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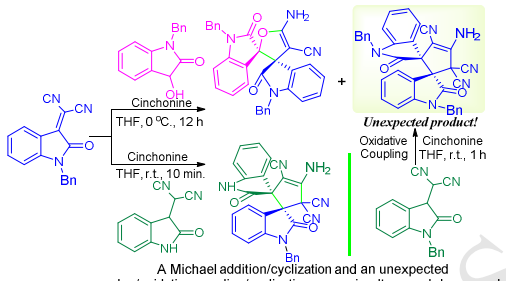


A Michael addition/cyclization and an unexpected redox/oxidative coupling/cyclization were simultaneously happened.

Stereoselective Construction of Bi-spirooxindole Frameworks via a Michael Addition/Cyclization and an Unexpected Redox/Oxidative Coupling/Cyclization

Xiao-Qian Zhu[a], Jia-Shou Wu[b], Jian-Wu Xie [a,*]

[a]*Key Laboratory of the Ministry of Education for Advanced Catalysis Materials, Department of Chemistry and Life Science, Zhejiang Normal University, Jinhua 321004, P. R. China; E-mail: xiejw@zjnu.cn*

[b] *School of Pharmaceutical and Chemical Engineering, Taizhou University, Taizhou 318000, Zhejiang, P. R. of China.*

KEYWORDS: Spirooxindoles Michael addition Domino reactions

ABSTRACT: A series of polyheterocyclic bi-spirooxindole derivatives with skeletal diversity and molecular complexity were prepared via a cascade synthesis strategy. The key step transfer hydrogenation is smoothly fulfilled by using 3-hydroxyoxindole derivatives as the hydrogen source and the oxidative coupling happened by using simple and green molecular oxygen as the oxidant. The plausible mechanisms for the unexpected redox/oxidative coupling/cyclization were also given.

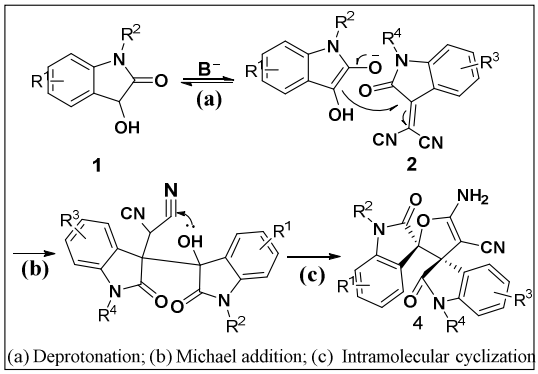
1. Introduction

It is a major challenge to develop novel synthetic methods for the construction of new analogues of bioactive heterocyclic compounds in synthetic organic and medicinal chemistry. The reactions that generate new spirocyclic ring units and maximize molecular complexity with a minimum of operations are not only noteworthy but also fundamental for the construction of spiro heterocyclic molecule frameworks. The spirooxindole core is a privileged heterocyclic ring system featured in numerous clinical pharmaceuticals and natural spirooxindole alkaloids with diverse and important biological profiles. Natural products and pharmaceuticals possessing the spirooxindole skeleton show a wide spectrum of considerable bioactivities, such as anticonvulsant,[1] antimicrobial,[2] antitumor,[3] antiviral,[4] anti-HIV,[5] and antitubercular.[6] Some additional biologically active spirocyclic oxindoles have also been described in a broader-context review.[7] Moreover, the unique potential of the C3 position of the oxindole core to be used both as an electrophile and nucleophile

and their easy availability have made them valuable building blocks for the construction of spiro-fused cyclic frameworks.[8-13] Thus, more and more general and versatile synthetic methodologies to access analogous compounds possessing the spirocyclic oxindole skeleton have been devoted over the past few decades.[7,8] Among various spirocyclic oxindoles, bi-spirooxindole was a very interesting subgroup member, in which the two oxindole moieties can exist at a new formed cyclic ring. The dispirocyclopentyl-3,3-bisoxindoles with two oxindoles at 1,3-position of cyclopentyl ring have been reported in several works.[9-13] As part of our heterocyclic chemistry and medicinal chemistry research program,[14] we required a robust facile synthesis of bi-spirooxindole derivatives wherein we could vary the different substitutions. Herein we develop a cascade synthesis strategy for construction of bi-spirooxindoles with skeletal diversity and molecular complexity.

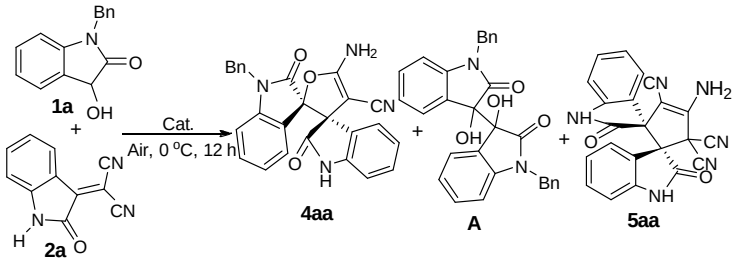
2. Result and discussion

Scheme 1 Potential strategy for the domino 3-hydroxyoxindoles **1** with α,α-dicyanoolefins **2**.



The 3-alkyl- or 3-arylsubstituted oxindoles have recently been identified as versatile synthons to construct spirocyclic oxindole skeleton at the C3 position of oxindole.[15] However, 3-hydroxyoxindole **1a**, which contains a valuable hydroxy moiety at C3, has rarely been used as a nucleophile in analogous reaction pathways, and remains to be explored.[16] In addition, the readily available α,α-dicyanoolefins have been developed as attractive precursors for the construction of various cyclic compounds by our group[17] and others[18]. As such, we envisioned that the new domino Michael addition-cyclization reactions would be possible between 3-hydroxyoxindoles **1** and α,α-dicyanoolefins **2**, giving a facile protocol to 2,3-dihydrofuranyl bi-spirooxindole derivatives **4** with multiple substitutions (**Scheme 1**).

Table 1 Reaction of *N*-benzyl-3-hydroxyoxindole 1a and α,α-dicyanoolefin 2a under different conditions [a]



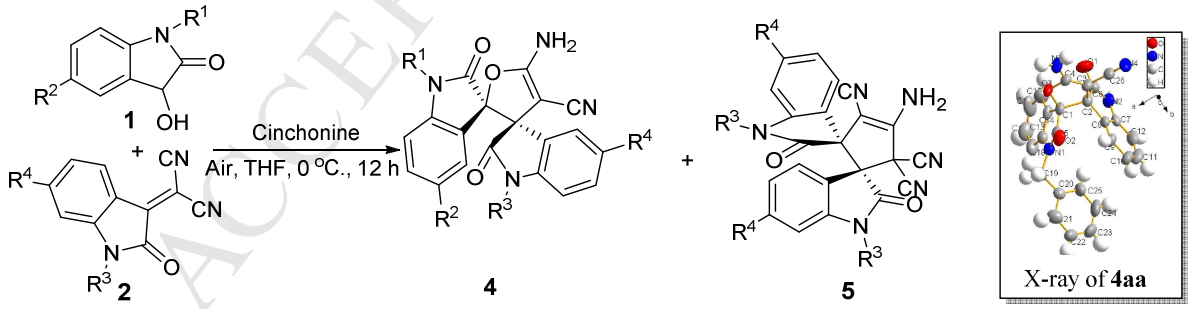
Entry	Base	Solvent	Yield(**4aa**/**A**/**5aa**)[b]	Dr(**4aa**/**A**/**5aa**)[c]
1	K_2CO_3	THF	30/21/-	>99:1/>99:1/-
2	KOH	THF	-	-/-/-
3	Cs_2CO_3	THF	-	-/-/-
4	TEA	THF	-/34/-	-/>99:1/-
5	DBU	THF	-/45/-	-/>99:1/-
6	**QN**	THF	34/trace/11	>99:1/-/>99:1
7	**CN**	THF	36/trace/17	>99:1/-/>99:1
8	**CN**	DCM	trace	-/-/-
9	**CN**	Toluene	trace	-/-/-
10	**CN**	acetone	29/-/10	>99:1/-/>99:1
11	**CN**	CH_3CN	23/-/14	>99:1/-/>99:1
12	**CN**	1,4-dioxane	21/trace/13	>99:1/-/>99:1
13[d]	**CN**	THF	71/trace/18	>99:1/-/>99:1
14[e]	**CN**	THF	63/trace/23	>99:1/-/>99:1
15[f]	**CN**	THF	60/trace/25	>99:1/-/>99:1

[a] Otherwise noted, reactions performed with 0.10 mmol of **1a**, 0.10 mmol of **2a,** 20 mol% base in solvent (1.0 mL) at 0 °C under air atmosphere for 12 h; [b] Isolated yields. [c] Determined by ^{1}H NMR. [d] 1.5 eq. of **1a**.. [e] 2.0 eq. of **1a**. [f] 2.5 eq. of **1a**.

First, we investigated the reactivity profile of 3-hydroxyoxindole **1a**, which was easily derived from isatin, under different reaction conditions in order to evaluate our reasoning. The oxidative coupling of *N*-benzyl-3-hydroxyoxindole **1a** easily happened to lead to the isatide **A** at room temperature under basic conditions,[19] we evaluated the new domino Michael addition-cyclization reaction at a lower temperature. As such, the model reaction of 3-hydroxyoxindole **1a** with electron-deficient α,α-dicyanoolefin **2a** was firstly carried out in the presence of K_2CO_3 in THF at 0 °C for 12 h (Table 1, entry 1). Besides oxidative coupling product **A**, the desired product **4aa** was also obtained in 30% yield with a high diastereoselectivity. Then a series of bases and organic solvents were screened for this domino reaction. However, when the stronger

bases, such as KOH, Cs_2CO_3, were used, the reaction became complicated and no main products were isolated (entries 2-3). Then the tertiary amines, such as TEA, DBU, were used as catalysts, only the oxidative coupling product **A** was isolated (entries 4-5). To our surprise, when the domino reaction was catalyzed by a milder, less basic organic catalyst quinine (**QN**), besides the desired product **4aa**, an unexpected product 1,5-cyclopent[2]ene bi-spirooxindole **5aa** was isolated and trace amount of product **A** was observed simultaneously (entry 6). With application of the organic base cinchonine (**CN**), both the yields of **4aa** and **5aa** were improved and high diastereoselectivities were also observed (entry 7). Subsequently, we investigated the effects of commonly used solvents. The domino reaction proceeded smoothly in the polar solvents (entries 10-12), while the non-polar solvents such as toluene and CH_2Cl_2, were inert to this reaction (entries 8 and 9). If the amount of *N*-benzyl-3-hydroxyoxindole **1a** is increased to 1.5 equivalents in the domino reaction, the yield was significantly improved and the total yields were up to 89% (entry 13). Continue to increase the amount of *N*-benzyl-3-hydroxyoxindole **1a**, similar results were obtained (entries 14-15). Hence, running the domino reaction in THF at 0 ^oC with 20 mol% cinchonine as the catalyst and 1.5 equivalents of **1a** appeared to be the optimal reaction conditions.

Table 2 Reaction scopes in the domino reaction of 3-hydroxyoxindoles 1 with α,α-dicyanoolefins 2 [a]

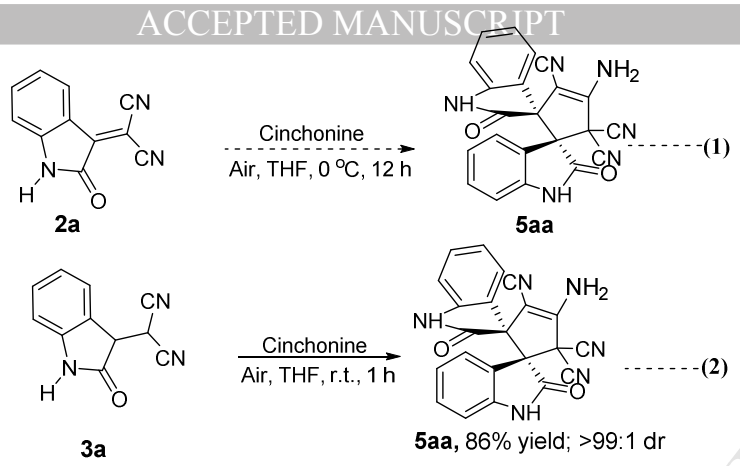


Entry	R^1	R^2 (**1**)	R^3	R^4 (**2**)	**4/5**	Yield/%[b]/dr[c]
1	Bn	H (**1a**)	H	H (**2a**)	**4aa**	71/>99:1
					5aa	18/>99:1
2	Bn	H (**1a**)	C_4H_9	H (**2b**)	**4ab**	51/>99:1
					5bb	15/>99:1
3	Bn	H (**1a**)	Bn	H (**2c**)	**4ac**	58/>99:1
					5cc	13/>99:1
4	CH_3	H (**1b**)	H	H (**2a**)	**4ba**	51/>99:1

					5aa	trace
5	CH_3	H (**1b**)	Bn	H (**2c**)	**4bc**	68/>99:1
					5cc	trace
6	C_4H_9	H (**1c**)	Bn	H (**2c**)	**4cc**	42/>99:1
					5cc	trace
7	Allyl	H (**1d**)	Bn	H (**2c**)	**4dc**	63/>99:1
					5cc	trace
8	C_6H_5CO	H (**1e**)	Bn	H (**2c**)	**4ec/5cc**	-
9	Bn	Me (**1f**)	H	Me (**2d**)	**4fd**	75/>99:1
					5dd	trace
10	Bn	Cl (**1g**)	H	Cl (**2e**)	**4ge**	63/>99:1
					5ee	11/>99:1

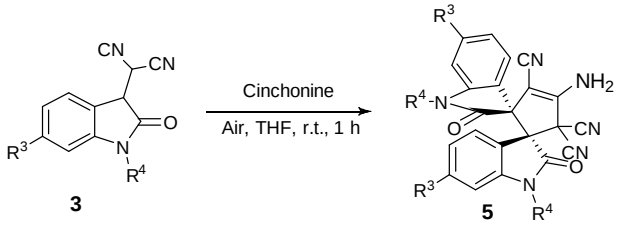
[a] Otherwise noted, reactions performed with 0.15 mmol of **1**, 0.10 mmol of **2,** 20 mol% cinchonine in THF (1.0 mL) at 0 ^{o}C under air atmosphere for 12 h. [b] Isolated yields. [c] Determined by ^{1}H NMR.

With the optimized reaction conditions in hand, we explored the scope of the domino reaction by using various 3-hydroxyoxindole derivatives **1** and electron-deficient α,α-dicyanoolefin derivatives **2**, and the results are summarized in Table 2. All the products were obtained with excellent diastereoselectivities (>99:1). α,α-Dicyanoolefin derivatives **2** that bear different substituents at the *N*-position performed well under the reaction conditions to give both products **4** and **5** (entries 1-3). It turned out that the substituents on the *N*-position of 3-hydroxyoxindole derivatives **1** had a significant influence on the domino reaction with the optimized reaction conditions (entries 4-10). Only trace amount of products **5** was obtained with other substituents on the *N*-position or C5 position of 3-hydroxyoxindole derivatives **1** (entries 4-7, 9), while the products **4** were obtained in moderate to good yields. Replace benzyl with benzoyl on the *N*-position of 3-hydroxyoxindole derivatives **1**, no products were obtained.



Having presented the domino reaction to afford the unexpected products **5**, more experiments were conducted to gain some insight into the mechanism of this domino reaction. Under the optimized reaction conditions, no reaction occurred for the electron-deficient α,α-dicyanoolefin **2a** (Eq. 1). To our surprise, the domino coupling/cyclization of 2-(2-oxoindolin-3-yl)-malononitrile **3a** took place smoothly to give unexpected product **5aa** in 86% yield when the reaction was catalyzed by cinchonine at room temperature for 1 hour (Eq. 2). Subsequently, the scope of the unexpected domino reaction was explored. As shown in Table 3, the reactions occurred smoothly to provide the structurally diverse corresponding bi-spirooxindoles **5** in moderate to excellent diastereoselectivities (>99:1) and good yields (64-86% yields, entries 1-7). The 2-(2-oxoindolin-3-yl)malononitrile derivatives **3** that bear different substituents at the C5 and *N* positions have a little effect on the yields. An alkyl at the nitrogen atom slightly improved the reactivity as well as the electron-donating substituent on the C5 position (entries 2, 4, 6). To our surprise, only trace amount of product **5aa** was observed when the reaction was carried out under argon atmosphere (entry 8).

Table 3 Reaction scopes in the domino redox/oxidative coupling/cyclization of 2-(2-oxoindolin-3-yl)-malononitriles 3[a]

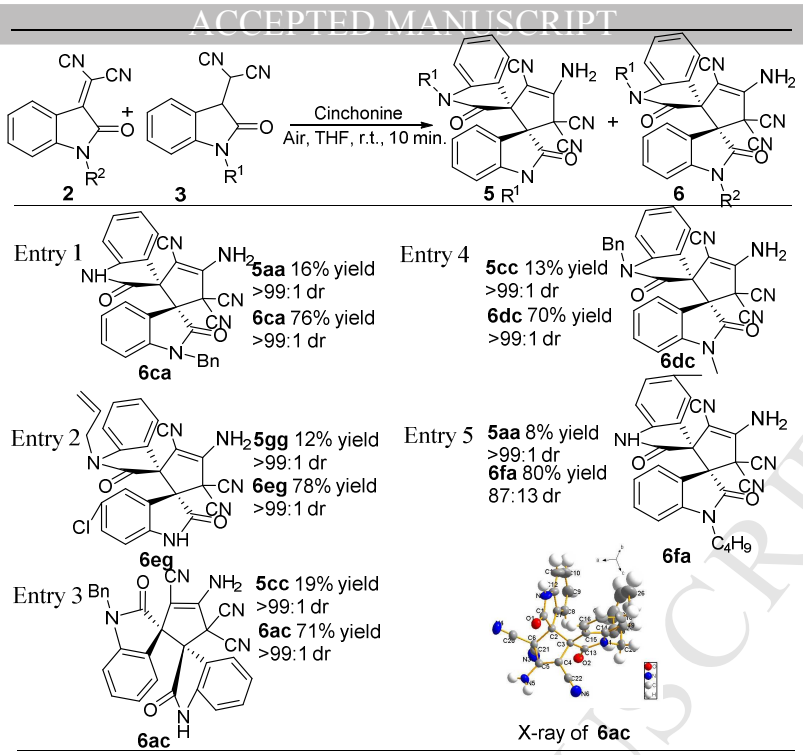


Entry	R^3	R^4 (**3**)	**5**	Yield/%[b]	dr[c]
1	H	H (**3a**)	**5aa**	86	>99:1
2	H	C_4H_9 (**3b**)	**5bb**	85	>99:1
3	H	Bn(**3c**)	**5cc**	76	>99:1
4	Me	H (**3d**)	**5dd**	83	>99:1
5	Cl	H(**3e**)	**5ee**	71	>99:1
6	H	CH_3 (**3f**)	**5ff**	83	>99:1
7	H	Allyl(**3g**)	**5gg**	64	>99:1
8[d]	H	H (**3a**)	**5aa**	trace	-

[a] Otherwise noted, reactions performed with 0.15 mmol of **3**, 20 mol% cinchonine in THF (1.0 mL) at room temperature under air atmosphere for 1 h. [b] Isolated yields. [c] Determined by ^{1}H NMR. [d] Under argon atmosphere.

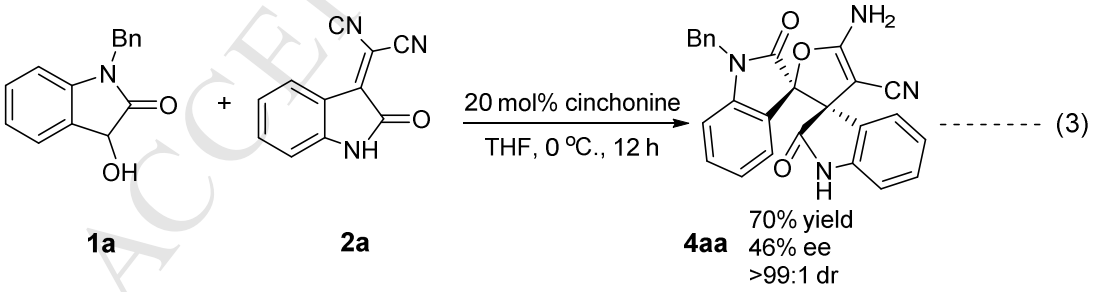
Prompted by the above results, we envisioned that the new domino reaction would be possible between electron-deficient α,α-dicyanoolefins **2** and 2-(2-oxoindolin-3-yl)-malononitriles **3** under the same reaction conditions, giving a facile protocol to both products **5** and **6** (Table 4). As such, the reaction of 2-(2-oxoindolin-3- yl)-malononitriles **3a** with electron-deficient α,α-dicyanoolefin **2c** was firstly carried out at room temperature. To our delight, we found that the reaction generally exhibited high efficiency. Both products **5aa** and **6ca** with excellent total yields were obtained in 10 minutes (Entry 1). In all cases, high yields ranging from 83 to 92% were achieved under the optimized conditions, and the rate of the reactions was very fast. Of particular interest was that excellent diastereoselectivity (>99:1) could be obtained for most of the cases except **6fa** (Entry 5, 87:13 dr).

Table 4 Reaction scopes in the domino reaction of α,α-dicyanoolefins 2 2-(2-oxoindolin-3-yl)-malononitriles 3[a, b]



[a] Otherwise noted, reactions performed with 0.10 mmol of **2**, 0.10 mmol of **3,** 20 mol% cinchonine in THF (1.0 mL) at room temperature under air atmosphere for 10 min.. [b] Isolated yields.

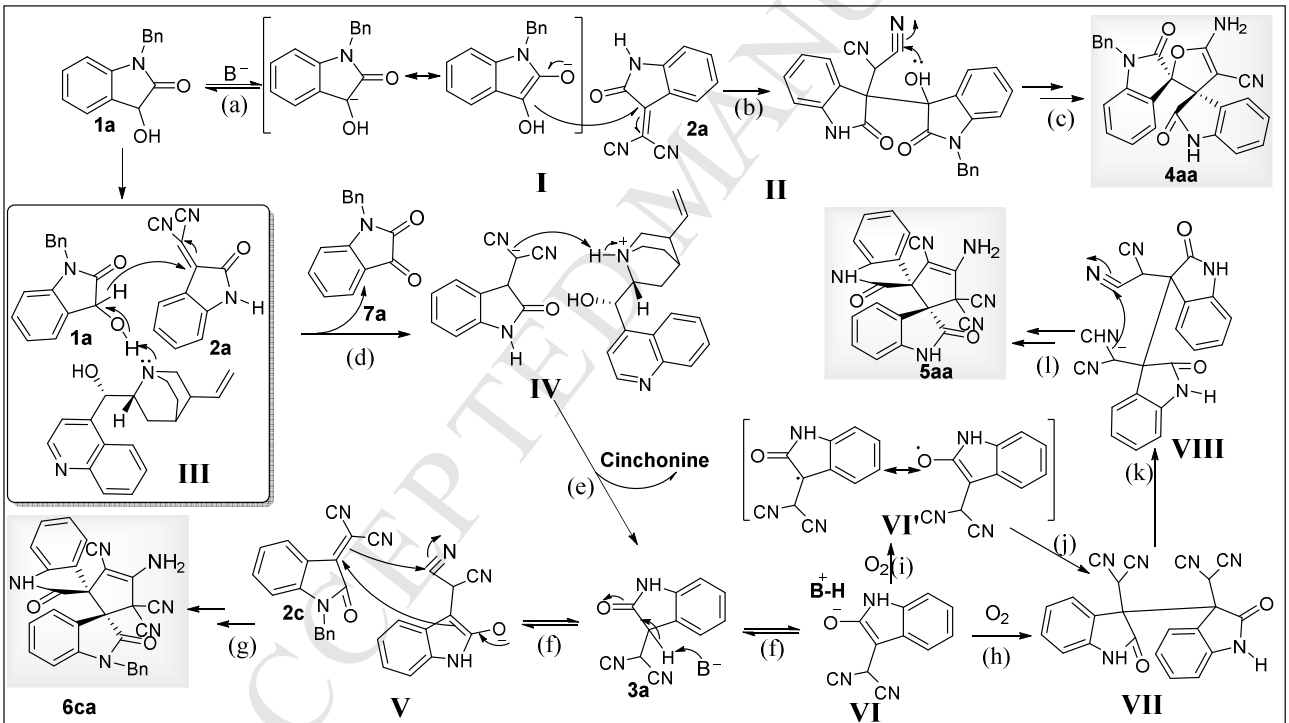
Recently, many organocatalytic asymmetric strategies have been developed for the construction of bi-spirooxindoles in an enantioselective manner.[20] A few organocatalysts have also been screened for the domino reaction (see Supporting information). However, only a moderate enantioselectivity (46% ee) was also obtained in the presence of cinchonine (Eq. 3). Asymmetric oganocatalytic the domino reaction catayzed by other novel catalysts is under way in our laboratory.



On the basis of the experimental observations and the control experiments (see supporting information, **Scheme S1**), a possible mechanism was proposed to explain the domino reaction **(Scheme 2)**. On the one hand, deprotonation of **1a** by cinchonine followed by a domino Michael/intramolecular cyclization/proton transfer to form 2,3-dihydrofuranyl bi-spirooxindole 4**aa** (a-c). On the other hand, the

N-benzyl-3-hydroxyoxindole **1a** was deprotonated by cinchonine (**III**) and the hydride transfer to the electron-deficient α,α-dicyanoolefin **2a** to produce *N*-benzyl isatin **7a** and intermediate **VI**. Subsequently, the ion **VI** acquires a proton to form **3a** (d-e). After that, the deprotonative activation of compound **3a** under basic conditions followed by a domino Michael/intramolecular cyclization/proton transfer to form compound **6ca** (f-g). Simultaneously, an unexpected oxidative coupling (an oxidative dimerization pathway or a radical process) happened to form intermediate **VII** (h-j), following a domino intramolecular cyclization/proton transfer to produce product **5aa** under base conditions (k-l). Nevertheless, the real reaction mechanism still remains to be explored.

Scheme 2 Proposed mechanisms



Conclusion

In summary, we have developed a facile and mild synthesis of bi-spirooxindole frameworks, including 2,3-dihydrofuranyl bi-spirooxindoles and 1,5-cyclopent[2]ene bi-spirooxindoles, that are potentially relevant to natural product synthesis via a Michael addition/cyclization, as well as developed an unexpected

redox/oxidative coupling/cyclization to afford 1,5-cyclopent[2]ene bi-spirooxindoles. Both domino reactions employ very simple and readily available substrates and tolerate a range of functional groups to produce substituted bi-spirooxindole frameworks in moderate to good yields with excellent diastereoselectivities. The plausible mechanisms for the Michael addition/cyclization and the unexpected oxidative coupling/cyclization were given. Further development of this reaction including studies on the reaction mechanism and scopes, is being pursued and will be reported in due course.

4. Experiment procesure

4.1 General

NMR spectra were recorded with tetramethylsilane as the internal standard. TLC was performed on glass-backed silica plates. Column chromatography was performed using silica gel (150-200 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR spectra were recorded at 600 MHz, and ^{13}C NMR spectra were recorded at 150 MHz. Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) or D6-DMSO (δ = 2.50 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.0 ppm) or D6-DMSO resonance (δ = 39.5 ppm) for ^{13}C NMR spectroscopy. Coupling constants (*J*) are given in Hz. ESI-HRMS spectrometer was measured with an ion trap mass spectrometer.

4.1 **Typical procedure for the synthesis compounds 4 and 5.**

(Table 2, entry 1) Catalyst **cinchonine** (5.88 mg, 20 mol%) was added to the solution of *N*-benzyl-3-hydroxyoxindole **1a** (36.0 mg, 0.15 mmol) and α,α-dicyanoolefin **2a** (20.0 mg, 0.10 mmol) in THF (1.0 mL) at 0 ^{o}C under air atmosphere. The mixture was stirred at 0 ^{o}C for 12 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **4aa** (30.0 mg) and **5aa** (7.0 mg)**.**

5'-Amino-1-benzyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4aa**); (30.0 mg) Yield 71%; ^{1}H NMR (400 MHz, D6-DMSO) δ 10.44 (s, 1H), 7.99 (s, 2H), 7.62 (d, *J* = 7.6 Hz, 1H), 7.38 (d, *J*

= 7.6 Hz, 1H), 7.31 – 7.20 (m, 2H), 7.17 (dd, *J* = 10.8, 7.2 Hz, 3H), 7.05 (s, 1H), 6.94 (s, 1H), 6.80 – 6.70 (m, 3H), 6.60 (d, *J* = 7.9 Hz, 1H), 4.95 (d, *J* = 16.0 Hz, 1H), 4.49 (d, *J* = 16.1 Hz, 1H).^{13}C NMR (101 MHz, D6-DMSO) δ 177.5, 171.7, 171.0, 143.8, 143.5, 135.3, 132.2, 130.4, 129.0, 127.7, 127.5, 127.3, 127.1, 127.0, 126.8, 123.9, 123.4, 122.7, 121.7, 118.1, 110.3, 88.8, 63.2, 53.5, 43.1. IR (KBr) cm^{-1} 3413, 3325, 3290, 2196, 1721, 1567, 1615, 1468, 754, 695； ESI-HRMS: calcd. for $C_{26}H_{18}N_4O_3$ + H 435.1452, found 435.1457; ee = 46%; $[\alpha]^{20}_D$ = -25.4 (c = 1.10, MeOH) The enantiomeric ratio was determined by HPLC on Chiralpak OJ column (30% 2-propanol/hexane, 1 mL/min), t_{major} = 19.548 min, t_{minor} = 36.789 min.

5'-Amino-1-benzyl-1''-butyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4ab**); (25.0 mg) Yield 51%; ^{1}H NMR (600 MHz, D6-DMSO) δ 7.98 (s, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.5 Hz, 1H), 7.36 – 7.31 (m, 1H), 7.24 (td, *J* = 7.8, 1.0 Hz, 1H), 7.18 (d, *J* = 7.2 Hz, 1H), 7.15 (t, *J* = 7.3 Hz, 2H), 7.01 (dt, *J* = 20.9, 7.6 Hz, 2H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.73 (d, *J* = 7.3 Hz, 2H), 6.58 (d, *J* = 7.9 Hz, 1H), 4.88 (d, *J* = 16.0 Hz, 1H), 4.48 (d, *J* = 16.1 Hz, 1H), 3.60 (dd, *J* = 13.8, 7.4 Hz, 1H), 3.37 – 3.29 (m, 2H), 1.27 – 1.10 (m, 4H), 0.67 (t, *J* = 7.3 Hz, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 175.6, 171.8, 171.0, 144.5, 143.7, 135.3, 132.1, 130.6, 128.9, 127.7, 127.4, 127.1, 126.7, 123.4, 123.1, 123.2, 121.5, 117.8, 110.2, 109.4, 89.0, 62.8, 53.3, 43.1, 29.4, 19.5, 14.1. IR (KBr) cm^{-1} 3404, 3305, 2971, 2931, 1678, 1640, 1616, 1094, 698, 580; ESI-HRMS: calcd. for $C_{30}H_{26}N_4O_3$ + H 491.2078, found 491.2069.

5'-Amino-1,1''-dibenzyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4ac**); (30.1 mg) Yield 58%; ^{1}H NMR (600 MHz, D6-DMSO) δ 8.05 (s, 2H), 7.56 (d, *J* = 7.6 Hz, 1H), 7.42 (d, *J* = 7.5 Hz, 1H), 7.31 (td, *J* = 7.8, 1.2 Hz, 1H), 7.22 (td, *J* = 7.8, 1.2 Hz, 1H), 7.16 – 7.10 (m, 3H), 7.08 (d, *J* = 7.7 Hz, 1H), 7.07 – 7.03 (m, 2H), 6.98 (ddd, *J* = 5.7, 4.4, 2.3 Hz, 2H), 6.72 (d, *J* = 7.5 Hz, 2H), 6.68 (d, *J* = 7.5 Hz, 2H), 6.65 (d, *J* = 7.9 Hz, 1H), 6.62 (d, *J* = 7.9 Hz, 1H), 4.94 (d, *J* = 16.1 Hz, 1H), 4.89 (d, *J* = 16.1 Hz, 1H), 4.57 (d, *J* = 16.2 Hz, 1H), 4.52 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (150 MHz, D6-DMSO) δ 175.9, 171.9, 171.0, 145.0, 143.8, 135.5, 135.2, 132.2, 130.6, 130.5, 129.6, 128.9, 127.7, 127.5, 127.1, 126.8,125.9, 125.3, 124.8,

124.4, 123.7, 123.3, 121.7, 117.8, 110.4, 110.1, 89.0, 63.1, 53.5, 43.1. .IR (KBr) cm^{-1} 3415, 3325, 3296, 2196, 1720, 1568, 1615, 1470, 756, 699; ESI-HRMS: calcd. for $C_{33}H_{24}N_4O_3$ + H 525.1921, found 525.1917.

5'-Amino-1-methyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4ba**); (18.2 mg) Yield 51%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.43 (s, 1H), 7.94 (s, 2H), 7.59 (d, *J* = 7.5 Hz, 1H), 7.39 (t, *J* = 7.7 Hz, 1H), 7.33 (d, *J* = 7.6 Hz, 1H), 7.20 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 6.99 (t, *J* = 7.6 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 6.68 (d, *J* = 7.7 Hz, 1H), 2.92 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 177.3, 171.7, 171.1, 144.6, 143.3, 132.2, 130.4, 126.9, 126.2, 123.7, 123.2, 122.3, 121.4, 118.1, 110.2, 109.5, 88.7, 63.0, 53.6, 26.2. IR (KBr) cm^{-1} 3334, 3172, 2188, 1720, 1665, 1612, 1470, 1102, 753, 539; ESI-HRMS: calcd. for $C_{20}H_{14}N_4O_3$ +Na 381.0958, found 381.0951.

5'-Amino-1''-benzyl-1-methyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4bc**); (30.5 mg) Yield 68%; ^{1}H NMR (600 MHz, D6-DMSO) δ 8.04 (s, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.41 (d, *J* = 7.3 Hz, 2H), 7.19 – 7.09 (m, 4H), 7.02 (t, *J* = 7.7 Hz, 2H), 6.89 (d, *J* = 7.9 Hz, 1H), 6.75 (d, *J* = 7.4 Hz, 2H), 6.58 (d, *J* = 7.9 Hz, 1H), 4.95 (d, *J* = 16.1 Hz, 1H), 4.56 (d, *J* = 16.1 Hz, 1H), 2.87 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 175.8, 172.0, 171.2, 144.7, 143.7, 138.6, 135.6, 132.2, 130.5, 128.9, 127.6, 127.1, 127.0, 126.2, 124.7, 123.6, 123.4, 123.3, 123.1, 121.5, 110.9, 109.9, 109.7, 88.9, 62.9, 55.3, 53.8, 43.2, 26.3. IR (KBr) cm^{-1} 3394, 3298, 2189, 1784, 1640, 1614, 1095, 1007, 597; ESI-HRMS: calcd. for $C_{27}H_{20}N_4O_3$+H 449.1608, found 449.1605.

5'-Amino-1''-benzyl-1-butyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4cc**); (20.6 mg) Yield 42%; ^{1}H NMR (600 MHz, D6-DMSO) δ 7.98 (s, 2H), 7.53 (d, *J* = 7.6 Hz, 1H), 7.46 – 7.36 (m, 2H), 7.15 (ddd, *J* = 23.0, 11.3, 4.4 Hz, 5H), 7.06 – 6.91 (m, 3H), 6.70 (d, *J* = 7.4 Hz, 2H), 6.56 (d, *J* = 7.8 Hz, 1H), 4.92 (d, *J* = 16.1 Hz, 1H), 4.54 (d, *J* = 16.1 Hz, 1H), 3.57 (dd, *J* = 14.5, 6.9 Hz, 1H), 3.32 – 3.24 (m, 1H), 1.61 – 1.11 (m, 4H), 0.68 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (150 MHz, D6-DMSO) δ 175.9, 171.7, 171.1, 144.4, 143.7, 135.6, 132.3, 130.3, 128.9, 127.6, 127.3, 127.0, 126.7, 123.3, 123.2, 123.0, 121.6,117.3, 109.8,

88.7, 63.0, 53.5, 43.1, 29.3, 19.6, 14.0. IR (KBr) cm^{-1} 3396, 3335, 2188, 1725, 1618, 1613, 1513, 1176, 753, 700; ESI-HRMS: calcd. for $C_{30}H_{26}N_4O_3$ + H 491.2078, found 491.2071.

1-Allyl-5'-amino-1''-methyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4dc**); (29.9 mg) Yield 63%; ^{1}H NMR (600 MHz, D6-DMSO) δ 7.97 (s, 2H), 7.50 (d, *J* = 7.2 Hz, 1H), 7.38 – 7.21 (m, 4H), 7.03 (dt, *J* = 20.9, 7.6 Hz, 2H), 6.86 (d, *J* = 7.8 Hz, 1H), 6.75 (d, *J* = 7.9 Hz, 1H), 5.49 – 5.40 (m, 1H), 4.88 (dd, *J* = 10.4, 1.0 Hz, 1H), 4.48 (dd, *J* = 17.3, 1.0 Hz, 1H), 4.30 – 4.22 (m, 1H), 3.90 (dd, *J* = 16.7, 5.3 Hz, 1H), 2.91 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 175.7, 171.7, 171.2, 146.2, 144.6, 143.7, 132.2, 131.0, 130.5, 126.6, 126.2, 123.7, 123.3, 123.1, 122.9, 121.1, 120.7, 119.3, 118.6, 117.9, 117.3, 110.6, 110.2, 109.3, 88.8, 62.9, 52.9, 41.7, 26.4. IR (KBr) cm^{-1} 3397, 3335, 2188, 1727, 1618, 1615, 1513, 1176, 753, 700; ESI-HRMS: calcd. for $C_{29}H_{22}N_4O_3$ + H 475.1765, found 475.1761.

5'-Amino-1-benzyl-5'',6-dimethyl-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4fd**); (37.0 mg) Yield 80%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.36 (s, 1H), 7.90 (s, 2H), 7.42 (s, 1H), 7.18 (dd, *J* = 15.7, 8.3 Hz, 2H), 7.12 (t, *J* = 7.5 Hz, 2H), 7.06 (d, *J* = 8.0 Hz, 2H), 6.71 (d, *J* = 7.5 Hz, 2H), 6.60 (d, *J* = 7.8 Hz, 1H), 6.47 (d, *J* = 8.0 Hz, 1H), 4.97 (d, *J* = 16.2 Hz, 1H), 4.43 (d, *J* = 16.2 Hz, 1H), 2.21 (s, 3H), 2.08 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 177.5, 171.7, 171.0, 141.6, 141.0, 135.5, 134.6, 133.5, 132.3, 131.5, 130.7, 128.9, 127.9, 127.6, 126.8, 125.9, 125.1, 124.0, 121.7, 118.2, 110.0, 109.9, 89.0, 63.2, 53.6, 43.0, 21.1; IR (KBr) cm^{-1} 3416, 3340, 2193, 1719, 1670, 1614, 1468, 1178, 1008, 749, 699, 500; ESI-HRMS: calcd. for $C_{28}H_{22}N_4O_3$ + H 463.1765, found 463.1769.

5'-Amino-1-benzyl-5'',6-dichloro-2,2''-dioxodispiro[indoline-3,2'-furan-3',3''-indoline]-4'-carbonitrile (**4ge**); (31.6 mg) Yield 63%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.80 (s, 1H), 8.12 (s, 2H), 7.55 (d, *J* = 2.2 Hz, 1H), 7.42 (dd, *J* = 8.5, 2.2 Hz, 1H), 7.38 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.31 (d, *J* = 2.1 Hz, 1H), 7.23 – 7.16 (m, 3H), 6.78 (dd, *J* = 12.0, 7.8 Hz, 3H), 6.72 (d, *J* = 8.5 Hz, 1H), 5.05 (d, *J* = 16.1 Hz, 1H), 4.49 (d, *J* = 16.1 Hz, 1H).^{13}C NMR (150 MHz, D6-DMSO) δ 177.1, 171.0, 170.8, 142.8, 142.3, 134.9, 132.3, 130.8, 129.1,

128.0, 127.7, 127.2, 127.1, 127.0, 126.9, 126.8, 125.6, 123.2, 112.2, 112.1, 88.0, 63.3, 52.9, 43.3.IR (KBr) cm^{-1} 3381, 3274, 2187, 1718, 1670, 1604, 1424, 1177, 1012, 750, 536; ESI-HRMS: calcd. for $C_{26}H_{16}Cl_2N_4O_3$+ H 503.0672, found 503.0679.

1,1'-Dibenzyl-3,3'-dihydroxy-[3,3'-biindoline]-2,2'-dione (**A**); (21.4 mg) Yield 45%; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.69 (d, *J* = 7.6 Hz, 1H), 7.59 (d, *J* = 7.6 Hz, 1H), 7.16 – 7.11 (m, 2H), 7.09 (dd, *J* = 11.4, 7.0 Hz, 2H), 6.98 (dt, *J* = 10.9, 7.7 Hz, 4H), 6.93 (t, *J* = 7.7 Hz, 1H), 6.86 (t, *J* = 7.7 Hz, 1H), 6.50 (d, *J* = 7.6 Hz, 4H), 6.40 (d, *J* = 7.8 Hz, 1H), 6.36 (d, *J* = 7.9 Hz, 1H), 5.91 (s, 2H), 5.13 (dd, *J* = 30.6, 16.1 Hz, 2H), 4.32 (d, *J* = 16.2 Hz, 1H), 4.23 (d, *J* = 16.1 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 172.1, 170.6, 143.8, 143.8, 134.6, 134.2, 131.5, 130.1, 128.7, 128.6, 127.9, 127.3, 127.1, 126.3, 126.2, 123.7, 123.5, 122.9, 121.6, 109.7, 109.6, 90.3, 43.8; ESI-HRMS: calcd. for $C_{30}H_{24}N_2O_4$+ H 477.1809, found 477.1801.

4.2 **Typical procedure for the synthesis compounds 5.**

(Table 3, entry 1) Catalyst **cinchonine** (5.88 mg, 20 mol%) was added to the solution of 2-(2-oxoindolin-3-yl)-malononitrile **3a** (40.0 mg, 0.20 mmol) in THF (1.0 mL) at room temperature under air atmosphere. The mixture was stirred for 1 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **5aa** (33.7 mg)**.**

4'-Amino-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbonitrile (**5aa**); (33.7 mg) Yield 86%; ^{1}H NMR (600 MHz, D6-DMSO) δ 11.27 (s, 1H), 10.81 (s, 1H), 8.41 (s, 2H), 7.75 (d, *J* = 7.8 Hz, 1H), 7.42 – 7.34 (m, 2H), 7.24 (dd, *J* = 7.7, 1.1 Hz, 1H), 7.16 (dd, *J* = 7.8, 0.8 Hz, 1H), 7.04 (dd, *J* = 7.7, 0.8 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.71 (d, *J* = 7.7 Hz, 1H). ^{13}C NMR (150 MHz, D6-DMSO) δ 176.7, 173.0, 153.8, 143.3, 143.2, 132.0, 131.0, 127.0, 126.9, 123.4, 123.0, 122.9, 119.8, 115.4, 112.6, 111.8, 110.9, 110.6, 76.3, 62.8, 62.4, 46.8. IR (KBr) cm^{-1} 3416, 3319, 3294, 2193, 1711, 1568, 1616, 1468, 760, 693; ESI-HRMS: calcd. for $C_{22}H_{12}N_6O_2$ + Na 415.0914, found 415.0911.

4'-amino-1,1''-dibutyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbo

nitrile **(5bb)**; (42.8 mg) Yield 85%; ^{1}H NMR (600 MHz, D6-DMSO) δ 8.49 (s, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.42 (t, *J* = 7.6 Hz, 1H), 7.33 (d, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.05 (t, *J* = 7.9 Hz, 2H), 6.91 (d, *J* = 7.7 Hz, 1H), 3.64 – 3.54 (m, 3H), 3.50 (dd, *J* = 13.9, 6.8 Hz, 1H), 1.36 (ddd, *J* = 22.5, 14.8, 7.5 Hz, 4H), 1.21 – 1.12 (m, 2H), 1.05 (ddd, *J* = 30.7, 13.9, 7.0 Hz, 2H), 0.81 (dd, *J* = 13.3, 6.5 Hz, 6H).^{13}C NMR (150 MHz, D6-DMSO) δ 174.9, 171.1, 154.0, 144.2, 144.0, 132.2, 131.2, 126.9, 126.7, 123.5, 123.3, 122.5, 118.9, 115.2, 112.3, 111.8, 110.3, 109.9, 76.1, 62.22, 61.9, 60.2, 46.9, 29.4, 29.2, 19.8, 19.8, 14.0, 113.9. IR (KBr) cm^{-1} 3417, 3322, 3290, 2195, 1720, 1565, 1617, 1464, 758, 697; ESI-HRMS: calcd. for $C_{30}H_{28}N_6O_2$ + Na 527.2166, found 527.2167.

4'-Amino-1,1''-dibutyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbo nitrile (**5cc**); (43.5 mg) Yield 76%; ^{1}H NMR (400 MHz, D6-DMSO) δ 8.59 (s, 2H), 7.74 (d, *J* = 7.6 Hz, 1H), 7.35 (d, *J* = 7.2 Hz, 2H), 7.26 – 7.18 (m, 7H), 7.11 – 7.04 (m, 3H), 7.01 (dd, *J* = 9.2, 5.7 Hz, 3H), 6.84 (d, *J* = 7.9 Hz, 1H), 6.77 (d, *J* = 7.9 Hz, 1H), 4.98 – 4.76 (m, 4H). ^{13}C NMR (150 MHz, D6-DMSO) δ 175.3, 171.4, 154.1, 143.8, 143.5, 135.5, 135.0, 132.1, 131.2, 129.0, 128.2, 128.5, 128.1, 127.6, 127.6, 127.5, 127.4, 126.9, 126.5, 124.1, 123.9, 122.5, 118.9, 115.2, 112.4, 111.8, 111.0, 110.5, 76.1, 62.6, 62.2, 47.1, 43.5 (d, *J* = 7.4 Hz). IR (KBr) cm^{-1} 3417, 3320, 3296, 2191, 1727, 1565, 1618, 1464, 755, 693; ESI-HRMS: calcd. for $C_{36}H_{24}N_6O_2$ + Na 595.1853, found 595.1844.

4'-Amino-5,5''-dimethyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricar bonitrile (**5dd**) (Table 3, entry 4); (34.9 mg) Yield 83%; ^{1}H NMR (400 MHz, D6-DMSO) δ 11.18 (s, 1H), 10.72 (s, 1H), 8.35 (s, 2H), 7.54 (s, 1H), 7.18 – 7.09 (m, 2H), 7.00 (d, *J* = 7.8 Hz, 1H), 6.67 (d, *J* = 7.9 Hz, 1H), 6.56 (d, *J* = 7.9 Hz, 1H), 2.26 (s, 3H), 2.21 (s, 3H). ^{13}C NMR (150 MHz, D6-DMSO) δ 176.7, 173.1, 153.8, 140.9, 140.7, 132.3, 131.9, 131.6, 131.3, 127.6, 127.5, 123.64, 120.0, 115.5, 112.69, 111.9, 110.6, 110.3, 76.4, 62.8, 62.4, 55.3, 46.9, 21.3. IR (KBr) cm^{-1} 3416, 33203, 3292, 2194, 1725, 1569, 1619, 1465, 757, 693; ESI-HRMS: calcd. for $C_{24}H_{16}N_6O_2$ + Na 443.1227, found 443.1219.

4'-Amino-5,5''-dichloro-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarb onitrile (**5ee**); (32.7 mg) Yield 71%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.95 (s, 1H), 10.82 (s, 1H), 8.11 (s, 2H), 7.50 (s, 1H), 7.42 (d, *J* = 8.3 Hz, 1H), 7.34 (d, *J* = 7.2 Hz, 2H), 6.84 – 6.73 (m, 2H). ^{13}C NMR (150 MHz, D6-DMSO) δ 177.09, 172.79, 170.98, 142.22 (d, *J* = 10.9 Hz), 132.31, 130.61, 127.25, 126.76 – 126.29 (m), 125.78, 123.55, 117.73, 112.51, 111.97, 88.33, 63.08, 60.24, 52.93. ^{13}C NMR (150 MHz, D6-DMSO) δ 177.0, 172.7, 170.9, 142.2, 142.1, 132.3, 130.6, 127.2, 126.7, 126.6, 125.7, 123.5, 117.7, 112.5, 111.9, 88.3, 63.0, 60.2, 52.9; IR (KBr) cm^{-1} 3413, 3327, 3293, 2195, 1727, 1561, 1619, 1461, 755, 696; ESI-HRMS: calcd. for $C_{22}H_{10}Cl_2N_6O_2$ + Na 483.0135, found 483.0127.

4'-Amino-1,1''-dimethyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricar bonitrile (**5ff**); (34.9 mg) Yield 83%; ^{1}H NMR (600 MHz, D6-DMSO) δ 8.60 (s, 2H), 7.47 (td, *J* = 7.8, 1.0 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.25 (td, *J* = 7.8, 1.1 Hz, 2H), 7.19 (dd, *J* = 7.9, 7.3 Hz, 1H), 7.03 (d, *J* = 7.9 Hz, 1H), 6.92 (d, *J* = 7.8 Hz, 1H), 6.73 (t, *J* = 7.6 Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 3.05 (s, 3H), 3.00 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 173.5, 168.0, 154.5, 144.70, 143.6, 132.1, 131.0, 126.4, 125.4, 123.0, 122.1, 115.2, 111.9, 110.6, 110.2, 109.2, 75.8, 62.7, 62.3, 47.1, 27.1, 27.0; IR (KBr) cm^{-1} 3416, 3321, 3289, 2191, 1720, 1564, 1612, 1469, 755, 690; ESI-HRMS: calcd. for $C_{24}H_{16}N_6O_2$+H 421.1408, found 421.1411.

1,1''-Diallyl-4'-amino-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbo nitrile (**5gg**); (30.2 mg) Yield 64%; ^{1}H NMR (400 MHz, D6-DMSO) δ 8.52 (s, 2H), 7.71 (d, *J* = 7.4 Hz, 1H), 7.42 (td, *J* = 7.9, 0.9 Hz, 1H), 7.29 (t, *J* = 7.8 Hz, 2H), 7.17 (t, *J* = 7.5 Hz, 1H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.93 (d, *J* = 7.9 Hz, 1H), 6.80 (d, *J* = 7.8 Hz, 1H), 5.56 (ddd, *J* = 17.0, 10.7, 5.4 Hz, 2H), 5.01 (ddd, *J* = 10.4, 5.4, 1.0 Hz, 2H), 4.75 (ddd, *J* = 27.1, 17.3, 1.0 Hz, 2H), 4.36 – 4.08 (m, 4H). ^{13}C NMR (101 MHz, D6-DMSO) δ 174.7, 171.0, 154.0, 143.7, 143.5, 132.2, 131.1 (d, *J* = 12.1 Hz), 130.6, 126.9, 126.8, 123.9, 123.6, 122.4, 118.8, 118.1, 117.5, 115.2, 112.3, 111.7, 110.8, 110.4, 75.8, 62.4, 62.2, 46.9, 42.3, 42.2; IR (KBr) cm^{-1} 3413, 3325, 3294, 2198, 1728, 1563, 1613, 1466, 757, 691; ESI-HRMS: calcd. for $C_{28}H_{20}N_6O_2$ + Na 495.1540,

found 495.1539.

4.3 **Typical procedure for the synthesis compounds 6.**

(Table 4, entry 1) Catalyst **cinchonine** (5.88 mg, 20 mol%) was added to the solution of α,α-dicyanoolefin **2c** (28.5 mg, 0.10 mmol) and 2-(2-oxoindolin-3-yl)-malononitrile **3a** (20 mg, 0.10 mmol) in THF (1.0 mL) at 0 ^{o}C. The mixture was stirred at 0 ^{o}C under air atmosphere for 12 h. Then the reaction mixture was concentrated and the residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 4:1) to give **6ca** (36.6 mg)**.**

4'-Amino-1-benzyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbonitrile (**6ca**); (36.6 mg) Yield 76%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.83 (s, 1H), 8.49 (s, 2H), 7.81 (d, *J* = 7.7 Hz, 1H), 7.35 (t, *J* = 7.7 Hz, 1H), 7.28 – 7.15 (m, 7H), 7.04 (d, *J* = 6.9 Hz, 2H), 6.92 (t, *J* = 7.6 Hz, 1H), 6.80 (d, *J* = 7.9 Hz, 1H), 6.69 (d, *J* = 7.7 Hz, 1H), 4.90 (d, *J* = 15.9 Hz, 1H), 4.82 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (150 MHz, D6-DMSO) δ 175.2, 171.3, 154.1, 144.3, 143.8, 135.5, 132.2, 131.3, 129.0, 127.95, 127.4, 126.7, 126.4, 124.0, 123.7, 122.6, 118.8, 115.2, 112.4, 111.9, 110.5, 110.3, 62.6, 62.2, 46.8, 43.5; IR (KBr) cm^{-1} 3417, 3326, 3297, 2198, 1724, 1565, 1619, 1463, 756, 693; ESI-HRMS: calcd for $C_{29}H_{18}N_6O_2$ + Na 505.1383, found 505.1379.

*4'-Amino-1''-benzyl-1-methyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbonitrile (**6dc**)*; (34.7 mg) Yield 70%; ^{1}H NMR (600 MHz, D6-DMSO) δ 8.57 (s, 2H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.46 (d, *J* = 7.7 Hz, 1H), 7.35 (d, *J* = 7.6 Hz, 1H), 7.23 (dd, *J* = 10.5, 7.9 Hz, 4H), 7.09 (dd, *J* = 14.4, 6.6 Hz, 2H), 7.07 – 7.03 (m, 2H), 7.02 (d, *J* = 4.1 Hz, 2H), 6.74 (d, *J* = 7.6 Hz, 1H), 4.84 (q, *J* = 15.9 Hz, 2H), 3.07 (s, 3H).^{13}C NMR (150 MHz, D6-DMSO) δ 175.2, 171.3, 154.1, 144.3, 143.8, 135.5, 132.2, 131.3, 129.0, 127.9, 127.4, 126.7, 126.4, 124.0, 123.7, 122.6, 118.8, 115.2, 112.4, 111.9, 110.5, 110.3, 62.6, 62.2, 46.8, 43.5, 26.8. IR (KBr) cm^{-1} 3418, 3316, 3288, 2187, 1719, 1558, 1619, 1459, 750, 701; ESI-HRMS: calcd for $C_{30}H_{20}N_6O_2$ + H 497.1721, found 497.1713.

1''-Allyl-4'-amino-5-chloro-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tri carbonitrile (**6eg**); (36.0 mg) Yield 78%; ^{1}H NMR (600 MHz, D6-DMSO) δ 11.54 (s, 1H), 8.60 (s, 2H), 7.65 (s, 1H), 7.47 (dd, *J* = 20.7, 8.0 Hz, 2H), 7.38 (t, *J* = 7.7 Hz, 1H), 7.17 (t, *J* = 7.6 Hz, 1H), 6.90 (dd, *J* = 13.8, 8.1 Hz, 2H), 5.69 (ddd, *J* = 15.5, 9.7, 4.5 Hz, 1H), 5.09 (d, *J* = 10.4 Hz, 1H), 4.74 (d, *J* = 17.2 Hz, 1H), 4.49 (d, *J* = 16.5 Hz, 1H), 4.22 – 4.10 (m, 1H). ^{13}C NMR (150 MHz, D6-DMSO) δ 174.7, 172.6, 153.9, 143.7, 142.1, 132.1, 131.4, 130.9, 127.3, 127.2, 126.7, 123.9, 122.4, 121.4, 117.3, 115.1, 112.6, 112.2, 111.7, 110.4, 75.7, 62.3, 62.1, 46.7, 42.2; IR (KBr) cm^{-1} 3420, 3317, 3285, 2187, 1724, 1560, 1621, 1459, 761, 702; ESI-HRMS: calcd. for $C_{25}H_{15}ClN_6O_2$ + H 467.1018, found 467.1011.

4'-Amino-1''-benzyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tricarbonitrile (**6ac**) (34.2 mg) Yield 71%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.47 (s, 1H), 7.64 (s, 2H), 6.80 (d, *J* = 7.7 Hz, 1H), 6.58 (dd, *J* = 7.7, 0.7 Hz, 1H), 6.52 (td, *J* = 7.8, 1.1 Hz, 1H), 6.43 – 6.31 (m, 5H), 6.23 (td, *J* = 7.7, 0.8 Hz, 1H), 6.18 – 6.14 (m, 3H), 5.98 (d, *J* = 7.8 Hz, 1H), 5.88 (d, *J* = 7.9 Hz, 1H), 1.69 – 1.66 (m, 1H). ^{13}C NMR (151 MHz, D6-DMSO) δ 175.3, 173.0, 154.1, 143.8, 143.1, 135.4, 132.1, 131.2, 129.0, 127.9, 127.4, 127.1, 126.8, 123.8, 123.3, 122.8, 119.6, 115.2, 112.5, 111.9, 111.1, 110.4, 76.36, 62.4, 55.2, 46.9, 43.5, 40.1. (KBr) cm^{-1} 3422, 3329, 3288, 2181, 1716, 1617, 1571, 1460, 757, 695; ESI-HRMS: calcd for $C_{29}H_{18}N_6O_2$ + H 483.1564, found 483.1567.

4'-Amino-1-butyl-5''-methyl-2,2''-dioxodispiro[indoline-3,1'-cyclopentane-2',3''-indolin]-3'-ene-3',5',5'-tri carbonitrile (**6fa**); (37.0 mg) Yield 80%; ^{1}H NMR (600 MHz, D6-DMSO) δ 10.71 (s, 1H), 8.43 (s, 2H), 7.79 (d, *J* = 7.4 Hz, 1H), 7.46 (d, *J* = 7.5 Hz, 1H), 7.21 (d, *J* = 7.4 Hz, 1H), 7.08 (s, 2H), 7.01 (d, *J* = 7.1 Hz, 1H), 6.59 – 6.53 (m, 1H), 3.70 – 3.51 (m, 2H), 2.22 (s, 3H), 1.36 (s, 2H), 1.21 – 1.06 (m, 2H), 0.89 – 0.75 (m, 3H). ^{13}C NMR (150 MHz, D6-DMSO) δ 176.6, 171.2, 153.8, 144.1, 140.8, 132.2, 131.5, 131.3, 127.5, 126.8, 123.6, 123.2, 119.2, 115.5, 112.4, 111.8, 110.4, 110.3, 76.3, 62.8, 61.9, 46.9, 29.4, 21.2, 19.8, 14.0. IR (KBr) cm^{-1} 3418, 3324, 3297, 2189, 1725, 1559, 1614, 1458, 760, 701; ESI-HRMS: calcd. for $C_{27}H_{22}N_6O_2$ + Na

485.1696, found 485.1693.

1-Benzylindoline-2,3-dione (**7a**) 18.9 mg, yield 8%; The ^{1}H NMR spectra agreed well with the corresponding literature values.[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, *J* = 7.4 Hz, 1H), 7.48 (td, *J* = 7.9, 1.1 Hz, 1H), 7.35 (d, *J* = 4.6 Hz, 5H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 4.94 (s, 2H).

5. Supplementary data

Supplementary data (^{1}H NMR, ^{13}C NMR spectra and X-ray structural data for **4aa** and **6ac**) associated with this article can be found in the online version, at XXXX.

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