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Synthesis of indole-linked β-cyano-enones: a pathway to indolyl-2-pyrrolones†

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Herein, we report for the first time an additive- and catalyst-free dehydrogenative multicomponent reaction of arylglyoxal, malononitrile, and indoles for the one-pot synthesis of indole-linked β-cyano-enones in DMF medium. The reaction was performed at 100 °C in DMF, forming one C–C single bond and one C=C double bond in a single-flask. Furthermore, we developed an efficient method for the synthesis of indolyl-2-pyrrolones having a hydroxyl group-containing chiral carbon center from the β-cyano-enones using trifluoroacetic acid and water as reaction medium. The β-cyano-enones were also further transformed into indolyl-1,2-diketones *via* a base-mediated reaction, which yielded indolyl quinoxalines upon reaction with *o*-phenylenediamine (OPD).

Introduction

β-Cyano-enones are considered as important intermediates due to the presence of a nitrile group, an electron-deficient alkene, and a ketone functionality, which can act as 1,4-di electrophilic carbon sites. These 1,4-dielectrophilic compounds have great potential like common dielectrophilic synthons, such as 1,3- or 1,5-dicarbonyl compounds for the synthesis of novel organic compounds.[1] β-Cyano-enones are also found in many dyes and pharmaceuticals.[2] For example, compound **I** is used as a near-infrared dye,[2a] and compound **II** is a calcium channel blocker[3] as shown in Fig. 1a.

Nitrogen-containing heterocycles such as indole and pyrrolones are the most common scaffolds in natural products and synthetic bioactive molecules. Considering their importance, the design and development of new methods for synthesizing indole-containing and pyrrolone-containing molecules has remained an important area of research in organic synthesis. Pyrrolones are an important pharmacophore in drug design and discovery and are the building blocks of numerous bioactive molecules and natural products (Fig. 1b).[4]

Pyrrolone derivatives exhibit diverse medicinal properties such as antibacterial, anticancer, anti-inflammatory, and antiviral.[5] Similarly, indole derivatives show antibacterial, α-amylase and monooxime inhibition, antimalarial and anti-tumor activities.[6]

The linking of two or more distinct heterocyclic moieties to provide a hybrid molecule with more than one pharmacophore

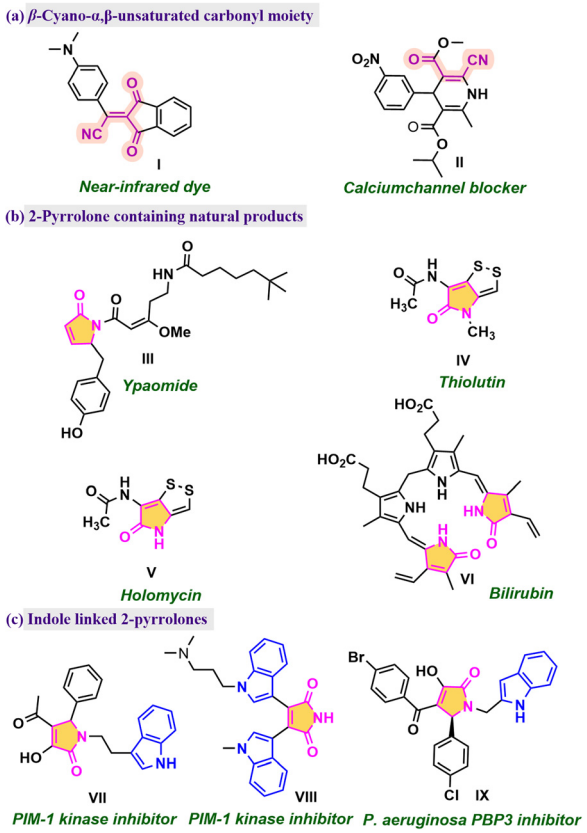

Fig. 1 (a) Examples of β-cyano-α,β-unsaturated carbonyls in dye and pharmaceutics. (b) Examples of 2-pyrolones containing natural products. (c) Examples of bioactive indole-linked 2-pyrrolones.

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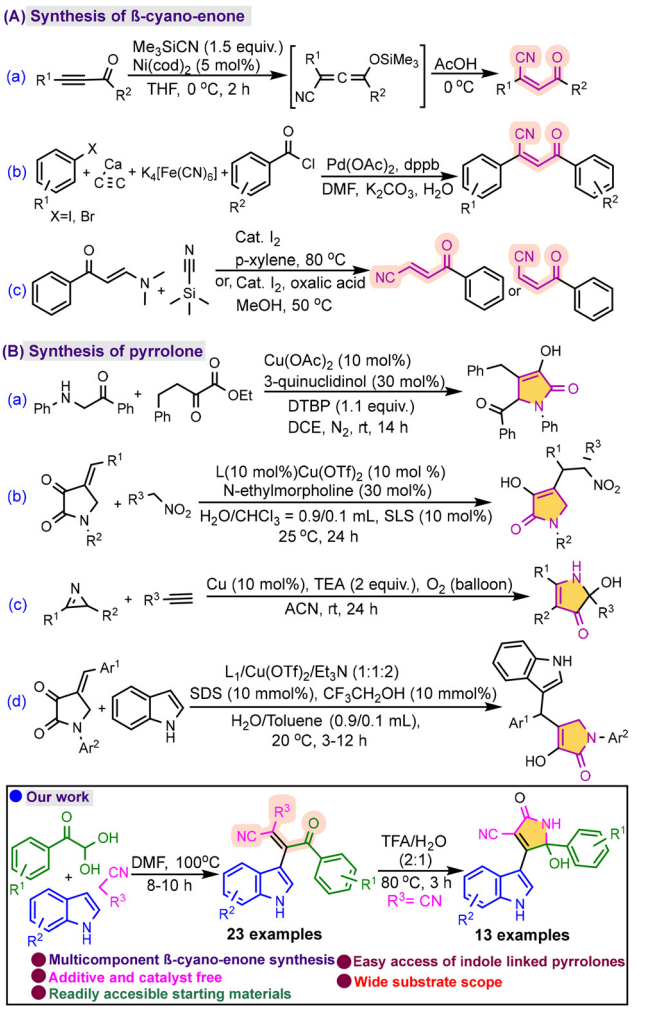
has recently gained considerable interest. Often these hybrid molecules exhibit promising biological activities.[7] Many indole-linked pyrrolone hybrids are known with notable pharmacological activities such as PIM-1 kinase inhibitor,[8] *P. aeruginosa* PBP3 inhibitor[9] *etc.* (Fig. 1c). The literature shows that the syntheses of indole-linked-2-pyrrolones are relatively unexplored.

Multicomponent reactions are the preferred strategy for synthesizing complex organic molecules for their virtues such as high efficiency, better atom economy, lesser waste production, and cost-effective use of time and energy.[10] As part of our ongoing research[11] for the synthesis of fused and functionalized heterocycles, we aimed to develop a method for the synthesis of indole linked β-cyano-enones and molecular hybrids of indole–pyrrolone from commercially available starting materials involving indole, aryl glyoxal, and malononitrile.

A comparison between recently reported works with our present methodology is shown in Scheme 1. Arai *et al.* reported the synthesis of β-cyano-enones from the reaction of ynones with Me_3SiCN in the presence of $Ni(cod)_2$ as a catalyst as shown in (Scheme 1A, eqn (a)).[12] Lu *et al.* developed a palladium-catalyzed four-component reaction for the synthesis of β-cyano enones using aryl halides, calcium carbide, potassium hexacyanoferrate(II) and aroyl chlorides as shown in Scheme 1A, eqn (b).[13] Likewise, Liu *et al.* reported the synthesis of β-cyano enones from the enaminone and TMSCN using molecular iodine as a catalyst (Scheme 1A, eqn (c)).[14]

Similar to β-cyano-enones, a few recent methods for the preparation of pyrrolones are shown in Scheme 1B. Baidya and co-workers reported the synthesis of densely functionalized pyrrolones by reacting α-amino ketones with α-keto esters at room temperature in the presence of copper/organo cooperative catalysts (Scheme 1B, eqn (a)).[15] Huang *et al.* reported a method for the synthesis of nitro-substituted pyrrolones using a chiral copper catalyst involving asymmetric 1,4-Michael addition reactions (Scheme 1B, eqn (b)).[16] Sujatha *et al.* synthesized highly functionalized pyrrolones by Cu-catalyzed azirine–alkyne ring-expansion reaction in the presence of molecular oxygen (Scheme 1B, eqn (c)).[17] Likewise, Mansaray *et al.* reported indole-linked pyrrolidone synthesis by Michael's addition reaction of 2,3-dioxopyrrolidine with indole in aqueous media (Scheme 1B, eqn (d)).[18]

To the best of our knowledge, to date, there is no report for the efficient synthesis of indole-linked β-cyano-enones and a straightforward approach for accessing indole-linked densely substituted pyrrolones without involving any metal or hazardous reagents. Herein, we report for the first time indole-linked highly substituted pyrrolone synthesis proceeding *via* an acid-catalyzed cyclization of our synthesized multicomponent β-cyano-enones.

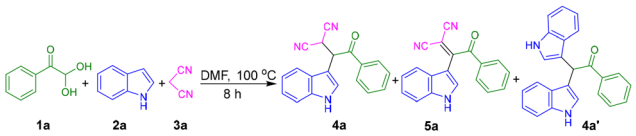


Scheme 1 Comparison of our methodology with some reported methods for the synthesis of (A) β-cyano-enones. (B) Substituted 2-pyrrolones.

Results and discussion

We began our investigation using the model substrates phenylglyoxal monohydrate (**1a**), indole (**2a**), and malononitrile (**3a**) (Table 1). In a DMF medium keeping the reaction temperature at 100 °C, an indole-substituted β,β-dicyano-enone (**5a**) was formed with an 83% yield within 8 hours (Table 1, entry 1). Interestingly, when the reaction was performed for 4 h, we observed the desired product **5a** with only a 29% yield, along with the corresponding three-component indole-substituted β,β-dicyanoketone (**4a**) as the major product (Table 1, entry 2). An attempt to perform this reaction at room temperature failed to yield the desired product **5a**. Instead, it produced **4a** with an 80% yield, along with a trace amount of the pseudo-three-component side product **4a′** (Table 1, entry 3). Next, the reaction at 50 °C in DMF produced only tri-substituted methane **4a** with 82% of yield (Table 1, entry 4). We also realized that the compound **4a** on heating at 100 °C in DMF for 5 h converted to our desired product **5a**. When the reaction was conducted at a higher temperature of 130 °C in DMF, the reaction time decreased to 5 h, though the observed yield dropped to 75% (Table 1, entry 5). After this, different organic solvents were screened by replacing DMF for this reaction.

Table 1 Optimization of the reaction conditions for the synthesis of β-cyano-enones[a]



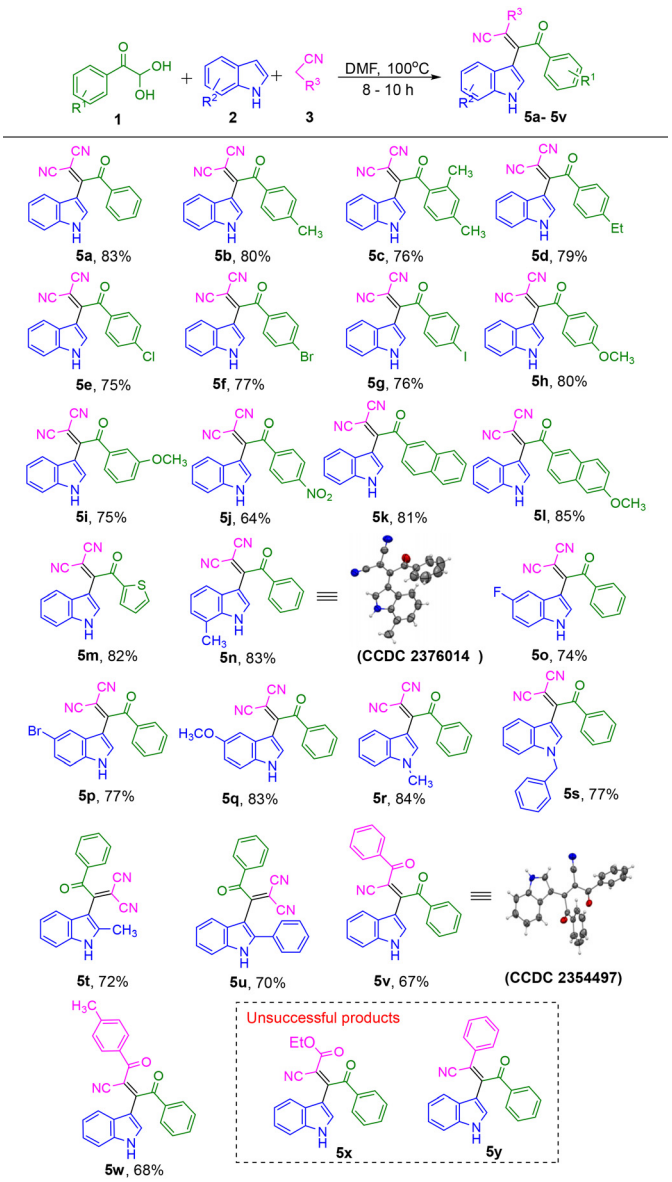
Entry	Deviation from standard conditions	Yield[b] 4a/5a/4a′
1	None	Nil/83/nil
2	4 h instead of 8 h	60/29/nil
3	Room temp. instead of 100 °C	80/nil/trace
4	50 °C instead of 100 °C	82/nil/trace
5[c]	130 °C instead of 100 °C	Nil/75/nil
6	DMSO instead of DMF	30/51/nil
7[d]	ACN instead of DMF	55/nil/20
8[d]	EtOH instead of DMF	52/nil/23
9[d]	EtOH : H_2O (1 : 1) instead of DMF	55/nil/21
10	PEG 400 instead of DMF	65/trace/nil
11	2-Pyrrolidone instead of DMF	Nil/74/nil
12	Presence of 20 mol% $FeCl_3$	Nil/71/nil
13	Presence of 20 mol% NH_2SO_3H	20/60/nil
14	Presence of 20 mol% Cs_2CO_3	Nil/74/nil

[a] Reaction conditions: **1a** (0.25 mmol), **2a** (0.25 mmol), and **3a** (0.25 mmol) in 2 mL solvent. [b] Isolated yield. [c] Reaction continued for 5 h. [d] Heated at 80 °C instead of 100 °C.

Replacing DMF by DMSO we observed the formation of a mixture of two products **4a** (30%) and **5a** (51%) (Table 1, entry 6). Solvents like acetonitrile, EtOH, and EtOH/H_2O (1 : 1) did not provide **5a** even after 8 h of heating at 80 °C. In these cases, the formation of **4a** and **4a′** were observed (Table 1, entries 7–9). Using PEG 400 instead of DMF, only a trace amount of **5a** was observed (Table 1, entry 10). 2-Pyrrolidone instead of DMF produced **5a** with 74% of yield (entry 11). Further, the effect of acid and base catalysts was investigated by performing the reaction in the presence of 20 mol% of $FeCl_3$, NH_2SO_3H, and Cs_2CO_3. These attempts did not provide expected yields (Table 1, entries 12–14).

Using the optimized reaction conditions for the synthesis of β-cyano-enones (Table 1, entry 1), the scope and generality of this method was further investigated by varying the arylglyoxal, indole, and malononitrile. The results are summarized in Table 2. Arylglyoxals with *para* methyl, *ortho*, *para* dimethyl and *para* ethyl substituents produced the desired products **5b**, **5c** and **5d** with yields of 80%, 76% and 79% respectively. Likewise, halogens (–Cl, –Br, and –I) substituted arylglyoxal reacted efficiently and produced the desired products **5e**, **5f**, and **5g** in good yields of 75%, 77%, and 76% respectively. *para*-Methoxy phenylglyoxal provided the corresponding product **5h** with a very good yield of 80%. When the aryl glyoxal had –OCH_3 group at *meta* position, it produced **5i** with 75% of yield. In contrast, an electron-withdrawing –NO_2 group at the *para* position of phenylglyoxal gave a moderate yield of 64% for product **5j**. Bulkier arylglyoxals, such as 2-naphthyl glyoxal and 6-methoxy-2-naphthyl glyoxal, afforded the corresponding products **5k** and **5l** with very good yields of 81% and

Table 2 Substrate scope for the multicomponent synthesis of indole linked β-cyano-enones[a,b]



[a] Reaction conditions: **1** (0.25 mmol), **2** (0.25 mmol), and **3** (0.25 mmol) in 2 mL DMF, stirring at 100 °C temperature for 8–10 h. [b] Isolated yield.

85%, respectively. Then, to check the feasibility of this reaction for heteroaryl glyoxal we performed the reaction with 2-thiophene glyoxal hydrate. It provided the product **5m** with 82% yield.

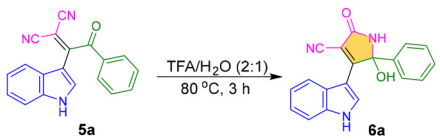
Next, the effect of substituents on the indole was examined. Products **5n**, **5o**, **5p**, and **5q** having Me, –F, –Br, and –OMe substituent in the indole were prepared in good to very good yields. Likewise, indoles having, *N*-Me, and *N*-Bn substituents also provided the corresponding desired products **5r** and **5s** in good to very good yields. 2-Methyl indole and 2-Ph indole also produced the corresponding products **5t** and **5u** in good

yields. Interestingly, the reaction worked even after replacing malononitrile with benzoyl acetonitrile and its derivatives. Products **5v** and **5w** were obtained at 67% and 68% respectively. It is noteworthy to mention that replacing malononitrile by ethyl cyanoacetate or benzyl nitrile did not provide the corresponding expected β-cyanoenones **5x** and **5y**. All the synthesized products were fully characterized using ^{1}H, ^{13}C{^{1}H} NMR and HRMS. In addition to these, the structure of the compounds **5n** and **5v** were further confirmed by single crystal XRD analysis.

Next, we turned our attention to utilizing these β-cyanoenones **5** for the synthesis of indole-linked 2-pyrrolones. Initially, we optimized the reaction conditions using different reaction conditions (Table 3). The optimum condition was achieved using TFA/H_2O (2 : 1) as the reaction medium keeping the reaction at 80 °C for 3 h. At room temperature, instead of heating, we observed 20% yield of **6a** after continuing the reaction for 24 h (Table 3, entry 2). In the TFA/H_2O (1 : 1) solvent system, we got an 80% yield of **6a** (Table 3, entry 3). When the reaction was conducted in only TFA, the observed yield dropped to 40% (Table 3 entry 4). The reaction did not work in H_2O and 50% AcOH in H_2O solvent (Table 3, entries 5 and 6). However, in AcOH/H_2O in a 2 : 1 ratio, the trace amount of **6a** was obtained after continuing the reaction at 120 °C for 24 h. In only AcOH, instead of TFA/H_2O (2 : 1), product **6a** was observed with a 25% of yield after keeping the reaction at 120 °C for 24 h (Table 3, entry 8).

Initially, 5-hydroxy-4-(1*H*-indol-3-yl)-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile **6a** was synthesized using optimum reaction conditions. Next, substrate scope was studied by using different substituents at phenyl and indole rings (Table 4). 4-Ethyl substituent at the *para* position of phenyl ring produced **6b** with 87% of yield. Halogen groups such as –Cl and –I at the *para* position of the phenyl ring produced **6c** and **6d** with 80% and 82% of yield respectively. The

Table 3 Optimization of the reaction conditions for the synthesis of **6a** [a]

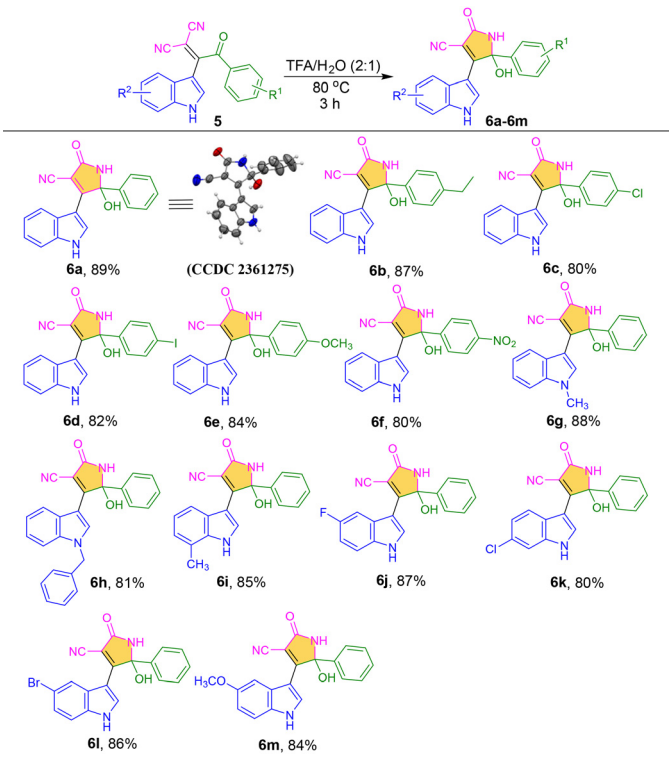


5a **6a**

Entry	Deviation from standard condition	Yield[b]
1	None	86
2[c]	Room temperature instead of 80 °C	20
3	TFA/H_2O (1 : 1) instead of TFA/H_2O (2 : 1)	80
4	TFA instead of TFA/H_2O (2 : 1)	40
5[c]	H_2O instead of TFA/H_2O (2 : 1)	Nil
6[c]	AcOH/H_2O (1 : 1) instead of TFA/H_2O (2 : 1)	Nil
7[c,d]	AcOH/H_2O (2 : 1) instead of TFA/H_2O (2 : 1)	Trace
8[c,d]	AcOH instead of TFA/H_2O (2 : 1)	25

[a] Reaction conditions: **5a** (0.25 mmol) in 2 mL solvent. [b] Isolated yield of **6a**. [c] Reaction continued for 24 h. [d] Heated at 120 °C instead of 80 °C.

Table 4 Synthesis of indolyl-2-pyrrolones from β-cyanoenones[a,b]



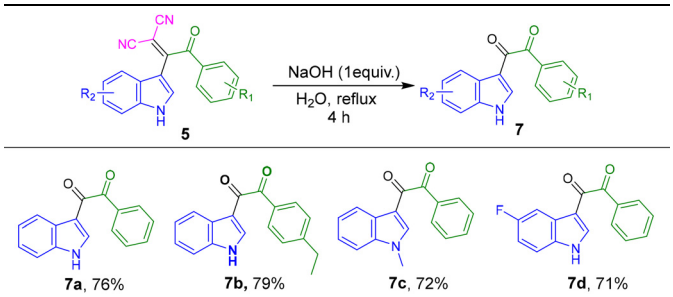
[a] Reaction conditions: **5** (0.1 mmol) in 1 mL TFA/H_2O (2 : 1), stirring at 80 °C temperature for 3 h. [b] Isolated yield.

electron-releasing and withdrawing groups such as –OCH_3 and –NO_2 substituted products **6e** and **6f** were obtained with 84% and 80% of yield respectively. *N*-CH_3 and *N*-Bn substituted indolyl products **6g** and **6h** were observed with 88% and 81% yield. 7-Me-indolyl product **6i** was found with 85% of yield. 5-F, 6-Cl and 5-Br indolyl-pyrrolones **6j**, **6k** and **6l** were obtained with 87%, 80% and 86% of yield respectively. 5-OCH_3 indolyl-pyrrolone **6m** was found with 84% of yield. It is noteworthy to mention, that when β-cyano-enones **5v** was tried in this process, the intended result did not occur. Since there is just one –CN group in *trans* to the benzoyl group (**5v** XRD structure), the cyclization did not proceed. All the products were fully characterized by ^{1}H NMR, ^{13}C{^{1}H} NMR and HRMS. The exact structure of compound **6a** was further confirmed by single-crystal XRD analysis.

After, preparing the set of indolyl-2-pyrrolone derivatives in an acidic medium we performed a reaction of β-cyano-enone **5a** with an aqueous NaOH solution, and the reaction was performed under reflux conditions. Within 4 h, the 1,2-diketone product **7a** was obtained with 76% of yield. Next, using this strategy, other indole-linked 1,2-diketones **7b–7d** were prepared in good yields (Table 5). It is interesting to note that in this process an alkene has broken to generate the ketone functional group in the presence of a simple base.

Next, product **7** was reacted with *o*-phenylenediamine (OPD) **8a** in MeOH solvent to get the indolyl quinoxaline **9a** in

Table 5 Synthesis of indolyl-1,2-diketone from β-cyano-enones[a,b]



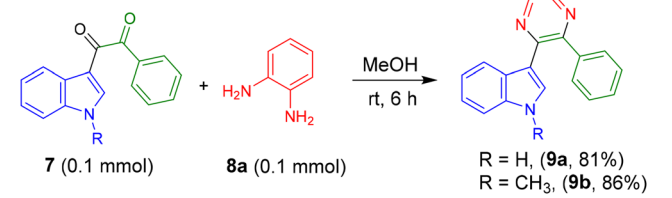
[a] Reaction conditions: **5** (0.1 mmol) in 1 mL H_2O, stirring at 100 °C temperature for 4 h. [b] Isolated yield.

81% yield (Scheme 2). Similarly, product **9b** was synthesized in 86% yield.

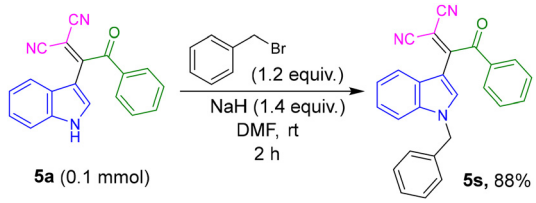
After the synthesis of functionalized pyrrolone and quinoxaline with the synthesized multicomponent product β-cyano-enones, we aimed for the further functionalization of the indole of the synthesized β-cyano-enones. Upon reacting the β-cyano-enone **5a** with benzyl bromide in DMF at room temperature. It provided *N*-benzylated indole linked β-cyano-enone **5s** in 88% yield (Scheme 3).

A gram-scale synthesis for **5a** was performed employing 1.065 g (7 mmol) **1a**, 820 mg (7 mmol) **2a** with 462 mg (7 mmol) **3a**. The target product **5a** was obtained with a 52% yield, confirming the viability of the protocol for large-scale application (Scheme 4).

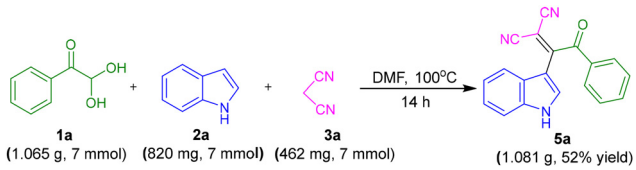
DMF is a versatile solvent that shows extraordinary properties in many reactions. It is also used as a reagent, a catalyst, and a stabilizer which can provide various units such as HCO_2, O, CO, $H^{\bullet}$, H^{-}, NMe_2, $CONMe_2$, Me, CHO, *etc.*[19] To



Scheme 2 Synthesis of indolyl-quinoxalines from indolyl-1,2-diketones.



Scheme 3 *N*-Benzylation of β-cyano-enone (**5a**).



Scheme 4 Gram-scale synthesis of **5a**.

understand the role of the solvent in our multicomponent reaction, a series of control experiments were conducted. For this, the conversion of β,β-dicyano-ketone (**4a**) to β,β-dicyano-enone (**5a**) was chosen. The reactions were performed using a 10 mL sealed tube. In DMF solvent, both under open air and nitrogen (N_2) atmosphere at 100 °C, the desired product **5a** was obtained with an 87% yield (Fig. 2a and b). These results suggest that dehydrogenative oxidation is not occurring *via* air oxidation. In contrast, when the reaction was performed in toluene or 1,4-dioxane, product **5a** was not observed (Fig. 2c and d), indicating that thermal conditions alone are insufficient for the conversion. However, when the reaction was conducted in DMF in the presence of 1 equiv. of dimethylamine, **5a** was produced even at room temperature with a 70% yield (Fig. 2e). To further investigate the role of dimethylamine, a reaction was performed in toluene in the presence of dimethylamine, resulting in the unexpected formation of **5a** (Fig. 2f and g). At room temperature, after 8 h, a yield of 60% of **5a** was observed (Fig. 2f). When the reaction was performed at 100 °C, the yield increased to 65% (Fig. 2g).

Based on the above observations and literature reports,[20] we propose that DMF undergoes partial decomposition under

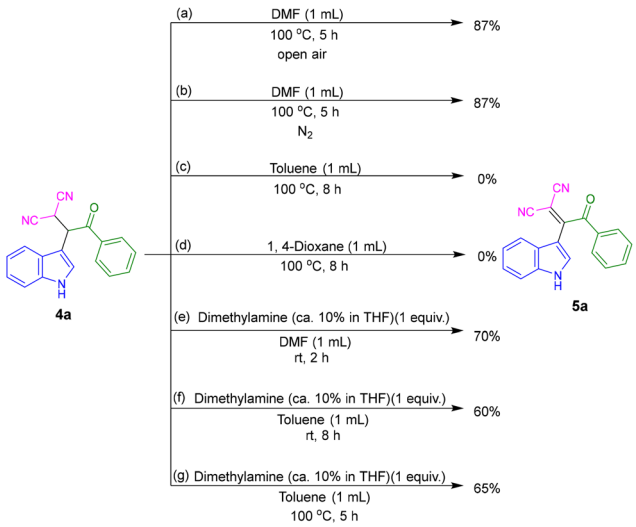
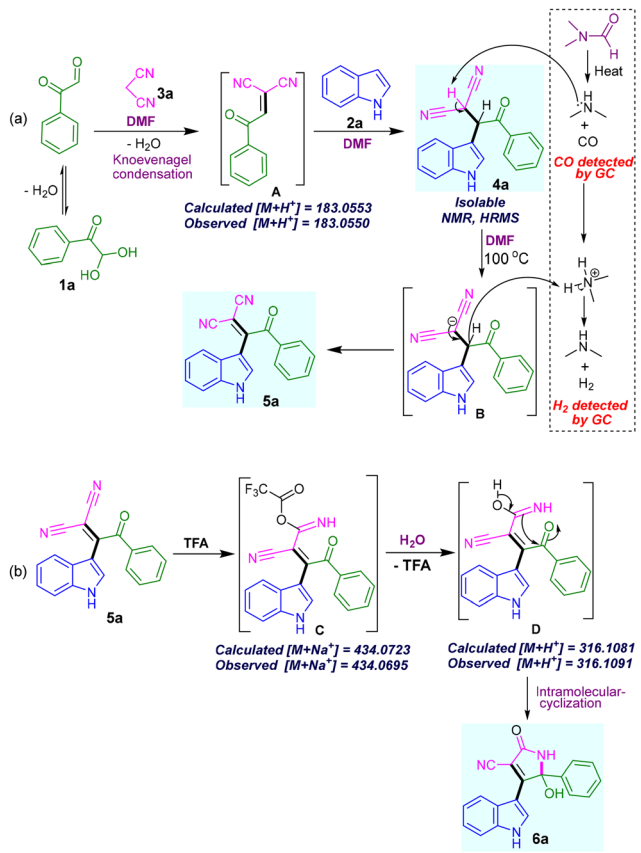


Fig. 2 Controlled experiments for the conversion of β,β-dicyano-ketone **4a** (0.1 mmol) to β, β-dicyano-enone **5a** using (a) 1 mL DMF at 100 °C for 5 h. (b) 1 mL DMF at 100 °C under N_2 atmosphere for 5 h. (c) 1 mL toluene at 100 °C for 8 h. (d) 1 mL 1,4-dioxane at 100 °C for 8 h. (e) 1 equiv. dimethylamine, 1 mL DMF at rt for 2 h. (f) 1 equiv. dimethylamine, 1 mL toluene at rt for 8 h. (g) 1 equiv. dimethylamine, 1 mL toluene at 100 °C for 5 h.

heating conditions to generate dimethylamine and carbon monoxide, thereby creating weakly basic conditions. The decomposition of DMF at 100 °C is further supported by gas chromatography (GC) analysis. The detection of carbon monoxide in the GC analysis, shown in Fig. S5 of the ESI,† provides evidence for the thermal decomposition of DMF.

We have proposed a mechanism in Scheme 5 based on our observation and the literature report.[21] We believe, initially, Knoevenagel condensation between phenylglyoxal **1a** and malononitrile **3a** takes place to provide intermediate **A**. Then Michael-type reaction with indole **2a** provides the product **4a**. Product **4a** was isolated and fully characterized. The compound **4a** upon heating at 100 °C in DMF solvent provides highly conjugated product **5a** (Scheme 5a). The liberated H_2 gas was detected by GC (Fig. S3 in ESI†). Based on the literature[19,20] and preliminary experiments (Fig. 2), it is believed that the trace amount of dimethylamine is generated from the DMF under heating conditions. It makes the basic environment for abstracting the most acidic proton from the **4a** followed by hydride elimination to form the desired product **5a**. Based on the literature on acid-catalyzed selective conversion of nitriles to amides,[22] we have proposed the mechanism for forming compound **6a** (Scheme 5b). Adding trifluoroacetate (TFA) to one of the nitriles followed by hydration reaction produces intermediate **D**. Which upon intramolecular cyclization provides desired densely substituted pyrrolone **6a**.



Scheme 5 Proposed reaction mechanisms. (a) Synthesis of β,β-dicyano-enone **5a**. (b) Synthesis of indolyl-2-pyrrolones **6a** from β,β-dicyano-enone **5a**.

Conclusions

In summary, we have developed a metal-free dehydrogenative multicomponent reaction for synthesizing indole-linked β-cyano-enones using readily available starting materials: arylglyoxal, indole, and malononitrile. These β-cyano-enones can be further transformed into medicinally relevant indole-linked 2-pyrrolones featuring a hydroxyl group containing chiral carbon centre. The reaction conditions are straightforward, with a broad substrate scope. Additionally, we have established a method for converting the β-cyano-enones into indole-substituted 1,2-diketones, which can subsequently be transformed into indole-linked quinoxalines.

Experimental section

General information

All the starting materials were procured from commercial suppliers such as TCI, Sigma Aldrich, Alfa Aesar, bldpharm, and Chemscene and used without further purification. Anhydrous sodium sulfate was used to dry organic extracts. Solvents were removed by using a rotary evaporator under reduced pressure. Heating reactions were performed using a silicone oil bath using a heating cum magnetic stirrer. The progress of reactions was monitored by TLC. Melting points were determined using the automated SRS EZ-Melt instrument. ^{1}H NMR spectra were recorded using Bruker 400 MHz or JEOL 500 MHz spectrometers, while $^{13}C\{^1H\}$ NMR spectra were obtained at 100 MHz or 125 MHz in DMSO-d_6 or $CDCl_3$. Chemical shifts are referenced in δ ppm downfield. Multiplicities were designated as follows: dd (doublet of doublets), td (triplet of doublets), s (singlet), d (doublet), t (triplet), m (multiplet), bs (broad singlet), and coupling constants (J, in Hz) were indicated. HRMS data were acquired utilizing a BRUKER Impact HD mass spectrometer (ESI, positive mode) or SCIEX Model-X500R QTOF. Column chromatographic purifications were performed using SRL silica gel (100–200 mesh). Single crystal XRD was recorded using BRUKER AXS D8 quest system or BRUKER D8 venture diffractometer system. Gas Chromatography (GC) was performed using Centurion Scientific, 5800 Gas Chromatograph.

Experimental procedure

General experimental procedure for the synthesis of 5a

Phenylglyoxal monohydrate **1a** (38 mg, 0.25 mmol), indole **2a** (29 mg, 0.25 mmol), and malononitrile **3a** (17 mg, 0.25 mmol) were taken in a 10 mL round bottom flask. Then 2 mL of DMF was added and stirred at 100 °C for 8 h. The progress of the reaction was monitored using TLC. After completion of the reaction, the reaction mixture was quenched with ice-cold

water and extracted with ethyl acetate (3 × 20 mL). Then combined organic layer was washed with brine solution and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using a rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as the stationary phase and different ratios of hexane/ethyl acetate mixture as eluent. The other derivatives **5b–5w** were made using similar methods.

General experimental procedure for the synthesis of 6a

In a 10 mL glass sealed tube, 1.0 mL TFA/H_2O (2 : 1) mix solvent was cooled by placing an ice bath. β,β-Dicyano-enones **5a** (0.1 mmol, 30 mg) was added keeping the reaction temperature at 0 °C. Then the reaction tube was stirred for 3 h keeping the reaction temperature at 80 °C. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into 20 mL of water and neutralized by saturated $NaHCO_3$ solution. Then the product was extracted with ethyl acetate (3 × 20 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using a rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as the stationary phase and different ratios of hexane/ethyl acetate mixture as eluent. The other derivatives **6b–6m** were made using similar methods.

General experimental procedure for the synthesis of 7a

In a 10 mL of glass sealed tube 4 mg (1 equiv.) of NaOH was dissolved in 1 mL of distilled water. Then β,β-dicyano-enones **5a** (0.1 mmol, 30 mg) was added. The reaction mixture was heated at 100 °C for 4 h. Progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was poured in 20 mL of water. Then the product was extracted with ethyl acetate (3 × 20 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as stationary phase and hexane/ethyl acetate (9 : 1) mixture as eluent. The other derivatives **7b–7d** were made using similar methods.

General experimental procedure for the synthesis of indolylquinoxalines (9a)

In a 10 mL of glass sealed tube, **7a** (0.1 mmol, 25 mg) and *o*-phenylenedimine **8a** (OPD) (0.1 mmol, 11 mg) were dissolved in 1 mL of MeOH. Then the reaction mixture was stirred at room temperature for 6 h. Progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was poured in 20 mL of water. Then the product was extracted with ethyl acetate (3 × 20 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as stationary phase and hexane/ethyl acetate (9.5 : 0.5) mixture as eluent. The other derivative **9b** was also made using similar methods.

Procedures for *N*-benzylation of β-cyano-enone (5a)

In a 10 mL of glass sealed tube 5 mg (1.4 equiv.) of NaH (63–67% oil dispersion) and 30 mg (0.1 mmol) of **5a** were dissolved in 1 mL of DMF. Then 14 μL (0.12 mmol) of benzyl bromide was added and started stirring for 2 h. Progress of the reaction was monitored by TLC. After completion of the reaction, reaction mixture was poured in 20 mL of ice cold water. Then the product was extracted with ethyl acetate (3 × 20 mL) and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as stationary phase and hexane/ethyl acetate (8.5 : 1.5) mixture as eluent.

General procedures for the gram-scale synthesis of compound 5a

Phenylglyoxal monohydrate **1a** (1.065 g, 7 mmol), indole **2a** (820 mg, 7 mmol), and malononitrile **3a** (462 mg, 7 mmol) were taken in a 100 mL round bottom flask. Then 30 mL of DMF was added and stirred at 100 °C for 14 h. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was quenched with ice-cold water and extracted with ethyl acetate (3 × 80 mL). Then combined organic layer was washed with brine solution and dried over anhydrous sodium sulfate. The solvent was evaporated under reduced pressure using a rotary evaporator and collected for reuse, and the solid crude product was purified by column chromatography using silica gel as stationary phase and hexane/ethyl acetate (8 : 2) mixture as eluent.

Characterization data

2-(1-(1*H*-Indol-3-yl)-2-oxo-2-phenylethyl)malononitrile (4a). Purified by column chromatography. Eluent: hexane/ethyl acetate (8.5 : 1.5). Yield 61 mg (82%); light brown solid; mp 156–158 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.93 (d, J = 7.2 Hz, 2H), 7.74 (d, J = 8.1 Hz, 1H), 7.50 (t, J = 7.4 Hz, 1H), 7.40 (d, J = 7.1 Hz, 1H), 7.35 (t, J = 8.5 Hz, 2H), 7.29–7.23 (m, 2H), 7.22 (d, J = 2.8 Hz, 1H), 5.48 (d, J = 7.7 Hz, 1H), 4.61 (d, J = 7.7 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.2, 136.5, 134.3, 134.1, 129.1, 128.9, 125.2, 124.9, 123.6, 121.4, 118.1, 112.6, 112.4, 112.1, 107.1, 47.2, 26.6. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{14}N_3O^+$, 300.1131; found, 300.1160.

2,2-Di(1*H*-indol-3-yl)-1-phenylethan-1-one (4a′).[23] Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). White solid; mp 212 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, J = 7.2 Hz, 2H), 8.03 (s, 2H), 7.56 (d, J = 7.9 Hz, 2H), 7.52 (t, J = 7.4 Hz, 1H), 7.41 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 8.1 Hz, 2H), 7.18 (t, J = 7.6 Hz, 2H), 7.08 (t, J = 7.1 Hz, 2H), 6.92 (s, 2H), 6.52 (s, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 198.7, 137.1, 136.7, 133.0, 128.9, 128.8, 126.8, 124.1, 122.4, 119.8, 119.1, 114.4, 111.5, 42.2.

2-(1-(1*H*-Indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5a). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 62 mg (83%); yellow solid; mp 200–202 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.99 (s, 1H), 8.73 (s, 1H), 8.08

(d, J = 5 Hz, 2H), 7.77 (t, J = 10 Hz, 1H), 7.61–7.58 (m, 3H), 7.26–7.21 (m, 2H), 7.11 (t, J = 10 Hz, 1H) ppm. $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.9, 164.1, 137.1, 136.0, 135.3, 133.2, 129.8, 129.7, 124.1, 123.8, 123.1, 119.7, 115.1, 113.9, 113.8, 108.1, 69.9 ppm. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{19}H_{11}N_3NaO^+$, 320.0794; found, 320.0824.

2-(1-(1*H*-Indol-3-yl)-2-oxo-2-(*p*-tolyl)ethylidene)malononitrile (5b). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 62 mg (80%); yellow solid; mp 215–217 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 12.98 (s, 1H), 8.73 (s, 1H), 7.96 (d, J = 10 Hz, 2H), 7.58 (d, J = 10 Hz, 1H), 7.40 (d, J = 5 Hz, 2H), 7.24 (t, J = 10 Hz, 1H), 7.20 (d, J = 10 Hz, 1H), 7.10 (t, J = 10 Hz, 1H), 2.38 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.4, 164.4, 147.2, 137.1, 135.2, 130.9, 130.4, 129.9, 124.1, 123.9, 123.1, 119.7, 115.2, 114.0, 113.8, 108.2, 69.7, 21.5 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O^+$, 312.1131; found, 312.1154.

2-(2-(2,4-Dimethylphenyl)-1-(1*H*-indol-3-yl)-2-oxoethylidene) malononitrile (5c). Purified by column chromatography. Eluent: hexane/ethyl acetate (8.5 : 1.5). Yield 62 mg (76%); yellow solid; mp 195–197 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 12.97 (s, 1H), 8.72 (s, 1H), 7.71 (d, J = 8.1 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.31 (s, 1H), 7.25 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 8.2 Hz, 1H), 7.12 (t, J = 7.1 Hz, 2H), 2.71 (s, 3H), 2.33 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 193.6, 165.6, 145.9, 141.2, 136.9, 135.2, 133.6, 129.2, 127.4, 124.0, 123.9, 122.9, 119.7, 115.3, 113.9, 113.7, 108.5, 69.5, 21.7, 21.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}N_3O^+$, 326.1288; found, 326.1287.

2-(2-(4-Ethylphenyl)-1-(1*H*-indol-3-yl)-2-oxoethylidene) malononitrile (5d). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 64 mg (79%); yellow solid; mp 197–199 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 12.98 (s, 1H), 8.72 (s, 1H), 7.98 (d, J = 10 Hz, 2H), 7.58 (d, J = 10 Hz, 1H), 7.43 (d, J = 10 Hz, 2H), 7.26–7.21 (m, 2H), 7.11 (t, J = 10 Hz, 1H), 2.68 (q, J = 10 Hz, 2H), 1.17 (t, J = 10 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.4, 164.4, 152.9, 137.1, 135.2, 131.1, 130.0, 129.2, 124.1, 123.8, 123.1, 119.7, 115.2, 114.0, 113.8, 108.2, 69.7, 28.4, 14.8 ppm. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{16}N_3O^+$, 326.1288; found, 326.1295.

2-(2-(4-Chlorophenyl)-1-(1*H*-indol-3-yl)-2-oxoethylidene)malononitrile (5e). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 62 mg (75%); yellow solid; mp 213–215 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 13.02 (s, 1H), 8.71 (s, 1H), 8.10 (d, J = 8.7 Hz, 2H), 7.67 (d, J = 8.7 Hz, 2H), 7.59 (d, J = 8.1 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.20 (d, J = 8.1 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 191.9, 163.3, 141.2, 137.1, 135.5, 131.9, 131.6, 130.0, 124.2, 123.8, 123.2, 119.7, 115.1, 113.9, 113.8, 107.9, 70.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{11}ClN_3O^+$, 332.0585; found, 332.0582.

2-(2-(4-Bromophenyl)-1-(1*H*-indol-3-yl)-2-oxoethylidene)malononitrile (5f). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 72 mg (77%); yellow solid; mp 217–219 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 13.02 (s, 1H), 8.72 (s, 1H), 8.01 (d, J = 8.7 Hz, 2H), 7.82 (d, J = 8.7 Hz, 2H), 7.59 (d, J = 7.2 Hz, 1H), 7.26 (t, J = 8.2 Hz, 1H), 7.20 (d, J = 8.2 Hz, 1H), 7.12 (t, J = 7.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.2, 163.3, 137.1, 135.5, 132.9, 132.3, 131.6, 130.7, 124.2, 123.8, 123.2, 119.7, 115.1, 113.96, 113.86, 107.9, 70.0. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{11}BrN_3O^+$, 376.0080; found, 376.0104.

2-(1-(1*H*-Indol-3-yl)-2-(4-iodophenyl)-2-oxoethylidene)malononitrile (5g). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 80 mg (76%); yellow solid; mp 248–250 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 13.01 (s, 1H), 8.72 (s, 1H), 8.00 (d, J = 8.6 Hz, 2H), 7.82 (d, J = 8.7 Hz, 2H), 7.59 (d, J = 8.1 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.19 (d, J = 8.2 Hz, 1H), 7.12 (t, J = 7.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.6, 163.3, 138.8, 137.1, 135.5, 132.5, 131.1, 124.1, 123.7, 123.2, 119.6, 115.1, 113.9, 113.8, 107.9, 106.2, 69.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{11}IN_3O^+$, 423.9941; found, 423.9943.

2-(1-(1*H*-Indol-3-yl)-2-(4-methoxyphenyl)-2-oxoethylidene) malononitrile (5h). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 65 mg (80%); yellow solid; mp 215–217 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 12.95 (s, 1H), 8.72 (s, 1H), 8.03 (d, J = 9.0 Hz, 2H), 7.58 (d, J = 8.2 Hz, 1H), 7.25–7.21 (m, 2H), 7.11–7.09 (m, 3H), 3.85 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 190.9, 165.3, 164.6, 137.0, 135.2, 132.5, 126.2, 124.0, 123.9, 123.0, 119.8, 115.3, 115.1, 114.1, 113.7, 108.2, 69.6, 55.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O_2^+$, 328.1081; found, 328.1080.

2-(1-(1*H*-Indol-3-yl)-2-(3-methoxyphenyl)-2-oxoethylidene) malononitrile (5i). Purified by column chromatography. Eluent: hexane/ethyl acetate (8.5 : 1.5). Yield 61 mg (75%); yellow solid; mp 219–221 °C. ^1H NMR (500 MHz, DMSO-d_6 + $CDCl_3$) δ 12.98 (s, 1H), 8.72 (s, 1H), 7.62–7.57 (m, 3H), 7.49 (t, J = 8.0 Hz, 1H), 7.35 (dd, J = 8.2, 2.7 Hz, 1H), 7.27–7.22 (m, 2H), 7.12 (t, J = 7.7 Hz, 1H), 3.83 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.6, 163.9, 159.9, 137.0, 135.2, 134.5, 130.9, 124.0, 123.8, 123.0, 122.8, 121.9, 119.7, 115.1, 113.9, 113.7, 113.4, 108.1, 69.9, 55.6. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_{20}H_{13}N_3O_2Na^+$, 350.0900; found, 350.0916.

2-(1-(1*H*-Indol-3-yl)-2-(4-nitrophenyl)-2-oxoethylidene)malononitrile (5j). Purified by column chromatography. Eluent: hexane/ethyl acetate (7.5 : 2.5). Yield 55 mg (64%); yellow solid; mp 246–248 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 13.05 (s, 1H), 8.73 (s, 1H), 8.35 (s, 4H), 7.59 (d, J = 8.1 Hz, 1H), 7.26 (t, J = 7.6 Hz, 1H), 7.21 (d, J = 8.1 Hz, 1H), 7.12 (t, J = 7.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.2, 162.5, 151.6, 137.4, 137.2, 135.8, 131.4, 124.9, 124.4, 123.7, 123.4, 119.7, 114.9, 114.0, 113.9, 107.9, 70.5. HRMS (ESI-TOF) m/z: [M] calcd for $C_{19}H_{10}N_4O_3$, 342.0747; found, 342.0751.

2-(1-(1*H*-Indol-3-yl)-2-(naphthalen-2-yl)-2-oxoethylidene)malononitrile (5k). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 70 mg (81%); yellow solid; mp 247–249 °C. ^1H NMR (500 MHz, DMSO-d_6) δ 13.02 (s, 1H), 8.81 (s, 1H), 8.78 (s, 1H), 8.14 (t, J = 5 Hz, 3H), 8.04 (d, J = 8.2 Hz, 1H), 7.74 (t, J = 6.9 Hz, 1H), 7.64 (t, J = 7.0 Hz, 1H), 7.58 (d, J = 7.8 Hz, 1H), 7.22 (t, J = 7.8 Hz, 2H), 7.07 (t, J = 10 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.9, 164.1, 137.0, 136.2, 135.4, 133.6, 132.1, 130.7, 130.3, 130.2, 129.7, 127.9, 127.6, 124.0, 123.9, 123.2, 123.1, 119.7, 115.3, 114.2, 113.8, 108.4,

69.9. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{23}H_{14}N_3O^+$, 348.1131; found, 348.1148.

2-(1-(6,7-Dihydro-1*H*-indol-3-yl)-2-(6-methoxynaphthalen-2-yl)-2-oxoethylidene)malononitrile (5l). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 80 mg (85%); yellow solid; mp 160–162 °C. ^{1}H NMR (500 MHz, DMSO-d_6 + $CDCl_3$) δ 12.98 (s, 1H), 8.79 (s, 1H), 8.66 (s, 1H), 8.09–7.99 (m, 3H), 7.57 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 2.7 Hz, 1H), 7.27 (dd, J = 9.1, 2.6 Hz, 1H), 7.22 (t, J = 8.5 Hz, 2H), 7.06 (t, J = 7.7 Hz, 1H), 3.91 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6 + $CDCl_3$) δ 192.4, 164.4, 160.7, 138.4, 137.0, 135.2, 133.4, 131.9, 128.7, 128.4, 127.4, 124.0, 123.0, 120.2, 119.8, 115.4, 114.2, 113.8, 108.4, 106.5, 69.8, 55.7. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{24}H_{16}N_3O_2^+$, 378.1237; found, 378.1266.

2-(1-(1*H*-Indol-3-yl)-2-oxo-2-(thiophen-2-yl)ethylidene)malononitrile (5m). Purified by column chromatography. Eluent: hexane/ethyl acetate (8.5 : 1.5). Yield 62 mg (82%); yellow solid; mp 227–230 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.97 (s, 1H), 8.72 (s, 1H), 8.33 (d, J = 4.9 Hz, 1H), 7.99 (d, J = 2.7 Hz, 1H), 7.59 (d, J = 8.1 Hz, 1H), 7.30–7.25 (m, 3H), 7.15 (t, J = 7.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 184.6, 162.8, 140.0, 138.6, 137.0, 135.4, 129.9, 124.0, 123.9, 123.0, 119.6, 115.1, 113.9, 113.7, 108.2, 70.2. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{17}H_9N_3OSNa^+$, 326.0359; found, 326.0381.

2-(1-(7-Methyl-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5n). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 65 mg (83%); yellow solid; mp 155–157 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.08 (s, 1H), 8.68 (s, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.77 (t, J = 7.6 Hz, 1H), 7.59 (t, J = 7.8 Hz, 2H), 7.07–6.99 (m, 3H), 2.49 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.9, 164.1, 136.4, 135.9, 134.6, 133.2, 129.8, 129.7, 124.7, 123.7, 123.25, 123.22, 117.2, 115.2, 108.5, 70.1, 16.6. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O^+$, 312.1131; found, 312.1108.

2-(1-(5-Fluoro-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5o). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 58 mg (74%); yellow solid; mp 227–229 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.06 (s, 1H), 8.70 (s, 1H), 8.09 (d, J = 7.5 Hz, 2H), 7.79 (t, J = 7.5 Hz, 1H), 7.61 (t, J = 7.0 Hz, 3H), 7.14 (t, J = 7.8 Hz, 1H), 6.96 (d, J = 7.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.6, 163.8, 158.6 (d, J = 236 Hz), 136.5, 136.2, 133.8, 133.1, 129.9, 129.8, 124.4 (d, J = 10 Hz), 115.3 (d, J = 10 Hz), 114.8, 113.8, 112.3 (d, J = 26 Hz), 107.9, 105.3 (d, J = 26 Hz), 71.1. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{19}H_{11}FN_3O^+$, 316.0881; found, 316.0865.

2-(1-(5-Bromo-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5p). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 72 mg (77%); yellow solid; mp 260–262 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 13.08 (s, 1H), 8.66 (s, 1H), 8.09 (d, J = 7.1 Hz, 2H), 7.80 (t, J = 7.5 Hz, 1H), 7.62 (t, J = 7.8 Hz, 2H), 7.55 (d, J = 8.6 Hz, 1H), 7.44 (s, 1H), 7.40 (d, J = 8.6 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.5, 163.6, 136.2, 136.1, 135.9, 133.0, 129.9, 129.8, 126.7, 125.4, 122.3, 115.7, 115.5, 114.7, 113.6, 107.2, 71.9. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{19}H_{11}BrN_3O^+$, 376.0080; found, 376.0097.

2-(1-(5-Methoxy-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5q). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 68 mg (83%); yellow solid; mp 227–229 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.91 (s, 1H), 8.61 (s, 1H), 8.09 (d, J = 7.1 Hz, 2H), 7.79 (t, J = 7.4 Hz, 1H), 7.61 (t, J = 8.4 Hz, 2H), 7.48 (d, J = 8.9 Hz, 1H), 6.89 (dd, J = 8.9, 2.4 Hz, 1H), 6.69 (d, J = 2.4 Hz, 1H), 3.57 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.9, 163.9, 155.8, 136.0, 135.3, 133.2, 131.8, 129.8, 124.6, 115.2, 114.5, 114.2, 113.2, 108.0, 102.8, 68.8, 55.1. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O_2^+$, 328.1081; found, 328.1088.

2-(1-(1-Methyl-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5r). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 65 mg (84%); yellow solid; mp 190–192 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 8.67 (s, 1H), 8.05 (d, J = 8.5 Hz, 2H), 7.77 (t, J = 7.5 Hz, 1H), 7.66 (d, J = 9.2 Hz, 1H), 7.60 (t, J = 7.5 Hz, 2H), 7.33 (t, J = 7.7 Hz, 1H), 7.29 (d, J = 8.2 Hz, 1H), 7.18 (t, J = 7.7 Hz, 1H), 3.99 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, DMSO-d_6) δ 192.9, 163.4, 138.2, 137.8, 136.1, 133.3, 129.85, 129.82, 124.2, 123.5, 120.1, 115.0, 114.1, 112.4, 107.2, 69.6, 34.3. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O^+$, 312.1131; found, 312.1116.

2-(1-(1-Benzyl-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5s). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 75 mg (77%); yellow solid; mp 195–197 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.03 (d, J = 7.2 Hz, 2H), 7.67 (t, J = 7.4 Hz, 1H), 7.52 (t, J = 7.5 Hz, 2H), 7.40–7.30 (m, 5H), 7.26–7.20 (m, 3H), 7.11 (t, J = 8.27 Hz, 1H), 5.43 (s, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 192.8, 164.0, 137.2, 135.8, 135.7, 134.3, 134.0, 130.0, 129.6, 129.4, 128.9, 127.4, 125.5, 124.7, 123.9, 121.2, 115.3, 113.2, 111.6, 108.9, 51.9. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{26}H_{18}N_3O^+$, 388.1444; found, 388.1414.

2-(1-(2-Methyl-1*H*-indol-3-yl)-2-oxo-2-phenylethylidene)malononitrile (5t). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 56 mg (72%); yellow solid; mp 198–200 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.58 (s, 1H), 7.88 (d, J = 7.5 Hz, 2H), 7.70 (t, J = 7.4 Hz, 1H), 7.54 (t, J = 7.8 Hz, 2H), 7.41 (d, J = 8.7 Hz, 2H), 7.22–7.12 (m, 2H), 2.55 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.7, 165.1, 144.3, 136.1, 135.8, 133.6, 129.6, 124.9, 123.5, 122.1, 119.7, 114.2, 113.7, 112.3, 106.9, 77.1, 15.2. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{20}H_{14}N_3O^+$, 312.1131; found, 312.1137.

2-(2-Oxo-2-phenyl-1-(2-phenyl-1*H*-indol-3-yl)ethylidene)malononitrile (5u). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 65 mg (70%); red solid; mp 192–194 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.97 (s, 1H), 7.65–7.63 (m, 1H), 7.48–7.43 (m, 3H), 7.40–7.33 (m, 6H), 7.24–7.20 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.9, 164.6, 144.6, 136.2, 134.8, 134.5, 130.6, 129.9, 129.4, 129.31, 129.29, 128.7, 125.3, 124.8, 122.9, 120.9, 113.7, 112.9, 112.3, 108.3. HRMS (ESI-TOF) *m*/*z*: $[M + H]^+$ calcd for $C_{25}H_{16}N_3O^+$, 374.1288; found, 374.1298.

(*Z*)-2-Benzoyl-3-(1*H*-indol-3-yl)-4-oxo-4-phenylbut-2-enenitrile (5v). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 63 mg (67%); yellow solid; mp 218–220 °C.

^{1}H NMR (500 MHz, DMSO-d_6) δ 12.71 (s, 1H), 8.67 (s, 1H), 7.96 (d, J = 7.2 Hz, 2H), 7.87 (d, J = 7.1 Hz, 2H), 7.66 (t, J = 7.5 Hz, 1H), 7.59–7.52 (m, 4H), 7.46 (t, J = 7.8 Hz, 2H), 7.41 (d, J = 8.1 Hz, 1H), 7.22 (t, J = 7.2 Hz, 1H), 7.10 (t, J = 7.3 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 193.8, 187.9, 162.4, 137.1, 136.4, 135.4, 134.4, 133.8, 133.2, 128.9, 128.6, 128.5, 124.2, 123.5, 122.2, 120.6, 119.5, 113.4, 109.3, 101.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{25}H_{17}N_2O_2^+$, 377.1285; found, 377.1301.

(*Z*)-3-(1*H*-Indol-3-yl)-2-(4-methylbenzoyl)-4-oxo-4-phenylbut-2-enenitrile (5w). Purified by column chromatography. Eluent: hexane/ethyl acetate (8 : 2). Yield 66 mg (68%); yellow solid; mp 212–214 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.70 (s, 1H), 8.65 (s, 1H), 7.95 (d, J = 7.1 Hz, 2H), 7.79 (d, J = 8.2 Hz, 2H), 7.59–7.53 (m, 2H), 7.45 (t, J = 7.7 Hz, 2H), 7.40 (d, J = 8.1 Hz, 1H), 7.34 (d, J = 8.2 Hz, 2H), 7.22 (t, J = 7.0 Hz, 1H), 7.09 (t, J = 7.7 Hz, 1H), 2.38 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 193.9, 187.5, 162.2, 143.9, 137.1, 135.4, 134.1, 133.8, 133.6, 129.1, 128.97, 128.94, 128.6, 124.2, 123.5, 122.2, 120.6, 119.6, 113.4, 109.3, 101.9, 21.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{26}H_{19}N_2O_2^+$, 391.1441; found, 391.1465.

5-Hydroxy-4-(1*H*-indol-3-yl)-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6a). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 28 mg (89%); pale yellow solid; mp 344–346 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 9.32 (s, 1H), 8.05 (d, J = 8.1 Hz, 1H), 7.99 (d, J = 3.2 Hz, 1H), 7.58 (s, 1H), 7.46 (t, J = 8.6 Hz, 3H), 7.30 (t, J = 7.6 Hz, 2H), 7.24–7.13 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.5, 166.4, 141.0, 136.6, 132.7, 128.4, 128.1, 125.3, 124.7, 123.0, 121.9, 121.1, 115.9, 112.7, 106.5, 96.9, 89.5. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{14}N_3O_2^+$, 316.1081; found, 316.1084.

5-(4-Ethylphenyl)-5-hydroxy-4-(1*H*-indol-3-yl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6b). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 30 mg (87%); pale yellow solid; mp 248–250 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 9.26 (s, 1H), 8.06 (d, J = 7.8 Hz, 1H), 8.00 (d, J = 3.3 Hz, 1H), 7.51 (s, 1H), 7.45 (d, J = 7.3 Hz, 1H), 7.38 (d, J = 8.2 Hz, 2H), 7.22–7.12 (m, 4H), 2.54–2.48 (m, 2H), 1.09 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.6, 166.4, 143.6, 138.4, 136.5, 132.7, 127.8, 125.3, 124.8, 122.9, 121.9, 121.1, 115.9, 112.7, 106.5, 96.8, 89.5, 27.7, 15.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{21}H_{18}N_3O_2^+$, 344.1394; found, 344.1396.

5-(4-Chlorophenyl)-5-hydroxy-4-(1*H*-indol-3-yl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6c). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 28 mg (80%); yellow solid; mp 216–218 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.18 (s, 1H), 9.34 (s, 1H), 8.05 (d, J = 7.9 Hz, 1H), 8.01 (d, J = 3.2 Hz, 1H), 7.69 (s, 1H), 7.48 (t, J = 9.2 Hz, 3H), 7.35 (d, J = 8.6 Hz, 2H), 7.18 (dt, J = 21.3, 6.8 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.3, 166.0, 140.1, 136.6, 132.74, 132.72, 128.4, 127.4, 124.7, 123.1, 121.9, 121.2, 115.8, 112.8, 106.4, 96.9, 89.1. HRMS (ESI-TOF) m/z: $[M + H^+]$ calcd for $C_{19}H_{13}ClN_3O_2^+$, 350.0691; found, 350.0702.

5-Hydroxy-4-(1*H*-indol-3-yl)-5-(4-iodophenyl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6d). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 36 mg (82%); light brown solid; charred at 350 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 9.33 (s, 1H), 8.04 (d, J = 8.9 Hz, 1H), 8.01 (s, 1H), 7.67 (d, J = 4.6 Hz, 2H), 7.64 (s, 1H), 7.46 (d, J = 7.8 Hz, 1H), 7.27 (d, J = 8.6 Hz, 2H), 7.18 (dt, J = 21.5, 7.0 Hz, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.3, 165.9, 140.9, 137.2, 136.6, 132.7, 127.7, 124.6, 123.1, 121.9, 121.2, 112.8, 106.4, 96.9, 94.6, 89.3. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{13}IN_3O_2^+$, 442.0047; found, 442.0042.

5-Hydroxy-4-(1*H*-indol-3-yl)-5-(4-methoxyphenyl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6e). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 29 mg (84%); orange solid; mp 226–228 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.15 (s, 1H), 9.25 (s, 1H), 8.03 (d, J = 7.8 Hz, 1H), 7.98 (d, J = 3.2 Hz, 1H), 7.49 (s, 1H), 7.45 (d, J = 7.3 Hz, 1H), 7.37 (d, J = 8.9 Hz, 2H), 7.22–7.13 (m, 2H), 6.84 (d, J = 8.9 Hz, 2H), 3.67 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.7, 166.3, 158.9, 136.6, 132.9, 132.6, 126.7, 124.8, 122.9, 121.9, 121.1, 115.9, 113.7, 112.7, 106.5, 96.8, 89.5, 55.1. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{16}N_3O_3^+$, 346.1186; found, 346.1204.

5-Hydroxy-4-(1*H*-indol-3-yl)-5-(4-nitrophenyl)-2-oxo-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6f). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 29 mg (80%); yellow solid; mp 232–235 °C. ^{1}H NMR (400 MHz, DMSO-d_6 + $CDCl_3$) δ 12.21 (s, 1H), 9.47 (s, 1H), 8.15 (d, J = 9.0 Hz, 2H), 8.06 (d, J = 7.1 Hz, 2H), 7.94 (s, 1H), 7.77 (d, J = 9.0 Hz, 2H), 7.46 (d, J = 7.1 Hz, 1H), 7.22–7.14 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6 + $CDCl_3$) δ 166.4, 165.3, 148.1, 147.1, 136.6, 132.7, 126.8, 124.5, 123.5, 122.9, 121.9, 121.1, 115.6, 112.6, 106.2, 97.2, 88.9. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{13}N_4O_4^+$, 361.0931; found, 361.0901.

5-Hydroxy-4-(1-methyl-1*H*-indol-3-yl)-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6g). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 29 mg (88%); light brown solid; mp 261–263 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.32 (s, 1H), 8.10 (s, 1H), 8.03 (d, J = 7.9 Hz, 1H), 7.61 (s, 1H), 7.49 (t, J = 7.5 Hz, 3H), 7.28 (q, J = 8.4, 7.8 Hz, 3H), 7.21 (q, J = 7.2 Hz, 2H), 3.82 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.4, 166.1, 140.9, 137.1, 135.8, 128.4, 128.1, 125.3, 125.1, 123.0, 122.1, 121.4, 115.9, 111.2, 105.5, 96.8, 89.6, 33.4. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{20}H_{16}N_3O_2^+$, 330.1237; found, 330.1243.

4-(1-Benzyl-1*H*-indol-3-yl)-5-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6h). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 33 mg (81%); pale yellow solid; mp 224–226 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.35 (s, 1H), 8.29 (s, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.61 (s, 1H), 7.53 (d, J = 8.1 Hz, 1H), 7.47 (d, J = 8.4 Hz, 2H), 7.30–7.16 (m, 8H), 7.08 (d, J = 7.5 Hz, 2H), 5.48 (s, 2H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.4, 165.9, 140.9, 136.6, 136.2, 135.4, 128.6, 128.3, 128.0, 127.8, 127.3, 125.5, 125.4, 123.0, 121.9, 121.4, 115.7, 111.5, 105.7, 97.3, 89.6, 49.5. HRMS (ESI-TOF) m/z: $[M + H^+]$ calcd for $C_{26}H_{20}N_3O_2^+$, 406.1550; found, 406.1578.

5-Hydroxy-4-(7-methyl-1*H*-indol-3-yl)-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6i). Purified by column chromato-

graphy. Eluent: hexane/ethyl acetate (7 : 3). Yield 28 mg (85%); yellow solid; mp 275–277 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.17 (s, 1H), 9.32 (s, 1H), 7.93 (d, J = 3.3 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.59 (s, 1H), 7.47 (d, J = 7.5 Hz, 2H), 7.30 (t, J = 7.5 Hz, 2H), 7.22 (t, J = 7.3 Hz, 1H), 7.06 (t, J = 7.6 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.6, 166.4, 141.1, 135.9, 132.1, 128.4, 128.1, 125.3, 124.6, 123.6, 121.9, 121.3, 119.5, 115.9, 106.9, 97.0, 89.6, 16.7. HRMS (ESI-TOF) m/z: [M + H$^+$] calcd for $C_{20}H_{16}N_3O_2^+$, 330.1237; found, 330.1262.

4-(5-Fluoro-1*H*-indol-3-yl)-5-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6j). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 29 mg (87%); pale yellow solid; mp 232–234 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.34 (s, 1H), 9.31 (s, 1H), 8.10 (s, 1H), 7.78 (d, J = 10.9 Hz, 1H), 7.61 (s, 1H), 7.47 (t, J = 7.3 Hz, 3H), 7.30 (t, J = 7.5 Hz, 2H), 7.23 (t, J = 7.3 Hz, 1H), 7.06 (t, J = 9.0 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 166.4, 166.2, 158.4, 158.2, 157.8 (d, J = 232.5 Hz), 140.8, 134.4, 133.4, 128.5, 128.3, 125.3 (d, J = 17.5 Hz), 118.6, 116.2, 116.0, 114.0 (d, J = 10 Hz), 111.2 (d, J = 26.25 Hz), 107.4 (d, J = 25 Hz), 106.8, 97.0, 89.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{13}FN_3O_2^+$, 334.0986; found, 334.1000.

4-(6-Chloro-1*H*-indol-3-yl)-5-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6k). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 28 mg (80%); yellow solid; mp 186–188 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.20 (s, 1H), 9.36 (s, 1H), 8.04 (s, 1H), 8.01 (d, J = 8.7 Hz, 1H), 7.60 (s, 1H), 7.51 (d, J = 2.1 Hz, 1H), 7.47 (d, J = 7.0 Hz, 2H), 7.30 (t, J = 7.4 Hz, 2H), 7.23 (t, J = 7.2 Hz, 1H), 7.17 (dd, J = 8.7, 2.0 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.2, 166.1, 140.6, 137.0, 133.4, 128.4, 128.2, 127.6, 125.3, 123.4, 123.3, 121.3, 115.7, 112.4, 106.5, 97.9, 89.5. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{13}ClN_3O_2^+$, 350.0691; found, 350.0689.

4-(5-Bromo-1*H*-indol-3-yl)-5-hydroxy-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6l). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 34 mg (86%); yellow solid; mp 270–272 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.31 (s, 1H), 9.34 (s, 1H), 8.22 (d, J = 2.0 Hz, 1H), 8.07 (s, 1H), 7.60 (s, 1H), 7.48 (d, J = 7.1 Hz, 2H), 7.42 (d, J = 8.6 Hz, 1H), 7.30 (t, J = 7.8 Hz, 3H), 7.24 (t, J = 7.2 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 166.1, 165.9, 140.5, 135.3, 133.6, 128.4, 128.2, 126.2, 125.5, 125.3, 124.4, 115.8, 114.6, 113.7, 106.0, 97.7, 89.4. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{19}H_{13}N_3O_2Br^+$, 394.0186; found, 394.0199.

5-Hydroxy-4-(5-methoxy-1*H*-indol-3-yl)-2-oxo-5-phenyl-2,5-dihydro-1*H*-pyrrole-3-carbonitrile (6m). Purified by column chromatography. Eluent: hexane/ethyl acetate (7 : 3). Yield 29 mg (84%); pale yellow solid; mp 230–232 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.05 (s, 1H), 9.25 (s, 1H), 7.97 (d, J = 3.3 Hz, 1H), 7.55 (d, J = 10.5 Hz, 2H), 7.48 (d, J = 7.9 Hz, 2H), 7.35–7.29 (m, 3H), 7.24 (t, J = 7.2 Hz, 1H), 6.82 (d, J = 8.8 Hz, 1H), 3.74 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 166.4, 166.3, 154.7, 141.2, 133.1, 131.3, 128.4, 128.0, 125.4, 125.2, 116.2, 113.3, 112.8, 106.6, 104.3, 95.7, 89.4, 55.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{20}H_{16}N_3O_3^+$, 346.1186; found, 346.1162.

1-(1*H*-Indol-3-yl)-2-phenylethane-1,2-dione (7a). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 19 mg (76%); pale yellow solid; mp 191–193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.90 (s, 1H), 8.48 (d, J = 8.8 Hz, 1H), 8.09 (d, J = 7.1 Hz, 2H), 7.91 (d, J = 3.3 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.52–7.45 (m, 3H), 7.40–7.34 (m, 2H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6 + $CDCl_3$) δ 193.9, 188.4, 137.0, 136.5, 134.2, 133.5, 130.2, 128.7, 125.6, 123.9, 122.9, 122.1, 113.7, 112.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{12}NO_2^+$, 250.0863; found, 250.0872.

1-(4-Ethylphenyl)-2-(1*H*-indol-3-yl)ethane-1,2-dione (7b). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 22 mg (79%); pale yellow solid; mp 147–149 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H), 8.22–8.19 (m, 1H), 8.15 (s, 1H), 7.88 (d, J = 8.3 Hz, 2H), 7.56–7.54 (m, 1H), 7.43 (d, J = 8.3 Hz, 2H), 7.33–7.28 (m, 2H), 2.70 (q, J = 7.6 Hz, 2H), 1.20 (t, J = 7.6 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, DMSO-d_6) δ 193.7, 188.9, 151.5, 137.8, 136.9, 130.8, 129.9, 128.6, 125.0, 123.8, 122.8, 121.2, 112.8, 112.6, 28.4, 15.1. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{18}H_{16}NO_2^+$, 278.1176; found, 278.1146.

1-(1-Methyl-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (7c). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 19 mg (72%); pale yellow solid; mp 191–193 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.49–8.46 (m, 1H), 8.10 (d, J = 7.0 Hz, 2H), 7.81 (s, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.50 (t, J = 7.8 Hz, 2H), 7.41–7.39 (m, 3H), 3.84 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 193.9, 187.7, 139.7, 137.9, 134.4, 133.6, 130.5, 128.9, 126.5, 124.4, 123.6, 122.8, 113.0, 110.1, 33.9. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{17}H_{14}NO_2^+$, 264.1019; found, 264.1018.

1-(5-Fluoro-1*H*-indol-3-yl)-2-phenylethane-1,2-dione (7d). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 19 mg (71%); white solid; mp 194–195 °C. ^{1}H NMR (500 MHz, DMSO-d_6) δ 12.52 (s, 1H), 8.25 (s, 1H), 7.97 (d, J = 7.0 Hz, 2H), 7.89 (dd, J = 9.5, 2.6 Hz, 1H), 7.75 (t, J = 7.4 Hz, 1H), 7.62–7.56 (m, 3H), 7.18 (td, J = 9.2, 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, DMSO-d_6) δ 193.7, 188.3, 159.1 (d, J = 235 Hz), 139.3, 134.8, 133.6, 132.8, 129.8, 129.2, 125.7 (d, J = 11.25 Hz), 114.2 (d, J = 10 Hz), 112.64, 112.61, 112.0 (d, J = 25 Hz), 106.3, 106.2 (d, J = 25). HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{16}H_{11}FNO_2^+$, 268.0768; found, 268.0748.

2-(1*H*-Indol-3-yl)-3-phenylquinoxaline (9a). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 26 mg (81%); pale yellow solid; mp 195–197 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56–8.53 (m, 1H), 8.28 (s, 1H), 8.19 (d, J = 8.2 Hz, 1H), 8.11 (d, J = 6.5 Hz, 1H), 7.73 (dt, J = 23.4, 6.8 Hz, 2H), 7.64–7.62 (m, 2H), 7.44–7.39 (m, 3H), 7.36–7.33 (m, 1H), 7.29–7.27 (m, 2H), 6.73 (d, J = 2.9 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 153.9, 149.6, 141.7, 140.4, 139.8, 136.1, 129.9, 129.4, 129.2, 128.99, 128.91, 128.7, 127.9, 126.7, 123.3, 122.3, 121.5, 114.9, 111.2. HRMS (ESI-TOF) m/z: [M + H]$^+$ calcd for $C_{22}H_{16}N_3^+$, 322.1339; found, 322.1346.

2-(1-Methyl-1*H*-indol-3-yl)-3-phenylquinoxaline (9b). Purified by column chromatography. Eluent: hexane/ethyl acetate (9 : 1). Yield 29 mg (86%); pale yellow solid; mp 193–195 °C. ^{1}H

NMR (400 MHz, $CDCl_3$) δ 8.51 (d, J = 7.1 Hz, 1H), 8.17 (d, J = 8.3 Hz, 1H), 8.10 (d, J = 8.2 Hz, 1H), 7.74 (t, J = 7.6 Hz, 1H), 7.69 (d, J = 8.3 Hz, 1H), 7.64 (d, J = 9.5 Hz, 2H), 7.47–7.41 (m, 3H), 7.31–7.27 (m, 2H), 6.60 (s, 1H), 3.64 (s, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 153.8, 149.6, 141.8, 140.5, 139.7, 137.2, 132.4, 129.8, 129.4, 129.1, 129.0, 128.8, 128.7, 127.4, 122.8, 122.6, 121.3, 113.5, 109.4, 33.2. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{18}N_3^+$, 336.1495; found, 336.1488.

Author contributions

L. H. C. and N. M. conceived and designed the experiments. N. M., V. K., and D. A. performed the experiments, analyzed the data, and prepared the figures. N. M. drafted the manuscript. L. H. C. acquired funding, supervised the laboratory work, revised the manuscript, and prepared the final version.

Data availability

The data underlying this study are available in the published article and its online ESI.†

Conflicts of interest

There are no conflicts to declare.

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