**SYNTHESIS, CHARACTERIZATION AND ANTIMICROBIAL
EVALUATION OF SOME NOVEL 4-HYDROXYQUINOLIN-2(1H)-ONES**

Magdy A. Ibrahim,* Hany M. Hassanin, and Youssef A. Alnamer

Department of Chemistry, Faculty of Education, Ain Shams University, Roxy 11711,

Cairo, Egypt

e-mail address: magdy_ahmed1977@yahoo.com

Tel.: +2 01007887204; fax: +2 022581243.

(A) Spectroscopic and characterization of the synthesized compounds:

6-Methyl-4,5-dioxo-5,6-dihydro-4H-pyrano[3,2-c]quinoline-3-carboxaldehyde (3)

Phosphoryl chloride (5 mL, 5.4 mmol) was added drop-wise to a stirred cold DMF (15 mL) in an ice-bath, then the mixture was stirred at room temperature for 30 min. A solution of 3-acetyl-1-methyl-4-hydroxyquinolin-2(1H)-one (**2**) (1.0 g, 4 mmol), in DMF (10 mL) was added drop-wise with continuous stirring. After completion of addition, the reaction mixture was stirred at room temperature for 2 h and heated under reflux, on a boiling water-bath, for 2 h. The mixture was left to cool at room temperature and poured onto crushed ice (*ca.* 50 g). The brown solid so obtained was filtered, dried and crystallized from ethanol to give compound **3** as pale yellow crystals, yield 0.65 g (64 %), m.p. 258-259 °C. IR (KBr, cm⁻¹): 3082 (CH_{arom}), 2982, 2905 (CH_{alph.}), 1684 (HC=O), 1650 (C=O_{γ-pyrone}), 1633 (C=O_{quinolone}) and 1619 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.58 (s, 3H, CH₃), 7.39 (t, 1H, *J*=7.2 Hz, H-9), 7.60 (d, 1H, *J*=8.7 Hz, H-7), 7.84 (t, 1H, *J*=7.2 Hz, H-8), 8.11 (d, 1H, *J*=8.1 Hz, H-10), 8.81 (s, 1H, H-2), 10.08 (s, 1H, CH=O). Mass spectrum, *m/z* (*I_r* %): 255 (M⁺, 11), 227 (57), 214 (9), 198 (18), 173 (7), 143 (13), 132 (8), 115 (13), 104 (18), 94 (13), 80 (100%), 77 (24) and 64 (68). Anal. Calcd. for C₁₄H₉NO₄ (255.23); C, 65.88; H, 3.55; N, 5.49%. Found: C, 65.84; H, 3.47; N, 5.35%.

4-Hydroxy-1-methyl-3-(1*H*-pyrazol-4-ylcarbonyl)quinolin-2(1*H*)-one (5)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and hydrazine hydrate (0.1 mL, 2 mmol) in absolute ethanol was heated under reflux for 15 min. The solid obtained during heating was filtered and crystallized from ethanol to give compound **5** as yellow crystals, yield (0.34 g, 63%), m.p. > 300 °C. IR (KBr, cm⁻¹): 3423 (OH), 3166 (NH), 3029 (CH_{arom.}), 2965, 2920 (CH_{aliph.}), 1628 (C=O_{quinolone}), 1624 (C=O_{hydrogen bonded} and C=N), and 1574 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300MHz): 3.66 (s, 3H, CH₃), 7.34 (t, 1H, *J*=7.2 Hz, H-6), 7.54-7.63 (m, 2H, H-8 and H-7), 8.17 (d, 1H, *J*=7.8 Hz, H-5), 8.53 (s, 2H, H-3_{pyrazole} and H-5_{pyrazole}), 9.63 (bs, 1H, NH exchangeable with D₂O). Mass spectrum, *m/z* (*I_r* %): 269 (M⁺, 2), 252 (2), 238 (5), 211 (4), 199 (4), 173 (2), 154 (4), 127 (5), 118 (5), 104 (7), 94 (7), 80 (83), 91 (16), 77 (10) and 64 (100). Anal. Calcd. for C₁₄H₁₁N₃O₃ (269.26); C, 62.45; H, 4.12; N, 15.61%. Found: C, 62.28; H, 3.87; N, 15.27%.

4-Hydroxy-1-methyl-3-[(1-phenyl-1*H*-pyrazol-4-yl)carbonyl]quinolin-2(1*H*)-one (6)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and phenyl hydrazine (0.22 mL, 2 mmol) in absolute ethanol (20 mL) containing few drops of triethylamine was heated under reflux for 2 h. The solid obtained after cooling was filtered and crystallized from methanol to give compound **6** as orange crystals, yield (0.39 g, 66%), m.p. 198-199 °C. IR (KBr, cm⁻¹): 3447 (OH), 3015 (CH_{arom.}), 1636 (C=O_{quinolone}), 1624 (C=O_{hydrogen bond}), 1598 (C=N) and 1559 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.59 (s, 3H, CH₃), 6.62 (t, 1H, *J*=6.6 Hz, Ar-H), 6.78 (d, 1H, *J*=6.6 Hz, Ar-H), 7.02 (t, 1H, *J*=7.5 Hz, Ar-H), 7.34-7.56 (m, 4H, Ar-H), 7.90 (d, 1H, *J*=8.1 Hz, Ar-H), 8.06 (d, 1H, *J*=7.8 Hz, H-5), 8.25 (s, 1H, H-3_{pyrazole}) and 9.14 (s, 1H, H-5_{pyrazole}). Mass spectrum, *m/z* (*I_r* %): 345 (M⁺, 100), 328 (6), 314 (8), 268 (5), 253 (84), 201 (33), 171 (25), 144 (48), 133 (12), 117 (27), 104 (40), 93 (53), 80 (44), 77 (98) and 64 (28). Anal. Calcd. for C₂₀H₁₅N₃O₃ (345.36); C, 69.56; H, 4.38; N, 12.17%. Found: C, 69.27; H, 4.24; N, 11.88%.

4-Hydroxy-1-methyl-3-[(1-(7-chloroquinolin-4-yl)-1H-pyrazol-4-yl)carbonyl]quinolin-2(1H)-one (9)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 7-chloro-4-hydrazinoquinoline (**7**) (0.36 g, 2 mmol) in absolute ethanol (20 mL) containing few drops of triethylamine was heated under reflux for 2 h. The solid obtained during heating was filtered and crystallized from DMF/H₂O to give compound **9** as orange-red crystals, yield (0.46 g, 53%), m.p. 206-207 °C. IR (KBr, cm⁻¹): 3452 (OH), 3060 (CH_{arom.}), 1657 (C=O_{quinolone}), 1622 (C=O_{hydrogen bonded}), 1595 (C=N) and 1566 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.60 (s, 3H, CH₃), 7.33 (t, 1H, *J*=7.2 Hz, H-6_{quinolone}), 7.57 (d, 1H, *J*=8.4 Hz, Ar-H), 7.76-7.81 (m, 3H, Ar-H), 8.13 (d, 1H, *J*=7.8 Hz, H-5_{quinolone}), 8.23 (s, 1H, H-8_{quinoline}), 8.33 (d, 1H, *J*=9.3 Hz, H-5_{quinoline}), 8.45 (s, 1H, H-3_{pyrazole}), 9.08 (d, 1H, *J*=8.1 Hz, H-2_{quinoline}), 9.13 (s, 1H, H-5_{pyrazole}). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 28.8, 113.6, 115.0, 116.3, 117.1, 120.4, 121.6, 124.6, 125.8, 126.1, 128.4, 128.9, 130.9, 133.8, 137.0, 139.4, 140.2, 148.2, 152.2, 161.2, 164.2, 184.0. Mass spectrum, *m/z* (*I*_r %): 430 (M⁺, 73), 403 (19), 268 (4), 253 (100), 230 (18), 201 (35), 175 (12), 162 (10), 134 (15), 117 (14), 104 (28), 91 (9), 80 (25), 77 (30), 64 (16). Anal. Calcd. for C₂₃H₁₅ClN₄O₃ (430.85); C, 64.12; H, 3.51; N, 13.00%. Found: C, 64.01; H, 3.24; N, 12.79%.

4-Hydroxy-1-methyl-3-[(1-(5,6-diphenyl-1,2,4-triazin-3-yl)-1H-pyrazol-4-yl)carbonyl]quinolin-2(1H)-one (10)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 3-hydrazino-5,6-diphenyl-1,2,4-triazine (**8**) (0.49 g, 2 mmol) in absolute ethanol (20 mL) containing few drops of triethylamine was heated under reflux for 2 h. The solid obtained after cooling was filtered and crystallized from DMF/EtOH to give compound **10** as yellow crystals, yield (0.56 g, 56%), m.p. 231-232 °C. IR (KBr, cm⁻¹): 3447 (OH), 3058 (CH_{arom.}), 2926, 2885 (CH_{aliph.}), 1653 (C=O_{quinolone}), 1622

70 (C=O_{hydrogen bond}), 1594 (C=N) and 1544 (C=C). ¹H NMR (DMSO-*d*₆, δ , 300 MHz): 3.63 (s, 3H,
 71 CH₃), 7.28 (t, 1H, *J*= 6.6 Hz, Ar-H), 7.41-7.55 (m, 10H, Ar-H), 7.61 (d, 1H, *J*= 6.6 Hz Ar-H),
 72 7.71 (t, 1H, *J*=7.8 Hz, Ar-H), 8.11 (d, 1H, *J*=7.8 Hz, H-5_{quinolone}), 8.38 (s, 1H, H-3_{pyrazole}) and
 73 9.35 (s, 1H, H-5_{pyrazole}). Mass spectrum, *m/z* (*I*_r %): 500 (M⁺, 9), 485 (9), 472 (9), 459 (10), 403
 74 (12), 350 (11), 324 (11), 286 (12), 238 (13), 220 (13), 203 (14), 178 (100), 151 (19), 132 (10),
 75 121 (13), 104 (12), 80 (13), 76 (12) and 64 (5). Anal. Calcd. for C₂₉H₂₀N₆O₃ (500.52); C, 69.59;
 76 H, 4.03; N, 16.79%. Found: C, 69.31; H, 3.81; N, 16.54%.

77 **3-[(2-Aminopyrimidin-5-yl)carbonyl]-4-hydroxy-1-methyl-quinolin-2(1*H*)-one (11)**

78 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and guanidine hydrochloride (0.19 g, 2 mmol)
 79 in ethanolic potassium hydroxide solution (20 mL, 1%) was heated under reflux for 4h. After
 80 cooling at room temperature, the reaction mixture was poured onto crushed ice and neutralized
 81 with concentrated HCl. The precipitate so formed was filtered and crystallized from ethanol to
 82 give compound **11** as pale brown crystals, yield (0.38 g, 64%), m.p. 256-257 °C. IR (KBr, cm⁻¹):
 83 3436, 3161 (bs, OH, NH₂), 2940 (CH_{aliph.}), 1641 (C=O_{quinolone}), 1625 (C=O_{hydrogen bonded}), 1585
 84 (C=N) and 1570 (C=C). ¹H NMR (DMSO-*d*₆, δ , 300 MHz): 3.56 (s, 3H, CH₃), 6.92 (bs, 2H,
 85 NH₂ exchangeable with D₂O), 7.24 (t, 1H, *J*=7.2 Hz, H-6), 7.49 (d, 1H, *J*=8.1 Hz, H-8), 7.78 (t,
 86 1H, *J*=7.2 Hz, H-7), 8.13 (d, 1H, *J*=7.8 Hz, H-5), 8.28 (s, 1H, H-4_{pyrimidine}), 8.56 (s, 1H, H-
 87 6_{pyrimidine}). Mass spectrum, *m/z* (*I*_r %): 296 (M⁺, 9), 282 (10), 268 (38), 253 (15), 240 (39), 224
 88 (17), 215 (12), 202 (30), 184 (47), 156 (22), 134 (30), 117 (21), 104 (63), 91 (34), 77 (100) and
 89 64 (41). Anal. Calcd. for C₁₅H₁₂N₄O₃ (296.29); C, 60.81; H, 4.08; N, 18.91%. Found: C, 60.50;
 90 H, 4.11; N, 18.65%.

91 **{5-[(4-Hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]pyrimidin-2-yl}**
 92 **cyanamide (12)**

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and cyanoguanidine (0.17 g, 2 mmol) in ethanolic potassium hydroxide solution (20 mL, 1%) was heated under reflux for 4h. After cooling at room temperature, the reaction mixture was poured onto crushed ice and neutralized with concentrated HCl. The precipitate so formed was filtered and crystallized from ethanol to give compound **12** as pale brown crystals, yield (0.37 g, 58%), m.p 294-295 °C. IR (KBr, cm⁻¹): 3442 (OH, NH), 3070 (CH_{arom.}), 2923 (CH_{aliph.}), 2188 (C≡N), 1676 (C=O_{quinolone}), 1648 (C=O_{hydrogen bonded}), 1612 (C=N) and 1561 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.62 (s, 3H, CH₃), 7.51 (t, 1H, *J*=8.4 Hz, H-6), 7.73 (d, 1H, *J*=8.4 Hz, H-8), 7.82 (t, 1H, *J*=7.8 Hz, H-7), 8.08 (s, 1H, H-4_{pyrimidine}), 8.14 (d, 1H, *J*=7.8 Hz, H-5), 8.73 (s, 1H, H-6_{pyrimidine}), 11.34 (bs, 1H, NH exchangeable with D₂O). Mass spectrum, *m/z* (*I*_r %): 321 (M⁺, 37), 302 (48), 294 (46), 282 (56), 276 (37), 262 (59), 246 (49), 192 (49), 171 (44), 132 (40), 118 (44), 105 (41), 93 (37), 80 (100), 77 (42) and 64 (68). Anal. Calcd. for C₁₆H₁₁N₅O₃ (321.30); C, 59.81; H, 3.45; N, 21.80%. Found: C, 59.62; H, 3.18; N, 21.44%.

4-Hydroxy-1-methyl-3-[(2-thioxo-1,2-dihydropyrimidin-5-yl)carbonyl]quinolin-2(1*H*)-one (13)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and thiourea (0.15 g, 2 mmol) in ethanolic potassium hydroxide solution (20 mL, 1%) was heated under reflux for 4 h. After cooling at room temperature, the reaction mixture was poured onto crushed ice and neutralized with concentrated HCl. The precipitate so formed was filtered and crystallized from ethanol to give compound **13** as orange crystals, yield (0.35 g, 56%), m.p. 290-291 °C. IR (KBr, cm⁻¹): 3448 (OH, NH), 3073 (CH_{arom.}), 1676 (C=O_{quinolone}), 1636 (C=O_{hydrogen bonded}), 1614 (C=N), 1559 (C=C) and 1200 (C=S). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.59 (s, 3H, CH₃), 7.29 (t, 1H, *J*=7.2 Hz, H-6), 7.51 (d, 1H, *J*=7.8 Hz, H-8), 7.77 (t, 1H, *J*=8.7 Hz, H-7), 8.09 (d, 1H, *J*=8.1 Hz, H-5),

8.32 (s, 1H, H-4_{pyrimidine}), 8.88 (s, 1H, H-6_{pyrimidine}) and 12.28 (bs, 2H, NH and OH exchangeable with D₂O). Mass spectrum, m/z (*I_r* %): 313 (*M*⁺, 71), 295 (76), 282 (85), 268 (100), 256 (83), 226 (89), 214 (69), 201 (70), 192 (76), 116 (89), 93 (83), 78 (85) and 63 (77). Anal. Calcd. for C₁₅H₁₁N₃O₃S (313.34); C, 57.50; H, 3.54; N, 13.41; S, 10.32%. Found: C, 57.41; H, 3.37; N, 13.27; S, 10.13%.

4-Hydroxy-1-methyl-3-([1,2,4]triazolo[4,3-*a*]pyrimidin-6-ylcarbonyl)quinolin-2(1*H*)-one (14)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 3-aminotriazole (0.17 g, 2 mmol) in absolute ethanol (20 mL) was heated under reflux for 4 h. The solid obtained during heating was filtered and crystallized from ethanol to give compound **14** as pale yellow crystals, yield (0.45 g, 70%), m.p. 239 °C. IR (KBr, cm⁻¹): 3447 (OH), 3081 (CH_{arom.}), 1636 (C=O_{quinolone} and C=O_{hydrogen bond}), 1618 (C=N) and 1556 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.55 (s, 3H, CH₃), 7.37 (t, 1H, *J*=7.2 Hz, H-6), 7.60 (d, 1H, *J*=8.7 Hz, H-8), 7.81 (t, 1H, *J*=7.5 Hz, H-7), 8.16 (d, 1H, *J*=7.5 Hz, H-5), 8.82 (s, 1H, H-4_{pyrimidine}), 9.18 (s, 1H, H-6_{pyrimidine}), 9.88 (s, 1H, H-3_{triazole}). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 28.9, 113.5, 115.2, 121.0, 121.8, 122.1, 123.4, 124.8, 134.2, 139.0, 141.2, 155.1, 157.7, 160.8, 184.0. Mass spectrum, m/z (*I_r* %): 321 (*M*⁺, 9), 320 (100), 304 (34), 202 (8), 147 (13), 134 (18), 117 (18), 104 (26), 92 (29), 77 (86) and 64 (49). Anal. Calcd. for C₁₆H₁₁N₅O₃ (321.29); C, 59.81; H, 3.45; N, 21.80%. Found: C, 59.65; H, 3.50; N, 21.49%.

3-[(2-Azidopyrimidin-5-yl)carbonyl]-4-hydroxy-1-methylquinolin-2(1*H*)-one (16)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 5-aminotetrazole monohydrate (0.21 g, 2 mmol) in absolute ethanol (20 mL) was heated under reflux for 4 h. The solid obtained during heating was filtered and crystallized from DMF/MeOH to give compound **16** as pale yellow

139 crystals, yield (0.39 g, 61%), m.p. 239-240 °C. IR (KBr, cm^{-1}): 3455 (OH), 3060 ($\text{CH}_{\text{arom.}}$), 2144
140 (N_3 azido), 1638 ($\text{C}=\text{O}_{\text{quinolone}}$ and $\text{C}=\text{O}_{\text{hydrogen bond}}$), 1617 ($\text{C}=\text{N}$) and 1596 ($\text{C}=\text{C}$). ^1H NMR
141 ($\text{DMSO}-d_6$, δ , 300 MHz): 3.55 (s, 3H, CH_3), 7.37 (t, 1H, $J=7.2$ Hz, H-6), 7.60 (d, 1H, $J=8.4$ Hz,
142 H-8), 7.79 (t, 1H, $J=7.2$ Hz, H-7), 8.14 (d, 1H, $J=8.4$ Hz, H-5), 8.99 (s, 1H, H-4_{pyrimidine}), 9.35 (s,
143 1H, H-6_{pyrimidine}). Mass spectrum, m/z (I_r %): 322 (M^+ , 36), 308 (40), 295 (44), 280 (44), 252
144 (45), 220 (41), 201 (47), 147 (42), 135 (52), 116 (40), 104 (44), 92 (42), 80 (100) and 64 (88).
145 Anal. Calcd. for $\text{C}_{15}\text{H}_{10}\text{N}_6\text{O}_3$ (322.28); C, 55.90; H, 3.13; N, 26.08%. Found: C, 55.71; H, 3.02;
146 N, 25.76%.

147 **4-Hydroxy-1-methyl-3-(pyrimido[1,2-*a*]benzimidazol-3-ylcarbonyl)quinolin-2(1*H*)-one (17)**

148 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 2-aminobenzimidazole (0.27 g, 2 mmol) in
149 absolute ethanol (20 mL) containing one crystal of *p*-TsOH was heated under reflux for 4 h. The
150 solid obtained during heating was filtered and crystallized from DMF to give compound **17** as
151 yellow crystals, yield (0.44 g, 59%), m.p. 280-281 °C. IR (KBr, cm^{-1}): 3421 (OH), 3064
152 ($\text{CH}_{\text{arom.}}$), 1645 ($\text{C}=\text{O}_{\text{quinolone}}$), 1630 ($\text{C}=\text{O}_{\text{hydrogen bond}}$), 1603 ($\text{C}=\text{N}$) and 1559 ($\text{C}=\text{C}$). ^1H NMR
153 ($\text{DMSO}-d_6$, δ , 300 MHz): 3.64 (s, 3H, CH_3), 7.02-7.87 (m, 6H, Ar-H), 8.25 (d, 1H, Ar-H), 8.46
154 (d, 1H, Ar-H), 8.88 (s, 1H, H-4_{pyrimidine}) and 9.51 (s, 1H, H-6_{pyrimidine}). Mass spectrum, m/z (I_r %):
155 370 (M^+ , 4), 342 (100), 313 (22), 299 (24), 218 (9), 169 (6), 161 (11), 142 (9), 133 (12), 116 (9),
156 104 (14), 91 (10), 80 (16), 77 (20) and 64 (19). Anal. Calcd. for $\text{C}_{21}\text{H}_{14}\text{N}_4\text{O}_3$ (370.37); C, 68.10;
157 H, 3.81; N, 15.13%. Found: C, 67.72; H, 3.52; N, 15.00%.

158 **1-Benzyl-5-[(4-hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]-2-oxo-1,2-**
159 **dihydro-pyridine-3-carbonitrile (18)**

160 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and *N*-benzyl-2-cyanoacetamide (0.35 g, 2
161 mmol) in absolute ethanol containing few drops of TEA was heated under reflux under water

bath for 4 h. The solid obtained after cooling was filtered and crystallized from DMF/EtOH to give compound **18** as pale brown crystals, yield (0.52 g, 63%), m.p. 168 °C. IR (KBr, cm⁻¹): 3446 (OH), 3082 (CH_{arom.}), 2943 (CH_{aliph.}), 2214 (C≡N), 1648 (C=O_{pyridone} and C=O_{quinolone}), 1630 (C=O_{hydrogen bonded}), 1608 (C=N), and 1558 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.56 (s, 3H, CH₃), 3.72 (s, 2H, CH₂), 7.02-7.72 (m, 8H, Ar-H), 7.95 (s, 1H, H-4_{pyridine}), 8.03 (d, 1H, *J*=7.8 Hz, H-5_{quinolone}), 8.27 (s, 1H, H-6_{pyridine}), 12.58 (bs, 1H, OH exchangeable with D₂O). Mass spectrum, *m/z* (*I*_r %): 412 (M⁺, 81), 321 (64), 305 (70), 266 (91), 201 (64), 181 (100), 173 (81), 144 (64), 120 (88), 105 (94) and 77 (78). Anal. Calcd. for C₂₄H₁₇N₃O₄ (411.42); C, 70.07; H, 4.16; N, 10.21%. Found: C, 69.85; H, 3.87; N, 10.13%.

2-[(4-Hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]pyrido[1,2-*a*]benzimidazole-4-carbonitrile (19**)**

A mixture of aldehyde **3** (0.51 g, 2 mmol) and 1*H*-benzimidazol-2-ylacetonitrile (0.32 g, 2 mmol) in absolute ethanol containing few drops of TEA was heated under reflux for 4h. The solid obtained after cooling was filtered and crystallized from DMF to give compound **19** as pale brown crystals, yield (0.49 g, 62 %), m.p. 294-295 °C. IR (KBr, cm⁻¹): 3064 (CH_{arom.}), 2926, 2885 (CH_{aliph.}), 2235 (C≡N), 1644 (C=O_{quinolone}), 1633 (C=O_{hydrogen bonded}), 1592 (C=N), and 1557 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.58 (s, 3H, CH₃), 7.37 (t, 1H, *J*=7.2 Hz, Ar-H), 7.47 (t, 1H, *J*=8.4 Hz, Ar-H), 7.53-7.68 (m, 2H, Ar-H), 7.79 (t, 1H, *J*=8.1 Hz, Ar-H), 7.96 (d, 1H, *J*=8.1 Hz, Ar-H), 8.14 (d, 1H, *J*=8.4 Hz, Ar-H), 8.59 (s, 1H, H-4_{pyridine}), 8.63 (d, 1H, Ar-H) and 9.90 (s, 1H, H-6_{pyridine}). ¹³C NMR (DMSO-*d*₆, δ, 75 MHz): 28.9, 99.3, 108.7, 113.4, 114.9, 115.1, 115.8, 119.7, 121.8, 122.2, 122.7, 124.5, 127.3, 129.5, 133.3, 135.7, 137.6, 140.7, 144.9, 145.1, 160.8, 163.1, 190.8. Mass spectrum, *m/z* (*I*_r %): 394 (M⁺, 100), 365 (18), 351 (5), 338 (5), 193

(56), 134 (10), 117 (6), 104 (15), 91 (9), 80 (22), 77 (29), and 64 (37). Anal. Calcd. for $C_{23}H_{14}N_4O_3$ (394.39); C, 70.05; H, 3.58; N, 14.21%. Found: C, 69.78; H, 3.43; N, 13.84%.

6-[(4-Hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (22a)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 6-aminouracil (0.49 g, 2 mmol) in absolute ethanol (20 mL) containing one crystal *p*-toluenesulfonic acid was heated under reflux for 2 h. The precipitate so formed during heating was filtered and crystallized from DMF/H₂O to give compound **22a** as yellow crystals, yield (0.42 g, 58%), m.p. > 300 °C. IR (KBr, cm⁻¹): 3407 (OH), 3306, 3180 (2NH), 3052 (CH_{arom.}), 1736 (C=O_{pyrimidine}), 1678 (C=O_{pyrimidine}), 1638 (C=O_{quinolone} and C=O_{hydrogen bonded}), 1610 (C=N) and 1559 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.66 (s, 3H, CH₃) 7.34 (t, 1H, *J*=7.2 Hz, H-6_{quinolone}), 7.57 (d, 1H, *J*=8.4 Hz, H-8_{quinolone}), 7.75 (t, 1H, *J*=7.2 Hz, H-7_{quinolone}), 8.07 (d, 1H, *J*=7.8 Hz, H-5_{quinolone}), 8.36 (s, 1H, H-4_{pyridine}) 8.92 (s, 1H, H-2_{pyridine}), 10.03 (bs, 1H, NH exchangeable with D₂O), 11.41 (bs, 1H, NH exchangeable with D₂O). Mass spectrum, *m/z* (*I_r* %): 364 (M⁺, 10), 334 (14), 318 (11), 308 (12), 294 (11), 250 (13), 228 (15), 202 (16), 188 (14), 137 (13), 121 (15), 93 (20), 80 (100) and 64 (68). Anal. Calcd. for $C_{18}H_{12}N_4O_5$ (364.32); C, 59.34; H, 3.32; N, 15.38%. Found: C, 59.17; H, 3.11; N, 14.90%.

6-[(4-Hydroxy-1-methyl-2-oxo-1,2-dihydroquinolin-3-yl)carbonyl]-1,3-dimethylpyrido [2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (22b)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 6-amino-1,3-dimethyluracil (0.31 g, 2 mmol) in absolute ethanol (20 mL) containing one crystal *p*-toluenesulfonic acid was heated under reflux for 30 min. The solid obtained during heating was filtered and crystallized from DMF/EtOH to give compound **22b** as yellow crystals, yield (0.50 g, 64%), m.p. > 300 °C. IR

(KBr, cm^{-1}): 3255 (OH), 2949 ($\text{CH}_{\text{aliph.}}$), 1708 ($\text{C}=\text{O}_{\text{pyrimidine}}$), 1660 ($\text{C}=\text{O}_{\text{pyrimidine}}$), 1633 ($\text{C}=\text{O}_{\text{quinolone}}$ and $\text{C}=\text{O}_{\text{hydrogen bond}}$), 1603 ($\text{C}=\text{N}$) and 1559 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO}-d_6$, δ , 300 MHz): 3.55 (s, 3H, CH_3), 3.65 (s, 3H, $\text{CH}_3_{\text{pyrimidine}}$), 3.69 (s, 3H, $\text{CH}_3_{\text{pyrimidine}}$), 7.33 (t, 1H, $J=7.2$ Hz, H-6_{quinolone}), 7.57 (d, 1H, $J=8.1$ Hz, H-8_{quinolone}), 7.75 (t, 1H, $J=7.2$ Hz, H-7_{quinolone}), 8.06 (d, 1H, $J=6.6$ Hz, H-5_{quinolone}), 8.43 (s, 1H, H-2_{pyridine}) and 9.02 (s, 1H, H-4_{pyridine}). ^{13}C NMR ($\text{DMSO}-d_6$, δ , 75 MHz): 28.1, 28.8, 29.4, 115.1, 121.8, 121.9, 124.6, 129.4, 130.6, 130.9, 133.4, 133.6, 155.8, 156.4, 156.9, 157.4, 160.2, 184.2, 189.2. Mass spectrum, m/z (I_r %): 392 (M^+ , 42), 391 (100), 375 (31), 364 (66), 335 (18), 321 (9), 278 (8), 252 (9), 218 (6), 202 (6), 161 (6), 146 (10), 134 (16), 132 (15), 117 (12), 104 (28), 91 (17), 80 (29), 77 (44) and 64 (33). Anal. Calcd. for $\text{C}_{20}\text{H}_{16}\text{N}_4\text{O}_5$ (392.37); C, 61.22; H, 4.11; N, 14.28%. Found: C, 61.13; H, 4.05; N, 14.07%.

3-[(2,3-Dihydro-1H-1,4-diazepin-6-yl)carbonyl]-4-hydroxy-1-methyl-quinolin-2(1H)-one (23)

A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and ethylenediamine (0.12 mL, 2 mmol) in absolute ethanol (20 mL) was heated under reflux for 15 min. The solid obtained during heating was filtered and crystallized from DMF to give compound **23** as yellow crystals, yield (0.46 g, 77%), m.p. 289-290 °C. IR (KBr, cm^{-1}): 3447 (OH) 3200 (NH), 2966, 2925 ($\text{CH}_{\text{aliph.}}$), 1663 ($\text{C}=\text{O}_{\text{quinolone}}$), 1625 ($\text{C}=\text{O}_{\text{hydrogen bonded}}$), 1620 ($\text{C}=\text{N}$), and 1567 ($\text{C}=\text{C}$). ^1H NMR ($\text{DMSO}-d_6$, δ , 300 MHz): 3.59 (s, 3H, CH_3), 3.69 (s, 4H, $\text{NCH}_2\text{-CH}_2\text{N}$), 5.84 (bs, 1H, NH exchangeable with D_2O), 6.99 (t, 1H, $J=7.2$ Hz, H-6_{quinolone}), 7.21 (d, 1H, $J=8.1$ Hz, H-8_{quinolone}), 7.42 (t, 1H, $J=6.9$ Hz, H-7_{quinolone}), 7.95 (d, 1H, $J=7.8$ Hz, H-5_{quinolone}) and 8.18 (s, 2H, H-5_{diazepine} and H-7_{diazepine}). Mass spectrum, m/z (I_r %): 297 (M^+ , 49), 282 (13), 270 (50), 250 (15), 243 (22), 227 (32), 218 (39), 205 (19), 196 (25), 162 (39), 141 (25), 131 (100), 101 (10), 97 (8), 81 (11), and 73 (25).

229 Anal. Calcd. for C₁₆H₁₅N₃O₃ (297.32); C, 64.64; H, 5.09; N, 14.13%. Found: C, 64.47; H, 5.16;
230 N, 14.04%.

231 **5-Methyl-14*H*-quinolino[3',4':5,6]pyrano[2,3-*b*][1,5]benzodiazepine-6,7(5*H*)-dione (25)**

232 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and *o*-phenylenediamine (0.22 g, 2 mmol) in
233 glacial acetic acid was heated under reflux for 30 min. The solid obtained during heating was
234 filtered and crystallized from DMF to give compound **25** as orange crystals, yield (0.45 g, 66%),
235 m.p. 299-300 °C. IR (KBr, cm⁻¹): 3120 (NH), 1642 (C=O_{γ-pyrone}), 1632 (C=O_{quinolone}), 1590
236 (C=N) and 1574 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.68 (s, 3H, CH₃), 6.50 (d, 1H,
237 *J*=9.0 Hz, Ar-H), 7.12 (d, 1H, *J*=8.7 Hz, Ar-H), 7.31 (t, 1H, *J*=7.2 Hz, Ar-H), 7.44-7.73 (m, 3H,
238 Ar-H), 8.03 (d, 1H, *J*=7.5 Hz, Ar-H), 8.13 (d, 1H, *J*=7.2 Hz, Ar-H), 8.77 (s, 1H, CH=N) and
239 12.11 (bs, 1H, NH exchangeable with D₂O). Mass spectrum, *m/z* (*I*_r %): 343 (*M*⁺-1, 52), 297
240 (40), 271 (57), 264 (56), 234 (44), 215 (100), 201 (77), 175 (64), 146 (60), 133 (46), 104 (35)
241 and 77 (38). Anal. Calcd. for C₂₀H₁₃N₃O₃ (343.34); C, 69.97; H, 3.82; N, 12.24%. Found: C,
242 69.68; H, 3.57; N, 12.01%.

243 **5-Methylquinolino[3',4':5,6]pyrano[2,3-*b*][1,5]benzoxazepine-6,7(5*H*)-dione (26)**

244 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and 2-aminophenol (0.22 g, 2 mmol) in glacial
245 acetic acid (15 mL) was heated under reflux for 2 h. The solid so formed after cooling was
246 filtered and crystallized from DMF to give compound **26** as orange-red crystals, yield (0.41 g,
247 60%), m.p. 295-296 °C. IR (KBr, cm⁻¹): 2917 (CH_{aliph.}), 1654 (C=O_{γ-pyrone}), 1621 (C=O_{quinolone}),
248 1609 (C=N) and 1559 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.66 (s, 3H, CH₃), 7.26-7.45
249 (m, 4H, Ar-H), 7.63-7.68 (m, 2H, Ar-H), 7.81 (t, 1H, *J*= 7.8 Hz, Ar-H), 8.07 (d, 1H, *J*=7.5 Hz,
250 Ar-H) and 8.51 (s, 1H, CH=N). Mass spectrum, *m/z* (*I*_r %): 344 (*M*⁺, 22), 330 (28), 301 (25), 293

251 (35), 237 (33), 216 (21), 133 (22), 91 (100), 77 (51) and 64 (53). Anal. Calcd. for C₂₀H₁₂N₂O₄
252 (344.33); C, 69.77; H, 3.51; N, 8.14%. Found: C, 69.39; H, 3.30; N, 7.86%.

253 **5-Methylquinolino[3',4':5,6]pyrano[2,3-*b*][1,5]benzothiazepine-6,7(5*H*)-dione (27).**

254 A mixture of carboxaldehyde **3** (0.51 g, 2 mmol) and *o*-aminothiophenol (0.25 mL, 2 mmol) in
255 glacial acetic acid was heated under reflux for 2h. The solid obtained after cooling was filtered
256 and crystallized from DMF to give compound **27** as pale brown crystals, yield (0.34 g, 47%),
257 m.p. 286-287 °C. IR (KBr, cm⁻¹): 3010 (CH_{arom.}), 2970, 2945 (CH_{aliph.}), 1640 (C=O_{γ-pyrone}), 1632
258 (C=O_{quinolone}), 1595 (C=N) and 1547 (C=C). ¹H NMR (DMSO-*d*₆, δ, 300 MHz): 3.62 (s, 3H,
259 CH₃), 7.23-7.87 (m, 7H, Ar-H), 8.09 (d, 1H, Ar-H) and 8.59 (s, 1H, CH=N). Mass spectrum, m/z
260 (*I*_r %): 360 (M⁺, 1), 322 (21), 302 (17), 289 (8), 265 (7), 248 (13), 217 (56), 213 (34), 202 (64),
261 117 (15), 104 (30), 93 (16), 80 (100), 110 (100), 77 (49) and 64 (45). Anal. Calcd. for
262 C₂₀H₁₂N₂O₃S (360.39); C, 66.66; H, 3.36; N, 7.77; S, 8.90%. Found: C, 66.31; H, 3.13; N, 7.38;
263 S, 8.55%.

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265 **(B) Copies of some IR, MS and ¹H-NMR spectral data for the synthesized compounds:**

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268 **Figure S1: IR spectrum of compound 3.**

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271 **Figure S2: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound 3.**

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274 **Figure S3: Mass spectrum of compound 3.**

Figure S4: IR spectrum of compound **5**.

Figure S5: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **5**.

Figure S6: Mass spectrum of compound **5**.

Figure S7: IR spectrum of compound **6**.

Figure S8: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **6**.

Figure S9: Mass spectrum of compound **6**.

Figure S10: IR spectrum of compound **9**.

Figure S11: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **9**.

Figure S12: Mass spectrum of compound **9**.

Figure S13: IR spectrum of compound **10**.

Figure S14: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **10**.

Figure S15: Mass spectrum of compound **10**.

Figure S16: IR spectrum of compound **11**.

Figure S17: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **11**.

Figure S18: Mass spectrum of compound **11**.

Figure S19: IR spectrum of compound **12**.

Figure S20: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **12**.

Figure S21: Mass spectrum of compound **12**.

Figure S22: IR spectrum of compound **13**.

Figure S23: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **13**.

Figure S24: Mass spectrum of compound **13**.

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Figure S25: IR spectrum of compound **14**.

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Figure S26: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **14**.

Figure S27: ^{13}C -NMR spectrum (75.0 MHz; $\text{DMSO-}d_6$) of compound **14**.

Figure S28: Mass spectrum of compound **14**.

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Figure S29: IR spectrum of compound **16**.

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Figure S30: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **16**.

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Figure S31: Mass spectrum of compound **16**.

Figure S32: IR spectrum of compound **17**.

Figure S33: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **17**.

Figure S34: Mass spectrum of compound 17.

Figure S35: IR spectrum of compound 18.

Figure S36: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound 18.

Figure S37: Mass spectrum of compound 18.

Figure S38: IR spectrum of compound 19.

Figure S39: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **19**.

Figure S40: ^{13}C -NMR spectrum (75.0 MHz; $\text{DMSO}-d_6$) of compound **19**.

Figure S41: Mass spectrum of compound 19.

Figure S42: IR spectrum of compound 22a.

Figure S43: ¹H-NMR spectrum (300.00 MHz; DMSO-d₆) of compound 22a.

Figure S44: Mass spectrum of compound 22a.

Figure S45: IR spectrum of compound 22b.

Figure S46: ^1H -NMR spectrum (300.00 MHz; $\text{DMSO}-d_6$) of compound **22b**.

Figure S47: Mass spectrum of compound **22b**.

Figure S48: IR spectrum of compound **23**.

Figure S49: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **23**.

Figure S50: Mass spectrum of compound **23**.

Figure S51: IR spectrum of compound **25**.

Figure S52: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **25**.

Figure S53: Mass spectrum of compound **25**.

Figure S54: IR spectrum of compound **26**.

Figure S55: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **26**.

Figure S56: Mass spectrum of compound **26**.

Figure S57: IR spectrum of compound **27**.

Figure S58: ¹H-NMR spectrum (300.00 MHz; DMSO-*d*₆) of compound **27**.