

On Triazoles. XIII [1].
The Reaction of 5-Benzalimino-1,2,4-triazoles
with Substituted Acetyl Chlorides [2]

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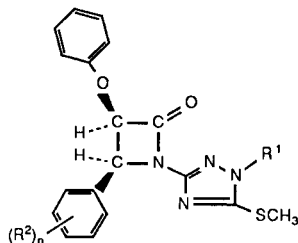
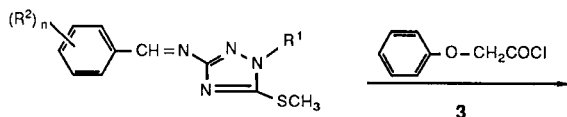
The reaction of Schiff bases prepared from 1- and 2-substituted-5-amino-1,2,4-triazoles with phenoxyacetyl chlorides in the presence of triethylamine and a mixture of phosphorus oxychloride and dichloroacetic acid in dimethylformamide to yield β -lactam **4**, a dihydro-1,2,4-triazolo[4,3-*a*]pyrimidine-5(1*H*)-one **5**, a 1,2,4-triazolo[1,5-*a*]pyrimidin-5(3*H*)-one **9** and the corresponding 1,2,4-triazolo[4,3-*a*]pyrimidine-5(1*H*)-one **10** derivatives was studied.

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In a previous paper of this series [3] we have described the synthesis of different **1** and **2** type Schiff bases. Starting from biological considerations, in hope of preparing the corresponding β -lactam derivatives the above Schiff bases were reacted by the known method [4] with phenoxyacetyl chloride (**3**) in the presence of triethylamine.

Nevertheless the expected β -lactam derivatives **4a-c** were obtained in the case of Schiff bases **1a-c** only which were substituted at the position 2 of the triazole ring (Scheme 1), while in case of the Schiff base **2a** substituted in position 1 of the triazole ring, a 1,4-type cycloaddition occurred to yield the corresponding 6,7-dihydro-1,2,4-triazolo[4,3-*a*]pyrimidin-5-one **5** derivative (Scheme 2).

Scheme 1

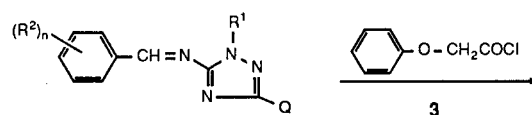


4a-c

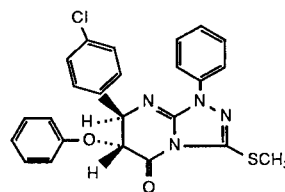
- a**, R^1 = methyl, $(R^2)_n$ = H
b, R^1 = methyl, $(R^2)_n$ = 4-chloro
c, R^1 = methyl, $(R^2)_n$ = 4-(2-dimethylaminoethoxy)

The structure of derivatives **4a-c** (Scheme 1) is consistent, in addition to the other spectral data with the

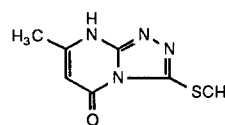
Scheme 2



2a $Q = SCH_3$, $R^1 = Ph$, $(R^2)_n = Cl$



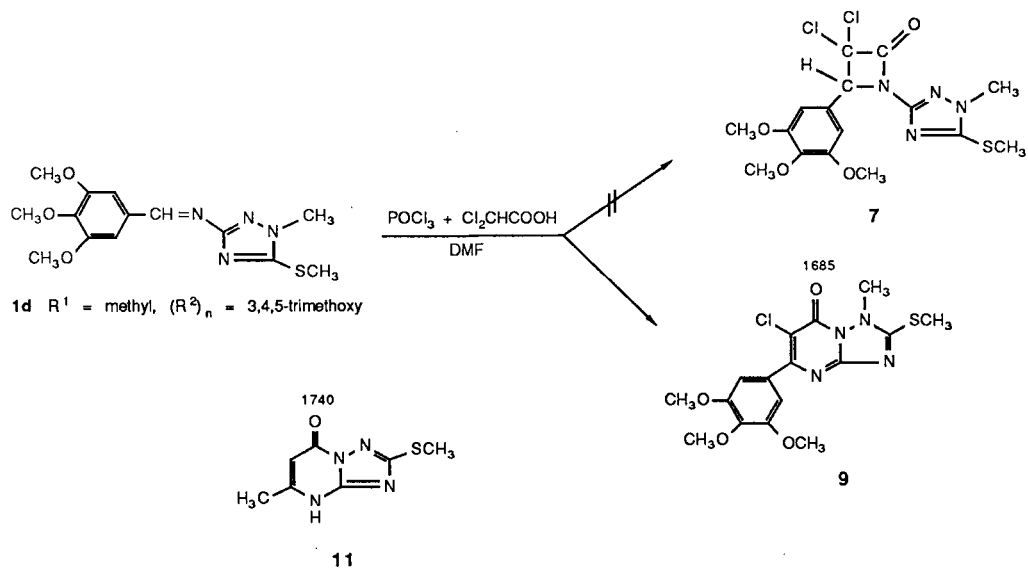
1745 **5**



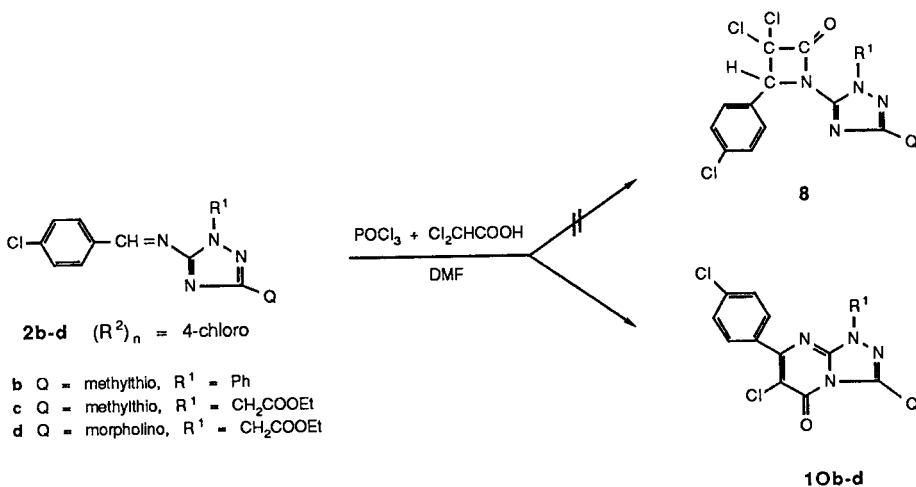
1720 **6**

β -lactam carbonyl bands appearing at $1770-1775\text{ cm}^{-1}$. The *cis* configuration of the azetidinone-ring substituents was deduced from the $J_{H,H}$ coupling constants of the azetidinone-ring protons being of the value of 4.5-5 Hz (see Experimental) [5]. The structure of derivative **5** (Scheme 2) is again consistent - besides all other spectral data - with the ir carbonyl band of 1745 cm^{-1} (compare *e.g.* with the ν C=O band of the corresponding dehydro-derivative **6** appearing at 1720 cm^{-1} [6] where the carbonyl frequency is lowered by a conjugated double bond). The *trans* configuration of the dihydropyrimidinone substituents was deduced from the $J_{H,H}$ coupling constants of the dihydropyrimidinone protons being of the value of ≈ 11 ppm.

Scheme 3



Scheme 4



Taking into account the strong antiinflammatory activity of some 3,3-dichloroazetidinone derivatives [7] the Schiff bases were reacted by the known method [8] with the mixture of phosphorus oxychloride and dichloroacetic acid in dimethylformamide but instead of the expected 3,3-dichloroazetidinone derivatives **7** and **8** (Schemes 3 and 4) the corresponding triazolo-pyrimidinone derivatives **9** and **10** were formed.

The structure of derivative **9** obtained is - besides all other spectral data - again in accordance with the carbonyl band appearing at 1685 cm^{-1} if we take into consideration that this derivative has one more conjugated double bond than the known derivative **11** which absorbs at 1740 cm^{-1} (Scheme 3) [6] and the 3,4,5-trimethoxyphenyl group is also conjugated through the pyrimidinone double bond to the carbonyl group present in **9**.

The situation is the same with the carbonyl bands of derivatives **10b-d** appearing between $1685\text{--}1700\text{ cm}^{-1}$ having again an extra conjugated double bond as compared with the analogous derivative **6** absorbing at 1720 cm^{-1} (Scheme 2 and 4).

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are uncorrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained with a Varian Cary 118 and a Pye Unicam SP 8-150 instrument. The ^1H -nmr and the ^{13}C -nmr measurements were performed using Varian XL-100, Bruker WM-250 and Bruker WP-80 SY instruments. The electron impact mass spectra were recorded on a Varian MAS SM-1 spectrometer.

5-[4-(2-Dimethylaminoethoxy)benzalimino]-2-methyl-3-methylthio-2H-1,2,4-triazole[**1c**, $\text{R}^1 = \text{CH}_3$, $(\text{R}^2)_n = 4(2\text{-dimethylaminoethoxy})$].

A mixture of 4.18 g (0.029 mole) of 5-amino-2-methyl-3-methylthio-2*H*-1,2,4-triazole [3], 5.63 g (0.0291 mole) of 4-(2-dimethylaminoethoxy)benzaldehyde [9] 50 ml of 2-propanol and 3 drops of piperidine was refluxed for 16 hours. The solution obtained was evaporated *in vacuo* to dryness and the residue recrystallised from ethyl acetate to yield 8.3 g (90%) of the title product, mp 96-97°; ir: ν C=N = 1620, 1610 and 1580 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.32 (s, 6H, N(CH₃)₂), 2.69 (s, 3H, SCH₃), 3.71 (s, 3H, NCH₃), 2.65 (t, 2H, NCH₂), 4.08 (t, 2H, OCH₂), 6.85-7.95 (dd, 4H, ArH), 9.07 (s, 1H, CH).

Anal. Calcd. for C₁₅H₂₁N₅S (MW, 303.42): C, 59.38, H, 6.98, N, 23.08, S, 10.57. Found: C, 59.44, H, 7.05, N, 22.94, S, 10.48.

Ethyl[5-(4-Chlorobenzalimino)-3-morpholino-1*H*-1,2,4-triazol-1-yl]acetate (2d, Q = morpholino, R' = CH₂COOEt, (R₂)_n = 4-chloro).

The solution of 5.1 g (0.02 mole) of ethyl (5-amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)acetate (preparation see below), 3.09 g (0.022 mole) of 4-chlorobenzaldehyde and 1 drop of piperidine in 20 ml of 2-propanol was refluxed for 3 hours. After cooling the crystals precipitated were filtered off to yield 5.45 g (72%) of the title product, mp 171-172° (2-propanol); ir: ν C=O = 1750 cm^{-1} , ν C=N = 1620 and 1595 cm^{-1} ; pmr (DMSO-*d*₆): δ ppm 1.20 (t, 3H, CH₃), 3.20 (t, 4H, NCH₂), 3.61 (t, 4H, OCH₂), 4.20 (qa, 2H, CH₂CH₃), 5.05 (s, 2H, NCH₂), 7.55 and 8.1 (AB, 4H, ArH), 9.1 (s, 1H, CH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 207 (15.2), 282 (18.3), 356 (9.3).

Anal. Calcd. for C₁₇H₂₀ClN₅O₃ (MW, 377.84): C, 54.04; H, 5.34; N, 18.54; Cl, 9.38. Found: C, 54.13, H, 5.32, N, 18.79; Cl, 9.25.

Ethyl(5-Amino-3-morpholino-1*H*-1,2,4-triazol-1-yl)acetate.

To a solution of 20 ml of dimethylformamide and 3.0 g (0.01 mole) of 80% sodium hydride, 16.9 g (0.01 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole [10] was added at 0° with stirring. The stirring was continued for 30 minutes at 0°, then 10.6 ml (12.2 g, 0.01 mole) of ethyl chloroacetate was dropped into the reaction mixture maintaining the same temperature with stirring. The stirring was continued for further 2 hours leaving the reaction mixture to warm to the room temperature. After standing overnight 200 ml of water was added to the reaction mixture, the product was extracted with ethyl acetate, dried and evaporated *in vacuo* to dryness to yield 17.0 g (67%) of the title product, mp 171-172° (ethanol); ir: ν C=O = 1748 cm^{-1} , ν C=N = 1665 and 1595 cm^{-1} , ν NH₂ = 3380 cm^{-1} ; pmr (DMSO-*d*₆): δ ppm 1.22 (t, 3H, CH₃), 3.15 (t, 4H, NCH₂), 3.65 (t, 4H, OCH₂), 4.17 (qa, 2H, CH₂CH₃), 4.65 (s, 2H, NCH₂CO), 6.22 (bs, 2H, NH₂); cmr (DMSO-*d*₆): δ ppm 15.9 (CH₃), 48.5 (NCH₂), 49.3 (NCH₂CO), 62.9 (OCH₂CH₃), 67.8 (OCH₂), 158.1 (triazole C₅), 164.7 (triazole C₃), 170.3 (C=O) [11]; uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 218 sh (6.5); uv (10% ethanol + 90% hydrochloric acid) 214 (9.5).

Anal. Calcd. for C₁₀H₁₇N₅O₃ (MW, 225.28): C, 47.05; H, 6.71; N, 27.43. Found: C, 47.23; H, 6.95; N, 27.56.

cis-1-(2-Methyl-3-methylthio-2*H*-1,2,4-triazol-5-yl)-2-phenyl-3-phenoxyazetid-4-one (4a, R' = methyl, (R₂)_n = H).

To a solution of 9.29 g (0.04 mole) of 5-benzalimino-2-methyl-3-methylthio-2*H*-1,2,4-triazole (1a, R' = methyl, (R₂)_n = H) [3] in 120 ml of absolute dichloromethane and 11.0 ml = 8.0 g (0.08 mole) of anhydrous triethylamine the solution of 8.5 g (0.05 mole) of phenoxyacetyl chloride dissolved in 140 ml of absolute dichloroethane was added dropwise with stirring at 0° under nitrogen stream during the period of 5 hours. The stirring was continued and the reaction mixture was let to warm slowly to room temperature. After standing overnight 100 ml of water was added, the layers were separated, the organic layer was washed twice with 100 ml portions of water, dried over anhydrous potassium carbonate and evaporated *in vacuo* to dryness. The residue was recrystallised from acetonitrile to yield 3.3 g (23%) of the title product, mp 187-188°; ir: ν C=O = 1775 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.60 (s, 3H, SCH₃), 3.64 (s, 3H, NCH₃), 5.55 [d (J = 4.5 Hz), 1H, CH²], 7.30 [d (J = 4.5 Hz), 1H, CH²], 6.7-7.2 (m, 9H, ArH).

Anal. Calcd. for C₁₉H₁₈N₄O₂S (MW, 366.43): C, 62.28; H, 4.95; N, 15.29; S, 8.75. Found: C, 62.33; H, 5.18; N, 15.06; S, 8.95.

cis 1-(2-Methyl-3-methylthio-2*H*-1,2,4-triazol-5-yl)-2-(4-chlorophenyl)-3-phenoxyazetid-4-one (4b, R' = methyl, (R₂)_n = 4-chloro).

To a solution of 8.00 g (0.03 mole) of 5-(4-chlorobenzalimino)-2-methyl-3-methylthio-2*H*-1,2,4-triazole (1b, R' = methyl, (R₂)_n = 4-chloro) [3] in 120 ml of absolute dichloromethane and 11.0 ml = 8.0 g (0.08 mole) of anhydrous triethylamine the solution of 8.5 g (0.05 mole) of phenoxyacetyl chloride dissolved in 140 ml of absolute dichloromethane was added dropwise while stirring at 0° under nitrogen atmosphere during a period of 5 hours. The stirring was continued and the reaction mixture was let to warm slowly to room temperature. After standing overnight 100 ml of water was added the layers were separated, the organic layer was washed twice with 100 ml portions of water, dried over anhydrous potassium carbonate and evaporated *in vacuo* to dryness. The residue was recrystallised from acetonitrile to yield 4.1 g (34%) of the title product, mp 185-186°; ir: ν C=O = 1770 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.60 (s, 3H, SCH₃), 3.64 (s, 3H, NCH₃), 5.54 [d (J = 4.5 Hz), 1H, CH²], 7.28 [d (J = 4.5 Hz), 1H, CH²], 6.9-7.2 (m, 5H, ArH), 7.6 and 7.9 (AB, 4H, ArH).

Anal. Calcd. for C₁₉H₁₇ClN₄O₂S (MW, 400.89): C, 56.93; H, 4.27; N, 13.98; S, 7.98; Cl, 8.84. Found: C, 57.09; H, 4.44; N, 14.24; S, 8.10; Cl, 8.98.

cis 1-(2-Methyl-3-methylthio-2*H*-1,2,4-triazol-5-yl)-2-[4-(2-dimethylaminoethoxy)phenyl]-3-phenoxyazetid-4-one (4c, R' = methyl, (R₂)_n = 4-(2-dimethylaminoethoxy)).

To a solution of 9.4 g (0.029 mole) of 5-[4-(dimethylaminoethoxy)benzalimino]-2-methyl-3-methylthio-2*H*-1,2,4-triazole [1c, R' = methyl, (R₂)_n = 4-(dimethylaminoethoxy)] in 350 ml of absolute dichloromethane and 9.7 ml = 7.0 g (0.07 mole) of anhydrous triethylamine the solution of 10.25 g (0.6 mole) of phenoxyacetyl chloride dissolved in 100 ml of absolute dichloromethane was added dropwise while stirring at 0° under nitrogen stream during a period of 5 hours. The stirring was continued and the reaction mixture was let to warm slowly to the room temperature. After standing overnight 100 ml of water was added, the layers were separated, the organic layer was washed twice with 100 ml portions of water, dried over anhydrous potassium carbonate and evaporated *in vacuo* to dryness. 15.2 g of honey-like product was obtained which was chromatographed on a silica-gel column (eluent: benzene-ethyl acetate 2:1) to obtain 8.0 g (60%) of chromatographically pure title product which crystallised upon standing. It melted after recrystallisation from acetonitrile at 134-135°; ir: ν C=O = 1770 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.33 (s, 6H, N(CH₃)₂), 2.58 (s, 3H, SCH₃), 3.64 (s, 3H, NCH₃), 2.68 (t, 2H, NCH₂), 4.00 (t, 2H, OCH₂), 5.53 [d (J = 5 Hz), 1H, CH²], 7.25 [d (J = 5 Hz), 1H, CH²], 6.8-7.4 (m, 9H, ArH).

Anal. Calcd. for C₂₂H₂₇N₅O₃S (MW, 453.57): C, 60.91; H, 6.00; N, 15.44; S, 7.07. Found: C, 60.25; H, 6.16; N, 15.26; S, 7.11.

trans-6,7-Dihydro-7-(4-chlorophenyl)-3-methylthio-1-phenyl-6-phenoxy-1,2,4-triazolo[4,3-*a*]pyrimidine-5(1*H*)-one (5).

To a solution of 6.56 g (0.02 mole) of 5-(4-chlorobenzalimino)-3-methylthio-1-phenyl-1*H*-1,2,4-triazole (2a, Q = methylthio, R' = phenyl, (R₂)_n = 4-chloro) [3] in 100 ml of absolute dichloromethane and 8.25 ml = 6.0 g (0.06 mole) of anhydrous triethylamine the solution of 6.82 g (0.04 mole) of phenoxyacetyl chloride dissolved in 30 ml of absolute dichloromethane was added dropwise while stirring the reaction mixture at 0° under nitrogen stream during a period of 5 hours. The stirring was continued and the reaction mixture let to warm slowly to the room temperature. After standing overnight 100 ml of water was added, the layers were separated, the organic layer was washed twice with 100 ml portions of water, dried over anhydrous potassium carbonate and evaporated *in vacuo* to dryness. The residue was recrystallised from acetonitrile to yield 3.6 g (39%) of the title product, mp 174-175°; ir: ν C=O = 1745 cm^{-1} , ν C=N = 1690, 1600 and 1535 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.53 (s, 3H, SCH₃), 4.58 [d (J \approx 11 Hz), 1H, CH²], 5.03 [d (J \approx 11 Hz), 1H, CH²], 6.6-8.1 (m, 14H, ArH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 216 sh (30.6), 270 (15.1), 280 sh (12.0), 320 (1.9); uv (10% ethanol + 90% 0.1 N sodium hydroxide): max nm ($\epsilon \cdot 10^{-3}$) 258 (8.9).

Anal. Calcd. for $C_{24}H_{19}ClN_4O_2S$ (MW, 462.97): C, 62.26; H, 4.14; N, 12.10; S, 6.91; Cl, 7.66. Found: C, 62.30; H, 4.29; N, 11.97; S, 6.99; Cl, 7.82.

6-Chloro-3-methyl-2-methylthio-7-(3,4,5-trimethoxyphenyl)-1,2,4-triazolo[1,5-*a*]pyrimidine-5(3*H*)-one (**9**).

To a solution of 10 ml of dimethylformamide, 0.57 ml (0.95 g, 0.0062 mole) of phosphorus oxychloride and 0.5 ml (0.8 g, 0.0062 mole) of dichloroacetyl chloride prepared at 0° 2.0 g (0.0062 mole) of 3-methyl-2-methylthio-5-(3,4,5-trimethoxybenzalimino)-2*H*-1,2,4-triazole (**1d**, $R^1 = \text{methyl}$, (R^2)_n = 3,4,5-trimethoxy) [3] was added in small portions followed by warming the reaction mixture to 70-80° for 1 hour with stirring. After cooling the crystals precipitated were filtered off to yield 1.13 g (46%) of the title product, mp 235-237° (acetonitrile); ir: $\nu C=O = 1685 \text{ cm}^{-1}$, $\nu C=N = 1590$ and 1575 cm^{-1} ; pmr (deuteriochloroform): δ ppm 2.65 (s, 3H, SCH₃), 2.80 (s, 3H, NCH₃), 3.86 [s, 6H, OCH₃ (m)], 4.23 [s, 3H, (OCH₃ (p))], 7.00 (s, 2H, ArH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 217 sh (25.9), 235 sh (18.9), 275 (24.5), 304 sh (14.6); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 241 (24.9), 269 (24.0), 296 sh (13.6); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 220 (34.1), 228 sh (32.6), 248 sh (22.8), 277 (10.8), 294 sh (9.8).

Anal. Calcd. for $C_{16}H_{17}ClN_4O_2S$ (MW, 396.86): C, 44.82; H, 4.32; N, 14.12; Cl, 8.93; S, 8.08. Found: C, 44.75; H, 4.26; N, 14.21; Cl, 8.98; S, 7.97.

6-Chloro-7-(4-chlorophenyl)-1-phenyl-3-methylthio-1,2,4-triazolo[4,3-*a*]pyrimidine-5(1*H*)-one (**10b**, Q = methylthio, $R^1 = \text{phenyl}$).

To a solution of 10 ml of dimethylformamide, 0.82 ml (1.38 g, 0.009 mole) of phosphorus oxychloride and 0.74 ml (0.009 mole) of dichloroacetic acid prepared at 0° 2.0 g (0.0061 mole) of 5-(4-chlorobenzalimino)-3-methylthio-1-phenyl-1*H*-1,2,4-triazole (**2b**, Q = methylthio, $R^1 = \text{phenyl}$, (R^2)_n = 4-chloro) [3] was added in small portions. The reaction mixture was then warmed to 60-70° for 30 minutes with stirring. After cooling the crystals precipitated were filtered off to yield 1.25 g (51%) of the title product, mp 252-254° (dioxane); ir: $\nu C=O = 1685 \text{ cm}^{-1}$; pmr (DMSO-*d*₆): δ ppm 2.69 (s, 3H, SCH₃), 7.60 and 7.78 (AB, 4H, ArH), 7.38-8.09 (m, 5H, ArH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 264 (53.6), 358 (24.4); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 268 (24.0), 380 (19.1); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 280 (22.8), 386 (21.2).

Anal. Calcd. for $C_{18}H_{12}Cl_2N_4OS$ (MW, 403.30): C, 53.61; H, 3.00; N, 13.89; Cl, 17.58; S, 7.95. Found: C, 53.73; H, 3.08; N, 13.71; Cl, 17.55; S, 7.89.

Ethyl (6-Chloro-7-(4-chlorophenyl)-3-methylthio-1,2,4-triazolo[4,3-*a*]pyrimidin-5(1*H*)-one-1-yl)acetate (**10c**, Q = methylthio, $R^1 = \text{CH}_2\text{COOEt}$).

To a solution of 10 ml of dimethylformamide, 0.82 ml (1.38 g, 0.009 mole) of phosphorus oxychloride and 0.74 ml (1.16 g, 0.009 mole) of dichloroacetic acid prepared at 0° the solution of 1.69 g (0.005 mole) of ethyl [5-(4-chlorobenzalimino)-3-methylthio-1*H*-1,2,4-triazole-1-yl]acetate (**2c**, Q = methylthio, $R^1 = \text{CH}_2\text{COOEt}$, (R^2)_n = 4-chloro) [3] in 5 ml of dimethylformamide was added with stirring. The reaction mixture was stirred for further 3 hours leaving it to warm to the room temperature. After standing overnight 30 ml of water was dropped to the reaction mixture with cooling to keep its temperature below 20°. The crystals precipitated were filtered off to yield 1.35 g (65%) of the title product, mp 163-164° (2-propanol); ir: $\nu C=O = 1730$ and 1700 cm^{-1} , $\nu C=N = 1600$ and 1520 cm^{-1} ; pmr (deuteriochloroform): δ ppm 1.28 (t, 3H, CH₂CH₃) 2.60 (s, 3H, SCH₃), 4.25 (qa, 2H, CH₂CH₃), 4.88 (s, 2H, NCH₃), 7.40 and 7.68 (AB, 4H, ArH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 261 (30.9), 342 (8.3); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 261 (29.3), 338 (8.5); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 261 (28.4), 342 (8.1).

Anal. Calcd. for $C_{16}H_{14}Cl_2N_4O_3S$ (MW, 413.29): C, 46.50; H, 3.41; N, 13.56; S, 7.76; Cl, 17.16. Found: C, 46.66; H, 3.56; N, 13.44; S, 7.82; Cl, 17.03.

Ethyl (6-Chloro-7-(4-chlorophenyl)-3-morpholino-1,2,4-triazolo[4,3-*a*]pyrimidine-5(1*H*)-one-1-yl)acetate (**10d**, Q = morpholino, $R^1 = \text{CH}_2\text{COOEt}$).

To a solution of 5 ml of dimethylformamide, 0.82 ml (1.38 g, 0.009 mole) of phosphorus oxychloride and 0.74 ml (1.16 g, 0.009 mole) of dichloroacetic acid prepared at 0° the solution of 1.89 g (0.005 mole) of ethyl[5-(4-chlorobenzalimino)-3-morpholino-1*H*-1,2,4-triazole-1-yl]acetate (**2d**, Q = morpholino, $R^1 = \text{CH}_2\text{COOEt}$, (R^2)_n = 4-chloro) in 5 ml of dimethylformamide was added with stirring. During the addition the temperature of the reaction mixture arose to 80° at which temperature it was kept with stirring for 2 hours. After cooling 10 ml of water was dropped to the reaction mixture with cooling to keep the temperature of the reaction mixture below 20°. The crystals precipitated were filtered off to yield 0.85 g (38%) of the title product, mp 197-199° (dimethylformamide); ms: $M^+ = 451$ (60%), ($M-18$)⁺ = 433 (100%); ir: $\nu C=O = 1755$ and 1690 cm^{-1} , $\nu C=N = 1620$ and 1555 cm^{-1} ; pmr (deuteriochloroform): δ ppm 1.25 (t, 3H, CH₃), 3.40 (t, 4H, NCH₂), 3.80 (t, 4H, OCH₂), 4.20 (qa, 2H, OCH₂CH₃), 4.80 (s, 2H, NCH₂CO), 7.37 and 7.65 (AB, 4H, ArH); uv (ethanol): λ max nm ($\epsilon \cdot 10^{-3}$) 260 (30.2), 342 (8.1); uv (10% ethanol + 90% 0.1 *N* hydrochloric acid): λ max nm ($\epsilon \cdot 10^{-3}$) 259 (27.8), 338 (8.2); uv (10% ethanol + 90% 0.1 *N* sodium hydroxide): λ max nm ($\epsilon \cdot 10^{-3}$) 259 (27.8), 345 (7.7).

Anal. Calcd. for $C_{19}H_{19}Cl_2N_5O_4$ (MW, 452.31): C, 50.45; H, 4.23; N, 15.48; Cl, 15.68. Found: C, 50.32; H, 4.20; N, 15.55; Cl, 15.61.

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