Supporting Information
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Experimental

Melting points were measured with a Stuart melting point apparatus and are uncorrected. The IR spectra were recorded using a FTIR Bruker–vector 22 spectrophotometer as KBr pellets. The $^1$H and $^{13}$C NMR spectra were recorded in DMSO–d$_6$ as solvent on Varian Gemini NMR spectrometer at 400 MHz and 100 MHz, respectively, using TMS as internal standard. Chemical shifts are reported as δ values in ppm. The elemental analyses were performed at the Micro analytical center, Cairo University.

**Synthesis of 9,10-dimethoxy-4-methyl-2-aryl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4a-g):**

A mixture of aldehydes 1a-g (1 mmol) and 2-(6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)acetonitrile 2 (1 mmol) was heated in acetic acid (10 mL) for 5 minute, then 3-aminocrotononitrile 2 (1 mmol) was added and the heating was continued at reflux for 3 h. The excess solvent was evaporated at reduced pressure. The crude product was crystallized from EtOH.

**9,10-Dimethoxy-4-methyl-2-phenyl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4a):** Yellow crystals, Yield (75%); mp 208-210 °C; IR (KBr): ν 2182 (CN); $^1$H NMR (400 MHz, DMSO-d$_6$) δ 2.31 (s, 3H, CH$_3$), 2.88-2.91 (m, 2H, CH$_2$), 3.54-3.59 (m, 1H, CH$_2$), 3.75 (s, 3H, CH$_3$O), 3.88 (s, 3H, CH$_3$O), 4.46 (s, 1H, H-2), 7.02 (s, 1H, Ar-H), 7.34-7.42 (m, 5H, Ph), 7.63 (s, 1H, Ar-H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 18.9 (Me), 28.6 (C-7), 42.1 (C-2), 44.2 (C-6), 56.1 (OMe), 56.2 (OMe), 82.2 (C-1), 85.1 (C-3), 111.2 (C-11), 111.3 (C-8), 119.6 (CN), 120.3 (CN), 121.6 (Ar-C), 127.8 (Ar-C), 128.3 (Ar-C), 129.5 (Ar-C), 131.8 (Ar-C), 143.7 (Ar-C), 146.3 (C10), 147.1 (C9), 150.4 (C4), 151.3 (C11b). Anal. Calcd. for C$_{24}$H$_{21}$N$_3$O$_2$ (383.5): C, 75.18; H, 5.52; N, 10.96. Found: C, 75.04; H, 5.60; N, 10.87.

**9,10-Dimethoxy-4-methyl-2-(p-tolyl)-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4b):** Yellow crystals, Yield (70%); mp 224-226 °C; IR (KBr): ν 2182 (CN); $^1$H NMR (400 MHz, DMSO-d$_6$) δ 2.30 (s, 6H, 2CH$_3$), 2.85-2.93 (m, 2H, CH$_2$), 3.55-3.60 (m, 1H, CH$_2$), 3.74 (s, 3H, CH$_3$O), 3.75-3.82 (m, 1H, CH$_2$), 3.83 (s, 3H, CH$_3$O), 4.40 (s, 1H, H-2), 7.01 (s, 1H, Ar-H), 7.19-7.24 (m, 4H, Ar), 7.60 (s, 1H, Ar-H); $^{13}$C NMR (100 MHz, DMSO-d$_6$) δ 18.9, 21.1, 28.7, 41.8, 44.2, 56.1, 56.2, 82.4, 85.2, 111.2, 111.3,
119.6, 120.3, 121.6, 127.7, 130.0, 131.8, 137.6, 140.9, 146.1, 147.1, 150.2, 151.3. Anal. Calcd. for C_{25}H_{23}N_{3}O_{2} (397.5): C, 75.55; H, 5.83; N, 10.57. Found: C, 75.42; H, 5.75; N, 10.49.

9,10-Dimethoxy-2-(4-methoxyphenyl)-4-methyl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4c): Yellow crystals, Yield (78%); mp 180-182 °C; IR (KBr): ν 2181 (CN); \(^1\)H NMR (400 MHz, DMSO-d6) δ 2.30 (s, 3H, CH3), 2.86-2.90 (m, 2H, CH2), 3.56-3.72 (m, 1H, CH2), 3.75 (s, 3H, CH3O), 3.76 (s, 3H, CH3O), 3.77-3.81 (m, 1H, CH2), 3.83 (s, 3H, CH3O), 4.39 (s, 1H, H-2), 6.95 (d, 2H), 7.01 (s, 1H, Ar-H), 7.26 (d, 2H) and 7.60 (s, 1H, Ar-H); \(^13\)C NMR (100 MHz, DMSO-d6) δ 18.9, 28.6, 41.4, 44.1, 55.6, 56.1, 56.2, 82.6, 85.4, 111.2, 111.3, 114.8, 119.6, 120.3, 121.6, 129.0, 131.7, 136.0, 145.9, 147.1, 150.0, 151.2, 159.4. Anal. Calcd. for C_{25}H_{23}N_{3}O_{3} (413.5): C, 72.62; H, 5.61; N, 10.16. Found: C, 72.50; H, 5.73; N, 10.22.

2-(2,4-Dimethoxyphenyl)-9,10-dimethoxy-4-methyl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4d): Orange crystals, Yield (68%); mp 150-152 °C; IR (KBr): ν 2180 (CN); \(^1\)H NMR (400 MHz, DMSO-d6) δ 2.27 (s, 3H, CH3), 2.84-2.94 (m, 2H, CH2), 3.41-3.60 (m, 2H, CH2), 3.74 (s, 3H, CH3O), 3.76 (s, 3H, CH3O), 3.77 (s, 3H, CH3O), 3.84 (s, 3H, CH3O), 4.65 (s, 1H, H-2), 6.55 (dd, 1H), 6.61 (d, 1H), 7.01 (s, 1H, Ar-H), 7.12 (s, 1H) and 7.61 (s, 1H, Ar-H); \(^13\)C NMR (100 MHz, DMSO-d6) δ 18.8, 28.7, 35.6, 44.1, 55.6, 56.1, 56.5, 81.6, 84.5, 99.1, 106.1, 111.2, 111.3, 119.7, 120.3, 121.6, 123.8, 130.2, 131.6, 146.5, 147.1, 150.4, 151.1, 158.0, 160.6. Anal. Calcd. for C_{26}H_{25}N_{3}O_{4} (443.5): C, 70.41; H, 5.68; N, 9.47. Found: C, 70.29; H, 5.56; N, 9.35.

2-(4-Chlorophenyl)-9,10-dimethoxy-4-methyl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4e): Yellow crystals, Yield (75%); mp 200-202 °C; IR (KBr): ν 2182 (CN); \(^1\)H NMR (400 MHz, DMSO-d6) δ 2.31 (s, 3H, CH3), 2.87-2.91 (m, 2H, CH2), 3.54-3.60 (m, 1H, CH2), 3.75 (s, 3H, CH3O), 3.77-3.83 (m, 1H, CH2), 3.85 (s, 3H, CH3O), 4.54 (s, 1H, H-2), 7.02 (s, 1H, Ar-H), 7.38 (d, 2H), 7.46 (d, 2H) and 7.61 (s, 1H, Ar-H); \(^13\)C NMR (100 MHz, DMSO-d6) δ 18.9, 28.6, 41.3, 44.2, 56.1, 56.2, 81.7, 84.6, 111.2, 111.3, 119.4, 120.1, 121.4, 129.4, 129.8, 131.9, 133.0, 142.7, 146.4, 147.1, 150.8, 151.4. Anal. Calcd. for C_{24}H_{20}ClN_{3}O_{2} (417.9): C, 68.98; H, 4.82; Cl, 8.48; N, 10.06. Found: C, 68.84; H, 4.75; Cl, 8.39; N, 10.18.

9,10-Dimethoxy-4-methyl-2-(4-nitrophenyl)-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4f): Yellow crystals, Yield (72%); mp 194-196 °C; IR (KBr): ν 2180 (CN); \(^1\)H NMR (400 MHz, DMSO-d6) δ 2.32 (s, 3H, CH3), 2.90-2.93 (m, 2H, CH2), 3.57-
3.63 (m, 1H, CH₂), 3.75 (s, 3H, CH₃O), 3.76-3.80 (m, 1H, CH₂), 3.83 (s, 3H, CH₃O), 4.78 (s, 1H, (s, 1H, H-2), 7.03 (s, 1H, Ar-H), 7.62 (d, 2H), 7.68 (s, 1H, Ar-H) and 8.26 (d, 2H); ¹³C NMR (100 MHz, DMSO-d₆) δ 19.0, 28.5, 41.6, 44.3, 56.1, 56.2, 81.0, 83.9, 111.2, 111.3, 119.3, 119.9, 121.2, 124.7, 129.3, 132.0, 147.0, 147.1, 147.6, 150.4, 151.4, 151.5. Anal. Calcd. for C₂₄H₂₀N₄O₄ (428.4): C, 67.28; H, 4.71; N, 13.08. Found: C, 67.35; H, 4.63; N, 13.20.

2-(Benzo[d][1,3]dioxol-5-yl)-9,10-dimethoxy-4-methyl-6,7-dihydro-2H-pyrido[2,1-a]isoquinoline-1,3-dicarbonitrile (4g): Yellow crystals, Yield (76%); mp 219-220 °C; IR (KBr): ν 2180 (CN); ¹H NMR (400 MHz, DMSO-d₆) δ 2.30 (s, 3H, CH₃), 2.85-2.90 (m, 2H, CH₂), 3.53-3.60 (m, 1H, CH₂), 3.75 (s, 3H, CH₃O), 3.78 (m, 1H, CH₂), 3.83 (s, 3H, CH₃O), 4.39 (s, 1H, H-2), 6.03 (s, 2H, -OCH₂O-), 6.80-6.93 (m, 3H, Ar-H), 7.01 (s, 1H, Ar-H), 7.60 (s, 1H, Ar-H);¹³C NMR (100 MHz, DMSO-d₆) δ 18.9, 28.6, 41.9, 44.1, 56.1, 56.2, 82.4, 85.2, 101.6, 108.3, 108.9, 111.2, 111.3, 119.6, 120.3, 121.2, 121.6, 131.8, 138.0, 146.0, 147.1, 147.4, 148.3, 150.2, 151.3. Anal. Calcd. for C₂₅H₂₁N₃O₄ (427.5): C, 70.25; H, 4.95; N, 9.83. Found: C, 70.18; H, 4.82; N, 9.74.
$^1$H NMR spectrum of compound 4a
$^{13}$C NMR spectrum of compound 4a
HMBC spectrum of compound 4a
$^1$H NMR spectrum of compound 4b
$^{13}$C NMR spectrum of compound 4b
$^1$H NMR spectrum of compound 4c
$^{13}$C NMR spectrum of compound 4c
$^1$H NMR spectrum of compound 4d
$^{13}$C NMR spectrum of compound 4d
\(^1\)H NMR spectrum of compound 4e
$^{13}$C NMR spectrum of compound 4e
$^1$H NMR spectrum of compound 4f
$^{13}$C NMR spectrum of compound 4f
$^1$H NMR spectrum of compound 4g
$^{13}$C NMR spectrum of compound 4g