

# Supporting Information

for

## **A new and facile synthetic approach to substituted 2-thioxoquinazolin-4-ones by the annulation of a pyrimidine derivative**

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## **Experimental part**

**General procedure for the synthesis of 7-amino-2,3-dihydro-2-thioxo-1,3-di(2-methylphenyl)quinazolin-4(1*H*)-one, 2a:**

A mixture of 1,3-di(2-methylphenyl)-1,3-dihydro-2-thioxo-5-ethoxymethylene-pyrimidine-4,6-dione (**1a**) (0.4 g, 0.001 mol) and malononitrile (0.3 g, 0.004 mol) were heated under reflux in the presence of NH<sub>4</sub>OAc (1 equiv), AcOH (1 equiv) and ZnCl<sub>2</sub> (6 equiv) at 120 °C for 6 h (monitored by TLC). The reaction mixture was diluted with CHCl<sub>3</sub> and water. The organic layer

was separated and dried over anhydrous  $\text{Na}_2\text{SO}_4$ . The solvent was concentrated in vacuo and then purified by column chromatography with PE and EA as eluent. Compound **2a** was obtained as an amorphous yellow solid in 83% yield, mp 180–182 °C; IR/KBr/ $\text{cm}^{-1}$ : 3346, 3225, 2951, 1682, 1647, 1510, 1416, 1331, 1273, 1157, 1107, 881, 808;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  9.38 (1H, d,  $J = 7.6$  Hz), 8.18 (1H, d,  $J = 7.6$  Hz), 7.32 (1H, m), 7.25–7.32 (5H, m, Ar), 7.09–7.14 (3H, m, Ar), 2.40 (3H, s,  $\text{CH}_3$ ), 2.37 (3H, s,  $\text{CH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  181.14, 163.49, 162.46, 160.79, 138.76, 138.75, 137.14, 136.38, 130.27, 128.41, 128.37, 93.42, 60.46, 21.36, 21.35; Mass(EI):  $m/z$  374  $[\text{M}+1]$ .

Compounds **2b** and **2c** were prepared similarly.

**7-Amino-2,3-dihydro-2-thioxo-1,3-di(4-chlorophenyl)quinazolin-4(1H)-one (2b):** Yield: 85%; mp 220–221 °C; IR/KBr/ $\text{cm}^{-1}$ : 3050, 2980, 1705, 1622, 1562, 1319, 1269, 1092, 810;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  12.19 (1H, d,  $J = 7.6$  Hz), 8.79 (1H, d,  $J = 7.6$  Hz), 7.46 (1H, m), 7.19–7.34 (3H, m, Ar), 6.93–7.12 (5H, m, Ar), 3.86 (3H, s,  $\text{OCH}_3$ ), 3.83 (3H, s,  $\text{OCH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  180.85, 163.58, 162.58, 161.06, 130.53, 130.30, 130.06, 130.11, 128.88, 128.66, 128.19, 121.44, 121.31, 112.96, 112.61, 93.57, 56.52, 56.34; Mass(EI) :  $m/z$  415  $[\text{M}+1]$ .

**7-Amino-2,3-dihydro-2-thioxo-1,3-di(2-methoxyphenyl)quinazolin-4(1H)-one (2c):** Yield: 78%; mp 188–190 °C; IR/KBr/ $\text{cm}^{-1}$ : 3072, 2941, 2839, 1686, 1651, 1452, 1327, 1021, 750;  $^1\text{H}$  NMR (400 MHz,  $\text{CDCl}_3$ ):  $\delta$  12.19 (1H, d,  $J = 7.6$  Hz), 8.79 (1H, d,  $J = 7.6$  Hz), 7.46 (1H, m), 7.19–7.34 (3H, m, Ar), 6.93–7.12 (5H, m, Ar), 3.86 (3H, s,  $\text{OCH}_3$ ), 3.83 (3H, s,  $\text{OCH}_3$ );  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta$  180.85, 163.58, 162.58, 161.06, 130.53, 130.30, 130.06, 130.11, 128.88, 128.66, 128.19, 121.44, 121.31, 112.96, 112.61, 93.57, 56.52, 56.34; Mass(EI):  $m/z$  405.

**General procedure for the synthesis of 7-hydroxy-2,3-dihydro-2-thioxo-1,3-di(2-methylphenyl)quinazolin-4(1*H*)-one (3a):**

1,3-Di(2-methylphenyl)-1,3-dihydro-2-thioxo-5-ethoxymethylene-pyrimidine-4,6-dione (**1a**) (0.4 g, 0.001 mol) and ethylcyanoacetate (0.3 mL, 2.6 mol) were heated under reflux in the presence of NH<sub>4</sub>OAc, AcOH and ZnCl<sub>2</sub> (6 equiv) at 120 °C for 6 h in an oil bath. The reaction mixture was treated as above. The organic layer was dried over anhydrous Na<sub>2</sub>SO<sub>4</sub> and the solvent was concentrated in vacuo and then purified by column chromatography with PE and EA as eluent. The product **3a** was obtained as an amorphous yellow solid in 82% yield, mp 170–171 °C; IR/KBr/cm<sup>-1</sup>: 3379, 3034, 1686, 1645, 1612, 1456, 1329, 1265, 810; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 12.23 (1H, d, *J* = 7.6 Hz), 8.74 (1H, d, *J* = 7.6 Hz), 7.35 (1H, m), 7.21–7.31 (5H, m, Ar), 7.03–7.18 (3H, m, Ar), 2.48 (3H, s, CH<sub>3</sub>), 2.41 (3H, s, CH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 180.94, 164.03, 161.62, 153.02, 138.81, 138.48, 137.45, 137.15, 136.38, 135.22, 130.75, 130.32, 130.20, 128.37, 128.31, 117.99, 94.44, 21.39, 20.98; Mass(EI): *m/z* 375 [M+1].

Compounds **3b**, **3c** and **3d** were prepared similarly.

**7-Hydroxy-2,3-dihydro-2-thioxo-1,3-di(4-chlorophenyl)quinazolin-4(1*H*)-one (3b):** Yield: 87%; mp 210–212 °C; IR/KBr/cm<sup>-1</sup>: 3030, 1708, 1571, 1440, 1319, 1260, 780; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 12.19 (1H, d, *J* = 7.6 Hz), 8.72 (1H, d, *J* = 7.6 Hz), 7.53 (1H, m), 7.42–7.51 (4H, m, Ar), 7.17–7.28 (4H, m, Ar); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 180.25, 163.68, 161.04, 153.24, 137.82, 137.06, 136.02, 135.01, 134.70, 133.10, 130.48, 130.13, 130.07, 129.83, 119.37, 94.78; Mass(EI): *m/z* 416 [M+1].

**7-Hydroxy-2,3-dihydro-2-thioxo-1,3-di(2-methoxyphenyl)quinazolin-4(1*H*)-one (3c):**

Yield: 80%; mp 160–162 °C; IR/KBr/cm<sup>-1</sup>: 3576, 3069, 2941, 1686, 1649, 1450, 1331, 1281, 1018, 750; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 12.18 (1H, d, *J* = 7.6 Hz), 8.79 (1H, d, *J* = 7.6 Hz), 7.46 (1H, m), 7.39–7.44 (4H, m, Ar), 7.05–7.33 (4H, m, Ar), 3.87 (3H, s, OCH<sub>3</sub>), 3.82 (3H, s, OCH<sub>3</sub>); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 180.61, 163.23, 161.62, 155.04, 154.84, 152.03, 56.29, 56.12; Mass(EI): *m/z* 406 [M+1].

**7-Hydroxy-2,3-dihydro-2-thioxo-1,3-diphenylquinazolin-4(1*H*)-one (3d):**

Yield: 76%; mp 192–194 °C; IR/KBr/cm<sup>-1</sup>: 3512, 3035, 2911, 1678, 1645, 725; <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 12.12 (1H, d, *J* = 7.6 Hz), 8.69 (1H, d, *J* = 7.6 Hz), 7.52 (1H, m), 7.28–7.46 (4H, m, Ar), 7.15–7.24 (4H, m, Ar); <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ 179.88, 163.59, 161.12, 152.82, 137.66, 137.12, 135.06, 92.71; Mass(EI): *m/z* 347 [M+1].

**Table 1:** Characteristic data of quinazolines (**2a–c** and **3a–d**).

Compound	mp (°C)	Yield (%)	Molecular formula (mol. Mass)
<b>2a</b>	180–182	83	C <sub>22</sub> H <sub>19</sub> N <sub>3</sub> OS (373)
<b>2b</b>	220–221	85	C <sub>20</sub> H <sub>13</sub> N <sub>3</sub> Cl <sub>2</sub> OS (414)
<b>2c</b>	188–190	78	C <sub>22</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub> S (405)
<b>3a</b>	170–171	82	C <sub>22</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub> S (374)
<b>3b</b>	210–212	87	C <sub>20</sub> H <sub>12</sub> N <sub>2</sub> Cl <sub>2</sub> O <sub>2</sub> S (415)
<b>3c</b>	160–162	80	C <sub>22</sub> H <sub>18</sub> N <sub>2</sub> O <sub>4</sub> S (406)
<b>3d</b>	192–194	76	C <sub>20</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> S (346)