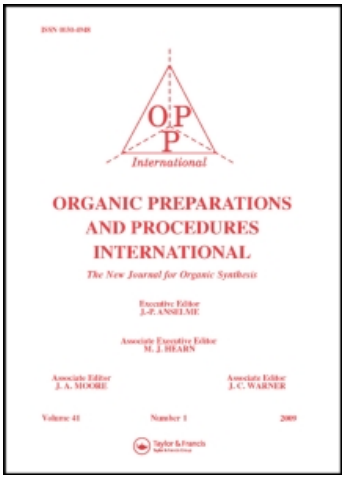

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

SYNTHESIS OF NOVEL 1,2,4-TRIAZOLOQUINAZOLINE RING SYSTEMS

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To cite this Article Reiter, József and Pongo, László(1989) 'SYNTHESIS OF NOVEL 1,2,4-TRIAZOLOQUINAZOLINE RING SYSTEMS', Organic Preparations and Procedures International, 21: 2, 163 — 171
To link to this Article: DOI: 10.1080/00304948909356362
URL: http://dx.doi.org/10.1080/00304948909356362

ORGANIC PREPARATIONS AND PROCEDURES INT. 21(2), 163-171 (1989)

SYNTHESIS OF NOVEL 1,2,4-TRIAZOLOQUINAZOLINE RING SYSTEMS †

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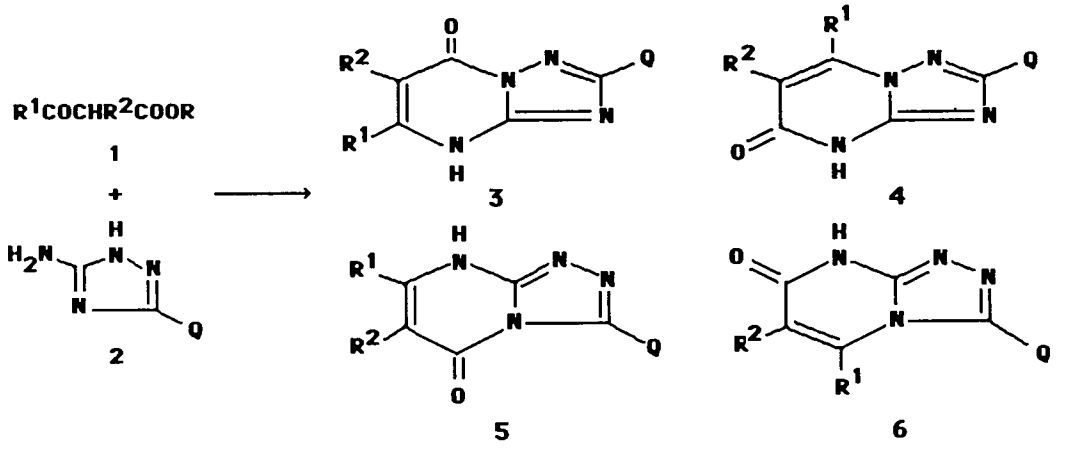
The reaction of β-ketoesters (**1**) with 5-amino-3-Q-1*H*-1,2,4-triazoles (**2**) may lead to four type of condensed ring dervatives **3-6** (Scheme 1). These compounds can exist in different tautomeric forms arising from the triazolo-pyrimidinone skeleton. The structure of **3** ($R^1 = CH_3$, $R^2 = H$) and **4** ($R^1 = CH_3$, $R^2 = H$) type products obtained from alkyl acetoacetates (**1**, $R^1 = CH_3$, $R^2 = H$) and different triazoles **2** was established in a previous paper of this series[1] with the help of their UV and ^{13}C-NMR spectra. It was stated[1] that the UV spectra of these derivatives **3** and **4** ($R^1 = CH_3$, $R^2 = H$) in ethanol or methanol were characterised by two absorption bands appearing at about 230 and 270 nm and at 208 and 290 nm, respectively; they differed significantly from those of the corresponding spectra of derivatives **5** and **6** ($R^1 = CH_3$, $R^2 = H$) characterised by three and one absorption bands, respectively.

Scheme 1

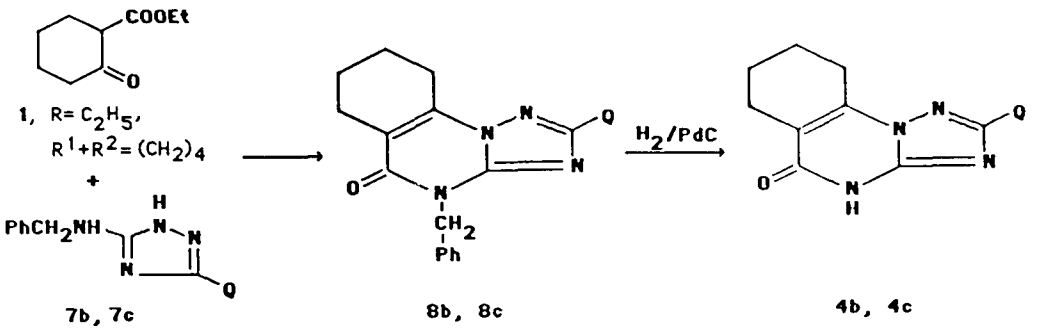


a) Q= H, $R^1+R^2=(CH_2)_4$ b) Q= methylthio, $R^1+R^2=(CH_2)_4$ c) Q= morpholino, $R^1+R^2=(CH_2)_4$

It was also stated[1] that in the ^{13}C-NMR spectra of the [1,5-a] type derivatives **3** and **4** ($R^1 = CH_3$, $R^2 = H$) taken in DMSO-d_6 solution, the triazolo carbon atom 2 appeared at about 163 ppm while that of the analoguous triazolo carbon atom 3 of the [4,3-a] type derivatives **5** and **6** ($R^1 = CH_3$, $R^2 = H$) is at about 143 ppm, thus offering a possibility of an easy differentiation between them. The differentiation between the "ring acylated" derivatives **3** and **5** ($R^1 = CH_3$, $R^2 = H$) and those of the isomeric "acylamino" derivatives **4** and **6** ($R^1 = CH_3$, $R^2 = H$) was made possible by the chemical shifts of the carbonyl carbon atoms that appeared at about 154 and 160 ppm, respectively.[1] These guidelines were used in the structure elucidation of the products of type **3** and **4** obtained from ethyl 2-oxocyclopentanecarboxylate [**1**, $R = C_2H_5$, $R^1 + R^2 = (CH_2)_3$] and their tetrahydrothiophene analogues [**1**, $R = CH_3$, $R^1 + R^2 = CH_2SCH_2$ and CH_2CH_2S, respectively] with derivatives **2**.[2] However, there remained considerable confusion regarding the structure of the products obtained from other homocyclic β-ketoesters, e. g. from the reaction of ethyl 2-oxocyclohexanecarboxylate [**1**, $R = C_2H_5$, $R^1 + R^2 = (CH_2)_4$] and derivatives **2**. Thus structure **3a** [Q = H, $R^1 + R^2 = (CH_2)_4$] initially proposed without evidence[3] for the product obtained from the reaction of **1** [$R = C_2H_5$, $R^1 + R^2 = (CH_2)_4$] and 5-amino-1*H*-1,2,4-triazole (**2**, Q = H) was later modified to structures **4a** or **6a** [Q = H, $R^1 + R^2 = (CH_2)_4$] on the basis of an analogy with tetrazoles,[4] later structure **3a** [Q = H, $R^1 + R^2 = (CH_2)_4$] was resurrected[5] without evidence, and finally structure **3a** [Q = H, $R^1 + R^2 = (CH_2)_4$] was assigned on the basis of ^{1}H-NMR.[6]

As a continuation of our studies in the 1,2,4-triazole series, ethyl 2-oxocyclohexanecarboxylate [**1**, $R = C_2H_5$, $R^1 + R^2 = (CH_2)_4$] was reacted with 5-amino-3-methylthio- and 3-morpholino-1*H*-1,2,4-triazoles [**2**, Q = methylthio and morpholino, respectively] in acetic acid to yield the corresponding 2-methylthio- and 2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]- quinazoline-5(10*H*)-ones [**3b**, Q = methylthio, $R^1 + R^2 = (CH_2)_4$ and **3c**, Q = morpholino, $R^1 + R^2 = (CH_2)_4$, respectively] as main products. The UV spectra of **3b** [Q = methylthio, $R^1 + R^2 = (CH_2)_4$, λ_{max}= 232 and 274 nm] and **3c** [Q = morpholino, $R^1 + R^2 = (CH_2)_4$, λ_{max}= 227 and 270 nm] in ethanol fully supported the proposed structure **3** (see the UV rule[1] mentioned above). The ^{13}C-NMR spectra of the above derivatives also nicely followed the previous conclusion[1] concerning the chemical shifts of the triazole carbon atom 2 and that of the carbonyl carbon atom {for **3b** [Q= methylthio, $R^1 + R^2 = (CH_2)_4$, δ C_2= 163.1 ppm and δ C=O = 155.4 ppm], and for **3c** [Q= morpholino, $R^1 + R^2 = (CH_2)_4$, δ C_2= 164.0 ppm and δ C=O = 155.2 ppm]} giving a further unequivocal proof of their structure.

Scheme 2



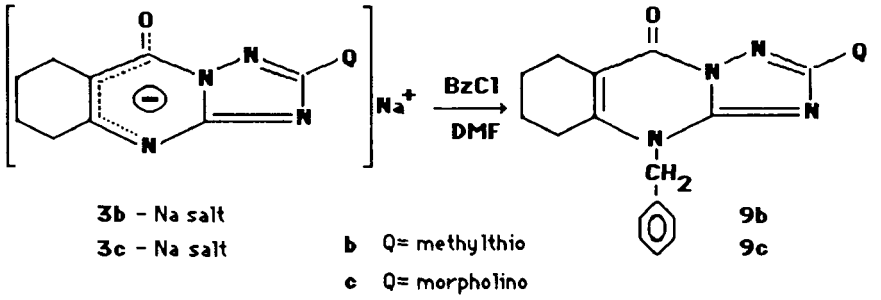
b) Q= methylthio c) Q= morpholino

The isomeric 2-methylthio- and 2-morpholino-5,6,7,8-tetrahydro-1,2,4-triazolo[1,5-a]quinazoline-9(10*H*)-ones [**4b**, Q =methylthio, $R^1 + R^2 = (CH_2)_4$ and **4c**, Q = morpholino, $R^1 + R^2 = (CH_2)_4$, respectively] representing the novel 1,2,4-triazolo[1,5-a]quinazoline ring system formed in the above reactions in extremely low yields, were not separated but were prepared by an other synthetical route. Thus ethyl 2-oxocyclohexanecarboxylate [**1**, R = C_2H_5, $R^1 + R^2 = (CH_2)_4$] was reacted with 5-benzylamino-3-methylthio- and 5-benzylamino-3-morpholino-1*H* -1,2,4-triazole [**7b** (Q = methylthio) and **7c** (Q = morpholino), respectively] (Scheme 2) to yield 10-benzyl-2-methylthio- and 10-benzyl-2-morpholino-5,6,7,8-tetrahydro-1,2,4-triazolo[1,5-a]quinazoline-9(10*H*)-one [**8e**, Q = methylthio, $R^1 + R^2 = (CH_2)_4$ and **8f**, Q = morpholino, $R^1 + R^2 = (CH_2)_4$, respectively]. These benzyl derivatives were then hydrogenated to yield the expected 2-methylthio- and 2-morpholino-5,6,7,8-tetrahydro-1,2,4-triazolo[1,5-a]quinazoline-9(10*H*)-ones [**4b**, Q =methylthio, $R^1 + R^2 = (CH_2)_4$ and **4c**, Q = morpholino, $R^1 + R^2 = (CH_2)_4$, respectively] (Scheme 2).

The UV spectra of **4b** [Q = methylthio, $R^1 + R^2 = (CH_2)_4$, λ_{max} = 206 and 292 nm] and **4c** [Q = morpholino, $R^1 + R^2 = (CH_2)_4$, λ_{max}= 205 and 308 nm] taken in ethanol were again in full agreement with that expected[1] for structure **4** (see the UV rule above). Also the ^{13}C-NMR spectra of **4b** (δ C_2 = 161.9 ppm, δ C=O = 160.5 ppm) and **4c** (δ C_2 = 164.6 ppm, δ C=O = 160.3 ppm) in DMSO-d_6 solution corroborated unequivocally the proposed structures (see the ^{13}C-NMR rule above).

The isomeric 10-benzyl-2-methylthio- and 10-benzyl-2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazoline-5(10*H*)-ones [**9b**, Q = methylthio, $R^1 + R^2 = (CH_2)_4$ and **9c**, Q = morpholino, $R^1 + R^2 = (CH_2)_4$, respectively] were prepared by the direct benzylation of the sodium salts of **3b** and **3c** [$R^1 + R^2 = (CH_2)_4$, Q = methylthio and Q = morpholino, respectively] with benzyl chloride in dimethylformamide (Scheme 3).

Scheme 3



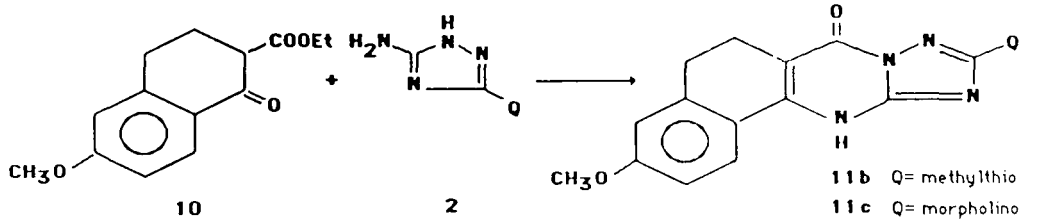
3b - Na salt
3c - Na salt

b Q= methylthio
c Q= morpholino

9b
9c

The position of the benzyl groups in **8b**, **8c**, **9b** and **9c** was unequivocally established with the help of the proton coupled ^{13}C-NMR spectra. The equivalence of the UV spectra of **3b** and **3c** with those of **9b** and **9c**, as well as of **4b** and **4c** with those of **8b** and **8c**, respectively (See Experimental) demonstrated unequivocally the dominant tautomeric structures of derivatives **3b-f** and **4b-c**, respectively, in DMSO-d_6 and in ethanol. The corresponding 2-methylthio- and 2-morpholino-6,7-dihydro-9-methoxy-benzo(h)-1,2,4-triazolo[5,1-b]quinazoline-5(12*H*)-ones (**11b** and **11c**, Q = methylthio and morpholino, respectively) (Scheme 4) representing also a novel, the benzo(h)-1,2,4-triazolo[5,1-b]quinazoline ring system were obtained from the reaction of 5-amino-3-methylthio- and 5-amino-3-morpholino-1*H*-1,2,4- triazole (**2**, Q = methylthio and morpholino, respectively) with ethyl 6-methoxy-1-oxo-1,2,3,4-tetrahydro-2-naphtoate (**10**).[7] Unfortunately the triazolo-pyrimidinone chro-

Scheme 4



10

2

11b Q= methylthio
11c Q= morpholino

mophore of these derivatives was overwhelmed by that of the 4-methoxyphenylacrylic acid and thus their UV spectra were not characteristic for any of the **3** - **6** type structures. However, their ^{13}C-NMR spectra [**11b** (Q= methylthio, δ C_2 = 162.0 ppm, δ C=O = 154.4 ppm) and **11c** (Q = morpholino, δ C_2 = 164.4 ppm, δ C=O = 154.1 ppm)] in DMSO-d_6 proved again unequivocally the proposed structure **11b** and **11c**.

EXPERIMENTAL SECTION

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 recorded on a Varian Cary 118 and Pye Unicam SP 8-150 instruments. The ^{1}H-nmr and the ^{13}C-nmr measurements were performed using Varian XL-100, Bruker WM-250 and Bruker WP-80 SY instruments.

2-METHYLTHIO-6,7,8,9-TETRAHYDRO-1,2,4-TRIAZOLO[5,1-b]QUINAZOLINE-5(10H)-ONE (3b). - A mixture of 1.3 g (0.01 mole) of 5-amino-3-methylthio-1*H*-1,2,4-triazole (2, Q = methylthio)[8] 1.70 g (0.01 mole) of ethyl 2-oxocyclohexanecarboxylate [1, R= C_2H_5, $R^1 + R^2 = (CH_2)_4$] and 4 ml of glacial acetic acid was refluxed for 2 hrs. During the reaction the starting materials had dissolved and the still hot solution began to crystallise. After cooling the precipitated crystals were collected, washed with water and recrystallized from dimethylformamide to yield 1.96 g (83 %) of the title *product*, mp. 308-310°. IR: 1690 cm^{-1} (C=O); ^{1}H-NMR (DMSO-d_6) : δ 1.71 (m, 4H, $CH_2^{7,8}$), 2.38 (t, 2H, CH_2^{9}), 2.52 (t, 2H, CH_2^{6}), 2.59 (s, 3H, SCH_3), 12.8 (bs, 1H, NH). ^{13}C-NMR (DMSO-d_6) : δ 13.4 (SCH_3), 20.9 ($CH_2^{7,8}$), 21.2 (CH_2^{6}), 26.3 (CH_2^{9}), 106.0 (C^{5a}), 146.7 (C^{9a}), 150.3 (C^{10a}), 155.4 [C^{5} (keto)], 163.1 (C_2); UV(EtOH): λ max (nm, ε.10^{-3}): 232 (28.2), 274 (11.4); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 232 (27.4), 271 (12.7); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 234 (30.0), 289 (11.4).

Anal. Calcd. for $C_{10}H_{12}N_4OS$: C, 50.83; H, 5.12; N, 23.71; S, 13.57
Found: C, 51.02; H, 5.23; N, 23.77; S, 13.45

2-MORPHOLINO-6,7,8,9-TETRAHYDRO-1,2,4-TRIAZOLO[5.1-b]QUINAZOLINE-5(10H)-ONE (3c). - A mixture of 1.69 g (0.01 mole) of 5-amino-3-morpholino-1*H*-1,2,4-triazole (2, Q = morpholino)[8] 1.70 g (0.01 mole) of ethyl 2-oxocyclohexanecarboxylate [1, R= C_2H_5, $R^1 + R^2 = (CH_2)_4$] and 4 ml of glacial acetic acid was refluxed for 2 hrs. The starting material dissolved at the beginning of the reaction and shortly after the hot mixture began to crystallize. After cooling the precipitated crystals were collected and washed thoroughly with water and isopropanol to afford 2.32 g (84 %) of the title *product*, mp. 335- 337°. IR: 1665 cm^{-1}(C=O). ^{1}H-NMR (DMSO-d_6) : δ ~1.70 (m, 4H, $CH_2^{7,8}$), 2.36 (t, 2H, CH_2^{9}), 2.56 (t, 2H, CH_2^{6}), 3.38 (t, 4H, NCH_2), 3.69 (t, 4H, OCH_2), ~12.6 (b, 1H, NH). ^{13}C-NMR (DMSO-d_6): δ 20.5 (CH_2^{6}), 20.8 (CH_2^{8}), 20.9 (CH_2^{7}), 25.7 (CH_2^{9}), 45.5 (NCH_2), 65.1 (OCH_2), 106.0 (C^{5a}), 144.8 (C^{9a}), 149.2 (C^{10a}), 155.2 [C^{5}(keto)], 164.0 (C^{2}). UV(EtOH): λ max (nm, ε.10^{-3}): 227 (29.9), 270 (12.1); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 227 (29.9), 270 (12.9); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 226 (36.8), 281 (10.5).

Anal. Calcd. for $C_{13}H_{17}N_5O_2$: C, 56.71; H, 6.22; N, 25.44
Found: C, 56.55; H, 6.18; N, 25.36

2-METHYLTHIO-5,6,7,8-TETRAHYDRO-1,2,4-TRIAZOLO[1,5-a]QUINAZOLINE-9(10H)-ONE **(4b).** - A solution of 0.33 g (0.001 mole) of 10-benzyl-2-methylthio-5,6,7,8-tetrahydro-1,2,4-triazolo[1,5-a]-quinazoline-9(10*H*)-one (**8b**) in 120 ml of methanol to which was added 1 g of Selcat F (10 % Palladium catalyst on charcoal) was hydrogenated at room temperatute on 1.4 MPa for 6 hrs. The catalyst was filtered off and washed twice with 5 ml portions of hot dimethylformamide. The combined filtrates were evaporated *in vacuo* to dryness and the residue was chromatographed on a silica-gel column (eluent: a 1: 2 mixture of benzene and ethyl acetate) to yield 0.04 g (17 %) of the title *product* which after recrystallisation from acetonitrile melted at 261-263°. IR: 1680 cm^{-1} (C=O). ^{1}H-NMR (DMSO-d_6: δ 1.72 (m, 4H, $CH_2^{6,7}$), 2.35 (t, 2H, CH_2^5), 2.57 (s, 3H, SCH_3), 2.78 (t, 2H, CH_2^8). ^{13}C-NMR (DMSO-d_6: δ 13.5 (SCH_3), 20.4 (CH_2^8), 20.9 (CH_2^6), 21.6 (CH_2^7), 23.6 (CH_2^5), 112.4 (C^{8a}), 144.1 (C^{4a}), 148.7 (C^{10a}), 160.5 (C=O), 161.9 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 206 (27.1), 292 (9.6); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 206 (28.7), 289 (9.9); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 288 (10.0).

Anal. Calcd. for $C_{10}H_{12}N_4OS$: C, 50.83; H, 5.12; N, 23,71; S, 13.57
Found: C, 50.98; H, 5.22; N, 23.61; S, 13.45

2-MORPHOLINO-5,6,7,8-TETRAHYDRO-1,2,4-TRIAZOLO[1,5-a]QUINAZOLINE-9(10H)-ONE **(4c).** - A solution of 0.37 g (0.001 mole) of 10-benzyl-2-morpholino-5,6,7,8-tetrahydro-1,2,4-triazolo[1,5-a]-quinazoline-9(10*H*)-one (**8c**) in 350 ml of methanol to which was added 1 g of Selcat F (10 % Palladium catalyst on charcoal) was hydrogenated at room temperature on 0.6 MPa for 6 hrs. The catalyst was filtered off and washed twice with 10 ml portions of hot dimethylformamide. The combined methanol dimethylformamide filtrates were evaporated *in vacuo* to dryness to yield 0.25 g (91 %) of the title *product* which after recrystallisation from acetonitrile melted at 260-262°. IR: 1650 cm^{-1} (C=O). ^{1}H-NMR (DMSO-d_6: δ 1.70 (m, 4H, $CH_2^{6,7}$), 2.31 (t, 2H, CH_2^5), 2.73 (t, 2H, CH_2^8), 3.32 (t, 4H, NCH_2), 3,68 (t, 4H, OCH_2). ^{13}C-NMR (DMSO-d_6: δ 20.4 (CH_2^8), 20.9 (CH_2^6), 21.3 (CH_2^7), 23.6 (CH_2^5), 45.9 (NCH_2), 65.5 (OCH_2), 110.5 (C^{8a}), 144.0 (C^{4a}), 148.1 (C^{10a}), 160.3 (C=O), 164.6 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 205 (29.4), 308 (10.2); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 205 (31.0), 304 (10.9); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 294 (9.6).

Anal. Calcd. for $C_{13}H_{17}N_5O_2$: C, 56.72; H, 6.22; N, 25.44
Found: C, 56.65; H, 6.30; N, 25.36

10-BENZYL-2-METHYLTHIO-5,6,7,8-TETRAHYDRO-1,2,4-TRIAZOLO[1,5-a]QUINAZOLINE-9(10H)-ONE **(8b).** - A mixture of 2.2 g (0.01 mole) of 5-benzylamino-3-methylthio-1*H* -1,2,4-triazole (**7b**, Q= methylthio)[9] and 4 ml of ethyl 2-oxocyclohexanecarboxylate [1, R= C_2H_5, R^1 + R^2= $(CH_2)_2$] was refluxed for 15 min. To the still hot solution 10 ml of 2-propanol was added and it was allowed to crystallise. The crystals were collected and recrystallised from acetonitrile to yield 2.4 g (74 %) of the title product, mp. 129-130°. IR: 1665 cm^{-1} (C=O). ^{1}H-NMR(DMSO-d_6: δ 1.75 (m, 4H, $CH_2^{6,7}$), 2.39 (t, 2H, CH_2^5), 2.57 (s, 3H, SCH_3), 2.81 (t, 2H,

CH_2^8), 5.23 (s, 2H, NCH_2), 7.2-7.4 (m, 5H, ArH). ^{13}C-NMR(DMSO-d_6: δ 13.5 (SCH_3), 20.3 (CH_2^8), 20.9 (CH_2^6), 21.9 (CH_2^7), 23.5 (CH_2^5), 46.1 (NCH_2), 112.1 (C^{8a}), 143.4 (C^{4a}), 149.7 (C^{10a}), 158.8 (C=O), 161.7 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 206 (27.8), 287 (9.9); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}) : 206 (30.4), 284 (10.6); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 284 (10.8).

Anal. Calcd. for $C_{17}H_{18}N_4OS$: C, 62.55; H, 5.56; N, 17.17; S, 9.82

Found: C, 62.63; H, 5.68; N, 17.03; S, 9.76

10-BENZYL-2-MORPHOLINO-5,6,7,8-TETRAHYDRO-1,2,4-TRIAZOLO[1,5-a]QUINAZOLINE-9(10H)-ONE **(8c)** . - A mixture of 1.30 g (0.005 mole) of 5-benzylamino-3-morpholino-1*H* -1,2,4- triazole (**7c**, Q= morpholino)[1] and 3 ml of ethyl 2-oxocyclohexanecarboxylate [1, R= C_2H_5, R^1 + R^2= $(CH_2)_4$] was refluxed 10 min. The solution obtained was evaporated *in vacuo* to dryness and the crystals obtained were recrystallised from acetonitrile to yield 1.2 g (66 %) of the title product, mp. 162-164°. IR: 1664 cm^{-1}(C=O). ^{1}H-NMR (DMSO-d_6: δ 1.70 (m, 4H, $CH_2^{6,7}$), 2.35 (t, 2H, CH_2^5), 2.75 (t, 2H, CH_2^8), 3.40 (t, 4H, NCH_2), 3.68 (t, 4H, OCH_2), 5.21 (s, 2H, NCH_2), 7.2-7.4 (m, 5H, ArH). ^{13}C-NMR (DMSO-d_6: δ 20.3 (CH_2^8), 20.9 (CH_2^6), 21.7 (CH_2^7), 23.5 (CH_2^5), 45.8 (NCH_2), 66.0 (OCH_2), 110.0 (C^{8a}), 143.6 (C^{4a}), 148.8 (C^{10a}), 158.8 (C=O), 164.0 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 206 (33.6), 310 (9.9); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 206 (38.1), 306 (11.2); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 306 (11.1).

Anal. Calcd. for $C_{20}H_{23}N_5O_2$: C, 65.73; H, 6.34; N, 19.17

Found: C, 65.58; H, 6.21; N, 19.11

10-BENZYL-2-METHYLTHIO-6,7,8,9-TETRAHYDRO-1,2,4-TRIAZOLO[5,1-b]QUINAZOLINE-5(10H)-ONE **(9b)**. - To a solution of 5.16 g (0.02 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo-[5,1-b]quinazoline-5(10*H*)-one sodium salt (**3b**-Na salt) (prepared by dissolving **3b** in hot 1*N* sodium hydroxide solution, allowing it to cool and collecting the sodium salt precipitated and drying the product) in 50 ml of dimethylformamide 2.88 ml (3.16 g, 0.025 mole) of benzyl chloride was added at room temperature and it was allowed to stand for 3 days. To the solution thus obtained 50 ml of water was added dropwise with stirring. The precipitated crystals were collected and washed with water to afford 2.55 g (39 %) of the title *product* , mp. 220-222° (acetonitrile). IR: 1680 cm^{-1}(C=O); ^{1}H-NMR (DMSO-d_6: δ 1.65 (m, 4H, $CH_2^{7,8}$), 2.45 (t, 2H, CH_2^9), 2.59 (s, 3H, SCH_3), 2.63 (t, 2H, CH_2^6), 5.48 (s, 2H, NCH_2), 7.2-7.4 (m, 5H, ArH). ^{13}C-NMR (DMSO-d_6: δ 13.3 (SCH_3), 20.5 (CH_2^8), 21.1 (CH_2^7), 21.9 (CH_2^6), 25.0 (CH_2^9), 108.7 (C^{5a}), 147.6 (C^{9a}), 152.2 (C^{10a}), 154.5 (C=O), 163.0 (C^2).; UV(EtOH): λ max (nm, ε.10^{-3}): 238 (21.8), 280 (10.3); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 237 (20.8), 280 (11.5); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 238 (20.5). 280 (11.3).

Anal. Calcd. for $C_{17}H_{18}N_4OS$: C, 62.55; H, 5.56; N, 17.17; S, 9.82

Found: C, 62.45; H, 5.62; N, 17.22; S, 9.73

***10-BENZYL-2-MORPHOLINO-6,7,8,9-TETRAHYDRO-1,2,4-TRIAZOLO[5.1-b]QUINAZOLINE-5(10H)-ONE* (9c).** - To a solution of 5.95 g (0.02 mole) of 2-morpholino-6,7,8,9-tetrahydro-1,2,4-triazolo-[5,1-b]quinazoline-5(10*H*)-one sodium salt (3c-Na salt) (prepared by dissolving 3c in hot 1*N* sodium hydroxide solution, allowing it to cool and collecting the sodium salt precipitated and drying the product) in 50 ml of dimethylformamide 2.88 ml (3.16 g, 0.025 mole) of benzyl chloride was added at room temperature and it was allowed to stand for 3 days. To the solution thus obtained 50 ml of water was added dropwise with stirring. The precipitated crystals were collected and washed with water to give 4.15 g (57 %) of the title *product* , mp. 213-215° (acetonitrile). IR: 1670 cm^{-1} (C=O). ^{1}H-NMR(DMSO-d_6: δ 1.63 (m, 4H, $CH_2^{7,8}$), 2.42 (t, 2H, CH_2^9), 2.57 (t, 2H, CH_2^6), 3.38 (t, 4H, NCH_2), 3.67 (t, 4H, OCH_2), 5.44 (s, 2H, NCH_2), 7.25-7.4 (m, 5H, ArH). ^{13}C-NMR(DMSO-d_6: δ 20.5 (CH_2^8), 21.1 (CH_2^7), 21.9 (CH_2^6), 24.9 (CH_2^9), 45.7 (NCH_2), 48.9 (NCH_2), 65.4 (OCH_2), 108.5 (C^{5a}), 146.1 (C^{9a}), 151.3 (C^{10a}), 154.7 (C=O), 163.8 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 236 (29.0), 280 (13.0); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 236 (30.1), 280 (14.2); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 236 (30.1), 280 (14.3).

Anal. Calcd. for $C_{20}H_{23}N_5O_2$: C, 65.73; H, 6.34; N, 19.17
Found: C, 65.80; H, 6.45; N, 19.05

***2-METHYLTHIO-6,7-DIHYDRO-9-METHOXY-BENZO(h)-1,2,4-TRIAZOLO[5,1-b]QUINAZOLINE-5(12H)-ONE* (11b).** - The solution of 1.3 g (0.01 mole) of 5-amino-3-methylthio-1*H* -1,2,4-triazole (2, Q= methylthio)[8] and 2.48 g (0.01 mole) of ethyl 6-methoxy-1-oxo-1,2,3,4-tetrahydro-2-naphthoate (10)[7] in 3 ml of dimethylformamide and 1 ml of glacial acetic acid was refluxed for 10 hrs. After cooling 30 ml of water was added to the reaction mixture, the precipitated crystals were collected and recrystallized from dimethylformamide to yield 2.55 g (81 %) of the title product, mp. 305-308°. IR: 1660 cm^{-1} (C=O); ^{1}H-NMR (DMSO-d_6: δ 2.64 (s, 3H, SCH_3), 2.54 (t, 2H, CH_2^7), 2.77 (t, 2H, CH_2^6), 3.85 (s, 3H, OCH_3), 7.02 + 7.98 (d+d, 3H, ArH); ^{13}C-NMR (DMSO-d_6: δ 13.1 (SCH_3), 15.7 (OCH_3), 19.2 (C^7), 27.3 (C^6), 104.3 (C^{5a}), 142.2 (C^{11b}), 150.9 (C^{12a}), 154.4 [C^5(keto)], 162.0 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 260 (25.8), 303 (18.2), 323sh (13.9); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 233 (18.5), 249sh (13.7), 296sh (13.7), 329 (20.2); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 258 (29.4), 302 (19.1), 323sh (14.1), 337sh (9.2).

Anal. Calcd. for $C_{15}H_{14}N_4O_2S$: C, 57.31; H, 4.49; N, 17.82; S, 10.20
Found: C, 57.54; H, 4.56; N, 17.53; S, 9.93

***2-MORPHOLINO-6,7-DIHYDRO-9-METHOXY-BENZO(h)-1,2,4-TRIAZOLO[5,1-b]QUINAZOLINE-5(12H)-ONE* (11c).** - The solution of 1.69 g (0.01 mole) of 5-amino-3-morpholino-1*H* -1,2,4-triazole (2, Q= morpholino)[8] and 2.48 g (0.01 mole) of ethyl 6-methoxy-1-oxo-1,2,3,4-tetrahydro-2-naphthoate (10)[7] in 3 ml of dimethylformamide and 1 ml of glacial acetic acid was refluxed for 10 hrs. After cooling 30 ml of water was add-

ed to the reaction mixture, the precipitated crystals were collected and recrystallized from dimethylformamide to yield 2.36 g (67 %) of the title product, mp. 302-305°. IR: 1665 cm^{-1} (C=O); ^{1}H-NMR (TFA: δ 3.0 (m, 4H, CH_2CH_2), 3.80 (t, 4H, NCH_2), 4.02 (s, 3H, OCH_3), 4.1 (t, 4H, OCH_2), 7.05 + 7.85 (dd, 3H, ArH); ^{13}C-NMR (DMSO-d_6: δ 15.7 (OCH_3), 19.2 (C^7), 27.4 (C^6), 45.8 (NCH_2), 65.4 (OCH_2), 104.5 (C^{5a}), 142.0 (C^{11b}), 150.0 (C^{12a}), 154.1 [C^5(keto)], 164.4 (C^2); UV(EtOH): λ max (nm, ε.10^{-3}): 228sh (16.4), 232sh (15.8), 312 (18.7); UV(10 % EtOH+90 % hydrochloric acid): λ max (nm, ε.10^{-3}): 228sh (16.7), 320 (18.7); UV(10 % EtOH+90 % sodium hydroxide): λ max (nm, ε.10^{-3}): 248 (18.1), 304 (17.8).

Anal. Calcd. for $C_{18}H_{19}N_5O_3$: C, 61.18; H, 5.42; N, 19.82
Found: C, 61.07; H, 5.33; N, 19.85

ACKNOWLEDGEMENT. -The authors wish to express their thanks to Miss Ilona Sztruhár for recording the UV spectra, to Mrs Zsoltné Bíró for recording the IR spectra to Mr István Parragi for recording the NMR spectra and to Mrs Jánosné Ifjú and Mrs Lászloné Nyikos for technical assistance.

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(Received November 30, 1987; in revised form January 23, 1989)