temperature and diluted with ether. The precipitated crystals were washed successively with glacial acetic acid and ether to give 5.2 g (53%) of snow-white crystals of II with mp 165°C (from glacial acetic acid). IR spectrum: 1830 (C=O); 1740 (O==C==O); 1610, 1530 (O==C==N); 1100 cm⁻¹ (C=O). Found: C 40.6; H 5.7; Cl 11.0; N 4.3%. C₁₁H₁₇Cl₁NO₈. Calculated: C 40.3; H 5.5; Cl 10.8; N 4.3%.

LITERATURE CITED

RESEARCH ON AMINOMETHYLENE DERIVATIVES OF AZOLES.
24.* CYCLIZATION OF THIOHIPPURIC ACID IN THE PRESENCE OF THE VILSMEIER REAGENT

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It is shown that, in contrast to hippuric acid, thiohippuric acid reacts with dimethylformamide in the presence of phosphorus oxychloride to give three compounds, viz., 2-phenyl-4-dimethylaminomethylene-5-thiazolone, 2-phenyl-4-dimethylamino-methyleneoxazole-5-thione, and 2-phenyl-4-formyl-5-chlorothiazole. The pathways of their formation are discussed. The structures of the compounds obtained and the transformations of 2-phenyl-4-formyl-5-chlorothiazole were studied. 2-Phenyl-4-formyl-5-hydroxy(mercapto)thiazoles and their methyl derivatives, as well as 2-phenyl-4-dimethylaminomethylenethiazole-5-thione, were synthesized from the latter.

Hippuric acid readily undergoes cyclodehydration in the presence of N-methylformanilide and phosphorus oxychloride to 2-phenyl-5-oxazolone, which is then aminomethylated to give an aminomethylene derivative (I) [2]. The reaction of hippuric acid with the adduct from dimethylformamide (DMF) and phosphorus oxychloride proceeds similarly and leads to II.

We used thiohippuric acid to obtain 2-phenyl-4-dimethylaminomethylene-5-thiazolone (III) under the conditions of the formation of II. It was found that in this case one ob-

*See [1] for Communication 23.
tains three products, the ratio of which changes only slightly as a function of the reaction conditions. Chromatographic separation and identification of the resulting compounds showed that, in addition to the expected III, 2-phenyl-4-dimethylaminomethyleneoxazole-5-thione (IV) and 2-phenyl-4-formyl-5-chlorothiazole (V) are obtained. With respect to its properties, IV is identical to the substance obtained from 2-phenyl-4-formyl-5-mercaptooxazole and dimethylamine [3], whereas III is identical to the product of the reaction of 2-phenyl-5-thiazolone with the Vilsmeier reagent from DMF and phosphorus oxychloride. The presence of V in the reaction products is explained by chlorination of 2-phenyl-4-dimethylaminomethylene-5-thiazolone (III) with phosphorus oxychloride, as in the case of other similar compounds [4], and is confirmed by a specially designed experiment.

Thus cyclization of thiohippuric acid in the presence of DMF and phosphorus oxychloride leads to both thiazole and oxazole derivatives in an approximately equal ratio. The production of oxazole derivative IV under the conditions used is evidently associated with recycling of 2-phenyl-5-thiazolone to 2-phenyloxazole-5-thione, which then undergoes aminof ormation:

- [Chemical structure diagram]

It has been noted that if previously prepared 2-phenyl-5-thiazolone or its hydrobromide are subjected to aminof ormation [5], only a thiazole derivative (III) is obtained. Instead of the hydrobromide, it is more convenient to use the hydrochloride, which is obtained by cyclization of thiohippuric acid with phosphorus trichloride; in this case the reaction can be carried out either up to the formation of III or in one step to give 2-phenyl-4-formyl-5-chlorothiazole (V). The chlorine atom in the latter compound is easily replaced by hydroxy, methoxy, and mercapto groups to give the corresponding derivatives (VI–VIII). Compounds IX and X are obtained by reaction of VIII with methyl iodide and dimethylamine:

- [Chemical structure diagram]

Two approximately equally intense absorption bands of C=O, C=N, and C=C bonds are observed in the IR spectrum of II, just as in the case of I [6], and this indicates the existence of Z and E stereoisomers. The conversion to the corresponding thione (IV) is accompanied by a change in the ratio of the intensities of the bands of the vibrations of these groups, evidently in the direction of the E isomer as a consequence of the large size of the sulfur atom as compared with the oxygen atom. The presence of two stereoisomers is also confirmed by the data from the electronic spectra of II and IV (Table I), in which two maxima are observed for the closely located absorption bands. Judging from the data from the IR and electronic spectra, the thiazole derivatives (III, X) also exist in the form of two stereoisomers with, however, predominance of the E isomer.

The corresponding thiazole derivatives are more deeply colored than the oxazole derivatives, and replacement of the carbonyl oxygen atom by sulfur leads to 40–50 nm deepening of the color in ethanol and 50–70 nm deepening of the color in heptane (Table I) as a consequence of the large contribution of the dipolar resonance hybrid for sulfur-containing compounds (IV, X).

EXPERIMENTAL

2-Phenyl-4-dimethylaminomethylene-5-oxazolone (II). A 1.8-g (10 mmole) sample of hippuric acid was added with stirring at -20°C to the adduct obtained from 4.4 g (60 mmole) of DMF