On Triazoles. XXXIX [1,2]. Synthesis and Structure of Some 1,2,4-Triazolo[1,5-*a*]pyrimidin-5-one Oximes

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Some 1,2,4-triazolo[1,5-*a*]pyrimidin-5-one derivatives **1** and their alicyclic condensed ring analogues **2-3** were converted through the corresponding "imino chlorides" **4-6** to the oximes **7-9**. The "*E*" isomeric structure of the products obtained was proven with the use of cmr using the spectral data of the corresponding "benzyloximino" derivatives **10-12** prepared as model compounds.

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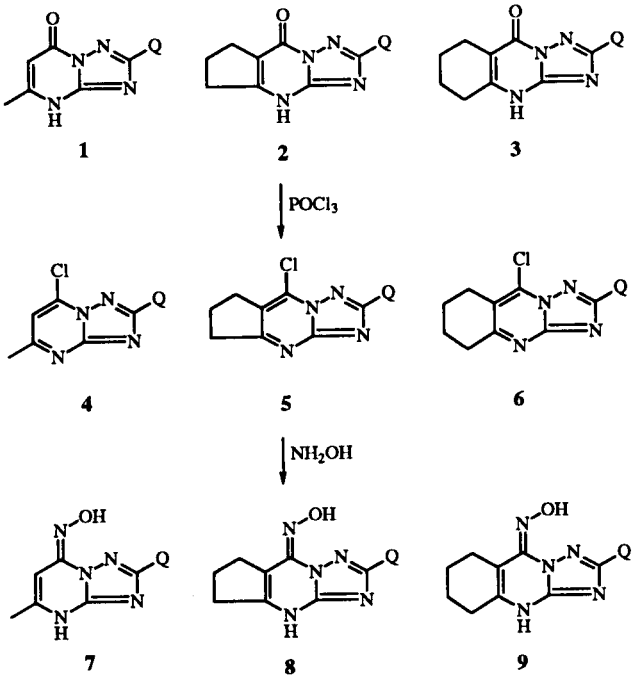
In the previous papers of this series [3-5], we described the synthesis and structure elucidation of some 1,2,4-triazolo[1,5-*a*]pyrimidin-5-one derivatives **1** and their alicyclic condensed ring analogues **2-3** (Scheme 1). Biological considerations led us to decide to convert them into the corresponding 5-oximes **7-9**. However, probably due to their unusual "amide" character, neither their reaction with hydroxylamine in different water-methanol or water-ethanol mixtures, nor their reaction with hydroxylamine hydrochloride in acetic acid in the presence of sodium acetate led to the formation of the expected oximes.

Scheme 1

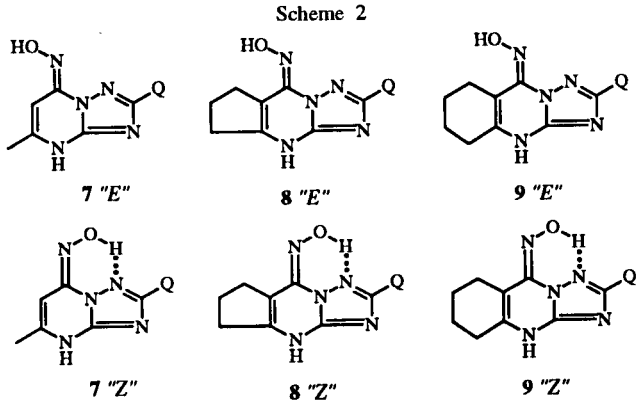


a, Q = methylthio **b**, Q = morpholino

Thus the "amides" **1-3** were converted with phosphorus oxychloride to the corresponding "imino-chlorides" **4-6** that reacted readily with hydroxylamine in acetonitrile-water, methanol-water or dimethylformamide-water solutions to yield the corresponding oximes **7-9** (Scheme 1).

Even the oximes **7-9** may exist in two, "*E*" or "*Z*" isomeric structures (Scheme 2) in the above reactions in all cases only one isomer was obtained. As we wished to convert deriatives **7-9** by Beckmann rearrangement to novel ring systems [6] we needed to know their exact structures.

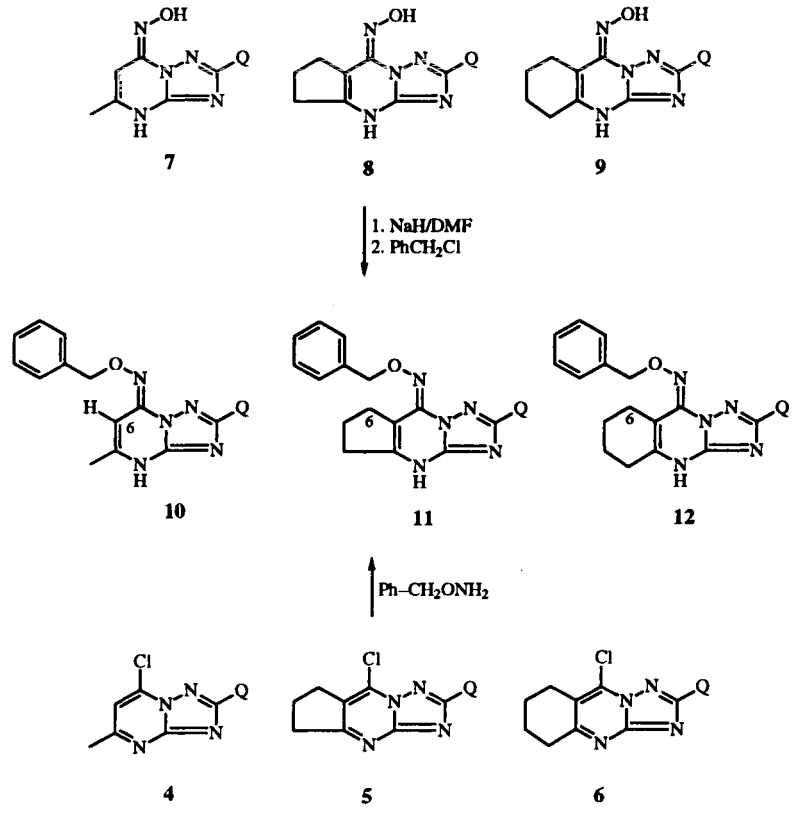
Scheme 2



It was known from the literature [7] that the "*E*" and "*Z*" α-CH_2 carbon atoms of the cyclohexanone oxime appeared with very different chemical shifts (32.3 and 27.5 ppm, respectively). This difference was also visible in differently substituted cyclohexanone oxime derivatives [8]. However, this rule was not applicable in our case as we had in the α-positions to the oxime moiety a nitrogen atom and a quaternary carbon atom. Thus we decided to make some DNOE experiments by irradiating the OH signals of oximes **7-9**. Nevertheless, no DNOE enhancement was observed neither on the corresponding CH-6 protons of derivatives **7**, nor on the CH_2-6 protons of derivatives **8** and **9** indicating that our derivatives **7-9** had to have the "*Z*" isomeric structure that could be stabilized by an intramolecular H-bond (Scheme 2).

However, it was also known that the absence of DNOE enhancement may be - accidentally - due to ineligible recording conditions. To exclude the possibility of misinterpretation caused by recording conditions the OH groups of oximes **7-9** were enlarged by introducing an *O*-benzyl group to yield derivatives **10-12** (Scheme 3). This could be done either by direct *O*-benzylation of the

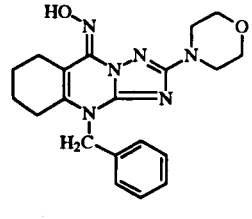
Scheme 3



sodium salts of the corresponding oximes **7-9** with benzyl chloride, or by the reaction of the "imino-chlorides" **4-6** with benzyloxamine (Scheme 3).

In both reactions the same "*E*" *O*-benzyloxy derivatives were obtained as proven by the positive DNOE enhancements observed on the CH-6 protons of derivatives **10** and on the CH_2-6 protons of derivatives **11** and **12** after irradiation of the benzyloxy CH_2 protons (See Experimental). It should be mentioned that during the benzylation of **9b** besides the expected **12b** a byproduct, namely the *N*-benzyl derivative **13** (Scheme 4) was also isolated.

Scheme 4



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However, eventhough the *O*-benzylated derivatives **10-12** obtained from derivatives **7-9** definitely had "*E*" isomeric structures, there still remained the possibility of conversion of the originally present "*Z*" structures to the "*E*"-configuration during the formation of the sodium salts in their alkylation reactions.

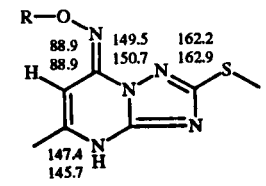
Finally, the cmr spectra helped to definitely solve the above question. Thus, if the "*Z*" isomeric structure stabilized by an intramolecular H-bond between the OH group and the triazole N-3 atoms were present the electron density of the N-3 atoms of derivatives **7-9** would be decreased causing a strong upfield shift of the carbon atoms 2, while the electron density of the oximino nitrogen atoms would be increased causing a downfield shift of the carbon atoms 5 and through the conjugated double bonds of that of carbon atoms 7, 8a and 9a, respectively.

The practically negligible changes in the chemical shifts of carbon atoms 2, 5, 7 and 9a, respectively, of derivatives **10** and **12** as compared with those of parent oximes **7** and **9** (Scheme 5) proved unequivocally the "*E*" isomeric structure of compounds **7** and **9**.

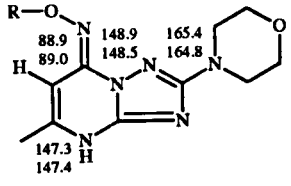
In derivatives **11** a slight upfield shift of carbon atoms 2, 5 and 8a as compared with those of **8**, respectively, was observed. This is just the opposite to that of expected for "*Z*" structures. On the other hand these upfield shifts could be easily explained by taking in account that the cyclopentane ring condensed to the 1,2,4-triazolo[1,5-*a*]-pyrimidine moiety is practically coplanar with it causing a steric hindrance between the benzyl CH_2 and cyclopentane CH_2-6 groups. This is also visible on the upfield shift

of the corresponding CH_2-6 carbon atoms of **11** (Scheme 5). Altogether, derivatives **8** may also be present in the "*E*" isomeric structure.

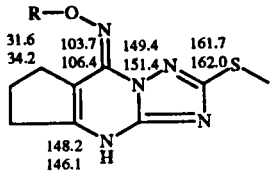
Scheme 5



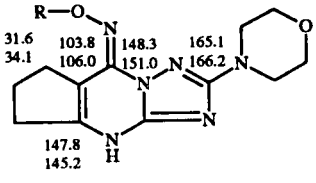
7a, R = H
10a, R = benzyl



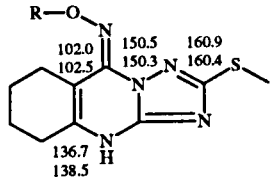
7b, R = H
10b, R = benzyl



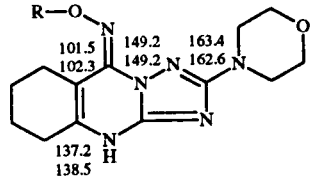
8a, R = H
11a, R = benzyl



8b, R = H
11b, R = benzyl



9a, R = H
12a, R = benzyl



9b, R = H
12b, R = benzyl

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are not corrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The pmr and cmr measurements were performed using a Bruker WM-250 instrument. The ms spectra were observed with a Kratos MS 25 RFA double focusing instrument in EI and CI mode.

5-Chloro-7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**4a**).

To a stirred suspension of 150 g (0.75 mole) of 7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidin-5(8*H*)-one (**1a**) [5] and 500 ml (5.5 moles) of phosphorus oxychloride, 20 ml (0.25 mole) of pyridine was added dropwise within 10 minutes. The orange suspension obtained was heated to 85° and allowed to at this temperature with stirring for 6 hours. The orange solution obtained was cooled to ambient temperature and poured with stirring onto 3000 g of crushed ice. The product was extracted with 5 x 100 ml portions of chloroform, the combined organic phases were extracted with ice cold water, saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (117 g) was passed through a short silica gel column (eluent a 3:1 mixture of benzene and acetonitrile) to yield 102 g (62%) of 5-chloro-7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]-pyrimidine (**4a**), mp 136-137°; ir: ν C=N = 1595 and 1505 cm^{-1}; pmr (deuteriochloroform): δ, ppm 2.59 (s, 3H, CH_3), 2.66 (s, 3H, SCH_3), 7.55 (s, 1H, CH-7); cmr (deuteriochloroform): δ, ppm 13.9 (SCH_3), 24.9 (CH_3), 110.2 (C-6), 137.5 (C-7), 156.3 (C-8a), 164.4 (C-2), 169.8 (C-5); ms: (EI) m/z 214 (100%, M^+), 213 (10%), 169 (80%).

Anal. Calcd. for $C_7H_7ClN_4S$ (MW 214.68): C, 39.16; H, 3.29; N, 26.10; S, 14.94; Cl, 16.51. Found: C, 39.03; H, 3.41; N, 26.23; S, 15.08; Cl, 16.55.

5-Chloro-7-methyl-2-morpholino-1,2,4-triazolo[1,5-*a*]pyrimidine (**4b**).

To a stirred suspension of 109 g (0.47 mole) of 7-methyl-2-morpholino-1,2,4-triazolo[1,5-*a*]pyrimidin-5(8*H*)-one (**1b**) [5] and 150 ml (1.65 moles) of phosphorus oxychloride, 10 ml (0.125 mole) of pyridine was added dropwise within 10 minutes. The yellow suspension obtained was heated to 85° and allowed to react at this temperature with stirring for 6 hours. The deep red solution obtained was cooled to ambient temperature and poured with stirring onto 3000 g of crushed ice. The product was extracted with 5 x 100 ml portions of chloroform, the combined organic phases were extracted with ice cold water and saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (100.2 g) was passed through a short silica gel column (eluent a 3:2 mixture of benzene and chloroform) to yield 87.8 g (74%) of 5-chloro-7-methyl-2-morpholino-1,2,4-triazolo[1,5-*a*]pyrimidine (**4b**), mp 176-177°; ir: ν C=N = 1614, 1572 and 1508 cm^{-1}, ν COC = 1117 cm^{-1}; pmr (deuteriochloroform): δ, ppm 2.59 (s, 3H, CH_3), 3.68 (t, 4H, NCH_2), 3.79 (t, 4H, OCH_2), 6.83 (s, 1H, CH); cmr (deuteriochloroform): δ, ppm 24.4 (CH_3), 45.7 (NCH_2), 66.3 (OCH_2), 108.4 (C-6), 136.5 (C-7), 156.0 (C-8a), 162.4 (C-2), 167.7 (C-5).

Anal. Calcd. for $C_{10}H_{12}ClN_5O$ (MW 253.69): C, 47.35; H, 4.77; N, 27.61; Cl, 13.97. Found: C, 47.29; H, 4.86; N, 27.63; Cl, 13.95.

5-Chloro-2-methylthio-6,7-dihydro-8*H*-cyclopenta[1,2-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidine (**5a**).

To a stirred suspension of 166.8 g (0.75 mole) of 2-methylthio-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one (**2a**) [3] and 350 ml (3.8 mole) of phosphorus oxychloride, 20 ml (0.25 mole) of pyridine was added dropwise within 10 minutes. The suspension obtained was heated to 85° and reacted at this temperature with stirring for 6 hours. The orange solution obtained was cooled to ambient temperature and poured with stirring onto 3000 g of crushed ice. The product was extracted with 5 x 100 ml portions of chloroform, the combined organic phases were extracted with ice cold water, saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (151 g) was passed through a short silica gel column (eluent a 5:1 mixture of benzene and acetonitrile) to yield 137.1 g (73%) of 5-chloro-2-methylthio-6,7-dihydro-8*H*-cyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**5a**), mp 121-122°; ir: ν C=N = 1614 and 1528 cm^{-1}; pmr (deuteriochloroform): δ, ppm 2.19 (qi, 2H, CH_2-7), 2.64 (s, 3H, SCH_3), 3.10 (t, 2H, CH_2-8), 3.15 (t, 2H, CH_2-6); cmr (deuterio-

chloroform): δ, ppm 13.8 (SCH_3), 22.9 (C-7), 28.1 (C-8), 35.1 (C-6), 123.1 (C-5a), 132.9 (C-8a), 156.7 (C-9a), 168.4 (C-2), 173.0 (C-5); ms: (EI) m/z 240 (100%, M^+), 239 (50%), 195 (58%).

Anal. Calcd. for $C_9H_9ClN_4S$ (MW 240.72): C, 44.91; H, 3.77; N, 23.28; S, 13.32; Cl, 14.73. Found: C, 45.07; H, 3.88; N, 23.20; S, 13.36; Cl, 14.63.

5-Chloro-2-morpholino-6,7-dihydro-8*H*-cyclopenta[1,2-*d*]-[1,2,4]triazolo[1,5-*a*]pyrimidine (**5b**).

To a stirred suspension of 210.2 g (0.8 mole) of 2-morpholino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]-pyrimidin-5-one (**2b**) [3] and 500 ml (5.5 moles) of phosphorus oxychloride, 20 ml (0.25 mole) of pyridine was added dropwise within 10 minutes. The yellow suspension obtained was heated to 85° and reacted at this temperature with stirring for 6 hours. The red solution obtained was cooled to ambient temperature and poured with stirring onto 3000 g of crushed ice. The product was extracted with 5 x 100 ml portions of chloroform, the combined organic phases were extracted with ice cold water, saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (163 g) was passed through a short silica gel column (eluent a 3:1 mixture of benzene and acetonitrile) to yield 155.6 g (69%) of 5-chloro-2-morpholino-6,7-dihydro-8*H*-cyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**5b**), mp 218-218.5°; ir: ν C=N = 1618 and 1566 cm^{-1}, ν COC = 1117 cm^{-1}; pmr (deuteriochloroform): δ, ppm 2.16 (qi, 2H, CH_2-7), 2.98 (t, 2H, CH_2-8), 3.03 (t, 2H, CH_2-6), 3.50 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2); cmr (deuteriochloroform): δ, ppm 22.8 (C-7), 28.2 (C-8), 35.1 (C-6), 45.8 (NCH_2), 66.4 (OCH_2), 121.4 (C-5a), 132.5 (C-8a), 156.4 (C-9a), 167.4 (C-2), 170.8 (C-5).

Anal. Calcd. for $C_{12}H_{14}ClN_5O$ (MW 279.73): C, 51.53; H, 5.04; N, 25.04; Cl, 12.67. Found: C, 51.68; H, 5.04; N, 25.13; Cl, 12.66.

5-Chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]-quinazoline (**6a**).

To a stirred suspension of 201.6 g (0.85 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline-5(10*H*)-one (**3a**) [4] and 500 ml (5.5 moles) of phosphorus oxychloride, 20 ml (0.25 mole) of pyridine was added dropwise within 10 minutes. The orange suspension obtained was heated to 85° and reacted at this temperature with stirring for 6 hours. The orange solution obtained was cooled to ambient temperature and poured with stirring onto 3000 g of crushed ice. The product was extracted with 5 x 100 ml portions of chloroform, the combined organic phases were extracted with ice cold water, saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (211 g) was passed through a short silica gel column (eluent a 5:1 mixture of benzene and acetonitrile) to yield 189.2 g (87%) of 5-chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6a**), mp 136-137°; ir: ν C=N = 1605 and 1510 cm^{-1}; pmr (deuteriochloroform): δ, ppm 1.83 (qi, 4H, CH_2-7 and 8), 2.66 (s, 3H, SCH_3), 2.80 (t, 2H, CH_2-9), 2.93 (t, 2H, CH_2-6); cmr (deuteriochloroform): δ, ppm 13.8 (SCH_3), 21.8* (C-8), 21.9* (C-7), 25.2 (C-9), 33.5 (C-6), 117.9 (C-5a), 136.1 (C-9a), 154.4 (C-10a), 164.7 (C-2), 168.9 (C-5).

Anal. Calcd. for $C_{10}H_{11}ClN_4S$ (MW 254.74): C, 47.15; H, 4.35; N, 21.99; Cl, 13.92; S, 12.59. Found: C, 47.12; H, 4.33; N, 22.10; Cl, 13.88; S, 12.87.

5-Chloro-2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]-quinazoline (**6b**).

To a stirred suspension of 13.78 g (0.05 mole) of 2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]-quinazoline-5(10*H*)-one (**3b**) [4] and 45 ml (0.5 mole) of phosphorus oxychloride, 1 ml (0.0125 mole) of pyridine was added dropwise within 10 minutes. The yellow suspension obtained was heated to 85° and reacted at this temperature with stirring for 6 hours. The orange solution obtained was cooled to ambient temperature and poured with stirring onto 100 g of crushed ice. The product was extracted with 5 x 50 ml portions of chloroform, the combined organic phases were extracted with ice cold water and saturated sodium hydrogen carbonate solution, and dried over anhydrous sodium sulfate. The solvent was evaporated *in vacuo* to dryness, and the residue (14.1 g) was passed through a short silica gel column (eluent a 5:1 mixture of benzene and chloroform) to yield 12.08 g (82%) of 5-chloro-2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6b**), mp 166-167°; ir: ν C=N 1610, 1564 and 1516 cm^{-1}, ν COC = 1113 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.84 (qi, 4H, CH_2-7 and 8), 2.72 (t, 2H, CH_2-9), 2.86 (t, 2H, CH_2-6), 3.46 (t, 4H, NCH_2), 3.74 (t, 4H, OCH_2); cmr (DMSO-d_6): δ, ppm 21.4* (C-8), 21.5* (C-7), 24.6 (C-9), 32.8 (C-6), 45.5 (NCH_2), 65.6 (OCH_2), 116.1 (C-5a), 135.0 (C-9a), 153.6 (C-10a), 162.3 (C-2), 167.0 (C-5).

Anal. Calcd. for $C_{13}H_{16}ClN_5O$ (MW 293.76): C, 53.15; H, 5.49; N, 23.84; Cl, 12.07. Found: C, 53.08; H, 5.46; N, 23.94; Cl, 12.06.

(*E*)-7-Methyl-2-methylthio-5-oximino-8*H*-1,2,4-triazolo[1,5-*a*]-pyrimidine (**7a**).

To a solution of 4.28 g (0.02 mole) of 5-chloro-7-methyl-2-methylthio-1,2,4-triazolo[1,5-*a*]pyrimidine (**4a**) in 60 ml of acetonitrile a water solution of 1.32 g (0.04 mole) of hydroxylamine [prepared fresh by mixing a solution of 2.76 g (0.04 mole) of hydroxylamine hydrochloride in 8 ml of water and 2.12 g (0.02 mole) of sodium carbonate in 16 ml of water] was added in one portion at 65°. The reaction mixture crystallized immediately. After cooling, the crystals that precipitated were filtered and washed with a 1:1 mixture of chloroform and methanol to yield 2.03 g (84%) of (*E*)-7-methyl-2-methylthio-5-oximino-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine, mp 260-262° (dimethylformamide); ir: ν OH = 3490 cm^{-1}, ν C=N = 1683, 1630 and 1605 cm^{-1}, ν N-O = 993 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.28 (s, 3H, CH_3), 2.59 (s, 3H, SCH_3), 6.05 (s, 1H, CH), 9.9 (bs, 1H, OH), 10.5 (bs, 1H, NH); cmr (DMSO-d_6): δ, ppm 13.5 (SCH_3), 19.9 (CH_3), 88.9 (C-6), 144.9 (C-8a), 147.4 (C-7), 150.7 (C-5), 162.9 (C-2); ms: (EI) m/z 211 (100%, M^+), 195 (90%).

Anal. Calcd. for $C_7H_9N_5OS$ (MW 211.25): C, 39.80; H, 4.29; N, 33.15; S, 15.18. Found: C, 39.93; H, 4.55; N, 33.02; S, 15.16.

(*E*)-7-Methyl-2-morpholino-5-oximino-8*H*-1,2,4-triazolo-[1,5-*a*]pyrimidine (**7b**).

To a solution of 2.53 g (0.01 mole) of 5-chloro-7-methyl-2-morpholino-1,2,4-triazolo[1,5-*a*]pyrimidine (**4b**) in 40 ml of acetonitrile a water solution of 0.66 g (0.02 mole) of hydroxylamine [prepared fresh by mixing a solution of 1.38 g (0.02 mole) of hydroxylamine hydrochloride in 4 ml of water and 1.06 g (0.01 mole) of sodium carbonate in 8 ml of water] was added in one portion at 45°. The reaction mixture crystallized immediately. After cooling, the crystals that precipitated were filtered, and washed with a 1:1 mixture of chloroform and

methanol to yield 2.03 g (84%) of *(E)*-7-methyl-2-morpholino-5-oximino-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**7b**), mp 270-272° (dimethylformamide); ir: ν OH = 3420 cm^{-1}, ν C=N = 1680, 1640, 1599 and 1576 cm^{-1}, ν COC = 1117 cm^{-1}, ν N-O = 922 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.29 (s, 3H, CH_3), 3.37 (t, 4H, NCH_2), 3.66 (t, 4H, OCH_2), 6.05 (s, 1H, CH), 9.5 (bs, 1H, OH), 10.5 (b, 1H, NH); cmr (DMSO-d_6): δ, ppm 18.6 (CH_3), 46.1 (NCH_2), 65.8 (OCH_2), 89.0 (CH), 144.2 (C-8a), 147.3 (C-7), 148.5 (C-5), 164.8 (C-2); ms: (EI) m/z 250 (13%, M^+), 234 (47%), 233 (10%), 177 (100%).

Anal. Calcd. for $C_{10}H_{14}N_6O_2$ (MW 250.26): C, 47.99; H, 5.64; N, 33.58. Found: C, 48.12; H, 5.88; N, 33.61.

(E)-2-Methylthio-5-oximino-6,7,8,9-tetrahydrocyclopenta-[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**8a**).

To a solution of 24.1 g (0.1 mole) of 5-chloro-2-methylthio-6,7-dihydro-8*H*-cyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**5a**) in 120 ml of methanol a water solution of 6.6 g (0.2 mole) of hydroxylamine [prepared fresh by mixing a solution of 13.8 g (0.2 mole) of hydroxylamine hydrochloride in 15 ml of water and 10.6 g (0.1 mole) of sodium carbonate in 25 ml of water] was added in one portion at 50°. The reaction mixture crystallized immediately. After cooling the crystals that precipitated were filtered, and washed with a 1:1 mixture of chloroform and methanol to yield 16.5 g (69%) of *(E)*-2-methylthio-5-oximino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo-[1,5-*a*]-pyrimidine (**8a**), mp 260-262° (dimethylformamide); ir: ν OH = 3450 cm^{-1}, ν C=N = 1672, 1620 and 1606 cm^{-1}, ν N-O = 973 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.00 (qi, 2H, CH_2-7), 2.57 (s, 3H, SCH_3), 2.72 (t, 2H, CH_2-8), 3.15 (t, 2H, CH_2-6), 9.9 (bs, 1H, OH), 10.5 (bs, 1H, NH); cmr (DMSO-d_6): δ, ppm 15.7 (SCH_3), 24.9 (C-7), 30.7 (C-8), 34.2 (C-6), 106.4 (C-5a), 143.4 (C-9a), 148.2 (C-8a), 151.4 (C-5), 162.0 (C-2); ms: (EI) m/z 237 (14%, M^+), 221 (100%), 220 (54%).

Anal. Calcd. for $C_9H_{11}N_5OS$ (MW 237.29): C, 45.56; H, 4.67; N, 29.51; S, 13.51. Found: C, 45.48; H, 4.72; N, 29.63; S, 13.47.

(E)-2-Morpholino-5-oximino-6,7,8,9-tetrahydrocyclopenta-[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**8b**).

To a solution of 13.98 g (0.05 mole) of 5-chloro-2-morpholino-6,7-dihydro-8*H*-cyclopenta[1,2-*d*][1,2,4]triazolo-[1,5-*a*]pyrimidine (**5b**) in 250 ml of dimethylformamide a water solution of 3.3 g (0.1 mole) of hydroxylamine [prepared fresh by mixing a solution of 6.9 g (0.1 mole) of hydroxylamine hydrochloride in 8 ml of water and 5.3 g (0.05 mole) of sodium carbonate in 10 ml of water] was added in one portion at 50-60°. The reaction mixture crystallized immediately. After cooling the crystals that precipitated were filtered, and washed with a 1:1 mixture of chloroform and methanol to yield 9.03 g (65%) of *(E)*-2-morpholino-5-oximino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]-pyrimidine (**8b**), mp 282-284° (dimethylformamide); ir: ν OH = 3420 cm^{-1}, ν C=N = 1639 and 1579 cm^{-1}, ν COC = 1118 cm^{-1}, ν N-O = 973 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.00 (qi, 2H, CH_2-7), 2.73 (t, 2H, CH_2-8), 3.13 (t, 2H, CH_2-6), 3.40 (m, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 9.75 (bs, 1H, OH), 10.2 (bs, 1H, NH); cmr (DMSO-d_6): δ, ppm 22.3 (C-7), 29.9 (C-8), 34.1 (C-6), 45.9 (NCH_2), 65.7 (OCH_2), 105.0 (C-5a), 144.6 (C-9a), 147.8 (C-8a), 151.0 (C-5), 166.5 (C-2); ms: (EI) m/z 276 (30%, M^+), 260 (66%), 203 (100%).

Anal. Calcd. for $C_{12}H_{16}N_6O_2$ (MW 276.30): C, 52.17; H, 5.84; N, 30.42. Found: C, 52.09; H, 5.98; N, 30.30.

(E)-2-Methylthio-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**9a**).

To a solution of 5.09 g (0.02 mole) of 5-chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6a**) in 25 ml of dimethylformamide, a water solution of 1.32 g (0.04 mole) of hydroxylamine [prepared fresh by mixing a solution of 2.76 g (0.04 mole) of hydroxylamine hydrochloride in 6 ml of water and 2.12 g (0.02 mole) of sodium carbonate in 15 ml of water] was added in one portion at 40°. The reaction mixture crystallized immediately. After cooling the crystals that precipitated were filtered, and washed with a 1:1 mixture of chloroform and methanol to yield 4.95 g (93%) of *(E)*-2-methylthio-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**9a**), mp 231-233° (dimethylformamide); ir: ν OH = 3420 cm^{-1}, ν C=N = 1671, 1637 and 1599 cm^{-1}, ν N-O = 977 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.65 (m, 4H, CH_2-7 and 8), 2.15 (m, 2H, CH_2-9), 2.34 (t, 2H, CH_2-6), 2.65 (s, 3H, SCH_3), 10.3 (bs, 1H, OH), 11.4 (bs, 1H, NH); cmr (DMSO-d_6): δ, ppm 13.5 (SCH_3), 21.2* (C-8), 21.5* (C-7), 22.0* (C-9), 25.9 (C-6), 102.5 (C-5a), 135.4 (C-10a), 136.7 (C-9a), 150.3 (C-5), 160.4 (C-2); ms: (EI) m/z 251 (45%, M^+), 235 (98%), 234 (100%).

Anal. Calcd. for $C_{10}H_{13}N_5OS$ (MW 251.31): C, 47.79; H, 5.21; N, 27.87; S, 12.76. Found: C, 47.64; H, 5.33; N, 27.94; S, 12.71.

(E)-2-Morpholino-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**9b**).

To a solution of 7.20 g (0.025 mole) of 5-chloro-2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6b**) in 60 ml of dimethylformamide prepared at 100° an aqueous solution of 1.65 g (0.05 mole) of hydroxylamine [prepared fresh by mixing a solution of 3.45 g (0.05 mole) of hydroxylamine hydrochloride in 10 ml of water and 2.65 g (0.025 mole) of sodium carbonate in 20 ml of water] was added in one portion. The reaction mixture was allowed to cool with stirring to room temperature. The crystals that precipitated were filtered, and washed with acetonitrile to yield 2.84 g (39%) of *(E)*-2-morpholino-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]-quinazoline (**9b**), mp 236-238° (dimethylformamide); ir: ν OH = 3420 cm^{-1}, ν C=N = 1666 and 1612 cm^{-1}, ν COC = 1118 cm^{-1}, ν N-O = 984 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.65 (m, 4H, CH_2-7 and 8), 2.15 (t, 2H, CH_2-9), 2.36 (t, 2H, CH_2-6), 3.36 (t, 4H, NCH_2), 3.69 (t, 4H, OCH_2), 10.95 (bs, 1H, OH), 11.2 (bs, 1H, NH); cmr (DMSO-d_6): δ, ppm 21.1 (C-7 and 8), 21.5 (C-9), 25.9 (C-6), 45.9 (NCH_2), 65.6 (OCH_2), 102.3 (C-5a), 135.4 (C-10a), 137.2 (C-9a), 149.2 (C-5), 162.6 (C-2); ms: (EI) m/z 290 (32%, M^+), 274 (45%), 273 (37%), 217 (100%).

Anal. Calcd. for $C_{13}H_{18}N_6O_2$ (MW 290.33): C, 53.78; H, 6.25; N, 28.95. Found: C, 53.70; H, 6.31; N, 29.04.

(E)-5-Benzyloximino-7-methyl-2-methylthio-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**10a**).

To a solution of 2.11 g (0.01 mole) of *(E)*-7-methyl-2-methylthio-5-oximino-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**7a**) in 10 ml of dry dimethylformamide, 0.38 g (0.01 mole) of sodium hydride (60% suspension in paraffin oil, Fluka) was added in small portions with stirring at room temperature. The reaction mixture foamed while the temperature rose to 35°. After its cooling to 20°, 1.26 g (0.01 mole) of benzyl chloride was

added dropwise with stirring to the reaction mixture while the temperature rose to 50°. The reaction mixture was stirred for 3 hours at room temperature, then 20 ml of water was added and the product was extracted with three 10 ml portions of benzene. The combined benzene layers were extracted with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness. The residue was recrystallized from acetonitrile to yield 1.24 g (41%) of *(E)*-5-benzyloximino-7-methyl-2-methylthio-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**10a**), mp 218-219°; ir: ν C=N = 1614 and 1496 cm^{-1}, ν N-O = 908 cm^{-1}; pmr (DMSO-d_6): δ, ppm 2.18 (s, 3H, CH_3), 2.55 (s, 3H, SCH_3), 5.04 (s, 2H, $PhCH_2O$), 6.05 (s, 1H, CH), 7.36-7.43 (m, 5H, PhH), 10.6 (NH); irradiated at 5.04 ppm DNOE at 2.18 (5%, CH_3), 6.05 (3%, CH) and 7.43 (9%, *o*-PhH) ppm; irradiated at 6.05 ppm DNOE at 2.18 (10%, CH_3), 5.04 (2%, $PhCH_2O$) and 7.43 (2%, *o*-PhH) ppm; cmr (DMSO-d_6): δ, ppm 13.4 (SCH_3), 18.6 (CH_3), 75.1 ($PhCH_2O$), 88.9 (C-6), 127.4 (*p*-PhC), 128.1 (*o*-PhC), 128.7 (*m*-PhC), 138.1 (*s*-PhC), 143.6 (C-8a), 145.7 (C-7), 149.5 (C-5), 162.2 (C-2); ms: (EI) m/z 301 (25%, M^+), 195 (78%), 106 (70%), 105 (72%), 91 (100%).

Anal. Calcd. for $C_{14}H_{15}N_5OS$ (MW 301.37): C, 55.80; H, 5.02; N, 23.24; S, 10.64. Found: C, 55.88; H, 5.15; N, 23.20; S, 10.66.

(E)-5-Benzyloximino-7-methyl-2-morpholino-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**10b**).

To a suspension of 1.59 g (0.01 mole) of *O*-benzylhydroxylamine hydrochloride [9] in 20 ml of methanol, 1.1 ml (0.011 mole) of triethylamine was added dropwise with stirring at room temperature. The reaction mixture was heated to 40° at which temperature 2.54 g (0.01 mole) of 5-chloro-7-methyl-2-morpholino-1,2,4-triazolo[1,5-*a*]pyrimidine (**4b**) was added in small portions. The reaction was completed by heating the mixture at 65° for 2 hours. The solution obtained was evaporated *in vacuo* to dryness and the residue (5.05 g) was recrystallized from 20 ml of 2-propanol to yield 2.24 g (66%) of *(E)*-5-benzyloximino-7-methyl-2-morpholino-8*H*-1,2,4-triazolo[1,5-*a*]pyrimidine (**10b**), mp 223-225°; ir: ν C=N = 1600 and 1498 cm^{-1}, ν COC = 1117 cm^{-1}, ν N-O = 916 cm^{-1}; pmr (deuteriochloroform + DMSO-d_6): δ, ppm 2.34 (s, 3H, CH_3), 3.62 (t, 4H, NCH_2), 3.65 (t, 4H, OCH_2), 5.17 (s, 2H, $PhCH_2O$), 6.11 (s, 1H, CH), 7.35-7.46 (m, 5H, PhH), 8.3 (b, 1H, NH); irradiated at 5.17 ppm DNOE at 6.11 (3%, CH) and 7.35 (8.5%, *o*-PhH) ppm; cmr (deuteriochloroform + DMSO-d_6): δ, ppm 19.7 (CH_3), 45.6 (NCH_2), 66.0 (OCH_2), 78.7 ($PhCH_2O$), 88.8 (C-6), 128.6 (*p*-PhC), 129.0 (*o*-PhC), 129.5 (*m*-PhC), 134.1 (*s*-PhC), 144.6 (C-8a), 147.4 (C-7), 148.9 (C-5), 165.4 (C-2); ms: (EI) m/z 340 (16%, M^+), 234 (44%), 106 (83%), 105 (82%), 91 (50%), 77 (100%).

Anal. Calcd. for $C_{17}H_{20}N_6O_2$ (MW 340.39): C, 59.99; H, 5.92; N, 24.69. Found: C, 60.04; H, 6.05; N, 24.62.

(E)-5-Benzyloximino-2-methylthio-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**11a**).

To a suspension of 5.75 g (0.02 mole) of *(E)*-2-methylthio-5-oximino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo-[1,5-*a*]pyrimidine (**8a**) in 10 ml of dimethylformamide, 0.76 g (0.02 mole) of sodium hydride (60% suspension in paraffin oil, Fluka) was added in small portions at room temperature with stirring. During the addition the reaction mixture foamed and the temperature rose to 35°. After cooling to 20°, 2.52 ml (0.02 mole) of benzyl chloride was added dropwise into the reaction mixture. During the addition the temperature of the mixture rose to 50°. The mixture was stirred at this temperature for 30 minutes, then 20 ml of water was added to it and extracted with three 10 ml portions of chloroform. The combined organic layers were extracted with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness. The residue (7.4 g) was recrystallized from acetonitrile to yield 2.30 g (35%) of *(E)*-5-benzyloximino-2-methylthio-6,7,8,9-tetrahydrocyclopenta-[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**11a**), mp 206-208°; ir: ν C=N = 1664 and 1609 cm^{-1}, ν N-O = 863 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.98 (qi, 2H, CH_2-7), 2.55 (s, 3H, SCH_3), 2.65 (t, 2H, CH_2-8), 3.06 (t, 2H, CH_2-6), 4.98 (s, 2H, $PhCH_2O$), 7.36-7.38 (m, 5H, PhH), 12.1 (b, 1H, NH); irradiation at 4.98 ppm DNOE at 3.06 (3%, CH_2-6) and 7.37 (8.5%, *o*-PhH) ppm; cmr (DMSO-d_6): δ, ppm 13.3 (SCH_3), 21.7 (C-7), 29.9 (C-8), 31.6 (C-6), 75.3 ($PhCH_2O$), 103.7 (C-5a), 128.0 (*p*-PhC), 128.3 (*o*- and *m*-PhC), 138.1 (*s*-PhC), 143.2 (C-9a), 146.1 (C-8a), 149.4 (C-5), 161.7 (C-2); ms: (EI) m/z: 327 (10%, M^+), 221 (80%), 106 (92%), 105 (90%), 77 (100%); (CI) m/z 328 [15%, $(M+1)^+$], 222 (2%), 107 (100%).

Anal. Calcd. for $C_{16}H_{17}N_5OS$ (MW 327.41): C, 58.70; H, 5.23; N, 21.39; S, 9.79. Found: C, 58.63; H, 5.31; N, 21.44; S, 9.83.

(E)-5-Benzyloximino-2-morpholino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**11b**).

To a suspension of 1.59 g (0.01 mole) of *O*-benzylhydroxylamine hydrochloride [9] in 20 ml of methanol, 1.1 ml (0.011 mole) of triethylamine was added dropwise with stirring at room temperature. The reaction mixture was heated to 40° at which temperature 2.79 g (0.01 mole) of 5-chloro-2-morpholino-6,7-dihydro-8*H*-cyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**5b**) was added in small portions. The reaction was completed by heating the mixture at 65° for 3 hours. After cooling the crystals that precipitated were filtered and washed with methanol to yield 1.45 g (39%) of *(E)*-5-benzyloximino-2-morpholino-6,7,8,9-tetrahydrocyclopenta[1,2-*d*][1,2,4]triazolo[1,5-*a*]pyrimidine (**11b**), mp 204-205° (acetonitrile); ir: ν C=N = 1651 and 1603 cm^{-1}, ν COC = 1118 cm^{-1}, ν N-O = 968 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.99 (qi, 2H, CH_2-7), 2.67 (t, 2H, CH_2-8), 3.07 (t, 2H, CH_2-6), 3.54 (t, 4H, NCH_2), 3.70 (t, 4H, OCH_2), 5.00 (s, 2H, $PhCH_2O$), 7.28-7.42 (m, 5H, PhH), 11.1 (NH); irradiation at 5.00 ppm DNOE at 3.07 (3%, CH_2-6) and 7.40 (10%, *o*-PhH) ppm; cmr (DMSO-d_6): δ, ppm 21.8 (C-7), 30.0 (C-8), 31.6 (C-6), 45.9 (NCH_2), 65.7 (OCH_2), 75.4 ($PhCH_2O$), 103.8 (C-5a), 127.8 (*p*-PhC), 128.2 (*o*-PhC), 128.5 (*m*-PhC), 138.1 (*s*-PhC), 143.7 (C-9a), 145.2 (C-8a), 148.3 (C-5), 165.1 (C-2); ms: (EI) m/z 366 (12%, M^+), 260 (52%), 203 (98%), 106 (72%), 105 (80%), 77 (100%); (CI) m/z 367 [7%, $(M+1)^+$], 261 (100%), 107 (17%).

Anal. Calcd. for $C_{19}H_{22}N_6O_2$ (MW 366.43): C, 62.28; H, 6.05; N, 22.94. Found: C, 62.34; H, 6.21; N, 22.87.

(E)-Benzyloximino-2-methylthio-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12a**). From **9a**.

To a suspension of 2.51 g (0.01 mole) of *(E)*-2-methylthio-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**9a**) in 10 ml of dimethylformamide 0.38 g (0.01 mole) of sodium hydride (60% suspension in paraffin oil, Fluka) was added in small portions at room temperature with stirring. During the addition the reaction mixture foamed and the temperature rose to 35°. After cooling the mixture to 20°, 1.25 ml (0.01 mole) of benzyl chloride was added dropwise to the reaction mixture. During the addition the temperature of the mixture rose

to 50°. The mixture was stirred at this temperature for 40 minutes then 30 ml of water was added and it was extracted with three 10 ml portions of chloroform. The combined organic layers were extracted with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 1.15 g (32%) of *(E)*-benzyloximino-2-methylthio-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12a**), mp 302-304°; ir: ν C=N = 1676, 1624 and 1600 cm^{-1}, ν N-O = 983 cm^{-1}; pmr (deuteriochloroform + DMSO-d_6): δ, ppm 1.62 (m, 4H, CH_2-7 and 8), 2.14 (m, 2H, CH_2-9), 2.33 (m, 2H, CH_2-6), 2.54 (s, 3H, SCH_3), 5.00 (s, 2H, $PhCH_2O$), 7.28-7.36 (m, 5H, PhH), 11.4 (b, 1H, NH); irradiation at 5.00 ppm DNOE at 2.33 (2%, CH_2-6) and 7.36 (5.5%, *o*-PhH) ppm; cmr (DMSO-d_6): δ, ppm 13.5 (SCH_3), 21.2* (C-8), 21.5* (C-7), 22.0* (C-9), 26.0 (C-6), 75.6 ($PhCH_2O$), 102.0 (C-5a), 127.4 (*p*-PhC), 127.6 (*o*-PhC), 128.2 (*m*-PhC), 136.5 (*s*-PhC), 137.5 (C-10a), 138.5 (C-9a), 150.5 (C-5), 160.9 (C-2); ms: (EI) m/z 341 (7%, M^+), 235 (100%), 234 (36%), 106 (48%), 105 (50%), 91 (22%), 77 (58%).

Anal. Calcd. for $C_{17}H_{19}N_5OS$ (MW 341.44): C, 59.80; H, 5.61; N, 20.51; S, 9.39. Found: C, 59.83; H, 5.59; N, 20.48; S, 9.30.

(E)-Benzyloximino-2-methylthio-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12a**). From **6a**.

To a solution of 2.04 g (0.0166 mole) of *O*-benzylhydroxylamine [10] and 2 ml of triethylamine in 50 ml of dimethylformamide 2.54 g (0.005 mole) of 5-chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6a**) was added at 40° in small portions. The reaction was completed by stirring the mixture at 90° for 1 hour. After cooling 30 ml of water was added to the mixture, the crystals that precipitated were filtered and washed with acetonitrile to yield 2.20 g (65%) of *(E)*-benzyloximino-2-methylthio-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12a**), mp 301-303°. The product is identical (mixed mp, ir) with that of obtained from **9a**.

(E)-5-Benzyloximino-2-morpholino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12b**). From **6b**.

To a solution of 1.02 g (0.0083 mole) of *O*-benzylhydroxylamine [10] and 1 ml of triethylamine in 25 ml of dimethylformamide 1.47 g (0.005 mole) of 5-chloro-2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**6b**) was added at 40° in small portions. The reaction was completed by stirring the mixture at 90° for 1 hour. After cooling, 30 ml of water was added to the mixture, the crystals that precipitated were filtered and washed with acetonitrile to yield 1.2 g (63%) of *(E)*-5-benzyloximino-2-morpholino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12b**), mp 342-344° (dimethylformamide); ir: ν C=N = 1672, 1624 and 1556 cm^{-1}, ν COC = 1106 cm^{-1}, ν N-O = 983 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.62 (m, 4H, CH_2-7 and 8), 2.13 (m, 2H, CH_2-9), 2.32 (m, 2H, CH_2-6), 3.34 (m, 4H, NCH_2), 3.70 (m, 4H, OCH_2), 4.97 (s, 2H, $PhCH_2O$), 7.29-7.51 (m, 5H, PhH), 11.2 (b, 1H, NH); irradiated at 4.97 ppm DNOE at 2.32 (2%, CH_2-6) and 7.35 (5%, *o*-PhH) ppm; cmr (DMSO-d_6): δ, ppm 20.9 (C-8), 21.3 (C-7), 21.7 (C-9), 25.6 (C-6), 46.0 (NCH_2), 65.3 (OCH_2), 75.2 ($PhCH_2O$), 101.5 (C-5a), 126.8 (*p*-PhC), 126.9 (*o*-PhC), 127.7 (*m*-PhC), 135.7 (*s*-PhC), 138.0 (C-10a), 138.5 (C-9a), 149.2 (C-5), 163.4 (C-2); ms: (EI) m/z 380 (3%, M^+), 274 (50%), 217 (100%), 189 (30%), 107 (40%), 106 (37%), 77 (50%).

Anal. Calcd. for $C_{20}H_{24}N_6O_2$ (MW 380.45): C, 63.14; H, 6.36; N, 22.09. Found: C, 63.08; H, 6.50; N, 22.14.

(E)-10-Benzyl-2-morpholino-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**13**), and *(E)*-5-Benzyloximino-2-morpholino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12b**). From **9b**.

To a suspension of 2.61 g (0.009 mole) of *(E)*- 2-morpholino-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**9b**) in 20 ml of dimethylformamide, 0.38 g (0.01 mole) of sodium hydride (60% suspension in paraffin oil, Fluka) was added in small portions at room temperature with stirring. During the addition the reaction mixture foamed and the temperature rose to 35°. After cooling to 20°, 1.25 ml (0.01 mole) of benzyl chloride was added dropwise to the reaction mixture. During the addition the temperature of the mixture rose to 30°. The mixture was stirred at this temperature for 40 minutes then 30 ml of water was added and it was extracted with three 10 ml portions of chloroform. The combined organic layers were extracted with water, dried over anhydrous sodium sulfate and evaporated *in vacuo* to dryness to yield 2.45 g of a honey like product that after the addition of 8 ml of acetonitrile crystallized. The crystals were filtered and washed with acetonitrile to yield 0.56 g (16%) of *(E)*-10-benzyl-2-morpholino-5-oximino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**13**), that after recrystallization from a 3:1 mixture of acetonitrile and dimethylformamide melted at 196-198°; ir: ν C=N = 1643 cm^{-1}, ν COC = 1116 cm^{-1}; pmr (DMSO-d_6): δ, ppm 1.55 (m, 2H, CH_2-8), 1.62 (m, 2H, CH_2-7), 2.20 [t (J = 6.0 Hz), 2H, CH_2-9], 2.35 [t, (J = 6 Hz), CH_2-6], 3.31 [t (J = 4.8 Hz), 4H, NCH_2), 3.65 [t (J = 4.8 Hz), 4H, OCH_2], 5.21 (s, 2H, $PhCH_2$), 7.19-7.37 (m, 5H, PhH), 10.9 (b, 1H, NH); irradiation at 5.21 ppm DNOE at 7.36 ppm, but irradiation at 2.35 ppm, no DNOE enhancement observed; cmr (DMSO-d_6): δ, ppm 20.9* (C-8), 21.5* (C-7), 22.4* (C-9), 24.5 (C-6), 45.9 (NCH_2), 65.6 (OCH_2), 48.1 ($PhCH_2$), 105.2 (C-5a), 126.1 (*p*-PhC), 127.5 (*o*-PhC), 129.0 (*m*-PhC), 136.6* (*s*-PhC), 137.0* (C-9a and 10a), 150.9 (C-5), 161.7 (C-2); ms: (EI) m/z 380 (53%, M^+), 363 (85%), 273 (35%), 215 (15%), 113 (21%), 91 (100%); (CI) m/z 381 [100%, $(M+1)^+$], 365 (88%).

Anal. Calcd. for $C_{20}H_{24}N_6O_2$ (MW 380.45): C, 63.14; H, 6.36; N, 22.09. Found C, 63.10; H, 6.45; N, 22.20.

The mother liquor was evaporated to dryness and the residue chromatographed on a short silica gel column (eluent chloroform) to yield 0.52 g (15%) of *(E)*-5-benzyloximino-2-morpholino-6,7,8,9-tetrahydro-10*H*-1,2,4-triazolo[5,1-*b*]quinazoline (**12b**), mp 341-344° (dimethylformamide). The product is identical (mixed mp, ir) with that of obtained from **6b**.

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