JOC The Journal of Organic Chemistry

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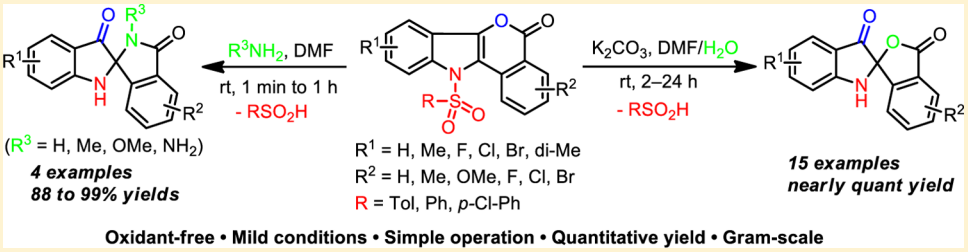
Ring-Contraction Disproportionation/Spirocyclization Cascade Reaction of Isochromeno[4,3-*b*]indol-5(11*H*)-ones: Synthesis of N-Unsubstituted Spirocycles

Xiang Zhang,[†] Guangshuai Zhou,[†] Yong Zhang,[†] Daisy Zhang-Negrerie,[†] Yunfei Du,*[,†,‡] and Kang Zhao*[,†]

[†]Tianjin Key Laboratory for Modern Drug Delivery & High-Efficiency, School of Pharmaceutical Science and Technology, Tianjin University, Tianjin 300072, China

[‡]Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Tianjin 300072, China

Supporting Information



ABSTRACT: An efficient ring-contraction reaction of isochromeno[4,3-*b*]indol-5(11*H*)-ones via a nucleophile-induced disproportionation/spirocyclization cascade process has been developed under mild conditions. The process realized the conversion of isochromeno[4,3-*b*]indol-5(11*H*)-ones into N-unsubstituted spiro[indoline-2,1′-isobenzofuran]-3,3′-diones and spiro[indoline-2,1′-isoindoline]-3,3′-diones in the absence of a transition-metal catalyst or oxidant. Gram-scale reaction further demonstrated the practicability of the protocol.

Syntheses of molecules of ever-increasing sensitivity or complexity demand the availability of a variety of protecting groups to ensure the survival of the functional groups, especially those common ones such as the hydroxyl and amino group.[1] One of the well-known protecting groups that has been widely used in organic synthesis, particularly in the total syntheses of complex natural products and pharmaceutical reagents, is the sulfonyl group (RSO_2-).[2] A survey of the literature showed that (1) RSO_2- can be removed under reductive conditions (Na/naphthalide[3] or powdered magnesium[4]) or harsh acidic conditions[5] but in many cases is of limited usage due to its poor tolerance of functional groups; (2) sulfonyl groups attached to the nitrogen atom in an indole or pyrrole can be deprotected under basic conditions;[6] (3) as leaving groups, sulfonyl groups can also be removed through a base-mediated disproportionation process or *β*-elimination reactions.[7] The last strategy, offering less harsh reactions conditions, is more promising in organic synthesis for its higher functional-group tolerance.

Recently, we disclosed a cascade annulation[8] and also a follow-up reaction of *trans*-aminocarboxylation[9] of internal alkynes, both of which afforded spiro and fused heterocycles with high efficiency and wide substrate scopes. In both works, sulfonyl groups were involved as an indispensible protecting group for the construction of target molecules. However, removing the sulfonyl group in the final product was unachievable under the above-mentioned reductive or acidic conditions, due to the presence of the reactive internal carbonyl, ketal, and lactone moieties. Herein, we report an efficient nucleophile-induced cascade reaction of isochromeno-[4,3-*b*]indol-5(11*H*)-ones, where sulfonyl groups functioned as a protecting group in the early stage of the process and were eliminated as a leaving group at a later stage, which further facilitated a spirocyclization reaction, all in one-pot, under mild, transition-metal-free conditions. To the best of our knowledge, this is the first report of such a ring-contraction rearrangement of isochromeno[4,3-*b*]indol-5(11*H*)-ones.

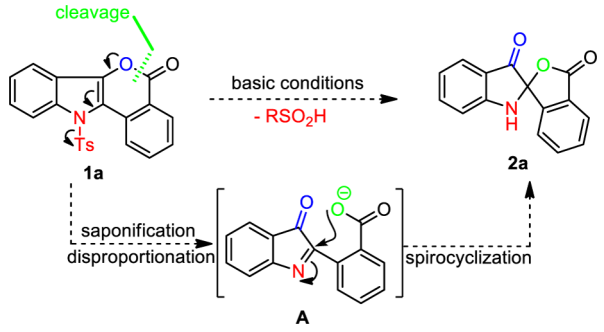
Based on the methodologies developed in our previous work,[8,9] we envisaged that isochromeno[4,3-*b*]indol-5(11*H*)-one **1a** would undergo a saponification/tosyl deprotection process in a basic environment to generate an imine intermediate **A**, followed by an intramolecular cyclization reaction to yield the N-unprotected 3′*H*-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione **2a** (Scheme 1).

In order to systematically investigate and better understand the transformations for the synthesis of N-unsubstituted spiroheterocycles, we designed and synthesized **1a**, the structurally simplest isochromeno[4,3-*b*]indol-5(11*H*)-one, as the model substrate. To our delight, treatment of **1a** with

Received: August 9, 2016
Published: October 18, 2016

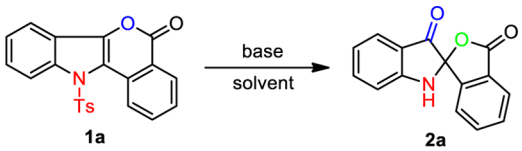
DOI: 10.1021/acs.joc.6b01957
J. Org. Chem. 2016, 81, 11397−11403

Scheme 1. Conjectured Cascade Process of Saponification/Disproportionation/Spirocyclization Reactions



aqueous KOH solution resulted in **2a** in 25% yield (Table 1, entry 1). Solvent-screening studies revealed that the reaction would not occur in dry DMF, THF, or MeCN, indicating that water is indispensible for the conversion (not shown). However, as the solubility of **1a** in H_2O was very low at room temperature, we aspired to improve the yield by running the reaction at a higher temperature but unfortunately observed decomposition of the substrate (Table 1, entry 2). Applying a two-component solvent of DMF and H_2O (9:1) led to a much improved yield. Base-screening studies showed that K_2CO_3 was by far the best base among a list of many common bases, including KF, CsF, Li_2CO_3, Na_2CO_3, NaOH, KOH, NaOMe, 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), and pyridine, affording **2a** in nearly quantitative yield (Table 1, entries 3–12). The two strongest bases, NaOH and KOH, led to significantly decreased yields, although the reaction time was shortened (Table 1, entries 13 and 14). In addition, other bases, such as $NaHCO_3$, NaOAc, K_2HPO_4, piperidine, TEA, etc., are not effective in the conversion of **1a** to **2a** (not shown). Finally, the reaction yield was found to be sensitive to the ratio of DMF and water (Table 1, entries 13 and 14). In summary, the optimized conditions were as follows: room temperature, K_2CO_3 as the base, and a mixture of DMF and H_2O in 9:1 ratio as the solvent (Table 1, entry 7). The purity of **2a** was high enough with no further purification (by column chromatography) necessary.

Table 1. Optimization of Reaction Conditions[a]



entry	base/Nu	solvent	time (h)	yield (%)[b]
1	KOH	H_2O	24	25
2[c]	KOH	H_2O	2	trace
3[d]	KF	DMF/H_2O (9/1)	48	NR
4[d]	CsF	DMF/H_2O (9/1)	48	trace
5[d]	Li_2CO_3	DMF/H_2O (9/1)	48	trace
6[d]	Na_2CO_3	DMF/H_2O (9/1)	48	NR
7[d]	K_2CO_3	DMF/H_2O (9/1)	12	99
8[d]	NaOH	DMF/H_2O (9/1)	0.5	36
9[d]	KOH	DMF/H_2O (9/1)	0.5	30
10[d]	NaOMe	DMF/H_2O (9/1)	0.05	70
11[d]	DBU	DMF/H_2O (9/1)	0.5	trace
12[d]	pyridine	DMF/H_2O (9/1)	48	NR
13[e]	K_2CO_3	DMF/H_2O (4/1)	48	74
14[f]	K_2CO_3	DMF/H_2O (15/1)	18	85

[a]Reaction conditions: substrate **1a** (0.4 mmol), base (1.2 mmol) in solvent (4 mL) at rt unless otherwise stated. [b]Isolated yield by extraction with EtOAc without further purification by column chromatography. [c]Reaction was conducted at 90 °C. [d]DMF (3.6 mL) and H_2O (0.4 mL) as solvent. [e]DMF (3.2 mL) and H_2O (0.8 mL) as solvent. [f]DMF (3750 μL) and H_2O (250 μL) as solvent.

Under the optimized conditions, a series of isochromeno[4,3-*b*]indol-5(11*H*)-ones **1** were studied to investigate the substituent scope of this newly established method (Table 2). Results showed that the protocol was applicable across a broad range of substrates, with the spiro products being smoothly generated in near quantitative yield for all substrates **2a–m**. While neither the R^1 or R^2 exerted any negative effect on the (quantitative) yield of the product, there was observed a consistent correlation between the electronic nature of R^2 and the reaction time; namely, electron-withdrawing halogen R^2 groups sped up the reactions (**2g–j**), while those of electron-donating (−Me and −OMe) slowed down the reactions (**2k–m**). This observation was in complete agreement with the mechanism of the reaction as an electron-withdrawing R^2 group would benefit the reaction during the saponification step by increasing the electrophilicity of the substrate to facilitate the nucleophilic attack at the carbonyl carbon.

Replacement of the tosyl group with other sulfonyl groups (*p*-$ClPhSO_2$, $PhSO_2$) also gave the expected product **2a** in quantitative yield. However, substrate **1p** (where R = 1-butanesulfonyl) yielded a mixture of two products, with **2a** in moderate yield accompanied by a side product of the N-unprotected starting substrate **3a** in 42% yield. This remarkably high-yield, easy-to-handle, one-pot process was found to be suitable for gram-scale production.

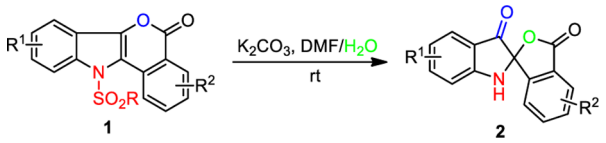
The next part of our systematic study addressed the scope of the nucleophile (Scheme 2). We were pleased to find that other nitrogen nucleophiles, such as ammonium hydroxide ($NH_3\cdot H_2O$),[10] methylamine ($MeNH_2$) in aqueous solution, and methoxyamine ($MeONH_2$), all gave the corresponding N,N′-unsubstituted ketal in excellent yields and in most cases finished the reaction almost instantly (Scheme 2a–d).[11,12] On the other hand, sulfur nucleophiles, such as Na_2S and $(NH_4)_2S$, failed to furnish the *N*,*S*-ketal product. In these reactions, the deprotected isochromeno[4,3-*b*]indol-5(11*H*)-one **3a** was formed instead as the sole product[13] (Scheme 2e).

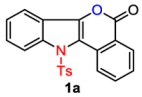
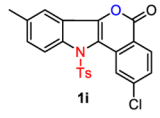
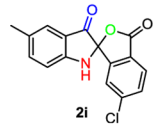
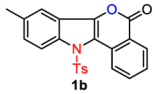
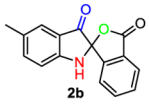
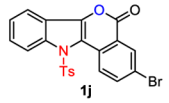
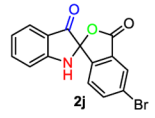
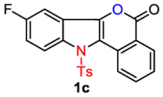
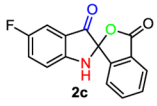
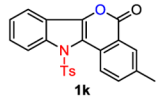
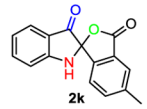
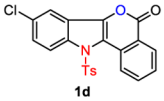
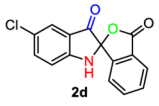
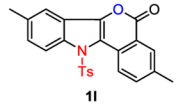
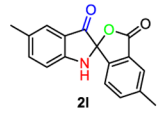
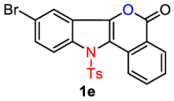
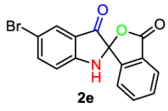
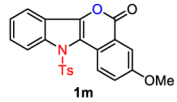
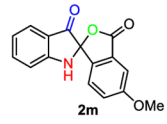
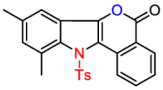
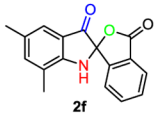
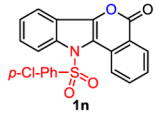
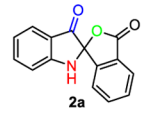
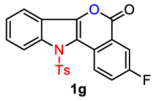
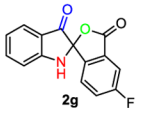
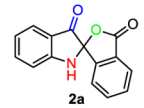
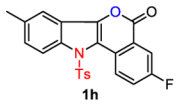
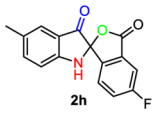
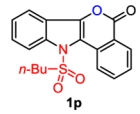
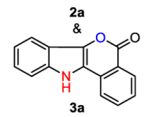
The proposed mechanism depicted in Scheme 3 can be used for reference to explain why water is indispensible for the ring-contraction reaction of **1a**. First, the hydroxide ion, generated in situ from the reaction of potassium carbonate (K_2CO_3) and H_2O (step 1), reacts with **1a** to form an acid intermediate **B** after saponification of the isochromeno ring (step 2). Then intermediate **B** undergoes a disproportionation/spirocyclization cascade process to form the precursor **A** (steps 3 and 4). Finally, the water-promoted protonation of **A** delivers product **2a** (step 5). Here, the suitable basic aqueous solution, generated in the K_2CO_3–H_2O–DMF system, is crucial for the formation and survival of the intermediates, which ensure the smooth occurrence of the ring opening and intramolecular cyclization phases.

A control experiment was carried out where methanol was used in place of H_2O, which gave the methyl 2-(2-methoxy-3-oxoindolin-2-yl)benzoate **5a** in a quantitative yield (Scheme 4). This result supported the proposed formation of intermediates **C** (or **A**) and **A′** in the cascade process.

DOI: 10.1021/acs.joc.6b01957
J. Org. Chem. 2016, 81, 11397–11403

Table 2. Scope of the K_2CO_3-Mediated Ring-Contraction Reaction[a]



Substrate **1**	Product **2**	T (h)	Yield (%)[b]	Substrate **1**	Product **2**	T (h)	Yield (%)[b]
 **1a**	 **2a**	12	99	 **1i**	 **2i**	2	99
 **1b**	 **2b**	12	98	 **1j**	 **2j**	3	98
 **1c**	 **2c**	12	99	 **1k**	 **2k**	8	99
 **1d**	 **2d**	12	99	 **1l**	 **2l**	18	99
 **1e**	 **2e**	12	99	 **1m**	 **2m**	24	99
 **1f**	 **2f**	12	98	 **1n**	 **2a**	8	99
 **1g**	 **2g**	12	98	 **1o**	 **2a**	18	99
 **1h**	 **2h**	2	99	 **1p**	 **2a** & **3a**	24	**2a** (55%[c]) **3a** (42%[c])

[a]All reactions were carried out with substrate **1** (0.4 mmol), K_2CO_3 (1.2 mmol) in DMF (3.6 mL) and H_2O (0.4 mL) at rt. [b]After extraction with EtOAc without further purification by column chromatography. [c]Isolated yield.

Lastly, treatment of product **2a** with zinc powder, activated with 3 M HCl solution, led to the formation of **3a** in 82% yield (Scheme 5).[14] This finding could serve to provide additional means for forming N-unprotected isochromeno[4,3-*b*]indol-5(11*H*)-one derivatives. Then, a possible mechanism of this transformation has also been put forward and depicted in Scheme 5. First, the internal ketone moiety in **2a** is activated by a proton to form the corresponding oxonium salt **E**. Then an electron push−pull effect of **E** leads to the ring enlargement of the five-membered lactone subunit, giving an iminium salt **F**, which will be easily reduced to 3-hydroxy indoline derivative **G** in the Zn/H^+ system. Finally, the desired product **3a** can be obtained via dehydration of the intermediate **G**. Alternatively, the generated intermediate **E** might as well undergo an oxonium ion reduction process to form the intermediate **H** after the activation of the resulting alcohol. Then the intermediate **H** can be converted to the desired product **3a** via the ring-expansion/isomerization process, accompanied by the release of one molecule of H_2O and proton.

In conclusion, a new strategy has been disclosed for the ring-contraction reactions of isochromeno[4,3-*b*]indol-5(11*H*)-ones via an unusual nucleophile-induced disproportionation/spiro-cyclization cascade process forming a variety of N-unsubstituted spiro[indoline-2,1′-isobenzofuran]-3,3′-diones and spiro-[indoline-2,1′-isoindoline]-3,3′-diones. The advantage of this method includes one-pot, mild conditions, simple operation, transition-metal- and oxidant-free, excellent yields at gram scale.

EXPERIMENTAL SECTION

General Information. ^1H and ^{13}C NMR spectra were recorded on a 600 MHz spectrometer at 25 °C. Chemical shifts values are given in ppm and referred as the internal standard to TMS: 0.00 ppm. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet). The coupling constants *J*, are

DOI: 10.1021/acs.joc.6b01957
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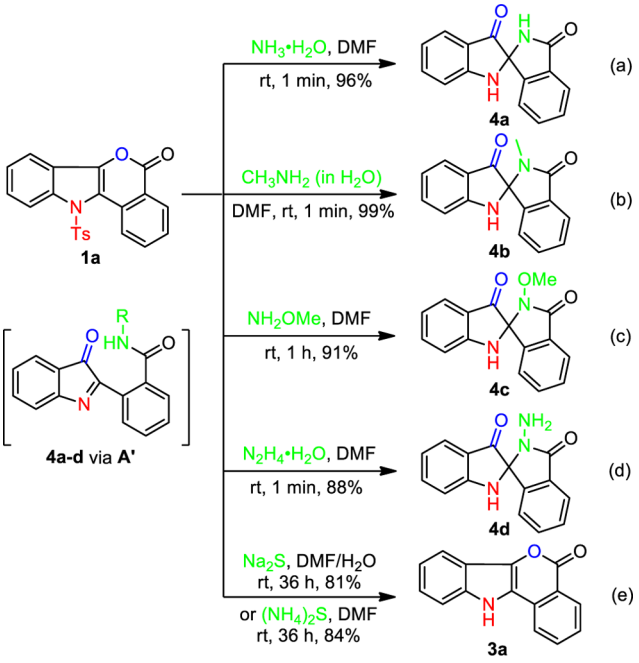
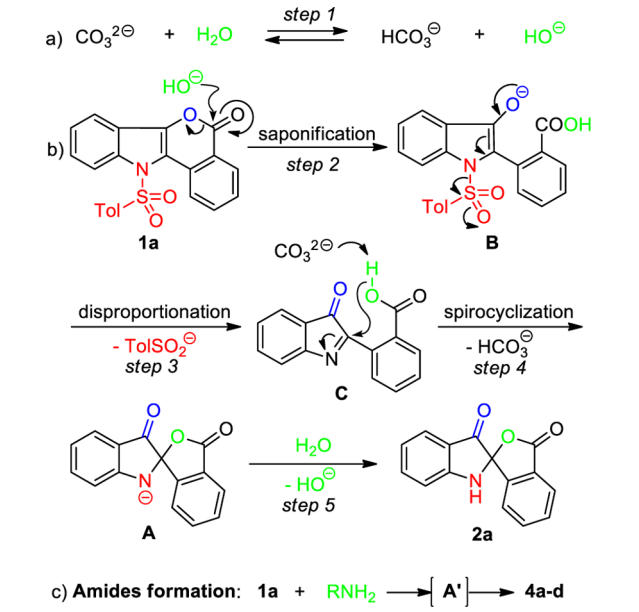
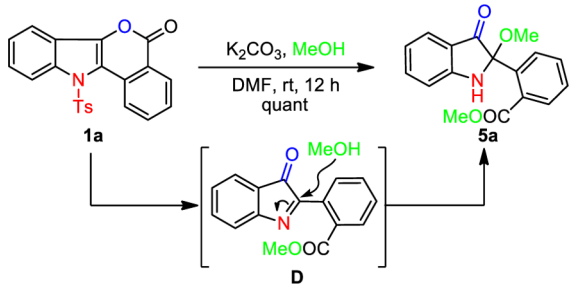
Scheme 2. Additional Ring-Contraction Reactions Forming *N,N′*-Ketals



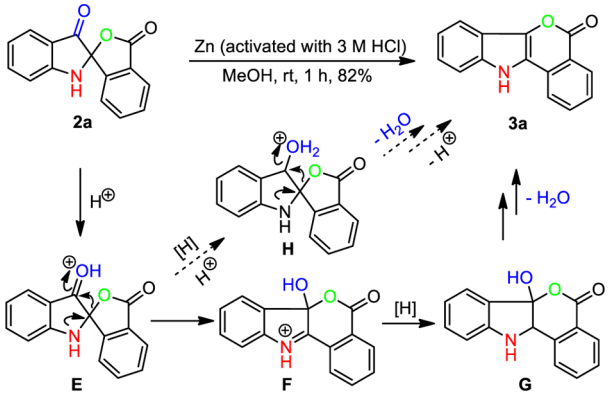
Scheme 3. Proposed Mechanism for the Formation of 2a and 4a−d



Scheme 4. Control Reaction of Saponification and Nucleophilic Substitution



Scheme 5. Zinc-Mediated Reductive Ring-Expansion Reaction of 2a



reported in Hertz (Hz). High resolution mass spectrometry (HRMS) was obtained on a Q-TOF micro spectrometer. Melting points were determined with a Micromelting point apparatus. TLC plates were visualized by exposure to ultraviolet light. Reagents and solvents were purchased as reagent grade and were used without further purification. Flash column chromatography was performed over silica gel (200−300 m) using a mixture of ethyl acetate (EtOAc) and petroleum ether (PE).

Preparation of Substrates 1. *General Procedure.* Substrates **1a−p** were prepared in a manner adapted from our previously reported procedure.[9] The properties and NMR data of **1a−p** were consistent with those in the known publication.

Construction of Products 2. *Construction of Spiro Products* ***2****. General Procedure.* To a solution of substrate **1** (0.4 mmol) in the DMF (3.6 mL) and H_2O (0.4 mL) was added K_2CO_3 (166 mg, 1.2 mmol) at room temperature. Then the mixture was stirred for 2−24 h until the total consumption of the substrate. The resulting mixture was diluted with water (30 mL), acidified with 3 M HCl pH 3−5, and extracted with EtOAc (30 mL × 2). The combined organic phase was then washed with water (30 mL × 2) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give product **2** as bright yellow solids (except for **2p**). The purity of **2** was high enough with no further purification (by column chromatography) necessary.

Gram-Scale Formation of Spiro Products ***2a****. General Procedure.* To a solution of substrate **1a** (2.23g, 5.2 mmol) in the DMF (27.0 mL) and H_2O (3.0 mL) was added K_2CO_3 (11.0 g, 8 mmol) at room temperature. Then the mixture was stirred for 8 h until the total consumption of the substrate. The resulting mixture was diluted with water (30 mL), acidified with 3 M HCl to pH 3−5, and extracted with EtOAc (100 mL × 2). The combined organic phase was then washed with water (100 mL × 2) and brine (50 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give product **2a** as a bright yellow solid (1.3 g, > 99%). The purity of **2a** was high enough with no further purification (by column chromatography) necessary.

Construction of Spiro Products ***4****. General Procedure.* To a solution of substrate **1** (0.4 mmol) in DMF (4 mL) was added amine (4 mmol, 10 equiv) at room temperature. Then the mixture was stirred for a few seconds to 1 h until the total consumption of the substrate. The resulting mixture was diluted with water (30 mL), acidified with 3 M HCl to pH 3−5, and extracted with EtOAc (30 mL × 2). The combined organic phase was then washed with water (30 mL × 2) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give product **4** as bright yellow solids. The purity of **4** was high enough with no further purification (by column chromatography) necessary.

Sulfur Nucleophile-Mediated Tosyl Deprotection of ***1a****. General Procedure.* To a solution of substrate **1** (0.4 mmol) in DMF (4 mL) was added a sulfur nucleophile (4 mmol, 10 equiv) at room temperature. Then the mixture was stirred for 36 h until the total

DOI: 10.1021/acs.joc.6b01957
J. Org. Chem. 2016, 81, 11397−11403

consumption of the substrate. The resulting mixture was diluted with water (30 mL) and extracted with EtOAc (30 mL × 2). The combined organic phase was then washed with water (30 mL × 2) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of EtOAc and PE (40/60, v/v) as eluent to give compound **3a** as a bright yellow solid.

*Synthesis of Compound **5a**. General Procedure.* To a solution of substrate **1a** (0.4 mmol) in DMF (4 mL) and MeOH (2 mL) was added K_2CO_3 (166 mg, 1.2 mmol) at room temperature. Then the mixture was stirred for 12 h. The resulting mixture was diluted with water (30 mL) and extracted with EtOAc (30 mL × 2). The combined organic phase was then washed with water (30 mL × 2) and brine (30 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated in vacuo to give the crude product **5a** as a white solid.

*Zn-Mediated Reductive Ring Expansion of **2a**. General Procedure.* To a solution of substrate **2a** (0.4 mmol) in methanol (10 mL) was added zinc powder (8.0 mmol, 20 equiv) activated with aqueous HCl (3 M) solution at room temperature. Then the mixture was stirred for 1 h, filtered, and concentrated in vacuo. The residue was purified by column chromatography on silica gel using a mixture of EtOAc and PE (40/60, v/v) as eluent to give compound **3a** as a bright yellow solid (82%).

Spectral Data of Products. *Spectral Data of Compounds **2**. 3′H-Spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2a**).* Following the general procedure, **2a** was obtained as a bright yellow solid: yield 100 mg, 99%, mp 234−236 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.52 (s, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.82 (t, J = 7.4 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 8.2 Hz, 1H), 7.58 (d, J = 8.0 Hz, 1H), 7.03 (d, J = 8.1 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 194.4, 168.1, 161.3, 143.4, 139.6, 135.3, 131.3, 126.8, 125.6, 125.2, 122.8, 112.0, 116.8, 112.4, 94.1; HRMS (ESI) calcd for $C_{15}H_{10}NO_3$ $[M + H]^+$ 252.0655, found 252.0657.

*5-Methyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2b**).* Following the general procedure, **2b** was obtained as a bright yellow solid: yield 106 mg, 98%, mp 190−191 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.32 (s, 1H), 7.98 (d, J = 7.5 Hz, 1H), 7.81 (t, J = 7.4 Hz, 1H), 7.75 (t, J = 7.4 Hz, 1H), 7.53 (d, J = 7.6 Hz, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.40 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.3, 168.1, 159.7, 143.6, 140.7, 135.3, 131.3, 129.2, 126.8, 125.2, 124.8, 122.6, 117.0, 112.4, 94.6, 19.9; HRMS (ESI) calcd for $C_{16}H_{12}NO_3$ $[M + H]^+$ 266.0812, found 266.0811.

*5-Fluoro-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2c**).* Following the general procedure, **2c** was obtained as a bright yellow solid: yield 108 mg, 99%, mp 238−239 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.47 (s, 1H), 7.99 (d, J = 7.6 Hz, 1H), 7.83 (t, J = 7.4 Hz, 1H), 7.76 (t, J = 7.4 Hz, 1H), 7.59 (dd, J = 15.3, 8.2 Hz, 2H), 7.47 (d, J = 7.0 Hz, 1H), 7.08 (dd, J = 8.5, 3.1 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 194.3, 168.0, 158.1, 156.2 (d, J = 238.1 Hz), 143.2, 135.4, 131.4, 127.2 (d, J = 25.4 Hz), 126.7, 125.3, 122.8, 117.2 (d, J = 7.9 Hz), 114.0 (d, J = 7.5 Hz), 110.7 (d, J = 23.2 Hz), 94.9; HRMS (ESI) calcd for $C_{15}H_9FNO_3$ $[M + H]^+$ 270.0561, found 270.0560.

*5-Chloro-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2d**).* Following the general procedure, **2d** was obtained as a bright yellow solid: yield 114 mg, 99%, mp 213-214 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.66 (s, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.83 (t, J = 7.4 Hz, 1H), 7.76 (t, J = 7.5 Hz, 1H), 7.69 (dd, J = 8.6, 2.1 Hz, 1H), 7.65 (s, 1H), 7.62 (d, J = 7.5 Hz, 1H), 7.07 (d, J = 8.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 193.6, 167.9, 159.9, 143.1, 139.0, 135.4, 131.5, 126.6, 125.3, 124.6, 123.7, 122.9, 118.0, 114.2, 94.3; HRMS (ESI) calcd for $C_{15}H_9{}^{35}ClNO_3$ $[M + H]^+$ 286.0265, found 286.0266.

*5-Bromo-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2e**).* Following the general procedure, **2e** was obtained as a bright yellow solid: yield 132 mg, 99%, mp 196−197 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.68 (s, 1H), 7.99 (d, J = 7.5 Hz, 1H), 7.83 (t, J = 7.4 Hz, 1H), 7.78 (dd, J = 21.1, 9.2 Hz, 3H), 7.62 (d, J = 7.6 Hz, 1H), 7.02 (d, J = 8.6 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 193.4, 167.9, 160.2, 143.1, 141.6, 135.4, 131.5, 127.6, 126.6, 125.3, 122.9, 118.5, 114.6, 111.0, 94.1; HRMS (ESI) calcd for $C_{15}H_9{}^{79}BrNO_3$ $[M + H]^+$ 329.9760, found 329.9763.

*5,7-Dimethyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2f**).* Following the general procedure, **2f** was obtained as a bright yellow solid: yield 112 mg, 98%, mp 178−179 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.17 (s, 1H), 7.98 (d, J = 7.6 Hz, 1H), 7.80 (d, J = 7.3 Hz, 1H), 7.75 (d, J = 7.5 Hz, 1H), 7.52 (d, J = 7.6 Hz, 1H), 7.35 (s, 1H), 7.23 (s, 1H), 2.25 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.6, 168.2, 158.8, 143.9, 140.9, 135.3, 131.2, 129.1, 126.8, 125.1, 122.8, 121.9, 121.8, 116.7, 94.7, 19.9, 15.5; HRMS (ESI) calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0968, found 280.0967.

*5′-Fluoro-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2g**).* Following the general procedure, **2g** was obtained as a bright yellow solid: yield 108 mg, 98%, mp 201−202 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.52 (s, 1H), 7.88 (d, J = 7.3 Hz, 1H), 7.72−7.65 (m, 3H), 7.60 (d, J = 7.6 Hz, 1H), 7.04 (d, J = 8.1 Hz, 1H), 6.95 (t, J = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 194.0, 166.9 (d, J = 3.5 Hz), 163.7 (d, J = 249.1 Hz), 161.2, 139.6, 139.3, 129.2 (d, J = 9.4 Hz), 125.6, 125.4 (d, J = 9.0 Hz), 123.1 (d, J = 24.3 Hz), 120.1, 116.8, 112.5, 111.9 (d, J = 24.4 Hz), 94.0; HRMS (ESI) calcd for $C_{15}H_9FNO_3$ $[M + H]^+$ 270.0561, found 270.0558.

*5′-Fluoro-5-methyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2h**).* Following the general procedure, **2h** was obtained as a bright yellow solid: yield 113 mg, 99%, mp 190−192 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.33 (s, 1H), 7.87 (d, J = 7.3 Hz, 1H), 7.68 (t, J = 8.7 Hz, 1H), 7.63 (dd, J = 8.2, 4.2 Hz, 1H), 7.51 (d, J = 8.1 Hz, 1H), 7.40 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.0, 166.9, 163.7 (d, J = 249.0 Hz), 159.6, 140.7, 139.4, 129.3, 129.2 (d, J = 9.2 Hz), 125.2 (d, J = 10.5 Hz), 124.9, 123.0 (d, J = 23.6 Hz), 116.9, 112.5, 111.9 (d, J = 23.5 Hz), 94.5, 19.9; HRMS (ESI) calcd for $C_{16}H_{11}FNO_3$ $[M + H]^+$ 284.0717, found 284.0718.

*6′-Chloro-5-methyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2i**).* Following the general procedure, **2i** was obtained as a bright yellow solid: yield 120 mg, 99%, mp 200−202 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.30 (s, 1H), 7.99 (d, J = 8.2 Hz, 1H), 7.80 (d, J = 8.2 Hz, 1H), 7.77 (s, 1H), 7.50 (d, J = 8.2 Hz, 1H), 7.40 (s, 1H), 6.96 (d, J = 8.2 Hz, 1H), 2.28 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 193.7, 167.0, 159.6, 145.5, 140.7, 140.3, 131.7, 129.3, 126.9, 125.8, 124.9, 123.3, 117.0, 112.6, 94.1, 19.9; HRMS (ESI) calcd for $C_{16}H_{11}{}^{35}ClNO_3$ $[M + H]^+$ 300.0422, found 300.0425.

*5′-Bromo-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2j**).* Following the general procedure, **2j** was obtained as a bright yellow solid: yield 131 mg, 99%, mp 193−194 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.51 (s, 1H), 8.21 (s, 1H), 8.00 (d, J = 8.1 Hz, 1H), 7.67 (t, J = 7.6 Hz, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.58 (d, J = 8.2 Hz, 1H), 7.05 (d, J = 8.1 Hz, 1H), 6.95 (t, J = 7.3 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 193.8, 166.5, 161.2, 142.4, 139.7, 138.1, 129.1, 127.9, 125.6, 125.0, 124.5, 120.1, 116.7, 112.5, 94.1; HRMS (ESI) calcd for $C_{15}H_9{}^{79}BrNO_3$ $[M + H]^+$ 329.9760, found 329.9761.

*5′-Methyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2k**).* Following the general procedure, **2k** was obtained as a bright yellow solid: yield 106 mg, 99%, mp 194−195 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.44 (s, 1H), 7.78 (s, 1H), 7.65 (t, J = 7.7 Hz, 1H), 7.62 (d, J = 7.8 Hz, 1H), 7.58 (d, J = 7.6 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.01 (d, J = 8.1 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 2.46 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.6, 168.1, 161.3, 141.6, 140.8, 139.5, 136.2, 127.1, 125.5, 125.1, 122.4, 119.9, 116.9, 112.4, 94.0, 20.7; HRMS (ESI) calcd for $C_{16}H_{12}NO_3$ $[M + H]^+$ 266.0812, found 266.0810.

*5,5′-Dimethyl-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2l**).* Following the general procedure, **2l** was obtained as a bright yellow solid: yield 112 mg, 99%, mp 233−235 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.28 (s, 1H), 7.78 (s, 1H), 7.61 (d, J = 7.7 Hz, 1H), 7.49 (d, J = 8.1 Hz, 1H), 7.41−7.37 (m, 2H), 6.94 (d, J = 8.2 Hz, 1H), 2.46 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.5, 168.2, 159.6, 141.5, 141.0, 140.6, 136.1, 129.1, 127.1, 125.0, 124.8, 122.3, 117.0, 112.4, 94.5, 20.7, 19.9; HRMS (ESI) calcd for $C_{17}H_{14}NO_3$ $[M + H]^+$ 280.0968, found 280.0965.

DOI: 10.1021/acs.joc.6b01957
J. Org. Chem. 2016, 81, 11397−11403

*5′-Methoxy-3′H-spiro[indoline-2,1′-isobenzofuran]-3,3′-dione (**2m**).* Following the general procedure, **2m** was obtained as a bright yellow solid: yield 112 mg, 99%, mp 209−210 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.45 (s, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.57 (d, J = 7.6 Hz, 1H), 7.48−7.43 (m, 2H), 7.35 (d, J = 8.3 Hz, 1H), 7.00 (d, J = 8.1 Hz, 1H), 6.93 (t, J = 7.4 Hz, 1H), 3.89 (s, 3H); ^{13}C NMR (151 MHz, DMSO) δ 194.6, 167.9, 161.7, 161.2, 139.5, 135.3, 128.7, 125.5, 123.9, 123.2, 119.9, 116.9, 112.4, 107.8, 94.0, 56.0; HRMS (ESI) calcd for $C_{16}H_{12}NO_4$ $[M + H]^+$ 282.0761, found 282.0763.

*Spectral Data of Compound **3a**. Isochromeno[4,3-b]indol-5(11H)-one (**3a**).* Following the general procedure, **3a** was obtained as a yellow solid after purification by silica gel chromatography (40% EtOAc/PE): mp >280 °C (lit.[15] 304−305 °C); ^{1}H NMR (600 MHz, DMSO) δ 12.01 (s, 1H), 8.28 (d, J = 7.9 Hz, 1H), 8.08 (d, J = 7.8 Hz, 1H), 7.97 (t, J = 7.5 Hz, 1H), 7.75 (d, J = 7.9 Hz, 1H), 7.60 (t, J = 7.5 Hz, 1H), 7.55 (d, J = 8.2 Hz, 1H), 7.33 (t, J = 7.5 Hz, 1H), 7.18 (t, J = 7.3 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 161.5, 135.4, 135.1, 133.6, 130.9, 130.5, 127.4, 124.4, 120.7, 120.0, 118.9, 117.1, 117.0, 115.8, 112.3; HRMS (ESI) calcd for $C_{15}H_{10}NO_2$ $[M + H]^+$ 236.0706, found 236.0705.

*Spectral Data of Compounds **4**. Spiro[indoline-2,1′-isoindoline]-3,3′-dione (**4a**).* Following the general procedure, **4a** was obtained as a bright yellow solid: yield 96 mg, 96%, mp 244−245 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.93 (s, 1H), 7.96 (s, 1H), 7.75−7.70 (m, 1H), 7.60 (t, J = 7.7 Hz, 1H), 7.58−7.54 (m, 2H), 7.52 (d, J = 7.7 Hz, 1H), 7.21 (d, J = 4.9 Hz, 1H), 6.96 (d, J = 8.2 Hz, 1H), 6.84 (t, J = 7.4 Hz, 1H); ^{13}C NMR (150 MHz, DMSO) δ 197.5, 169.4, 161.6, 143.5, 138.8, 132.6, 132.4, 129.7, 125.0, 123.1, 121.2, 118.5, 117.8, 112.3, 79.3; HRMS (ESI) calcd for $C_{15}H_{11}N_2O_2$ $[M + H]^+$ 251.0815, found 251.0813.

*2′-Methylspiro[indoline-2,1′-isoindoline]-3,3′-dione (**4b**).* Following the general procedure, **4b** was obtained as a bright yellow solid: yield 105 mg, 99%, mp 243−244 °C; ^{1}H NMR (600 MHz, DMSO) δ 7.97 (s, 1H), 7.77 (d, J = 6.6 Hz, 1H), 7.65 (t, J = 7.6 Hz, 1H), 7.57 (dt, J = 15.4, 7.7 Hz, 3H), 7.25 (d, J = 6.8 Hz, 1H), 7.07 (d, J = 8.2 Hz, 1H), 6.90 (t, J = 7.3 Hz, 1H), 2.69 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 196.7, 167.1, 162.2, 141.6, 139.2, 132.4, 132.0, 129.9, 124.9, 123.1, 121.1, 119.1, 118.3, 112.8, 82.6, 24.2; HRMS (ESI) calcd for $C_{16}H_{13}N_2O_2$ $[M + H]^+$ 265.0972, found 265.0974.

*2′-Methoxyspiro[indoline-2,1′-isoindoline]-3,3′-dione (**4c**).* Following the general procedure, **4c** was obtained as a bright yellow solid: yield 102 mg, 91%, mp 204−205 °C; ^{1}H NMR (600 MHz, DMSO) δ 8.28 (s, 1H), 7.85 (d, J = 7.1 Hz, 1H), 7.64 (dd, J = 14.2, 6.8 Hz, 3H), 7.52 (d, J = 7.7 Hz, 1H), 7.30 (d, J = 7.0 Hz, 1H), 7.09 (d, J = 8.2 Hz, 1H), 6.89 (t, J = 7.4 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 194.9, 165.2, 162.2, 139.2, 138.5, 133.5, 130.3, 129.5, 125.0, 123.5, 121.5, 119.1, 117.5, 112.5, 82.5, 65.3; HRMS (ESI) calcd for $C_{16}H_{13}N_2O_3$ $[M + H]^+$ 281.0921, found 281.0922.

*2′-Aminospiro[indoline-2,1′-isoindoline]-3,3′-dione (**4d**).* Following the general procedure, **4d** was obtained as a bright yellow solid: yield 93 mg, 88%, mp 199−200 °C; ^{1}H NMR (600 MHz, DMSO) δ 7.89 (s, 1H), 7.76 (d, J = 5.0 Hz, 1H), 7.61 (d, J = 7.8 Hz, 1H), 7.59−7.55 (m, 2H), 7.49 (d, J = 7.6 Hz, 1H), 7.27−7.22 (m, 1H), 7.00 (d, J = 8.2 Hz, 1H), 6.84 (t, J = 7.4 Hz, 1H), 4.67 (s, 2H); ^{13}C NMR (150 MHz, DMSO) δ 197.0, 166.7, 162.5, 139.9, 138.7, 132.4, 131.4, 129.8, 124.7, 122.9, 121.4, 118.5, 118.5, 112.5, 83.1; HRMS (ESI) calcd for $C_{15}H_{12}N_3O_2$ $[M + H]^+$ 266.0924, found 266.0923.

*Spectral Data of Compounds **5a**. Methyl 2-(2-Methoxy-3-oxoindolin-2-yl)benzoate (**5a**).* Following the general procedure, **5a** was obtained as a white solid: yield 119 mg, quant, mp 147−149 °C; ^{1}H NMR (600 MHz, DMSO) δ 7.90 (d, J = 7.6 Hz, 1H), 7.83 (d, J = 7.4 Hz, 1H), 7.79 (t, J = 7.5 Hz, 1H), 7.73 (t, J = 7.3 Hz, 2H), 7.67 (t, J = 7.3 Hz, 1H), 7.60 (d, J = 7.9 Hz, 1H), 7.50 (t, J = 7.5 Hz, 1H), 6.62 (s, 1H), 3.66 (s, 3H), 3.07 (s, 3H); ^{13}C NMR (150 MHz, DMSO) δ 166.1, 140.6, 135.3, 133.0, 132.8, 131.7, 130.5, 130.2, 128.0, 127.4, 127.4, 127.1, 123.9, 123.4, 88.0, 52.1, 50.5; HRMS (ESI) calcd for $C_{17}H_{16}NO_4$ $[M + H]^+$ 298.1074, found 298.1075.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01957.

NMR spectra for all new compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Authors

*E-mail: duyunfeier@tju.edu.cn.

*E-mail: kangzhao@tju.edu.cn.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We acknowledge the National Natural Science Foundation of China (#21472136), Tianjin Research Program of Application Foundation and Advanced Technology (#15JCZDJC32900), and the National Basic Research Projects (#2014CB932201) for their financial support.

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DOI: 10.1021/acs.joc.6b01957
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(11) We also carried out the reaction of **1a** and aniline in DMF; however, no reaction occurred though the mixture was heated to 100 °C for 36 h.
(12) The reaction of **1a** with $BocNH_2$ at rt gave no desired product. Further increasing the temperature to 100 °C for 24 h led to the formation of **4a** in 96% yield. This phenomenon was generated due to the decomposition of the $BocNH_2$ to NH_3, which followed the sequence to form product **4a**.
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DOI: 10.1021/acs.joc.6b01957
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