Supporting Information

Synthesis of indoline-piperidinones via a novel Ugi, ring expansion, pseudo-Dieckmann condensation and rearrangement cascade reaction

Jie Lei,a,b Gui-Ting Song,a Ya-Fei Luo,a Dian-Yong Tang,a Wei Yan,b Hong-yu Li,*b Zhong-Zhu Chen,*a Zhi-Gang Xu*a

aCollege of Pharmacy, National & Local Joint Engineering Research Center of Targeted and Innovative Therapeutics, Chongqing Key Laboratory of Kinase Modulators as Innovative Medicine, Chongqing University of Arts and Sciences, Chongqing 402160, China.

bDepartment of Pharmaceutical Sciences, College of Pharmacy, University of Arkansas for Medical Sciences, Little Rock, AR 72205, USA

*e-mail: HLi2@uams.edu; 18883138277@163.com; xzg@cqwu.edu.cn

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General Experimental

$^1$H and $^{13}$C NMR were recorded on a Bruker 400 spectrometer. $^1$H NMR data are reported as follows: chemical shift in ppm ($\delta$), multiplicity ($s =$ singlet, $d =$ doublet, $t =$ triplet, $m =$ multiplet), coupling constant (Hz), relative intensity. $^{13}$C NMR data are reported as follows: chemical shift in ppm ($\delta$). LC/MS analyses were performed on a Shimadzu-2020 LC-MS instrument using the following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 4.6 mm); a linear gradient from 10% water and 90% acetonitrile to 75% acetonitrile and 25% water over 6.0 min; flow rate of 0.5 mL/min; UV photodiode array detection from 200 to 400 nm. High-resolution mass spectra (HRMS) were recorded on Thermo Scientific Exactive Plus System. The products were purified by Biotage Isolera™ Spektra Systems and hexane/EtOAc solvent systems. All reagents and solvents were obtained from commercial sources and used without further purification. All microwave irradiation experiments were carried out in a Biotage® Initiator Classic microwave apparatus with continuous irradiation power from 0 to 400W with utilization of the standard absorbance level of 250W maximum power. The reactions were carried out in 10 mL glass tubes, sealed with microwave cavity. The reaction was irradiated at a required ceiling temperature using maximum power for the stipulated time. Then it was cooled to 50 °C with gas jet cooling.
Experimental Sections

(a) General procedures for compound 7.

Glyoxylate acid (1.0 mmol), isonitrile (1.0 mmol), ethyl glyoxylate (2.0 mmol) and methyl-2-aminobenzoate (1.0 mmol) were mixed and stirred overnight in MeOH (2.0 mL) at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under nitrogen blowing. Then the crude residue was subjected to DBU (2.0 equiv.) and DMF (3.0 mL) solution under microwave irradiation condition at 80 °C for 10 min. After the microwave vial was cooled to room temperature, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford the relative targeted product 7.

(b) General procedures for compound 10.

Benzoylformic acid (1.0 mmol), formaldehyde (4.0 mmol), benzyl isocyanide (1.0 mmol), and methyl-2-aminobenzoate (1.0 mmol) were mixed and stirred overnight in MeOH (2.0 mL) at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under reduced pressure and the product 9a was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) (350 mg of white solid was obtained and the yield was 82%). Then, the product 9a (86 mg, 0.2 mmol) was subjected to DBU (0.4 mmol, 2.0 equiv.) and DMF (1.0 mL) solution under microwave irradiation condition at 140 °C for 10 min. After the microwave vial was cooled to room temperature, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (20-100%) to afford the relative targeted product 10 (64 mg, 78% yield) as yellow solid.

(c) General procedures for compound 12.
1a (1.0 mmol), 2 (2.0 mmol), 3 (1.0 mmol), and aniline 11 (1.0 mmol) were mixed and stirred overnight in MeOH (2.0 mL) at room temperature. The reaction mixture was monitored by TLC. When the reaction was completed, the solvent was removed under reduced pressure. Then, the product 5v was subjected to DBU (2.0 mmol, 2.0 equiv.) and DMF (5.0 mL) solution under microwave irradiation condition at 80 °C for 10 min. After the microwave vial was cooled to room temperature, the residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (0-100%) to afford final product 12 (217 mg, 59% yield) as yellow solid.
NMR Characterization Data and Figures of Products

**Methyl 2-(N-(1-(benzylamino)-3-ethoxy-1,3-dioxopropan-2-yl)-2-oxo-2-phenylacetamido)benzoate**

![Methyl 2-(N-(1-(benzylamino)-3-ethoxy-1,3-dioxopropan-2-yl)-2-oxo-2-phenylacetamido)benzoate](image)

Compound 5a (white solid, 421 mg, yield 87%, R\(_f\) = 0.20 (EA/Hex= 20%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 7.89 - 7.83 (m, 2H), 7.83 - 7.78 (m, 1H), 7.64 (d, \(J = 4.3\) Hz, 1H), 7.53 - 7.48 (m, 1H), 7.42 - 7.35 (m, 4H), 7.20 - 7.13 (m, 3H), 6.81 (d, \(J = 6.8\) Hz, 2H), 5.77 (s, 1H), 4.49 - 4.41 (m, 2H), 4.24 (dd, \(J = 14.3, 7.2\) Hz, 1H), 3.94 (dd, \(J = 14.3, 4.3\) Hz, 1H), 3.78 (s, 3H), 1.42 (t, \(J = 7.1\) Hz, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 189.53, 167.44, 167.15, 166.63, 163.01, 136.94, 135.81, 134.48, 133.10, 132.87, 131.57, 130.64, 130.36, 130.06, 129.77, 129.51, 129.31, 128.59, 128.00, 127.34, 65.09, 62.52, 52.82, 43.88, 14.15. HRMS (ESI) m/z calcd for C\(_{28}\)H\(_{27}\)N\(_2\)O\(_7\)\(^+\) (M+H)\(^+\) 503.1813, found 503.1811.

**2-Benzyl-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione**

![2-Benzyl-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione](image)

Compound 7a (dark yellow solid, 262 mg, yield 69%, R\(_f\) = 0.29 (EA/Hex=15%)) \(^1\)H NMR (400 MHz, d\(_6\)-DMSO) \(\delta\) 8.36 (d, \(J = 8.2\) Hz, 1H), 7.88-7.82 (m, 1H), 7.78 (d, \(J = 7.5\) Hz, 1H), 7.46-7.39 (m, 8H), 7.34 (t, \(J = 7.4\) Hz, 2H), 7.29 (d, \(J = 7.1\) Hz, 1H), 5.15 (s, 2H). \(^{13}\)C NMR (100 MHz, d\(_6\)-DMSO) \(\delta\) 182.35, 163.25, 147.57, 146.58, 137.98, 136.98, 136.09, 131.21,129.29, 129.13, 128.85, 128.26, 127.96, 127.83, 126.40, 125.11, 123.80, 118.11, 116.74, 44.71. HRMS (ESI) m/z calcd for
C_{24}H_{17}N_{2}O_{3}^+ (M+H)^+ 381.1234, found 381.1238.

2-Benzyl-4-(p-tolyl)pyrimido[1,6-a]indole-1,3,5(2H)-trione

![Structure](image)

Compound 7b (dark yellow solid, 288 mg, yield 73%, R_f = 0.21 (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.48 (d, \(J = 8.2\) Hz, 1H), 7.79-7.68 (m, 2H), 7.60-7.54 (m, 2H), 7.35-7.27 (m, 7H), 7.26 (s, 1H), 5.26 (s, 2H), 2.42 (s, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 181.79, 163.03, 147.28, 146.40, 139.91, 137.53, 136.23, 134.60, 130.46, 129.54, 128.81, 128.56, 128.01, 126.03, 125.01, 124.66, 123.49, 119.98, 117.09, 45.06, 21.56. HRMS (ESI) m/z calcd for C\(_{25}\)H\(_{19}\)N\(_2\)O\(_3\)\(^+\) (M+H)^+ 395.1390, found 395.1391.

2-Phenethyl-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

![Structure](image)

Compound 7c (light yellow solid, 251 mg, yield 64%, R_f = 0.24 (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 8.48 (d, \(J = 8.2\) Hz, 1H), 7.85-7.69 (m, 2H), 7.48 (dd, \(J = 4.2, 2.3\) Hz, 3H), 7.44-7.39 (m, 2H), 7.37-7.29 (m, 5H), 7.25-7.21 (m, 1H), 4.35-4.24 (m, 2H), 3.09-2.94 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 181.81, 162.78, 147.09, 146.50, 138.10, 137.65, 134.79, 130.47, 129.68, 129.02, 128.62, 128.05, 127.70, 126.69, 126.09, 125.09, 123.42, 119.69, 117.04, 43.33, 33.82. HRMS (ESI) m/z calcd for C\(_{25}\)H\(_{19}\)N\(_2\)O\(_3\)\(^+\) (M+H)^+ 395.1390, found 395.1391.
2-Benzyl-4-(4-bromophenyl)pyrimido[1,6-α]indole-1,3,5(2H)-trione

Compound 7d (dark yellow solid, 275 mg, yield 61%, R$_f$ = 0.23 (EA/Hex=15%))  $^1$H NMR (400 MHz, CDCl$_3$) δ 8.47 (d, $J$ = 8.2 Hz, 1H), 7.81-7.69 (m, 2H), 7.62-7.53 (m, 4H), 7.36-7.27 (m, 6H), 5.25 (s, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 181.71, 162.62, 147.12, 146.47, 137.79, 136.03, 134.89, 132.26, 131.30, 129.52, 128.60, 128.10, 126.51, 126.23, 125.16, 124.27, 123.23, 118.45, 117.13, 45.13. HRMS (ESI) m/z calcd for C$_{24}$H$_{16}$BrN$_2$O$_3$ $^+$ (M+H)$^+$ 459.0339, found 459.0335.

2-Benzyl-4-(4-methoxyphenyl)pyrimido[1,6-α]indole-1,3,5(2H)-trione

Compound 7e (light yellow solid, 308 mg, yield 75%, R$_f$ = 0.23 (EA/Hex=15%))  $^1$H NMR (400 MHz, CDCl$_3$) δ 8.48 (d, $J$ = 8.2 Hz, 1H), 7.78 (d, $J$ = 7.1 Hz, 1H), 7.75-7.69 (m, 1H), 7.60-7.55 (m, 2H), 7.41 (d, $J$ = 8.8 Hz, 2H), 7.32 (qd, $J$ = 8.6, 3.9 Hz, 4H), 6.99 (d, $J$ = 8.8 Hz, 2H), 5.26 (s, 2H), 3.87 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) δ 181.82, 163.14, 160.89, 147.25, 146.30, 137.48, 136.22, 134.27, 132.29, 129.51, 128.56, 128.01, 126.01, 124.98, 123.56, 119.82, 119.64, 117.09, 113.53, 55.32, 45.08. HRMS (ESI) m/z calcd for C$_{25}$H$_{19}$N$_2$O$_4$ $^+$ (M+H)$^+$ 411.1339, found 411.1339.

2-Cyclohexyl-4-phenylpyrimido[1,6-α]indole-1,3,5(2H)-trione
Compound 7f (dark yellow solid, 253 mg, yield 68%, Rf = 0.22 (EA/Hex=15%))  
1H NMR (400 MHz, CDCl3) δ 8.47 (d, J = 8.2 Hz, 1H), 7.81-7.68 (m, 2H), 7.44 (m, 5H), 7.32 (t, J = 7.3 Hz, 1H), 4.93-4.86 (m, 1H), 2.49 (qd, J = 12.4, 3.3 Hz, 2H), 1.88 (d, J = 13.2 Hz, 2H), 1.78-1.70 (m, 2H), 1.47-1.34 (m, 2H), 1.33-1.18 (m, 2H).  
13C NMR (100 MHz, CDCl3) δ 182.03, 163.37, 147.42, 146.75, 137.55, 134.64, 130.53, 129.53, 128.08, 127.97, 125.89, 124.96, 123.47, 119.86, 117.17, 55.47, 28.67, 26.40, 25.27.  
HRMS (ESI) m/z calcd for C23H21N2O3+ (M+H)+ 373.1547, found 373.1546.

2-Cyclohexyl-4-(4-methoxyphenyl)pyrimido[1,6-a]indole-1,3,5(2H)-trione

Compound 7g (dark yellow solid, 260 mg, yield 65%, Rf = 0.30 (EA/Hex=15%))  
1H NMR (400 MHz, CDCl3) δ 8.37 (t, J = 8.9 Hz, 1H), 8.32 (d, J = 8.7 Hz, 1H), 7.69 (d, J = 7.5 Hz, 1H), 7.63 (t, J = 7.7 Hz, 1H), 7.33 (d, J = 8.7 Hz, 2H), 6.91 (d, J = 8.7 Hz, 2H), 3.80 (s, 1H), 3.78 (s, 3H), 1.89 (dd, J = 12.3, 3.0 Hz, 1H), 1.80 (d, J = 10.1 Hz, 2H), 1.69-1.63 (m, 3H), 1.40-1.24 (m, 4H).  
13C NMR (100 MHz, CDCl3) δ 185.06, 162.53, 159.74, 146.35, 145.53, 136.37, 132.89, 131.27, 124.76, 123.84, 122.58, 118.95, 116.11, 112.78, 112.42, 54.28, 47.37, 31.70, 27.64, 25.37, 24.26, 23.74.  
HRMS (ESI) m/z calcd for C24H23N2O4+(M+H)+ 403.1652, found 403.1653.

4-(Benzo[d][1,3]dioxol-5-yl)-2-cyclohexylpyrimido[1,6-a]indole-1,3,5(2H)-trione
Compounds 7h (red solid, yield 67%, 280 mg, \(R_f = 0.15\) (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.46\) (d, \(J = 8.3\) Hz, 1H), \(7.78\) (d, \(J = 7.5\) Hz, 1H), \(7.73\) (t, \(J = 7.9\) Hz, 1H), \(7.32\) (t, \(J = 7.5\) Hz, 1H), \(6.96\)–\(6.88\) (m, 3H), \(6.03\) (s, 2H), \(4.90\)–\(4.83\) (m, 1H), \(2.53\)–\(2.43\) (m, 2H), \(1.88\) (d, \(J = 10.3\) Hz, 2H), \(1.73\) (d, \(J = 9.6\) Hz, 3H), \(1.45\)–\(1.35\) (m, 3H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 181.99, 163.39, 148.85, 147.42, 147.33, 146.58, 137.50, 134.48, 125.86, 125.07, 124.94, 123.50, 121.29, 119.61, 117.15, 111.04, 108.07, 101.41, 55.46, 28.64, 26.37, 25.26. HRMS (ESI) m/z calcd for C\(_{24}\)H\(_{21}\)N\(_2\)O\(_5\)\(^+\) (M+H)\(^+\) 417.1445, found 417.1448.

4-(Benzo[d][1,3]dioxol-5-yl)-2-phenethylpyrimido[1,6-a]indole-1,3,5(2H)-trione

Compounds 7i (red solid, yield 74%, 322 mg, \(R_f = 0.18\) (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta 8.48\) (d, \(J = 8.2\) Hz, 1H), \(7.81\) (d, \(J = 7.5\) Hz, 1H), \(7.76\) (t, \(J = 7.8\) Hz, 1H), \(7.38\)–\(7.29\) (m, 5H), \(7.24\) (dd, \(J = 6.0, 2.9\) Hz, 1H), \(6.96\)–\(6.91\) (m, 2H), \(6.90\) (d, \(J = 2.5\) Hz, 1H), \(6.04\) (s, 2H), \(4.39\)–\(4.21\) (m, 2H), \(3.07\)–\(2.88\) (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \(\delta 181.79, 162.83, 149.00, 147.50, 147.01, 146.34, 138.08, 137.62, 134.63, 129.02, 128.62, 126.70, 126.08, 125.08, 123.47, 120.98, 119.47, 117.03, 110.97, 108.17, 101.47, 43.34, 33.81. HRMS (ESI) m/z calcd for C\(_{26}\)H\(_{19}\)N\(_2\)O\(_5\)\(^+\) (M+H)\(^+\) 439.1288, found 439.1281.
**4-(Benzo[d][1,3]dioxol-5-yl)-2-(2,6-dimethylphenyl)pyrimido[1,6-a]indole-1,3,5(2H)-trione**

![Chemical Structure]

Compound *7j* (red solid, yield 59%, 258 mg, R<sub>f</sub> = 0.20 (EA/Hex=15%)) ¹H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.42 (d, <i>J</i> = 8.2 Hz, 1H), 7.85 (d, <i>J</i> = 7.6 Hz, 1H), 7.74 (t, <i>J</i> = 7.8 Hz, 1H), 7.37 (t, <i>J</i> = 7.5 Hz, 1H), 7.32-7.27 (m, 1H), 7.21 (d, <i>J</i> = 7.5 Hz, 2H), 7.03 (dd, <i>J</i> = 8.1, 1.7 Hz, 1H), 6.98 (d, <i>J</i> = 1.5 Hz, 1H), 6.90 (d, <i>J</i> = 8.1 Hz, 1H), 6.03 (s, 2H), 2.20 (s, 6H). ¹³C NMR (100 MHz, CDCl<sub>3</sub>) δ 181.70, 162.16, 149.15, 147.43, 146.29, 146.18, 137.72, 135.37, 135.28, 132.83, 129.31, 128.76, 126.19, 125.44, 125.12, 123.62, 120.63, 119.74, 117.22, 111.19, 108.06, 101.49, 17.86. HRMS (ESI) m/z calcd for C<sub>26</sub>H<sub>19</sub>N<sub>2</sub>O<sub>5</sub>⁺ (M+H)<sup>+</sup> 439.1288, found 439.1289.

**4-(Benzo[d][1,3]dioxol-5-yl)-2-benzylpyrimido[1,6-a]indole-1,3,5(2H)-trione**

![Chemical Structure]

Compound *7k* (red solid, 264 mg, yield 62%, R<sub>f</sub> = 0.32 (EA/Hex=15%)) ¹H NMR (400 MHz, CDCl<sub>3</sub>) δ 8.47 (d, <i>J</i> = 8.2 Hz, 1H), 7.78 (d, <i>J</i> = 7.5 Hz, 1H), 7.75 – 7.68 (m, 1H), 7.57 (d, <i>J</i> = 6.7 Hz, 2H), 7.31 (dd, <i>J</i> = 15.3, 8.3 Hz, 4H), 6.94 (dd, <i>J</i> = 8.2, 1.3 Hz, 1H), 6.89 (d, <i>J</i> = 7.6 Hz, 2H), 6.03 (s, 2H), 5.25 (s, 2H). ¹³C NMR (100 MHz, CDCl<sub>3</sub>) δ 181.71, 162.98, 148.99, 147.47, 147.19, 146.30, 137.57, 136.15, 134.67, 129.53, 128.57, 128.04, 126.08, 125.13, 125.04, 123.44, 120.96, 119.51, 117.09, 111.00, 108.14, 101.46, 45.10. HRMS (ESI) m/z calcd for C<sub>25</sub>H<sub>17</sub>N<sub>2</sub>O<sub>5</sub>⁺ (M+H)<sup>+</sup>
425.1132, found 425.1131.

4-(4-Bromophenyl)-2-phenethylpyrimido[1,6-a]indole-1,3,5(2H)-trione

\[
\text{O} \quad \text{N} \quad \text{N} \\
\text{N} \quad \text{O} \quad \text{O} \\
\text{Br}
\]

Compound 7l (red solid, 303 mg, yield 64%, \( R_f = 0.27 \) (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.48 (d, \( J = 8.2 \) Hz, 1H), 7.80 (d, \( J = 7.6 \) Hz, 1H), 7.76 (d, \( J = 8.0 \) Hz, 1H), 7.61 (d, \( J = 8.4 \) Hz, 2H), 7.38-7.32 (m, 5H), 7.30 (d, \( J = 8.4 \) Hz, 3H), 4.31-4.27 (m, 2H), 3.04-2.99 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 181.79, 162.46, 146.93, 146.50, 137.97, 137.84, 134.84, 132.21, 131.31, 129.00, 128.63, 126.72, 126.52, 126.23, 125.20, 124.25, 123.25, 118.39, 117.07, 43.43, 33.30. HRMS (ESI) \( m/z \) calcd for C\(_{25}\)H\(_{18}\)BrN\(_2\)O\(_3\)\(^+\) (M+H\(^+\)) 473.0495, found 473.0492.

4-(4-methoxyphenyl)-2-phenethylpyrimido[1,6-a]indole-1,3,5(2H)-trione

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\text{O} \quad \text{N} \quad \text{N} \\
\text{N} \quad \text{O} \quad \text{O} \\
\text{OMe}
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Compound 7m (red solid, 285 mg, yield 67%, \( R_f = 0.21 \) (EA/Hex=15%)) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) \(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 8.48 (d, \( J = 8.2 \) Hz, 1H), 7.80 (d, \( J = 7.6 \) Hz, 1H), 7.75 (t, \( J = 7.8 \) Hz, 1H), 7.41 (d, \( J = 8.6 \) Hz, 2H), 7.36-7.30 (m, 5H), 7.23 (d, \( J = 6.9 \) Hz, 1H), 7.00 (d, \( J = 8.6 \) Hz, 2H), 4.34-4.24 (m, 2H), 3.88 (s, 3H), 3.06-2.97 (m, 2H). \(^{13}\)C NMR (100 MHz, CDCl\(_3\)) \( \delta \) 181.87, 162.97, 160.88, 147.05,
4-(4-Bromophenyl)-2-(2,6-dimethylphenyl)pyrimido[1,6-a]indole-1,3,5(2H)-trione

Compound 7n (red solid, 330 mg, yield 70%, R_f = 0.23 (EA/Hex=15%)) ¹H NMR (400 MHz, CDCl₃) δ 8.42 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 7.5 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.59 (d, J = 8.4 Hz, 2H), 7.37 (t, J = 7.4 Hz, 3H), 7.33-7.24 (m, 2H), 7.21 (d, J = 7.4 Hz, 2H), 2.20 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 181.69, 161.81, 146.46, 146.11, 137.96, 135.59, 135.33, 132.68, 132.43, 131.21, 129.39, 128.80, 126.36, 126.17, 125.25, 124.43, 123.40, 118.64, 117.26, 17.86. HRMS (ESI) m/z calcd for C₂₆H₂₁N₂O₄⁺ (M+H)⁺ 425.1496, found 425.1492.

2-(2,6-Dimethylphenyl)-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

Compound 7o (red solid, 280 mg, yield 71%, R_f = 0.25 (EA/Hex=15%)) ¹H NMR (400 MHz, CDCl₃) δ 8.43 (d, J = 8.2 Hz, 1H), 7.84 (d, J = 7.6 Hz, 1H), 7.75 (t, J = 7.8 Hz, 1H), 7.48 (d, J = 2.2 Hz, 5H), 7.37 (t, J = 7.5 Hz, 1H), 7.34-7.27 (m, 1H), 7.21 (d, J = 7.5 Hz, 2H), 2.22 (s, 6H). ¹³C NMR (100 MHz, CDCl₃) δ 181.73, 162.10, 146.46, 146.26, 137.77, 135.51, 135.38, 132.82, 130.70,
129.84, 129.30, 128.76, 127.94, 127.32, 126.21, 125.14, 123.55, 119.96, 117.23, 17.86. HRMS (ESI) m/z calcd for C_{25}H_{19}N_{2}O_{3}^{+} (M+H)^{+} 395.1390, found 395.1392.

2-(2,6-Dimethylphenyl)-4-(4-methoxyphenyl)pyrimido[1,6-α]indole-1,3,5(2H)-trione

Compound 7p (dark yellow solid, 260 mg, yield 61%, R_{f} = 0.29 (EA/Hex=15%)) ^{1}H NMR (400 MHz, CDCl$_{3}$) δ ^{1}H NMR (400 MHz, CDCl$_{3}$) δ 8.43 (d, J = 8.2 Hz, 1H), 7.85 (d, J = 7.6 Hz, 1H), 7.74 (t, J = 7.8 Hz, 1H), 7.50 (d, J = 8.7 Hz, 2H), 7.37 (t, J = 7.5 Hz, 1H), 7.3-7.28 (m, 1H), 7.21 (d, J = 7.4 Hz, 2H), 6.99 (d, J = 8.7 Hz, 2H), 3.87 (s, 3H), 2.21 (s, 6H). ^{13}C NMR (100 MHz, CDCl$_{3}$) δ 181.81, 162.34, 161.06, 146.29, 137.64, 135.40, 132.90, 132.54, 129.28, 128.76, 126.12, 125.06, 123.74, 120.05, 119.33, 117.22, 113.43, 55.33, 17.87. HRMS (ESI) m/z calcd for C_{26}H_{21}N_{2}O_{4}^{+} (M+H)^{+} 425.1496, found 425.1432.

2-Butyl-4-phenylpyrimido[1,6-α]indole-1,3,5(2H)-trione

Compound 7q (yellow solid, 264 mg, R$_{f}$=Me, yield 69%; R$_{f}$=Et, yield 65%, R$_{f}$ = 0.35 (EA/Hex = 15%)) ^{1}H NMR (400 MHz, CDCl$_{3}$) δ 8.46 (d, J = 8.2 Hz, 1H), 7.79 - 7.69 (m, 2H), 7.46 (dd, J = 6.7, 2.8 Hz, 3H), 7.41 (dt, J = 3.9, 2.7 Hz, 2H), 7.32 (t, J = 7.5 Hz, 1H), 4.12 - 4.01 (m, 2H), 1.70 (tt, J = 7.7, 6.6 Hz, 2H), 1.42 (dq, J = 14.8, 7.4 Hz, 2H), 0.96 (t, J = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, CDCl$_{3}$) δ 181.87, 162.80, 147.19, 146.48, 137.59, 134.67, 130.46, 129.60, 127.96, 127.69, 125.99, 125.01, 123.34,
119.62, 116.99, 41.87, 29.68, 20.24, 13.72. HRMS (ESI) m/z calcd for C_{21}H_{19}N_{2}O_{3}^+(M+H)^+ 374.1390, found 374.1391.

8-Bromo-2-cyclohexyl-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

![Chemical structure of compound 7r](image)

Compound 7r (yellow solid, 280 mg, yield 72%, R_1 = 0.28 (EA/Hex= 10%)) 1H NMR (400 MHz, CDCl_3) δ 8.72 (s, 1H), 7.60 (d, J = 8.1 Hz, 1H), 7.45 (dd, J = 5.2, 1.1 Hz, 4H), 7.41 – 7.37 (m, 2H), 4.85 (ddd, J = 12.0, 8.7, 3.6 Hz, 1H), 2.49 – 2.40 (m, 2H), 1.87 (d, J = 12.8 Hz, 2H), 1.70 (s, 2H), 1.43 – 1.33 (m, 4H). 13C NMR (100 MHz, CDCl_3) δ 180.76, 163.01, 132.80, 131.18, 130.42, 129.67, 129.33, 128.41, 127.95, 127.63, 125.71, 122.19, 120.56, 55.60, 29.56, 28.57, 26.44. HRMS (ESI) m/z calcd for C_{23}H_{20}BrN_{2}O_{3}^+(M+H)^+ 451.0652, found 451.0649.

2-Cyclohexyl-7-methoxy-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

![Chemical structure of compound 7s](image)

Compound 7s (yellow solid, 174 mg, yield 52%, R_1 = 0.30 (EA/Hex= 10%)) 1H NMR (400 MHz, CDCl_3) δ 8.34 (d, J = 8.7 Hz, 1H), 7.47 – 7.42 (m, 3H), 7.42 – 7.36 (m, 2H), 7.27 (d, J = 2.8 Hz, 1H), 7.18 (d, J = 2.5 Hz, 1H), 4.90 – 4.81 (m, 1H), 3.83 (s, 3H), 2.54 – 2.42 (m, 2H), 1.86 (d, J = 12.9 Hz, 2H), 1.72 (d, J = 13.5 Hz, 2H), 1.45 – 1.34 (m, 4H). 13C NMR (100 MHz, CDCl_3) δ 181.86, 163.29, 157.78, 141.00, 131.21, 130.29, 129.40, 127.90, 124.96, 118.12, 107.17, 55.84, 55.31, 29.62, 28.60, 26.33. HRMS (ESI) m/z calcd for C_{24}H_{23}N_{2}O_{3}^+(M+H)^+ 403.1652, found 403.1652.
2-Cyclohexyl-8-methoxy-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

![Chemical Structure](image)

Compound 7t (yellow solid, 167 mg, yield 50%, R\textsubscript{f} = 0.35 (EA/Hex = 10%)) \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.47 (d, \(J = 8.2\) Hz, 1H), 7.81–7.68 (m, 2H), 7.44 (m, 4H), 7.32 (t, \(J = 7.3\) Hz, 1H), 4.93–4.86 (m, 1H), 3.78 (s, 3H), 2.49 (qd, \(J = 12.4, 3.3\) Hz, 2H), 1.88 (d, \(J = 13.2\) Hz, 2H), 1.78–1.70 (m, 2H), 1.47–1.34 (m, 2H), 1.33–1.18 (m, 2H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 182.03, 163.37, 147.42, 146.75, 137.55, 134.64, 130.53, 129.53, 128.08, 127.97, 125.89, 124.96, 123.47, 119.86, 117.17, 59.23, 55.47, 28.67, 26.40, 25.27. HRMS (ESI) m/z calcd for C\textsubscript{24}H\textsubscript{23}N\textsubscript{2}O\textsubscript{3} \((\text{M+H})^{+}\) 403.1652, found 403.1652.

2-Benzyl-7-methyl-4-phenylpyrimido[1,6-a]indole-1,3,5(2H)-trione

![Chemical Structure](image)

Compound 7u (yellow solid, 151 mg, yield 57%, R\textsubscript{f} = 0.35 (EA/Hex = 10%)) \textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}) \(\delta\) 8.47 (s, 1H), 7.81–7.68 (m, 2H), 7.57 (d, \(J = 6.6\) Hz, 2H), 7.30 (ddd, \(J = 16.7, 9.5, 3.8\) Hz, 8H), 5.26 (s, 2H), 2.42 (s, 3H). \textsuperscript{13}C NMR (100 MHz, CDCl\textsubscript{3}) \(\delta\) 181.79, 163.37, 147.28, 146.40, 139.91, 137.53, 136.23, 134.60, 130.46, 129.54, 128.81, 128.56, 128.01, 126.03, 125.01, 124.66, 123.49, 119.98, 117.09, 45.06, 21.56. HRMS (ESI) m/z calcd for C\textsubscript{25}H\textsubscript{19}N\textsubscript{2}O\textsubscript{3} \((\text{M+H})^{+}\) 395.1390, found 395.1391.

Methyl 2-(N-(2-(benzylamino)-2-oxoethyl)-2-oxo-2-phenylacetamido)benzoate
Compound 9a (white solid, 350 mg, yield 82%, $R_f$ = 0.25 (EA/Hex=30%)) $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.86 (dd, $J = 10.1$, 4.2 Hz, 3H), 7.52 (dd, $J = 9.9$, 4.1 Hz, 2H), 7.46-7.42 (m, 1H), 7.40 (d, $J = 7.8$ Hz, 2H), 7.36 (d, $J = 7.0$ Hz, 1H), 7.33 (d, $J = 7.1$ Hz, 2H), 7.30 (d, $J = 3.2$ Hz, 3H), 7.23-7.19 (m, 1H), 4.90 (d, $J = 8.9$ Hz, 1H), 4.52 (dd, $J = 8.0$, 4.7 Hz, 2H), 4.23 (t, $J = 8.5$ Hz, 1H), 3.68 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 189.41, 167.68, 166.62, 165.69, 140.19, 138.02, 134.41, 133.59, 133.01, 131.62, 130.73, 130.28, 129.96, 128.99, 128.64, 128.60, 127.77, 127.40, 53.74, 52.49, 43.64. HRMS (ESI) m/z calcd for C$_{25}$H$_{23}$N$_2$O$_5$ $^+$ (M+H)$^+$ 431.1601, found 431.1607.

Methyl

2-((1-benzyl-2,5-dioxo-4-phenyl-2,5-dihydro-1H-pyrrol-3-yl)amino)benzoate

Compound 10 (yellow solid, 64 mg, yield 78%, $R_f$ = 0.29 (EA/Hex=15%)) $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 10.40 (s, 1H), 7.98 (s, 1H), 7.47 (d, $J = 6.5$ Hz, 2H), 7.37-7.29 (m, 2H), 7.26 (s, 1H), 7.19 (d, $J = 6.5$ Hz, 3H), 7.11 (s, 2H), 6.90 (s, 2H), 6.12 (s, 1H), 4.80 (s, 2H), 3.98 (s, 3H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 171.68, 168.13, 168.04, 138.96, 136.56, 134.87, 132.45, 130.90, 129.89, 129.71, 128.84, 128.66, 127.87, 127.80, 127.49, 122.02, 120.89, 116.98, 106.24, 52.47, 41.92. HRMS (ESI) m/z calcd for C$_{25}$H$_{21}$N$_2$O$_4$ $^+$ (M+H)$^+$ 413.1496, found 413.1495.

1-Phenethyl-3-phenyl-4-(phenylamino)-1H-pyrrole-2,5-dione
Compound 12 (yellow solid, 91 mg, yield 59%, $R_f = 0.30$ (EA/Hex= 10%)) $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ $^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.35 – 7.23 (m, 6H), 7.16 – 7.08 (m, 3H), 7.06 – 6.93 (m, 5H), 6.63 (d, $J = 7.5$ Hz, 2H), 3.86 (dd, $J = 8.7$, 6.9 Hz, 2H), 3.06 – 2.94 (m, 2H). $^{13}$C NMR (100 MHz, CDCl$_3$) $\delta$ 172.03, 168.35, 138.19, 136.28, 135.97, 129.72, 129.33, 128.91, 128.58, 128.30, 127.32, 126.64, 124.49, 121.50, 102.64, 39.57, 34.85. HRMS (ESI) m/z calcd for C$_{24}$H$_{21}$N$_2$O$_3$ $(M+H)^+$ 369.1598, found 369.1597.
$^1$H NMR and $^{13}$C NMR spectrum of 5a.
$^1$H NMR and $^{13}$C NMR spectrum of 7a.
$^1$H NMR and $^{13}$C NMR spectrum of 7b.
$^1$H NMR and $^{13}$C NMR spectrum of 7c.
$^1$H NMR and $^{13}$C NMR spectrum of 7d.
$^1$H NMR and $^{13}$C NMR spectrum of 7e.
$^1$H NMR and $^{13}$C NMR spectrum of 7f.
$^1\text{H NMR}$ and $^{13}\text{C NMR}$ spectrum of 7g.
$^1$H NMR and $^{13}$C NMR spectrum of 7h.
$^1$H NMR and $^{13}$C NMR spectrum of 7i.
$^1$H NMR and $^{13}$C NMR spectrum of 7j.
$^1$H NMR and $^{13}$C NMR spectrum of 7k.
$^1$H NMR and $^{13}$C NMR spectrum of 71.
\(^1\)H NMR and \(^{13}\)C NMR spectrum of 7m.
$^1$H NMR and $^{13}$C NMR spectrum of 7n.
$^1$H NMR and $^{13}$C NMR spectrum of 7o.
$^1$H NMR and $^{13}$C NMR spectrum of 7p.
$^1$H NMR and $^{13}$C NMR spectrum of 7q.
$^1$H NMR and $^{13}$C NMR spectrum of 7r.
$^{1}$H NMR and $^{13}$C NMR spectrum of 7s.
$^1$H NMR and $^{13}$C NMR spectrum of 7t.
$^1$H NMR and $^{13}$C NMR spectrum of 7u.
$^1$H NMR and $^{13}$C NMR spectrum of 9a.
$^1$H NMR and $^{13}$C NMR spectrum of 10.
$^1$H NMR and $^{13}$C NMR spectrum of 12.