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QUINAZOLINES. 2*. UNSYMMETRIC 1,3-DIALKYL-6-CHLOROSULFONYL-QUINAZOLINE-2,4-DIONES IN NUCLEOPHILIC SUBSTITUTION REACTIONS

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The corresponding 6-chlorosulfonylquinazoline-2,4-diones were synthesized by the reactions of 1-methylquinazoline-2,4-dione and its 3-alkyl-substituted derivatives with chlorosulfonic acid. Treatment of the products with nucleophilic agents (water or ammonia, aliphatic and cyclic amines) gave 2,4-dioxoquinazolin-6-sulfonic acids or their amides.

Keywords: amides of 2,4-dioxoquinazoline-6-sulfonic acid, 2,4-dioxoquinaxoline-6-sulfonic acids, unsymmetrical 1,3-dialkylquinazoline-2,4-diones, 6-chlorosulfonylquinazoline-2,4-diones, nucleophilic and electrophilic substitution.

High biological activity and the wide spectrum of activity of derivatives of quinazoline [2-7] has resulted in a considerable interest in them. Recently we carried out the chlorosulfonation of symmetrical 1,3-dialkylquinazoline-2,4-diones and studied some chemical conversions of the 6-chlorosulfonyl derivatives produced [1]. In a continuation of our study on the electrophilic substitution of this series of compounds we have studied the chlorosulfonation of unsymmetrical 1-methylquinazoline-2,4-dione (**1**) and its 3-alkyl-substituted derivatives **2a,b** and also the behavior of the 6-chlorosulfonyl derivatives **3a-c** obtained with respect to nucleophilic reagents.

The starting compound was not successfully obtained by direct alkylation of quinazoline-2,4-dione because of the formation of a complex mixture of products, so it was made by cyclization of N-methylanthranilic acid (**4**) with sodium cyanate in basic media. Unsymmetrical 3-alkyl-1-methylquinazoline-2,4-diones **2a,b** were synthesized by subsequent alkylation of compound **1** with alkyl iodides in conditions of phase-transfer catalysis [8].

We have shown that, like the symmetrical 1,3-dialkylquinazoline-2,4-diones [1], their unsymmetrical analogs **1** and **2a,b** reacted with chlorosulfonic acid to give the corresponding 6-chlorosulfonyl derivatives **3a-c**. The intermediate 2,4-dioxoquinazoline-6-sulfonic acids **5a-c** were not isolated, despite variation in the composition of the reagents and the conditions of the reaction.

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* For Communication 1 see [1].

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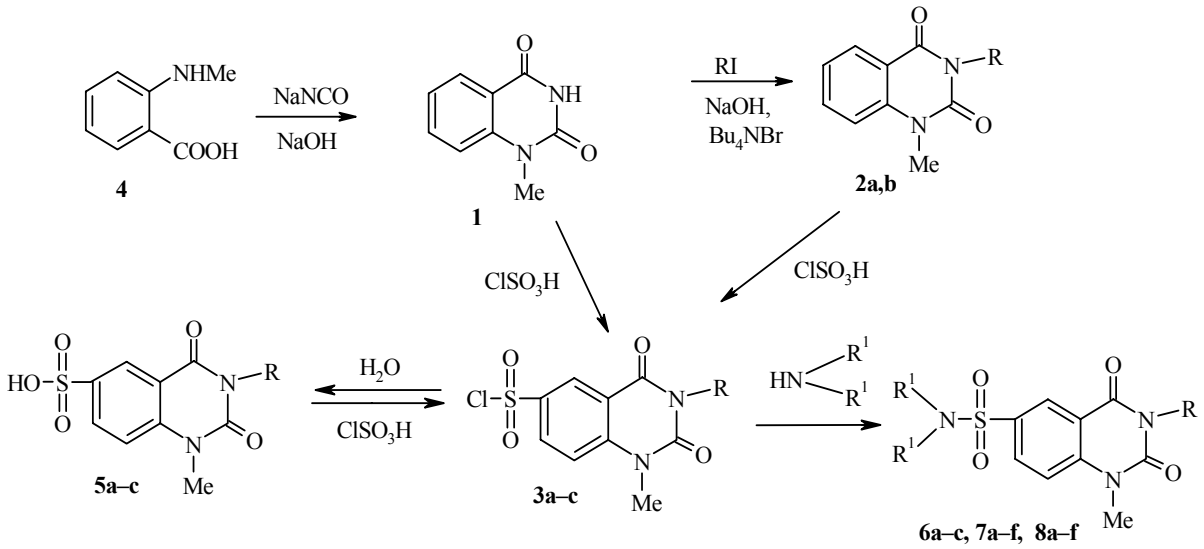


2 a R = *n*-Pr, **b** R = *n*-Bu; **3**, **5 a** R = H, **b** R = *n*-Pr, **c** R = *n*-Bu; **6a–c** R^1 = H, **a** R = H, **b** R = *n*-Pr, **c** R = *n*-Bu; **7**, **8 a**, **d** R = H, **b**, **e** R = *n*-Pr, **c**, **f** R = *n*-Bu; **7a–c** R^1 = Et, **d–f** R^1 = *n*-Bu; **8 a–c** $R^1 + R^1 = (CH_2)_5$, **d–f** $R^1 + R^1 = (CH_2)_2O(CH_2)_2$

The sulfonic acids **5a-c** were synthesized in high yields (Table 1) by hydrolysis of the corresponding 6-sulfonyl chlorides **3a-c**. It was established that the rate of hydrolysis depended on the substituent R. For example, if it was sufficient for conversion of the sulfonyl chloride **3a** (R =H) into the sulfonic acid **5a** to heat the reaction mixture for 2 h, hydrolysis of compounds **3b,c** (**b** R = *n*-Pr, **c** R = *n*-Bu) required 4 and 6 h respectively.

The sulfonic acids **5a-c** were easily converted into the corresponding chlorosulfonyl derivatives **3a-c** in almost quantitative yields by treatment with chlorosulfonic acid.

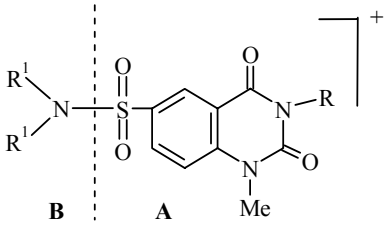
The reactions of compounds **3a-c** with ammonia, aliphatic and cyclic amines occurred readily and did not depend on the substituent R. Treatment of the sulfonyl chlorides **3a-c** with a concentrated aqueous solution of ammonia led to the corresponding 6-sulfamidoquinazoline-2,4-diones **6a-c**. On reaction of compounds **3a-c** with aliphatic amines in the presence of triethylamine at room temperature N,N-dialkylamides of 2,4-dioxo-6-sulfonic acids **7a-f** were formed and with piperidine and morpholine the N-piperidino- and N-morpholino-substituted amides **8a-f** of the same acids respectively were formed.

The compositions and structures of compounds **3**, **5-8** were confirmed by IR and ^{1}H NMR spectroscopy, mass spectrometry, and the results of elemental analysis.

In the IR spectra of compounds **3**, **5-8** there are bands characteristic of absorptions of asymmetric and symmetric vibrations of the SO_2 group in the 1100-1400 cm^{-1} region. In the case of the sulfonic acids **5a-c** there are also bands for the absorption of the stretching of the S-O group (600-700 cm^{-1} (Table 2).

In the mass spectra of the quinazolinediones **3**, **5-8** there are peaks of the molecular ions and fragments which completely confirm the proposed structure. Independent of the nature of the substituent R and the character of the amide substituent, these spectra show a uniform fragmentation with rupture of the SO_2-$N(R^1)_2$ bond and the formation of fragments **A** [M^+-$N(R^1)_2$] and **B** [$N(R^1)_2$].

It should be noted that in the case of compounds **6a-c** and **8a-c** the molecular ion M^+ is the maximum peak, whereas in the compounds **7a-f** and **8d-f** it is the peak for fragment A. In the case of fragmentation the sulfonic chloride **3a** with no substituent at position 3, rupture of the S-Cl bond occurs whereas in the alkylated derivatives **3b,c** the 3-R substituent is lost.



6–8

TABLE 1. Physicochemical Characteristics of the Compounds Synthesized, **3**, **5-8**

Compound	Empirical formula	Found, % / Calculated, %	mp °C (solvent for recrystallization)	Yield, %
3a	$C_9H_7ClN_2O_4S$	9.87 / 10.20	208-210 (heptane)	86*
3b	$C_{12}H_{13}ClN_2O_4S$	9.15 / 8.84	136-138 (hexane)	88*
3c	$C_{13}H_{15}ClN_2O_4S$	8.26 / 8.47	128-130 (benzene)	94*
5a	$C_9H_8N_2O_5S$	11.25 / 10.93	314-316 (water)	96
5b	$C_{12}H_{14}N_2O_5S$	9.12 / 9.39	220-222 (water)	88
5c	$C_{13}H_{16}N_2O_5S$	9.22 / 8.97	113–115 (water)	85
6a	$C_9H_9N_3O_4S$	16.21 / 16.47	338-340 (ethanol)	41
6b	$C_{12}H_{15}N_3O_4S$	13.85 / 14.14	264-266 (aqueous ethanol)	76
6c	$C_{13}H_{17}N_3O_4S$	13.11 / 13.50	212-214 (aqueous ethanol)	86
7a	$C_{13}H_{17}N_3O_4S$	13.69 / 13.50	304-306 (methanol)	89
7b	$C_{16}H_{23}N_3O_4S$	12.21 / 11.89	200-202 (methanol)	94
7c	$C_{17}H_{25}N_3O_4S$	11.68 / 11.44	162-164 (aqueous methanol)	83
7d	$C_{17}H_{25}N_3O_4S$	11.09 / 11.44	186-188 (ethanol)	89
7e	$C_{20}H_{31}N_3O_4S$	10.58 / 10.26	202-204 (aqueous methanol)	90
7f	$C_{21}H_{33}N_3O_4S$	10.23 / 9.92	180-182 (aqueous ethanol)	86
8a	$C_{14}H_{17}N_3O_4S$	12.77 / 13.00	320-322 (ethanol	90
8b	$C_{17}H_{23}N_3O_4S$	11.81 / 11.50	224-226 (aqueous methanol)	70
8c	$C_{18}H_{25}N_3O_4S$	10.83 / 11.08	204-206 (aqueous methanol)	87
8d	$C_{13}H_{15}N_3O_5S$	13.20 / 12.92	334-336 (benzene)	80
8e	$C_{16}H_{21}N_3O_5S$	11.68 / 11.44	194-196 (ethanol)	91
8f	$C_{17}H_{23}N_3O_5S$	10.74 / 11.02	170-172 (aqueous methanol)	98

* Yield by method A.

TABLE 2. Spectral Characteristics of Compounds **3**, **5-8**

Compound	IR spectrum, ν, cm^{-1}		Mass spectrum, *m/z* (I_{rel}, %)
	$SO_2(as)$, $SO_2(s)$, C–S	S–O, NH_2	
3a	1370, 1180, 710	—	274 $[M]^+$ (82) (for ^{35}Cl)
3b	1365, 1170, 720	—	316 $[M]^+$ (72)
3c	1375, 1175, 725	—	330 $[M]^+$ (78)
5a	1233, 1063, 744	650	256 $[M]^+$ (45)
5b	1245, 1026, 733	670	298 $[M]^+$ (47)
5c	1247, 1026, 728	675	312 $[M]^+$ (44)
6a	1338, 1164, 756	3565	255 $[M]^+$ (100)
6b	1345, 1164, 749	3370	297 $[M]^+$ (100)
6c	1365, 1168, 752	3360	311 $[M]^+$ (100)
7a	1366, 1175, 744	—	311 $[M]^+$ (13)
7b	1358, 1161, 748	—	353 $[M]^+$ (15)
7c	1338, 1161, 751	—	367 $[M]^+$ (20)
7d	1341, 1166, 752	—	367 $[M]^+$ (18)
7e	1340, 1160, 749	—	409 $[M]^+$ (19)
7f	1339, 1160, 750	—	423 $[M]^+$ (22)
8a	1342, 1166, 749	—	323 $[M]^+$ (100)
8b	1342, 1165, 747	—	365 $[M]^+$ (100)
8c	1342, 1166, 749	—	379 $[M]^+$ (100)
8d	1345, 1153, 743	—	325 $[M]^+$ (7)
8e	1348, 1165, 748	—	367 $[M]^+$ (10)
8f	1348, 1164, 748	—	381 $[M]^+$ (9)

In the ^1H NMR spectra of compounds **3**, **5-8** (Table 3) there are characteristic signals of the protons of the quinazoline unit: the H-5 doublet at 8.13-8.34 (^3J = 2.2-2.3 Hz), a doublet of doublets for H-7 at 7.92-8.04 (^3J = 8.6-9.0 and ^4J = 2.2-2.3 Hz) and also a doublet for H-8 at 7.32-7.62 ppm (^3J = 8.6-9.0 Hz).The signal of the protons of the alkyl substituents R and R^1 appear at relatively strong field (0.46-3.57 ppm) and the proton of the NH group at weak field (11.66-11.83 ppm).

EXPERIMENTAL

IR spectra of Nujol mulls were recorded on a Perkin-Elmer 2000 Fourier spectrometer, ^1H NMR spectra of CD_3COOD solutions with TMS as internal standard on Unity 400^+ (400 MHz) machine. Mass spectra were recorded on a Kratos MS-30 machine with direct insertion into the ion source (energy of ionization 70eV). The course of reactions and purity of the compounds synthesized were monitored by TLC on Silufol UV-254 strips with a 10:1 benzene-acetone eluant, and development with 1 g $KMnO_4$ in 4ml H_2SO_4 and 96 ml H_2O.

1-Methylquinqzoline-2,4-dione (1). Sodium cyanate (0.91 g, 14 mmol) in water (18 ml) was added to a solution of N-methylanthranilic acid (**4**) (1.51 g, 10 mmol) and acetic acid (0.1 ml) in water (53 ml) with stirring. The temperature of the reaction mixture reached 40°C and NaOH (11.68 g, 292 mmol) was added in portions, the reaction temperature reaching 75°C. Stirring was continued without cooling for 4 h, after which the crystals were filtered off and dissolved in boiling water (30 ml). The solution was carefully acidified with ~50% H_2SO_4 to pH 1-2. The precipitated crystals were filtered off, washed with water and recrystallized from 50% MeCOOH to give compound **1** (1.47 g, 84%); mp 276-278°C (mp 277-279°C [9]).

3-Alkyl-1-methylqunazoline-2,4-diones 2a,b. An alkyl iodide (15 mmol) was added to a mixture of compound **1** (1.76 g, 10 mmol), a solution of NaOH (2 g, 50 mmol) in water (20 ml), tetrabutylammonium bromide (1.28, 4 mmol) and benzene (40 ml). The reaction mixture was heated to 60°C and held at this

TABLE 3. ^{1}H NMR Spectra of Compounds **3**, **5-8**

Com-pound	^{1}H NMR spectrum, δ, ppm (*J*, Hz)
1	2
3a	11.86 (1H, s, NH); 8.26 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.95 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.6, H-7); 7.40 (1H, d, $J_{8,7}$ = 8.6, H-8); 3.44 (3H, s, 1-CH_3)
3b	8.29 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.96 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.6, H-7); 7.35 (1H, d, $J_{8,7}$ = 8.6, H-8); 3.95 (2H, t, *J* = 7.2, 3-C<u>H</u>$_2$CH$_2$CH$_3$); 3.51 (3H, s, 1-CH_3); 1.64 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 0.87 (3H, t, *J* = 7.2, 3-CH$_2$CH$_2$C<u>H</u>$_3$)
3c	8.25 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.92 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.6, H-7); 7.40 (1H, d, $J_{8,7}$ = 8.6, H-8); 3.90-3.96 (2H, m, 3-C<u>H</u>$_2$C$_3$H$_7$); 3.50 (3H, s, 1-CH_3); 1.55 (2H, m, 3-CH$_2$C<u>H</u>$_2$C$_2$H$_5$); 1.31 (2H, m, 3-C$_2$H$_4$C<u>H</u>$_2$CH$_3$); 0.90 (3H, m, 3-C$_3$H$_6$C<u>H</u>$_3$)
5a	11.67 (1H, s, NH); 8.19 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.95 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.31 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.35 (3H, s, 1-CH_3)
5b	8.21 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.96 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.32 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.97 (2H, t, *J* = 7.2, 3-C<u>H</u>$_2$CH$_2$CH$_3$); 3.37 (3H, s, 1-CH_3); 1.69 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 0.89 (3H, t, *J* = 7.2, 3-CH$_2$CH$_2$C<u>H</u>$_3$)
5c	8.20 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.95 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.32 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.91–3.97 (2H, m, 3-C<u>H</u>$_2$C$_3$H$_7$); 3.37 (3H, s, 1-CH_3); 1.57 (2H, m, 3-CH$_2$C<u>H</u>$_2$C$_2$H$_5$); 1.32 (2H, m, 3-C$_2$H$_4$C<u>H</u>$_2$CH$_3$); 0.91 (3H, m, 3-C$_3$H$_6$C<u>H</u>$_3$)
6a	11.66 (1H, br. s, NH); 8.34 (1H, d, $J_{5,7}$ = 2.2, H-5); 8.04 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.54 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.41 (3H, s, 1-CH_3)
6b	8.32 (1H, d, $J_{5,7}$ = 2.2, H-5); 8.03 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.55 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.96 (2H, t, *J* = 7.2, 3-C<u>H</u>$_2$CH$_2$CH$_3$); 3.42 (3H, s, 1-CH_3); 1.70 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 0.90 (3H, t, *J* = 7.2, 3-CH$_2$CH$_2$C<u>H</u>$_3$)
6c	8.31 (1H, d, $J_{5,7}$ = 2.2, H-5); 8.01 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.9, H-7); 7.53 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.90-3.97 (2H, m, 3-C<u>H</u>$_2$C$_3$H$_7$); 3.41 (3H, s, 1-CH_3); 1.58 (2H, m, 3-CH$_2$C<u>H</u>$_2$C$_2$H$_5$); 1.31 (2H, m, 3-C$_2$H$_4$C<u>H</u>$_2$CH$_3$); 0.90 (3H, m, 3-C$_3$H$_6$C<u>H</u>$_3$)
7a	11.79 (1H, s, NH); 8.19 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.02 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.54 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.41 (3H, s, 1-CH_3); 2.45 (4H, q, *J* = 6.9, N(C<u>H</u>$_2$CH$_3$)$_2$); 1.00 (6H, t, *J* = 7.2, N(CH$_2$C<u>H</u>$_3$)$_2$
7b	8.27 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.02 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.55 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.86 (2H, t, *J* = 3.6, 3-C<u>H</u>$_2$C$_2$H$_5$); 3.48 (3H, s, 1-CH_3); 2.45 (4H, m, N(C<u>H</u>$_2$)$_2$); 1.56 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 1.02 0.84 (3H, t, *J* = 7.1, 3-C$_2$H$_4$C<u>H</u>$_3$); 1.01 (6H, t, *J* = 7.3, N(CH$_2$C<u>H</u>$_3$)$_2$)
7c	8.27 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.02 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.55 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.87-3.91 (2H, m, 3-C<u>H</u>$_2$C$_3$H$_7$); 3.48 (3H, s, 1-CH_3); 2.44 (4H, q, *J* = 7.3, N(C<u>H</u>$_2$)$_2$); 1.51-1.54 (2H, m, 3-CH$_2$C<u>H</u>$_2$C$_2$H$_5$); 1.29 (2H, m, 3-C$_2$H$_4$C<u>H</u>$_2$CH$_3$); 1.02 (6H, t, *J* = 7.3, N(CH$_2$C<u>H</u>$_3$)$_2$);
7d	11.8 (1H, s, NH); 8.18 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.03 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 9.0, H-7); 7.54 (1H, d, $J_{8,7}$=9.0, H-8); 3.41 (3H, s, 1-CH_3); 3.01 (4H, m, N(C<u>H</u>$_2$)$_2$); 1.32-1.44 (4H, m, N(CH$_2$C<u>H</u>$_2$)$_2$); 0.95-1.24 (4H, m, N(C$_2$H$_4$C<u>H</u>$_2$)$_2$); 0.78-0.84 (6H, m, N(C$_3$H$_6$C<u>H</u>$_3$)$_2$)
7e	8.26 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.02 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.55 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.88 (2H, t, *J* = 7.3, 3-C<u>H</u>$_2$C$_2$H$_5$); 3.49 (3H, s, 1-CH_3); 3.02-3.22 (4H, m, N(C<u>H</u>$_2$)$_2$); 1.56 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 1.50-1.65 (4H, m, N(CH$_2$C<u>H</u>$_2$)$_2$); 1.35-1.45 (4H, m, N(C$_2$H$_4$C<u>H</u>$_2$)$_2$); 1.23 (3H, t, *J* = 7.1, 3-C$_2$H$_4$C<u>H</u>$_3$); 0.75-0.85 (6H, m, N(C$_3$H$_6$C<u>H</u>$_3$)$_2$)
7f	8.28 (1H, d, $J_{5,7}$ = 2.3, H-5); 8.02 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.55 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.85-3.95 (2H, m, 3-C<u>H</u>$_2$C$_3$H$_7$); 3.49 (3H, s, 1-CH_3); 3.01-3.10 (4H, m, N(C<u>H</u>$_2$)$_2$); 1.50–1.60 (2H, m, 3-CH$_2$C<u>H</u>$_2$C$_2$H$_5$); 1.36-1.46 (4H, m, N(CH$_2$C<u>H</u>$_2$)$_2$); 1.31 (2H, m, 3-C$_2$H$_4$C<u>H</u>$_2$CH$_3$); 1.16-1.28 (4H, m, N(C$_2$H$_4$C<u>H</u>$_2$)$_2$); 0.90 (3H, m, 3-C$_3$H$_6$C<u>H</u>$_3$); 0.76-0.86 (6H, m, N(C$_3$H$_6$C<u>H</u>$_3$)$_2$)
8a	11.83 (1H, s, NH); 8.13 (1H, d, $J_{5,7}$ = 2.3, H-5); 7.96 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.7, H-7); 7.57 (1H, d, $J_{8,7}$ = 8.7, H-8); 3.59 (4H, t, *J* = 6.5, N(C<u>H</u>$_2$)$_2$); 3.42 (3H, s, 1-CH_3); 2.83 (4H, t, *J* = 6.9, N(CH$_2$C<u>H</u>$_2$)$_2$); 2.45 (2H, m, N(C$_2$H$_4$)$_2$C<u>H</u>$_2$)
8b	8.20 (1H, d, $J_{5,7}$ = 2.3, H-5); 7.97 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.9, H-7); 7.59 (1H, d, $J_{8,7}$ = 8.9, H-8); 3.85 (2H, t, *J* = 7.2, 3-C<u>H</u>$_2$C$_2$H$_5$); 3.49 (3H, s, 1-CH_3); 2.86 (4H, t, *J* = 6.5, N(C<u>H</u>$_2$)$_2$); 2.45 (4H, t, *J* = 6.9, N(CH$_2$C<u>H</u>$_2$)$_2$); 1.62 (2H, m, 3-CH$_2$C<u>H</u>$_2$CH$_3$); 1.52 (2H, m, N(C$_2$H$_4$)$_2$C<u>H</u>$_2$); 0.85 (3H, t, *J* = 7.2, 3-C$_2$H$_4$C<u>H</u>$_3$)

TABLE 3 (continued)

1	2
8c	8.21 (1H, d, $J_{5,7}$ = 2.3, H-5); 7.95 (1H, dd, $J_{7,5}$ = 2.3, $J_{7,8}$ = 8.7, H-7); 7.58 (1H, d, $J_{8,7}$ = 8.7, H-8); 3.90 (2H, t, J = 7.3, 3-C$\underline{H}_2$C$_3$H$_7$); 3.49 (3H, s, 1-CH$_3$); 2.95 (4H, t, J = 6.5, N(C$\underline{H}_2$)$_2$); 1.57 (2H, m, 3-CH$_2$C$\underline{H}_2$C$_2$H$_5$); 1.44 (4H, dt, J = 6.9, N(CH$_2$C$\underline{H}_2$)$_2$); 1.31 (2H, m, 3-C$_2$H$_4$C$\underline{H}_2$CH$_3$); 1.25 (2H, m, N(C$_2$H$_4$)$_2$C$\underline{H}_2$); 0.93 (3H, t, J = 7.1, 3-C$_3$H$_6$C$\underline{H}_3$)
8d	11.83 (1H, s, NH); 8.14 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.97 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.8, H-7); 7.6 (1H, d, $J_{8,7}$ = 8.8, H-8); 3.58 (4H, t, J = 6.0, N(C$\underline{H}_2$)$_2$); 3.42 (3H, s, 1-CH$_3$); 2.82 (4H, t, J = 8.0, O(CH$_2$)$_2$)
8e	8.22 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.97 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.8, H-7); 7.62 (1H, d, $J_{8,7}$ = 8.8, H-8); 3.87 (2H, t, J = 7.2, 3-C$\underline{H}_2$C$_2$H$_5$); 3.58 (4H, t, J = 6.0, N(C$\underline{H}_2$)$_2$); 3.50 (3H, s, 1-CH$_3$); 2.82 (4H, t, J = 8.0, O(CH$_2$)$_2$); 1.55 (2H, q, J = 5.7, 3-CH$_2$C$\underline{H}_2$CH$_3$); 0.85 (3H, t, J = 7.2, 3-C$_2$H$_4$C$\underline{H}_3$)
8f	8.20 (1H, d, $J_{5,7}$ = 2.2, H-5); 7.96 (1H, dd, $J_{7,5}$ = 2.2, $J_{7,8}$ = 8.8, H-7); 7.61 (1H, d, $J_{8,7}$ = 8.8, H-8); 3.88 (2H, t, J = 7.3, 3-C$\underline{H}_2$C$_3$H$_7$); 3.58 (4H, t, J = 6.0, N(C$\underline{H}_2$)$_2$); 3.49 (3H, s, 1-CH$_3$); 2.84 (4H, t, J = 8.0, O(CH$_2$)$_2$); 1.52 (2H, m, 3-CH$_2$C$\underline{H}_2$C$_2$H$_5$); 1.26 (2H, m, 3-C$_2$H$_4$C$\underline{H}_2$CH$_3$); 0.85 (3H, t, J = 7.1, 3-C$_3$H$_6$C$\underline{H}_3$)

temperature for 6 h. After cooling, the organic layer was separated, washed with water until neutral and dried over Na_2SO_4. The benzene was evaporated and the residue was recrystallized. Product **2a** (1.98g 91%); mp 90-92°C (91-93° [9]) was obtained from *n*-propyl iodide, and compound **2b** (1.9 g, 82%); mp 70-72°C (71-73° [9]) from *n*-butyl iodide.

6-Chlorosulfonyl-1-methylquinazoline-2,4-dione (3a) and 3-Alkyl-6-chlorosulfonyl-1-methylquinazolin-2,4-diones 3b,c. Method A**.** Compounds **1** or **2a,b** (10 mmol) were added in portions to chlorosulfonic acid (5.83 g, 50 mmol) at 5-10°C with stirring at such a rate that the solution temperature did not exceed 15°C. The reaction mixture was then heated to 50-60°C, kept at this temperature for 6 h and then poured over broken ice. The precipitate of **3** was filtered off, washed with water, and crystallized.

Compounds **3a-c** were also obtained from the sulfoacids **5a-c** by method B (see below).

1-Methyl-2,4-dioxoquinazoline-6-sulfoacid (5a) and 3-Alkyl-1-methyl-2,4-dioxoquinazolinesulfoacids 5b,c. A mixture of compound **3** (10 mmol) and water (20 ml) was boiled for 2 h, the solvent was partially removed, the precipitate of product **5** was filtered off and recrystallized from water.

The sulfoacids **5a-c** were treated with chlorosulfonic acid by method B to give compounds **3a-c**.

Method B. Sulfoacids **5** (10 mmol) were added in portions to chlorosulfonic acid (2.33 g, 20 mmol), cooled to 0°C, at such a rate that the temperature did not exceed 10°C. The mixture was heated to 50-60°C, kept at this temperature for 2 h and poured onto broken ice. The precipitate of compound **3** was filtered off, washed with water, and recrystallized. The yields of compounds **3a-c** were close to quantitative. Samples of compounds **3a-c**, obtained by methods A and B were identical (there was no depression of the melting point with mixed probes).

1-Methyl-6-sulfamidoquinazoline-2,4-dione (6a) and 3-Alkyl-1-methyl-6-sulfamidoquinazoline-2,4-diones 6b,c. A mixture of compound **3** (10 mmol) and concentrated ammonia solution (100 ml) was heated with stirring on a boiling water bath for 6 h then kept at room temperature for 16 h. The precipitate of compound **6** was filtered off and recrystallized.

N,N-Diethyl- and N,N-Dibutylamides of 1-Methyl-2,4-dioxoquinazoline-6-sulfoacids 7a,d and 3-Alkyl-1-methyl-2,4-dioxoquinazoline-6-sulfoacids 7b,c,e,f. Diethyl- or dibutylamine (10 mmol) and triethylamine (1.01 g, 10 mmol) in acetone (15 ml) was added dropwise to a solution of compound **3** (10 mmol) in acetone (30 ml). The reaction mixture was stirred at room temperature for 2 h, the acetone was then evaporated, and water (100 ml) was added to the residue. The precipitate of compound **7** was filtered off and recrystallized.

N-Piperidides and N-Morpholides of 1-Methyl-2,4-dioxoquinazoline-6-sulfoacids 8a,d and 3-Alkyl-1-methyl2,4-dioxoquinazoline-6-sulfoacids 8b,c,e,f were synthesized analogously to the dialkylamides **7a-f** using piperidine (10 mmol) or morpholine (10 mmol) in place of the dialkylamines.

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