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Multi-component Tether Catalysis Synthesis of Highly Functionalized 4-(Pyridin-2-ylmethyl)-2-amino-pyrroles via Cascade Reaction is Accompanied by Decarboxylation

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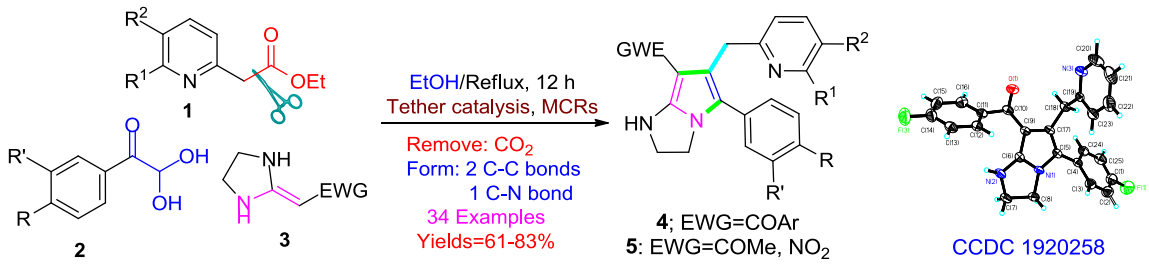
KEYWORDS: *2-Aminopyrroles, Tether catalysis, Cascade reaction, Decarboxylation, Heterocyclic ketene aminals.*



ABSTRACT: A multi-component tether catalysis protocol for the synthesis of 4-(pyridin-2-ylmethyl)-2-aminopyrroles (PMAPs) was constructed by simply refluxing a mixture of ethyl 2-(pyridin-2-yl)acetates **1** and various types of arylglyoxal monohydrates **2** and different heterocyclic ketene aminals **3** in EtOH solvent. Based on this reaction, a series of highly functionalized PMAPs was obtained through a novel cascade reaction accompanied by a decarboxylation mechanism. As a result, the pyridin-2-ylmethyl was successfully introduced in the target compounds, and a library of PMAPs was easily constructed using the cascade reaction described in this study. This protocol demonstrated that the most important feature was the decarboxylation reaction of the 2-(pyridin-2-yl)acetates **1**, which can be used in the synthesis of pyridin-2-ylmethyl-substituted heterocycles including pyrroles, pyridines, quinolones, and other heterocyclic compounds resembling those found in nature.

INTRODUCTION

Pyrrole derivatives are vital *N*-containing heterocycles and are a common structural motif in numerous natural products, biologically important molecules, and pharmaceuticals.[1] Examples are the central cannabinoid (CB1) receptor antagonist (Fig. 1, URB447), the anti-tumor agent neolamellarin A, and the antihyperlipidemic agent atorvastatin.[2] Consequently, a greater number of chemists and pharmacologists have been interested in these types of heterocycles and have constructed many protocols for the synthesis of pyrrole derivatives.[2-3] A general method involves the use of Paal-Knorr condensations to synthesize pyrroles.[4] Furthermore, *N*-sulfonyl-1,2,3-triazoles also have been widely used as the substrate to synthesize pyrroles.[5]

Currently, there has been an increasing number of protocols for synthesizing pyrroles.[6] Among pyrrole derivatives, there has been great interest in 2-aminopyrrole in recent years due to the 2-aminopyrrole skeleton being incorporated in many medicinal compounds, as well as its broad-spectrum and unique biological activities including mitogen-activated protein kinase kinase (MEK) inhibitor,[7] metallo-β-lactamase (MBL) inhibitor,[8] (Fig. 1), tumor necrosis factor (TNF)-α production inhibitor, phosphodiesterase (PDE) inhibitor,[9] protein kinase casein kinase 2 (CK2) inhibitor;[10] antagonist against corticotropin-releasing factor (CRF) receptors (Fig. 1);[11] and antimalarial, anti-bacterial, and cytotoxic activities.[12] As a result, an increasing number of procedures have been used to synthesize pyrroles[13-16] including (1) a multicomponent reaction base on nitrile or isocyanide-containing substrates and (2) cycloisomerization of alkyne and allene-containing substrates catalyzed by transition metal complexes. For example, Ye and co-workers reported a gold-catalyzed intermolecular ynamide amination-initiated *aza*-Nazarov cyclization to synthesize 2-aminopyrroles (Scheme 1).[16a] Zhu and co-workers described an oxidative Strecker reaction (mediated by 2-iodoxybenzoic acid and tetra-butylammonium

bromide) followed by a [4+1]-cycloaddition of the resulting *α,β*-unsaturated imidoyl cyanides with isocyanides to provide 2-aminopyrroles (Scheme 1).[16b] (3) Our group recently established a simple protocol that uses Morita–Baylis–Hillman (MBH) acetates reacted with heterocyclic ketene aminals (HKAs) *via* base-promoted tandem Michael addition, elimination, and aromatization for the facile synthesis of 2-aminopyrroles.[17]

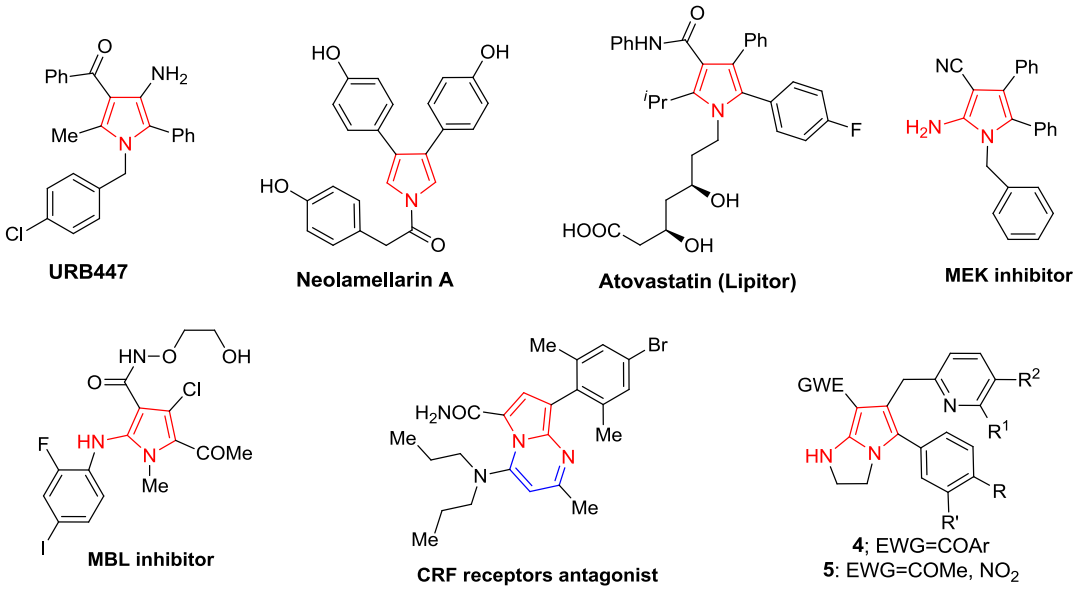
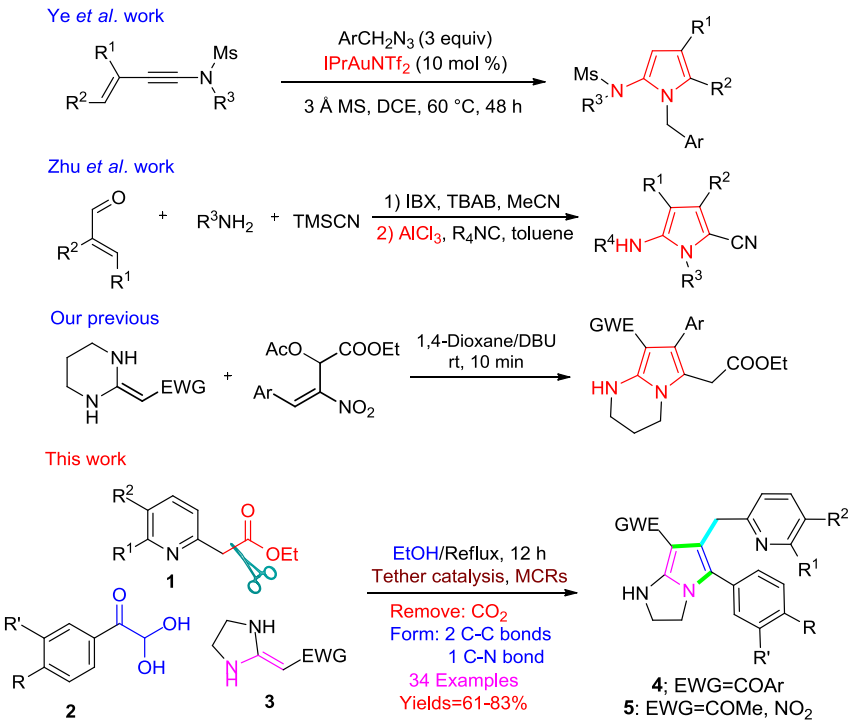


Figure 1. Biological activity of pyrroles and compounds **4–5**.

Pyridine derivatives are one of the most important classes of nitrogen heterocyclic compounds and are ubiquitous structural motifs in biologically active molecules or drugs.[18-21] Constructing hybrid molecules that are combined with the pyridine skeleton and 2-aminopyrrole skeleton may increase the chance for excellent biological activities. The hybrid molecules are 4-(pyridin-2-ylmethyl)-2-aminopyrroles (PMAPs). The reported methods for their synthesis usually have some shortcomings, such as the need for expensive transition metal additives and poor selectivity. Additionally, methods for synthesis of biological heterocycles substituted by pyridinylmethyl, quinolin-2-ylmethyl, and other benzyl groups are very rare. The scarcity may

be due to the fact that when using the alkylation agents, the *N*-alkylation products are always obtained rather that the *C*-alkylation products.

Scheme 1. Methods for the Construction of 2-Aminopyrrole Derivatives

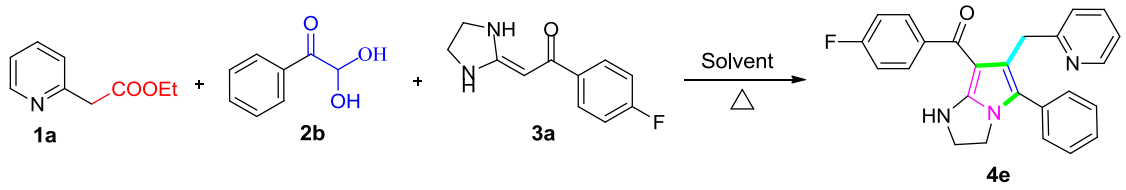


Heterocyclic ketene aminals (HKAs) are fascinating and versatile building blocks[22] and were widely used to synthesize various heterocycles with important biological activities including antitumor,[23] anti-anxiety,[24] anti-leishmanial,[25] antibacterial,[26] and pesticide.[27] To further extend the use of HKAs in synthesis, we herein report the construction of a library of functionalized 2-aminopyrrole derivatives based on multicomponent reactions between HKAs, ethyl 2-(pyridin-2-yl)acetates, and arylglyoxal monohydrates. The process occurs in refluxing ethanol without any added catalyst.

RESULTS AND DISCUSSION

In order to achieve optimal conditions, first, ethyl 2-(pyridin-2-yl)acetates **1a** (0.5 mmol), arylglyoxal monohydrate **2b** (0.5 mmol), and HKA **3a** were mixed without any added catalyst at reflux in different solvents including ethanol, acetonitrile, tetrahydrofuran (THF), 1,4-dioxane, and toluene. The results showed that ethanol was the most optimal solvent, and gave the product **4e** with a moderate yield (79%) (Table 1, entries 1–5). In an attempt to use a more environmentally friendly solvent, water was used as a solvent in this cascade reaction, and the results showed that we obtained a lower yield compared with ethanol (Table 1, entry 1 vs. 6). Next, a mixture of ethanol and water at different volume ratios served as the solvent and was screened at reflux without any other catalyst (Table 1, entries 7–9). The results showed that ethanol is the most optimal solvent when compared to other solvents, including the mixed solvents (Table 1, entry 1 vs. 2–9). Based on the optimal solvents, the basic catalyst including Et_3N, pyridine, and Cs_2CO_3 were applied in this reaction that was refluxed in ethanol for 12 hours (Table 1, entries 10–12). The results demonstrated that the basic catalyst could not promote the reaction at all, and a low yield (35–66%) was obtained. Next, acid catalysts including CH_3COOH, *p*-TsOH, and NH_2SO_3H were screened under the same conditions. The results revealed that these three catalysts also could not promote the yield of the cascade reaction (Table 1, entries 12–15). Comparing all of the conditions, we found that the optimal conditions were the use of ethanol as the solvent without any other catalyst at reflux for 12 hours (Table 1, entry 1 vs. 2–15).

Table 1. Optimized Conditions for the Synthesis of 4e[a]

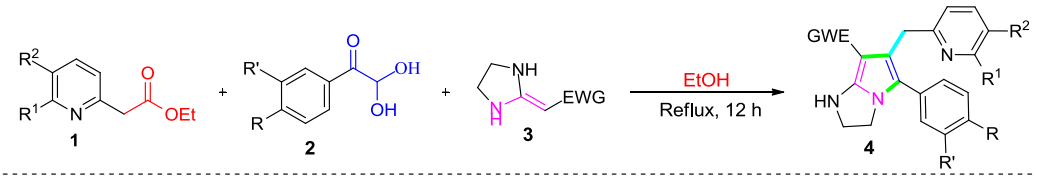


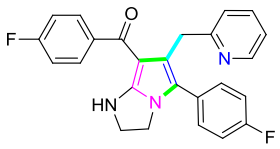
entry	solvent	catalyst	time/h	yield[b] (%)
1	EtOH	–	12	79
2	MeCN	–	12	54
3	THF	–	12	55
4	1,4-dioxane	–	12	42
5	toluene	–	12	61
6	H_2O	–	12	12
7	EtOH/H_2O=1:5	–	12	19
8	EtOH/H_2O=1:2	–	12	33
9	EtOH/H_2O=1:1	–	12	55
10	EtOH	Et_3N	12	57
11	EtOH	pyridine	12	35
12	EtOH	Cs_2CO_3	12	66
13	EtOH	CH_3COOH	12	49
14	EtOH	*p*-TsOH	12	0
15	EtOH	NH_2SO_3H	12	0

[a] Reagents and conditions: **1a** (0.5 mmol), **2b** (0.5 mmol), **3a** (0.5 mmol), catalyst (0.05 mmol), solvent (3.0 mL). [b] Isolated yield based on **3a**.

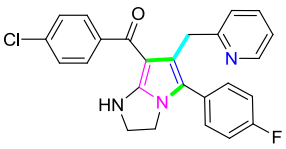
Once we determined the optimized conditions, we explored the scope and limitations of the cascade reaction of ethyl 2-(pyridin-2-yl)acetates **1** and arylglyoxal monohydrates **2** and HKAs **3** (Table 2). The results showed that the substituted groups of ethyl 2-(pyridin-2-yl)acetates **1** and arylglyoxal monohydrates **2** exerted only a slight effect on the yield of the target compounds **4**, and we almost could not arrive at obvious rules for the substituted group. In general, this cascade

Table 2. Synthesis of 4-(Pyridin-2-ylmethyl)-2-aminopyrroles 4

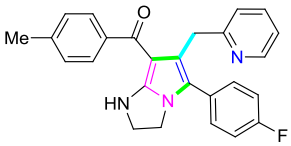




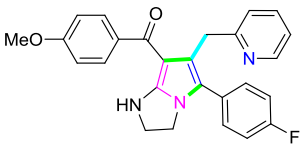
4a: yield=81%[a]



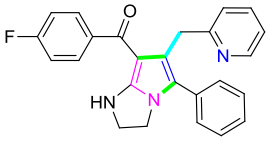
4b: yield=78%[a]



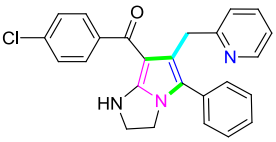
4c: yield=79%[a]



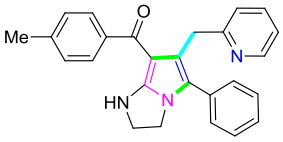
4d: yield=77%[a]



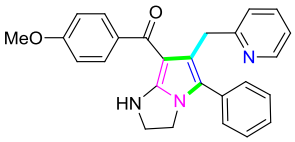
4e: yield=79%[a]
4e: yield=78%[b]



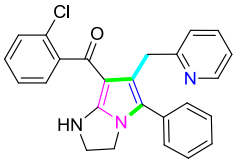
4f: yield=79%[a]



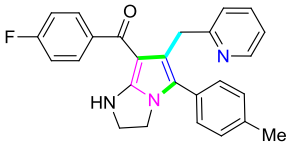
4g: yield=77%[a]



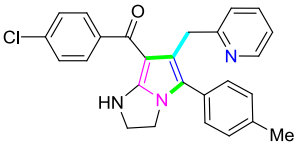
4h: yield=78%[a]



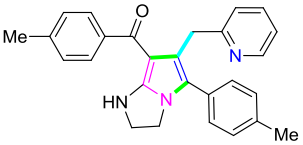
4i: yield=76%[a]



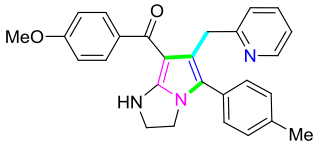
4j: yield=81%[a]



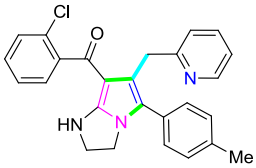
4k: yield=81%[a]



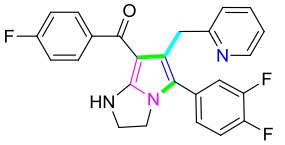
4l: yield=83%[a]



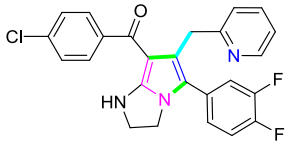
4m: yield=78%[a]



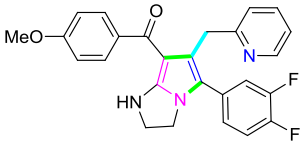
4n: yield=62%[a]



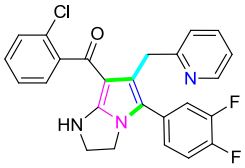
4o: yield=80%[a]



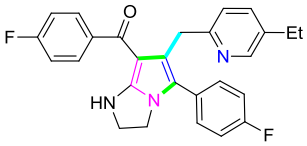
4p: yield=82%[a]



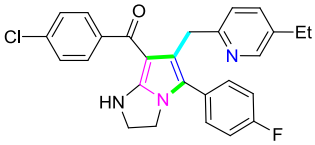
4q: yield=80%[a]



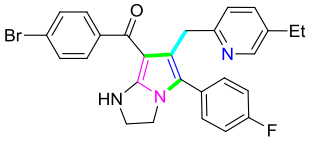
4r: yield=63%[a]



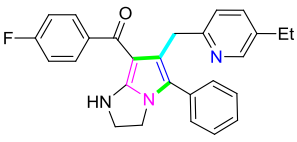
4s: yield=78%[a]



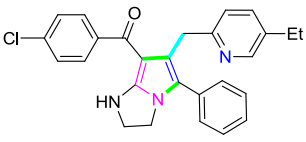
4t: yield=79%[a]



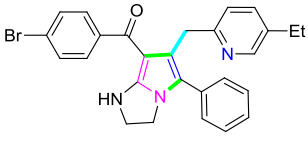
4u: yield=82%[a]



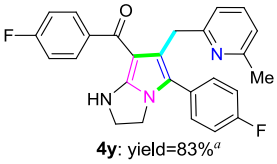
4v: yield=78%[a]



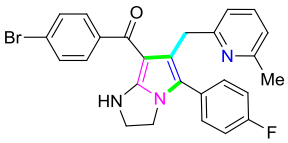
4w: yield=76%[a]



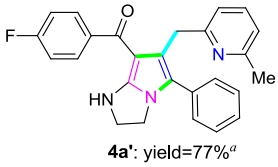
4x: yield=75%[a]



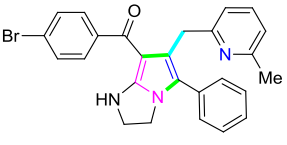
4y: yield=83%[a]



4z: yield=76%[a]



4a': yield=77%[a]

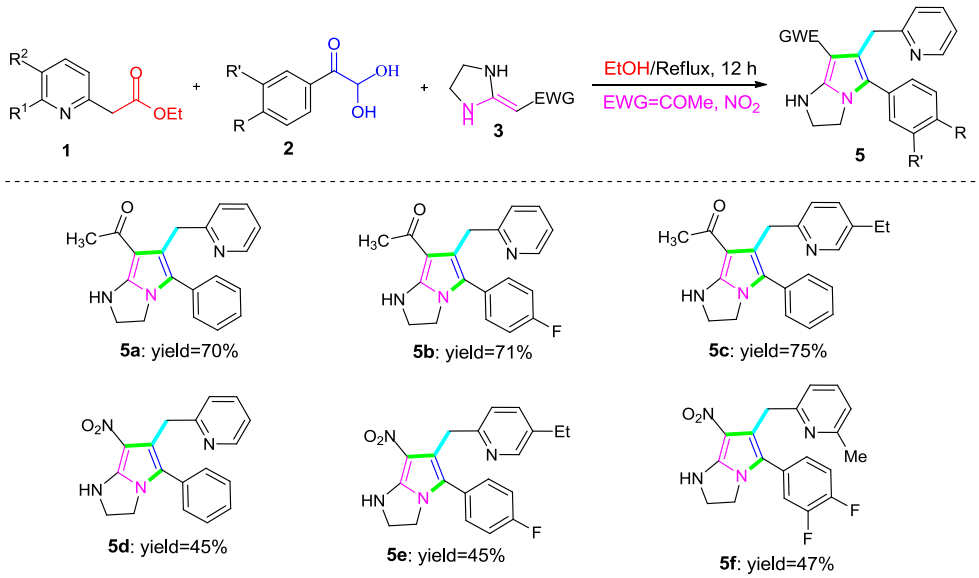


4b': yield=79%[a]

[a] **1–3** (0.5 mmol), EtOH (3.0 mL). [b] **1–3** (1.0 mmol), EtOH (5.0 mL).

reaction can smoothly proceed with the different structures of the 2-(pyridin-2-yl)acetates **1** and arylglyoxal monohydrates **2** to produce compounds **4** with moderate to good yield. The substituted group of HKAs **3** has a different effect on the yield of the target compounds. The effect of substitution on the aryl group of HKAs was also evaluated. Substitution at C-4 of the aryl group has a slight effect on the yield. When the substituents were at C-2 of the aryl group, yields were slightly lower (Table 2, **4i**, **4n** and **4r**). Overall, all of the substrates can be used in the reaction, and all will produce compounds **4** in moderate to good yield (Table 2, entries 1–28). To illustrate this new synthetic method, a larger scale (**1–3**, 1.0 mmol) synthesis of compound **4e** was carried out, and we obtained 309 mg compound **4e** with an increasing yield up to 78% (Table 2). Alkylglyoxal monohydrates **2e–2f** were used as substrates to test this cascade reaction, and the results showed that alkylglyoxal monohydrates **2e–2f** did not react with ethyl 2-(pyridin-2-yl)acetates **1a** and HKA **3a**, and we could not obtain the target compounds **4c'–4d'** (SI, Scheme S1).

Table 3. Synthesis of 4-(Pyridin-2-ylmethyl)-2-aminopyrroles 5[a-b]



[a] Reagents and conditions: **1–3** (0.5 mmol), EtOH (3.0 mL). [b] Isolated yield based on **3**.

To further explore the scope and limitations of the cascade reaction, a variety of HKAs **3** with electron-withdrawing groups was used as the substrate in this cascade reaction (Table 3). The results showed that all of the substituted groups of HKAs **3** had a slight influence on the yield of the reaction. Overall, different substituted HKAs can be used in the reaction and give compounds **5** with good yield (Table 3).

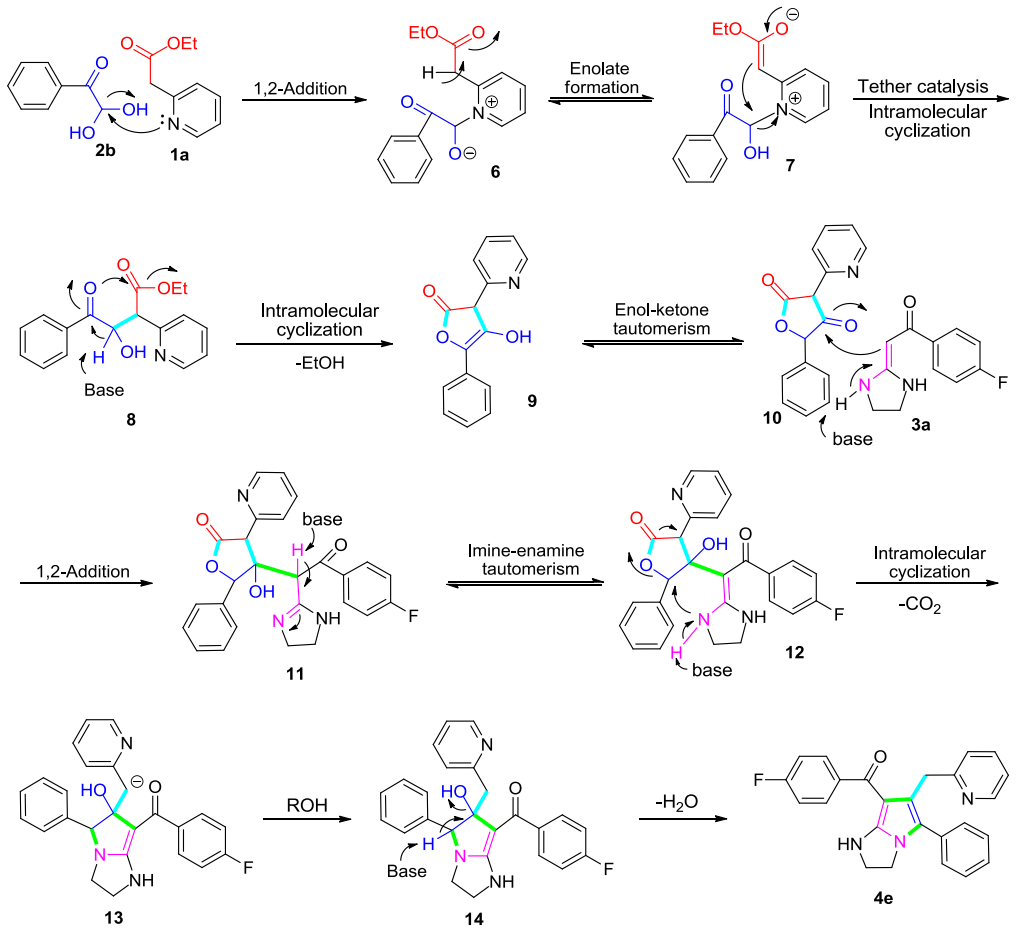
To determine the structure of PMAPs, compound **4a** was selected as a representative compound and characterized by X-ray crystallography (Supporting Information, Figure S1, CCDC 1920258).

To determine the tether catalysis mechanism, control experiments were performed using substrates **1d–1g** as reagents that were reacted with arylglyoxal monohydrate **2b** and HKA **3a**. Substrates **1d–1g** did not react with arylglyoxal monohydrate **2b** and HKA **3a** under the same conditions (SI, Scheme S2). Substrates **1a–1d** produced the target compounds with satisfactory yields (Table 2), but positive results were not obtained for substrates **1d–1g**. Thus, it was successfully demonstrated that intermediate **7** is necessary for the cascade reaction to proceed so that intermediates **8** and **9** can be formed (Scheme 2).

To explain the possible mechanism of the cascade reaction, we used target compound **4e** as a representative compound. The hypothesis for the mechanism of the cascade reaction is shown in Scheme 2. Initially, the 2-(pyridin-2-yl)acetate **1a** react with the arylglyoxal monohydrate **2b** *via* 1,2-addition to form the intermediate **6**. Next, the intermediate **7** is produced from intermediate **6** by enolate formation. Then, intermediate **7** gives compound **8** *via* an intramolecular tether-catalyzed cyclization reaction. Compound **9** is obtained from compound **8** through another intramolecular cyclization reaction and loses one molecule of ethanol. Compound **9** gives intermediate **10** *via* a enol-ketone tautomerization. Then, *α-C* of substrate **3a** attacks the carbonyl

group of intermediate **10** by a 1,2-addition reaction, and imine-enamine tautomerization follows to obtain intermediate **12**. The amino group of intermediate **12** subsequently attacks the intramolecular benzylic carbon, which results in the loss of one molecule of CO_2 to produce intermediate **13**. The intermediate **13** gets one proton from solvent to form intermediate **14**. Ultimately, intermediate **14** forms compound **4e** by losing one molecule of water.

Scheme 2. Proposed Mechanism of the Cascade Reaction



To probe the mechanism of this cascade reaction, 2,2-dihydroxy-1-phenylethanone (**2b)** and HKA (**3a**) and the solvent EtOH (3 mL) were charged in a round-bottom flask. Next, ethyl 2-(pyridin-2-yl)acetate (**1a**) was added. The reaction was refluxed only for 3 hours. Then, the reaction mixture was injected into the high-performance liquid chromatography-high resolution

mass spectrometry (HPLC-HRMS) system. The four molecular ion peaks that appeared in the high-resolution mass spectrum were: HRMS (TOF ES^+): *m/z* calcd. for $C_{17}H_{18}NO_4$ $[M+H]^+$, 300.1230; found, 300.1236; HRMS (TOF ES^+): *m/z* calcd. for $C_{17}H_{18}NO_4$ $[M+H]^+$, 300.1230; found, 300.1224; HRMS (TOF ES^+): *m/z* calcd. for $C_{17}H_{18}NO_4$ $[M+H]^+$, 300.1230; found, 300.1230. There are the HRMS spectra of intermediates **6**/**7**/**8**; HRMS (TOF ES^+): *m/z* calcd. for $C_{15}H_{12}NO_3$ $[M+H]^+$, 254.0812; found, 254.0816; HRMS (TOF ES^+): *m/z* calcd. for $C_{15}H_{12}NO_3$ $[M+H]^+$, 254.0812; found, 254.0819, which are the HRMS spectra of intermediate **9**/**10**; HRMS (TOF ES^+): *m/z* calcd. for $C_{26}H_{23}FN_3O_4$ $[M+H]^+$, 460.1667; found, 460.1663, which is the HRMS spectra of compound **11** or **12**; HRMS (TOF ES^+): *m/z* calcd. for $C_{25}H_{21}FN_3O$ $[M+H]^+$, 398.1663; found, 398.1661), which is the HRMS spectrum of target compound **4e** (supporting information, Figure S83−Figure S90). Based on the molecular ion peaks of intermediate **6–12**, the proposed mechanism of the cascade reaction is reasonable (Scheme 2).

This cascade reaction via a novel mechanism including a tether catalysis and a decarboxylation mechanism (Scheme 2). As a result, the pyridin-2-ylmethyl was successfully introduced in the target compounds, and a library of PMAPs was easily constructed using the cascade reaction described in this study. The novel mechanism was been confirmed by the high resolution mass spectrometry (HRMS) of intermediates **6–12** (Supporting information, Figure S84−Figure S89) and the control experiments (Supporting Information, Scheme S2). This protocol demonstrated that the most important feature was the tether catalysis and decarboxylation reaction of the 2-(pyridin-2-yl)acetates **1**. In future studies, these reactions will be used in this efficient and concise one-step protocol for the synthesis of pyridin-2-ylmethyl-substituted heterocycles including pyrroles, pyridines, quinolones, and other heterocyclic compounds resembling those found in nature.

■ CONCLUSIONS

In conclusion, we have developed a procedure consisting of an tether catalysis reaction for the synthesis of PMAPs by simply refluxing a mixture of ethyl 2-(pyridin-2-yl)acetates **1** and various types of arylglyoxal monohydrates **2** and different heterocyclic ketene aminals **3** in EtOH solvent (Scheme 2). Using this procedure, a series of highly functionalized PMAPs was obtained through a novel cascade reaction accompanying a decarboxylation mechanism. Consequently, the functionalized pyridin-2-ylmethyl was simply and rapidly introduced in the pyrrole skeleton, and the library of PMAPs was easily constructed using the cascade reaction described in this study. This protocol demonstrated that the most important feature was the decarboxylation reaction of the 2-(pyridin-2-yl)acetates **1**, and it can be used in the synthesis of pyridin-2-ylmethyl-substituted heterocycles including pyrroles, pyridines, quinolones, and other heterocyclic compounds resembling those found in nature.

■ EXPERIMENTAL SECTION

General Methods. All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX600. Chemical shifts (δ) are expressed in ppm, J values are given in Hz, and deuterated DMSO-d_6 were used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected; HRMS were performed on an Agilent LC/Msd TOF instrument.

The materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

The procedure for the synthesis of HKAs 3a–3g.[28a-b]

HKAs (**3a–3f**) were prepared according to the literature.[28a] The mixture of ketene dithioacetals (10 mmol) and 1,2-diaminoethane (12 mmol) in anhydrous toluene (40 mL) was stirred for about 8 hours at reflux. The mixture was cooled to room temperature and the product collected by filtration as a withe or yellow solid with 85–92%.

HKA (**3g**) were prepared according to the literature.[28b] The mixture of ketene dithioacetals (10 mmol) and 1,2-diaminoethane (12 mmol) in ethanol (40 mL) was stirred for about 8 hours at reflux. The mixture was cooled to room temperature and the product collected by filtration as a withe solid (**3g**) with 86%.

*1-(4-Fluorophenyl)-2-(imidazolidin-2-ylidene)ethanone (**3a**):*[28c] Withe solid (1.86 g, 90%); Mp: 206–208 °C [Lit. 206 °C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.25 (s, 1H, NH), 7.78–7.76 (m, 2H, ArH), 7.40 (s, 1H, NH), 7.17 (t, J = 8.8 Hz, 2H, ArH), 5.24 (s, 1H, CH), 3.61 (t, J = 8.3 Hz, 2H, CH_2), 3.45 (t, J = 8.3 Hz, 2H, CH_2); HRMS (TOF ES$^+$): *m/z* calcd for $C_{11}H_{12}FN_2O$ [$(M+H)^+$], 207.0928; found, 207.0928.

*1-(4-Chlorophenyl)-2-(imidazolidin-2-ylidene)ethanone (**3b**):*[28d] Withe solid (2.05 g, 92%); Mp: 236–237.5 °C [Lit. 238°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.26 (s, 1H, NH), 7.73 (d, J = 8.5 Hz, 2H, ArH), 7.42 (s, 1H, NH), 7.41 (d, J = 8.5 Hz, 2H, ArH), 5.25 (s, 1H, CH), 3.60 (d, J = 7.7 Hz, 2H, CH_2), 3.46 (d, J = 7.7 Hz, 2H, CH_2); HRMS (TOF ES$^+$): *m/z* calcd for $C_{11}H_{12}ClN_2O$ [$(M+H)^+$], 223.0633; found, 223.0634.

*1-(4-Bromophenyl)-2-(imidazolidin-2-ylidene)ethanone (**3c**):*[28d] Yellow solid (2.35 g, 88%); Mp: 272–274°C [Lit. 275°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.25 (s, 1H, NH), 7.66 (d, J = 8.4 Hz, 2H, ArH), 7.56 (d, J = 8.4 Hz, 2H, ArH), 7.43 (s, 1H, NH), 5.24 (s, 1H, CH), 3.61 (d, J = 7.7 Hz, 2H, CH_2), 3.46 (d, J = 7.7 Hz, 2H, CH_2); HRMS (TOF ES$^+$): *m/z* calcd for

$C_{11}H_{12}BrN_2O$ [$(M+H)^+$], 267.0128; found, 267.0128.

*2-(Imidazolidin-2-ylidene)-1-(p-tolyl)ethanone (**3d**)*:[28d] Withe solid (1.82 g, 90%); Mp: 244–245 °C [Lit. 245°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.26 (s, 1H, NH), 7.61 (d, J = 8.0 Hz, 2H, ArH), 7.33 (s, 1H, NH), 7.16 (d, J = 8.0 Hz, 2H, ArH), 5.24 (s, 1H, CH), 3.59 (d, J = 7.6 Hz, 2H, CH_2), 3.43 (d, J = 7.6 Hz, 2H, CH_2), 2.31 (s, 3H, CH_3); HRMS (TOF ES$^+$): *m/z* calcd for $C_{12}H_{14}N_2O$ [$(M+H)^+$], 203.1179; found, 203.1176.

*2-(Imidazolidin-2-ylidene)-1-(4-methoxyphenyl)ethanone (**3e**)*:[28d] Withe solid (1.99 g, 91%); Mp: 217–219 °C [Lit. 218°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.24 (s, 1H, NH), 7.68 (d, J = 8.6 Hz, 2H, ArH), 7.28 (s, 1H, NH), 6.90 (d, J = 8.6 Hz, 2H, ArH), 5.23 (s, 1H, CH), 3.77 (s, 3H, CH_3), 3.59 (t, J = 8.3 Hz, 2H, CH_2), 3.43 (t, J = 8.3 Hz, 2H, CH_2); HRMS (TOF ES$^+$): *m/z* calcd for $C_{12}H_{15}N_2O_2$ [$(M+H)^+$], 219.1128; found, 219.1128.

*1-(2-Chlorophenyl)-2-(imidazolidin-2-ylidene)ethan-1-one (**3f**)*:[28e] Yellow solid (1.89 g, 85%); Mp: 240–241 °C [Lit. 242°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 9.00 (s, 1H, NH), 7.46 (s, 1H, NH), 7.38–7.28 (m, 4H, ArH), 4.72 (s, 1H, CH), 3.61 (t, J = 8.5 Hz, 2H, CH_2), 3.44 (t, J = 8.5 Hz, 2H, CH_2); HRMS (TOF ES$^+$): *m/z* calcd for $C_{11}H_{12}ClN_2O$ [$(M+H)^+$], 223.0633; found, 223.0637.

*2-(Nitromethylene)imidazolidine (**3g**)*:[28b] White solid (1.11 g, 86%); Mp: 168–169 °C [Lit. 170°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.29 (s, 2H, NH), 6.34 (s, 1H, CH), 3.58 (s, 4H, CH_2); HRMS (TOF ES$^+$): *m/z*calcd for $C_4H_7N_3NaO_2$ [$(M+Na)^+$], 152.0430; found, 152.0434.

*1-(Imidazolidin-2-ylidene)propan-2-one(**3h**)*:[28f] White solid (87%); Mp: 145–147 °C [Lit. 148°C]; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.88 (s, 1H, NH), 7.07 (s, 1H, NH), 4.51 (s, 1H, CH), 3.50 (t, J = 8.1 Hz, 2H, CH_2), 3.35 (t, J = 8.1 Hz, 2H, CH_2), 1.73 (s, 3H, CH_3); HRMS (TOF ES$^+$): *m/z* calcd for $C_6H_{11}N_2O$ [$(M+H)^+$], 127.0866; found, 127.0866.

General procedure for the synthesis of 4-(pyridin-2-ylmethyl)-2-aminopyrroles 4–5. Arylglyoxal monohydrates **1** (0.5 mmol), ethyl 2-pyridylacetates **2** (0.5 mmol), and ethanol (3 mL) were placed into a 5-mL round-bottom flask. Then, heterocyclic ketene amines (HKAs) **3** (0.5 mmol) were added to this mixture, and the mixture was refluxed until the completion of the reaction, which was monitored by thin-layer chromatography (TLC, approximately 12 hours). The reaction mixture was cooled to room temperature. The mixture was extracted three times with ethyl acetate (25 mL). The combined organic extracts were washed with water and brine, and finally dried over $MgSO_4$. The solvent was removed in vacuum to afford a crude residue, which was purified by flash column chromatography to provide **4–5** with good yield of 61−83%.

*(4-Fluorophenyl)(5-(4-fluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4a**):* Yellow solid (168 mg, 81%); Mp: 173.0–173.5 °C; IR (KBr) 3435, 2962, 2368, 1598, 1528, 1417, 1249, 1164, 1079, 769cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 8.39–8.38 (m, 1H, NCH), 7.57 (d, J = 1.8 Hz, 1H, ArH), 7.53–7.47 (m, 4H, ArH), 7.23–7.17 (m, 4H, ArH), 7.12–7.04 (m, 2H, ArH), 5.72 (s, 1H, NH), 4.03 (t, J = 8.8 Hz, 4H, $ArCH_2$, NCH_2), 3.78 (t, J = 1.5 Hz, 2H, $NHCH_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6): δ = 187.2, 163.7 (d, J = 244.5 Hz), 162.0, 161.6 (d, J = 243.0 Hz), 153.9, 148.9, 138.4, 136.5, 130.4, 130.3, 128.1, 123.3, 122.6, 121.2, 119.6, 116.0, 115.6, 100.7, 49.1, 44.7, 34.8; ^{19}F NMR (470 MHz, DMSO-d_6) δ = 110.7, 115.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{20}F_2N_3O$ [$(M+H)^+$], 416.1569; found, 416.1569.

*(4-Chlorophenyl)(5-(4-fluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]-imidazol-7-yl)methanone (**4b**):* Yellow solid (168 mg, 78%); Mp: 214.1–210.5 °C; IR (KBr) 3434, 2896, 1592, 1506, 1416, 1299, 1227 1164, 1084, 1245, 764cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.31–8.30 (m, 1H, NCH), 7.52–7.49 (m, 1H, ArH), 7.42–7.40 (m, 6H, ArH),

7.39–7.34 (m, 2H, ArH), 7.16–7.13 (m, 1H, ArH), 7.04–7.96 (m, 1H, ArH), 5.70 (s, 1H, NH), 3.95 (t, J = 4.4 Hz, 4H, $ArCH_2$, NCH_2), 3.71–3.68 (m, 2H, $NHCH_2$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 187.1, 162.0, 161.6 (d, J = 241.5Hz), 154.1, 148.9, 140.6, 136.5, 135.2, 130.3 (d, J = 7.5 Hz), 129.7, 128.7, 128.1, 123.4, 122.6, 121.2, 119.5, 116.0 (d, J = 21.0Hz), 100.7, 49.1, 44.7, 34.8; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{20}ClFN_3O$ [$(M+H)^+$], 432.1273; found, 432.1264.

*(5-(4-Fluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(p-tolyl)methanone (**4c**):* Yellow solid (162 mg, 79%); Mp: 207.8–208.0 °C; IR (KBr) 3433, 1593, 1531, 1504, 1414, 1298, 1225, 1163, 1079, 763cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ= 8.32–8.31 (m, 1H, NCH), 7.50–7.47 (m, 1H, ArCH), 7.42–7.40 (m, 2H, ArH), 7.32 (d, J = 8.0 Hz, 2H, ArH), 7.15–7.11 (m, 4H, ArH), 7.03–7.01 (m, 4H, ArH), 6.95 (d, J = 7.8 Hz, 1H, ArH), 5.42 (s, 1H, NH), 3.98–3.92 (m, 4H, $ArCH_2$, NCH_2), 3.70–3.66 (m, 2H, $NHCH_2$), 2.27 (s,3H, $ArCH_3$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 188.4, 162.2, 161.5 (d, J = 243.0 Hz), 153.6, 148.9, 140.4, 139.2, 136.4, 130.2 (d, J = 7.5 Hz), 129.2, 128.2, 128.0, 123.1, 122.6, 121.2, 119.8, 115.9 (d, J = 21.0 Hz), 101.0, 49.1, 44.7, 34.7, 21.5; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}FN_3O$ [$(M+H)^+$], 412.1820; found, 412.1823.

*(5-(4-Fluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(4-methoxyphenyl)methanone (**4d**):* Yellow solid (164 mg, 77%); Mp: 180.1–180.5 °C; IR (KBr) 3419, 1595, 1529, 1503, 1417, 1305, 1251, 1162, 841, 770cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.32–8.31 (m, 1H, NCH), 7.50–7.47 (m, 1H, ArCH), 7.45–7.40 (m, 4H, ArCH), 7.13 (d, J = 8.9 Hz, 2H, ArH), 7.03–7.01 (m, 1H, ArCH), 6.97 (d, J = 7.9 Hz, 1H, ArH), 6.87–6.86 (m, 2H, ArH), 5.47 (s, 1H, NH), 4.00–3.93 (m, 4H, $ArCH_2$, NCH_2), 3.73 (s, 3H, $COCH_3$), 3.69–3.66 (m, 2H, $NHCH_2$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 187.7, 162.3, 161.6, 161.6 (d, J = 243.0

Hz), 153.2, 148.9, 136.5, 134.2, 130.2, 130.2, 128.3, 123.0, 122.7, 121.2, 120.1, 116.0 (d, J = 21.0 Hz), 113.9, 100.9, 55.7, 49.1, 44.7, 34.8; ^{19}F NMR (470 MHz, DMSO-d_6) δ = 115.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{23}FN_3O_2$ [(M+H)$^+$], 428.1769; found, 428.1766.

*(4-Fluorophenyl)(5-phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4e**):* Yellow solid (157 mg, 79%); Mp: 191.0–191.2 °C; IR (KBr) 3429, 2930, 1603, 1553, 1294, 1219, 1151, 763cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.39–8.38 (m, 1H, NCH), 7.58–7.56 (m, 1H, ArH), 7.53–7.51 (m, 2H, ArH), 7.43–7.41 (m, 1H, ArH), 7.37 (t, J = 7.5 Hz, 3H, ArH), 7.27 (d, J = 7.3 Hz, 1H, ArH), 7.19 (t, J = 8.9 Hz, 2H, ArH), 7.11–7.10 (m, 1H, ArH), 7.04 (d, J = 7.8 Hz, 1H, ArH), 5.73 (s, 1H, NH), 4.07–4.04 (m, 4H, ArCH$_2$, NCH$_2$), 3.79–3.76 (m, 2H, NHCH$_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.2, 162.9, 162.2, 154.0, 148.9, 138.4, 136.5, 131.7, 130.4 (d, J = 9.0 Hz), 129.0, 128.2, 127.2, 124.3, 122.5, 121.2, 119.5, 115.6, 115.5, 100.8, 49.1, 44.9, 34.9; ^{19}F NMR (470 MHz, DMSO-d_6) δ = 110.7; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{21}FN_3O$ [(M+H)$^+$], 398.1663; found, 398.1664.

*(4-Chlorophenyl)(5-phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4f**):* Yellow solid (163 mg, 79%); Mp: 190.2–190.8°C; IR (KBr) 3433, 2893, 1593, 1529, 1417, 1298, 1166, 1083, 643cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.38 (d, J = 4.1 Hz, 1H, NCH), 7.58 (d, J = 1.6 Hz, 1H, ArH), 7.46–7.41 (m, 3H, ArH), 7.38 (t, J = 5.1 Hz, 5H, ArH), 7.27 (d, J = 7.3Hz, 1H, ArH), 7.11 (d, J = 1.7 Hz, 1H, ArH), 7.04 (d, J = 7.9 Hz, 1H, ArH), 5.79 (s, 1H, NH), 4.05 (t, J = 3.4 Hz, 4H, ArCH$_2$, NCH$_2$), 3.78 (t, J = 7.5 Hz, 2H, NHCH$_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ =187.2, 162.1, 154.2, 148.9, 140.6, 136.5, 135.2, 131.6, 129.7, 129.0, 128.7, 128.2, 127.2, 124.5, 122.5, 121.2, 119.4, 100.8, 49.1, 44.9, 34.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{21}ClN_3O$ [(M+H)$^+$], 414.1368; found, 414.1364.

(5-Phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(p-tolyl)meth-

*anone (**4g**):* Yellow solid (151 mg, 77%); Mp: 226.5–226.8 °C; IR (KBr) 3322, 3057, 2893, 1599, 1535, 1415, 1298, 1168, 1079, 762cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.32–8.31 (m, 1H, NCH), 7.50–7.48 (m, 1H, ArCH), 7.34–7.27 (m, 6H, ArH), 7.19–7.17 (m, 1H, ArH), 7.12 (d, J = 7.7 Hz, 2H, ArH), 7.03–7.01 (m, 1H, ArH), 6.95 (d, J = 7.9 Hz, 1H, ArH), 5.42 (s, 1H, NH), 4.01–3.94 (m, 4H, $ArCH_2$, NCH_2), 3.70–3.67 (m, 2H, $NHCH_2$), 2.27 (s, 3H, $ArCH_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ= 188.4, 162.2, 153.7, 148.9, 140.4, 139.3, 136.4, 131.8, 129.2, 129.0, 128.1, 123.1, 127.1, 124.1, 122.5, 121.1, 119.8, 101.1, 49.1, 44.9, 34.9, 21.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{24}N_3O$ [(M+H)$^+$], 394.1914; found, 394.1912.

*(4-Methoxyphenyl)(5-phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4h**):* Yellow solid (159 mg, 78%); Mp: 165.1–165.4 °C; IR (KBr) 3435, 1598, 1527, 1417, 1303, 1249, 1164, 1079, 1034, 843, 769cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.32–8.31 (m, 1H, NCH), 7.50–7.47 (m, 1H, ArCH), 7.45–7.44 (m, 2H, ArCH), 7.35 (t, J = 1.1 Hz, 2H, ArH), 7.29 (t, J = 7.6 Hz, 2H, ArH), 7.18 (t, J = 7.3 Hz, 1H, ArH), 7.03–7.01 (m, 2H, ArH), 6.97 (d, J = 7.9Hz, 1H, ArH), 6.87 (t, J = 1.8 Hz, 2H, ArH), 5.47 (s, 1H, NH), 4.03–3.95 (m, 4H, $ArCH_2$, NCH_2), 3.73 (s, 3H, $COCH_3$), 3.70–3.67 (m, 2H, $NHCH_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ= 187.7, 162.4, 161.6, 153.3, 148.9, 136.4, 134.3, 131.8, 130.2, 129.0, 128.1, 127.0, 124.0, 122.5, 121.1, 120.0, 113.9, 101.1, 55.7, 49.1, 44.9, 34.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{24}N_3O_2$ [(M+H)$^+$], 410.1863; found, 410.1862.

*(2-Chlorophenyl)(5-phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4i**):* Yellow solid (156 mg, 76%); Mp: 169.4–169.9 °C; IR (KBr) 3383, 1611, 1534, 1478, 1414, 1361, 1254, 1219, 973, 743cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.25 (d, J = 2.4 Hz, 1H, NCH), 7.49 (t, J = 7.4 Hz, 1H, ArCH), 7.28–7.17 (m, 8H, ArCH), 7.04–6.96 (m, 4H, ArCH), 3.97 (t, 2H, NCH_2), 3.77 (d, J = 7.1 Hz, 4H, $ArCH_2$, NCH_2); ^{13}C{^{1}H} NMR (150

MHz, DMSO-d_6) δ= 185.4, 161.5, 155.5, 148.9, 141.7, 136.4, 131.5, 130.3, 130.0, 129.6, 129.0, 128.1, 128.0, 127.4, 127.3, 124.4, 122.3, 121.2, 101.4, 49.1, 44.7, 34.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{21}ClN_3O$ [(M+H)$^+$], 414.1368; found, 414.1364.

*(4-Fluorophenyl)(6-(pyridin-2-ylmethyl)-5-(p-tolyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4j**):* Yellow solid (166 mg, 81%); Mp: 179.0–179.2 °C; IR (KBr) 3433, 3262, 1604, 1539, 1502, 1418, 1223, 1156, 766 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.38–8.37 (m, 1H, NCH), 7.59–7.56 (m, 1H, ArH), 7.53–7.50 (m, 2H, ArH), 7.29 (d, *J* = 8.0 Hz, 2H, ArH), 7.20–7.17 (m, 4H, ArH), 7.11–7.09 (m, 1H, ArH), 7.03 (d, *J* = 7.9 Hz,1H, ArH), 5.70 (s, 1H, NH), 4.05–4.01 (m, 4H, $ArCH_2$, NCH_2), 3.78–3.75 (m, 2H, $NHCH_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ =187.1, 163.7 (d, *J* = 244.5 Hz), 162.3, 153.9, 148.9, 138.5, 136.4 (d, *J* = 9.0 Hz), 130.4 (d, *J* = 7.0 Hz), 129.6, 128.8, 128.2, 124.3, 122.4, 121.1, 119.0, 115.6, 115.4, 100.8, 49.1, 44.8, 34.9, 21.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{23}FN_3O$ [(M+H)$^+$], 412.1820; found, 412.1818.

*(4-Chlorophenyl)(6-(pyridin-2-ylmethyl)-5-(p-tolyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4k**):* Yellow solid (172 mg, 81%); Mp: 227.3–227.9 °C; IR (KBr) 3433, 2962, 1595, 1531, 1414, 1298, 1228, 1166, 1083, 632cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.30–8.29 (m, 1H, NCH), 7.49 (d, *J* = 1.8 Hz, 1H, ArH), 7.38–7.37 (m, 4H, ArH), 7.34–7.33 (m, 2H, ArH), 7.21 (d, *J* = 8.1 Hz, 2H, ArH), 7.10 (d, *J* = 8.0 Hz, 1H, ArH), 6.95 (d, *J* = 7.8 Hz, 1H, ArH), 5.70 (s, 1H, NH), 3.96–3.93 (m, 4H, $ArCH_2$, NCH_2), 3.70 (t, *J* = 4.6 Hz, 2H, $NHCH_2$), 2.22 (s, 3H, $ArCH_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ =187.1, 162.2, 154.0, 148.9, 140.7, 136.6, 136.5, 135.2, 129.7, 129.6, 128.7, 128.7, 128.2, 124.5, 122.4, 121.1, 118.9, 100.7, 49.1, 44.8, 34.9, 21.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{23}ClN_3O$ [(M+H)$^+$], 428.1524; found, 428.1518.

*(6-(Pyridin-2-ylmethyl)-5-(p-tolyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(p-tolyl)methanone (**4l**):* Yellow solid (169 mg, 83%); Mp: 166.1–166.9 °C; IR (KBr) 3385, 2927, 1595, 1532, 1415, 1298, 1167, 760cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.31–8.30 (m, 1H, NCH), 7.50–7.47 (m, 1H, ArCH), 7.31 (d, J = 8.0 Hz, 2H, ArH), 7.21 (d, J = 8.1 Hz, 2H, ArH), 7.12–7.08 (m, 4H, ArH), 7.02–7.00 (m, 1H, ArH), 6.94 (d, J = 7.9 Hz, 1H, ArH), 5.38 (s, 1H, NH), 3.99–3.91 (m, 4H, $ArCH_2$, NCH_2), 3.69–3.66 (m, 2H, $NHCH_2$), 2.26 (s, 3H, $ArCH_3$), 2.21 (s, 3H, $ArCH_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ= 188.4, 162.4, 153.5, 148.9, 140.3, 139.3, 136.4, 129.6, 129.2, 128.9, 128.9, 128.1, 124.1, 122.5, 121.1, 119.2, 101.1, 49.1, 44.8, 34.9, 21.5, 21.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}N_3O$ [(M+H)$^+$], 408.2070; found, 408.2075.

*(4-Methoxyphenyl)(6-(pyridin-2-ylmethyl)-5-(p-tolyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4m**):* Yellow solid (165 mg, 78%); Mp: 171.0–171.2 °C; IR (KBr) 3315, 2925, 1600, 1530, 1418, 1305, 1251, 1163, 1077, 1037, 841, 771cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.31–8.30 (m, 1H, NCH), 7.48–7.43 (m, 3H, ArCH), 7.21 (d, J = 8.1 Hz, 2H, ArH), 7.09 (d, J = 7.9 Hz, 2H, ArH), 7.01 (s, 2H, ArH), 6.95 (d, J = 7.9 Hz, 1H, ArH), 6.87–6.85 (m, 2H, ArH), 5.44 (s, 1H, NH), 4.01–3.92 (m, 4H, $ArCH_2$, NCH_2), 3.73 (s, 3H, $COCH_3$), 3.69 (t, J = 1.7 Hz, 2H, $NHCH_2$), 2.21 (s,3H, $ArCH_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ= 187.7, 162.5, 161.5, 153.1, 148.9, 136.4, 136.3, 134.3, 130.1, 129.6, 129.0, 128.1, 124.0, 122.5, 121.1, 119.5, 113.9, 101.0, 55.7, 49.1, 44.8, 34.9, 21.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{26}N_3O_2$ [(M+H)$^+$], 424.2020; found, 424.2017.

*(2-Chlorophenyl)(6-(pyridin-2-ylmethyl)-5-(p-tolyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4n**):* Yellow solid (132 mg, 62%); Mp: 205.1–205.2 °C; IR (KBr) 3343, 1546, 1527, 1470, 1414, 1282, 1229, 975, 749cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.24 (s, 1H, NCH), 7.49 (t, J = 7.6 Hz, 1H, ArCH), 7.24 (t, J = 6.7 Hz, 2H, ArCH), 7.16 (d, J = 7.4 Hz, 3H,

ArCH), 7.08 (d, *J* = 7.4 Hz, 3H, ArCH), 7.02 (t, *J* = 5.8 Hz, 3H, ArCH), 3.95 (t, *J* = 8.1 Hz, 2H, NCH_2), 3.76 (s, 4H, $ArCH_2$, NCH_2), 2.20 (s, 3H, $ArCH_3$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ= 185.3, 161.6, 155.4, 148.8, 141.7, 136.7, 136.4, 130.3, 129.9, 129.6, 128.6, 128.1, 128.0, 127.4, 124.4, 122.3, 121.2, 101.4, 49.1, 44.6, 34.5, 21.2; HRMS (TOF ES^+): *m/z* calcd for $C_{26}H_{23}ClN_3O$ [$(M+H)^+$], 428.1524; found, 428.1522.

*(5-(3,4-Difluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)-(4-fluorophenyl)methanone (**4o**):* Yellow solid (173 mg, 80%); Mp: 165.1–165.5 °C; IR (KBr) 3435, 1605, 1556, 1510, 1224, 1150, 768cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.41–8.40 (m, 1H, NCH), 7.61–7.58 (m, 2H, ArH), 7.54–7.52 (m, 2H, ArH), 7.44 (t, *J* = 8.8 Hz, 1H, ArH),7.31 (d, *J* = 1.2 Hz, 1H, ArH), 7.21–7.19 (m, 2H, ArH), 7.13–7.11 (m, 1H, ArH), 7.07 (d, *J* = 7.9 Hz, 1H, ArH), 5.75 (s, 1H, NH), 4.06 (t, *J* = 7.9 Hz, 4H, $ArCH_2$, NCH_2), 3.78–3.75 (m, 2H, $NHCH_2$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ =187.2, 163.3 (d, *J* = 246.0 Hz), 161.8, 154.0, 150.0 (d, *J* = 244.0 Hz), 149.0, 148.0 (d, *J* = 244.0 Hz), 138.3, 136.6, 130.4 (d, *J* = 9.0 Hz), 129.3, 125.1, 122.9, 122.3, 121.3, 120.8, 118.1 (d, *J* = 18.0 Hz), 117.0 (d, *J* = 18.0 Hz), 115.6 (d, *J* = 22.5 Hz), 100.8, 49.1, 44.8, 34.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ = 138.0 (d, *J* = -18.8 Hz), 140.7 (d, *J* = -18.8 Hz), 140.7; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{19}F_3N_3O$ [$(M+H)^+$], 434.1475; found, 434.1473.

*(4-Chlorophenyl)(5-(3,4-difluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4p**):* Yellow solid (184 mg, 82%); Mp: 209.3–209.8 °C; IR (KBr) 3433, 1592, 1525, 1469, 1416, 1278, 1223, 1091, 768cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.33 (d, *J* = 4.0 Hz, 1H, NCH), 7.58–7.50 (m, 2H, ArH), 7.40–7.35 (m, 5H, ArH), 7.23 (d, *J* = 6.0 Hz, 1H, ArH), 7.06–7.04 (m, 1H, ArH), 7.00 (d, *J* = 7.8 Hz, 1H, ArH), 5.72 (s, 1H, NH), 3.98 (t, *J* = 10.8 Hz, 4H, $ArCH_2$, NCH_2), 3.69 (t, *J* = 7.4 Hz, 2H, $NHCH_2$); $^{13}C\{^1H\}$ NMR (150

MHz, DMSO-d_6) 187.2, 161.7, 154.2, 149.8 (d, J = 243.0 Hz), 149.0, 149.5 (d, J = 243.0 Hz), 140.5, 136.6, 135.4, 129.8, 129.2, 128.8, 125.1, 122.9, 122.4, 121.3, 120.7, 118.1 (d, J = 18.0 Hz), 117.1 (d, J = 18.0 Hz), 100.7, 49.1, 44.8, 34.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{19}ClF_2N_3O$ [(M+H)$^+$], 450.1179; found, 450.1167.

*(5-(3,4-Difluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)-(4-methoxyphenyl)methanone (**4q**):* Yellow solid (178 mg, 80%); Mp: 205.9–206.3 °C; IR (KBr) 3324, 1594, 1525, 1469, 1417, 1376, 1304, 1252, 1161, 770cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.41 (t, J = 4.0 Hz, 1H, NCH), 7.65–7.62 (m, 1H, ArCH), 7.60–7.57 (m, 1H, ArCH), 7.52 (t, J = 6.8 Hz, 2H, ArH), 7.31 (d, J = 10.6 Hz, 1H, ArH), 7.13–7.07 (m, 2H, ArCH), 6.95 (d, J = 8.7 Hz, 1H, ArH), 5.60 (s, 1H, NH), 4.09–4.04 (m, 4H, $ArCH_2$, NCH_2), 3.81 (s, 3H, $COCH_3$), 3.76–3.73 (m, 2H, $NHCH_2$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.8, 162.0, 161.7, 153.3, 149.8 (d, J = 243.0 Hz), 149.5 (d, J = 243.0 Hz), 149.0, 136.6, 134.1, 130.2, 129.5, 125.0, 123.0, 121.9, 121.3, 121.3, 118.1 (d, J = 18.0 Hz), 117.0 (d, J = 18.0 Hz), 113.9, 101.0, 55.7, 49.1, 44.8, 34.6; ^{19}F NMR (470 MHz, DMSO-d_6) δ = 138.1 (d, J = -18.8 Hz), 141.2 (d, J = -18.8 Hz); HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{22}F_2N_3O_2$ [(M+H)$^+$], 446.1675; found, 446.1682.

*(2-Chlorophenyl)(5-(3,4-difluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a] -imidazol-7-yl)methanone (**4r**):* Yellow solid (141 mg, 63%); Mp: 175.1–175.7 °C; IR (KBr) 3383, 1606, 1530, 1475, 1416, 1271, 1220, 974, 750cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ= 8.36 (s, J = 3.5 Hz, 1H, NCH), 7.58 (t, J = 6.6 Hz, 2H, ArCH), 7.44–7.33 (m, 4H, ArCH), 7.23 (d, J = 6.0 Hz, 2H, ArCH), 7.19 (s, 1H, ArCH), 7.14–7.12 (m, 1H, ArCH), 7.06 (s, 1H, ArCH), 4.06 (t, J = 8.1 Hz, 2H, NCH_2), 3.83 (d, J = 8.0 Hz, 4H, $ArCH_2$, NCH_2); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 185.5, 161.1, 155.5, 150.6, 150.6, 149.8 (d, J = 243.0 Hz), 149.5 (d, J = 243.0 Hz), 141.6, 136.5, 130.4, 130.0, 129.6, 129.1, 128.0, 127.5, 125.0, 122.6, 122.4, 121.4,

118.1 (d, J = 18.0 Hz), 117.1 (d, J = 18.0 Hz), 101.4, 49.1, 44.6, 34.3; HRMS (TOF ES$^+$): *m/z* calcd for $C_{25}H_{19}ClF_2N_3O$ [(M+H)$^+$], 450.1179; found, 450.1174.

*(6-((5-Ethylpyridin-2-yl)methyl)-5-(4-fluorophenyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(4-fluorophenyl)methanone (**4s**):* Yellow solid (172 mg, 78%); Mp: 186.3–186.5 °C; IR (KBr) 3440, 1572, 1457, 1418, 1267, 1239, 1033, 753cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.25 (d, J = 1.7 Hz, 1H, NCH), 7.53–7.49 (m, 4H, ArH), 7.44–7.42 (m, 1H, ArH), 7.24–7.18 (m, 4H, ArH), 6.96 (d, J = 8.0 Hz, 1H, ArH), 5.73 (s, 1H, NH), 4.03 (t, J = 7.9 Hz, 4H, $ArCH_2$, NCH_2), 3.76 (t, J = 7.4 Hz, 2H, $NHCH_2$), 2.56–2.51 (m, 2H, CH_2CH_3), 1.16 (t, J = 7.6 Hz, 3H, CH_2CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.2, 163.7 (d, J = 246.0 Hz), 161.6 (d, J = 243.0 Hz), 159.4, 153.9, 148.4, 138.4, 136.0, 135.8, 130.4 (d, J = 9.0 Hz), 130.2 (d, J = 7.5 Hz), 128.2, 123.2, 122.2, 119.9, 116.0 (d, J = 21.0 Hz), 115.5 (d, J = 21.0 Hz), 100.7, 49.1, 44.7, 34.3, 25.4, 15.8; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{24}F_2N_3O$ [(M+H)$^+$], 444.1882; found, 444.1883.

*(4-Chlorophenyl)(6-((5-ethylpyridin-2-yl)methyl)-5-(4-fluorophenyl)-2,3-dihydro-1H-pyrrolo-[1,2-a]imidazol-7-yl)methanone (**4t**):* Yellow solid (181 mg, 79%); Mp: 189.1–189.6 °C; IR (KBr) 3443, 1593, 1564, 1439, 1418, 1277, 1203, 1081, 760cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.25 (d, J = 1.8 Hz, 1H, NCH), 7.51–7.49 (m, 2H, ArH), 7.46–7.41 (m, 5H, ArH), 7.22 (d, J = 8.8 Hz, 2H, ArH), 6.96 (d, J = 8.0 Hz, 1H, ArH), 5.78 (s, 1H, NH), 4.04–4.00 (m, 4H, $ArCH_2$, NCH_2), 3.77 (t, J = 7.5 Hz, 2H, $NHCH_2$), 2.56–2.53 (m, 2H, CH_2CH_3), 1.16 (t, J = 7.6 Hz, 3H, CH_2CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.1, 161.0 (d, J = 243.0 Hz), 159.3, 154.1, 148.4, 140.6, 136.1, 135.8, 135.2, 130.2 (d, J = 9.0 Hz), 129.7, 128.7, 128.1, 123.4, 122.2, 119.7, 116.0 (d, J = 21.0 Hz), 100.7, 49.1, 44.7, 34.3, 25.4, 15.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{24}ClFN_3O$ [(M+H)$^+$], 460.1586; found, 460.1586.

*(4-Bromophenyl)(6-((5-ethylpyridin-2-yl)methyl)-5-(4-fluorophenyl)-2,3-dihydro-1H-pyrrolo-[1,2-a]imidazol-7-yl)methanone (**4u**):* Yellow solid (206 mg, 82%); Mp: 201.1–201.6 °C; IR (KBr) 3433, 1597, 1542, 1433, 1416, 1289, 1204, 1086, 753cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.24 (d, J = 1.8 Hz, 1H, NCH), 7.55 (d, J = 8.3 Hz, 2H, ArH), 7.51–7.49 (m, 2H, ArH), 7.43–7.37 (m, 3H, ArH), 7.22 (d, J = 8.8 Hz, 2H, ArH), 6.96 (d, J = 8.0 Hz, 1H, ArH), 5.79 (s, 1H, NH), 4.03–3.99 (m, 4H, $ArCH_2$, NCH_2), 3.77 (t, J = 7.5 Hz, 2H, $NHCH_2$), 2.56–2.53 (m, 2H, CH_2CH_3), 1.16 (t, J = 7.6 Hz, 3H, CH_2CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.2, 161.6 (d, J = 243.0 Hz), 159.3, 154.1, 148.4, 141.0, 136.1, 135.8, 131.6, 130.2 (d, J = 7.5 Hz), 129.9, 128.1, 124.1, 123.4, 122.2, 119.7, 116.0 (d, J = 21.0 Hz), 100.6, 49.1, 44.7, 34.3, 25.4, 15.9; HRMS (TOF ES^{+}): *m/z* calcd for $C_{27}H_{24}BrFN_3O$ [$(M+H)^{+}$], 504.1081; found, 504.1083.

*(6-((5-Ethylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)(4-fluorophenyl)methanone (**4v**):* Yellow solid (165 mg, 78%); Mp: 161.9–162.5 °C; IR (KBr) 3443, 1560, 1453, 1419, 1247, 1227, 1037, 750cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.25 (s, 1H, NCH), 7.54–7.52 (m, 2H, ArH), 7.44–7.36 (m, 5H, ArH), 7.28–7.25 (m, 1H, ArH), 7.19 (t, J = 8.8 Hz, 2H, ArH), 6.96 (d, J = 8.0 Hz, 1H, ArH), 5.74 (s, 1H, NH), 4.03–4.07 (m, 4H, $ArCH_2$, NCH_2), 3.77(t, J = 7.7 Hz, 2H, $NHCH_2$), 2.56–2.51 (m, 2H, CH_2CH_3), 1.16 (t, J = 7.6 Hz, 3H, CH_2CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ = 187.2, 163.7 (d, J = 246.0 Hz), 159.5, 154.0, 148.4, 138.4, 135.8 (d, J = 36.0 Hz), 131.7, 130.4 (d, J = 9.0 Hz), 129.0, 128.2, 127.8, 127.1, 124.2, 122.0, 119.8, 115.5 (d, J = 21.0 Hz), 100.9, 49.1, 44.9, 34.4, 25.4, 15.8; HRMS (TOF ES^{+}): *m/z* calcd for $C_{27}H_{25}FN_3O$ [$(M+H)^{+}$], 426.1976; found, 426.1974.

*(4-Chlorophenyl)(6-((5-ethylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4w**):* Yellow solid (167 mg, 76%); Mp:210.2–210.5 °C; IR (KBr) 3433,

1597, 1542, 1433, 1416, 1289, 1204, 1086, 760cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.24 (d, J = 1.6 Hz, 1H, NCH), 7.46–7.41 (m, 4H, ArH), 7.37 (t, J = 7.6 Hz, 5H, ArH), 7.27 (t, J = 7.4 Hz, 1H, ArH), 6.96 (d, J = 7.0 Hz, 1H, ArH), 5.79 (s, 1H, NH), 4.06–4.02 (m, 4H, $ArCH_2$, NCH_2), 3.79–3.76 (m, 2H, $NHCH_2$), 2.57–2.53 (m, 2H, CH_2CH_3), 1.17(t, J = 7.6 Hz, 3H, CH_2CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ =187.1, 159.5, 154.2, 148.4, 140.7, 136.0, 135.7, 135.2, 131.7, 129.7, 129.0, 128.7, 128.2, 127.1, 124.4, 122.0, 119.7, 100.8, 49.1, 44.9, 34.4, 25.4, 15.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{25}ClN_3O$ [(M+H)$^+$], 442.1681; found, 442.1681.

*(4-Bromophenyl)(6-((5-ethylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4x**):* Yellow solid (182 mg, 75%); Mp: 200.5–200.9 °C; IR (KBr) 3446, 1587, 1532, 1434, 1417, 1289, 1204, 1086, 760cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.17 (d, J = 1.8 Hz, 1H, NCH), 7.48 (d, J = 1.7 Hz, 4H, ArH), 7.35 (d, J = 7.4 Hz, 3H, ArH), 7.31–7.28 (m, 4H, ArH), 7.19 (d, J = 7.4 Hz, 1H, ArH), 6.88 (d, J = 8.0 Hz, 1H, ArH), 5.72 (s, 1H, NH), 3.98–3.94 (m, 4H, $ArCH_2$, NCH_2), 3.71–3.68 (m, 2H, $NHCH_2$), 2.49–2.45 (m, 2H, CH_2CH_3), 1.09 (t, J = 7.6 Hz, 3H, CH_2CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ =187.2, 159.4, 154.2, 148.4, 141.0, 136.0, 135.7, 135.7, 131.6, 129.9, 129.0, 128.1, 127.2, 124.4, 124.1, 122.0, 119.6, 100.8, 49.1, 44.9, 34.4, 25.4, 15.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{25}BrN_3O$ [(M+H)$^+$], 486.1176; found, 486.1172.

*(4-Fluorophenyl)(5-(4-fluorophenyl)-6-((6-methylpyridin-2-yl)methyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)methanone (**4y**):* Yellow solid (178 mg, 83%); Mp: 184.9–185.5 °C; IR (KBr) 3443, 1594, 1443, 1418, 1253, 1217, 1079, 763cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 7.44–7.37 (m, 5H, ArH), 7.16–7.09 (m, 4H, ArH), 6.87 (d, J = 7.6 Hz, 1H, ArH), 6.75 (d, J = 7.7 Hz,1H, ArH),5.69 (s, 1H, NH), 3.96–3.90 (m, 4H, $ArCH_2$, NCH_2), 3.69 (t, J = 7.9 Hz, 2H,

NHCH$_2$), 2.30 (s, 3H, CH$_2$CH$_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-*d*$_6$) δ = 187.3, 163.7 (d, *J* = 244.5 Hz), 161.6 (d, *J* = 243.0 Hz), 161.3, 157.0, 153.9, 138.4, 136.8, 130.3 (d, *J* = 9.0 Hz), 130.3, 128.1, 123.3, 120.4, 119.6, 119.3, 115.9 (d, *J* = 21.0 Hz), 115.5 (d, *J* = 21.0 Hz), 100.7, 49.1, 44.7, 34.7, 24.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{22}F_2N_3O$ [(M+H)$^+$], 430.1725; found, 430.1717.

*(4-Bromophenyl)(5-(4-fluorophenyl)-6-((6-methylpyridin-2-yl)methyl)-2,3-dihydro-1H-pyrrolo-[1,2-a]imidazol-7-yl)methanone (**4z**):* Yellow solid (186 mg, 76%); Mp: 210.2–210.5 °C; IR (KBr) 3434, 1587, 1506, 1457, 1415, 1228, 1163, 1074, 1015cm^{-1}; ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ = 7.48–7.37 (m, 5H, ArH), 7.27 (d, *J* = 8.3 Hz, 2H, ArH), 7.15 (t, *J* = 8.9 Hz, 2H, ArH), 6.88 (d, *J* = 7.6 Hz, 1H, ArH), 6.74 (d, *J* = 7.7 Hz, 1H, ArH), 5.79 (s, 1H, NH), 3.96–3.87 (m, 4H, ArCH$_2$, NCH$_2$), 3.70 (t, *J* = 8.3 Hz, 2H, NHCH$_2$), 2.30 (s, 3H, CH$_2$CH$_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-*d*$_6$) δ = 187.3, 161.6 (d, *J* = 243.0 Hz), 161.2, 157.0, 154.2, 141.0, 136.8, 131.6, 130.3 (d, *J* = 9.0 Hz), 129.9, 128.1, 124.0, 123.4, 120.4, 119.3, 119.2, 115.9 (d, *J* = 22.5 Hz), 100.6, 49.1, 44.7, 34.7, 24.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{22}BrFN_3O$ [(M+H)$^+$], 490.0925; found, 490.0919.

*(4-Fluorophenyl)(6-((6-methylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]im-idazol-7-yl)methanone (**4a'**):* Yellow solid (158 mg, 77%); Mp: 171.9–172.5 °C; IR (KBr) 3469, 1572, 1593, 1449, 1416, 1257, 1207, 1070, 755cm^{-1}; ^{1}H NMR (600 MHz, DMSO-*d*$_6$) δ = 7.52–7.42 (m, 5H, ArH), 7.38 (t, *J* = 7.6 Hz, 2H, ArH), 7.27 (t, *J* = 7.3 Hz,1H, ArH), 7.18 (t, *J* = 7.8 Hz, 2H, ArH), 6.95 (d, *J* = 7.6 Hz, 1H, ArH), 6.82 (d, *J* = 7.7 Hz, 1H, ArH), 5.77 (d, *J* = 9.5 Hz, 1H, NH), 4.06–4.01 (m, 4H, ArCH$_2$, NCH$_2$), 3.79–3.77 (m, 2H, NHCH$_2$), 2.38 (s, 3H, CH$_2$CH$_3$); ^{13}C{^{1}H} NMR (150 MHz, DMSO-*d*$_6$) δ = 187.3, 163.7 (d, *J* = 246.0 Hz), 161.5, 156.9, 154.1, 136.8, 131.7, 130.3 (d, *J* = 9.0 Hz), 129.0, 128.2, 127.1, 124.3, 120.4, 119.5, 119.2,

115.5 (d, *J* = 21.0 Hz), 100.8, 49.1, 44.9, 34.8, 24.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{23}FN_3O$ [(M+H)$^+$], 412.1820; found, 412.1819.

*(4-Bromophenyl)(6-((6-methylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]im-idazol-7-yl)methanone (**4b'**):* Yellow solid (186 mg, 79%); Mp: 192.6–192.8 °C; IR (KBr) 3433, 1592, 1504, 1457, 1415, 1248, 1167, 1078, 1013 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 7.54 (d, *J* = 8.4 Hz, 2H, ArH), 7.47–7.41 (m, 3H, ArH), 7.39–7.34 (m, 4H, ArH), 7.27 (t, *J* = 7.3 Hz, 1H, ArH), 6.95 (d, *J* = 7.6 Hz, 1H, ArH), 6.81 (d, *J* = 1.2 Hz, 1H, ArH), 5.89 (s, 1H, NH), 4.06–3.98 (m, 4H, $ArCH_2$, NCH_2), 3.81–3.78 (m, 2H, $NHCH_2$), 2.38 (s, 3H, CH_2CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ =187.3, 161.3, 157.0, 154.3, 141.0, 136.8, 131.6, 131.6, 129.8, 129.0, 128.2, 127.2, 124.4, 124.0, 120.4, 119.2, 119.2, 100.8, 49.1, 44.9, 34.8, 24.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{26}H_{23}BrN_3O$ [(M+H)$^+$], 472.1019; found, 472.1018.

*1-(5-Phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)ethan-1-one (**5a**):* White solid (111 mg, 70%); Mp: 203.9–204.5 °C; IR (KBr) 1617, 1363, 701, 644, 611, 570 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.46 (d, *J* = 4.5 Hz, 1H, NCH), 7.64–7.61 (m, 1H, ArH), 7.39–7.34 (m, 4H, ArH), 7.25(t, *J* = 7.1 Hz, 1H, ArH), 7.14 (t, *J* = 4.8 Hz, 2H, ArH), 6.48 (s, 1H, NH), 4.14 (s, 2H, $ArCH_2$), 4.06 (t, *J* = 7.7 Hz, 2H, NCH_2), 3.90 (d, *J* = 7.0 Hz, 2H, $NHCH_2$), 2.14 (s, 3H, CH_3); ^{13}C{^{1}H} NMR (150 MHz, DMSO-d_6) δ =189.4, 162.5, 153.9, 149.0, 136.6, 131.8, 129.0, 128.1, 127.0, 123.5, 122.7, 121.2, 119.0, 102.3, 48.9, 45.0, 35.0, 29.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{20}N_3O$ [(M+H)$^+$], 318.1601; found, 318.1599.

*1-(5-(4-Fluorophenyl)-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)-ethan-1-one (**5b**):* White solid (119 mg, 71%); Mp: 181.2–181.5 °C; IR (KBr) 1617, 1361, 700, 634, 570 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) δ = 8.45 (d, *J* = 4.6 Hz, 1H, NCH), 7.64–7.61 (m, 1H, ArH), 7.46–7.44 (m, 2H, ArH), 7.22–7.13 (m, 4H, ArH), 6.47 (s, 1H, NH), 4.09 (s, 2H,

$ArCH_2$), 4.04 (t, J = 7.7 Hz, 2H, NCH_2), 3.89 (t, 2H, $NHCH_2$), 2.13 (s, 3H, CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 189.3, 162.3, 161.5 (d, J = 246.0 Hz), 153.8, 149.0, 136.6, 130.1 (d, J = 9.0 Hz), 128.3, 122.8, 122.5, 121.2, 119.1, 115.8 (d, J = 21.0 Hz), 102.1, 48.9, 44.8, 34.8, 29.6; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{19}FN_3O$ [$(M+H)^+$], 336.1507; found, 336.1507.

*1-(6-((5-Ethylpyridin-2-yl)methyl)-5-phenyl-2,3-dihydro-1H-pyrrolo[1,2-a]imidazol-7-yl)ethan-1-one (**5c**):* White solid (125 mg, 75%); Mp: 183.9–184.5 °C; IR (KBr) 1617, 1460, 1375, 1361, 701, 644 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.31 (d, J = 1.9 Hz, 1H, NCH), 7.48–7.47 (m, 1H, ArH), 7.40–7.34 (m, 4H, ArH), 7.25 (t, J = 7.3 Hz, 1H, ArH), 7.05 (d, J = 8.0 Hz, 1H, ArH), 6.47 (s, 1H, NH), 4.09–4.05 (m, 4H, $ArCH_2$, NCH_2), 3.91–3.88 (m, 2H, $NHCH_2$), 2.59–2.55 (m, 2H, CH_2CH_3), 2.13 (s, 3H, CH_3), 1.18 (t, J = 7.6 Hz, 3H, CH_2CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ =189.3, 159.8, 153.9, 148.5, 136.0, 135.9, 131.9, 129.0, 128.1, 127.0, 123.4, 122.2, 119.3, 102.3, 48.9, 45.0, 34.5, 29.6, 25.4, 15.8; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{24}N_3O$ [$(M+H)^+$], 346.1914; found, 346.1907.

*7-Nitro-5-phenyl-6-(pyridin-2-ylmethyl)-2,3-dihydro-1H-pyrrolo[1,2-a]imidazole(**5d**):* Yellow solid (72 mg, 45%); Mp: 163.9–164.5 °C; IR (KBr) 1616, 1560, 1361, 699, 643, 610 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.47 (d, J = 4.3 Hz, 1H, NCH), 7.92 (s, 1H, NH), 7.68 (t, J = 7.4 Hz, 1H, ArH), 7.48 (d, J = 7.8 Hz, 2H, ArH), 7.41 (t, J = 7.5 Hz, 2H, ArH), 7.33 (t, J = 7.4 Hz, 1H, ArH), 7.21–7.17 (m, 2H, ArH), 4.16 (s, 2H, $ArCH_2$), 4.13 (d, J = 5.4 Hz, 2H, NCH_2), 4.02 (t, J = 8.8 Hz, 2H, $NHCH_2$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ =161.1, 151.6, 149.3, 136.8, 130.5, 129.2, 128.3, 128.1, 124.2, 122.6, 121.6, 114.5, 113.0, 49.0, 45.4, 33.9; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{17}N_4O_2$ [$(M+H)^+$], 321.1346; found, 321.1339.

*6-((5-Ethylpyridin-2-yl)methyl)-5-(4-fluorophenyl)-7-nitro-2,3-dihydro-1H-pyrrolo[1,2-a]imidazole (**5e**):* Yellow solid (82 mg, 45%); Mp: 179.9–180.3 °C; IR (KBr) 1561, 1617, 1464, 1372,

1361, 697, 646 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 8.33 (s, 1H, NCH), 7.92 (s, 1H, NH), 7.79 (t, J = 8.7 Hz, 1H, ArH), 7.55–7.46 (m, 3H, ArH), 7.41 (s, 1H, ArH), 7.17 (d, J = 8.0 Hz, 1H, ArH), 4.15 (t, 2H, $ArCH_2$), 4.06 (s, 2H, NCH_2), 4.00 (t, J = 8.9 Hz, 2H, $NHCH_2$), 2.60–2.56 (m, 2H, CH_2CH_3), 1.18 (t, J = 7.6 Hz, 3H, CH_2CH_3); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 158.1, 155.0 (d, J = 243.0 Hz), 151.5, 148.7, 136.7, 136.1, 136.2, 125.5, 122.7, 122.1, 118.3 (d, J = 16.5 Hz), 117.6 (d, J = 18.0 Hz), 114.4, 48.9, 45.3, 33.2, 25.4, 15.7; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{20}FN_4O_2$ [$(M+H)^+$], 367.1565; found, 367.1559.

*5-(3,4-Difluorophenyl)-6-((6-methylpyridin-2-yl)methyl)-7-nitro-2,3-dihydro-1H-pyrrolo[1,2-a] -imidazole (**5f**):* Yellow solid (87 mg, 47%); Mp: 170.2–170.5 °C; IR (KBr) 1549, 1617, 1464, 671, 649 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) δ = 7.92 (s, 1H, NH), 7.60–7.54 (m, 3H8, ArH), 7.26 (t, J = 8.7 Hz, 2H, ArH), 7.04 (d, J = 7.6 Hz, 1H, ArH), 6.96 (d, J = 7.7 Hz, 1H, ArH), 4.13 (t, 2H, NCH_2), 4.04–3.99 (m, 4H, $ArCH_2$, $NHCH_2$), 2.44 (s, 3H, $ArCH_3$); $^{13}C\{^1H\}$ NMR (150 MHz, DMSO-d_6) δ = 162.9 (d, J = 243.0 Hz), 161.3 (d, J = 243.0 Hz), 160.3, 157.4, 151.4, 137.2, 130.6 (d, J = 9.0 Hz), 126.9, 123.3, 120.9, 119.3, 119.4, 116.1 (d, J = 21.0 Hz), 114.4, 113.0, 48.9, 45.3, 33.8, 24.6; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{17}F_2N_4O_2$ [$(M+H)^+$], 371.1314; found, 371.1310.

■ ASSOCIATED CONTENT

Supporting Information

Spectroscopic and analytical data as well as the original copy of ^1H and ^{13}C NMR spectra of all new compounds and X-ray crystallographicdata (CIF file) of compound **4a** (CCDC1920258). This material is available free of charge *via* the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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