JOC The Journal of Organic Chemistry

Note

pubs.acs.org/joc

Tandem Michael Addition–Ring Transformation Reactions of 3-Hydroxyoxindoles/3-Aminooxindoles with Olefinic Azlactones: Direct Access to Structurally Diverse Spirocyclic Oxindoles

Bao-Dong Cui,[†,§] Jian Zuo,[†,§] Jian-Qiang Zhao,[†,§] Ming-Qiang Zhou,[†,§] Zhi-Jun Wu,[‡] Xiao-Mei Zhang,[†] and Wei-Cheng Yuan*[,†]

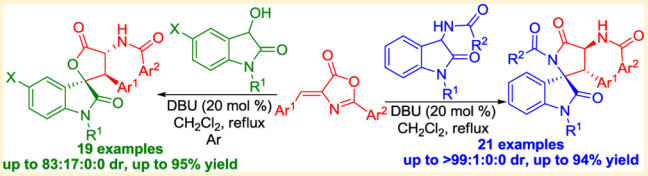
[†]National Engineering Research Center of Chiral Drugs, Chengdu Institute of Organic Chemistry, Chinese Academy of Sciences, Chengdu 610041, China

[‡]Chengdu Institute of Biology, Chinese Academy of Sciences, Chengdu 610041, China

[§]University of the Chinese Academy of Sciences, Beijing 100049, China

Supporting Information

ABSTRACT: An efficient method for the direct construction of two classes of spirocyclic oxindoles by the reactions of 3-hydroxyoxindoles/3-aminooxindoles and (*Z*)-olefinic azlactones through a tandem Michael addition–ring transformation process has been developed. With DBU as the catalyst, a range of spiro-butyrolactoneoxindoles and spiro-butyrolactamoxindoles, containing an oxygen or a nitrogen heteroatom, respectively, in the spiro stereocenter, were smoothly obtained with good to excellent diastereoselectivities in high yields.



The spirocyclic oxindole core is represented in some natural and unnatural compounds possessing important biological activities.[1] It has been shown that a defined spatial arrangement of the structural element greatly influences the properties of those compounds.[2] Accordingly, there has been a powerful inner impetus in organic chemists to develop creative approaches to access spirocyclic oxindoles, and a lot of methods for their generation have been designed.[3] Potentially promising skeletons are those containing a heteroatom (especially N or O) in the spiro stereocenter at the C3 position of the oxindole because of their importance for the synthesis of medicinally important compounds.[4,5] However, most of the studies have mainly focused on the synthesis of spirocyclic oxindoles bearing an all-carbon quaternary stereocenter at the C3 position of the oxindole. In contrast, the construction of spirocyclic oxindoles bearing a heteroatom at the C3 position is in need of further development.[6] Because of the correlation between molecular structure and biological activity,[7] it is strongly desired to develop an efficient method for the construction of spirocyclic oxindoles bearing a heteroatom at the spiro stereocenter.

We recently demonstrated that 3-aminooxindoles can serve as nucleophiles for the enantioselective synthesis of quaternary 3-aminooxindoles.[8] Some reports have shown that 3-hydroxyoxindoles can be used to prepare 3,3-disubstituted oxindoles[6e−k] and that olefinic azlactones can be applied as Michael acceptors.[9] Encouraged by these achievements and on the basis of our recent successes in preparing diverse spirocyclic oxindoles,[10] we reasoned that two classes of spirocyclic oxindoles could be constructed through a tandem Michael addition–ring transformation process involving the reactions of 3-hydroxyoxindoles/3-aminooxindoles and olefinic azlactones (Scheme 1).[11] Herein we report our progress in this area for preparing spiro-butyrolactoneoxindoles and spiro-butyrolactamoxindoles with acceptable results.

To optimize the reaction conditions, 3-hydroxyoxindole **1a** was reacted with (*Z*)-olefinic azlactone **2a** (Table 1). When the reaction was performed in CH_2Cl_2 at room temperature with 1,4-diazabicyclo[2.2.2]octane (DABCO) or 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the catalyst, spiro-butyrolactoneoxindole **3a** was obtained in a trace amount (entries 1–2). When the temperature was increased to 40 °C, **3a** was obtained in 60% yield with a 67:33:0:0 diastereomeric ratio (dr) (entry 3). Using 20 mol % DBU at 40 °C for 5 h afforded **3a** in 92% yield with 75:25:0:0 dr (entry 4). The reactions with other bases showed inferior results in terms of the yield and dr value compared with DBU as the catalyst (entries 4–6). Finally, with 20 mol % DBU as the catalyst, solvent screening revealed CH_2Cl_2 to be the most selective for the reaction (entry 4 vs entries 7–10).

With the optimized conditions in hand, we explored the substrate scope of the reaction of 3-hydroxyoxindoles and (*Z*)-olefinic azlactones (Table 2). The steric bulk of the substituent at N1 in **1a–c** had a slight influence on the diastereoselectivity but almost no effect on the reactivity (entries 1–3). Substrate **1d** incorporating a methyl group at the 5-position of the oxindole ring was tolerated and provided product **3d** with good results (entry 4). Afterward, we investigated the reactions of **1a** with (*Z*)-olefinic azlactones **2b–k**. It was observed that

Received: February 22, 2014
Published: May 2, 2014

   dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305–5314

Scheme 1. Synthetic Strategy for Spiro-Butyrolactoneoxindoles and Spiro-Butyrolactamoxindoles

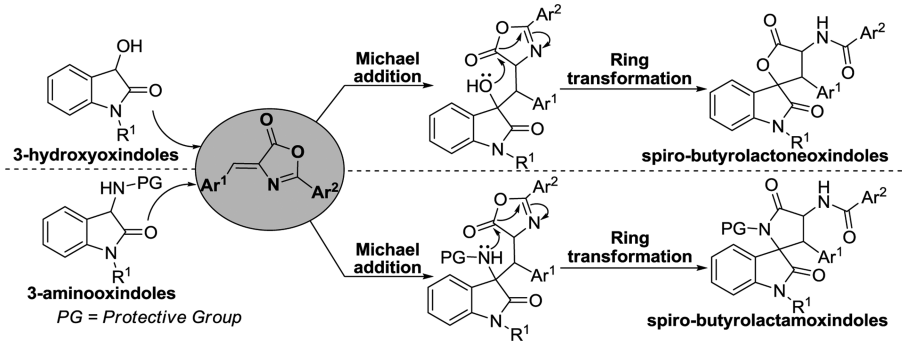
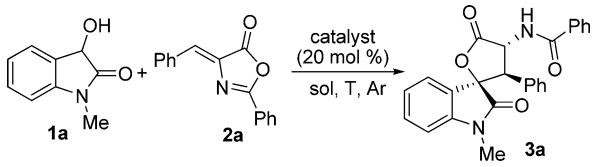


Table 1. Selected Optimiazation Studies[a]



no.	catalyst	sol.	T (°C)	t (h)	dr[b]	yield (%)[c]
1	DABCO	CH_2Cl_2	25	12	nd	trace
2	DBU	CH_2Cl_2	25	12	nd	trace
3	DABCO	CH_2Cl_2	40	12	67:33:0:0	60
4	DBU	CH_2Cl_2	40	5	75:25:0:0	92
5	Et_3N	CH_2Cl_2	40	8	71:29:0:0	75
6	DMAP	CH_2Cl_2	40	8	50:50:0:0	71
7	DBU	$CHCl_3$	40	5	50:50:0:0	87
8	DBU	DCE[d]	40	5	nd	trace
9	DBU	THF	40	5	67:33:0:0	75
10	DBU	toluene	40	8	50:50:0:0	51

[a]Conditions: **1a** (0.2 mmol), **2a** (0.24 mmol), and 20 mol % catalyst in 10 mL of solvent. [b]Determined by ^{1}H NMR spectroscopy. nd = not determined. [c]Isolated yields. [d]DCE = 1,2-dichloroethane.

regardless of whether an electron-withdrawing group (**2b**–**e**) or an electron-donating group (**2f**–**h**) was used as Ar^1 of the olefinic azlactone, the reactions proceeded well, giving spiro-butyrolactoneoxindoles **3e**–**k** in up to 93% yield and 83:17:0:0 dr (entries 5–11). 1-Naphthyl-based reactant **2i** also gave rise to the product **3l** in 85% yield with 67:33:0:0 dr (entry 12). Heteroaromatic subject **2j** was also successfully employed to react with **1a**, furnishing **3m** in excellent yield with 75:25:0:0 dr (entry 13). The structure and relative configuration of the product **3m** were determined by X-ray analysis.[12] A substituent on the Ar^2 group of the olefinic azlactone was well-tolerated (entry 14). Subsequently, we examined the reaction of olefinic azlactones **2l**–**p** with 3-hydroxyoxindole **1b** (entries 15–19). In a similar fashion, introduction of an electron-withdrawing or electron-donating group on Ar^2 of the olefinic azlactone did not affect the reactivity and stereoselectivity (entries 16–19).

The remarkable reactivity between 3-hydroxyoxindoles and (*Z*)-olefinic azlactones prompted us to explore another tandem reaction using 3-aminooxindoles **4** as nucleophiles for the construction of spiro-butyrolactamoxindoles (Table 3). Different substitutions at the N1 position of the 3-aminooxindole were well-tolerated (entries 1–4, 7, and 8), as were different groups at the N3 position (entries 5 and 6). A series of (*Z*)-olefinic azlactones bearing various β-aryl groups were able to undergo the Michael addition–ring transformation reaction under the standard conditions, generating spiro-butyrolactamoxindoles **5i**–**p** in good yields with excellent diastereoselectivities (entries 9–16). Two heteroaromatic azlactones, **2j** and **2r**, were also successfully employed in the tandem reaction (entries 17–19). A bulkier substituent such as naphthyl could be used to obtaining spiro-butyrolactamoxindole **5t** with excellent results (entry 20). Introduction of a substituent on the Ar^2 group of the olefinic azlactone had no effect on the stereoselectivity and reactivity (entry 21).

The formyl group incorporated on the butyrolactam ring could be readily deprotected by hydrolysis with 10% NaOH solution, leading to compound **6** in 56% yield with >99:1:0:0 dr (eq 1 in Scheme 2). Nevertheless, we performed an intermolecular competition experiment between 3-hydroxyoxindole **1a** and 3-aminooxindole **4a** by reacting them with **2g** under the standard conditions. The results revealed 3-hydroxyoxindole to be more reactive and to be preferentially converted (eq 2 in Scheme 2).

We also tried to develop an enantioselective version of the tandem Michael addition–ring transformation reaction. We selected the reaction of **4c** and **2a** with 10 mol % 6′-OH cinchona alkaloid **A** as the catalyst (Scheme 3). The product **5c** was obtained in 47% yield with >99:1:0:0 dr and 61% ee using xylene as the solvent at room temperature. The absolute configuration of **5c** was not determined at the moment.

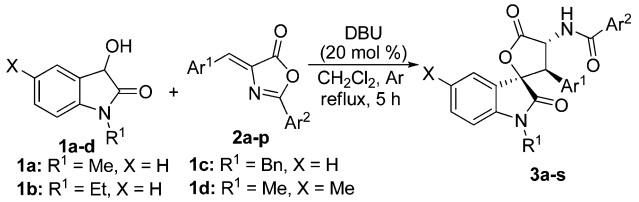
In conclusion, we have developed an efficient method for the direct construction of two classes of spirocyclic oxindoles with the reaction of 3-hydroxyoxindoles/3-aminooxindoles and (*Z*)-olefinic azlactones. The chemistry is based on Michael addition of the 3-hydroxyoxindole/3-aminooxindole to the (*Z*)-olefinic azlactone and sequential ring transformation. With DBU as the catalyst, the tandem reactions proceeded smoothly and delivered a wide range of spiro-butyrolactoneoxindoles and spiro-butyrolactamoxindoles, containing an oxygen heteroatom or a nitrogen heteroatom, respectively, in the spiro stereocenter, with very good to excellent diastereoselectivities in high yields. Additionally, a preliminary trial of an asymmetric version of the tandem Michael addition–ring transformation process was conducted, and it afforded the product in moderate yield with excellent diastereoselectivity and moderate enantioselectivity.

■ EXPERIMENTAL SECTION

General Methods. Reagents were purchased from commercial sources and were used as received, unless mentioned otherwise. Reactions were monitored by TLC. ^{1}H NMR and ^{13}C NMR (300 and 75 MHz, respectively) spectra were recorded in $CDCl_3$ and DMSO-d_6. ^{1}H NMR chemical shifts are reported in parts per million relative to tetramethylsilane (TMS) with the solvent resonance employed as the internal standard ($CDCl_3$ at 7.26 ppm, DMSO-d_6 at 2.50 ppm). Data

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305–5314

Table 2. Scope of 3-Hydroxyoxindoles with Olefinic Azlactones[a]



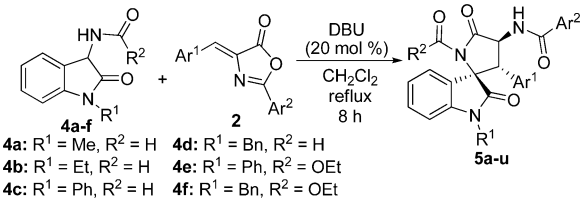
1a-d **2a-p** **3a-s**

1a: R^1 = Me, X = H **1b:** R^1 = Et, X = H **1c:** R^1 = Bn, X = H **1d:** R^1 = Me, X = Me

no.	1	Ar^1/Ar^2 (2)	3/yield[c] (%)	dr[b]
1	**1a**	Ph/Ph (**2a**)	**3a**/92	75:25:0:0
2	**1b**	Ph/Ph (**2a**)	**3b**/93	50:50:0:0
3	**1c**	Ph/Ph (**2a**)	**3c**/90[d]	67:33:0:0
4	**1d**	Ph/Ph (**2a**)	**3d**/91	75:25:0:0
5	**1a**	2-FC_6H_4/Ph (**2b**)	**3e**/93	75:25:0:0
6	**1a**	2-BrC_6H_4/Ph (**2c**)	**3f**/87	80:20:0:0
7	**1a**	2,4-$Cl_2C_6H_3$/Ph (**2d**)	**3g**/83	80:20:0:0
8	**1a**	4-CNC_6H_4/Ph (**2e**)	**3h**/91	50:50:0:0
9	**1a**	4-MeC_6H_4/Ph (**2f**)	**3i**/91	80:20:0:0
10	**1a**	4-$MeOC_6H_4$/Ph (**2g**)	**3j**/88	83:17:0:0
11	**1a**	 /Ph (**2h**)	**3k**/91	75:25:0:0
12	**1a**	1-naphthyl/Ph (**2i**)	**3l**/85	67:33:0:0
13	**1a**	2-thienyl/Ph (**2j**)	**3m**/95[e]	75:25:0:0
14	**1a**	Ph/3-FC_6H_4 (**2k**)	**3n**/93	75:25:0:0
15	**1b**	4-ClC_6H_4/Ph (**2l**)	**3o**/89	80:20:0:0
16	**1b**	Ph/4-BrC_6H_4 (**2m**)	**3p**/91	80:20:0:0
17	**1b**	Ph/2-MeC_6H_4 (**2n**)	**3q**/92	67:33:0:0
18	**1b**	Ph/4-MeC_6H_4 (**2o**)	**3r**/90	75:25:0:0
19	**1b**	Ph/4-$MeOC_6H_4$ (**2p**)	**3s**/94	67:33:0:0

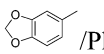
[a]See the Experimental Section for experimental details. [b]Determined by ^{1}H NMR spectroscopy. [c]Isolated yields. [d]Run for 8 h. [e]The structure and relative configuration of **3m** were determined by single-crystal X-ray analysis.[12]

Table 3. Scope of 3-Aminooxindoles with Olefinic Azlactones[a]



4a-f **2** **5a-u**

4a: R^1 = Me, R^2 = H **4b:** R^1 = Et, R^2 = H **4c:** R^1 = Ph, R^2 = H **4d:** R^1 = Bn, R^2 = H **4e:** R^1 = Ph, R^2 = OEt **4f:** R^1 = Bn, R^2 = OEt

no.	4	Ar^1/Ar^2 (2)	5/yield[c] (%)	dr[b]
1	**4a**	Ph/Ph (**2a**)	**5a**/93	>99:1:0:0
2	**4b**	Ph/Ph (**2a**)	**5b**/92[d]	92:8:0:0
3	**4c**	Ph/Ph (**2a**)	**5c** /90	>99:1:0:0
4	**4d**	Ph/Ph (**2a**)	**5d**/94	>99:1:0:0
5	**4e**	Ph/Ph (**2a**)	**5e**/87	95:5:0:0
6	**4f**	Ph/Ph (**2a**)	**5f**/92	>99:1:0:0
7	**4a**	2,4-$Cl_2C_6H_3$/Ph (**2d**)	**5g**/90	>99:1:0:0
8	**4c**	2,4-$Cl_2C_6H_3$/Ph (**2d**)	**5h**/86	96:4:0:0
9	**4d**	2-FC_6H_4/Ph (**2b**)	**5i**/91	>99:1:0:0
10	**4d**	4-ClC_6H_4/Ph (**2l**)	**5j** /87	94:6:0:0
11	**4d**	4-CNC_6H_4/Ph (**2e**)	**5k**/92	94:6:0:0
12	**4c**	3-$MeOC_6H_4$/Ph (**2q**)	**5l**/88	>99:1:0:0
13	**4c**	4-$MeOC_6H_4$/Ph (**2g**)	**5m**/86	96:4:0:0
14	**4d**	4-MeC_6H_4/Ph (**2f**)	**5n**/90	>99:1:0:0
15	**4d**	4-$MeOC_6H_4$/Ph (**2g**)	**5o**/89	>99:1:0:0
16	**4d**	 /Ph (**2h**)	**5p**/87	>99:1:0:0
17	**4b**	2-thienyl/Ph (**2j**)	**5q**/85	92:8:0:0
18	**4d**	2-thienyl/Ph (**2j**)	**5r**/88	>99:1:0:0
19	**4c**	2-furyl/Ph (**2r**)	**5s**/82	94:6:0:0
20	**4d**	1-naphthyl/Ph (**2i**)	**5t**/93	>99:1:0:0
21	**4d**	Ph/4-BrC_6H_4 (**2m**)	**5u**/82	>99:1:0:0

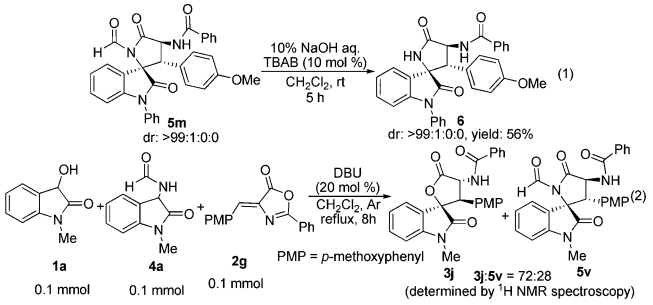
[a]See the Experimental Section for experimental details. [b]Determined by ^{1}H NMR spectroscopy. [c]Isolated yields. [d]The structure and relative configuration of the product **5b** were determined by X-ray analysis.[12]

are reported as follows: chemical shift (multiplicity, coupling constant(s) in Hz, integration). Multiplicities are abbreviated as follows: s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, m = multiplet. ^{13}C NMR chemical shifts are reported in parts per million from tetramethylsilane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ at 77.20 ppm, DMSO-d_6 at 39.51 ppm). Melting points were recorded on a melting point apparatus.

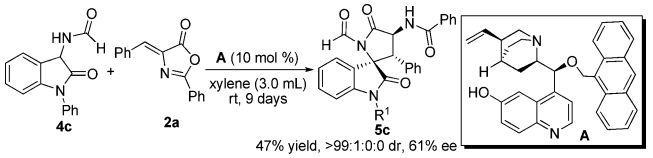
Synthesis of Substrates 4a–d. *N-(1-Methyl-2-oxoindolin-3-yl)formamide (**4a**).* A solution of 3-amino-1-methylindolin-2-one hydrochloride (2.5 g, 12.6 mmol) in ethyl formate (100 mL) was heated to reflux under an Ar atmosphere, and Et_3N (2.1 mL, 15.1 mmol) was added to the resulting mixture. The mixture was refluxed for 15 h and then concentrated, and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 1:1) to give **4a** (1.7 g, 71% yield) as a white solid. Mp 175.8–177.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.11 (s, 3H), 5.24 (d, J = 8.1 Hz, 1H), 6.97–7.04 (m, 2H), 7.17 (d, J = 7.2 Hz, 1H), 7.27–7.32 (m, 1H), 8.18 (s, 1H),

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305–5314

Scheme 2. Transformation of 5m and the Competition Experiment with 1a and 4a



Scheme 3. Catalytic Enantioselective Variant



8.78 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.2, 50.6, 108.4, 122.2, 123.4, 126.8, 128.7, 144.0, 161.3, 173.4; HRMS (ESI-TOF) calcd for $C_{10}H_{10}N_2NaO_2$ [M + Na]$^+$ 213.0634, found 213.0629.

*N-(1-Ethyl-2-oxoindolin-3-yl)formamide (**4b**).* The method for the synthesis of **4b** was similar to that for **4a**. Product **4b** (0.87 g, 91% yield) was obtained from 3-amino-1-ethylindolin-2-one hydrochloride (1.0 g, 4.7 mmol) as a white solid. Mp 140.3−141.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.15 (t, J = 7.2 Hz, 3H), 3.70 (q, J = 7.2 Hz, 2H), 5.24 (d, J = 8.1 Hz, 1H), 7.00−7.10 (m, 2H), 7.20 (d, J = 7.2 Hz, 1H), 7.28−7.35 (m, 1H), 8.19 (s, 1H), 8.82 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.4, 34.2, 50.6, 108.5, 122.0, 123.6, 126.9, 128.7, 143.0, 161.2, 173.0; HRMS (ESI-TOF) calcd for $C_{11}H_{12}N_2NaO_2$ [M + Na]$^+$ 227.0791, found 227.0789.

*N-(2-Oxo-1-phenylindolin-3-yl)formamide (**4c**).* The method for the synthesis of **4c** was similar to that for **4a**. Product **4c** (0.8 g, 82% yield) was obtained from 3-amino-1-phenylindolin-2-one hydrochloride (1.0 g, 3.8 mmol) as a white solid. Mp 174.3−175.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 5.43 (d, J = 8.1 Hz, 1H), 6.72 (d, J = 7.8 Hz, 1H), 7.06−7.11 (m, 1H), 7.23−7.30 (m, 2H), 7.41−7.49 (m, 3H), 7.56−7.61 (m, 2H), 8.25 (s, 1H), 8.98 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 50.9, 108.8, 122.8, 123.9, 126.6, 126.7, 128.0, 128.7, 129.6, 134.5, 143.8, 161.4, 173.0; HRMS (ESI-TOF) calcd for $C_{15}H_{12}N_2NaO_2$ [M + Na]$^+$ 275.0791, found 275.0786.

*N-(1-Benzyl-2-oxoindolin-3-yl)formamide (**4d**).* The method for the synthesis of **4d** was similar to that for **4a**. Product **4d** (0.65 g, 67% yield) was obtained from 3-amino-1-benzylindolin-2-one hydrochloride (1.0 g, 3.6 mmol) as a white solid. Mp 139.8−141.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.85 (d, J = 15.9 Hz, 1H), 4.96 (d, J = 15.9 Hz, 1H), 5.37 (d, J = 8.1 Hz, 1H), 6.81 (d, J = 7.8 Hz, 1H), 7.00−7.03 (m, 1H), 7.17−7.42 (m, 7H), 8.23 (s, 1H), 8.98 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 42.8, 50.9, 109.0, 122.3, 123.5, 126.8, 127.2, 127.3, 128.5, 129.1, 136.1, 142.9, 161.3, 173.6; HRMS (ESI-TOF) calcd for $C_{16}H_{14}N_2NaO_2$ [M + Na]$^+$ 289.0947, found 289.0953.

Synthesis of Substrates 4e and 4f. *Ethyl N-(2-Oxo-1-phenylindolin-3-yl)carbamate (**4e**).* To a solution of 3-amino-1-phenylindolin-2-one hydrochloride (1.4 g, 5.4 mmol) in $CHCl_3$ (30 mL) was added Et_3N (1.2 mL, 8.1 mmol) at 0 °C under an Ar atmosphere. The resulting mixture was vigorously stirred for 15 min, and then ethyl carbonochloridate (0.6 mL, 5.95 mmol) was slowly added to the mixture via syringe. The resultant mixture was allowed to stir for 1 h and then concentrated, and the residue was purified by flash chromatography (petroleum ether/ethyl acetate = 2:1) to give **4e** (0.8 g, 50% yield) as a white solid. Mp 181.9−183.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.25 (s, 3H), 4.17 (q, J = 7.2 Hz, 2H), 5.20 (d, J = 6.9 Hz, 1H), 5.52 (d, J = 7.5 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 7.08−7.13 (m, 1H), 7.21−7.23 (m, 1H), 7.41−7.44 (m, 4H), 7.50−7.55 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 54.1, 61.6, 109.5, 123.3, 124.6, 126.2, 126.5, 128.2, 129.1, 129.6, 134.3, 143.8, 156.4, 173.8; HRMS (ESI-TOF) calcd for $C_{17}H_{16}N_2NaO_3$ [M + Na]$^+$ 319.1053, found 319.1053.

*Ethyl N-(1-Benzyl-2-oxoindolin-3-yl)carbamate (**4f**).* The method for the synthesis of **4f** was similar to that for **4e**. Product **4f** (1.0 g, 63% yield) was obtained from 3-amino-1-benzylindolin-2-one hydrochloride (1.4 g, 5.1 mmol) as a white solid. Mp 125.9−127.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.26 (s, 3H), 4.11−4.19 (m, 2H), 4.86 (d, J = 15.6 Hz, 1H), 4.97 (d, J = 15.6 Hz, 1H), 5.17 (d, J = 6.9 Hz, 1H), 5.37 (d, J = 6.9 Hz, 1H), 6.71 (d, J = 7.8 Hz, 1H), 7.01−7.06 (m, 1H), 7.17−7.22 (m, 1H), 7.27−7.39 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 14.4, 44.1, 53.9, 61.6, 109.3, 122.9, 124.3, 126.4, 127.3, 127.6, 128.7, 129.1, 135.4, 142.8, 156.4, 174.4; HRMS (ESI-TOF) calcd for $C_{18}H_{18}N_2NaO_3$ [M + Na]$^+$ 333.1210, found 333.1197.

General Procedure for the Synthesis of Compounds 3. In an ordinary vial equipped with a magnetic stirring bar, compound **1** (0.2 mmol, 1.0 equiv), compound **2** (0.24 mmol, 1.2 equiv), and catalyst (DBU, 20 mol %) were dissolved in 10 mL of CH_2Cl_2, and then the mixture was refluxed for the indicated time under an Ar atmosphere. After completion of the reaction as indicated by TLC, the solvent was removed in vacuo, and the diastereomeric ratio (dr) was determined by ^{1}H NMR analysis of the crude mixture. The product **3** was isolated by flash chromatography on silica gel (petroleum ether/ethyl acetate = 10/1−3/1).

*N-(1′-Methyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3a**).* White solid (75.9 mg, 92% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 215.8−216.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.17 (s, 3H), 4.68 (d, J = 13.2 Hz, 1H), 6.10 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.91 (d, J = 7.8 Hz, 1H), 7.01−7.14 (m, 6H), 7.23−7.28 (m, 1H), 7.46−7.59 (m, 3H), 7.73 (d, J = 7.5 Hz, 1H), 7.89 (d, J = 7.2 Hz, 2H), 9.32 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 27.0, 50.6, 52.4, 83.5, 109.8, 123.4, 123.9, 125.9, 127.7, 127.8, 128.3, 128.9, 131.4, 132.4, 132.5, 133.3, 143.7, 166.6, 172.2, 172.8; IR (KBr) ν 3390, 3064, 2928, 2853, 1786, 1732, 1667, 1617, 1545, 1471, 1377, 1316, 1205, 1096, 1003, 706, 694 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{20}N_2NaO_4$ [M + Na]$^+$ 435.1315, found 435.1303.

*N-(1′-Ethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3b**).* White solid (79.3 mg, 93% yield), 50:50:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 158.1−159.6 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (one diastereomer) 0.55 (t, J = 7.2 Hz, 3H), 3.27−3.34 (m, 1H), 3.47−3.54 (m, 1H), 4.57 (d, J = 12.6 Hz, 1H), 5.96 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.89−6.91 (m, 2H), 7.03 (d, J = 7.8 Hz, 1H), 7.15−7.20 (m, 3H), 7.29−7.34 (m, 1H), 7.47−7.60 (m, 4H), 7.68 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 9.17 (d, J = 8.4 Hz, 1H); δ (the other diastereomer) 1.11 (t, J = 6.9 Hz, 3H), 3.62−3.74 (m, 1H), 3.77−3.84 (m, 1H), 4.67 (d, J = 13.2 Hz, 1H), 6.11 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.94 (d, J = 7.8 Hz, 1H), 6.98−7.03 (m, 1H), 7.05−7.15 (m, 4H), 7.22−7.27 (m, 2H), 7.46−7.56 (m, 3H), 7.73 (d, J = 7.2 Hz, 1H), 7.89 (d, J = 7.2 Hz, 2H), 9.33 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (one diastereomer) 111.6, 34.0, 50.3, 53.3, 83.6, 109.6, 123.7, 124.0, 124.5, 127.2, 127.7, 128.3, 128.5, 128.7, 130.9, 131.9, 132.1, 132.8, 143.1, 166.3, 171.6, 172.9; δ (the other diastereomer) 12.2, 34.7, 50.1, 52.1, 83.0, 109.3, 122.8, 123.7, 125.7, 127.3, 127.5, 127.9, 128.2, 128.3, 128.5, 129.9, 131.0, 131.9, 132.0, 132.8, 142.1, 166.1, 171.4, 172.4; IR (KBr) ν 3359, 3062, 2934, 1801, 1728, 1650, 1616, 1531, 1489, 1469, 1375, 1162, 1027, 753, 698 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{22}N_2NaO_4$ [M + Na]$^+$ 449.1472, found 449.1472.

*N-(1′-Benzyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3c**).* White solid (87.9 mg, 90% yield), 67:33:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 145.8−147.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (one diastereomer) 4.48 (d, J = 16.2 Hz, 1H), 4.72 (d, J = 12.6 Hz, 1H), 4.90 (d, J = 16.2 Hz, 1H), 6.06 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.48 (d, J = 7.2 Hz, 2H), 6.71 (d, J = 7.5 Hz, 1H), 7.01 (d, J = 7.5 Hz, 2H), 7.07−7.16 (m, 3H), 7.21−7.41 (m, 5H), 7.48−7.60 (m, 3H),

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305−5314

7.73 (d, J = 7.2 Hz, 1H), 7.84−7.87 (m, 2H), 9.21 (d, J = 8.4 Hz, 1H); δ (the other diastereomer) 4.73 (d, J = 13.2 Hz, 1H), 4.85 (d, J = 15.9 Hz, 1H), 5.04 (d, J = 15.9 Hz, 1H), 6.11 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.96−7.10 (m, 5H), 7.20−7.22 (m, 3H), 7.30−7.36 (m, 3H), 7.38−7.41 (m, 1H), 7.48−7.51 (m, 2H), 7.54−7.56 (m, 1H), 7.80 (d, J = 7.2 Hz, 1H), 7.87−7.90 (m, 2H), 9.34 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (one diastereomer) 43.2, 50.9, 53.2, 84.0, 110.7, 124.2, 124.4, 125.1, 126.7, 127.6, 128.5, 128.9, 129.0, 129.2, 131.2, 132.3, 132.5, 133.2, 135.1, 143.8, 166.7, 172.6, 173.2; δ (the other diastereomer) 43.3, 50.5, 52.0, 83.0, 110.0, 123.0, 123.6, 125.9, 127.3, 127.4, 127.6, 127.8, 128.4, 128.5, 128.6, 130.0, 131.0, 131.8, 131.9, 132.8, 135.3, 142.4, 166.1, 171.9, 172.3; IR (KBr) ν 3401, 3061, 2927, 1799, 1707, 1653, 1617, 1512, 1488, 1469, 1382, 1368, 1170, 1023, 753, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{24}N_2NaO_4$ [M + Na]$^+$ 511.1628, found 511.1627.

*N-(1′,5′-Dimethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro-[furan-2,3′-indolin]-4-yl)benzamide (**3d**).* White solid (77.6 mg, 91% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 259.2−260.5 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.41 (s, 3H), 2.81 (s, 3H), 4.63 (d, J = 12.6 Hz, 1H), 5.90 (dd, J = 8.4 Hz, 12.3 Hz, 1H), 6.88 (d, J = 8.1 Hz, 1H), 6.95−6.97 (m, 2H), 7.19−7.21 (m, 3H), 7.29 (d, J = 8.1 Hz, 1H), 7.47−7.57 (m, 4H), 7.84−7.86 (m, 2H), 9.19 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 21.1, 26.3, 51.2, 53.1, 84.1, 109.8, 124.3, 125.2, 127.6, 128.0, 128.1, 128.7, 128.9, 129.0, 130.5, 131.7, 132.4, 132.5, 133.2, 133.4, 142.3, 166.7, 172.3, 173.2; IR (KBr) ν 3273, 3061, 2926, 1784, 1739, 1644, 1603, 1552, 1499, 1332, 1201, 1111, 999, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{22}N_2NaO_4$ [M + Na]$^+$ 449.1472, found 449.1478.

*N-(3-(2-Fluorophenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3e**).* White solid (80.1 mg, 93% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 120.2−121.5 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.89 (s, 3H), 5.01 (d, J = 12.6 Hz, 1H), 5.93 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.97 (d, J = 7.8 Hz, 2H), 7.21−7.29 (m, 3H), 7.45−7.65 (m, 6H), 7.81−7.84 (m, 2H), 9.19 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.1, 45.2, 51.1, 83.3, 109.6, 115.5 (d, J = 22.2 Hz, 1C), 118.0 (d, J = 13.7 Hz, 1C), 123.4, 123.7, 124.6 (d, J = 3.5 Hz, 1C), 124.7, 127.2, 128.7, 128.9, 130.6 (d, J = 8.6 Hz, 1C), 132.0 (d, J = 28.1 Hz, 1C), 132.7, 143.9, 161.0 (d, J = 245.8 Hz, 1C), 166.4, 172.1, 172.5; IR (KBr) ν 3376, 3063, 2934, 1801, 1728, 1657, 1616, 1530, 1494, 1472, 1380, 1239, 1165, 753, 693 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}FN_2NaO_4$ [M + Na]$^+$ 453.1221, found 453.1214.

*N-(3-(2-Bromophenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3f**).* White solid (85.5 mg, 87% yield), 80:20:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 117.9−119.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.94 (s, 3H), 5.39 (d, J = 12.3 Hz, 1H), 5.65 (dd, J = 7.8 Hz, 12.3 Hz, 1H), 6.95 (d, J = 7.8 Hz, 1H), 7.14−7.26 (m, 2H), 7.39−7.57 (m, 6H), 7.71 (d, J = 7.2 Hz, 2H), 7.81 (d, J = 7.2 Hz, 2H), 9.24 (d, J = 7.8 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.1, 50.4, 53.6, 83.8, 109.6, 122.9, 123.3, 126.0, 127.2, 128.0, 128.6, 129.4, 130.5, 130.8, 131.8, 132.1, 132.7, 133.2, 143.8, 166.4, 172.1, 172.5; IR (KBr) ν 3339, 3061, 2925, 1802, 1727, 1654, 1616, 1530, 1491, 1472, 1377, 1241, 1160, 752, 693 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}BrN_2NaO_4$ [M + Na]$^+$ 513.0420, found 513.0413.

*N-(3-(2,4-Dichlorophenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3g**).* White solid (79.9 mg, 83% yield), 80:20:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 180.4−181.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.96 (s, 3H), 5.30 (d, J = 12.3 Hz, 1H), 5.72 (dd, J = 8.1 Hz, 12.3 Hz, 1H), 7.00 (d, J = 7.8 Hz, 1H), 7.23−7.28 (m, 1H), 7.43−7.61 (m, 6H), 7.64−7.70 (m, 2H), 7.80 (d, J = 7.8 Hz, 2H), 9.20 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.6, 48.1, 53.3, 83.8, 110.2, 123.4, 123.9, 125.9, 127.6, 128.1, 128.5, 129.1, 129.6, 131.1, 132.3, 132.6, 133.0, 134.4, 136.2, 144.2, 166.8, 172.3, 172.6; IR (KBr) ν 3381, 3065, 2930, 1801, 1725, 1650, 1616, 1531, 1473, 1378, 1329, 1166, 1009, 752, 694 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{18}Cl_2N_2NaO_4$ [M + Na]$^+$ 503.0536, found 503.0531.

*N-(3-(4-Cyanophenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3h**).* White solid (79.6 mg, 91% yield), 50:50:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 256.8−258.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (one diastereomer) 3.16 (s, 3H), 4.73 (d, J = 12.9 Hz, 1H), 6.14 (dd, J = 8.1 Hz, 12.9 Hz, 1H), 6.92 (d, J = 7.8 Hz, 1H), 6.97−7.03 (m, 1H), 7.24−7.29 (m, 3H), 7.44−7.55 (m, 3H), 7.63 (d, J = 8.1 Hz, 2H), 7.77 (d, J = 7.5 Hz, 1H), 7.86 (d, J = 7.5 Hz, 2H), 9.34 (d, J = 8.1 Hz, 1H); δ (the other diastereomer) 2.86 (s, 3H), 4.71 (d, J = 12.3 Hz, 1H), 5.93 (dd, J = 8.1 Hz, 12.3 Hz, 1H), 7.04 (d, J = 7.8 Hz, 1H), 7.13 (d, J = 8.4 Hz, 2H), 7.31−7.36 (m, 1H), 7.46−7.56 (m, 4H), 7.69−7.75 (m, 3H), 7.80−7.85 (m, 2H), 9.22 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (one diastereomer) 27.0, 50.6, 52.4, 83.1, 109.9, 111.2, 118.6, 123.4, 123.5, 126.0, 127.8, 128.9, 129.0, 131.7, 132.5, 132.8, 133.1, 138.4, 143.6, 166.6, 171.9, 172.3; δ (the other diastereomer) 26.0, 50.6, 52.6, 83.2, 109.8, 111.3, 118.2, 123.3, 124.0, 124.4, 127.1, 127.3, 128.6, 128.7, 132.1, 132.4, 132.7, 136.9, 144.1, 166.3, 171.6, 172.2; IR (KBr) ν 3369, 3062, 2935, 1801, 1725, 1658, 1616, 1531, 1491, 1471, 1377, 1311, 1243, 1161, 1007, 754, 694 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{19}N_3NaO_4$ [M + Na]$^+$ 460.1268, found 460.1252.

*N-(1′-Methyl-2′,5-dioxo-3-(p-tolyl)-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3i**).* White solid (77.6 mg, 91% yield), 80:20:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 105.8−107.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.15 (s, 3H), 2.86 (s, 3H), 4.56 (d, J = 12.6 Hz, 1H), 5.94 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.84 (d, J = 8.1 Hz, 2H), 6.98−7.01 (m, 3H), 7.29−7.34 (m, 1H), 7.47−7.57 (m, 4H), 7.66 (d, J = 7.2 Hz, 1H), 7.82−7.85 (m, 2H), 9.15 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 20.9, 26.4, 51.3, 53.1, 84.0, 110.1, 124.2, 124.3, 124.7, 127.6, 128.0, 128.4, 129.0, 129.5, 132.2, 132.5, 133.2, 138.0, 144.7, 166.7, 172.5, 173.3; IR (KBr) ν 3377, 3056, 2931, 1806, 1732, 1650, 1616, 1516, 1494, 1470, 1343, 1256, 1164, 978, 754, 696 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{22}N_2NaO_4$ [M + Na]$^+$ 449.1472, found 449.1472.

*N-(3-(4-Methoxyphenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3j**).* White solid (77.9 mg, 88% yield), 83:17:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 285.6−287.1 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.16 (s, 3H), 3.57 (s, 3H), 4.59 (d, J = 13.2 Hz, 1H), 6.04 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.69 (d, J = 8.7 Hz, 2H), 6.91−7.01 (m, 3H), 7.05 (d, J = 7.5 Hz, 1H), 7.25−7.30 (m, 1H), 7.45−7.58 (m, 3H), 7.74 (d, J = 7.2 Hz, 1H), 7.87−7.89 (m, 2H), 9.28 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.5, 50.5, 51.5, 54.9, 83.2, 109.4, 113.9, 123.0, 123.6, 123.7, 125.5, 127.3, 128.5, 128.7, 131.0, 132.0, 132.9, 143.3, 158.6, 166.1, 171.8, 172.5; IR (KBr) ν 3383, 3068, 2936, 1806, 1725, 1635, 1616, 1533, 1517, 1492, 1472, 1380, 1259, 1150, 1026, 830, 719 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{22}N_2NaO_5$ [M + Na]$^+$ 465.1421, found 465.1402.

*N-(3-(Benzo[d][1,3]dioxol-5-yl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)benzamide (**3k**).* White solid (83.1 mg, 91% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 242.8−244.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.16 (s, 3H), 4.58 (d, J = 13.2 Hz, 1H), 5.86 (s, 2H), 5.99 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.48 (d, J = 8.1 Hz, 1H), 6.68 (d, J = 6.6 Hz, 2H), 6.95 (d, J = 7.8 Hz, 1H), 7.03−7.08 (m, 1H), 7.28−7.33 (m, 1H), 7.46−7.59 (m, 3H), 7.78 (d, J = 7.5 Hz, 1H), 7.89 (d, J = 7.2 Hz, 2H), 9.29 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.6, 50.7, 51.7, 83.1, 101.1, 107.5, 108.3, 109.5, 121.4, 123.0, 123.6, 125.7, 127.4, 128.5, 131.1, 132.0, 132.8, 143.3, 146.7, 147.3, 166.2, 171.8, 172.3; IR (KBr) ν 3290, 3065, 2895, 1798, 1724, 1664, 1615, 1541, 1493, 1471, 1376, 1245, 1160, 936, 758 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{20}N_2NaO_6$ [M + Na]$^+$ 479.1214, found 479.1201.

*N-(1′-Methyl-3-(naphthalen-1-yl)-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl) benzamide (**3l**).* White solid (78.6 mg, 85% yield), 67:33:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 255.6−257.1 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ (one diastereomer) 2.76 (s, 3H), 5.65 (d, J = 12.6 Hz, 1H), 6.06 (dd, J = 8.4 Hz, 12.3 Hz, 1H), 6.71 (d, J = 6.9 Hz, 1H), 7.18−7.35 (m, 4H), 7.41−7.62 (m, 5H), 7.75−7.87 (m, 6H), 9.13 (d, J

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305−5314

= 8.1 Hz, 1H); δ (the other diastereomer) 2.85 (s, 3H), 5.51 (d, J = 12.9 Hz, 1H), 6.37 (dd, J = 8.1 Hz, 12.9 Hz, 1H), 6.65 (d, J = 7.8 Hz, 1H), 6.95−7.00 (m, 1H), 7.10−7.15 (m, 1H), 7.28−7.37 (m, 2H), 7.41−7.46 (m, 2H), 7.49−7.54 (m, 1H), 7.64−7.74 (m, 3H), 7.77−7.93 (m, 5H), 9.33 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ (one diastereomer) 25.9, 46.9, 52.7, 84.2, 109.6, 122.3, 123.5, 123.7, 124.7, 125.2, 125.4, 125.6, 125.9, 126.9, 127.1, 128.6, 129.0, 131.7, 132.0, 132.1, 132.7, 133.2, 143.9, 166.4, 172.5, 172.8; δ (the other diastereomer) 26.3, 47.2, 51.1, 83.1, 109.1, 122.4, 122.7, 123.6, 124.8, 125.7, 125.9, 126.1, 126.6, 127.3, 128.0, 128.1, 128.4, 128.7, 130.7, 131.8, 131.9, 132.8, 133.0, 142.8, 166.2, 172.4, 172.6; IR (KBr) ν 3367, 3058, 2929, 1801, 1716, 1671, 1616, 1526, 1492, 1471, 1379, 1325, 1163, 1011, 778, 693 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{29}H_{22}N_2NaO_4$ $[M + Na]^+$ 485.1472, found 485.1471.

*N-(1′-Methyl-2′,5-dioxo-3-(thiophen-2-yl)-4,5-dihydro-3H-spiro-[furan-2,3′-indolin]-4-yl)benzamide (**3m**).* White solid (79.5 mg, 95% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 134.3−135.8 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.96 (s, 3H), 4.80 (d, J = 12.3 Hz, 1H), 5.78 (dd, J = 8.4 Hz, 12.3 Hz, 1H), 6.88−6.92 (m, 2H), 7.10 (d, J = 7.8 Hz, 1H), 7.31−7.36 (m, 2H), 7.52−7.61 (m, 5H), 7.85−7.88 (m, 2H), 9.25 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.1, 48.7, 52.6, 83.0, 109.9, 123.3, 123.9, 124.4, 126.4, 126.6, 127.0, 127.2, 128.7, 132.2, 132.8, 133.8, 144.7, 166.4, 171.8, 172.2; IR (KBr) ν 3360, 3062, 2928, 1802, 1727, 1651, 1616, 1530, 1491, 1471, 1383, 1244, 1162, 1004, 753, 709 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{23}H_{18}N_2NaO_4S$ $[M + Na]^+$ 441.0879, found 441.0877.

*N-(3-(3-Fluorophenyl)-1′-methyl-2′,5-dioxo-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl) benzamide (**3n**).* White solid (80.1 mg, 93% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 138.4−139.8 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.15 (s, 3H), 4.64 (d, J = 13.2 Hz, 1H), 6.08 (dd, J = 8.1 Hz, 13.2 Hz, 1H), 6.89 (d, J = 7.8 Hz, 1H), 6.97−7.15 (m, 6H), 7.22−7.27 (m, 1H), 7.38−7.44 (m, 1H), 7.48−7.57 (m, 1H), 7.67 (d, J = 9.6 Hz, 1H), 7.74 (d, J = 7.5 Hz, 2H), 9.41 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.6, 50.4, 51.9, 83.2, 109.4, 114.2 (d, J = 22.9 Hz, 1C), 119.0 (d, J = 20.9 Hz, 1C), 123.0, 123.5, 123.6 (d, J = 2.6 Hz, 1C), 125.7, 127.4, 127.9, 128.5, 130.8 (d, J = 8.0 Hz, 1C), 131.0, 132.0, 135.1 (d, J = 6.8 Hz, 1C), 143.3, 162.0 (d, J = 243.2 Hz, 1C), 164.9, 171.8, 172.3; IR (KBr) ν 3282, 3069, 2928, 1797, 1727, 1663, 1615, 1536, 1486, 1471, 1376, 1331, 1152, 1003, 802, 749 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{19}FN_2NaO_4$ $[M + Na]^+$ 453.1221, found 453.1218.

*N-(3-(4-Chlorophenyl)-1′-ethyl-2′,5-dioxo-4,5-dihydro-3H-spiro-[furan-2,3′-indolin]-4-yl)benzamide (**3o**).* White solid (82.0 mg, 89% yield), 80:20:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 252.2−253.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.11 (t, J = 6.9 Hz, 3H), 3.66−3.82 (m, 2H), 4.64 (d, J = 13.2 Hz, 1H), 6.09 (dd, J = 8.1 Hz, 13.2 Hz, 1H), 6.97−7.11 (m, 4H), 7.21−7.28 (m, 3H), 7.46−7.57 (m, 3H), 7.78 (d, J = 7.5 Hz, 1H), 7.88 (d, J = 7.2 Hz, 2H), 9.33 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.6, 35.2, 50.6, 52.1, 83.2, 109.9, 123.3, 123.9, 126.2, 127.8, 128.8, 128.9, 129.9, 131.5, 131.6, 132.4, 133.0, 133.2, 142.5, 166.6, 171.7, 172.6; IR (KBr) ν 3357, 3057, 2927, 1797, 1717, 1667, 1618, 1520, 1489, 1469, 1384, 1334, 1162, 1021, 752, 725 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{21}ClN_2NaO_4$ $[M + Na]^+$ 483.1082, found 483.1067.

*4-Bromo-N-(1′-ethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro-[furan-2,3′-indolin]-4-yl)benzamide (**3p**).* White solid (92.0 mg, 91% yield), 80:20:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 117.9−119.4 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.55 (t, J = 7.2 Hz, 3H), 3.29−3.33 (m, 1H), 3.47−3.54 (m, 1H), 4.55 (d, J = 12.6 Hz, 1H), 5.95 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.88−6.91 (m, 2H), 7.02 (d, J = 7.8 Hz, 1H), 7.16−7.20 (m, 3H), 7.29−7.34 (m, 1H), 7.47−7.52 (m, 1H), 7.67 (d, J = 6.9 Hz, 1H), 7.72 (d, J = 8.7 Hz, 2H), 7.79 (d, J = 8.7 Hz, 2H), 9.27 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.0, 34.3, 50.7, 53.7, 84.0, 110.0, 124.1, 124.3, 124.9, 126.3, 128.1, 128.7, 128.9, 129.7, 131.2, 132.1, 132.3, 143.5, 165.8, 171.9, 173.2; IR (KBr) ν 3350, 3062, 2935, 1801, 1725, 1664, 1616, 1533, 1484, 1469, 1375, 1211, 1162, 1012, 752, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{21}BrN_2NaO_4$ $[M + Na]^+$ 527.0577, found 527.0577.

*N-(1′-Ethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)-2-methylbenzamide (**3q**).* White solid (81.1 mg, 92% yield), 67:33:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 115.6−117.1 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.57 (t, J = 6.9 Hz, 3H), 2.24 (s, 3H), 3.26−3.33 (m, 1H), 3.46−3.55 (m, 1H), 4.50 (d, J = 12.6 Hz, 1H), 5.93 (dd, J = 8.7 Hz, 12.6 Hz, 1H), 6.90−6.92 (m, 2H), 7.03 (d, J = 7.8 Hz, 1H), 7.19−7.34 (m, 8H), 7.46−7.51 (m, 1H), 7.64 (d, J = 7.2 Hz, 1H), 8.86 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.0, 19.6, 34.4, 50.4, 53.7, 83.9, 110.0, 124.1, 124.4, 124.9, 126.1, 127.2, 128.0, 128.8, 128.9, 130.4, 131.2, 131.3, 132.3, 135.8, 135.9, 143.5, 169.7, 171.9, 173.2; IR (KBr) ν 3347, 3063, 2924, 1766, 1712, 1670, 1614, 1532, 1489, 1468, 1383, 1316, 1190, 730, 698 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{24}N_2NaO_4$ $[M + Na]^+$ 463.1628, found 463.1617.

*N-(1′-Ethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)-4-methylbenzamide (**3r**).* White solid (79.3 mg, 90% yield), 75:25:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 117.2−118.6 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.55 (t, J = 6.9 Hz, 3H), 2.34 (s, 3H), 3.28−3.33 (m, 1H), 3.47−3.54 (m, 1H), 4.57 (d, J = 12.6 Hz, 1H), 5.96 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.89−6.91 (m, 2H), 7.02 (d, J = 7.8 Hz, 1H), 7.18−7.20 (m, 3H), 7.28−7.34 (m, 3H), 7.47−7.49 (m, 1H), 7.67 (d, J = 6.6 Hz, 1H), 7.75 (d, J = 8.1 Hz, 2H), 9.08 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.0, 21.4, 34.3, 50.6, 53.7, 84.0, 110.0, 124.1, 124.5, 124.9, 127.6, 128.1, 128.7, 128.8, 129.5, 130.5, 131.3, 132.2, 142.5, 143.5, 166.6, 172.0, 173.4; IR (KBr) ν 3371, 3061, 2931, 1801, 1724, 1648, 1614, 1535, 1490, 1469, 1375, 1211, 1161, 1018, 751, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{24}N_2NaO_4$ $[M + Na]^+$ 463.1628, found 463.1625.

*N-(1′-Ethyl-2′,5-dioxo-3-phenyl-4,5-dihydro-3H-spiro[furan-2,3′-indolin]-4-yl)-4-methoxybenzamide (**3s**).* White solid (85.8 mg, 94% yield), 67:33:0:0 dr (as determined by ^{1}H NMR spectroscopy of the crude product); mp 108.4−109.8 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.09 (t, J = 6.9 Hz, 3H), 3.61−3.68 (m, 1H), 3.76−3.83 (m, 4H), 4.64 (d, J = 13.2 Hz, 1H), 6.06 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.91−7.11 (m, 9H), 7.20−7.25 (m, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.85 (d, J = 8.7 Hz, 2H), 9.14 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.2, 34.7, 50.0, 52.2, 55.5, 83.0, 109.4, 113.7, 122.8, 123.8, 125.1, 125.7, 127.5, 127.9, 128.4, 129.3, 131.0, 132.1, 142.2, 162.1, 165.7, 171.4, 172.6; IR (KBr) ν 3354, 3066, 2919, 1797, 1718, 1660, 1605, 1528, 1508, 1471, 1330, 1257, 1175, 1025, 850, 798, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{24}N_2NaO_5$ $[M + Na]^+$ 479.1577, found 479.1576.

General Procedure for the Synthesis of Compounds 5. In an ordinary vial equipped with a magnetic stirring bar, compound **4** (0.15 mmol, 1.0 equiv), compound **2** (0.18 mmol, 1.2 equiv), and catalyst (DBU, 20 mol %) were dissolved in 10 mL of CH_2Cl_2, and then the mixture was refluxed for the indicated time. After completion of the reaction as indicated by TLC, the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 10/1−2/1) on silica gel to yield the product **5**.

*N-(1′-Formyl-1-methyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5a**).* White solid (61.3 mg, 93% yield), >99:1:0:0 dr; mp 278.5−279.8 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.13 (s, 3H), 4.37 (d, J = 13.2 Hz, 1H), 6.02 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.79 (d, J = 7.8 Hz, 1H), 6.95−6.99 (m, 3H), 7.04−7.14 (m, 4H), 7.44−7.55 (m, 3H), 7.66 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 2H), 9.08 (s, 1H), 9.24 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.5, 51.9, 52.2, 65.7, 108.5, 122.4, 124.0, 124.5, 127.3, 127.9, 128.1, 128.5, 129.7, 131.7, 132.0, 132.9, 143.2, 159.1, 166.2, 172.6, 172.7; IR (KBr) ν 3362, 3061, 2925, 1765, 1713, 1665, 1615, 1536, 1492, 1472, 1382, 1341, 1253, 1096, 752, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{21}N_3NaO_4$ $[M + Na]^+$ 462.1424, found 462.1432.

*N-(1-Ethyl-1′-formyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5b**).* White solid (62.6 mg, 92% yield), 92:8:0:0 dr; mp 268.5−269.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.08 (t, J = 6.9 Hz, 3H), 3.64−3.78 (m, 2H), 4.38 (d, J = 13.2 Hz, 1H),

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305−5314

6.03 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.82 (d, J = 7.8 Hz, 1H), 6.94−7.14 (m, 7H), 7.46−7.55 (m, 3H), 7.67 (d, J = 7.2 Hz, 1H), 7.87 (d, J = 7.2 Hz, 2H), 9.08 (s, 1H), 9.25 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.0, 34.6, 52.0, 52.2, 65.6, 108.6, 122.2, 124.2, 124.8, 127.4, 127.9, 128.0, 128.1, 128.5, 129.7, 131.6, 132.0, 132.9, 142.2, 159.1, 166.2, 172.3, 172.7; IR (KBr) ν 3377, 3062, 2931, 1763, 1705, 1666, 1615, 1530, 1490, 1469, 1379, 1338, 1316, 1286, 1097, 713, 698 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{27}H_{23}N_3NaO_4$ [M + Na]$^+$ 476.1581, found 476.1588.

*N-(1′-Formyl-2,5′-dioxo-1,3′-diphenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5c**).* White solid (67.7 mg, 90% yield), >99:1:0:0 dr; mp 296.2−297.6 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.47 (d, J = 12.9 Hz, 1H), 6.11 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.40 (d, J = 7.8 Hz, 1H), 6.99−7.15 (m, 7H), 7.24 (d, J = 7.8 Hz, 2H), 7.43−7.54 (m, 4H), 7.57−7.63 (m, 2H), 7.76 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.8 Hz, 2H), 9.16 (s, 1H), 9.29 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 52.2, 52.3, 65.9, 108.9, 123.1, 123.8, 125.2, 126.4, 127.4, 128.0, 128.1, 128.2, 128.5, 128.6, 128.7, 129.9, 130.0, 131.7, 132.1, 132.9, 133.8, 143.1, 159.4, 166.3, 172.4, 172.5; IR (KBr) ν 3351, 3062, 2924, 1769, 1708, 1667, 1614, 1533, 1500, 1467, 1378, 1317, 1259, 1026, 755, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{23}N_3NaO_4$ [M + Na]$^+$ 524.1581, found 524.1583.

*N-(1-Benzyl-1′-formyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5d**).* White solid (72.7 mg, 94% yield), >99:1:0:0 dr; mp 231.2−232.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.45 (d, J = 13.2 Hz, 1H), 4.86 (d, J = 15.9 Hz, 1H), 4.97 (d, J = 15.9 Hz, 1H), 6.04 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 6.92−7.06 (m, 7H), 7.24−7.29 (m, 5H), 7.44−7.55 (m, 3H), 7.73 (d, J = 7.2 Hz, 1H), 7.87 (d, J = 7.2 Hz, 2H), 9.14 (s, 1H), 9.27 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.4, 52.2, 52.6, 65.8, 109.3, 122.5, 124.1, 124.9, 127.4, 127.5, 128.0, 128.1, 128.4, 128.5, 128.6, 129.7, 131.5, 132.0, 132.9, 135.6, 142.5, 159.3, 166.3, 172.6, 172.9; IR (KBr) ν 3369, 3062, 2926, 1801, 1728, 1649, 1615, 1532, 1489, 1469, 1383, 1330, 1181, 1163, 998, 752, 698 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_3NaO_4$ [M + Na]$^+$ 538.1737, found 538.1756.

*Ethyl 4′-Benzamido-2,5′-dioxo-1,3′-diphenylspiro[indoline-3,2′-pyrrolidine]-1′-carboxylate (**5e**).* White solid (71.2 mg, 87% yield), 95:5:0:0 dr; mp 196.8−198.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.05 (t, J = 6.9 Hz, 3H), 4.13 (q, J = 6.9 Hz, 2H), 4.38 (d, J = 13.2 Hz, 1H), 5.99 (dd, J = 8.7 Hz, 13.2 Hz, 1H), 6.42 (d, J = 7.2 Hz, 1H), 7.02−7.14 (m, 7H), 7.22 (d, J = 7.8 Hz, 2H), 7.44−7.54 (m, 4H), 7.58−7.63 (m, 2H), 7.78 (d, J = 7.2 Hz, 1H), 7.85 (d, J = 7.8 Hz, 2H), 9.18 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.9, 52.1, 55.0, 63.2, 68.1, 108.8, 123.1, 124.5, 125.0, 126.2, 127.3, 128.0, 128.2, 128.5, 129.8, 130.0, 131.7, 131.9, 133.0, 133.8, 142.7, 149.8, 166.2, 169.7, 173.2; IR (KBr) ν 3386, 3060, 2925, 1806, 1731, 1668, 1613, 1529, 1501, 1374, 1337, 1316, 1268, 1218, 1039, 751, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{27}N_3NaO_5$ [M + Na]$^+$ 568.1843, found 568.1865.

*Ethyl 4′-Benzamido-1-benzyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidine]-1′- carboxylate (**5f**).* White solid (77.2 mg, 92% yield), >99:1:0:0 dr; mp 85.8−87.4 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 0.96 (t, J = 6.9 Hz, 3H), 3.95−4.05 (m, 2H), 4.33 (d, J = 13.2 Hz, 1H), 4.78 (d, J = 15.9 Hz, 1H), 4.89 (d, J = 15.9 Hz, 1H), 5.88 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.64 (d, J = 7.8 Hz, 1H), 6.91−7.08 (m, 7H), 7.17−7.28 (m, 5H), 7.44−7.50 (m, 3H), 7.70 (d, J = 7.2 Hz, 1H), 7.82 (d, J = 7.2 Hz, 2H), 9.13 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 13.7, 43.5, 51.8, 52.6, 63.0, 68.0, 109.2, 122.5, 124.2, 125.3, 127.3, 127.5, 128.0, 128.4, 128.5, 129.7, 131.6, 131.9, 133.0, 135.6, 142.4, 149.6, 166.2, 169.8, 173.8; IR (KBr) ν 3332, 3062, 2927, 1764, 1730, 1708, 1676, 1616, 1544, 1488, 1469, 1369, 1298, 1260, 1183, 1032, 749, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{34}H_{29}N_3NaO_5$ [M + Na]$^+$ 582.1999, found 582.2022.

*N-(3′-(2,4-Dichlorophenyl)-1′-formyl-1-methyl-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5g**).* White solid (68.6 mg, 90% yield), >99:1:0:0 dr; mp 333.8−335.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.08 (s, 3H), 4.81 (d, J = 12.6 Hz, 1H), 6.09 (dd, J = 8.4 Hz, 12.3 Hz, 1H), 6.85 (d, J = 7.8 Hz, 1H), 6.92−6.97 (m, 1H), 7.15−7.20 (m, 2H), 7.39−7.58 (m, 5H), 7.83−7.85 (m, 3H), 9.10 (s, 1H), 9.32 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 26.6, 47.4, 53.5, 64.9, 108.5, 122.0, 123.9, 125.2, 126.5, 127.4, 128.5, 128.7, 129.5, 129.9, 132.0, 132.2, 132.8, 133.1, 135.3, 143.3, 159.2, 166.2, 172.1, 172.6; IR (KBr) ν 3333, 3061, 2933, 1764, 1717, 1662, 1615, 1532, 1492, 1472, 1381, 1337, 1297, 1254, 755, 695 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{26}H_{19}Cl_2N_3NaO_4$ [M + Na]$^+$ 530.0645, found 530.0670.

*N-(3′-(2,4-Dichlorophenyl)-1′-formyl-2,5′-dioxo-1-phenylspiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5h**).* White solid (73.6 mg, 86% yield), 96:4:0:0 dr; mp 278.2−279.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.95 (d, J = 12.6 Hz, 1H), 6.19 (dd, J = 8.1 Hz, 12.3 Hz, 1H), 6.49 (d, J = 7.8 Hz, 1H), 6.99−7.04 (m, 1H), 7.10−7.15 (m, 1H), 7.24−7.29 (m, 3H), 7.45−7.63 (m, 8H), 7.85 (d, J = 7.2 Hz, 2H), 7.96 (d, J = 7.2 Hz, 1H), 9.18 (s, 1H), 9.37 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 47.5, 53.7, 65.2, 108.9, 122.7, 123.7, 125.9, 126.3, 126.7, 127.4, 128.6, 128.8, 129.4, 129.9, 130.0, 132.1, 132.3, 132.8, 133.4, 134.0, 135.4, 143.2, 159.5, 166.2, 172.0, 172.2; IR (KBr) ν 3351, 3061, 2923, 1771, 1727, 1705, 1668, 1615, 1516, 1483, 1466, 1331, 1303, 1223, 756, 702 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{21}Cl_2N_3NaO_4$ [M + Na]$^+$ 592.0801, found 592.0817.

*N-(1-Benzyl-3′-(2-fluorophenyl)-1′-formyl-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5i**).* White solid (72.8 mg, 91% yield), >99:1:0:0 dr; mp 218.3−219.5 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.76 (d, J = 12.9 Hz, 1H), 4.83 (d, J = 16.2 Hz, 1H), 4.94 (d, J = 16.2 Hz, 1H), 6.11 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.56 (d, J = 7.8 Hz, 1H), 6.90−6.97 (m, 3H), 7.01−7.13 (m, 2H), 7.22−7.33 (m, 6H), 7.45−7.58 (m, 3H), 7.78 (d, J = 7.5 Hz, 1H), 7.86−7.88 (m, 2H), 9.15 (s, 1H), 9.31 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.3, 45.0, 52.4, 65.3, 109.2, 115.1 (d, J = 21.9 Hz, 1C), 119.0 (d, J = 14.3 Hz, 1C), 122.3, 123.9, 125.1, 127.0, 127.4, 128.4, 128.6, 129.8, 130.0, 130.1, 132.1, 132.8, 135.6, 142.6, 159.3, 161.1 (d, J = 244.6 Hz, 1C), 166.2, 172.3, 172.7; IR (KBr) ν 3387, 3067, 2921, 1765, 1719, 1661, 1614, 1519, 1489, 1468, 1338, 1309, 1257, 754, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{24}FN_3NaO_4$ [M + Na]$^+$ 556.1643, found 556.1653.

*N-(1-Benzyl-3′-(4-chlorophenyl)-1′-formyl-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5j**).* White solid (71.8 mg, 87% yield), 94:6:0:0 dr; mp 190.2−191.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.40 (d, J = 12.9 Hz, 1H), 4.87 (d, J = 15.9 Hz, 1H), 4.97 (d, J = 15.9 Hz, 1H), 6.00 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.68 (d, J = 7.8 Hz, 1H), 6.95−7.00 (m, 3H), 7.08−7.13 (m, 3H), 7.24−7.29 (m, 5H), 7.45−7.50 (m, 2H), 7.53−7.58 (m, 1H), 7.77 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 2H), 9.14 (s, 1H), 9.26 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.3, 51.7, 52.7, 65.6, 109.4, 122.6, 123.8, 124.9, 127.3, 127.4, 127.5, 128.1, 128.5, 128.6, 129.9, 130.2, 130.6, 132.1, 132.7, 132.8, 135.6, 142.3, 159.3, 166.3, 172.3, 172.7; IR (KBr) ν 3367, 3067, 2931, 1765, 1719, 1665, 1618, 1535, 1489, 1471, 1378, 1339, 1298, 1253, 753, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{24}ClN_3NaO_4$ [M + Na]$^+$ 572.1348, found 572.1361.

*N-(1-Benzyl-3′-(4-cyanophenyl)-1′-formyl-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5k**).* White solid (74.6 mg, 92% yield), 94:6:0:0 dr; mp 192.3−193.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.49 (d, J = 12.9 Hz, 1H), 4.85 (d, J = 15.9 Hz, 1H), 5.00 (J = 15.9 Hz, 1H), 6.08 (dd, J = 8.1 Hz, 12.9 Hz, 1H), 6.69 (d, J = 7.8 Hz, 1H), 6.94−6.99 (m, 1H), 7.06−7.13 (m, 1H), 7.17 (d, J = 8.4 Hz, 2H), 7.28−7.31 (m, 5H), 7.45−7.58 (m, 5H), 7.80 (d, J = 7.2 Hz, 1H), 7.84−7.87 (m, 2H), 9.15 (s, 1H), 9.30 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.4, 52.1, 52.5, 65.5, 109.4, 110.8, 118.2, 122.7, 123.5, 125.0, 127.4, 127.5, 127.6, 128.5, 128.6, 129.4, 130.0, 131.9, 132.1, 132.7, 135.6, 137.4, 142.2, 159.3, 166.3, 172.1, 172.5; IR (KBr) ν 3262, 3063, 2925, 1769, 1722, 1698, 1652, 1614, 1540, 1489, 1468, 1334, 1309, 1252, 1029, 751, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{24}N_4NaO_4$ [M + Na]$^+$ 563.1690, found 563.1689.

*N-(1′-Formyl-3′-(3-methoxyphenyl)-2,5′-dioxo-1-phenylspiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5l**).* White solid (70.2 mg, 88% yield), >99:1:0:0 dr; mp 171.2−172.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.59 (s, 3H), 4.46 (d, J = 12.9 Hz, 1H), 6.10 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.46 (d, J = 7.8 Hz, 1H), 6.66−6.70 (m, 3H), 7.00−7.04 (m, 1H), 7.06−7.13 (m, 2H), 7.26 (d, J = 7.5 Hz, 2H), 7.48−7.62 (m, 6H), 7.79 (d, J = 7.2 Hz, 1H), 7.89 (d, J = 7.2 Hz, 2H), 9.17 (s,

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305−5314

1H), 9.31 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 52.2, 52.3, 55.0, 65.8, 108.9, 113.5, 113.6, 120.4, 123.0, 123.8, 125.2, 126.4, 127.4, 128.6, 128.7, 129.4, 129.9, 130.0, 132.1, 132.9, 133.3, 133.9, 143.1, 158.9, 159.4, 166.3, 172.4; IR (KBr) ν 3375, 3061, 2922, 1765, 1715, 1702, 1664, 1613, 1528, 1499, 1466, 1377, 1330, 1294, 1261, 1028, 751, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_3NaO_5$ [M + Na]$^+$ 554.1686, found 554.1667.

*N-(1′-Formyl-3′-(4-methoxyphenyl)-2,5′-dioxo-1-phenylspiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5m**).* White solid (68.6 mg, 86% yield), 96:4:0:0 dr; mp 264.3−265.8 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.60 (s, 3H), 4.39 (d, J = 13.2 Hz, 1H), 6.04 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.46 (d, J = 7.8 Hz, 1H), 6.72 (d, J = 8.7 Hz, 2H), 7.00−7.06 (m, 3H), 7.09−7.14 (m, 1H), 7.26 (d, J = 7.5 Hz, 2H), 7.45−7.56 (m, 4H), 7.59−7.64 (m, 2H), 7.77 (d, J = 7.2 Hz, 1H), 7.87 (d, J = 7.2 Hz, 2H), 9.15 (s, 1H), 9.25 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 51.8, 52.4, 55.0, 65.9, 108.9, 113.6, 123.1, 123.3, 124.0, 125.1, 126.5, 127.4, 128.6, 128.7, 129.2, 129.9, 130.0, 132.0, 132.9, 133.9, 143.1, 158.8, 159.4, 166.2, 172.5; IR (KBr) ν 3371, 3063, 2928, 1769, 1712, 1660, 1614, 1517, 1501, 1467, 1315, 1256, 1231, 1028, 754, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{25}N_3NaO_5$ [M + Na]$^+$ 554.1686, found 554.1670.

*N-(1-Benzyl-1′-formyl-2,5′-dioxo-3′-(p-tolyl)spiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5n**).* White solid (71.5 mg, 90% yield), >99:1:0:0 dr; mp 199.8−201.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 2.07 (s, 3H), 4.36 (d, J = 13.2 Hz, 1H), 4.84 (d, J = 15.9 Hz, 1H), 4.94 (d, J = 15.9 Hz, 1H), 5.97 (dd, J = 8.4 Hz, 13.2 Hz, 1H), 6.61 (d, J = 7.8 Hz, 1H), 6.81−6.87 (m, 4H), 6.92−6.97 (m, 1H), 7.04−7.09 (m, 1H), 7.20−7.29 (m, 5H), 7.43−7.56 (m, 3H), 7.71 (d, J = 7.2 Hz, 1H), 7.84 (d, J = 7.2 Hz, 2H), 9.11 (s, 1H), 9.21 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 20.9, 43.6, 52.3, 53.1, 66.1, 109.7, 122.8, 124.5, 125.1, 127.6, 127.7, 127.8, 128.6, 128.8, 128.9, 129.0, 130.1, 132.3, 133.2, 135.9, 137.5, 142.8, 159.6, 166.5, 173.0, 173.2; IR (KBr) ν 3270, 3063, 2925, 1762, 1719, 1704, 1655, 1615, 1548, 1487, 1333, 1319, 1308, 1250, 1026, 752, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{27}N_3NaO_4$ [M + Na]$^+$ 552.1894, found 552.1899.

*N-(1-Benzyl-1′-formyl-3′-(4-methoxyphenyl)-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5o**).* White solid (72.8 mg, 89% yield), >99:1:0:0 dr; mp 87.2−88.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.57 (s, 3H), 4.36 (d, J = 13.2 Hz, 1H), 4.87 (d, J = 16.2 Hz, 1H), 4.94 (d, J = 16.2 Hz, 1H), 5.96 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.57 (d, J = 8.4 Hz, 2H), 6.66 (d, J = 7.8 Hz, 1H), 6.89 (d, J = 8.4 Hz, 2H), 6.95−7.00 (m, 1H), 7.07−7.13 (m, 1H), 7.28−7.32 (m, 5H), 7.45−7.58 (m, 3H), 7.73 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.5 Hz, 2H), 9.13 (s, 1H), 9.23 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.3, 51.8, 52.9, 54.9, 65.8, 109.3, 113.4, 122.5, 123.1, 124.2, 124.8, 127.4, 127.5, 128.5, 128.6, 129.6, 129.7, 132.0, 132.9, 135.6, 142.5, 158.7, 159.3, 166.2, 172.6, 172.9; IR (KBr) ν 3337, 3062, 2930, 1762, 1714, 1668, 1614, 1534, 1516, 1468, 1340, 1313, 1252, 1181, 1026, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{27}N_3NaO_5$ [M + Na]$^+$ 568.1843, found 568.1838.

*N-(3′-(Benzo[d][1,3]dioxol-5-yl)-1-benzyl-1′-formyl-2,5′-dioxospiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5p**).* White solid (73.0 mg, 87% yield), >99:1:0:0 dr; mp 213.5−214.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.33 (d, J = 13.2 Hz, 1H), 4.87 (d, J = 16.2 Hz, 1H), 4.93 (d, J = 16.2 Hz, 1H), 5.84−5.94 (m, 3H), 6.41 (d, J = 8.1 Hz, 1H), 6.55−6.58 (m, 2H), 6.65 (d, J = 7.8 Hz, 1H), 6.95−7.00 (m, 1H), 7.09−7.14 (m, 1H), 7.27−7.30 (m, 5H), 7.44−7.56 (m, 3H), 7.75 (d, J = 7.2 Hz, 1H), 7.86 (d, J = 7.2 Hz, 2H), 9.10 (s, 1H), 9.23 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.4, 52.0, 53.1, 65.8, 101.1, 107.9, 108.2, 109.4, 122.5, 124.1, 124.9, 125.2, 127.2, 127.4, 127.5, 128.5, 128.6, 129.8, 132.0, 132.9, 135.6, 142.5, 146.8, 146.9, 159.3, 166.2, 172.4, 172.9; IR (KBr) ν 3330, 3064, 2925, 1761, 1719, 1702, 1658, 1615, 1504, 1490, 1335, 1307, 1243, 1040, 753, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{33}H_{25}N_3NaO_6$ [M + Na]$^+$ 582.1636, found 582.1646.

*N-(1-Ethyl-1′-formyl-2,5′-dioxo-3′-(thiophen-2-yl)spiro[indoline-3,2′-pyrrolidine]-4′-yl)benzamide (**5q**).* White solid (58.6 mg, 85% yield), 92:8:0:0 dr; mp 223.5−234.9 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 1.14 (t, J = 6.9 Hz, 3H), 3.75 (q, J = 6.9 Hz, 2H), 4.59 (d, J = 12.9 Hz, 1H), 5.78 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.75−6.77 (m, 1H), 6.80 (s, 1H), 6.94−7.02 (m, 2H), 7.22−7.24 (m, 2H), 7.47−7.57 (m, 3H), 7.63 (d, J = 7.2 Hz, 1H), 7.88 (d, J = 6.9 Hz, 2H), 9.06 (s, 1H), 9.28 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 12.0, 34.7, 47.6, 54.5, 65.4, 108.8, 122.3, 124.0, 124.9, 126.3, 126.6, 126.8, 127.3, 128.4, 128.6, 130.1, 132.0, 132.9, 134.5, 142.8, 159.1, 166.3, 171.8, 171.9; IR (KBr) ν 3326, 3063, 2926, 1771, 1718, 1703, 1675, 1616, 1540, 1492, 1469, 1297, 1263, 1026, 755, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{25}H_{21}N_3NaO_4S$ [M + Na]$^+$ 482.1145, found 482.1122.

*N-(1-Benzyl-1′-formyl-2,5′-dioxo-3′-(thiophen-2-yl)spiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5r**).* White solid (68.8 mg, 88% yield), >99:1:0:0 dr; mp 275.6−277.1 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.65 (d, J = 12.9 Hz, 1H), 4.85 (d, J = 16.2 Hz, 1H), 5.02 (d, J = 16.2 Hz, 1H), 5.73 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.67−6.75 (m, 3H), 6.97−7.02 (m, 1H), 7.13−7.28 (m, 7H), 7.46−7.58 (m, 3H), 7.71 (d, J = 7.2 Hz, 1H), 7.87 (d, J = 7.2 Hz, 2H), 9.12 (s, 1H), 9.30 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.4, 48.1, 55.1, 65.5, 109.5, 122.7, 123.9, 125.0, 126.6, 127.1, 127.4, 127.5, 128.5, 128.6, 130.1, 132.1, 132.9, 134.3, 135.5, 142.9, 159.3, 166.3, 171.7, 172.5; IR (KBr) ν 3310, 3064, 2923, 1770, 1718, 1702, 1672, 1614, 1541, 1489, 1468, 1298, 1265, 1025, 719, 699 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{30}H_{23}N_3NaO_4S$ [M + Na]$^+$ 544.1301, found 544.1319.

*N-(1′-Formyl-3′-(furan-2-yl)-2,5′-dioxo-1-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5s**).* White solid (60.5 mg, 82% yield), 94:6:0:0 dr; mp 175.6−177.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.47 (d, J = 12.6 Hz, 1H), 5.86 (dd, J = 8.4 Hz, 12.6 Hz, 1H), 6.18 (s, 1H), 6.29 (d, J = 3.0 Hz, 1H), 6.59 (d, J = 7.8 Hz, 1H), 6.98−7.03 (m, 1H), 7.15−7.20 (m, 1H), 7.38−7.41 (m, 3H), 7.49−7.59 (m, 4H), 7.62−7.67 (m, 3H), 7.91 (d, J = 7.2 Hz, 2H), 9.14 (s, 1H), 9.39 (d, J = 8.4 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 46.4, 52.3, 64.6, 108.5, 108.9, 110.4, 123.0, 123.6, 125.1, 126.6, 127.4, 128.7, 130.0, 132.1, 132.9, 134.1, 143.4, 143.6, 147.9, 159.5, 166.4, 171.8, 172.1; IR (KBr) ν 3356, 3063, 2928, 1773, 1716, 1668, 1616, 1545, 1491, 1465, 1292, 1268, 1026, 755, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{29}H_{21}N_3NaO_5$ [M + Na]$^+$ 514.1373, found 514.1389.

*N-(1-Benzyl-1′-formyl-3′-(naphthalen-1-yl)-2,5′-dioxospiro-[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (**5t**).* White solid (78.9 mg, 93% yield), >99:1:0:0 dr; mp 305.6−307.2 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.39 (d, J = 16.2 Hz, 1H), 4.63 (d, J = 16.2 Hz, 1H), 5.45 (d, J = 12.9 Hz, 1H), 6.18−6.25 (m, 2H), 6.77 (d, J = 7.2 Hz, 2H), 6.92−7.01 (m, 4H), 7.06−7.11 (m, 1H), 7.18−7.23 (m, 1H), 7.38−7.53 (m, 6H), 7.65 (d, J = 8.1 Hz, 1H), 7.77−7.90 (m, 4H), 8.06 (d, J = 8.4 Hz, 1H), 9.18 (s, 1H), 9.25 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.1, 46.0, 54.2, 65.9, 109.3, 122.4, 122.6, 124.4, 124.5, 126.5, 126.6, 127.1, 127.3, 127.6, 128.3, 128.4, 128.5, 128.8, 132.4, 132.8, 133.1, 135.1, 142.1, 159.4, 166.3, 172.7, 173.4; IR (KBr) ν 3357, 3067, 2924, 1768, 1720, 1698, 1668, 1615, 1538, 1490, 1468, 1334, 1315, 1298, 780, 757, 715 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{36}H_{27}N_3NaO_4$ [M + Na]$^+$ 588.1894, found 588.1900.

*N-(1-Benzyl-1′-formyl-2,5′-dioxo-3′-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)-4-bromobenzamide (**5u**).* White solid (73.1 mg, 82% yield), >99:1:0:0 dr; mp 286.8−288.3 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 4.39 (d, J = 13.2 Hz, 1H), 4.85 (d, J = 15.9 Hz, 1H), 4.95 (d, J = 15.9 Hz, 1H), 6.00 (dd, J = 8.4 Hz, 12.9 Hz, 1H), 6.62 (d, J = 7.8 Hz, 1H), 6.92−7.09 (m, 7H), 7.26−7.32 (m, 5H), 7.69−7.81 (m, 5H), 9.12 (s, 1H), 9.34 (d, J = 8.1 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 43.4, 52.1, 52.7, 65.8, 109.3, 122.5, 124.0, 124.9, 125.9, 127.4, 127.5, 128.0, 128.1, 128.3, 128.5, 129.5, 129.7, 131.5, 131.7, 132.0, 135.6, 142.4, 159.3, 165.4, 172.5, 172.9; IR (KBr) ν 3367, 3056, 2924, 1769, 1718, 1706, 1658, 1615, 1528, 1485, 1467, 1335, 1315, 1301, 1012, 751, 727, 697 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{32}H_{24}BrN_3NaO_4$ [M + Na]$^+$ 616.0842, found 616.0860.

Procedure for the Catalytic Asymmetric Reaction of 3-Aminooxindole 4c and (*Z*)-Olefinic Azlactone 2a. In an ordinary vial equipped with a magnetic stirring bar, a solution of **4c** (0.10 mmol), **2a** (0.12 mmol), and catalyst **A** (5 mg, 10 mol %, 0.01 mmol) in 3 mL of xylene was stirred at room temperature for 9 days. Then the reaction mixture was directly purified by flash chromatography (petroleum ether/ethyl acetate = 10/1−2/1) on silica gel to yield

dx.doi.org/10.1021/jo500432c | J. Org. Chem. 2014, 79, 5305−5314

chiral product **5c** (23.6 mg, 47% yield) as a white solid with >99:1 dr and 61% ee. $[\alpha]_D^{20}$ = +2.5 (*c* 0.50, $CHCl_3$); the ee was determined by HPLC (Chiralpak OD-H, *i*-PrOH/hexane = 20/80, flow rate = 1.0 mL/min, λ = 254 nm, t_{minor} = 8.0 min, t_{major} = 7.2 min); the ^{1}H NMR and ^{13}C NMR data for chiral compound **5c** were same as those of the racemic compound **5c**.

Synthesis of *N*-(3′-(4-Methoxyphenyl)-2,5′-dioxo-1-phenylspiro[indoline-3,2′-pyrrolidin]-4′-yl)benzamide (6). To a solution of compound **5m** (0.11 mmol, 59 mg) in CH_2Cl_2 (12 mL) were successively added 10% NaOH(aq) (11 mL) and TBAB (3.5 mg, 0.011 mmol). The resulting mixture was stirred at the room temperature for 5 h. After completion of the reaction as indicated by TLC, the mixture was extracted with CH_2Cl_2, and the combined organic layers were dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash chromatography on silica gel (petroleum ether/ethyl acetate = 2/1) to yield product **6** as a white solid (31.0 mg, 56% yield, >99:1:0:0 dr). Mp 301.2−302.7 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 3.59 (s, 3H), 4.31 (d, *J* = 12.6 Hz, 1H), 5.80 (dd, *J* = 9.0 Hz, 12.6 Hz, 1H), 6.48 (d, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 8.7 Hz, 2H), 7.00 (d, *J* = 8.7 Hz, 2H), 7.05−7.15 (m, 2H), 7.27 (d, *J* = 7.5 Hz, 2H), 7.42−7.55 (m, 5H), 7.59−7.64 (m, 2H), 7.88 (d, *J* = 7.2 Hz, 2H), 8.76 (s, 1H), 9.02 (d, *J* = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 51.1, 54.8, 55.0, 65.5, 109.1, 113.5, 123.3, 125.0, 125.3, 126.4, 127.4, 127.6, 128.4, 128.5, 129.0, 129.5, 130.0, 131.7, 133.4, 133.9, 142.3, 158.5, 166.3, 173.2, 174.8; IR (KBr) ν 3359, 3061, 2928, 1731, 1705, 1659, 1614, 1543, 1515, 1500, 1466, 1254, 1033, 750, 700 cm^{-1}; HRMS (ESI-TOF) calcd for $C_{31}H_{25}N_3NaO_4$ $[M + Na]^+$ 526.1737, found 526.1747.

Competition Experiment with 1a and 4a. In an ordinary vial equipped with a magnetic stirring bar, **1a** (0.1 mmol, 1.0 equiv), **4a** (0.1 mmol, 1.0 equiv), **2g** (0.1 mmol, 1.0 equiv), and catalyst (DBU, 20 mol %) were dissolved in 10 mL of CH_2Cl_2, and then the mixture was refluxed for 8 h under an Ar atmosphere. After completion of the reaction as indicated by TLC, the solvent was removed in vacuo, and the ratio of **3j** and **5v** was determined by ^{1}H NMR analysis of the crude mixture.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for the products and single-crystal X-ray crystallography data for **3m** and **5b**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: yuanwc@cioc.ac.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We are grateful for financial support from the National Natural Science Foundation of China (21372217) and the Sichuan Youth Science and Technology Foundation (2011JQ0046 and 2013JQ0021).

■ REFERENCES

(1) (a) Lin, H.; Danishefsky, S. J. *Angew. Chem., Int. Ed.* **2003**, *42*, 36. (b) Galliford, C. V.; Scheidt, K. A. *Angew. Chem., Int. Ed.* **2007**, *46*, 8748. (c) Badillo, J. J.; Hanhan, N. V.; Franz, A. K. *Curr. Opin. Drug Discovery Dev.* **2010**, *13*, 758. (d) Rottmann, M.; McNamara, C.; Yeung, B. K. S.; Lee, M. C. S.; Zou, B.; Russell, B.; Seitz, P.; Plouffe, D. M.; Dharia, N. V.; Tan, J.; Cohen, S. B.; Spencer, K. R.; Gonzalez-Paez, G. E.; Lakshminarayana, S. B.; Goh, A.; Suwanarusk, R.; Jegla, T.; Schmitt, E. K.; Beck, H. P.; Brun, R.; Nosten, F.; Renia, L.; Dartois, V.; Keller, T. H.; Fidock, D. A.; Winzeler, E. A.; Diagana, T. T. *Science* **2010**, *329*, 1175. (e) Singh, G. S.; Desta, Z. Y. *Chem. Rev.* **2012**, *112*, 6104.

(2) Peddibhotla, S. *Curr. Bioact. Compd.* **2009**, *5*, 20.

(3) For reviews of the construction of spirocyclic oxindoles, see: (a) Marti, C.; Carreira, E. M. *Eur. J. Org. Chem.* **2003**, 2209. (b) Trost, B. M.; Brennan, M. K. *Synthesis* **2009**, 3003. (c) Liu, Y.-L.; Zhou, J. *Adv. Synth. Catal.* **2010**, *352*, 1381. (d) Alba, A.-N. R.; Rios, R. *Chem.—Asian J.* **2011**, *6*, 720. (e) Ball-Jones, N. R.; Badillo, J. J.; Franz, A. K. *Org. Biomol. Chem.* **2012**, *10*, 5165. (f) Dalpozzo, R.; Bartoli, G.; Bencivenni, G. *Chem. Soc. Rev.* **2012**, *41*, 7247. (g) Hong, L.; Wang, R. *Adv. Synth. Catal.* **2013**, *355*, 1023.

(4) For selected examples containing a nitrogen atom at the C3 position of the oxindole unit, see: (a) Ochi, M.; Kawasaki, K.; Kataoka, H.; Uchio, Y.; Nishi, H. *Biochem. Biophys. Res. Commun.* **2001**, *283*, 1118. (b) Bernard, K.; Bogliolo, S.; Ehrenfeld, J. *Br. J. Pharmacol.* **2005**, *144*, 1037. (c) Czarna, A.; Beck, B.; Srivastava, S.; Popowicz, G. M.; Wolf, S.; Huang, Y.; Bista, M.; Holak, T. A.; Dömling, A. *Angew. Chem., Int. Ed.* **2010**, *49*, 5352. (d) Vintonyak, V. V.; Warburg, K.; Kruse, H.; Grimme, S.; Hübel, K.; Rauh, D.; Waldmann, H. *Angew. Chem., Int. Ed.* **2010**, *49*, 5902. (e) Crosignani, S.; Jorand-Lebrun, C.; Page, P.; Campbell, G.; Colovray, V.; Missotten, M.; Humbert, Y.; Cleva, C.; Arrighi, J.-F.; Gaudet, M.; Johnson, Z.; Ferro, P.; Chollet, A. *ACS Med. Chem. Lett.* **2011**, *2*, 644.

(5) For selected examples containing an oxygen atom at the C3 position of the oxindole unit, see: (a) Heindel, N. D.; Minatelli, J. A. *J. Pharm. Sci.* **1981**, *70*, 84. (b) Jimenez, J. I.; Huber, U.; Moore, R. E.; Patterson, G. M. L. *J. Nat. Prod.* **1999**, *62*, 569. (c) Jiang, X.; Cao, Y.; Wang, Y.; Liu, L.; Shen, F.; Wang, R. *J. Am. Chem. Soc.* **2010**, *132*, 15328. (d) Franz, A. K.; Dreyfuss, P. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **2007**, *129*, 1020. (e) Quasdorf, K. W.; Huters, A. D.; Lodewyk, M. W.; Tantillo, D. J.; Garg, N. K. *J. Am. Chem. Soc.* **2012**, *134*, 1396. (f) Rana, S.; Natarajan, A. *Org. Biomol. Chem.* **2013**, *11*, 244.

(6) For selected examples, see: (a) Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R. *Org. Lett.* **2009**, *11*, 3874. (b) Mouri, S.; Chen, Z.; Mitsunuma, H.; Furutachi, M.; Matsunaga, S.; Shibasaki, M. *J. Am. Chem. Soc.* **2010**, *132*, 1255. (c) Jung, H. H.; Buesking, A. W.; Ellman, J. A. *Org. Lett.* **2011**, *13*, 3912. (d) Shen, K.; Liu, X.; Wang, G.; Lin, L.; Feng, X. *Angew. Chem., Int. Ed.* **2011**, *50*, 4684. (e) Bergonzini, G.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2012**, *51*, 971. (f) Trost, B. M.; Hirano, K. *Org. Lett.* **2012**, *14*, 2446. (g) Retini, M.; Bergonzini, G.; Melchiorre, P. *Chem. Commun.* **2012**, *48*, 3336. (h) Chen, D.; Xu, M.-H. *Chem. Commun.* **2013**, *49*, 1327. (i) Yamaguchi, E.; Mowat, J.; Luong, T.; Krische, M. J. *Angew. Chem., Int. Ed.* **2013**, *52*, 8428. (j) Wang, Q.-L.; Peng, L.; Wang, F.-Y.; Zhang, M.-L.; Jia, L.-N.; Tian, F.; Xu, X.-Y.; Wang, L.-X. *Chem. Commun.* **2013**, *49*, 9422. (k) Silvi, M.; Chatterjee, I.; Liu, Y.; Melchiorre, P. *Angew. Chem., Int. Ed.* **2013**, *52*, 10780.

(7) For selected reviews, see: (a) Kitson, R. R. A.; Millemaggi, A.; Taylor, R. J. K. *Angew. Chem., Int. Ed.* **2009**, *48*, 9426. (b) Elford, T. G.; Hall, D. G. *Synthesis* **2010**, 893.

(8) Cui, B.-D.; Han, W.-Y.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *J. Org. Chem.* **2013**, *78*, 8833.

(9) For selected examples, see: (a) Shi, F.; Dai, A.-X.; Zhang, S.; Zhang, X.-H.; Tu, S.-J. *Eur. J. Med. Chem.* **2003**, *38*, 597. (b) Yadav, L. D. S.; Singh, A. *Tetrahedron Lett.* **2003**, *44*, 5637. (c) Tu, S.; Zhang, J.; Jia, R.; Jiang, B.; Zhang, Y.; Jiang, H. *Org. Biomol. Chem.* **2007**, *5*, 1450. (d) Yadav, L. D. S.; Rai, V. K. *Tetrahedron* **2007**, *63*, 6924. (e) Jiang, H.; Gschwend, B.; Albrecht, Ł.; Hansen, S. G.; Jørgensen, K. A. *Chem.—Eur. J.* **2011**, *17*, 9032. (f) Alba, A.-N. R.; Calbet, T.; Font-Bardía, M.; Moyano, A.; Rios, R. *Eur. J. Org. Chem.* **2011**, 2053. (g) Steurer, M.; Jensen, K. L.; Worgull, D.; Jørgensen, K. A. *Chem.—Eur. J.* **2012**, *18*, 76. (h) Halskov, K. S.; Johansen, T. K.; Davis, R. L.; Steurer, M.; Jensen, F.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2012**, *134*, 12943. (i) Uraguchi, D.; Ueki, Y.; Sugiyama, A.; Ooi, T. *Chem. Sci.* **2013**, *4*, 1308. (j) Dell'Amico, L.; Albrecht, Ł.; Naicker, T.; Poulsen, P. H.; Jørgensen, K. A. *J. Am. Chem. Soc.* **2013**, *135*, 8063.

(10) (a) Chen, W.-B.; Wu, Z.-J.; Pei, Q.-L.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2010**, *12*, 3132. (b) Chen, W.-B.; Wu, Z.-J.; Hu, J.; Cun, L.-F.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2011**, *13*, 2472. (c) Han, Y.-Y.; Chen, W.-B.; Han, W.-Y.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2012**, *14*, 490. (d) Han, Y.-Y.; Han, W.-Y.; Hou,

X.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2012**, *14*, 4054. (e) Liu, X.-L.; Han, W.-Y.; Zhang, X.-M.; Yuan, W.-C. *Org. Lett.* **2013**, *15*, 1246. (f) Chen, W.-B.; Han, W.-Y.; Han, Y.-Y.; Zhang, X.-M.; Yuan, W.-C. *Tetrahedron* **2013**, *69*, 5281. (g) Han, W.-Y.; Li, S.-W.; Wu, Z.-J.; Zhang, X.-M.; Yuan, W.-C. *Chem.—Eur. J.* **2013**, *19*, 5551.

(11) For selected reviews of the application of tandem reactions in organic synthesis, see: (a) Enders, D.; Grondal, C.; Hüttl, M. R. M. *Angew. Chem., Int. Ed.* **2007**, *46*, 1570. (b) Grondal, C.; Jeanty, M.; Enders, D. *Nat. Chem.* **2010**, *2*, 167. (c) Westermann, B.; Ayaz, M.; van Berkel, S. S. *Angew. Chem., Int. Ed.* **2010**, *49*, 846. (d) Moyano, A.; Rios, R. *Chem. Rev.* **2011**, *111*, 4703. (e) Pellissier, H. *Chem. Rev.* **2013**, *113*, 442.

(12) See the Supporting Information for details about the single-crystal X-ray analyses of products **3m** and **5b** in this paper.