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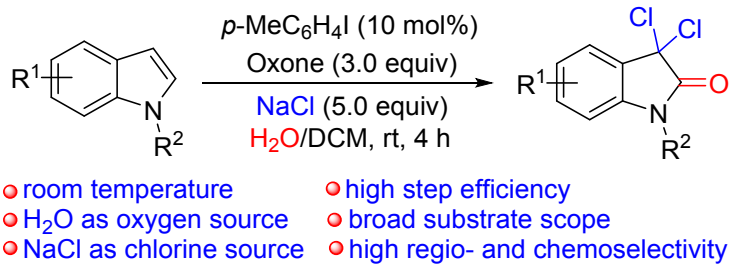
# An environmentally friendly protocol for 2,3-difunctionlization of indole derivatives

Wen-Wu Sun,* Na Chen, Ting-Ting Wei, Guo-Jing You, Hao Yang, Ji-Kai Liu,* Bin Wu*

School of Pharmaceutical Sciences, South-Central University for Nationalities, Wuhan 430074, China

E-mail: 2016027@mail.scuec.edu.cn (Wen-Wu Sun); jkliu@mail.kib.ac.cn (Ji-Kai Liu)

2015084@mail.scuec.edu.cn (Bin Wu)




ABSTRACT: An environmentally friendly and highly regioselective C-3 dichlorination and C-2 oxidation of *N*-substituted indoles has been established by using NaCl as a chlorine source and $H_2O$ as an oxygen source. A series of 3,3-dichloro-2-oxindoles were obtained in moderate to excellent yields. The gram-scale synthesis and derivatization reaction were explored. The possible mechanism for this reaction was elucidated.

## INTRODUCTION

3,3-Dihalo-2-oxindoles have been widely used in medicine and agriculture industry, and they are also important intermediates in organic synthesis.[1] Given the pharmaceutical relevance of this structure unit, the development of novel methodologies for the synthesis of 3,3-dichloro-2-oxindoles has attracted considerable attention from organic chemists in the past few years.[2] In 2005, Padwa reported a nucleophilic addition-[3,3]-sigmatropic rearrangement-cyclization reaction of vinyl sulfilimines with dichloroketene, producing diverse $\gamma$-lactam derivatives.[3] Murphy described (dichloroiodo)benzene

($PhICl_2$)-mediated *a,a*-dichlorination of isatin-3-*p*-tosylhydrazones or isatin-3-hydrazones leading to the formation of 3,3-dichloroindolin-2-ones.[4] Phosphorus pentachloride ($PCl_5$),[1e, 5] sulfonylchloride ($SO_2Cl_2$),[6] chlorosulfonic acid ($ClSO_3H$)[7] and tungsten(VI) chloride ($WCl_6$)[8] were used as chlorine sources for chlorination of isatins. The halogenation–decarboxylation of indolecarboxylic acids with 1,3-dichloro-5,5-dimethylhydantoin (DCDMH) and phenyliodine diacetate (PIDA) was also achieved.[9] However, these transformations inherently required prefunctional substrates or highly toxic reagents. To address these issues, it is highly desirable to develop superior procedures for the construction of 3,3-dichloro-2-oxindoles from simple and readily available indoles.

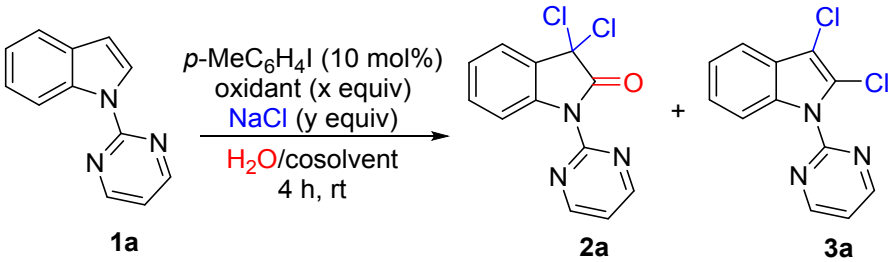
In 2015, Finn reported only one example of the synthesis of 3,3-dichloro-2-oxindole from indole with $NaN_3$, NaClO, and AcOH.[10] Yu's group described a hypervalent iodine-mediated chlorooxidation of indoles.[11] We recently demonstrated an efficient route to 3,3-dichloro-2-oxindoles from *N*-substituted indoles using $PhICl_2$ as oxidation reagent and chlorine source.[12] In 2017, our group employed aryliodide, selectfluor and amine·$(HF)_x$ to generate $PhIF_2$ in situ to synthesize 3,3-difluoro-2-oxindoles.[13] With our continuous interest in the synthesis of 3,3-dihalo-2-oxindoles, we herein report a 4-iodotoluene promoted water-phase C-3 dichlorination and C-2 oxidation of *N*-substituted indoles at room temperature. Compared with the previous reports, this method has several advantages: (1) water is acted as an oxygen source and solvent; (2) NaCl, an environmentally friendly reagent, is used as a chlorine source; (3) Oxone, a nontoxic, cheap and stable reagent, is used as an oxidant; (4) the reaction conditions are mild and easy to operate.

## RESULTS AND DISCUSSION

Our original idea was to develop a transition-metal catalyzed C($sp^2$)−H bonds activation at C3 position of indoles with 2-aminopyrimidine as directing group, but in the end, a metal-free synthetic strategy to

oxindoles has been developed via the $PhICl_2$-mediated C-2 oxidation and C-3 dichlorination of N-substituted indoles.[12] In this project, we plan to further develop an easily-handled aryliodide-catalyzed procedure for oxindole synthesis (Table 1). The desired product **2a** was obtained in 6% yield, along with 6% of **3a** in the presence of *p*-$MeC_6H_4I$ (10 mol%) and Oxone (1.1 equiv) (entry 1). Next, a series of cosolvents (DCM, DCE, MeCN, EtOAc, THF, MeOH, EtOH, $CF_3CH_2OH$ and AcOH) were screened (entry 2-10), giving rise to a slightly higher yield (15%) of **2a** when DCM was used. Increasing the loading of Oxone led to a significant improvement of the product **2a** in 85% yield (entry 11-13). The desired product **2a** was obtained in 83% when *p*-$MeC_6H_4I$ was replaced by PhI (entry 14). Compound **3a** was the major product when the amount of NaCl decreased to 2.0 equivalents. A slightly lower yield was obtained when KCl was used as the chlorine source (entry 17). Further attempts of other oxidants revealed that the performance of *m*-CPBA, $NaIO_4$ and $K_2S_2O_8$ was limited (entries 18-20). The 3,3-dichloro-2-oxindole **2a** was formed in 54% yield in the absence of *p*-$MeC_6H_4I$ (entry 21). These results indicated that aryliodide could effectively promote the reaction via in-situ generation of *p*-$MeC_6H_4ICl_2$ since it has better stability than chlorine cation ($Cl^+$).

**Table 1.** Optimization of the reaction conditions.[a, b]




**1a** **2a** **3a**

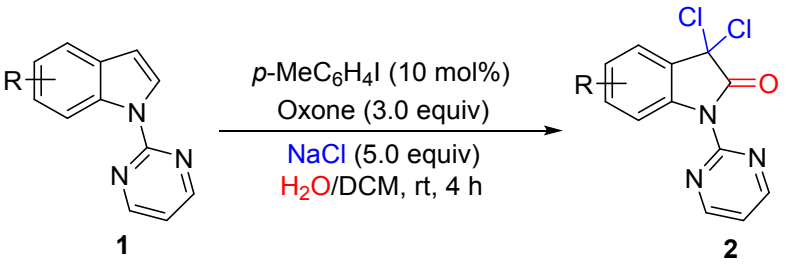
| Entry | ArI | Oxidant (x equiv) | Chlorine source (y equiv) | Cosolvent | Yield [%] of **2a**/**3a** |
|---|---|---|---|---|---|
| 1 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | - | 6/6 |
| 2 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | DCM | 15/20 |
| 3 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | DCE | 11/ 9 |
| 4 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | MeCN | 8/7 |

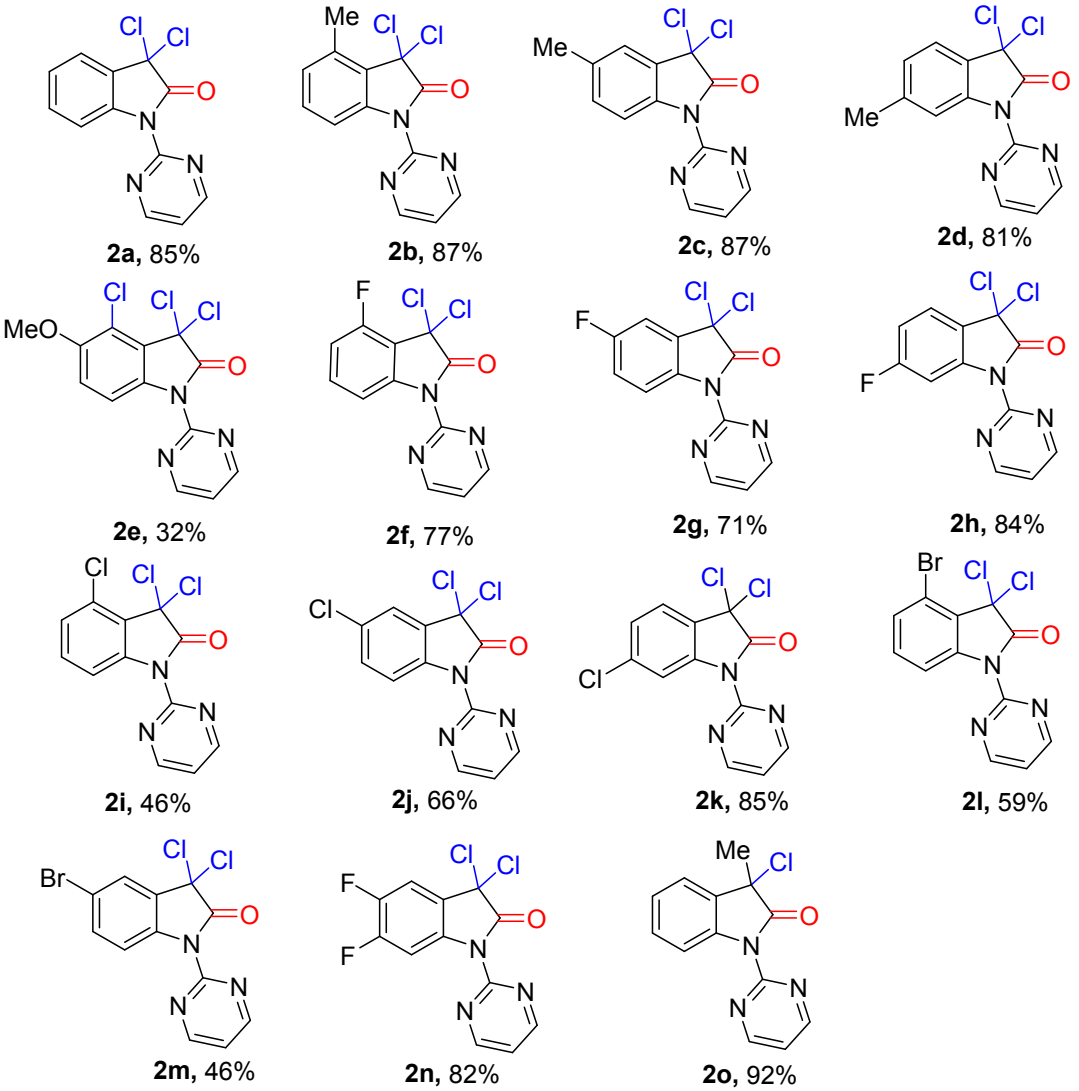
| | | | | | |
|---|---|---|---|---|---|
| 5 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | EtOAc | -/- |
| 6 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | THF | 7/trace |
| 7 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | MeOH | 11/7 |
| 8 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | EtOH | trace/6 |
| 9 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | $CF_3CH_2OH$ | 9/trace |
| 10 | *p*-$MeC_6H_4I$ | Oxone (1.1) | NaCl (5.0) | AcOH | -/- |
| 11 | *p*-$MeC_6H_4I$ | Oxone (1.5) | NaCl (5.0) | DCM | 30/43 |
| 12 | *p*-$MeC_6H_4I$ | Oxone (2.5) | NaCl (5.0) | DCM | 65/10 |
| 13 | *p*-$MeC_6H_4I$ | Oxone (3.0) | NaCl (5.0) | DCM | 85/- |
| 14 | PhI | Oxone (3.0) | NaCl (5.0) | DCM | 83/- |
| 15 | *p*-$MeC_6H_4I$ | Oxone (3.0) | NaCl (2.0) | DCM | 11/61 |
| 16 | *p*-$MeC_6H_4I$ | Oxone (3.0) | NaCl (3.0) | DCM | 26/53 |
| 17 | *p*-$MeC_6H_4I$ | Oxone (3.0) | KCl (5.0) | DCM | 69/8 |
| 18 | *p*-$MeC_6H_4I$ | *m*-CPBA (3.0) | NaCl (5.0) | DCM | -/- |
| 19 | *p*-$MeC_6H_4I$ | $NaIO_4$ (3.0) | NaCl (5.0) | DCM | -/- |
| 20 | *p*-$MeC_6H_4I$ | $K_2S_2O_8$ (3.0) | NaCl (5.0) | DCM | -/- |
| 21 | - | Oxone (3.0) | NaCl (5.0) | DCM | 54/- |

[a] Reaction conditions: **1a** (0.1 mmol), ArI (10 mol%), oxidant (x equiv), chlorine source (y equiv) and cosolvent (0.2 mL) in $H_2O$ (1.0 mL), 4 h, room temperature. [b] Isolated yield.

With the optimized reaction conditions in hand, the substrate scope and limitation of this protocol were explored. As depicted in Table 2, the indole substrates bearing different groups on the phenyl ring afforded the desired products **2a**-**2o** in moderate to excellent yields. The substrates with methyl group on the phenyl ring gave the corresponding products **2b**-**2d** up to 87% yield under the standard reaction conditions. These results showed that the position of the methyl group has a less effect on the reaction. However, the strong electron-donating group, OMe moiety, on the indole ring led to the polyhalogeno-substituted products **3e** in 32% yield. A strong electron-donating group may increase the electron cloud density in the *ortho*-position of phenyl ring, which is beneficial to the electrophilic substitution reaction on the phenyl ring. The F, Cl and Br substituted groups on the indole backbone were tolerated to afford the products **2f**-**2n** in moderate to good yields. **2o** was obtained in 92% yield by using 3-methyl-1-(pyrimidin-2-yl)-1H-indole **1o** as the substrate under our standard reaction conditions.

**Table 2.** Substrate scope.[a, b]



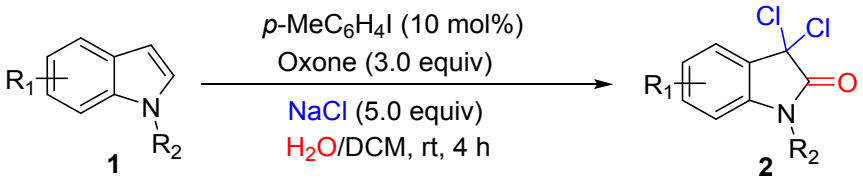



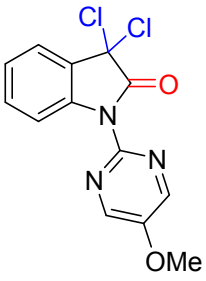

[a] Reaction conditions: **1** (0.1 mmol), *p*-$MeC_6H_4I$ (10 mol%), Oxone (3.0 equiv), NaCl (5.0 equiv) and DCM (0.2 mL) in $H_2O$ (1.0 mL), 4 h, room temperature. [b] Isolated yield.

Next, the effect of the *N*-substituent group on indole was investigated on this reaction (Table 3). There was less effect on the reaction with methoxy group substituted on the pyrimidine ring. The yields of the products were up to 89%. Generally, substrates with electron-donating or electron-withdrawing group substituted on the pyrimidine ring gave the corresponding products **2p**-**2w** in good yields. Under the

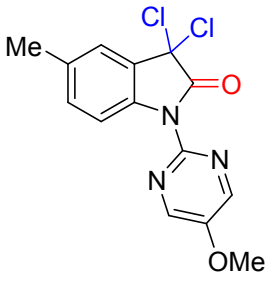
standard reaction conditions, 1-phenyl-1H-indole afforded the product **2x** in 71% yield. 1-Methylindole was reacted to provide **2y** in 53% yield. The polyhalogeno-substituted products **2z** was obtained in 57% yield. The indole was converted to a nearly 2:1 mixture of 3,3-dichloroindolin-2-one (**2aa**) and 3,3,5-trichloroindolin-2-one (**2aa'**).

**Table 3.** Substrate scope. [a, b]

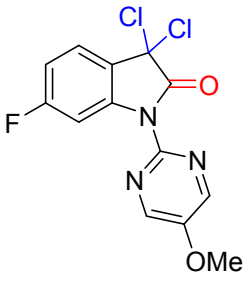




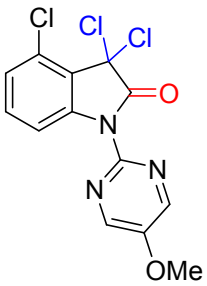
**2p,** 82%



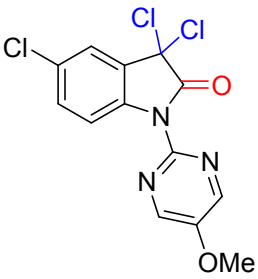
**2q,** 65%



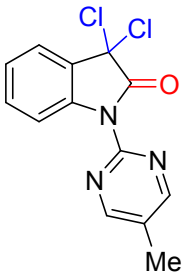
**2r,** 72%



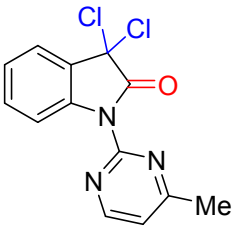
**2s,** 73%



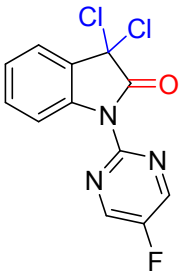
**2t,** 89%



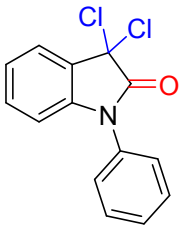
**2u,** 73%



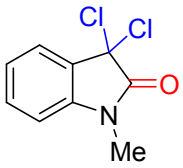
**2v,** 78%



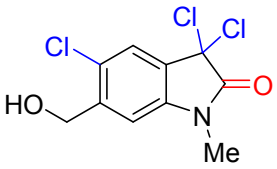
**2w,** 80%



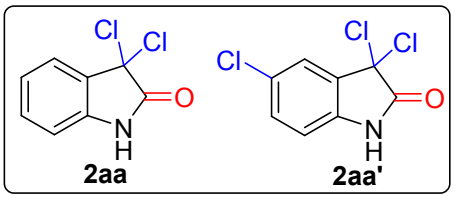
**2x,** 71%



**2y,** 53%



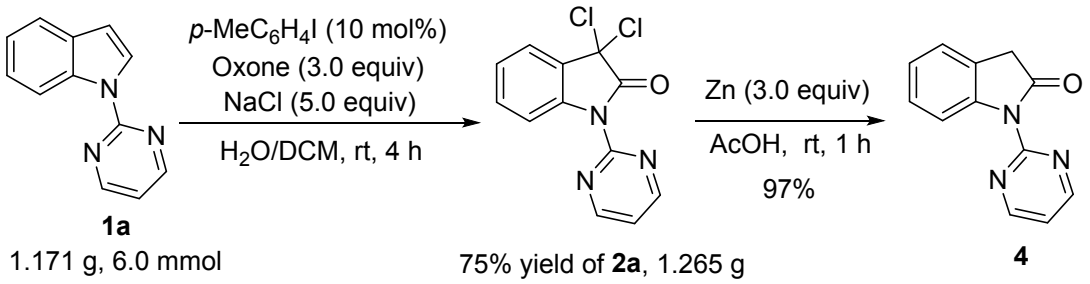
**2z,** 57%



**2aa/2aa'** = 2/1, 39%

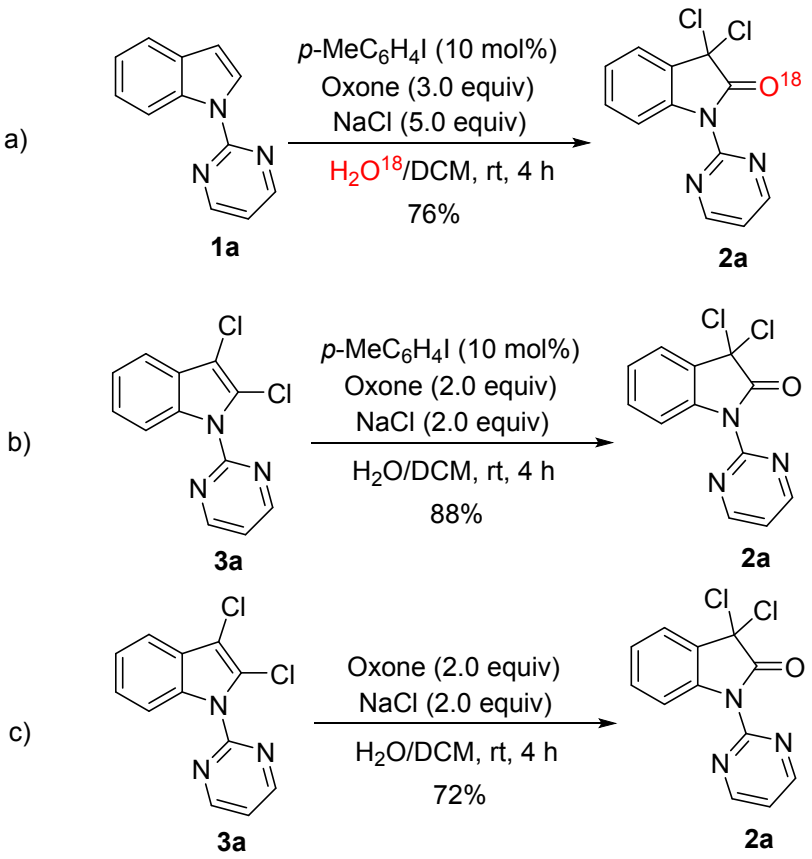
[a] Reaction conditions: **1** (0.1 mmol), *p*-$MeC_6H_4I$ (10 mol%), Oxone (3.0 equiv), NaCl (5.0 equiv) and DCM (0.2 mL) in $H_2O$ (1.0 mL), 4 h, room temperature. [b] Isolated yield.

In order to illustrate the practicality of this method, the gram-scale reaction was carried out with **1a** as the substrate under our standard reaction conditions to afford the product **2a** in 75% yield. When **2a** was treated with 3.0 equivalents of zinc powder in AcOH, **2a** was reduced to the corresponding product **4** in 97% yield (Scheme 1).




**Scheme 1**. Gram-scale synthesis and reduction of 3,3-dichloro-2-oxindole

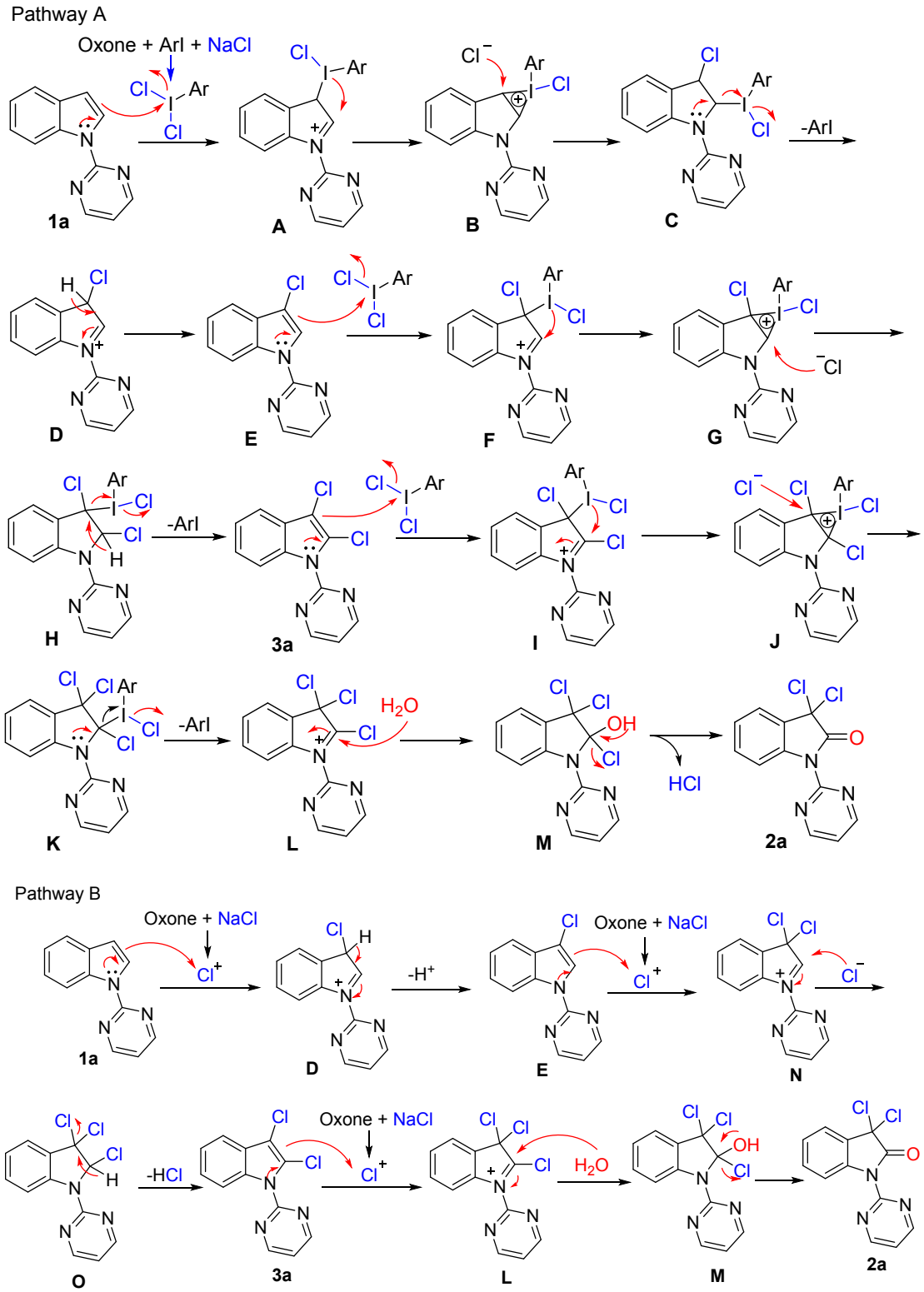
To further investigate the mechanism, a $H_2O^{18}$-labeling experiment was carried out with 10 mol% of *p*-$MeC_6H_4I$, 3.0 equivalents of Oxone and 5.0 equivalents of NaCl in a co-solvent of $H_2O^{18}$ and DCM at room temperature for 4 h. The desired product **2a** was obtained in 76% yield (Scheme 2a). The high resolution mass spectrometry (HRMS) indicated that the oxygen at the C-2 position of **2a** largely stemmed from $H_2O^{18}$ (see supporting information). With **3a** as substrate, in the presence or absence of *p*-$MeC_6H_4I$, the reaction produced **2a** in 88% and 76% yield, respectively (Scheme 2b and 2c). These results showed that **3a** was the intermediate compound and *p*-$MeC_6H_4I$ could promote this reaction. The production of the polyhalogeno-substituted 3,3-dichloro-2-oxindoles **2e**, **2aa**'and **2z** indicated that the electrophilic chlorine cation ($Cl^+$) was generated in situ.




**Scheme 2**. Mechanistic studies.

Based on the mechanistic studies and previous results, [12, 14] two possible mechanisms can be proposed, as shown in Scheme 3. In pathway A, as we stated early,[12] the electrophilic addition of **1a** towards the in-situ generated $ArICl_2$ forms **C**, which is then converted to **D** after the loss of one molecule of ArI via intramolecular nucleophilic substitution reaction. ArI is further oxidized to produce $ArICl_2$, which participates in the next electrophilic addition reaction to form **H**. The rearomatization of **H** affords **3a** by the loss of one molecule of ArI. Compound **3a** reacts with a third $PhICl_2$ to afford **K** and **K** losses one molecule of ArI to afford **L**. **L** reacts with $H_2O$ to yield the final product **2a**. The other possibility is that the in situ generated $ArICl_2$ reacts with the electron-rich double bond of indole **1a** to form **D,** which is further converted to the intermediate **E**. **E** could be transformed to **N** via electrophilic addition with another chlorine cation ($Cl^+$), followed by the attack of a chlorine anion at the C-2 of indole ring to produce **O**. The rearomatization of **O** affords **3a** by the loss of one proton. Compound **3a** reacts with a

third chlorine cation ($Cl^+$) to afford **L**. Subsequently, **L** is attacked by $H_2O$, followed by the removal of one hydrochloride (HCl), affording 3,3-dichloro-2-oxindoles **2a** ( Scheme 3, pathway B).




**Scheme 3**. Plausible mechanism.

## CONCLUSION

In summary, an efficient route to the synthesis of 3,3-disubstituted 2-oxindoles has been established via 2,3-difunctionlization of indoles by using the $ArICl_2$ and/or chlorine cation ($Cl^+$) generated in situ. Moreover, this method provides an environmentally friendly synthesis of 2-oxindole derivatives in moderate to excellent yield with a wide range of functional group tolerance. The gram-scale synthesis and derivatization reaction have been studied. Further investigation of the anti-inflammatory activity of these 3,3-disubstituted 2-oxindoles is underway.

## EXPERIMENTAL SECTION

**Materials and Methods.** Unless otherwise specified, all reactions were carried out under an air atmosphere. All chemicals and solvents that are commercially available were used without further purification. Analytical thin-layer chromatography (TLC) was performed on silica gel plates (GF254) using UV light (254 and 365 nm). Flash chromatography was conducted on silica gel (300−400 mesh). $^1H$ NMR spectra were recorded at 500 MHz and 600 MHz in $CDCl_3$ and dimethyl sulfoxide (DMSO)-$d_6$. $^{13}C$ NMR spectra were recorded at 150 MHz in $CDCl_3$ and DMSO-$d_6$ using tetramethylsilane (TMS) or residual solvent signals as internal standard. *J* values are given in hertz. All melting points are uncorrected. IR spectra were measured for samples as KBr pellets. High-resolution mass spectra (HRMS) were obtained using electrospray ionization (ESI) [quantitative time-of-flight (Q-TOF)] ionization sources. All substrates were prepared according to the literature procedures.[12]

**General procedure for the synthesis of 3,3-dichloro-2-oxindoles:**

To a 10 mL of round-bottom flask equipped with a stirrer was charged with substrate **1** (0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol) and NaCl (29.2 mg, 0.5 mmol). Then, $H_2O$

(1.0 mL) and DCM (0.2 mL) were added to the reaction flask. The reaction mixture was stirred at room temperature for 4 h and monitored by TLC. Next, the reaction mixture was extracted with $CH_2Cl_2$ (3 × 10 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$, and concentrated under vacuum. The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2**.

**3,3-Dichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2a**)[12]: The general procedure described above was followed using substrate **1a** (19.5 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2a** (23.5 mg, 85% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.8 Hz, 2H), 7.74 (d, *J* = 5.7 Hz, 1H), 7.73 (d, *J* = 4.9 Hz, 1H), 7.42 (t, *J* = 7.9 Hz, 1H), 7.35 (t, *J* = 4.8 Hz, 1H), 7.29 (t, *J* = 7.6 Hz, 1H).

**3,3-Dichloro-4-methyl-1-(pyrimidin-2-yl)indolin-2-one** (**2b**): The general procedure described above was followed using substrate **1b** (20.8 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2b** (25.6 mg, 87% yield). Yellow soild; mp:105-107 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.8 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 1H), 7.36 (t, *J* = 4.9 Hz, 1H), 7.30 (t, *J* = 7.9 Hz, 1H), 7.05 (d, *J* = 7.7 Hz, 1H), 2.68 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 167.3, 158.8, 155.1, 138.5, 137.4, 131.3, 127.4,

125.2, 119.7, 110.7, 75.2, 17.6. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{10}Cl_2N_3O$ 294.0201; Found 294.0195; IR(KBr) $\nu$($cm^{-1}$):1757, 1566, 1404, 1356, 1198, 787, 673.

**3,3-Dichloro-5-methyl-1-(pyrimidin-2-yl)indolin-2-one (2c)**[12]: The general procedure described above was followed using substrate **1c** (20.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2c** (25.5 mg, 87% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.8 Hz, 2H), 7.65 (d, *J* = 8.3 Hz, 1H), 7.56 – 7.50 (m, 1H), 7.33 (t, *J* = 4.8 Hz, 1H), 7.21 (dd, *J* = 8.3 and 0.96 Hz, 1H), 2.41 (s, 3H).

**3,3-Dichloro-6-methyl-1-(pyrimidin-2-yl)indolin-2-one** (**2d**)[12]: The general procedure described above was followed using substrate **1d** (20.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2d** (23.7 mg, 81% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.92 (d, *J* = 4.8 Hz, 2H), 7.61 (d, *J* = 7.8 Hz, 1H), 7.52 (s, 1H), 7.36 (t, *J* = 4.8 Hz, 1H), 7.10 (d, *J* = 7.8 Hz, 1H), 2.41 (s, 3H).

**3,3,6-Trichloro-5-methoxy-1-(pyrimidin-2-yl)indolin-2-one** (**2e**): The general procedure described above was followed using substrate **1e** (22.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the

product **2e** (11.0 mg, 32% yield). White solid; mp:109-110 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.8 Hz, 2H), 7.71 (d, *J* = 8.9 Hz, 1H), 7.35 (t, *J* = 4.8 Hz, 1H), 6.98 (d, *J* = 8.9 Hz, 1H), 3.94 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.6, 158.8, 155.2, 153.2, 132.5, 125.9, 122.0, 119.6, 114.0, 112.4, 74.1, 56.8. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_9Cl_3N_3O_2$ 343.9760; Found 343.9755; IR(KBr) *v*($cm^{-1}$): 2924, 1757, 1460, 1263, 748.

**3,3-Dichloro-4-fluoro-1-(pyrimidin-2-yl)indolin-2-one** (**2f**): The general procedure described above was followed using substrate **1f** (21.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2f** (22.9 mg, 77% yield). White solid; mp: 106-107 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.92 (d, *J* = 4.8 Hz, 2H), 7.58 – 7.53 (m, 1H), 7.43 (td, *J* = 8.3 and 5.5 Hz, 1H), 7.38 (t, *J* = 4.8 Hz, 1H), 6.98 (t, *J* = 8.7 Hz, 1H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.7, 159.0 (d, *J* = 257.3 Hz), 158.9, 155.0, 139.6 (d, *J* = 5.9 Hz), 133.4 (d, *J* = 8.9 Hz), 119.9, 115.5 (d, *J* = 17.6 Hz), 112.7 (d, *J* = 18.8 Hz), 109.5 (d, *J* = 3.5 Hz), 71.5. $^{19}$F NMR (470 MHz, $CDCl_3$) δ -114.5. HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_7Cl_2FN_3O$ 297.9950; Found 297.9944; IR(KBr) *v*($cm^{-1}$):1771, 1466, 1402, 1200, 781.

**3,3-Dichloro-5-fluoro-1-(pyrimidin-2-yl)indolin-2-one** (**2g**): The general procedure described above was followed using substrate **1g** (21.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2g** (21.1 mg, 71% yield). Yellow solid; mp:104-105 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.8

Hz, 2H), 7.82 (dd, *J* = 8.9 and 4.2 Hz, 1H), 7.45 (dd, *J* = 7.1 and 2.8 Hz, 1H), 7.36 (t, *J* = 4.8 Hz, 1H), 7.14 (td, *J* = 8.8 and 2.8 Hz, 1H). $^{13}C\{1H\}$NMR (150 MHz, $CDCl_3$) δ 167.0, 160.1 (d, *J* = 246.3 Hz), 158.8, 155.2, 134.0 (d, *J* = 2.7 Hz), 123.0 (d, *J* = 8.6 Hz), 119.6, 118.6 (d, *J* = 23.2 Hz), 115.6 (d, *J* = 7.7 Hz), 112.4 (d, *J* = 25.5 Hz), 73.8. $^{19}F$ NMR (470 MHz, $CDCl_3$) δ -115.5. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_7Cl_2FN_3O$ 297.9950; Found 297.9944; IR(KBr) *v*($cm^{-1}$):1767, 1568, 1483, 1402, 1352, 1167, 831.

**3,3-Dichloro-6-fluoro-1-(pyrimidin-2-yl)indolin-2-one** (**2h**)[12]: The general procedure described above was followed using substrate **1h** (21.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2h** (25.1 mg, 84% yield). Yellow oil, $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.91 (d, *J* = 4.9 Hz, 2H), 7.71 (dd, *J* = 8.5 and 5.4 Hz, 1H), 7.59 (dd, *J* = 9.6 and 2.4 Hz, 1H), 7.37 (t, *J* = 4.8 Hz, 1H), 6.99 (td, *J* = 8.6 and 2.4 Hz, 1H).

**3,3,4-Trichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2i**)[12]: The general procedure described above was followed using substrate **1i** (23.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2i** (14.6 mg, 46% yield). White solid, mp 167-169 °C; $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.92 (d, *J* = 4.8 Hz, 2H), 7.65 (d, *J* = 8.2 Hz, 1H), 7.42-7.33 (m, 2H), 7.25 (d, *J* = 8.6 Hz, 1H).

**3,3,5-Trichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2j**)[12]: The general procedure described above was followed using substrate **1j** (21.1 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2j** (20.8 mg, 66% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.89 (d, *J* = 4.8 Hz, 2H), 7.76 (d, *J* = 8.7 Hz, 1H), 7.69 (d, *J* = 2.2 Hz, 1H), 7.38 (dd, *J* = 8.8 and 2.3 Hz, 1H), 7.36 (t, *J* = 5.0 Hz, 1H).

**3,3,6-Trichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2k**)[12]: The general procedure described above was followed using substrate **1k** (21.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2k** (26.7 mg, 85% yield). Yellow solid; mp 160-162 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.92 (d, *J* = 4.9 Hz, 2H), 7.84 (d, *J* = 1.9 Hz, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.38 (t, *J* = 4.8 Hz, 1H), 7.28 (dd, *J* = 8.2 and 1.8 Hz, 1H).

**4-bromo-3,3-Dichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2l**): The general procedure described above was followed using substrate **1l** (27.4 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2l** (21.0 mg, 59% yield). Yellowish solid; mp:110-111 $^o$C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.92 (d, *J* = 4.8 Hz, 2H), 7.68 (dd, *J* = 8.2 and 0.9 Hz, 1H), 7.44 (dd, *J* = 8.2 and 0.9 Hz, 1H), 7.38 (t, *J* = 4.8 Hz, 1H), 7.29 (t, *J* = 8.2 Hz, 1H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.6, 158.9, 154.7, 140.2, 132.5, 129.7,

125.8, 120.9, 120.0, 112.3, 74.9. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_7BrCl_2N_3O$ 357.9150; Found 357.9149; IR(KBr) $\nu$($cm^{-1}$):1759, 1599, 1445, 1404, 1161, 785, 673.

**5-bromo-3,3-Dichloro-1-(pyrimidin-2-yl)indolin-2-one** (**2m**): The general procedure described above was followed using substrate **1m** (27.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2m** (16.5 mg, 46% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.90 (d, $J$ = 4.9 Hz, 2H), 7.85 (d, $J$ = 2.1 Hz, 1H), 7.72 (d, $J$ = 8.7 Hz, 1H), 7.54 (dd, $J$ = 8.7 and 2.1 Hz, 1H), 7.36 (t, $J$ = 4.9 Hz, 1H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.6, 158.8, 155.1, 137.1, 134.6, 130.3, 128.0, 119.7, 118.0, 115.7, 73.5. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_7BrCl_2N_3O$ 357.9150; Found 357.9146; IR(KBr) $\nu$($cm^{-1}$):2924, 1773, 1472, 1404, 816.

**3,3-Dichloro-5,6-difluoro-1-(pyrimidin-2-yl)indolin-2-one** (**2n**)[12]: The general procedure described above was followed using substrate **1n** (23.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$, and concentrated under vacuum. The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2n** (26.0 mg, 82% yield). Yellow oil, $^1$H NMR (600 MHz, DMSO-$d_6$) δ 9.02 (d, $J$ = 4.9 Hz, 2H), 8.22 (dd, $J$ = 9.3 and 7.7 Hz, 1H), 7.81 (dd, $J$ = 11.1 and 6.7 Hz, 1H), 7.65 (t, $J$ = 4.9 Hz, 1H).

**3-Chloro-3-methyl-1-(pyrimidin-2-yl)indolin-2-one** (**2o**)[12]: The general procedure described above was followed using substrate **1o** (20.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2o** (23.9 mg, 92% yield). Yellow oil, $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.90 (d, *J* = 4.8 Hz, 2H), 7.72 (d, *J* = 8.1 Hz, 1H), 7.52 (dd, *J* = 7.5 and 1.3 Hz, 1H), 7.36 (td, *J* = 7.9 and 1.4 Hz, 1H), 7.31 (t, *J* = 4.9 Hz, 1H), 7.23 (td, *J* = 7.6 and 1.0 Hz, 1H), 2.04 (s, 3H).

**3,3-Dichloro-1-(5-methoxypyrimidin-2-yl)indolin-2-one** (**2p**): The general procedure described above was followed using substrate **1p** (22.8 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2p** (25.3 mg, 82% yield). Yellow soild; mp: 91-92 °C; $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.54 (s, 2H), 7.71 (dd, *J* = 7.7 and 1.3 Hz, 1H), 7.47 (d, *J* = 8.1 Hz, 1H), 7.39 (td, *J* = 7.9 and 1.4 Hz, 1H), 7.29 – 7.24 (m, 1H), 3.99 (s, 3H). $^{13}C\{1H\}$NMR (150 MHz, $CDCl_3$) δ 167.4, 152.2, 147.7, 144.7, 138.6, 131.7, 128.5, 125.1, 124.9, 112.7, 74.5, 56.4. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{10}Cl_2N_3O_2$ 310.0150; Found 310.0143; IR(KBr) *v*($cm^{-1}$):1757, 1609, 1452, 1427, 1290, 1177, 754.

**3,3-Dichloro-1-(5-methoxypyrimidin-2-yl)-5-methylindolin-2-one** (**2q**): The general procedure described above was followed using substrate **1q** (23.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford

the product **2q** (21.2 mg, 65% yield). Yellow oil, $^1$H NMR (600 MHz, $CDCl_3$) δ 8.53 (s, 2H), 7.52 (s, 1H), 7.39 (d, *J* = 8.2 Hz, 1H), 7.19 (d, *J* = 8.2 Hz, 1H), 3.99 (s, 3H), 2.40 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 167.5, 152.0, 148.0, 144.7, 136.2, 135.1, 132.2, 128.5, 125.3, 112.6, 74.7, 56.4, 21.0. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{14}H_{12}Cl_2N_3O_2$ 324.0307; Found 324.0300; IR(KBr) *v*($cm^{-1}$): 2926, 1763, 1422, 1277, 748.

**3,3-Dichloro-6-fluoro-1-(5-methoxypyrimidin-2-yl)indolin-2-one** (**2r**): The general procedure described above was followed using substrate **1r** (24.3 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2r** (23.6 mg, 72% yield). Orange solid; mp:99-100 °C; $^1$H NMR (600 MHz, $CDCl_3$) δ 8.54 (s, 2H), 7.69 (dd, *J* = 8.5 and 5.3 Hz, 1H), 7.31 (dd, *J* = 9.4 and 2.3 Hz, 1H), 6.96 (td, *J* = 8.7 and 2.3 Hz, 1H), 4.00 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 167.3, 164.3 (d, *J* = 250.9 Hz), 152.2, 146.6 (d, *J* = 276.5 Hz), 144.7, 140.1 (d, *J* = 12.6 Hz), 126.6 (d, *J* = 10.3 Hz), 124.3 (d, *J* = 3.3 Hz), 112.0 (d, *J* = 23.4 Hz), 101.8 (d, *J* = 29.5 Hz), 73.8, 56.4. $^{19}$F NMR (470 MHz, $CDCl_3$) δ -114.6. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_9Cl_2FN_3O_2$ 328.0056; Found 328.0049; IR(KBr) *v*($cm^{-1}$):1765, 1605, 1497, 1422, 1281, 1099.

**3,3,4-Trichloro-1-(5-methoxypyrimidin-2-yl)indolin-2-one** (**2s**): The general procedure described above was followed using substrate **1s** (25.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the

product **2s** (25.0 mg, 73% yield). Yellow oil. $^1$H NMR (600 MHz, $CDCl_3$) δ 8.53 (s, 2H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 7.21 (d, *J* = 7.9 Hz, 1H), 4.00 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.7, 152.5, 147.4, 144.8, 140.5, 132.8, 132.4, 126.1, 124.5, 111.0, 73.7, 56.5. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_9Cl_3N_3O_2$ 343.9760; Found 343.9785; IR(KBr) *v*($cm^{-1}$):1757, 1603, 1452, 1421, 1358, 1281.

**3,3,5-Trichloro-1-(5-methoxypyrimidin-2-yl)indolin-2-one** (**2t**): The general procedure described above was followed using substrate **1t** (26.0 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2t** (30.5 mg, 89% yield). Yellow oil. $^1$H NMR (600 MHz, $CDCl_3$) δ 8.53 (s, 2H), 7.68 (d, *J* = 2.2 Hz, 1H), 7.49 (d, *J* = 8.7 Hz, 1H), 7.36 (dd, *J* = 8.7 and 2.2 Hz, 1H), 3.99 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 166.8, 152.2, 147.6, 144.7, 137.1, 131.7, 130.5, 130.0, 125.1, 114.3, 73.6, 56.4. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_9Cl_3N_3O_2$ 343.9760; Found 342.9763. IR(KBr) *v*($cm^{-1}$):1773, 1474, 1452, 1422, 1356, 1277.

**3,3-Dichloro-1-(5-methylpyrimidin-2-yl)indolin-2-one** (**2u**): The general procedure described above was followed using substrate **1u** (20.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2u** (21.3 mg, 73% yield). Lavender solid; mp:109-111 °C; $^1$H NMR (600 MHz, $CDCl_3$) *δ* 8.73 (s, 2H), 7.73 (dd, *J* = 7.6 and 1.3 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 1H), 7.41 (td, *J* = 7.9 and 1.4 Hz, 1H), 7.30 – 7.27

(m, 1H), 2.42 (s, 3H). $^{13}C\{1H\}$NMR (150 MHz, $CDCl_3$) δ 167.3, 158.7, 153.0, 138.3, 131.7, 129.5, 128.6, 125.2, 124.9, 113.2, 74.5, 15.4. HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{13}H_{10}Cl_2N_3O$ 294.0201; Found 294.0193; IR(KBr) $\nu$($cm^{-1}$):1755, 1422, 1364, 1177, 752.

**3,3-Dichloro-1-(4-methylpyrimidin-2-yl)indolin-2-one** (**2v**)[12]: The general procedure described above was followed using substrate **1v** (20.9 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2v** (23.0 mg, 78% yield). Yellow oil. $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.73 (d, $J$ = 5.1 Hz, 1H), 7.71 (d, $J$ = 7.6 Hz, 1H), 7.65 (d, $J$ = 8.2 Hz, 1H), 7.41 (t, $J$ = 7.9 Hz, 1H), 7.28 (d, $J$ = 7.6 Hz, 1H), 7.19 (s, 1H), 2.64 (s, 3H).

**3,3-Dichloro-1-(5-fluoropyrimidin-2-yl)indolin-2-one** (**2w**): The general procedure described above was followed using substrate **1w** (21.4 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2w** (23.8 mg, 80% yield). Yellow oil. $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 2H), 7.74 (d, $J$ = 8.5 Hz, 1H), 7.64 (d, $J$ = 8.1 Hz, 1H), 7.43 (t, $J$ = 8.6 Hz, 1H), 7.31 (t, $J$ = 8.0 Hz, 1H). $^{13}C\{1H\}$NMR (150 MHz, $CDCl_3$) δ 167.3, 156.7, 155.4 (d, $J$ = 132.6 Hz), 150.8 (d, $J$ = 3.6 Hz), 146.6 (d, $J$ = 22.1 Hz), 138.0, 131.8, 128.5, 125.3 (d, $J$ = 75.1 Hz), 113.2, 74.3. $^{19}F$ NMR (470 MHz, $CDCl_3$) δ -138.0. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_7Cl_2FN_3O$ 297.9950; Found 297.9943; IR(KBr) $\nu$($cm^{-1}$):1773, 1420, 1261, 750.

**3,3-dichloro-1-phenylindolin-2-one** (**2x**)[9a]: The general procedure described above was followed using substrate **1x** (38.6 mg, 0.2 mmol), *p*-$MeC_6H_4I$ (4.5 mg, 0.2 mmol), Oxone (364.4 mg, 0.6 mmol), NaCl (58.4 mg, 1.0 mmol), $H_2O$ (2.0 mL) and DCM (0.4 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2x** (39.6 mg, 71% yield). Orange solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 7.6 and 0.9 Hz, 1H), 7.56 (t, *J* = 7.7 Hz, 2H), 7.50 – 7.42 (m, 3H), 7.34 (td, *J* = 7.8 and 1.3 Hz, 1H), 7.23 (td, *J* = 7.6 and 0.9 Hz, 1H), 6.83 (d, *J* = 8.0 Hz, 1H).

**3,3-Dichloro-1-methylindolin-2-one** (**2y**)[4a]: The general procedure described above was followed using substrate **1y** (13.1 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 20:1) to afford the product **2y** (11.5 mg, 53% yield). Orange oil. $^1$H NMR (600 MHz, $CDCl_3$) δ 7.63 (d, *J* = 7.5 Hz, 1H), 7.41 (t, *J* = 7.7 Hz, 1H), 7.19 (t, *J* = 7.6 Hz, 1H), 6.87 (d, *J* = 7.9 Hz, 1H), 3.27 (s, 3H).

**3,3,5-Trichloro-6-(hydroxymethyl)-1-methylindolin-2-one** (**2z**): The general procedure described above was followed using substrate **1z** (16.2 mg, 0.1 mmol), *p*-$MeC_6H_4I$ (2.2 mg, 0.1 mmol), Oxone (182.2 mg, 0.3 mmol), NaCl (29.2 mg, 0.5 mmol), $H_2O$ (1.0 mL) and DCM (0.2 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2z** (16.0 mg, 57% yield). Yellow oil. $^1$H NMR (600 MHz, $CDCl_3$) δ 7.59 (s, 1H), 7.15 (s, 1H), 4.83 (d, *J* = 0.9 Hz, 2H), 3.28 (s, 3H). $^{13}$C{1H}NMR (150 MHz, $CDCl_3$) δ 168.7, 142.9, 139.6, 128.9,

126.9, 125.5, 108.6, 73.4, 62.2, 27.3. HRMS(ESI) m/z: $[M+H]^+$Calcd for $C_{10}H_9Cl_3NO_2$ 279.9699; Found 279.9699; IR(KBr) $\nu$($cm^{-1}$): 3472, 1763, 1730, 1614, 1460, 827, 669.

**3,3-dichloroindolin-2-one** (**2aa**) and **3,3,5-trichloroindolin-2-one** (**2aa'**)[9a]: The general procedure described above was followed using substrate **1aa** (23.4 mg, 0.2 mmol), *p*-$MeC_6H_4I$ (4.5 mg, 0.2 mmol), Oxone (364.4 mg, 0.6 mmol), NaCl (58.4 mg, 1.0 mmol), $H_2O$ (2.0 mL) and DCM (0.4 mL). The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 5:1) to afford a mixture of **2aa** and **2aa'** (**2aa**/**2aa'** = 2/1, 16.8 mg, 39% yield). Orange solid. $^1$H NMR (500 MHz, $CDCl_3$) δ 9.13 (s, 0.5H), 8.95 (s, 1.0H), 7.62 (dd, *J* = 7.6 and 1.1 Hz, 1H), 7.60 (d, *J* = 2.1 Hz, 0.5H), 7.37 (td, *J* = 7.7 and 1.0 Hz, 1H), 7.34 (dd, *J* = 8.5 and 2.0 Hz, 0.5H), 7.18 (td, *J* = 7.7 and 0.8 Hz, 1H), 6.98 (d, *J* = 7.9 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 0.5H).

**Gram-scale synthesis and derivation of 3,3-dichloro-2-oxindole:**

To a 100 mL of round-bottom flask equipped with a stirrer was charged with substrate **1a** (1.171 g, 6.0 mmol), *p*-$MeC_6H_4I$ (0.131 g, 0.6 mmol), Oxone (11.069 g, 18.0 mmol) and NaCl (1.752 g, 30.0 mmol). Then, $H_2O$ (30.0 mL) and DCM (6.0 mL) were added to the reaction flask. The reaction mixture was stirred at room temperature for 4 h and monitored by TLC. Then, the reaction mixture was extracted with $CH_2Cl_2$ (3 × 50 mL). The combined organic phase was dried over anhydrous $Na_2SO_4$, and concentrated under vacuum. The residue was purified by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 10:1) to afford the product **2a** (1.265 g, 75% yield).

In a 10 mL of round-bottom flask was placed substrate **2a** (28.0 mg, 0.1 mmol), Zn (19.6 mg, 0.3 mmol) and AcOH (1.0 mL). The reaction mixture was stirred at room temperature for 1 h. Then the reaction

mixture was neutralized by addition of aqueous saturated sodium bicarbonate and extracted with $CH_2Cl_2$. The combined extracts were dried over $Na_2SO_4$ and concentrated. Purification by flash chromatography (Silica gel, eluent: petroleum ether: ethyl acetate = 4 : 1) afforded the product **4** (20.5 mg, 97% yield). White solid; mp:108-110 $^oC$. $^1H$ NMR (600 MHz, $CDCl_3$) δ 8.82 (d, J = 4.8 Hz, 2H), 7.52 (d, J = 8.1 Hz, 1H), 7.27 – 7.18 (m, 3H), 7.06 (t, J = 7.7 Hz, 1H), 3.71 (s, 2H). $^{13}C\{1H\}$NMR (150 MHz, $CDCl_3$) δ 173.9, 158.6, 155.9, 142.3, 127.7, 124.4, 123.8, 123.7, 118.9, 112.4, 36.4. HRMS (ESI) m/z: $[M+H]^+$Calcd for $C_{12}H_{10}N_3O$ 212.0824; Found 212.0819; IR(KBr) $\nu$($cm^{-1}$): 1740, 1566, 1483, 1412, 1368, 1088, 750.

## ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI:, including $H_2O^{18}$-labeling experiments, $^1H$ NMR and $^{13}C$ NMR spectra for new compounds.

## AUTHOR INFORMATION

### Corresponding Author

*E-mail: 2016027@mail.scuec.edu.cn.

*E-mail: jkliu@mail.kib.ac.cn.

*E-mail: 2015084@mail.scuec.edu.cn.

### Notes

The authors declare no competing financial interest.

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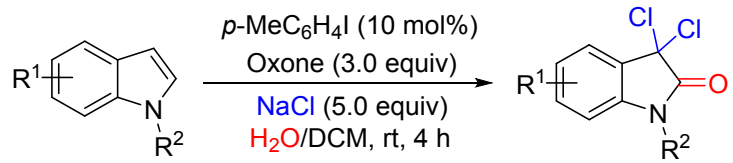


- room temperature
- $H_2O$ as oxygen source
- NaCl as chlorine source
- high step efficiency
- broad substrate scope
- high regio- and chemoselectivity

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