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LETTERS TO THE EDITOR

Azoles and Azines: CXXVIII.[1] Reaction of 2-Aryl-4-hydroxy-6*H*-1,3-thiazin-6-ones with 6-Bromo-4-oxo-4*H*-chromene-3-carbaldehyde

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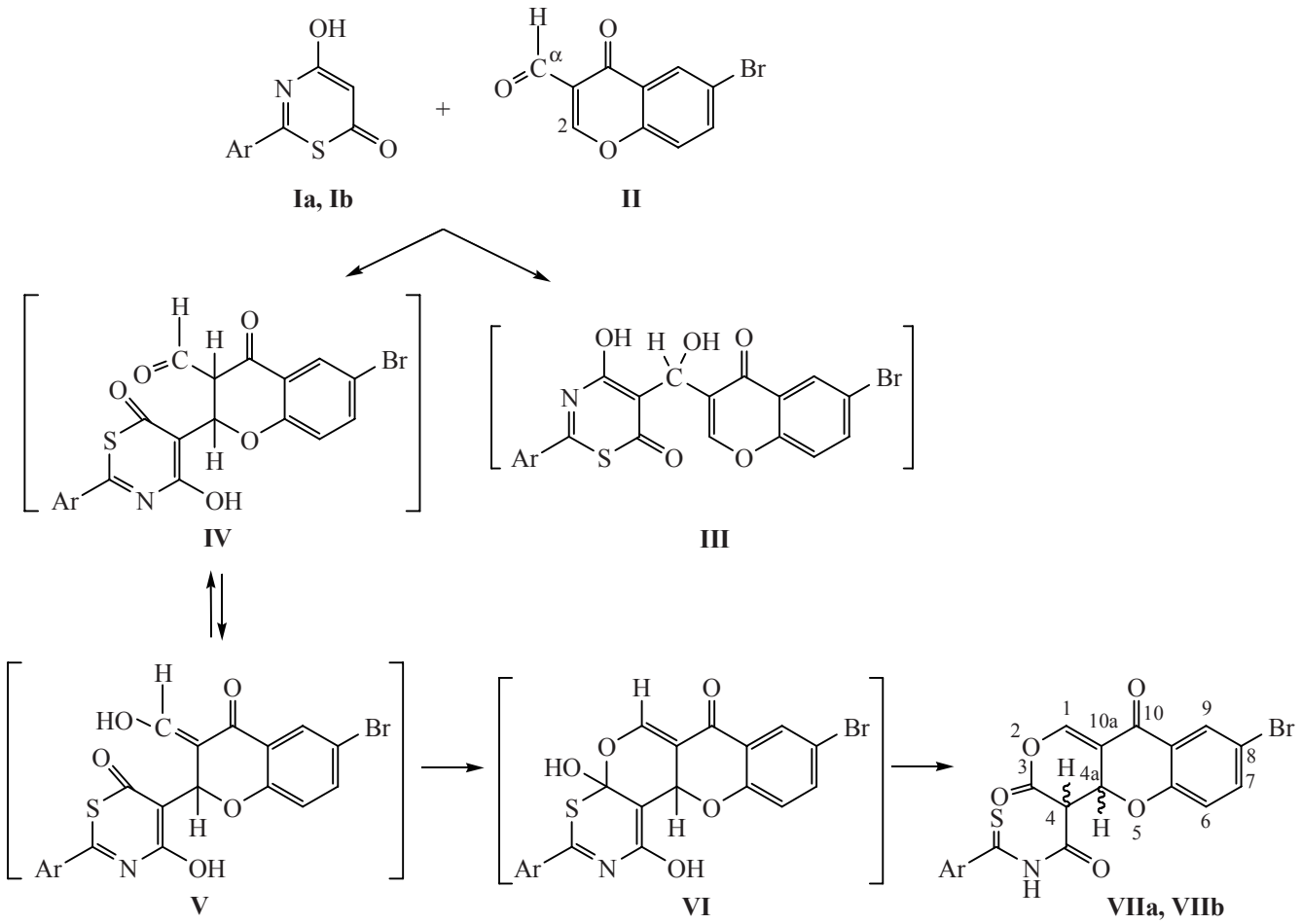
We previously studied reactions of 2-aryl-4-hydroxy-6*H*-1,3-thiazin-6-ones with aliphatic and aromatic aldehydes [2]; in these studies, specific attention was given to reactions of such 1,3-thiazines with salicylaldehyde derivatives [3], taking into account possible closure of coumarin ring in the reactions with malonic acid derivatives, including cyclic ones (e.g., barbituric acid or 2-aryl-4-hydroxy-6*H*-1,3-thiazin-6-ones). Derivatives of 3-formylchromone also attract strong theoretical and practical interest due to the presence of double carbon–carbon bond (C^2=C^3) activated by two carbonyl groups, which is capable of taking up nucleophilic reagents, including compounds with an activated methylene group [4]. Reactions of such chromones with polyhydroxypyrimidines (which can be regarded as cyclic analogs of malonic acid) give rise only to the corresponding ylidene derivatives as a result of condensation at the aldehyde group [5]. Reactions of 4-hydroxy-6*H*-1,3-thiazin-6-ones with substituted 3-formylchromones were not studied.

We have found that 2-aryl-4-hydroxy-6*H*-1,3-thiazin-6-ones **Ia** and **Ib** react with 6-bromo-4-oxo-4*H*-chromene-3-carbaldehyde (**II**) in polar aprotic solvents (such as DMSO or pyridine) to give 3,10-dioxo-*N*-thioaroyl-4,4a-dihydro-3*H*,10*H*-pyrano[4,3-*b*]chromene-4-carboxamides **VIIa** and **VIIb** in 60–70% yield. It should be noted that the formation of such products is quite surprising, taking into account that the reaction of 3-formylchromone with barbituric acid leads to the formation of 5-(4-oxochromene-3-ylmethylidene)barbituric acid [5].

[1] For communication CXXVII, see [1].

The mass spectra of pyranochromenes **VIIa** and **VIIb** contained the molecular ion peaks whose subsequent fragmentation involved elimination of $[ArC{\equiv}S]^+$ and HNCO or successive elimination of $[ArC{\equiv}NH]^+$, S, and CO. Compounds **VIIa** and **VIIb** characteristically displayed in the ^{1}H NMR spectra singlets at δ 12.5–12.9 (NH) and 8.6–8.9 ppm (1-H) and doublets at δ 7.1–7.3 (4-H) and 6.5–6.6 ppm (4a-H). In addition, signals from protons in the benzene rings of the chromene and benzothioyl fragments were present in the region δ 6.6–8.2 ppm, their intensity ratio being 1:1. In the ^{13}C NMR spectra of **VIIa** and **VIIb**, signals from carbon atoms in the carbonyl and thiocarbonyl groups appeared at δ_C 159–161 and 198–202 ppm, respectively; carbon nuclei in the pyran ring resonated at δ_C 160–165 (C^3), 110–115 (C^4), 91–98 (C^{4a}), and 115–118 ppm (C^{12}); and aromatic carbon signals were located in the region δ_C 112–158 ppm. The IR spectra of crystalline compounds **VIIa** and **VIIb** contained absorption bands belonging to vibrations of the imide NH group [~3400 cm^{-1} (N–H), 1650–1660 cm^{-1} (amide **I**), and 1560–1570 cm^{-1} (amide **II**)] and lactone fragment [1720–1740 cm^{-1} (C=O) and 1240–1250 cm^{-1} (C–O–C). In the UV spectra of **VIIa** and **VIIb** in acetonitrile were observed three absorption maxima at λ 210, 280–300, and 340 nm.

A probable mechanism of formation of compounds **VII** implies addition of thiazine molecule **I** at the C^2=C^3 bond of chromone, transformation of adduct **IV** into hydroxymethylidene tautomer **V**, intramolecular attack on C^6 in the thiazine ring by the enol oxygen atom, and cleavage of the C^6–S bond in intermediate **VI**.



Ar = 4-MeOC$_6$H$_4$ (**a**), Ph (**b**).

It would be reasonable to presume that, like other aldehydes, 3-formylchromones should react with thiazines at the aldehyde group. However, this reaction path does not occur. With a view to rationalize the observed behavior of 6-bromo-4-oxo-4*H*-chromene-3-carbaldehyde (**II**) in reactions with 2-aryl-4-hydroxy-6*H*-1,3-thiazin-6-ones **Ia** and **Ib** we performed PM3 quantum-chemical calculations of charges on atoms, orbital coefficients of atoms in the lowest unoccupied molecular orbital (LUMO), and energies of the initial compounds and presumed intermediates. Although the calculated charge on the aldehyde carbonyl carbon atom in molecule **II** (0.353) is almost twice as large as that on C^2 (0.175), adduct **IV** formed by addition of thiazine at the C^2=C^3 bond of **II** is more stable (E = –71.6 and –111.7 kcal mol^{-1} for the neutral species and anion, respectively) than adduct **III** at the aldehyde group (E = –74.9 and –76.4 kcal mol^{-1} for the neutral molecule and anion respectively. On the other hand, the contribution of C^2 into the LUMO of **II** (0.54) is much greater then the contribution of the aldehyde carbonyl carbon atom (0.16). Thus the results of quantum-chemical calculations suggest orbital thermodynamic control over the examined reactions.

8-Bromo-*N*-(4-methoxyphenylcarbonothioyl)-3,10-dioxo-4,4a-dihydro-3*H*,10*H*-pyrano[4,3-*b*]chromene-4-carboxamide (VIIa). 6-Bromo-4-oxo-4*H*-chromene-3-carbaldehyde (**II**), 2 mmol, was added to a solution of 2 mmol of 4-hydroxy-2-(4-methoxyphenyl)-6*H*-1,3-thiazin-6-one (**Ia**) in 10 ml of pyridine, and the mixture was heated for 30 min at 70°C. The mixture was cooled to room temperature, diluted with 30 ml of ethanol, and stirred. The precipitate was filtered off, washed on a filter with ethanol, dried, and recrystallized from 1,4-dioxane. Yield 65%, R_f 0.78 (acetonitrile–methylene chloride, 1:7), mp 241°C. ^{1}H NMR spectrum, δ, ppm: 6.6 d (1H, 4a-H), 7.5 m (5H, Ph), 7.2 d (1H, 4-H), 7.7 d (1H, 6-H), 7.8 s (1H, 9-H), 8.1 d (1H, 7-H), 8.5 s (1H, 1-H), 12.6 s (1H, NH). ^{13}C

NMR spectrum, δ_C, ppm: 55.8 (OMe), 91.5, 111.2, 113.5, 115.7, 118.3, 121.0, 125.8, 131.0, 134.8, 135.5, 136.2, 148.8, 153.4, 153.9, 160.2, 160.6, 163.8, 201.2 (C=S). UV spectrum (ethanol), λ_{max}, nm ($\varepsilon \times 10^{-4}$): 215 (1.32), 285 (1.25), 340 (1.09). IR spectrum (KBr), ν, cm^{-1}: 1682, 1725, 3300. Found, %: C 57.5; H 3.10; N 3.23; S 7.6. $C_{21}H_{14}ClNO_6S$. Calculated, %: C 56.8; H 3.18; N 3.16; S 7.2.

8-Bromo-3,10-dioxo-*N*-(phenylcarbonothioyl)-4,4a-dihydro-3*H*,10*H*-pyrano[4,3-*b*]chromene-4-carboxamide (VIIb) was synthesized in a similar way. Yield 65%. R_f 0.81 (acetonitrile–methylene chloride, 1:7). mp 232°C. ^{1}H NMR spectrum, δ, ppm: 6.6 d (1H, 4a-H), 7.5 m (5H, Ph), 7.2 d (1H, 4-H), 7.7 d (1H, 6-H), 7.8 s (1H, 9-H), 8.1 d (1H, 7-H), 8.5 s (1H, 1-H), 12.6 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 55.8 (OMe), 91.3, 110.7, 113.8, 115.5, 117.5, 120.5, 125.2, 130.0, 134.5, 135.5, 136.8, 148.3, 153.2, 153.5, 160.3, 160.4, 163.1, 200.2 (C=S). UV spectrum (ethanol), λ_{max}, nm ($\varepsilon \times 10^{-4}$): 218 (1.35), 288 (1.28), 340 (1.08). IR spectrum (KBr), ν, cm^{-1}: 1680, 1720, 3300. Found, %: C 52.8; H 3.6; N 3.3; S 7.2. $C_{20}H_{12}ClNO_5S$. Calculated, %: C 51.6; H 2.9; N 2.9; S 6.6.

The IR spectra of crystalline samples were recorded on an IKS-29 spectrometer. The UV spectra were measured on an SF-2000 spectrophotometer. The ^{1}H and ^{13}C NMR spectra were recorded from solutions in DMSO-d_6 on a Bruker AM-500 instrument at 500 and 125 MHz, respectively; the chemical shifts were determined relative to tetramethylsilane. The progress of reactions and the purity of products were monitored by TLC using Sorbfil plates.

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