**Research Paper** 



# An iodine-promoted one-pot and metal-free access to indolin-2-ones

Yong Zhang<sup>1</sup>, Xi Zong<sup>2</sup> and Min Ji<sup>1</sup>

# Abstract

A new method for the synthesis of indolin-2-ones has been realized by an  $I_2$ -promoted oxidative reaction from  $I_2,3,3$ -tetramethyl-3*H*-indolium iodides. This transformation proceeded smoothly under metal-free and peroxide-free conditions in a cascade manner.

### **Keywords**

 $\mathsf{I}_2\text{-}\mathsf{promoted},$  indolin-2-one, metal-free, one-pot, peroxide-free

Date received: 17 May 2019; accepted: 21 August 2019



# Introduction

Indolin-2-one rings have been recognized as crucial motifs in diverse natural products and pharmaceutically relevant entities.<sup>1-3</sup> Several drug discovery programs in industry and academia are anchored around the indolin-2-one scaffold, and drugs such as Sunitinib and Nintedanib are in clinical use for targeted anticancer therapies.4,5 A number of methods for the synthesis of indolin-2-one have been reported. Classical synthetic methods include the derivatization of other heterocycles (such as Wolff-Kishner reduction of isatin and oxidation of indole), Friedel-Crafts cyclizations of  $\alpha$ -haloacetanilides, and variations in the Fischer indole synthesis.<sup>6-8</sup> Cyclizations of 2-haloacryloylanilide derivatives by a variety of radical initiators have also been used to prepare indolin-2-ones.9-12 In recent years, metal-mediated activations/cyclizations on precrafted advanced precursors have been a commonly pursued approach (Scheme 1). Notable examples are Cu-catalyzed intermolecular C-H cyclization (Scheme 1(a)),13 Pd-catalyzed insertion of isocyanide (Scheme 1(b)),<sup>14</sup> ruthenium-catalyzed intramolecular alkene hydroarylation (Scheme 1(c)),15 and Femediated hydrometallation-cyclization (Scheme 1(d)).<sup>16</sup> In addition, Ni-catalyzed aromatic C-H alkylation (Scheme 1(e)) and Ir-catalyzed radical cyclization under visible light (Scheme 1(f)) have also been used to construct indolin-2-one rings.17,18

Recently, due to the need for "greener chemistry," chemists are beginning to develop transformations under metalfree conditions. Iodine, a cheap, nontoxic, and abundant halogen, is attracting more and more attention, especially in oxidative coupling reactions to form new carbon-carbon (C-C) or carbon-heteroatom (C-X) bonds.<sup>19,20</sup> An in situ iodination usually occurs in iodine-mediated oxidative couplings, followed by in situ oxidation to generate an electrophilicaldehydegroup.<sup>21-23</sup>1,2,3,3-Tetramethyl-3H-indolium iodide, a well-known synthetic agent of many fluorescent dyes, is considered to contain an activated methyl group which can react with an aldehyde or carbonyl group.<sup>24,25</sup> In our previous research, the activated C-2 methyl group reacted with molecular iodine to form an aldehyde via Kornblum oxidation in the presence of dimethyl sulfoxide (DMSO).<sup>26</sup> Based on these results, we report an I<sub>2</sub>-promoted

# Corresponding author:

Min Ji, School of Biological Science and Medical Engineering, Southeast University, Nanjing 210009, China. Email: jiminseu@163.com

Journal of Chemical Research 1–6 © The Author(s) 2019 Article reuse guidelines: sagepub.com/journals-permissions DOI: 10.1177/1747519819875862 journals.sagepub.com/home/chl



School of Biological Science and Medical Engineering, Southeast University, Nanjing, China

<sup>&</sup>lt;sup>2</sup>Suzhou Key Laboratory of Biomaterials and Technologies & Collaborative Innovation Center of Suzhou Nano Science and Technology, Suzhou, China



**Scheme 1.** Representative recent approaches for accessing indolin-2-ones. Source: (a) Theunissen et al.,<sup>13</sup> (b) Kong et al.,<sup>14</sup> (c) Kilaru et al.,<sup>15</sup> (d) Gui et al.,<sup>16</sup> (e) Liu et al.,<sup>17</sup> and (f) Dong et al.<sup>18</sup>

one-pot method for the synthesis of indolin-2-ones under metal-free conditions.

# **Results and discussion**

The reaction is demonstrated by using 1,2,3,3-tetramethyl-3H-indol-1-ium iodide (1a) in the presence of molecular iodine (3.0 equiv.) in DMSO at 100°C for 2 h (Table 1, entry 1). We next studied the effect of the temperature on reaction (Table 1, entries 2 and 3), and only at a higher temperature was the product obtained. An acid, methanesulfonic acid, could effectively promote the reaction by lowering the reaction temperature (Table 1, entries 4 and 5). An additive, N-methyl-1,2benzenediamine dihydrochloride (2a), was added to the reaction system and a higher yield was observed (Table 1, entries 6 and 7). Subsequently, the addition of water or 3-Å molecular sieves (Table 1, entries 8 and 9) led to a drastic reduction in the yield, suggesting the unusual role of water in the reaction system. We then screened the amount of iodine at 70°C (Table 1, entries 12-15) and found that 2.0 equiv. was optimum. Further increasing the amount of I<sub>2</sub> had no effect on the yield, and no reaction occurred in the absence of I<sub>2</sub> (Table 1, entry 15), indicating that iodine was essential. When additive was reduced to catalytic amounts (Table 1, entries 16 and 17), only small amounts of products were obtained. The addition of pyridine greatly decreased the yield, suggesting the importance of acidic conditions (Table 1, entry 18). In addition, several reactions were performed in different solvents so as to ascertain the unusual role of DMSO in this process (see Table S1 in Supplementary material). The amount of I<sub>2</sub> was increased to 7.0 equiv.,

and the reaction time was prolonged to 3.0 h (Table 1, entries 19 and 20). However, the indolin-2-one was not completely converted into the iodide product. To further optimize this reaction, we explored the influence of various additives (see Table S2 in Supplementary material). After several experimental iterations, optimum reaction conditions were found: **1a** (1.0 mmol), **2a** (1.2 mmol), I<sub>2</sub> (2.0 mmol), DMSO (3 mL), and 70°C (Table 1, entry 6).

With optimized conditions in hand, the generality and scope of the reaction were investigated (Table 2). 1,2,3,3-Tetramethyl-3H-indol-1-ium iodides 1 with electron-donating or electron-withdrawing groups on the phenyl ring participated in the reaction to afford the corresponding products 3b-m. Compared to electrondonating groups (e.g. 3b, 3d, and 3h) on the phenyl ring or on the fused ring (3i), electron-withdrawing groups (e.g. 3c, 3e, 3f, and 3g) tended to offer the products with higher yields. Furthermore, 7-substituted substrates (e.g. 3h, 3j, and 3k) participated in the transformation as well, but the yields were slightly lower than those obtained with 5-substituted substrates. When the 7-position of the substrate was substituted by a bromine atom, no iodide product could be obtained (3j). Finally, a substituent on the nitrogen and a bulky group at the 3-position are well tolerated, but their reactions afforded the target products in lower yields (31 and 3m).

To gain more information about the reaction mechanism, a model reaction of **1a** (0.2 mmol) with  $I_2$  (0.4 mmol) in DMSO- $d_6$  was tracked by <sup>1</sup>H nuclear magnetic resonance (NMR; see Figure S1 in Supplementary material). As the reaction proceeded, a signal around 10 ppm rapidly appeared, indicating the existence of an aldehyde group due to the release of formaldehyde in the reaction system.

Table I. Optimization of the reaction conditions<sup>a</sup>.



Entry	<b>2a</b> (equiv.)	l <sub>2</sub> (equiv.)	Temperature (°C)	Time (h)	Ratio a'/b' <sup>b</sup>	Yield (%) <sup>c</sup>
I	_	3	100	2	63:37	25
2	-	2	70	1.5	-	0
3	-	2	70	2	n.d.	Trace
4	-	3	100	2	50:50	35d
5	-	2	70	0.5	80:20	<b>34</b> <sup>d</sup>
6	1.2	2	70	0.5	61:38	50
7	1.2	2	70	2	40:60	45
8	1.2	2	70	0.5	n.d.	Trace <sup>e</sup>
9	1.2	2	70	0.5	n.d.	Trace <sup>f</sup>
10	1.2	2	100	0.5	25:75	42
11	1.2	2	50	I	88:12	18
12	1.2	I	70	0.5	77:23	35
13	1.2	1.5	70	0.5	65:35	36
14	1.2	3	70	0.5	60:40	44
15	1.2	-	70	0.5	-	0
16	0.1	2	70	0.5	50:50	3
17	0.2	2	70	1.5	56:44	9
18	1.2	2	70	0.5	n.d.	Trace <sup>g</sup>
19	1.2	5	70	I	14:68 <sup>h</sup>	_
20	1.2	7	70	3	12:69 <sup>h</sup>	-

DMSO: dimethyl sulfoxide; HPLC: high-performance liquid chromatography.

<sup>a</sup>Reaction conditions: **I a** (I mmol), **2a**, and DMSO (3 mL).

<sup>b</sup>Ratio of a' to b' in the isolated product is determined by HPLC.

clsolated yield of 3a. n.d.= not determined.

<sup>d</sup>Methanesulfonic acid (2.0 mmol) was added.

<sup>e</sup>H<sub>2</sub>O (I mL) was added.

<sup>f</sup>3-Å molecular sieves were added.

<sup>g</sup>Pyridine (0.1 mL) was added.

<sup>h</sup>Ratio of a' to b' in the reaction solution was determined by HPLC.

With the aforementioned results and previous reports in mind,<sup>26</sup> a possible mechanism is proposed in Scheme 2 using 1,2,3,3,5-pentamethyl-3*H*-indol-1-ium iodide **1b** as an example. Initially, the substrate indolium iodide **1b** reacted with  $I_2$  to afford the intermediate 2-iodomethyl indolium iodide **A**. Subsequently, the intermediate **A** underwent a nucleophilic substitution reaction with the nucleophilic oxygen atom of DMSO to form the alkoxysulfonium salt **B**, which was then attacked by  $H_2O$  to give the intermediate **C** was unstable and underwent C–C bond cleavage to give the final indolin-2-one **3b**, along with the release of formaldehyde and dimethyl sulfide.

In conclusion, a molecular  $I_2$  promoted C–C bond cleavage has been developed to construct indolin-2-ones from simple and readily available indolinium iodides. In addition, the reaction performs well in the absence of any metal or peroxide. Further studies to elucidate a detailed mechanism and further explorations of this  $I_2$ /DMSO-promoted oxidative reaction are currently underway in our laboratory.

# **Experimental analysis**

All reagents and solvents were obtained from commercial suppliers and were used without further purification. The method of preparing starting compounds 1 is given in Supplementary material. NMR spectra were recorded on a Bruker FT-NMR 400 spectrometer with chemical shifts reported in ppm relative to the internal standard tetra-methylsilane (TMS). HRMS was determined on a Waters GCT Premier spectrometer.

# General procedure for the synthesis of indolin-2-ones **3**

A mixture of quaternary salt 1 (1.0 mmol), 2a (1.2 mmol), and iodine (2 mmol) in DMSO (3 mL) was stirred at 70°C. After the reaction was complete (monitored by thin-layer chromatography (TLC)), the mixture was cooled to room temperature and quenched with saturated aqueous Na<sub>2</sub>S<sub>2</sub>O<sub>3</sub>, then extracted with ethyl acetate ( $3 \times 20$  mL). The



Scheme 2. A plausible reaction mechanism.

# Table 2. Substrate scope<sup>a</sup>.

Entry	Substrate I (R <sup>1</sup> )	Product <b>3</b> (R <sup>1</sup> )	Yield (%) <sup>b</sup>
I	<b>Ib</b> (5-Me)	<b>3b</b> (5-Me)	43
2	<b>I c</b> (5-Cl)	<b>3c</b> (5-Cl)	55
3	<b>I d</b> (5-OMe)	<b>3d</b> (5-OMe)	40
4	le (5-Br)	<b>3e</b> (5-Br)	56
5	If (5-CF <sub>3</sub> )	<b>3f</b> (5-CF <sub>3</sub> )	52
6	<b>I</b> g (5,7-diCl)	<b>3g</b> (5,7-diCl)	54
7	<b>I h</b> (5,7-diMe)	<b>3h</b> (5,7-diMe)	39
8			42
9	<b>li</b> (7-Br)	<b>3i</b> (7-Br)	45
10	Ik (7-Me)	$ \begin{array}{c}                                     $	4 ¢
11		$ \begin{array}{c}                                     $	40°
12			4 c
		0.42 · I	
		3m	

DMSO: dimethyl sulfoxide; NMR: nuclear magnetic resonance.

<sup>a</sup>Reaction was performed with 1 (1.0 mmol), 2a (1.2 mmol), and  $l_2$  (2 mmol) in DMSO (3 mL) at 70°C for 0.5 h. <sup>b</sup>Yields of isolated products.

<sup>c</sup>The ratio was determined by <sup>1</sup>H NMR spectroscopy.

combined organic layers were washed with brine, dried over anhydrous  $Na_2SO_4$ , and evaporated. The residue was purified by column chromatography using ethyl acetate and petroleum ether to yield the desired pure product.

*1,3,3-Trimethylindolin-2-one* and *7-iodo-1,3,3-trimethylindolin-2-one* (mixture obtained from entry 7 in Table 1, **3a**): Brown oil, 50% yield; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm H}$  7.71 (d, *J*=1.7Hz, 1H), 7.61 (dd, *J*=8.2, 1.8Hz, 1H), 7.35–7.31 (m, 0.67H), 7.26 (td, *J*=7.7, 1.3Hz, 0.67H), 7.04 (td, *J*=7.6, 1.3Hz, 0.67H), 7.00 (d, *J*=7.8Hz, 0.67H), 6.87 (d, *J*=8.2Hz, 1H), 3.13 (s, 2H), 3.11 (s, 3H), 1.26 (s, 10H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm C}$  180.6, 180.1, 142.9, 142.8, 138.4, 136.6, 135.7, 131.4, 128.1, 122.8, 122.6, 111.4, 108.8, 85.8, 44.0, 26.5, 26.4, 24.6, 24.3; LC-MS: *t*<sub>R</sub>=3.94min, *m/z*=176.1 [M + H]<sup>+</sup>; *t*<sub>R</sub>=4.48min, *m/z*=302.0 [M + H]<sup>+</sup>; HRMS (ESI<sup>+</sup>): *m/z* [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>14</sub>NO<sup>+</sup> and C<sub>11</sub>H<sub>13</sub>INO<sup>+</sup>: 176.1075 and 302.0042, found: 176.1074 and 302.0040.

1,3,3,5-Tetramethylindolin-2-one (**3b**):<sup>16</sup> Brown oil, 43% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ): δ<sub>H</sub> 7.18 (s, 1H), 7.09 (d, *J*=7.9 Hz, 1H), 6.91 (d, *J*=7.9 Hz, 1H), 3.13 (s, 3H), 2.31 (s, 3H), 1.27 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ): δ<sub>C</sub> 180.5, 140.5, 135.7, 131.5, 128.2, 123.5, 108.5, 43.9, 26.4, 24.6, 21.2; HRMS (ESI<sup>+</sup>): *m/z* [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>16</sub>NO<sup>+</sup>: 190.1226, found: 190.1230.

5-*Chloro-1,3,3-trimethylindolin-2-one* (**3c**):<sup>16</sup> White solid, 55% yield; m.p. 141–143°C (lit.<sup>16</sup> 140–143°C); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm H}$  7.52 (d, *J*=2.1 Hz, 1H), 7.35 (dd, *J*=8.3, 2.2 Hz, 1H), 7.06 (d, *J*=8.3 Hz, 1H), 3.15 (s, 3H), 1.30 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm C}$  180.3, 141.8, 137.8, 127.9, 126.8, 123.4, 110.3, 44.2, 26.5, 24.2; HRMS (ESI<sup>+</sup>): *m*/*z* [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>13</sub>ClNO<sup>+</sup>: 210.0680, found: 210.0683.

5-*Methoxy*-1,3,3-*trimethylindolin*-2-one (**3d**):<sup>16</sup> Yellow oil, 40% yield; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm H}$  7.02 (d, *J*=2.5 Hz, 1H), 6.90 (d, *J*=8.4 Hz, 1H), 6.81 (dd, *J*=8.4, 2.5 Hz, 1H), 3.72 (s, 3H), 3.09 (s, 3H), 1.24 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm C}$  180.3, 156.0, 137.0, 136.2, 112.3, 110.4, 109.1, 56.0, 44.3, 26.4, 24.5; HRMS (ESI<sup>+</sup>): *m*/*z* [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>16</sub>NO<sub>2</sub><sup>+</sup>: 206.1176, found: 206.1183.

5-Bromo-1,3,3-trimethylindolin-2-one (**3e**):<sup>16</sup> White solid, 56% yield; m.p. 152–154°C (lit.<sup>16</sup> 152–154°C); <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_{\rm H}$  7.63 (s, 1H), 7.47 (d, J=8.2 Hz, 1H), 7.01 (d, J=8.3 Hz, 1H), 3.14 (s, 3H), 1.29 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_{\rm C}$  180.2, 142.3, 138.2, 130.7, 126.0, 114.6, 110.8, 44.2, 26.5, 24.2; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>13</sub>BrNO<sup>+</sup>: 254.0175, found: 254.0174.

*1,3,3-Trimethyl-5-(trifluoromethyl)indolin-2-one* (**3f**):<sup>27</sup> Light yellow solid, 52% yield; m.p. 38–40°C (lit.<sup>27</sup> 37–39°C); <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm H}$  7.80 (s, 1H), 7.68 (d, *J*=8.2 Hz, 1H), 7.22 (d, *J*=8.2 Hz, 1H), 3.20 (s, 3H), 1.33 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm C}$  180.8, 146.5, 136.6, 126.0, 125.9, 123.3, 122.9, 120.0, 109.1, 44.0, 26.6, 24.1; HRMS (ESI<sup>+</sup>): *m/z* [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>13</sub>F<sub>3</sub>NO<sup>+</sup>: 244.0944, found: 244.0943.

5,7-Dichloro-1,3,3-trimethylindolin-2-one (**3g**): Yellow oil, 54% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  7.56 (d, J=1.9 Hz, 1H), 7.44 (d, J=1.9 Hz, 1H), 3.46 (s, 3H), 1.31

(s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  180.7, 140.4, 137.9, 129.1, 127.2, 122.7, 115.1, 44.3, 29.5, 24.3; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>12</sub>Cl<sub>2</sub>NO<sup>+</sup>: 244.0290, found: 244.0290.

1,3,3,5,7-Pentamethylindolin-2-one (**3h**):<sup>16</sup> Yellow oil, 39% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_{\rm H}$  7.00 (s, 1H), 6.83 (s, 1H), 3.35 (s, 3H), 2.52 (s, 3H), 2.25 (s, 3H), 1.23 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_{\rm C}$  181.1, 138.1, 136.4, 131.9, 131.4, 121.4, 119.7, 43.2, 29.3, 24.9, 20.9, 18.8; HRMS (ESI<sup>+</sup>): m/z [M+H]<sup>+</sup> calcd for C<sub>13</sub>H<sub>18</sub>NO<sup>+</sup>: 204.1383, found: 204.1391.

1,1,3-Trimethyl-1,3-dihydro-2H-benzo[e]indol-2-one (**3i**): Yellow oil, 42% yield; <sup>1</sup>H NMR (400 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm H}$  8.02 (d, *J*=8.5 Hz, 1H), 7.98 (s, 1H), 7.96 (s, 1H), 7.57– 7.53 (m, 1H), 7.47 (d, *J*=8.6 Hz, 1H), 7.39 (t, *J*=7.5 Hz, 1H), 3.28 (s, 3H), 1.54 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO-*d*<sub>6</sub>):  $\delta_{\rm C}$  181.7, 140.5, 130.5, 130.0, 129.3, 129.1, 127.5, 126.6, 123.7, 122.4, 110.9, 45.4, 26.7, 24.1; HRMS (ESI<sup>+</sup>): *m/z* [M+H]<sup>+</sup> calcd for C<sub>15</sub>H<sub>16</sub>NO<sup>+</sup>: 226.1226, found: 226.1230.

7-Bromo-1,3,3-trimethylindolin-2-one (**3j**): Light yellow oil, 45% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  7.44 (d, J=8.1 Hz, 1H), 7.40 (d, J=7.2 Hz, 1H), 7.00 (t, J=7.7 Hz, 1H), 3.49 (s, 3H), 1.30 (s, 6H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  181.1, 140.0, 139.1, 133.4, 124.4, 122.5, 101.9, 43.7, 29.8, 24.7; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>11</sub>H<sub>13</sub>BrNO<sup>+</sup>: 254.0175, found: 254.0174.

1,3,3,7-Tetramethylindolin-2-one and 5-Iodo-1,3,3,7tetramethylindolin-2-one (mixture, **3k**): Yellow oil, 41% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  7.56 (d, J=1.3 Hz, 0.68H), 7.41 (s, 0.68H), 7.18 (d, J=7.1 Hz, 1H), 7.02 (d, J=7.5 Hz, 1H), 6.94 (t, J=7.5 Hz, 1H), 3.43 (s, 3H), 3.40 (s, 2H), 2.57 (s, 3H), 2.53 (s, 2H), 1.25 (s, 10H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  181.2, 180.7, 140.6, 140.5, 139.5, 138.9, 136.3, 131.6, 129.3, 123.0, 122.5, 120.7, 120.0, 85.9, 43.3, 43.1, 29.3, 24.9, 24.6, 19.0, 18.4; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>16</sub>NO<sup>+</sup> and C<sub>12</sub>H<sub>15</sub>INO<sup>+</sup>: 190.1226 and 316.0193, found: 190.1228 and 316.0192.

*1-Ethyl-3,3-dimethylindolin-2-one* and *1-Ethyl-5-iodo-3,3-dimethylindolin-2-one* (mixture, **31**): Yellow oil, 40% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_{\rm H}$  7.76 (d, J=1.5 Hz, 0.8H), 7.63 (dd, J=8.2, 1.5 Hz, 0.8H), 7.38 (d, J=7.3 Hz, 1H), 7.28 (d, J=7.5 Hz, 1H), 7.09–7.06 (m, 2H), 6.96 (d, J=8.2 Hz, 0.8H), 3.78–3.67 (m, 3.6H), 1.29 (s, 10.8H), 1.19–1.13 (m, 5.4H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_{\rm C}$  180.3, 179.7, 141.8,141.6, 138.6, 136.6, 135.9, 131.6, 128.1, 123.0, 122.4, 111.5, 108.9, 85.7, 44.0, 43.8, 34.4, 34.3, 24.5, 24.2, 13.0, 12.9; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>12</sub>H<sub>16</sub>NO<sup>+</sup> and C<sub>12</sub>H<sub>15</sub>INO<sup>+</sup>: 190.1226 and 316.0193, found: 190.1226 and 316.0190.

*l'-Methylspiro[cyclohexane-1,3'-indolin]-2'-one* and *5'-Iodo-1'-methylspiro [cyclohexane-1,3'-indolin]-2'-one* (mixture, **3m**): Yellow oil, 41% yield; <sup>1</sup>H NMR (400 MHz, DMSO- $d_6$ ):  $\delta_H$  7.69 (d, J=1.6 Hz, 0.42H), 7.57 (dd, J=8.2, 1.7 Hz, 0.42H), 7.43 (d, J=7.3 Hz, 1H), 7.24–7.20 (m, 1H), 6.99–6.93 (m, 2H), 6.81 (d, J=8.2 Hz, 0.42H), 3.06 (s, 3H), 3.03 (s, 1.26H), 1.88–1.43 (m, 14.2H); <sup>13</sup>C NMR (100 MHz, DMSO- $d_6$ ):  $\delta_C$  179.9, 179.2, 143.0, 142.8, 137.9, 136.5, 135.2, 132.0, 127.9, 123.9, 122.2, 111.3, 108.7, 85.5, 46.9, 46.8, 33.1, 32.9, 26.3, 25.3, 21.0, 20.9; HRMS (ESI<sup>+</sup>): m/z [M + H]<sup>+</sup> calcd for C<sub>14</sub>H<sub>18</sub>NO<sup>+</sup> and C<sub>14</sub>H<sub>17</sub>INO<sup>+</sup>: 216.1383 and 342.0349, found: 216.1385 and 342.0348.

#### **Declaration of conflicting interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

### Funding

The author(s) disclosed receipt of the following financial support for the research, authorship, and/or publication of this article: This work was supported by the National Natural Science Foundation of China (Grant No. 81671745).

### **ORCID** iD

Yong Zhang (D) https://orcid.org/0000-0003-4594-9415

### Supplemental material

Supplemental material for this article, which contains the NMR spectra and preliminary study of reaction mechanism, is available online.

### References

- 1. Dounay AB and Overman LE. Chem Rev 2003; 103: 2945.
- Cerchiaro G and Ferreira AMdC. J Brazil Chem Soc 2006; 17: 1473.
- 3. Higuchi K and Kawasaki T. Nat Prod Rep 2007; 24: 843.
- 4. Faivre S, Niccoli P, Castellano D, et al. *Ann Oncol* 2017; 28: 339.

- Roth GJ, Binder R, Colbatzky F, et al. *J Med Chem* 2015; 58: 1053.
- 6. Crestini C and Saladino R. Synth Comm 1994; 24: 2835.
- 7. Vazquez E and Payack JF. Tetrahedron Lett 2004; 45: 6549.
- Beckett AH, Daisley RW and Walker J. *Tetrahedron* 1968; 24: 6093.
- Jones K, Wilkinson J and Ewin R. *Tetrahedron Lett* 1994; 35: 7673.
- Clark AJ, Davies DI, Jones K, et al. J Chem Soc Chem Comm 1994; 1: 41.
- Jones K, Brunton SA and Gosain R. *Tetrahedron Lett* 1999; 40: 8935.
- 12. Nishio T, Iseki K, Araki N, et al. *Helv Chim Acta* 2005; 88: 35.
- 13. Theunissen C, Wang J and Evano G. Chem Sci 2017; 8: 3465.
- Kong W, Wang Q and Zhu J. Angew Chem Int Edit 2016; 55: 9714.
- Kilaru P, Acharya SP and Zhao P. Chem Commun 2018; 54: 924.
- 16. Gui Q, Hu L, Chen X, et al. Asian J Org Chem 2015; 4: 870.
- 17. Liu C, Liu D, Zhang W, et al. Org Lett 2013; 15: 6166.
- 18. Dong W, Liu Y, Hu B, et al. Chem Commun 2015; 51: 4587.
- 19. Finkbeiner P and Nachtsheim BJ. Synthesis 2013; 45: 979.
- 20. Breugst M and von der Heiden D. *Chem Eur J* 2018; 24: 9187.
- 21. Wu X, Geng X, Zhao P, et al. Org Lett 2017; 19: 4584.
- 22. Zhang J, Wu X, Gao Q, et al. Org Lett 2017; 19: 408.
- 23. Wu X, Gao Q, Geng X, et al. Org Lett 2016; 18: 2507.
- 24. Gaur P, Kumar A, Dey G, et al. *ACS Appl Mater Inter* 2016; 8: 10690.
- 25. Shivashimpi GM, Pandey SS, Ogomi Y, et al. J Photoch Photobio A 2014; 273: 1.
- 26. Liu H, Chen H, Li Y, et al. Tetrahedron Lett 2015; 56: 2332.
- 27. Chen J, Wei Y, Xu G, et al. Chem Commun 2016; 52: 6455.