HETEROCYCLES, Vol. 75, No. 8, 2008, pp. 1953 - 1961. © The Japan Institute of Heterocyclic Chemistry
Received, 12th February, 2008, Accepted, 8th April, 2008, Published online, 11th April, 2008. COM-08-11365

SYNTHESIS OF NEW THIAZOLO[3,2-*a*]PYRIMIDIN-5-ONE DERIVATIVES IN REACTION OF 3-ALLYL-2-THIOURACILS CYCLIZATION

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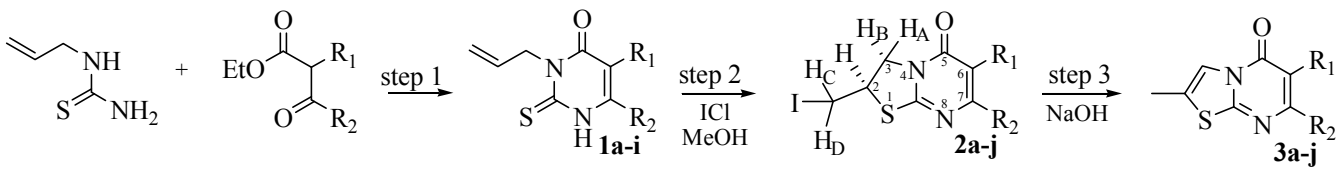
Abstract – The series of thiazolo[3,2-*a*]pyrimidin-5-one derivatives in cyclization reaction of 3-allyl-2-thiouracil derivatives with iodine monochloride, and then hydrogen iodide elimination from intermediate reaction product has been obtained. On the basis of the studies of reaction kinetics, the elimination reaction mechanism has been proposed. Moreover, the influence of substituent on the reaction elimination rate has been investigated.

INTRODUCTION

A lot of thiazolo[3,2-*a*]pyrimidin-5-one derivatives are biologically active compounds. Ritanserin (6-(2-(4-(bis(4-fluorophenyl)methylene)piperidin-1-yl)ethyl)-7-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one) is one of the antagonist of $5HT_2$ serotonine receptors.[1] Setoperone (6-(2-(4-(4-fluorobenzoyl)-piperidin-1-yl)ethyl)-7-methyl-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one) is a strong antagonist of D_2 dopamine receptors and it is effective as far as treatment of patients with chronic schizophrenia is concerned.[2] Other thiazolo[3,2-*a*]pyrimidin-5-one derivatives display antibacterial,[3] antiviral,[4,5] and analgetic activities[6] as well as hypotensive.[7] The above-mentioned information has induced us to become interested in the synthesis of thiazolo[3,2-*a*]pyrimidin-5-one derivatives), which determined the material to biological research. Scheme 1 shows the way of synthesis of thiazolo[3,2-*a*]pyrimidin-5-one



Scheme 1. Synthesis of thiazolo[3,2-*a*]pyrimidin-5-one derivatives – compound **a**(R_1=R_2= -$(CH_2)_3$-), **b**(R_1=R_2= -$(CH_2)_4$-), **c**(R_1=R_2= -$(CH_2)_5$-), **d**(R_1=H, R_2=$CH_2C_6H_{11}$), **e**(R_1=H, R_2=$CH_2C_6H_5$), **f**(R_1=H, R_2=Me), **g**(R_1=Me, R_2=H), **h**(R_1=R_2=H), **i**(R_1=R_2=Me), **j**[†](R_1=NO_2, R_2=Me)

[†] see Scheme 4.

derivatives. The first step of synthesis is condensation of 1-allylthiourea with appropriate 3-oxoesters which leads to obtaining 3-allyl-2-thiouracil derivatives (**1a-i**). The second step is closing of thiazole ring in compounds (**1a-i**). In this way 2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one derivatives (**2a-i**) are obtained. The third step is elimination of hydrogen iodide from derivatives (**2a-j**) which leads to obtaining 2-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one derivatives (**3a-j**).

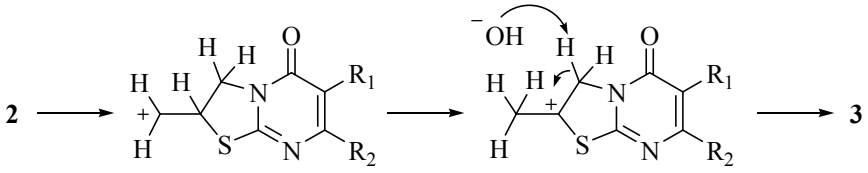
RESULTS AND DISCUSSION

At first the reactions of synthesis of thiazole ring (step 2) were carried out in iodine methanolic solution. First efforts showed that the time in which fading the reaction mixture is coming had been quite long (about 7 hours). Analysing the mechanism proposed by Skaric at al.[8] it was thought that since to form 2',3'-iodonium ion, which forms during the initial step of reaction of 3-allyl-2-thiouracil with iodine, ion I^+ is required, it is valid to use in the reaction a compound which is easier to obtain this ion form. Therefore, iodine monochloride as a compound to cause thiazole ring closing was used on the ground of higher polarization of this molecule and, consequently, it was easier for it to form 2',3'-iodonium ion. The reaction was carried out in anhydrous methanol because in these conditions (protic solvent) the attack of nucleofilic sulphur atom of 3-allyl-2-thiouracil molecule on carbocation (2',3'-iodonium ion), which had risen at the initial step of the reaction, was more probable (in comparison with the attack of Cl^-) ion coming from iodine monochloride dissociation. The assumptions concerning the course of the reaction were confirmed. The reaction with iodine monochloride in anhydrous methanol at the boiling point followed directly after substrates mixing (after adding next portions of ICl bleaching reaction of mixture followed immediately, which confirms that iodonic cation forms very fast).

The earliest elimination tests of hydrogen halide (conducted in the presence of 1-benzylpiperazine and potassium carbonate) from the compounds analogous to (**2**) led to the derivatives with double bond exocyclic which next were submitted to isomerization under the influence of concentrated sulfuric acid.[9] Searching for a more suitable method of synthesis of 2-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one derivatives we made an attempt to carry out a reaction in the presence of NaOH. The first experiments based on the observation of UV light spectrum change showed during the reaction that the elimination in the presence of stechiometric amount of NaOH was not observed. Elimination reaction is possible after adding ten fold excess of NaOH and successive increase in base concentration does not interfere with the reaction. Spectral analysis of the obtained products shows that the elimination of hydrogen iodide from compounds (**2**) under the influence of ten fold base excess of NaOH leads directly to the products with endocyclic double bond (**3**).

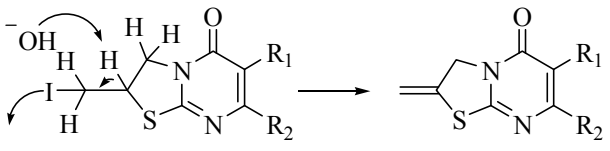
The fact that elimination reaction of hydrogen iodide from 2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]-pyrimidin-5-one derivatives occurs selectively towards the product with endocyclic double bond has

encouraged us to discussion on the reaction mechanism. In order to carry out the research on reaction kinetics UV absorption measurements were used. There is a possibility of precise measurement on account of substrate and product demonstrate maximum absorption at various wavelength. Absorbance measurements were run at 330 nm. Within this range thiazolo[3,2-*a*]pyrimidin-5-one derivatives demonstrate maximum absorption whereas 2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one derivatives do not absorb. The reaction order was marked with graphic method. For all tested elimination reaction the dependence f(t)=log C_s (where C_s stands for substrate concentration after time t) is linear, which means that the examined reaction is the first-order reaction. Experimental determination of reaction order confirmed initial speculations put forward on the basis of the fact that one of the substrates appears in large excess (most reactions of this type are first-order ones). Experimental determination of reaction order and establishing on the basis of H^1-NMR and MS Spectrum analysis that the only one of its product is the compound with endocyclic double bond lets us expect that it follows E1 mechanism (such types of reactions follow according to the first-order kinetics). In this case at the first reaction molecule ionization takes place and primary carbocation is formed. This carbocation complies regrouping to the most stable intermediate product (positive charge on tertiary carbon atom). The next step of the reaction involves losing proton by a base and forming endocyclic double bond (Scheme 2).



Scheme 2. Suggested mechanism of HI elimination from the 2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one derivatives

However, the mechanism of presented reaction is contradicted by the structure of a molecule. It is known that primary halogen derivative (such as a substrates) practically do not comply E1 elimination. For this type of compounds in these conditions of reaction (ten fold base excess) substitution reaction is privileged, not the elimination one. Established in a clear way and not raising any doubts elimination products structure argues that the reaction occurs according to the presented above mechanism. If the reaction



Scheme 3. The course of reaction of HI elimination from the 2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one derivatives according to E2 mechanism

occurred according to E2 mechanism, carbocation would not be formed and consequently rearrangement with creation of intermediate product with positive charge on C-2 would not be possible so elimination product structure would be a compound with exocyclic double bond (Scheme 3).

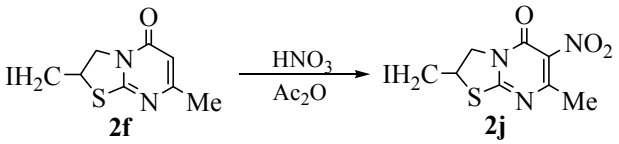
The fact to reflect well on E1 mechanism is that C-I bond is the weakest one among all carbon-halogen bonds (bond dissociation energy is 234 kJ/mol) and thereby ionization of iododerivative molecule is possible. Moreover, the presence of nitrogen and oxygen atoms containing free electron pair in molecule gives possibility of electron delocalization what facilitates molecule ionization and forming of tertiary carbocation. Taking into consideration the relation between half-life time $t_{0,5}$ and reaction rate constant for the first-order reaction k value was calculated for the elimination reactions which were carried out (Table 1).

Table 1. Experimentally define velocity constant for reaction **2a-j →3a-j**

Entry	Reaction **2→3**	$k \cdot 10^4$ [s^{-1}]
1	**a**	3.5
2	**b**	2.8
3	**c**	3.1
4	**d**	6.2
5	**e**	5.8
6	**f**	6.6
7	**g**	10.3
8	**h**	22.4
9	**i**	1.9
10	**j**	90.0

Experimentally determined reaction rate constant values show that elimination reaction occurs 2-5 fold faster in case of iodomethyl derivatives with a proton bonded to a C-6 atom and C-7 substituent atom (reactions **d-f**, Table 1), and derivative with C-6 methyl group and proton bonded to a C-7 atom (reaction **g**, Table 1) in comparison with the 6,7 – disubstituent derivatives (reactions **a-c** and **i**, Table 1). The differences in elimination reaction rate depending on the presence of C-6, C-7 substituent group, which were observed, induced us to make an attempt to synthesis of 2-(iodomethyl)-2,3-dihydrothiazolo-[3,2-*a*]pyrimidin-5-one derivative containing C-6 electron withdrawing group in order to confirm that these differences are not accidental. Attempting at 3-allyl-2-thiouracil derivative (**1f**) nitration and 1-allylthiourea with 2-nitro-3-oxoester condensation failed so nitroderivative **2j** (R_1=NO_2, R_2=Me) was obtained in nitration reaction of **2f** derivative (Scheme 4). Kinetic measurements proved the influence of

substituent on the reaction elimination rate. In case of derivatives with C-6 nitro group this reaction occurs 14-fold faster in comparison with analogous derivative with C-6 proton (reaction **f**, Table 1) and almost 50-fold faster in comparison with derivatives with C-6 methyl group (reaction **i**, Table 1). An electron density on nitrogen atoms in pyrimidine ring is not decrease by C-6 nitro group (Scheme 1, compound **2**) in comparison to C-5 and C-6 alkyl groups. These electrons stabilize carbocation on thiazole ring. So we explain increase reaction elimination rate compound **2j** compared to compund **2i**.



2f **2j**

Scheme 4. Synthesis of 2-(iodomethyl)-7-methyl-6-nitro-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one

EXPERIMENTAL

Synthesis of 3-allyl-2-thiouracils: 3-Allyl-2-thiouracil derivatives (**1a-g**, **i**) were synthesized according to the literature.[10,11] 3-Allyl-2-thiouracil (**1h**) was synthesized according to the literature.[12] Synthesis of 2-iodomethyl-2,3-dihydrothiazolo[3,2-*a*]pyrimidine-5-on derivatives (**2a-i**) – general procedure: The mixture of 3-allyl-2-thiouracil (0.03 mol) and MeOH (50 mL) was heated and solution of 0.03 mol ICl in MeOH (10 mL) was added dropwise and refluxed until the mixture was faded. Half volume of the solvent was evaporated under reduced pressure and precipitated solid was filtered, dissolved in water (50 mL) and neutralized with 2 M NaOH. A crude product was isolated through extraction with CH_2Cl_2 and crystallized from EtOH.

2-(Iodomethyl)-6,7-trimethylene-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2a**) Yield 41%, mp 130-132 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max}\cdot10^3$) = 250 (8.71), 291 (7.17), ^1H NMR ($CDCl_3$) δ ppm: 2.06 (m, 2H, C^6C^7-C$\underline{H_2}$-), 2.80 (m, 4H, $C^6C^7$2x-C$\underline{H_2}$-), 3.38 (dd, 1H, -C$\underline{H_C}$I), 3.51 (dd, 1H, -C$\underline{H_D}$I), 4.10 (m, 1H, C^2-$\underline{H}$), 4.35 (dd, 1H, $C^3\underline{H_A}$), 4.57 (dd, 1H, $C^3\underline{H_B}$), MS: (70 eV) *m/z* = 334 (100%, $M^{+\cdot}$)

2-(Iodomethyl)-6,7-tetramethylene-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2b**) Yield 30%, mp 148-150 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max}\cdot10^3$) = 248 (10.26), 285 (8.72), ^1H NMR ($CDCl_3$) δ ppm: 1.75 (m, 4H, $C^6C^7$2x -C$\underline{H_2}$-), 2.51 (m, 4H, $C^6C^7$2x -C$\underline{H_2}$-), 3.36 (dd, 1H, -C$\underline{H_C}$I), 3.50 (dd, 1H, -C$\underline{H_D}$I), 4.07 (m, 1H, C^2-$\underline{H}$), 4.33 (dd, 1H, $C^3\underline{H_A}$), 4.57 (dd, 1H, $C^3\underline{H_B}$), MS: (70eV) *m/z* = 348 (100%, $M^{+\cdot}$)

2-(Iodomethyl)-6,7-pentamethylene-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2c**) Yield 35%, mp 99-102 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max}\cdot10^3$) = 248 (9.51), 297 (8.33), ^1H NMR ($CDCl_3$) δ ppm: 1.60 (m, 4H, $C^6C^7$2x -C$\underline{H_2}$-), 1.82 (m, 2H, C^6C^7-C$\underline{H_2}$-), 2.72 (m, 4H, $C^6C^7$2x -C$\underline{H_2}$-), 3.38 (dd, 1H, -C$\underline{H_C}$I), 3.50 (dd, 1H, -C$\underline{H_D}$I), 4.10 (m, 1H, C^2-$\underline{H}$), 4.34 (dd, 1H, $C^3\underline{H_A}$), 4.56 (dd, 1H, $C^3\underline{H_B}$), MS: (70

eV) *m/z* = 362 (*100%, $M^{+\cdot}$)*

7-(Cyclohexylmethyl)-2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2d**) Yield 16%, mp 97-99 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 240 (6.50), 287 (5.81), ^{1}H NMR ($CDCl_3$) δ ppm: 0.94 (m, 2H, C^7-CH_2-), 1.18 (m, 3H, C^7-CH_2-$C_6\underline{H}_{11}$), 1.65 (m, 6H, C^7-CH_2-$C_6\underline{H}_{11}$), 2.31 (d, 2H, C^7-CH_2-$C_6\underline{H}_{11}$), 3.39 (dd, 1H, -C$\underline{H}_C$I), 3.52 (dd, 1H, -C$\underline{H}_D$I), 4.12 (m, 1H, C^2-$\underline{H}$), 4.36 (dd, 1H, $C^3\underline{H}_A$), 4.55 (dd, 1H, $C^3\underline{H}_B$), 5.98 (s, 1H, C^6-$\underline{H}$), MS: (70 eV) *m/z* = 390 (4.6%, $M^{+\cdot}$), 308 (100%, $M^{+\cdot}$-82)

7-Benzyl-2-(iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2e**) Yield 6%, mp 45-46 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 288 (6.97), ^{1}H NMR ($CDCl_3$) δ ppm: 3.78 (s, 2H, C^7-$C\underline{H}_2$-), 3.37 (dd, 1H, -C$\underline{H}_C$I), 3.49 (dd, 1H, -C$\underline{H}_D$I), 4.09 (m, 1H, C^2-$\underline{H}$), 4.33 (dd, 1H, $C^3\underline{H}_A$), 4.52 (dd, 1H, $C^3\underline{H}_B$), 5.93 (s, 1H, C^6-$\underline{H}$), 7.22-7.33 (m, 5H, C^7-CH_2-$C_6\underline{H}_5$), MS: (70eV) *m/z* = 384 (100%, $M^{+\cdot}$)

2-(Iodomethyl)-7-methyl-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2f**) Yield 25%, mp 121-122.5 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 239 (7.47), 286 (7.73), ^{1}H NMR ($CDCl_3$) δ ppm: 2.23 (d, 3H, C^7-$C\underline{H}_3$), 3.38 (dd, 1H, -C$\underline{H}_C$I), 3.53 (dd, 1H, -C$\underline{H}_D$I), 4.11 (m, 1H, C^2-$\underline{H}$), 4.36 (dd, 1H, $C^3\underline{H}_A$), 4.55 (dd, 1H, $C^3\underline{H}_B$), 6.03 (4, 1H, C^6-$\underline{H}$), MS: (70 eV) *m/z* = 308 (39.3%, $M^{+\cdot}$), 181 (100%, $M^{+\cdot}$-127)

2-(Iodomethyl)-6-methyl-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2g**) Yield 21%, mp 141-144 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 237 (9.41), 290.5 (9.84), ^{1}H NMR ($CDCl_3$) δ ppm: 2.05 (s, 3H, C^6-$C\underline{H}_3$), 3.40 (dd, 1H, -C$\underline{H}_C$I), 3.53 (dd, 1H, -C$\underline{H}_D$I), 4.16 (m, 1H, C^2-$\underline{H}$), 4.41 (dd, 1H, $C^3\underline{H}_A$), 4.61 (dd, 1H, $C^3\underline{H}_B$), 7.63 (s, 1H, C^7-$\underline{H}$), MS (CI - isobutane): *m/z* = 308 (72%, $M^{+\cdot}$), 181 (100%, $M^{+\cdot}$-127)

2-(Iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2h**) Yield 47%, mp 138-139 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 226 (8.34), 290 (8.89), ^{1}H NMR ($CDCl_3$) δ ppm: 3.40 (dd, 1H, -C$\underline{H}_C$I), 3.52 (dd, 1H, -C$\underline{H}_D$I), 4.13 (m, 1H, C^2-$\underline{H}$), 4.39 (dd, 1H, $C^3\underline{H}_A$), 4.58 (dd, 1H, $C^3\underline{H}_B$), 6.20 (d, 1H, C^6-$\underline{H}$), 7.74 (d, 1H, C^7-$\underline{H}$), MS (CI - isobutane): *m/z* = 294 (65.5%, $M^{+\cdot}$), 167 (100%, $M^{+\cdot}$-127)

2-(Iodomethyl)-6,7-dimethyl-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2i**) Yield 10%, mp 109-110 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 246 (10.50), 288.5 (9.80), ^{1}H NMR ($CDCl_3$) δ ppm: 2.01 (s, 3H, C^6-$C\underline{H}_3$), 2.24 (s, 3H, C^7-$C\underline{H}_3$), 3.38 (dd, 1H, -C$\underline{H}_C$I), 3.50 (dd, 1H, -C$\underline{H}_D$I), 4.08 (m, 1H, C^2-$\underline{H}$), 4.33 (dd, 1H, $C^3\underline{H}_A$), 4.56 (dd, 1H, $C^3\underline{H}_B$), MS (70eV): *m/z* = 322 (83.8%, $M^{+\cdot}$), 195 (100%, $M^{+\cdot}$-127)

Synthesis of 2-(iodomethyl)-7-methyl-6-nitro-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2j**) was synthesized from **2f** by method described earlier.[13] The solution of the crude product in ethanol was neutralized (Amberlit IRA-410 (OH^-)). Volatiles were evaporated and the residue was recrystallized (EtOH) to give **2j**. Yield 35%, mp 173-174 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 212 (15.10), 300 (9.60), ^{1}H NMR ($CDCl_3$) δ ppm: 2.40 (s, 3H, C^7-$C\underline{H}_3$), 3.42 (dd, 1H, -C$\underline{H}_C$I), 3.55 (dd, 1H, -C$\underline{H}_D$I), 4.25 (m, 1H, C^2-$\underline{H}$), 4.45 (dd, 1H, $C^3\underline{H}_A$), 4.61 (dd, 1H, $C^3\underline{H}_B$), MS (CI - isobutane): *m/z* = 353 (55.6%, $M^{+\cdot}$), 244 (100%, $M^{+\cdot}$- 109)

Synthesis of 2-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one derivatives (**3a-i**) – General procedure: 2-(Iodomethyl)-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2a-i**) 0.001 mol was dissolved in EtOH (50 mL) and NaOH 0.01 mol (5 mL 2 M solution in water) was added. The mixture was stirred for 12 h at rt. The solvent was evaporated under reduced pressure and neutralized with 2 M H_2SO_4. A crude product was isolated through extraction with chloroform and cristallized from EtOH.

2-Methyl-6,7-trimethylene-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3a**) Yield 42%, mp 159-161 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 219 (18.46), 234 (20.49), 313 (14.23), 323.5 (13.28), ^1H NMR ($CDCl_3$) δ ppm: 2.11 (m, 2H, C^6C^7-C<u>H</u>$_2$-), 2.91 (m, 4H, $C^6C^7$2x -C<u>H</u>$_2$-), 2.42 (d, 3H, C^2-C<u>H</u>$_3$), 7.68 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 206 (100%, $M^{+\cdot}$)

2-Methyl-6,7-tetramethylene-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one) (**3b**) Yield 34%, mp 127-129 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 219 (16.69), 231 (17.44), 312 (12.53), 323 (11.40), ^1H NMR ($CDCl_3$) δ ppm: 1.75 (m, 4H, $C^6C^7$2x -C<u>H</u>$_2$-), 2.62 (m, 4H, $C^6C^7$2x -C<u>H</u>$_2$-), 2.40 (d, 3H, C^2-C<u>H</u>$_3$), 7.60 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 220 (100%, $M^{+\cdot}$)

2-Methyl-6,7-pentamethylene-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3c**) Yield 45%, mp 124-125 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 218 (16.98), 238 (19.81), 319 (14.08), 330.5 (12.90), ^1H NMR ($CDCl_3$) δ ppm: 1.65 (m, 4H, $C^6C^7$2x -C<u>H</u>$_2$-), 1.85 (m, 2H, C^6C^7-C<u>H</u>$_2$-), 2.83 (m, 4H, $C^6C^7$2x -C<u>H</u>$_2$-), 2.41 (d, 3H, C^2-C<u>H</u>$_3$), 7.62 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 234 (100%, $M^{+\cdot}$)

7-(Cyclohexylmethyl)-2-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3d**) Yield 27%, mp 93-95 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 216 (20.11), 232 (21.40), 312.5 (18.24), 322.5 (25.60), ^1H NMR ($CDCl_3$) δ ppm: 0.95 (m, 2H, C^7-CH_2-), 1.24 (m, 3H, C^7-CH_2-C_6<u>H</u>$_{11}$), 1.65 (m, 6H, C^7-CH_2-C_6<u>H</u>$_{11}$), 2.45 (d, 2H, C^7-CH_2-C_6<u>H</u>$_{11}$), 2.43 (d, 3H, C^2-C<u>H</u>$_3$), 6.08 (4, 1H, C^6-<u>H</u>), 7.65 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 262 (9%, $M^{+\cdot}$), 180 (100%, $M^{+\cdot}$-82)

7-Benzyl-2-methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3e**) Yield 50%, mp 138-139 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 317.5 (16.36), 329.5 (15.38), ^1H NMR ($CDCl_3$) δ ppm: 2.42 (d, 3H, C^2-C<u>H</u>$_3$), 3.90 (s, 2H, C^7-C<u>H</u>$_2$-), 6.06 (s, 1H, C^6-<u>H</u>), 7.24-7.34 (m, 5H, C^7-CH_2-C_6<u>H</u>$_5$), 7.64 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 256 (100%, $M^{+\cdot}$)

2,7-Dimethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3f**) Yield 33%, mp 159-161 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 215 (13.32), 229 (13.93), 311 (11.14), 321 (11.09), ^1H NMR ($CDCl_3$) δ ppm: 2.35 (d, 3H, C^7-C<u>H</u>$_3$), 2.42 (d, 3H, C^2-C<u>H</u>$_3$), 6.12 (4, 1H, C^6-<u>H</u>), 7.65 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 180 (100%, $M^{+\cdot}$)

2,6-Dimethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3g**) Yield 50%, mp 144-146 ^oC, UV (H_2O + 5% EtOH): λ_{max}[nm] (ε_{max} $\cdot 10^3$) = 213 (15.41), 229.5 (13,85), 256 (5.36), 318 (15.07), 322.5 (14.09), ^1H NMR ($CDCl_3$) δ ppm: 2.14 (s, 3H, C^6-C<u>H</u>$_3$), 2.43 (d, 3H, C^2-C<u>H</u>$_3$), 7.67 (4, 1H, C^3-<u>H</u>), 7.86 (s, 1H, C^7-<u>H</u>),

MS (CI - isobutane): *m/z* = 180 (100%, $M^{+\cdot}$)

2-Methyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3h**) Yield 51%, mp 183-183.5 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 206 (10.80), 227.5 (9.15), 253.5 (4.07), 316 (10.27), 329.5 (10.04), ^{1}H NMR ($CDCl_3$) δ ppm: 2.45 (d, 3H, C^2-C<u>H</u>$_3$), 6.26 (d, 1H, C^7-<u>H</u>), 7.71 (4, 1H, C^3-<u>H</u>), 7.95 (d, 1H, C^6-<u>H</u>), MS (70eV): *m/z* = 166 (100%, $M^{+\cdot}$)

2,6,7-Trimethyl-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3i**) Yield 37%, mp 148-150 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 217 (15.91), 231.5 (17.04), 316 (12.84), 326 (11.77), ^{1}H NMR ($CDCl_3$) δ ppm: 2.12 (s, 3H, C^6-C<u>H</u>$_3$), 2.36 (s, 3H, C^7-C<u>H</u>$_3$), 2.40 (d, 3H, C^2-C<u>H</u>$_3$), 7.60 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 194 (100%, $M^{+\cdot}$)

Synthesis of 2,7-dimethyl-6-nitro-5*H*-thiazolo[3,2-*a*]pyrimidin-5-one (**3j**) 2-(Iodomethyl)-7-methylnitro-2,3-dihydrothiazolo[3,2-*a*]pyrimidin-5-one (**2j**) 0.0002 mol was dissolved in EtOH (10 mL) and NaOH 0.002 mol (1 mL 2 M solution in water) was added. The mixture was stirred for 5 min at rt, water (5 mL) was added and neutralized with 0.5 M H_2SO_4. A crude product was isolated through extraction with CH_2Cl_2 and cristallized from EtOH. Yield 40%, mp 161-163 °C, UV (H_2O + 5% EtOH): λ_{max}[nm] ($\varepsilon_{max} \cdot 10^3$) = 222 (32.8), 330 (16.2), 359 (16.5), ^{1}H NMR ($CDCl_3$) δ ppm: 2.54 (s, 3H, C^7-C<u>H</u>$_3$), 2.50 (d, 3H, C^2-C<u>H</u>$_3$), 7.79 (4, 1H, C^3-<u>H</u>), MS (70eV): *m/z* = 225 (100%, $M^{+\cdot}$)

Research of reaction of HI elimination kinetics was conducted through measurement of UV absorption change in EtOH solutions of different concentrations ($1 \cdot 10^{-4}$ and $5 \cdot 10^{-5}$ mol/L). Tenfold excess of NaOH was applied. A changes of absorption was measured at 330 nm at 25 °C, The application to kinetics measurements in spectrofotometer *Aquarius 7250* Cecil Instruments was used.

Results given in Table 1 – mean from three independent measurements.

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