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REACTION OF 5,6-DIHYDROXY-2,2,9,9-TETRAMETHYL-4,6-DECADIENE-3,8-DIONE WITH *o*-AMINOPHENOL AND *o*-AMINOTHIOPHENOL

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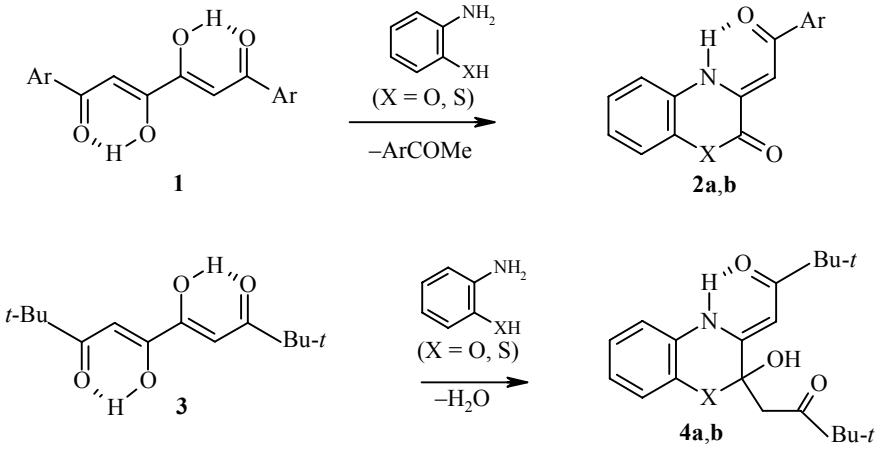
Keywords: 2-hydroxy-2-pivaloylmethyl-3-pivaloylmethylene-3,4-dihydro-2H-1,4-benzoxazine, 2-hydroxy-2-pivaloylmethyl-3-pivaloylmethylene-3,4-dihydro-2H-1,4-benzothiazine, 5,6-dihydroxy-2,2,9,9-tetramethyl-4,6-decadiene-3,8-dione, *o*-aminophenol, *o*-aminothiophenol.

The action of *o*-aminophenol or *o*-aminothiophenol on 1,6-diaryl-3,4-dihydroxy-2,4-hexadiene-1,6-diones (1,6-diarylhexane-1,3,4,7-tetraones) **1** leads to the formation of 3-aroylmethylene derivatives of 3,4-dihydro-2H-1,4-benzoxazin-2-one **2a** [1, 2] or 3,4-dihydro-2H-1,4-benzothiazin-2-one **2b** [2-4]. We have found that the reaction of readily available 5,6-dihydroxy-2,2,9,9-tetramethyl-4,6-decadiene-3,8-dione (**3**) [5,6] with *o*-aminophenol or *o*-aminothiophenol unexpectedly gives stable cyclic O- or S-acetals, namely, 2-hydroxy-3,4-dihydro-2-pivaloylmethyl-3-pivaloylmethylene-2H-1,4-benzoxazine (**4a**) and 2-hydroxy-2-pivaloylmethyl-3-pivaloylmethylene-3,4-dihydro-2H-1,4-benzothiazine (**4b**).

Products **4a** and **4b** are probably formed as the result of initial nucleophilic attack of the amino or thiol group of the reagent at $C_{(3)}$ or, equally likely, $C_{(4)}$ atom of the dienol form of 1,3,4,6-tetraketone **3** with subsequent heterocyclization and splitting off a water molecule from the hemiaminal unit of the intermediate but without elimination of the corresponding methyl ketone as in the case of the formation of compounds **2a** and **2b**.



1 **2a**,**b** **3** **4a**,**b**

2, **4 a** X = O, **b** X = S

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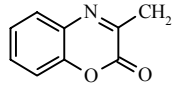
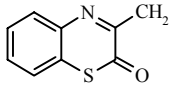
A computer prediction of biological activity [7] suggests that azines **4a** and **4b** may have fibrinolytic activity and may be cardiovascular stimulants and lipid metabolism regulators. The calculated *P*(A) effect probability is 0.6-0.7.

2-Hydroxy-2-pivaloylmethyl-3-pivaloylmethylene-3,4-dihydro-2H-1,4-benzoxazine (4a). Mixture of compound **3** (1.02 g, 4.0 mmol) [5, 6] and *o*-aminophenol (0.44 g, 4.0 mmol) was heated in a mixture of ethanol (40 ml) and acetic acid (1 ml) until dissolution and then heated at reflux for 3-4 min. The solvent was evaporated off and the residue was crystallized from 1:1 ethanol–water to give 1.10 g (80%) of compound **4a**; mp 133-134°C. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm, (*J*, Hz): 1.08 (18H, s, 6CH_3 in *t*-Bu); 3.26, 3.60 (2H, dd, J_{AB} = 13.0, CH_2); 5.50 (1H, s, CH); 6.84-6.94, 7.11-7.14 (4H, m, C_6H_4); 7.46 (1H, s, OH); 12.51 (1H, s, NH). Mass spectrum, *m/z* (*I*, %): (ion peaks with *I* > 5% are given): 345 (22) $[M]^+$, 245 (10) $[M - (CH_3)_3C–COCH_3]^+$, 219 (12), 218 (100) $[M - (CH_3)_3C–COCH_2CO]^+$, 204 (37) $[M - (CH_3)_3C–CO–(CH_3)_2=CH_2]^+$, 189 (5), 188 (43) $[M - (CH_3)_3C–COCH_3–(CH_3)_3C]^+$, 186 (13), 161 (6), 160 (12) [], 133 (7), 132 (10) $[C_8H_6NO]^+$, 85 (11) $[(CH_3)_3C–CO]^+$, 67 (6), 65 (5), 57 (88) $[(CH_3)_3C]^+$.

Found, %: C 69.80; H 7.64; N 4.21. $C_{20}H_{27}NO_4$. Calculated, %: C 69.54; H 7.88; N 4.05.

2-Hydroxy-2-pivaloylmethyl-3-pivaloylmethylene-3,4-dihydro-2H-1,4-benzothiazine (4b). Mixture of 5,6-dihydroxy-2,2,9,9-tetramethyl-4,6-decadiene-3,8-dione **3** (0.51 g, 2.0 mmol) and *o*-aminothiophenol (0.25 g, 2.0 mmol) was heated in a mixture of ethanol (20 ml) and acetic acid (1 ml) until dissolution, heated at reflux for 3-4 min, and cooled. The precipitate was filtered off and crystallized from 2-propanol to give 0.54 g (75%) of compound **4b**; mp 132-133°C. IR spectrum (vaseline oil), ν, cm^{-1}: 3390 (OH), 1685, 1623, 1565-1590 (CO, C=C), 1470. ^{1}H NMR spectrum (500 MHz, DMSO-d_6), δ, ppm, (*J*, Hz): 0.97 (9H, s, 3CH_3 in *t*-Bu); 1.13 (9H, s, 3CH_3 in *t*-Bu); 2.96, 3.22 (2H, dd, J_{AB} = 11.5, CH_2); 5.77 (1H, s, CH); 6.95-6.98, 7.12-7.21 (4H, m, C_6H_4); 7.05 (1H, s, OH); 12.60 (1H, s, NH). Mass spectrum, *m/z* (*I*, %) (only ion peaks with *I* > 5% are given): 361 (8) $[M]^+$, 235 (14), 234 (100) $[M - (CH_3)_3C–COCH_2–CO]^+$, 204 (6) $[M - (CH_3)_3C–COCH_3–(CH_3)_3C]^+$, 202 (7), 176 (12) [], 149 (5), 148 (6) $[C_8H_6NS]^+$, 85 (5) $[(CH_3)_3C–CO]^+$, 57 (82) $[(CH_3)_3C]^+$.

Found, %: C 66.78; H 7.29; N 4.16. $C_{20}H_{27}NO_3S$. Calculated, %: C 66.45; H 7.53; N 3.87.

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