On Triazoles. X [1]. The Reaction of 5-Amino-1,2,4-triazoles with Tetrahydrothiophene β-Keto Esters [2]

Klára Esses-Reiter and József Reiter*

EGIS Pharmaceuticals, H-1475 Budapest, P. O. Box 100, Hungary

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Three novel ring systems, namely the thieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine, the thieno[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidine and the thieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine were synthesised. The structure of compounds obtained was proved with the help of their uv and cmr spectra using model compounds prepared for this purpose.

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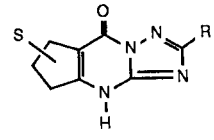
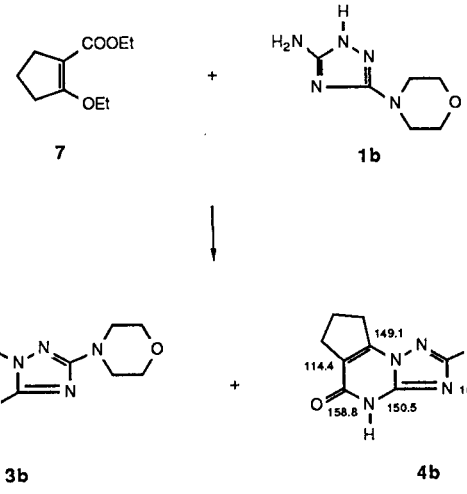
The reaction of 5-amino-1*H*-1,2,4-triazole (**1**, R = H) with ethyl 2-ketocyclopentanecarboxylate (**2**) to give 6,7,8,9-tetrahydrocyclopenta[1,2-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidine-5-one (**3**, R = H) (Scheme 1) is known from the literature [3]. However this reaction may - in principal - lead to any of the products **3-6** (R = H). Nevertheless the above authors gave no physico-chemical data of the product obtained nor any proof of its structure. As we wanted to use these derivatives as model compounds during the structure-elucidation of the planned novel **I** type condensed-ring derivatives (Scheme 2) we decided to repeat the above reaction with 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) and 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) and to prove the structure of the products obtained unambiguously.

In this reaction in case of R = methylthio besides the main product **3a** a small amount of **4a** was also formed which was also isolated. On the other hand in case of R = morpholino the sole product of the reaction that could be isolated was **3b**. The analogous **4b** was obtained as the by-product of the reaction of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) with ethyl 2-ethoxycyclopent-1-enecarboxylate (**7**) [8] (Scheme 3). The ir and pmr spectra of the above products (see Experimental) were in agreement with their proposed structures **3a-4b** but were not characteristic for any of them. On the other hand the uv (Scheme 5) and cmr (Schemes 1 and 3) spectra of derivatives **3a**, **3b**, **4a** and **4b** were fully analogous with those of

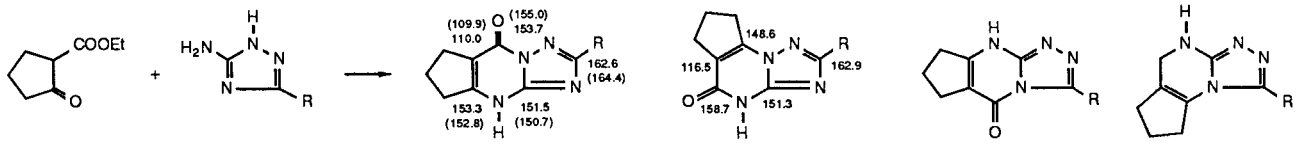
Scheme 2



Scheme 3



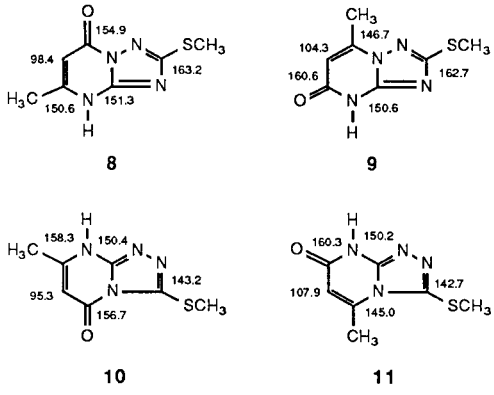
Scheme 1



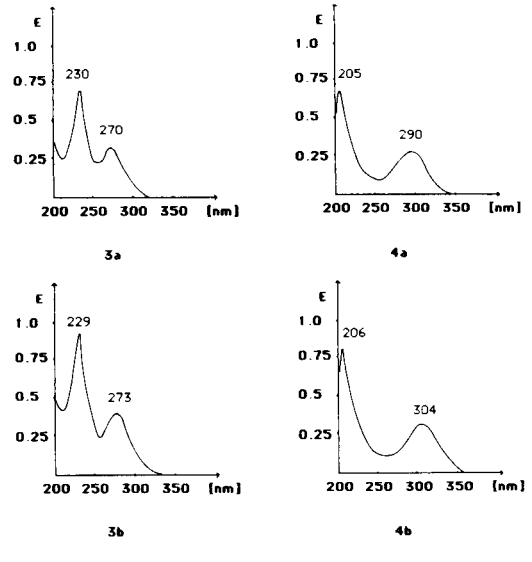
2 **1a**, R = methylthio; **1b**, R = morpholino **3a**, R = methylthio; **3b**, R = morpholino **4a**, R = methylthio **5** **6**

the analogues **8** and **9**, respectively, and differed significantly from those of **10** and **11** (Schemes 4 and 6), derivatives of previously proved structure [4] giving an unequivocal proof of their isomeric and tautomeric structure. Reacting methyl 4-oxotetrahydrothiophene-3-carboxylate (**12**), synthesised by Dieckmann condensation [5] of methyl 3-[3'-(methoxycarbonylmethyl)thio]propionate with 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1a**) a mixture of a main product **13a** and a small amount of **14a** (Scheme 7) was obtained which were separated. Repeating the above reaction with 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1b**) the formation of only one product **13a** was again observed.

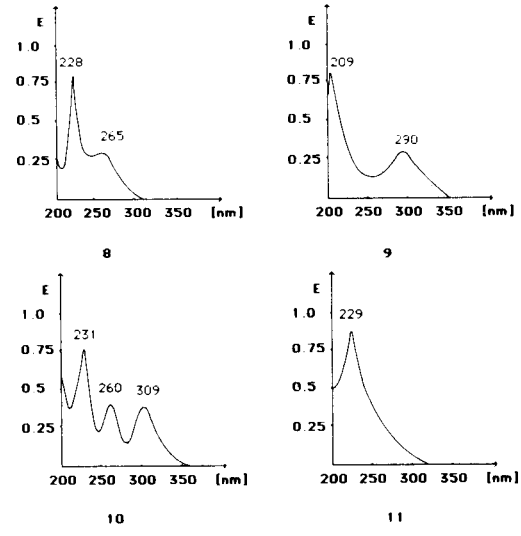
Scheme 4



Again the ir and pmr data of the products were in accordance with the proposed structures **13a**, **13b** and **14a**, respectively, but were again not characteristic for any of them. Fortunately their uv (Scheme 8) and cmr (Scheme 7) spectra were fully analogous with those of derivatives **3a** and **4a**, respectively (Scheme 1 and 5), helping to prove unequivocally the structure of these derivatives, too.

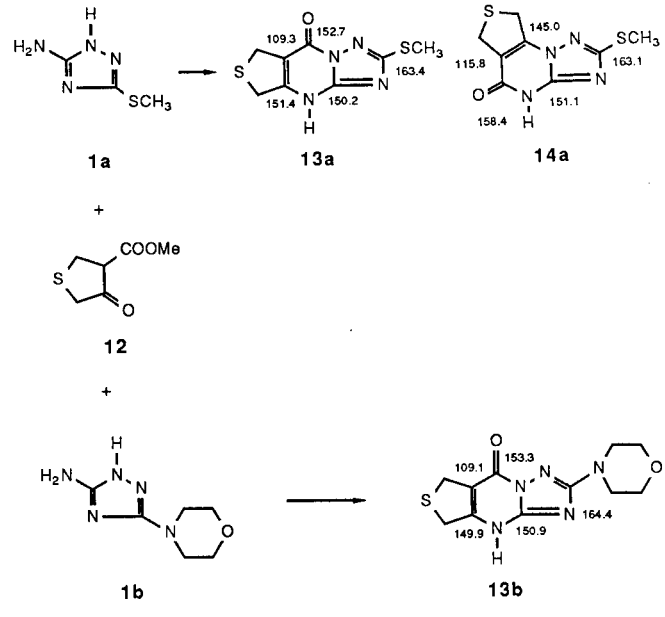


Scheme 5



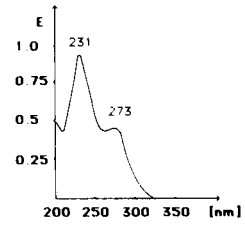
Scheme 6

Scheme 7

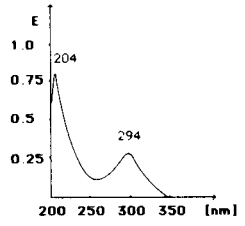


Derivatives **13a-b** and **14a** are the first representatives of two new condensed ring systems, namely the thieno-[3,4-*b*]-1,2,4-triazolo[1,5-*a*]pyrimidine and the thieno[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidine ring systems [6].

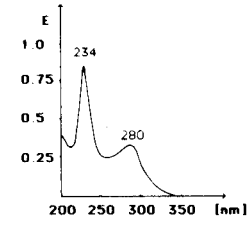
To prove its tautomeric structure derivative **13a** was *N*-methylated to yield **15a** (Scheme 9). The position of the methyl group in **15a** was proved unequivocally with the help of the proton coupled cmr spectra on the basis of the β-coupling causing a change of the multiplicity of the quaternary carbon atoms 8a and 9a. As the uv spectrum of **15a** (Scheme 10) is fully analogous with that of **13a** (Scheme 8)



13a

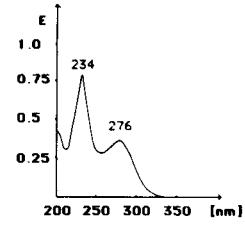


14a

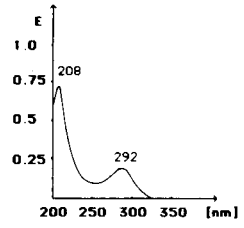


13b

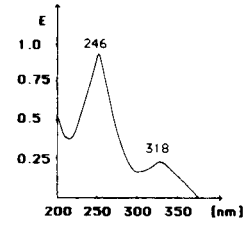
Scheme 8



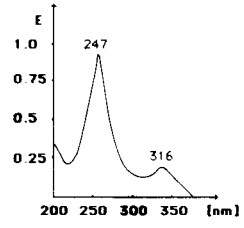
15a



17a



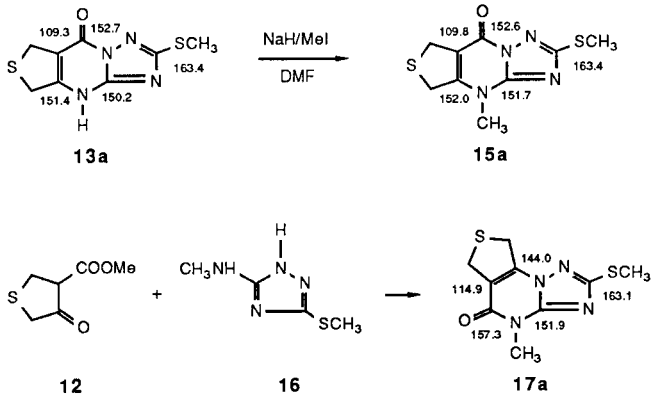
19a



20a

Scheme 10

Scheme 9

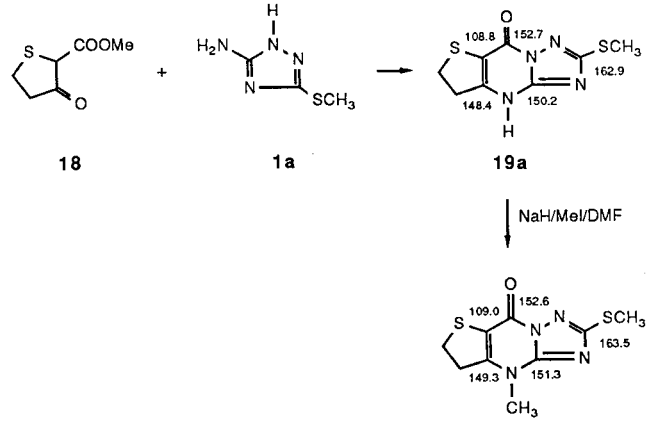


13a 15a

it has to have 9*H*-tautomeric structure. As the uv spectrum of **13b** (Scheme 8) is also analogous to that of **13a** (Scheme 8) and **15a** (Scheme 10) it has to have also the 9*H*-tautomeric structure. The tautomeric structure of **14a** was proved by the analogy of its uv spectra (Scheme 8) with that of **17a** (Scheme 10) prepared as a model compound from methyl 4-oxotetrahydrothiophene-3-carboxylate (**12**) and 5-methylamino-3-methylthio-1*H*-1,2,4-triazole (**16**) (Scheme 9).

Reacting the mother liquor of **12** containing methyl 3-oxotetrahydrothiophene-2-carboxylate (**18**) as the by-product of the Dieckmann condensation [5] with 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1a**) a 2:1 mixture (proved by pmr, see Experimental) of **13a** and **19a** was obtained which could not be separated. However the presence of **19a** containing again a novel ring system, namely the thieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine ring system, could be easily detected by the cmr spectra (Scheme 11) extracting the signals corresponding to **13a** as well as by differential uv spectra (Scheme 10) using instead of solvent the solution of **13a** in a proper concentration as reference.

Scheme 11



The tautomeric structure of **19a** was again proved by its methylation to obtain a 4:1 mixture (proved by pmr, see Experimental) of **15a** and **20a** that could be again not separated but using the differential methods described above the uv and cmr spectra of **20a** could be well detected. The analogy of the uv spectra of **19a** and **20a** (Scheme 10) gives again an unequivocal proof for the tautomeric structure of **19a**.

It should be mentioned that the uv spectra of derivatives containing the 7,8-dihydrothieno[3,2-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidine-5(9*H*)-one ring (**19a** and **20a**) suffered a

batochromic shift as compared with those of the analogous derivatives **13a** and **15a** containing the 6,8-dihydrothieno-[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidine-5(9*H*)-one ring (Schemes 8 and 10). This fact can be well explained by taking into account the loan electron pair of the sulfur atom which is in case of **19a** and **20a** conjugated with the chromophore present in the molecule.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using a 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.

2-Methylthio-6,7,8,9-tetrahydrocyclopenta[1,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one (**3a**) and 2-Methylthio-5,6,7,9-tetrahydrocyclopenta[1,2-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-8-one (**4a**).

To the solution of 13.0 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1a**) [7] in 40 ml of acetic acid 15.6 g (0.1 mole) of ethyl 2-ketocyclopentane carboxylate (**2**) was added and refluxed for 1/4 hour. After 2-3 minutes the refluxing solution began to crystallise. The crystals which precipitated were filtered off while still hot to yield 12.4 g (56%) of 2-methylthio-6,7,8,9-tetrahydrocyclopenta[1,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one (**3a**), mp 315-317°. The mother liquor was refluxed for further 2 hours to yield after cooling a further crop of **3a**, mp 314-317°; ir: ν C=O = 1691 cm^{-1}; pmr (DMSO-d$_6$): δ, ppm 2.09 (qi, 2H, CH$_2^7$), 2.58 (s, 3H, SCH$_3$), 2.66 (t, 2H, CH$_2^8$), 2.90 (t, 2H, CH$_2^6$), 13.3 (b, 1H, NH); cmr (DMSO-d$_6$): δ ppm 13.3 (SCH$_3$), 21.4 (CH$_2^7$), 26.6 (CH$_2^8$), 31.1 (CH$_2^6$), 110.0 (C^{5a}), 151.5 (C^{9a}), 153.3 (C^{8a}), 153.7 (C=O), 162.6 (C^2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 230 (25.3), 270 (12.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ.10^{-3}) 228 (28.2), 270 (13.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ.10^{-3}) 227 (28.2), 282 (11.1).

Anal. Calcd. for $C_9H_{10}N_4OS$ (MW. 222.27): C, 48.63; H, 4.54; N, 25.21; S, 14.43. Found: C, 48.78; H, 4.66; N, 25.32; S, 14.18.

The mother liquor of **3a** was diluted with 300 ml of water and extracted three times with 100 ml portions of benzene. The benzene layers were collected, dried over anhydrous sodium sulfate and evaporated to dryness to yield 1.6 g (7%) of 2-methylthio-5,6,7,9-tetrahydrocyclopenta-[1,2-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-8-one (**4a**), which after recrystallization from dimethylformamide melted at 283-285°; ir: ν C=O 1650 cm^{-1}; pmr (DMSO-d$_6$): δ ppm 2.13 (qi, 2H, CH$_2^6$), 2.56 (s, 3H, SCH$_3$), 2.68 (t, 2H, CH$_2^5$), 3.10 (t, 2H, CH$_2^7$), 12.9 (bs, 1H, NH); cmr (DMSO-d$_6$): δ, ppm 13.3 (SCH$_3$), 20.9 (CH$_2^6$), 27.7 (CH$_2^5$), 29.7 (CH$_2^7$), 116.5 (C^{7a}), 148.6 (C^{4a}), 151.3 (C^{9a}), 158.7 (C=O), 162.9 (C^2); uv (ethanol): λ max nm (ϵ.10^{-3}) 205 (29.0), 290 (11.1); uv (10% ethanol + 90% hydrochloric acid): λ max nm (ϵ.10^{-3}) 205 (29.7), 290 (12.3); uv (10% ethanol + 90% sodium hydroxide): λ max nm (ϵ.10^{-3}) 285 (9.2).

Anal. Calcd. for $C_9H_{10}N_4OS$ (MW.222.27): C, 48.63; H, 4.54; N, 25.21; S, 14.43. Found: C, 48.62; H, 4.76; N, 25.11; S, 14.48.

2-Morpholino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5-one (**3b**).

To the solution of 16.9 g (0.1 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1b**) [7] in 40 ml of acetic acid 15.6 g (0.1 mole) of ethyl 2-ketocyclopentanecarboxylate (**2**) was added and refluxed with stirring for 1/2 hour. After 15 minutes the refluxing solution began to cystallize. The crystals precipitated were filtered off while hot to yield 13.0 g (50%) of the title product, mp >350°. The mother liquor was refluxed for further 2 hours to yield after cooling a further 7.9 g (30%) crop of **3b**, mp >350°; ir: ν C=O = 1653 cm^{-1}; pmr (DMSO-d$_6$): δ, ppm 2.06 (qi, 2H, CH$_2^7$), 2.65 (t, 2H, CH$_2^8$), 2.85 (t, 2H, CH$_2^6$), 3.38 (t, 4H, NCH$_2$), 3.69 (t, 4H, OCH$_2$), 12.9 (bs, 1H, NH); cmr (DMSO-d$_6$): δ ppm 21.4 (CH$_2^7$), 26.7 (CH$_2^6$), 31.0 (CH$_2^8$), 45.8 (NCH$_2$), 65.4 (OCH$_2$), 109.9 (C^{5a}), 150.7 (C^{8a}), 152.8 (C^{9a}), 155.0 (C=O), 164.2 (C^2); uv (ethanol): λ max nm (ϵ.10^{-3}) 229 (28.6), 273 (12.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ.10^{-3}) 228 (29.0), 274 (13.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ.10^{-3}) 229 (35.8), 282 (9.9).

Anal. Calcd. for $C_{12}H_{15}N_5O_2$ (MW. 261.28): C, 55.16; H, 5.79; N, 26.81. Found: C, 55.32; H, 5.86; N, 26.67.

2-Morpholino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5-one (**3b**) and 2-Morpholino-5,6,7,9-tetrahydrocyclopenta-[1,2-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-8-one (**4b**).

The mixture of 6.76 g (0.04 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1b**) [7] and 7.36 g (0.04 mole) of ethyl 2-ethoxycyclopent-1-enecarboxylate [8] was refluxed for 15 minutes. The reaction mixture crystallised after about 5 minutes while hot. To the still hot reaction mixture 10 ml of ethanol was added, and the crystals precipitated were filtered off to yield 6.2 g (59%) of the mixture of **3b** and **4b**. This was dissolved in 40 ml of hot 5% sodium hydroxide solution in ethanol and allowed to crystallise. The crystals precipitated were filtered off to yield 4.1 g of the sodium salt of **3b**, mp >350°. The mother liquor was evaporated to dryness, the residue was dissolved in 20 ml of water (charcoal), filtered and acidified with acetic acid to *p*H = 4. The crystals precipitated after standing were filtered off and recrystallised from dimethylformamide to yield 0.89 g of **4b**, mp 241-243°; ir: ν C=O = 1690 cm^{-1}; pmr (DMSO-d$_6$): δ ppm 2.10 (qi, 2H, CH$_2^6$), 2.65 (t, 2H, CH$_2^5$), 3.03 (t, 2H, CH$_2^7$), 3.33 (t, 4H, NCH$_2$), 3.67 (t, 4H, OCH$_2$), 12.6 (bs, 1H, NH); cmr (DMSO-d$_6$): δ ppm 21.1 (CH$_2^6$), 27.7 (CH$_2^5$), 29.9 (CH$_2^7$), 45.9 (NCH$_2$), 65.5 (OCH$_2$), 114.4 (C^{7a}), 149.1 (C^{4a}), 150.5 (C^{8a}), 158.8 (C=O), 165.2 (C^2); uv (ethanol): λ max nm (ϵ.10^{-3}) 206 (25.1), 304 (10.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ.10^{-3}) 203 (27.8), 302 (10.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ.10^{-3}) 221 (26.1), 290 (8.7).

Anal. Calcd. for $C_{12}H_{15}N_5O_2$ (MW. 261.28): C, 55.16; H, 5.79; N, 26.81. Found: C, 55.22; H, 5.97; N, 26.76.

2-Methylthio-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**13a**) and 2-Methylthio-5,7-dihydrothieno[3,4-*e*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-8(9*H*)-one (**14a**).

The mixture of 8.0 g (0.05 mole) of methyl 4-ketotetrahydrothiophene-3-carboxylate (**12**) [5], 6.5 g (0.05 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1a**) [7] and 5 ml of acetic acid was refluxed with stirring for 15 minutes. The crystals of **1a** were dissolved during the first two minutes of heating and the solution crystallised after 10 minutes while hot. To the still hot reaction mixture 15 ml of 2-propanol was added and the crystals were immediately filtered off to yield 8.65 g (72%) of 2-methylthio-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**13a**), which after recrystallisation from dimethylformamide melted at >350°; ir: ν C=O = 1663 cm^{-1}; pmr (DMSO-d$_6$): δ, ppm 2.61 (s, 3H, SCH$_3$), 4.00 (t, 2H, SCH$_2^8$), 4.25 (t, 2H, SCH$_2^6$), 13.2 (b, 1H, NH); cmr (DMSO-d$_6$): δ, ppm 13.4 (SCH$_3$), 32.0 (t, CH$_2^8$), 35.3, (t, CH$_2^6$), 109.3 (tt, C^{5a}), 150.2 (s, C^{9a}), 151.4 (tt, C^{8a}), 152.7 (d, C=O), 163.4 (qa, C^2); uv (ethanol): λ max (ϵ.10^{-3}) 231 (25.1), 273 (9.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ.10^{-3}) 230 (23.4), 268 (10.9), uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ.10^{-3}) 234 (28.4), 284 (9.5).

Anal. Calcd. for $C_8H_8N_4OS_2$ (MW. 240.31): C, 39.98; H, 3.36; N, 23.32; S, 26.69. Found: C, 40.07; H, 3.54; N, 23.21; S, 26.53.

The mother liquor (containing the 2-propanol washings) crystallised upon standing to yield 1.3 g (11%) of 2-methylthio-5,7-dihydrothieno-[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-8(9*H*)-one (**14a**), which after recrystallisation from dimethylformamide melted at 308-310°; ir: ν C=O = 1663 cm^{-3}; pmr (DMSO-d$_6$): δ, ppm 2.60 (s, 3H, SCH$_3$), 4.05 (t, 2H, CH$_2^5$), 4.49 (t, 2H, CH$_2^7$); cmr (DMSO-d$_6$): δ, ppm 13.5 (SCH$_3$), 36.4 (CH$_2^5$), 37.5 (CH$_2^7$), 115.8 (C^{7a}), 145.0 (C^{4a}), 151.1 (C^{9a}), 158.4 (C=O), 163.1 (C^2); uv (ethanol): λ max nm (ϵ.10^{-3}) 204 (31.3), 294 (11.6); uv: (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ.10^{-3}) 204 (32.0), 294 (11.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ.10^{-3}) 221 (46.3), 288 (10.7).

Anal. Calcd. for $C_8H_8N_4OS_2$ (MW. 240.31): C, 39.98; H, 3.36; N, 23.32; S, 26.69. Found: C, 38.87; H, 3.41; N, 23.36; S, 26.61.

2-Morpholino-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**13b**).

The mixture of 16.0 g (0.1 mole) of methyl 4-ketotetrahydrothiophene-3-carboxylate (**12**) [5], 16.9 g (0.1 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1b**) [7] and 15 ml of acetic acid was refluxed with stirring for 15 minutes. The crystals of **1b** were dissolved in the hot reaction mixture within 1-2 minutes and the refluxing solution began to crystallise after about 5 minutes. The still hot reaction mixture was diluted with 30 ml of 2-propanol and the crystals precipitated filtered off while hot to yield 18.4 g (66%) of the title product, mp >350°. The product was dissolved in 200 ml of hot 1 *N* sodium hydroxide and allowed to crystallise. After cooling the crystals were filtered off, washed with 2-propanol and dried to yield 17.5 g of the sodium salt of **13b**, mp >350°. The sodium salt was dissolved in 400 ml of warm water and acidified still warm with 5 ml of acetic acid to yield 15.1 g of pure **13b**, mp >350°; ir: ν C=O = 1655 cm^{-1}; pmr (DMSO-d_6): δ, ppm 3.41 (t, 4H, NCH_2), 3.71 (t, 4H, OCH_2), 3.97 (t, 2H, SCH_2^8), 4.22 (t, 2H, SCH_2^6); cmr (DMSO-d_6): δ, ppm 32.2 (C^6), 35.5 (C^8), 45.7 (NCH_2), 65.5 (OCH_2), 109.1 (t, C^{5a}), 149.9 (t, C^{8a}), 150.9 (s, C^{9a}), 153.3 (s, C=O), 164.4 (m, C^2); uv (methanol): λ max nm ($\epsilon.10^{-3}$) 234 (24.8), 280 (6.4); uv (10% methanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 229 (22.3), 276 (9.6); uv (10% methanol + 90% sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 230 (27.6), 284 (7.9).

Anal. Calcd. for $C_{11}H_{13}N_5O_2S$ (MW. 279.32): C, 47.30; H, 4.69; N, 25.08; S, 11.48. Found: C, 47.51; H, 4.77; N, 24.89; S, 11.42.

2-Methylthio-9-methyl-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**15a**).

To the suspension of 1.20 g (0.005 mole) of 2-methylthio-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**13a**) in 100 ml of dry dimethylformamide 0.25 g (0.0083 mole) of 80% sodium hydride suspension in toluene was added in one portion. To the solution obtained after the hydrogen evolution 1.6 g (0.7 ml = 0.011 mole) of methyl iodide was added by dropping it to the reaction mixture at room temperature. The reaction was completed by stirring it at 40° for 1 hour. After cooling to the room temperature 100 ml of water was added to the reaction mixture and let to crystallise. The crystals precipitated overnight were filtered off to yield 0.65 g (47%) of the title product, which after recrystallisation from the mixture of 2-propanol and dimethylformamide melted at 273-275°; ir: ν C=O = 1686 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.63 (s, 1H, SCH_3), 3.74 (s, 3H, NCH_3), 4.08 (t, 2H, SCH_2^8), 4.48 (t, 2H, SCH_2^6); cmr (DMSO-d_6): δ, ppm 13.3 (SCH_3), 32.5 (SCH_2^8), 35.0 (NCH_3), 35.3 (SCH_2^6), 109.8 (t, C^{5a}), 151.7 (qa, C^{9a}), 152.0 (m, C^{8a}), 152.6 (s, C=O), 163.4 (qa, C^2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 234 (26.1), 276 (10.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 234 (25.5), 274 (11.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 234 (16.3), 274 (8.4).

Anal. Calcd. for $C_9H_{10}N_4OS_2$ (MW. 254.33): C, 42.50; H, 3.96; N, 22.03; S, 25.22. Found: C, 42.57; H, 4.03; N, 21.89; S, 25.09.

2-Methylthio-9-methyl-5,7-dihydrothieno[3,4-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-8(9*H*)-one (**17a**).

The mixture of 0.56 g (0.004 mole) of 5-methylamino-3-methylthio-1*H*-1,2,4-triazole (**16**) [8] and 0.96 g (0.006 mole) of methyl 4-oxotetrahydrothiophene-3-carboxylate (**12**) [5] was heated to 160° for 5 minutes. The melt obtained crystallised after the addition of 5 ml of ethanol to the hot reaction mixture. After cooling the crystals precipitated were filtered off and recrystallised from dimethylformamide to yield 0.95 g (93%) of the title *product*, mp 176-178°; ir: ν C=O = 1655 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.59 (s, 3H, SCH_3), 3.48 (s, 3H, NCH_3), 4.03 (t, 2H, SCH_2^5), 4.47 (t, 2H, SCH_2^7); cmr (DMSO-d_6): δ, ppm 13.3 (SCH_3), 29.7 (SCH_2^5), 33.6 (SCH_2^7), 34.1 (NCH_3), 114.9 (C^{7a}), 144.0 (C^{4a}), 151.9 (C^{9a}), 157.3 (C=O), 163.1 (C_2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 208 (26.1), 292 (8.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 206 (33.0), 289 (9.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 288 (8.8).

Anal. Calcd. for $C_9H_{10}N_4OS_2$ (MW. 254.33): C, 42.50: H, 3.96; N, 22.03; S, 25.22. Found: C, 42.39; H, 4.02; N, 22.14; S, 25.06.

2-Methylthio-7,8-dihydrothieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**19a**).

The mixture of 22 g (~0.17 mole) of the evaporated mother liquor of the recrystallisation of methyl 4-ketotetrahydrothiophene-3-carboxylate (**12**) [5] containing besides **12** the isomeric methyl 3-ketotetrahydrothiophene-2-carboxylate (**18**), 30.1 g (0.17 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1a**) [7] and 150 ml of acetic acid was refluxed for 3 hours. After cooling the crystals precipitated were filtered off to yield 14.5 g (35%) of the 1:2 mixture of the title product and the isomeric 2-methylthio-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**13a**), mp 308-318°. The product was dissolved in 240 ml of hot 1*N* sodium hydroxide solution to yield after cooling 16.1 g of the mixture of the sodium salts of **13a** and **19a** melting at 230-247°. The above mixture (0.5 g) of sodium salts was dissolved in 15 ml of water and acidified with acetic acid to *p*H = 4 to yield 0.35 g of the *product* melting at 310-316°; ir: ν C=O = 1663 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.61 (s, SCH_3**13a**), 2.62 (s, SCH_3**19a**), 3.4 (m, CH_2CH_2**19a**), 4.00 (t, SCH_2**8,13a**), 4.25 (t, SCH_2**6,13a**), The ratio of intensities of signals at δ 2.61 and δ 2.62 was 2:1; cmr (DMSO-d_6): **19a** signals only δ, ppm 13.4 (SCH_3), 29.2 (CH_2^8), 34.9 (CH_2^7), 108.8 (C^{5a}), 148.4 (C^{8a}), 150.9 (C^{9a}), 152.7 (C=O), 162.9 (C^2); uv (ethanol-differential): λ max nm 246 and 318 (The ratio of intensities ~3:1).

Anal. Calcd. for $C_8H_8N_4OS_2$ (MW. 240.31): C, 39.98; H, 3.36; S, 26.69. Found: C, 40.21; H, 3.55; S, 26.51.

2-Methylthio-9-methyl-7,8-dihydrothieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**20a**).

To the solution of 1.31 g (0.005 mole) of the mixture of sodium salts of 2-methylthio-7,8-dihydrothieno[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**19a**) and 2-methylthio-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-5(9*H*)-one (**13a**) in 10 ml of dry dimethylformamide 1.41 g (0.63 ml = 0.01 mole) of methyl iodide was added in one portion with stirring. The reaction mixture turned within 1-2 minutes yellow and began to crystalise. After 30 minutes of stirring at room temperature the crystals were filtered off to yield 0.73 g (57%) of the product, which melted after recrystallisation from dimethylformamide at 257-265°. The product is a 1:5 mixture of 2-methylthio-9-methyl-7,8-dihydrothieno-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**20a**) and 2-methylthio-9-methyl-6,8-dihydrothieno[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one (**15a**); ir: ν C=O = 1684 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.62 (s, SCH_3**20a**), 2.63 (s, SCH_3**15a**), 3.49 (t, CH_2**20a**), 3.54 (t, SCH_2**20a**), 3.72 (s, NCH_3**20a**), 3.74 (s, NCH_3**15a**), 4.08 (t, SCH_2**15a**), 4.48 (t, SCH_2**15a**), The ratio of intensities of the signals at δ 2.62 and δ 2.63 as well as at δ 3.72 and δ 3.74 was 1:4; cmr (DMSO-d_6): **20a** signals only δ, ppm 13.2 (SCH_3), 28.3 (CH_2^8), 35.0 (SCH_2), 109.9 (t, C^{5a}), 149.3 (m, C^{8a}), 151.3 (qa, C^{9a}), 152.6 (s, C=O), 163.5 (qa, C^2); uv (ethanol-differential): λ max nm 247 and 316. The ratio of intensities ~3:1.

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[6] US. Patent 2,444,607 (see ref [3]) claims the synthesis of a compound having the **19** type ring system, namely the 7,8-dihydrothieno-[3,2-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(9*H*)-one describing it in the Patent Specification by its structural formula but giving neither the physical data, nor method for its preparation, nor any proof that the structure proposed for it is correct. Consequently this reference was neglected.

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