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A simple *N*-alkylation method of highly insoluble cyclic amides based on the high solubility of their easily isolable tetraalkylammonium and tetraalkylphosphonium salts was elaborated. The method has a rather wide scope, it is not influenced by the identity of the different rings attached to the 1,2,4-triazolo[1,5-*a*]-pyrimidinone moiety of isomers **1** and **2**, nor the presence of the triazole substituents. It proceeds smoothly without any unwanted by-products, at relatively low temperatures, and is not sensitive to moisture. The method allows an easy isolation of all possible *N*-alkylated derivatives **3**, **7**, and **8**. Spectral analysis of isomers **3**, **7**, and **8** showed that our previous results concerning the formation of **3** type *N*-alkylated derivatives as main products of the *N*-alkylations as well as the tautomeric structure of the non-alkylated isomers **1** and **2** is correct. However, it also showed that the isolation of a single *N*-alkylated isomer **3** and its comparison with the corresponding non-alkylated derivative to prove its tautomeric structure may lead to mistakes.

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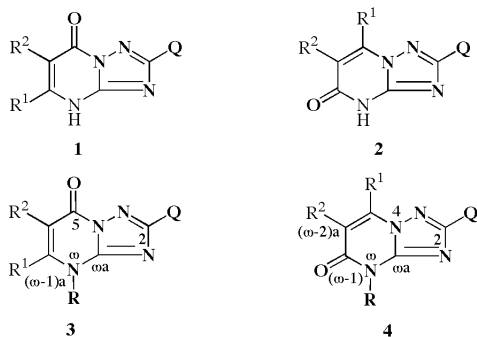
Elucidation of the tautomeric structure of different 6- and 7-substituted [1,2,4]triazolo[1,5-*a*]pyrimidin-5-ones of type **1** (**1**, $R^1, R^2 = \text{alkyl}$) [3], their [1,2,4]triazolo[1,5-*a*]pyrimidin-7-one isomers of type **2** (**2**, $R^1, R^2 = \text{alkyl}$) [3], cycloalka[*d*]- (**1**, $R^1 + R^2 = (\text{CH}_2)_{3-10}$)[4,5], and cycloalka[*e*]- analogues (**2**, $R^1 + R^2 = (\text{CH}_2)_{3-10}$)[4,5], and the corresponding nitrogen (**1** and **2**, $R^1 + R^2 = (\text{CH}_2)_n\text{-NR-}(\text{CH}_2)_m$)[6-8] and sulphur (**1** and **2**, $R^1 + R^2 = (\text{CH}_2)_n\text{-S-}(\text{CH}_2)_m$)[9,10] containing hetero analogues required model

above alkylations strongly depended on the solubility of the sodium salts in dimethylformamide, which can lead to difficulty during isolation of the products from the very diluted dimethylformamide containing solutions. Moreover the above methods enabled the isolation of the main *N*-alkylated products only. Luckily the isolated *N*-alkylated products of type **3** and **4** (Scheme 1) contain the same chromophore systems as derivatives **1** and **2**, respectively, making their structure elucidation possible [2-10]. However, in spite of their similarities, doubts still remained concerning the validity of identifying the above structural pairs by comparing the spectral data. To solve this problem unambiguously we wanted to synthesize all possible *N*-alkylated isomers of type **1** and that of their *O*-alkylated analogues, *i.e.* derivatives **7-9** as well as compounds **3** (Scheme 3).

It was known [11] that the *N*-alkylation of different cyclic amides can be performed in two-phase (liquid-liquid or solid-liquid) systems using phase transfer catalysts (quaternary ammonium or phosphonium salts).

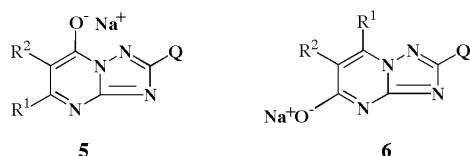
Brändström [12] successfully isolated the stoichiometric crystalline tetrabutylammonium salts (**10**) of weak CH-acids like methyl 2,4-dioxovalerate (**10z**, $X = \text{COCH}_3$, $Y = \text{COOMe}$) and methyl cyanoacetate (**10w**, $X = \text{CN}$,

Scheme 1

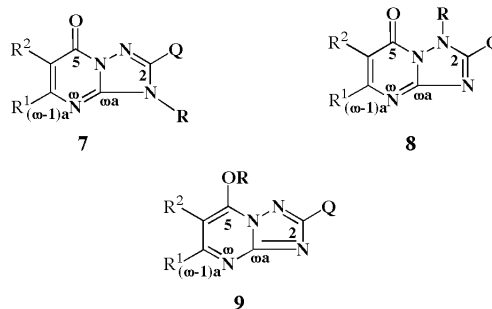


compounds of "fixed" tautomeric structures, like that of derivatives **3** and **4** (Scheme 1). They were synthesized by the *N*-alkylation of the corresponding sodium salts **5** and **6** (Scheme 2) prepared either *in situ* with sodium hydride in dimethylformamide [2,4,6-9] or in advance in hot sodium hydroxide solution [3,6,10]. However, the yields of the

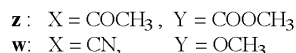
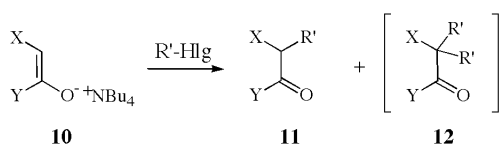
Scheme 2



Scheme 3



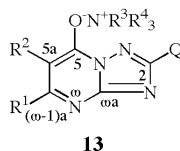
Scheme 4



$\text{Y} = \text{OMe}$) (Scheme 4) that were fairly soluble in chloroform and their chloroform solutions could be C-alkylated at room temperature to yield monoalkylated derivatives (**11z** and **11w**, respectively) as well as a small amount of the dialkylated products (**12z** and **12w**, respectively).

The above results led us to the idea that derivatives **1** could also form crystalline stoichiometric tetraalkylammonium salts (**13**) (Scheme 5) that may be soluble in simple low boiling organic solvents and thus could have been N-alkylated to produce the mixture of derivatives **3**, **7** and **8** (Schemes 1 and 3).

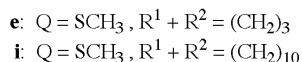
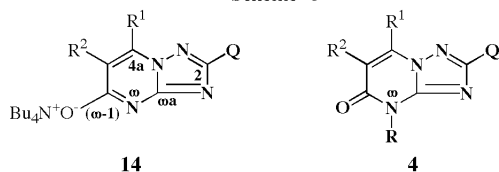
Scheme 5



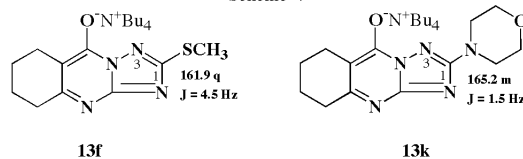
The tetraalkylammonium salts **13**, which are derivatives of **1**, were prepared by simple shaking of the corresponding amides **1** in a mixture of 1 *N* sodium hydroxide solution and the corresponding quaternary ammonium salt in chloroform at room temperature for 5–10 minutes. After separating the phases the chloroform layer was washed with water, dried and evaporated *in vacuo* to dryness to yield the corresponding tetraalkylammonium salts (**13**). Compounds **13** were usually obtained in crystalline form that was pure enough for N-alkylation (Table I, for their spectral data see Table II). However, if necessary, they could easily be recrystallised from an appropriate solvent (ethyl acetate, diisopropyl ether, etc.).

Comparing the different tetraalkylammonium salts (**13**) the tetrabutylammonium ones proved to be the most convenient. The corresponding benzyltriethylammonium or tetraethylammonium salts were a bit more soluble in

Scheme 6

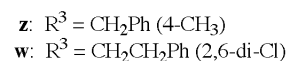
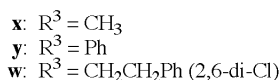
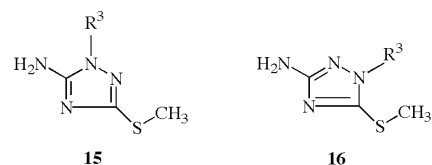


Scheme 7



water thereby lowering their yields when extracted with chloroform. However, in some cases [*e.g.* in case of 2-amino-1,2,4-triazolo[5,1-*b*]quinazolin-5-one (**1j**, $\text{Q} = \text{amino}$, $\text{R}^1 + \text{R}^2 = (\text{CH}_2)_4$] even the tetrabutylammonium salt was fairly soluble in water thus it was necessary to extract the reaction mixture several times with chloroform.

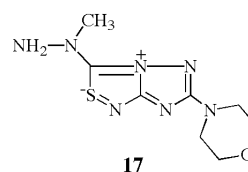
Scheme 8



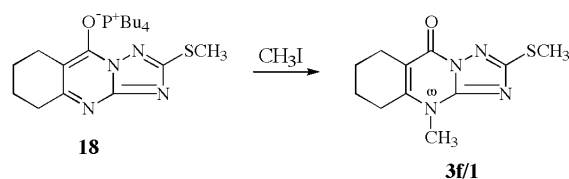
The tetrabutylammonium salts **13** ($\text{R}^3 = \text{R}^4 = \text{butyl}$, Scheme 5) obtained were nicely soluble even at room temperature in all common low boiling organic solvents such as acetonitrile, 2-propanol, benzene, dichloromethane, etc., enabling their N-alkylation with alkyl halides in homogeneous systems either at room temperature or at the boiling points of the corresponding solvents. The reactions were not sensitive to moisture, proceeded smoothly without any unwanted by-products, the N-alkylations reaction time was relatively short and the main products usually crystallised in pure form from the reaction mixtures. Because the only by-product of the reaction was the corresponding tetrabutylammonium halogenide, all N-alkylated isomers could be easily isolated by evaporating the mother liquors to dryness and chromatography of the residues (Tables V, VII and IX, for their spectral data see Tables VI, VIII and X).

As expected the most reactive alkyl halides, such as methyl iodide reacted just at room temperature giving, within a few minutes, high yields (up to 85%) of the main alkylated products, while the reaction of alkyl chlorides was a bit more sluggish requiring boiling of the reaction mixtures.

Scheme 9

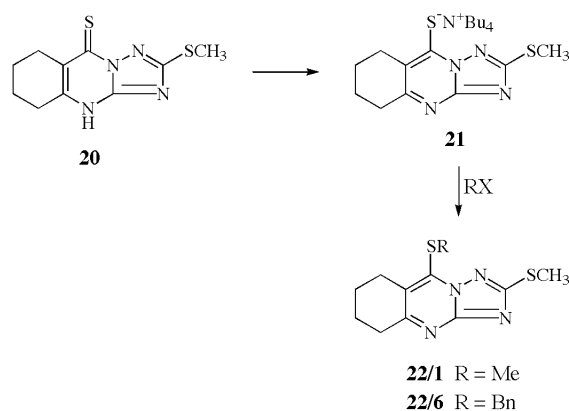


Scheme 10

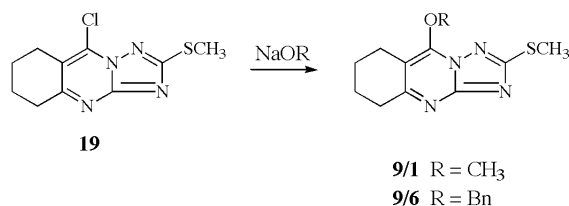


To compare the productivity of our new *N*-alkylation method with those *N*-alkylation methods known from the literature we compared the yields of the *N*-benzylated products of **1f** [Q = methylthio, R¹+ R² = (CH₂)₄] obtained with benzyl chloride using different type alkylations (Table III).

Scheme 12



Scheme 11



As the data in Table III show, in addition to the simple reaction conditions, our method gave, in some cases, better yields of the main *N*-benzylated product **3f/6**. Also, isomers **7f/6** and **8f/6** could be isolated from the mother liquors (see Note [13]).

To prove the rather wide scope of our *N*-alkylation reaction, tetrabutylammonium salts of five different 2-methylthio-cycloalka[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-ones (**13e-i**, Q = methylthio, R¹+ R² = (CH₂)_{3,4,5,6}, and 10,

Table I

Compound	R ¹	R ²	Q	Lit mp (°C)	Yield (%)	Mp (°C) (cryst. from)	Molecular Formula (MW)	Analysis			
								C	Calcd/Found H	N	S
13a	Me	H	SMe		87	99-101 (EtOAc)	C ₂₃ H ₄₃ N ₅ OS	63.12	9.90	16.00	7.33
							437.70	63.32	10.11	15.88	7.26
13b	Me	H	SiPr		94	59-66 (iPr ₂ O)	C ₂₅ H ₄₇ N ₅ OS	64.47	10.17	15.04	6.88
							465.75	64.36	10.42	14.99	6.77
13c	Me	H	SBu		94	57-60.5 (cyclohexane)	C ₂₆ H ₄₉ N ₅ OS	65.09	10.29	14.60	6.68
							479.78	64.89	10.44	14.68	6.57
13d	-(CH ₂) ₄ -		H		91	123-126 (EtOAc)	C ₂₅ H ₄₅ N ₅ O	69.56	10.51	16.22	
							431.67	69.67	10.76	16.08	
13e	-(CH ₂) ₃ -		SMe		85	110.5-111.5 (EtOAc)	C ₂₅ H ₄₅ N ₅ OS	64.75	9.78	15.10	6.91
							463.73	64.66	9.98	15.01	7.13
13f	-(CH ₂) ₄ -		SMe		95	105-107 (EtOAc)	C ₂₆ H ₄₇ N ₅ OS	65.37	9.92	14.66	6.71
							477.76	65.44	10.21	14.75	6.54
13g	-(CH ₂) ₅ -		SMe	[5] 127-138	100	127-138	C ₂₇ H ₄₉ N ₅ OS	65.94	10.04	14.24	6.52
							491.79	66.05	10.28	14.08	6.67
13h	-(CH ₂) ₆ -		SMe	[5] 100-110	98	100-110	C ₂₈ H ₅₁ N ₅ OS	66.49	10.16	13.85	6.34
							505.82	66.66	10.35	13.72	6.28
13i	-(CH ₂) ₁₀ -		SMe	[5] oily crystals	100	oily crystals	C ₃₂ H ₅₉ N ₅ OS	68.40	10.58	12.46	5.71
							561.92	68.26	10.76	12.32	5.54
13j	-(CH ₂) ₄ -		NH ₂		96	oil	C ₂₅ H ₄₆ N ₆ O	67.22	10.38	18.81	
							446.69	67.37	10.62	18.95	
13k	-(CH ₂) ₄ -		M		98	163-166 (EtOAc)	C ₂₉ H ₅₂ N ₆ O ₂	67.40	10.14	16.26	
							516.78	67.32	10.35	16.22	
13l	-(CH ₂) ₁₀ -		M		93	96-99 (ether/EtOAc)	C ₃₅ H ₆₄ N ₆ O ₂	69.96	10.73	13.98	
							600.94	70.12	10.89	14.06	
13m	-(CH ₂) ₃ -S-		SMe		98	121-124 (EtOAc)	C ₂₅ H ₄₅ N ₅ OS ₂	60.56	9.15	14.13	12.93
							495.80	60.51	9.44	14.02	13.04
13n	-CH ₂ NBn(CH ₂) ₂ -		SMe		91	95-99 (ether/EtOAc)	C ₃₂ H ₅₂ N ₆ OS	67.56	9.21	14.77	5.64
							568.88	67.44	9.33	14.68	5.66

M: morpholin-4-yl.

Table III
Comparison of Different type *N*-Benzylations of **1f** [Q = methylthio, R¹+R² = (CH₂)₄] with Benzyl Chloride

Method	Type of Salt	Deprot. Agent	Solvent	Reaction Conditions	Isolated yield of 3f/6	Isolated yield of 7f/6	Isolated yield of 8f/6
Traditional	Na ⁺	NaH	DMF	70°, 10 hours 150°, 4 hours	50 % 39 %		
Classical PTC	Na ⁺	NaOH/ Bu ₄ N ⁺ Br ⁻ (catalytic amount)	CH ₂ Cl ₂ /H ₂ O	60°, 12 hours	60 %		
Our New Method	Bu ₄ N ⁺ Salt stoichio- metric		CH ₃ CN 2-PrOH Benzene	80°, 1 hour 80°, 1 hour 80°, 1 hour	61 % 61 % 67 %	4.7 %	0.7 %

Derivatives **7** and **8** were isolated by column chromatography

Table IV
The Ratio of Isolated Isomeric *N*-Alkylated Products **3**, **7** and **8** Formed During the Alkylation of Some Tetrabutylammonium Salts **13** with Benzyl Chloride in Acetonitrile

Compound	R ¹	R ²	Q	Isolated Yield (%)		
				3/6	7/6	8/6
13b [a]	Me	H	SiPr	58	6	1.3
13e	-(CH ₂) ₃ -		SMe	77	3	0.5
13f	-(CH ₂) ₄ -		SMe	61	4.7	0.7
13g	-(CH ₂) ₅ -		SMe	56	15	2.3
13h	-(CH ₂) ₆ -		SMe	54	15	3
13i	-(CH ₂) ₁₀ -		SMe	32	24	5.2
13k	-(CH ₂) ₄ -		M	76	0.6	10
13l	-(CH ₂) ₁₀ -		M	41	2	19
13m	-(CH ₂) ₃ -S-		SMe	52	13	0.2

[a] Alkylated with 4-chlorobenzyl chloride. Derivatives **7** and **8** were isolated by column chromatography. M = morpholin-4-yl.

respectively, R³ = R⁴ = *n*-butyl) (Scheme 5) were *N*-benzylated in boiling acetonitrile, and in each case all three *N*-benzylated isomers [**3e-i/6**, **7e-i/6** and **8e-i/6**, Q = methylthio, R = benzyl, R¹+ R² = (CH₂)_{3,4,5,6}, and **10**, respectively] were isolated (Table IV).

Next the isomeric tetrabutylammonium salts **14e** and **14i** (Q = methylthio, R¹+ R² = (CH₂)₃ and (CH₂)₁₀, respectively,) (Scheme 6) derived from derivatives of type **2** were in case of **14e** *N*-benzylated with benzyl chloride in boiling acetonitrile to yield the expected *ω*-*N*-benzylated main product **4e/6** (Q = methylthio, R¹+ R² = (CH₂)₃, R = benzyl) with 70% yield and in case of **14i** *N*-methylated in acetonitrile at room temperature with methyl iodide to yield **4i/1** (Q = methylthio, R¹+ R² = (CH₂)₁₀, R = methyl) with 62% yield.

Our *N*-alkylation reaction proceeds independently of the identity of the Q substituents in derivatives **1** as proved by the *N*-alkylation of the corresponding 2-(morpholin-4-yl)-cycloalka[*d*][1,2,4]triazolo[1,5-*a*]pyrimidin-5-one tetrabutylammonium salts **13k** and **13l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively, R³ = R⁴ = *n*-butyl] (Scheme 5) to yield as main products again the

ω-*N*-alkylated derivatives **3k** and **3l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively] (Scheme 1, Table IV). However, quite unexpectedly, in these cases the corresponding 1-*N*-benzylated products **7k** and **7l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively] (Scheme 3) were not the most abundant minor products of the reaction as observed in the previous experiments, but just to the contrary in the mother liquors of **3k** and **3l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively] derivatives **8k** and **8l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively] were present in approximately 10-20% yield and those of derivatives **7k** and **7l** [Q = morpholin-4-yl, R¹+ R² = (CH₂)₄ and (CH₂)₁₀, respectively] were present in very low concentrations (Table IV). This fact is contrary to previous literary observations [14], where the nitrogen atom at position 3 of the 1,2,4-triazolo[1,5-*a*]pyrimidin-5-ones can be only hardly alkylated.

A possible explanation for the results above can be given by taking in account the coplanarity of the 2-*S*-methyl substituents with the 1,2,4-triazolo[1,5-*a*]pyrimidinone moiety of **13f** (Scheme 7), which is

Table V

Compound	R ¹	R ²	R	Q	Lit mp (°C)	Reaction time (hours)	Yield (%)	Mp (°C) (cryst from)	Molecular Formula (MW)	C	Analysis			
											Calcd/Found	H	N	S
3a/1	Me	H	Me	SMe	Lit [3] 213-215	12 (25 °C)	78	212-214 (CH ₃ CN)	C ₈ H ₁₀ N ₄ OS	45.70	4.79	26.65	15.25	
									210.26	45.84	4.88	26.52	15.09	
3a/3	Me	H	<i>n</i> -Bu	SMe		6	62	147-148 (EtOAc)	C ₁₁ H ₁₆ N ₄ OS	52.36	6.39	22.20	12.71	
									252.34	52.44	6.55	22.09	12.60	
3a/6	Me	H	Bn	SMe	Lit [3] 145-147	6	53	151.5-153 (EtOAc)	C ₁₄ H ₁₄ N ₄ OS	58.72	4.93	19.57	11.20	
									286.36	58.80	5.11	19.55	11.32	
3b/7	Me	H	Bn (4-Cl)	SiPr		7	58	170-172 (CH ₃ CN)	C ₁₆ H ₁₇ ClN ₄ OS	55.09	4.91	16.06	9.19	
									348.86	54.92	4.88	16.21	9.24	
3c/1	Me	H	Me	SBu		5	56	147-148 (ⁱ Pr ₂ O/EtOAc)	C ₁₁ H ₁₆ N ₄ OS	52.36	6.39	22.20	12.71	
									252.34	52.33	6.54	22.16	12.88	
3c/3	Me	H	<i>n</i> -Bu	SBu		6	55	77.5-78 (<i>n</i> -hexane)	C ₁₄ H ₂₂ N ₄ OS	57.11	7.53	19.03	10.89	
									294.42	57.23	7.66	18.90	10.91	
3d/6	-(CH ₂) ₄ -		Bn	H		3	38	198-199 (CH ₃ CN)	C ₁₆ H ₁₆ N ₄ O	68.55	5.75	19.99		
									280.33	68.50	5.93	20.11		
3e/6	-(CH ₂) ₃ -		Bn	SMe		30	77	221.5-222.5 (CH ₃ CN)	C ₁₆ H ₁₆ N ₄ OS	61.52	5.16	17.93	10.26	
									312.40	61.48	5.43	18.02	10.11	
3f/1	-(CH ₂) ₄ -		Me	SMe	Bu ₄ N-salt	0.15 (25°C)	85	259-260 (CH ₃ CN)	C ₁₁ H ₁₄ N ₄ OS	52.78	5.64	22.38	12.81	
									250.32	52.88	5.75	22.30	12.77	
3f/2	-(CH ₂) ₄ -		ⁱ Pr	SMe	Bu ₄ P-salt	1	65							
									34	16	206.5-207.5 (EtOAc)	C ₁₃ H ₁₈ N ₄ OS	56.09	6.52
3f/4	-(CH ₂) ₄ -		allyl	SMe		1.5	79	168.5-169 (CH ₃ CN)	C ₁₃ H ₁₆ N ₄ OS	56.13	6.67	20.23	11.47	
									278.38	56.50	5.84	20.27	11.60	
3f/6	-(CH ₂) ₄ -		Bn	SMe	Lit [4] 220-222	1	61	222-224 (CH ₃ CN)	C ₁₇ H ₁₈ N ₄ OS	56.42	5.90	20.21	11.64	
									276.36	62.55	5.56	17.16	9.82	
3g/6	-(CH ₂) ₅ -		Bn	SMe	Lit [5] 201-202	1	56	201-202 (CH ₃ CN)	C ₁₈ H ₂₀ N ₄ OS	62.48	5.60	17.25	10.01	
									326.42	63.50	5.92	16.46	9.42	
3h/6	-(CH ₂) ₆ -		Bn	SMe	Lit [5] 167.5-169	1.5	54	167.5-169 (CH ₃ CN)	C ₁₉ H ₂₂ N ₄ OS	63.55	6.11	16.40	9.38	
									340.45	64.38	6.26	15.81	9.05	
3i/6	-(CH ₂) ₁₀ -		Bn	SMe	Lit [5] 186-188	1	32	186-188 (CH ₃ CN)	C ₂₃ H ₃₀ N ₄ OS	64.40	6.52	15.99	8.94	
									410.59	67.28	7.36	13.65	7.81	
3j/5	-(CH ₂) ₄ -	<i>n</i> -Hex	NH ₂			4	27	227-229 (CH ₃ CN)	C ₁₅ H ₂₃ N ₅ O	67.33	7.56	13.58	7.88	
									289.38	62.26	8.01	24.20		
3k/6	-(CH ₂) ₄ -		Bn	M	Lit [4] 213-215	4	76	209-211 (CH ₃ CN)	C ₂₀ H ₂₃ N ₅ O ₂	62.36	7.95	24.30		
									365.44	65.74	6.34	19.16		
3l/6	-(CH ₂) ₁₀ -		Bn	M	Lit [5] 245.5-247.5	2	41	245.5-247.5 (CH ₃ CN)	C ₂₆ H ₃₅ N ₅ O ₂	65.66	6.35	19.02		
									449.60	69.46	7.85	15.58		
3m/6	-(CH ₂) ₃ -S-		Bn	SMe	Lit [10] 236-238	8	52	239-241 (CH ₃ CN)	C ₁₆ H ₁₆ N ₄ OS ₂	69.62	7.88	15.51		
									344.46	55.79	4.68	16.27	18.62	
3n/6	-CH ₂ -NBn-(CH ₂) ₂ -		Bn	SMe	Lit [7] 165-166	6	46	165-168(d) (CH ₃ CN)	C ₂₃ H ₂₃ N ₅ OS	55.84	4.78	16.33	18.58	
									417.54	66.16	5.55	16.77	7.68	
										66.02	5.67	16.68	7.62	

M = Morpholin-4-yl, Bn = benzyl, Bn(4-Cl) = 4-chlorobenzyl, *n*-Hex = *n*-hexyl

consistent with the X-ray diffraction spectra of some analogous derivatives **15** and **16** (Scheme 8) [15-16], thus enabling conjugation of the lone electron pair of the sulphur atom with the 1,2,4-triazolo[1,5-*a*]pyrimidinone ring system. This conjugation lowers the negative charge (and consequently the nucleophilicity) of the nitrogen atom at position 3. On the contrary, the 2-morpholin-4-yl moiety of analogues **13k** (Scheme 7) is strongly twisted out of the plain compared to the 1,2,4-triazolo[1,5-*a*]pyrimidinone ring system analogously to **17** (Scheme 9) (for its X-ray diffraction spectra see [1]) thereby strongly decreasing the conjugation of the lone electron pair of the

nitrogen atom with the conjugated double bonds of the heterocyclic ring system. Consequently, it has little influence on the negative charge of the nitrogen atom at position 3 which is now more negative (and thus more nucleophilic) than the nitrogen atom at position 1.

The above facts are corroborated by the cmr spectra as well. Thus while the coupling constant of the carbon atom at position 2 of **13f** coupled with the planar *S*-methyl protons is 4.5 Hz (Scheme 7) the coupling constant of the analogous carbon atom at position 2 of **13k** coupled with the strongly twisted morpholin-4-yl NCH₂ protons is only 1.5 Hz (Scheme 7).

Table VI

Compound	IR, ν (cm ⁻¹)	CH ₂ -5	CH ₂ - (ω -2)	¹ H-NMR (δ , ppm)	Other	R	Q	C-2	C-5	C-5a	C-6	(ω -1)	(ω -1)a	ω a	R	Q	UV(EtOH) $\lambda_{\max}$ (ϵ ·10 ⁻³)
3a/1	1709	5.85d	2.45d	3.80s(3H)	2.67s (3H)	164.2	154.2	100.4	18.9	150.5	152.2	34.0	13.6	233 (26.7)			
	1612	(6-H)	(7-Me)												(0.8Hz)	(7-Me)	
	1554	(0.8Hz)															
3a/3	1701	5.82d	2.45d	4.17t(2H)	2.69s (3H)	164.8	154.5	101.3	18.8	149.8	152.1	47.7;30.5	13.5	234 (26.2)			
	1606	(0.7Hz)	(7-Me)												(7-Me)		
	1555	(6-H)															
3a/6	1712	5.85s	2.34s	0.99t(3H)	2.67s (3H)	164.8	154.3	101.3	18.7	150.6	152.8	50.6	13.6	234.5 (26.7)			
	1613	(6-H)	(7-Me)												(7-Me)		
	1559	(7-Me)															
3b/7	1709	5.88s	2.34s	5.43s(2H)	4.03m (1H)	164.2	154.4	101.8	19.0	150.2	152.7	50.2	36.7	235.5 (26.8)			
	1565	(6-H)	(7-Me)												(C-6)		
	1464																
3c/1	1683	5.83d	2.42s	3.79s(3H)	3.27t	164.2	154.4	100.7	18.9	150.4	152.3	34.0	30.9	233.5 (27.0)			
	1610	(6-H)	(7-Me)												(7-Me)		
	1572																
3c/3	1700	5.84d	2.44s	4.17t(2H)	3.27t	164.3	154.4	101.0	18.5	149.8	151.9	47.7;30.2	30.9	235 (27.1)			
	1607	(6-H)	(7-Me)												(7-Me)		
	1555																
3d/6	1692	2.64m	2.66m	1.75m (4H)	8.03s (1H)	151.8	156.0	109.7	22.2	147.9	151.6	49.8	13.2	209 (25.1)			
	1613		7.1m(2H)												25.7	134.7(s)	249 (4.9)
	1571		7.35m(3H)												31.3	128.1(p)	284 (13.2)
3e/6	1689	2.89t	2.93t	2.15m (CH ₂ -7)	2.69s (3H)	164.6	153.8	112.9	27.4	153.5	152.9	51.8	13.8	237 (25.6)			
	1614		7.2-7.35m												26.1	134.5(s)	281 (13.6)
	1567		(5H)												146.7	128.5(p)	
3f/1	1680	2.60t	2.68t	1.75m	2.68s (3H)	164.5	155.2	109.7	22.3	146.7	152.2	33.3	14.1	236.5 (26.1)			
	1614			1.90m										281.5 (10.8)			
3f/2	1565			(2x2H)													
	1691	2.63t	2.72t	4.8m(1H)	2.69s (3H)	164.2	155.4	109.6	22.7	146.2	150.2	51.2	14.1	238 (27.6)			
	1604			1.68d(6H)								19.7	283 (12.3)				
3f/4	1560	2.60t	2.72t	(2x2H)	2.67s (3H)	164.4	155.0	109.4	22.1	146.6	151.4	48.4	13.8				
				1.87m													
				1.75m													
3f/6	1685	2.59t	2.62t	(2x2H)	2.68s (3H)	164.6	155.2	109.8	21.9	146.8	152.2	49.6	13.7	237.5 (27.8)			
	1614			(CH ₂ -7,8)								117.9(CH ₂ =)	282.5 (13.0)				
	1567			7.3-7.4m								134.7(s)					
3g/6	1691	2.86m	2.82m	5.48s(2H)	2.61s (3H)	164.5	154.9	114.6	24.1	153.2	152.0	51.1t	13.8	236.5 (27.8)			
	1609			1.46m								128.0(p)		282.5 (13.0)			
	1565			1.22m								135.0(s)					
3h/6	1680	2.8m	2.8m	5.50s(2H)	2.69s (3H)	164.7	154.7	113.2	25.2	149.2	152.5	50.8	13.9	236 (29.3)			
	1603			1.75m								128.0(p)		282.5 (12.8)			
	1562			1.5m								135.3(s)					

Table VI (continued)

Compound	IR,ν (cm ⁻¹)	CH ₂ -5	CH ₂ - (ω-2)	¹ H-NMR (δ, ppm)	R	Q	C-2	C-5	C-5a	C-6	¹³ C-NMR (δ, ppm)	(ω-1)	(ω-1)a	ωa	R	Q	UV(EtOH) λ _{max} (ε·10 ⁻³)
3i/6	1692	2.67m	2.67m	1.75m	5.52s(2H)	2.67s(3H)	164.8	155.5	113.7	25.2	27.4	149.9	152.5	152.5	50.9	14.0	239 (30.5)
	1601			1.5m	7.1m(2H)										135.5(s)		285 (13.1)
	1556			(4+12H)	7.3m(3H)										128.1(p)		
3j/5	1661	2.60t	2.67t	1.70m	4.06t(2H)	4.88s(2H)	163.0	155.5	109.5	22.4	26.2	145.0	150.5	150.5	46.6; 31.3;		229 (31.7)
	1601			(4H)	1.90m(2H)										28.6; 25.4;		281 (11.2)
	1576				1.35m(6H)										22.2; 13.9		
3k/6	1680	2.55t	2.60t	1.75m	0.89t(3H)	3.58m(NCH ₂)	164.3	155.4	109.7	22.0	25.3	145.2	151.4	151.4	49.4	45.8	234 (31.1)
	1549			(4H)	5.42s(2H)	3.77m(OCH ₂)									135.0(s)	66.1	278 (13.5)
					7.15m(2H)										127.8(p)		
3l/6	1668	2.6m	2.6m	1.7m	5.48s(2H)	3.56m(NCH ₂)	164.4	155.7	113.6	25.0	27.4	148.4	151.8	151.8	50.6	46.0	238 (27.8)
	1570			1.5m	7.1m(2H)	3.76m(OCH ₂)									135.7(s)	66.3	285 (10.9)
	1547			(4+12H)	7.3m(3H)										128.0(p)		
3m/6	1678	2.90m	2.70t	2.15m	5.51s(2H)	2.66s(3H)	164.7	152.3	108.1	24.9* (C-7)	24.8*	140.7	151.5	151.5	49.9	13.5	257 (21.9)
	1605	(CH ₂ -7)		(CH ₂ -8)	7.15m(2H)										134.3(s)		324 (6.3)
	1554				7.35m(3H)										127.8(p)		
3n/6	1677	2.73s	3.39s	2.73s	5.27s(2H)	2.68s(3H)	164.8	154.8	107.7	22.0	50.6	144.5	152.3	152.3	49.7	13.7	237.5 (29.5)
	1616			(CH ₂ -7)	7.05m(2H)										134.2(s)		279.5 (12.9)
	1566				7.3m(3H)										136.7(s)		

Our *N*-alkylation reaction can be performed with the corresponding tetrabutylphosphonium salt **18** (Scheme 10) as well. It was prepared analogously to the tetrabutylammonium salts using tetrabutylphosphonium bromide instead of the corresponding quaternary tetraalkylammonium salts. This salt was also crystalline and soluble in common organic solvents. Its *N*-alkylation in acetonitrile provided again as the main product the ω-*N*-alkylated derivative **3f/1** (Scheme 10) that crystallised from the reaction mixtures. However, the yield of this reaction was a bit lower than that made with the corresponding tetrabutylammonium salt (see the alkylations of **13f** to yield **3f/1**, Table V).

The *O*-alkylated derivatives **9** (Scheme 3) representing the fourth possible isomer required for the structure elucidation of the *N*-alkylated products were obtained by analogy to the known methods [17-19] from the corresponding 5-chloro derivative **19** (Scheme 11).

At last the methylation and benzylation of the tetrabutylammonium salt (**21**) of a thioamide, namely the 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]-quinazolin-5(10*H*)-thione (**20**) prepared by analogy to a known method [20] was attempted. However, even though the alkylation proceeded smoothly, in this case no *N*-alkylation occurred but instead the *S*-alkyl derivatives **22/1** and **22/6** (R = methyl and benzyl, respectively) were obtained in high (86%) yield (Scheme 12).

The uv and cmr spectra of isomers **3**, **7**, **8** and **9** proved the correctness of structures based on the analogy of the uv and cmr spectral data of derivatives **3** and **1** reported previously [3-10]. As expected they were very different from each other. Thus the uv maxima of derivatives **3** recorded in ethanolic solution appeared as reported previously [3-8] with two maxima at 229-237 and 272-285 nm (Table VI). The only exceptions observed were from derivative **3d/6**, the Q = H substituent did not contain a lone electron pair, and consequently a hypsochromic shift of the spectra was observed, and that of compound **3m/6** where, just to contrary, the lone electron pair of the sulphur atom of the thiacyclohexane moiety is conjugated to the triazolo-pyrimidinone chromophore thus causing a bathochromic shift of the spectra. The uv spectra of derivatives **7** recorded under the same conditions were characterised also with two uv maxima appearing at 221-227.5 and 284-291 nm (Table VIII), derivatives **8** showed four uv maxima at 206-219, 240.5-246.5, 270.5-276.5 and 291.5-301 nm (Table X) (the exceptions formed again derivatives **7d/6**, **7m/6** and **8m/6** for the reasons discussed above), while derivatives **9** showed three uv maxima at 210, 239-241 and 285-300 nm (see Experimental).

In the cmr spectra of derivatives **3** the carbon atoms 2, 5, (ω-1)a and ωa (see Scheme 1, Table VI) appeared as expected [3-8] at 163.0-164.8, 153.8-156.0, 144.5-153.5 and 150.2-152.8 ppm, respectively. Again the only exceptions were compound **3d/6**, where the carbon atom 2 of which appeared as a consequence of the CH group at

Table VII

Compound	R ¹	R ²	R	Q	Lit. mp	Reaction time (hours)	Yield (%)	Mp (°C) (cryst from)	Molecular Formula (MW)	Analysis			
										C	Calcd/ H	Found N	S
7a/3	Me	H	<i>n</i> -Bu	SMe		6	15	105-107 (<i>c</i> -hexane/ ether)	C ₁₁ H ₁₆ N ₄ OS 252.34	52.36	6.39	22.20	12.71
										52.44	6.56	22.09	12.65
7b/7	Me	H	Bn (4-Cl)	S ⁱ Pr		7	6	121-124 (<i>c</i> -hexane/ EtOAc)	C ₁₆ H ₁₇ ClN ₄ OS 348.86	55.09	4.91	16.06	9.19
										55.11	5.09	16.11	9.06
7c/1	Me	H	Me	SBu		5	3	123-125 (<i>n</i> -hexane/ ether)	C ₁₁ H ₁₆ N ₄ OS 252.34	52.36	6.39	22.20	12.71
										52.28	6.44	22.25	12.77
7c/3	Me	H	<i>n</i> -Bu	SBu		6	10	77.5-79 (<i>n</i> -hexane)	C ₁₄ H ₂₂ N ₄ OS 294.42	57.11	7.53	19.03	10.89
										57.08	7.65	19.11	10.94
7d/6	-(CH ₂) ₄ -		Bn	H		3	23	170-171.5 (EtOAc)	C ₁₆ H ₁₆ N ₄ O 280.33	68.55	5.75	19.99	
										68.46	5.83	19.78	
7e/6	-(CH ₂) ₃ -		Bn	SMe		30	3	168-170 (ⁱ Pr ₂ O)	C ₁₆ H ₁₆ N ₄ OS 312.40	61.52	5.16	17.93	10.26
										61.65	5.32	17.88	10.31
7f/1	-(CH ₂) ₄ -		Me	SMe		1 (25°C)	3	197-200 (EtOAc)	C ₁₁ H ₁₄ N ₄ OS 250.32	52.78	5.64	22.38	12.81
										52.86	5.78	22.28	12.77
7f/2	-(CH ₂) ₄ -		ⁱ Pr	SMe		34	14	182-184 (EtOAc)	C ₁₃ H ₁₈ N ₄ OS 278.38	56.09	6.52	20.13	11.52
										55.98	6.59	20.32	11.66
7f/4	-(CH ₂) ₄ -		allyl	SMe		1.5	4	134-135.5 (ether)	C ₁₃ H ₁₆ N ₄ OS 276.36	56.50	5.84	20.27	11.60
										56.44	5.96	20.18	11.47
7f/6	-(CH ₂) ₄ -		Bn	SMe		1	5	171-173 (<i>c</i> -hexane)	C ₁₇ H ₁₈ N ₄ OS 326.42	62.55	5.56	17.16	9.82
										62.60	5.79	17.08	9.86
7g/6	-(CH ₂) ₅ -		Bn	SMe		1	15	184-187 (EtOAc)	C ₁₈ H ₂₀ N ₄ OS 340.45	63.50	5.92	16.46	9.42
										63.47	6.07	16.55	9.48
7h/6	-(CH ₂) ₆ -		Bn	SMe	[5] 223-224	1.5	15	223-224 (benzene)	C ₁₉ H ₂₂ N ₄ OS 354.48	64.38	6.26	15.81	9.05
										64.44	6.52	15.88	9.02
7i/6	-(CH ₂) ₁₀ -		Bn	SMe	[5] 211-213	1	24	211-213 (benzene)	C ₂₃ H ₃₀ N ₄ OS 410.59	67.28	7.36	13.65	7.81
										67.39	7.54	13.70	7.76
7j/5	-(CH ₂) ₄ -		<i>n</i> -Hex	NH ₂		4	5	207-209 (CH ₃ CN)	C ₁₅ H ₂₃ N ₅ O 289.38	62.26	8.01	24.20	
										62.36	8.35	24.32	
7k/6	-(CH ₂) ₄ -		Bn	M		4	0.6	197-199 (ether)	C ₂₀ H ₂₃ N ₅ O ₂ 365.44	65.74	6.34		
										65.77	6.45		
7l/6	-(CH ₂) ₁₀ -		Bn	M		2	2	143-145 (ether)	C ₂₆ H ₃₅ N ₅ O ₂ 449.60	69.46	7.85		
										69.38	7.89		
7m/6	-(CH ₂) ₃ -S-		Bn	SMe		8	13	192-194 (EtOAc/ CH ₃ CN)	C ₁₆ H ₁₆ N ₄ OS ₂ 344.46	55.79	4.68	16.27	18.62
										55.84	4.85	16.23	18.66
7n/6	-CH ₂ -NBn-(CH ₂) ₂ -		Bn	SMe		6	8	148-151(d) (CH ₃ CN)	C ₂₃ H ₂₃ N ₅ OS 417.54	66.16	5.55	16.77	7.68
										66.24	5.68	16.85	7.62

M = morpholin-4-yl, Bn = benzyl, Bn (4-Cl) = 4-chlorobenzyl, *n*-Hex = *n*-hexyl.

151.8 ppm, and derivative **3m/6**, where as a consequence of the thiacyclohexane sulphur atom attached to the triazolo-pyrimidinone ring system carbon atoms 5 and (ω-1)a appeared at 152.3 and 140.7 ppm, respectively.

In the cmr spectra of derivatives **7** the carbon atoms 2, 5, (ω-1)a and ωa (see Scheme 3, Table VIII) appeared at 152.4-155.1, 154-157.1, 159.3-168.5 and 145.3-150.0 ppm, respectively, and in those of derivatives **8** appeared at 163.8-166.3, 154.0-157.6, 161.3-171.0 and 151.7-155.6 ppm, respectively (Table X) (the only exceptions formed again derivatives **7d/6**, **7m/6** and **8m/6** for the reasons discussed above), while in those of derivatives **9** they appeared at 167.6, 150.4-151.5, 165.6-165.7 and 156.1-156.2, respectively (see Experimental).

From the four chemical shifts corresponding to carbon atoms 2, 5, (ω-1)a and ωa at least one always differed significantly from all others, making possible a reliable basis to differentiate between isomers **3**, **7**, **8** and **9**. The present results corroborated the structural decisions made earlier [3-10]. However, they also showed that the chemical shifts of the carbon atoms 2 and 5 of derivatives **3** and **8** are very similar, thus a decision based on comparison of only these two spectral data might lead to mistakes.

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

Table VIII

Compound	IR, ν (cm^{-1})	CH_2 -6	CH_2 -7 (ω -1)	^1H -NMR (δ , ppm)	R	Q	C-2	C-5	C-5a	C-6	ω -1	(ω -1)a	^{13}C -NMR (δ , ppm)	R	Q	UV(EtOH) $\lambda_{\text{max}}(\epsilon \cdot 10^{-3})$
7a/3		6.06s (6-H)	2.35s (7-Me)	Other	R	Q	C-2	C-5	C-5a	C-6	ω -1	(ω -1)a	^{13}C -NMR (δ , ppm)	R	Q	UV(EtOH) $\lambda_{\text{max}}(\epsilon \cdot 10^{-3})$
7b/7	1699 1601 1537	6.09s (6-H)	2.36s (7-Me)	3.99t(2H) 1.81m(2H) 1.40m(6H) 0.99t(3H) 5.12s(2H) 7.34s(4H)	3.99t(2H) 1.81m(2H) 1.40m(6H) 0.99t(3H) 5.12s(2H) 7.34s(4H)	2.82s(3H) 4.23m(1H) 1.48d(6H) (7Hz)	153.3	155.9	102.5 (C-6)	24.0 (7-Me)	163.5	149.1	43.0 29.9 19.4 13.2 45.8 134.8(s) 132.3(s)	43.0 29.9 19.4 13.2 45.8 134.8(s) 132.3(s)	13.5 39.1 23.3 31.3 30.4 21.5 13.2 31.1 30.2 21.3 13.0	223 (24.7) 284 (12.2) 222.5 (30.7) 285 (12.7) 223 (24.6) 284 (11.5)
7c/1	1693 1599 1536	6.08s (6-H)	2.35s (7-Me)	3.57s(3H)	3.57s(3H)	3.44t(2H) 1.80m(2H) 1.50m(2H) 0.96t(3H)	153.4	156.2	103.0 (C-6)	24.0 (7-Me)	163.7	149.5	28.8	28.8	31.3 30.4 21.5 13.2	223 (24.6) 284 (11.5)
7c/3	1686 1593 1534	6.06s (6-H)	2.34s (7-Me)	3.99t(2H) 1.8m(2H) 1.4m(6H) 0.98t(3H)	3.99t(2H) 1.8m(2H) 1.4m(6H) 0.98t(3H)	3.44t(2H) 1.8m(2H) 1.5m(2H) 0.96t(3H)	152.8	156.0	102.5 (C-6)	23.8 (7-Me)	163.5	149.1	42.8 29.8 19.2 13.0	42.8 29.8 19.2 13.0	31.1 30.2 21.3 13.0	224 (23.6) 284.5 (12.0)
7d/6	1675 1601 1549	2.63t	2.72t	1.8m (4H)	5.25s(2H) 7.3-7.4m (5H)	8.20s	141.0	156.8	111.7	22.4	32.5	160.8	145.8	47.2 133.8(s) 128.8(p)	47.2 133.8(s) 128.8(p)	209 (25.8) 255 (4.9) 289.5 (12.6)
7e/6	1714 1688 1595 1533	2.92t	2.92t	2.13m (7.5Hz)	5.17s(2H) 7.3-7.4m(5H)	2.76s(3H)	153.1	154.0	114.7	27.1	35.0	168.5	150.0	46.4 133.4(s) 128.6(p)	46.4 133.4(s) 128.6(p)	224.5 (23.9) 284 (12.1)
7f/1	1679 1600 1542	2.66m	2.66m	1.8m (4H)	3.55s(3H)	2.82s(3H)	153.4	156.0	111.7	22.3	32.2	159.3	147.2	28.6	13.4	226 (25.6) 287 (11.3)
7f/2	1678 1597 1547	2.64t	2.68t	1.78m (4H)	4.66m(1H) 1.62d(6H)	2.81s(3H)	152.5	156.3	111.6	22.5	32.6	159.5	146.9	48.7 19.9	14.2	227 (25.6) 288 (11.8)
7f/4		2.65t	2.68t	1.8m (4H)	4.58d(2H) 5.3m(2H) 5.9m(1H)	2.80s(3H)	153.2	156.2	112.0	22.4	32.3	159.6	146.9	44.7 129.3(CH) 119.6(CH ₂ =)	13.7	
7f/6	1695 1607	2.65m	2.71m	1.82m (CH ₂ -7,8)	5.13s(2H) 7.3-7.4m(5H)	2.75s(3H)	153.1	156.0	111.8	22.3	32.2	159.5	147.1	46.0 133.5(s) 128.6(p)	13.6	227 (23.6) 288 (12.5)
7g/6	1539 1684 1598	2.87m	2.87m	1.85m 1.65m	5.14s(2H) 7.3-7.4m(5H)	2.75s(3H)	153.2	156.0	116.4	26.9	38.7	166.2	146.8	46.1 133.5(s) 128.4(p)	13.7	225 (24.4) 291 (12.2)
7h/6	1529 1679 1602	2.82m	2.82m	(2+4H) 1.75m 1.43m	5.15s(2H) 7.3-7.4m(5H)	2.76s(3H)	153.3	155.9	114.6	26.4	34.8	163.4	147.7	46.3 133.8(s) 128.6(p)	13.9	228 (26.1) 289 (12.3)
7i/6	1530 1672 1607 1529	2.69m	2.69m	(4+4H) 1.85m 1.78m 1.4m (12H)	5.11s(2H) 7.3-7.4m(5H)	2.75s(3H)	153.2	156.5	115.0	26.4	31.6	162.8	147.2	46.2 133.8(s) 128.5(p)	13.7	225 (23.3) 291 (14.0)

Table VIII (continued)

Compound	IR, ν (cm^{-1})	CH_2 -6	CH_2 - (ω -1)	$^1\text{H-NMR}$ (δ , ppm)	Other	R	Q	C-2	C-5	C-5a	C-6	ω -1	(ω -1) α	$^{13}\text{C-NMR}$ (δ , ppm)	R	Q	UV(EtOH) $\lambda_{\text{max}}(\epsilon \cdot 10^{-3})$
7j/5	1643	2.58t	2.66t	1.8m (4H) 1.3m(6H) 0.85t(3H) 5.17s(2H) 7.2m(2H) 7.3m(3H) 5.14s(2H) 7.3-7.4m(5H)	3.92t(2H) 1.8m(2H) 1.3m(6H) 0.85t(3H) 5.17s(2H) 7.2m(2H) 7.3m(3H)	6.56s(2H)	152.8	156.9	111.3	22.2	31.9	159.3	145.3	41.3; 31.0 27.6; 25.8 22.0; 13.5	46.6 134.3(s) 128.1(p)	49.4 65.7	221 (29.5) 285 (10.1)
7k/6	1672	2.65m	2.65m	1.8m (4H) 1.8m 1.4m (16H) 2.20m (CH_2 -8) 1510	5.13s(2H) 7.35s(5H)	3.23(NCH_2) 3.71(OCH_2)	154.7	156.4	112.5	22.4	32.2	159.3	147.0	46.6 134.3(s) 128.1(p)	49.4 65.7	224 (26.7) 284 (12.5)	
7l/6	1580	2.64t	2.69t	1.8m 1.4m (16H) 2.20m (CH_2 -8) 1510	5.13s(2H) 7.35s(5H)	3.23(NCH_2) 3.72(OCH_2)	155.1	157.1	116.0	26.5	31.6	162.9	147.3	46.9 134.7(s) 128.5(p)	49.6 65.9	227.5 (23.4) 290.5 (11.4)	
7m/6	1670	2.98m (CH_2 -7)	2.82t	2.75s (CH_2 -7) 1510	5.10s(2H) 7.3-7.45m (10H)	2.75s(3H)	154.1	153.5	110.1	26.4 (C-7)	32.2	154.3	146.4	46.6 133.8(s) 128.9(p)	13.9	250.5 (25.0) 283.5 (7.4) 322 (9.9)	
7n/6	1603	2.75s	3.53s	2.75s (CH_2 -7) 1510	5.10s(2H) 7.3-7.45m (10H)	2.75s(3H)	153.5	155.8	109.9	22.5	57.2	157.3	148.0	46.1 133.5(s) 137.6(s)	13.6	227 (26.8) 288 (12.5)	

spectrophotometer. The ultraviolet spectra were obtained by a Varian Cary 1E UV-VIS spectrophotometer. The pmr and cmr measurements were performed, if not stated otherwise, in deuteriochloroform solutions using tetramethylsilane as internal standard. Bruker WM-250 and Varian VXR-400 instruments, standard Varian HSQC, HMBC and selective INEPT programs were used. Ms spectra were acquired using a KRATOS MS 25 RFA double focusing instrument in EI and CI mode. The dry-column flash chromatographies were performed according to [21]. As adsorbents Aluminium oxide 60 G neutral (Merck 1090 for thin layer chromatography) and Silica gel 60 H (Merck 7736 for thin layer chromatography) were used. For preparative thin layer chromatography pre-coated Merck plates were used under the same conditions as for tlc measurements.

Typical Experiments for the Synthesis of Tetrabutylammonium Salts (**13**).

2-Methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one tetrabutylammonium Salt (**13f**).

Using Tetrabutylammonium Hydrogen Sulphate.

A solution of 37.35 g (0.11 mole) of tetrabutylammonium hydrogen sulphate (Fluka) in 100 ml of water was cooled to 5° and at this temperature a solution of 8.80 g (0.22 mole) of sodium hydroxide in 50 ml of water precooled to 5° was added to it. To the solution obtained 23.63 g (0.1 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one (**1f**, $\text{R}^1 + \text{R}^2 = -(\text{CH}_2)_4$, Q = methylthio) [4] and 100 ml of chloroform was added in one portion and the mixture was intensively stirred for 10 minutes. The lactame dissolved within a short time during which the organic phase turned yellow. The phases were separated, the water phase was extracted with 50 ml of chloroform, the combined chloroform phases were washed with 50 ml of water, dried over sodium sulphate and evaporated *in vacuo* to dryness to yield 45.5 g (95%) of crystalline tetrabutylammonium salt (mp 92-105°) that after recrystallisation from 110 ml of ethyl acetate yielded 40.3 g (84%) of pure 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one tetrabutylammonium salt (**13f**, $\text{R}^1 + \text{R}^2 = -(\text{CH}_2)_4$, Q = methylthio) that melted at 105-107° (for the physical data of all **13** type tetrabutylammonium salts see Table I, for their spectral data see Table II).

Using Tetrabutylammonium Bromide.

To a solution of 3.23 g (0.01 mole) of tetrabutylammonium bromide (Fluka) in 10 ml of water a solution of 0.44 g (0.011 mole) of sodium hydroxide in 10 ml of water was added at room temperature. To the solution obtained 2.36 g (0.01 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one (**1f**, $\text{R}^1 + \text{R}^2 = -(\text{CH}_2)_4$, Q = methylthio) [4] and 10 ml of chloroform was added in one portion and the mixture was intensively shaken for 5 minutes. The phases were separated, the aqueous phase was extracted with 10 ml of chloroform, the combined chloroform phases were washed with 5 ml of water, dried over sodium sulphate and evaporated *in vacuo* to dryness to yield 4.38 g (92%) of crystalline tetrabutylammonium salt that after recrystallisation from 12 ml of ethyl acetate yielded 3.55 g (74%) of pure 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one tetrabutylammonium salt (**13f**, $\text{R}^1 + \text{R}^2 = -(\text{CH}_2)_4$, Q = methylthio), mp 105-107° that was identical with that of obtained in the previous experiment.

Table IX

Compound	R ¹	R ²	R	Q	Lit. Mp (°C)	Reaction time (hours)	Yield (%)	Mp (°C) (cryst from)	Molecular Formula (MW)	C	Analysis Calcd/Found		S
											H	N	
8b/7	Me	H	Bn (4-Cl)	SiPr		7	1.3	141-144 (ether)	C ₁₆ H ₁₇ ClN ₄ OS 348.86	55.09 55.17	4.91 5.08		
8e/6		-(CH ₂) ₃ -	Bn	SMe		30	0.5	145-148 (n-hexane)	C ₁₆ H ₁₆ N ₄ OS 312.40	61.52 61.48	5.16 5.22		
8f/1		-(CH ₂) ₄ -	Me	SMe		1	0.5	174-177 (c-hexane)	C ₁₁ H ₁₄ N ₄ OS 250.32	52.78 52.66	5.64 5.73		
8f/6		-(CH ₂) ₄ -	Bn	SMe		1	0.7	151-152.5 (ether)	C ₁₇ H ₁₈ N ₄ OS 326.42	62.55 62.63	5.56 5.65		
8g/6		-(CH ₂) ₅ -	Bn	SMe		1	2.3	143-145 (c-hexane/ ether)	C ₁₈ H ₂₀ N ₄ OS 340.45	63.50 63.38	5.92 5.99	16.46 16.38	
8h/6		-(CH ₂) ₆ -	Bn	SMe		1.5	3	136-139 (ether)	C ₁₉ H ₂₂ N ₄ OS 354.48	64.38 64.45	6.26 6.44	15.81 15.74	9.05 8.98
8i/6		-(CH ₂) ₁₀ -	Bn	SMe	[5] 128-130	1	5.2	128-130 (ether)	C ₂₃ H ₃₀ N ₄ OS 410.58	67.28 67.12	7.36 7.51	13.65 13.60	7.81 7.69
8k/6		-(CH ₂) ₄ -	Bn	M		4	10	186-188 (ⁱ Pr ₂ O/ EtOAc)	C ₂₀ H ₂₃ N ₅ O ₂ 365.44	65.74 65.79	6.34 6.45	19.16 19.11	
8l/6		-(CH ₂) ₁₀ -	Bn	M		2	19	180-182 (ether)	C ₂₆ H ₃₅ N ₅ O ₂ 449.60	69.46 69.44	7.85 7.98	15.58 15.48	
8m/6		-(CH ₂) ₃ -S-	Bn	SMe		8	0.2	166-169 (ether)	C ₁₆ H ₁₆ N ₄ OS ₂ 344.46	55.79 55.69	4.68 4.75		

Bn (4-Cl) = 4-chlorobenzyl, M: morpholin-4-yl.

A Typical Experiment for the *N*-Alkylation of Tetrabutylammonium Salts **13**.

10-Benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one (**3f/6**), 1-Benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(1*H*)-one (**7f/6**), and 3-Benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(3*H*)-one (**8f/6**).

To a solution of 3.07 g (0.0064 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one tetrabutylammonium salt (**13f**, R¹ + R² = -(CH₂)₄-, Q = methylthio) in 6.5 ml of acetonitrile 1.27 g (0.01 mole) of benzyl chloride was added and the mixture refluxed for 1 hour. The crystals that precipitated after cooling were filtered off and washed with acetonitrile to yield 1.27 g (61%) of 10-benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-one (**3f/6**, R¹ + R² = -(CH₂)₄-, Q = methylthio, R = benzyl), mp 222-224° (acetonitrile) (for the physical data of all 3 type derivatives see Table V, for their spectral data see Table VI).

The mother liquor was evaporated to dryness and the residue was partitioned between 20 ml of chloroform and 10 ml of water. The phases were separated, the chloroform layer was washed (in order to get rid of the water soluble tetrabutylammonium chloride) with 2 x 10 ml of water, dried over sodium sulphate and evaporated *in vacuo* to dryness. The residue was chromatographed on a Silica gel 60 H column (eluent different mixtures of benzene and chloroform of increasing polarities) to yield 98 mg (4.7%) of 1-benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(1*H*)-one (**7f/6**, R¹ + R² = -(CH₂)₄-, Q = methylthio, R = benzyl) mp 171-173° (cyclohexane) (for the physical data of all 7 type derivatives see Table VII, for their

spectral data see Table VIII), and 14.5 mg (0.7%) of 3-benzyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(3*H*)-one (**8f/6**, R¹ + R² = -(CH₂)₄-, Q = methylthio, R = benzyl), mp 151-152.5° (ether) (for the physical data of all 8 type derivatives see Table IX, for their spectral data see Table X).

Tetrabutylammonium Salts of the Isomeric Cyclopenta- and Cyclododeca[e]-1,2,4-triazolo[1,5-*a*]pyrimidin-8- and -15-ones (**14e** and **14i**, respectively).

Derivatives **14e** and **14i** were prepared analogously to the tetrabutylammonium salts **13** starting from 2-methylthio-6,7-dihydro-5*H*-cyclopenta[e]-1,2,4-triazolo[1,5-*a*]pyrimidin-8(9*H*)-one **2e** (R¹ + R² = -(CH₂)₃-, Q = methylthio) [9] and 2-methylthio-5,6,7,8,9,10,11,12,13,14-decahydro-cyclododeca[e]-1,2,4-triazolo[1,5-*a*]pyrimidin-15(16*H*)-one **2i** (R¹ + R² = -(CH₂)₁₀-, Q = methylthio) [5], respectively. Derivative **14e** was isolated in crystalline form, while the oily **14i** was methylated directly to **4i/1**.

2-Methylthio-6,7-dihydro-5*H*-cyclopenta[e]-1,2,4-triazolo[1,5-*a*]pyrimidin-8(9*H*)-one Tetrabutylammonium Salt (**14e**).

Compound **14e** was obtained in 81% yield, mp 112-115° (ethyl acetate/ether); pmr: δ, ppm 0.95 (t, 12H, 4 x CH₃), 1.40 (m, 8H, (CH₂)₄), 1.63 [m, 8H, (CH₂)₄], 2.11 (m, 2H, CH₂-6), 2.58 (s, 3H, SCH₃), 2.82 (t, 2H, CH₂-7), 3.08 (t, 2H, CH₂-5), 3.35 (m, 8H, 4 x NCH₂); cmr: δ, ppm 13.3 (4 x CH₃), 13.9 (SCH₃), 19.4 (4x CH₃CH₂), 21.5 (C-6), 23.7 (4 x NCH₂CH₂), 28.8 and 29.6 (C-5 and C-7), 58.5 (4 x NCH₂), 117.6 (C-7a), 144.2 (C-4a), 159.7 (C-9a), 161.6 (C-8), 169.8 (C-2).

Anal. Calcd. for C₂₅H₄₅N₅OS (MW 463.73): C, 64.75, H, 9.78, N, 15.10, S, 6.91. Found: C, 64.70, H, 9.98, N, 14.97, S, 7.02.

Table X

Compound	IR, ν (cm^{-1})	CH_2 -6	CH_2 -7 (ω -1)	Other	$^1\text{H-NMR}$ (δ , ppm)		$^{13}\text{C-NMR}$ (δ , ppm)										$\lambda_{\text{max}}(\epsilon, 10^{-3})$	UV(EtOH)
					R	Q	C-2	C-5	C-5a	C-6	ω -1	(ω -1)a	ω a	R	Q			
8b/7	1687	5.93s (6-H)	2.34s (7-Me)		5.80s(2H)	4.25m(1H)	165.9	157.1	102.4 (C-6)	27.0	24.2 (7-Me)	164.0	155.6	52.3	40.0	219 (21.4);		
	1580				7.30m(4H)	1.55d(6H) (6.8Hz)								134.9(s)	23.1	246.5 (17.8);		
														132.1(s)		266sh (11.3);		
8e/6	1677	2.82m	2.89m	2.09m (CH_2 -7)	5.89s(2H)	2.82s(3H)	163.8	156.1	114.2	27.0	35.1	171.0	155.0	53.1	14.5	295.5 (7.7);		
	1563				7.3-7.4m(5H)									133.7(s)		206 (24.9);		
	1521													128.7(p)		241 (18.1);		
8f/1	1673	2.56m	2.72m	1.8m (4H)	4.20s(3H)	2.79s(3H)	163.7	157.2	111.3	22.3	32.4	162.0	152.9	36.9	14.2	270.5 (12.0);		
	1582															291.5 (9.0);		
	1530															208.5 (17.4);		
8f/6	1663	2.55t	2.70t	1.75m (CH_2 -7,8)	5.85s(2H)	2.81s(3H)	164.2	157.0	111.7	22.2	32.3	161.8	153.1	52.9	14.4	241(20.1);		
	1575				7.2-7.4m(5H)		q	t			m	s		133.6(s)		244.5 (19.6);		
	1525													128.6(p)		275 (12.4);		
8g/6	1666	2.81m	2.81m	1.83m	5.88s(2H)	2.81s(3H)	164.1	157.1	116.2	27.2	38.9	168.4	152.9	52.9	14.5	296 (10.1);		
	1571			1.66m	7.2-7.4m(5H)									133.6(s)		206.5 (25.7);		
	1515			1.57m										128.7(p)		240.5 (16.4);		
8h/6	1664	2.75m	2.78m	1.8m	5.85s(2H)	2.81s(3H)	164.5	156.8	114.5	26.3	34.8	165.5	153.5	53.0	14.5	272 (10.2);		
	1577			1.67m	7.2-7.4m(5H)									133.5(s)		301 (8.9);		
	1523			1.45m										128.7(p)		206 (27.5);		
8i/6	1661	2.63m	2.63m	1.85m	5.84s(2H)	2.81s(3H)	164.6	157.6	115.1	26.6	31.9	165.1	153.2	53.2	14.6	241 (18.8);		
	1580			1.7m	7.2-7.4m(5H)									133.6(s)		272.5 (11.8);		
	1516			1.4m (12H)										129.4(p)		298 (10.0);		
8k/6	1660	2.56m	2.56m	1.74m (4H)	5.29s(2H)	3.71m (NCH_2)	166.1	157.1	112.2	22.1	32.0	161.3	154.6	54.7	48.6	207.5 (26.3);		
	1631				7.1m(2H)	3.84m (OCH_2)								131.8(s)		244.5 (17.3);		
	1569				7.3m(3H)									128.8(p)		276.5 (10.7);		
8l/6	1526															301 (9.3);		
	1657	2.54t	2.61t	1.7m	5.26s(2H)	3.74m (NCH_2)	166.3	157.3	115.4	26.4	31.3	164.5	154.5	54.8	48.6	236 (16.0);		
	1626			1.4m (16H)	7.05m(2H)	3.85m (OCH_2)								131.4(s)		263.5 (16.0);		
8m/6	1562				7.2m(3H)									128.8(p)		295 (10.2);		
	1526																	
8n/6	1665	2.97m (CH_2 -7)	2.81t	2.18m (CH_2 -8)	5.84s(2H)	2.81s(3H)	164.1	154.0	109.8	26.4 (C-7)	32.1	156.2	151.7	53.2	14.6	207 (30.5);		
	1578				7.35m(5H)									133.4(s)		240 (20.6);		
														128.8(p)		267.5 (20.8);		
																299.5 (14.5);		
																242 (19.6);		
																312 (11.0);		
																331.5 (12.1);		

9-Benzyl-2-methylthio-6,7-dihydro-5H-cyclopenta[e]-1,2,4-triazolo[1,5-a]pyrimidin-8(9H)-one (**4e/6**).

This compound was prepared analogously to derivatives **3** by benzylation of a solution of 250 mg (0.00054 mole) of 2-methylthio-6,7-dihydro-5H-cyclopenta[e]-1,2,4-triazolo[1,5-a]pyrimidin-8(9H)-one tetrabutylammonium salt **14e** ($R^1 + R^2 = -(CH_2)_3$, Q = methylthio). Yield after dry column flash chromatography (adsorbent Silica gel 60 H, eluent a 1:1 mixture of benzene and chloroform) 118 mg (70%), mp 149–151° (cyclohexane/ethyl acetate). ir: ν C=O = 1668 cm^{-1} ; pmr: δ , ppm 2.21 (m, 2H, CH₂-6), 2.63 (s, 3H, SCH₃), 2.87 (t, 2H, CH₂-7), 3.16 (t, 2H, CH₂-5), 5.35 (s, 2H, PhCH₂), 7.25 (m, 3H, PhH-3',4',5'), 7.6 (m, 2H, PhH-2',6'); cmr: δ , ppm 14.0 (SCH₃), 21.3 (C-6), 28.2 (C-7), 30.1 (C-5), 46.5 (PhCH₂), 116.6 (C-7a), 127.9 (PhC-4'), 128.3 (PhC-2',6'), 129.2 (PhC-3',5'), 135.5 (PhC-1'), 148.0 (C-4a), 152.0 (C-9a), 157.8 (C-8), 163.9 (C-2).

Anal. Calcd. for C₁₆H₁₆N₄OS (MW 312.40): C, 61.52, H, 5.16, N, 17.93, S, 10.26. Found: C, 61.32, H, 5.34, N, 18.03, S, 10.09.

2-Methylthio-5,6,7,8,9,10,11,12,13,14-decahydrocyclo-dodeca[e]-1,2,4-triazolo[1,5-a]pyrimidin-15(16H)-one tetrabutylammonium salt (**14i**) and its Methylation to 16-Methyl-2-methylthio-5,6,7,8,9,10,11,12,13,14-decahydro-cyclo-dodeca[e]-1,2,4-triazolo[1,5-a]pyrimidin-15(16H)-one (**4i/1**).

Compound **14i** was prepared analogously to **14e** starting from 1.00 g (0.0031 mole) of 2-methylthio-5,6,7,8,9,10,11,12,13,14-decahydrocyclo-dodeca[e]-1,2,4-triazolo[1,5-a]pyrimidin-15(16H)-one **2i** ($R^1 + R^2 = -(CH_2)_{10}$, Q = methylthio) [5]. The oily **14i** was directly methylated analogously to **14e** to give an overall yield 62%, of **4i/1**, mp 100–102° (acetonitrile). ir: ν C=O = 1663 cm^{-1} ; pmr: δ , ppm 1.45 (m, 12H, CH₂-7,8,9,10,11,12), 1.73 (m, 2H, CH₂-13), 1.94 (m, 2H, CH₂-6), 2.57 (t, 2H, CH₂-14), 2.62 (s, 3H, SCH₃), 2.96 (t, 2H, CH₂-5), 3.64 (s, 3H, NCH₃); cmr: δ , ppm 13.9 (SCH₃), 22.0, 22.1, 24.2, 24.7, 24.9, 25.2, 25.5, 25.8, 25.9 (two signals) (C-5 - C-14), 29.8 (NCH₃), 116.0 (C-14a), 145.8 (C-4a), 150.2 (C-16a), 160.4 (C-15), 162.6 (C-2).

Anal. Calcd. for C₁₇H₂₆N₄OS (MW 334.49): C, 61.05, H, 7.84, N, 16.75, S, 9.59. Found: C, 61.14, H, 7.95, N, 16.65, S, 9.72.

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

To a solution of 0.115 g (0.005 mole) of sodium in 5 ml of absolute methanol 1.27 g (0.005 mole) of 5-chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazoline (**19**) [22] was added, and the mixture stirred at 20° for 90 minutes. The crystals that precipitated after addition of 10 ml water to the reaction mixture were filtered off and washed with water to yield 1.02 g (81%) of the title product, that decomposed after recrystallisation from 2-propanol at 106–109°; pmr: δ , ppm 1.85 (m, 4H, CH₂-7,8), 2.69 (s, 3H, SCH₃), 2.72 (t, 2H, CH₂-6), 2.94 (t, 2H, CH₂-9), 4.48 (s, 3H, OCH₃); cmr: δ , ppm 13.5 (SCH₃), 21.4 (C-7 and C-8), 21.7 (C-6), 32.8 (C-9), 60.9 (OCH₃), 106.8 (C-5a), 151.5 (C-5), 156.2 (C-10a), 165.7 (C-9a), 167.6 (C-2); uv (EtOH): λ_{max} [nm] ($\epsilon \cdot 10^{-3}$) 210 (28.0), 239 (33.6), 285 (9.0).

Anal. Calcd. for C₁₁H₁₄N₄OS (MW 250.32): C, 52.78, H, 5.64, N, 22.38, S, 12.81. Found: C, 52.92, H, 5.87, N, 22.17, S, 12.78.

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

To a mixture of 0.144 g (0.006 mole) of sodium hydride (240 mg of 60% suspension Fluka washed with petroleum ether) and 15 ml of absolute ether 0.65 g (0.006 mole) of freshly distilled benzylalcohol was added. The mixture was stirred at room temperature until the evolution of hydrogen ceased, at which time 1.27 g (0.005 mole) of 5-chloro-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazoline (**19**) [22] was added to the reaction mixture which was stirred at 20° for an additional 3 hours. The reaction mixture obtained was passed through a short silica gel column and the column washed with 4 x 30 ml of ether. The combined ether solutions were evaporated *in vacuo* to dryness, the residue triturated with a mixture of cyclohexane and diisopropyl ether and filtered to yield 0.98 g (60%) of the title product, mp 94–98° (dec); pmr (hexadeuteriobenzene): δ , ppm 1.21 (m, 2H, CH₂-7), 1.27 (m, 2H, CH₂-8), 2.18 (t, 2H, CH₂-6), 2.53 (s, 3H, SCH₃), 2.63 (t, 2H, CH₂-9), 5.50 (s, 2H, OCH₂), 7.05 (m, 2H, PhH-2',6'), 7.20 (m, 3H, PhH-3',4',5'); pmr (deuteriochloroform): δ , ppm 1.80 (m, 4H, CH₂-7,8), 2.60 (t, 2H, CH₂-6), 2.74 (s, 3H, SCH₃), 2.92 (t, 2H, CH₂-9), 5.88 (s, 2H, OCH₂), 7.35 (m, 5H, PhH); cmr (deuteriochloroform): δ , ppm 13.8 (SCH₃), 21.6 (C-7), 21.9 (C-6 and C-8), 33.0 (C-9), 74.9 (OCH₂), 108.1 (C-5a), 128.46 and 128.50 (PhC-2',6' and 3',5'), 128.9 (PhC-4'), 134.8 (PhC-1'), 150.4qi (C-5), 156.1s (C-10a), 165.6m (C-9a), 167.6q (C-2); uv (EtOH): λ_{max} [nm] ($\epsilon \cdot 10^{-3}$) 210 (24.4), 241 (30.2), 300 (8.6).

Anal. Calcd. for C₁₇H₁₈N₄OS (MW 326.42): C, 62.55, H, 5.56, N, 17.16, S, 9.82. Found: C, 62.82, H, 5.67, N, 16.98, S, 10.02.

2-Methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazolin-5(10H)-one Tetrabutylphosphonium Salt (**18**).

This compound was prepared analogously to the tetrabutylammonium salt **13f** ($R^1 + R^2 = -(CH_2)_4$, Q = methylthio) using 3.40 g (0.01 mole) of tetrabutylphosphonium bromide instead of tetrabutylammonium bromide. Yield: 93%, mp 110–114° (ethyl acetate). pmr: δ , ppm 0.92 (t, 12H, 4 x CH₃), 1.45 (m, 16H, 8 x CH₂), 1.75 (m, 4H, CH₂-7,8), 2.25 (m, 8H, 4 x PCH₂), 2.62 (m, 7H, SCH₃ + CH₂-6,9); cmr: δ , ppm 13.0 [s, 4 x CH₃, ⁴J(C,P) $\approx$ 0 Hz], 13.6 (SCH₃), 18.2 [d, PCH₂, ¹J(C,P) = 47.4 Hz], 22.6 (C-7), 22.8 (C-8), 23.0 (C-6), 23.2 [d, PCH₂CH₂, ²J(C,P) = 4.4 Hz], 23.5 [d, PCH₂CH₂CH₂, ³J(C,P) = 15.4 Hz], 32.6 (C-9), 103.4 (C-5a), 157.4 (C-10a), 157.8 (C-9a), 158.3 (C-5), 161.6 (C-2).

10-Methyl-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazolin-5(10H)-one (**3f/1**).

The alkylation was provided analogously to the alkylation of the corresponding derivative **13f** in acetonitrile using the tetrabutylphosphonium salt **18** and methyl iodide as the alkylation agent. Yield: 65%, mp 258–260° (see also Table V). The product is identical with **3f/1** ($R^1 + R^2 = -(CH_2)_4$, Q = methylthio, R = methyl) obtained from the corresponding tetrabutylammonium salt **13f** ($R^1 + R^2 = -(CH_2)_4$, Q = methylthio).

2-Methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazolin-5(10H)-thione (**20**).

To a suspension of 10.7 g (0.024 mole) of phosphorus pentasulfide in 40 ml of bis(2-methoxyethyl)ether (diglyme) 4.73 g (0.020 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-b]quinazolin-5(10H)-one (**1f**, $R^1 + R^2 = -(CH_2)_4$, Q = methylthio) [4] was added followed by 8.07 g (0.096 mole) of

sodium hydrogen carbonate in little portions allowing the carbon dioxide evolved to leave the mixture. The suspension was heated with stirring at 110° for 40 hours. After cooling 150 ml of water was added to the reaction mixture by dropping it through a dropping funnel (the hydrogen sulphide liberated was trapped in 10% sodium hydroxide solution). The crystals separated were filtered off and washed thoroughly with water and acetonitrile to yield after recrystallisation from dimethylformamide 2.70 g (53%) of pure 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-thione (**20**), mp 277-283° (dec). MS (EI): M^+ = 252; pmr (DMSO- d_6): δ , ppm 1.72 (m, 4H, CH₂-7,8), 2.58 (s, 3H, SCH₃), 2.65 (m, 4H, CH₂-6,9); cmr (DMSO- d_6): δ , ppm 13.5 (SCH₃), 22.1 (C-7), 22.7 (C-8), 27.5 (C-6), 30.9 (C-9), 118.7 (C-5a), 151.3 and 151.5 (C-9a and C-10a), 163.6 (C-2), 171.8 (C-5); uv (EtOH): $\lambda_{\max}$ [nm]($\epsilon \cdot 10^{-3}$) 254 (21.0), 294 (6.0), 336 (23.2).

Anal. Calcd. for C₁₀H₁₂N₄S₂ (MW 252.30): C, 47.60, H, 4.79, N, 22.21, S, 25.41. Found: C, 47.56, H, 4.88, N, 22.20, S, 25.32.

2-Methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-thione Tetrabutylammonium Salt (**21**).

To a solution of 3.74 g (0.011 mole) of tetrabutylammonium hydrogen sulphate in 10 ml of water a pre-cooled solution of 0.88 g (0.022 mole) of sodium hydroxide in 8 ml of water was added and the solution obtained cooled to 5°. After that 2.52 g (0.01 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-thione (**20**) and 10 ml of chloroform was added and the resulting yellow suspension was intensively stirred until the thione dissolved (about 5 minutes). The phases were separated, the aqueous layer was washed with 10 ml of chloroform, the combined chloroform layers with 5 ml of water and dried over sodium sulphate. After evaporating the solvent *in vacuo* the residue was dissolved in 10 ml of ethyl acetate and left to stand overnight. The crystals that precipitated were filtered off and washed with cold ethyl acetate to yield 4.48 g (90%) of the product, mp 106-109°. pmr: δ , ppm 0.91 (t, 12H, 4 x CH₃), 1.29 (m, 8H, 4 x CH₂CH₂), 1.51 (m, 8H, NCH₂CH₂), 1.8 (m, 4H, CH₂-7,8), 2.65 (s, 3H, SCH₃), 2.74 (m, 2H, CH₂-6), 2.86 (m, 2H, CH₂-9), 3.14 (m, 8H, 4 x NCH₂); cmr: δ , ppm 13.6 (4x CH₃), 14.1 (SCH₃), 19.6 (CH₃CH₂), 23.0 (C-7), 23.5 (C-8), 23.9 (4x NCH₂CH₂), 28.3 (C-6), 33.5 (C-9), 58.7 (4 x NCH₂), 119.7 (C-5a), 154.2 and 156.6 (C-9a and C-10a), 163.7 (C-2), 167.8 (C-5).

Anal. Calcd. for C₂₆H₄₇N₅S₂ (MW 493.83): C, 63.24, H, 9.59, N, 14.18, S, 12.99. Found: C, 63.42, H, 9.66, N, 14.04, S, 13.09.

2,5-Bis(methylthio)-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**22/1**).

To a solution of 493 mg (0.001 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5-(10*H*)-thione tetrabutylammonium salt (**21**) in 1.2 ml of acetonitrile 170 mg (0.0012 mole) of methyl iodide was added and the solution stirred at room temperature for 5 minutes. The mixture was evaporated to dryness, the residue was dry column flash chromatographed on a Silica gel 60 H layer (eluent benzene-chloroform 1:1) to yield a crystalline product that was triturated with ether and filtered off. By this method 229 mg (86%) of pale yellow 2,5-bis(methylthio)-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**22/1**) was obtained, mp 118-120°; ms (EI): M^+ = 266; pmr: δ , ppm 1.9 (m, 4H, CH₂-7,8), 2.71 (s, 3H, 2-SCH₃), 2.85 (s, 3H, 5-SCH₃), 2.87 (m, 2H, CH₂-6), 2.95 (m, 2H, CH₂-9); cmr: δ ,

ppm 13.8 (2-SCH₃), 16.0 (5-SCH₃), 21.9 (C-7), 22.2 (C-8), 26.1 (C-6), 33.4 (C-9), 120.5 (C-5a), 143.1 (C-5), 154.2 (C-10a), 162.7 (C-9a), 167.4 (C-2).

Anal. Calcd. for C₁₁H₁₄N₄S₂ (MW 266.39): C, 49.60, H, 5.30, N, 21.03, S, 24.07. Found: C, 49.65, H, 5.46, N, 21.07, S, 23.96.

5-Benzylthio-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**22/6**).

To a solution of 493 mg (0.001 mole) of 2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazolin-5(10*H*)-thione tetrabutylammonium salt (**21**) in 1.2 ml of acetonitrile 152 mg (0.0012 mole) of benzyl chloride was added and the solution stirred at room temperature for 1 hour. The mixture was evaporated to dryness, the residue was dry column flash chromatographed on a Silica gel 60 H layer (eluent benzene-chloroform 1:1) to yield a crystalline product that was triturated with diisopropyl ether and filtered off. By this method 294 mg (86%) of pale yellow 5-benzylthio-2-methylthio-6,7,8,9-tetrahydro-1,2,4-triazolo[5,1-*b*]quinazoline (**22/6**) was obtained, mp 98-99.5°; pmr: δ , ppm 1.75 (m, 4H, CH₂-7,8), 2.67 (m, 2H, CH₂-6), 2.76 (s, 3H, SCH₃), 2.92 (m, 2H, CH₂-9), 4.64 (s, 2H, SCH₂), 7.05 (m, 2H, PhH-2',6'), 7.20 (m, 3H, PhH-3',4',5'); cmr: δ , ppm 14.0 (SCH₃), 21.8 (C-7), 22.2 (C-8), 26.4 (C-6), 33.5 (C-9), 36.8 (SCH₂), 122.5 (C-5a), 127.6 (PhC-4'), 128.6 and 128.8 (PhC-2' and PhC-3'), 136.5 (PhC-1'), 141.2 (C-5), 154.3 (C-10a), 163.1 (C-9a) 167.8 (C-2).

Anal. Calcd. for C₁₇H₁₈N₄S₂ (MW 342.49): C, 59.62, H, 5.30, N, 16.36, S, 18.72. Found: C, 59.66, H, 5.42, N, 16.29, S, 18.70.

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