# SYNTHESIS OF DIHYDRO-1,3-THIAZINE DERIVATIVES. III*

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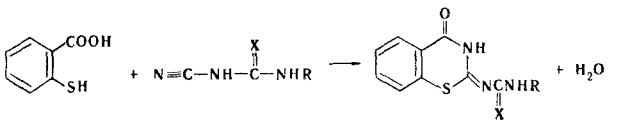
2-Carbamoylimino- and 2-thiocarbamoylimino-4-oxo-3,4-dihydro-2H-benzo[e]-1,3-thiazine derivatives were obtained by condensation of thiosalicylic acid with 3-alkyl(aryl)-substituted cyanoureas and cyanothioureas. 2-Hydroxy-3-mercaptoquinoline-4-carboxylic acid reacts similarly.

2-Substituted 4-oxodihydrobenzo(naphtho)-1,3-thiazine derivatives were obtained by reaction of o-mercaptocarboxylic acids with cyanamide and its derivatives [1-3]. Compounds of this type are of definite interest since they have fungicidal action and are also effective antioxidants for cured rubbers [4, 5].

In the present research, we have studied the reaction of thiosalicylic acid (I) and 2-hydroxy-3-mercaptoquinoline-4-carboxylic acid (II) with various cyano derivatives. Acid I reacts with 3-alkyl(aryl)-substituted cyanoureas and cyanothioureas to give 2-substituted 4-oxo-3,4-dihydro-2H-benzo[e]-1,3-thiazine (III-VII):



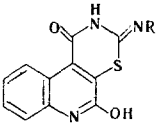
I III-VII

III X=O, R=$C_6H_5$; IV X=O, R=α-$C_{10}H_7$; V X=O, R=$CH_3$; VI X=S, R=$CH_2$—CH=$CH_2$; VII X=S, R=$C_6H_5$

Condensation of acid I with 1,6-bis(cyanocarbamoylimino)hexane gave 1,6-bis(4-oxo-2,3,4-dihydro-2H-benzo[e]-1,3-thiazinyl-2-carbamoylimino)hexane (VIII).

When III-VIII are heated with dilute hydrochloric acid, the group in the 2 position is replaced by oxygen. The resulting 2,4-dioxo-2,3,4-dihydro-2H-benzo[e]-1,3-thiazine (IX) is then hydrolyzed to acid I. The thiazine ring is cleaved during alkaline hydrolysis to give the salt of acid I.

3-Substituted 1-oxo-5-hydroxy-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinolines (X-XV) are obtained in the condensation of acid II with cyanamide, cyanourea, and 3-alkyl(aryl)-substituted cyanoureas.



X-XV

X R=H; XI R=$CONH_2$; XII R=$CONHC_6H_5$; XIII R=$CONHC_{10}H_7$-α; XIV R=$CSNHCH_3$; XV R=$CSNHC_6H_5$

When X-XV are heated with dilute hydrochloric acid or alkali, the thiazine ring is cleaved to give the starting acid (II).

*See [1] for communication II.

†Deceased.

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TABLE 1. 2-Substituted 4-Oxo-3,4-dihydro-2H-benzo[e]-1,3-thiazines (III-IX) and 3-Substituted 1-Oxo-5-hydroxy-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinolines (X-XV)

| Compound | Decomposition temp., °C | Empirical formula | Found, % | | Calc., % | | Yield, % |
|---|---|---|---|---|---|---|---|
| | | | N | S | N | S | |
| III | 234 | $C_{15}H_{11}N_3O_2S$ | 13,8 | 10,8 | 14,2 | 10,8 | 36 |
| IV | 185 | $C_{10}H_9N_3OS_2$ | 16,5 | 12,5 | 16,7 | 12,8 | 44 |
| V | 175 | $C_{12}H_{11}N_3OS_2$ | 15,0 | 23,4 | 15,2 | 23,1 | 45 |
| VI | 277 | $C_{19}H_{11}N_3OS_2$ | 11,8 | 9,2 | 12,1 | 9,2 | 40 |
| VII | 203 | $C_{13}H_{11}N_3OS_2$ | 13,2 | 20,5 | 13,4 | 20,3 | 40 |
| VIII | 212 | $C_{24}H_{22}N_6O_4S_2$ | 16,2 | 12,2 | 16,0 | 12,2 | 64 |
| IX | 296 | $C_{11}H_7N_3O_2S$ | 17,5 | 13,5 | 17,1 | 13,1 | 51 |
| X | 300 | $C_{12}H_8N_4O_3S$ | 19,5 | 11,3 | 19,4 | 11,1 | 76 |
| XI | 256 | $C_{11}H_{12}N_4O_3S$ | 16,6 | 8,9 | 16,5 | 9,1 | 65 |
| XII | 236 | $C_{22}H_{15}N_4O_3S$ | 13,7 | 7,5 | 13,5 | 7,7 | 45 |
| XIII | 312 | $C_{13}H_{10}N_4O_2S_2$ | 17,8 | 19,9 | 17,6 | 19,1 | 40 |
| XIV | 260 | $C_{18}H_{12}N_4O_2S_2$ | 14,8 | 16,3 | 14,8 | 16,1 | 38 |

Dicyanamide could not be introduced into the condensation with II because of the low activity of the nitrile group.

## EXPERIMENTAL

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

2-Phenylcarbamoylimino-4-oxo-3,4-dihydro-2H-benzo[e]-1,3-thiazine (III). A 3.8-g (0.025 mole) sample of acid I, 4.6 g (0.025 mole) of the sodium salt of phenylcyanourea, 10 ml of water, and 3 ml of acetic acid were introduced into 25 ml of dimethylformamide (DMF), and the resulting solution was refluxed for 2 h. The DMF was removed by steam distillation, the solution was cooled, and the precipitated III was removed by filtration. The filtrate was acidified with hydrochloric acid, and another certain amount of the same compound was isolated. Crystallization from acetic acid gave colorless needles.

Compounds IV, V, and VIII (see Table 1) were similarly obtained.

The synthesized compounds are weakly colored substances that are soluble in acetic acid, pyridine, and DMF, and insoluble in alcohols and water.

2-Allylthiocarbamoylimino-4-oxobenzo-3,4-dihydro-2H-benzo[e]-1,3-thiazine (VI). An 8.2-g (0.05 mole) sample of the sodium salt of 3-allylcyanothiourea dissolved in 25 ml of water and 3 ml of acetic acid was added to a solution of 6.7 g (0.05 mole) of acid I in 50 ml of alcohol, and the mixture was heated on a boiling-water bath for 1 h. It was then cooled, and the precipitated VI was separated.

Compound VII was similarly obtained.

2,4-Dioxo-3,4-dihydro-2H-benzo[e]-1,3-thiazine (IX). A 3-g sample of VIII was added to 30 ml of acetic acid, 10 ml of concentrated hydrochloric acid was added, and the mixture was refluxed for 10 min. Water (50 ml) was added to the cooled reaction mass, and the precipitate was separated, washed with sodium bicarbonate solution, and dissolved in 1 N of alkali solution. Acidification with hydrochloric acid precipitated IX. Crystallization from alcohol gave 0.7 g (67%) of colorless crystals with mp 209-212°. The compound was identified by a mixed-melting-point determination [2].

Compounds III-VIII were similarly hydrolyzed.

1-Oxo-3-imino-5-hydroxy-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (X). A 1.29-g (0.03 mole) sample of fused cyanamide was added dropwise to a refluxing solution of 5.52 g (0.025 mole) of acid II in 25 ml of dioxane, after which the mixture was heated for 2.5 h, At the end of the reaction, the dioxane was removed by vacuum distillation on a water bath, the solution was cooled, and the precipitated X was separated. Water (100 ml) was added to the filtrate, and a certain amount of the same substance was precipitated. The product was purified by refluxing with activated charcoal in DMF.

1-Oxo-3-methylthiocarbamoylimino-5-hydroxy-2,3-dihydro-1H-1,3-thiazino[6,5-c]quinoline (XIV). A 6.9-g (0.06 mole) sample of the sodium salt of methylcyanothiourea and 50 ml of glacial acetic acid were added to a solution of 11.4 g (0.05 mole) of acid II in 40 ml of dioxane, and the mixture was heated at 105-110° for 4-4.5 h and allowed to stand for 24 h. The precipitated XIV was separated and reprecipitated from DMF.

Compounds XI-XIII and XV (see Table 1) were similarly obtained. The compounds obtained were hydrolyzed as described above.

Compounds X-XV were light-brown and soluble in pyridine, DMF, dioxane, and alcohols, and insoluble in benzene, ether, and water.

The IR spectra of XII and XV contained absorption bands characteristic for the quinoline ring at 1635, 1600, 1505, and 1415 $cm^{-1}$ and bands characteristic for the stretching vibrations of the C = O group at 1715-1720 $cm^{-1}$. The band at 3260 $cm^{-1}$ is, in all likelihood, due to the vibration of the ring NH bond, while the absorption band at 1330 $cm^{-1}$ should pertain to the C = S stretching vibrations [6].

## LITERATURE CITED


1. A. E. Kretov, A. P. Momsenko, A. S. Bespalyi, and Yu. A. Levin, Khim. Geterotsikl. Soedin., 641 (1973).
2. A. E. Kretov and A. S. Bespalyi, Zh. Obshch. Khim., 33, 213 (1963).
3. E. V. Vladzimirskaya, Zh. Obshch. Khim., 33, 3149 (1963).
4. A. S. Bespalyi, Master's Dissertation [in Russian], Dnepropetrovsk (1965).
5. E. V. Utlenko, Master's Dissertation [in Russian], Dnepropetrovsk (1968).
6. L. Bellamy, Infrared Spectra of Complex Molecules [Russian translation], Inostr. Lit., Moscow (1957).