5. K. V. Vatsuro and G. L. Mishchenko, Name Reactions in Organic Chemistry [in Russian], Moscow (1976), p. 180.
6. J. Berson, J. Am. Chem. Soc., 74, 358 (1952).
7. G. N. Dorofeenko, É. A. Zvezdina, M. P. Zhdanova, V. V. Derbenev, and E. S. Matskovskaya, Khim. Geterotsikl. Soedin., No. 8, 1036 (1974).
8. V. P. Mamaev and A. L. Vais, Khim. Geterotsikl. Soedin., No. 11, 1555 (1975).

ACTION OF ACIDIC AND ALKALINE AGENTS ON DIOXONAPHTHOFURAN DERIVATIVES

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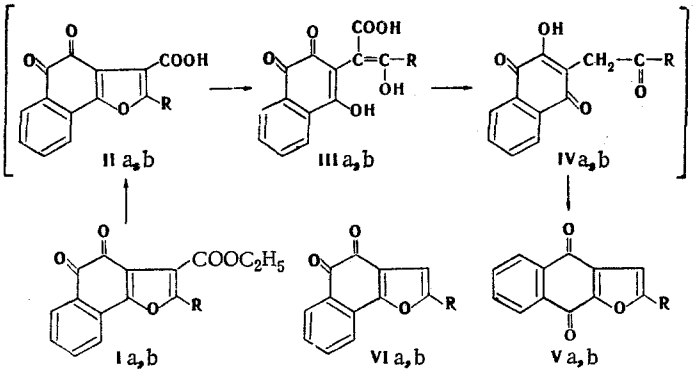
UDC 547.728.2:542.938

The action of sulfuric and polyphosphoric acids and sodium hydroxide on 3-carbethoxy-4,5-dioxonaphthofuran derivatives was studied. 2-Methyl- and 2-phenyl-3-carboxy-4,5-dioxonaphthofurans were obtained by the action of sulfuric acid on the indicated compounds. The action of alkali on 2-methyl- and 2-phenyl-3-carbethoxy-4,5-dioxonaphthofurans and 2-phenyl-4,9-dioxonaphthofurans leads to the formation of 2-hydroxy-3-acetonyl- and 2-hydroxy-3-phenacyl-1,4-dioxonaphthalenes.

In connection with the interest in diverse quinones as potential antiviral agents [1] we studied the transformations of quinones in the naphthofuran series. During an attempt to decarbethoxylate 3-carbethoxy-4,5-dioxonaphthofurans Ia, b via the method described for derivatives of other classes [2] we observed only hydrolysis of the ester group and the formation of the corresponding acids.

In an attempt to carry out decarbethoxylation by the action of polyphosphoric acid (PPA) on Ia, b, instead of the expected 2-methyl- and 2-phenyl-4,5-dioxonaphthofurans, we obtained the previously described [3] 4,9-dioxonaphthofuran derivatives Va, b. The reaction evidently proceeds through a step involving the formation of IIa, b. The formation of 4,9-dioxonaphthofurans Va, b can be explained by opening of the furan ring in IIa, b by decarboxylation of the resulting carboxylic acids IIIa, b and cyclization of the resulting intermediate hydroxynaphthoquinone derivatives IVa, b. We obtained hydroxynaphthoquinones IVa, b [3] by the action of alkali on 4,5-dioxonaphthofuran derivatives Ia, b. 4,9-Dioxonaphthofurans Va, b were isolated by the action of PPA on IVa, b at 170°C. When this reaction is carried out at 60°C, 4,5-dioxonaphthofuran derivatives VIb are formed along with Va, b.



I-V a $R=CH_3$; I-VI b $R=C_6H_5$

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 0009-3122/80/1606-0578$07.50

EXPERIMENTAL

The IR spectra of mineral oil suspensions of the compounds were recorded with a UR-10 spectrometer. The UV spectra of solutions of the compounds in alcohol were recorded with an EPS-3 spectrophotometer. The mass spectra were recorded with an MKh-1303 mass spectrometer with direct introduction of the samples into the ion source at an ionizing-electron energy of 30 eV. The purity of the products obtained was verified by thin-layer chromatography (TLC) on Silufol UV-254.

2-Methyl-3-carboxy-4,5-dioxonaphthofuran (IIa). A 2-ml sample of concentrated H_2SO_4 was added to a suspension of 2.84 g (1 mmole) of Ia [4] in 50 ml of acetic acid, and the mixture was refluxed for 1 h. A total of 25 ml of the solvent was then removed by distillation, and the concentrate was cooled and diluted with two volumes of water. The precipitate was removed by filtration to give 1.87 g (73%) of a product with mp 220°C (from methanol). Found %: C 65.7; H 3.2, M 256. $C_{14}H_8O_5$. Calculated %: C 65.6; H 3.1, M 256.

2-Phenyl-3-carboxy-4,5-dioxonaphthofuran (IIb). This compound was similarly obtained from 1.1 g (3 mmole) of Ib [4]. Workup gave 0.68 g (68%) of a product with mp 216°C (from methanol). Found %: C 71.4; H 3.4, M 318. $C_{19}H_{10}O_5$. Calculated %: C 71.7; H 3.2, M 318.

2-Methyl-4,9-dioxonaphthofuran (Va). A 0.95-g (3 mmole) sample of Ia was added with stirring at 100°C to PPA, prepared from 4 g of phosphoric anhydride and 8.4 ml of orthophosphoric acid, after which the temperature was raised to 170°C, and the mixture was maintained at this temperature for 15 min. It was then poured into ice water, and the aqueous mixture was neutralized with ammonium hydroxide. The resulting precipitate was removed by filtration, washed with water, dried, and chromatographed with a column filled with aluminum oxide (elution with chloroform). Workup gave 0.08 g (11%) with mp 246-247°C. IR spectrum: 1650 cm^{-1} (CO). Molecular weight 212. According to the data in [3], this compound had mp 246-247°C.

2-Phenyl-4,9-dioxonaphthofuran (Vb). A) This compound was obtained under conditions similar to those in the preceding experiment from 1.1 g (3 mmole) of Ib. Workup gave 0.57 g (63%) of a product with mp 251-253°C. IR spectrum: 1670 cm^{-1} (CO). Molecular weight 274. According to the data in [3], this compound had mp 252-253°C.

B) Reaction under conditions similar to those in the preparation of Va gave 0.65 g (67.3%) from 1.1 g (3 mmole) of IVb. No melting-point depression was observed for a mixture of samples obtained by methods A and B.

2-Hydroxy-3-acetonyl-1,4-dioxonaphthalene (IVa). A 10-ml sample of 2 N sodium hydroxide was added to a suspension of 1.42 g (5 mmole) of Ia in 10 ml of water, and the mixture was refluxed for 3 h. It was then cooled and made weakly acidic with dilute hydrochloric acid. The reaction product was extracted with chloroform. Purification was carried out with a column filled with silica gel (elution with chloroform) to give 0.40 g (36.5%) of a product with mp 176-177°C. IR spectrum: 1640, 1680, 1700 (CO); 3200 cm^{-1} (OH). UV spectrum, λ_{max} (log ε): 252 (4.29), and 278 nm (4.26). Molecular weight 230. According to the data in [3], this compound had mp 176.5-177.5°C.

2-Hydroxy-3-phenacyl-1,4-dioxonaphthalene (IVb). A) This compound was obtained under conditions similar to those in the preceding experiment from 1.72 g (5 mmole) of Ib. Workup gave 0.79 g (54%) of a product with mp 179-180°C. IR spectrum: 1660, 1635 (CO); 3200 cm^{-1} (OH). Molecular weight 292. According to the data in [3], this compound had mp 182-183°C.

B) A 0.27-g (1 mmole) sample of Vb was dissolved in 7.5 ml of DMF at 60°C, after which 2 ml of 40% sodium hydroxide solution was added, and the mixture was refluxed for 30 min. It was then cooled, and the unconverted Vb was removed by filtration. The filtrate was made weakly acid with concentrated hydrochloric acid, and the resulting precipitate was removed by filtration and recrystallized from methanol to give 0.11 g (37%) of product. No melting-point depression was observed for a mixture of samples obtained by methods A and B.

2-Phenyl-4,5-dioxonaphthofuran (VIb). A 0.56-g (2 mmole) sample of IVb was added at 60°C to PPA, prepared from 2.8 g of phosphoric anhydride and 5.6 ml of orthophosphoric acid, and the mixture was stirred at this temperature for 1 h. It was then poured into water, and the resulting precipitate was removed by filtration, washed with water, dried, and chromatographed with a column filled with aluminum oxide (elution with chloroform) to give 0.39 g

(62.3%) of Vb, with mp 251-253°C, and 0.16 g (29.6%) of VIb with mp 221-222°C. IR spectrum: 1670 cm^{-1} (CO). UV spectrum, λ_{max} (log ε): 224 (4.38), 226 (4.37), and 340 nm (4.47). Molecular weight 274. According to the data in [3], this compound had mp 219-220°C.

LITERATURE CITED

1. A. N. Grinev, Khim.-Farm. Zh., 4, 6 (1970).
2. A. N. Grinev, I. A. Zaitsev, N. K. Venevtseva, and A. P. Terent'ev, Zh. Obshch. Khim., 28, 1853 (1958).
3. E. F. Pratt and G. R. Rice, J. Am. Chem. Soc., 79, 5489 (1957).
4. A. N. Grinev, Shi-Tszyun' Khun', and A. P. Terent'ev, Zh. Obshch. Khim., 32, 1951 (1962).

DERIVATIVES OF CONDENSED PYRIMIDINE, PYRAZINE, AND PYRIDINE SYSTEMS. 39.* SYNTHESIS AND STRUCTURES OF 9-OXO-5H-6,7,8,9-TETRAHYDRO-PYRIMIDO[4,5-b][1,4]THIAZINES

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UDC 547.859'869.2.07

A number of 9-oxo-5H-6,7,8,9-tetrahydropyrimido[4,5-b][1,4]benzothiazines were synthesized by the reaction of 5-amino-6-mercaptopyrimidines with 2-halo-substituted cyclohexane-1,3-diones. It is demonstrated by means of the IR and UV spectra that these compounds exist primarily in the enamino ketone form.

Substances that display both antibacterial and pharmacological activity are found among pyrimido[5,4-b][1,4]benzothiazines and the isomeric pyrimido[4,5-b][1,4]benzothiazines [2-4]. No information regarding the synthesis and biological properties of pyrimidobenzothiazines that contain a partially or completely saturated benzene ring is available; in particular, no data on 6,7,8,9-tetrahydropyrimido[4,5-b][1,4]benzothiazines (I) are available.

In a continuation of our research [5] on the synthesis of pyrimido[4,5-b][1,4]thiazine derivatives we have shown that the reaction of 5-amino-6-mercaptopyrimidines (II) with 2-halo-substituted cyclohexane-1,3-diones (III) is a convenient method for the preparation of I [6]. The inertness of halogen in the 2 position of cyclohexane-1,3-diones, which are capable of enolization, is well known [7, 8]. In addition, it has been observed that the reaction of pyrimidine derivatives IIa-d, which contain substituents such as Cl, OCH_3, and $N(CH_3)_2$ in the 4 position, with 2-bromodimedone and 2-bromodihydroresorcinol proceeds under mild conditions and leads to the production of Ia-f in satisfactory yields (Table 1). We were unable to isolate any intermediates in this case. However, intermediate sulfide IV was obtained in the reaction of pyrimidine IIe with 2-bromodimedone under the conditions of the synthesis of Ia-f.

*See [1] for communication 38.

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 755-760, June, 1980. Original article submitted March 15, 1979; revision submitted January 22, 1980.

0009-3122/80/1606-0580$07.50