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SHORT COMMUNICATIONS

Synthesis of New Thiazolopyrimidines Proceeding from 4-Aryl-Substituted 3,4-Dihydropyrimidine-2(1*H*)-thiones

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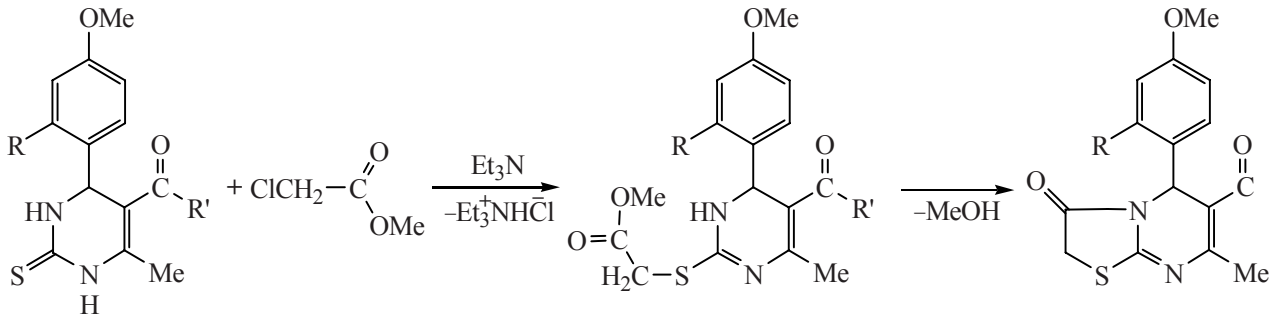
Recently a number of publications grew considerably in the field of the chemistry of 4-aryl-3,4-dihydropyrimidin-2-ones and 4-aryl-3,4-dihydropyrimidine-2-thione obtained by the three-component Biginelli condensation. It is not only due to their preparative accessibility but also to their wide range of pharmacological action (analgesic, antibacterial, antihypertension etc.) [1–3]. The presence of several reactive nucleophilic centers also attracts attention to, e.g., 4-aryl-3,4-dihydropyrimidine-2-thiones for it makes possible carry out both versatile mono- and dialkylation and acetylation [4, 5] and also very promising cyclizations. For instance, a method was described of a cyclization of 4-phenyl-3,4-dihydropyrimidine-2(1*H*)-thione into 3,5-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidine by boiling in DMF with chloroacetic acid [6].

Aiming to preparation from 4-aryl-substituted 3,4-dihydropyrimidine-2(1*H*)-thiones of new 3,5-dihydro-2*H*-thiazolo[3,2-*a*]pyrimidines derivatives we developed a new preparatively more accessible method consisting in the boiling of toluene solutions of 4-aryl-substituted 3,4-dihydropyrimidine-2(1*H*)-thiones with a slight excess of methyl chloroacetate in the presence of triethylamine.

It was expected that the reaction would stop at the formation of one of intermediate products of S- or N-alkylation whose formation depended on the solvents and acceptors used affecting apparently the process of thione-thiol transition [5]. However in 86–90% yield the target cyclization products **IIa–IId** were isolated.

The formation of 3,5-dihydro-2*H*-thiazolo[3,2-*a*]-pyrimidines **IIa–IId** was proved by the lack in the IR spectra of the absorption bands of amino groups and also the absence in the ^{1}H NMR spectra of the signals of ester methoxy group and of N^{3}H protons observed in the initial compounds and in their monoalkylated products as doublets in the region 9.2 ppm. The methylene protons CH_2 of the thiazole ring turned out to be nonequivalent and thus appeared as a doublet of doublets with a coupling constant of 17.7 Hz.



Ia–Id **IIa–IId**

R = H, R' = OEt (**a**); R = OMe, R' = OEt (**b**); R = H, R' = Me (**c**); R = OMe, R' = Me (**d**).

Ethyl 7-methyl-5-(4-methoxyphenyl)-3-oxo-3,5-dihydro-2*H*-thiazolo[3,2-*a*]-pyrimidine-6-carboxylate (IIa). A mixture of 0.80 g (2.6 mmol) of 2-thione **Ia**, 0.304 g (2.8 mmol)of methyl chloroacetate, and 0.9 g (9 mmol) of triethylamine in 10 ml of anhydrous toluene was heated at reflux for 4 h. The precipitated crystals of triethylamine hydrochloride were filtered off, washed with a small quantity of benzene. On distilling off the solvent the residue was crystallized by adding hexane. Yield 0.81g (90%). After three recrystallizations from ethanol light-orange transparent crystals were obtained, mp 126–127°C. IR spectrum, ν, cm^{-1}: 1736, 1700, 1544, 1241, 1171. ^{1}H NMR spectrum, δ, ppm: 1.11 t (3H, CH_3, *J* 7.1 Hz), 2.33 s (3H, CH_3), 3.71 s (3H, OCH_3), 4.01 q (2H, CH_2CH_3), 4.10 d.d (2H, SCH_2, *J* 17.7 Hz), 5.83 s (1H, H^5), 6.88 d, 7.16 d (4H_{arom}, *J* 8.62 Hz). Found, %: C 59.17; H 5.56; N 8.32. $C_{17}H_{18}N_2O_4S$. Calculated, %: C 58.94; H 5.24; N 8.09.

Ethyl-5-(2,4-dimethoxyphenyl)-7-methyl-3-oxo-3,5-dihydro-2*H*-thiazolo[3,2-*a*]-pyrimidine-6-carboxylate (IIb) was similarly obtained from 2.02 g (6 mmol) of 2-thione **Ib**, 0.66 g (6.1mmol) of methyl chloroacetate, and 1.23 g (12mmol) of triethylamine. Yield 89%. After three recrystallizations from ethanol orange transparent crystals were obtained, mp 129–130°C. IR spectrum, ν, cm^{-1}: 1730, 1697, 1548, 1301, 1076. ^{1}H NMR spectrum, δ, ppm: 1.13 t (3H, CH_2CH_3, *J* 7.1 Hz), 2.23 s (3H, CH_3), 3.71 s (3H, OCH_3), 3.73 s (3H, OCH_3), 3.98 q (2H, CH_2CH_3), 4.01 d.d (2H, SCH_2, *J* 17.6 Hz), 5.95 s (1H, H^5), 6.46 d, 6.52 s, 7.09 d (3H_{arom}, *J* 8.41 Hz). Found, %: C 57.79; H 5.60; N 7.12. $C_{18}H_{20}N_2O_5S$. Calculated, %: C 57.43; H 5.36; N 7.44.

6-Acetyl-7-methyl-5-(4-methoxyphenyl)-2*H*-thiazolo[3,2-*a*]pyrimidin-3(5*H*)-one (IIc) was similarly obtained from 1.38 g (5 mmol) of 2-thione **Ic**, 0.55 g (5.1mmol) of methyl chloroacetate, and 1.5 g (15mmol) of triethylamine. Yield 86%. After three recrystallizations from ethanol dark brown transparent crystals were obtained, mp 121–122°C. IR spectrum, ν, cm^{-1}: 1732, 1695, 1550, 1300, 1084. ^{1}H NMR spectrum, δ, ppm: 2.19 s (3H, CH_3), 2.32 s [3H, C(O)CH_3], 3.71 s (3H, OCH_3), 4.10 d.d (2H, SCH_2, *J* 17.72 Hz), 5.97 s (1H, H^5), 6.88 d, 7.18 d (4H_{arom}, *J* 8.73 Hz). Found, %: C 61.18; H 5.51; N 8.42. $C_{16}H_{16}N_2O_3S$. Calculated, %: C 60.74; H 5.10; N 8.85.

6-Acetyl-5-(2,4-dimethoxyphenyl)-7-methyl-2*H*-thiazolo[3,2-*a*]pyrimidin-3(5*H*)-one (IId) was similarly obtained from 1.53 g (5.0 mmol) of 2-thione **Id**, 0.55 g (5.1mmol) of methyl chloroacetate, and 1.5 g (15.0mmol) of triethylamine. Yield 84%. After three recrystallizations from ethanol dark brown transparent crystals were obtained, mp 131–133°C. IR spectrum, ν, cm^{-1}: 1742, 1656, 1585. ^{1}H NMR spectrum, δ, ppm: 2.15 s (3H, CH_3), 2.17 s [3H, C(O)CH_3], 3.72 s (3H, OCH_3), 3.74 s (3H, OCH_2, 4.05 d.d (2H, SCH_2, *J* 17.62 Hz), 6.10 s (1H, H^5), 6.48 d, 6.54 s, 7.06 d (3H_{arom}, *J* 8.4 Hz). Found, %: C 59.31; H 5.56; N 8.37. $C_{17}H_{18}N_2O_4S$. Calculated, %: C 58.94; H 5.24; N 8.09.

^{1}H NMR spectra were registered on a spectrometer Bruker DRX-500 at operating frequency 500 MHz in DMSO-d_6, internal reference TMS. IR spectra were recorded on a Fourier spectrophotometer Avatar-320 from pellets with KBr. Monitoring the reaction progress and checking the purity of compounds obtained was performed by TLC on Sorbfil plates.

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