CATALYZED LIQUID-PHASE OXIDATION OF DIALKYLTHIOPHENES

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The oxidation of 3-methyl-2-ethylthiophene with molecular oxygen in glacial acetic acid in the presence of a cobalt-bromide catalyst was investigated. It was established that there is a dependence of the rate of oxidation of this compound on its concentration, on the catalyst (cobalt acetate) concentration, and on the initiator (NaBr) concentration. The principal oxidation products are 3-methyl-2-acetothienone (III) and 1-(3-methyl-2-thienyl)ethyl acetate, which were isolated and characterized. The reactivity of 3-methyl-2-ethylthiophene in the oxidation reaction is higher than that of 4-methyl-2-ethylthiophene.

Monoalkylthiophenes are readily oxidized by molecular oxygen in acetic acid with a cobalt-bromide catalyst [1, 2]. The oxidation process leads to the formation of carboxylic acids in the case of methylthiophenes and to ketones in the case of ethylthiophenes. Alcohols, aldehydes, and esters have been detected among the intermediates of the oxidation reaction. Continuing our study of the liquid-phase oxidation of thiophene derivatives we obtained some experimental data on the oxidation of dialkylthiophenes. We selected 3-methyl-2-ethylthiophene (I) and 4-methyl-2-ethylthiophene (II) as the subjects of our investigation.

The oxidation of the indicated compounds was carried out in glacial acetic acid at 70-95°C with oxygen at atmospheric pressure in the presence of divalent cobalt acetate in conjunction with added sodium bromide. The amounts of the catalyst (cobalt acetate) and the initiator (sodium bromide) were varied within the ranges, respectively, of $2 \cdot 10^{-2}$ to $1 \cdot 10^{-1}$ and $2.5 \cdot 10^{-3}$ to $2.5 \cdot 10^{-2}$ mole/liter. The volume fraction of thiophene I ranged from 2.5 to 40%.

The rate of oxidation was measured volumetrically from the degree of oxygen absorption. The quantitative percentages of the substances in the reaction products were determined by gas-liquid chromatography (GLC). The principal products of the oxidation of I are 3-methyl-2-acetothienone (III) and 1-(3-methyl-2-thienyl)ethyl acetate (IV). In addition, we detected 3-formyl-2-acetothienone (VII), which are probably side products or intermediates.

In the case of the absorption of 1 mole of O_2 per mole of I the process is, as a rule, slowed down or stopped completely at the step involving the formation of ketone III and ester IV. The accumulation in the mixture of ketone III and ester IV, as well as other oxygen-containing intermediates in the oxidation of thiophene I, evidently slows down the further development of the process. Ketone III and ester IV were isolated in pure form and identified. The very small percentages of the remaining substances and the extremely rapid resinification of some of them made it impossible to isolate them in pure form.

Virtually no oxygen absorption is observed in the case of oxidation of thiophenes I and II in the absence of added bromide. The introduction of bromide (NaBr) made it possible to carry out the oxidation process in one step without an induction period and at a rather high rate (Fig. 1). It is important to note that in the presence of bromide (NaBr) the rate of oxidation increases not only as the initiator concentration is increased but also as the catalyst (cobalt acetate) concentration is increased (Figs. 2 and 3).

The experimental data obtained made it possible to establish the reaction order, which was found to be 0.5 in NaBr, 1.0 in $Co(OAc)_2$, and 0.5 in $C_7H_{10}S$ (Figs. 2-4).

The curves of the accumulation of 3-methyl-2-acetothienone (III) and 1-(3-methyl-2-thienyl)ethyl acetate (IV) start from zero, whereas the sum of the rates of their formation

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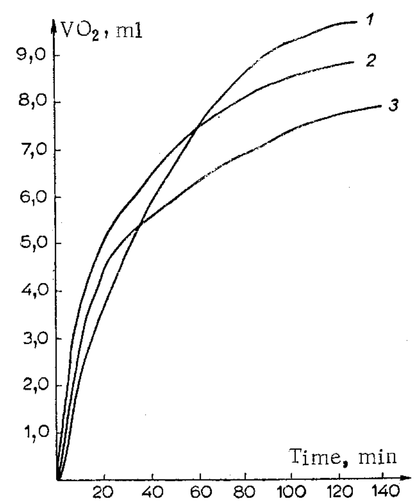

Fig. 1

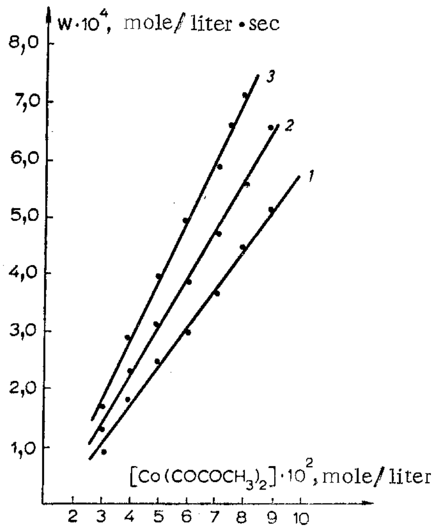

Fig. 2

Fig. 1. Kinetics of oxygen absorption during the oxidation of 3-methyl-2-ethylthiophene (0.195 mole/liter), 4-methyl-2-ethylthiophene (0.195 mole/liter), and 2-ethylthiophene (0.195 mole/liter) with $[Co(OCOCH_3)_2] = 8 \cdot 10^{-2}$ mole/liter and $[NaBr] = 1 \cdot 10^{-2}$ mole/liter at 90°C: 1) 2-ethylthiophene; 2) 3-methyl-2-ethylthiophene; 3) 4-methyl-2-ethylthiophene.

Fig. 2. Dependence of the rate of oxidation of 3-methyl-2-ethylthiophene (0.389 mole/liter) on the cobalt acetate concentration at 90°C for NaBr concentrations of $0.5 \cdot 10^{-2}$ (1), $1.0 \cdot 10^{-2}$ (2), and $1.5 \cdot 10^{-2}$ mole/liter (3).

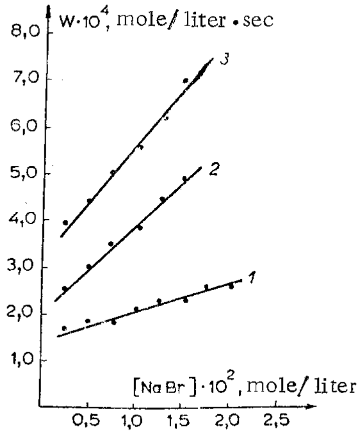

Fig. 3. Dependence of the rate of oxidation of 3-methyl-2-ethylthiophene (0.389 mole/liter) on the NaBr concentration at 90°C for $Co(OCOCH_3)_2$ concentrations of $4 \cdot 10^{-2}$ (1), $6 \cdot 10^{-2}$ (2), and $8 \cdot 10^{-2}$ mole/liter (3).

is equal to the rate of consumption of 3-methyl-2-ethylthiophene (I), and this constitutes indirect evidence for the parallel formation of the product (Fig. 5). Alcohol V formed as a result of the oxidation undergoes quantitative esterification and is contained in the final mixture in the form of the acetate. Virtually no oxidation of the methyl group of I is observed. The further oxidation of the methyl group of III under the reaction conditions is hindered by the effect of the electron-acceptor $COCH_3$ carbonyl group. However, in this case the high percentage in the reaction products of alcohol V, which ties up peroxide radi-

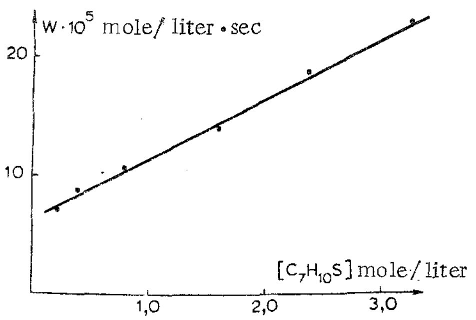

Fig. 4.

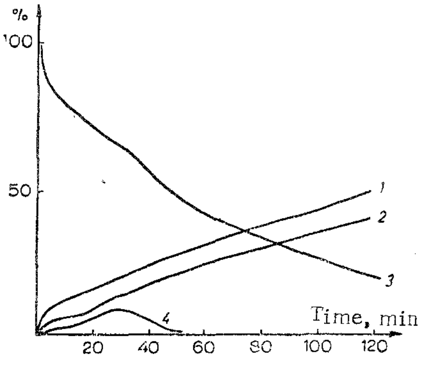

Fig. 5

Fig. 4. Dependence of the rate of oxidation of 3-methyl-2-ethylthiophene on its concentration for $[Co(OCOCH_3)_2] = 8 \cdot 10^{-2}$ and $[NaBr] = 1.55 \cdot 10^{-2}$ mole/liter.

Fig. 5. Rate of consumption of 3-methyl-2-ethylthiophene (0.195 mole/liter) and accumulation of the products of its oxidation at 90°C for $[Co(OCOCH_3)_2] = 8 \cdot 10^{-2}$ and $[NaBr] = 1 \cdot 10^{-2}$ mole/liter: 1) 1-(3-methyl-2-thienyl)ethyl acetate; 2) 3-methyl-2-acetothienone; 3) 3-methyl-2-ethylthiophene; 4) 1-(3-methyl-2-thienyl)-ethanol.

cals and breaks the oxidation chain, may also be of significance. This is confirmed by the fact that the addition of ketone III lowers the rate of oxidation significantly, while the addition of 1-(3-methyl-2-thienyl)ethanol (V) and its acetate completely suppresses the oxidation reaction. The presence in the products of oxidation of vinylthiophene VI, which are formed as a result of dehydration of alcohol V, reduces the degree of oxidation, as in the case of vinyltoluene [3]. It should be noted that ketone III under conditions similar to those in the oxidation of thiophene I is readily oxidized in the presence of a cobalt-bromide catalyst to give the corresponding keto acids. Under the same conditions, alcohol V and its acetate IV are oxidized with difficulty; only 0.1-0.15 mole of O_2 per mole of substance is absorbed after 3 h.

The reactivities of 3-methyl-2-ethylthiophene (I) and the previously investigated 2-ethylthiophene [1] differ only slightly (Fig. 1). The increase in the rate of oxidation of thiophene I in the initial step of the process as compared with 2-ethylthiophene is apparently explained by the effect of the electron-donor substituent (the CH_3 group). It is interesting to note the certain decrease in the oxidation rate on passing from 3-methyl-2-ethylthiophene (I) to 4-methyl-2-ethylthiophene (II). A decrease in the oxidation rate on passing from the ortho isomer to the meta isomer is also observed in the dialkylbenzene series [5] and is explained by the stability of the intermediate peroxide radical.

EXPERIMENTAL

The reaction products were subjected to chromatographic analysis with an LKhM-8MD chromatograph (model 5). The carrier-gas (helium) flow rate in all cases was 40 ml/min, the detectors were a G-26 catharometer and a flame-ionization device, and the stainless steel columns (300 by 0.3 cm) were filled with N-super Chromaton impregnated with SE-30 silicone elastomer (5%); the temperature-rise rate was 6 deg/min from 90 to 160°C. The IR spectra of the substances in CCl_4 were recorded with a UR-20 spectrometer.

Oxidation was carried out in a closed system with a gasometric apparatus by a previously described method [4]. The cobalt acetate, sodium bromide, and glacial acetic acid were purified by the method in [4].

The starting 3-methyl-2-ethylthiophene (I) had bp 161°C, d_4^{20} 0.9815, and n_D^{20} 1.5103 (bp 158-161°C and $n_D^{22.5}$ 1.5225 [6]). The 4-methyl-2-ethylthiophene (II) had bp 160-161°C and n_D^{20} 1.5204 (bp 160-161°C and $n_D^{22.5}$ 1.5218 [6]). The 2-ethylthiophene had bp 135-137°C and n_D^{20} 1.5120 (bp 135-136°C and n_D^{20} 1.5124 [7]).

<u>3-Methyl-2-acetothienone (III).</u> This compound was obtained by the method in [8]. A 19.6-g (0.2 mole) sample of 3-methyl-2-ethylthiophene was treated with 20.4 g (0.2 mole) of

acetic anhydride in the presence of 2 g of 85% orthophosphoric acid, as a result of which we obtained 76% of a mixture containing 80% 3-methyl-2-acetothienone and 20% 4-methyl-2-acetothienone. Distillation with a rectification column gave 17.2 g (65%) of 3-methyl-2-acetothienone with bp 77-78°C (3 mm) and n_D^{20} 1.5608 [bp 72-73°C (2 mm) and n_D^{20} 1.5618 [8]]. The 2,4-dinitrophenylhydrazone had mp 196-197°C (from ethanol), while the semicarbazone had mp 207-208.5°C.

1-(3-Methyl-2-thienyl)ethyl Acetate (IV). A 3.98-g (0.028 mole) sample of 1-(3-methyl-2-thienyl)ethanol (V) was treated with 5.71 g (0.057 mole) of acetic anhydride in 10 ml of pyridine, as a result of which we obtained IV, with bp 86-87°C (10 mm) and n_D^{20} 1.5146, in 64% yield. Found: C 59.1; H 6.0; S 17.4%. Calculated: C 59.0; H 6.0; S 17.5%.

1-(3-Methyl-2-thienyl)ethanol (V). This compound was obtained by reduction of ketone III with sodium borohydride in absolute methanol and had bp 83.5-85°C (5 mm) and n_D^{20} 1.5361. The phenylurethane had mp 85-87°C (from hexane). Found: C 59.3; H 7.0; S 22.4%. Calculated: C 59.2; H 7.0; S 22.5%.

3-Methyl-2-vinylthiophene (VI). This compound was obtained by the method in [9] by heating 1-(3-methyl-2-thienyl)ethanol (V) with fused KOH and had bp 71-72°C (10 mm) and n_D^{20} 1.5728. Found: C 67.5; H 6.6; S 25.7%. Calculated: C 67.8; H 6.5; S 25.8%.

3-Formyl-2-acetothienone (VII). This compound was obtained by the method in [10] and had mp 47-48°C (from benzene–hexane).

Isolation of 3-Methyl-2-acetothienone (III) and 1-(3-Methyl-2-thienyl)ethyl Acetate (IV) from the Products of Oxidation of 3-Methyl-2-ethylthiophene (I). A solution of 64 ml of cobalt acetate ($8 \cdot 10^{-2}$ mole/liter) in acetic acid, 10 ml of a solution of sodium bromide ($1 \cdot 10^{-2}$ mole/liter) in acetic acid, 6 ml of acetic acid, and 2 ml (0.195 mole/liter) of thiophene I were placed in a flask with a jacket connected to a gasometer through drying bottles filled with calcium chloride and potassium hydroxide, and the reaction mixture was heated to 90°C as oxygen was passed through it; the oxidation process was carried out with vigorous shaking for 2 h. At the end of the process the reaction products were analyzed by GLC. Acetic acid and I and III-VII were detected. The acetic acid was removed from the contact solution by distillation at reduced pressure to two thirds of its original volume, the residue was diluted with ether, and the precipitate was separated. The ether solution was washed with a 10% solution of sodium carbonate and with water until the wash waters gave a neutral reaction, after which it was dried over calcium chloride. The ether was removed by distillation to half the original volume and the mixture was separated with a preparative chromatograph. The stainless steel columns (600 by 1.0 cm) were filled with N-super Chromaton (0.400-0.630 mm) impregnated with SE-30 silicone elastomer (5%); the temperature of the thermostat of the columns was 120°C. Vacuum fractionation of the third fraction gave 3-methyl-2-acetothienone (III) with bp 98-99°C (14 mm) and n_D^{20} 1.5610; the 2,4-dinitrophenylhydrazone had mp 198°C, and the semicarbazone had mp 208°C. Found: C 59.9; H 5.6; S 22.5%. Calculated: C 60.0; H 5.7; S 22.9%. The IR spectrum was identical to the IR spectrum of a sample obtained by an independent method. Fraction V was 1-(3-methyl-2-thienyl)ethyl acetate (IV). Vacuum fractionation gave a product with bp 91-92°C and n_D^{20} 1.5144. Found: C 59.1; H 6.1; S 17.4%. Calculated: C 59.0; H 6.0; S 17.5%. The IR spectrum was identical to the IR spectrum of a sample obtained by an independent method.

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SYNTHESIS AND REACTIONS OF 1-ALKYL-SUBSTITUTED 1,5-DIKETONES WITH SULFUROUS REAGENTS

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1-Alkyl-substituted 1,5-diketones react with sulfurous reagents (H_2S and P_4S_{10}) to give thiopyrylium salts primarily via a mechanism that is competitive with disproportionation. The reaction depends on the nature of the acidic reagent. Some properties of the compounds obtained are described.

The character of the chemical transformations of 1,5-diarylpentanediones in reactions with nucleophilic reagents has recently been the subject of intensive study [1, 2]. In reactions with sulfurous reagents (P_xS_y, H_2S) thiopyrylium salts are formed via two competitive mechanisms that are determined by the structural peculiarities of the 1,5-dicarbonyl compounds and the reaction conditions [3]. The conversion of 1,5-dialdehydes (glutaraldehyde and its alkyl-substituted derivatives) with H_2S/HCl has been given an interpretation by Strating and Molenaar [4] that differs from what we have observed [1, 3]. One might have expected that 1,5-dialkyl- or 1,5-alkylarylpentanediones would display certain specific characteristics under acid-catalysis conditions.

Taking into account the information stated above, as well as the interest in thiopyrylium salts in connection with their extensive practical importance [5], we synthesized unsymmetrical α-alkyl-substituted 1,5-diketones I and II and studied their heterocyclization with sulfurous reagents, viz., hydrogen sulfide and phosphorus pentasulfide, under various conditions. The selection of 1,5-diketones I and II, which have a tert-butyl substituent in the α position relative to the carbonyl group, was due to the fact that the presence of other alkyl substituents such as a methyl or methylene group usually leads to carbocyclization [6]. The tert-butyl group in the α position of diketones I and II prevents carbocyclization of the latter; however, the Michael reaction is hindered as a consequence of steric factors, as a result of which the yields reach only 40-46%.

TABLE 1. Reaction of Alkyl-Substituted Diketones I and II with Sulfurous Reagents and of 4H-Thiopyrans IV and V with Acids

Starting compounds	Reagents	Solvent*	Reaction time, h	Reaction products (yield, %)
II	$H_2S/HClO_4$	CH_3COOH†	70	VIII (81)
I	P_4S_{10}	Dioxane	22	V (2,3) IX (80,5)
II	P_4S_{10}	Dioxane	17	IV (2) X (63)
I	P_4S_{10}	Pyridine	25	III (65)
II	P_4S_{10}	Pyridine	2,5	IV (72)
IV	CH_3COOH	CH_3COOH	20	XII (82)
V	CH_3COOH	CH_3COOH	25	XI (76)
IV	$HClO_4$	CH_3COOH†	70	VIII (83)
IV	CF_3COOH	Cl_3COOH†	30	VI (24) XV (61)

*The reaction was carried out at 100°C.

†At 20°C.

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