hz, 1H), 7.21 (t, *J* = 7.3 Hz, 2H), 7.14 (d, *J* = 7.2 Hz, 2H), 6.73 (d, *J* = 8.6 Hz, 1H), 6.46 (s, 1H), 3.91 (s, 3H), 3.80 (s, 3H), 2.79 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.77, 167.00, 162.86, 154.24, 146.61, 135.20, 128.79, 127.82, 127.50, 126.61, 110.76, 110.60, 109.68, 107.34, 97.39, 89.68, 65.93, 55.69, 53.38, 51.57, 26.26; IR (KBr, thin film) ν/cm^{-1}: 2921, 2851, 1755, 1722, 1627, 1600, 1509, 1375, 1214, 1095, 582; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1215; $[\alpha]_D^{20}$ = 35.0 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 208 nm), t_R (major) = 15.5 min, t_R (minor) = 17.7 min, 92% ee).

(*R*)-Ethyl-4′,4′-dicyano-1-methyl-2-oxo-4′,5′-dihydro-spiro-[indoline-3,3′-pyrrole]-2′-carboxylate (5l). The product was obtained following the general procedure. White solid. Mp 134–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.52 (t, *J* = 7.8 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.19 (t, *J* = 7.7 Hz, 1H), 7.01 (d, *J* = 7.9 Hz, 1H), 5.11 (s, 2H), 4.20–4.09 (m, 2H), 3.33 (s, 3H), 1.14 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.63, 163.77, 158.81, 144.87, 131.84, 125.28, 123.82, 121.21, 112.77, 111.52, 109.54, 70.26, 69.65, 63.01, 43.04, 27.20, 13.64; IR (KBr, thin film) ν/cm^{-1}: 2986, 1727, 1713, 1636, 1612, 1564, 1494, 1374, 1153, 1098, 574; HRMS (ESI) calcd for $C_{17}H_{14}N_4NaO_3$ (M + Na)$^+$: 345.0958, found: 345.0943; $[\alpha]_D^{20}$ = 23.0 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm, t_R (major) = 26.7 min, t_R (minor) = 22.4 min, 12% ee).

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-2′-(4-methoxyphenyl)-1-methyl-2-oxo-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5m). The product was obtained following the general procedure. White solid. Mp 216–218 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.15 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 6.99–6.94 (m, 3H), 6.90–6.51 (m, 3H), 6.04 (d, *J* = 7.7 Hz, 1H), 3.83 (s, 3H), 3.75 (s, 3H), 3.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 173.52, 170.00, 160.86, 152.44, 145.17, 131.11, 128.68, 128.07, 122.48, 122.20, 119.53, 113.92, 109.82, 109.01, 108.80, 91.33, 64.26, 55.37, 53.79, 51.00, 26.93; IR (KBr, thin film) ν/cm^{-1}: 2918, 2835, 2025, 1718, 1637, 1614, 1512, 1494, 1374, 1260, 1162, 1068, 950, 542; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1237; $[\alpha]_D^{20}$ = 16.7 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 70/30, 0.8 mL min^{-1}, 230 nm), t_R (major) = 22.9 min, t_R (minor) = 44.3 min, 92% ee).

(2′*R*,3*R*)-methyl-4′,4′-dicyano-2′-(4-methoxyphenyl)-1-methyl-2-oxo-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5m′). The product was obtained following the general procedure. White solid. Mp 232–234 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.09 (s, 1H), 7.54 (d, *J* = 7.2 Hz, 2H), 7.29–7.25 (m, 1H), 7.04 (d, *J* = 7.1 Hz, 2H), 6.93 (d, *J* = 6.4 Hz, 1H), 6.74 (d, *J* = 7.3 Hz, 2H), 3.80 (s, 3H), 3.76 (s, 3H), 2.87 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 170.19, 167.05, 159.81, 154.07, 145.09, 131.81, 127.94, 126.82, 126.27, 123.71, 119.62, 113.23, 110.51, 109.57, 109.27, 89.85, 65.76, 55.16, 53.43, 51.53, 26.41; IR (KBr, thin film) ν/cm^{-1}: 2922, 2849, 2025, 1730, 1639, 1613, 1512, 1493, 1372, 1254, 1177, 1098, 951, 543; HRMS (ESI) calcd for $C_{23}H_{18}N_4NaO_4$ (M + Na)$^+$: 437.1220, found: 437.1232; $[\alpha]_D^{20}$ = 87.5 (*c* 1.0, $CHCl_3$); The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 80/20, 0.8 mL min^{-1}, 230 nm), t_R (major) = 26.1 min, t_R (minor) = 22.5 min, 89% ee).

Methyl-2′-(4-chlorophenyl)-4′,4′-dicyano-1-methyl-2-oxo-2′,4′-dihydrospiro[indoline-3,3′-pyrrole]-2′-carboxylate (5n/5n′). The product was obtained as an inseparable mixture of **5n** and **5n′** following the general procedure. White solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ, for **5n**: 8.18 (s, 1H), 7.48–7.39 (m, 1H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.04–6.89 (m, 4H), 6.07 (d, *J* = 7.7 Hz, 1H), 3.76 (s, 3H), 3.31 (s, 3H); for **5n′**: 7.48–7.39 (m, 1H), 7.33 (d, *J* = 8.5 Hz, 2H), 7.04–6.89 (m, 4H), 6.14 (d, *J* = 7.8 Hz, 1H), 5.77 (d, *J* = 12.8 Hz, 1H), 3.71 (s, 3H), 3.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 176.89, 173.14, 169.61, 168.14, 165.55, 158.31, 153.27, 145.12, 144.34, 136.52, 136.29, 133.55, 131.40, 129.96, 129.43, 129.27, 128.84, 128.74, 127.79, 126.32, 123.85, 122.65, 122.64, 119.24, 115.64, 109.48, 109.26, 108.66, 108.62, 90.96, 78.03, 64.11, 62.26, 61.75, 54.01, 53.80, 51.17, 29.70, 27.01, 26.62; IR (KBr, thin film) ν/cm^{-1}: 2921, 2920, 2851, 2050, 2025, 1726, 1634, 1629, 1615, 1546, 1469, 1384, 1357, 1215, 1163, 1075, 1015, 547, 523. HRMS (ESI) calcd for $C_{22}H_{15}ClN_4NaO_3$ (M + Na)$^+$: 441.0725, found: 441.0728; The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 80/20, 0.8 mL min^{-1}, 230 nm), **5n**: t_R (major) = 26.6 min, t_R (minor) = 40.7 min, 96% ee; **5n′**: t_R (major) = 19.4 min, t_R (minor) = 17.4 min, 97% ee.

(2′*S*,3*R*)-Methyl-4′,4′-dicyano-1-methyl-2-oxo-2′-phenylspiro-[indoline-3,3′-pyrrolidine]-2′-carboxylate (6a). 5a (38.4 mg, 0.100 mmol) was added into CH_3CN (1 mL) and H_2O (50 μL), stirred for 10 min, then $NaBH_3CN$ (12.6 mg, 0.200 mmol) and acetic acid (50 μL) were added and stirred for 2 h at room temperature. After the evaporation of the solvent under vacuum, extracted with EtOAc (5 mL) for three times. The mixture was washed with NaOH (1 M) and brine. And the organic layer was dried over anhydrous Na_2SO_4. After evaporation of the solvent under vacuum, the residue was separated by flash chromatography over silica gel to give **7a** as a white solid. Mp 162–164 °C; $[\alpha]_D^{20}$ = 37.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.57 (d, *J* = 5.8 Hz, 2H), 7.40–7.32 (m, 2H), 7.27 (dd, *J* = 10.5, 4.3 Hz, 2H), 6.96 (d, *J* = 7.9 Hz, 1H), 6.82 (t, *J* = 7.7 Hz, 1H), 6.19 (d, *J* = 7.7 Hz, 1H), 4.57 (d, *J* = 1.0 Hz, 1H),

4.04 (d, J = 1.0 Hz, 1H), 3.67 (s, 3H), 3.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 174.10, 171.41, 144.39, 135.99, 130.75, 129.19, 128.73, 128.62, 127.87, 122.46, 120.83, 113.54, 111.97, 108.68, 75.99, 63.83, 53.28, 44.02, 29.68, 26.77; IR (KBr, thin film) ν/cm^{-1}: 3395, 1741, 1712, 1611, 1564, 1493, 1472, 1376, 1242, 1098, 577; HRMS (ESI) calcd for $C_{22}H_{19}N_4O_3$ $(M + H)^+$: 387.1452, found: 387.1450; The enantiomeric excess was determined by HPLC with Chiralpak AD column (hexane–*i*PrOH = 85/15, 0.8 mL min^{-1}, 254 nm, t_R (major) = 17.4 min, t_R (minor) = 19.2 min, 94% ee).

Acknowledgements

We thank the National Natural Science Foundation of China (Nos. 20972195, 21172270) and Guangdong Engineering Research Center of Chiral Drugs for the financial supports of this study.

Notes and references

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