On Triazoles. XVII [1]. The Reaction of 5-Amino-1,2,4-Triazoles with *N*-Heterocyclic β-Oxo-esters

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Received March 7, 1988

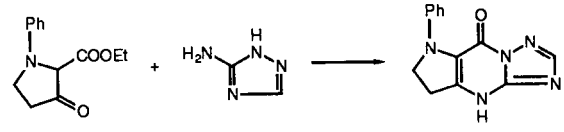
Pyrrolo[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidinone (**3d**), pyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidinone (**3e**) and pyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidinone (**4e**) derivatives representing three new ring systems were synthesised. Their structure was proved by comparing their uv and cmr spectra with those of the known benzo- and thieno-1,2,4-triazolo[1,5-*a*]pyrimidinones used as model compounds.

J. Heterocyclic Chem., **25**, 1497 (1988).

In the previous papers of this series [2,3] we have studied the reaction of 5-amino-3-R-1*H*-1,2,4-triazoles **1** with different homocyclic [**2a** (Y = CH_2) and **2b** (Y = CH_2CH_2)] and heterocyclic [**2c** (Y = S)] β-oxo-esters containing a sulphur heteroatom (Scheme 1) to yield the mixture of derivatives **3a** (Y = CH_2) and **4a** (Y = CH_2), **3b** (Y = CH_2CH_2) and **4b** (Y = CH_2CH_2) and **3c** (Y = S) and **4c** (Y = S), respectively. The structure of products obtained was unambiguously proved by comparing their uv and cmr spectra with the four possible bicyclic **3-6** type triazolopyrimidinones [4] of known structure. It should be mentioned that during these reactions the formation of the **5a-c** and **6a-c** type tricyclic derivatives was not observed. In hope to change the sulphur atom of the thiophene ring of **3c** or **4c** to a nitrogen one the reaction of **1** (R = methylthio and morpholino) was repeated with ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**, Y = N-Ph) to yield derivatives **3d** (Y = N-Ph, R = methylthio and morpholino) representing a novel ring system.

It should be mentioned that an analogous reaction of the isomeric ethyl 1-phenyl-3-oxo-2-pyrrolidinecarboxylate (**7**) with 3-amino-2*H*-1,2,4-triazole (**1**, R = H) to yield a tricyclic derivative **8** was reported previously [5,6] (Scheme 2). However the above authors gave neither spectroscopic nor physico-chemical data for the starting materials, and to the products obtained. As the ethyl 1-phenyl-3-oxo-2-pyrrolidinecarboxylate (**7**) used as starting material of the above reaction was prepared by the Dieckman condensation of diethyl *N*-phenyl-3-azaadipate (**9**) [7,8] in which reaction both the ethyl 1-phenyl-3-oxo-2-pyrrolidinecarboxylate (**7**) and the corresponding ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**, Y = *N*-Ph) could be formed (Scheme 3) and the above authors gave no proof of the structure of the product obtained; its structure was highly ambiguous.

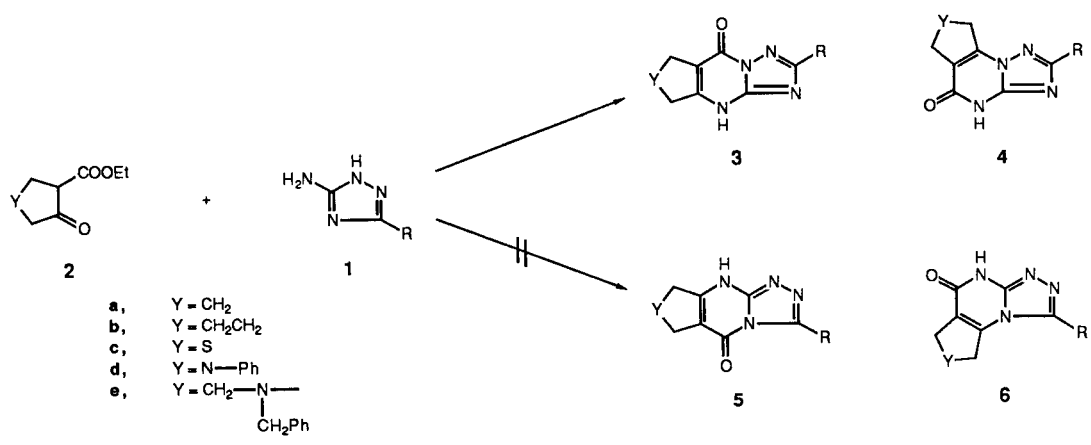
Scheme 2



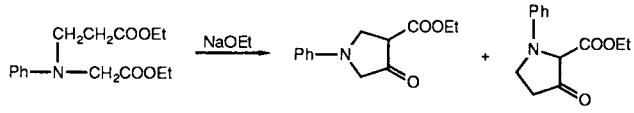
7 **1**, R = H **8**

We repeated the Dieckman condensation of the diethyl *N*-phenyl-3-azaadipate (**9**) (Scheme 3). The melting point

Scheme 1

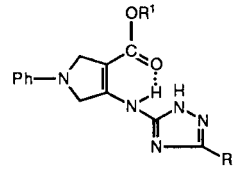


Scheme 3



9 2d 7

of the product obtained was identical with that of the product mentioned in the literature (69-70°, lit [7,8] mp 69-70°). Its ir, pmr and cmr spectra were consistent with the β-oxo-ester structure appearing completely in the enolate form (in DMSO-d_6 solution) stabilised by a six membered chelate system. However, it was not possible to decide unambiguously whether it corresponded to the structure **2d** (Y = *N*-Ph) or to the structure **7** as the observed symmetricity of the pyrrolidine CH_2 groups could be accidentally caused by the chelate system. The final decision between the structures **2d** (Y = *N*-Ph) and **7** was given by X-ray measurements [9] to prove structure **2d** (Y = *N*-Ph) of this derivative. The structure of products **3d** (Y = *N*-Ph, R = methylthio and morpholino) obtained above was proved on the basis of the analogy of their uv spectra with those of the known [2] **3a** (Y = CH_2, R = methylthio and morpholino) and **3c** (Y = S, R = methylthio and morpholino), respectively [uv (ethanol): λ max nm (ε.10^{-3}), **3d** (R = methylthio): 244 (24.8) and 283 (10.6), **3d** (R = morpholino): 247 (25.7) and 281 (9.7); **3a** (R = methylthio): 230 (25.3) and 270 (12.0), **3a** (R = morpholino): 229 (28.6) and 273 (12.1); **3c** (R = methylthio): 231 (25.1) and 273 (9.2), **3c** (R = morpholino): 234 (24.8) and 280 (6.4)] and that of the good agreement of the chemical shifts of their C-2 and carbonyl carbon atoms [**3d**, (R = methylthio): δ C-2 = 162.1 ppm, δ C=O = 155.7 ppm; **3d** (R = morpholino): δ C-2 = 166.0 ppm, δ C=O = 155.7 ppm] with the cmr rule [expected: δ C-2 ≈ 163 ppm, δ C=O ≈ 154 ppm] stated by us previously [4]. These data proved also unambiguously the tautomeric structure of derivatives **3d** (Y = *N*-Ph, R = methylthio and morpholino) [2-4]. The by-products of the above reactions provided in 1-butanol as solvent were the cyclic enamines **10a-b** (R^1 = *n*-butyl, R = methylthio and morpholino, respectively) formed by transesterification of the corresponding intermediates **10c-d** (R^1 = ethyl, R = methylthio and morpholino, respectively). The real intermediates **10c-d** (R^1 = ethyl, R = methylthio and morpholino, respectively) of the reactions of **2d** and **1** (R = methylthio and morpholino, respectively) were isolated from the reaction mixture of the reactions provided in dimethylformamide as solvent to give a nice proof of its supposed mechanism.



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Repeating the reaction of **1** (R = methylthio and morpholino, respectively) with ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride [**2e**.HCl, Y = $CH_2N(CH_2Ph)$] (Scheme 1) besides the corresponding derivatives **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] obtained as main products of the reactions the isomeric derivatives **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] were also isolated from the reaction mixtures both representing novel ring systems.

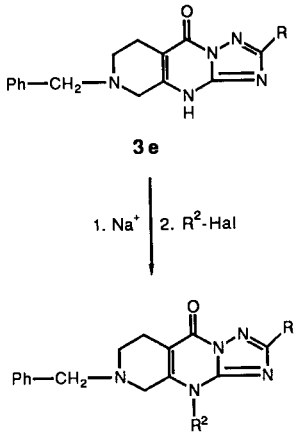
The uv spectra of **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] and **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] [uv (ethanol): λ max nm (ε.10^{-3}): **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio]: 232 (29.5) and 278 (8.8); **3e** [Y = $CH_2N(CH_2Ph)$, R = morpholino]: 232 (24.7) and 277 (7.5); **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio]: 204 (18.5) and 308 (8.6); **4e** (Y = $CH_2N(CH_2Ph)$, R = morpholino): 205 (19.0) and 310 (9.8)] were fully analogous with those of the known [3] **3b** (Y = CH_2CH_2, R = methylthio and morpholino, respectively) [uv (ethanol): λ max nm (ε.10^{-3}): **3b** (Y = CH_2CH_2, R = methylthio): 232 (28.2) and 274 (11.4); **3b** (Y = CH_2CH_2, R = morpholino): 227 (29.9) and 270 (12.1)] and **4b** (Y = CH_2CH_2, R = methylthio and morpholino, respectively) [uv (ethanol): λ max nm (ε.10^{-3}): **4b** (Y = CH_2CH_2, R = methylthio): 206 (27.1) and 292 (9.6); **4b** (Y = CH_2CH_2, R = morpholino): 205 (29.4) and 308 (10.2)] suggesting the structures shown on Scheme 1.

Their structure was finally proved again with the help of the cmr spectra in which the carbonyl groups of derivatives **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino] appeared at 154.1 and 155.1 ppm, respectively (expected [4] δ C=O ≈ 154 ppm), and those of derivatives **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino] appeared at 159.6 and 159.6 ppm, respectively (expected [4] δ C=O ≈ 160 ppm), while the C-2 carbon atoms appeared in **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino] at 163.0 and 164.1 ppm, respectively (expected [4] δ C-2 ≈ 163 ppm), and in **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino], appeared at 164.4 and 164.4 ppm, respectively (expected [4] δ C-2 ≈ 163 ppm), following perfectly the cmr rule stated previously [4].

The tautomeric structure of derivatives **3e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] and **4e** [Y = $CH_2N(CH_2Ph)$, R = methylthio and morpholino, respectively] was corroborated by the identity of their uv spectra with those of their *N*-alkylated deriva-

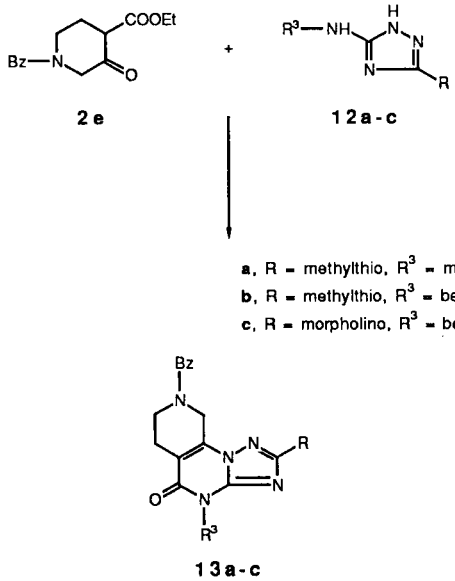
tives **11** (R^1 = alkyl, R = methylthio and morpholino, respectively) prepared by the direct alkylation of the corresponding derivatives **3e** (Scheme 4) where the position of the alkylation was proved with the help of their proton coupled cmr spectra and those of derivatives **13** (R = methylthio and morpholino) (Scheme 5) prepared by the reaction of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride **2e.HCl** [Y = $CH_2N(CH_2Ph)$] or its base with the corresponding 5-R^3-amino-3-R-1*H*-1,2,4-triazoles (**12**, R = methylthio and morpholino, R^3 = methyl and benzyl, respectively).

Scheme 4



a, R = methylthio
b, R = morpholino

Scheme 5



EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using Bruker IFS 113-V spectrophotomer. The ultraviolet spectra were obtained by a Pye Unicam SP 8-150 and a Perkin-Elmer 555 instrument. The pmr and the cmr measurements were performed using a Bruker WM-250 and Bruker WP-80 SY instruments. The X-ray measurements were performed using a Nicolet R 3 diffractometer.

7,8-Dihydro-2-methylthio-7-phenyl-6*H*-pyrrolo[3,4-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidine-5(9*H*)-one (**3d**, R = methylthio) and Butyl 1-Phenyl-4-(3-methylthio-1*H*-1,2,4-triazol-5-yl)imino-3-pyrrolidinecarboxylate (**10a**, R = methylthio, R^1 = butyl).

A mixture of 1.30 g (0.01 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) [9], 2.33 g (0.01 mole) of ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**) [8] and 10 ml of 1-butanol was refluxed for 5 hours. After cooling the crystals precipitated were filtered off and recrystallised by dissolving them in hot dimethylformamide and precipitating with acetonitrile to yield 1.35 g (45%) of **3d** (R = methylthio), mp 308-310°; ir: ν CO = 1666 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.53 (s, 3H, SCH_3), 4.20 (s, 2H, CH_2-8), 4.54 (s, 2H, CH_2-6), 6.7 (m, 3H, ArH), 7.25 (t, 2H, ArH), 9.65 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 13.0 (SCH_3), 49.7* (CH_2-6), 51.7* (CH_2-8), 110.7 (C-5a), 111.2 (*m*-C-Ph), 116.2 (*p*-C-Ph), 128.7 (*o*-C-Ph), 146.0 (s-C-Ph), 148.9 (C-8a), 151.4 (C-9a), 155.7 (C=O), 162.1 (C-2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 244 (24.8), 283 (10.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 246 (23.7), 285 (10.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 242 (28.4), 282 (11.1).

Anal. Calcd. for $C_{14}H_{13}N_5OS$ (MW 299.35): C, 56.17; H, 4.38; N, 23.40; S, 10.71. Found: C, 56.23; H, 4.49; N, 23.29; S, 10.59.

The combined mother liquors were evaporated *in vacuo* to dryness and the residue was recrystallised from acetonitrile to yield 1.14 g (33%) of **10a** (R = methylthio, R^1 = butyl), mp 138-140°; ir: ν CO = 1650 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.95 (t, 3H, CCH_3), 1.4 (m, 2H, CH_3CH_2), 1.7 (m, 2H, CCH_2C), 2.61 (s, 3H, SCH_3), 4.20 (t, 2H, OCH_2), 4.28 (bs, 2H, pyrrolidine CH_2-2), 4.79 (bs, 2H, pyrrolidine CH_2-5), 6.57 (d, 2H, *o*-Ph), 6.70 (t, 1H, *p*-Ph), 7.24 (t, 2H, *m*-Ph), 9.8 (s, 1H, NH); cmr (DMSO-d_6) (s-coupling only): δ ppm 13.4 (qa, SCH_3), 14.1 (qa, CCH_3), 18.5 (t, CH_2CH_2), 30.3 (t, CH_2CH_2), 50.8 (t, pyrrolidine C-2), 54.3 (t, pyrrolidine C-5), 63.0 (t, OCH_2), 95.0 (s, pyrrolidine C-3), 110.8 (d, *m*-C-Ph), 115.8 (d, *p*-C-Ph), 129.1 (d, *o*-C-Ph), 146.1 (s, s-C-Ph), 150.8 (s, pyrrolidine C-4), 151.3 (s, triazole C-5), 157.6 (s, triazole C-3), 165.1 (s, C=O); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 250 (9.3), 290 (7.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 240 sh (8.2), 293 (4.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 250 (9.1), 290 (5.9).

Anal. Calcd. for $C_{18}H_{23}N_5O_2S$ (MW 373.47): C, 57.88; H, 6.21; N, 18.75; S, 8.58. Found: C, 57.78; H, 6.19; N, 18.82; S, 8.53.

7,8-Dihydro-2-morpholino-7-phenyl-6*H*-pyrrolo[3,4-*d*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-5(9*H*)-one (**3d**, R = morpholino) and Butyl 1-Phenyl-4-(3-morpholino-1*H*-1,2,4-triazol-5-yl)imino-3-pyrrolidinecarboxylate (**10b**, R = morpholino, R^1 = butyl).

A mixture of 1.69 g (0.01 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) [10], 2.33 g (0.01 mole) of ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**) [8] and 10 ml of 1-butanol was refluxed for 5 hours. After cooling the crystals precipitated were filtered off and recrystallised by dissolving them in hot dimethylformamide and precipitating with acetonitrile to yield 0.94 g (28%) of **3d** (R = morpholino), mp 320°; ir: ν CO = 1670 cm^{-1}; pmr (DMSO-d_6): δ ppm 3.78 (t, 4H, NCH_2), 4.06 (t, 4H, OCH_2), 4.38 (s, 2H, CH_2-8), 4.48 (s, 2H, CH_2-6), 7.5-7.8 (m, 5H, Ph), 8.1 (s, 1H, NH); cmr (TFA): δ ppm 49.7 (NCH_2), 64.9 (C-6), 66.2 (C-8), 69.5 (OCH_2), 109.0 (C-5a), 110.7 (*m*-C-Ph), 124.1 (*p*-C-Ph), 129.2 (*o*-C-Ph), 139.9 (s-Ph), 144.2 (C-8a), 154.6 (C-9a), 155.7 (C=O), 166.0 (C-2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 247 (25.7), 281 (9.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 246 (32.7), 282 (11.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 238 (36.4),

280 (12.9).

Anal. Calcd. for $C_{17}H_{18}N_6O_2$ (MW 338.36): C, 60.34; H, 5.36; N, 24.84. Found: C, 60.51; H, 5.41; N, 24.82.

The combined mother liquors were evaporatd *in vacuo* to dryness and the residue was chromatographed on a silica gel column (eluent a 1:2 mixture of benzene and ethyl acetate) to obtain after recrystallisation from 2-propanol 1.35 g (33%) of **10b** (R = morpholino, R^1 = butyl), mp 201-203° (R_f = 0.52); ir: ν CO = 1660 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.98 (t, 3H, CH_3), 1.4 (m, 2H, CH_3CH_2), 1.7 (m, 2H, CCH_2C), 3.4 (t, 4H, NCH_2), 3.8 (t, 4H, OCH_2), 4.18 (bs, 2H, pyrrolidine CH_2-5), 4.2 (t, 2H, OCH_2), 4.74 (bs, 2H, pyrrolidine CH_2-2), 6.50 (d, 2H, *o*-Ph), 6.70 (t, 1H, *p*-Ph), 7.24 (t, 2H, *m*-Ph), 9.65 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 13.5 (CCH_3), 18.6 (CH_3CH_2), 30.3 (CH_2CH_2), 50.8 (pyrrolidine C-2), 54.4 (pyrrolidine C-5), 63.0 (OCH_2), 93.8 (pyrrolidine C-3), 110.9 (*m*-C-Ph), 115.8 (*p*-C-Ph), 129.1 (*o*-C-Ph), 146.2 (s-C-Ph), 151.6 (pyrrolidine C-4), 155.4 (triazole C-5), 157.6 (triazole C-3), 165.3 (C=O); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 247 (11.8), 290 (9.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 235 (9.6), 282 (4.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 249 (12.6), 288 (5.1).

Anal. Calcd. $C_{21}H_{28}N_6O_3$ (MW 412.49): C, 61.14; H, 6.84; N, 20.38; Found: C, 60.96; H, 6.80; N, 20.13.

Ethyl 1-Phenyl-4-(3-methylthio-1*H*-1,2,4-triazol-5-yl)imino-3-pyrrolidinecarboxylate (**10c**, R = methylthio, R^1 = ethyl).

A mixture of 6.50 g (0.05 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) [9], 11.66 g (0.05 mole) of ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**) [8] and 25 ml of dimethylformamide was heated at 80-100° with stirring for 6 hours. The solution obtained was evaporated *in vacuo* to dryness, the residue was treated with acetone, the crystals precipitated were filtered off, resolved in dimethylformamide and precipitated again with acetonitrile to yield 4.01 g (23%) of the title *product*, which after two recrystallisations from 2-propanol melted at 179-181°; ir: ν C=O= 1657 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.27 (t, 3H, CCH_3), 2.63 (s, 3H, SCH_3), 4.20 (qa, 2H, CCH_2), 4.18 (bs, 2H, pyrolidine C-5), 4.71 (bs, 2H, pyrrolidine C-2), 6.53 (d, 2H, *o*-Ph), 6.70 (t, 1H, *p*-Ph), 7.22 (t, 2H, *m*-Ph), 9.6 (bs, 1H, NH), 13.7 (bs, 1H, triazole NH); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 14.3 (CCH_3), 50.8 (pyrrolidine C-2), 54.4 (pyrrolidine C-5), 59.4 (OCH_2), 94.6 (pyrrolidine C-3), 110.9 (*m*-C-Ph), 115.9 (*p*-C-Ph), 129.1 (*o*-C-Ph), 146.1 (s-C-Ph), 151.3 (pyrrolidine C-4), 152.3 (triazole C-5), 157.8 (triazole C-3), 165.3 (C=O); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 246 (21.0) and 288 (18.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 240 (22.5) and 270sh (4.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 242 (23.4) and 278 (8.7).

Anal. Calcd. for $C_{16}H_{19}N_5O_2S$ (MW 345.43): C, 55.63; H, 5.54; N, 20.27; S, 9.28. Found: C, 55.72; H, 5.42; N, 20.38; S, 9.25.

Ethyl 1-Phenyl-4-(3-morpholino-1*H*-1,2,4-triazol-5-yl)imino-3-pyrrolidinecarboxylate (**10d**, R = morpholino, R^1 = ethyl).

A mixture of 8.46 g (0.05 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) [10], 11.66 g (0.05 mole) of ethyl 1-phenyl-4-oxo-3-pyrrolidinecarboxylate (**2d**) [8] and 25 ml of dimethylformamide was heated at 80-100° with stirring for 6 hours. The solution obtained was evaporated *in vacuo* to drynes, the residue was treated with acetone, the crystals precipitated were filtered off, and recrystallised twice from 2-propanol (charcoal) to yield 4.20 g (22%) of the title *product*, mp 174-176°; ir: ν C=O= 1670 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.21 (t, 3H, CH_3), 3.30 (t, 4H, NCH_2), 3.65 (t, 4H, OCH_2), 4.15 (s, 2H, pyrrolidine C-5), 4.20 (qa, 2H, OCH_2CH_3), 4.67 (s, 2H, pyrrolidine C-2), 6.5-7.2 (m, 5H, ArH), 9.5 (s, 1H, NH), 11.8 (s, 1H, triazole NH); cmr (DMSO-d_6): δ ppm 14.4 (CCH_3), 46.1 (NCH_2), 50.8 (pyrrolidine C-2), 54.4 (pyrrolidine C-5), 59.3 (OCH_2CH_3), 65.3 (OCH_2), 94.1 (pyrrolidine C-3), 110.9 (*m*-C-Ph), 115.9 (*p*-C-Ph), 129.2 (*o*-C-Ph), 146.3 (s-C-Ph), 151.3 (pyrrolidine C-4), 152.3 (triazole C-5), 158.3 (triazole C-3), 165.3 (C=O); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 248 (22.6) and 296 (17.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 242 (21.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 235 (23.2) and 276 sh (9.2).

Anal. Calcd. for $C_{19}H_{24}N_6O_3$ (MW 384.44): C, 59.36; H, 6.29; N, 21.86. Found: C, 59.36; H, 6.29; N, 21.79.

8-Benzyl-2-methylthio-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-5(10*H*)-one [**3e**, Y = $CH_2N(CH_2Ph)$, R = methylthio] and 6-Benzyl-2-methylthio-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-9(10*H*)-one [**4e**, Y = $CH_2N(CH_2Ph)$, R = methylthio].

A mixture of 39.1 g (0.03 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) [9], 89.3 g (0.03 mole) of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride [**2e**, Y = $CH_2N(CH_2Ph)$] [11] and 110 ml of acetic acid was refluxed with stirring for 6.5 hours. The solution obtained crystallised upon cooling. The crystals were filtered off, washed with acetone, dissolved in hot pyridine and again precipitated with acetone to yield after filtration 89.3 g (91%) of 8-benzyl-2-methylthio-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one [**3e**, Y = $CH_2N(CH_2Ph)$, R = methylthio], mp 232-234°; ir: ν CO = 1678 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.51 (t, 2H, CH_2-6), 2.57 (s, 3H, SCH_3), 2.77 (t, 2H, CH_2-7), 3.47 (s, 2H, CH_2-9), 3.75 (s, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 20.0 (CH_2-6), 49.2* (CH_2-7), 49.4* (NCH_2), 59.6 (CH_2-9), 103.5 (C-5a), 128.6 (*m*-Ph), 129.6 (*o*-Ph), 131.1 (*p*-Ph), 137.0 (s-Ph), 141.4 (C-9a), 150.2 (C-10a), 154.1 (C=O), 163.0 (C-2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 232 (29.5), 278 (8.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 232 (26.1), 278 (10.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 234 (30.9), 287 (10.2).

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, 58.81; H, 5.27; N, 21.41; S, 9.87.

The mother liquor was evaporated *in vacuo* to dryness and the residue was recrystallised from the mixture of dimethylformamide and acetonitrile to obtain 0.2 g (2%) of 6-benzyl-2-methylthio-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9(10*H*)-one (**4e**, Y = $CH_2N(CH_2Ph)$, R = methylthio), which after recrystallisation from acetonitrile melted at 248-250°; ir: ν C=O= 1678 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.41 (t, 2H, CH_2-8), 2.51 (s, 3H, SCH_3), 2.70 (t, 2H, CH_2-7), 3.58 (s, 2H, CH_2-5), 3.72 (s, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH); cmr (DMSO-d_6): δ ppm 13.1 (SCH_3), 21.3 (C-8), 48.5* (C-7), 48.6* (NCH_2), 60.2 (C-5), 108.4 (C-8a), 126.5 (*o*-Ph), 127.7 (*p*-Ph), 128.2 (*m*-Ph), 138.9 (s-Ph), 141.2 (C-4a), 148.1 (C-10a), 159.6 (C=O), 164.4 (C-2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 204 (18.5) and 308 (8.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 205 (21.1) and 310 (9.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon.10^{-3}$) 295 (8.1).

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, 58.52; H, 5.27; N, 21.47; S, 9.70.

8-Benzyl-2-morpholino-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-5(10*H*)-one [**3e**, Y = $CH_2N(CH_2Ph)$, R = morpholino] and 6-Benzyl-2-morpholino-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-9(10*H*)-one [**4e**, Y = $CH_2N(CH_2Ph)$, R = morpholino].

A mixture of 50.8 g (0.3 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) [10], 89.3 g (0.3 mole) of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride [**2e**, Y = $CH_2N(CH_2Ph)$] [11] and 220 ml of acetic acid was refluxed with stirring for 7 hours. After cooling the crystals precipitated were filtered off, washed with acetone, dissolved in hot pyridine and precipitated again with acetone to yield after filtration 78.9 g (72%) of 8-benzyl-2-morpholino-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one [**3e**, Y = $CH_2N(CH_2Ph)$, R = morpholino], mp 315-317°; ir: ν CO = 1684 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.50 (t, 2H, CH_2-6), 2.71 (t, 2H, CH_2-7), 3.30 (t, 4H, NCH_2), 3.59 (s, 2H, CH_2-9), 3.62 (t, 4H, OCH_2), 3.74 (s, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH), 12.8 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 21.1 (CH_2-6), 45.7 (NCH_2), 48.7* (CH_2-7), 51.0* (NCH_2), 60.4 (CH_2-9), 103.9 (C-5a), 126.7 (*m*-Ph), 127.9 (*o*-Ph), 128.4 (*p*-Ph), 137.4 (s-Ph), 143.1 (C-9a), 149.5 (C-10a), 155.1 (C=O), 164.1 (C-2); uv (ethanol): λ max nm ($\epsilon.10^{-3}$) 232 (24.7), 277 (7.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon.10^{-3}$) 228 (27.1), 279 (10.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide):

λ max nm (ε.10⁻³) 232 (28.1), 284 (10.6).

Anal. Calcd. for $C_{19}H_{22}N_6O_2$ (MW 366.43): C, 62.28; H, 6.05; N, 22.94. Found: C, 62.38; H, 6.09; N, 22.78.

The mother liquor was evaporated *in vacuo* to dryness and the residue was recrystallised from the mixture of dimethylformamide and acetonitrile to obtain 0.33 g (3%) of 6-benzyl-2-morpholino-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9(10*H*)-one (**4e**, Y = $CH_2N(CH_2Ph)$, R = morpholino), which after recrystallisation from dimethylformamide melted at 223-225°; ν C=O = 1684 cm⁻¹; pmr (DMSO-d_6): δ ppm 2.45 (t, 2H, CH_2-8), 2.75 (t, 2H, CH_2-7), 3.40 (t, 4H, NCH_2), 3.64 (s, 2H, CH_2-5), 3.70 (t, 4H, OCH_2), 3.74 (s, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH), 12.8 (bs, 1H, NH); cmr (DMSO-d_6): δ ppm 21.3 (C-8), 45.6 (NCH_2), 48.1* (C-7), 48.6* (NCH_2), 60.4 (C-5), 65.2 (OCH_2), 108.3 (C-8a), 126.8, 127.9, 128.3 (*o,m,p*-Ph), 137.5 (s-Ph), 141.3 (C-4a), 148.2 (C-10a), 159.6 (C=O), 164.4 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 205 (19.0) and 310 (9.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 206 (20.9) and 312 (10.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 296 (8.6).

Anal. Calcd. for $C_{19}H_{22}N_6O_2$ (MW 366.43): C, 62.28; H, 6.05; N, 22.94. Found: C, 62.37; H, 6.13; N, 22.81.

8,10-Dibenzyl-2-methylthio-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11a**, R = methylthio, R^2 = benzyl).

A mixture of 0.87 g (0.0025 mole) of 8-benzyl-2-methylthio-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one sodium salt (**3e.Na**, Y = $CH_2N(CH_2Ph)$, R = methylthio; prepared by dissolving of 8-benzyl-2-methylthio-6,7,8,9-tetradropyrido[3,4-*d*]-1,2,4-triazolo-[1,5-*a*]pyrimidin-5(10*H*)-one (**3e**, Y = $CH_2N(CH_2Ph)$, R = methylthio) in a slight excess of methanolic sodium hydroxyde solution, evaporating to dryness and recrystallisation from 2-propanol, to yield the sodium salt, mp 231-233°), 0.58 ml (0.63 g, 0.005 mole) of benzyl chloride and 3 ml of dimethylformamide was refluxed with stirring for 1 hour. After cooling 5 ml of water was added to the reaction mixture, the separated oily product was extracted with ethyl acetate, the organic layer was washed with water, dried, evaporated *in vacuo* to dryness and the residue was recrystallised from 2-propanol to yield 0.6 g (58%) of the title *product*, mp 165-166°; ir: ν C=O= 1677 cm⁻¹; pmr (DMSO-d_6): δ ppm 2.50 (m, overlaped by DMSO, CH_2-6), 2.63 (s, 3H, SCH_3), 2.65 (t, 2H, CH_2-7), 3.54 (s, 2H, CH_2-9), 3.65 and 5.39 (s, 2H, NCH_2), 7.15-7.35 (m, 10H, ArH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 21.9 (C-6), 47.8, 49.2 and 50.1 (C-7 + NCH_2), 60.3 (C-9), 106.6 (C-5a), 126.4 and 128.1 (*o*-Ph), 127.0 and 127.6 (*p*-Ph), 128.7 (two peaks, *m*-Ph), 135.0 and 137.0 (s-Ph), 145.2 (C-9a), 152.2 (C-10a), 154.1 (C=O), 163.1 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 233 (26.8) and 276 (11.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 235 (27.7) and 274 (11.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 234 (22.4) and 274 (10.4).

Anal. Calcd. for $C_{23}H_{23}N_5OS$ (MW 417.52): C, 66.16; H, 5.55; N, 16.77; S, 7.68. Found: C, 66.23; H, 5.60; N, 16.72; S, 7.55.

8-Benzyl-2-morpholino-10-(3-dimethylaminopropyl)-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11b**, R = morpholino, R^2 = 3-dimethylaminopropyl).

To a mixture of 14.66 g (0.04 mole) of 8-benzyl-2-morpholino-6,7,8,9-tetrahydropyrido-[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3e**, Y = $CH_2N(CH_2Ph)$, R = morpholino) and 50 ml of dimethylformamide 1.5 g (0.05 mole) of sodium hydride (80% suspension in paraffin oil) was added and heated with stirring at 60-70° for 3 hours. After cooling 6.08 g (0.05 mole) of 3-dimethylaminopropyl chloride (in form of 41.5% solution in xylene) was added to the reaction mixture and refluxed with stirring for 30 hours. After cooling the crystals precipitated were filtered off, the filtrate was diluted with 100 ml of water, extracted with 6 x 60 ml of chloroform, the combined chloroform extracts were treated with charcoal, dried over sodium sulphate and evaporated *in vacuo* to dryness. The residue was recrystallised from 2-propanol to yield 5.8 g (32%) of the title *product*, mp 167-169°; ir ν CO = 1672 cm⁻¹; pmr (DMSO-d_6): δ ppm 1.85 (qi, 2H, CCH_2C), 2.13 (s, 6H, NCH_3), 2.24 (t, 2H, NCH_2), 2.74 (b, 4H, CH_2-6 and CH_2-7), 3.56 (s, 2H, CH_2-9), 3.60 (t, 4H, NCH_2), 3.74 (s, 2H, NCH_2), 3.78 (t, 4H, OCH_2), 4.05 (t, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH); cmr (deuteriochloroform): δ ppm 22.1 (C-6), 25.8 (CCH_2C), 44.2 (NCH_2), 44.7 (NCH_3), 45.8 (NCH_2), 48.6 (C-7), 50.4 (NCH_2), 55.7 (NCH_2), 61.5 (C-9), 66.0 (OCH_2), 106.9 (C-5a), 127.1 (*m*-Ph), 128.1 (*o*-Ph), 128.5 (*p*-Ph), 137.0 (s-Ph), 142.6 (C-9a), 150.4 (C-10a), 154.8 (C=O), 164.3 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 234 (28.1), 280 (10.6); uv (10% ethanol + 90 % 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 232 (29.9), 280 (11.2); uv (10% etahnol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 234 (31.0), 282 (12.3).

Anal. Calcd. for $C_{24}H_{33}N_7O_2$ (MW 451.58): C, 63.84; H, 7.37; N, 21.71. Found: C, 63.92; H, 7.48; N, 21.65.

8-Benzyl-2-morpholino-10-(1-dimethylamino-2-propyl)-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11b**, R = morpholino, R^2 = 1-dimethylamino-2-propyl).

Prepared as (**11b**, R = morpholino, R^2 = 3-dimethylaminopropyl) using instead of 3-dimethylaminopropyl chloride 6.06 g (0.05 mole) of 1-dimethylamino-2-propyl chloride as a 38.8% solution in xylene, yield 8.35 g (37%), mp 170-172° (2-propanol); ir: ν CO = 1674 cm⁻¹; pmr (deuteriochloroform): δ ppm 0.90 (d, 3H, CCH_3), 2.00 (s, 6H, NCH_3), 2.30 (d, 2H, NCH_2), 2.52 (t, 2H, CH_2-6), 2.58 (t, 2H, CH_2-7), 2.7 (m, 1H, CH), 3.40 (m, 4H, NCH_2), 3.60 (s, 2H, CH_2-9), 3.70 (m, 4H, OCH_2), 3.78 (s, 2H, NCH_2), 7.3-7.4 (m, 5H, ArH); cmr (deuteriochloroform): δ ppm 9.8 (CCH_3), 22.1 (C-6), 40.2 (NCH_3), 45.9 (NCH_2), 48.4* (C-7), 49.0* (NCH_2), 50.3* (NCH_2), 57.6 (CH), 60.7 (C-9), 65.6 (OCH_2), 105.9 (C-5a), 127.1 (*m*-Ph), 128.3 (*o*-Ph), 128.9 (*p*-Ph), 137.8 (s-Ph), 144.6 (C-9a), 151.1 (C-10a), 154.6 (C=O), 164.0 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 236 (30.1), 280 (7.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 232 (27.1), 282 (11.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 236 (29.2), 284 (12.4).

Anal. Calcd. for $C_{24}H_{33}N_7O_2$ (MW 451.58): C, 63.84; H, 7.37; N, 21.71. Found: C, 63.75; H, 7.30; N, 21.61.

8-Benzyl-2-morpholino-10-(2-pyrrolidinoethyl)-6,7,8,9-tetrahydropyrido-[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11b**, R = morpholino, R^2 = 2-pyrrolidinoethyl).

Prepared as (**11b**, R = morpholino, R^2 = 3-dimethylaminopropyl) using instead of 3-dimethylaminopropyl chloride 8.02 g (0.06 mole) of 2-pyrrolidinoethyl chloride as a 20.1% solution in xylene, yield 7.60 g (41%), mp 184-186° (2-propanol); ir: ν CO = 1670 cm⁻¹; pmr (deuteriochloroform): δ ppm 1.72 (m, 4H, CH_2''), 2.44 (m, 4H, NCH_2''), 2.74 (t, 2H, NCH_2'), 2.75 (bs, 4H, CH_2-6 + CH_2-7), 3.60 (s, 6H, CH_2-9 + NCH_2), 3.74 (m, 6H, NCH_2 + OCH_2), 4.66 (m, 2H, NCH_2'), 7.3-7.4 (m, 5H, ArH); cmr (deuteriochloroform): δ ppm 22.0 (C-6), 23.7 (CH_2''), 45.5 (NCH_2'), 46.0 (NCH_2), 49.2 (C-7), 50.9 (NCH_2), 53.9 (CH_2'), 54.3 (NCH_2''), 66.4 (OCH_2), 107.2 (C-5a), 127.5 (*m*-Ph), 128.5 (*o*-Ph), 128.9 (*p*-Ph), 137.4 (s-Ph), 143.2 (C-9a), 150.7 (C-10a), 155.2 (C=O), 164.6 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 234 (26.4), 280 (10.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 234 (21.8), 278 (12.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 234 (23.1), 280 (9.7).

Anal. Calcd. for $C_{28}H_{33}N_7O_2$ (MW 463.59): C, 64.77, H, 7.18, N, 21.15. Found: C, 64.59; H, 7.07; N, 21.1.

8-Benzyl-2-morpholino-10-(3-morpholinopropyl)-6,7,8,9-tetrahydropyrido[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11b**, R = morpholino, R^2 = 3-morpholinopropyl).

Prepared as (**11b**, R = morpholino, R^2 = 3-dimethylaminopropyl) using instead of 3-dimethylaminopropyl chloride 6.70 g (0.045 mole) of 3-morpholinopropyl chloride, yield 10.27 g (52%), mp 157-159° (2-propanol); ir: ν CO = 1677 cm⁻¹; pmr (DMSO-d_6): δ ppm 1.80 (b, 2H, CH_2'), 2.30 (t, 2H, NCH_2), 2.52 (t, 2H, CH_2-6), 2.65 (t, 2H, CH_2-7), 3.40 (t, 8H, NCH_2), 3.56 (s, 2H, CH_2-9), 3.66 (t, 8H, OCH_2), 3.74 (s, 2H, NCH_2), 4.05 (t, 2H, NCH_2'), 7.2-7.4 (m, 5H, ArH); cmr (DMSO-d_6): δ ppm 23.7 (C-6), 25.5 (CH_2'), 46.3 (NCH_2), 47.4 (NCH_2), 49.4 (C-7), 51.8* (NCH_2), 51.9* (NCH_2'), 54.4 (NCH_2'), 62.0 (C-9), 67.2 and 67.7 (OCH_2), 107.6 (C-5a), 128.8 (*m*-Ph), 129.4 (*o*-Ph), 130.0 (*p*-Ph), 139.3 (s-Ph), 145.6 (C-9a), 152.5 (C-10a), 156.2 (C=O), 165.6 (C-2); uv (ethanol); λ max nm (ε.10⁻³) 235 (29.7), 282 (12.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 234 (27.3), 282 (11.0); uv (10% ethanol + 90% 0.1 *N*

sodium hydroxide): λ max nm (ε.10⁻³) 236 (29.0), 282 (11.8).

Anal. Calcd. for $C_{26}H_{35}N_7O_3$ (MW 493.61): C, 63.27; H, 7.15; N, 19.86. Found: C, 63.11; H, 7.06; N, 19.97.

8-Benzyl-2-morpholino-10-(2-piperidinoethyl)-6,7,8,9-tetrahydropyrido-[3,4-*d*]-1,2,4-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**11b**, R = morpholino, R^2 = 2-piperidinoethyl).

Prepared as (**11b**, R = morpholino, R^2 = 3-dimethylaminopropyl) using instead of 3-dimethylaminopropyl chloride 13.29 g (0.09 mole) of 2-piperidinoethyl chloride as a 17.3% solution in xylene, yield 9.55 g (50%), mp 172-174° (2-propanol); ir: ν CO = 1670 cm⁻¹; pmr (deuteriochloroform): δ ppm 1.4-1.6 (m, 6H, *m,p*-CH_2), 2.32 (m, 4H, NCH_2), 2.54 (t, 2H, NCH_2'), 2.75 (b, 4H, CH_2-6 + CH_2-7), 3.60 (t, 4H, NCH_2), 3.57 (s, 2H, CH_2-9), 3.74 (s, 2H, NCH_2), 3.78 (t, 4H, OCH_2), 4.05 (t, 2H, NCH_2'), 7.3-7.4 (m, 5H, ArH); cmr (deuteriochloroform): δ ppm 22.4 (t, C-6), 24.0 (t, pip. CH_2-4), 46.1 (t, morph. NCH_2), 49.0 (t, C-7), 51.0 (t, benzyl NCH_2), 55.0 (t, pip. NCH_2), 56.6 (t, NCH_2'), 62.0 (t, C-9), 66.4 (t, OCH_2), 107.3 (s, C-5a), 126.9 (d, *m*-Ph), 128.0 (d, *o*-Ph), 129.4 (d, *p*-Ph), 137.3 (s, s-Ph), 143.2 (s, C-9a), 150.7 (s, C-10a), 155.3 (s, C=O), 164.6 (s, C-2); uv (ethanol): λ max nm (ε.10⁻³) 234 (33.5), 281 (13.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 234 (32.9), 280 (13.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 234 (34.7), 282 (14.7).

Anal. Calcd. for $C_{26}H_{35}N_7O_2$ (MW 477.61): C, 65.38; H, 7.39; N, 20.53. Found: C, 65.48; H, 7.27; N, 20.61.

6-Benzyl-10-methyl-2-methylthio-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9(10*H*)-one (**13a**, R = methylthio, R^3 = methyl).

A mixture of 2.88 g (0.02 mole) of 5-methylamino-3-methylthio-1*H*-1,2,4-triazole (**12a**, R = methylthio, R^3 = methyl) [12], 5.96 g (0.02 mole) of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate hydrochloride [11] and 10 ml of acetic acid was refluxed with stirring for 6 hours. After cooling the solution was made alkaline with 20 ml of concentrated ammonium hydroxide solution, the crystals precipitated were filtered off, washed with water and recrystallised from 2-propanol to yield 4.23 g (62%) of the title *product*, mp 148-150°; ir: ν CO = 1670 cm⁻¹; pmr (deuteriochloroform): δ ppm 2.59 (s, 3H, SCH_3), 2.66 (t, 2H, CH_2-7), 2.78 (t, 2H, CH_2-8), 3.38 (s, 3H, NCH_3), 3.65 (s, 2H, NCH_2), 3.80 (s, 2H, CH_2-5), 7.2-7.4 (m, 5H, ArH); cmr (deuteriochloroform): δ ppm 14.2 (SCH_3), 22.6 (C-8), 30.2 (NCH_3), 49.0* (C-7), 49.5* (NCH_2), 61.8 (C-5), 110.9 (C-8a), 127.7 (*m*-Ph), 128.7 (*o*-Ph), 129.0 (*p*-Ph), 137.2 (s, Ph), 141.0 (C-4a), 150.7 (C-10a), 159.7 (C=O), 163.7 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 203 (24.5) and 286 (10.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 204 (21.4) and 284 (10.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 288 (9.7).

Anal. Calcd for $C_{17}H_{19}N_5OS$ (MW 341.45): C, 59.80; H, 5.61; N, 20.51; S, 9.39. Found: C, 59.71; H, 5.67; N, 20.39; S, 9.44.

6,10-Dibenzyl-2-methylthio-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]pyrimidin-9(10*H*)-one (**13b**, R = methylthio, R^3 = benzyl).

A mixture of 1.10 g (0.005 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**12a**, R = methylthio, R^2 = benzyl) [12] and 1.61 g (0.0065 mole) of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate (prepared from the corresponding hydrochloride [11] by partitioning it between benzene and cold 5 *N* sodium hydroxide solution, washing, drying and evaporating the benzene layer to dryness) was heated at 150° for 15 minutes. The still hot melt was dissolved in 20 ml of 2-propanol and treated with charcoal. After cooling the crystals precipitated were filtered off and recrystallised from acetonitrile to yield 1.3 g (62%) of the title *product*, mp 124-125°; ir: ν C=O = 1670 cm⁻¹, ν C=N = 1570 and 1515 cm⁻¹; pmr (DMSO-d_6): δ ppm 2.53 (t, 2H, CH_2-8), 2.56 (s, 3H, SCH_3), 2.77 (t, 2H, CH_2-7), 3.35 (s, 2H, CH_2-5), 3.78 (s, 2H, NCH_2-5), 5.26 (s, 2H, NCH_2-10), 7.28-7.40 (m, 10H, ArH); cmr (DMSO-d_6): δ ppm 13.2 (SCH_3), 22.0 (C-8), 46.1 (NCH_2), 48.1* (NCH_2), 48.5* (C-7), 60.3 (C-5), 110.2 (C-8a), 127.0, 127.4, 127.8, 128.1, 128.2 and 128.6 (*o,m,p*-Ph), 135.6 and 137.5 (s-Ph), 141.0 (C-4a), 150.0 (C-10a), 158.5 (C=O), 162.1 (C-2); uv (ethanol): λ max nm (ε.10⁻³) 205 (38.7) and 290 (8.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 204 (40.2) and 293 (9.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 302 (8.1).

Anal. Calcd. for $C_{23}H_{23}N_5OS$ (MW 417.52): C, 66.17; H, 5.55; N, 16.77; S, 7.68. Found: C, 66.03; H, 5.62; N, 16.59; S, 7.71.

6,10-Dibenzyl-2-morpholino-5,6,7,8-tetrahydropyrido[4,3-*e*]-1,2,4-triazolo[1,5-*a*]-pyrimidin-9(10*H*)-one (**13c**, R = morpholino, R^3 = benzyl).

A mixture of 1.30 g (0.005 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole (**12c**, R = morpholino, R^3 = benzyl) [4] and 1.61 g (0.0065 mole) of ethyl 1-benzyl-3-oxo-4-piperidinecarboxylate (preparation see in **13b**) was heated at 150° for 10 minutes. The still hot melt was dissolved in 10 ml of 2-propanol, treated with charcoal and 10 ml of ethyl acetate was added to the warm solution. After cooling the crystals precipitated were filtered off and recrystallised from acetonitrile to yield 1.35 g (59%) of the title *product*, mp 149-151°; ir: ν C=O = 1664 cm⁻¹; pmr (DMSO-d_6): δ ppm 2.53 (t, 2H, CH_2-8), 2.73 (t, 2H, CH_2-7), 3.33 (s, 2H, CH_2-5), 3.36 (t, 4H, NCH_2), 3.65 (t, 4H, OCH_2), 3.75 (s, 2H, NCH_2-5), 5.23 (s, 2H, NCH_2-10), 7.30-7.38 (m, 10H, ArH); cmr (DMSO-d_6): δ ppm 22.1 (C-8), 45.3 (NCH_2), 45.8 (C-7), 48.5 and 48.9 (NCH_2), 60.6 (C-5), 65.5 (OCH_2), 108.1 (C-8a), 126.8, 127.4, 127.8, 128.0, 128.2 and 128.5 (*o,m,p*-Ph), 135.9 and 137.5 (s-Ph), 141.3 (C-4a), 149.2 (C-10a), 158.5 (C=O), 164.3 (C-2); uv ethanol): λ max nm (ε.10⁻³) 205 (39.9) and 308 (8.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε.10⁻³) 205 (36.8) and 312 (8.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε.10⁻³) 308 (4.6).

Anal. Calcd. for $C_{26}H_{28}N_6O_2$ (MW 456.55): C, 68.40; H, 6.18; N, 18.41. Found: C, 68.31; H, 6.10; 18.36.

Acknowledgement.

The authors wish to express their thanks to Mrs. Dr. Andrea Csokán-Hollós for recording the uv spectra, to Miss Monika Sipos for recording the ir spectra, to Mr. István Pallagi and to Mr. Attila Fürjes for recording the nmr spectra, to Prof. Pál Sohár for helpful nmr discussions, to Dr. Erich Paulus for the X-ray investigations, to Mrs. Lászlóné Zalavári for performing the elementar analyses and to Mrs. Lászlóné Kartali and Mrs. Lászlóné Nyikos for technical assistance.

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