EXPERIMENTAL

Azlactone derivatives I-III were synthesized by the Erlenmeyer—Plochl reaction by condensation of the corresponding aromatic or heterocyclic aldehydes with hippuric acid or substituted hippuric acids in acetic anhydride in the presence of anhydrous sodium acetate [10, 11]. Azlactams IV were obtained by reaction of azlactones with ammonia in the presence of sodium carbonate under pressure for 30 h by the method in [12]. The characteristics of the new compounds are presented in Table 3.

The IR spectra of KBr pellets and solutions of the compounds in CCl_4 and $CHCl_3$ (c = 0.01 mole/liter) at 700-1900 cm^{-1} were recorded with a UR-20 spectrometer in cuvettes with NaCl windows and a layer thickness of 0.1 cm.

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REACTION OF 2-CYCLOPROPYLTHIOPHENES WITH MERCURIC ACETATE

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The reaction of 2-cyclopropylthiophene with mercuric acetate in methanol takes place only in the thiophene ring. 5-Methyl-2-cyclopropylthiophene undergoes mercuration in both the heterocyclic ring and in the three-carbon ring (the Levina reaction).

It is known [1, 2] that 4-substituted 2-nitrophenylcyclopropanes (Ia-c) readily undergo rearrangement ot the corresponding o-nitrosopropiophenones under the influence of concentrated sulfuric acid. At the same time, a similar rearrangement cannot be realized in the case of 3-nitro-2-cyclopropylthiophenes (IIa-c) even under more severe conditions [3].*

*Compounds IIa-c did not undergo rearrangement under the influence of sulfuric acid even at 20-25°C (the starting compounds were recovered), whereas nitrophenylcyclopropanes Ia-c undergo rearrangement at —30 to —10°C.

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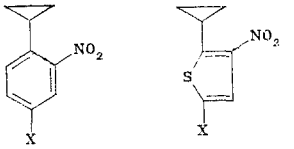


I a-c II a-c

I, II a X=Br; b X=Ac; c X=CH_3

It is important to note that neither rearrangement nor disruption of the three-carbon ring occurred in the case of cyclopropylthiophenes IIa-c under the severe conditions used.

Whereas the hindrance to realization of the rearrangement of 3-nitro-2-cyclopropylthiophenes (IIa-c) under the influence of sulfuric acid can be explained by the absence of nucleophilic assistance of the o-nitro groups in opening of the cyclopropane ring [4] due to an increase in the distance between the nitro group and the cyclopropyl ring, it is not so easy to explain the general resistance of the three-carbon ring to the action of concentrated sulfuric acid.

One of the possible explanations of the increased stability of the small ring in substituted nitrothiophenes IIa-c may evidently be associated with protonation of the thiophene ring under the rearrangement conditions. For example, it is known [5] that both thiophene itself and alkylthiophenes are capable of forming such stable σ complexes with protic acids (of the $HAlCl_4$ type) that these complexes can exist for a long time in solutions at 20°C. In all likelihood, under the conditions of sulfuric acid isomerization used in the case of o-nitrophenylcyclopropanes Ia-c, thiophenes IIa-c are protonated in the heterocyclic ring considerably more readily than in the cyclopropane ring,* and this promotes retention of the latter under the adopted conditions.

This assumption, incidentally, is confirmed by data on the behavior of phenyl- and thienylcyclopropanes when they are treated with 75% sulfuric acid. Thus it has been shown [7] that the action of 75% sulfuric acid on phenylcyclopropane at 20°C converts it virtually quantitatively to a mixture of dimeric hydrocarbons, the formation of which is initiated by opening of the cyclopropane ring. Under the same conditions, as specially demonstrated in the present research, 2-cyclopropylthiophene — a heteroanalog of phenylcyclopropane — undergoes 70% sulfonation in the heterocyclic ring, and 30% of the starting compound is recovered unchanged.†

This result shows, first of all, that the thiophene ring in 2-cyclopropylthiophene is more active than the phenyl ring in phenylcyclopropane in electrophilic reactions and, second, that protonation, which is necessary for cleavage of the three-carbon ring in the starting compound, either does not occur or the protonated small ring is resistant to opening under the adopted reaction conditions.

In connection with the data discussed above it seemed of interest to study the behavior of cyclopropylthiophenes in reactions with other electrophilic reagents under conditions for which the small ring in phenylcyclopropanes also is opened.

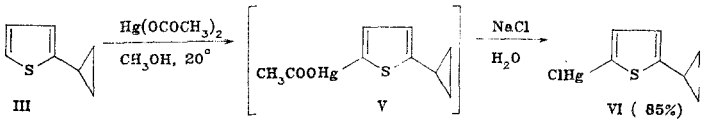
In conformity with the formulated problem we studied the reaction of 2-cyclopropyl- and 5-methyl-2-cyclopropylthiophenes (III, IV) with mercuric acetate.

It is known that structural analogs of cyclopropylthiophenes III and IV, viz., phenylcyclopropane and p-tolylcyclopropane, readily undergo the Levina reaction under the influence of mercuric acetate to give derivatives of γ-mercurated alcohols or the alcohols themselves; products of mercuration of the phenyl ring are not formed in this case. For example, the reaction of the indicated hydrocarbons with mercuric acetate in methanol led exclusively to 1-methoxy-1-aryl-3-mercuriacetates [8, 9].

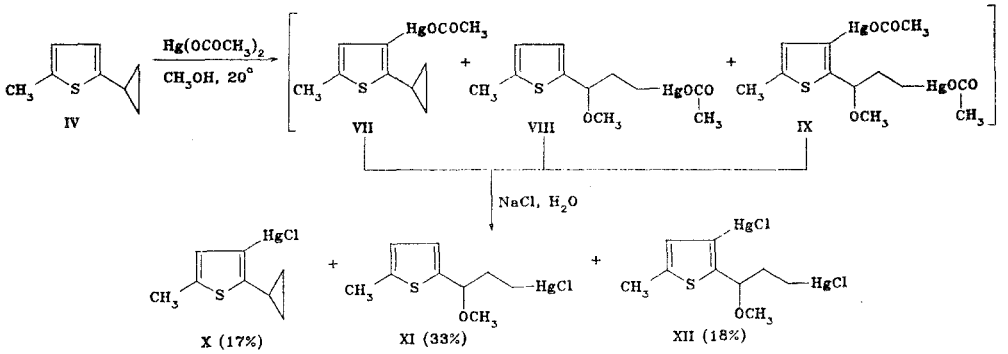
We found that only 5-acetoxymercuri-2-cyclopropylthiophene (V) is formed from 2-cyclopropylthiophene (III) under the same conditions; complete conversion of the starting substrate does not occur even after 120 h, and ∿20% of cyclopropylthiophene III is recovered from the reaction mixture.

*It has been proved that opening of the cyclopropane ring under the influence of acids occurs through its prior protonation [6].

†This reaction was carried out only qualitatively; it was intended to obtain dimeric compounds of 2-cyclopropylthiophene.



In contrast to thiophene III, the conversion of 5-methyl-2-cyclopropylthiophene (IV) under the influence of mercuric acetate under the same conditions does not proceed so selectively. In this case the addition of mercuric acetate and methanol fragments to the cyclopropane ring occurs in addition to mercuration in the thiophene ring; both thiophene IV and the initially formed product of its mercuration in the ring (VII) undergo addition in the three-membered ring in this case.

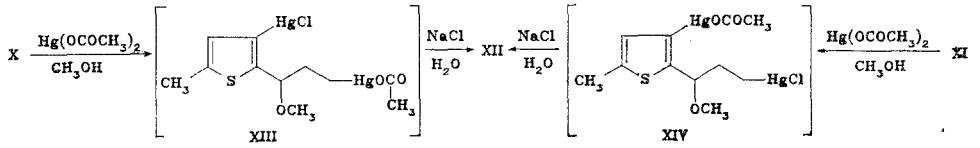


Just as in the preceding experiment, a significant amount (∿15%) of starting IV is recovered from the reaction mixture.

When the reaction temperature is raised to 65°C, the process is complete in 2.5-3 h, and the compositions of the reaction mixtures do not change in this case. However, it was noted that when mercuration is carried out with heating, primarily monomercuri derivatives VII and VIII are formed 2 h after the start of the reaction, and ∿1.5 times more VII than VIII is formed. The amount of bismercuri derivative IX increases when the reaction time is increased.

The structures of the compounds obtained as a result of mercuration were confirmed both by the results of physicochemical methods of investigation and by chemical transformations.

For example, we were able to prove that bismercuri derivative IX is formed from both VII and from adduct VIII during the transformation of substrate IV — treatment of individual mercurichlorides X and XI under the adopted mercuration conditions led primarily to bis-(mercurichloride) XII (in this case evidently through the corresponding acetoxymercuri derivatives XIII and XIV).



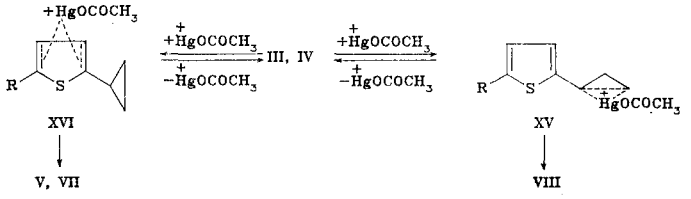
However, an attempt to realize bromodemercuration, which is often used to confirm the structures of organomercury compounds [10], by the action of bromine in chloroform was unsuccessful — even monosubstituted mercurihalides X and XI gave multicomponent mixtures, from which we were unable to isolate individual compounds.

Thus the three-carbon ring in thienylcyclopropanes proves to be considerably more resistant to the action of mercuric acetate than the three-carbon ring in phenylcyclopropanes.

It should be noted that this sort of resistance of the cyclopropane ring to the action of a mercurating agent is also observed for 1,2-diphenyl- and 1,2,3-triphenylcyclopropanes [11]; mercuration of the aromatic rings also occurs in this case. However, the reasons for this reaction pathway are evidently different for di- and polyphenylated cyclopropanes and for thienylcyclopropanes. In fact, whereas in the case of polyphenylcyclopropanes the resistance of the small ring to the action of mercuric acetate, as Shabarov and co-workers [11] validly assume, is due to an increase in the degree of conjugation of the small ring with the phenyl rings and the steric hindrance, created by the phenyl substituents relative

to the three-membered ring, to the formation of a π complex of mercuric acetate with the cyclopropane ring; these factors evidently do not have a decisive effect in the case of thienylcyclopropanes. In all likelihood, as a result of the higher π-donor character of the thiophene ring, the complex of cyclopropylthiophene with a mercury salt is primarily formed through the heterocyclic aromatic ring rather than through the small ring, as in the case of monophenylated cyclopropanes [12].

At the same time, the character of the substitution and the nature of the substituents in mercurated XI and XII indicate that they were formed from the corresponding 5-methyl-2-cyclopropylthiophenes (IV and VII) through mercurinium ions of the XV type* and that, consequently, complexes with the participation of the small ring can be formed in the mercuration of cyclopropylthiophenes. In this connection it must be assumed that equilibrium interconversions of complexes XV and XVI are realized under the reaction conditions.



III, V R=H; IV, VII, VIII R=CH_3

The formation of products of addition to the cyclopropane fragment in the reaction of 5-methyl-2-cyclopropylthiophene (IV) with mercuric acetate and the absence of side compounds in the transformation of 2-cyclopropylthiophene (III) indicate that electron-donor substituents in the thiophene ring facilitate the Levina reaction. This result is in agreement with the results obtained in the corresponding mercuration of substituted monophenylated cyclopropanes [12].

It is interesting that, in contrast to nitration [13], the mercuration of 2-cyclopropylthiophene (III) is a selective process that takes place in the α position of the thiophene ring.

EXPERIMENTAL

The PMR spectra of solutions of the compounds in CCl_4, $CDCl_3$, d_6-DMSO, and d_5-pyridine were recorded with a JNM-60 spectrometer with hexamethyldisiloxane as the internal standard.

2-Cyclopropylthiophene (III). This compound, with bp 60-61°C (9 mm), was obtained in 31% yield by the method described in [3]. 5-Methyl-2-cyclopropylthiophene (IV), with bp 74-75°C (15 mm), was synthesized in 28% yield by the method described in [14].

Reaction of 2-Cyclopropylthiophene (III) with Mercuric Acetate. A 2.7-g (8.5 mmole) sample of mercuric acetate was added to a solution of 1 g (8 mmole) of III in 50 ml of methanol, and the mixture was stirred at 20°C for 120 h. It was then poured into a saturated solution of NaCl (100 ml), and the reaction products were extracted with chloroform. The extract was dried with $MgSO_4$, the solvent was evaporated, and the residue (2.6 g) was chromatographed with a column packed with silica gel by successive elution with CCl_4 and CCl_4–$CHCl_3$ mixtures (4:1, 2:1, 1:1, 1:2, and 1:4, respectively) to give 0.2 g (19%) of 2-cyclopropylthiophene (III)† and 1.96 g (85%) of 2-cyclopropyl-5-chloromercurithiophene (VI) with mp 141-142°C (from benzene). PMR spectrum: 0.56-1.43 (m, 4H) and 2.03-2.57 ppm (m, 1H, cyclopropane ring protons) and 7.07 ppm (broad s, 2H, degenerate AB system, thiophene ring β protons). Found: C 23.4; H 2.0; Hg 55.6%. C_7H_7ClHgS. Calculated: C 23.4; H 2.0; Hg 55.8%.

Reaction of 5-Methyl-2-cyclopropylthiophene (IV) with Mercuric Acetate. A 5-g (15.6 mmole) sample of mercuric acetate was added to a solution of 2 g (14.5 mmole) of IV in 100 ml of methanol, and the mixture was stirred at 20°C for 120 h. It was then poured into a saturated solution of NaCl, and the mixture was extracted with chloroform–benzene (1:1).

*An alternative pathway for the formation of products of addition of mercuric acetate to the small ring — through prior ipso attack of the mercury-containing cation at the 5 position and subsequent opening of the small ring — is not acceptable in this case, since it should lead to mercuri derivatives with a different order of addition of the corresponding fragments.

†Identified from the PMR spectra of a sample of this product and a genuine sample.

The extract was dried with $MgSO_4$, the solvents were evaporated, and the residue (4.2 g) was chromatographed with a column packed with silica gel by means of the eluants indicated in the preceding experiment to give 0.3 g (15%) of starting IV (identified from comparison of the PMR spectra of this product and a genuine sample), 0.8 g (17%) of 5-methyl-2-cyclopropyl-3-chloromercurithiophene (X) [mp 87-88°C. PMR spectrum: 0.53-1.24 (m, 4H), and 1.77-2.31 (m, 1H, cyclopropane ring protons); 2.39 (s, 3H, CH_3); 6.57 ppm (s, 1H, thiophene ring β-H). Found: C 25.5; H 2.3; Hg 53.3%. C_8H_9ClHgS. Calculated: C 25.7; H 2.4; Hg 53.7%], 1.65 g (33%) of 1-(5-methyl-2-thienyl)-1-methoxy-3-chloromercuripropane (XI) [mp 78-79°C. PMR spectrum: 1.61-1.95 (m, 2H, $-CH_2-HgCl$); 1.99-2.33 (m, 2H, $-CH-CH_2-CH_2-$); 2.46 (m, 3H, CH_3); 3.25 (s, 3H, $-OCH_3$); 4.23 (t, 1H, $-CH-CH_2-CH_2-$); 6.57-6.86 ppm (m, 2H, thiophene ring β-H). Found: C 26.7; H 3.2; Hg 49.0%. $C_9H_{13}ClHgOS$. Calculated: C 26.7; H 3.2; Hg 49.4%], and 1.42 g (∿18%)* of 1-(5-methyl-3-chloromercuri-2-thienyl)-1-methoxy-3-chloromercuripropane (XII) with R_f 0.3 [silica gel, elution with benzene–acetone (30:1)] [PMR spectrum: 1.56-2.01 (m, 2H, $-CH_2-CH_2-HgCl$); 2.07-2.59 (m, 5H, $-CH-CH_2-CH_2$ and CH_3); 3.17 (s, 3H, OCH_3); 4.45 (t, 111, $-CH-CH_2-CH_2$); 6.92 ppm (broad s, 1H, thiophene ring β-H). The product was easily electrified. Found: C 17.6; H 1.9; Hg 60.6%. $C_9H_{12}Cl_2Hg_2OS$. Calculated: C 16.8; H 1.9; Hg 62.6%.

Reaction of 5-Methyl-2-cyclopropyl-3-chloromercurithiophene (X) with Mercuric Acetate. A 0.4-g (1.27 mmole) sample of mercuric acetate was dissolved in 30 ml of methanol, 0.5 g (1.3 mmole) of X in 15 ml of the same solvent was added to the solution, and the mixture was allowed to stand for 120 h. Workup by a method similar to that described above and chromatography with a column packed with silica gel gave 0.08 g (16%) of starting X and 0.51 g (71%) of bismercuri derivative XII, the physicochemical characteristics of which were in agreement with those for the sample obtained in the preceding experiment.

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*This substance was difficult to purify by crystallization or chromatography and contained XI as an impurity.