SYNTHESIS OF DIHYDRO-1,3-THIAZINE DERIVATIVES. II*

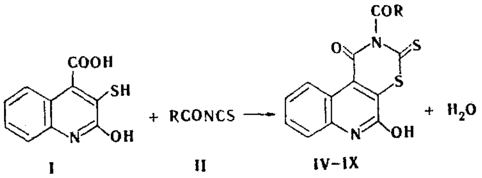
A. E. Kretov,† A. P. Momsenko,
A. S. Bespalyi, and Yu. A. Levin

UDC 547.831.88.9'869.07:542.953

1-Oxo-3-thioxo-5-hydroxy-2-acyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinolines were obtained for the first time by condensation of 2-hydroxy-3-mercaptoquinoline-4-carboxylic acid with acyl isothiocyanates. Alkyl and acyl isothiocyanates react with 1-methyl-2-oxo-3-mercapto-1,2-dihydroquinoline-4-carboxylic acid to give 1,5-dioxo-3-thioxo-2-alkyl (acyl)-6-methyl-2,3,5,6-tetrahydro-1H-1,3-thiazino[6,5-c]quinolines.

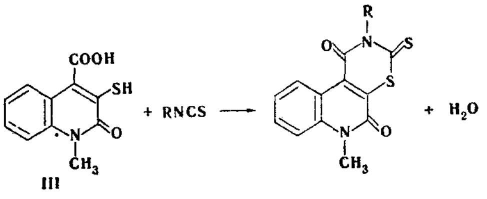
Alkyl isothiocyanates react readily with various mercaptocarboxylic acids to give thiazolidine and 1,3-thiazine derivatives [1-5]. The latter have found application as valuable accelerators for the vulcanization of rubber and as reagents for analytical chemistry [6, 7]. In this connection, it seemed of interest to study the previously undescribed reaction of acyl isothiocyanates with mercaptocarboxylic acids.

We found that the chief products in the condensation of acyl isothiocyanates (II) with 2-hydroxy-3-mercaptoquinoline-4-carboxylic acid (I) are 1-oxo-3-thioxo-5-hydroxy-2-acyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinolines (IV-IX):



IV $R=CH_3$; V $R=C_2H_5$; VI $R=n\text{-}C_3H_7$; VII $R=n\text{-}C_4H_9$; VIII $R=i\text{-}C_4H_9$;
IX $R=C_6H_5$

Another direction of the reaction can also be assumed: formation of a nitrogen–carbon bond proceeds at the hydroxyl group of acid I rather than at the carboxyl group. However, IV-IX do not dissolve in cold alkalis, and this indicates the absence of a carboxyl group. To confirm the scheme presented above, we studied the reaction of alkyl and acyl isothiocyanates with 1-methyl-2-oxo-3-mercapto-1,2-dihydroquinoline-4-carboxylic acid (III). It was shown that acid III reacts similarly with isothiocyanates II to give 1,5-dioxo-3-thioxo-2,3,5,6-tetrahydro-1H-1,3-thiazino[6,5-c]quinolines:



X $R=CH_2CH{=}CH_2$; XI $R=CH_2CH(CH_3){=}CH_2$; XII $R=C_6H_5$; XIII $R=COCH_3$;
XIV $R=COC_2H_5$; XV $R=COC_3H_7\text{-}n$; XVI $R=COC_6H_5$

---

*See [1] for communication I.

†Deceased.

Kursk Polytechnic Institute. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, pp. 641-643, May, 1973. Original article submitted January 11, 1972.

TABLE 1. 1-Oxo-3-thioxo-5-hydroxy-2-acyl-2,3-dihydro-(IV-IX) and 1,5-Dioxo-3-thioxo-2,3,5,6-tetrahydro-1H-1,3-thiazino[6,5-c]-quinolines (X-XVI)

Compound	Decomposition temp., °C	Empirical formula	Found, %		Calc., %		Yield, %
			N	S	N	S	
IV	225—227	$C_{13}H_8N_2O_3S_2$	9,4	20,8	9,2	21,0	73
V	215—220	$C_{14}H_{10}N_2O_3S_2$	9,0	20,4	8,8	20,1	58
VI	257—259	$C_{15}H_{12}N_2O_3S_2$	8,0	18,9	8,4	19,3	66
VII	295—298	$C_{16}H_{14}N_2O_3S_2$	8,2	18,8	8,1	18,5	60
VIII	238—240	$C_{16}H_{14}N_2O_3S_2$	8,4	18,9	8,1	18,5	72
IX	320—321	$C_{18}H_{10}N_2O_3S_2$	7,9	17,7	7,6	17,4	40
X	240—242	$C_{15}H_{12}N_2O_2S_2$	8,5	20,6	8,9	20,3	63
XI	235—237	$C_{16}H_{14}N_2O_2S_2$	8,4	18,9	8,5	19,4	56
XII	302—305	$C_{18}H_{12}N_2O_2S_2$	7,9	17,9	8,0	18,2	75
XIII	228—230	$C_{14}H_{10}N_2O_3S_2$	8,9	20,2	8,8	20,0	68
XIV	236—238	$C_{15}H_{12}N_2O_3S_2$	8,6	19,0	8,5	19,3	59
XV	250—253	$C_{16}H_{14}N_2O_3S_2$	8,1	18,1	8,1	18,5	65
XVI	300—302	$C_{18}H_{12}N_2O_3S_2$	7,8	16,5	7,4	16,9	47

The IR spectra of VI-IX contain intense absorption bands at 1690-1770 cm^{-1}, which can be assigned to the stretching vibrations of the C = O group. According to [8], the bands at 1340-1360 cm^{-1} should apparently be assigned to the stretching vibrations of the thio keto group (C = S). The interpretation of the absorption bands of the $N-\underset{|}{C}=S$ group at 1450-1470 cm^{-1} is complicated, since absorption bands characteristic for the deformation and stretching vibrations of the quinoline ring [9] also appear in this region. Absorption bands at 1600, 1500, 1440, 1300, 1240, and 1200 cm^{-1} are observed for the latter. The spectra of VI and IX contain absorption bands at 3170-3250 cm^{-1}, which are characteristic for the OH group and are absent in the spectra of X-XVI. An absorption band at 1340 cm^{-1}, which is characteristic for the stretching vibrations of the thio keto group, is detected in the spectra of X-XVI. Absorption bands that are characteristic for the quinoline ring appear at 1600, 1570, 1260, 1220, and 1200 cm^{-1}, along with a band at 1680 cm^{-1}, which is characteristic for the stretching vibrations of the C = O group.

Concentrated acids and alkalis cleave the thiazine ring of IV-XVI to give acids I and III. When IV is oxidized with hydrogen peroxide in acetic acid, the sulfur in the thio keto group is replaced by oxygen to give 1,3-dioxo-5-hydroxy-2-acetyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (XVIII). Compounds X-XVI are similarly oxidized. More prolonged heating during the oxidation also leads to cleavage of the thiazine ring to give acids I and III.

EXPERIMENTAL

The spectra of potassium bromide pellets of the investigated compounds (3% concentrations) were measured with a UR-10 spectrometer with KBr, NaCl, and LiF prisms.

1-Oxo-3-thioxo-5-hydroxy-2-acetyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (IV). A mixture of 11.5 g (0.05 mole) of acid I and 7.1 g (0.07 mole) of acetyl isothiocyanate in 20 ml of dioxane was heated on a boiling-water bath for 5 h, after which the mixture was allowed to stand for 24 h. The precipitated IV was removed by filtration and washed with ether. The filtrate was diluted with sodium bicarbonate solution, and another certain quantity of the same substance was isolated. Recrystallization from aqueous dioxane gave a brown powder. Compounds V-IX (see Table 1) were similarly obtained.

1,5-Dioxo-3-thioxo-2-allyl-6-methyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (X). A mixture of 4.7 g (0.02 mole) of acid III, 3 ml (0.03 mole) of allyl isothiocyanate, and 10 ml of dioxane was heated on a boiling-water bath for 3-3.5 h, after which it was allowed to stand for 24 h. The precipitated X was separated and washed with ether, and the filtrate was diluted with bicarbonate solution to give an additional amount of the same substance. Crystallization from dioxane gave shiny cherry-colored leaflets.

Compounds XI-XVI (see Table 1) were similarly obtained.

Compounds IV-XVI were obtained as colored solids. They were soluble in pyridine, dimethylformamide, and dioxane, less soluble in alcohol, and insoluble in benzene, ether, and water.

Hydrolysis of 1-Oxo-3-thioxo-5-hydroxy-2-isovaleryl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (VIII). A 2.8-g sample of VIII was heated in 10 ml of 20% sodium hydroxide on a boiling-water bath for 1 h, after which the mixture was cooled and acidified with hydrochloric acid to give 1.2 g (70%) of acid I, which was identified by a mixed-melting-point determination. The filtrate was steam-distilled, and the distillate yielded 0.7 g (85%) of isovaleric acid. Compounds IV-XVI were similarly hydrolyzed.

1,3-Dioxo-5-hydroxy-2-acetyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (XVII). A 2-g sample of IV was heated with 5 ml of acetic acid and 10 ml of dioxane up to the boiling point, and 7 ml of 30% hydrogen peroxide was added. A vigorous reaction began after a few seconds, and all of the solid dissolved. The solution was cooled and diluted with 100 ml of water, and the precipitated XVII was removed by filtration to give 1.54 g (81%) of light-brown crystals (from aqueous dioxane) with mp 195-197°. Found: N 9.6; S 11.4%. $C_{13}H_8N_2O_4S$. Calculated: N 9.7; S 11.1%.

Compounds V-XVI were similarly oxidized. Oxidation of X gave 1,3,5-trioxo-2-allyl-5-methyl-2,3-dihydro-1H-1,3-thiazino[6,5-c]dihydroquinoline (XVIII). The yield was 1.6 g (84%). Crystallization from dioxane gave a red powder with mp 200°. Found: N 9.1; S 10.9%. $C_{15}H_{12}N_2O_3S$. Calculated: N 9.3; S 10.6%.

LITERATURE CITED

1. A. E. Kretov, A. P. Momsenko, A. S. Bespalyi, and Yu. A. Levin, Khim. Geterotsikl. Soedin., 99 (1968).
2. R. Andreasch and A. Zipser, Montash., 24, 499 (1903).
3. R. Andreasch and A. Zipser, Monatsh., 25, 159 (1904).
4. R. Andreasch and A. Zipser, Monatsh., 26, 1191 (1905).
5. A. E. Kretov, A. S. Bespalyi, Yu. A. Levin, and A. P. Momsenko, Khim. Geterotsikl. Soedin., 1053 (1967).
6. C. Granacher and C. Kouniniotis, Ber., 60, 1021 (1927).
7. A. P. Momsenko and M. A. Shashkin, Trudy Kurskogo Politekhn. Instit., 1, 94 (1968).
8. L. Bellamy, IR Spectra of Complex Molecules [Russian translation], Inostr. Lit., Moscow (1957), pp. 310, 413.
9. L. I. Arestov and A. A. Shamshurin, Khim. Geterotsikl. Soedin., 288, 292 (1968).