LIQUID-PHASE CATALYTIC OXIDATION OF

2 - METHOXYMETHYLTHIOPHENE

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The oxidation of 2-methoxymethylthiophene with molecular oxygen in the presence of a cobalt bromide catalyst in the kinetic region at 65-100°C was investigated. It is shown that the principal products are 2-formylthiophene and methylthiophene-2-carboxylate in a ratio of 1:2. The composition of the products does not depend on the oxidation temperature and changes as the starting concentration of 2-methoxymethylthiophene and the amount of cobalt bromide catalyst are changed.

Continuing our study of the liquid-phase catalytic oxidation of heterocyclic sulfur- and selenium-containing compounds, we investigated the oxidation of 2-methoxymethylthiophene (I). No similar studies have been reported. The selection of I as the subject of the study was due to the practical application of the products of its oxidation as inhibitors of steel corrosion [1, 2], low-temperature plasticizers for rubbers [3], and biologically active substances that have organoleptic properties [4, 5]. At the same time, ethers are intermediates in the oxidation of alkylthiophenes, from which carboxylic acids are formed in the extreme stages of the oxidation [6].

The liquid-phase oxidation of ether I was carried out in glacial acetic acid at 65-105°C and atmospheric oxygen pressure in the presence of cobalt acetate and sodium bromide. We studied the effect of the temperature in order to obtain data on the kinetics of accumulation of the aldehyde, ester, and acid, as well as on the role of the cobalt bromide catalyst in the formation of the indicated products. The rate of the reaction was measured from the oxygen absorption with a gasometric apparatus. The products of decomposition of ether I were analyzed by gas-liquid chromatography with monomethyl succinate (II) as the internal standard. The principal products of oxidation of ether I were 2-formylthiophene (III) and methylthiophene-2-carboxylate (IV). 2-Acetoxymethylthiophene (V), which vanishes 15 min after the start of the reaction during which methanol is formed in the mixture, was observed as an intermediate in the initial step of the oxidation (Fig. 1). Peroxide compounds and 2-hydroxymethylthiophene were not detected during the reaction. It is apparent from Fig. 1 that ether I is converted primarily to aldehyde III and ester IV in the first minutes of the oxidation and that the 1:2 ratio of these compounds that is established in the tenth minute does not change up to the end of the process. Although oxygen absorption is complete at the fortieth minute, the formation of aldehyde III and ester IV continues, while their ratio remains the same. An increase in the temperature from 70 to 95°C also does not affect the ratio of aldehyde III and ester IV, although their overall percentage in the contact mixture increases (Fig. 2).

The oxidation of ester V, obtained by an independent method, under similar conditions leads to the production of acid VI and, in smaller amounts, aldehyde III. Methanol was not detected in the reaction products. The oxidation of aldehyde III under the same conditions leads to the formation of acid VI. Thus, the kinetic curves of the accumulation of esters IV and V are typical for a consecutive reaction. However, the kinetics of the accumulation of aldehyde III constitute evidence for its consecutive-parallel formation.

We studied the effect of cobalt acetate and sodium bromide cumulatively on the formation of the products of oxidation of ether I for $[\text{Co}^{2^+}] = 9.6 \cdot 10^{-3} - 1.6 \cdot 10^{-1}$ and $[\text{NaBr}] = 0.1 \cdot 10^{-3} - 7.65 \cdot 10^{-2}$ mole/liter. The percentage of ester IV in the oxidation products increases from 1.4 to 1.8% by weight and the percentage of aldehyde III decreases as the cobalt acetate concentration is increased from $3.5 \cdot 10^{-2}$ to $1.12 \cdot 10^{-1}$ mole/liter. Aldehyde III is not formed at cobalt acetate concentrations above $5 \cdot 10^{-2}$ mole/liter. It is evidently converted to the corresponding acid, the percentage of which in the contact mixture increases. The percentage of alde-

Moscow Physicotechnical Institute, Dolgoprudnyi 141700. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 924-928, July, 1980. Original article submitted September 24, 1979.



Fig. 1. Dependence of the consumption and accumulation of products of the oxidation of ether I (according to GLC data) for $[Co(OAc)_2] = 4.7 \cdot 10^{-2} \text{ mole/liter}, [NaBr] = 1.5 \cdot 10^{-3} \text{ mole/liter}, and [C_6H_8OS] = 0.219 \text{ mole/liter} at 95^{\circ}C: 1)$ ester IV; 2) aldehyde III; 3) methanol; 4) ether I; 5) ester V.

hyde III decreases by a factor of two as the sodium bromide concentration is increased from $0.9 \cdot 10^{-3}$ to $2 \cdot 10^{-2}$ mole/liter, while the amount of ester IV formed does not change. The percentage of ester IV increases from 0.52 to 2.8% by weight as the concentration of starting ether I in the contact mixture is increased from 0.5 to 9.6%, and the percentage of aldehyde III in the oxidation products increases from 0 to 1.7% by weight. Aldehyde III is not detected in the final mixture at concentrations of starting ether I below 2.5%, while at concentrations greater than 6% the aldehyde undergoes appreciable resinification, and the overall yield of oxidation products decreases.

It is characteristic that the oxidation of ether I takes place without appreciable induction periods. As the products of oxidation of ether I accumulate, the rate of oxidation of I decreases, i.e., some of the oxidation products have an inhibiting effect that is reinforced considerably as the temperature is lowered. The addition of alcohol and ester IV to the contact mixture in the initial stage of the process leads to a sharp decrease in the reaction rate.

The dependence of the change in the initial rate of oxidation of ether I on the temperature (70, 80, and 90°C) in Arrhenius coordinates makes it possible to calculate the activation energy of the process. The effective activation energy of the oxidation of the developed stage of the reaction is 7.6 kcal/mole.

To ascertain the kinetic principles of the process we studied the effect of the concentrations of the cobalt bromide catalyst and the starting compound. The reaction is first-order in Co^{2^+} , 0.5-order in NaBr, and first-order in $\text{C}_6\text{H}_8\text{OS}$. A linear dependence of the initial rate of the reaction on the concentrations of the catalyst and the starting compound is observed.

In the oxidation of ether I we noted the phenomenon of synergism in the case of the action of cobalt and manganese acetates; manganese acetate was used in 2% by weight amounts relative to the cobalt acetate concentration in the presence of the NaBr initiator. This catalyst composition made it possible to increase the rate of oxidation by a factor of 1.7.

The scheme of the oxidation of ether I can be presented on the basis of the experimental data. The oxidation of the ether is accompanied by parallel-consecutive reactions, viz., oxidation, destruction, esterification, and condensation. A product of destructive oxidation, viz., methanol, is formed. Primarily the α -CH bond undergoes oxidation to give oxygen-containing functional groups. Destructive oxidation becomes more intensive with time, and oxygen-containing compounds are formed; however, cleavage of the thiophene ring is not observed.

Like hydrocarbons, ethers are oxidized via a free-radical mechanism, and the intermediates are evidently hydroperoxides [7]; in the case of oxidation with metal bromide catalysts the catalytically active particles are not metal ions in a higher valence form (Co^{3^+} ions in this case) but rather the [$Co^{3^+}Br^-$] complex [8]. The composition of the products of oxidation of ether I is basically the same as in the case of ethers of the aliphatic and aromatic series [9].



Fig. 2. Dependence of the yields of the principal products of the oxidation of 2-methoxymethylthiophene on the temperature (according to GLC data) for $[Co(OAc)_2] = 4.7 \cdot 10^{-2}$ mole/liter, $[NaBr] = 1.5 \cdot 10^{-3}$ mole/liter at 70°C (2, 3, and 5) and 95°C (1, 4, and 6): 1, 2) ester IV; 3, 6) ether I; 4, 5) aldehyde III.

The primary intermediate in the oxidation of ether I is evidently the corresponding hydroperoxide, the subsequent transformation of which at relatively low temperatures (up to 60° C) leads to the formation of an aldehyde and methanol. At temperatures above 100° C, in addition to the aldehyde, considerable amounts of thiophenecarboxylic acid, ester, and methanol, the percentage of which increases as the temperature is raised, are detected in the oxidation products. At 95°C the amount of ester reaches 41.3%, the amount of al-dehyde reaches 28.1%, and the amount of methanol reaches 11.4%. The formation of the ester may occur as a result of decomposition of the hydroperoxide, recombination of peroxide radicals, and esterification of the acid by the corresponding alcohol. The possibility of the formation of the aldehyde

as a result of recombination of radicals also is not excluded:

$$\sum_{i=1}^{2} C_{H-OCH_3} + C$$

This pathway is likely, since the alcohol and ester are detected in the products in the early stages. The acids accumulate evidently as a result of both monomolecular decomposition of the hydroperoxide and further oxidation of the resulting aldehyde. The formation of these products can be explained by the following reactions:



EXPERIMENTAL

The method used to carry out the oxidation was described in [10]. The IR spectra of the compounds in carbon tetrachloride were recorded with a UR-10 spectrometer. The reaction products were identified by chromatography. Analysis by gas-liquid chromatography (GLC) was performed with an LKhM-8MD chromatograph (models 1 and 5) with a catharometer as the detector and stainless-steel columns (2 m by 2 mm and 3 m by 3 mm) filled with 7% polyethylene glycol sebacate on acid-washed Chromosorb (60-80 mesh) and 5%

XE-60 on Chromaton N-AW (0.20-0.25 mm). The column temperature was maintained at 130°C or was varied from 70 to 140°C at a rate of 8 deg/min. The carrier gas was helium, and the flow rate was 30 ml/min. Ester II, the constants of which were in agreement with the literature data, was used as the internal standard. Preparative separation of the substances by GLC was realized with a PAKhV-07 chromatograph; the stationary phase was 7% polyethylene glycol sebacate on Chromosorb (60-80 mesh), the column (2 m by 8 mm) temperature was 150°C, the vaporizer temperature was 200°C, the carrier gas was helium, and the flow rate was 200 ml/min.

The glacial acetic acid was frozen out and distilled with a rectification column. Chemically pure-grade $Co(CH_3COO)_2 \cdot 4H_2O$ was used without additional purification. The sodium bromide was calcined to constant weight at 130-150°C. The solvents were purified by the methods in [11].

2-Methoxymethylthiophene (I) was obtained by the method in [12] and had bp $36-38 \,^{\circ}C$ (3 mm), n_D^{20} 1.5195, and d_4^{20} 1.0607. IR spectrum: 2830 (CH₃) and 1235 cm⁻¹ (C-O-C). Found: C 56.2; H 6.3; S 25.2%. C₆H₈OS. Calculated: C 56.3; H 6.3; S 25.0%. According to the data in [12], this compound had bp 54-55°C (8 mm) and n_D^{25} 1.5190.

2-Formylthiophene (III) was obtained by the method in [13] and had bp 56-58°C (2 mm) and n_D^{20} 1.5930 [bp 97-100°C (27 mm) and n_D^{20} 1.5937 [13]]. IR spectrum: 1700 (C = O) and 1400 cm⁻¹ (CHO). Found: C 53.3; H 3.4; S 28.3%. C₅H₄OS. Calculated: C 53.6; H 3.6; S 28.6%.

Thiophene-2 carboxylic acid (VI) was obtained by the method in [14] and had mp 126°C (from water). IR spectrum: 1710 cm⁻¹ (C=O). Found: C 46.9; H 3.2; S 25.3%. C₅H₄O₂S. Calculated: C 46.7; H 3.2; S 25.0%. According to the data in [14], this compound had mp 128°C.

Methylthiophene-2-carboxylate (IV) was obtained by the method in [15] and had bp 47-50°C (10 mm) and n_C^{20} 1.5425. IR spectrum: 1735 cm⁻¹ (C=O). Found: C 50.5; H 4.3; S 23.1%. C₆H₆O₂S. Calculated: C 50.7; H 4.2; S 22.5%. According to the data in [15], this compound had bp 40°C (0.5 mm) and n_D^{20} 1.5420.

2-Acetoxymethylthiophene (V) was obtained by the method in [16] and had bp 89-91°C (9 mm) and n_D^{20} 1.5170 [bp 92-97°C (11 mm) and n_D^{25} 1.5159 [16]]. IR spectrum: 1730 (C=O) and 1220 cm⁻¹ (C=O-C). Found: C 53.9; H 5.5; S 20.1%. C₇H₈O₂S. Calculated: C 53.9; H 5.1; S 20.5%.

Isolation of the Products of Oxidation of Ether I. A thermostatted flask was charged with 1.24 g of cobalt acetate and 0.015 g of sodium bromide in 96 ml of glacial acetic acid, and 2.8 g of ether I was added at 95°C. Oxidation was carried out with molecular oxygen at 95 ± 0.5 °C with vigorous shaking for 1 h. At the end of the reaction, the acetic acid was removed by distillation, and 30 ml of water was added to a part of the residue. The aqueous mixture was extracted with ether (three 30-ml portions), and the ether extracts were combined, washed with water, and dried with MgSO₄. The solvent was removed, and the residue was subjected to preparative chromatography to give 1.04 g of ester IV with bp 47-50°C (2 mm) and n_D^{20} 1.5452. Found: C 50.4; H 4.2; S 22.5%. C₆H₆O₂S. Calculated: C 50.7; H 4.1; S 22.5%. Also obtained was 0.63 g of aldehyde III with bp 57-60°C (2 mm) and n_D^{20} 1.5930. Found: C 53.8; H 3.6; S 28.2%. C₅H₄OS. Calculated: C 53.5; H 3.6; S 28.6%. The IR spectra of III and IV were in complete agreement with the spectra of these compounds obtained by independent methods. A part of the residual contact solution after removal of the acetic acid was extracted with ether (three 20-ml portions), and the ether extracts were washed with a small amount of ice water. The ether was removed by distillation to give acid VI with mp 123-125°C (from water). No melting-point depression was observed for a mixture of this product with a sample obtained from 2acetylthiophene by the method in [14], and the IR spectra of the two samples coincided completely.

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HYDROXYMETHYLATION AND AMINOMETHYLA-

TION OF 2-IMINO-5-ARYLIDENETHIAZOLIDIN-

4 - ONES

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The hydroxymethylation and aminomethylation of 2-imino-5-arylidenethiazolidin-4-ones lead to the formation of 2-hydroxymethylimino- and 2-piperidinomethylimino-5-arylidenethiazolidin-4-ones. The structures of the synthesized compounds are discussed on the basis of the spectral data.

UDC 547.789.1.3.5

In [1] it was shown that the aminomethylation of 2-imino-5-benzylidenethiazolidin-4-one (Ia) in benzene leads to the formation of 3-aminomethyl derivatives, while aminomethylation products could not be isolated when the reaction was carried out in ethanol or acetic acid. The hydroxymethylation of 2-imino-5-arylidene-thiazolidin-4-ones Ia-c has not been previously studied.



The hydroxymethyl derivatives (IIa-c) that we obtained (Table 1) were found to be unstable substances that undergo decomposition to the starting Ia-c during chromatography in thin layers of silica gel and during attempts to determine their melting points or recrystallize them. According to the derivatographic data, the weight loss of a solid sample, which begins at 110-115°C, corresponds to splitting out of one molecule of formaldehyde. The formation of unstable adducts with formaldehyde has also been demonstrated for the similarly constructed 3-aryl-2-iminothiazolidin-4-ones [3].

In contrast to IIa-c, aminomethyl derivatives IIIa-c have fixed melting (decomposition) points; however,

^{*}Deceased.

Lensovet Leningrad Technological Institute, Leningrad 198013. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 7, pp. 929-932, July, 1980. Original article submitted May 14, 1979; revision submitted February 19, 1980.