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Copper-Catalyzed Synthesis of Indoly Diketones via C–H Oxidation/Diacylation of Indoles with Arylglyoxal Hydrates

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An expedient protocol for Cu-catalyzed C–H oxidation/diacylation of indoles with arylglyoxal hydrates to construct indolyl diketones is developed. The methodology exhibits the synthetic utility by the synthesis of an indole-alkaloid 1,2-di(1*H*-indol-3-yl)ethane-1,2-dione and offers a straightforward means to produce different indolyl nitrogen-containing heterocycles such as indolyl quinoxaline, indolyl hydantoin and indolyl imidazole in high yields. Preliminary mechanistic studies indicate that two proposed pathways are involved in this process.

Introduction

The indole moiety is ubiquitous in natural products, pharmaceuticals and agrochemicals.[1] Consequently, much attention has been paid to the functionalization of indoles. Among numerous efforts, transition-metal-catalyzed direct C(3)–H bond functionalization of indoles has emerged as a powerful tool in organic synthesis.[2] For the past few years, C3-acylation of indole has been widely reported because of the versatile chemical transformations[3] of 3-acylindoles and their important applications in pharmaceutical compounds and natural products.[4]

Usually, 3-acylindoles can be prepared by the mono- and di-acylation of indoles. Many methods have been developed to realize the mono-acylation of indoles to provide 3-acylindoles.[5] Recently, a few examples have been reported to construct indolyl diketones by utilizing the diacylation of indoles approach. Two representative approaches have been first established by Li's group. One involves Cu-catalyzed C–H oxidation/cross-coupling of indoles with secondary anilines using TBHP as an oxidant under air atmosphere;[6] Pd-catalyzed oxidative cross-coupling of indoles with tertiary anilines using $Cu(OAc)_2$ as an oxidant provides a complementary method to the synthesis of diacylation of indoles.[3b] Recently, Wu's group developed a direct oxidative cross-coupling of N-substituted indoles with methyl ketones to construct indolyl diketones in the presence of molecular iodine and pyrrolidine.[7] Subsequently, Jiang and his co-workers reported a copper-catalyzed aerobic oxidative C3-dicarbonylation of indoles and α-hydroxyketones.[8] In addition, arylglyoxals, aromatic α-keto aldehydes containing both aldehyde and ketone functional groups, have been also used as the diacylating agents for the diacylation of indoles and N-substituted indoles using pyrrolidine or morpholine as catalyst or CuBr-pyridine catalytic system by Mupparapu et al.[9] and Yang et al.[10]

Although significant advances have been achieved, there are still some disadvantages, such as poor tolerance of functional groups (OH, CN, NO_2), the use of expensive palladium catalyst and an excess of oxidant, a long reaction time, and particularly for the introduction of a protecting group for N-position of indole. Moreover, we found that all reactions proceeded under oxidative conditions, or/and in the presence of an alkali additive (pyridine) or an alkali catalyst (pyrrolidine, morpholine). However, an acidic additive (HOAc) was used only in Li's work on the diacylation of indoles.[3b] These findings inspired us to explore more explicit reaction mechanism and develop an efficient approach to obtain indolyl diketones.

Recently, we developed a Cu-catalyzed decarboxylative C3-acylation of free (N–H) indoles with α-oxocarboxylic acids.[11] As part of our ongoing interest in the development of new C–H bond functionalization of indoles, we report herein an efficient protocol for the Cu-catalyzed C–H oxidation/diacylation of indoles with arylglyoxal hydrates under air atmosphere to afford indolyl diketones in moderate to good yields.

Results and discussion

Our investigation commenced with the reaction of indole (**1a**) and 2-(4-bromophenyl)-2-oxoacetaldehyde hydrate (**2a**). In the initial experiment, the treatment of indole **1a** with substrate **2a** in different solvents such as toluene, dioxane and DMSO under air atmosphere afforded only a trace amount of the desired product 1-(4-bromophenyl)-2-(1*H*-indol-3-yl)ethane-

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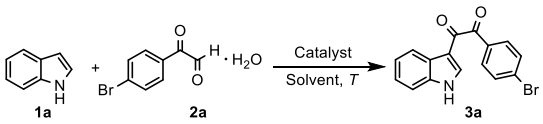
1,2-dione **3a** (Table 1, entries 1–3). Inspired by Li's and Cao's works,[3b,12] HOAc was added in the above reaction system. Much to our satisfaction, the combination of toluene/HOAc or dioxane/HOAc (4.0/0.5, v/v) increased the yield of **3a** to 55% and 60%, respectively (Table 1, entries 4 and 5). The results indicated that the acid system could effectively promote the diacylation of indole. To our delight, the yield of **3a** was enhanced significantly to 80% in dioxane/HOAc in the presence of 20 mol% of $Cu(OAc)_2·H_2O$ (Table 1, entry 6). Moreover, other Cu catalysts were also evaluated. The results suggested that $Cu(OAc)_2·H_2O$ exhibited the highest catalytic activity, and the appropriate amount of $Cu(OAc)_2·H_2O$ was 20 mol% (Table 1, entries 7–13). Subsequently, the stronger acids such as TFA (CF_3CO_3H) and TfOH (CF_3SO_3H) were also tested. The results showed that the reaction activity was suppressed (Table 1, entries 14 and 15). In addition, the reaction temperature was also examined. Unfortunately, elevating the temperature did not improve the yield; lowering the reaction temperature did result in low yield (Table 1, entries 16 and 17). Further experiments showed that the reaction atmosphere plays a crucial role in this transformation, in the presence of sole N_2 or O_2, only moderate yields were obtained (Table 1, entries 18 and 19). Therefore, all reactions were performed in the presence of $Cu(OAc)_2·H_2O$ (20 mol%) in dioxane/HOAc (4.0/0.5, v/v) at 100 °C under air atmosphere.

Using the optimized reaction conditions, the diacylation of a series of indoles was performed, and the results were summarized in Table 2. The reaction afforded the corresponding products **3aa**-**3ka** in moderate to good yields. It was observed that free (N–H) indoles with electron-rich groups such as 5-OCH_3, 5-CH_3, 4-CH_3, 7-CH_3 and 2-CH_3 exhibited high reactivity and furnished the desired products **3ba**–**3fa** in good yields. Moreover, the diacylation of an N-substituted indole such as N-methylindole could also proceed smoothly to provide the target product **3ga** in good yield. However, electron-rich 6-methoxyindole showed low efficiency and gave the corresponding product **3ha** only in moderate yield. Particularly, the diacylation process was compatible with the sensitive OH, CN group and electron-deficient NO_2 group, although only moderate yields of products **3ia, 3ja** and **3ka** were obtained, which were hard to be obtained by other reported methods. The above experiment results demonstrated that although the electronic properties of the indole rings had a strong influence on the yield, the reaction exhibited high tolerance towards various functional groups.

Subsequently, the scope with respect to arylglyoxal hydrates was investigated under the optimized conditions. Arylglyoxal hydrates with both electron-donating groups and electron-withdrawing groups smoothly underwent diacylation to generate the desired products **3ab**–**3al** in moderate to good yields. It was noticed that arylglyoxal hydrates with electron-deficient groups (Cl, F, I, NO_2 and $COOCH_3$) were well-tolerated to deliver the desired products **3ab**–**3ag** in relatively high yields. Importantly, halogen substituents on the arylglyoxal hydrates remained intact, which could potentially be used for further functionalization. Moderate yields of products **3ag**–**3ai** were obtained when arylglyoxal hydrates with electron-rich groups (CH_3 and OCH_3) reacted with indoles. It is worth noting that *ortho*- or *meta*-substituted 2-(2,4-dimethylphenyl)-2-oxo-acetaldehyde hydrate, 2-(3-chlorophenyl)-2-oxoacetaldehyde hydrate and 2-(3-methylphenyl)-2-oxoacetaldehyde hydrate also provided the target product **3ak**, **3ac** and **3aj** in 60%, 70% and 60% yields, respectively. Furthermore, electron-rich indoles bearing 5-OCH_3, 4-OH, 2-CH_3 and N-CH_3 groups also successfully reacted with arylglyoxal hydrates bearing *p*-NO_2, *p*-Cl, *p*-CH_3 and *p*-OCH_3 groups under the optimized reaction conditions, thus providing the corresponding products **3bb**–**3gi** in moderate to good yields.

Table 1 Optimization of Reaction Conditions[a]



1a 2a 3a

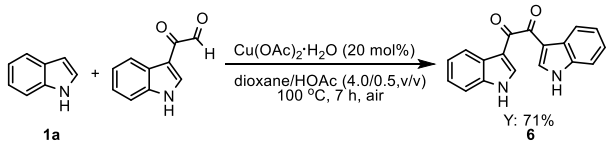
Entry	Catalyst	Solvent (v/v mL)	Temp. (°C)	Yield[b] (%)
1	—	toluene (4.5)	100	trace
2	—	dioxane (4.5)	100	trace
3	—	DMSO (4.5)	100	trace
4	—	toluene/HOAc (4.0/0.5)	100	55
5	—	dioxane/HOAc (4.0/0.5)	100	60
6	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	100	80
7	CuO	dioxane/HOAc (4.0/0.5)	100	76
8	$Cu_2(OH)_2CO_3$	dioxane/HOAc (4.0/0.5)	100	56
9	CuI	dioxane/HOAc (4.0/0.5)	100	46
10	Cu_2O	dioxane/HOAc (4.0/0.5)	100	39
11	$CuCl_2·2H_2O$	dioxane/HOAc (4.0/0.5)	100	—
12	$CuSO_4·5H_2O$	dioxane/HOAc (4.0/0.5)	100	—
13[c]	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	100	69
14	$Cu(OAc)_2·H_2O$	dioxane/TFA (4.0/0.5)	100	20
15	$Cu(OAc)_2·H_2O$	dioxane/TfOH (4.0/0.5)	100	trace
16	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	120	78
17	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	80	40
18[d]	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	100	55
19[e]	$Cu(OAc)_2·H_2O$	dioxane/HOAc (4.0/0.5)	100	62

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), catalyst (20 mol%), solvent (4.5 mL), 100 °C, 6 h, under air atmosphere. [b] Isolated yields. [c] $Cu(OAc)_2·H_2O$ (10 mol%) was used. [d] The reaction was performed under N_2 atmosphere. [e] The reaction was performed under O_2 atmosphere.

To demonstrate the synthetic utility of the method, the diacylation was applied for the synthesis of 1,2-di(1*H*-indol-3-yl)ethane-1,2-dione **6**, an indole alkaloid from the marine sponge *Smenospongia* sp.[13] Moreover, **6** is also an important intermediate for the construction of anion sensors including indolylquinoxalines[14a] and indolocarbazolequinoxalines.[14b] The treatment of indole **1a** with 2-(1*H*-indol-3-yl)-2-oxoacetaldehyde afforded the product **6** in 71% yield under the standard conditions (Scheme 1).[15] Gratifyingly, the obtained indolyl diketone products were further used to construct indolyl nitrogen-containing heterocycles including indolyl quinoxaline (**7**),[8] indolyl hydantoin (**8**) and indolyl imidazole (**9**)[16] in 90%, 85% and 88% yields, respectively, by the reaction of indolyl diketones with *o*-phenylenediamine, urea, benzaldehyde and ammonium acetate under conventional heating or microwave irradiation conditions (Scheme 2).

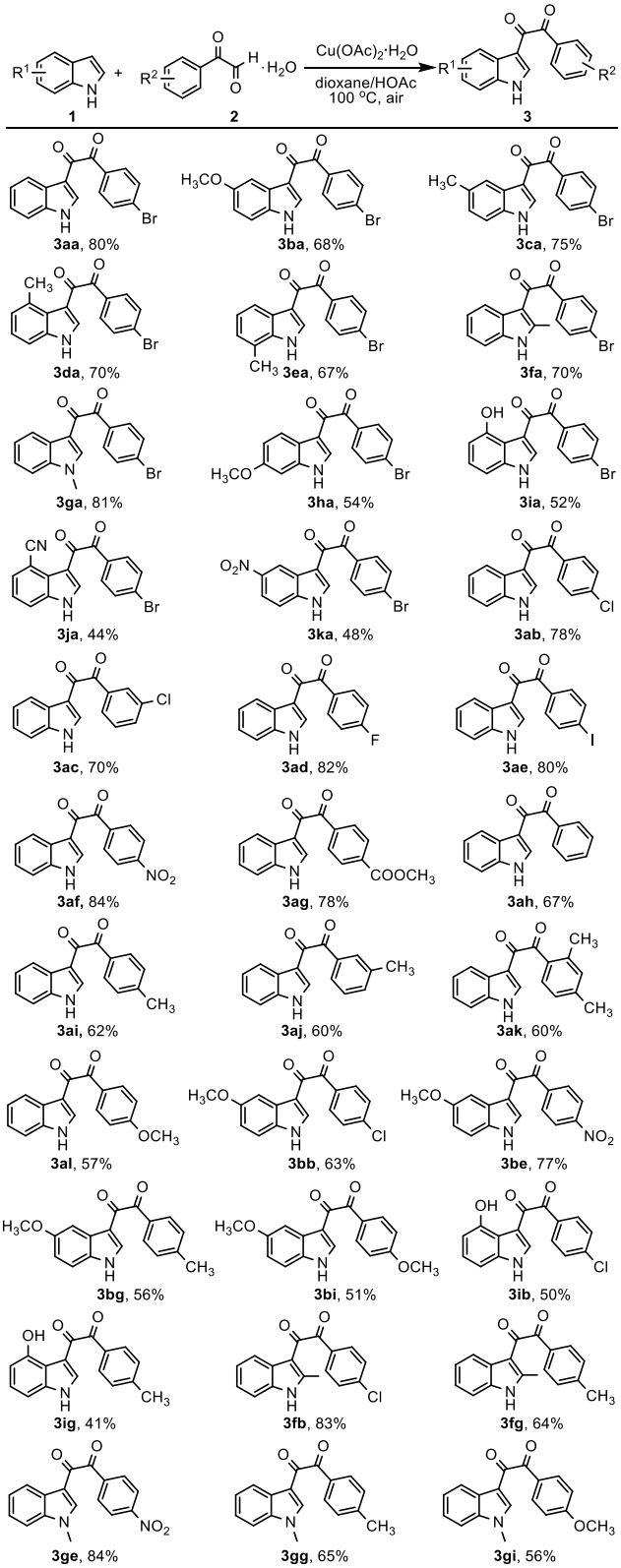
To gain further insight into the reaction mechanism, representative LC-MS analyses were shown in Figure 1A. Interestingly, two isomeric intermediates **4a** (major) and **5a** (minor) were detected under all reaction conditions (Figure S2–S3 in supporting information). It is noteworthy that Ivonin et al. first reported the two isomers and indolyl diketone by the reaction of indole with phenylglyoxal hydrate and subsequent isomerization or oxidation under basic condition such as NEt_3 and KOH (Figure 1B).[17] Recently, Mupparapu et al. reported another similar result that the aminocatalytic reaction of indole and phenylglyoxal hydrate with pyrrolidine as catalyst in toluene or morpholine as catalyst in DMSO afforded indolyl diketone via three-component intermediate **10** and **11** (detected by LC-MS result) transformed by iminium ion.[9] However, our detailed experiment results demonstrated that the different intermediates were obtained in different solvents in this reaction system (Figure 1C, detailed LC-MS results in Figure S4-S7). The three-component intermediates **10** and **11** were detected by LC-MS results with pyrrolidine or morpholine as catalyst in DMSO, while two isomeric intermediates **4a** and **5a** were detected by LC-MS results with pyrrolidine or morpholine as catalyst in toluene. Furthermore, the two intermediates **4a** and **5a** were also detected under acidic conditions in our reaction systems. The result indicated that both acid and base could promote the formation of the two intermediates **4a** and **5a**. Another control experiment was also performed to prove the crucial role of HOAc. The product **3a** was obtained in 65% yield in dioxane without HOAc and the two isomeric intermediates **4a** and **5a** were also detected by LC-MS result (Figure 1D, LC-MS result in Figure S8). These results demonstrated that both $Cu(OAc)_2{\cdot}H_2O$ and HOAc played a role of promotor for the formation of the two isomeric intermediates **4a** and **5a**; moreover, $Cu(OAc)_2{\cdot}H_2O$/air or only air played a role of the oxidant for the subsequent formation of the product **3a** (the result *vs* Table 1, entries 2 and 5).

Based on the above experimental results, a plausible mechanism was proposed as shown in Scheme 3. Initially, the reaction of indole **1a** and 2-(4-bromophenyl)-2-oxoacetaldehyde hydrate **2a** in the presence of $Cu(OAc)_2{\cdot}H_2O$ (**path a**) or HOAc (**path b**) resulted in the formation of two isomeric intermediates **4a** and **5a** (**4a** could be converted to **5a** in the presence of $Cu(OAc)_2{\cdot}H_2O$ or HOAc), followed by further rapid oxidation by $Cu(OAc)_2{\cdot}H_2O$/air (**path a**) or only air (**path b**) to afford the desired product **3a**. Finally, $Cu(OAc)_2{\cdot}H_2O$ was reduced to Cu_2O after the reaction in **path a**. Notably, a precipitate was collected after the reaction at a 4 mmol scale and was analyzed by XRD (X-ray powder diffraction). The significant diffraction peak was assigned to Cu_2O (see Figure S1 in supporting information). The result suggested that $Cu(OAc)_2{\cdot}H_2O$ can be considered as both the catalyst and the oxidant in the reaction.

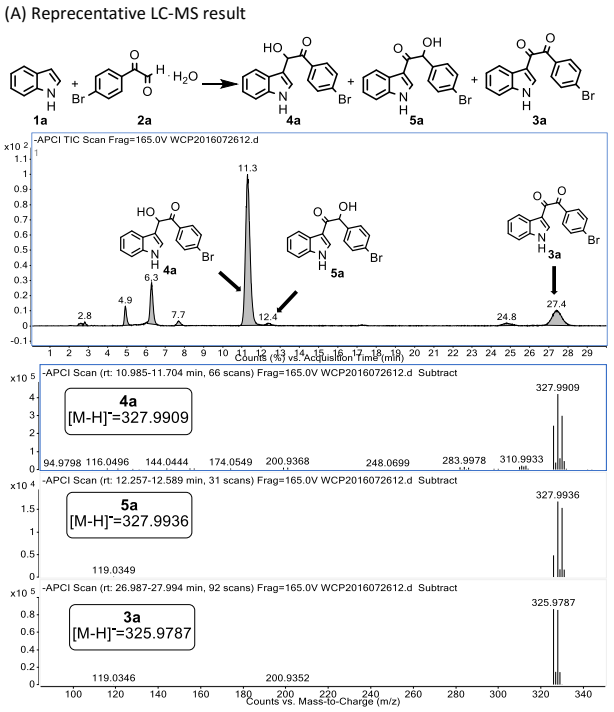


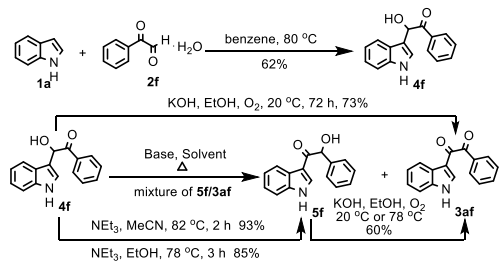
Scheme 1 Synthesis of the indole alkaloid **6** by Cu-catalyzed C–H oxidation/diacylation

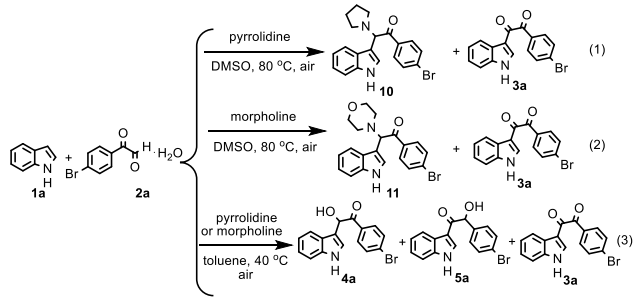
Table 2 Cu-catalyzed C–H oxidation/diacylation of Indoles with arylglyoxal hydrates[a]



[a] Conditions: **1** (0.5 mmol), **2** (0.6 mmol), $Cu(OAc)_2{\cdot}H_2O$ (20 mol%), dioxane/HOAc (4.0/0.5, v/v, 4.5 mL), 100 °C, under air atmosphere; the isolated yields are given.







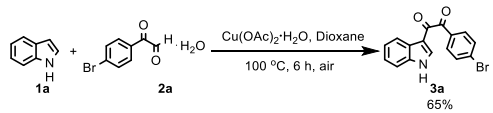
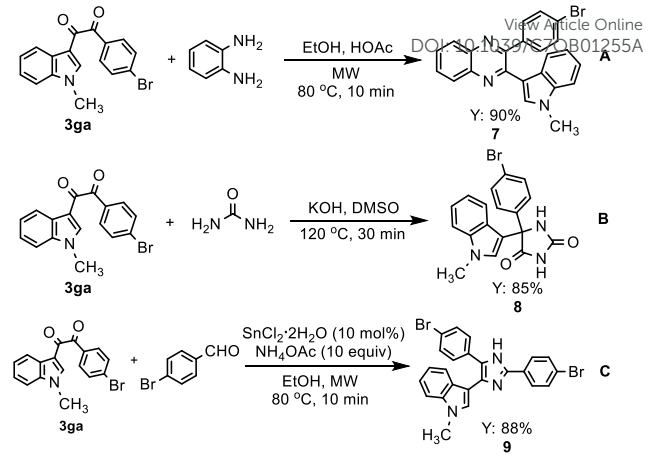


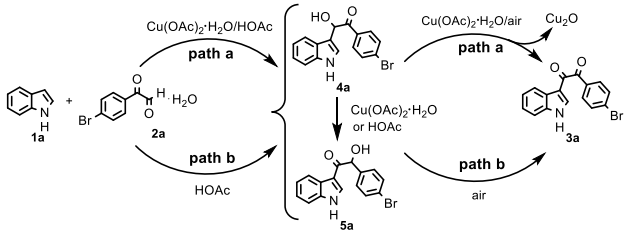
Figure 1 (A) Reprecentative LC-MS result. (B) Ivonin's work on two isomeric intermediates. (C) Detailed experiment results on the different intermediates by LC-MS results. (D) Control experiment.

Conclusions

In conclusion, we have successfully established an efficient Cu-catalyzed C–H oxidation/diacylation of indoles with arylglyoxals hydrates under air atmosphere. The reaction provides a new and expedient alternative synthetic method for indolyl diketones in moderate to good yields with a broad substrate scope and good tolerance of functional groups. Furthermore, the synthetic utility of the reaction is also achieved by the synthesis of the natural alkaloid 1,2-di(1*H*-indol-3-yl)ethane-1,2-dione. Gratifyingly, the obtained indolyl diketone products could be further used to construct indolyl nitrogen-containing heterocycles such as indolyl quinoxaline, indolyl hydantoin and indolyl imidazole in high yields. Preliminary mechanistic studies indicate that two proposed pathways are involved in this process. Further investigations on the detailed reaction mechanism and studies on transition-metal-catalyzed C–H functionalization of indoles are currently underway in our laboratory.



Scheme 2 Synthetic application of indolyl diketones



Scheme 3 Plausible reaction mechanism

Experimental

General procedure for the synthesis of product 3

A dried 25mL two-neck round bottom flask was charged with indole **1** (0.5 mmol), arylglyoxal hydrates **2** (0.6 mmol), $Cu(OAc)_2 \cdot H_2O$ (20.0 mg, 20 mol%) and dioxane/HOAc (4.0/0.5, v/v, 4.5 mL) under air atmosphere. The reaction mixture was stirred at 100 °C. After completion of the reaction, the reaction mixture was cooled to room temperature and diluted with ethyl acetate and water. The aqueous phase was extracted with ethyl acetate. The combined organic extracts were washed with saturated brine, dried with anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude products were purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 10/1, v/v) to afford the corresponding products **3**.

1-(4-bromophenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (3aa)[9]

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Yellow solid, m.p.: 205.1-206.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.44 (s, 1H), 8.20 (s, 2H), 7.89 (d, *J*=8.5 Hz, 2H), 7.79 (d, *J*=8.0 Hz, 2H), 7.55 (dd, *J*=2.0, 5.5 Hz, 1H), 7.30 (dd, *J*=3.5, 3.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.30, 188.21, 138.64, 137.48, 132.74, 132.52, 132.08, 129.40, 125.54, 124.37, 123.37, 121.67, 113.25, 112.95. HRMS (ESI) for $C_{16}H_{10}NO_2NaBr$ ([M+Na]$^+$): calcd 349.9793, 351.9772, found 349.9803, 349.9780.

1-(4-bromophenyl)-2-(5-methoxy-1*H*-indol-3-yl)ethane-1,2-dione (3ba)

Yellow solid, m.p.: 201.6-202.3 °C. ^{1}H NMR (500 MHz, acetone-d_6): δ 8.02 (s, 1H), 7.94 (d, *J*=8.0 Hz, 2H), 7.82 (s, 1H), 7.76 (d, *J*=8.0 Hz, 2H), 7.46 (d, *J*=8.5 Hz, 1H), 6.91 (d, *J*=8.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 192.77, 187.70, 156.87, 137.04, 132.69, 131.85, 131.63, 128.90, 126.51, 113.91, 113.22, 113.11, 103.45, 55.06. HRMS (ESI) for $C_{17}H_{12}NO_3NaBr$ ([M+Na]$^+$): calcd 379.9898, 381.9878, found 379.9900, 381.9884.

1-(4-bromophenyl)-2-(5-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3ca)

Grey solid, m.p.: 226.4-227.8 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.33 (s, 1H), 8.12 (d, *J*=3.0 Hz, 1H), 8.03 (s, 1H), 7.87 (d, *J*=8.5 Hz, 2H), 7.80 (d, *J*=9.0 Hz, 2H), 7.42 (d, *J*=8.0 Hz, 2H), 7.13 (d, *J*=7.5 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.34, 188.12, 138.49, 135.77, 132.72, 132.58, 132.44, 132.05, 129.34, 125.82, 125.80, 121.45, 112.86, 112.58, 21.74. HRMS (ESI) for $C_{17}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 363.9949, 365.9929, found 363.9940, 365.9925.

1-(4-bromophenyl)-2-(4-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3da)

Yellow solid, m.p.: 152.8-154.8 °C. ^{1}H NMR (500 MHz, acetone-d_6): δ 8.01 (s, 1H), 7.91 (d, *J*=7.0 Hz, 2H), 7.75 (d, *J*=7.0 Hz, 2H), 7.36 (d, *J*=8.0 Hz, 1H), 7.17 (dd, *J*=7.0, 7.0 Hz, 1H), 7.04 (d, *J*=6.5 Hz, 1H), 2.90 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 193.86, 188.08, 139.09, 138.26, 132.83, 132.60, 132.22, 131.52, 128.81, 124.62, 124.39, 124.24, 114.57, 109.95, 22.50. HRMS (ESI) for $C_{17}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 363.9949, 365.9929, found 363.9940, 365.9925.

1-(4-bromophenyl)-2-(7-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3ea)

Yellow solid, m.p.: 229.9-230.5 °C. ^{1}H NMR (500 MHz, acetone-d_6): δ 8.13 (d, *J*=8.0 Hz, 1H), 8.05 (s, 1H), 7.93 (d, *J*=7.0 Hz, 2H), 7.75 (d, *J*=7.5 Hz, 2H), 7.19 (dd, *J*=6.5, 7.5 Hz, 1H), 7.10 (d, *J*=7.0 Hz, 1H), 2.51 (s, 3H); ^{13}C NMR (125 MHz, acetone-d_6) δ 192.79, 187.91, 136.67, 136.57, 132.67, 132.18, 131.61, 128.92, 125.34, 124.66, 123.15, 122.02, 119.29, 113.59, 15.93. HRMS (ESI) for $C_{17}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 363.9949, 365.9929, found 363.9940, 365.9925.

1-(4-bromophenyl)-2-(2-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3fa)

Yellow solid, m.p.: 235.9-236.4 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.42 (s, 1H), 7.86 (d, *J*=8.5 Hz, 2H), 7.79 (d, *J*=8.5 Hz, 3H), 7.44 (d, *J*=7.5 Hz, 1H), 7.19 (dd, *J*=7.5, 2.0 Hz, 1H), 7.19 (dd, *J*=7.5, 2.0 Hz, 1H), 7.15 (dd, *J*=7.5, 2.0 Hz, 1H), 2.48 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.76, 190.17, 149.37, 136.77, 134.01, 133.16, 132.68, 130.64, 127.77, 124.36, 123.86, 121.29, 113.25, 110.93, 15.67. HRMS (ESI) for $C_{17}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 363.9949, 365.9929, found 363.9940, 365.9925.

1-(4-bromophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3ga)

Yellow solid, m.p.: 160.4-161.4 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.24 (s, 1H), 8.22 (d, *J*=7.0 Hz, 1H), 7.88 (d, *J*=8.5 Hz, 2H), 7.80 (d, *J*=8.5 Hz, 2H), 7.61 (d, *J*=7.5 Hz, 1H), 7.39-7.33 (m, 2H), 3.86 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.23, 188.53, 142.76, 139.13, 133.70, 133.38, 132.98, 130.39, 126.88, 125.34, 124.68, 122.71, 112.68, 34.85. HRMS (ESI) for $C_{17}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 363.9949, 365.9929, found 363.9940, 365.9925.

1-(4-bromophenyl)-2-(6-methoxy-1*H*-indol-3-yl)ethane-1,2-dione (3ha)

Yellow solid, m.p.: 220.3-220.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.24 (s, 1H), 8.05 (d, *J*=8.0 Hz, 2H), 7.87 (d, *J*=8.5 Hz, 2H), 7.79 (d, *J*=8.5 Hz, 2H), 7.02 (s, 1H), 6.93 (d, *J*=8.5 Hz, 1H), 3.80 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.28, 188.00, 157.58, 138.51, 137.84, 132.72, 132.57, 132.05, 129.34, 122.30, 119.34, 113.06, 112.99, 96.40, 55.84. HRMS (ESI) for $C_{17}H_{12}NO_3NaBr$ ([M+Na]$^+$): calcd 379.9898, 381.9878, found 379.9900, 381.9884.

1-(4-bromophenyl)-2-(4-hydroxy-1*H*-indol-3-yl)ethane-1,2-dione (3ia)

Brown solid, m.p.: 203.5-204.6 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.98 (s, 1H), 8.52 (s, 1H), 7.59 (d, *J*=8.0 Hz, 2H), 7.51 (s, 1H), 7.41 (d, *J*=8.0 Hz, 2H), 7.24-7.19 (m, 2H), 6.75 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.92, 167.22, 143.52, 137.31, 131.80, 128.42, 126.97, 122.78, 116.88, 113.21, 108.85, 108.55, 105.26, 100.28. HRMS (ESI) for $C_{16}H_{10}NO_3NaBr$ ([M+Na]$^+$): calcd 365.9742, 367.9721, found 365.9728, 367.9705.

3-(2-(4-bromophenyl)-2-oxoacetyl)-1*H*-indole-4-carbonitrile (3ja)

Yellow solid, m.p.: 256.9-257.8 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.95 (s, 1H), 8.41 (s, 1H), 7.90 (d, *J*=7.5 Hz, 3H), 7.82 (d, *J*=8.5 Hz, 2H), 7.79 (d, *J*=7.5 Hz, 1H), 7.79 (dd, *J*=7.0, 7.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.10, 187.47, 141.11, 138.43, 132.77, 132.16, 130.97, 129.55, 124.57, 124.12, 119.22, 118.70, 112.66, 104.41. HRMS (ESI) for $C_{17}H_9N_2O_2NaBr$ ([M+Na]$^+$): calcd 374.9745, 376.9725, found 374.9741, 376.9723.

1-(4-bromophenyl)-2-(5-nitro-1*H*-indol-3-yl)ethane-1,2-dione (3ka)

Brown solid, m.p.: 266.5-268.4 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.98 (s, 1H), 9.05 (s, 1H), 8.50 (s, 1H), 8.19 (dd, *J*=9.0, 2.0 Hz, 1H), 7.92 (d, *J*=8.0 Hz, 2H), 7.80 (d, *J*=8.5 Hz, 2H), 7.73 (d, *J*=9.0 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.41, 188.04, 143.91, 141.89, 140.61, 132.75, 132.25, 132.17, 129.68, 125.17, 119.68, 117.90, 114.08, 114.05. HRMS (ESI) for $C_{16}H_9N_2O_4NaBr$ ([M+Na]$^+$): calcd 394.9643, 394.9623 found 394.9637, 396.9614.

1-(4-chlorophenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (3ab)[6,9]

Yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.48 (s, 1H), 8.24-8.23 (m, 2H), 8.01-7.98 (m, 2H), 7.71-7.68 (m, 2H), 7.60-7.59 (m, 1H), 7.36-7.31 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.09, 188.23, 140.08, 138.62, 137.47, 132.20, 132.05, 129.79, 125.52, 124.37, 123.36, 121.64, 113.24, 112.93. HRMS

(ESI) for $C_{16}H_{10}NO_2NaCl$ ([M+Na]$^+$): calcd 306.0298, 308.0268, found 306.0290, 308.0258.

1-(3-chlorophenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (3ac)

Yellow solid, m.p.: 216.7-218.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.49 (s, 1H), 8.25 (m, 2H), 7.96 (s, 1H), 7.92 (d, *J*=6.5 Hz, 1H), 7.82 (d, *J*=8.0 Hz, 1H), 7.63 (dd, *J*=7.5, 8.0 Hz, 1H), 7.58 (d, *J*=6.5 Hz, 1H), 7.34-7.33 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.06, 187.10, 170.13, 138.20, 136.83, 134.68, 134.11, 133.75, 131.00, 128.63, 128.48, 124.89, 123.76, 122.76, 121.04, 112.61, 112.22. HRMS (APCI) for $C_{16}H_{11}NO_2Cl$ ([M+H]$^+$): calcd 284.0478, 286.0449, found 284.0476, 286.0450.

1-(4-fluorophenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (3ad)[6]

Yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.44 (s, 1H), 8.23-8.20 (m, 2H), 8.07-8.05 (m, 2H), 7.57-7.55 (m, 1H), 7.46-7.42 (m, 2H), 7.34-7.30 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.73, 189.44, 167.17 (d, *J*=252.5 Hz), 139.40, 138.38, 134.26 (d, *J*=10.0 Hz), 131.20 (d, *J*=2.5 Hz), 126.46, 125.25, 124.24, 122.56, 117.75 (d, *J*=21.3 Hz), 114.14, 113.91. HRMS (ESI) for $C_{16}H_{10}NO_2NaF$ ([M+Na]$^+$): calcd 290.0593, found 290.0589.

1-(1*H*-indol-3-yl)-2-(4-iodophenyl)ethane-1,2-dione (3ae)

Yellow solid, m.p.: 219.9-220.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.45 (s, 1H), 8.22-8.20 (m, 2H), 8.02-8.00 (m, 2H), 7.73-7.70 (m, 2H), 7.57-7.54 (m, 1H), 7.34-7.29 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.67, 189.25, 139.54, 138.38, 133.70, 132.59, 126.42, 125.29, 124.27, 122.56, 114.16, 113.86, 106.73, 105.22. HRMS (ESI) for $C_{16}H_{10}NO_2NaI$ ([M+Na]$^+$): calcd 397.9654, found 397.9652.

1-(1*H*-indol-3-yl)-2-(4-nitrophenyl)ethane-1,2-dione (3af)

Brown solid, m.p.: 238.6-239.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.52 (s, 1H), 8.40 (d, *J*=8.5 Hz, 2H), 8.29 (s, 1H), 8.22 (d, *J*=8.5 Hz, 3H), 7.57 (d, *J*=5.5 Hz, 1H), 7.33 (dd, *J*=3.5, 3.5 Hz, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.50, 187.15, 151.06, 139.09, 138.19, 137.50, 131.68, 125.60, 124.59, 124.49, 123.48, 121.70, 113.30, 112.77. HRMS (ESI) for $C_{16}H_{10}N_2O_4Na$ ([M+Na]$^+$): calcd 317.0538, found 317.0537.

Methyl 4-(2-(1*H*-indol-3-yl)-2-oxoacetly)benzoate (3ag)

Yellow solid, m.p.: 352.3-353.9 °C. ^{1}H NMR (500 MHz, C_3D_6O): δ 11.45 (s, 1H), 8.40-8.39 (m, 1H), 8.22-8.16 (m, 5H), 7.63 (dd, *J*=3.0, 3.5 Hz, 1H), 7.37 (dd, *J*=3.0, 3.0 Hz, 2H), 3.95 (s, 3H); ^{13}C NMR (125 MHz, C_3D_6O) δ 192.29, 186.98, 164.88, 136.60, 136.57, 136.36, 134.17, 129.32, 129.00, 125.00, 123.41, 122.27, 121.11, 112.74, 111.78, 51.26. HRMS (APCI) for $C_{18}H_{14}NO_4$ ([M+H]$^+$): calcd 308.0923, found 308.0923.

1-(1*H*-indol-3-yl)-2-phenylethane-1,2-dione (3ah)[6,9]

Brown solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.37 (s, 1H), 8.21 (d, *J*=5.5 Hz, 1H), 8.15 (d, *J*=3.0 Hz, 1H), 7.96 (d, *J*=7.0 Hz, 2H), 7.74-7.71 (m, 1H), 7.60-7.54 (m, 3H), 7.32-7.29 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.45, 189.01, 138.31, 137.47, 135.10, 133.51, 130.18, 129.59, 125.51, 124.30, 123.28, 121.63, 113.22, 113.09. HRMS (ESI) for $C_{16}H_{11}NO_2Na$ ([M+Na]$^+$): calcd 272.0687, found 272.0689.

1-(1*H*-indol-3-yl)-2-(*p*-tolyl)ethane-1,2-dione (3ai)[6]

Yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.42 (s, 1H), 8.23 (d, *J*=6.0 Hz, 1H), 8.16 (d, *J*=3.0 Hz, 1H), 7.88 (d, *J*=8.0 Hz, 2H), 7.58-7.56 (m, 1H), 7.41 (d, *J*=8.0 Hz, 2H), 7.35-7.30 (m, 2H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.16, 189.30, 145.91, 138.15, 137.44, 131.03, 130.30, 130.15, 125.49, 124.26, 123.24, 121.62, 113.20, 113.12, 21.83. HRMS (ESI) for $C_{17}H_{13}NO_2Na$ ([M+Na]$^+$): calcd 286.0844, found 286.0840.

1-(1*H*-indol-3-yl)-2-(*m*-tolyl)ethane-1,2-dione (3aj)

Yellow solid, m.p.: 317.1-318.8 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.43 (s, 1H), 8.22 (d, *J*=3.0 Hz, 1H), 8.17 (s, 1H), 7.78-7.76 (m, 2H), 7.56-7.53 (m, 3H), 7.33-7.31 (m, 2H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.49, 190.15, 145.65, 138.36, 136.95, 134.48, 134.34, 131.23, 131.07, 128.12, 126.48, 125.37, 124.12, 122.14, 113.44, 113.36, 22.20. HRMS (APCI) for $C_{17}H_{14}NO_2$ ([M+H]$^+$): calcd 264.1025, found 264.1022.

1-(2,4-dimethylphenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (3ak)

Yellow solid, m.p.: 192.5-194.1 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.39 (s, 1H), 8.20-8.16 (m, 2H), 7.59 (d, *J*=8.0 Hz, 1H), 7.56 (dd, *J*=7.0, 2.0 Hz, 1H), 7.33-7.28 (m, 2H), 7.24 (s, 1H), 7.15 (d, *J*=8.0 Hz, 1H), 2.59 (s, 3H), 2.35 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 197.50, 190.74, 145.35, 141.60, 138.78, 138.31, 134.31, 134.20, 131.06, 128.08, 126.54, 125.09, 124.06, 122.49, 114.08, 114.03, 22.55, 22.49. HRMS (ESI) for $C_{18}H_{15}NO_2Na$ ([M+Na]$^+$): calcd 300.1000, found 299.9994.

1-(1*H*-indol-3-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3al)[6,9]

Yellow solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.40 (s, 1H), 8.23 (dd, *J*=6.0, 2.5 Hz, 1H), 8.15 (d, *J*=3.0 Hz, 1H), 7.97-7.94 (m, 2H), 7.59-7.55 (m, 1H), 7.35-7.30 (m, 2H), 7.15-7.12 (m, 2H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.15, 189.55, 164.79, 138.01, 137.42, 132.66, 126.34, 125.53, 124.20, 123.19, 121.61, 114.98, 113.22, 113.18, 56.21. HRMS (ESI) for $C_{17}H_{13}NO_3Na$ ([M+Na]$^+$): calcd 302.0793, found 302.0795.

1-(4-chlorophenyl)-2-(5-methoxy-1*H*-indol-3-yl)ethane-1,2-dione (3bb)

Yellow solid, m.p.: 194.1-195.0 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.36 (s, 1H), 8.12 (d, *J*=3.0 Hz, 1H), 7.98 (d, *J*=8.5 Hz, 2H), 7.73 (s, 1H), 7.67 (d, *J*=8.5 Hz, 2H), 7.45 (d, *J*=9.0 Hz, 1H), 6.94 (dd, *J*=9.0, 2.5 Hz, 1H), 3.83 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.10, 188.04, 156.71, 140.05, 138.49, 132.20, 132.05, 131.60, 129.78, 126.48, 114.10, 114.04, 112.81, 103.58, 55.86. HRMS (ESI) for $C_{17}H_{12}NO_3NaCl$ ([M+Na]$^+$): calcd 336.0403, 338.0374, found 336.0416, 338.0381.

1-(5-methoxy-1*H*-indol-3-yl)-2-(4-nitrophenyl)ethane-1,2-dione (3be)

Yellow solid, m.p.: 236.1-236.9 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.43 (s, 1H), 8.42 (dd, *J*=9.0, 4.0 Hz, 2H), 8.23 (dd, *J*=9.0, 4.0 Hz, 3H), 7.75 (s, 1H), 7.48 (dd, *J*=9.0, 3.5 Hz, 1H), 6.97 (dd, *J*=9.0, 2.5 Hz, 1H), 3.85 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.53, 186.96, 156.81, 151.06, 138.92, 138.23, 132.21, 131.67, 126.56, 124.59, 114.18, 114.10, 112.64, 103.66, 55.89. HRMS (ESI) for $C_{17}H_{12}N_2O_5Na$ ([M+Na]$^+$): calcd 347.0644, found 347.0656.

1-(5-methoxy-1*H*-indol-3-yl)-2-*p*-tolylethane-1,2-dione (3bg)

Brown solid, m.p.: 165.4-167.3 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.27 (s, 1H), 8.03 (d, *J*=3.5 Hz, 1H), 7.85 (d, *J*=8.0 Hz, 2H), 7.71 (s, 1H), 7.43 (d, *J*=9.0 Hz, 1H), 7.38 (d, *J*=8.0 Hz, 2H), 6.92 (dd, *J*=9.0, 2.5 Hz, 1H), 3.81 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.17, 189.10, 156.63, 145.86, 138.02, 132.19, 131.08, 130.28, 130.13, 126.43, 114.00, 113.97, 113.00,

103.57, 55.87, 21.82. HRMS (ESI) for $C_{18}H_{15}NO_3Na$ ([M+Na]$^+$): calcd 316.0950, found 316.0963.

1-(5-methoxy-1*H*-indol-3-yl)-2-(4-methoxyphenyl)ethane-1,2-dione (3bi)

Brown solid, m.p.: 212.8-213.6 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.28 (s, 1H), 8.04 (d, *J*=3.0 Hz, 1H), 7.95 (d, *J*=9.0 Hz, 2H), 7.73 (s, 1H), 7.45 (d, *J*=9.0 Hz, 1H), 7.13 (d, *J*=9.0 Hz, 2H), 6.95 (dd, *J*=8.5, 2.5 Hz, 1H), 3.88 (s, 3H), 3.84 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.16, 189.37, 164.76, 156.59, 137.94, 132.64, 132.15, 126.38, 126.27, 114.97, 113.95, 113.06, 103.53, 56.23, 55.86. HRMS (ESI) for $C_{18}H_{15}NO_4Na$ ([M+Na]$^+$): calcd 332.0899, found 332.0898.

1-(4-chlorophenyl)-2-(4-hydroxy-1*H*-indol-3-yl)ethane-1,2-dione (3ib)

Yellow solid, m.p.: 196.3-197.4 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.98 (s, 1H), 8.52 (s, 1H), 7.51-7.44 (m, 5H), 7.25-7.20 (m, 2H), 6.76 (s, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.97, 167.22, 143.53, 136.88, 134.15, 128.87, 128.12, 126.97, 116.90, 113.22, 108.86, 108.56, 105.22, 100.29. HRMS (ESI) for $C_{16}H_{10}NO_3NaCl$ ([M+Na]$^+$): calcd 322.0247, 324.0217, found 322.0258, 324.0220.

1-(4-hydroxy-1*H*-indol-3-yl)-2-p-tolylethane-1,2-dione (3ig)

Yellow solid, m.p.: 192.2-193.6 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.95 (s, 1H), 8.33 (s, 1H), 7.51 (s, 1H), 7.37 (d, *J*=8.0 Hz, 2H), 7.24-7.18 (m, 4H), 6.75 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 196.50, 167.26, 143.40, 138.68, 134.99, 129.25, 126.79, 126.09, 116.87, 113.23, 109.09, 108.25, 105.89, 100.25, 21.20. HRMS (ESI) for $C_{16}H_{10}NO_3NaCl$ ([M+Na]$^+$): calcd 302.0793, found 302.0805.

1-(4-chlorophenyl)-2-(2-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3fb)

Yellow solid, m.p.: 243.9-244.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.44 (s, 1H), 7.95 (d, *J*=8.0 Hz, 2H), 7.79 (s, 1H), 7.68 (d, *J*=8.0 Hz, 2H), 7.45 (d, *J*=8.0 Hz, 1H), 7.21 (dd, *J*=7.0, 2.5 Hz, 1H), 7.16 (dd, *J*=7.0, 2.5 Hz, 1H), 2.49 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.63, 189.27, 148.44, 140.39, 135.83, 131.91, 131.73, 130.15, 126.82, 123.44, 122.94, 120.34, 112.32, 109.97, 14.73. HRMS (ESI) for $C_{17}H_{12}NO_2NaCl$ ([M+Na]$^+$): calcd 320.0454, 322.0425, found 320.0447, 322.0414.

1-(2-methyl-1*H*-indol-3-yl)-2-p-tolylethane-1,2-dione (3fg)

Yellow solid, m.p.: 188.9-189.6 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.38 (s, 1H), 7.84 (d, *J*=8.0 Hz, 2H), 7.80 (s, 1H), 7.44 (d, *J*=8.0 Hz, 1H), 7.40 (d, *J*=8.0 Hz, 2H), 7.20 (dd, *J*=7.5, 2.5 Hz, 1H), 7.15 (dd, *J*=7.5, 2.5 Hz, 1H), 2.49 (s, 3H), 2.39 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 195.59, 190.19, 148.01, 146.16, 135.78, 130.84, 130.46, 130.00, 126.86, 123.31, 122.79, 120.38, 112.24, 110.11, 21.84, 14.65. HRMS (ESI) for $C_{18}H_{15}NO_2Na$ ([M+Na]$^+$): calcd 300.1000, found 300.1009.

1-(1-methyl-1*H*-indol-3-yl)-2-(4-nitrophenyl)ethane-1,2-dione (3ge)[7]

Yellow solid, m.p.: 198.9-200.0 °C ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.42 (d, *J*=9.0 Hz, 2H), 8.37 (s, 1H), 8.27 (d, *J*=7.5 Hz, 1H), 8.23 (d, *J*=8.5 Hz, 2H), 7.67 (d, *J*=8.0 Hz, 1H), 7.44-7.39 (m, 2H), 3.91 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 192.53, 186.54, 151.10, 142.26, 138.26, 138.09, 131.67, 126.01, 124.64, 124.55, 123.90, 121.83, 111.85, 111.58, 34.00. HRMS (ESI) for $C_{17}H_{12}N_2O_4Na$ ([M+Na]$^+$): calcd 331.0695, found 331.0706.

1-(1-methyl-1*H*-indol-3-yl)-2-p-tolylethane-1,2-dione (3gg)[7]

Yellow solid, m.p.: 114.2-115.3 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.24 (d, *J*=7.5 Hz, 1H), 8.21 (s, 1H), 7.95 (d, *J*=8.5 Hz, 2H), 7.64 (d, *J*=7.5 Hz, 1H), 7.41-7.35 (m, 2H), 7.14 (d, *J*=8.5 Hz, 2H), 3.89 (s, 3H), 3.88 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 193.12, 188.99, 164.83, 141.30, 138.14, 132.65, 126.26, 125.94, 124.26, 123.59, 121.74, 115.01, 112.04, 111.68, 56.24, 33.83. HRMS (ESI) for $C_{18}H_{15}NO_2Na$ ([M+Na]$^+$): calcd 300.1000, found 300.1009.

1-(4-methoxyphenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (3gi)[7]

Yellow solid, m.p.: 123.7-125.0 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.25 (d, *J*=7.5 Hz, 1H), 8.23 (s, 1H), 7.88 (d, *J*=8.0 Hz, 2H), 7.64 (d, *J*=8.0 Hz, 1H), 7.43-7.36 (m, 4H), 3.89 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 194.13, 188.73, 145.98, 141.41, 138.17, 130.96, 130.29, 130.18, 125.92, 124.31, 123.64, 121.75, 111.96, 111.70, 33.85, 21.83. HRMS (ESI) for $C_{18}H_{15}NO_3Na$ ([M+Na]$^+$): calcd 316.0950, found 316.0963.

1-(4-bromophenyl)-2-hydroxy-2-(1*H*-indol-3-yl)ethanone (4a)[17a]

Recrystallization from benzene, white solid, m.p.: 158.5-160.1 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.10 (s, 1H), 7.94 (d, *J*=8.5 Hz, 2H), 7.61 (d, *J*=8.5 Hz, 3H), 7.37-7.32 (m, 2H), 7.06 (dd, *J*=7.0, 7.5 Hz, 1H), 6.98 (dd, *J*=7.5, 7.5 Hz, 1H), 6.33 (d, *J*=5.5 Hz, 1H), 5.64 (d, *J*=5.5 Hz, 1H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 198.69, 136.80, 134.50, 131.99, 130.98, 128.78, 127.40, 126.03, 125.32, 121.80, 119.61, 119.44, 113.46, 112.08, 70.30. HRMS (ESI) for $C_{16}H_{12}NO_2NaBr$ ([M+Na]$^+$): calcd 351.9949, found 351.9945.

1,2-di(1*H*-indol-3-yl)ethane-1,2-dione (6)[13,15b]

Yellow solid, m.p.: 279.1-280.5 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.23 (s, 2H), 8.26 (m, 2H), 8.20 (s, 2H), 7.53 (m, 2H), 7.28 (m, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 189.24, 137.78, 137.70, 126.15, 123.86, 122.84, 121.78, 113.05, 113.01. HRMS (ESI) for $C_{24}H_{17}N_2O_2Na$ ([M+Na]$^+$): calcd 311.0796, found 311.0792.

General procedure for the synthesis of product 7

A mixture of 1-(4-bromophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (0.15 mmol, 51.33 mg) and *o*-phenylenediamine (0.225 mmol, 24.33 mg) was dissolved in HOAc (1 mL) and EtOH (5 mL). The reaction mixture was stirred at 80 °C for 10 min under microwave irradiation (a Biotage Initiator 8 reactor from Sweden). After the completion of the reaction, water (6 mL) was added. The solid was filtered under reduced pressure and washed with small portions of a mixture of cooled EtOH/H_2O (1:1, v:v). The crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5/1, v/v) to afford the target product 2-(4-bromophenyl)-3-(1-methyl-1*H*-indol-3-yl)quinoxaline in 90% yield. Yellow solid, m.p.: 196.1-196.8 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 8.19 (d, *J*=8.0 Hz, 1H), 8.08 (d, *J*=8.5 Hz, 1H), 8.02 (d, *J*=8.0 Hz, 1H), 7.81 (dd, *J*=7.0, 7.5 Hz, 1H), 7.74 (dd, *J*=7.0, 7.5 Hz, 1H), 7.62 (d, *J*=8.5 Hz, 2H), 7.56 (d, *J*=8.0 Hz, 2H), 7.46 (d, *J*=8.5 Hz, 1H), 7.21 (dd, *J*=7.5, 7.5 Hz, 1H), 7.11 (dd, *J*=8.0, 7.5 Hz, 1H), 7.00 (s, 1H), 3.69 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 153.43, 150.14, 142.25, 140.41, 140.35, 138.18, 133.99, 132.76, 132.59, 131.64, 130.37, 130.03, 129.60, 127.83,

123.81, 123.69, 123.06, 121.99, 113.74, 111.56, 34.25. HRMS (APCI) for $C_{23}H_{17}N_3Br$ ($[M+H]^+$): calcd 414.0606, 416.0585, found 414.0616, 416.0588.

General procedure for the synthesis of product 8

A mixture of 1-(4-bromophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (0.15 mmol, 51.33 mg), urea (0.30 mmol, 18.02 mg) and KOH (0.60 mmol, 33.70 mg) was dissolved in DMSO (3 mL). The reaction mixture was stirred at 120 °C for 30 min. After the completion of the reaction, the reaction mixture was poured into cold water. The solution was acidified with glacial acetic acid. The solid was filtered under reduced pressure and washed with cold water. The product was recrystallized from ethanol. The product 5-(4-bromophenyl)-5-(1-methyl-1*H*-indol-3-yl)imidazolidine-2,4-dione was obtained in 85% yield. Off-white solid, m.p.: 269.8-270.5 °C. IR (KBr, cm^{-1}) *v* 3264 (NH), 1763 (C=O), 1711 (C=O); ^{1}H NMR (500 MHz, DMSO-d_6): δ 11.10 (s, 1H), 9.14 (s, 1H), 7.62 (d, *J*=8.5 Hz, 2H), 7.44 (dd, *J*=7.5, 6.0 Hz, 3H), 7.21-7.15 (m, 2H), 7.05 (s, 1H), 6.98 (dd, *J*=8.0, 7.5 Hz, 1H), 3.75 (s, 3H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 175.37, 156.55, 139.11, 137.72, 131.70, 129.40, 129.15, 125.38, 122.16, 121.89, 120.00, 119.69, 113.43, 110.60, 66.91, 32.89. HRMS (APCI) for $C_{18}H_{15}N_3O_2Br$ ($[M+H]^+$): calcd 384.0348, 386.0327, found 384.0343, 386.0325.

General procedure for the synthesis of product 9

A mixture of 1-(4-bromophenyl)-2-(1-methyl-1*H*-indol-3-yl)ethane-1,2-dione (0.15 mmol, 51.33 mg), 4-bromobenzaldehyde (0.15 mmol, 27.27 mg), NH_4OAc (10 equiv, 1.50 mmol, 115.62 mg) and $SnCl_2{\cdot}2H_2O$ (10 mol%, 3.4 mg) was dissolved in EtOH (6 mL). The reaction mixture was stirred at 80 °C for 10 min under microwave irradiation (a Biotage Initiator 8 reactor from Sweden). After the completion of the reaction, water (6 mL) was added. The solid was filtered under reduced pressure and washed with small portions of a mixture of cooled EtOH/H_2O (1:1, v:v). The crude product was purified by flash column chromatography on silica gel (petroleum ether/ethyl acetate, 5/1, v/v) to afford the target product 3-(2,5-bis(4-bromophenyl)-1*H*-imidazol-4-yl)-1-methyl-1*H*-indole in 88% yield. NMR spectrum show that the imidazole ring exists in prototropic tautomers. Light yellow solid, m.p.: 308.5-308.9 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ 12.73, 12.70 (s, 1H), 8.07, 8.03 (d, *J*=8.5 Hz, 2H), 7.71, 7.68 (d, *J*=7.5 Hz, 3H), 7.56 (dd, *J*=8.0, 6.5 Hz, 3H), 7.50 (dd, *J*=7.5, 7.0 Hz, 0.58H), 7.44 (dd, *J*=4.5, 3.5 Hz, 0.34H), 7.39 (d, *J*=8.0 Hz, 1.74H), 7.22 (dd, *J*=6.5, 8.0 Hz, 0.89H), 7.15 (dd, *J*=7.5, 7.5 Hz, 0.20H), 7.11 (d, *J*= 8.0 Hz, 0.85H), 7.01 (dd, *J*= 7.0, 8.0 Hz, 0.87H), 6.97 (dd, *J*= 7.5, 7.5 Hz, 0.87H), 3.91 (s, 2.65H), 3.81 (s, 0.45H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 144.62, 137.13, 136.41, 135.04, 132.14, 131.86, 131.36, 130.11, 130.05, 129.67, 128.36, 127.56, 127.39, 126.48, 123.51, 122.26, 121.73, 121.66, 120.21, 120.09, 119.47, 119.27, 110.74, 104.65, 33.16. HRMS (APCI) for $C_{24}H_{18}N_3Br_2$ ($[M+H]^+$): calcd 505.9867, 507.9847, 509.9827, found 505.9923, 507.9959, 509.9891.

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