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NOVEL HETEROCYCLIC SYSTEMS BASED ON 8-R-4,5-DIHYDRO-4,4-DIMETHYL-[1,2]DITHIOLO[3,4-*c*]QUINOLINE-1-THIONES

S. M. Medvedeva, E. V. Leshcheva, Kh. S. Shikhaliev, and A. S. Solov'ev

Based on the reaction of 8-R-4,5-dihydro-4,4-dimethyl[1,2]dithiolo[3,4-c]quinoline-1-thiones with oxalyl chloride followed by the reactions of 1,3-dipolar cycloaddition and diene synthesis with participation of acetylenedicarboxylic acid dimethyl ester, we have developed approaches to synthesis of novel polycondensed heterocyclic systems: [1,2]dithiolo[3,4-c]pyrrolo[3,2,1-ij]quinoline-4,5-dione, 6-(1,3-dithiol-2-ylidene)-1,2-dioxo-5-thioxo-7H-pyrrolo[3,2,1-ij]quinoline and 4,5-dioxospiro(pyrrolo)-[3,2,1-ij]thiopyrano[2,3-c]quinoline-11,2'-[1,3]dithiole.

Keywords: acetylenedicarboxylic acid dimethyl ester, 4,5-dioxospiro(pyrrolo)[3,2,1-*ij*]thiopyrano-[2,3-*c*]quinoline-11,2'-[1,3]dithiole, 6-(1,3-dithiol-2-ylidene)-1,2-dioxo-5-thioxo-7H-pyrrolo[3,2,1-*ij*]-quinoline, [1,2]dithiolo[3,4-*c*]pyrrolo[3,2,1-*ij*]quinoline-4,5-dione, [1,2]dithiolo[3,4-*c*]quinoline-1-thione, oxalyl chloride.

Many substances with a broad spectrum of biological action have been observed among substituted 4,4-dimethyl[1,2]dithiolo[3,4-*c*]quinoline-1-thiones, and these compounds furthermore exhibit antioxidant activity and also are radical polymerization regulators [1, 2]. With the aim of obtaining novel polycondensed heterocyclic systems, we have continued work on further modification of these compounds.

We reported earlier [3] that acylation of 8-R-4,4-dimethyl-4,5-dihydro[1,2]dithiolo[3,4-*c*]quinoline-1-thiones **1a-c** by oxalyl chloride, as in the case of simple acyl chlorides [4], occurs exclusively at the nitrogen atom of the dihydroquinoline ring and is accompanied by spontaneous cyclization according to a Stolle reaction [5]. The best solvent in this case is absolute toluene, in which the process goes to completion within 1.5-2 h. The reaction does not require the use of Lewis acids, which are typically used as catalysts. This is possibly connected with the fact that the limiting step of the two-step Stolle reaction in the case of 8-R-4,4-dimethyl-4,5-dihydro[1,2]dithiolo[3,4-*c*]quinoline-1-thiones **1a-f** is the first acylation reaction, with formation of the corresponding intermediate chlorooxalyl amides **2a-f.**

As a result, derivatives of a novel condensed heterocyclic system were synthesized in good yields (60-80%): 2-R^1-3-R^2-7,7-dimethyl-10-thioxo-4,5,7,10-tetrahydro[1,2]dithiolo[3,4-*c*]pyrrolo[3,2,1-*ij*]quinoline-4,5-diones **3a-f** (Scheme 1).

Their structure is supported by the combination of IR, ^{1}H NMR, and mass spectral data. In the IR spectra of compounds **3a-f** (Table 1), the frequencies of the stretching vibrations of the thioketone group are observed in the 1230-1240 cm^{-1} region, and the vibrations of the two carbonyl groups of the isatin moiety are observed at 1740-1750 cm^{-1} and 1760-1770 cm^{-1}.

Voronezh State University, Voronezh 394006, Russia; e-mail: shikh@online.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 610-615, April, 2006. Original article submitted April 29, 2003; revision submitted February 6, 2006.

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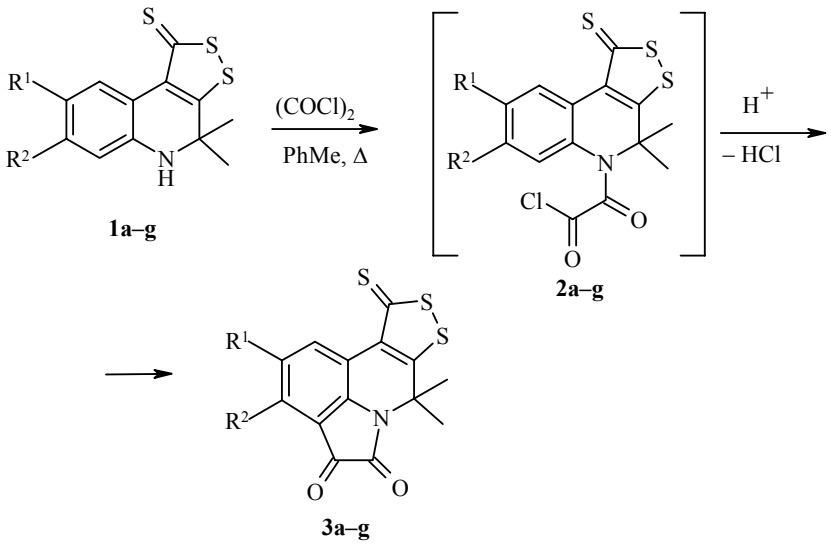
Scheme 1



1-3 a-d, **g** R^2 = H, **a** R^1 = H, **b** R^1 = Me, **c** R^1 = OMe, **d** R^1 = OEt, **e** R^1 = H, R^2 = Me, **f** R^1 = R^2 = Me; **g** R^1 = PhCOO

In the ^{1}H NMR spectra of dithiolopyrroloquinolines **3a-f** (Table 1), compared with the starting dithiolquinolines **1a-f** the signal from the N–H proton in the 5.5-6.2 ppm region is missing, while in the aromatic region we observe the characteristic set of signals reduced by 1 proton. The chemical shift of the $C_{(1)}$–H proton, which experiences the anisotropic effect of the adjacent thioketone group, is shifted further downfield, all the way down to values of 9.50 ppm.

The yields and characteristics of the synthesized compounds **3d-g** are given in Table 2.

TABLE 1. IR and ^{1}H NMR Spectra of Compounds **3a-g**

Com-pound	IR spectrum, ν, cm^{-1}			^{1}H NMR spectrum, δ, ppm (*J*, Hz)
	C=S	C(1)=O	C(2)=O	
3a	1235	1740	1770	2.13 (6H, s, $C(CH_3)_2$); 6.97 (1H, d, *J* = 7.1, 3-CH); 7.13 (1H, t, *J* = 7.1, 2-CH); 9.41 (1H, d, *J* = 7.1, 1-CH)
3b	1230	1745	1763	2.00 (6H, s, $C(CH_3)_2$); 2.39 (3H, s, 2-CH_3); 7.19 (1H, s, 3-CH); 9.43 (1H, s, 1-CH)
3c	1225	1748	1770	2.12 (6H, s, $C(CH_3)_2$); 3.82 (3H, s, 2-CH_3O); 7.05 (1H, s, 3-CH); 9.45 (1H, s, 1-CH)
3d	1230	1740	1765	1.25 (3H, t, *J* = 7.0, $OCH_2\underline{CH_3}$); 2.02 (6H, s, $C(CH_3)_2$); 4.25 (2H, q, *J* = 7.0, $O\underline{CH_2}CH_3$); 7.01 (1H, s, 3-CH); 9.40 (1H, s, 1-CH)
3e	1228	1745	1770	2.00 (6H, s, $C(CH_3)_2$); 2.32 (3H, s, 3-CH_3); 7.11 (1H, d, *J* = 7.2, 2-CH); 9.43 (1H, d, *J* = 7.2, 1-CH)
3f	1230	1748	1760	2.09 (6H, s, $C(CH_3)_2$); 2.28, 2.43 (6H, 2s, 2,3-$(CH_3)_2$); 9.45 (1H, s, 1-CH)
3g	1225	1740	1765	2.15 (6H, s, $C(CH_3)_2$); 7.55-8.30 (6H, m, arom.); 9.70 (1H, s, 1-CH)

TABLE 2. Characteristics and Yields of Compounds **3a-g**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	Yield, %
		C, %	H, %	N, %	M*		
3a	$C_{14}H_9NO_2S_3$	52.74 / 52.64	2.92 / 2.84	4.43 / 4.38	319 / 319.43	295-300	65
3b	$C_{15}H_{11}NO_2S_3$	54.17 / 54.03	3.45 / 3.33	4.30 / 4.20	333 / 333.46	254-256	74
3c	$C_{15}H_{11}NO_3S_3$	51.47 / 51.65	3.09 / 3.17	4.17 / 4.01	349 / 349.46	278-279	68
3d	$C_{16}H_{13}NO_3S_3$	52.95 / 52.87	3.56 / 3.61	3.72 / 3.85	363 / 363.49	270-272	62
3e	$C_{15}H_{11}NO_2S_3$	54.11 / 54.03	3.27 / 3.33	4.29 / 4.20	333 / 333.46	305-307	58
3f	$C_{16}H_{13}NO_2S_3$	55.46 / 55.31	3.89 / 3.77	4.12 / 4.03	347 / 347.49	233-235	70
3g	$C_{21}H_{13}NO_4S_3$	57.31 / 57.39	3.06 / 2.98	3.23 / 3.19	439 / 439.52	268-270	74

* Mass spectrometrically.

The presence of a 1,2-dithiolethione ring in the structure of the tetracyclic compounds **3a-g** obtained makes it possible to modify them further, in particular using the 1,3-dipolar cycloaddition reaction.

We have established that compounds **3a-f**, like the starting [1,2]dithiolo[3,4-*c*]quinoline-1-thiones **1a-f** [6], even at room temperature readily undergo a 1,3-dipolar cycloaddition reaction with acetylenedicarboxylic acid dimethyl ester (ADM). Due to the poor solubility of compounds **3a-f** and in order to accordingly avoid secondary reactions, the reaction was carried out in DMF.

As a result, we isolated derivatives of a novel heterocyclic system in moderate yields (40-50%): dimethyl 2-(8-R^1-9-R^2-4,4-dimethyl-1,2-dioxo-5-thioxo-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-*ij*]quinolin-6-ylidene)-1,3-dithiole-4,5-dicarboxylates **4a-f**.

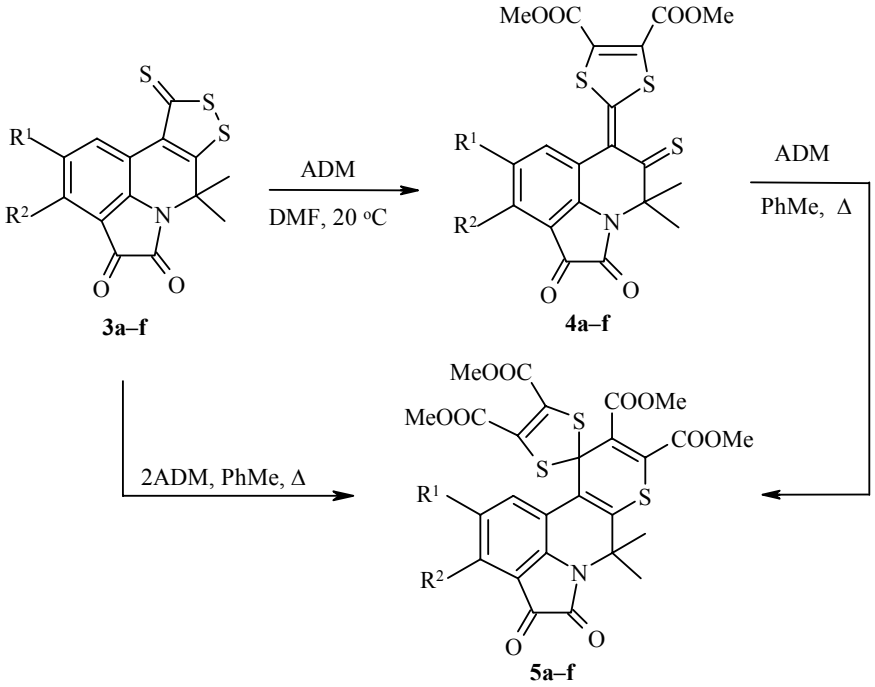
Carrying out the reaction at higher temperatures, as expected, leads to the appearance of one more competing product in addition to compounds **4a-f.** This product may be just the expected adduct from cycloaddition of one more ADM molecule to the diene system of products **4a-f**.

We have established that compounds **4a-f** react with the ADM molecule in a Diels–Alder reaction when the reagents are boiled in toluene. We can unambiguously assign the structure of a novel condensed heterocyclic system to the adducts formed in this case: dimethyl (2-R^1,3-R^2-4',5'-dimethoxycarbonyl-7,7-dimethyl-4,5-dioxo-4,5,7,11-tetrahydrospiro(pyrrolo)[3,2,1-*ij*]thiopyrano[2,3-*c*]quinoline-11,2'-[1,3]dithiole)-9,10-dicarboxylates **5a-f**. The latter are also obtained in one step by reaction of pyrrolo[3,2,1-*ij*]quinoline-4,5-diones **3a-f** with a two-fold excess of ADM in boiling toluene. In this case, the yields of the target products **5a-f** are practically the same in the first and second variants, and are rather high (60-80%) (Scheme 1).

In the ^{1}H NMR spectra of ylidenes **4a-f** (Table 3), compared with the spectra of starting 10-thioxoquinoline-4,5-diones **3a-f**, the chemical shifts of the aromatic protons return to the "normal" region, in the range from 7.0 ppm to 7.8 ppm, and in the 3.8-3.9 ppm region the chemical shifts of the methoxycarbonyl groups appear as two singlets.

In the ^{1}H NMR spectra of the bisadducts **5a-f** in the 3.8-3.9 ppm region, we already observe a multiplet of chemical shifts for the four methoxycarbonyl groups. Their magnetic nonequivalence is obviously explained by inversion of both the spiro-1,3-dithiole and the dihydrothiopyran rings. Table 4 gives the characteristics and yields of the synthesized compounds **4a-f** and **5a-f**.

Scheme 1



4, 5 a-d R^2 = H; **a** R^1 = H, **b** R^1 = Me, **c** R^1 = OMe, **d** R^1 = OEt, **e** R^1 = H, R^2 = Me, **f** R^1 = R^2 = Me

TABLE 3. ^{1}H NMR Spectra of Compounds **4a-f, 5a-f**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
4a	2.10 (6H, s, $C(CH_3)_2$); 3.81, 3.88 (6H, 2s, OCH_3); 6.99 (1H, d, *J* = 7.1, 3-CH); 7.15 (1H, t, *J* = 7.1, 2-CH); 7.71 (1H, d, *J* = 7.1, 1-CH)
4b	2.05 (6H, s, $C(CH_3)_2$); 2.33 (3H, s, 2-CH_3); 3.83, 3.90 (6H, 2s, OCH_3); 7.19 (1H, s, 3-CH); 7.63 (1H, s, 1-CH)
4c	2.12 (6H, s, $C(CH_3)_2$); 3.80, 3.82, 3.88 (9H, 3s, CH_3O); 7.05 (1H, s, 3-CH); 7.73 (1H, s, 1-CH)
4d	1.22 (3H, t, *J* = 7.0, $OCH_2\underline{CH_3}$); 2.02 (6H, s, $C(CH_3)_2$); 3.81, 3.88 (6H, 2s, OCH_3); 4.28 (2H, q, *J* = 7.0, $O\underline{CH_2}CH_3$); 7.01 (1H, s, 3-CH); 7.70 (1H, s, 1-CH)
4e	2.00 (6H, s, $C(CH_3)_2$); 2.35 (3H, s, 3-CH_3); 3.80, 3.86 (6H, 2s, OCH_3); 7.11 (1H, d, *J* = 7.2, 2-CH); 7.43 (1H, d, *J* = 7.2, 1-CH)
4f	2.09 (6H, s, $C(CH_3)_2$); 2.23, 2.40 (6H, 2s, 2,3-$(CH_3)_2$); 3.84, 3.90 (6H, 2s, OCH_3); 9.45 (1H, s, 1-CH)
5a	2.13 (6H, s, $C(CH_3)_2$); 3.8-3.9 (12H, m, OCH_3); 6.97 (1H, d, *J* = 7.0, 3-CH); 7.13 (1H, t, *J* = 7.0, 2-CH); 7.51 (1H, d, *J* = 7.0, 1-CH)
5b	2.05 (6H, s, $C(CH_3)_2$); 2.33 (3H, s, 2-CH_3); 3.8-3.9 (12H, m, OCH_3); 7.19 (1H, s, 3-CH); 7.43 (1H, s, 1-CH)
5c	2.15 (6H, s, $C(CH_3)_2$); 3.82-3.95 (15H, m, OCH_3); 7.05 (1H, s, 3-CH); 7.51 (1H, s, 1-CH)
5d	1.22 (3H, t, *J* = 7.0, $OCH_2\underline{CH_3}$); 2.09 (6H, s, $C(CH_3)_2$); 3.8-3.9 (12H, m, OCH_3); 4.20 (2H, m, $O\underline{CH_2}CH_3$); 7.01 (1H, s, 3-CH); 7.50 (1H, s, 1-CH)
5e	2.00 (6H, s, $C(CH_3)_2$); 2.30 (3H, s, 3-CH_3); 3.8-3.9 (12H, m, OCH_3); 7.11 (1H, d, *J* = 7.2, 2-CH); 7.47 (1H, d, *J* = 7.2, 1-CH)
5f	2.09 (6H, s, $C(CH_3)_2$); 2.26, 2.49 (6H, 2s, 2,3-$(CH_3)_2$); 3.8-3.9 (12H, m, OCH_3); 9.45 (1H, s, 1-CH)

TABLE 4. Characteristics and Yields of Synthesized Compounds **4a-f** and Adducts **5a-f**

Compound	Empirical formul	Found, % / Calculated, %				mp, °C	Yield, %
		C, %	H, %	N, %	M*		
4a	$C_{20}H_{15}NO_6S_3$	52.18 / 52.05	3.34 / 3.28	3.12 / 3.03	461 / 461.54	172-173	42
4b	$C_{21}H_{17}NO_6S_3$	53.18 / 53.04	3.72 / 3.60	2.87 / 2.95	475 / 475.57	184-186	53
4c	$C_{21}H_{17}NO_7S_3$	51.40 / 51.31	3.54 / 3.49	2.78 / 2.85	491 / 491.57	179-181	45
4d	$C_{22}H_{19}NO_7S_3$	52.37 / 52.26	3.87 / 3.79	2.84 / 2.77	505 / 505.60	173-174	50
4e	$C_{21}H_{17}NO_6S_3$	53.13 / 53.04	3.74 / 3.60	2.83 / 2.95	475 / 475.57	187-188	47
4f	$C_{22}H_{19}NO_6S_3$	54.10 / 53.97	4.03 / 3.91	2.91 / 2.86	489 / 489.60	182-183	40
5a	$C_{26}H_{21}NO_{10}S_3$	51.87 / 51.73	3.64 / 3.51	2.48 / 2.32	603 / 603.65	184-185	70
5b	$C_{27}H_{23}NO_{10}S_3$	52.61 / 52.50	3.81 / 3.75	2.34 / 2.27	617 / 617.68	228-230	65
5c	$C_{27}H_{23}NO_{11}S_3$	51.24 / 51.18	3.73 / 3.66	2.31 / 2.27	633 / 633.68	199-201	68
5d	$C_{28}H_{25}NO_{11}S_3$	52.03 / 51.92	3.77 / 3.89	2.24 / 2.16	647 / 647.71	210-211	62
5e	$C_{27}H_{23}NO_{10}S_3$	52.63 / 52.50	3.80 / 3.75	2.39 / 2.27	617 / 617.68	225-226	60
5f	$C_{28}H_{25}NO_{10}S_3$	53.37 / 53.24	3.89 / 3.96	2.36 / 2.22	631 / 631.71	289-290	72

* Mass spectrometrically.

EXPERIMENTAL

The course of the reaction and the purity of the substances obtained were monitored by TLC on Silufol UV-254 plates, with chloroform or ethyl acetate as the eluent. The IR spectra were taken on a Specord M-80 in nujol. The ^{1}H NMR spectra were taken on a Bruker AC-300 (300 MHz) in DMSO-d_6, internal standard TMS. The mass spectra were taken on an LKB-9000, ionizing electron energy 70 eV.

The starting [1,2]dithiolo[3,4-*c*]quinoline-1-thiones **1a-g** were obtained as described in [1].

2-R^1-R^2-7,7-Dimethyl-10-thioxo-4,5,7,10-tetrahydro[1,2]dithiolo[3,4-*c*]pyrrolo[3,2,1-*ij*]quinoline-4,5-diones 3a-g. A mixture of the corresponding [1,2]dithiolo[3,4-*c*]quinoline-1-thione **1a-f** (0.01 mol) and oxalyl chloride (0.011 mol) in absolute toluene (30 ml) was boiled for 1.5-2 h and then cooled down; the precipitate was filtered out and recrystallized from DMF.

Dimethyl 2-(8-R^1-9-R^2-4,4-Dimethyl-1,2-dioxo-5-thioxo-1,2,5,6-tetrahydro-4H-pyrrolo[3,2,1-*ij*]-quinolin-6-ylidene)-1,3-dithiole-4,5-dicarboxylates 4a-f. A mixture of the corresponding compound **3a-f** (0.01 mol) was dissolved in DMF (50 ml), ADM (0.01 mol) was added dropwise at room temperature, and the reaction mixture was allowed to stand overnight. When the reaction was complete (monitored by TLC), the reaction mixture was poured into water (200 ml), the precipitate was filtered out, dried, and recrystallized from dioxane.

Dimethyl (2-R^1-3-R^2-4',5'-Dimethoxycarbonyl-7,7-dimethyl-)-4,5-dioxo-4,5,7,11-tetrahydro-spiro(pyrrolo)[3,2,1-*ij*]thiopyrano[2,3-*c*]quinoline-11,2'-[1,3]dithiole)-9,10-dicarboxylates 5a-f. A. A mixture of the diene **4a-f** (0.01 mol) and ADM (0.01 mol) in toluene (30 ml) was boiled for 4-5 h, the toluene was distilled off under reduced pressure, and the residue was crystallized from dioxane.

B. A mixture of [1,2]dithiolo[3,4-*c*]quinoline-1-thione **3a-f** (0.01 mol) and ADM (0.02 mol) in toluene (30 ml) was boiled for 4-5 h, the toluene was distilled off under reduced pressure, and the residue was crystallized from dioxane.

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