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Synthesis of some 3-(thiazol-4-yl)-4-hydroxycoumarins

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Abstract: In this work, an easy and efficient procedure for the synthesis of eight 3-(thiazol-4-yl)-4-hydroxychromen-2-one derivatives is presented. 3-Acetyl-4-hydroxychromen-2-one (**1**) was brominated with phenyltrimethylammonium tribromide to afford 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**). Compound **2** reacts with thiourea, thioacetamide and ammonium dithiocarbamate to afford 3-(2-aminothiazol-4-yl)-4-hydroxychromen-2-one (**3**), 4-hydroxy-3-(2-methylthiazol-4-yl)chromen-2-one (**4a**) and 4-hydroxy-3-(2-mercaptothiazol-4-yl)chromen-2-one (**5**), respectively. In a similar manner, compound **2** was treated with four mono-N-substituted thioureas and thiobenzamide to give the corresponding 3-(thiazol-4-yl)-4-hydroxychromen-2-one derivatives.

Keywords: Hantzsch reaction, 3-(2-bromoacetyl)-4-hydroxychromen-2-one, 3-(thiazol-4-yl)-4-hydroxycoumarins.

INTRODUCTION

Derivatives of 2-aminothiazolines are important pharmacological compounds and precursors in the synthesis of medications,[1] such as the antibiotic sulfathiazole and the anthelmintic thiabedazole. Moreover, recent research indicates that they are also inhibitors of enzymes, such as kinurenin 3-hydroxylase.[2] On the other hand, derivatives of 4-hydroxy-chromen-2-one are known as anti-coagulants and anti-tumour compounds.[3–5] The 2-aminothiazolines are obtained by means of the Hantzsch reaction,[6–8] which is the reaction of α-haloketones with thioureas.

For these reasons, in the present work, the reaction of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) with thioureas, thioacetamides and ammonium dithiocarbamate have been investigated.

* Serbian Chemical Society active member.

RESULTS AND DISCUSSION

*Preparation of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**)*

Compound **2** was synthesized as yellow crystals (m.p. 144–146 ºC) from 3-acetyl-4-hydroxychromen-2-one (**1**) and used as a suitable synthone for further reactions. The 4-hydroxycoumarin nucleus is very susceptible to electrophilic substitution,[9,10] and the preparation of **2** using bromine is difficult and not regiospecific. Thus, 3-acetyl-4-hydroxychromen-2-one (**1**) reacts with bromine in a conventional manner (bromine/acetic acid) to give substitution products at the aromatic nucleus as the major product.[11] For example, 3-acetyltropolone and 4-acetyltropolone were reacted with bromine to afford the corresponding substitution products at the tropolone nucleus as the main products.[12,13] For this reason, **1** was treated with phenyltrimethylammonium tribromide[14–19] (Fig. 1). The reaction was carried out at room temperature using tetrahydrofuran, as the solvent. The structure of **2** was determined on the basis of spectral data, as well as elemental analysis.

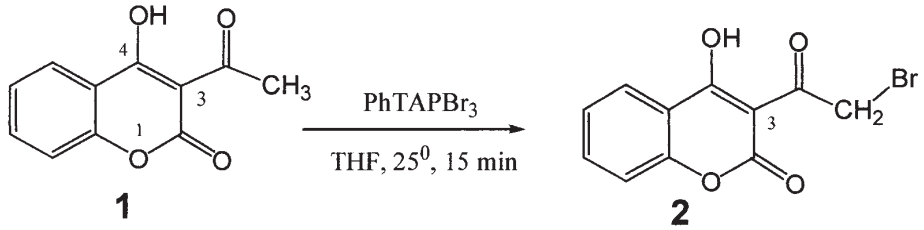

Fig. 1. Preparation of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (2).

*Reaction of compound **2** with thioureas affording **3a–e***

3-(2-Bromoacetyl)-4-hydroxychromen-2-one (**2**) reacts with thiourea to afford 3-(2-amino-thiazol-4-yl)-4-hydroxychromen-2-one hydrobromide* (**3a**), as yellow needles (m.p. 255–257 ºC), in 60 % yield. This reaction was carried out in boiling ethanol during 30 min. Compound **3a** also gave positive coloration with iron(III) chloride solution (Fig. 2).

In the reaction of compound **2** with 1-methylthiourea under identical experimental conditions as above, 4-hydroxy-3-(2-methylaminothiazol-4-yl)chromen-2-one (**3b**), (m.p. 218–220 ºC), in 67 % yield was obtained. (R_f = 0.42; silica gel, methyl ethyl ketone:toluene = 1:9, v/v).

In a similar manner, **2** reacted with three arylthiourea derivatives affording the corresponding 3-(2-arylthiazol-4-yl)chromen-2-ones (**3c**, **3d** and **3e**) in different yields (70, 63 and 74 %, respectively). The derivatives formed in these reactions were identified as 4-hydroxy-3-(2-phenylaminothiazol-4-yl)chromen-2-one (**3c**), 4-hydroxy-3-(2-*p*-tolylaminothiazol-4-yl)chromen-2-one (**3d**) and 4-hydroxy-3-[2-(4-methoxyphenyla-

* 2-Aminothiazolines, as aromatic amines have low basicity.[20] Especially secondary aromatic amines, compounds **3b–3e**, have very low basicity. For this reason, only primary amine, compound **3a**, was identified (TLC) and isolated as a salt.

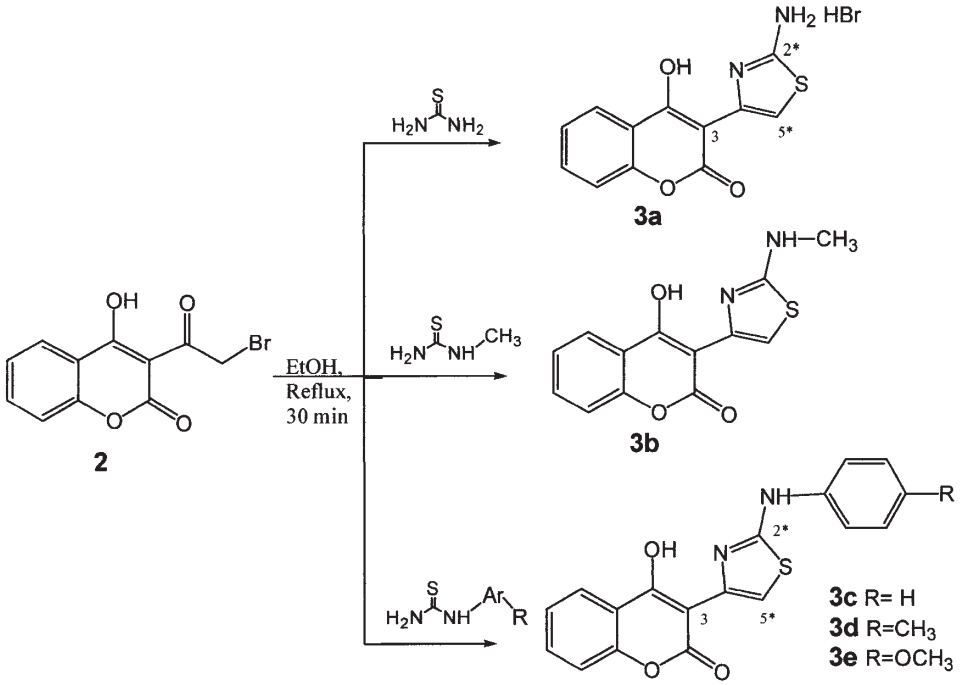

Fig. 2. Reaction of compound **2** with thioureas.

mino)thiazol-4-yl]chromen-2-one (**3e**). The identities of these compounds were established by spectral data and elemental analysis.

*Reaction of compound **2** with thioacetamide, thiobenzamide and ammonium dithiocarbamate*

The reaction of **2** with thioacetamide and thiobenzamide gave 4-hydroxy-3-(2-methylthiazol-4-yl)chromen-2-one (**4a**) and 4-hydroxy-3-(2-phenylthiazol-4-yl)chromen-2-one (**4b**). The derivatives **4a** (yellow needles; m.p. 182–184 ºC) and **4b** (yellow needles; m.p. 189–191 ºC) were isolated in 72 and 74 % yield, respectively (Fig. 3).

Finally, compound **2** was also reacted with ammonium dithiocarbamate to give 4-hydroxy-3-(2-mercaptothiazol-4-yl)chromen-2-one (**5**), (m.p. 204–206 ºC) in 81 % yield. (R_f = 0.42; silica gel, methyl ethyl ketone:toluene, 1:9, v/v) (Fig. 4).

EXPERIMENTAL

Melting points were recorded on a Kofler-hot stage apparatus and are uncorrected. Microanalysis of carbon, hydrogen and nitrogen was carried out with a Carlo Erba 1106 microanalyser. The IR spectra were run on Perkin-Elmer Grating Spectrophotometers Model 137 and Model 337, ν in cm^{-1}. The NMR spectra were recorded on a Varian Gemini 200 spectrometer (^1H at 200 MHz, ^{13}C at 50 MHz), in $CDCl_3$ and DMSO-d_6 solutions, using TMS ($SiMe_4$) as the internal standard. Chemical shifts are given in δ ppm, *J*, coupling constants in hertz (Hz), abbreviations: *s*-singlet, *d*-doublet, *t*-triplet, *q*-quartet, *m*-multiplet and *br*-broadened). Abbreviations used: PhTAPBr$_3$-phenyltrimethylam-

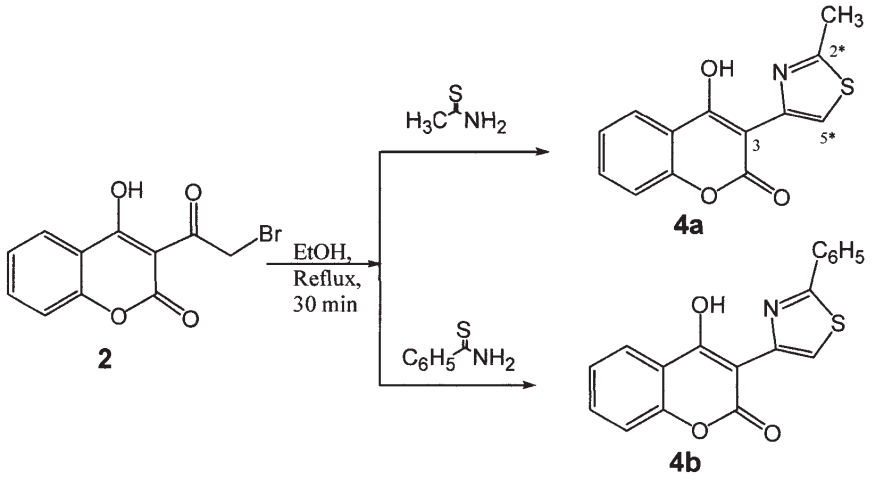

Fig. 3. Reaction of compound **2** with thioacetamide and thiobenzamide.

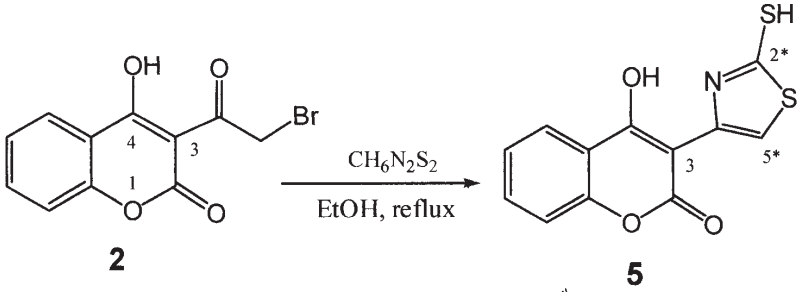

Fig. 4. Reaction of compound **2** with ammonium dithiocarbamate.

monium tribromide, DMSO-dimethylsulphoxide, EtOH-ethanol, $CDCl_3$-deuterochloroform. The reactions were monitored by thin-layer chromatography (TLC) using Kieselgel G nach Stahl, r.t.-room temperature.

*Starting compound: 3-Acetyl-4-hydroxychromen-2-one (**1**)*

To a solution of 4-hydroxychromen-2-one (3 g, 1.86 mmol) in acetic acid (16 mL) phosphorus oxychloride (5.6 mL) was added. The mixture was heated at reflux for 30 min. After cooling, the precipitate was collected and recrystallized from ethanol, to give 3-acetyl-4-hydroxychromen-2-one (**1**), white needles, in a yield of 2.7 g (90 %); m.p. 134–136 ºC; IR (KBr); ν max 3185, 2950, 1705, 1700, 1610, 1560, 1460, 1310, 1130, 950, 840, 820, 770 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$): δ 2.43 (*s*, 3H, CH_3), 7.35 (*ddd*, 1H, H-C(6), $^3J_{6,5}$ = 7.8, $^4J_{6,8}$ = 1.2, $^3J_{6,7}$ = 7.4), 7.42 (*dd*, 1H, H–C(8), $^3J_{7,8}$ = 8.35, $^4J_{6,8}$ = 1.2), 7.42 (1H, *ddd*, H-C(7) $^3J_{7,8}$ = 8.35, $^3J_{7,6}$ = 7.4, $^4J_{7,5}$ = 1.6), 7.69 (*dd*, H, H-C(5), $^3J_{5,6}$ = 7.8, $^4J_{5,7}$ = 1.6), 15.7 (OH, exchanges readily with D_2O). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 28.33 (CH_3), 160.10 (CO), 177.32 (C-4), 116.91 (C-8), 159.65 (C-2), 154.10 (C-9), 136.85 (C-7), 116.09 (C-5), 124.82 (C-6), 114.41 (C-10), 101.91 (C-3). MS, *m*/*z* 204 (M^+, 100) 189 (74), 161 (43), 120 (17), 119 (31), 92 (56), 78 (33), 43 (28). Anal: Calcd. for $C_{11}H_8O_4$: C, 64.71; H, 3.95. Found C, 64.92; H, 3.68.

*3-(2-Bromoacetyl)-4-hydroxychromen-2-one (**2**)*

Phenyltrimethylammonium tribromide (3.8 g, 9.80 mmol) was added to solution of 3-acetyl-4-hydroxychromen-2-one (**1**) (2.0 g, 9.80 mmol) in tetrahydrofuran (b.p. 60 ºC, 40 mL) over a

period of 15 min, at room temperature (25 ºC). A precipitate was deposited from the solution, and the colour of the solution changed into pale yellow. After stirring for 20 min and standing for 30 min, cold water (100 mL) was added to the reaction mixture. The precipitate was collected, washed with water and recrystallized from ethanol to afford 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) as light yellow needles, in a yield of 2.51 g (90 %); m.p. 144–146 ºC, IR (KBr); ν max 3185, 1725, 1685, 1560, 1437, 1200, 1032, 945, 842, 822, 771 cm^{-1}. ^{1}H-NMR (200 MHz, $CDCl_3$); δ 4.28 (*s*, 2H, CH_2), 7.31 (*ddd*, 1H, H-C(6), $^3J_{6,5}$ = 7.38, $^4J_{6.8}$ = 1.16, $^3J_{6,7}$ = 7.32), 7.39 (*dd*, 1H, H-C(8), $^3J_{7,8}$ = 8.35, $^4J_{6,8}$ = 1.16), 7.42 (*ddd*, 1H, H-C(7), $^3J_{7,8}$ = 8.35, $^3J_{7,6}$ = 7.37, $^4J_{7,5}$ = 1.63), 7.69 (*dd*, H-C(5), 1H, $^3J_{5,6}$ = 7.89, $^4J_{5,7}$ = 1.63), 15.7 (OH, exchanges readily with D_2O). ^{13}C-NMR (50 MHz, $CDCl_3$): δ 33.41 (CH_2), 183.50 (CO), 185.32 (C-4), 115.91 (C-8), 158.65 (C-2), 153.00 (C-9), 134.85 (C-7), 125.09 (C-5), 124.82 (C-6), 119.41 (C-10), 100.91 (C-3). Anal: Calcd. for $C_{11}H_7O_4Br$ (M_r 281.95): C, 46.67; H, 2.49. Found C, 46.92; H, 2.38.

*3-(2-Amino-thiazol-4-yl)-4-hydroxychromen-2-one hydrobromide (**3a**)*

To a solution of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) (3.5 mmol) in absolute ethanol (60 mL), thiourea (3.5 mmol) was added. The mixture was heated at reflux for 30 min. After cooling, the precipitate was collected and recrystallized from ethanol–10 % sodium hydroxide, to give 3-(2-aminothiazol-4-yl)-4-hydroxychromen-2-one (**3**) as yellow needles, in a yield of 0.71 g (60 %); m.p. 255–257 ºC, IR (KBr): ν max 3433, 3381, 3241, 3122, 1698, 1609, 1524, 1405, 1328, 1294, 1165, 1072, 950 cm^{-1}. ^{1}H-NMR (200 MHz, DMSO-d_6): δ 7.37–7.29 (*m*, 2H, H-C(6), H-C(8), $^4J_{6,8}$ = 1.16, $^3J_{6,5}$ = 7.90, $^3J_{6,7}$ = 7.35, $^3J_{8,7}$ = 8.35), 7.21 (*s*, 1H, H-C(5')), 7.44 (*ddd*, 1H, H-C(7) $^3J_{6,7}$ = 7.35, $^4J_{7,5}$ = 1.63, $^3J_{8,7}$ = 8.35), 8.58 (1H, *bs*, NH_2, exchanges slowly with D_2O), 15.87 (H, *s*, OH, exchanges readily with D_2O). ^{13}C-NMR (50 MHz, DMSO-d_6) δ 165.42 (C-2'), 140.67 (C-4'), 108.56 (C-5'), 154.28 (C-2), 93.86 (C-3), 163.09 (C-4), 123.76 (C-5), 124.06 (C-6), 132.11 (C-7), 116.34 (C-8), 120.23 (C-9), 152.05 (C-10). Anal: Calcd. for $C_{12}H_8N_2O_3S$ (M_r 260.27, recrystallized from ethanol–10 % sodium carbonate): C, 55.37; H, 3.10; N, 10.76. Found: C, 55.12; H, 2.98; N, 10.38.

*4-Hydroxy-3-(2-methylaminothiazol-4-yl)chromen-2-one (**3b**)*

This compound was obtained from the reaction of **2** with 1-methylthiourea as yellow needles (from ethanol) in a yield of 0.52 g (65 %); m.p. 216–218 ºC, R_f = 0.25 (silica gel, methyl ethyl ketone:toluene, 1:9), IR (KBr): ν max 3433, 3381, 3155, 3116 (OH and NH), 1698 (C=O), 1630, 1513, 1409, 1340, 1299, 1185, 1092, 960 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.98 (3H, CH_3, *s*), 7.29–7.82 (4H, *m*, H-C(6), H-C(7), H-C(5), H-C(8), $^4J_{7,5}$ = 1.63, $^4J_{6,8}$ = 1.18, $^3J_{8,7}$ = 8.35, $^3J_{6,5}$ = 7.89, $^3J_{6,7}$ = 7.37), 7.36 (1H, *s*, H-C(5'), 11.01 (H, *bs*, NH), 16.36 (H, *s*, OH). ^{13}C-NMR (DMSO-d_6) ppm: 159.42 (C-2'), 109.46 (C-5')), 141.67 (C–4')). 156.32 (C-2), 168.39 (C-4), 32.34 (CH_3). Anal: Calcd. for $C_{13}H_{10}N_2O_3S$ (M_r 274.30, recrystallized from ethanol): C, 56.92; H, 3.67; N, 10.26. Found: C, 56.62; H, 3.98; N, 10.28.

*4-Hydroxy-3-(2-phenylaminothiazol-4-yl)chromen-2-one (**3c**)*

This compound was obtained from the reaction of **2** with 1-phenylthiourea as yellow needles (from ethanol) in a yield of 0.42 g (70 %); m.p. 224–226 ºC, R_f = 0.64 (silica gel, methyl ethyl ketone:toluene, 1:9), IR (KBr): ν max 3483 (NH), 3261 (OH), 3030, 1684 (C=O), 1615, 1533, 1459, 1165, 1072, 966 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.37–7.85 (4H, *m*, H-C(6), H-C(7), H-C(5), H-C(8), $^4J_{7,5}$ = 1.63, $^4J_{6,8}$ = 1.17, $^3J_{8,7}$ = 8.34, $^3J_{6,5}$ = 7.78, $^3J_{6,7}$ = 7.35), 6.8–7.2 (5H, *m*, phenyl), 8.11 (1H, *s*, H-C(5')), 10.31 (1H, *bs*, NH), 12.85 (H, *s*, OH). ^{13}C-NMR (DMSO-d_6): ppm 159.42 (C-2'), 119.36 (C-5'), 150.37 (C-4'), 156.32 (C-2), 168.78 (C-4). Anal: Calcd. for $C_{18}H_{12}N_2O_3S$ (M_r 336.36, recrystallized from ethanol): C, 64.27; H, 3.61; N, 8.33. Found: C, 63.98; H, 3.78; H, 8.28.

*4-Hydroxy-3-(2-*p*-tolylaminothiazol-4-yl)chromen-2-one (**3d**)*

This compound was obtained from the reaction of **2** with 1-(4-methylphenyl)thiourea as yellow needles (from ethanol) in a yield of 0.78 g (63 %); m.p. 208–210 ºC, R_f = 0.58 (silica gel, methyl

ethyl ketone:toluene, 1:9), IR (KBr) ν max 3287 (OH), 3147 (NH), 3082, 1692 (C=O), 1621, 1591, 1432, 1356, 1106, 1052, 866 cm^{-1}. ^{1}H-NMR (DMSO-d_6): δ: 2.23 (3H, *s*, CH_3), 7.29–7.82 (4H, *m*, H-C(6), H-C(7), H-C(5), H-C(8), $^4J_{7,5}$ = 1.63, $^4J_{6,8}$ = 1.15, $^3J_{8,7}$ = 8.37, $^3J_{6,5}$ = 7.89, $^3J_{6,7}$ = 7.34), 7.12–7.21 (4H, AB*q*, phenyl, ^3J = 8.41), 8.24 (1H, *s*, H-C(5'), 9.86 (1H, *bs*, NH), 14.22 (1H, *bs*, OH). ^{13}C-NMR (DMSO-d_6): ppm 20.67 (CH_3), 153.92, (C-2'), 118.56 (C-5'), 150.67 (C-4'). 145.62 (C-1, phenyl), 129.78 (C-4, phenyl). Anal. Calcd. for $C_{19}H_{14}N_2O_3S$ (M_r 350.07, recrystallized from ethanol): C, 64.13; H, 4.03; N, 7.99. Found: C, 63.99; H, 4.10; N, 8.13.

4-Hydroxy-3-[*2-(4-methoxyphenylamino)thiazol-4-yl*]*chromen-2-one (**3e**)*

This compound was obtained from the reaction of **2** with 1-(4-methoxyphenyl)thiourea as pale orange needles (from ethanol) in a yield of 0.964 g (74 %); m.p. 198–200 ºC, R_f = 0.46 (silica gel, methyl etyl ketone:toluene, 1:9), IR (KBr): ν max 3476 (NH), 3251 (OH), 3076, 1686 (C=O), 1665, 1563, 1459, 1365, 1002, 846 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.35–7.85 (4H, *m*, H-C(6), H-C(7), H-C(5), H-C(8), $^4J_{7,5}$ = 1.61, $^4J_{6,8}$ = 1.15, $^3J_{8,7}$ = 8.31, $^3J_{6,5}$ = 7.85, $^3J_{6,7}$ = 7.33), 6.81–7.05 (4H, AB*q*, phenyl, ^3J = 8.90), 8.17 (1H, *s*, H-C(5')), 10.09 (H, *bs*, HN), 14.85 (H, *bs*, OH). ^{13}C-NMR (DMSO-d_6): ppm 154.52 (C-2'), 118.86 (C-5'), 150.27 (C-4'), 153.32 (C-4), 139.78 (C-1). Anal: Calcd. for $C_{18}H_{12}N_2O_3S$ (M_r 366.07, recrystallized from ethanol): C, 62.28; H, 3.85, N, 7.65. Found: C, 62.56; H, 3.79; N, 7.48.

*Reaction of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) with thioamides*

A mixture of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) (1 g, 3.5 mmol) and thioamide (3.5 mmol) in absolute ethanol (90 mL) was heated for 30–40 min under reflux. After cooling, the precipitate was collected and recrystallized to give 4-hydroxy-3-(thiazol-4-yl)chromen-2-one (**4a-b**).

4-Hydroxy-3-(2-methylthiazol-4-yl)chromen-2-one (***4a***). This compound was obtained from the reaction of **2** with thioacetamide as orange needles (from ethanol) in a yield of 0.186 g (72 %); m.p. 224–226 ºC, R_f = 0.32 (silica gel, methyl ethyl ketone:toluene, 1:9), IR (KBr) ν max 3191 (OH), 3030, 1684, (C=O), 1615, 1533, 1459, 1390, 1165, 1072, 966 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 2.43 (3H, *s*, CH_3), 7.28–7.85 (4H, *m*, $^4J_{7,5}$ = 1.62, H-C(6), H-C(7), H-C(5), H-C(8), $^4J_{6,8}$ = 1.15, $^3J_{8,7}$ = 8.37, $^3J_{6,5}$ = 7.9, $^3J_{6,7}$ = 7.39), 8.43 (1H, *bs*, H-C(5')), 15.36 (1H, *bs*, OH). ^{13}C-NMR (DMSO-d_6): ppm 162.02 (C-2'), 111.96 (C-5'), 144.27 (C4'), 154.32 (C-2), 167.99 (C-4), 18.38 (CH_3). Anal: Calcd. for $C_{13}H_9NO_3S$ (M_r 259.28 recrystallized from ethanol): C, 60.22; H, 3.50; N, 5.40. Found: C, 59.86; H, 3.82; N, 5.28.

4-Hydroxy-3-(2-phenylthiazol-4-yl)chromen-2-one (***4b***). This compound was obtained from the reaction of **2** with thiobenzamide as orange needles (from ethanol) in a yield of 0.186 g (72 %); m.p. 209–211 ºC, R_f = 0.45 (silica gel, methyl ethyl ketone:toluene, 1:9); IR (KBr) ν max 3165 (OH), 3011, 1691 (C=O), 1619, 1532, 1439, 1373, 1163, 1077, 969 cm^{-1}. ^{1}H-NMR (DMSO-d_6) δ: 7.10–7.82 (9H, *m*, phenyl and H-C(6), H-C(7), H-C(5), H-C(8)), 8.29 (1H, *s*, H-C(5')), 15.19 (1H, *s*, OH). ^{13}C-NMR (DMSO-d_6): ppm 167.12 (C-2'), 112.96 (C-5'), 144.87 (C-4'), 155.92 (C-2), 168.77 (C-4). Anal: Calcd. for $C_{18}H_{11}NO_3S$ (M_r 321.35, recrystallized from ethanol): C, 67.28; H, 3.45; N, 4.36. Found: C, 66.92; H, 3.81; N, 4.28.

*4-Hydroxy-3-(2-mercaptothiazol-4-yl)chromen-2-one (**5**)*

A mixture of 3-(2-bromoacetyl)-4-hydroxychromen-2-one (**2**) (0.285 g, 1 mmol) and ammonium dithiocarbamate (0.110 g, 1 mmol) in absolute ethanol (30 mL) was heated for 30 min under reflux. The precipitate was collected and recrystallized from 70 % ethanol to afford 4-hydroxy-3-(2-mercaptothiazol-4-yl)chromen-2-one (**5**) as yellow-orange needles, in a yield of 0.39 g (39 %); m.p. 212–214 ºC, R_f = 0.42 (silica gel, methyl ethyl ketone:toluene, 1:9), IR (KBr) ν max 3305 (OH), 3021, 1682 (C=O), 1621, 1533, 1474, 1396, 1166, 1067, 962 cm^{-1}. ^{1}H-NMR (DMSO): δ 3.43 (1H, *s*, SH), 8.26 (1H, *s*, H-C(5')), 15.23 (1H, *s*, OH). ^{13}C-NMR (DMSO) ppm: 153.12 (C-2'), 112.86 (C-5'), 144.37 (C–4'). 156.22 (C-2), 168.77 (C-4). Anal: Calcd. for $C_{12}H_7NO_3S$ (M_r 277.32, recrystallized from ethanol): C, 51.97; H, 2.54; N, 5.05. Found: C, 51.55; H, 2.91; N, 5.28.

CONCLUSION

In conclusion, eight 3-(thiazol-4-yl)-4-hydroxychromen-2-one derivatives were prepared in good yields in the reaction of 3-(2-bromoacetyl)-4-hydroxychromen-2-one with thioureas, thioacetamide, thiobenzamide and ammonium dithiocarbamate. The obtained coumarin derivatives can be used as potentially bioactive compounds and as precursors in the synthesis of medications.

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SINTEZE NEKIH 3-(TIAZOL-4-IL)-4-HIDROKSI-KUMARINA

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U ovom radu smo prikazali jednostavan i efikasan na~in za sintezu osam derivata 3-(tiazol-4-il)-4-hidroksi-hromen-2-ona. 3-Acetil-4-hidroksi-hromen-2-on (**1**) je bromovan sa feniltrimetilamonijumtribromidom daju}i 3-(2-bromacetil)-4-hidroksi-hromen-2-on (**2**) koji reakcijom sa tioureom, tioacetamidom i amonijumditiokarbamatom daje 3-(2-amino-tiazol-4-il)-4-hidroksi-hromen-2-on (**3a**), 4-hidroksi-3-(2-metil-tiazol-4-il)-hromen-2-on (**4a**) i 4-hidroksi-3-(2-merkapto-tiazol-4-il)-hromen-2-on (**5**). Na isti na~in ~etiri mono N-supstituisana derivata tiouree i tiobenzamida su dala odgovaraju}e derivate 3-(tiazol-4-il)-4-hidroksi-hromen-2-ona u visokom prinosu.

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