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Rh(III)-Catalyzed C−H Activation/Cyclization of Indoles and Pyrroles: Divergent Synthesis of Heterocycles

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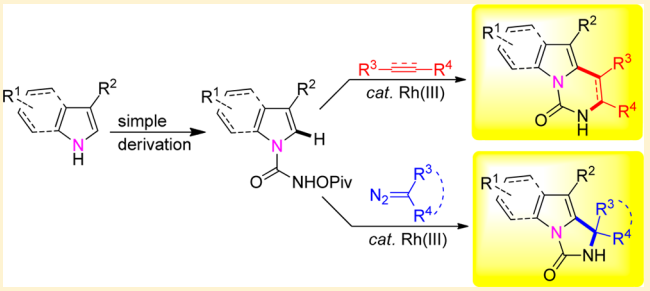
Supporting Information

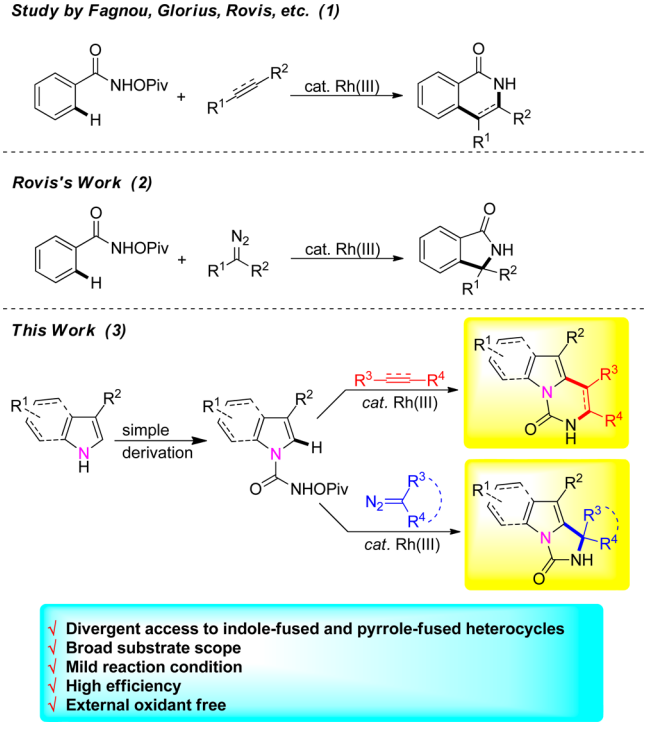
ABSTRACT: We report herein a new strategy of the Rh(III)-catalyzed C−H activation/cyclization of indoles and pyrroles, for the divergent synthesis of privileged heterocycles. A simple derivation of indoles and pyrroles to *N*-carboxamides with oxidative bidentate directing group could enable rhodacycle formation and late-stage redox-neutral cyclization with alkynes, alkenes and diazo compounds, for access to five- and six-membered fused heterocycles, such as pyrimido[1,6-*a*]indol-1(2*H*)-one, 3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one, and 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones. Kinetic isotope effect study was conducted, and a plausible mechanism was proposed. Furthermore, this protocol was applied to concise synthesis of 5-HT3 receptor antagonist in gram-scale.



INTRODUCTION

Indoles and pyrroles are probably the most ubiquitous heterocycles in nature and have been referred as privileged structures in drug discovery,[1] and consequently, there are many powerful methodologies for the synthesis of these scaffolds.[2] Polycyclic indole-fused and pyrrole-fused heterocycles, such as pyrimido[1,6-*a*]indol-1(2*H*)-one, 3,4-dihydropyrimido[1,6-*a*]-indol-1(2*H*)-one, 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one and the pyrrole-containing analogues, are an integral part of many biologically active natural molecules and synthetic compounds, drugs (Figure 1), acting as fluorescent material, antihypertensive agent, 5-HT_3 receptor antagonist, CNS depressant, etc.[3] Construction of these polycyclic heterocycles either requires multistep synthesis or suffers from narrow substrate scope.[4] Therefore, the development of new approaches that allow rapid establishment of these scaffolds in simple operation from readily available precursors remains challenge and importance.

Recently, the Rh(III)-catalyzed functionalization of aryl C−H bond has enjoyed tremendous advance owing to their wide applications to the rapid assembly of various complex molecular structures, particular in the fields of medicinal chemistry.[5,6] The pioneering works on Rh(III)-catalyzed C−H/O−H and C−H/N−H cyclizations were reported by Miura and Satoh, Fagnou and Jones.[7] Particularly, Rh(III)-catalyzed cyclization of benzamides has been well developed by Fagnou, Glorius, Rovis and so on, to access various nitrogen-containing heterocycles with the fashion of external oxidant free (eq 1).[8] These protocols involve a sequence of C−H activation of benzamides to generate rhodacycles and subsequent annulation reaction with alkenes, alkynes and allenes, etc. More recently, Rovis established a coupling of benzamides and donor/acceptor diazo compounds to form γ-lactams via Rh(III)-catalyzed C−H activation (eq 2).[9]



Indoles and pyrroles have been popular molecules in transition-metal catalyzed C−H functionalization owing to their numerous biological activities,[10−13] despite this fact, unique C−H functionalization for these compounds toward new heterocycle skeletal construction still remains rare. In

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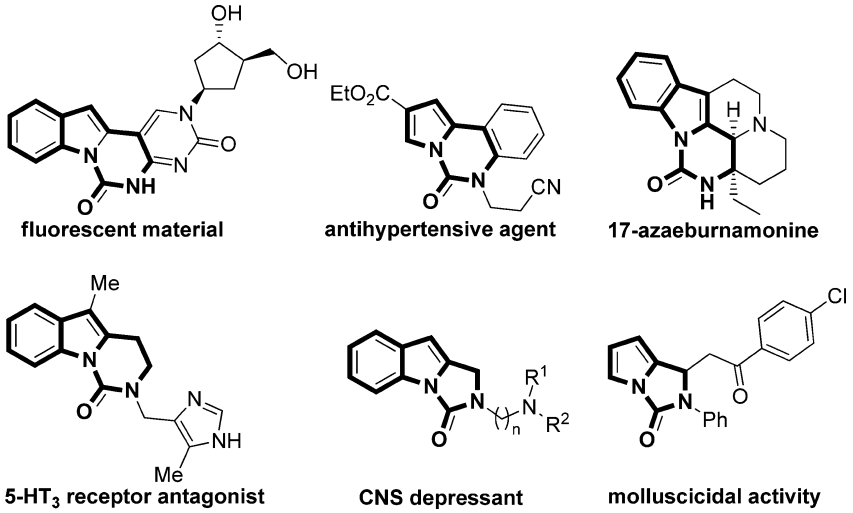


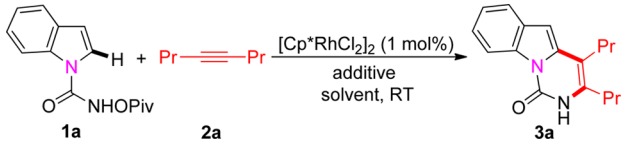
Figure 1. Selected examples of natural products and pharmaceuticals containing polycyclic indole-fused and pyrrole-fused heterocycles.

continuation of our interest in Rh(III)-catalyzed C−H functionalization toward biologically interesting small molecule synthesis,[14] we proposed that a simple derivation of indoles and pyrroles to their *N*-carboxamide derivatives as oxidative bidentate directing group could enable a Rh(III)-catalyzed C−H activation of indoles and pyrroles at 2-position, and a further coupling with various alkynes, alkenes and diazo compounds would deliver interesting heterocycles. Herein, we wish to report a divergent synthesis of heterocycles via Rh(III)-catalyzed C−H activation/cyclization of indoles and pyrroles (eq 3).

RESULTS AND DISCUSSION

We initially commenced our study by investigating *N*-(pivaloyloxy)-1*H*-indole-1-carboxamide **1a** and 4-octyne **2a**, with $[Cp^*RhCl_2]_2$ as catalyst and MeOH as solvent. However, no new products were observed, and the starting materials were recovered (Table 1, entry 1). To our delight, the addition of equivalent amount of NaOAc resulted in a formation of cyclic pyrimido[1,6-*a*]indol-1(2*H*)-one product **3a** in 87% yield (Table 1, entry 2), and this was attributed to a C−H activation/cyclization of **1a**. The result encouraged us to further optimize the reaction condition. Variation of additives showed that KOAc led to the formation of product in a slightly lower yield (Table 1, entry 3), while CsOAc was superior to afford the product in 93% yield (Table 1, entry 4). Replacing CsOAc with CsOPiv gave a comparable yield (Table 1, entry 5). Further screening of solvents revealed that EtOH, TFE and CH_3CN were inferior to MeOH (Table 1, entries 6−8).

Table 1. Optimization of Reaction Conditions[a]



entry	solvent	additive	yield (%)[b]
1	MeOH	none	0
2	MeOH	NaOAc (1 equiv)	87
3	MeOH	KOAc (1 equiv)	83
4	**MeOH**	**CsOAc (1 equiv)**	**93**
5	MeOH	CsOPiv (1 equiv)	90
6	EtOH	CsOAc (1 equiv)	80
7	TFE[c]	CsOAc (1 equiv)	51
8	CH_3CN	CsOAc (1 equiv)	37

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.4 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), additive, solvent (2 mL), at rt for 8 h. [b]Isolated yield. [c]TFE = trifluoroethanol.

With the optimized reaction condition in hand, we next investigated the generality of this scope for pyrimido[1,6-*a*]indol-1(2*H*)-one synthesis. As shown in Table 2, both symmetrical and unsymmetrical alkynes with valuable functional groups such as hydroxyl, ester, could proceed smoothly in this transformation to provide the corresponding pyrimido-[1,6-*a*]indol-1(2*H*)-one products in good to excellent yields (**3a**−**3h**, 50−95%). Moreover, the insertion of an aryl-alkyl disubstituted alkyne occurred regioselectively with the sp^2 center being installed at the 3-position (**3d** and **3e**). The reaction was also compatible with terminal alkynes with terminal end being located at the 4-position (**3f**−**3h**), except for that *n*-hexyne was used to afford a mixture of regioisomers (**3i** and **3j**). A variety of *N*-carboxamides of indoles were also well applicable to access diverse pyrimido[1,6-*a*]indol-1(2*H*)-ones. For example, the *N*-carboxamides derived from 5-methylindole, 5-methoxyindole, 4-benzyloxyindole and 3-methylindole could proceed efficiently to generate polysubstituted privileged pyrimido[1,6-*a*]indol-1(2*H*)-ones in good to excellent yields (**3k**−**3q**, 68−97%). The *N*-(pivaloyloxy)-1*H*-pyrrole-1-carboxamide **1g** was also employed in this Rh(III)-catalyzed C−H activation/cyclization process to construct pyrrolo[1,2-*c*]pyrimidin-1(2*H*)-ones in good to excellent yields (**3r**−**3v**, 64−98%), which usually required multistep synthesis in traditional methods. Moreover, the structure of **3f** was unambiguously confirmed by single X-ray analysis (see Supporting Information), identical to characterization. Considering the wealth of these pyrimido[1,6-*a*]indol-1(2*H*)-ones in pharmaceuticals, this process represents a simple and straightforward entry to these compounds with ample structural diversity.

Since alkenes were another ideal coupling partners in Rh(III)-catalyzed C−H activation/cyclization, this scope was extended by investigating the use of alkenes under the standard reaction condition (Table 3). Gratifyingly, alkenes performed well in this reaction to deliver the partially saturated 3,4-

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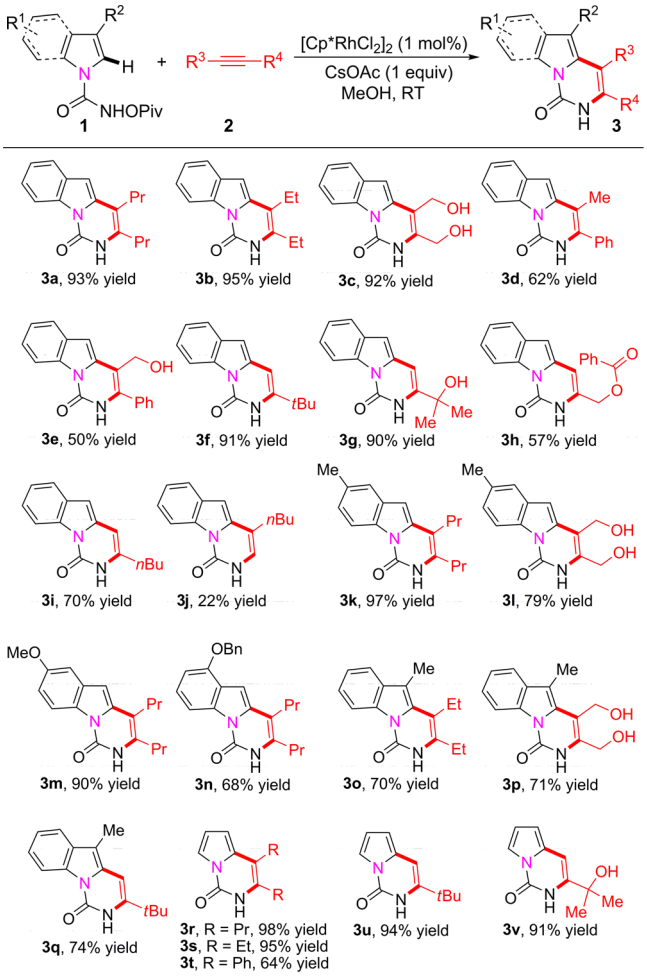
Table 2. Rh(III)-Catalyzed Synthesis of Pyrimido[1,6-*a*]indol-1(2*H*)-one[a]



[a]Reaction conditions: **1** (0.2 mmol), **2** (0.4 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), CsOAc (0.2 mmol), MeOH (2 mL), at rt for 2−5 h, isolated yields.

dihydropyrimido[1,6-*a*]indol-1(2*H*)-ones, contrary to related systems where *β*-hydride elimination occurred giving rise to Heck-type adducts.[10b] Interestingly, the unsubstituted 3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-ones can be synthesized at ambient pressure using a balloon of ethylene gas (**5a**, **5f**, **5h**, **5j**, **5k**, **5n**, **5o**). The reaction tolerated with valuable functional groups, such as ester, cyano, hydroxyl, thus offering ample opportunities for further derivation. When the unsymmetrical alkenes participated, the products formed with regioselectivity ranging from 5.9:1 (**5p**) to >20:1 (**5l** and **5m**). Moreover, the structure of **5k** was unambiguously confirmed by single X-ray analysis (see Supporting Information), in addition to standard characterization. It should be noted that 3,4-dihydropyrimido-[1,6-*a*]indol-1(2*H*)-one represents core structure of various biologically interesting scaffolds, and this synthetic method makes a direct access toward the construction of these compounds.

With these results in hand, we next tried to extend the divergent synthesis scope of this transformation using diazo compounds to deliver interesting heterocycles. Considering that this Rh(III)-catalyzed transformation of *N*-carboxamides of indoles and pyrroles includes the formation of rhodacycles intermediate, we postulated that the rhodium species could be captured by diazo compounds for insertion.[9,14b] By slightly changing the reaction condition using CH_3CN as solvent, the reaction performed smoothly at room temperature to furnish the polycyclic 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-ones in moderate to excellent yields (Table 4, 49−93%). As shown in Table 4, donor/acceptor diazo compounds were broadly tolerated with reasonable scope. Differential substitution on the ester gave the corresponding products in high yields (**7a**−**7d**), and a wide range of substituents on the aromatic ring were tolerated (**7e**−**7h**), with valuable functional group, such as chloro, bromo, ester, nitro. When alkyl substituted diazo was used, the reaction condition should be slightly elevated by increasing the temperature to 50 °C (**7i**). Interestingly, the cyclic diazo substrate delivered the spiro oxindole-fused products in good yields (**7j**). Differentially substituted indole and pyrrole derived *N*-carboxamides were well applicable to furnish the polysubstituted products in good yields (**7k**−**7u**) with extraordinary structural diversities, and definitely would facilitate the process in drug discovery. Moreover, the structure of **7a** was confirmed by X-ray analysis (see Supporting Information).

A practical synthesis of 5-HT_3 receptor antagonist was also carried out to demonstrate the synthetic utility of this protocol (Scheme 1). Under the standard reaction condition, 3,4-dihydro pyrimido[1,6-*a*]indol-1(2*H*)-one **5k** was obtained in simple operation. **5k** was then converted to **8** and a subsequent deprotection of **8** soon led to the formation of 5-HT_3 receptor antagonist **9** in gram-scale. Obviously, this strategy opens a new avenue to this pharmaceuticals synthesis with readily available starting materials and high efficiency, and therefore could be applied to divergent synthesis of 5-HT_3 receptor antagonist.

Considering this Rh(III)-catalyzed divergent synthesis includes a C−H activation step, kinetic isotope effect (KIE) study was conducted to probe the mechanism. As shown in Scheme 2, a deuterium labeled [**D**]-**1a** was synthesized with 83% D incorporation and was subject to the parallel experiments. A primary KIE value (1.44) was obtained, suggesting that C−H bond cleavage occurs during the rate-determining step.[15]

On the basis of these experiments and literature precedents,[8,16] a plausible mechanism for this divergent synthesis was proposed in Scheme 3. The initial rhodium dicarboxylate was generated from $[Cp^*RhCl_2]_2$ and CsOAc, and a carboxylate-assisted C−H activation of *N*-carboxamides of indoles and pyrroles **1** occurred via a concerted metalation/deprotonation (CMD) pathway to form rhodacycle A.[17] A shows divergent reactivity: (1) In the presence of alkynes and alkenes, A is coordinated with alkynes **2** or alkenes **4** to give complex B. The subsequent insertion delivers rhodium species C. Then a C−N bond formation takes place to afford D along with N−O bond cleavage. The final step is protonation of D to furnish pyrimido[1,6-*a*]indol-1(2*H*)-one **3** or 3,4-dihydropyrimido[1,6-*a*]indol-1(2*H*)-one **5** with concomitant Rh(III) catalysis regeneration; (2) In the presence of diazo compounds **6**, a diazo insertion occurs with extrusion of N_2 to form Rh-carbene E, which would undergo a 1,1-migratory insertion to generate rhodium species F.[9,14b] Then a C−N bond formation takes place to afford G along with N−O bond cleavage. Finally, G is protonated to furnish the 1*H*-imidazo-[1,5-*a*]indol-3(2*H*)-one product **7** with regeneration of Rh(III) catalysis.

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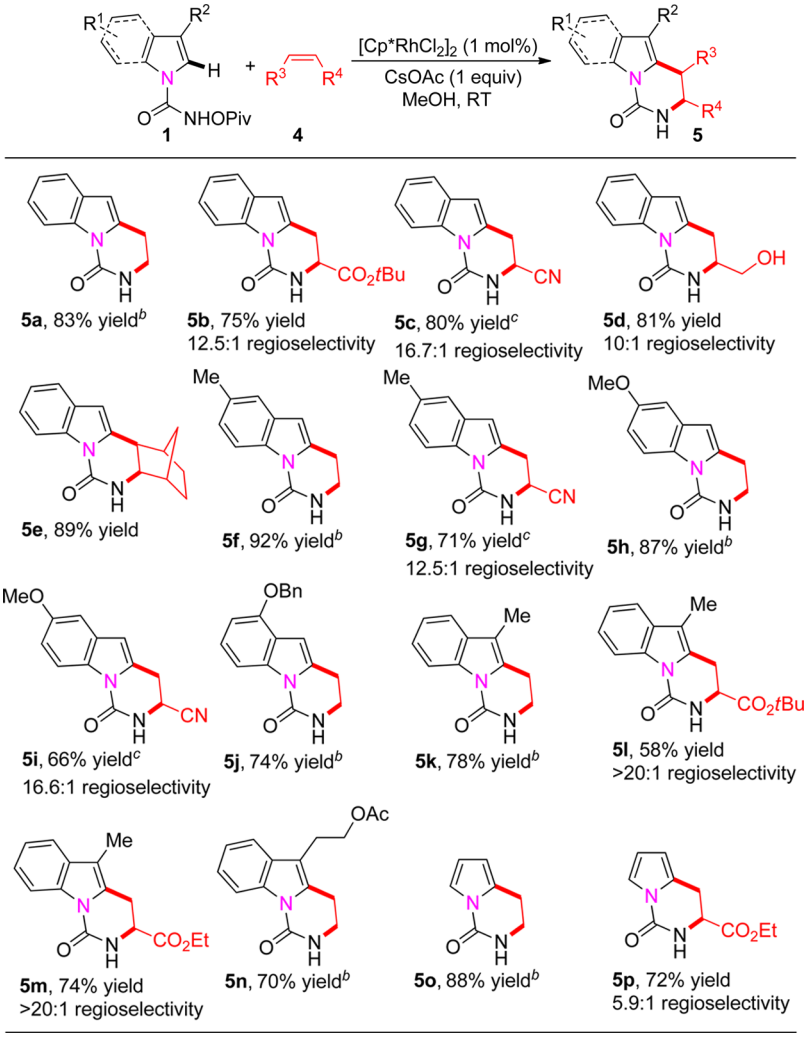
Table 3. Rh(III)-Catalyzed Synthesis of 3,4-Dihydropyrimido[1,6-*a*]indol-1(2*H*)-one[a]



[a]Reaction conditions: **1** (0.2 mmol), **4** (0.4 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), CsOAc (0.2 mmol), MeOH (2 mL), at rt for 2−5 h, isolated yield, regioselectivity determined by ^1H NMR of isolated products. [b]Balloon of ethylene gas was used. [c]Run at 50 °C for 14 h.

CONCLUSION

In summary, we have established divergent synthesis of heterocycles, via Rh(III)-catalyzed C−H activation/cyclization of indoles and pyrroles to couple with various alkynes, alkenes and diazo compounds. This protocol makes a feature of readily available starting materials, mild reaction condition, broad substrate scope and external oxidant free. KIE study was conducted and a plausible mechanism was proposed. Furthermore, this protocol was applied to a concise synthesis of 5-HT_3 receptor antagonist in gram-scale.

EXPERIMENTAL SECTION

Infrared spectra were obtained on a FTIR spectrometer. ^1H NMR and ^{13}C NMR spectra were recorded on 500 or 400 NMR machine. HRMS were performed on TOF LC−MS apparatus (ESI). Melting points were measured with micro melting point apparatus.

Typical Procedure for Synthesis of 3. $[Cp^*RhCl_2]_2$ (1.3 mg, 1 mol %), *N*-(pivaloyloxy)-1*H*-indole-1-carboxamide **1a** (52 mg, 0.2 mmol), CsOAc (38.4 mg, 0.2 mmol) were added to a vial. MeOH (2 mL) was added, followed by addition of 4-octyne **2a** (58.5 μL, 0.4 mmol). The mixture was kept at room temperature under air. After completion within 5 h, it was diluted with CH_2Cl_2 and transferred to a round-bottom flask. Silica was added to the flask, and volatiles were evaporated under a vacuum. The purification was performed by flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:6) as eluent to give pyrimido[1,6-*a*]indol-1(2*H*)-one product **3a** as a yellow solid (49.8 mg, 93% yield).

Typical Procedure for Synthesis of 5. $[Cp^*RhCl_2]_2$ (1.3 mg, 1 mol %), *N*-(pivaloyloxy)-1*H*-indole-1-carboxamide **1a** (52 mg, 0.2 mmol), CsOAc (38.4 mg, 0.2 mmol) were added to a vial. MeOH (2 mL) was added, followed by addition of *t*-butyl acrylate **2b** (58 μL, 0.4 mmol). The mixture was kept at room temperature under air. After completion within 5 h, it was diluted with CH_2Cl_2 and transferred to a round-bottom flask. Silica was added to the flask and volatiles were evaporated under a vacuum. The purification was performed by flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:2) as eluent to give **5b** as a yellow solid (42.9 mg, 75% yield).

Typical Procedure for Synthesis of 7. $[Cp^*RhCl_2]_2$ (1.3 mg, 1 mol %), *N*-(pivaloyloxy)-1*H*-indole-1-carboxamide **1a** (52 mg, 0.2 mmol), CsOAc (38.4 mg, 0.2 mmol) were added to a vial. CH_3CN (2 mL) was added, followed by addition of diazo compound **6a** (70.4 mg, 0.4 mmol). The mixture was kept at room temperature under air. After completion within 5 h, it was diluted with CH_2Cl_2 and transferred to a round-bottom flask. Silica was added to the flask, and volatiles were evaporated under a vacuum. The purification was performed by flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:5) as eluent to give **7a** as a yellow solid (55.7 mg, 91% yield).

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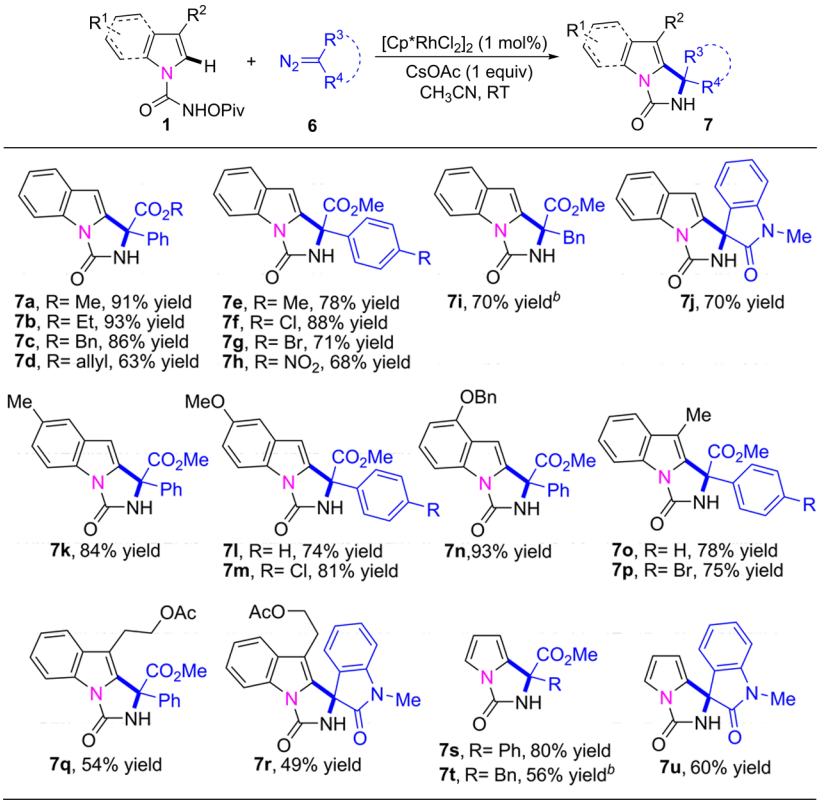
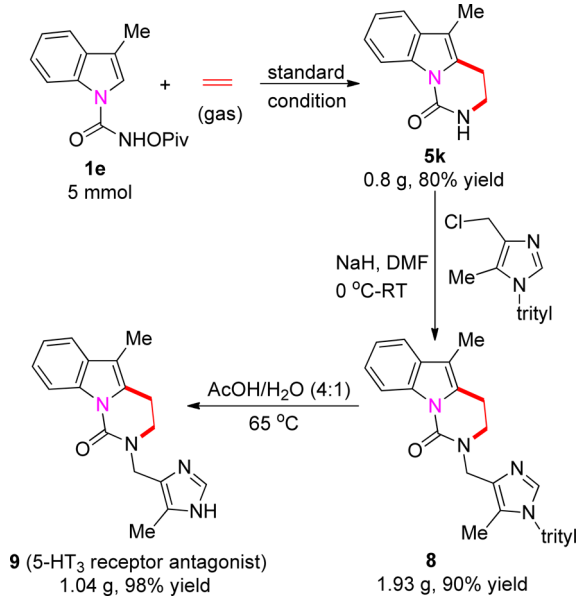
Table 4. Rh(III)-Catalyzed Synthesis of 1*H*-imidazo[1,5-*a*]indol-3(2*H*)-one[a]

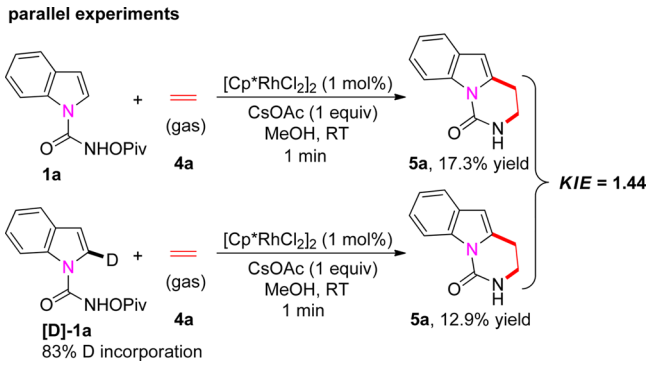


[a]Reaction conditions: **1** (0.2 mmol), **6** (0.4 mmol), $[Cp^*RhCl_2]_2$ (1 mol %), CsOAc (0.2 mmol), CH_3CN (2 mL), at rt for 3−5 h, isolated yield. [b]Run at 50 °C for 8 h.

Scheme 1. Practical Synthesis of 5-HT_3 Receptor Antagonist



Scheme 2. Kinetic Isotope Effect Study



Synthesis of 5-HT_3 Receptor Antagonist 9. $[Cp^*RhCl_2]_2$ (31 mg, 1 mol %), 3-methyl-*N*-(pivaloyloxy)-1*H*-indole-1-carbox-amide **1e** (1.37 g, 5 mmol) and CsOAc (0.96 g, 5 mmol) were added to two necked flask, which was then evacuated and backfilled with balloon of ethylene gas. MeOH (30 mL) was added, and the solution was kept at rt to be completed within 3 h. The solution was concentrated and subject to flash column chromatography on silica gel using ethyl acetate/petroleum ether (v/v, 1:2) as eluent to give **5k** as a yellow solid (0.8 g, 80% yield). A 100 mL three-necked flask with a stir-bar was charged with NaH (0.32 g, 8 mmol), which was then evacuated and backfilled with Argon for three times. Anhydrous DMF (30 mL) was added, and the solution was cooled to 0 °C. Then DMF solution (5 mL) of **5k** (0.8 g, 4 mmol) was added dropwise to the reaction solution over 30 min and kept at that temperature for another 30 min. Afterward, it was warmed to 50 °C and kept for 2 h. The reaction solution was cooled to 0 °C, and DMF solution (5 mL) of 4-(chloromethyl)-5-methyl-1-trityl-1*H*-imidazole (1.488 g, 4 mmol) was added. Afterward, the solution was warmed to 50 °C and kept for 1 h. The reaction mixture was then diluted with H_2O (100 mL) to give a precipitate. The precipitate collected was dissolved in CH_2Cl_2. The organic layer was washed with H_2O and brine, dried over $MgSO_4$, and evaporated in vacuo. The residue was subject to column chromatography on silica gel (2% MeOH−CH_2Cl_2) to get **8** (1.93 g, 90%) as white solid. A solution of **8** (1.93 g, 3.6 mmol) in AcOH−H_2O (4:1, 50 mL) was heated at 65 °C for 8 h. After evaporation of the solvent, the residue was neutralized with aqueous $NaHCO_3$ solution and extracted with CH_2Cl_2. The organic layer was washed with H_2O and

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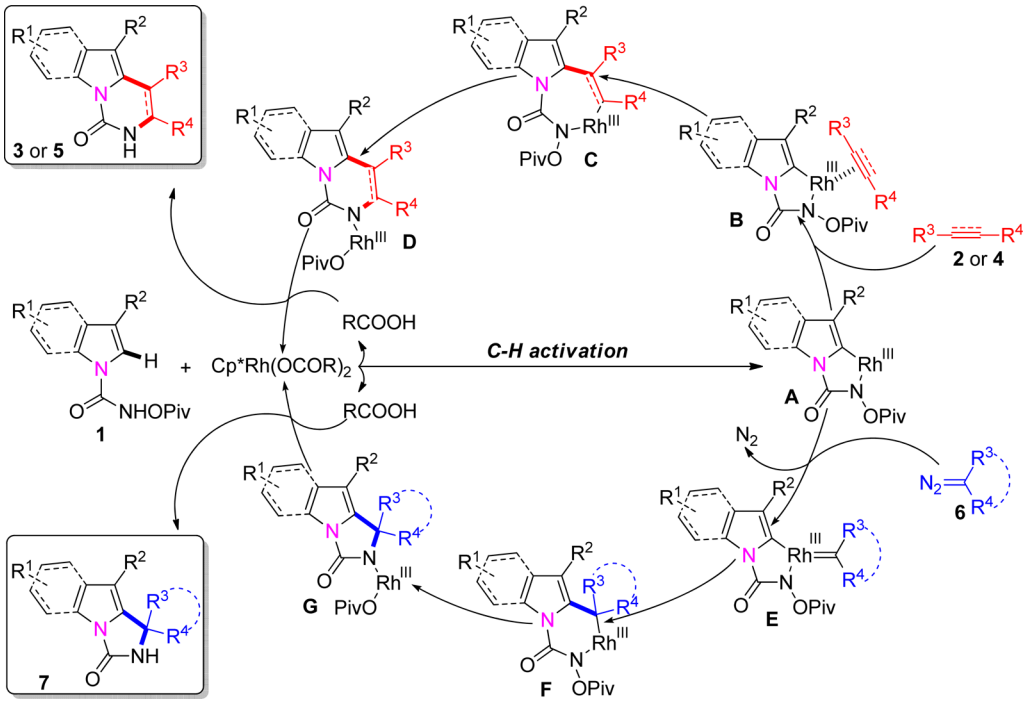
Scheme 3. Proposed Mechanism



brine, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (5% MeOH−CH_2Cl_2) to give the product **9** as white solid (1.04 g, 98% yield).

*3,4-Dipropylpyrimido[1,6-a]indol-1(2H)-one (**3a**).* Yellow solid (93% yield, 50 mg): mp 182−184 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.42 (s, 1H), 8.67 (d, J = 8.0 Hz, 1H), 7.66 (d, J = 7.2 Hz, 1H), 7.39−7.26 (m, 2H), 6.50 (s, 1H), 2.64−2.59 (m, 4H), 1.87−1.81 (m, 2H), 1.73−1.67 (m, 2H), 1.13 (t, J = 7.2 Hz, 3H), 1.05 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.1, 138.1, 134.2, 133.0, 130.9, 123.8, 121.9, 119.6, 116.1, 108.0, 96.1, 31.7, 29.2, 22.9, 22.2, 14.4, 14.1; IR (KBr) ν 3214, 3111, 2962, 2871, 1686, 1643, 1616, 1605, 1578, 1554, 1451, 1407, 1379, 1200, 782, 737 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{17}H_{20}N_2O$ ([M + H]$^+$), 269.1649, found 269.1647.

*3,4-Diethylpyrimido[1,6-a]indol-1(2H)-one (**3b**).* Yellow solid (95% yield, 45.6 mg): mp 217−219 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.91 (s, 1H), 8.64 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 8.0 Hz, 1H), 7.38−7.30 (m, 2H), 6.51 (s, 1H), 2.64 (q, J = 7.6 Hz, 4H), 1.38 (t, J = 7.6 Hz, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.9, 137.7, 134.9, 133.2, 131.0, 123.8, 122.1, 119.6, 116.1, 109.0, 96.0, 23.0, 20.3, 14.4, 13.5; IR (KBr) ν 3215, 3112, 2963, 1698, 1643, 1602, 1578, 1555, 1450, 1380, 1206, 825, 783, 756, 745 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O$ ([M + H]$^+$), 241.1336, found 241.1337.

*3,4-Bis(hydroxymethyl)pyrimido[1,6-a]indol-1(2H)-one (**3c**).* Gray solid (92% yield, 44.9 mg): mp 143−145 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.59 (s, 1H), 8.51 (d, J = 8.4 Hz, 1H), 7.67 (d, J = 7.2 Hz, 1H), 7.34−7.24 (m, 2H), 6.74 (s, 1H), 5.26 (t, J = 6.0 Hz, 1H), 4.96 (t, J = 5.6 Hz, 1H), 4.54 (d, J = 5.2 Hz, 2H), 4.43 (d, J = 5.6 Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz), δ 147.7, 137.1, 136.1, 132.2, 130.3, 123.4, 121.7, 119.6, 115.3, 107.7, 96.5, 56.6, 55.4; IR (KBr) ν 2962, 2926, 2855, 1694, 1652, 1449, 1377, 1261, 1094, 1026. 803 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{13}H_{12}N_2O_3$ ([M + H]$^+$), 245.0921, found 245.0921.

*4-Methyl-3-phenylpyrimido[1,6-a]indol-1(2H)-one (**3d**).* Pale green solid (62% yield, 34 mg): mp 255−257 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.91 (s, 1H), 8.56 (d, J = 7.6 Hz, 1H), 7.69 (d, J = 7.2 Hz, 1H), 7.52−7.46 (m, 5H), 7.36−7.28 (m, 2H), 6.68 (s, 1H), 2.09 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 147.7, 138.1, 134.0, 133.1, 132.5, 130.2, 129.5, 128.9, 128.3, 123.5, 121.9, 119.7, 115.4, 102.7, 96.7, 13.0; IR (KBr) ν 3205, 3112, 1694, 1654, 1630, 1601, 1450, 1406, 1367, 768, 732, 700 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{14}N_2O$ ([M + H]$^+$), 275.1179, found 275.1178.

*4-(Hydroxymethyl)-3-phenylpyrimido[1,6-a]indol-1(2H)-one (**3e**).* White solid (50% yield, 29 mg): mp 235−237 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.98 (s, 1H), 8.57 (d, J = 8.4 Hz, 1H), 7.72−7.51 (m, 6H), 7.37−7.28 (m, 2H), 6.84 (s, 1H), 5.18 (t, J = 5.2 Hz, 1H), 4.36 (d, J = 5.2 Hz, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 147.6, 137.1, 136.2, 132.4, 132.2, 130.4, 129.3, 128.2, 123.5, 121.8, 119.7, 115.3, 107.6, 97.1, 56.9; IR (KBr) ν 3345, 3187, 1690, 1630, 1602, 1575, 1452, 1408, 1210, 770, 758, 745 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{14}N_2O_2$ ([M + H]$^+$), 291.1128, found 291.1129.

*3-(tert-Butyl)pyrimido[1,6-a]indol-1(2H)-one (**3f**).* Gray solid (91% yield, 43.7 mg): mp 240−242 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.23 (s, 1H), 8.85 (d, J = 7.6 Hz, 1H), 7.65 (d, J = 8.4 Hz, 1H), 7.34−7.38 (m, 2H), 6.49 (s, 1H), 6.29 (d, J = 1.6 Hz, 1H), 1.47 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.3, 146.5, 136.2, 132.7, 131.2, 123.9, 122.1, 119.7, 116.0, 97.2, 93.7, 34.5, 28.6; IR (KBr) ν 3213, 3118, 2965, 1693, 1645, 1605, 1578, 1557, 1398, 1081, 820, 770 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O$ ([M + H]$^+$), 241.1336, found 241.1335.

*3-(2-Hydroxypropan-2-yl)pyrimido[1,6-a]indol-1(2H)-one (**3g**).* Gray solid (90% yield, 43.6 mg): mp 176−178 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.03 (s, 1H), 8.60−8.58 (m, 1H), 7.62−7.60 (m, 1H), 7.38−7.31 (m, 2H), 6.35 (s, 1H), 6.18 (d, J = 1.6 Hz, 1H), 2.88 (s, 1H), 1.65 (s, 6H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 149.3, 143.1, 135.3, 132.8, 131.0, 124.0, 122.5, 119.8, 116.0, 98.3, 93.8, 70.5, 29.3; IR (KBr) ν 3555, 3211, 3111, 2963, 1691, 1646, 1606, 1579, 1560, 1449, 1397, 1352, 1192, 834, 779, 756 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{14}H_{14}N_2O_2$ ([M + H]$^+$), 243.1128, found 243.1128.

*(1-Oxo-1,2-dihydropyrimido[1,6-a]indol-3-yl)methyl benzoate (**3h**).* White solid (57% yield, 36.2 mg): mp 209−211 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 11.17 (s, 1H), 8.52 (d, J = 8.8 Hz, 1H), 8.06−8.04 (m, 2H), 7.71−7.67 (m, 2H), 7.58−7.54 (m, 2H), 7.33−7.29 (m, 2H), 6.73 (s, 1H), 6.68 (s, 1H), 5.14 (s, 2H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 165.3, 148.0, 135.3, 133.6, 133.4, 132.3, 130.2, 129.5, 129.3, 128.8, 123.6, 122.1, 119.8, 115.3, 98.0, 97.9, 62.5; IR (KBr) ν 3210, 3104, 2966, 1701, 1652, 1561, 1449, 1389, 1269, 1096, 781, 719, 707 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{14}N_2O_3$ ([M + H]$^+$), 319.1077, found 319.1078.

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3-Butylpyrimido[1,6-a]indol-1(2H)-one (**3i**). Brown solid (70% yield, 33.6 mg): mp 170−172 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.33 (s, 1H), 8.63 (d, J = 8.0 Hz, 1H), 7.64 (d, J = 7.2 Hz, 1H), 7.37−7.32 (m, 2H), 6.44 (s, 1H), 6.19 (s, 1H), 2.58 (t, J = 7.6 Hz, 2H), 1.83−1.74 (m, 2H), 1.54−1.48 (m, 2H), 1.02 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.4, 138.9, 136.2, 132.8, 131.1, 123.9, 122.0, 119.6, 116.0, 96.6, 96.5, 32.7, 29.9, 22.4, 13.9; IR (KBr) ν 3206, 2956, 1701, 1651, 1618, 1606, 1577, 1451, 1402, 817, 777, 755 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O$ ([M + H]$^+$), 241.1336, found 241.1333.

4-Butylpyrimido[1,6-a]indol-1(2H)-one (**3j**). Brown solid (22% yield, 10.6 mg): mp 150−152 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.94 (d, J = 3.6 Hz, 1H), 8.71−8.69 (m, 1H), 7.69−7.67 (m, 1H), 7.40−7.36 (m, 2H), 6.59 (m, 2H), 2.56 (t, J = 7.2 Hz, 2H), 1.72−1.64 (m, 2H), 1.48−1.39 (m, 2H), 0.97 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.8, 137.0, 133.2, 130.4, 123.9, 122.6, 120.6, 119.9, 116.2, 112.5, 97.2, 30.4, 28.7, 22.6, 14.0; IR (KBr) ν 3211, 3103, 2955, 1696, 1651, 1561, 1451, 1400, 1206, 796, 772 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O$ ([M + H]$^+$), 241.1336, found 241.1337.

7-Methyl-3,4-dipropylpyrimido[1,6-a]indol-1(2H)-one (**3k**). Yellow solid (97% yield, 54.7 mg): mp 202−204 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.08 (s, 1H), 8.50 (d, J = 8.4 Hz, 1H), 7.42 (s, 1H), 7.14 (dd, J_1 = 8.4 Hz, J_2 = 1.6 Hz, 1H), 6.41 (s, 1H), 2.59 (t, J = 7.2 Hz, 4H), 2.51 (s, 3H), 1.84−1.78 (m, 2H), 1.71−1.65 (m, 2H), 1.10 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.9, 138.1, 133.9, 133.3, 131.3, 131.2, 123.5, 119.3, 115.7, 108.0, 95.8, 31.7, 29.2, 22.9, 22.2, 21.8, 14.4, 14.1; IR (KBr) ν 3215, 3104, 2961, 2871, 1703, 1638, 1617, 1578, 1554, 1371, 1262, 1096, 1031, 798 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{22}N_2O$ ([M + H]$^+$), 283.1805, found 283.1805.

3,4-Bis(hydroxymethyl)-7-methylpyrimido[1,6-a]indol-1(2H)-one (**3l**). Yellow solid (79% yield, 41 mg): mp 185−187 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.52 (s, 1H), 8.37 (d, J = 8.4 Hz, 1H), 7.44 (s, 1H), 7.10−7.07 (m, 1H), 6.65 (s, 1H), 5.27 (s, 1H), 4.95 (s, 1H), 4.53 (s, 2H), 4.42 (s, 2H), 2.43 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 147.6, 137.1, 135.9, 132.4, 130.5, 123.2, 119.3, 114.9, 107.7, 96.1, 56.5, 55.4, 21.3; IR (KBr) ν 3320, 2958, 1686, 1644, 1617, 1575, 1400, 1045, 1008, 802 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{14}H_{14}N_2O_3$ ([M + H]$^+$), 259.1077, found 259.1080.

7-Methoxy-3,4-dipropylpyrimido[1,6-a]indol-1(2H)-one (**3m**). Brown solid (90% yield, 53.6 mg): mp 195−196 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 10.51 (br, s, 1H), 8.52 (d, J = 8.8 Hz, 1H), 7.09 (d, J = 2.4 Hz, 1H), 6.94 (dd, J_1 = 9.2 Hz, J_2 = 2.0 Hz, 1H), 6.42 (s, 1H), 3.90 (s, 3H), 2.59 (m, 4H), 1.85−1.79 (m, 2H), 1.71−1.65 (m, 2H), 1.11 (t, J = 7.2 Hz, 3H), 1.04 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 156.7, 149.9, 138.8, 134.3, 131.9, 127.8, 116.8, 111.2, 107.9, 101.6, 95.8, 55.7, 31.7, 29.2, 22.9, 22.2, 14.4, 14.1; IR (KBr) ν 3209, 3104, 2956, 2871, 1687, 1640, 1614, 1585, 1548, 1479, 1439, 1376, 1262, 1093, 1033, 804 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{22}N_2O_2$ ([M + H]$^+$), 299.1754, found 299.1754.

6-(Benzyloxy)-3,4-dipropylpyrimido[1,6-a]indol-1(2H)-one (**3n**). Yellow solid (68% yield, 51 mg): mp 248−249 °C; ^{1}H NMR (400 MHz, DMSO-d_6), δ 10.62 (s, 1H), 8.10 (d, J = 8.4 Hz, 1H), 7.54−7.35 (m, 5H), 7.15 (t, J = 8.0 Hz, 1H), 6.93 (d, J = 7.6 Hz, 1H), 6.54 (s, 1H), 5.27 (s, 2H), 2.54 (t, J = 7.2 Hz, 2H), 2.44 (t, J = 7.2 Hz, 2H), 1.59 (sext, J = 7.2 Hz, 4H), 0.96 (quint, J = 7.2 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6), δ 150.6, 147.9, 137.2, 136.6, 134.8, 133.4, 128.4, 127.8, 127.7, 122.2, 121.0, 108.6, 106.3, 105.0, 92.0, 69.3, 30.3, 28.1, 22.5, 21.9, 13.9, 13.5; IR (KBr) ν 3435, 3215, 3113, 2961, 1700, 1641, 1498, 1364, 1266, 1044, 768, 693 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{24}H_{26}N_2O_2$ ([M + Na]$^+$), 397.1896, found 397.1892.

3,4-Diethyl-5-methylpyrimido[1,6-a]indol-1(2H)-one (**3o**). White solid (70% yield, 35.6 mg): mp 222−224 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.15 (s, 1H), 8.65 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 7.2 Hz, 1H), 7.40−7.31 (m, 2H), 2.78 (q, J = 7.6 Hz, 2H), 2.60 (q, J = 7.6 Hz, 2H), 2.57 (s, 3H), 1.34 (t, J = 7.6 Hz, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 149.7, 134.0, 132.4, 132.3, 123.4, 122.5, 117.5, 116.1, 109.9, 105.0, 100.1, 22.9, 19.7, 13.6, 10.0; IR (KBr) ν 3223, 3128, 2963, 1695, 1654, 1631, 1452, 1420, 1371, 1261, 1097, 1030, 802, 751 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{16}H_{18}N_2O$ ([M + Na]$^+$), 277.1311, found 277.1306.

3,4-Bis(hydroxymethyl)-5-methylpyrimido[1,6-a]indol-1(2H)-one (**3p**). Yellow solid (71% yield, 36.6 mg): mp 230−232 °C; ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.42 (s, 1H), 8.52 (d, J = 8.0 Hz, 1H), 7.65 (d, J = 7.6 Hz, 1H), 7.36−7.25 (m, 2H), 5.26 (t, J = 5.6 Hz, 1H), 4.97 (t, J = 5.2 Hz, 1H), 4.59 (d, J = 5.2 Hz, 2H), 4.42 (d, J = 5.6 Hz, 2H), 2.56 (s, 3H); ^{13}C NMR (DMSO-d_6, 400 MHz) δ 147.8, 135.8, 131.9, 131.6, 131.4, 123.0, 121.9, 117.6, 115.2, 108.3, 105.2, 56.6, 54.4, 8.9; IR (KBr) ν 3358, 2962, 1684, 1654, 1635, 1617, 1547, 1458, 1383, 1263, 1004, 804 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{14}H_{14}N_2O_3$ ([M + H]$^+$), 259.1077, found 259.1074.

3-(tert-Butyl)-5-methylpyrimido[1,6-a]indol-1(2H)-one (**3q**). White solid (74% yield, 37.6 mg): mp 226−228 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.44 (s, 1H), 8.61−8.59 (m, 1H), 7.60−7.58 (m, 1H), 7.41−7.31 (m, 2H), 6.21 (d, J = 2.0 Hz, 1H), 2.38 (s, 3H), 1.44 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.0, 145.1, 132.3, 132.1, 131.9, 123.5, 122.2, 117.7, 115.8, 104.9, 91.9, 34.4, 28.7, 8.4; IR (KBr) ν 3223, 3123, 2967, 1781, 1693, 1651, 1605, 1482, 1455, 1378, 1262, 1081, 813, 749 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{16}H_{18}N_2O$ ([M + Na]$^+$), 277.1311, found 277.1311.

3,4-Dipropylpyrrolo[1,2-c]pyrimidin-1(2H)-one (**3r**). Yellow solid (98% yield, 42.7 mg): mp 120−122 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.89 (s, 1H), 7.55−7.54 (m, 1H), 6.63 (t, J = 3.6 Hz, 1H), 6.25−6.24 (m, 1H), 2.54−2.49 (m, 4H), 1.74−1.58 (m, 4H), 1.03−0.97(m, 6H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.3, 133.9, 130.1, 114.5, 113.5, 109.1, 102.0, 31.3, 29.2, 23.0, 22.4, 14.4, 13.9; IR (KBr) ν 3212, 3110, 2960, 1708, 1640, 1617, 1554, 1404, 1353, 831, 776, 711 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{13}H_{18}N_2O$ ([M + H]$^+$), 219.1492, found 219.1491.

3,4-Diethylpyrrolo[1,2-c]pyrimidin-1(2H)-one (**3s**). White solid (95% yield, 36.1 mg): mp 175−177 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.97 (s, 1H), 7.57−7.56 (m, 1H), 6.63 (t, J = 3.6 Hz, 1H), 6.27−6.26 (m, 1H), 2.59−2.55 (m, 4H), 1.28 (t, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.3, 133.6, 131.1, 114.6, 113.6, 110.1, 101.8, 22.6, 20.3, 14.6, 13.8; IR (KBr) ν 3210, 3113, 2963, 1693, 1654, 1640, 1406, 1349, 1261, 1093, 1031, 802, 707 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{11}H_{14}N_2O$ ([M + H]$^+$),191.1179, found 191.1180.

3,4-Diphenylpyrrolo[1,2-c]pyrimidin-1(2H)-one (**3t**). Pale green solid (64% yield, 36.6 mg): mp 205−206 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.00 (s, 1H), 7.62 (q, J = 1.6 Hz, 1H), 7.28−7.23 (m, 10H), 6.63 (t, J = 3.2 Hz, 1H), 6.19 (q, J = 1.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.2, 135.0, 133.8, 133.4, 130.7, 129.4, 129.3, 128.7, 128.6, 128.5, 127.7, 115.2, 114.7, 112.3, 106.0; IR (KBr) ν 3214, 3066, 2958, 1717, 1654, 1616, 1597, 1405, 1349, 1262, 1032, 800, 700 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{14}N_2O$ ([M + H]$^+$), 287.1179, found 287.1180.

3-(tert-Butyl)pyrrolo[1,2-c]pyrimidin-1(2H)-one (**3u**). Green solid (94% yield, 35.7 mg): mp 155−157 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.86 (br, s, 1H), 7.55 (m, 1H), 6.62 (t, J = 3.2 Hz, 1H), 6.26−6.24 (m, 2H), 1.36 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 142.4, 131.9, 114.8, 113.3, 103.1, 94.3, 34.1, 28.8; IR (KBr) ν 3214, 2970, 1781, 1694, 1663, 1641, 1495, 1402, 1082, 1026, 822, 804, 717 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{11}H_{14}N_2O$ ([M + H]$^+$), 191.1179, found 191.1179.

3-(2-Hydroxypropan-2-yl)pyrrolo[1,2-c]pyrimidin-1(2H)-one (**3v**). Pale yellow oil (91% yield, 34.9 mg): ^{1}H NMR (DMSO-d_6, 400 MHz) δ 10.40 (br, s, 1H), 7.45−7.42 (m, 1H), 6.59 (t, J = 3.2 Hz, 1H), 6.42 (d, J = 1.6 Hz, 1H), 6.26−6.24 (m, 1H), 5.28 (s, 1H), 1.43 (s, 6H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 146.7, 142.1, 131.3, 114.4, 112.7, 103.0, 92.8, 68.9, 28.9; IR (KBr) ν 3379, 2978, 1694, 1641, 1560, 1402, 1333, 1159, 824, 717 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{10}H_{12}N_2O_2$ ([M + H]$^+$), 193.0972, found 193.0972.

3,4-Dihydropyrimido[1,6-a]indol-1(2H)-one (**5a**). Yellow solid (83% yield, 31.2 mg): mp 126−128 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.35 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.31−7.20 (m, 2H), 6.74 (s, 1H), 6.34 (s, 1H), 3.55−3.52 (m, 2H), 3.10 (t, J = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.7, 135.4, 134.8, 129.3, 123.6, 122.8, 120.0, 115.3, 103.3, 39.4, 23.2; IR (KBr) ν 3231, 3118,

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1694, 1654, 1596, 1473, 1420, 1333, 1300, 1194, 791, 758 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{11}H_{10}N_2O$ ($[M + H]^+$), 187.0866, found 187.0867.

*tert-Butyl 1-oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indole-3-carboxylate (**5b**).* Yellow solid (75% yield, 42.9 mg): mp 143−145 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.33 (d, J = 8.0 Hz, 1H), 7.48 (d, J = 7.6 Hz, 1H), 7.29−7.19 (m, 2H), 6.36 (s, 1H), 6.04−6.01 (m, 1H), 4.24−4.21 (m, 1H), 3.44−3.39 (m, 1H), 3.20−3.13 (m,1H), 1.46(s, 9H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 168.7, 150.8, 135.4, 132.4, 129.3, 124.0, 123.0, 120.1, 115.4, 104.2, 83.6, 53.1, 28.0, 26.6; IR (KBr) ν 3384, 3235, 3131, 2982, 1728, 1706, 1676, 1596, 1454, 1414, 1370, 1156, 802, 747 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{16}H_{18}N_2O_3$ ($[M + H]^+$), 287.1390, found 287.1389.

*1-Oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indole-3-carbonitrile (**5c**).* White solid (80% yield, 33.7 mg): mp 181−182 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.71 (d, J = 4.4 Hz, 1H), 8.19 (d, J = 8.4 Hz, 1H), 7.59−7.57 (m, 1H), 7.29−7.20 (m, 2H), 6.62 (s, 1H), 5.03−5.00 (m, 1H), 3.45−3.44 (m, 2H); ^{13}C NMR (DMSO-d_6, 400 MHz) δ 149.5, 134.6, 132.2, 128.8, 123.7, 122.8, 120.4, 119.2, 114.5, 104.6, 40.7, 26.2; IR (KBr) ν 3224, 3119, 2925, 1713, 1677, 1600, 1456, 1415, 1329, 1220, 814, 755 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{12}H_9N_3O$ ($[M + H]^+$), 212.0819, found 212.0828.

*3-(Hydroxymethyl)-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (**5d**).* Gray solid (81% yield, 35 mg): mp 141−143 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.20 (d, J = 8.0 Hz, 1H), 7.84 (s, 1H), 7.51 (d, J = 7.6 Hz, 1H), 7.19−7.15 (m, 2H), 6.47 (s, 1H), 5.06 (m, 1H), 3.81−3.76 (m, 1H), 3.62−3.56 (m, 1H), 3.51−3.46 (m, 1H), 3.37−3.29 (m, 1H), 3.25−3.19 (m, 1H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 150.9, 137.2, 134.6, 128.9, 122.9, 122.1, 120.0, 114.6, 102.0, 60.9, 40.4, 35.9; IR (KBr) ν 3269, 2881, 1694, 1593, 1572, 1479, 1455, 1325, 1211, 1048, 802, 759 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{12}H_{12}N_2O_2$($[M + H]^+$), 217.0972, found 217.0972.

*1,3,4,4a,5,12b-Hexahydro-1,4-methanoindolo[1,2-c]quinazolin-6(2H)-one (**5e**).* White solid (89% yield, 44.9 mg): mp 212−213 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.40 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.6 Hz,1H), 7.28−7.18 (m, 2H), 6.35 (s, 1H), 6.20−5.92 (m, 1H), 3.72 (d, J = 8.8 Hz, 1H), 3.25 (d, J = 8.8 Hz, 1H), 2.47 (s, 1H), 2.31 (s, 1H), 1.66−1.61 (m, 3H), 1.50−1.47 (m, 1H), 1.29−1.21 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 150.4, 137.6, 135.2, 129.8, 123.5, 122.8, 119.8, 116.1, 104.1, 58.0, 47.3, 45.8, 39.6, 33.5, 28.9, 25.4; IR (KBr) ν 3221, 3105, 2960, 2873, 1710, 1584, 1563, 1453, 1439, 1330, 1309, 1082, 1034, 787, 749 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{16}H_{16}N_2O$ ($[M + H]^+$), 253.1336, found 253.1332.

*7-Methyl-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (**5f**).* Yellow solid (92% yield, 36.8 mg): mp 170−171 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.20 (d, J = 8.4 Hz, 1H), 7.29 (s, 1H), 7.10 (dd, J_1= 8.4 Hz, J_2= 1.2 Hz, 1H), 6.48−6.40 (m, 1H), 6.26 (d, J = 0.8 Hz, 1H), 3.55−3.51 (m, 2H), 3.08 (t, J = 6.4 Hz, 2H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.6, 134.8, 133.6, 132.2, 129.5, 125.0, 120.0, 114.9, 103.1, 39.5, 23.2, 21.5; IR (KBr) ν 3235, 3122, 2917, 1702, 1598, 1476, 1421, 1324, 1196, 1045, 798, 751, 701 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{12}H_{12}N_2O$ ($[M + H]^+$), 201.1023, found 201.1023.

*7-Methyl-1-oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indole-3-carbonitrile (**5g**).* Yellow solid (71% yield, 32 mg): mp 205−207 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.65 (d, J = 4.0 Hz, 1H), 8.05 (d, J = 8.0 Hz, 1H), 7.35 (s, 1H), 7.08 (dd, J_1= 8.4 Hz, J_2= 1.2 Hz, 1H), 6.53(s, 1H), 4.99 (q, J = 4.4 Hz, 1H), 3.42 (d, J = 4.0 Hz, 2H), 2.38 (s, 3H); ^{13}C NMR (DMSO-d_6, 100 MHz) δ 149.5, 132.9, 132.2, 131.7, 129.1, 124.9, 120.2, 119.2, 114.2, 104.3, 40.8, 26.2, 21.0; IR (KBr) ν 3239, 3138, 2986, 2200, 1719, 1653, 1597, 1409, 1334, 1287, 1195, 1057, 811, 753 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{13}H_{11}N_3O$ ($[M + H]^+$), 226.0975, found 226.0977.

*7-Methoxy-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (**5h**).* Pale yellow solid (87% yield, 37.6 mg): mp 164−165 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.20 (d, J = 8.8 Hz, 1H), 6.97 (d, J = 2.8 Hz, 1H), 6.89 (q, J = 2.4 Hz, 1H), 6.45 (s, 1H), 6.26 (s, 1H), 3.85 (s, 3H), 3.55−3.51 (m, 2H), 3.07 (t, J = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 156.0, 152.5, 135.5 130.1, 115.9, 112.1, 103.2, 102.9, 55.8, 39.5, 23.2; IR (KBr) ν 3235, 3116, 1691, 1598, 1480, 1421, 1333, 1322, 1245, 1200, 1167, 1130, 815, 778 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{12}H_{12}N_2O_2$ ($[M + H]^+$), 217.0972, found 217.0973.

*7-Methoxy-1-oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indole-3-carbonitrile (**5i**).* White solid (66% yield, 31.8 mg): mp 208−209 °C; ^1H NMR (DMSO-d_6, 400 MHz) δ 8.63 (d, J = 4.0 Hz, 1H), 8.05 (d, J = 8.8 Hz, 1H), 7.10 (d, J = 2.4 Hz, 1H), 6.88 (dd, J_1= 9.2 Hz, J_2= 2.8 Hz, 1H), 6.54(s, 1H), 4.99 (q, J = 4.0 Hz, 1H), 3.78 (s, 3H), 3.42 (d, J = 4.4 Hz, 2H); ^{13}C NMR (DMSO-d_6, 400 MHz) δ 155.6, 149.4, 132.8, 129.8, 129.2, 119.3, 115.1, 112.2, 104.5, 103.1, 55.3, 40.8, 26.2; IR (KBr) ν 3194, 3118, 2962, 2200, 1716, 1599, 1479, 1439, 1333, 1205, 1169, 1036, 861, 806, 746 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{13}H_{11}N_3O_2$ ($[M + H]^+$), 242.0924, found 242.0927.

*6-(Benzyloxy)-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (**5j**).* White solid (78% yield, 45.5 mg): mp 185−187 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, J = 8.0 Hz, 1H), 7.48 (m, 2H), 7.42−7.33 (m, 3H), 7.18 (t, J = 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 6.53 (s, 1H), 5.82 (s, 1H), 5.21 (s, 2H), 3.56−3.52 (m, 2H), 3.10 (t, J = 6.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.2, 150.5, 136.3, 135.6, 132.0, 127.5, 126.8, 126.3, 123.4, 118.7, 107.8, 103.7, 99.5, 69.0, 38.6, 22.1; IR (KBr) ν 3223, 3118, 1688, 1577, 1493, 1435, 1242, 1043, 771, 748 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{16}N_2O_2$ ($[M + H]^+$), 293.1285, found 293.1287.

*5-Methyl-3,4-dihydropyrimido[1,6-a]indol-1(2H)-one (**5k**).* White solid (78% yield, 31.2 mg): mp 185−186 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.32 (d, J = 8.0 Hz, 1H), 7.46 (d, J = 7.2 Hz, 1H), 7.31−7.22 (m, 2H), 6.26 (s, 1H), 3.57−3.53 (m, 2H), 3.03 (t, J = 6.4 Hz, 2H), 2.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 152.71, 135.0, 130.5, 130.2, 123.8, 122.5, 118.1, 115.2, 110.8, 39.4, 21.3, 8.5; IR (KBr) ν 3230, 3118, 2918, 1694, 1653, 1625, 1479, 1423, 1335, 1198, 1081, 781, 755, 740 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{12}H_{12}N_2O$ ($[M + H]^+$), 201.1023, found 201.1022.

*tert-Butyl 5-methyl-1-oxo-1,2,3,4-tetrahydropyrimido[1,6-a]-indole-3-carboxylate (**5l**).* White solid (58% yield, 34.8 mg): mp 157−159 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.28 (d, J = 6.8 Hz, 1H), 6.57 (d, J = 6.0 Hz, 1H), 6.45−6.37 (m, 2H), 5.26 (s, 1H), 3.92−3.89 (m, 1H), 3.23−3.18 (m, 1H), 2.99−2.93 (m, 1H), 2.26 (s, 3H), 1.65 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.9, 150.9, 135.0, 130.5, 127.9, 124.2, 122.7, 118.2, 115.3, 111.9, 83.6, 53.1, 28.1, 24.8, 8.5; IR (KBr) ν 3239, 3125, 2977, 2920, 1735, 1695, 1629, 1459, 1226, 1158, 756 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{17}H_{20}N_2O_3$ ($[M + Na]^+$), 323.1366, found 323.1369.

*Ethyl 5-methyl-1-oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indole-3-carboxylate (**5m**).* Yellow solid (74% yield, 40.2 mg): mp 116−118 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.31 (s, 1H), 7.46−7.44 (m, 1H), 7.32−7.22 (m, 2H), 6.09 (s, 1H), 4.35−4.24 (m, 3H), 3.44−3.39 (m, 1H), 3.16−3.10(m, 1H), 2.22 (s, 3H), 1.30(t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 150.9, 135.0, 130.5, 127.7, 124.2, 122.7, 118.3, 115.3, 112.1, 62.4, 52.5, 24.5, 14.2, 8.5; IR (KBr) ν 3246, 3125, 2965, 1752, 1735, 1710, 1691, 1459, 1426, 1343, 1191, 1025, 805, 756 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O_3$ ($[M + H]^+$), 273.1234, found 273.1236.

*2-(1-Oxo-1,2,3,4-tetrahydropyrimido[1,6-a]indol-5-yl)ethyl acetate (**5n**).* Pale yellow solid (70% yield, 38 mg): mp 137−139 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.34 (d, J = 7.6 Hz, 1H), 7.51 (d, J = 7.2 Hz, 1H), 7.31−7.22 (m, 2H), 6.28 (s, 1H), 4.26 (t, J = 7.2 Hz, 2H), 3.58−3.54 (m, 2H), 3.08 (t, J = 6.4 Hz, 2H), 3.00 (t, J = 7.2 Hz, 2H), 2.03 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.1, 152.4, 135.2, 131.8, 129.5, 124.0, 122.7, 118.1, 115.5, 111.1, 63.8, 39.5, 23.7, 21.5, 21.1; IR (KBr) ν 3247, 3122, 2917, 1732, 1690, 1618, 1458, 1233, 1041, 802, 760 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{16}N_2O_3$ ($[M + H]^+$), 273.1235, found 273.1234.

*3,4-Dihydropyrrolo[1,2-c]pyrimidin-1(2H)-one (**5o**).* White solid (88% yield, 24 mg): mp 79−81 °C; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.29 (dd, J_1 = 3.2 Hz, J_2 = 1.2 Hz, 1H), 6.69 (br, s, 1H), 6.18 (t, J = 3.2 Hz, 1H), 5.99−5.98 (m, 1H), 3.52−3.48 (m, 2H), 2.94 (t, J = 6.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 151.6, 128.8, 117.4, 110.9, 107.9, 39.9, 22.2; IR (KBr) ν 3222, 2968, 1760, 1702, 1572, 1436, 1322, 1261, 1106, 801, 733, 698 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_7H_8N_2O$ ($[M + H]^+$), 137.0710, found 137.0709.

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*Ethyl 1-oxo-1,2,3,4-tetrahydropyrrolo[1,2-c]pyrimidine-3-carboxylate (**5p**).* Pale yellow oil (72% yield, 30 mg): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.30−7.29 (m, 1H), 6.30−6.26 (m, 1H), 6.17 (t, J = 3.2 Hz, 1H), 6.02−6.01 (m, 1H), 4.33−4.20 (m, 3H), 3.34−3.29 (m, 1H), 3.11−3.05 (m, 1H), 1.28(t, J = 7.2 Hz, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.8, 149.8, 126.2, 117.9, 111.3, 108.9, 62.4, 53.0, 25.5, 14.2; IR (KBr) ν 3143, 2963, 2926, 1747, 1732, 1714, 1698, 1575, 1417, 1261, 1095, 1027, 801, 727 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{10}H_{12}N_2O_3$ ([M + H]$^+$), 209.0921, found 209.0920.

*Methyl 3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7a**).* Pale brown solid (91% yield, 55.7 mg): mp 204−205 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (d, J = 8.0 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.57−7.54 (m, 2H), 7.42−7.31 (m, 4H), 7.26 (m, 1H), 6.99 (s, 1H), 6.74 (s, 1H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6, 151.5, 137.7, 137.5, 133.3, 130.6, 129.3, 125.6, 124.3, 123.2, 121.5, 112.9, 101.8, 67.3, 53.9; IR (KBr) ν 3325, 1759, 1584, 1479, 1450, 1260, 743, 701 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{14}N_2O_3$ ([M + H]$^+$), 307.1077, found 307.1071.

*Ethyl 3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7b**).* Pale yellow solid (93% yield, 59.5 mg): mp 205−206 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.0 (d, J = 8.0 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.56−7.54 (m, 2H), 7.42−7.36 (m, 3H), 7.34−7.32 (m, 1H), 7.28−7.25 (m, 1H), 4.31−4.25 (m, 2H), 1.30−1.26 (t, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.0, 151.5, 137.9, 133.3, 130.6, 129.3, 125.6, 124.2, 123.2, 121.5, 112.9, 101.7, 67.2, 63.3, 14.1; IR (KBr) ν 3320, 2847, 1755, 1729, 1486, 1394, 800, 747, 696 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_3$ ([M + H]$^+$), 321.1234, found 321.1235.

*Benzyl 3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7c**).* Pale yellow solid (86% yield, 65.7 mg): mp 152−154 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (d, J = 8.0 Hz, 1H), 7.60 (d, J = 8.0 Hz, 1H), 7.50−7.49 (m, 2H), 7.36−7.33 (m, 4H), 7.31−7.28 (m, 3H), 7.26−7.23 (m, 3H), 6.72−6.70 (m, 2H), 5.23−5.22 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.8, 151.4, 137.6, 137.5, 134.6, 133.3, 129.28, 128.83, 128.79, 128.4, 125.6, 124.3, 123.2, 121.6, 68.8, 67.3; IR (KBr) ν 3232, 3123, 1732, 1478, 1451, 1384, 1211, 751, 696 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{24}H_{18}N_2O_3$ ([M + H]$^+$), 383.1390, found 383.1380.

*Allyl 3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7d**).* Pale yellow solid (63% yield, 41.8 mg): mp 171−173 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (dd, J_1 = 8.0 Hz, J_2 = 0.8 Hz, 1H), 7.63−7.55 (m, 3H), 7.41−7.23 (m, 5H), 6.93 (s, 1H), 6.75 (s, 1H), 5.91−5.81(m, 1H), 5.28−5.21 (m, 2H), 4.71−4.69 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 168.7, 151.4, 137.6, 137.55, 133.3, 130.8, 130.6, 129.32, 129.29, 125.6, 124.3, 123.2, 121.6, 119.8, 113.0, 101.9, 67.5, 67.2; IR (KBr) ν 3341, 2962, 1744, 1454, 1400, 1265, 1092, 726, 702, 662, 519 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{20}H_{16}N_2O_3$ ([M + H]$^+$), 333.1234, found 333.1246.

*Methyl 3-oxo-1-(p-tolyl)-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7e**).* Pale yellow solid (78% yield, 49.9 mg): mp 155−157 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 8.0 Hz, 1H), 7.44−7.42 (m, 2H), 7.35−7.31 (m, 1H), 7.28−7.24 (m, 1H), 7.19 (s, 1H), 7.17 (s, 1H), 7.13 (s, 1H), 6.72 (s, 1H), 3.81 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.7, 151.5, 139.3, 137.8, 134.6, 133.3, 130.6, 129.9, 125.5, 124.2, 123.2, 121.5, 112.9, 101.7, 67.1, 53.9, 21.2; IR (KBr) ν 3270, 2956, 2850, 1731, 1454, 1356, 1258, 1093, 820, 777, 749 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_3$ ([M + H]$^+$), 321.1234, found 321.1232.

*Methyl 1-(4-chlorophenyl)-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]-indole-1-carboxylate (**7f**).* Pale yellow solid (88% yield, 59.8 mg): mp 116−118 °C; ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.99 (dd, J_1 = 8.0 Hz, J_2 = 0.5 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.52−7.50 (m, 2H), 7.39−7.36 (m, 2H), 7.35−7.34 (m, 1H), 7.30−7.26 (m, 1H), 7.02 (s, 1H), 6.73 (d, J = 0.5 Hz, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.3, 151.5, 137.3, 136.1, 135.4, 133.3, 130.6, 129.5, 127.1, 121.5, 123.4, 121.6, 113.0, 101.9, 66.7, 54.1; IR (KBr) ν 3301, 1740, 1493, 1455, 1407, 1249, 780, 749 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{13}ClN_2O_3$ ([M + H]$^+$), 341.0687, found 341.0685.

*Methyl 1-(4-bromophenyl)-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7g**).* Pale yellow solid (71% yield, 54.5 mg): mp 157−158 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, J = 7.6 Hz, 1H), 7.62 (d, J = 8.0 Hz, 1H), 7.52−7.50 (m, 2H), 7.54−7.51 (m, 2H), 7.48−7.45 (m, 1H), 7.37−7.33 (m, 1H), 7.30−7.26 (m, 2H), 6.74 (s, 1H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.2, 151.6, 137.2, 136.6, 133.2, 132.4, 130.6, 127.4, 124.5, 123.6, 123.4, 121.6, 113.0, 101.9, 66.8, 54.1; IR (KBr) ν 3228, 3131, 1741, 1480, 1452, 1436, 1407, 1245, 778, 755 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{13}BrN_2O_3$ ([M + H]$^+$), 385.0182, found 385.0183.

*Methyl 1-(4-nitrophenyl)-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]-indole-1-carboxylate (**7h**).* Brown solid (68% yield, 47.7 mg): mp 185−186 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.23−8.20 (m, 2H), 7.95 (d, J = 8.0 Hz, 1H), 7.81−7.78 (m, 2H), 7.60 (d, J = 8.0 Hz, 1H), 7.47(s, 1H), 7.35−7.31 (m, 1H), 7.28−7.22(m, 1H), 6.76 (s, 1H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 168.7, 151.7, 148.3, 144.1, 136.25, 133.2, 130.6, 127.0, 124.8, 124.4, 123.6, 121.8, 113.0, 102.3, 66.8, 54.4; IR (KBr) ν 3230, 3127, 1747, 1527, 1449, 1401, 1354, 1261, 1217, 1096, 787, 745 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{13}N_3O_5$ ([M + H]$^+$), 352.0928, found 352.0935.

*Methyl 1-benzyl-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7i**).* Pale yellow oil (70% yield, 44.8 mg): ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.93 (d, J = 7.6 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.34−7.24 (m, 5H), 7.19−7.18 (m, 2H), 6.63 (s, 1H), 5.88 (s, 1H), 3.78 (s, 3H), 3.67 (d, J = 13.6 Hz, 1H), 3.20 (d, J = 13.2 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 151.6, 138.3, 133.8, 133.2, 130.5, 129.9, 128.9, 128.1, 124.1, 123.1, 121.5, 112.9, 99.9, 65.6, 53.5, 45.5; IR (KBr) ν 3328, 1740, 1480, 1452, 1403, 1355, 1305, 1261, 748, 702 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_3$ ([M + H]$^+$), 321.1234, found 321.1235.

*1′-Methylspiro[imidazo[1,5-a]indole-1,3′-indoline]-2′,3(2H)-dione (**7j**).* Pink solid (70% yield, 42.4 mg): mp 212−214 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.98 (d, J = 7.6 Hz, 1H), 7.63−7.50 (m, 3H), 7.37−7.26 (m, 4H), 7.08 (s, 1H), 6.73 (s, 1H), 3.83 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.3, 151.5, 137.3, 136.1, 135.4, 133.2, 130.6, 129.4, 127.1, 124.5, 123.4, 121.6, 113.0, 101.9, 66.7, 54.1; IR (KBr) ν 3239, 1736, 1613, 1492, 1450, 1406, 750, 721 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{18}H_{13}N_3O_2$ ([M + Na]$^+$), 326.0900, found 326.0902.

*Methyl 7-methyl-3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]-indole-1-carboxylate (**7k**).* White solid (84% yield, 53.8 mg): mp 202−204 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, J = 8.0 Hz, 1H), 7.55−7.52 (m, 2H), 7.40−7.38 (m, 4H), 7.17 (dd, J_1 = 8.4 Hz, J_2 = 1.2 Hz, 1H), 6.65 (s, 1H), 6.61 (s, 1H), 3.83 (s, 3H), 2.46 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 151.5, 137.81, 137.75, 133.7, 132.9, 129.4, 128.9, 125.8, 125.7, 121.4, 112.6, 101.7, 67.3, 54.0, 21.8; IR (KBr) ν 3225, 3120, 1732, 1449, 1251, 1226, 1098, 794, 698, 665 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_3$ ([M + H]$^+$), 321.1234, found 321.1246.

*Methyl 7-methoxy-3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7l**).* Pale yellow solid (74% yield, 49.7 mg): mp 202−204 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.88 (d, J = 8.8 Hz, 1H), 7.57−7.54 (m, 2H), 7.42−7.34 (m, 3H), 7.09−7.08 (m, 2H), 6.97 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 6.68 (s, 1H), 3.86 (s, 3H), 3.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.6, 156.3, 151.5, 138.5, 137.5, 134.1, 129.2, 125.6, 125.4, 113.53, 113.46, 104.0, 101.6, 67.2, 55.9, 53.9; IR (KBr) ν 3226, 3124, 1736, 1584, 1478, 1410, 1249, 1135, 817, 698 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_4$ ([M + H]$^+$), 337.1183, found 337.1185.

*Methyl 1-(4-chlorophenyl)-7-methoxy-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]-indole-1-carboxylate (**7m**).* Yellow solid (81% yield, 59.9 mg): mp 160−162 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, J = 8.8 Hz, 1H), 7.53−7.51 (m, 2H), 7.38−7.36 (m, 2H), 7.07 (d, J = 2.4 Hz, 1H), 6.98 (dd, J_1 = 8.8 Hz, J_2 = 2.4 Hz, 1H), 6.64 (s, 1H), 6.53 (s, 3H), 3.86 (s, 3H), 3.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.3, 156.5, 151.2, 138.0, 136.2, 135.5, 134.1, 129.5, 127.1, 125.5, 113.7, 113.6, 104.1, 101.8, 66.6, 55.9, 54.1; IR (KBr) ν 3252, 1731, 1479, 1441, 1417, 1262, 1204, 1130, 1094, 1014, 905, 850 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}ClN_2O_4$ ([M + H]$^+$), 371.0793, found 371.0783.

*Methyl 8-(benzyloxy)-3-oxo-1-phenyl-2,3-dihydro-1H-imidazo-[1,5-a]indole-1-carboxylate (**7n**).* Pale yellow solid (93% yield, 76.6 mg): mp 168−170 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.62 (d, J = 8.0

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Hz, 1H), 7.57−7.54 (m, 2H), 7.53−7.51 (m, 2H), 7.45−7.34 (m, 6H), 7.26 (t, 1H), 6.92 (s, 1H), 6.78 (d, J = 7.6 Hz, 1H), 6.73 (s, 1H), 5.22 (s, 2H), 3.83 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.6, 152.5, 151.5, 137.5, 137.1, 136.0, 129.3, 128.7, 128.1, 127.7, 125.6, 125.3, 123.9, 106.3, 104.7, 99.4, 70.3, 67.2, 54.0; IR (KBr) ν 3416, 1736, 1450, 1436, 1401, 1241, 806, 750, 705 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{25}H_{20}N_2O_4$ ([M + H]$^+$), 413.1496, found 413.1499.

*Methyl 9-methyl-3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7o**).* White solid (78% yield, 49.9 mg): mp 176−178 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.87 (d, J = 8.0 Hz, 1H), 7.45 (d, J = 8.0 Hz, 1H), 7.28−7.24 (m, 4H), 7.24−7.21 (m, 2H), 7.19−7.15 (t, 1H), 6.73−6.66 (m, 1H), 3.73 (s, 1H), 2.16 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 170.1, 151.4, 137.0, 134.4, 132.4, 130.2, 129.30, 129.26, 126.0, 124.3, 122.7, 119.5, 112.8, 111.1, 67.8, 53.5, 9.0; IR (KBr) ν 3249, 1732, 1629, 1454, 1406, 1350, 1308, 1253, 756, 740, 695 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{16}N_2O_3$ ([M + H]$^+$), 321.1234, found 321.1239.

*Methyl 1-(4-bromophenyl)-9-methyl-3-oxo-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7p**).* White solid (75% yield, 59.7 mg): mp 182−183 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.96 (d, J = 8.0 Hz, 1H), 7.56 (d, J = 7.6 Hz, 1H), 7.28−7.24 (m, 4H), 7.52−7.50 (m, 2H), 7.38−7.34 (m, 1H), 7.31−7.29 (m, 1H), 7.27−7.24 (t, 1H), 6.56 (s, 1H), 3.86 (s, 3H), 2.25 (s, 3H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.8, 151.2, 136.1, 134.4, 132.5, 131.9, 130.2, 127.9, 124.6, 123.6, 122.9, 119.6, 112.8, 111.4, 67.3, 53.7, 9.0; IR (KBr) ν 3232, 3131, 1755, 1738, 1453, 1402, 1351, 1255, 1236, 1009, 756, 746 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{19}H_{15}BrN_2O_3$ ([M + H]$^+$), 399.0339, found 399.0325.

*Methyl 9-(2-acetoxyethyl)-3-oxo-1-phenyl-2,3-dihydro-1H-imidazo[1,5-a]indole-1-carboxylate (**7q**).* Yellow solid (54% yield, 42.3 mg): mp 143−144 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (d, J = 8.0 Hz, 1H), 7.68(d, J = 8.0 Hz, 1H), 7.40−7.33 (m, 6H), 7.31−7.26 (m, 1H), 6.65 (s, 1H), 4.14−4.10 (m, 2H), 3.92 (s, 3H), 3.13−3.06 (m, 1H), 3.02−2.94 (m, 1H), 1.99 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 171.0, 169.6, 151.1, 137.1, 133.7, 129.54, 129.45, 126.0, 124.6, 123.0, 120.2, 112.9, 111.0, 67.9, 63.3, 53.9, 24.0, 21.1; IR (KBr) ν 3338, 2955, 1755, 1734, 1457, 1399, 1246, 1023, 744, 694 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{22}H_{20}N_2O_5$ ([M + Na]$^+$), 415.1264, found 415.1255.

*2-(1′-Methyl-2′,3-dioxo-2,3-dihydrospiro[imidazo[1,5-a]indole-1,3′-indolin]-9-yl)ethyl acetate (**7r**).* Pink solid (49% yield, 38.1 mg): mp 142−144 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, J = 8.0 Hz, 1H), 7.44(d, J = 8.0 Hz, 1H), 7.36−7.24 (m, 2H), 7.20−7.16 (m, 2H), 7.01 (t, J = 7.6 Hz, 1H), 6.92 (d, J = 8.0 Hz, 1H), 6.40 (s, 1H), 3.86−3.73 (m, 1H), 3.72−3.67 (m, 1H), 3.25 (s, 3H), 2.51−2.44 (m, 1H), 2.39−2.31 (m, 1H), 1.85 (s, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 172.7, 170.9, 152.6, 143.9, 135.0, 133.4, 131.4, 130.8, 125.9, 125.0, 124.4, 124.2, 123.0, 119.6, 113.1, 109.4, 108.1, 62.9, 27.3, 23.3, 21.1; IR (KBr) ν 3238, 2946, 1732, 1693, 1613, 1471, 1454, 1237, 1034, 752 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{22}H_{19}N_3O_4$ ([M + Na]$^+$), 412.1268, found 412.1257.

*Methyl 3-oxo-1-phenyl-2,3-dihydro-1H-pyrrolo[1,2-c]imidazole-1-carboxylate (**7s**).* Pale yellow solid (80% yield, 41 mg): mp 134−136 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.50−7.47 (m, 2H), 7.41−7.35 (m, 1H), 7.22 (s, 1H), 7.11 (dd, J_1 = 2.8 Hz, J_2 = 1.2 Hz, 1H), 6.45−6.44 (m, 1H), 6.41 (dd, J_1 = 3.2 Hz, J_2 = 1.2 Hz, 1H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 169.7, 151.3, 137.5, 132.8, 129.17, 129.15, 125.6, 116.3, 112.5, 106.5, 122.9, 67.3, 53.8; IR (KBr) ν 3246, 3123, 1753, 1719, 1449, 1429, 1243, 755, 740, 697 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{14}H_{12}N_2O_3$ ([M + H]$^+$), 257.0921, found 257.0931.

*Methyl 1-benzyl-3-oxo-2,3-dihydro-1H-pyrrolo[1,2-c]imidazole-1-carboxylate (**7t**).* Pink solid (56% yield, 30 mg): mp 129−130 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29−7.27 (m, 3H), 7.14−7.11 (m, 2H), 7.00 (dd, J_1 = 2.8 Hz, J_2 = 0.8 Hz, 1H), 6.39−6.37 (m, 1H), 6.28 (dd, J_1 = 3.6 Hz, J_2 = 1.2 Hz, 1H), 3.76 (s, 3H), 3.57 (d, J = 13.6 Hz, 1H), 3.12 (d, J = 13.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 400 MHz) δ 169.8, 151.1, 134.0, 133.5, 129.8, 128.9, 128.0, 116.2, 112.4, 104.6, 65.6, 53.4, 45.2; IR (KBr) ν 3194, 1756, 1717, 1424, 1261, 1246, 1152, 781, 762, 697 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{15}H_{14}N_2O_3$ ([M + H]$^+$), 271.1077, found 271.1084.

*Methyl spiro[indoline-3,1′-pyrrolo[1,2-c]imidazole]-2,3′(2′H)-dione (**7u**).* Gray solid (60% yield, 30.3 mg): mp 213-215 °C; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.43−7.39 (m, 1H), 7.19 (d, J = 7.6 Hz, 1H), 7.12−7.08 (m, 2H), 6.94 (d, J = 7.6 Hz, 1H), 6.36 (t, 1H), 6.20−6.17 (m, 1H), 5.80 (dd, J1 = 3.6 Hz, J2 = 0.8 Hz, 1H), 3.27 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 173.1, 152.7, 144.0, 133.3, 131.0, 126.5, 125.0, 124.0, 116.6, 112.9, 109.2, 103.2, 63.1, 27.2; IR (KBr) ν 3318, 3117, 1736, 1614, 1493, 1471, 1412, 1366, 1309, 1218, 1108, 790, 760, 688 cm^{-1}; HRMS (ESI) (m/z) calcd for $C_{14}H_{11}N_3O_2$ ([M + Na]$^+$), 276.0743, found 276.0749.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Characterization data, including CIF files for compounds **3f**, **5k** and **7a**. 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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