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SYNTHESIS OF REGIOISOMERIC 3-PHENACYLIDENE-2,3-DIHYDRO-4H-BENZOTHIAZIN-2-ONE AND 2-PHENACYLIDENE-2,3-DIHYDRO-4H-BENZOTHIAZIN-3-ONE

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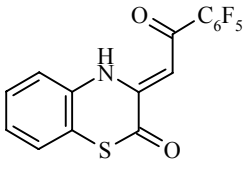
The action of *o*-aminothiophenol hydrochloride on the copper salt of the enolic form of methyl pentafluorobenzoylpyruvate leads to the formation of 3-pentafluorobenzoylmethylene-2,3-dihydro-4H-1,4-benzothiazin-2-one (**1**) [1]. The reaction of 3-*p*-toluoyl-1,2-dihydro-4H-pyrrolo[5,1-*c*][1,4]benzoxazine-1,2,4-trione with *o*-aminothiophenol gives the *o*-hydroxyphenylamide of 2,4-dioxo-3-(3-oxo-2,3-dihydro-4H-1,4-benzothiazin-2-ylidene)-4-*p*-tolylbutanoic acid (**2**) [2]. Prior to our investigations [3, 4], no other acylmethylene derivatives of 1,4-benzothiazinones had been reported. We also note that the report on the preparation of 2-aroylmethylene-2,3-dihydro-4H-1,4-benzothiazin-3-ones (**3**) in the reaction of aroylpyruvic acids or 5-aryl-2,3-dihydro-2,3-furandiones with *o*-aminothiophenol [5] is unreliable. According to our results, this reaction leads to the formation of acyclic enaminoacids, amides, cyclic O,S-hemiacetals, and 1,4-benzothiazine-2,3-dione [3, 6].

We have obtained 3-phenacylidene-2,3-dihydro-4H-1,4-benzothiazin-2-one (**4**) upon brief heating of a mixture of 1,6-diphenyl-3,4-dihydroxy-2,4-hexadiene-1,6-dione (**5**) with *o*-aminothiophenol in acetic acid at reflux. An equilibrium of two tautomers was found for **4** in DMSO solution featuring the predominant enamino form **A** with an NH-chelate ring and –N–H···O=C< intramolecular hydrogen bond and 26% imino form **B**.

The action of *o*-aminothiophenol on the ethyl ester of 2-carbamoyl-3,4-dihydroxy-6-oxo-6-phenyl-2,4-hexadienoic acid (**6**) gave 2-phenacylidene-2,3-dihydro-4H-1,4-benzothiazin-3-one (**3a**), which is regioisomeric to **4**. The yield of **3a** was 64%.



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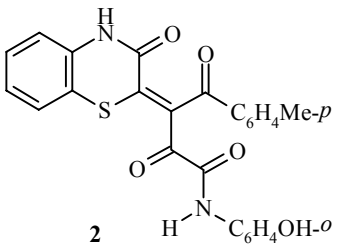

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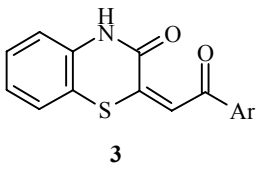

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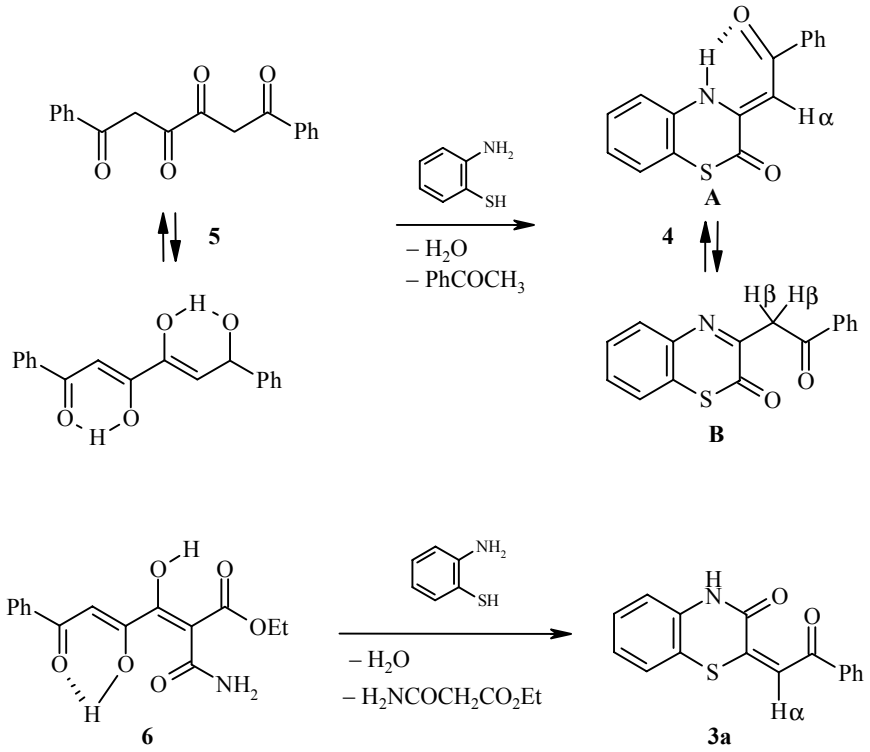
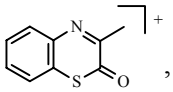
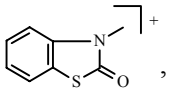


Products **3a** and **4** are probably formed as the result of initial nucleophilic attack of $C_{(3)}$ (or equally likely, $C_{(4)}$) of the dienol form of 1,3,4,6-tetraketone **5** or the most electrophilic site at $C_{(3)}$ of the substrate **6** by the amino group of *o*-aminothiophenol with subsequent heterocyclization and hydrolytic removal of acetophenone or, respectively, ethylmalonamide.

The resultant benzothiazinones **3a** and **4** have bacteriostatic activity relative to Staphylococcus aureus and colibacillus [3]. Regioisomer **4** is highly active.

2-Phenacylidene-2,3-dihydro-4H-1,4-benzothiazin-3-one (3a). A mixture of ethyl ester **6** (1.53 g, 5.0 mmol) [7] and *o*-aminothiophenol (0.63 g, 5.0 mmol) was heated until complete dissolution in ethanol (80 ml) and then heated at reflux for 3 h. After cooling, the precipitate formed was filtered off to give 0.90 g (64%) **3a**; mp 273-274°C (dioxane). IR spectrum (vaseline mull), ν, cm^{-1}: 3228 (CONH), 1668 (CONH), 1616, 1592 (C_6H_5COCH=), 1576, 1532, 1504, 1460, 1378, 1256, 1232. ^1H NMR spectrum at 300.13 MHz (DMSO-d_6), δ, ppm: 7.12-7.31, 7.47-7.65, 8.03 (9H, m, C_6H_5, C_6H_4); 8.23 (1H, s, CH^{α}); 11.62 (1H, s, NH). Mass spectrum, *m/z* (*I*, %), peaks for ions with $I > 5\%$ are given: 282 (8) $[M + H]^+$, 281 (37) $[M]^+$, 254 (5), 253 (29) $[M - CO]^+$, 252 (26) $[M - CO - H]^+$, 220 (7), 204 (16) $[M - C_6H_5]^+$, 176 (26) $[M - C_6H_5CO]^+$, 147 (15), 131 (11), 129 (9), 127 (8), 121 (7), 106 (7), 105 (80) $[C_6H_5 - C{\equiv}O]^+$, 104 (9), 96 (5), 90 (6), 89 (6), 78 (11), 77 (100) $[C_6H_5]^+$, 76 (7), 69 (12), 65 (6). Found, %: C 68.15; H 3.87; N 4.91. $C_{16}H_{11}NO_2S$. Calculated, %: C 68.31; H 3.94; N 4.98.

3-Phenylacylidene-2,3-dihydro-4H-1,4-benzothiazin-2-one (4). A mixture of **5** (0.59 g, 2.0 mmol) [8] and *o*-aminothiophenol (0.25 g, 2.0 mmol) was heated in acetic acid (10 ml) until completely dissolved and then heated at reflux for 3-4 min. After cooling, the precipitate was filtered off to give 0.40 g (71%) **4**; mp 154-155°C (ethanol). IR spectrum (vaseline mull), δ, cm^{-1}: 1630-1590 ($C_{(2)}$=O), C_6H_5CO), 1582, 1560, 1540, 1460, 1378, 1300. ^1H NMR spectrum at 300.13 MHz (DMSO-d_6), δ, ppm: 5.06 (2H, s, CH_2^{β}, imino form **4B**, 26%); 7.48 (1H, s, CH^{α}, enamino form **4A**, 74%); 7.57-7.70, 8.03-8.28 (9H, m, C_6H_5, C_6H_4). The NH group proton was not observed in the spectrum (a diffuse signal at 13.6 ppm is found for analog **1** [1]). Mass spectrum, *m/z* (*I*, %), peaks for ions with $I > 5\%$ are given: 282 (7) $[M + H]^+$, 281 (34) $[M]^+$, 253 (20) $[M - CO]^+$, 252 (13) $[M - CO - H]^+$,

236 (7), 162 (10) [M - $C_6H_5COCH_2$]$^+$ or  , 150 (14),  , 147 (14), 136 (7), 135 (26), 134 (11), 131 (11), 108 (10), 106 (8), 105 (100) [C_6H_5 - C≡O]$^+$, 102 (36), 77 (56) [C_6H_5]$^+$, 75 (5), 69 (46) 65 (5). Found, %: C 68.62; H 4.25; N 5.17. $C_{16}H_{11}NO_2S$. Calculated, %: C 68.31; H 3.94; N 4.98.

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