On Triazoles XLIII [1]. Synthesis of 1,2,4-Triazolyl Isoquinolinium Zwitter Ions

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Type **8** isoquinolinium zwitter ions were synthesised by the reaction of type **1** diketones or type **2** pyrylium salts with different 5-amino-3-Q-1*H*-1,2,4-triazoles. Spectroscopic and X-ray diffraction evidence was given for the zwitter ion structure of the products obtained. The position of the negative charge on the 1,2,4-tiazolium ring was proved by comparison of the cmr and uv spectra of the products obtained with the three possible *N*-benzyl derivatives **14-16** prepared for this purpose.

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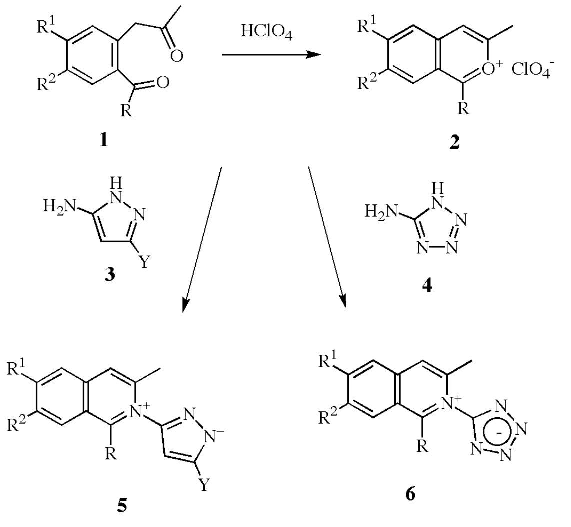
Recently, we have reported on the synthesis of pyrazolyl (**5**) and tetrazolyl (**6**) isoquinolinium zwitter ions by the reaction of the **1** type *ortho*-acylphenylacetones or the **2** type pyrylium salts formed from **1** with perchloric acid and different 3-amino-pyrazoles (**3**) and 5-amino-tetrazoles (**4**), respectively [2] (Scheme 1).

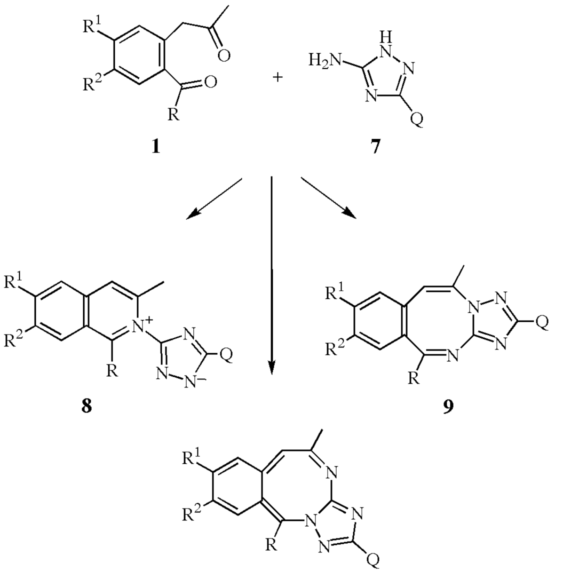
Scheme 1



In an effort to synthesise the corresponding 5'-Q-1,2,4-triazol-3'-yl-isoquinolinium salts (**8**), the above reaction was repeated with different 5-amino-3-Q-1*H*-1,2,4-triazoles (**7**) (Scheme 2, Table 1). In all reactions of **1** (or **2**) and **7** a single product was obtained. However, in the above reactions **9** and **10** type triazolo-benzodiazocines could also be formed hence, their formation had to be excluded.

For this purpose the product formed in the reaction of the simplest 5-amino-1*H*-1,2,4-triazole (amitrole, **7/4**, Q = H) and the 1-(4-chlorophenyl)-6,7-dimethoxy-3-methylpyrylium perchlorate (**2**, R = 4-chlorophenyl, R^1 = R^2 = methoxy), namely derivative **8/4** (R = 4-chlorophenyl, R^1 = R^2 = methoxy, Q = H) was chosen (Scheme 3). Its pmr and NOEDIF spectra (Scheme 3) helped to exclude structure **10/4** but on the basis of those experiments both structures **8/4** and **9/4** are possible. Even using both the cmr and proton carbon correlated spectra (Scheme 4) it is impossible to choose between structures **8/4** and **9/4**.

Scheme 2



To solve this structural problem unequivocally X-ray diffraction analysis was performed on **8/46** [R = 4-chlorophenyl, R^1 = R^2 = methoxy, Q = 4-(2-hydroxyethyl)piperazin-1-yl] monohydrate (Scheme 5) that formed suitable crystals [3]. It can be seen from its picture that the 1-(4-chlorophenyl) and 2-(1,2,4-triazolium-3'-yl) rings are nearly perpendicular to the plane of the isoquinolinium ring. The delocalisation of the loan electron pair through the 1,2,4-triazole moiety is rather small as seen from the different CN bond lengths of the triazole ring. The most basic nitrogen atom of the triazole ring at position 1 is connected by an H-bond to the hydrogen atom of water in the crystal. The unsymmetrical delocalisation of the loan electron pair in the 5-membered 1,2,4-triazolium heteroring is analogous to that observed previously [2] in the pyrazolium-3-yl series.

After recognition of the localisation of the negative charge on the 1,2,4-triazole ring in crystalline form the question arose whether it is also localised in solutions.

In our previous work [4-6] we succeeded in proving the tautomeric structures of 5-amino-3-Q-1*H*-1,2,4-triazoles (**7**) by comparison of their cmr and uv spectra with different

Table I

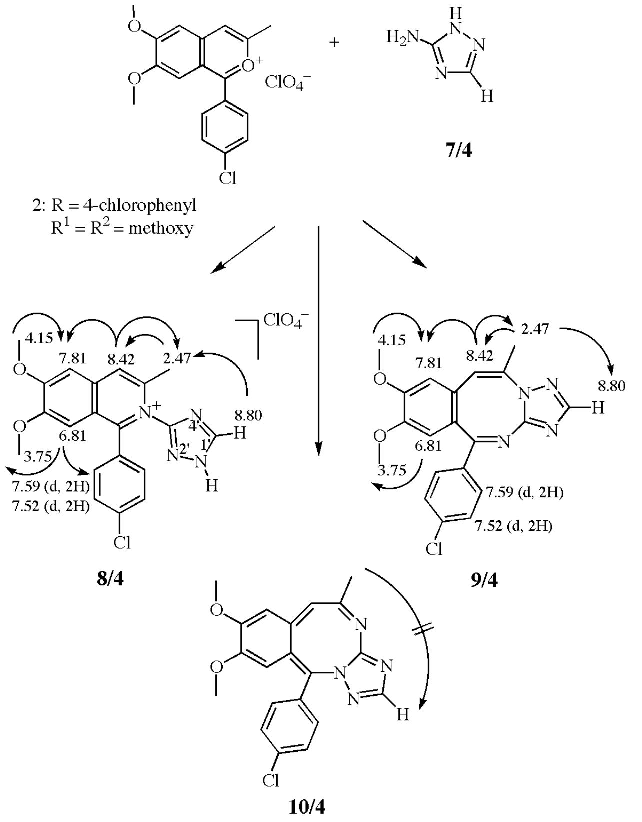
Synthetical and Analytical Data of the Triazole-3-yl-isoquinolinium Zwitter Ions **8**

Compound	R	R^1	R^2	Q	Yield % Method	Mp (°C) (cryst. from)	Molecular formula (MW)	Analysis % Calcd./Found					
								C	H	N	Cl	F	S
8/1	Methyl	Methoxy	Methoxy	Hydrogen	54	269-272	$C_{15}H_{16}N_4O_2$	63.37	5.67	19.71			
					D	(acetone)	(284.32)	63.22	5.54	19.88			
8/2	4-Fluoro-	Methoxy	Methoxy	Hydrogen	66	199-201	$C_{20}H_{17}FN_4O_2$	65.93	4.70	15.38		5.21	
	phenyl				B	(EtOAc)	(364.38)	65.72	4.93	15.51		4.99	
8/3	2-Chloro-	Methoxy	Methoxy	Hydrogen	74	147-150	$C_{20}H_{17}ClN_4O_2$	60.23	4.80	14.05	8.89		
	phenyl				A	(CH_3CN)	•H_2O	60.11	4.89	14.21	9.02		
							(398.85)						
8/4	4-Chloro-	Methoxy	Methoxy	Hydrogen	74	285-288	$C_{20}H_{17}ClN_4O_2$	49.91	3.77	11.64	14.73		
	phenyl				D	(2-PrOH)	•$HClO_4$	49.78	3.58	11.41	14.96		
							(481.30)						
8/5	Methyl	Methoxy	Methoxy	Methylthio	57	178-183	$C_{16}H_{18}N_4O_2S$	52.44	6.05	15.29			8.75
					D	(DMF/	•2 H_2O	52.32	6.28	15.11			8.93
						CH_3CN)	(330.41)						
8/6	4-Methyl-	Methoxy	Methoxy	Methylthio	81	216-219	$C_{22}H_{22}N_4O_2S$	65.00	5.46	13.78			7.89
	phenyl				B	(CH_3CN)	(406.51)	64.89	5.22	13.89			7.75
8/7	4-Fluoro-	Methoxy	Methoxy	Methylthio	58	184-187	$C_{21}H_{19}FN_4O_2S$	61.45	4.67	13.65		4.63	7.81
	phenyl				C	(2-PrOH)	(410.47)	61.37	4.73	13.50		4.81	7.63
8/8	2-Chloro-	Methoxy	Methoxy	Methylthio	69	181-183	$C_{21}H_{19}ClN_4O_2S$	56.69	4.76	12.59	7.97		7.21
	phenyl				A	(CH_3CN)	•H_2O	56.58	4.66	12.36	7.85		7.03
							(444.94)						
8/9	3-Chloro-	Methoxy	Methoxy	Methylthio	76	177-180	$C_{21}H_{19}ClN_4O_2S$	56.69	4.76	12.59	7.97		7.21
	phenyl				D	(EtOH)	•H_2O	56.55	4.94	12.68	8.06		7.40
							(444.94)						
8/10	3-Chloro-	Methylenedioxy		Methylthio	68	298-300	$C_{20}H_{15}ClN_4O_2S$	56.01	4.00	13.06	8.27		7.48
	phenyl				A	(CH_3CN/	•H_2O	56.19	4.21	13.19	8.05		7.60
						Et_2O)	(428.90)						
8/11	4-Chloro-	Methoxy	Methoxy	Methylthio	73	159-162	$C_{21}H_{19}ClN_4O_2S$	59.08	4.49	13.12	8.30		7.51
	phenyl				D	(EtOH)	(426.93)	58.88	4.31	12.89	8.42		7.39
8/12	Methyl	Methoxy	Methoxy	Ethylthio	47	126-129	$C_{17}H_{20}N_4O_2S$	56.34	6.12	15.46			8.85
					D	(CH_3CN)	•H_2O	56.27	6.00	15.61			8.68
							(362.45)						
8/13	4-Fluoro-	Methoxy	Methoxy	Ethylthio	62	171-174	$C_{22}H_{21}FN_4O_2S$	62.25	4.99	13.20		4.48	7.55
	phenyl				C	(CH_3CN)	(424.50)	62.13	5.13	13.07		4.27	7.67
8/14	2-Chloro-	Methoxy	Methoxy	Ethylthio	67	179-181	$C_{22}H_{21}ClN_4O_2S$	59.93	4.80	12.71	8.04		7.27
	phenyl				B	(CH_3CN/	(440.96)	59.79	4.91	12.54	7.90		7.00
						EtOAc)							
8/15	3-Chloro-	Methoxy	Methoxy	Ethylthio	48	143-145	$C_{22}H_{21}ClN_4O_2S$	59.93	4.80	12.71	8.04		7.27
	phenyl				D	(EtOAc)	(440.96)	59.74	4.89	12.58	8.26		7.42
8/16	4-Chloro-	Methoxy	Methoxy	Ethylthio	70	162-165	$C_{22}H_{21}ClN_4O_2S$	59.93	4.80	12.71	8.04		7.27
	phenyl				D	(EtOAc)	(440.96)	59.81	4.91	12.65	8.24		7.03
8/17	4-Methoxy-	Methoxy	Methoxy	1-Hexylthio	52	174-177	$C_{27}H_{32}N_4O_3S$	65.83	6.55	11.37			6.51
	phenyl				B	(CH_3CN)	(492.65)	65.65	6.43	11.18			6.73
8/18	4-Nitro-	Methoxy	Methoxy	1-Hexylthio	58	143-146	$C_{26}H_{29}N_5O_4S$	61.52	5.76	13.80			6.32
	phenyl				B	(2-PrOH)	(507.62)	61.24	5.88	13.56			6.19
8/19	Methyl	Methoxy	Methoxy	2-Propylthio	41	142-145	$C_{18}H_{22}N_4O_2S$	57.43	6.43	14.88			8.52
					D	(CH_3CN)	•H_2O	57.29	6.26	14.99			8.30
							(376.48)						
8/20	4-Fluoro-	Methoxy	Methoxy	2-Propylthio	61	208-210	$C_{23}H_{23}FN_4O_2S$	63.00	5.29	12.78		4.33	7.31
	phenyl				C	(Dioxane)	(438.53)	63.22	5.40	12.64		4.23	7.53
8/21	2-Chloro-	Methoxy	Methoxy	2-Propylthio	76	153-156	$C_{23}H_{23}ClN_4O_2S$	60.72	5.10	12.31	7.79		7.05
	phenyl				A	(CH_3CN)	(454.98)	60.81	5.21	12.19	7.68		6.96
8/22	3-Chloro-	Methoxy	Methoxy	2-Propylthio	47	138-141	$C_{23}H_{23}ClN_4O_2S$	58.41	5.33	11.85	7.50		6.78
	phenyl				D	(EtOAc)	•H_2O	58.63	5.45	11.97	7.66		6.51
							(473.00)						
8/23	4-Chloro-	Methoxy	Methoxy	2-Propylthio	66	187-190	$C_{23}H_{23}ClN_4O_2S$	60.72	5.10	12.31	7.79		7.05
	phenyl				D	(EtOAc)	(454.98)	60.54	5.29	12.48	7.71		7.14
8/24	2-Chloro-	Methoxy	Methoxy	Dimethyl-	59	188-190	$C_{22}H_{22}ClN_5O_2$	62.34	5.23	16.52	8.36		
	phenyl			amino	A	(2-PrOH/	(423.91)	62.52	5.43	16.68	8.14		
						EtOAc)							

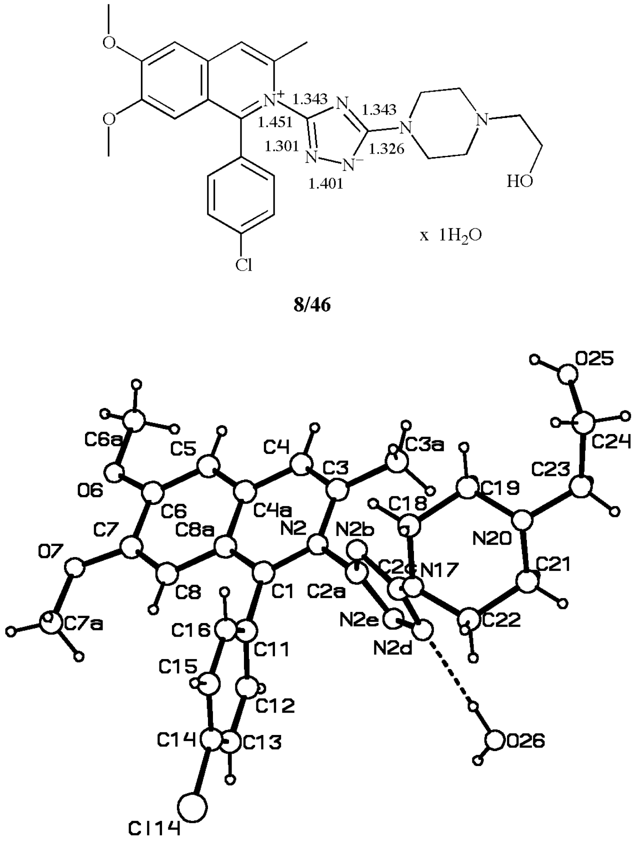
Table I (cintinued)

Compound	R	R^1	R^2	Q	Yield % Method	Mp (°C) (cryst. from)	Molecular formula (MW)	Analysis % Calcd./Found					
								C	H	N	Cl	F	S
8/25	4-Fluorophenyl	Methoxy	Methoxy	Diethylamino	61 C	152-154 (CH_3CN)	$C_{24}H_{26}FN_5O_2$ •H_2O (453.52)	63.56 63.42	6.22 6.12	15.44 15.59		4.19 4.00	
8/26	2-Chlorophenyl	Methoxy	Methoxy	Diethylamino	55 A	163-166 (CH_3CN/ EtOAc)	$C_{24}H_{26}ClN_5O_2$ •H_2O (469.98)	61.34 61.21	6.01 5.89	14.90 14.76	7.54 7.66		
8/27	4-Methoxyphenyl	Methoxy	Methoxy	Diethylamino	76 B	149-151 (CH_3CN)	$C_{25}H_{29}N_5O_3$ •H_2O (465.56)	64.50 64.58	6.71 6.50	15.04 15.10			
8/28	3,4-Dimethoxyphenyl	Methoxy	Methoxy	Diethylamino	63 C	155-158 (CH_3CN)	$C_{26}H_{31}N_5O_4$ •H_2O (495.58)	63.01 62.89	6.71 6.59	14.13 14.27			
8/29	2-Chlorophenyl	Methoxy	Methoxy	Diallylamino	80 B	112-115 (EtOAc)	$C_{26}H_{26}ClN_5O_2$ •H_2O (494.00)	63.22 63.14	5.71 5.83	14.18 14.04	7.18 7.30		
8/30	4-Chlorophenyl	Methoxy	Methoxy	Diallylamino	80 B	119-122 (EtOAc)	$C_{26}H_{26}ClN_5O_2$ •H_2O (494.00)	63.22 63.09	5.71 5.60	14.18 14.37	7.18 7.00		
8/31	4-Fluorophenyl	Methoxy	Methoxy	Phenylamino	58 C	213-215 (DMF)	$C_{26}H_{22}FN_5O_2$ (455.50)	68.56 68.64	4.87 4.75	15.38 15.52		4.17 4.06	
8/32	2-Chlorophenyl	Methoxy	Methoxy	Cyclohexylamino	63 B	183-186 (EtOAc)	$C_{26}H_{28}ClN_5O_2$ •HCl (514.46)	60.70 60.58	5.68 5.61	13.61 13.85	13.78 13.91		
8/33	4-Chlorophenyl	Methoxy	Methoxy	Phenylamino	61 B	212-215 (CH_3CN)	$C_{26}H_{22}ClN_5O_2$ •H_2O (489.97)	63.74 63.61	4.94 4.78	14.29 14.42	7.24 7.30		
8/34	4-Nitrophenyl	Methoxy	Methoxy	Phenylamino	80 B	215-218 (DMF)	$C_{26}H_{22}N_6O_4$ •H_2O (500.52)	62.39 62.25	4.83 4.72	16.79 16.84			
8/35	4-Methoxyphenyl	Methoxy	Methoxy	Phenylamino	55 C	186-188 (CH_3CN)	$C_{27}H_{25}N_5O_3$ (467.53)	69.36 69.20	5.39 5.50	14.98 14.84			
8/36	3,4-Dimethoxyphenyl	Methoxy	Methoxy	Phenylamino	59 C	221-223 (EtOH)	$C_{28}H_{27}N_5O_4$ (497.56)	67.59 67.47	5.47 5.54	14.08 14.21			
8/37	4-Fluorophenyl	Methoxy	Methoxy	Benzylamino	60 C	166-169 (CH_3CN)	$C_{27}H_{24}FN_5O_2$ •H_2O (487.54)	66.52 66.59	5.38 5.29	14.36 14.50		3.90 3.99	
8/38	2-Chlorophenyl	Methoxy	Methoxy	Benzylamino	62 A	161-164 (EtOH)	$C_{27}H_{24}ClN_5O_2$ •HCl (522.44)	62.07 61.90	4.82 4.77	13.41 13.54	13.57 13.43		
8/39	3,4-Dimethoxyphenyl	Methoxy	Methoxy	Benzylamino	61 C	151-154 (CH_3CN)	$C_{29}H_{29}N_5O_4$ (511.59)	68.09 67.89	5.71 5.60	13.69 13.85			
8/40	2-Chlorophenyl	Methoxy	Methoxy	Piperidin-1-yl	70 B	143-146 (CH_3CN)	$C_{25}H_{26}ClN_5O_2$ •H_2O (481.99)	62.30 62.22	5.86 5.96	14.53 14.67	7.36 7.14		
8/41	3-Chlorophenyl	Methoxy	Methoxy	Piperidin-1-yl	48 B	139-141 (CH_3CN)	$C_{25}H_{26}ClN_5O_2$ •H_2O (481.99)	62.30 62.17	5.86 5.73	14.53 14.40	7.36 7.51		
8/42	3-Chlorophenyl	Methoxy	Methoxy	Morpholin-4-yl	74 A	145-148 (CH_3CN)	$C_{24}H_{24}ClN_5O_3$ •H_2O (483.96)	59.56 59.66	5.42 5.34	14.47 14.40	7.33 7.41		
8/43	3,4-Dichlorophenyl	Methoxy	Methoxy	Morpholin-4-yl	59 C	224-226 (Dioxane)	$C_{24}H_{23}Cl_2N_5O_3$ •HCl (536.85)	53.70 53.61	4.51 4.40	13.05 13.22	19.81 19.92		
8/44	2-Chlorophenyl	Methoxy	Methoxy	4-Methylpiperazin-1-yl	58 B	175-178 (CH_3CN/ EtOAc)	$C_{25}H_{27}ClN_6O_2$ •H_2O (497.00)	60.42 60.30	5.88 6.00	16.91 17.06	7.13 7.21		
8/45	2-Chlorophenyl	Methoxy	Methoxy	4-(2-Hydroxyethyl)piperazine-1-yl	57 C	189-192 (EtOAc)	$C_{26}H_{29}ClN_6O_3$ •H_2O (527.03)	59.25 59.12	5.93 5.78	15.95 15.89	6.73 6.92		
8/46	4-Chlorophenyl	Methoxy	Methoxy	4-(2-Hydroxyethyl)piperazine-1-yl	67 C	168-170 (CH_3CN/ EtOAc)	$C_{26}H_{29}ClN_6O_3$ •2H_2O (545.04)	57.30 57.17	6.10 6.32	15.42 15.30	6.50 6.61		

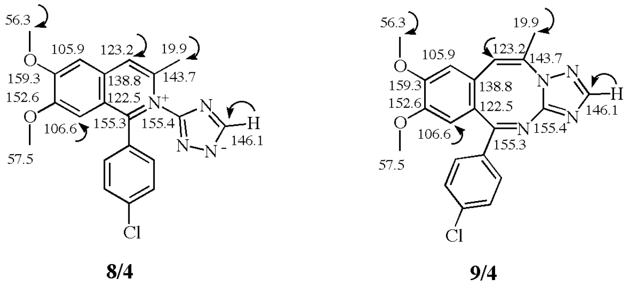
Scheme 3



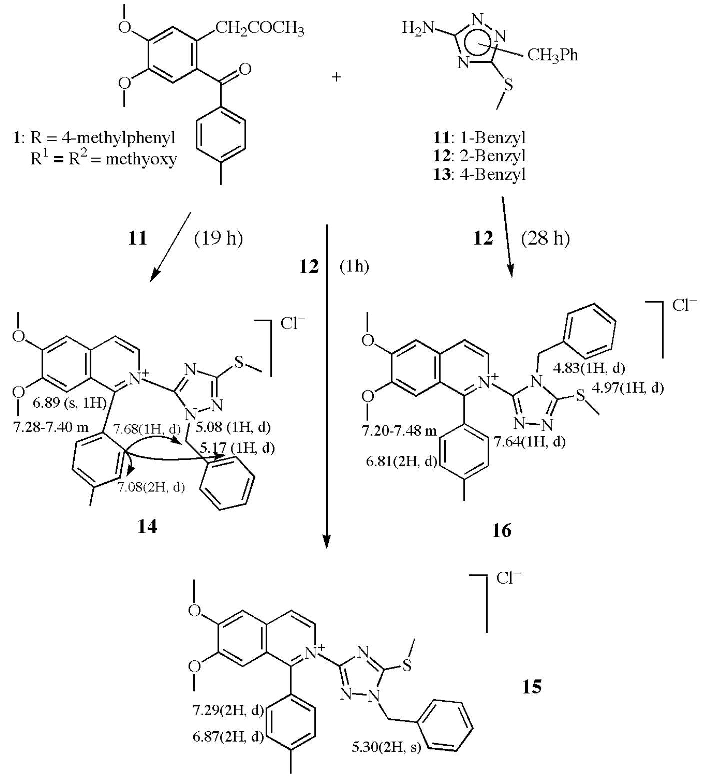
Scheme 5



Scheme 4



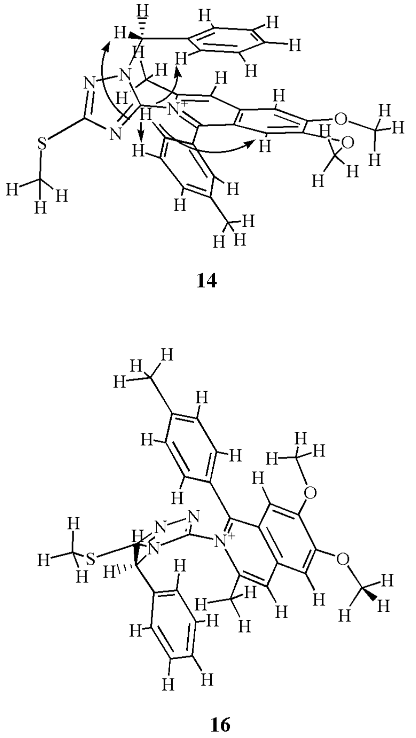
Scheme 6



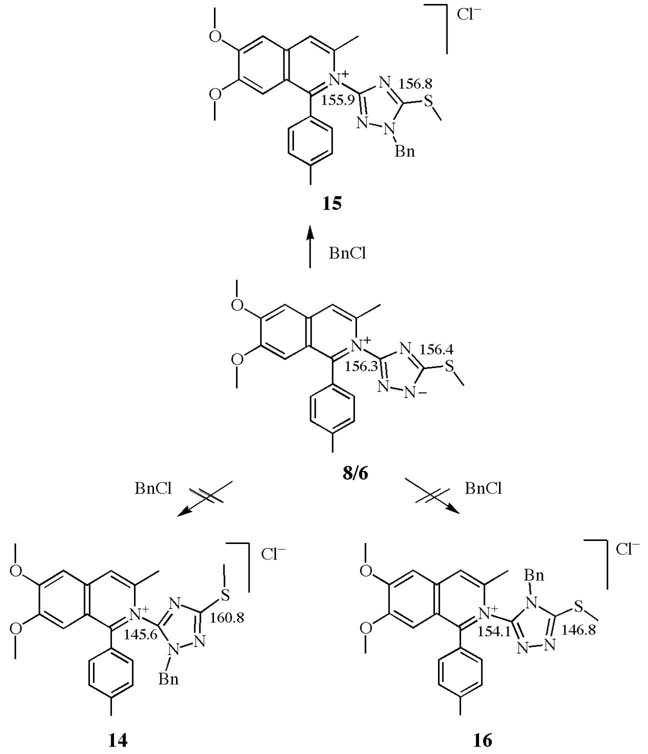
N-alkylated isomers. However, the rules elaborated for simple 5-amino-3-Q-1*H*-1,2,4-triazoles **7** could not be used directly in the case of derivatives **8** because their zwitter ion character strongly influences their cmr and uv spectra.

To overcome this problem the isomeric *N*-benzylated (1,2,4-triazol-3'-yl)isoquinolinium salts **14**, **15** and **16** were synthesised by the reaction of 1-[4,5-dimethoxy-2-(4-methylbenzoyl)]phenyl-acetone [**1**, R = (4-methylphenyl), R^1 = R^2 = methoxy] with the isomeric 5'-amino-*N*-benzyl-3'-methylthio-1,2,4-triazoles **11**, **12** and **13**, respectively (Scheme 6). Interestingly, while the reaction of **1** with **12** proceeded smoothly, the analogous reactions of **1** with **11** and **13** respectively required long reaction times, probably due to steric hindrance.

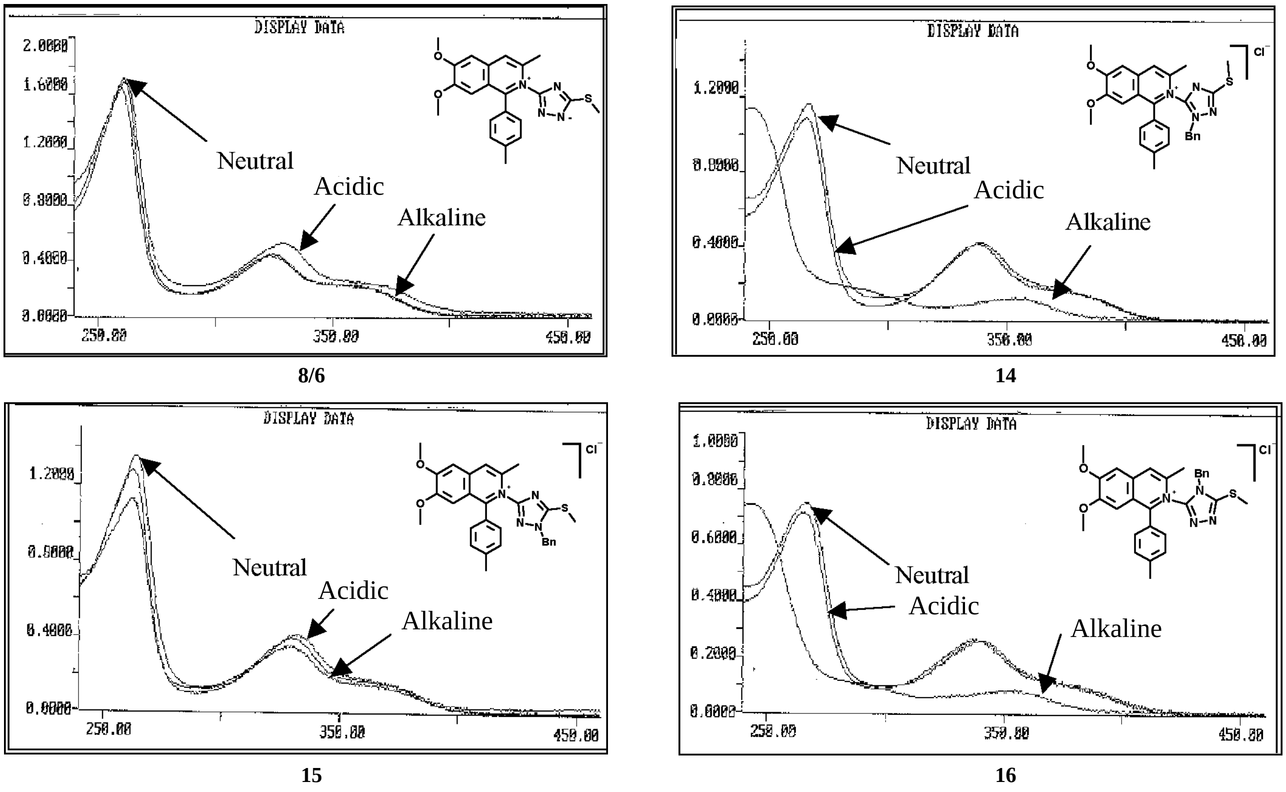
Scheme 7



Scheme 8



Scheme 9



8/6 **14**

15 **16**

Figuree 1. Uv spectra of derivatives **8/6**, **14**, **15** and **16** taken in ethanol, in a 9:1 mixture of 0.1 M hydrochloric acid and ethanol, and a 9:1 mixtue of 0.1 M sodium hydroxide and ethanol.

Table II
^{1}H NMR and ^{13}C NMR spectral data of derivatives **8**

Compound	H-4	H-5	H-8	R	Q	other	C-1	C-3	C-4	C-5 C-6	C-7 C-8	C-3' C-5'	R	Q	other
8/1	8.15 s [2]	7.71 s	7.63 s	2.81 s	9.14 (s, 1H)	2.35 s 4.06 s 4.11 s	157.2 [2]	142.6	121.5	105.8 158.7	152.3 106.5	155.5 147.0	18.1		19.6 56.7 57.1 121.5 137.0
8/2	7.73 s [2]	7.65 s	6.83 s	7.23 (dd, 2H, J = 8.9, 8.9 Hz) 7.49 (dd, 2H, J = 8.9, 5.1 Hz)	8.29 (s, 1H)	2.46 s 3.77 s 4.15 s	155.0 [2]	144.5	122.3	105.3 157.9	152.0 106.2	155.6 150.9	115.3 (q, J = 22.4 Hz) 126.7 (q, J = 3.8 Hz) 133.0 (q, J = 9.1 Hz) 162.8 (q, J = 248 Hz)		19.7 55.7 56.8 122.2 137.6
8/3	7.70 s [2]	7.62 s	6.63 s	7.28-7.47 (m, 4H)	8.21 (s, 1H)	2.53 s 3.76 s 4.16 s	152.7 [2]	144.8	122.3	104.9 158.0	152.4 105.1	154.2 151.0	125.8, 128.6 129.0, 131.2 131.3, 132.7		19.4 55.6 56.5 122.0 137.2
8/4	8.42 s [2]	7.81 s	6.81 s	7.52 (d, 2H, J = 8.4 Hz) 7.59 (d, 2H, J = 8.4 Hz)	8.80 (s, 1H)	2.47 s 3.75 s 4.15 s	155.3 [2]	143.7	123.2	105.9 159.3	152.6 106.6	155.4 146.1	128.4, 128.7 132.2, 136.0		19.9 56.3 57.5 122.5 138.8
8/5	7.98 s [2]	7.59 s	7.54 s	2.71 (s, 3H)	2.31 (s, 3H)	2.50 s 4.01 s 4.06 s	157.0 [2]	143.2	121.1	105.3 157.5	151.7 106.0	155.4 156.3	17.6	14.7	19.4 56.2 56.5 120.5 135.7
8/6	8.26 s [2]	7.72 s	6.83 s	2.35 (s, 3H) 7.24 (d, 2H, J = 7.9 Hz) 7.33 (d, 2H, J = 7.9 Hz)	2.30 (s, 3H)	2.40 s 3.69 s 4.11 s	155.3 [2]	144.4	122.2	105.6 158.0	152.0 106.9	156.3 156.4	127.5, 128.5 130.3, 139.8	15.4	19.9 21.2 55.9 57.1 122.2 137.5
8/7	8.26 s [2]	7.68 s	6.79 s	7.21 (dd, 2H, J = 8.8, 8.9 Hz) 7.46 (dd, 2H, J = 8.8, 5.2 Hz)	2.35 (s, 3H)	2.50 s 3.75 s 4.13 s	155.0 [2]	144.4	122.4	105.3 158.1	152.1 106.2	154.9 157.0	115.0 (q, J = 23.4 Hz) 126.3 (q, J = 4.0 Hz) 132.4 (q, J = 8.9 Hz) 162.8 (q, J = 250.0 Hz)	15.5	19.9 55.8 56.9 122.2 137.7
8/8	8.37 s [2]	7.77 s	6.54 s	7.38-7.60 (m, 4H)	2.28 (s, 3H)	2.47 s 3.68 s 4.12 s									
	8.01 s [1]	7.41 s	6.63 s	7.25-7.46 (m, 4H)	2.45 (s, 3H)	2.61 s 3.79 s 4.16 s	153.5 [1]	145.6	122.4	104.7 158.3	152.6 105.4	154.8 158.6	126.3, 129.0 129.1, 131.5 131.6, 133.3	15.7	20.3 56.1 57.1 122.4 137.5
8/9	8.38 s [2]	7.69 s	6.77 s	7.37-7.51 (m, 4 H)	2.37 (s, 3H)	2.51 s 3.76 s 4.13 s	154.8 [2]	144.5	122.6	105.4 158.2	152.3 106.0	154.0 157.2	128.5, 129.4 129.8, 130.2 131.8, 132.9	15.7	19.9 56.0 57.0 122.1 137.9
8/10	8.32 s [2]	7.71 s	6.80 s	7.30-7.58 (m, 4H)	2.30 (s, 3H)	2.42 s 6.41 (s, 2H)	154.6 [2]	145.0	123.6	104.4 158.1	151.4 102.8	155.0 156.7	129.1, 129.8 130.2, 130.3 132.3, 132.6	15.5	19.7 103.9 124.0 140.1
	7.85 s [1]	7.28 s	6.90 s	7.32-7.43 (m, 4H)	2.48 (s, 3H)	2.61 s 6.28 (s, 2H)	154.6 [1]	146.5	122.8	104.8 159.1	151.2 102.5	155.9 156.6	128.2, 129.5 130.0, 130.7 131.3, 134.1	16.0	20.5 103.6 124.2 139.8

Table II (continued)

Compound	H-4	H-5	H-8	R	Q	other	C-1	C-3	C-4	C-5 C-6	C-7 C8	C-3' C-4'	R	Q	other
8/11	8.31 s [2]	7.72 s	6.84 s	7.49 (d, 2H, J = 8.1 Hz) 7.51 (d, 2H, J = 8.1 Hz)	2.35 (s, 3H)	2.49 s 3.78 s 4.15 s	154.5 [2]	144.0	122.0	105.1 157.8	151.9 106.3	154.3 156.1	127.4, 128.8 131.6, 134.6	15.1	19.2 55.6 56.6 121.7 137.2
	7.86 s [1]	7.26 s	6.83 s	7.38 (d, 2H, J = 7.8 Hz) 7.42 (d, 2H, J = 7.8 Hz)	2.48 (s, 3H)	2.62 s 3.81 s 4.16 s	155.9 [1]	146.0	122.6	104.5 159.0	152.5 106.5	154.9 158.5	128.3, 128.5 131.3, 136.9	15.9	20.5 56.3 57.0 121.9 137.7
8/12	7.93 s [2]	7.54 s	7.47 s	2.86 (s, 3H)	1.37 (t, 3H, J = 7.3 Hz) 3.08 (q, 2H, J = 7.3 Hz)	2.47 s 4.10 s 4.14 s	156.0 [2]	143.6	121.3	105.0 157.5	151.9 105.0	155.4 157.2	17.6	14.9 26.7	19.6 56.1 56.5 120.6 136.1
8/13	8.29 s [2]	7.72 s	6.77 s	7.26 (dd, 2H, J = 8.8, 9.0 Hz) 7.49 (dd, 2H, J = 8.8, 5.3 Hz)	1.02 (t, 3H, J = 7.4 Hz) 2.72 (q, 2H, J = 7.4 Hz)	2.42 s 3.71 s 4.10 s	155.2 [2]	144.3	122.2	105.5 158.0	152.1 106.5	155.1 155.1	115.0 (q, J = 22.1 Hz) 126.7 (q, J = 3.4 Hz) 132.7 (q, J = 9.2 Hz) 162.5 (q, J = 248.0 Hz)	15.2 27.1	19.8 55.9 57.1 122.4 137.6
8/14	8.37 s [2]	7.77 s	6.55 s	7.32-7.60 (m, 4H)	1.01 (t, 3H, J = 7.3 Hz) 2.67 (q, 2H, J = 7.3 Hz)	2.47 s 3.68 s 4.12 s									
	8.00 s [1]	7.35 s	6.67 s	7.28-7.49 (m, 4H)	1.14 (t, 3H, J = 7.1 Hz) 2.89 (m, 2H)	2.65 s 3.81 s 4.19 s	153.8 [1]	146.0	122.3	104.6 158.4	152.7 105.7	154.9 157.5	126.5, 129.2 129.3, 131.6 131.8, 133.5	15.3 28.0	20.5 56.2 57.1 122.6 137.5
8/15	8.20 s [2]	7.61 s	6.79 s	7.35-7.48 (m, 4H)	1.11 (t, 3H, J = 7.4 Hz) 2.8 (q, 2H, J = 7.4 Hz)	2.56 s 3.78 s 4.16 s	154.9 [2]	144.7	122.6	105.2 158.4	152.4 105.9	154.2 156.4	128.3, 129.4 129.7, 130.2 131.7, 133.4	15.2 27.7	20.0 55.9 57.0 122.2 137.9
8/16	8.34 s [2]	7.79 s	6.82 s	7.52 (d, 2H, J = 8.8 Hz) 7.56 (d, 2H, J = 8.8 Hz)	1.07 (t, 3H, J = 7.2 Hz) 2.78 (q, 3H, J = 7.2 Hz)	2.48 s 3.77 s 4.15 s	155.0 [2]	144.2	122.4	105.4 157.9	152.0 106.2	154.6 155.1	127.9, 129.0 132.0, 134.9	15.1 27.1	19.7 55.8 57.0 121.9 137.5
8/17	8.28 s [2]	7.73 s	6.94 s	3.86 (s, 3H) 7.00 (d, 2H, J = 8.9 Hz) 7.42 (d, 2H, J = 8.9 Hz)	0.91 (t, 3H, J = 7.1 Hz) 1.22-1.53 (m, 8H) 2.80 (t, 2H, J = 6.9 Hz)	2.46 s 3.78 s 4.16 s	155.3 [2]	144.5	122.1	105.7 158.2	152.2 107.4	155.5 156.4	55.4, 113.4 122.6, 132.0 160.5	13.9 22.1 27.8 29.6 31.0 33.3	19.8 56.1 57.1 122.5 137.5
8/18	8.36 s [2]	7.73 s	6.71 s	7.76 (d, 2H, J = 8.8 Hz) 8.26 (d, 2H, J = 8.8 Hz)	0.85 (t, 3H, J = 6.6 Hz) 1.09-1.37 (m, 8H) 2.71 (t, 2H, J = 6.2 Hz)	2.47 s 3.71 s 4.11 s	153.4 [2]	144.4	122.8	105.5 158.2	152.3 105.9	154.8 155.7	122.9, 132.0 136.7, 148.0	13.8 22.0 27.6 29.2 30.8 32.8	19.6 56.0 57.0 121.9 137.8
8/19	8.01 s [2]	7.64 s	7.56 s	2.77 (s, 3H)	1.29 (d, 6H, J = 6.7 Hz) 3.49 (qi, 1H, J = 6.7 Hz)	2.34 s 4.03 s 4.08 s	155.7 [2]	143.3	120.7	105.4 157.6	151.8 106.2	155.6 156.3	17.7	23.3 37.1	19.4 56.3 56.6 121.3 136.0
8/20	7.91 s [1]	7.31 s	6.83 s	7.08 (dd, 2H, J = 8.8, 8.9 Hz) 7.48 (dd, 2H, J = 8.8, 5.2 Hz)	1.15 (d, 6H, J = 6.7 Hz) 3.34 (qi, 1H, J = 6.7 Hz)	2.59 s 3.80 s 4.17 s	155.0 [1]	145.8	121.9	104.6 158.4	152.4 106.5	156.0 157.0	115.5 (q, J = 24.6 Hz) 126.0 (q, J = 4.0 Hz), 132.2 (q, J = 7.1 Hz), 163.5 (q, J = 252.0)	23.3 38.5	20.5 56.2 57.1 122.7 137.7

Table I I (continued)

Compound	H-4	H-5	H-8	R	Q	other	C-1	C-3	C-4	C-5 C-6	C-7 C8	C-3' C-4'	R	Q	other
8/21	8.38 s [2]	7.78 s	6.55 s	7.30-7.60 (m, 4H)	1.02 (d, 6H, J = 6.2 Hz) 3.15 (m, 1H, J = 6.2 Hz)	2.45 s 3.68 s 4.12 s									
	8.06 s [1]	7.44 s	6.63 s	7.25-7.48 (m, 4H)	1.12 (d, 6H, J = 6.7 Hz) 3.18 (qi, 1H, J = 6.7 Hz)	2.60 s 3.79 s 4.17 s	153.5 [1]	145.7	122.4	104.8 158.3	152.6 105.4	155.0 156.7	126.3, 129.1 129.1, 131.5 131.6, 133.4	23.1 23.4 38.4	20.2 56.1 57.1 122.5 137.5
8/22	8.18 s [2]	7.58 s	6.79 s	7.36-7.46 (m, 4H)	1.12 (d, 6H, J = 6.6 Hz) 3.25 (qi, 1H, J = 6.6 Hz)	2.56 s 3.79 s 4.16 s	155.0 [2]	144.8	122.5	105.2 158.4	152.5 106.0	154.2 156.1	128.3, 129.4 129.7, 130.2 131.7, 133.6	23.2 38.3	20.0 56.0 57.0 122.2 137.9
8/23	8.33 s [2]	7.76 s	6.80 s	7.48 (d, 2H, J = 8.9 Hz) 7.52 (d, 2H, J = 8.9 Hz)	1.06 (d, 6H, J = 6.7 Hz) 3.18 (qi, 1H, J = 6.7 Hz)	2.45 s 3.75 s 4.13 s	154.8 [2]	144.2	122.4	105.4 157.9	152.0 106.2	154.6 155.0	127.9, 129.0 132.0, 135.0	23.1 37.7	19.7 55.8 57.0 121.9 137.5
8/24	8.32 s [2]	7.74 s	6.52 s	7.32-7.62 (m, 4H)	2.62 (s, 6H)	2.51 s 3.67 s 4.11 s	152.8 [2]	143.8	123.3	105.8 159.1	152.5 105.8	153.3 159.7	126.4, 128.5 129.2, 131.5 132.4, 133.4	37.8	19.3 56.0 57.1 122.3 138.5
	7.85 s [1]	7.24 s	6.65 s	7.26-7.51 (m, 4H)	2.84 (s, 6H)	2.72 s 3.78 s 4.15 s									
8/25	7.82 s [1]	7.22 s	6.84 s	7.10 (dd, 2H, J = 8.7, 8.7 Hz), 7.54 (dd, 2H, J = 8.7, 5.2 Hz)	1.00 (t, 6H, J = 7.1 Hz) 3.33 (d, 4H, J = 7.1 Hz)	2.69 s 3.79 s 4.15 s	156.2 [1]	146.2	122.7	104.3 158.0	152.1 106.5	151.3 166.8	115.3 (q, 21.4 Hz), 126.1(q, 4.2 Hz), 132.1(q, 9.0 Hz), 163.4 (q, 252.0 Hz)	12.2 42.2	20.2 56.1 56.9 121.8 137.4
8/26	8.32 s [2]	7.74 s	6.53 s	7.33-7.60 (m, 4H)	0.87 (t, 6H, J = 7.0 Hz) 3.12 (m, 4H, J = 7.0 Hz)	2.51 s 3.67 s 4.11 s									
	7.89 s [1]	7.29 s	6.65 s	7.29-7.49 (m, 4H)	1.00 (t, 6H, J = 7.0 Hz) 3.33 (m, 4H, J = 7.0 Hz)	2.71 s 3.78 s 4.15 s	152.6 [1]	146.3	122.6	104.5 158.1	151.3 105.7	154.0 166.7	126.3, 129.1 129.4, 131.5 131.6, 133.5	12.3 42.2	20.5 56.1 57.0 122.3 137.3
8/27	8.18 s [2]	7.68 s	6.90 s	3.79 (s, 3H) 6.94 (d, 2H, J = 8.9 Hz) 7.42 (d, 2H, J = 8.9 Hz)	0.92 (t, 6H, J = 7.0 Hz) 3.18 (q, 4H, J = 7.0 Hz)	2.47 s 3.72 s 4.09 s	152.0 [2]	144.9	121.9	105.6 157.8	151.8 107.4	156.4 165.9	55.5, 113.3 123.0 132.1 160.5	12.5 42.5	19.9 56.0 57.1 122.4 137.3
8/28	8.19 s [2]	7.64 s	7.06 s	3.68 (s, 3H) 3.72 (s, 3H) 6.99 (d, 1H, J = 8.2 Hz) 7.06 (dd, 1H, J = 1.8, 8.2 Hz), 7.11 (d, 1H, J = 1.8 Hz),	0.95 (t, 6H, J = 7.0 Hz) 3.19 (m, 4H, J = 7.0 Hz)	2.48 s 3.79 s 4.10 s	152.0 [2]	144.8	121.9	105.6 157.8	151.8 107.7	156.3 165.9	55.8, 56.0 111.1, 114.7 123.1, 124.3 148.2, 150.4	12.7 42.5	20.0 56.1 57.1 122.3 137.4
8/29	8.22 s [2]	7.63 s	6.59 s	7.29-7.50 (m, 4H)	3.82 (m, 4H) 4.98-5.05 (m, 4H), 5.67 (m, 2H)	2.62 s 3.72 s 4.13 s	152.4 [2]	144.8	122.7	104.9 158.0	151.5 105.3	152.7 165.1	126.2, 128.9 129.2, 131.4 131.5, 133.0	49.9 115.9 134.8	19.8 55.7 56.8 122.0 137.4
	7.92 s [1]	7.29 s	6.65 s	7.26-7.51 (m, 4H)	3.91 (m, 4H), 4.96-5.09 (m, 4H), 5.70 (m, 2H)	2.72s 3.78 s 4.16 s									
8/30	7.84 s [1]	7.24 s	6.83 s	7.39 (d, 2H, J = 8.8 Hz) 7.43 (d, 2H, J = 8.8 Hz)	3.94 (m, 4H) 5.04 (m, 4H) 5.70 (m, 2H)	2.69 s 3.80 s 4.15 s	152.4 [1]	146.2	122.6	104.4 158.2	151.5 106.4	155.9 166.9	128.4, 128.6 131.4, 135.1	50.2 115.8 136.6	20.3 56.1 56.9 121.9 137.5

Table II (continued)

Compound	H-4	H-5	H-8	R	Q	other	C-1	C-3	C-4	C-5 C-6	C-7 C8	C-3' C-4'	R	Q	other
8/31	8.26 s [2]	7.65 s	6.84 s	7.23 (dd, 2H, (J = 8.7, 8.7 Hz) 7.55 (dd, 2H, (J = 8.7, 5.3 Hz)	6.79 (t, 1H, J = 8.7 Hz) 7.16 (dd, 2H, J = 7.4, 8.7 Hz), 7.29 (d, 2H, J = 7.4 Hz)	8.25 s 3.88 s 4.14 s									
	7.88 s [1]	7.28 s	6.82 s	7.12-7.21 (m, 2H) 7.51 (dd, 2H, J = 8.4, 5.1 Hz)	6.79 (dt, 1H, J = 1.5, 7.0 Hz) 7.12-7.21 (m, 4H)	2.66 s 3.81 s 4.17 s	152.5 [1]	145.6	122.0	104.4 158.6	151.2 106.6	156.3 160.5	115.3 (q, 22.1 Hz), 125.8 (q, 3.9 Hz), 132.2 (q, 9.0 Hz) 162.3 (q, 251.1 Hz)	115.3 119.1 128.7 142.7	20.3 56.2 57.0 122.8 137.9
8/32	8.38 s [1]	7.80 s	6.60 s	7.33-7.55 (m, 4H)	1.11-1.37 (m, 4H), 1.50-1.90 (m, 4H) 3.36 (m, 1H) 6.44 (d, 1H, J = 7.5 Hz)	2.65 s 3.80 s 4.24 s	153.2 [1]	144.6	122.5	105.1 157.8	151.7 105.7	153.2 159.3	126.7, 128.4 129.6, 131.2 132.6, 133.7	24.4 24.5 25.4 32.6 32.7 51.9	20.1 56.2 57.7 123.4 138.6
8/33	8.26 s [2]	7.68 s	6.82 s	7.42 (d, 2H, J = 8.7 Hz) 7.49 (d, 2H, J = 8.7 Hz)	6.75 (dt, 1H, J = 6.7 Hz) 7.14-7.23 (m, 4H)	2.50 s 3.75 s 4.12 s	152.1 [2]	144.3	121.7	105.0 158.2	152.0 106.3	154.3 158.7	127.4, 127.6 131.2, 134.3	114.8 117.8 128.3 142.5	19.1 55.5 56.3 121.9 137.3
8/34	8.33 s [2]	7.74 s	6.78 s	7.79 (d,2H, J = 8.9 Hz) 8.26 (d, 2H, J = 8.9 Hz)	6.60 (t, 1H, J = 6.9 Hz) 7.05 (t, 2H, J = 6.9 Hz) 7.22 (d, 2H, J = 6.9 Hz)	2.59 s 3.74 s 4.14 s	152.6 [2]	144.6	122.6	105.6 158.4	151.3 106.5	153.5 160.4	122.9, 131.9 137.0, 148.2	114.8 117.1 128.1 143.1	19.6 56.2 57.1 122.0 137.7
8/35	8.26 s [2]	7.72 s	6.97 s	3.83 (s, 3H) 7.04 (d, 2H, J = 8.8 Hz) 7.32 (d, 2H, J = 8.8 Hz)	6.71 (dt, 1H, J = 7.9 Hz) 7.14 (t, 2H, J = 7.9 Hz) 7.51(d, 2H, J = 7.9 Hz)	2.58 s 3.78 s 4.18 s	154.0 [3]	144.0	122.2	104.9 160.2	153.1 107.3	157.6 159.6	55.5, 111.9 123.1 131.5, 160.4	114.5 117.5 129.6 139.1	20.0 56.4 57.3 120.4 136.6
	7.93 s [1]	7.37 s	6.97 bs 3H	3.82 (s, 3H) 6.81 (d, J = 8.7 Hz) 6.97 (bs, 3H)	6.81 (dt, 1H, J = 7.3 Hz) 6.97 (bs, 3H) 7.18 (dd, J = 7.3 Hz)										
8/36	7.98 s [2]	7.49 s	7.05 s	3.72 (s, 3H) 3.83 (s, 3H) 6.92 (d, 1H, J = 8.5 Hz) 7.06 (dd, 1H, J = 2.0, 8.5 Hz) 7.40 (bs, 1H)	6.78 (t, 1H, J = 7.3 Hz) 7.13 (d, 2H, J = 7.3 Hz) 7.26 (d, 2H, J = 7.3 Hz)	2.67 s 3.88 s 4.19 s	151.9 [2]	144.7	122.1	104.4 157.9	151.4 107.2	156.3 159.5	55.2, 55.6 110.7, 114.1 122.1, 123.3 148.2, 150.4	114.8 117.8 127.8 142.9	19.5 55.5 56.2 121.1 137.2
8/37	7.91 s [1]	7.21 s	6.74 s	7.13-7.35 (m, 4H)	4.38 (s, 2H) 7.01 (t, 2H, J = 8.0 Hz) 7.13-7.35 (m, 4H)	2.62 s 3.74 s 4.17 s	152.6 [1]	145.1	122.6	104.7 158.9	151.5 106.3	156.0 160.7	115.7 (20.0 Hz), 125.1 (3.6 Hz) 131.9 (3.6 Hz) 163.5 (254.2 Hz)	46.5 126.5 126.9 128.1 140.0	20.1 56.2 57.2 122.3 138.1
8/38	8.50 s [2]	7.88 s	6.59 s	7.19-7.59 (m, 9H)	4.38 (s, 2H) 7.19-7.59 (m, 9H)	2.63 s 3.74 s 4.17 s	152.6 [2]	143.7	123.4	104.8 157.7	152.2 105.8	152.9 159.1	126.9, 128.2 129.2, 131.4 132.5, 133.1	45.9 126.6 126.7 128.0 138.9	19.5 55.9 57.2 122.1 138.5
8/39	7.80 s [1]	7.26 s	7.02 s	3.78 (s, 3H) 3.79 (s, 3H) 7.16-7.28 (m, 3H)	4.42 (s, 2H) 6.86 (d, 1H, J = 7.8 Hz) 7.03 (d, 2H, J = 7.8 Hz) 7.16-7.28 (m, 2H)	2.63 s 3.91 s 4.14 s	152.5 [1]	146.1	121.5	104.6 158.5	151.9 107.9	157.6 165.1	56.5, 56.3 110.9, 114.3 123.0, 124.1 148.9, 151.1	48.7 126.6 127.4 128.5 140.9	20.5 56.0 57.0 122.5 137.7

Table II (continued)

Compound	H-4	H-5	H-8	R	Q	other	C-1	C-3	C-4	C-5 C-6	C-7 C8	C-3' C-4'	R	Q	other
8/40	8.32 s [2]	7.74 s	6.54 s	7.31-7.62 (m, 4H)	1.46 (m, 6H) 3.10 (m, 4H)	2.49 s 3.73 s 4.10 s									
	7.94 s [1]	7.33 s	6.63 s	7.28-7.49 (m, 4H)	1.51 (m, 6H) 3.21 (m, 4H)	2.68 s 3.78 s 4.16 s	152.7 [2]	146.2	122.6	105.7 158.3	151.6 104.6	153.9 167.7	126.4, 129.2 129.3, 131.7 131.7, 133.6	24.6 25.1 48.8	20.5 56.2 57.1 122.5 137.5
8/41	8.28 s [2]	7.72 s	6.80 s	7.44-7.58 (m, 4H)	1.46 (m, 6H) 3.10 (m, 4H)	2.60 s 3.73 s 4.10 s	152.3 [2]	145.0	122.4	105.7 158.2	152.0 105.9	154.5 167.4	129.5, 129.9 130.4, 130.4 132.7, 132.8	25.0 25.0 49.0	20.2 56.3 57.5 122.9 137.9
8/42	8.21 s [2]	7.63 s	6.81 s	7.38-7.51 (m, 4H)	3.17 (m, 4H) 3.65 (m, 4H)	2.60 s 3.77 s 4.13 s	152.0 [2]	144.5	122.2	104.9 157.8	151.4 105.6	153.9 166.8	128.1, 129.0 129.4, 129.8 131.6, 132.8	48.0 65.6	19.6 55.5 56.6 121.8 137.5
8/43	8.41 s [2]	7.81 s	6.89 s	7.57 (dd, 1H, J = 8.6, 1.9 Hz), 7.81 (d, 1H, J = 8.6 Hz), 7.83 (d, 1H, J = 1.9 Hz)	3.26 (m, 4H) 3.62 (m, 4H)	2.51 s 3.79 s 4.16 s									
	8.43 s [1]	7.88 s	6.78 s	7.24 (dd, 1H, J = 8.8, 1.7 Hz) 7.53 (d, 1H, J = 1.7 Hz) 7.60 (d, 1H, J = 8.8 Hz)	3.54 (m, 4H) 3.72 (m, 4H)	2.56 s 3.85 s 4.25 s	153.0 [1]	144.5	124.1	105.3 158.7	152.1 106.6	153.4 159.7	128.8, 129.3 130.8, 131.9 132.9, 136.0	46.7 65.8	19.9 56.3 57.9 122.3 139.4
8/44	8.32 s [2]	7.74 s	6.53 s	7.26-7.60 (m, 4H)	2.14 (s, 3H) 2.24 (m, 4H) 3.04 (m, 4H)	2.51 s 3.67 s 4.11 s									
	7.91 s [1]	7.30 s	6.65 s	7.25-7.47 (m, 4H)	2.28 (s, 3H) 2.44 (m, 4H) 3.31 (s, 4H)	2.70 s 3.79 s 4.15 s	152.5 [1]	146.0	122.4	105.5 158.0	151.7 104.4	153.8 167.7	126.2, 129.0 129.2, 131.4 131.4, 133.4	46.2 47.6 54.4	20.4 56.0 56.9 122.2 137.2
8/45	8.33 s [2]	7.74 s	6.54 s	7.38-7.61 (m, 4H)	2.35 (m, 6H) 3.02 (m, 4H) 3.50 (m, 2H)	2.50 s 3.67 s 4.11 s	152.5 [2]	146.1	122.1	104.2 158.2	151.6 105.7	153.9 167.6	126.3, 129.0 129.2, 131.5 131.6, 133.5	47.7 52.2 57.5 59.3	20.5 56.1 56.8 122.5 137.2
	7.84 s [1]	7.21 s	6.67 s	7.34-7.44 (m, 4H)	2.36 (t, 6H, J = 5.6 Hz) 3.27 (m, 4H) 3.64 (t, 2H, J = 5.6 Hz)	2.73 s 3.79 s 4.16 s									
8/46	8.26 s [2]	7.71 s	6.79 s	7.49 (bs, 4H)	2.49 (m, 6H) 3.07 (m, 4H) 3.44 (m, 2H)	2.47 s 3.72 s 4.09 s	152.2 [2]	144.8	122.6	105.6 158.0	152.0 106.5	154.9 166.9	128.0 129.5 132.3 135.0	47.9 52.7 58.7 60.9	19.8 56.0 57.1 122.1 137.6

[1] Taken in deuteriochloroform. [2] Taken in DMSO-d_6. [3] Taken in a mixture of deuteriochloroform and trifluoroacetic acid.

The steric hindrance in derivatives **14** and **16** is visible in their 3D structures near to global energy minimum, which were calculated by the conformational search option of HyperChem using MM+ molecular mechanics [7] (Scheme 7). These structures show that the 4-methylphenyl and the 1,2,4-triazol-3'-yl groups are nearly perpendicular to the plane of the isoquinolinium ring system and that the benzyl phenyls are nearly coplanar with the isoquinolinium ring system as well. As a consequence the benzyl CH_2 protons are non equivalent and appear as two doublets. Of course, this is not so in case of derivative **15** where the *N*-benzyl group is far away from the phenyl moiety thus the benzyl CH_2 appears as a singlet.

In the cmr spectra of isomers **14**, **15** and **16**, taken in DMSO-d_6 solution, the triazole carbon atoms appeared with very different chemical shifts that are characteristic for the site of *N*-benzylation (Scheme 8). Thus in derivative **14** the carbon atoms 3 and 5 appeared at 145.6 and 160.8 ppm, in the isomer **15** at 155.9 and 156.8, and in derivative **16** at 154.1 and 146.8 ppm, respectively. Comparing the above data with the corresponding chemical shifts of the non-benzylated derivative **8/6** (R = 4-methylphenyl, $R^1 = R^2$ = methoxy, Q = methylthio) appearing at 156.3 and 156.4 ppm, respectively, the analogy with derivative **15** is unequivocal. Consequently, it can be stated that **8/6** is present in DMSO-d_6 solution and also in 2*H*-tautomeric form. Similar observations were seen in the cmr spectra of all derivatives **8**, (it is compounds **8/1-8/46**) taken in DMSO-d_6 solution, (Table II) indicating that they have analogous tautomeric structures in solution.

The uv spectra of isomers **14-16** (R = 4-methylphenyl, $R^1 = R^2$ = methoxy, Q = methylthio) and that of derivative **8/6** taken in ethanolic and acidic solutions are completely analogues (Figure 1). However, if acquired in alkaline conditions, the uv spectrum of **15** remained unchanged, while the spectra of derivatives **14** and **16** underwent significant changes in both, the position of the maxima and the intensity of the maxima (Figure 1). As the uv spectrum of the non-benzylated derivative **8/6**, taken in alkaline conditions, remained unchanged it can be stated that derivative **8/6** also exists in the 2*H* tautomeric form in ethanolic solution (Figure 1). Because the uv spectra of all derivatives **8** (it is compounds **8/1-8/46**) taken in ethanolic solution are analogous to that of **8/6** they should have analogous structure in the above solution, as well.

The 2*H* tautomeric form of derivatives **8** is also in agreement with an experimental result. Namely, the *N*-benzylation of **8/6** with benzyl chloride led to **15** (Scheme 8).

EXPERIMENTAL

Melting points were determined on a Koffler-Boëtius micro apparatus and are not corrected. The infrared spectra were obtained as potassium bromide pellets using a Perkin-Elmer 577 spectrophotometer. The ultraviolet spectra were obtained using a Varian Cary 1E UV-VIS spectrophotometer. The mass spectra were recorded on a Kratos MS25RFA instrument using a direct inlet probe in EI or CI mode. The pmr and cmr measurements were performed using Varian Gemini-2000 and Varian Unity Inova instruments at 200 and 400 MHz, respectively. Standard Varian HSQC, HMBC, and HyperChem Ver. 4.0 programs were used. Dry-column flash chromatography was performed according to [8]. As adsorbent Kieselgel 60H (Merck 7736 for thin layer chromatography) was employed.

General Methods for the Synthesis of Triazol-3'-yl-isoquinolinium Zwitter Ions

Method A

A mixtue of 0.015 mole of the corresponding phenylacetone (**1**), 0.015 mole of the corresponding 5-amino-3-Q-1*H*-1,2,4-triazole (**7**) [6,9] and 20 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 50 ml of water was added to the reaction mixture. The crystals that precipitated were isolated by filtration, washed with a small amount of water and recrystallized from an appropriate solvent (Table I, for their spectral data see Table II).

Method B

A mixture of 0.015 mole of the corresponding phenylacetone (**1**), 0.015 mole of the corresponding 5-amino-3-Q-1*H*-1,2,4-triazole (**7**) [6,9] and 20 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 30 ml of water was added to the reaction mixture and it was made alkaline with 40 ml of 5 *N* sodium hydroxide solution. This mixture was extracted with 2x50 ml of chloroform, the collected organic phases were dried over anhydrous sodium sulphate, filtered and evaporated *in vacuo* to dryness. The residue was recrystallized from an appropriate solvent (Table I, for their spectral data see Table II).

Method C

A mixture of 0.015 mole of the corresponding phenylacetone (**1**), 0.015 mole of the corresponding 5-amino-3-Q-1*H*-1,2,4-triazole (**7**) [6,9] and 20 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 30 ml of water was added to the reaction mixture and it was made alkaline with 40 ml of 5 *N* sodium hydroxide solution. This mixture was extracted with 2x50 ml of chloroform, the collected organic phases were dried over anhydrous sodium sulphate, filtered and evaporated *in vacuo* to dryness. The residue was dry-column flash chromatographed on Kieselgel 60 H, as eluents different mixtures of chloroform and methanol of continuously increasing polarities were used. After evaporating the appropiate fractions *in vacuo* to dryness the residue was recrystallized from an appropriate solvent (Table I, for their spectral data see Table II).

Method D

A mixture of 0.015 mole of the corresponding pyrylium salt (**2**) [10], 0.015 mole of the corresponding 5-amino-3-Q-1*H*-1,2,4-triazole (**7**) [6,9] and 20 ml of acetic acid was refluxed with stirring for 4 hours. After cooling 30 ml of water was added to the reaction mixture and it was made alkaline with 40 ml of 5 *N* sodium hydroxide solution. This mixture was extracted with 2x50 ml of chloroform, the collected organic phases were dried over anhydrous sodium sulphate, filtered and evaporated *in vacuo* to dryness. The residue was recrystallized from an appropriate solvent (Table I, for their spectral data see Table II).

1-(Chlorophenyl)-6,7-dimethoxy-3-methyl-*N*-(1,2,4-triazol-3'-yl)isoquinolinium perchlorate (**8/4**).

A mixture of 0.01 mole of 1-(4-chlorophenyl)-6,7-dimethoxy-3-methyl-pyrylium perchlorate (**2**, R = 4-chlorophenyl, $R^1 = R^2$ = methoxy) [10], 0.01 mole of 5-amino-1*H*-1,2,4-triazole (**7/4**, Q = H) (Fluka) and 15 ml of acetic acid was refluxed with stirring for 2 hours. After cooling the crystals that precipitated were isolated by filtration and recrystallized from 40 ml of 2-propanol to yield 3.54 g (74%) of 1-(4-chlorophenyl)-6,7-dimethoxy-3-methyl-*N*-(1,2,4-triazol-3'-yl)isoquinolinium perchlorate (**8/4**) (Table I, for its spectral data see Table II).

6,7-Dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(2'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium Chloride (**14**).

A mixture of 5 mmoles of 1-[4,5-dimethoxy-2-(4-methylbenzoyl)]phenyl-acetone (**1**, R = 4-methylphenyl, $R^1 = R^2$ = methoxy), 5 mmole of 5-amino-1-benzyl-3-methylthio-1*H*-1,2,4-triazole (**11**) [4], 10 ml of acetonitrile and 2 ml of concentrated hydrochloric acid was refluxed with stirring for 19 hours. After cooling the reaction mixture was evaporated *in vacuo* to dryness. The residue was dry-column flash chromatographed on 30 g of Kieselgel 60 H, as eluents different mixtures of *n*-hexane, chloroform and methanol of continuously increasing polarities were used. After evaporation of the appropriate fractions *in vacuo* to dryness, the residue was recrystallized from 30 ml of ethyl acetate and filtered to yield 1.12 g (42%) of 6,7-dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(2'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium chloride (**14**), mp 168-171°; pmr (DMSO-d_6): δ 2.18 (s, 3H, CH_3-3), 2.41 (s, 3H, $PhCH_3$), 2.52 (s, 3H, SCH_3), 3.75 (s, 3H, OCH_3-7), 4.18 (s, 3H, OCH_3-6), 5.08 [d, (J = 14.6 Hz), 1H, $PhCH_2$-α_1)], 5.17 [d, (J = 14.6 Hz), 1H, $PhCH_2$-α_2)], 6.89 (s, 1H, H-8), 7.08 [d, (J = 7.8 Hz), 2H, PhH-3",5"], 7.28-7.40 (m, 6H, PhH-2" and BnH), 7.68 [d, (J = 7.8 Hz), 1H, PhH-6"], 7.88 (s, 1H, H-5), 8.40 (s, 1H, H-4); cmr (DMSO-d_6): δ, ppm 14.1 (SCH_3), 19.3 (CH_3-3), 21.3 ($PhCH_3$), 51.6 ($BzCH_2$), 56.3 (OCH_3-6), 57.7 (OCH_3-7), 106.2 (C-5), 107.1 (C-8), 123.1 (C-8a), 123.4 (C-4), 125.3, 128.7, 128.8, 129.3, 129.4, 129.9, 130.3, 133.2 (ArC), 139.6 (C-4a), 141.9 (PhC-4"), 142.8 (C-3), 145.6 (C-3'), 152.7 (C-7), 156.1 (C-1), 159.9 (C-6), 160.8 (C-5').

Anal. Calcd. for $C_{29}H_{29}ClN_4O_2S$ (MW 533.10): C, 65.34; H, 5.48; Cl, 6.65; N, 10.51; S, 6.01. Found: C, 65.14; H, 5.52; Cl, 6.57; N, 10.66; S, 5.97.

6,7-Dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(1'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium Chloride (**15**) from **1** and **12**.

A mixture of 1.7 mmoles of 1-[4,5-dimethoxy-2-(4-methylbenzoyl)]phenylacetone (**1**, R = 4-methylphenyl, $R^1 = R^2$ = methoxy), 1.7 mmole of 5-amino-2-benzyl-3-methylthio-2*H*-1,2,4-triazole (**12**) [4], 8 ml of acetonitrile and 0.3 ml of concentrated hydrochloric acid was refluxed with stirring for 1 hour. After cooling the reaction mixture was evaporated *in vacuo* to dryness. The residue was triturated with 5 ml of ethyl acetate and filtered to yield 0.87 g (96%) of 6,7-dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(1'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium chloride (**15**), mp 149-152°; pmr (DMSO-d_6): δ 2.40 (s, 3H, CH_3-3), 2.56 (s, 3H, $PhCH_3$), 2.57 (s, 3H, SCH_3), 3.72 (s, 3H, OCH_3-7), 4.15 (s, 3H, OCH_3-6), 5.30 (s, 2H, $PhCH_2$)], 6.83 (s, 1H, H-8), 6.87 [dd, (J = 1.8 and 6.8 Hz), 2H, PhH-3",5"], 7.24-7.40 (m, 7H, PhH-2",6" and BnH), 7.86 (s, 1H, H-5), 8.44 (s, 1H, H-4); cmr (DMSO-d_6): δ 15.7 (SCH_3), 19.9 (CH_3-3), 21.3 ($PhCH_3$), 52.3 ($BzCH_2$), 56.1 (OCH_3-6), 57.5 (OCH_3-7), 106.0 (C-5), 106.9 (C-8), 122.4 (C-8a), 122.8 (C-4), 126.5, 127.1, 128.2, 128.8, 129.0, 130.2, 134.4 (ArC), 138.7 (C-4a), 140.9 (PhC-4"), 143.3 (C-3), 152.4 (C-7), 154.5 (C-1), 155.9 (C-3'), 156.8 (C-5'), 159.2 (C-6).

Anal. Calcd. for $C_{29}H_{29}ClN_4O_2S$ (MW 533.10): C, 65.34; H, 5.48; Cl, 6.65; N, 10.51; S, 6.01. Found: C, 65.19; H, 5.35; Cl, 6.76; N, 10.42; S, 6.15.

6,7-Dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(1'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium Chloride (**15**) by Benzylation of **8/6**.

A mixture of 5 mmoles of 6,7-dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium zwitter ion (**8/6**), 7 mmoles of benzylchloride and 10 ml of acetonitrile was stirred at 40° for 13 hours. After cooling the crystals that precipitated were filtered off and washed with a small amount of acetonitrile to yield 1.52 g (57%) of 6,7-dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(1-benzyl-5-methylthio-1,2,4-triazol-3-yl)isoquinolinium chloride (**15**) mp 150-152°. The compound is identical (ir, mixed mp) with that of **15** obtained in the previous experiment.

6,7-Dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(4'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium Chloride (**16**).

A mixture of 7 mmoles of 1-[4,5-dimethoxy-2-(4-methylbenzoyl)]phenyl-acetone (**1**, R = 4-methylphenyl, $R^1 = R^2$ = methoxy), 8 mmoles of 5-amino-4-benzyl-3-methylthio-4*H*-1,2,4-triazole (**13**) [4], 15 ml of acetonitrile and 2 ml of concentrated hydrochloric acid was refluxed with stirring for 28 hours. After cooling the reaction mixture was evaporated *in vacuo* to dryness. The residue was dry-column flash chromatographed on 40 g of Kieselgel 60 H, as eluents different mixtures of *n*-hexane, chloroform and methanol of continuously increasing polarities were used. After evaporation of the appropiate fractions *in vacuo* to dryness, the residue was crystallized with 10 ml of ethyl acetate and filtered to yield 1.12 g (42%) of 6,7-dimethoxy-3-methyl-1-(4-methylphenyl)-*N*-(4'-benzyl-5'-methylthio-1,2,4-triazol-3'-yl)isoquinolinium chloride (**16**), mp 168-171°; pmr (DMSO-d_6): δ 2.11 (s, 3H, CH_3-3), 2.41 (s, 3H, $PhCH_3$), 2.52 (s, 3H, SCH_3), 3.75 (s, 3H, OCH_3-7), 4.18 (s, 3H, OCH_3-6), 4.83 [d, (J = 14.6 Hz), 1H, $PhCH_2$-α_1)], 4.97 [d, (J = 14.6 Hz), 1H, $PhCH_2$-α_2)], 6.81 [d, (J = 7.4 Hz), 2H, PhH-3",5"], 6.91 (s, 1H, H-8), 7.20-7.48 (m, 6H, PhH-2" and BnH), 7.64 [d, (J = 7.4 Hz), 1H, PhH-6"], 7.84 (s, 1H, H-5), 8.32 (s, 1H, H-4); cmr (DMSO-d_6): δ 15.1 (SCH_3), 19.5 (CH_3-3), 21.2 ($PhCH_3$), 47.5 ($BzCH_2$), 56.3 (OCH_3-6), 57.7 (OCH_3-7), 106.2 (C-5), 107.2 (C-8), 123.0 (C-8a), 123.3 (C-4), 125.2, 127.6, 128.9, 129.3, 129.5, 130.4, 130.9, 132.7 (ArC), 139.6 (C-4a), 141.9 (PhC-4"), 143.5 (C-3), 146.8 (C-5'), 152.6 (C-7), 154.1 (C-3'), 156.5 (C-1), 159.9 (C-6)

Anal. Calcd. for $C_{29}H_{29}ClN_4O_2S$ (MW 533.10): C, 65.34; H, 5.48; Cl, 6.65; N, 10.51; S, 6.01. Found: C, 65.17; H, 5.53; Cl, 6.77; N, 10.40; S, 6.14.

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REFERENCES AND NOTES

[1] For Part XLII see G. Berecz and J. Reiter, *J. Heterocyclic Chem.*, **38**, 199 (2001).

[2] I. Prauda and J. Reiter, *J. Heterocyclic Chem.*, **38**, 237 (2001).

[3] Gy. Argay and A. Kálmán (to be published).

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

[5] P. Dvortsák, J. Reiter, T. Somorai and P. Sohár, *Magn. Res. Chem.*, **23**, 194 (1985).

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

[7] HyperChem Ver. 4.0, HyperCube Inc, Toronto (1997.)

[8] L. M. Harwood, *Aldrichimica Acta*, **18**, 25 (1985); see also Vogel's Textbook of Practical Organic Chemistry, 5th Ed, Longman, 1989, p 220.

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

[10] E. V. Kuznetsov, I. V. Shcherbakova and A. T. Balaban, "Benzo[*c*]Pyrylium Salts: Syntheses, Reactions, and Physical Properties" in Advances in Heterocyclic Chemistry, Vol. **50**, p 161, Edited by A. R. Katritzky, Academic Press, 1990.