On Triazoles XXIV [1]. Synthesis of Cycloalka[1,2,4]triazolo[1,5-*a*]pyrimidinones [2]

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The uv and nmr spectral data of some 6,7,8,9,10,11-hexahydrocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one, 5,6,7,8,9,11-hexahydrocyclohepta[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-10-one, 6,7,8,9,10,11-hexahydrocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one, 5,6,7,8,9,10-hexahydrocycloocta[*e*][1,2,4]triazolo[1,5-*a*]-pyrimidin-11(12*H*)-one, 6,7,8,9,10,11,12,13,14,15-decahydrocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one and 5,6,7,8,9,10,11,12,13,14-decahydrocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one as well as their *N*-benzylated derivatives representing six novel ring systems were compared to prove their structure. The *N*-benzylation of the highly insoluble cyclic amides to yield the isomeric *N*-benzyl derivatives **3/1**, **3/2** and **3/3** distinguished by INAPT was performed through their readily soluble tetrabutylammonium salts.

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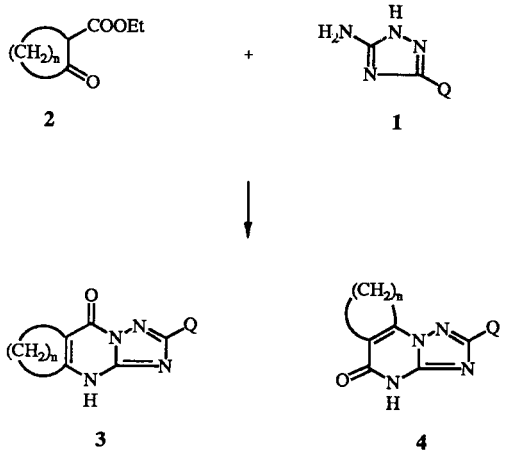
Recently we have discussed the reaction of 5-amino-3-Q-1*H*-1,2,4-triazoles **1** with alkyl 2-oxocyclopentanecarboxylates **2** (n = 3) [3] and alkyl 2-oxocyclohexanecarboxylates **2** (n = 4) [4] to yield in the acetic acid the corresponding 2-Q-6,7,8,9-tetrahydrocyclopenta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one **3** (n = 3) and 2-Q-6,7,8,9-tetrahydro[1,2,4]triazolo[5,1-*b*]quinazoline-5(10*H*)-one **3** (n = 4) derivatives as main products, besides a small amount of the corresponding isomeric 2-Q-5,6,7,9-tetrahydrocyclopenta[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-8-one **4** (n = 3) and 2-Q-5,6,7,8-tetrahydro[1,2,4]triazolo[1,5-*a*]quinazolin-9(10*H*)-one **4** (n = 4) derivatives, respectively (Scheme 1).

Scheme 1

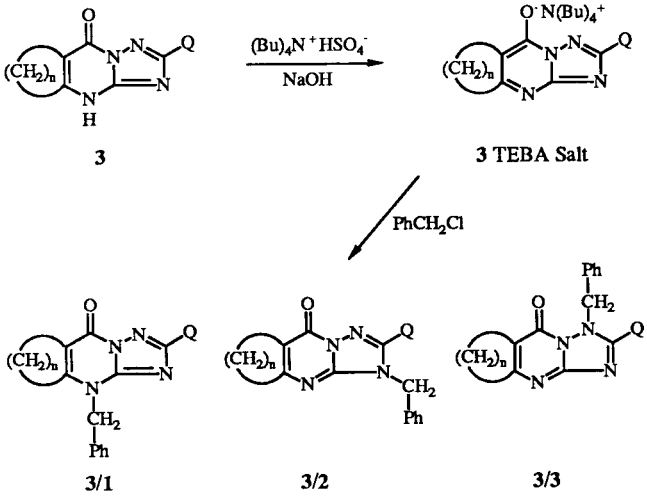


It was also shown [5] that the **3** type derivatives could be easily differentiated from the corresponding isomers **4** on the basis of their uv spectra taken in neutral conditions (*e.g.* in methanol or ethanol) which are characterised with two absorption bands appearing at about 230 and 270 nm, and at about 208 and 290 nm, respectively. A safe differentiation between derivatives **3** and **4** made also possible the cmr spectra [5] in which the triazole carbon atoms 2 appeared with the chemical shifts of about 163 ppm while the carbonyl bands of the "ring acylated" derivatives **3** appeared at about 154 ppm and those of the "acylamino" derivatives **4** at about 160 ppm, respectively. The above uv and cmr rules were corroborated by all **3** and **4** type condensed ring derivatives having a five- and six-membered homo-, or heterocyclic ring attached to the triazolo[1,5-*a*]-pyrimidinone ring system prepared thus far [1,3-7] with the exception of the uv spectra of those compounds where a free electron pair [1,3] or a double bond system [4] was conjugated to the triazolo[1,5-*a*]pyrimidinone chromophore causing a batochromic shift of their uv spectra.

However, the question arose, whether the above uv and cmr rules also work in case of such cycloalka[1,2,4]triazolo-[1,5-*a*]pyrimidinone ring systems in which a more flexible seven, eight or twelve membered cycloalkane ring was attached to the triazolo[1,5-*a*]pyrimidinone moiety?

Thus the 5-amino-3-(methylthio and morpholino)-1*H*-1,2,4-triazoles **1** (Q = methylthio and morpholino) were reacted in acetic acid with ethyl 2-oxocycloheptane **2** (n = 5), 2-oxocyclooctane **2** (n = 6) and 2-oxocyclododecane **2** (n = 10) carboxylates to yield as main products the corresponding **3** type 6,7,8,9,10,11-hexahydrocyclohepta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (n = 5), 6,7,8,9,10,11-hexahydrocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (n = 6), and 6,7,8,9,10,11,12,13,14,15-decahydrocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (n = 10) derivatives, respectively. The corresponding type **4** isomers that formed as minor products of these reactions could be in each case detected by tlc but were

Scheme 2



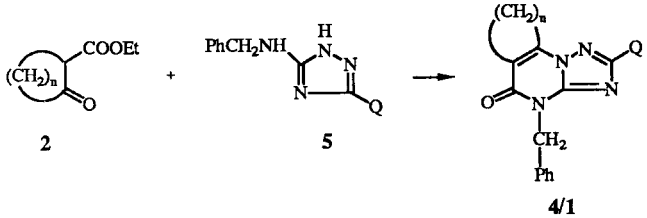
3 3 TEBA Salt

3/1 3/2 3/3

not isolated. However, simple melting of **1** (Q = methylthio) with ethyl 2-oxocyclododecanecarboxylate **2** (n = 10) led to a mixture of **3** (Q = methylthio, n = 10) and **4** (Q = methylthio, n = 10) more rich in **4** (Q = methylthio, n = 10) giving a possibility to isolate both isomers from this reaction mixture.

The spectra of derivatives obtained followed again nicely our uv and cmr rules [5] disscussed above. Thus the pairs of the uv maxima of all type **3** derivatives appeared between 232-234 and 272-278 nm, respectively, while the maxima of derivative **4** (Q = methylthio, n = 10) appeared at 206 and 290 nm. In the cmr spectra the triazole carbon atoms 2 of all derivatives appeared between 162.4 and 164.5 ppm, while the carbonyl groups of derivatives **3** were characterised with the chemical shifts appearing between 155.0-156.1 ppm and that of derivative **4** (Q = methylthio, n = 10) was characterized with the chemical shift of 161.5 ppm.

Scheme 3



2 5 4/1

To prove the tautomeric structure of derivatives **3** we tried to alkylate them by known methods [1,3-7] through their sodium salts. However, their terrible solubility even as sodium salts prompted us to elaborate a new method for their alkylation. It was known [8] that different CH-acid derivatives like enolates, β-diketones and β-cyanoacetates could be simply extracted as ion pairs in the form of tetrabutylammonium salts into chloroform or methylene chloride. This fact prompted us to convert the above cyclic amides into their tetrabutylammonium salts which led also to well soluble ionic enolates that could be easily extracted into chloroform and after evaporation of chloroform benzylated in acetonitrile as solvent to the mixture of the corresponding 1-benzyl **3/2**, 3-benzyl **3/3** and ω-benzyl **3/1** derivatives (Scheme 2), derivatives **3/1** being always the main products of the reaction. Isolation of all three benzylated 6,7,8,9,10,11,12,13,14,15-decahydrocyclododeca-[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one isomers **3/1**, **3/2**, **3/3** (Q = methylthio, n = 10, respectively) which were distinguished by INAPT method based on the irradiation of the cmr spectra with the pmr chemical shifts of the methylthio and benzyl CH_2 group (standard Bruker INAPT program was used) helped to prove on the basis of the identity of the uv spectra of the non-alkylated derivatives **3** and the corresponding ω-alkylated derivatives **3/1** the ω*H* dominant tautomeric structure of derivatives **3** in DMSO and ethanolic solutions. As expected the uv and cmr spectra of derivatives **3/1** followed again nicely the rules elaborated recently [5]. It should be mentioned that the observed essential differences among the uv and cmr spectra of the three possible *N*-benzyl isomers **3/1**, **3/2**, and **3/3**, respectively, gave a further proof for the validity of our earlier conclusions regarding the structure proving power of these spectral data, as well as the dominant tautomeric structures of all **3** type derivatives prepared previously [1,3-7].

The isomeric type **4** derivatives were prepared by simple melting of the corresponding 2-oxocycloalkanecarboxylates **2** (n = 5, 6 and 10, respectively) with 5-benzylamino-3-(methylthio and morpholino)-1*H*-1,2,4-triazoles **5** (Q = methylthio and morpholino) to yield as main product the corresponding ω-benzyl derivatives **4/1** (n = 5, 6, and 10). Their uv maxima (206-207 and 290-314 nm) and cmr data (δ C-2 = 162.4-164.4 and δ C=O = 159.2-160.2) were again in accordance with that of expected [5] proving their structure unequivocally. The analogy of the uv spectra of **4** (Q = methylthio, n = 10) (λ max = 206 and 290 nm) and **4/1** (Q = methylthio, n = 10) (λ max = 207 and 291 nm) proved again the 16*H* dominant tautomeric stucture of **4** (Q = methylthio, n = 10) in DMSO and ethanolic solutions.

Similarly to the alkylation experiments of derivatives **3**, **4/1** (Q = methylthio, n = 10) was also prepared by the benzylation of the tetrabutylammonium salt of **4** (Q = methylthio, n = 10).

It is worth mentioning that the full assignment of the methylene protons and carbon atoms of the 11-benzyl-6,7,8,9,10,11-hexahydrocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]-pyrimidin-5-ones and 11-benzyl-5,6,7,8,9,11-hexahydrocyclohepta[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-10-ones by 2D-nmr (standard Bruker COSY program was used) led to an unexpected result, namely that the flexible cyclo-

heptene ring should be twisted to cause a sterical closeness of the carbonyl group and the methylene groups 8 or 7, respectively, to cause a strong upfield shift of the corresponding methylene protons and carbon atoms in the pmr and cmr spectra.

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained by a Pye Unicam SP 8-150 instrument. The ^{1}H-nmr and the ^{13}C-nmr measurements were performed using Bruker WM-250 instrument. The ms spectra were recorded using a Kratos MS 25RFA instrument at 70 eV (Cl and El mode). All tlc determinations were performed on DC-Alufolien Kieselgel 60 F_{254} (Merck) plates. The spots were detected by uv.

6,7,8,9,10,11-Hexahydro-2-methylthiocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = methylthio, n = 5).

The mixture of 13.02 g (0.1 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [9], 18.42 g (0.1 mole) of ethyl 2-oxocycloheptanecarboxylate (**2**, n = 5) [10] and 30 ml of acetic acid was refluxed for 3 hours. The solution obtained during the reaction crystallised while hot. After cooling the crystals were collected, washed with acetic acid and acetone to yield 21.38 g (85%) of 6,7,8,9,10,11-hexahydro-2-methythiocyclohepta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = methylthio, n = 5) which after recrystallisation from dimethylformamide melted at 289-294° dec. Further reflux of the mother liquor for 5 hours yielded a second crop (1.20 g, 5%) of the title crystals, mp 277-286° dec; ir: 1660 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.47 (qi, 2H, CH_2-9), 1.60 (qi, 2H, CH_2-7), 1.74 (qi, 2H, CH_2-8), 2.52 (s, 3H, SCH_3), 2.66 (dt, 4H, CH_2-6 and 10), 12.7 (bs, 1H, NH); cmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 13.2 (SCH_3), 23.1 (C-6), 24.7 (C-9), 26.0 (C-7), 31.2 (C-10), 32.4 (C-8), 110.9 (C-5a), 149.3 (C-11a), 152.1 (C-10a), 155.4 (C=O), 163.5 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 233 (25.6), 274 (9.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 233 (26.2), 274 (11.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 287 (9.9); ms: M^+ = 250.

Anal. Calcd. for $C_{11}H_{14}N_4OS$ (MW. 250.32): C, 52.78; H, 5.64; N, 22.38; S, 12.81. Found: C, 52.53; H, 5.71; N, 22.30; S, 12.78.

11-Benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3/1**, Q = methylthio, n = 5).

To a solution of 1.70 g (0.005 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water the solution of 0.40 g (0.01 mole) of sodium hydroxide in 5 ml of water was added keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 1.25 g (0.005 mole) of 6,7,8,9,10,11-hexahydro-2-methylthiocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]-pyrimidin-5-one (**3**, Q = methylthio, n = 5). To the solution obtained 10 ml of chloroform was added, the mixture was stirred for 5 minutes, the phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 2.46 g (~ 100%) of 6,7,8,9,10,11-hexahydro-2-methylthiocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = methylthio, n = 5) tetrabutylammonium salt (mp 127-138°). This was dissolved in 5 ml of acetonitrile, to the solution obtained 0.95 g (0.86 ml ~ 0.0075 mole) of benzyl chloride was added and refluxed for 60 minutes. After cooling the crystals precipitated were filtered off and washed with cold acetonitrile to yield 0.89 g (52%) of 11-benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3/1**, Q = methylthio, n = 5), mp 201-202° (from acetonitrile); ir: ν C=O = 1690 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.22 (m, 2H, CH_2-9), 1.46 (m, 2H, CH_2-7), 1.65 (m, 2H, CH_2-8), 2.61 (s, 3H, SCH_3), 2.77 (m, 4H, CH_2-6 and 10), 5.48 (s, 2H, $PhCH_2$), 7.08 (dd, J = 7 and 1.5 Hz, 2H, *o*-PhH), 7.18-7.35 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ, ppm 13.8 (SCH_3), 24.1 (C-6), 24.3 (C-9), 25.9 (C-7), 29.3 (C-10), 31.3 (C-8), 51.1 ($PhCH_2$), 114.6 (C-5a), 126.2 (*o*-Ph), 128.0 (*p*-Ph), 128.9 (*m*-Ph), 135.0 (*s*-Ph), 152.0 (C-11a), 153.3 (C-10a), 154.9 (C=O), 164.5 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 238 (27.7), 284 (7.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 239 (27.5), 285 (13.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 286 (12.2).

Anal. Calcd. for $C_{18}H_{20}N_4OS$ (MW. 340.44): C, 63.50; H, 5.92; N, 16.46; S, 9.42. Found: C, 63.34; H, 5.80; N, 16.46; S, 9.49.

11-Benzyl-5,6,7,8,9,11-hexahydro-2-methylthiocyclohepta[*e*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-10-one (**4/1**, Q = methylthio, n = 5).

The mixture of 0.88 g (0.004 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [11] and 1.00 g (0.0054 mole) of ethyl 2-oxocycloheptanecarboxylate (**2**, n = 5) [10] was heated to 180-190° for 10 minutes. To the still hot yellow melt obtained 6 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 0.97 g (71%) of 11-benzyl-5,6,7,8,9,11-hexahydro-2-methylthiocyclohepta[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-10-one (**4/1**, Q = methylthio, n = 5), mp 132-133° (acetonitrile); ir: ν C=O = 1659 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.60 (qi, 2H, CH_2-8), 1.73 (m, 2H, CH_2-6), 1.83 (m, 2H, CH_2-7), 2.61 (s, 3H, SCH_3), 2.82 (m, 2H, CH_2-9), 3.20 (m, 2H, CH_2-5), 5.33 (s, 2H, $PhCH_2$), 7.15-7.35 (m, 3H, *m*- and *p*-PhH), 7.55 (dd, J = 8 Hz and 2 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 14.1 (SCH_3), 24.5 (C-6), 24.8 (C-9), 25.9 (C-8), 27.9 (C-5), 31.3 (C-7), 47.1 ($PhCH_2$), 117.7 (C-9a), 127.9 (*p*-Ph), 128.3 (*m*-Ph), 129.3 (*o*-Ph), 135.6 (*s*-Ph) 148.5 (C-4a), 149.7 (C-11a), 159.6 (C=O), 162.4 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 206 (26.2), 225 sh (12.2), 296 (8.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 204 (31.0), 225 sh (10.9), 295 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 291 (11.7).

Anal. Calcd. for $C_{18}H_{20}N_4OS$ (MW. 340.44): C, 63.50; H, 5.92; N, 16.46; S, 9.42. Found: C, 63.64; N, 5.90; N, 16.66; S, 9.38.

6,7,8,9,10,11-Hexahydro-2-morpholinocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = morpholino, n = 5).

The mixture of 3.38 g (0.02 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [12], 3.68 g (0.02 mole) of ethyl 2-oxocycloheptanecarboxylate (**2**, n = 5) [10] and 6 ml of acetic acid was refluxed for 2 hours. The solution obtained during the reaction crystallised while hot. After cooling the crystals precipitated were filtered off, washed with acetic acid and acetone to yield 4.51 g (78%) of 6,7,8,9,10,11-hexahydro-2-morpholinocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = morpholino, n = 5) which after recrystallisation from dimethylformamide melted at 337-347° dec. The mother liquor afforded

after standing for several hours a further crop (0.31 g, 5%) of the above material, mp 335-347° dec; ir; ν C=O = 1648 cm^{-1}; pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 1.45 (qi, 2H, CH_2-9), 1.58 (qi, 2H, CH_2-7), 1.74 (qi, 2H, CH_2-8), 2.67 (dt, 4H, CH_2-6 and 10), 3.40 (t, 4H, NCH_2), 3.65 (t, 4H, OCH_2), 12.4 (bs, 1H, NH); pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 23.1 (C-6), 24.8 (C-9), 26.1 (C-7), 31.3 (C-10), 32.2 (C-8), 45.4 (NCH_2), 65.4 (OCH_2), 110.9 (C-5a), 148.6 (C-11a), 150.6 (C-10a), 155.8 (C=O), 164.3 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 233 (29.2), 278 (8.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 232 (27.9), 272 (10.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 286 (8.3).

Anal. Calcd. for $C_{14}H_{19}N_5O_2$ (MW. 289.33): C, 58.11; H, 6.62; N, 24.21. Found: C, 57.96; H, 6.44; N, 24.41.

11-Benzyl-6,7,8,9,10,11-hexahydro-2-morpholinocyclohepta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3/1**, Q = morpholino, n = 5).

To a solution of 1.36 g (0.004 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water the solution of 0.32 g (0.008 mole) of sodium hydroxide in 5 ml of water was added keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 1.16 g (0.004 mole) of 6,7,8,9,10,11-hexahydro-2-morpholinocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = morpholino, n = 5). To the solution obtained 10 ml of chloroform was added, the mixture was stirred for 5 minutes, the phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 2.06 g (~97%) of 6,7,8,9,10,11-hexahydro-2-morpholinocyclohepta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3**, Q = morpholino, n = 5) tetrabutylammonium salt (mp 160-171°). This was dissolved in 5 ml of warm acetonitrile, to the solution obtained 0.76 g (0.69 ml ~ 0.006 mole) of benzyl chloride was added and refluxed for 90 minutes. After cooling the crystals precipitated were filtered off and washed with cold acetonitrile to yield 0.82 g (54%) of 11-benzyl-6,7,8,9,10,11-hexahydro-2-morpholinocyclohepta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**3/1**, Q = morpholino, n = 5), mp 225-227° (from acetonitrile); ir: ν C=O = 1674 cm^{-1}; pmr (deuteriochloroform): δ ppm, 1.27 (m, 2H, CH_2-9), 1.51 (m, 2H, CH_2-7), 1.73 (m, 2H, CH_2-8), 2.78 (t, 2H, CH_2-6), 2.84 (t, 2H, CH_2-10), 3.58 (t, 4H, NCH_2), 3.78 (t, 4H, OCH_2), 5.52 (s, 2H, $PhCH_2$), 7.16 (dd, J = 7.5 and 1.6 Hz, 2H, *o*-PhH), 7.15-7.40 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ ppm 24.2 (C-6), 24.6 (C-9), 26.1 (C-7), 29.3 (C-10), 31.5 (C-8), 46.1 (NCH_2), 51.0 ($PhCH_2$), 66.3 (OCH_2), 114.8 (C-5a), 126.3 (*o*-Ph), 128.0 (*p*-Ph), 129.0 (*m*-Ph), 135.6 (*s*-Ph), 151.6* (C-11a), 151.7* (C-10a), 155.4 (C=O), 164.6 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 238 (28.8), 284 (11.2); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 238 (30.0), 284 (12.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 286 (12.6).

Anal. Calcd. for $C_{21}H_{25}N_5O_2$ (MW. 379.45): C, 66.47; H, 6.64; N, 18.46. Found: C, 66.61; H, 6.36; N, 18.62.

11-Benzyl-5,6,7,8,9,11-hexahydro-2-morpholinocyclohepta[*e*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-10-one (**4/1**, Q = morpholino, n = 5).

The mixture of 0.985 g (0.0038 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole (**5**, Q = morpholino) [5] and 0.87 g (0.0047 mole) of ethyl 2-oxocycloheptanecarboxylate (**2**, n = 5) [10] was heated to 180-190° for 10 minutes. To the still hot yellow melt obtained 10 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 1.10 g (76%) of 11-benzyl-5,6,7,8,9,11-hexahydro-2-morpholinocyclohepta[*e*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-10-one (**4/1**, Q = morpholino, n = 5), mp 151-153° (acetonitrile); ir: ν C=O = 1661 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.60 (m, 2H, CH_2-8), 1.73 (m, 2H, CH_2-6), 1.84 (m, 2H, CH_2-7), 2.81 (t, 2H, CH_2-9), 3.14 (t, 2H, CH_2-5), 3.49 (t, 4H, NCH_2), 3.79 (t, 4H, OCH_2), 5.31 (s, 2H, $PhCH_2$), 7.27 (m, 3H, *m*- and *p*-PhH), 7.57 (dd, J = 8 Hz and 2 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 24.8 (C-6), 25.0 (C-9), 26.4 (C-8), 28.1 (C-5), 31.6 (C-7), 46.3 (NCH_2), 47.1 ($PhCH_2$), 66.4 (OCH_2), 115.9 (C-9a), 127.8 (*p*-Ph), 128.4 (*m*-Ph), 129.3 (*o*-Ph), 136.2 (*s*-Ph), 149.0 (C-4a), 149.2 (C-11a), 159.9 (C=O), 164.2 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 206 (27.9), 216 sh (11.5), 314 (8.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 205 (30.6), 216 (12.8), 311 (9.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 302 (11.1).

Anal. Calcd. for $C_{21}H_{25}N_5O_2$ (MW. 379.45): C, 66.47; H, 6.64; N, 18.46. Found: C, 66.70; H, 6.78; N, 18.27.

6,7,8,9,10,11-Hexahydro-2-methylthiocycloocta[*d*][1,2,4]triazolo-[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = methylthio, n = 6).

The mixture of 2.60 g (0.02 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [9], 3.97 g (0.02 mole) of ethyl 2-oxocyclooctanecarboxylate (**2**, n = 6) [13] and 6 ml of acetic acid was refluxed for 1 hour. The solution obtained during the reaction crystallised while hot. After cooling the crystals were collected, washed with acetic acid and acetone to yield 1.85 g (35%) of 6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = methylthio, n = 6) which after recrystallisation from dimethylformamide melted at 300-308° dec. Further reflux of the mother liquor for 6 hours yielded a second crop (0.90 g, 17%) of the title product, mp 288-293° dec; ir: ν C=O = 1659 cm^{-1}; pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 1.37 (m, 4H, CH_2-8 and 9), 1.58* (m, 2H, CH_2-10), 1.70* (m, 2H, CH_2-7), 2.54 (s, 3H, SCH_3), 2.60* (m, 2H, CH_2-6), 2.69* (m, 2H, CH_2-11), 12.7 (bs, 1H, NH); cmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 13.2 (SCH_3), 22.7, 25.0, 25.5, 28.7, 28.8, 29.0, (C-6 - C-11), 108.8 (C-5a), 149.0 (C-12a), 149.9 (C-11a), 155.0 (C=O), 163.4 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 234 (26.8), 274 (10.6); uv (10% ethanol + 90% 0.1 *N*-hydrochloric acid): λ max nm (E.10^{-3}) 234 (25.7), 274 (11.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 290 (10.7); ms: M^+ = 264.

Anal. Calcd. for $C_{12}H_{16}N_4OS$ (MW. 264.35): C, 54.52; H, 6.10; N, 21.20; S, 12.13. Found: C, 54.50; H, 5.99; N, 21.14; S, 12.39.

1-Benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-5(1*H*)-one (**3/2**, Q = methylthio, n = 6), and 12-Benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin5(12*H*)-one (**3/1**, Q = methylthio, n = 6).

To a solution of 1.36 g (0.004 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water a solution of 0.32 g (0.008 mole) of sodium hydroxide in 5 ml of water was added with cooling and stirring keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 1.06 g (0.004 mole) of 6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]-triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = methylthio, n = 6). To the solution obtained 10 ml of chloroform was added and the mixture was stirred for 5 minutes. The phases were separated,

the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.99 g (98%) of 6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]triazolo-[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = methylthio, n = 6) tetrabutylammonium salt (mp 100-110°). This was dissolved in 5 ml of acetonitrile, to the solution obtained 0.76 g (0.69 ml ~ 0.006 mole) of benzyl chloride was added and refluxed for 80 minutes.

After cooling the crystals precpitated were filtered off and washed with cold acetonitrile to yield 0.38 g (27%) of 1-benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]triazolo-[1,5-a]pyrimidin-5(1*H*)-one (**3/2**, Q = methylthio, n = 6) which after two recrystallisations from benzene melted at 223-224°; ir: ν C=O = 1662 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.43 (m, 4H, CH_2-8 and 9), 1.75 (m, 4H, CH_2-7 and 10), 2.76 (s, 3H, SCH_3), 2.82 (t, 4H, CH_2-6 and 11), 5.15 (s, 2H, $PhCH_2$), 7.34-7.36 (m, 5H, PhH); cmr (deuteriochloroform): δ, ppm 13.8 (SCH_3), 24.3, 26.1, 26.4, 29.5, 30.0, 34.8 (C-6-11), 46.3 ($PhCH_2$), 114.6 (C-5a), 128.2 (*o*-Ph), 128.6 (*p*-Ph), 128.8 (*m*-Ph), 133.8 (*s*-Ph), 147.7 (C-12a), 153.3 (C-2), 155.9 (C=O), 163.4 (C-11a); uv (ethanol): λ max nm ($E.10^{-3}$) 215 sh (22.5), 227 (25.7), 290 (12.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 215 sh (9.3), 232 (12.0), 286 (10.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 284 (5.0); ms: M^+ = 354.

Anal. Calcd. for $C_{19}H_{22}N_4OS$ (MW. 354.47): C, 64.37; H, 6.26; N, 15.81; S, 9.05. Found: C, 64.42; H, 6.35; N, 15.88; S, 8.99.

The mother liquor crystallised upon standing again to yield 0.38 g (27%) of 12-benzyl-6,7,8,9,10,11-hexahydro-2-methylthiocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3/1**, Q = methylthio, n = 6) which after recrystallisation from ethyl acetate melted at 167.5-169°; ir: ν C=O = 1692 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.45 (m, 4H, CH_2-8 and 9), 1.70 (m, 4H, CH_2-7 and 10), 2.68 (s, 3H, SCH_3), 2.79 (q, 4H, CH_2-6 and 11), 5.50 (s, 2H, $PhCH_2$), 7.11 (dd, J = 7 and 2 Hz, 2H, *o*-PhH), 7.25-7.40 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ, ppm 14.0 (SCH_3), 25.2 (C-6), 25.7 (C-10), 26.7 (C-8), 27.2 (C-7), 29.0 (C-11), 29.2 (C-9), 50.8 ($PhCH_2$), 113.2 (C-5a), 126.1 (*o*-Ph), 128.1 (*p*-Ph), 129.1 (*m*-Ph), 135.4 (*s*-Ph), 149.2 (C-12a), 152.5 (C-11a), 154.8 (C=O), 164.8 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 239 (26.3), 284 (11.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 239 (26.9), 285 (12.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 285 (11.2); ms: M^+ = 354.

Anal. Calcd. for $C_{19}H_{22}N_4OS$ (MW. 354.47): C, 64.37; H, 6.26; N, 15.81; S, 9.05. Found: C, 64.22; H, 6.25; N, 15.81; S, 9.09.

The mother liquors were evaporated *in vacuo* to dryness, the oily residue obtained was dissolved in chloroform, extracted with water, dried over anhydrous sodium sulfate, evaporated *in vacuo* to dryness and triturated with a small amount of diethyl ether containing some drops of acetonitrile to yield after filtration a further crop (0.20 g, 14%) of (**3/1**, Q = methylthio, n = 6), mp 165-169°.

12-Benzyl-5,6,7,8,9,10-hexahydro-2-methylthiocycloocta[*e*][1,2,4]-triazolo[1,5-*a*]pyrimidin-11(12*H*)-one (**4/1**, Q = methylthio, n = 6).

The mixture of 0.88 g (0.004 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**5**, Q = methylthio) [11] and 1.67 g (0.0084 mole) of ethyl 2-oxocyclooctanecarboxylate (**2**, n = 6) [13] was heated to 180-190° for 15 minutes. To the still hot yellow melt obtained 10 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 1.18 g (83%) of 12-benzyl-5,6,7,8,9,10-hexahydro-2-methylthiocycloocta[*e*][1,2,4]triazolo-[1,5-*a*]pyrimidin-11(12*H*)-one (**4/1**, Q = methylthio, n = 6), mp 136-137° (acetonitrile); ir: ν C=O = 1664 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.47 (m, 4H, CH_2-7 and 8), 1.70 (m, 2H, CH_2-9), 1.84 (m, 2H, CH_2-6), 2.62 (s, 3H, SCH_3), 2.71 (t, 2H, CH_2-10), 3.09 (t, 2H, CH_2-5), 5.35 (s, 2H, $PhCH_2$), 7.15-7.35 [m, 3H, *m*- and *p*-PhH], 7.55 (dd, J = 6.5 Hz and 1.3 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 14.1 (SCH_3), 24.4 (C-6), 26.0 (C-7), 26.1 (C-10), 26.3 (C-9), 27.8 (C-5), 29.3 (C-8), 46.9 ($PhCH_2$), 115.4 (C-10a), 127.9 (*p*-Ph), 128.3 (*m*-Ph), 129.1 (*o*-Ph), 135.6 (*s*-Ph), 145.8 (C-4a), 150.0 (C-12a), 159.2 (C=O), 162.6 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 206 (28.1), 226 sh (12.6), 290 (9.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 204 (30.4), 226 sh (11.2), 290 (9.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 288 (10.9).

Anal. Calcd. for $C_{19}H_{22}N_4OS$ (MW. 354.47): C, 64.37; H, 6.26; N, 15.81; S, 9.05. Found: C, 64.17; H, 6.07; N, 15.72; S, 9.07.

6,7,8,9,10,11-Hexahydro-2-morpholinocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = morpholino, n = 6).

The mixture of 3.38 g, (0.02 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [12], 3.97 g (0.02 mole) of ethyl 2-oxocyclooctanecarboxylate (**2**, n = 6) [13] and 6 ml of acetic acid was refluxed for 4 hours. The solution obtained during the reaction crystallised while hot. After cooling the crystals precipitated were filtered off, washed with acetic acid and acetone to yield 3.02 g (50%) of 6,7,8,9,10,11-hexahydro-2-morpholinocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = morpholino, n = 6) which after recrystallisation from dimethylformamide melted at 332-343° dec. Further boiling of the mother liquor for 3 hours afforded a second crop (0.45 g, 7%) of the above material, mp 332-341° dec; ir: ν C=O = 1652 cm^{-1}; pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 1.35 (m, 4H, CH_2-8 and 9), 1.55 (m, 2H, CH_2-10), 1.68 (m, 2H, CH_2-7), 2.58 (t, 2H, CH_2-6), 2.65 (t, 2H, CH_2-11), 3.42 (t, 4H, NCH_2), 3.67 (t, 4H, OCH_2); cmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 22.7, 25.0, 25.5, 28.8 (two peaks), 28.9 (C-6-C-11), 45.4 (NCH_2), 65.5 (OCH_2), 108.6 (C-5a), 147.6 (C-12a), 149.2 (C-11a), 155.4 (C=O), 162.4 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 233 (29.2), 278 (8.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 232 (27.9), 272 (10.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 286 (8.3).

Anal. Calcd. for $C_{15}H_{21}N_5O_2$ (MW. 303.36): C, 59.38; H, 6.98; N, 23.09. Found: C, 59.12; H, 6.74; N, 23.22.

12-Benzyl-6,7,8,9,10,11-hexahydro-2-morpholinocycloocta[*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3/1**, Q = morpholino, n = 6).

To a solution of 1.19 g (0.0035 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water a solution of 0.28 g (0.007 mole) of sodium hydroxide in 5 ml of water was added with cooling and stirring keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 1.06 g (0.0035 mole) of 6,7,8,9,10,11-hexahydro-2-morpholinocycloocta-[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = morpholino, n = 6). To the solution obtained 10 ml of chloroform was added and the mixture was stirred for 5 minutes, the phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.66 g (87%) of hygroscopic 6,7,8,9,10,11-hexahydro-2-morpholinocycloocta-[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3**, Q = morpholino,

n = 6) tetrabutylammonium salt. This was dissolved in 4 ml of acetonitrile, to the solution obtained 0.63 g (0.58 ml ~0.005 mole) of benzyl chloride was added and refluxed for 80 minutes and evaporated *in vacuo* to dryness. The oily residue obtained was dissolved in chloroform, extracted with water, dried over anhydrous sodium sulfate and evaporated again *in vacuo* to dryness. The oily residue obtained was triturated with a small amount of diethyl ether containing some drops of acetonitrile, the crystals precipitated were filtered off and washed with diethyl ether again containing some drops of acetonitrile to yield 0.66 g (48%) of 12-benzyl-6,7,8,9,10,11-hexahydro-2-morpholinocycloocta[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(12*H*)-one (**3/1**, Q = morpholino, n = 6) which after two recrystallisations from ethyl acetate melted at 192-194°; ir: ν C=O = 1680 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.43 (m, 4H, CH_2-8 and 9), 1.66 (m, 4H, CH_2-7 and 10), 2.75 (m, 4H, CH_2-6 and 11), 3.57 (t, 4H, NCH_2), 3.76 (t, 4H, OCH_2), 5.45 (s, 2H, $PhCH_2$), 7.12 (dd, J = 7 and 2 Hz, 2H, *o*-PhH), 7.25-7.35 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ, ppm 25.2 (C-6), 25.8 (C-10), 26.9 (C-8), 27.0 (C-7), 29.2 (C-11), 29.4 (C-9), 46.2 (NCH_2), 50.7 ($PhCH_2$), 66.5 (OCH_2), 113.4 (C-5a), 126.2 (*o*-Ph), 128.2 (*p*-Ph), 129.1 (*m*-Ph), 135.9 (*s*-Ph), 147.8 (C-12a), 152.0 (C-11a), 155.2 (C=O), 164.8 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 237 (28.8), 282 (12.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 237 (29.4), 282 (12.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 281 (11.4).

Anal. Calcd. for $C_{22}H_{27}N_5O_2$ (MW. 393.48): C, 67.15; H, 6.92; N, 17.80. Found: C, 67.10; H, 6.94; N, 18.00.

12-Benzyl-5,6,7,8,9,10-hexahydro-2-morpholinocycloocta[*e*][1,2,4]-triazolo[1,5-*a*]pyrimidin-11(12*H*)-one (**4/1**, Q = morpholino, n = 6).

The mixture of 1.04 g (0.004 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole (**5**, Q = morpholino) [5] and 1.67 g (0.0084 mole) of ethyl 2-oxocyclooctanecarboxylate (**2**, n = 6) [13] was heated to 180-190° for 15 minutes. To the still hot yellow melt obtained 10 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 1.45 g (92%) of 12-benzyl-5,6,7,8,-9,10-hexahydro-2-morpholinocycloocta[*e*][1,2,4]triazolo[1,5-*a*]-pyrimidin-11(12*H*)-one (**4/1**, Q = morpholino, n = 6), mp 166.5-168° (acetonitrile); ir: ν C=O = 1664 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.46 (m, 4H, CH_2-7 and 8), 1.68 (m, 2H, CH_2-9), 1.82 (m, 2H, CH_2-6), 2.69 (t, 2H, CH_2-10), 3.03 (t, 2H, CH_2-5), 3.50 (t, 4H, NCH_2), 3.80 (t, 4H, OCH_2), 5.32 (s, 2H, $PhCH_2$), 7.15-7.35 (m, 3H, *m*- and *p*-PhH), 7.54 (dd, J = 6 Hz and 1.2 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 24.5 (C-6), 26.2 (C-7 and 10), 26.5 (C-9), 27.8 (C-5), 29.5 (C-8), 46.3 (NCH_2), 46.8 ($PhCH_2$), 66.4 (OCH_2), 113.6 (C-10a), 127.7 (*p*-Ph), 128.3 (*m*-Ph), 129.1 (*o*-Ph), 136.2 (*s*-Ph), 146.3 (C-4a), 149.5 (C-12a), 159.4 (C=O), 164.5 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 206 (28.7), 226 sh (11.4), 311 (8.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 205 (29.6), 224 sh (11.4), 307 (8.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 302 (10.1).

Anal. Calcd. for $C_{22}H_{27}N_5O_2$ (MW. 393.48): C, 67.15; H, 6.92; N, 17.80. Found: C, 67.00; H, 7.02; N, 17.92.

6,7,8,9,10,11,12,13,14,15-Decahydro-2-methylthiocyclododeca-[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = methylthio, n = 10).

The mixture of 2.21 g (0.017 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [9], 5.45 g (0.0214 mole) of ethyl 2-oxocyclododecanecarboxylate (**2**, n = 10) [13] and 6 ml of acetic acid was refluxed for 5 hours. The solution obtained during the reaction crystallised while hot. After cooling the crystals were collected, washed with acetic acid and acetone to yield 1.66 g (30%) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16-*H*)-one (**3**, Q = methylthio, n = 10) which after recrystallisation from a 1:1 mixture of methanol and dimethylformamide melted at 288-294° dec; ir: ν C=O = 1658 cm^{-1}; pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 1.33 (m, 4H, CH_2-10 and 11). 1.39 (m, 4H, CH_2-9 and 12), 1.46 (m, 4H, CH_2-8 and 13), 1.66 (m, 2H, CH_2-14), 1.80 (m, 2H, CH_2-7), 2.59 (t, 2H, CH_2-6), 2.60 (s, 3H, SCH_3), 2.64 (t, 2H, CH_2-15); cmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 13.3 (SCH_3), 21.5, 22.2, 23.0, 24.3, 25.2 (two peaks), 25.6, 25.8, 25.9, 27.5 (C-6 - C-15), 109.5 (C-5a), 149.0 (C-16a), 150.2 (C-15a), 155.7 (C=O), 163.5 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 233 (27.1), 272 (10.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 232 (26.7), 272 (11.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 290 (10.8); ms: M^+ = 320.

Anal. Calcd. for $C_{16}H_{24}N_4OS$ (MW. 320.45): C, 59.97; H, 7.55; N, 17.48; S, 10.01. Found: C, 59.78; H, 7.24; N, 17.44; S, 10.18.

6,7,8,9,10,11,12,13,14,15-Decahydro-2-methylthiocyclododeca-[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = methylthio, n = 10) and 5,6,7,8,9,10,11,12,13,14-Decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4**, Q = methylthio, n = 10).

The mixture of 0.65 g (0.005 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (**1**, Q = methylthio) [9] and 2.03 g (0.008 mole) of ethyl 2-oxocyclododecanecarboxylate (**2**, n = 10) [13] was melted at 180-190° for 10 minutes. The still hot yellow melt obtained was dissolved in 10 ml of 2-propanol and let to crystallise. After cooling the crystals precipitated were collected to yield 1.22 g (76%) of crude product which was the mixture (based on tlc: eluent a 1:1 mixture of cyclohexane and ethyl acetate, R_f = 0.25 and 0.40, respectively) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = methylthio, n = 10) and 5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4**, Q = methylthio, n = 10). This was column chromatographed *in vacuo* on a thick layer made from 5 g of Kieselgel 60 H (Reanal) using a 3:1 mixture of cyclohexane and ethyl acetate as eluent to yield 0.41 g (25%) of 5,6,7,8,9,10,11,12,-13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4**, Q = methylthio, n = 10), mp 216-217.5° (methanol); ir: ν C=O = 1650 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.43 (m, 8H, CH_2-8,9,10 and 11), 1.49 (m, 4H, CH_2-7 and 12), 1.75 (m, 2H, CH_2-13), 1.95 (m, 2H, CH_2-6), 2.57 (t, 2H, CH_2-14), 2.65 (s, 3H, SCH_3), 2.97 (t, 2H, CH_2-5); cmr (DMSO-d_6): δ, ppm 14.3 (SCH_3), 22.5, 22.6, 24.2, 25.1, 25.4, 25.7, 26.0 (two peaks), 26.3 (two peaks) (C-5-C-19), 117.2 (C-14a), 147.4 (C-4a), 148.9 (C-16a), 161.5 (C=O), 162.9 (C-2); uv (ethanol): λ max nm (E.10^{-3}) 206 (29.2), 221 sh (14.0), 290 (11.0); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (E.10^{-3}) 205 (32.1), 222 sh (15.5), 282 (5.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (E.10^{-3}) 285 (8.6); ms: M^+ = 320.

Anal. Calcd. for $C_{16}H_{24}N_4OS$ (MW. 320.45): C, 59.97; H, 7.55; N, 17.48; S, 10.01. Found: C, 60.11; H, 7.75; N, 17.40; S, 9.89.

Continuing the chromatography using as eluent a 1:1 mixture of chloroform and methanol 0.70 g (44%) of 6,7,8,9,10,11,12,13,-14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]-pyrimidin-5(16*H*)-one (**3**, Q = methylthio, n = 10), mp 280-287° dec was obtained that was identical (ir) with that of (**3**, Q = methylthio, n = 10) obtained above.

1-Benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(1*H*)-one (**3/2**, Q = methylthio, n = 10), 3-Benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(3*H*)-one (**3/3**, Q = methylthio, n = 10), and 16-Benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3/1**, Q = methylthio, n = 10).

To a solution of 0.95 g (0.0028 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water a solution of 0.225 g (0.0056 mole) of sodium hydroxide in 5 ml of water was added with cooling and stirring keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 0.90 g (0.0028 mole) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = methylthio, n = 10). To the solution obtained 10 ml of chloroform was added and the mixture was stirred for 5 minutes. The phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.57 g (~100%) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16-*H*)-one (**3**, Q = methylthio, n = 10) tetrabutylammonium salt (oily crystals). This was dissolved in 3 ml of acetonitrile, to the solution obtained 0.51 g (0.46 ml, 0.004 mole) of benzyl chloride was added and refluxed for 60 minutes. The thick suspension obtained was diluted with 2 ml of acetonitrile and refluxed for further 30 minutes. After cooling the crystals precipitated were filtered off and washed with cold acetonitrile to yield 0.34 g (30%) of 1-benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(1*H*)-one (**3/2**, Q = methylthio, n = 10) which after recrystallisation first from ethanol, then from benzene melted at 211-213°; ir: ν C=O = 1672 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.33-1.39 (m, 8H, CH_2-9, 10, 11 and 12), 1.47 (m, 4H, CH_2-8 and 13), 1.76 (m, 4H, CH_2-7 and 14), 2.70 (m, 4H, CH_2-6 and 15), 2.75 (s, 3H, SCH_3), 5.11 (s, 2H, $PhCH_2$), 7.31-7.42 (m, 5H, PhH); cmr (deuteriochloroform): δ, ppm 13.7 (SCH_3), 22.2, 23.1, 23.7, 23.9, 25.1, 25.6, 26.0, 26.1, 26.4, 31.6 (C-6-C-15), 46.2 ($PhCH_2$), 115.0 (C-5a), 128.2 (*o*-Ph), 128.5 (*p*-Ph), 128.7 (*m*-Ph), 133.8 (*s*-Ph), 147.2 (C-16a), 153.2 (C-2), 156.5 (C=O), 162.8 (C-15a); uv (ethanol): λ max nm ($E.10^{-3}$) 214 sh (14.0), 227 (18.7), 290 (10.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 214 sh (11.0), 230 (11.7), 286 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 290 (4.2); ms: M^+ = 410.

The mother liquor was evaporated *in vacuo* to dryness, the oily residue obtained was dissolved in chloroform, extracted with water, dried over anhydrous sodium sulfate, evaporated *in vacuo* to dryness and the oily residue obtained was triturated with a small amount of diethyl ether containing some drops of acetonitrile to yield after filtration 0.42 g (36%) of crude 16-benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3/1**, Q = methylthio, n = 10). This was dissolved in dichloromethane, the solution was passed through a short silica gel column, evaporated *in vacuo* to dryness and the crystals obtained were recrystallised from acetonitrile, mp 186-188°; ir: ν C=O = 1692 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.50 (m, 12H, CH_2-8,9,10,11,12 and 13), 1.72 (m, 4H, CH_2-7 and 14), 2.66 (t, 2H, CH_2-6), 2.67 (s, 3H, SCH_3), 2.70 (t, 2H, CH_2-14), 5.52 (s, 2H, $PhCH_2$), 7.06 (dd, J = 7 and 2 Hz, 2H, *o*-PhH), 7.25-7.40 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ, ppm 14.0 (SCH_3), 22.2 (C-10), 22.5 (C-11), 25.2 (C-6), 26.6 (C-12), 26.7 (C-14), 26.8 (C-8), 27.2 (C-9), 27.4 (C-7 and 15), 28.0 (C-13), 50.9 ($PhCH_2$), 113.7 (C-5a), 126.1 (*o*-Ph), 128.1 (*p*-Ph), 129.1 (*m*-Ph), 135.5 (*s*-Ph), 149.9 (C-16a), 152.5 (C-15a), 155.5 (C=O), 164.9 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 238 (25.6), 282 (11.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 240 (25.1), 282 (11.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 290 (12.2); ms: M^+ = 410.

Anal. Calcd. for $C_{23}H_{30}N_4OS$ (MW. 410.57): C, 67.28; H, 7.37; N, 13.65; S, 7.81. Found: C, 67.47; H, 7.28; N, 13.76; S, 7.79.

The combined mother liquors were evaporated *in vacuo* again to dryness and the residue (200 mg) was chromatographed on a thick layer (Pre-Coated PLC Plates, Silica Gel 60 F_{254}, Merck 5717) in a 1:1 mixture of cyclohexane and ethyl acetate. The three benzyl isomers were characterised with R_f values of 0.30, 0.50 and 0.73 for **3/2**, **3/3**, and **3/1**, respectively. The spot with R_f = 0.50 was scratched down, extracted with chloroform, the chloroform was evaporated *in vacuo* to dryness, the residual crystals were triturated with diethyl ether and filtered to yield 0.06 g (5%) of 3-benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-methylthiocyclododeca[*d*]triazolo[1,5-*a*]pyrimidin-5(3*H*)-one (**3/3**, Q = methylthio, n = 10), mp 128-130°; ir: ν C=O = 1655 cm^{-1}, ν C=N = 1575 and 1510 cm^{-1}; pmr (deuteriochloroform), δ, ppm 1.27-1.55 (m, 12H, CH_2-8,9,10,11,12 and 13), 1.69 (qi, 2H, CH_2-7), 1.86 (qi, 2H, CH_2-14), 2.64 (dt, 4H, CH_2-6 and 15), 2.81 (s, 3H, SCH_3), 5.84 (s, 2H, $PhCH_2$), 7.27-7.36 (m, 5H, PhH); cmr (deuteriochloroform): δ, ppm 14.6 (SCH_3), 22.3, 23.1, 23.7, 24.3, 25.4, 25.7, 26.2, 26.3, 26.8, 31.9 (C-6 - C-15), 53.1 ($PhCH_2$), 115.2 (C-5a), 128.4 (*o*-Ph), 128.76 (*p*-Ph), 128.83 (*m*-Ph), 133.6 (*s*-Ph), 153.2 (C-16a), 157.6 (C=O), 164.6 (C-2), 165.1 (C-15a); uv (ethanol): λ max nm ($E.10^{-3}$) 208 (20.0), 244 (14.0), 276 (8.7), 299 (7.8); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 247 (13.8), 276 (8.5), 297 (7.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 251 (16.2), 272 sh (12.1); ms: M^+ = 410.

16-Benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4/1**, Q = methylthio, n = 10).

The mixture of 0.88 g (0.004 mole) of 5-benzylamino-3-methylthio-1*H*-1,2,4-triazole (**5**, Q = methylthio) [11] and 1.81 g (0.0071 mole) of ethyl 2-oxocyclododecanecarboxylate (**2**, n = 10) [13] was heated to 180-190° for 10 minutes. To the still hot yellow melt obtained 8 ml of 2-propanol was added. The solution obtained cyrstallised upon cooling to yield 1.40 g (85%) of 16-benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4/1**, Q = methylthio, n = 10), mp 182-184° (acetonitrile); ir: ν C=O = 1658 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.45 (m, 12H, CH_2-7,8,9,10,11 and 12), 1.72 (m, 2H, CH_2-13), 1.94 (m, 2H, CH_2-6), 2.55 (t, 2H, CH_2-14), 2.63 (s, 3H, SCH_3), 2.93 (t, 2H, CH_2-5), 5.35 (s, 2H, $PhCH_2$), 7.20-7.30 (m, 3H, *m*- and *p*-PhH), 7.59 (dd, J = 7 Hz and 1.5 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 14.2 (SCH_3), 22.1 (C-10), 22.2 (C-9), 24.5 (C-6), 24.8 (C-14),

25.0 (C-8), 25.3 (C-11), 25.7 (C-12), 25.9 (C-13), 26.0 (C-5 and 7), 46.9 ($PhCH_2$), 116.3 (C-14a), 128.0 (*p*-Ph), 128.4 (*m*-Ph), 129.5 (*o*-Ph), 135.7 (*s*-Ph) 146.0 (C-4a), 149.9 (C-16a), 160.0 (C=O), 162.5 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 209 (28.0), 225 sh (12.6), 291 (9.5); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 207 (39.4), 226 sh (11.7), 291 (9.8); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 289 (11.0).

Anal. Calcd. for $C_{23}H_{30}N_4OS$ (MW. 410.57): C, 67.28; H, 7.37; N, 13.65; S, 7.81. Found: C, 67.14; H, 7.23; N, 13.67; S, 7.84.

16-Benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4/1**, Q = methylthio, n = 10).

To a solution of 0.27 g (0.0008 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water a solution of 0.064 g (0.0016 mole) of sodium hydroxide in 5 ml of water was added with cooling and stirring keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 0.25 g (0.00078 mole) of 5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4**, Q = methylthio, n = 10). To the solution obtained 10 ml of chloroform was added and the mixture was stirred for 5 minutes, the phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 0.43 g (100%) of 5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16-*H*)-one (**4**, Q = methylthio, n = 10) tetrabutylammonium salt (yellow oil). This was dissolved in 2 ml of acetonitrile, to the solution obtained 0.127 g (0.001 mole) of benzyl chloride was added and refluxed for 2 hours. After cooling the crystals precipitated were filtered off and washed with cold acetonitrile to yield 0.20 g (62%) of 16-benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-methylthiocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4/1**, Q = methylthio, n = 10) which after two recrystallisations from ethyl acetate melted at 182-185°. The product was identical (ir) with that of **4/1** (Q = methylthio, n = 10) obtained above.

6,7,8,9,10,11,12,13,14,15-Decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = morpholino, n = 10).

The mixture of 3.38 g (0.02 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (**1**, Q = morpholino) [11], 7.43 g (0.0292 mole) of ethyl 2-oxocyclododecanecarboxylate (**2**, n = 10) [13] and 8 ml of acetic acid was refluxed for 2 hours. The solution obtained during the reaction crystallised while hot. After cooling the crystals precipitated were filtered off, washed with acetic acid and acetone to yield 2.76 g (38%) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = morpholino, n = 10) which after recrystallisation from the mixture of methanol and dimethylformamide melted at 308-318° dec. The mother liquor was diluted with 150 ml of acetonitrile, inoculated and let to stand in the refrigerator overnight. The crystals precipitated were collected to give a further croi (1.06 g, 15%) of the above material, mp 305-315° dec; ir: ν C=O = 1650 cm^{-1}; pmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 1.46 (m, 12H, CH_2-8,9,10,11,12 and 13), 1.67 (m, 2H, CH_2-14), 1.80 (m, 2H, CH_2-7), 2.50 (t, 2H, CH_2-6), 2.62 (t, 2H, CH_2-15), 3.48 (t, 4H, NCH_2), 3.74 (t, 4H, OCH_2); cmr (DMSO-d_6 + deuteriochloroform 1:3): δ, ppm 21.6, 22.2, 23.0, 24.2, 25.2 (two peaks), 25.6, 25.9, 26.0, 27.3 (C-6-C-15), 45.7 (NCH_2), 65.6 (OCH_2), 109.6 (C-5a), 147.6 (C-16a), 149.5 (C-15a), 156.1 (C=O), 164.5 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 232 (24.6), 276 (11.2), uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 232 (21.4), 272 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 290 (9.9).

Anal. Calcd. for $C_{19}H_{29}N_5O_2$ (MW. 359.46): C, 63.48; H, 8.13; N, 19.48. Found: C, 63.49; H, 8.04; N, 19.67.

16-Benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3/1**, Q = morpholino, n = 10).

To a solution of 1.02 g (0.003 mole) of tetrabutylammonium hydrogensulfate (Fluka) in 5 ml of water a solution of 0.24 g (0.006 mole) of sodium hydroxide in 5 ml of water was added with cooling and stirring keeping the temperature of the reaction mixture below 10°. This was followed by the addition of 1.08 g (0.003 mole) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = morpholino, n = 10). To the solution obtained 10 ml of chloroform was added and the mixture was stirred for 5 minutes, the phases were separated, the chloroform layer was dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.80 g (100%) of 6,7,8,9,10,11,12,13,14,15-decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3**, Q = morpholino, n = 10) tetrabutylammonium salt. This was dissolved in 3 ml of warm acetonitrile, to the solution obtained 0.57 g (0.52 ml ~0.0045 mole) of benzyl chloride was added, refluxed for 2 hours and evaporated *in vacuo* to dryness. The oily residue obtained was dissolved in chloroform, extracted with water, dried over anhydrous sodium sulfate and evaporated again *in vacuo* to dryness. The oily residue obtained was triturated with a small amount of diethyl ether containing some drops of acetonitrile, the crystals precipitated were filtered off and washed with diethyl ether again containing some drops of acetonitrile to yield 0.60 g (44%) of crude 16-benzyl-6,7,8,9,10,11,12,13,14,15-decahydro-2-morpholinocyclododeca[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5(16*H*)-one (**3/1**, Q = morpholino, n = 10). This was dissolved in dichloromethane, the solution obtained was passed through a short silica gel column, evaporated to dryness and the crystals obtained were recrystallised from acetonitrile, mp 245.5-247.5°; ir: ν C=O = 1678 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.48 (m, 12H, CH_2-8,9,10,11,12 and 13), 1.73 (m, 4H, CH_2-7 and 14), 2.61 (t, 2H, CH_2-6), 2.66 (t, 2H, CH_2-15), 3.55 (t, 4H, NCH_2), 3.75 (t, 4H, OCH_2), 5.48 (s, 2H, $PhCH_2$), 7.08 (dd, J = 7 and 2 Hz, 2H, *o*-PhH), 7.25-7.40 (m, 3H, *m*- and *p*-PhH); cmr (deuteriochloroform): δ, ppm 22.1 (C-10), 22.5 (C-11), 25.1 (C-6), 26.7 (C-12 and 14), 26.8 (C-8), 27.0 (C-9), 27.4 (C-7 and 15), 28.0 (C-13), 46.1 (NCH_2), 50.7 ($PhCH_2$), 66.4 (OCH_2), 113.7 (C-5a), 126.1 (*o*-Ph), 128.0 (*p*-Ph), 129.1 (*m*-Ph), 135.8 (*s*-Ph), 148.5 (C-16a), 151.8 (C-15a), 155.8 (C=O), 164.7 (C-2); uv (ethanol): λ max nm ($E.10^{-3}$) 237 (27.9), 282 (11.7); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($E.10^{-3}$) 237 (28.4), 282 (12.3); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($E.10^{-3}$) 283 (12.4).

Anal. Calcd. for $C_{26}H_{35}N_5O_2$ (MW. 449.58): C, 69.46; H, 7.85; N, 15.58. Found: C, 69.15; H, 7.66; N, 15.45.

16-Benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-morpholinocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)-one (**4/1**, Q = morpholino, n = 10).

The mixture of 1.04 g (0.004 mole) of 5-benzylamino-3-morpholino-1*H*-1,2,4-triazole (**5**, Q = morpholino) [5] and 1.65 g (0.0065 mole) of ethyl 2-oxocyclododecanecarboxylate (**2**, n = 10)

[13] was heated to 180-190° for 10 minutes. To the still hot yellow melt obtained 12 ml of 2-propanol was added. The solution obtained crystallised upon cooling to yield 1.60 g (89%) of 16-benzyl-5,6,7,8,9,10,11,12,13,14-decahydro-2-morpholinocyclododeca[*e*][1,2,4]triazolo[1,5-*a*]pyrimidin-15(16*H*)one (**4/1**, Q = morpholino, n = 10), mp 186-188° (acetonitrile); ir: ν C=O = 1664 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.40 (m, 12H, CH_2-7,8,9,10,11 and 12), 1.74 (m, 2H, CH_2-13), 1.93 (m, 2H, CH_2-6), 2.52 (t, 2H, CH_2-14), 2.85 (t, 2H, CH_2-5), 3.49 (t, 4H, NCH_2), 3.79 (t, 4H, OCH_2), 5.29 (s, 2H, $PhCH_2$), 7.20-7.35 (m, 3H, *m*- and *p*-PhH), 7.59 (dd, J = 7 Hz and 1.4 Hz, 2H, *o*-PhH); cmr (deuteriochloroform): δ, ppm 22.5 (C-9 and 10), 24.5 (C-6), 24.8 (C-14), 25.3 (C-8), 25.6 (C-11), 25.8 (C-12), 26.2 (C-7), 26.4 (C-5 and 13), 46.4 (NCH_2), 46.8 ($PhCH_2$), 66.4 (OCH_2), 114.4 (C-14a), 127.8 (*p*-Ph), 128.3 (*m*-Ph), 129.4 (*o*-Ph), 136.2 (*s*-Ph), 146.4 (C-4a), 149.3 (C-16a), 160.2 (C=O), 164.4 (C-2); uv (ethanol): λ max nm (ε. 10^{-3}) 206 (29.7), 228 sh (11.9), 310 (8.9); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm (ε. 10^{-3}) 206 (30.4), 226 sh (12.2), 310 (9.0); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm (ε. 10^{-3}) 304 (10.9).

Anal. Calcd. for $C_{26}H_{35}N_5O_2$ (MW. 449.58): C, 69.46; H, 7.85; N, 15.58. Found: C, 69.17; H, 7.73; N, 15.5.

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REFERENCES AND NOTES

[1] For Part XXIII. see J. Reiter and K. Esses-Reiter, *J. Heterocyclic Chem.*, **28**, 561 **(1991).**

[2] Presented on the 10th Symposium on the Chemistry of Heterocyclic Compounds, Košice (Czechoslovakia), 1990, see: Congress Abstracts Part II, p. 245.

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

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

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

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

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

[8] A. Brändström, P. Berntsson, S. Carlsson, A. Djurhuus, K. Gustavii, U. Junggren, B. Lamm and B. Samuelsson, *Acta Chem. Scand.*, **23**, 2202 (1969).

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

[10] V. Prelog and W. Hinden, *Helv. Chim. Acta*, **27**, 1856 (1944).

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

[12] J. Reiter, L. Pongó, T. Somorai and P. Dvortsák, *J. Heterocyclic Chem.*, **23**, 401 (1986).

[13] A. P. Krapcho, J. Diamanti, Ch. Cayen and R. Bingham, *Org. Synth, Coll. Vol.* **5**, 198 (1973).