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SHORT COMMUNICATIONS

Synthesis of Thiazolo[3,2-*a*]pyrimidines from 3,4-Dihydropyrimidine-2(1*H*)-thiones

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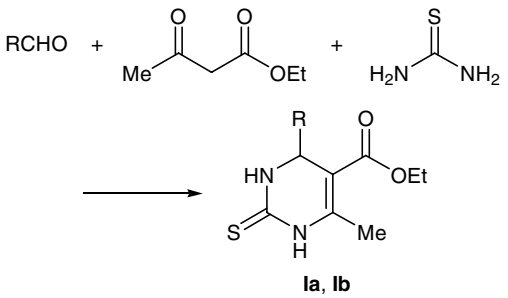
Some functional derivatives of dihydropyrimidinones are known to exhibit a broad spectrum of biological activity, such as antiviral, antitumor, and antibacterial [1–3]. 4-Aryldihydropyrimidinones were recently reported as a new class of calcium channel blocking agents [4, 5]. The potential of dihydropyrimidinones and dihydropyrimidinethiones and their derivatives as new pharmacologically active substances attracts interest of many researchers.

The most convenient procedure for the synthesis of 3,4-dihydropyrimidine-2(1*H*)-thiones (known as the Biginelli reaction) is based on one-pot three-component condensation of aldehydes with β-keto esters and thiourea. Following the procedure reported in [6] we synthesized 3,4-dihydropyrimidine-2(1*H*)-thiones **Ia** and **Ib** (Scheme 1) and converted them into fused thiazolo[3,2-*a*]pyrimidines **IIIa**, **IIIb**, **Va**, and **Vb** by treatment with halogen derivatives **II** and **IV** in dimethylformamide (Scheme 2).

Scheme 1.

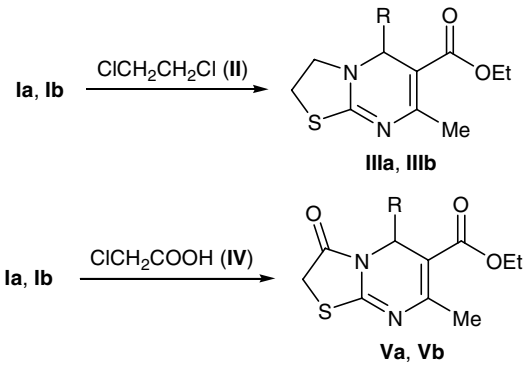


Ia, **Ib**

R = Me (**a**), Ph (**b**).

The progress of reactions was monitored by TLC, following the disappearance of the initial thiones. Compounds **IIIa**, **IIIb**, **Va**, and **Vb** are colorless high-melting crystalline substances; their structure was confirmed by the IR and NMR spectra. In the IR spectra of **IIIa**, **IIIb**, **Va**, and **Vb** we observed no absorption bands in the region 3200–3400 cm^{-1}, which are typical of stretching vibrations of the N–H bonds in the initial pyrimidines **Ia** and **Ib**.

Scheme 2.



R = Me (**a**), Ph (**b**).

Ethyl 5,7-dimethyl-2,3-dihydro-5*H*-[1,3]thiazolo-[3,2-*a*]pyrimidine-6-carboxylate (IIIa). A mixture of 0.9 ml (0.011 mol) of 1,2-dichloroethane, 2.14 g (0.01 mol) of dihydropyrimidinethione **Ia**, and 10 ml of DMF was heated for 4 h under reflux. The mixture was left overnight at room temperature and cooled to 0°C, and the precipitate was filtered off, washed with cold ethanol, and recrystallized from ethanol. Yield 65%, mp 219–220°C. IR spectrum, ν, cm^{-1}: 1670, 1533, 1280, 750. ^{1}H NMR spectrum, δ, ppm: 1.04 t (3H, CH_3), 1.35 d (3H, CH_3), 2.37 s (3H, CH_3), 3.2–3.54 m (4H, CH_2CH_2), 3.95 q (2H, OCH_2), 4.19 q (1H, 5-H). Found, %: C 55.07; H 6.59; N 11.70; S 13.41. $C_{11}H_{16}O_2N_2S$. Calculated, %: C 55.00; H 6.66; N 11.66; S 13.33.

Compound **IIIb** was synthesized in a similar way.

Ethyl 7-methyl-5-phenyl-2,3-dihydro-5*H*-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (IIIb). Yield 65%, mp 197–199°C. IR spectrum, ν, cm^{-1}: 1675, 1535, 1280, 755. ^1H NMR spectrum, δ, ppm: 1.02 t (3H, CH_3), 2.35 s (3H, CH_3), 3.1–3.51 m (4H, CH_2CH_2), 4.01 q (2H, OCH_2), 5.74 s (1H, 5-H), 7.45 m (5H, H_{arom}). Found, %: C 63.61; H 6.01; N 9.31; S 10.54. $C_{16}H_{18}O_2N_2S$. Calculated, %: C 63.57; H 5.96; N 9.27; S 10.59.

Ethyl 5,7-dimethyl-3-oxo-2,3-dihydro-5*H*-[1,3]-thiazolo[3,2-*a*]pyrimidine-6-carboxylate (Va). A mixture of 1.04 g (0.011 mol) of chloroacetic acid, 2.14 g (0.01 mol) of 3,4-dihydropyrimidinethione **Ia**, and 10 ml of DMF was heated for 4 h under reflux. The mixture was left to stand at room temperature and cooled to 0°C, and the precipitate was filtered off and washed with cold ethanol. Yield 60%, mp 200–202°C. IR spectrum, ν, cm^{-1}: 1715, 1670, 1530, 1275, 750. ^1H NMR spectrum, δ, ppm: 1.06 t (3H, CH_3), 1.41 d (3H, CH_3), 2.45 s (3H, CH_3), 3.8 s (2H, CH_2), 4.05 q (2H, OCH_2), 4.70 q (1H, 5-H). Found, %: C 51.89; H 5.57; N 11.09; S 12.63. $C_{11}H_{14}O_3N_2S$. Calculated, %: C 51.96; H 5.51; N 11.02; S 12.59.

Ethyl 7-methyl-3-oxo-5-phenyl-2,3-dihydro-5*H*-[1,3]thiazolo[3,2-*a*]pyrimidine-6-carboxylate (Vb) was synthesized in a similar was from dihydropyrimidinethione **Ib**. Yield 65%, mp 192–193°C. IR spectrum, ν, cm^{-1}: 1710, 1680, 1533, 1280, 755. ^1H NMR spectrum, δ, ppm: 1.05 t (3H, CH_3), 2.41 s (3H, CH_3), 3.75 s (2H, CH_2), 4.02 q (2H, OCH_2), 5.79 s (1H, 5-H), 7.35 m (5H, H_{arom}). Found, %: C 60.79; H 5.11; N 8.81; S 10.19. $C_{16}H_{16}O_3N_2S$. Calculated, %: C 60.75; H 5.06; N 8.86; S 10.12.

The ^1H NMR spectra were recorded from solutions in DMSO-d_6 on a Bruker-300 spectrometer (300 MHz) at 25°C. The IR spectra were measured on a Specord 75IR instrument from samples dispersed in mineral oil. The purity of the products was checked by TLC on Silufol UV-254 plates.

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