On Triazoles XXIII [1]. The Reaction of 5-Amino-1,2,4-triazoles with Thiacyclohexane β-Oxo Esters [2]

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Six novel isomeric ring systems, namely the thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine, the thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidine, the thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-**a**]pyrimidine, the thiopyrano[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidine, the thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine and the thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidine were synthesised. Spectroscopical evidence was given for the structure of compounds obtained.

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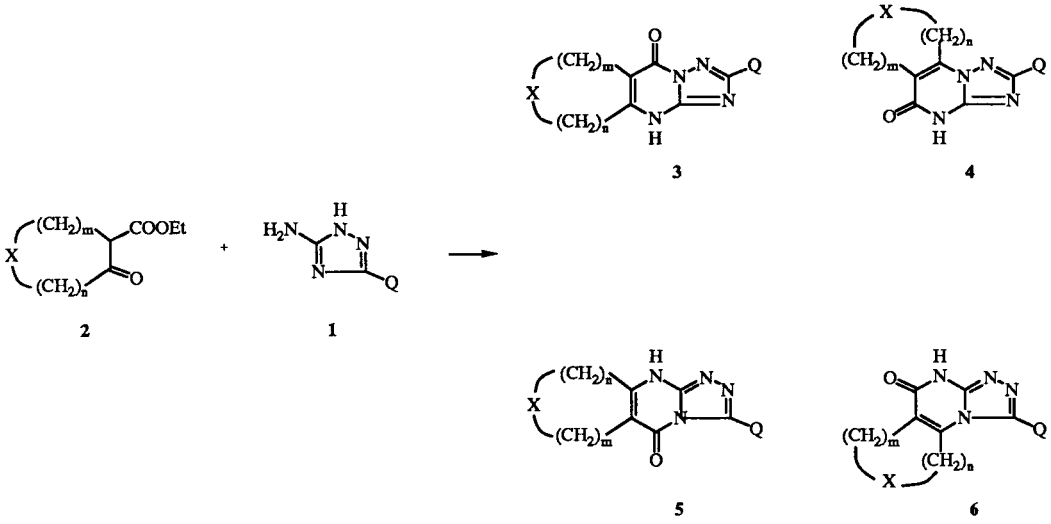
In some of the previous papers of this series [3-6] we have discussed the reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles (**1**) with different cyclic β-oxo esters **2** that may in principal lead to four type of condensed ring derivatives **3-6** (Scheme 1). It was pointed out that if providing the above reactions with homocyclic (**2**, X = CH_2, n + m = 2,3) [3,4] and different heterocyclic {**2**, X = S, n + m = 2 [3]; and **2**, X = N, n + m = 2,3 [5,6]} β-keto esters in acidic condition, *i.e.* in acetic acid or the mixture of acetic acid and dimethylformamide as solvent the main product was the corresponding derivative **3**, besides a small amount of derivative **4**.

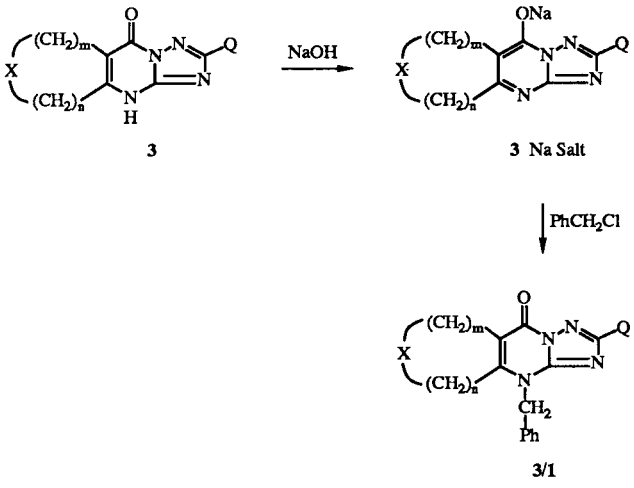
Using simple **3-6** type isomers it was also shown [7] that the ir and pmr spectra are not characteristic for any of these structures. On the other hand structures **3-6** could be easily differentiated on the basis of their uv and cmr spectra. Thus the uv spectra of the **3** type derivatives taken in neutral conditions (*e.g.* in methanol or ethanol) are characterised with two absorption bands appearing at about 230 and 270 nm, while those of the corresponding derivatives **4** are characterised with two absorption bands appearing at about 208 and 290 nm, respectively, significantly differing from the uv spectra of derivatives **5** and **6** characterised with three and one absorption maxima, respectively. In the cmr spectra of both derivatives **3** and **4** the triazole carbon atoms 2 appear with the chemical shifts of about 163 ppm strongly differing from those of the corresponding carbon atoms 3 of derivatives **5** and **6** appearing at about 143 ppm. The differentiation between the "ring acylated" structures **3** and **5** and those of the "acylamino" structures **4** and **6** made possible the carbonyl bands appearing at about 154 and 160 ppm, respectively. The above uv and cmr rules were corroborated by all **3** and **4** type condensed ring derivatives prepared thus far [3-6] with the exception of the uv spectra of those compounds where a free electron pair [3] or a double bond system [4] was conjugated to the triazolopyrimidone ring system causing a batochromic shift of their uv spectra.

As a continuation of the above studies we will now report about the reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with isomeric thiacyclohexane β-oxo-esters all leading to novel ring systems.

Scheme 1



Scheme 2



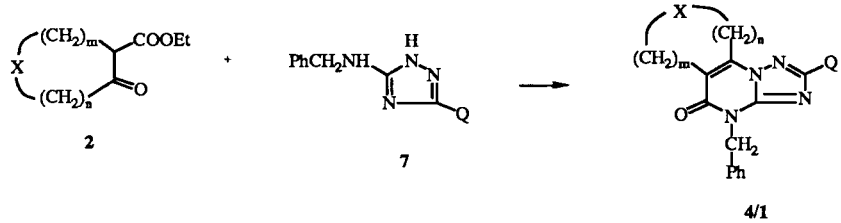
Thus the reaction of ethyl tetrahydrothiopyran-4-on-3-carboxylate **2** (X = S, m = 1, n = 2), synthesised by the known [8] Dieckmann condensation of diethyl β,β'-thiodipropionate with 5-amino-3-methylthio-, and 3-morpholino-1*H*-1,2,4-triazoles **1** (Q = methylthio and morpholino) in acetic acid lead to the formation of 8,9-dihydro-2-methylthio-, and 2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-ones **3** (Q = methylthio and morpholino, X = S, m = 1, n = 2) besides a small amount of 5,6-dihydro-2-methylthio-, and 2-morpholino-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-ones **4** (Q = methylthio and morpholino, X = S, m = 1, n = 2) the presence of which was proved by tlc but were not isolated from the reaction mixture (Scheme 1). The uv [λ max (ethanol): 232 and 268, and 231 and 276 nm, respectively] and cmr spectra (δ C-2 and δ C=O: 163.4 and 154.5 ppm, and 164.2 and 154.2 ppm, respectively) of **3** (Q = methylthio and morpholino, X = S, m = 1, n = 2) well followed the uv and cmr rules elaborated [7] recently, while the pmr spectra [δ CH_2-6 = 3.51s, δ CH_2-(8 + 9) = 2.89 bs (4H), and δ CH_2-6 = 3.50 s, δ CH_2-(8 + 9) = 2.85 bs (4H), respectively] fully supported the position of the sulfur atom 7 present.

The benzylation of the sodium salts of **3** (Q = methylthio and morpholino, X = S, m = 1, n = 2) led to the corresponding 10-benzyl derivatives **3/1** (Q = methylthio and morpholino, X = S, m = 1, n = 2), respectively, (Scheme 2) in which the position of the benzyl group was proved unequivocally with the help of gated cmr spectra. The uv and cmr spectra of derivatives **3/1** (Q = methylthio and morpholino, X = S, m = 1, n = 2) were fully analogues with those of the corresponding non-benzylated derivatives **3** (Q = methylthio and morpholino, X = S, m = 1, n = 2) proving unequivocally the 10*H*-dominant tautomeric structure of the latter ones in ethanolic and DMSO-d_6 solution shown in Scheme 2.

The isomeric *N*-benzyl derivatives **4/1** (Q = methylthio and morpholino, X = S, m = 1, n = 2) were prepared by simple smelting of the corresponding 5-benzylamino-3-Q-1*H*-1,2,4-triazoles **7** (Q = methylthio and morpholino) with ethyl tetrahydrothiopyran-4-one-3-carboxylate **2** (X = S, m = 1, n = 2) (Scheme 3). Their uv (λ max: 205 and 290, and 207 and 314 nm, respectively) and cmr (δ C-2 and δ C=O: 162.1 and 158.4, and 164.0 and 158.2 ppm, respectively) spectra again followed the rules elaborated previously [7] while the pmr spectra (δ CH_2-5 = 3.10 t, δ CH_2-6 = 2.94 t, δ CH_2-8 = 3.52 s, and δ CH_2-5 = 3.04 t, δ CH_2-6 = 2.92 t, δ CH_2-8 = 3.49 s, respectively) corroborated the position 7 of the sulphur atom present, proving their structures unequivocally.

Next ethyl γ-(carboethoxymethylthio)butyrate was cyclised in toluene analogously to the known method [9] to yield a product the structure of which was considered by the above authors to be either ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = 0, n = 3) or ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1). It should be mentioned that to the same product prepared in ether solution was later [10] assigned structure **2** (X = S, m = 0, n = 3). To the contrary of the previous experiments we have isolated from the reaction mixture both isomers, the known [10] ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = 0, n = 3) and ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1). On the basis of the enolic hydroxyl group pmr experiments showed that - probably due to the conjugation effect of the sulfur atom - **2** (X = S, m = 0, n = 3) was present in DMSO-d_6 solution dominantly in its enolic form (the ratio of the keto and enol forms ~ 1:7). To the contrary the dominant tautomeric form of **2** (X = S, m = 2, n = 1) was the keto form (the ratio of the keto and enol forms ~ 9:1). This is in accordance with their uv spectra, which in ethanolic solution showed in case of **2** (X = S, m

Scheme 3



= O, n = 3) an intensive enol absorption band at 302 nm (ε = 2020) besides a weak keto absorption at 240 nm (ε = 980), while in case of **2** (X = S, m = 2, n = 1) a strong keto absorption was observed only at 250 nm (ε = 2270). In basic condition both spectra suffered a batochromic shift accompanied with increase of intensity [see: **2** (X = S, m = O, n = 3) and **2** (X = S, m = 2, n = 1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max 307 nm (ε = 5020) and 287 nm (ε = 5440), respectively].

Providing the condensation of ethyl tetrahydrothiopyran-3-one-4-carboxylate (**2**, X = S, m = 2, n = 1) with 5-amino-3-methylthio-1*H*-1,2,4-triazole **1** (Q = methylthio) in acetic acid the expected 6,7-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 2, n = 1) was obtained (Scheme 1). Its uv [λ max (ethanol): 232 and 266 nm] and cmr spectra (δ C-2 and δ C=O = 163.5 and 155.4 ppm, respectively) again nicely followed the formerly elaborated [7] uv and cmr rules, and the pmr spectrum [δ CH_2-6 = 2.69 ppm (t, 2H), δ CH_2-7 = 2.87 ppm (t, 2H) and δ CH_2-9 = 3.69 (s, 2H)] proved the position of the sulfur atom 8 present.

The benzylation of the sodium salt of **3** (Q = methylthio, X = S, m = 2, n = 1) lead to the corresponding 10-benzyl derivative **3/1** (Q = methylthio, X = S, m = 2, n = 1) (Scheme 2) in which the position of the benzyl group was corroborated with gated cmr spectra. The analogy of the uv (λ max: 232 and 266, and 236 and 278 nm, respectively) and the cmr (δ C-2 and δ C=O: 163.2 and 154.4, and 165.4 and 155.0, respectively) of **3** (Q = methylthio, X = S, m = 2, n = 1) and **3/1** (Q = methylthio, X = S, m = 2, n = 1), respectively proved again the 10*H*-dominant tautomeric structure of **3** (Q = methylthio, X = S, m = 2, n = 1) in ethanolic and DMSO-d_6 solution shown in Scheme 2.

The isomeric *N*-benzyl derivative **4/1** (Q = methylthio, X = S, m = 2, n = 1) was obtained again by simple melting of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**7**, Q = methylthio) with ethyl tetrahydrothiopyran-3-one-4-carboxylate (**2**, X = S, m = 2, n = 1) (Scheme 3), Its uv [λ max nm (ethanol): 206 and 296] and cmr (δ C-2 and δ C=O: 162.0 and 159.2 ppm, respectively) spectra again perfectly followed the rules elaborated previously [7] giving an unequivocal evidence for its structure.

Reacting ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) with 5-amino-3-methylthio-1*H*-1,2,4-triazole **1** (Q = methylthio)) in acetic acid 7,8-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = O, n = 3) was obtained as the main product besides 6,7-dihydro-2-methylthio-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = methylthio, X = S, m = O, n = 3) (Scheme 2) that were separated [11]. The cmr spectra of both derivatives: **3** (Q = methylthio, X = S, m = O, n = 3; δ C-2 and δ C=O = 163.2 and 152.6 ppm, respectively) and **4** (Q = methylthio, X = S, m = O, n = 3, δ C-2 and δ C=O = 162.2 and 159.8 ppm, respectively) were in accordance with the cmr rules reported [7] and the pmr spectra corroborated the position of the sulfur atoms in the thiopyrane rings [see: **3** (Q = methylthio, X = S, m = O, n = 3); δ CH_2-7 = 2.95 ppm (t, 2H), δCH_2-8 = 2.11 ppm (qi, 2H) and δ CH_2-9 = 2.75 (t, 2H); **4** (Q = methylthio, X = S, m = O, n = 3); δ CH_2-5 = 2.95 ppm (t, 2H), δCH_2-6 = 2.12 ppm (qi, 2H) and δ CH_2-7 = 2.90 ppm (t, 2H)]. However, the higher maxima in the uv spectra of both derivatives taken in ethanol suffered a strong batochromic shift (λ max: 317 and 321 nm, respectively) as compared with those of the methylthio derivatives **3** and **4** (Q = methylthio, X = S, m = 1, n = 2 and X = S, m = 2, n = 1, respectively); (λ max: 268 and 268, and 290 and 296 nm, respectively) as well as the 2-methylthio-5,6,7,8-tetrahydrocyclohexa[1,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = methylthio, X = CH_2, m = O, n = 3); (λ max: 292 nm) described recently [4]. This is in accordance with that of observed previously [3] for 2-methylthio-7,8-dihydrothieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one **3** (Q = methylthio, X = S, m = O, n = 2); (λ max: 318 nm) as in these cases the loan electron pair of the sulfur atom is conjugated to the triazolopyrimidinone chromophore.

It should be mentioned that the uv spectra of all derivatives **3** and **4** are more or less influenced by the loan electron pair of the sulphur or nitrogen atom of the Q moiety, too. However, the character of the spectra remains in all cases unchanged giving a possibility to distinquish between them safely.

In all those cases, where Q stands for an alkylamino group (see: Q = 1,1-dimethyl-ethylamino, cyclohexylamino, benzylamino and 2-phenethylamino) further tautomeric structures arising from the amino-imino teutomerism of this group have also to be taken in account. However, in the pmr spectra of these derivatives a direct coupling was observed between the amino group and the alkyl moiety attached [see for **3** (Q = cyclohexylamino, benzylamino and phenethylamino, X = S, m = O, n = 3): δ NH = 6.30 **d**, 7.20 **t**, 6.72 **t**, respectively] excluding the possibility of imino tautomeric structures. In case of the remaining **3** (Q = 1,1-dimethylethylamino, X = S, m = O, n = 3) where the alkyl moiety bears no proton attached primarily to the amino group the above method was of no use. However, the complete analogy of all its spectra with the analogous derivatives **3** (X = S, m = O, n = 3) remained no doubt about its 10*H*-tautomeric structure shown on Scheme 1.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro ap-

paratus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained by a Pye Unicam SP 8-150 instrument. The ^{1}H-nmr and the ^{13}C-nmr measurements were performed using Brucker WM-250 and Brucker WP-80 SY instruments. All tlc determinations were performed on DC-Alufolien Kieselgel 60 F_{254} (Merck) plates. The spots were detected by uv.

Ethyl Tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) and Ethyl Tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1).

To the solution of 45.7 g (1.99 moles) of sodium in 1000 ml of absolute ethanol the solution of 389 g (1.66 moles) of ethyl γ-(carboethoxymethylthio)butyrate [9] in 500 ml of absolute toluene was added below 10°. The reaction was completed by stirring the reaction mixture at room temperature for 3 hours and at 50° for 1 hour. After standing overnight the reaction mixture was decomposed by pouring it with stirring to the mixture of 200 ml of concentrated hydrochloric acid and 2000 g of crushed ice, the phases were separated, the water phase was extracted two times with 300 ml portions of toluene, the combined toluene layers were washed with water and the solution of sodium hydrogen carbonate, dried and evaporated *in vacuo* to dryness to yield 262 g (84%) of an ioly product that is an ~6:1 mixture of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) and ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1) (gc). This was distilled *in vacuo* to yield 206 g of pure ethyl tetrahydrothiopyran-3-one-2-carboxylate (**2**, (X = S, m = O, n = 3), bp 118°/1 mm Hg (Lit [10], bp 117-120°/4 mm Hg); gc: Capillary column SP-2250, (CP-Sil-8 CB), internal diameter 0.32 mm, length 25 m, Carrier Nitrogen, Flow rate 20 ml/minute; Hydrogen 0.4 bar; Air 0.3 bar; Detector FID; Temperature program: 120°/3 minutes, raise by 20°/minutes to 250°; 250°/2 minutes stop; Retention times 4.93 and 5.40 sec (keto-enol); ir: ν C=O = 1745 cm^{-1} (ester-keto), 1720 cm^{-1} (ester-enol), 1650 cm^{-1} (keto); pmr (DMSO-d_6): δ, ppm 1.24 (t, CH_3-keto), 1.27 (t, CH_3-enol), 4.19 (q, OCH_2-enol), 4.20 (q, OCH_2-keto), 12.2 (bs, OH-enol), keto-enol ratio ~ 1:7; uv (ethanol): λ max nm (ε) 240 (980) (keto) and 302 (2020) (enol); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε) 307 (5020). The chromatography of the crude mixture of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) and ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1) on a silica-gel column (eluent benzene) lead first to ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3), R_f = 0.35, then to ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1), R_f = 0.30, which after recrystallisation from 2-propanol melted at 41-43°; gc (conditions see above) retention times 5.18 and 5.36 seconds (keto-enol); ir: ν C=O = 1739 cm^{-1} (keto-ester), 1726 cm^{-1} (enol-ester), 1690 cm^{-1} (keto); pmr (DMSO-d_6): δ, ppm 1.21 (t, CH_3-keto), 1.26 (t, CH_3-enol), 4.13 (q, OCH_2-enol), 4.14 (q, OCH_2-keto), 12.6 (bs, OH-enol), keto-enol ratio ~ 9:1; uv (ethanol): λ max nm (ε) 250 (2270); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε) 287 (5440).

Anal. Calcd. for $C_8H_{12}O_3S$ (MW 188.25): C, 51.04; H, 6.43; S, 17.03. Found: C, 50.97; H, 6.50; S, 17.11.

8,9-Dihydro-2-methylthio-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 1, n = 2).

To a solution of 1.30 g (0.01 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole **1** (Q = methylthio) [13] in 6 ml of acetic acid 1.88 g (0.01 mole) of ethyl tetrahydrothiopyran-4-one-3-carboxylate **2** (X = S, m = 1, n = 2) was added and the mixture refluxed for 60 minutes. The crystals precipitated were filtered while hot and washed with 2-propanol to yield 1.6 g (63%) of crude 8,9-dihydro-2-methylthio-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5-one **3** (Q = methylthio, X = S, m = 1, n = 2) contamined with a small amount of 5,6-dihydro-2-methylthio-8*H*, 10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = methylthio, X = S, m = 1, n = 2) (tlc: benzene-ethyl acetate 2:1, R_f = 0.26 and 0.30, respectively) that was dissolved in 12 ml of hot 10% sodium hydroxide solution, the sodium salt precipitated after cooling was filtered off (mp >350°), dissolved in 30 ml of water and the solution acidified with acetic acid. The crystals precipitated were filtered off, washed with water and dried to yield 1.0 g (39%) of pure 8,9-dihydro-2-methylthio-6*H*,10*H*-thiopyrano-[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 1, n = 2), mp 313-316°; ir: ν C=O = 1689 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.59 (s, 3H, SCH_3), 2.89 (bs, 4H, CH_2-8,9), 3.51 (s, 2H, CH_2-6); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 22.0 (CH_2-9), 23.4 (CH_2-8), 28.2 (CH_2-6), 104.8 (C-5a), 147.3 (C-9a), 150.3 (C-10a), 154.5 (C=O), 163.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 232 (25.2), 268 (8.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 231 (25.1), 268 (11.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 287 (14.4).

Anal. Calcd. for $C_9H_{10}N_4OS_2$ (MW 254.34): C, 42.50, H, 3.96; N, 22.03; S, 25.22. Found: C, 42.31; H, 4.08; N, 21.98; S, 25.32.

8,9-Dihydro-2-methylthio-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 1, n = 2) Na Salt.

Compound **3** (Q = methylthio, X = S, m = 1, n = 2) (1.35 g) was dissolved at 70° in 30 ml of 5% sodium hydroxide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2 ml of water to yield 1.4 g (95%) of the corresponding sodium salt, mp >350°.

10-Benzyl-8,9-dihydro-2-methylthio-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = 1, n = 2).

To a solution of 1.10 g (0.004 mole) of 8,9-dihydro-2-methylthio-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 1, n = 2) Na Salt in 5 ml of dimethylformamide 0.56 g (0.51 ml, 0.0045 mole) of benzyl chloride was added and the reaction mixture was refluxed for 4 hours. After cooling the mixture was diluted with 10 ml of water extracted twice with 25 ml portions of chloroform, the combined chloroform layers were extracted with 20 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness to yield 1.15 g (80%) of 10-benzyl-8,9-dihyro-2-methylthio-6*H*,10*H*-thiopyrano-[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = 1, n = 2) which after recrystallisation from acetonitrile melted at 221-223°; ir: ν C=O = 1658 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.59 (s, 3H, SCH_3), 2.87 (m, 4H, CH_2-8,9), 3.60 (s, 2H, CH_2-6), 5.54 (s, 2H, NCH_2), 7.2-7.4 (m, 5H, PhH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 22.9 (CH_2-9), 24.0 (CH_2-8), 26.7 (CH_2-6), 108.0 (C-5a), 126.1, 127.7, 128.8 and 135.5 (Ph), 148.0 (C-9a), 152.2 (C-10a), 153.7 (C=O), 163.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 237 (22.4), 280 (10.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 236 (26.8), 278 (11.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 239 (23.9), 279

(10.8).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 334.46): C, 55.79; H, 4.68; N, 16.27; S, 18.62. Found: C, 55.82; H, 4.78; N, 16.20; S, 18.60.

10-Benzyl-5,6-dihydro-2-methylthio-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = 1, n = 2).

The mixture of 1.10 g (0.005 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (Q = methylthio) [14] and 1.12 g, (0.005 mole) of ethyl tetrahydrothiopyran-4-one-3-carboxylate **2**, (X = S, m = 1, n = 2) (~84% pure, gc) was heated at 180-185° for 5 minutes. To the still hot melt 5 ml of 2-propanol was added. The solution obtained crystallised upon cooling. The crystals were filtered off to yield 0.72 g (42%) of 10-benzyl-5,6-dihydro-2-methylthio-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = 1, n = 2) which after recrystallisation from 2-propanol melted at 115-117°; ir: ν C=O = 1657 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.58 (s, 3H, SCH_3), 2.94 (t, 2H, CH_2-6), 3.10 (t, 2H, CH_2-5), 3.52 (s, 2H, CH_2-8), 5.25 (s, 2H, $PhCH_2$), 7.24-7.36 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 22.7* (C-5), 22.8* (C-6), 25.5 (C-8), 46.4 ($PhCH_2$), 111.0 (C-8a), 127.7, 128.0, 128.5 and 135.7 (Ph), 143.9 (C-4a), 149.7 (C-10a), 158.4 (C=O), 162.1 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 205 (24.2), 290 (8.1); uv (10% ethanol + 90% 0.1 *N*-hydrochloric acid): λ max nm (ε. 10^{-3}) 207 (30.1), 288 (9.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 289 (8.1).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 334.46): C, 55.79; H, 4.68; N, 16.27; S, 18.62. Found: C, 55.71; H, 4.70; N, 16.17; S, 18.75.

8,9-Dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 1, n = 2).

In a solution of 8.45 g (0.05 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole **1** (Q = morpholino) [14] in the mixture of 25 ml of acetic acid and 5 ml of dimethylformamide 9.41 g (0.05 mole) of ethyl tetrahydrothiopyran-4-one-3-carboxylate **2** (X = S, m = 1, n = 2) was added and the mixture refluxed for 5 hours. The crystals precipitated after cooling were filtered off and washed with acetonitrile to yield 12.0 g (82%) of crude 8,9-dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 1, n = 2) contamined with a small amount of 5,6-dihydro-2-morpholino-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = morpholino, X = S, m = 1, n = 2) (tlc: benzene-ethyl acetate 2:1, R_f = 0.15 and 0.18, respectively) that was dissolved in 120 ml of hot 5% sodium hydroxide solution, the sodium salt precipitated after cooling was filtered off (mp >350°), dissolved in 300 ml of water and the solution acidified with acetic acid. The crystals precipitated were filtered off, washed with water and dried to yield 10.1 g (69%) of pure 8,9-dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 1, n = 2), mp >360°; ir: ν C=O = 1660 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.85 (bs, 4H, CH_2-8,9), 3.38 (t, 4H, NCH_2), 3.50 (s, 2H, CH_2-6), 3.68 (t, 4H, OCH_2); cmr (DMSO-d_6): δ ppm 22.2 (C-9), 23.5 (C-8), 28.3 (C-6), 45.9 (NCH_2), 65.7 (OCH_2), 104.8 (C-5a), 146.2 (C-9a), 149.8 (C-10a), 155.1 (C=O), 163.7 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 231 (27.2), 276 (9.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 230 (24.5), 270 (8.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 233 (27.5), 289 (6.3).

Anal. Calcd. for $C_{12}H_{15}N_5O_2S$ (MW 293.35): C, 49.13; H, 5.15; N, 23.87; S, 10.93. Found: C, 49.25; H, 5.30; N, 23.79; S, 10.95.

8,9-Dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 1, n = 2) Na Salt.

Compound **3** (Q = morpholino, X = S, m = 1, n = 2) (2.40 g) was dissolved at 90° in 30 ml of 5% sodium hydroxide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2 ml of water to yield 2.25 g (87%) of the corresponding sodium salt, mp >350°.

10-Benzyl-8,9-dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = morpholino, X = S, m = 1, n = 2).

To a solution of 0.946 g (0.003 mole) of 8,9-dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 1, n = 2) Na Salt in 3 ml of dimethylformamide 0.456 g (0.41 ml, 0.0036 mole) of benzyl chloride was added and the reaction mixture was refluxed for 5 hours. After cooling the mixture was diluted with 10 ml of water extracted twice with 25 ml portions of chloroform, the combined chloroform layers were extracted with 20 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness to yield 0.65 g (57%) of 10-benzyl-8,9-dihydro-2-morpholino-6*H*,10*H*-thiopyrano[4,3-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = morpholino, X = S, m = 1, n = 2) which after recrystallisation from acetonitrile melted at 196-198°; ir ν C=O = 1678 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.84 (bs, 4H, CH_2-8,9), 3.39 (t, 4H, NCH_2), 3.57 (s, 2H, CH_2-6), 3.67 (t, 4H, OCH_2), 5.51 (s, 2H, $PhCH_2$), 7.22-7.38 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 23.2 (C-9), 24.2 (C-8), 26.7 (C-6), 45.9 (NCH_2), 49.2 ($PhCH_2$), 65.7 (OCH_2), 108.1 (C-5a), 126.3, 127.9, 129.2 and 135.7 (Ph), 146.9 (C-9a), 151.6 (C-10a), 154.2 (C=O), 164.2 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 236 (24.7), 281 (9.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 236 (27.0), 280 (10.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 282 (10.0).

Anal. Calcd. for $C_{19}H_{21}N_5O_2S$ (MW 383.48): C, 59.51; H, 5.52; N, 18.26; S, 8.36. Found: C, 59.48; H, 5.58; N, 18.17; S, 8.40.

10-Benzyl-5,6-dihydro-2-morpholino-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = morpholino, X = S, m = 1, n = 2).

The mixture of 3.50 g, (0.0145 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole **7** (Q = morpholino) [7] and 3.47 g (0.0149 mole) of ethyl tetrahydrothiopyran-4-one-3-carboxylate **2** (X = S, m = 1, n = 2) (~84% pure, gc) was heated at 170° for 10 minutes. To the still hot melt 20 ml of 2-propanol was added. The solution obtained crystallised upon cooling. The crystals were filtered off to yield 4.1 g (79%) of 10-benzyl-5,6-dihydro-2-morpholino-8*H*,10*H*-thiopyrano[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = morpholino, X = S, m = 1, n = 2) which after recrystallisation from dimethylformamide melted at 191-193°; ir: ν C=O = 1652 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.92 (t, 2H, CH_2-6), 3.04 (t, 2H, CH_2-5), 3.37 (t, 4H, NCH_2), 3.49 (s, 2H, CH_2-8), 3.68 (t, 4H, OCH_2), 5.22 (s, 2H, $PhCH_2$), 7.27-7.37 (m, 5H, ArH); cmr (DMSO-d_6): 22.5 (C-5), 22.8 (C-6), 25.5 (C-8), 45.8 (NCH_2), 46.1 ($PhCH_2$), 65.4 (OCH_2), 108.8 (C-8a), 127.4, 127.9, 128.3 and 135.8 (Ph), 144.0 (C-4a), 148.7 (C-10a), 158.2 (C=O), 164.0 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 209 (20.0), 228sh (10.7), 314 (8.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (21.5), 228 sh (11.2), 314 (8.7); uv

(10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 225 (9.7), 314 (9.1).

Anal. Calcd. for $C_{19}H_{21}N_5O_2S$ (MW 383.48): C, 59.51; H, 5.52; N, 18.26; S, 8.36. Found: C, 59.60; H, 5.71; N, 18.21; S, 8.24.

6,7-Dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 2, n = 1).

To a solution of 0.976 g (0.0075 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole **1** (Q = methylthio) [13] in 6 ml of acetic acid 1.368 g (0.0075 mole) of ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1) was added and the mixture refluxed for 30 minutes. The crystals precipitated were filtered while hot, washed with water and recrystallised from dimethylformamide to yield 1.2 g (63%) of 6,7-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 2, n = 1), mp 302-305°; ir: ν C=O = 1651 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.59 (s, 3H, SCH_3), 2.69 (t, 2H, CH_2-6), 2.87 (t, 2H, CH_2-7), 3.69 (s, 2H, CH_2-9); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 23.0 (CH_2-6), 24.5 (CH_2-7), 25.9 (CH_2-9), 106.1 (C-5a), 143.7 (C-9a), 149.6 (C-10a), 155.4 (C=O), 163.3 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 232 (23.9), 266 (9.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 232 (24.9), 268 (10.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 236 (26.5), 290 (9.3).

Anal. Calcd. for $C_9H_{10}N_4OS_2$ (MW 254.34): C, 42.50; H, 3.96; N, 22.03; S, 25.22. Found: C, 42.56; H, 4.11; N, 22.21; S, 25.09.

6,7-Dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 2, n = 1) Na Salt.

Compound **3** (Q = methylthio, X = S, m = 2, n = 1) (0.85 g) was dissolved at 70° in 15 ml of 5% sodium hydroxide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2 ml of water to yield 0.75 g (77%) of the corresponding sodium salt, mp 252-255°.

10-Benzyl-6,7-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = 2, n = 1).

To a solution of 1.10 g (0.004 mole) of 6,7-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 2, n = 1) Na Salt in 3 ml of dimethylformamide 0.56 g (0.51 ml, 0.0045 mole) of benzyl chloride was added and the reaction mixture was refluxed for 5 hours. After cooling the mixture was diluted with 10 ml of water extracted twice with 20 ml portions of chloroform, the combined chloroform layers were extracted with 20 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness to yield 0.75 g (54%) of 10-benzyl-8,9-dihydro-2-methylthio-6*H*,10*H*-thiopyrano[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = 2, n = 1) which after recrystallisation from acetonitrile melted at 225-226°; ir: ν C=O = 1682 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.60 (s, 3H, SCH_3), 2.80 (bs, 4H, CH_2-6,7), 3.72 (s, 2H, CH_2-9), 5.58 (s, 2H, $PhCH_2$), 7.22-7.36 (m, 5H, Ph); cmr (deuteriochloroform): δ ppm 14.1 (SCH_3), 24.2 (CH_2-6), 24.9 (CH_2-7), 25.4 (CH_2-9), 50.4 ($PhCH_2$), 110.5 (C-5a), 126.3, 128.6, 129.4 and 134.5 (Ph), 144.2 (C-9a), 152.0 (C-10a), 155.0 (C=O), 165.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-1}) 236 (25.8), 278 (11.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 236 (27.2), 278 (11.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 282 (12.0).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 344.46): C, 55.79; H, 4.68; N, 16.27; S, 18.62. Found: C, 55.88; H, 4.82; N, 16.05; S, 18.58.

10-Benzyl-7,8-dihydro-2-methylthio-5*H*,10*H*-thiopyrano[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = 2, n = 1).

The mixture of 0.88 g (0.004 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole **7** (Q = methylthio) [14] and 0.73 g (0.0039 mole) of ethyl tetrahydrothiopyran-3-one-4-carboxylate **2** (X = S, m = 2, n = 1) was heated to 175-180° for 10 minutes. To the still hot yellow melt obtained 8 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 1.0 g (74%) of 10-benzyl-7,8-dihydro-2-methylthio-5*H*,10*H*-thiopyrano-[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = 2, n = 1), mp 143-144°; ir: ν C=O = 1656 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.57 (s, 3H, SCH_3), 2.67 (t, 2H, CH_2-8), 2.86 (t, 2H, CH_2-7), 3.94 (s, 2H, CH_2-5), 5.23 (s, 2H, NCH_2), 7.2-7.4 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 13.6 (SCH_3), 23.2 (CH_2-5), 23.9 (CH_2-5,7), 46.4 (NCH_2), 112.6 (C-8a), 127.7, 127.9, 128.5 and 135.8 (Ph), 140.6 (C-4a), 149.3 (C-10a), 159.2 (C=O), 162.0 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 206 (28.9), 296 (8.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (21.9), 294 (7.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 295 (7.7).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 344.46): C, 55.79, H, 4.68; N, 16.27; S, 18.62. Found: C, 55.63; H, 4.54; N, 16.21; S, 18.67.

7,8-Dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 0, n = 3) and 6,7-Dihydro-2-methylthio-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = methylthio, X = S, m = 0, n = 3).

To the solution of 6.5 g (0.05 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [13] in the mixture of 2.5 ml of acetic acid and 12.5 ml of dimethylformamide 9.4 g (0.05 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = 0, n = 3) was added and refluxed for 60 minutes. After 2-3 minutes of refluxing the solution began to crystallise. The crystals precipitated were filtered while hot and washed with acetic acid and 2-propanol to yield 6.5 g (51%) of 7,8-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = 0, n = 3), mp >350° (after recrystallisation from dimethylformamide): ir: ν C=O = 1647 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.11 (qi, 2H, CH_2-8), 2.60 (s, 3H, SCH_3), 2.75 (t, 2H, CH_2-9), 2.95 (dt, 2H, CH_2-7); cmr (DMSO-d_6): δ ppm 12.9 (SCH_3), 21.5 (CH_2-8), 24.7 (CH_2-9), 25.6 (CH_2-7), 103.6 (C-5a), 141.6 (C-9a), 149.2 (C-10a), 152.3 (C=O), 163.0 (C-2); uv (ethanol); λ max nm (ε. 10^{-3}) 252 (31.0), 317 (8.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}), 253 (31.3), 316 (7.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 226 (37.9), 254 (12.7), 295 (10.4).

Anal. Calcd. for $C_9H_{10}OS_2$ (MW 254.34): C, 42.50; H, 3.96; N, 22.03; S, 25.22. Found: C, 42.73; H, 4.05; H, 21.85; S, 25.01.

The hot mother liquor of **3** (Q = methylthio, X = S, m = 0, n = 3) crystallised after cooling again to yield 1.8 g (14%) of 6,7-dihydro-2-methylthio-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4** (Q = methylthio, X = S, m = 0, n = 3), mp 334-338° after recrystallisation from dimethylformamide; ir: ν C=O = 1672 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.10 (qi, 2H, CH_2-6), 2.55 (s, 3H, SCH_3), 2.93 (t, 2H, CH_2-5), 2.99 (m, 2H,

CH_2-7), 12.8 (b, 1H, NH); cmr (DMSO-d_6): δ ppm 13.5 (SCH_3), 21.0 (CH_2-6), 23.0 (CH_2-5), 25.1 (CH_2-7), 112.3 (C-8a), 138.1 (C-4a), 147.5 (C-10a), 157.9 (C=O), 161.5 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 206 (21.8), 250sh (8.5), 321 (12.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 252 (9.1), 324 (12.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 312 (12.6).

Anal. Calcd. for $C_9H_{10}N_4OS_2$ (MW 254.34): C, 42.50; H, 3.96; N, 22.03; S, 25.22. Found: C, 42.55; H, 4.09; N, 22.11; S, 25.16.

7,8-Dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = O, n = 3) Na Salt.

Compound **3** (Q = methylthio, X = S, m = O, n = 3) (3.4 g) was dissolved at 70° in 7 ml of 10% sodium hydroxide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2 ml of water to yield 3.5 g (94%) of the corresponding sodium salt, mp >350°.

10-Benzyl-7,8-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = O, n = 3).

To a solution of 1.38 g (0.005 mole) of 7,8-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = methylthio, X = S, m = O, n = 3) Na Salt in 5 ml of dimethylformamide 0.70 g (0.63 ml, 0.0055 mole) of benzyl chloride was added and the reaction mixture was stirred at 70° for 8 hours. After cooling the mixture was diluted with 15 ml of water extracted twice with 15 ml portions of chloroform, the combined chloroform layers were extracted with 15 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness to yield 1.4 g (81%) of 10-benzyl-7,8-dihydro-2-methylthio-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = methylthio, X = S, m = O, n = 3) which after recrystallisation from dimethylformamide melted at 236-238° ir: ν CO = 1678 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.03 (qi, 2H, CH_2-8), 2.59 (s, 3H, SCH_3), 2.72 (t, 2H, CH_2-9), 2.89 (dt, 2H, CH_2-7), 5.53 (s, 2H, NCH_2), 7.21-7.36 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 13.8 (SCH_3), 22.7 (CH_2-8), 24.9* (CH_2-9), 25.0* (CH_2-7), 52.4 (NCH_2), 107.3 (C-5a), 126.6, 128.2, 129.3 and 135.8 (Ph), 142.8 (C-9a), 148.2 (C-10a), 152.1 (C=O), 164.0 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 256 (31.5), 322 (9.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 256 (32.7), 320 (9.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 257 (32.2), 320 (9.6).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 344.46): C, 55.79; H, 4.68; N, 16.27; S, 18.62. Found: C, 55.61; H, 4.75; N, 16.44; S, 18.57.

10-Benzyl-6,7-dihydro-2-methylthio-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = O, n = 3).

The mixture of 2.20 g (0.01 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole **7**, (Q = methylthio) [14] and 1.88 g (0.01 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) was heated to 175-180° for 8 minutes. To the still hot deep red melt 15 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 2.35 g (68%) of 10-benzyl-6,7-dihydro-2-methylthio-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = methylthio, X = S, m = O, n = 3), mp 154-156°; ir: ν C=O = 1650 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.11 (qi, 2H, CH_2-6), 2.58 (s, 3H, SCH_3), 2.94 (t, 2H, CH_2-5), 2.97 (t, 2H, CH_2-7), 5.25 (s, 2H, NCH_2), 7.23-7.38 (m, 5H, ArH); cmr (DMSO-d_6): δ ppm 13.7 (SCH_3), 21.0 (CH_2-6), 23.2 (CH_2-5), 25.5 (CH_2-7), 111.8 (C-8a), 127.8, 128.0, 128.6 and 135.6 (Ph), 138.2 (C-4a), 148.5 (C-10a), 156.8 (C=O), 161.3 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 209 (28.6), 248 sh (7.8), 324 (13.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (33.0), 245 sh (10.7), 322 (14.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}), 244 (9.6), 320 (12.5).

Anal. Calcd. for $C_{16}H_{16}N_4OS_2$ (MW 344.46): C, 55.79; H, 4.68; N, 16.27; S, 18.62. Found: C, 55.71; H, 4.79; N, 16.31; S, 18.53.

7,8-Dihydro-2-dimethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = dimethylamino, X = S, m = O, n = 3).

Prepared as **3** (Q = methylthio, X = S, m = O, n = 3) starting from 6.35 g (0.05 mole) of 5-amino-3-dimethylamino-1*H*-1,2,4-triazole **1** (Q = dimethylamino) [14]; the yield was 8.2 g (65%), mp >350° (after recrystallisation from dimethylformamide); ir: ν C=O = 1645 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.03 (qi, 2H, CH_2-8), 2.67 (t, 2H, CH_2-9), 2.91 (dt, 2H, CH_2-7), 2.96 (s, 6H, NCH_3), 12.9 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 21.8 (CH_2-8), 25.1 (CH_2-9), 25.9 (CH_2-7), 37.4 (NCH_3), 103.6 (C-5a), 140.8 (C-9a), 148.9 (C-10a), 152.9 (C=O), 164.7 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 255 (27.7), 305 (7.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 255 (26.4), 308 (7.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 246 (30.9), 273 sh (10.4), 313 (6.5).

Anal. Calcd. for $C_{10}H_{13}N_5OS$ (MW 251.31): C, 47.79; H, 5.21; N, 27.87; S, 12.76. Found: C, 47.99; H, 5.45; N, 27.66; S, 12.60.

7,8-Dihydro-2-dimethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = dimethylamino, X = S, m = O, n = 3) Na Salt.

Compound **3** (Q = dimethylamino, X = S, m = O, n = 3) (4.6 g) was dissolved at 70° in the mixture of 5 ml of dimethylformamide and 3 ml of 20% sodium hydroxide. The yellow solution obtained crystallised upon cooling. After addition of 5 ml of acetone the crystals precipitated were filtered off and washed with acetone to yield 4.5 g (90%) of the corresponding sodium salt, mp 350-360°.

10-Benzyl-7,8-dihydro-2-dimethylamino-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = dimethylamino, X = S, m = O, n = 3).

To a solution of 2.73 g (0.01 mole) of 7,8-dihydro-2-dimethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5-one **3** (Q = dimethylamino, X = S, m = O, n = 3) Na Salt in 5 ml of dimethylformamide 1.39 g (1.25 ml, 0.011 mole) of benzyl chloride was added and the reaction mixture was stirred at 60° for 9 hours. After cooling the mixture was diluted with 10 ml of water and the crystals precipitated were filtered off to yield 1.9 g (56%) of 10 benzyl-8,9-dihydro-2-dimethylamino-9*H*,-10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = dimethylamino, X = S, m = O, n = 3) which after recrystallisation from dimethylformamide melted at 269-272°; ir: ν C=O = 1662 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.02 (qi, 2H, C-8), 2.67 (t, 2H, C-9), 2.85 (dt, 2H, C-7), 2.97 (s, 6H, NCH_3), 5.50 (s, 2H, $PhCH_2$), 7.21-7.37 (m, 5H, PhH); cmr (DMSO-d_6): δ ppm 22.4 (C-8), 23.4 (C-9), 24.5 (C-7), 37.2 (CH_3), 49.4 (NCH_2), 106.5 (C-5a), 126.1, 127.5, 128.7 and 135.5 (Ph). 140.5 (C-9a), 150.9 (C-10a), 152.2 (C=O), 164.5 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 257

(27.9), 311 (9.5); uv (10% ethanol +90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 258 (24.7), 306 (8.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 259 (27.3), 310 (9.9).

Anal. Calcd. for $C_{17}H_{19}N_5OS$ (MW 341.44): C, 59.80; H, 5.61; N, 20.51; S, 9.39. Found: C, 59.72; H, 5.73; N, 20.55; S, 9.44.

2-Diethylamino-7,8-dihydro-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = diethylamino, X = S, m = O, n = 3).

Prepared as **3** (Q = methylthio, X = S, m = O, n = 3) starting from 7.76 g (0.05 mole) of 5-amino-3-diethylamino-1*H*-1,2,4-triazole **1** (Q = diethylamino) [14]; the yield was 8.53 g (61%) of crude product, mp 305-310°. The crude product was dissolved in 20 ml of hot 5% sodium hydroxide solution, filtered and let to crystallise. The sodium salt precipitated was filtered off (mp 330-335°), dissolved in 110 ml of warm water and acidified with acetic acid. The crystals precipitated were filtered off, washed with water and dried to yield 7.85 g (56%) of pure **3** (Q = diethylamino, X = S, m = O, n = 3), mp 310-312°; ir: ν C=O = 1651 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.12 (t, 6H, CH_3), 2.05 (qi, 2H, CH_2-8), 2.68 (t, 2H, CH_2-9), 2.92 (dt, 2H, CH_2-7), 3.43 (q, 4H, CH_2), 12.9 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 12.9 (CH_3), 21.8 (C-8), 25.2 (C-9), 26.0 (C-7), 41.7 (NCH_2), 103.4 (C-5a), 140.2 (C-9a), 149.0 (C-10a), 153.0 (C=O), 163.3 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 257 (27.5), 306 (7.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 258 (28.9), 310 (6.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 251 (35.0), 272 sh (11.4), 319 (6.8).

Anal. Calcd. for $C_{12}H_{17}N_5OS$ (MW 279.37): C, 51.59; H, 6.13; N, 25.07; S, 11.48. Found: C, 51.43; H, 6.28; N, 25.11; S, 11.36.

2-Diethylamino-7,8-dihydro-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = diethylamino, X = S, m = O, n = 3) Na Salt.

Compound **3** (Q = diethylamino, X = S, m = O, n = 3) (3.2 g) was dissolved at room temperature in 8 ml of 5% sodium hydroxide. The yellow solution obtained was evaporated *in vacuo* to dryness. To the honey-like product obtained 10 ml of 2-propanol was added which recrystallised. The crystals were filtered off and washed with 2 ml of 2-propanol to yield 3.2 g (92%) of the corresponding sodium salt, mp 325-330°.

10-Benzyl-7,8-dihydro-2-diethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = diethylamino, X = S, m = O, n = 3).

To a solution of 3.01 g (0.01 mole) of 7,8-dihydro-2-diethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = diethylamino, X = S, m = O, n = 3) Na Salt in 5 ml of dimethylformamide 1.39 g (1.25 ml, 0.011 mole) of benzyl chloride was added and the reaction mixture was stirred at 60° for 9 hours. After cooling the mixture was diluted with 10 ml of water and the crystals precipitated were filtered off to yield 2.55 g (69%) of 10-benzyl-8,9-dihydro-2-diethylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = diethylamino, X = S, m = O, n = 3) which after recrystallisation from dimethylformamide melted at 204-206°; ir: ν C=O = 1673 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.11 (t, 6H, CH_3), 2.01 (qi, 2H, CH_2-8), 2.69 (t, 2H, CH_2-9), 2.85 (dt, 2H, CH_2-7), 3.42 (qa, 4H, NCH_2), 5.49 (s, 2H, $PhCH_2$), 7.23-7.37 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 12.9 (CH_3), 22.4 (C-8), 24.4* (C-9), 24.5* (C-7), 41.7 (NCH_2), 49.5 ($PhCH_2$), 106.4 (C-5a), 126.3, 127.6, 128.8 and 135.6 (Ph), 140.3 (C-9a), 150.9 (C-10a), 152.1 (C=O), 163.1 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 259 (27.3), 310 (9.4); uv (10% ethanol + 90% 0.1 hydrochloric acid): λ max nm (ε. 10^{-3}) 257 (24.3), 308 (8.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 259 (26.9), 308 (9.6).

Anal. Calcd. for $C_{19}H_{23}N_5OS$ (MW 369.49): C, 61.76; H, 6.27; N, 18.95; S, 8.68. Found: C, 61.55; H, 6.38; N, 18.78; S, 8.70.

2-Diallylamino-7,8-dihydro-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = diallylamino, X = S, m = O, n = 3).

To the solution of 8.36 g (0.05 mole) of 5-amino-3-diallylamino-1*H*-1,2,4-triazole **1** (Q = diallylamino) [14] in 4 ml of acetic acid and 12 ml of dimethylformamide 9.4 g (0.05 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) was added and refluxed for 30 minutes. After cooling to 40° 12 ml of 2-propanol was added with stirring to the reaction mixture that began to crystallise. After cooling to laboratory temperature the crystals precipitated were filtered off and washed with 2-propanol to yield 11.7 g (77%) of 7,8-dihydro-2-diallylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5-one **3** (Q = diallylamino, X = S, m = O, n = 3), mp 270-273° (after recrystallisation from a 2:1 mixture of dimethylformamide and 2-propanol); ir ν C=O = 1647 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.07 (qi, 2H, CH_2-8), 2.71 (t, 2H, CH_2-9), 2.95 (dt, 2H, CH_2-7), 4.06 (d, 4H, CH_2), 5.20 (dd, 4H, C=CH_2), 5.90 (m, 2H, CH); cmr (DMSO-d_6): δ ppm 21.8 (CH_2-8), 25.2 (CH_2-9), 25.9 (CH_2-7), 49.4 (NCH_2), 103.7 (C-5a), 116.7 (CH=CH_2), 133.9 (CH), 140.0 (C-9a), 149.0 (C-10a), 153.0 (C=O), 163.7 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 257 (31.6), 300 (8.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 256 (30.1), 298 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 249 (36.1), 273 sh (12.2), 313 (6.6).

Anal. Calcd. for $C_{14}H_{19}N_5OS$ (MW 305.41): C, 55.06; H, 6.27; N, 22.93; S, 10.50. Found: C, 54.91; H, 6.24; N, 23.06; S, 10.44.

7,8-Dihydro-2-piperidino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-5-one **3** (Q = piperidino, X = S, m = O, n = 3).

To the solution of 16.7 g (0.1 mole) of 5-amino-3-piperidino-1*H*-1,2,4-triazole **1**, (Q = piperidino) [14] in 10 ml of acetic acid 18.8 g (0.1 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = O, n = 3) was added and refluxed for 10 minutes. The mixture was diluted while hot with 100 ml of water, the crystals precipitated were filtered off and washed with 2-propanol to yield 23.3 g (82%) of 7,8-dihydro-2-piperidino-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = piperidino, X = S, m = O, n = 3), mp >350° (after recrystallisation from dimethylformamide); ir: ν C=O = 1649 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.56 (m, 6H, piperidine CH_2-3′,4′,5′), 2.06 (qi, 2H, CH_2-8), 2.70 (t, 2H, CH_2-9), 2.93 (dt, 2H, CH_2-7), 3.45 (t, 4H, NCH_2); cmr (DMSO-d_6): δ ppm 21.4 (CH_2-8), 23.3 (piperidine C-4′), 24.1 (piperidine C-3′), 24.8 (CH_2-9), 25.5 (CH_2-7), 45.7 (piperidine NCH_2), 103.3 (C-5a), 139.9 (C-9a), 148.5 (C-10a), 152.5 (C=O), 163.8 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 254 (31.7), 303 (8.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 257 (29.3), 304 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 247 (33.0), 271 sh (11.2), 313 (5.2).

Anal. Calcd. for $C_{13}H_{17}N_5OS$ (MW 291.38): C, 53.59; H, 5.88; N, 24.04; S, 11.00. Found: C, 53.66; H, 6.01; N, 23.97; S, 11.12.

7,8-Dihydro-2-morpholino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = O, n = 3).

Prepared as **3** (Q = methylthio, X = S, m = 0, n = 3) starting from 8.46 (0.05 mole) of the 5-amino-3-morpholino-1*H*-1,2,4-triazole **1** (Q = morpholino) [14]; the yield was 9.5 g (65%), mp >350° (after recrystallisation from dimethylformamide); ir: ν C=O = 1645 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.07 (qi, 2H, CH_2-8), 2.71 (t, 2H, CH_2-9), 2.93 (dt, 2H, CH_2-7), 3.42 (t, 4H, NCH_2), 3.69 (t, 4H, OCH_2); cmr (DMSO-d_6): δ ppm 21.7 (CH_2-8), 25.1 (CH_2-9), 25.8 (CH_2-7), 45.7 (NCH_2), 65.4 (OCH_2), 103.8 (C-5a), 140.4 (C-9a), 148.9 (C-10a), 152.9 (C=O), 164.2 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 254 (28.2), 307 (6.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 254 (29.2), 310 (6.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 244 (31.7), 272 sh (10.6), 314 (6.7).

Anal. Calcd. for $C_{12}H_{15}N_5O_2S$ (MW 293.35): C, 49.13; H, 5.15; N, 23.87; S, 10.93. Found: C, 49.36; H, 5.22; N, 23.88; S, 10.84.

7,8-Dihydro-2-morpholino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 0, n = 3) Na Salt.

Compound **3** (Q = morpholino, X = S, m = 0, n = 3) (2.5 g) was dissolved at 70° in 40 ml of 10% sodium hydroxide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2-propanol to yield 2.45 g (91%) of the corresponding sodium salt, mp 315°.

10-Benzyl-7,8-dihydro-2-morpholino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = morpholino, X = S, m = 0, n = 3).

To a solution of 1.56 g (0.005 mole) of 7,8-dihydro-2-morpholino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = morpholino, X = S, m = 0, n = 3) Na Salt in 5 ml of dimethylformamide 0.70 g (0.63 ml, 0.0055 mole) of benzyl chloride was added and the reaction mixture was stirred at 120° for 3 hours. After cooling the mixture was diluted with 5 ml of water and the crystals precipitated were filtered of to yield 1.0 g (52%) of 10-benzyl-7,8-dihydro-2-morpholino-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = morpholino, X = S, m = 0, n = 3) which after recrystallisation from acetonitrile melted at 229-232°; ir: ν C=O = 1679 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.06 (qi, 2H, CH_2-8), 2.82 (t, 2H, CH_2-9), 2.91 (t, 2H, CH_2-7) 3.38 (t, 4H, NCH_2), 3.66 (t, 4H, OCH_2), 5.50 (s, 2H, $PhCH_2$), 7.21-7.36 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 22.3 (C-8), 24.4* (C-9), 24.5* (C-7), 45.6 (NCH_2), 49.5 ($PhCH_2$), 65.4 (OCH_2), 106.8 (C-5a), 126.1, 127.6, 128.8 and 135.5 (Ph), 140.9 (C-9a), 150.9 (C-10a), 152.8 (C=O), 164.0 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 256 (24.9), 312 (7.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 256 (24.7), 309 (7.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 256 (25.6), 310 (7.7).

Anal. Calcd. for $C_{19}H_{21}N_5O_2S$ (MW 383.48): C, 59.51; H, 5.52; N, 18.26; S, 8.36. Found: C, 59.78; H, 5.75; N, 18.22; S, 8.25.

10-Benzyl-6,7-dihydro-2-morpholino-5*H*,10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = morpholino, X = S, m = 0, n = 3).

The mixture of 1.30 g (0.005 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole **7** (Q = morpholino) [7] and 1.32 g (0.007 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = 0, n = 3) was heated at 160° for 5 minutes. The still hot melt was diluted with 10 ml of 2 propanol, the crystals precipitated were filtered off and recrystallised from acetonitrile to yield 1.35 g (70%) of 10-benzyl-6,7-dihydro-2-morpholino-5*H*,-10*H*-thiopyrano[2,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9-one **4/1** (Q = morpholino, X = S, m = 0, n = 3), mp 232-233°; ir: ν C=O = 1659 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.10 (qi, 2H, CH_2-6), 2.88 (t, 2H, CH_2-5), 2.96 (t, 2H, CH_2-7), 3.35 (t, 4H, NCH_2), 3.68 (t, 4H, OCH_2), 5.22 (s, 2H, $PhCH_2$), 7.25-7.40 (m, 5H, ArH); cmr (DMSO-d_6): 21.1 (C-6), 23.2 (C-5), 25.3 (C-7), 45.8 (NCH_2), 46.3 ($PhCH_2$), 65.4 (OCH_2), 109.0 (C-8a), 127.5, 127.9, 128.3 and 135.7 (Ph), 138.4 (C-4a), 147.5 (C-10a), 156.6 (C=O), 163.7 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 206 (22.3), 251 (7.2), 339 (9.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (17.7), 224 (8.5), 337 (9.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 246 (11.7), 240 (13.1).

Anal. Calcd. for $C_{19}H_{21}N_5O_2S$ (MW 383.48): C, 59.51; H, 5.52; N, 18.26; S, 8.36. Found: C, 59.63; H, 5.66; H, 18.32; S, 8.43.

7,8-Dihydro-2-(4-methylpiperazino)-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 4-methylpiperazino, X = S, m = 0, n = 3).

To the solution of 16.7 g (0.1 mole) of 5-amino-3-(4-methylpiperazino)-1*H*-1,2,4-triazole **1** (Q = 4-methylpiperazino) [14] in 15 ml of acetic acid 18.8 g (0.1 mole) of ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = S, m = 0, n = 3) was added and refluxed for 90 minutes. After cooling the reaction mixture was diluted with 200 ml of ethyl acetate that began to crystallise. The crystals precipitated were filtered off and washed with ethyl acetate to yield 30.0 g (98%) of 7,8-dihydro-2-(4-methylpiperazino)-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 4-methylpiperazino, X = S, m = 0, n = 3), mp 298-301° (after recrystallisation from 80% methanol). A very pure product was obtained when the crude material (30.0 g) was dissolved in the solution of 9 g of sodium hydroxide in 90 ml of methanol, the solution was treated with charcoal, filtered and evaporated *in vacuo* to dryness. The honey-like residue obtained crystallised after treating with 50 ml of 2-propanol. The crystals were filtered off and washed with 2-propanol to yield 28.0 g (85%) of 7,8-dihydro-2-(4-methylpiperazino)-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 4-methylpiperazino, X = S, m = 0, n = 3) sodium salt, mp >350°. This was dissolved in 60 ml of water and the solution was acidified to *p*H = 4 with acetic acid. The crystals precipitated were filtered off and washed with methanol to yield 25.1 g (82%) of 7,8-dihydro-2-(4-methylpiperazino)-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 4-methylpiperazino, X = S, m = 0, n = 3), mp 300-301°; ir: ν C = O = 1636 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.06 (qi, 2H, CH_2-8), 2.28 (s, 3H, NCH_3), 2.69 (t, 2H, CH_2-9), 2.93 (dt, 2H, CH_2-7), 3.43 (m, 8H, NCH_2); cmr (DMSO-d_6): δ ppm 22.0 (CH_2-8), 25.2 (CH_2-9), 26.5 (CH_2-7), 45.0 (NCH_3), 45.7 and 53.5 (NCH_2), 103.5 (C-5a), 141.5 (C-9a), 149.6 (C-10a), 153.0 (C=O), 164.1 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 250 (30.1), 292 (8.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 248 (29.1), 292 (5.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 242 (36.2), 270 sh (12.3), 300 (7.2).

Anal. Calcd. for $C_{13}H_{18}N_6OS$ (MW 306.39): C, 50.96; H, 5.92; N, 27.43; S, 10.47. Found: C, 51.12; H, 6.08; N, 27.34; S, 10.44.

7,8-Dihydro-2-(1,1-dimethylethylamino)-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 1,1-dimethylethylamino, X = S, m = 0, n = 3).

Prepared as **3** (Q = diallylamino, X = S, m = 0, n = 3) starting from 7.76 g (0.05 mole) of 5-amino-3-(1,1-dimethylethyl-

amino)-1*H*-1,2,4-triazole (**1**, Q = 1,1-dimethylethylamino) [14]; the yield was 8.7 g (62%), mp 317-320° (after recrystallisation from a 2:1 mixture of dimethylformamide and 2-propanol); ir ν C=O = 1684 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.30 (s, 9H, CH_3), 2.00 (qi, 2H, CH_2-8), 2.68 (t, 2H, CH_2-9), 2.88 (dt, 2H, CH_2-7), 6.25 (s, 1H, NH-exo), 12.6 (bs, 1H, NH-10); cmr (DMSO-d_6): δ ppm 21.8 (CH_2-8), 24.9 (CH_2-9), 25.8 (CH_2-7), 28.5 (CH_3), 50.0 (C-*tert*) 103.1 (C-5a), 140.4 (C-9a), 147.9 (C-10a), 152.8 (C=O), 162.1 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 253 (29.8), 308 (8.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 252 (29.1), 308 (7.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 242 (38.9), 270 sh (12.5), 314 (8.8).

Anal. Calcd. for $C_{12}H_{17}N_5OS$ (MW 279.37): C, 51.59; H, 6.13; N, 25.07; S, 11.48. Found: C, 51.53; H, 6.19; N, 24.96; S, 11.26.

7,8-Dihydro-2-cyclohexylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3**, (Q = 1-cyclohexylamino, X = S, m = 0, n = 3).

Prepared as **3** (Q = diallylamino, X = S, m = 0, n = 3) starting from 8.76 g (0.05 mole) of 5-amino-3-cyclohexylamino-1*H*-1,2,4-triazole **1** (Q = cyclohexylamino) [14]; the yield was 11.0 g (72%), mp 298-301° (after recrystallisation from dimethylformamide); ir: ν C=O = 1680 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.23 (m, 6H, piperidine CH_2-3'4'5'), 1.68 and 1.95 (two m, 4H, piperidine 2'6'), 2.06 (qi, 2H, CH_2-8), 2.67 (t, 2H, CH_2-9), 2.90 (dt, 2H, CH_2-7), 3.40 (m, 1H, CH), 6.30 (d, 1H, NH-exo), 12.6 (bs, 1H, NH-10); cmr (DMSO-d_6): δ ppm 21.5 (CH_2-8), 24.2 (piperidine CH_2-3'5'), 24.8 (CH_2-9), 25.0 (piperidine CH_2-4'), 25.7 (CH_2-7), 32.3 (piperidine CH_2-2'6'), 103.2 (C-5a), 140.0 (C-9a), 148.2 (C-10a), 152.6 (C=O), 162.2 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 253 (30.9), 305 (8.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 252 (29.9), 306 sh (8.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 243 (41.5), 270 sh (14.0), 314 (8.4).

Anal. Calcd. for $C_{14}H_{19}N_5OS$ (MW 305.41): C, 55.06; H, 6.27; N, 22.93; S, 10.50. Found: C, 55.30; H, 6.46; N, 23.06, S, 10.36.

7,8-Dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = benzylamino, X = S, m = 0, n = 3).

Prepared as **3** (Q = diallylamino, X = S, m = 0, n = 3) starting from 9.46 g (0.05 mole) of 5-amino-3-benzylamino-1*H*-1,2,4-triazole **1** (Q = benzylamino) [14]; the yield was 13.3 g (85%) of crude product that was dissolved in 75 ml of hot dimethylformamide, a solution of 20 ml of 10% sodium hydroxide was added to the still hot solution and let to crystallise. After cooling the sodium salt of 7,8-dihydro-2-benzylamino-9*H*,10*H*-thiopyrano-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = benzylamino, X = S, m = 0, n = 3) that crystallised as hemihydrite was filtered off (14.9 g, 82%, mp >360°), dissolved in 200 ml of hot water and the solution obtained acidified with acetic acid. The crystals precipitated were filtered off, washed with water and 2-propanol to yield 12.4 g (79%) of pure 7,8-dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = benzylamino, X = S, m = 0, n = 3), mp 332-335°; ir: ν C=O = 1665 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.05 (m, 2H, CH_2-8), 2.70 (t, 2H, CH_2-9), 2.93 (dt, 2H, CH_2-7), 4.22 (d, 2H, $NHCH_2$), 7.20 (t, 1H, NH-exo), 7.25-7.4 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 21.9 (CH_2-8), 25.2 (CH_2-9), 26.1 (CH_2-7), 45.7 (NCH_2), 103.4 (C-5a), 126.4, 127.0, 128.0 and 140.2 (Ph), 140.5 (C-9a), 148.8 (C-10a), 152.9 (C=O), 163.5 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 251 (30.1), 304 (8.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 246 (28.7), 300 (6.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 241 (42.0), 268 sh (14.2), 312 (9.2).

Anal. Calcd. for $C_{15}H_{15}N_5OS$ (MW 313.39): C, 57.49; H, 4.82; N, 22.35; S, 10.23. Found: C, 57.44; H, 5.01; N, 22.46; S, 9.98.

7,8-Dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = benzylamino, X = S, m = 0, n = 3) Na Salt Hemihydrate.

Compound **3** (Q = benzylamino, X = S, m = 0, n = 3) (4.13 g) was dissolved at 90° in the mixture of 5 ml of 10% sodium hydroxide and 20 ml of dimethylformamide. The yellow solution obtained crystallised upon cooling. The crystals precipitated were filtered off and washed with 2 ml of water to yield 4.2 g (88%) of the corresponding sodium salt hemihydrate (MW 363.40), mp >360°.

10-Benzyl-7,8-dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = benzylamino, X = S, m = 0, n = 3).

The mixture of 3.63 g (0.01 mole) of 7,8-dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5-one **3** (Q = benzylamino, X = S, m = 0, n = 3) Na Salt hemihydrate, 5 ml of dimethylformamide and 1.39 g (1.26 ml, 0.011 mole) of benzyl chloride was refluxed with stirring for 9 hours. After cooling the mixture was diluted with 30 ml of water, extracted three times with 50 ml portions of chloroform, the combined chloroform layers were extracted with 50 ml of water, dried over anhydrous sodium sulfate and evaporated to dryness to yield 2.6 g (64%) of10-benzyl-7,8-dihydro-2-benzylamino-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3/1** (Q = benzylamino, X = S, m = 0, n = 3) which after recrystallisation from acetonitrile melted at 273-275°; ir: ν C=O = 1658 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.00 (qi, 2H, CH_2-8), 2.67 (t, 2H, CH_2-9), 2.86 (t, 2H, CH_2-7), 4.39 (d, 2H, $NHCH_2$), 5.46 (s, 2H, NCH_2), 7.2-7.4 (m, 10H, ArH); cmr (DMSO-d_6): δ ppm 22.5 (CH_2-8), 24.5 (CH_2-9), 24.9 (CH_2-7), 45.7 ($NHCH_2$), 49.5 (NCH_2), 106.5 (C-5a), 126.2, 126.7, 127.3, 127.7, 128.2, 129.0, 135.7, 140.2 (2 x Ph), 140.6 (C-9a), 151.0 (C-10a), 152.4 (C=O), 163.6 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 254 (26.4), 310 (8.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 254 (27.3), 312 (6.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 260 (40.5), 312 (9.3).

Anal. Calcd. for $C_{22}H_{21}N_5OS$ (MW 403.51): C, 65.49; H, 5.25; N, 17.36; S, 7.95. Found: C, 65.33; H, 5.38; N, 17.30; S, 8.06.

7,8-Dihydro-2-(2-phenylethylamino)-9*H*,10*H*-thiopyrano[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one **3** (Q = 2-phenylethylamino, X = S, m = 0, n = 3).

Prepared as **3** (Q = diallylamino, X = S, m = 0, n = 3) starting from 10.16 g (0.05 mole) of 5-amino-3-(2-phenylethylamino)-1*H*-1,2,4-triazole **1** (Q = 2-phenylethylamino) [14]; the yield was 12.3 g (75%), mp 322-325° (after recrystallisation from dimethylformamide); ir: ν C=O = 1663 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.06 (qi, 2H, CH_2-8), 2.70 (t, 2H, CH_2-9), 2.90 (m, 4H, CH_2-7 and Ph-CH_2), 3.42 (q, 2H, $NHCH_2$), 6.72 (t, 1H, NH-exo), 7.2-7.4 (m, 5H, Ph); cmr (DMSO-d_6): δ ppm 21.9 (CH_2-8), 25.1 (CH_2-9), 26.0 (CH_2-7), 35.1 (CCH_2), 43.8 (NCH_2), 103.5 (C-5a), 125.8, 128.4, 128.5 and 139.6 (Ph), 140.3 (C-9a), 148.9 (C-10a), 152.9 (C=O), 163.1 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 252 (30.2), 306 (8.3);

uv (10% ethanol + 90% 0.1 *N*-hydrochloric acid): λ max nm (ϵ. 10^{-3}) 251 (30.2), 313 sh (8.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 242 (32.7), 270 sh (10.3), 314 (6.7).

Anal. Calcd. for $C_{16}H_{17}N_5OS$ (MW 327.41): C, 58.70; H, 5.23; N, 21.39; S, 9.79. Found: C, 58.86; H, 5.48; N, 21.50; S, 9.45.

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REFERENCES AND NOTES

[1] For Part **XXII**, see J. Reiter, L. Pongó and I. Pallagi, *J. Heterocyclic Chem.*, **27**, 1689 (1990).

[2] Different parts presented on the 10th international Congress of Heterocyclic Chemistry, Waterloo, Canada, 1985, see: Congress Abstracts p P5-135, on the 8th International IUPAC Conference on Organic Synthesis, Helsinki, Finland, 1990, see Congress Abstracts and on the 10th Symposium on the Chemistry of Heterocyclic Compounds, Košice, Czechoslovakia, 1990, see: Congress Abstracts, see also Hungarian Patent Appl. No 1016189, Appl: March 3, 1989.

[3] K. Esses-Reiter ad J. Reiter, *J. Heterocyclic Chem.*, **24**, 1503 (1987).

[4] J. Reiter and L. Pongó, *Org. Prep. Proced. Int.*, **20**, 465 (1988).

[5] J. Reiter and E. Rivó, *J. Heterocyclic Chem.*, **25**, 1497 (1988).

[6] J. Reiter and E. Rivó, *J. Heterocyclic Chem.*, **26**, 971 (1989).

[7] J. Reiter, L. Pongó and P. Dvortsák, *Tetrahedron*, **43**, 2497 (1987).

[8] G. M. Bennett and L. V. D. Scorah, *J. Chem. Soc.*, 194 (1927).

[9] N. J. Leonard and J. Figueras, Jr., *J. Am. Chem. Soc.*, **74**, 917 (1952).

[10] E. A. Fehnel, *J. Am. Chem. Soc.*, **74**, 1569 (1952).

[11] During having this paper is press M. T. Wu and coworkers published a paper [12] describing the reaction of 5-amino-1*H*-1,2,4-triazole **1** (Q = H) with ethyl tetrahydrothiopyran-3-one-2-carboxylate **2** (X = X, m = O, n = 3) in ethanol. Authors stated that only one detectable product was formed that was isolated tlc pure in 56% yield. The name of product was given incorrectly as 5,6-dihydro-9-hydroxy-7*H*-thiopyrano[3,2-*d*][1,2,4]triazolo[2,3,-*a*]pyrimidine although on the corresponding Scheme structure **3** (Q = H, X = S, m = O, n = 3) was assigned to it.

[12] M. T. Wu, M. MacCoss, T. J. Ikeler, J. Hirshfield, B. H. Arison and R. L. Tolman, *J. Heterocyclic Chem.*, **27**, 1559 (1990).

[13] J. Reiter, T. Somorai, Gy. Jerkovich and P. Dvortsák, *J. Heterocyclic Chem.*, **19**, 1157 (1982).

[14] J. Reiter, T. Somorai, P. Dvortsák and Gy. Bujtás, *J. Heterocyclic Chem.*, **22**, 385 (1985).