On Triazoles. XXVII [1].
The Acylation, Carbamoylation and Thiocarbamoylation of Tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidinones

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Isomeric 6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine-5(10*H*)-ones **3**, and -6(10*H*)-ones **4** were synthesised. Isomers **3** were converted to their 7-acyl **7**, 7-carbamoyl **8** and 7-thiocarbamoyl **9** derivatives.

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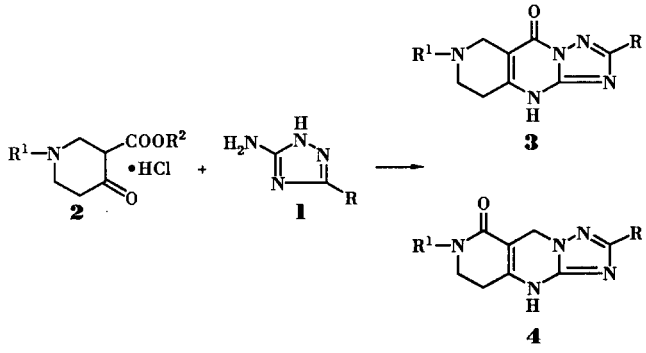
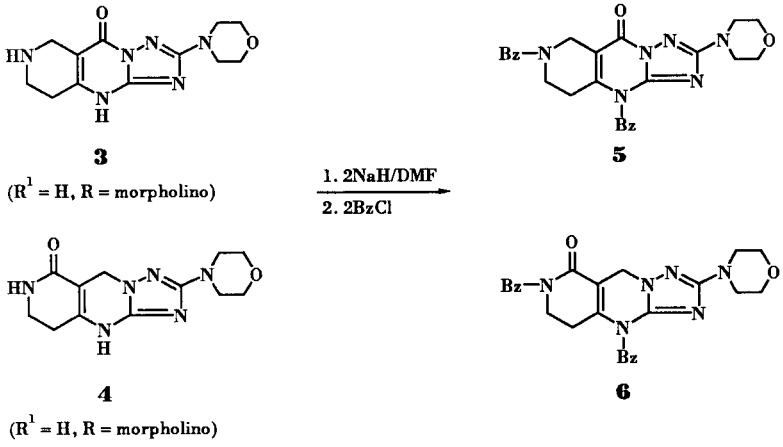
In a previous paper of this series [2] we have studied the reaction of 5-amino-3-R-1*H*-1,2,4-triazoles **1** with methyl 1-benzyl-4-oxo-3-piperidinecarboxylate hydrochloride (**2**, R^1 = benzyl, R^2 = methyl) to yield the mixture of tricyclic isomers **3** (R^1 = benzyl) and **4** (R^1 = benzyl), respectively, the latter one being formed by an unexpected rearrangement [2]. Repeating the above reaction with ethyl 4-oxo-3-piperidinecarboxylate hydrochloride (**2**, R^1 = H, R^2 = ethyl) [3] the analogues **3** (R^1 = H, R = methylthio and morpholino) and **4** (R^1 = H, R = methylthio and morpholino), respectively, were obtained (Scheme 1). Their pmr and uv spectra were completely analogous with those of the corresponding benzyl derivatives **3** (R^1 = benzyl) and **4** (R^1 = benzyl), respectively, prepared previously [2]. However, their extremely low solubility in all nmr solvents made it impractical to record their cmr spectra claimed [2] to be the most characteristic for their structure. To overcome this problem their disodium salts were benzylated to yield the dibenzyl derivatives **5** and **6** (Scheme 2) being in all respects (mp, mixed mp, ir) identical with those prepared previously [2].

As expected, the 7-NH group of derivatives **3** (R^1 = H, R = methylthio and morpholino) could be easily acylated, carbamoylated and thiocarbamoylated to yield the corresponding 7-acyl **7**, 7-carbamoyl **8** (X = O) and 7-thiocarbamoyl **9** (X = S) derivatives (Scheme 3). Their structures were consistent with the corresponding ir, pmr and cmr spectra recorded. The dramatic change in the chemical shifts of carbon atoms 6 and 8 of derivatives **7**, **8**, and **9** (**7**: δ C-6 = 37.5, δ C-8 = 36.5; **8**: δ C-6 = 40.1-40.7, δ C-8 = 38.6-40.8; **9**: δ C-6 = 43.5-44.7, δ C-8 = 43.1-44.0) as compared with those of derivatives **3** (R^1 = benzyl, R = methylthio and morpholino, respectively) (δ C-6 = 60.9-63.0, δ C-8 = 46.8-48.0) prepared previously [2] and the close analogy of their uv spectra with those of the corresponding starting materials **3** (R^1 = H, R = methylthio and morpholino, respectively) proved that the acylation, carbamoylation and thiocarbamoylation occurred on the ni-

Scheme 1

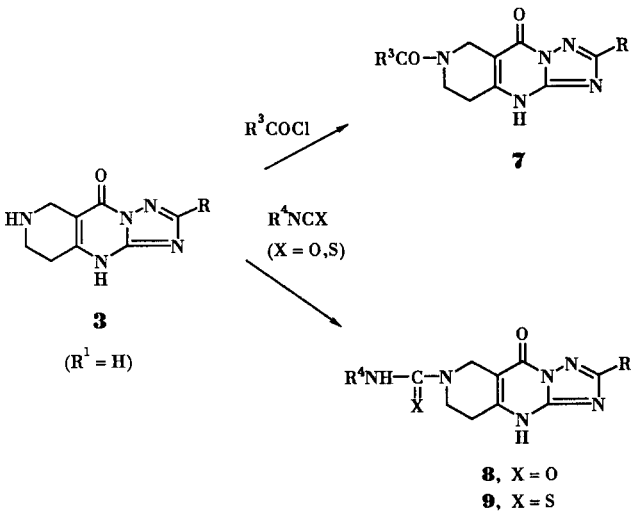


Scheme 2



trogen atom 7. Structure **8** (X = O, R = methylthio, R^4 = cyclohexyl) was also corroborated by its X-ray spectra [3].

Scheme 3



On the other hand, attempts to acylate, carbamoylate or thiocarbamoylate the isomers **4** (R^1 = H, R = methylthio and morpholino) resulted in the unchanged starting materials after workup of the reaction mixtures. This is probably due to the very low basicity of these derivatives as a consequence of which even if their acylation probably occurred, the acylated products spontaneously decomposed during the workup of the reaction mixtures.

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 spectrophotometer. 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 Bruker WM-250 and Bruker WP-80 SY instruments. The X-ray measurements were performed using an Enraf-Nonius diffractometer. All tlc determinations were carried out on Kieselgel GF_{254} (Merck) plates using a 12:6:1:1 (v/v/v/v) mixture of acetone, chloroform, methanol and water as eluent. The spots were detected by uv.

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

A solution of 16.92 g (0.1 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, R = morpholino) [4] and 20.77 g (0.1 mole) of ethyl 4-oxo-3-piperidinecarboxylate hydrochloride (Fluka) in 50 ml of acetic acid was refluxed for 13 hours. After cooling the crystals which precipitated were filtered off, washed with acetic acid and chloroform. To the crystals obtained [23.5 g (75%) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one hydrochloride] a solution of 3.0 g (0.075 mole) of sodium hydroxide in 250 ml of methanol was added and the mixture refluxed for 10 minutes while stirring. After cooling the crystals which precipitated were filtered off and washed with water and acetone to yield 21.0 g (72%) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), mp 308-310°; ir: ν C=O = 1653 cm^{-1}; pmr (deuteriotrifluoroacetic acid): δ ppm 3.30 (bs, 2H, CH_2-9), 3.62 (m, 4H, NCH_2), 3.80 (bs, 2H, CH_2-8), 3.95 (m, 4H, OCH_2), 4.40 (s, 2H, CH_2-6), 8.80 (s, 1H, NH-10); uv (ethanol): λ max nm (ϵ. 10^{-3}) 200 (11.1), 232 (17.1), 269 (5.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 200 (13.2), 230 (19.5), 276 (7.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 235 (16.5), 284 (6.5).

Anal. Calcd. for $C_{12}H_{16}N_6O_2$ (MW 276.30): C, 52.17; H, 5.84; N, 30.42. Found: C, 52.32; H, 5.88; N, 30.31.

The first acetic acid-chloroform filtrate of the reaction mixture was evaporated *in vacuo* to dryness, then 100 ml of ethanol was added to the residue and the evaporation *in vacuo* to dryness was repeated. Forty ml of 25% ammonium hydroxide was added to the residue, the crystals which precipitated were filtered off, washed with water and acetone, dissolved in hot hexamethylphosphoramide and precipitated again with acetonitrile to yield after collection of the crystals 1.94 g (7%) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(10*H*)-one (**4**, R = morpholino, R^1 = H), mp >360°; ir: ν C=O = 1668 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.86 (t, 2H, CH_2-9), 3.63 (m, 4H, NCH_2), 3.77 (t, 2H, CH_2-8), 4.08 (t, 4H, OCH_2), 4.97 (s, 2H, CH_2-5); uv (ethanol): λ max nm (ϵ. 10^{-3}) 201 (16.2), 236 sh (13.5), 309 (6.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 200 (15.7), 232 sh (11.5), 308 (7.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 222 (13.2), 356 (13.4).

Anal. Calcd. for $C_{12}H_{16}N_6O_2$ (MW 276.30): C, 52.17; H, 5.84; N, 30.42. Found: C, 51.98; H, 5.67; N, 30.40.

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

A solution of 13.02 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, R = methylthio) [5] and ethyl 4-oxo-3-piperidinecarboxylate (**2**, R^1 = H) in 50 ml of acetic acid was refluxed for 8 hours. After cooling the crystals which precipitated were filtered off, washed with acetic acid and chloroform, dissolved in 500 ml of hot water and neutralised while hot with 10% sodium bicarbonate solution. After cooling the crystals which precipitated were filtered off, washed with water and acetone, refluxed with 100 ml of hot hexamethylphosphoramide, cooled to room temperature, filtered and washed again with water and acetone to yield 13.8 g (58%) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H), mp 266-269°; ir: ν C=O = 1653 cm^{-1}; pmr (deuteriotrifluoroacetic acid): δ ppm 2.63 (s, 3H, SCH_3), 3.31 (t, 2H, CH_2-9), 3.80 (t, 2H, CH_2-8), 4.43 (s, 2H, CH_2-6), 8.2* (s, 1H, NH-7), 8.8* (s, 1H, NH-10); uv (ethanol): λ max nm (ϵ. 10^{-3}) 201 (10.8), 235 (15.7), 278 (6.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 200 (7.2), 234 (14.8), 276 (6.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 234 (15.4), 286 (5.7).

Anal. Calcd. for $C_9H_{11}N_5OS$ (MW 237.28): C, 45.56; H, 4.67; N, 29.52; S, 13.51. Found: C, 45.65; H, 4.75; N, 29.38; S, 13.55.

The first acetic acid-chloroform filtrate of the reaction mixture was evaporated *in vacuo* to a volume of about 10-15 ml, then 60 ml of 25% ammonium hydroxide was added to the residue. The

crystals which precipitated were filtered off, washed with water and acetone, dissolved in a little amount of hexamethylphosphoramide and precipitated again with acetone. The crystals which precipitated were collected, washed with water and acetone and dried to yield 1.66 g (7%) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(10*H*)-one (**4**, R = methylthio, R^1 = H), mp 314-317°; ir: ν C=O = 1666 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.71 (s, 3H, SCH_3), 2.86 (t, 2H, CH_2-9), 3.75 (t, 2H, CH_2-8), 5.08 (s, 2H, CH_2-5); uv (ethanol): λ max nm (ϵ. 10^{-3}) 201 (15.5), 236 (7.1), 306 (7.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 203 (14.6), 229 sh (9.8), 307 (8.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 221 (11.3), 358 (15.4).

Anal. Calcd. for $C_9H_{11}N_5OS$ (MW 237.28): C, 45.56; H, 4.67; N, 29.52; S, 13.51. Found: C, 45.55, H, 4.76; N, 29.55; S, 13.40.

7,10-Dibenzyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**5**).

To a mixture of 2.07 g (0.0075 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H) and 15 ml of dimethylformamide 0.675 g (0.0225 mole) of sodium hydride (80% suspension in paraffin oil) was added. The mixture was stirred at 60-70° for 30 minutes. After cooling to room temperauture 2.85 g (0.023 mole) of benzyl chloride was added by dropping it into the reaction mixture and it was stirred for further 5 hours at room temperature. After standing overnight 75 ml of water was added, the mixture obtained was extracted three times with 30 ml portions of chloroform, the combined chloroform layers were dried over anhydrous sodium sulfate, filtered, and evaporated *in vacuo* to dryness. The residue was recrystallised from dimethylformamide to yield 0.81 g (24%) of 7,10-dibenzyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**5**), mp 185-187°, lit [2] mp 185-187°, identical (mixed mp, ir).

7,10-Dibenzyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-6(10*H*)-one (**6**).

To a mixture of 2.20 g (0.008 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-6(10*H*)-one (**4**, R = morpholino, R^1 = H) and 8 ml of dimethylformamide 0.72 g (0.024 mole) of sodium hydride (80% suspension in paraffin oil) was added. The mixture was stirred at 40-50° for 30 minutes. After cooling to room temperature 3.80 g (0.03 mole) of benzyl chloride was added by dropping it into the reaction mixture and it was stirred for further 7 hours at room temperature. After standing overnight 40 ml of water was added, the mixture obtained was extracted five times with 15 ml portions of chloroform, the combined chloroform layers were treated with charcoal, dried over anhydrous sodium sulfate, filtered, and evaporated *in vacuo* to dryness. The residue was dissolved in 100 ml of ethanol, evaporated again to dryness *in vacuo* and recrystallised from 2-propanol to yield 1.52 g (40%) of 7,10-dibenzyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-6-(10*H*)-one (**6**), mp 142-144°, lit [2] mp 142-144°, identical (mixed mp, ir).

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

To a mixture of 0.83 g (0.003 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.5 g (0.005 mole, 0.69 ml) of triethylamine and 4 ml of dimethylformamide 0.39 g (0.005 mole, 0.55 ml) of acetyl chloride was added by dropping it into the reaction mixture while stirring at room temperature. The mixture was then stirred at 40-50° for 3.5 hours and allowed to stand at room temperature overnight. The crystals which precipitated were filtered off, washed with water, dissolved in 18 ml of hot dimethylformamide and precipitated again with 18 ml of acetonitrile to yield 0.39 g (41%) of 7-acetyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**7**, R = morpholino, R^3 = methyl), mp 310-313°, ir: ν C=O = 1664 and 1634 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.02 (s, 3H, CH_3), 2.70 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.65 (t, 4H, OCH_2), 3.70 (t, 2H, CH_2-8), 4.22 (s, 2H, CH_2-6); cmr (DMSO-d_6): δ ppm 21.1 (CH_3), 26.1 (C-9), 36.5 (C-8), 37.5 (C-6), 44.8 (NCH_2), 65.4 (OCH_2), 103.4 (C-5a), 144.2 (C-9a), 149.7 (C-10a), 154.1 (C-5), 164.3 (C-2), 168.6 ($COCH_3$); uv (ethanol): λ max nm (ϵ. 10^{-3}) 202 (14.3), 235 (25.5), 276 (9.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 201 (11.2), 233 (18.3), 275 (7.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 237 (20.2), 282 (6.8).

Anal. Calcd. for $C_{14}H_{18}N_6O_3$ (MW 318.34): C, 52.82; H, 5.70; N, 26.40. Found: C, 53.01; H, 5.88; N, 26.51.

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

To a mixture of 0.83 g (0.003 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.50 g (0.005 mole, 0.69 ml) of triethylamine, and 4 ml of dimethylformamide and 1 ml of hexamethylphosphoramide 0.46 g (0.005 mole, 0.43 ml) of propionyl chloride was added by dropping it into the reaction mixture while stirring at room temperature. The mixture was then stirred at room temperature for 6.5 hours. After standing overnight 25 ml of water was added to the reaction mixture, the crystals which separated were filtered off, washed with acetone, dissolved in 6 ml of hot dimethylformamide and precipitated again with 15 ml of acetonitrile to yield 0.63 g (63%) of 2-morpholino-7-propionyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**7**, R = morpholino, R^3 = ethyl), mp 278-280°, ir: ν C=O = 1672 and 1641 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.01 (t, 3H, CH_3), 2.42 (qa, 2H, CH_2CH_3), 2.65 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.70 (t, 6H, OCH_2 + CH_2-8), 4.28 (s, 2H, CH_2-6); cmr (DMSO-d_6): δ ppm 19.0 (CH_3), 26.0* (CH_2CH_3), 26.1* (C-9), 36.5 (C-8), 37.5 (C-6), 45.8 (NCH_2), 65.4 (OCH_2), 103.4 (C-5a), 144.2 (C-9a), 149.7 (C-10a), 154.1 (C-5), 164.3 (C-2), 170.8 (C=O); uv (ethanol): λ max nm (ϵ. 10^{-3}) 201 (13.4), 237 (23.6), 279 (9.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 202 (10.8), 233 (17.6), 274 (5.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 237 (18.7), 283 (5.6).

Anal. Calcd. for $C_{15}H_{20}N_6O_3$ (MW 332.36): C, 54.21; H, 6.07; N, 25.29. Found: C, 54.14; H, 6.04; N, 25.31.

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

To a mixture of 0.95 g (0.004 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H), 1.21 g (0.012 mole, 1.66 ml) of triethylamine and 5 ml of dimethylformamide 1.21 g (0.012 mole, 0.85 ml) of acetyl chloride was added by dropping it into the reaction mixture while stirring at room temperature. The mixture was

then stirred at 60-65° for 16 hours. After cooling the crystals which precipitated were filtered off, washed with water and acetone, dissolved in 4 ml of hot dimethylformamide and precipitated again with 15 ml of acetonitrile to yield 0.54 g (47%) of 7-acetyl-2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo-[1,5-*a*]pyrimidin-5(10*H*)-one (**7**, R = methylthio, R^3 = methyl), mp 284-286°; ir: ν C=O = 1661 and 1636 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.10 (s, 3H, CH_3CO), 2.59 (s, 3H, CH_3S), 2.65 (t, 2H, CH_2-9), 3.72 (t, 2H, CH_2-8), 4.32 (s, 2H, CH_2-6), cmr (DMSO-d_6): δ ppm 13.3 (CH_3S), 21.1 (CH_3CO), 26.3 (C-9), 36.5 (C-8), 37.5 (C-6), 103.5 (C-5a), 145.5 (C-9a), 150.4 (C-10a), 153.8 (C-5), 163.2 (C-2), 168.7 (C=O); uv (ethanol): λ max nm (ϵ. 10^{-3}) 202 (14.3), 236 (24.8), 275 (8.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 200 (11.0), 232 (19.0), 272 (6.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide); λ max nm (ϵ. 10^{-3}) 238 (20.3), 283 (6.8).

Anal. Calcd. for $C_{11}H_{13}N_5O_2S$ (MW 279.32): C, 47.30; H, 4.69; N, 25.07; S, 11.48. Found: C, 47.35; H, 4.51; N, 24.97; S, 11.42.

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

To a mixture of 0.71 g (0.003 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H), 0.50 g (0.005 mole, 0.69 ml) of triethylamine and 4 ml of dimethylformamide 0.46 g (0.005 mole, 0.43 ml) of propionyl chloride was added by dropping it into the reaction mixture while stirring at room temperature. The mixture was then stirred at 60-65° for 6.5 hours. After standing overnight 25 ml of water was added to the reaction mixture, the crystals which separated were filtered off, washed with acetonitrile, dissolved in 7 ml of hot dimethylformamide and precipitated again with 18 ml of acetonitrile to yield 0.58 g (63%) of 2-methylthio-7-propionyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-(10*H*)-one (**7**, R = methylthio, R^3 = ethyl), mp 276-278°, ir: ν C=O = 1668 and 1647 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.02 (t, 3H, CH_3), 2.44 (qa, 2H, $COCH_2$), 2.60 (s, 3H, SCH_3), 2.70 (t, 2H, CH_2-9), 3.70 (t, 2H, CH_2-8), 4.31 (s, 2H, CH_2-6); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 18.9 (CH_3), 25.6* ($COCH_2$), 26.2* (C-9), 36.5 (C-8), 37.5 (C-6), 103.5 (C-5a), 145.5 (C-9a), 150.3 (C-10a), 154.1 (C-5), 163.3 (C-2), 171.7 (C=O); uv (ethanol): λ max nm (ϵ. 10^{-3}) 203 (18.6), 235 (22.0), 278 (8.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 202 (13.8), 234 (18.6), 276 (7.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 237 (18.6), 284 (7.0).

Anal. Calcd. for $C_{12}H_{15}N_5O_2S$ (MW 293.36): C, 49.13; H, 5.15; N, 23.88; S, 10.93. Found: C, 48.99; H, 5.05; N, 24.01; S, 11.02.

2-Morpholino-7-(*n*-octadecylcarbamoyl)-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = *n*-octadecyl).

A mixture of 1.11 g (0.004 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 1.18 g (0.004 mole, 1.40 ml) of *n*-octadecylisocyanate, 2 ml of dimethylformamide and 3 ml of hexamethylphosphoramide was stirred at 120-130° for 2 hours. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with acetone, dissolved in 9 ml of hot dimethylformamide and precipitated again with 15 ml of acetonitrile to yield 1.14 g (58%) of 2-morpholino-7-(*n*-octadecylcarbamoyl)-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = *n*-octadecyl), mp 228-230°; ir: ν C=O = 1659 and 1634 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.84 (t, 3H, CH_3), 1.20 (m, 34H, -$(CH_2)_{17}$-), 2.62 (t, 2H, CH_2-9), 3.40 (t, 4H, morpholino NCH_2), 3.55 (t, 2H, CH_2-8), 3.70 (t, 4H, morpholino OCH_2), 4.18 (s, 2H, CH_2-6), 6.75 (t, 1H, CONH); cmr (DMSO-d_6): δ ppm 13.3 (CH_3), 21.5 (CH_3CH_2), 25.8 (C-9), 28.4-31.2 [CH_2-15 peaks], 39.6 (C-8), 40.7 (C-6), 44.8 ($NHCH_2$), 45.2 (NCH_2), 65.0 (OCH_2), 103.4 (C-5a), 143.8 (C-9a), 149.1 (C-10a), 153.7 (C-5), 155.6 (CONH), 164.2 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 200 (22.1), 235 (34.7), 279 (10.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 205 (19.2), 232 (28.1), 279 (9.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 235 (36.2), 282 (10.4).

Anal. Calcd. for $C_{31}H_{53}N_7O_3$ (MW 571.81): C, 65.12; H, 9.34; N, 17.15. Found: C, 65.23; H, 9.44; N, 17.06.

7-Cyclohexylcarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = cyclohexyl).

A mixture of 1.11 g (0.004 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.50 g (0.004 mole, 0.51 ml) of cyclohexylisocyanate, 2 ml of dimethylformamide and 3 ml of hexamethylphosphoramide was stirred at 130-140° for 2 hours. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with acetone, dissolved in 6 ml of hot dimethylformamide and precipitated again with 18 ml of acetonitrile to yield 0.80 g (50%) of 7-cyclohexylcarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = cyclohexyl), mp 258-260°; ir: ν C=O = 1674 and 1645 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.0-1.3 (m, 6H, cyclohexyl CH_2-3,4 and 5), 1.5-1.8 (m, 4H, cyclohexyl CH_2-2 and 6), 2.63 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.50 (b, 1H, CH), 3.60 (t, 2H, CH_2-8), 3.70 (t, 4H, OCH_2), 4.16 (s, 2H, CH_2-6), 6.45 (d, 1H, NH); cmr (DMSO-d_6): δ ppm 24.9 (*o*-CH), 25.2 (*p*-CH), 25.9 (C-9), 32.9 (*m*-CH), 39.0 (C-8), 40.1 (C-6), 45.8 (NCH_2), 49.2 (*s*-CH), 65.5 (OCH_2), 104.0 (C-5a), 144.3 (C-9a), 149.6 (C-10a), 154.2 (C-5), 156.8 (NHCO), 164.2 (C-2); uv (ethanol): λ max nm (ϵ. 10^{-3}) 200 (21.7), 235 (35.2), 277 (10.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 202 (17.5), 232 (26.3), 275 (8.7); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 233 (36.2), 285 (10.2).

Anal. Calcd. for $C_{19}H_{27}N_7O_3$ (MW 401.47): C, 56.84; H, 6.78; N, 24.42. Found: C, 56.98; H, 6.88; N, 24.32.

2-Morpholino-7-phenylcarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = phenyl).

A mixture of 0.83 g (0.003 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.36 g (0.003 mole, 0.34 ml) of phenylisocyanate, 3 ml of dimethylformamide and 1 ml of hexamethylphosphoramide was stirred at 130-140° for 2.5 hours. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with water and acetone, dissolved in 15 ml of hot dimethylformamide and precipitated again with 20 ml of acetonitrile to yield 1.01 g (85%) of 2-morpholino-7-phenylcarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-

(10*H*)-one (**8**, X = O, R = morpholino, R^4 = phenyl), mp 278-281°; ir: ν C=O = 1661 and 1640 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.75 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.70 (t, 6H, OCH_2 and CH_2-8), 4.36 (s, 2H, CH_2-6), 6.95 (t, 1H, *p*-PhH), 7.25 (t, 2H, *m*-PhH), 7.50 (d, 2H, *o*-PhH), 8.80 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 25.8 (C-9), 38.9 (C-8), 40.1 (C-6), 45.6 (NCH_2), 65.3 (OCH_2), 103.6 (C-5a), 119.7 (*o*-Ph), 121.6 (*p*-Ph), 126.9 (*m*-Ph), 140.1 (*s*-Ph), 144.2 (C-9a), 149.5 (C-10a), 154.0 (C-5), 154.9 (NHCO), 164.2 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 203 (31.6), 238 (38.7), 273 (9.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 203 (24.6), 234 (29.1), 274 (8.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): δ max nm (ε. 10^{-3}) 239 (33.2), 282 (7.1).

Anal. Calcd. for $C_{19}H_{21}N_7O_3$ (MW 395.42): C, 57.71; H, 5.35; N, 24.80. Found: C, 57.65; H, 5.23; N, 24.68.

2-Morpholino-7-(3-trifluoromethylphenylcarbamoyl)-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = 3-trifluoromethylphenyl).

A mixture of 1.11 g (0.004 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.75 g (0.004 mole, 0.56 ml) of 3-trifluoromethylphenylisocyanate, 2 ml of dimethylformamide and 3 ml of hexamethylphosphoramide was stirred at 120-130° for 8 hours. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with water and acetone, dissolved in 4 ml of hot dimethylformamide and precipitated again with 8 ml of acetonitrile to yield 0.46 g (25%) of 2-morpholino-7-(3-trifluoromethylphenylcarbamoyl)-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = 3-trifluoromethylphenyl), mp 266-268°; ir: ν C=O = 1664 and 1620 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.74 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.71 (bs, 4H, OCH_2), 3.74 (t, 2H, CH_2-8), 4.39 (s, 2H, CH_2-6), 7.32 (d, 1H, Ph-4H), 7.52 (t, 1H, Ph-5H), 7.82 (d, 1H, Ph-6H), 7.98 (s, 1H, Ph-2H), 9.10 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 25.9 (C-9), 38.6 (C-8), 40.6 (C-6), 45.8 (NCH_2), 65.5 (OCH_2), 103.6 (C-5a), 115.6 (2-Ph), 117.8* (4-Ph), 118.0* (6-Ph), 123.0 (CF_3), 128.5* (3-Ph), 129.1* (5-Ph), 141.2 (1-Ph), 144.3 (C-9a), 149.7 (C-10a), 154.1 (C-5), 154.6 (NHCO), 164.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 203 (26.9), 236 (31.3), 279 (8.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 203 (23.6), 232 (26.6), 273 (8.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 236 (38.2), 283 (8.6).

Anal. Calcd. for $C_{20}H_{20}F_3N_7O_3$ (MW 463.43): C, 51.84; H, 4.35; N, 21.16; F, 12.30. Found: C, 51.93; H, 4.54; N, 21.06; F, 12.35.

2-Methylthio-7-(*n*-octadecylcarbamoyl)-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = methylthio, R^4 = *n*-octadecyl).

Prepared as 2-morpholino-7-(*n*-octadecylcarbamoyl)-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = *n*-octadecyl) using 0.95 g (0.004 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidine-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield, 1.53 g (72%), mp 171-174°; ir: ν C=O = 1670 and 1649 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.85 (t, 3H, CH_3), 1.20 (m, 34H, $(CH_2)_{17}$), 2.59 (s, 3H, SCH_3), 2.65 (t, 2H, CH_2-9), 3.60 (t, 2H, CH_2-8), 4.20 (s, 2H, CH_2-6), 6.72 (t, 1H, NH); cmr (DMSO-d_6): δ ppm 13.1 (SCH_3), 13.7 (CH_3), 21.6 (CH_3CH_2), 25.8 (C-9), 28.4-31.2 (CH_2-15 peaks), 40.8 (C-8), 41.9 (C-6), 45.3 ($NHCH_2$), 103.5 (C-5a), 145.6 (C-9a), 150.2 (C-10a), 155.4 (C-5), 157.0 (NHCO), 165.2 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 203 (21.3), 232 (27.2), 278 (9.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 204 (19.3), 231 (28.0), 275 sh (8.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 232 (34.1), 281 (8.8).

Anal. Calcd. for $C_{28}H_{48}N_6O_2S$ (MW 532.79): C, 63.12; H, 9.08; N, 15.77; S, 6.02. Found: C, 63.25; H, 9.11; N, 15.71; S, 5.86.

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

Prepared as 7-cyclohexylcarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = cyclohexyl) using 0.95 g (0.004 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield: 1.15 g (79%), mp 239-241°; ir: ν C=O = 1672 and 1645 cm^{-1}; pmr (DMSO-d_6): δ ppm 1.0-1.3 (m, 6H, cyclohexyl CH_2-3,4,5), 1.5-1.8 (m, 4H, cyclohexyl CH_2-2,6), 2.66 (s, 3H, SCH_3), 2.68 (t, 2H, CH_2-9), 3.50 (b, 1H, cyclohexyl CH), 3.60 (t, 2H, CH_2-8), 4.20 (s, 2H, CH_2-6), 6.48 (d, 1H, NH); cmr (DMSO-d_6): δ ppm 13.5 (SCH_3), 25.0 (*o*-CH), 25.2 (*p*-CH), 26.2 (C-9), 32.9 (*m*-CH), 39.0 (C-8), 40.2 (C-6), 49.2 (*s*-CH), 104.1 (C-5a), 145.7 (C-9a), 150.4 (C-10a), 155.9 (C-5), 156.7 (NHCO), 163.3 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 204 (18.2), 237 (30.1), 279 (9.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (22.0), 233 (27.1), 276 (8.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 234 (39.6), 286 (8.3).

Anal. Calcd. for $C_{16}H_{22}N_6O_2S$ (MW 362.45): C, 53.02; H, 6.12; N, 23.19; S, 8.85. Found: C, 52.89; H, 6.18; N, 23.05; S, 9.02.

2-Methylthio-7-phenylcarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = methylthio, R^4 = phenyl).

Prepared as 2-morpholino-7-phenylcarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**8**, X = O, R = morpholino, R^4 = phenyl) using 1.18 g (0.005 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]-pyrimidine-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]-pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield: 1.09 g (61%), mp 265-269°; ir: ν C=O = 1657 and 1645 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.60 (s, 3H, SCH_3), 2.76 (t, 2H, CH_2-9), 3.74 (t, 2H, CH_2-8), 4.39 (s, 2H, CH_2-6), 6.95 (t, 1H, *p*-PhH), 7.25 (t, 2H, *m*-PhH), 7.50 (d, 2H, *o*-PhH), 8.80 (s, 1H, NH); cmr (DMSO-d_6): δ ppm 13.4 (SCH_3), 26.4 (C-9), 39.5 (C-8), 40.6 (C-6), 103.8 (C-5a), 119.9 (*o*-Ph), 121.9 (*p*-Ph), 128.1 (*m*-Ph), 140.3 (*s*-Ph), 146.2 (C-9a), 150.7 (C-10a), 154.0 (C-5), 155.0 (CONH), 163.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 203 (27.6), 236 (33.1), 279 (7.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 202 (21.0), 233 (25.5), 275 (7.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 238 (33.9), 282 (7.0).

Anal. Calcd. for $C_{16}H_{16}N_6O_2S$ (MW 356.40): C, 53.92; H, 4.53; N, 23.58; S, 9.00. Found: C, 53.76; H, 4.37; N, 23.55; S, 8.97.

7-(*n*-Butylthiocarbamoyl)-2-morpholino-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = *n*-butylthiocarbamoyl).

A mixture of 1.11 g (0.004 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R morpholino, R^1 = H), 0.46 g (0.004 mole, 1.40 ml) of *n*-butylisothiocyanate, 3 ml of dimethylformamide and 1 ml of hexamethylphosphoramide was stirred at 130-140° for 8 hours. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with water and acetone, dissolved in hot dimethylformamide and precipitated again with acetonitrile to yield 1.03 g (66%) of 7-(*n*-butylthiocarbamoyl)-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = *n*-butylthiocarbamoyl), mp 243-245°; ir: ν C=O = 1657, ν C=S = 1329 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.89 (t, 3H, CH_3), 1.35 (m, 2H, CH_3CH_2), 1.54 (m, 2H, CCH_2C), 2.62 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.50 (qa, 2H, $NHCH_2$), 3.70 (t, 4H, OCH_2), 4.08 (t, 2H, CH_2-8), 4.54 (s, 2H, CH_2-6), 7.95 (t, 1H, NH); cmr (DMSO-d_6), δ ppm 13.5 (CH_3), 19.4 (CH_3CH_2), 25.8 (C-9), 30.5 (CCH_2C), 43.2* (C-8), 43.6* (C-6), 45.0 (CH_2NH), 45.7 (NCH_2), 65.5 (OCH_2), 103.4 (C-5a), 144.4 (C-9a), 149.6 (C-10a), 154.0 (C-5), 164.3 (C-2), 181.8 (C=S); uv (ethanol): λ max nm (ϵ. 10^{-3}) 200 (22.1), 238 (37.5), 279 sh (9.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 200 (21.9), 232 (30.1), 276 (9.4); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 238 (47.2), 283 (9.1).

Anal. Calcd. for $C_{17}H_{25}N_7O_2S$ (MW 391.48): C, 52.16; H, 6.44; N, 25.04; S, 8.19. Found: C, 51.96; H, 6.32; N, 25.16; S, 8.02.

7-Allylthiocarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = allylthiocarbamoyl).

A mixture of 0.83 g (0.003 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.30 g (0.003 mole, 0.29 ml) of allylisothiocyanate, 3 ml of dimethylformamide and 1 ml of hexamethylphosphoramide was stirred at 130-140° for 4 hours. After standing overnight at room temperature 25 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with water and acetonitrile, dissolved in 3 ml of hot dimethylformamide and precipitated again with 13 ml of dioxane to yield 0.64 g (57%) of 7-allylthiocarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = allylthiocarbamoyl), mp 237-238°; ir: ν C=O = 1665 cm^{-3}, ν C=S = 1325 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.72 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 4.10 (t, 2H, CH_2-8), 4.12 (d, 2H, $NHCH_2$), 4.58 (s, 2H, CH_2-6), 5.16 (d, 2H, CH_2=), 5.90 (m, 1H, CH), 8.12 (t, 1H, CSNH), 13.0 (s, 1H, NH-10); cmr (DMSO-d_6): δ ppm 25.8 (C-9), 43.3* (C-8), 43.7* (C-6), 45.7 (NCH_2), 49.4 ($NHCH_2$), 65.4 (OCH_2), 103.4 (C-5a), 115.2 (CH_2=), 135.2 (CH), 144.3 (C-9a), 149.6 (C-10a), 153.9 (C-5), 164.3 (C-2), 182.0 (C=S); uv (ethanol): λ max nm (ϵ. 10^{-3}) 204 (19.1), 238 (34.3), 282 sh (8.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 202 (18.2), 232 (31.8), 278 sh (7.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 236 (36.9), 284 (9.2).

Anal. Calcd. for $C_{16}H_{21}N_7O_2S$ (375.45): C, 51.19; H, 5.64; N, 26.11; S, 8.54. Found: C, 51.12; H, 5.69; N, 26.07; S, 8.65.

2-Morpholino-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = phenyl).

A mixture of 1.11 g (0.004 mole) of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), 0.55 g (0.004 mole) of phenylisothiocyanate, 2 ml of dimethylformamide and 3 ml of hexamethylphosphoramide was stirred at 120-130° for 45 minutes. After standing overnight at room temperature 30 ml of water was added to the reaction mixture, the crystals which precipitated were filtered off, washed with water, dissolved in 4 ml of hot dimethylformamide and precipitated again with 8 ml of acetonitrile to yield 1.42 g (86%) of 2-morpholino-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = phenyl), mp 251-252°; ir: ν C=O = 1657 cm^{-1}, ν C=S = 1325 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.81 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.72 (t, 4H, OCH_2), 4.20 (t, 2H, CH_2-8), 4.73 (s, 2H, CH_2-6), 7.32 (m, 4H, *o*- and *m*-Ph), 7.51 (b, 1H, *p*-Ph), 9.62 (s, 1H, CSNH); cmr (DMSO-d_6): δ ppm 25.8 (C-9), 44.0* (C-8), 44.3* (C-6), 45.8 (NCH_2), 65.5 (OCH_2), 103.3 (C-5a), 124.1 (*p*-Ph), 125.0 (*o*-Ph), 127.7 (*m*-Ph), 140.8 (*s*-Ph), 144.3 (C-9a), 149.6 (C-10a), 154.0 (C-5), 164.4 (C-2), 182.3 (C=S); uv (ethanol): λ max nm (ϵ. 10^{-3}) 202 (26.8), 237 (30.7), 278 (11.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 201 (28.3), 228 (32.1), 273 sh (11.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 238 (36.7), 282 (9.3).

Anal. Calcd. for $C_{19}H_{21}N_7O_2S$ (MW 411.48): C, 55.46; H, 5.14; N, 23.83; S, 7.79. Found: C, 55.34; H, 5.32; N, 23.98; S, 7.92.

7-(2,6-Dimethylphenylthiocarbamoyl)-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = 2,6-dimethylphenyl).

Prepared as 2-morpholino-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = phenyl) using 0.49 g (0.003 mole) of 2,6-dimethylphenylisothiocyanate instead of phenylisothiocyanate, yield, 0.98 g (74%), mp 247-248°; ir: ν C=O = 1666 cm^{-1}, ν C=S = 1321 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.12 (s, 6H, CH_3), 2.80 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 4.18 (t, 2H, CH_2-8), 4.78 (s, 2H, CH_2-6), 7.05 (m, 3H, *m*-, *p*-PhH), 9.02 (s, 1H, CSNH), 13.0 (bs, 1H, NH-10); cmr (DMSO-d_6): δ ppm 18.1 (CH_3), 26.0 (C-9), 43.7 (C-8), 44.7 (C-6), 45.9 (NCH_2), 65.7 (OCH_2), 103.8 (C-5a), 126.5 (*m*-Ph), 127.7 (*p*-Ph), 136.5 (*o*-Ph), 138.3 (*s*-Ph), 144.6 (C-9a), 149.8 (C-10a), 154.2 (C-5), 164.6 (C-2), 181.5 (C=S); uv (ethanol): λ max nm (ϵ. 10^{-3}) 200 (26.2), 236 (34.7), 277 (10.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ϵ. 10^{-3}) 201 (28.6), 232 (32.2), 273 (10.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ϵ. 10^{-3}) 237 (37.7), 282 (7.8).

Anal. Calcd. for $C_{21}H_{25}N_7O_2S$ (MW 439.54): C, 57.39; H, 5.73; N, 22.31; S, 7.29. Found: C, 57.44; H, 5.82; N, 22.17; S, 7.13.

7-(*n*-Butylthiocarbamoyl)-2-methylthio-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = methylthio, R^4 = *n*-butylthiocarbamoyl).

Prepared as 7-(*n*-butylthiocarbamoyl)-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = *n*-butylthiocarbamoyl) using 0.71 g (0.003 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield 0.69 g (65%), mp 223-225°; ir: ν C=O = 1669 cm^{-1}, ν C=S = 1329 cm^{-1}; pmr (DMSO-d_6): δ ppm 0.89 (t, 3H, CH_3), 1.28 (m, 2H, CH_3CH_2), 1.54 (m, 2H, CCH_2C), 2.59 (s, 3H, SCH_3),

2.75 (t, 2H, CH_2-9), 3.50 (qa, 2H, $NHCH_2$), 4.08 (t, 2H, CH_2-8), 4.57 (s, 2H, CH_2-6), 7.95 (t, 1H, CSNH); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 13.5 (CH_3), 19.4 (CH_3CH_2), 26.0 (C-9), 30.6 (CCH_2C), 43.1* (C-8), 43.5* (C-6), 54.0 ($NHCH_2$), 103.5 (C-5a), 145.9 (C-9a), 150.4 (C-10a), 153.7 (C-2), 163.3 (C-2), 181.8 (C=S); uv (ethanol): λ max nm (ε. 10^{-3}) 202 (16.9), 236 (36.7), 275 (10.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 200 (16.4), 232 (28.4), 274 (9.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 238 (30.0), 283 (10.0).

Anal. Calcd. for $C_{14}H_{20}N_6OS_2$ (MW 352.48): C, 47.71; H, 5.72; N, 23.84; S, 18.19. Found: C, 47.65; H, 5.68; N, 23.80; S, 18.24.

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

Prepared as 7-allylthiocarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**7**, X = S, R = morpholino, R^4 = allylthiocarbamoyl) using 1.18 g (0.005 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield 0.42 g (25%), mp 221-224°; ir: ν C=O = 1676 cm^{-1}, ν C=S = 1323 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.60 (s, 3H, SCH_3), 2.80 (t, 2H, CH_2-9), 4.10 (t, 2H, CH_2-8), 4.25 (d, 2H, $NHCH_2$), 4.67 (s, 2H, CH_2-6), 5.10 (d, 2H, CH_2=), 5.90 (m, 1H, CH), 8.20 (t, 1H, CSNH); cmr (DMSO-d_6): δ ppm 13.3 (SCH_3), 26.0 (C-9), 43.3* (C-8), 43.7* (C-6), 47.6 ($NHCH_2$), 103.5 (C-5a), 115.2 (CH_2=), 135.2 (CH), 145.5 (C-9a), 150.4 (C-10a), 153.7 (C-5), 163.3 (C-2), 182.0 (C=S); uv (ethanol): λ max nm (ε. 10^{-3}) 203 (23.3), 236 (38.0), 278 (9.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 201 (16.4), 233 (27.6), 276 (6.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 235 (34.1), 283 (9.0).

Anal. Calcd. for $C_{13}H_{16}N_6OS_2$ (MW 336.43): C, 46.41; H, 4.79; N, 24.98; S, 19.06. Found: C, 46.54; H, 4.88; N, 24.92; S, 18.96.

2-Methylthio-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = methylthio, R^4 = phenyl).

Prepared as 2-morpholino-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = phenylthiocarbamoyl) using 0.95 g (0.004 mole) of 2-methylthio-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = methylthio, R^1 = H) instead of 2-morpholino-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**3**, R = morpholino, R^1 = H), yield, 1.45 g (97%) of 2-methylthio-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = methylthio, R^4 = phenyl), mp 249-252°; ir: ν C=O = 1686 cm^{-1}, ν C=S = 1324 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.59 (s, 3H, SCH_3), 2.75 (t, 2H, CH_2-9), 4.20 (t, 2H, CH_2-8), 4.74 (s, 2H, CH_2-6), 7.32 (m, 4H, *o*- and *m*-Ph), 7.51 (b, 1H, *p*-Ph), 9.60 (s, 1H, CSNH); uv (ethanol): λ max nm (ε. 10^{-3}) 201 (22.4), 238 (26.2), 277 (10.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 202 (23.8), 234 (28.2), 274 (9.9); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 236 (35.2), 282 (9.7).

Anal. Calcd. for $C_{16}H_{16}N_6OS_2$ (MW 372.47): C, 51.60; H, 4.33; N, 22.56; S, 17.22. Found: C, 51.55; H, 4.38; N, 22.51; S, 17.14.

7-Benzoylthiocarbamoyl-2-morpholino-6,7,8,9-tetrahydropyrido-[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = benzoyl).

Prepared as 2-morpholino-7-phenylthiocarbamoyl-6,7,8,9-tetrahydropyrido[4,3-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(10*H*)-one (**9**, X = S, R = morpholino, R^4 = phenyl) using 0.33 g (0.002 mole) of benzoylisothiocyanate instead of phenylisothiocyanate, yield, 0.54 g (61%), mp 305-307°; ir: ν C=O = 1663 cm^{-1}, ν C=S = 1310 cm^{-1}; pmr (DMSO-d_6): δ ppm 2.78 (t, 2H, CH_2-9), 3.40 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 3.75 (t, 2H, CH_2-8), 4.45 (s, 2H, CH_2-6), 7.5 (m, 5H, Ph H); uv (ethanol): λ max nm (ε. 10^{-3}) 201 (23.4), 232 (30.9), 278 (8.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 203 (23.0), 232 (27.2), 274 (6.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 237 (34.5), 284 (7.3).

Anal. Calcd. for $C_{20}H_{21}N_7O_3S$ (MW 439.49): C, 54.66; H, 4.82; N, 22.31; S, 7.29. Found: C, 54.72; H, 5.02; N, 22.21; S, 7.22

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