Reactions of Benzo and Dibenzo Derivatives of Five-Membered Aromatic Heterocycles with Ozone in the Liquid Phase

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Abstract—The ozonation reactions of benzo and dibenzo derivatives of pyrrole, furan, and thiophene in acetic acid solution have been studied. Peroxide compounds have been detected as the products. The mechanism of ozone interaction with these hetarenes has been proposed. The kinetics of ozonolytic reactions of benzologues of five-membered aromatic heterocycles (hetarenes) have been investigated. The reaction of ozone with the hetarenes obeys the bimolecular rate law and has the first order in each reactant. The effective rate constants and experimental stoichiometric coefficients for ozone have been found.

Benzo and dibenzo derivatives of five-membered hetarenes are characterized by usual electrophilic substitution reactions typical of aromatic compounds [1]. The electrophilic substitution reactions of these hetarenes proceed in the same way as for pyrrole, furan, and thiophene, but some peculiarities due to the stabilizing effect of the benzene ring caused by the electron-withdrawing action on the five-membered heterocycle should be noted.

Electrophilic substitution occurs exclusively in the 3-position of the heterocycle in the indole molecule (**I**), predominantly in the 2-position in benzofuran (**II**), and in the 3-position with a considerable impurity of the 2-isomer in thionaphthene (**III**) [1−3]. The electrophilic substitution and oxidation reactions of compounds **I−III**, as well as those of carbazole (**IV**), dibenzofuran (**V**), and dibenzothiophene (**VI**), have been reported [1−4], but there is a lack of data on the reaction of these compounds with ozone as an electrophilic oxidant. In this study, we examined the reaction of hetarenes **I−VI** with ozone in a solution of glacial acetic acid.

EXPERIMENTAL

The oxidation of hetarenes **I−VI** was carried out in a temperature-controlled reactor made as a glass column of a 0.1 dm^3 volume equipped with a finely porous separating wall for dispersing an ozone−air mixture and a reflux condenser. The reactor was charged with 0.05 dm^3 of glacial acetic acid and a calculated amount of hetarene; then, the ozone−air mixture was supplied at a rate of $3.3 \times 10^{-3} \text{ dm}^3/\text{s}$. The amount of the reactant hetarenes in solution was determined by GLC using an LKhM-80 chromatograph with FID on a 2-m column packed with polymethylphenylsiloxane (PMPS-6)-coated Chromaton N-AW. Peroxides were determined by iodometry after the reactor with air to remove ozone residue according to the published procedure [6]. The concentration of carboxylic acids was determined by alkalimetric titration with a 0.05 N sodium hydroxide solution after solvent evaporation. The IR spectra were recorded on a UR-20 spectrophotometer in KBr disks.

The ozone concentration in the gas phase was determined using the spectrophotometric method based on measuring the UV absorbance of gas flow in the range of 254−290 nm. The ozone uptake was determined as the difference of its concentrations at the reactor inlet and outlet, taking into account the air−ozone mixture feed rate. The kinetics of ozone consumption was studied using a Spektromom-202 spectrophotometer with a quartz-windowed flow cell placed in its measurement compartment. The cell material was Teflon. The ozone detection limit of the instrument was 10^{-7} mol/dm^3.

RESULTS AND DISCUSSION

The oxidation of compounds **I−III** with ozone was considered in [7−9]. It was shown that during the ozonation of benzo derivatives **I−III** in chloroform, the C−C heterocycle bond is cleaved and 1−1.8 mol of ozone per mole of hetarene is absorbed. The reactions of ozone with dibenzo derivatives **IV−VI** were not reported.

Earlier, in the investigation of the reaction of five-membered hetarenes [10] and their methyl derivatives

Stoichiometric characteristics of interaction of ozone with pyrrole, furan, thiophene, and their benzo **I−III** and dibenzo **IV−VI** derivatives in glacial acetic acid at 290 K. $[ArH]_0 = 1.0 \times 10^{-2}$; $[O_3]_0 = 4.0 \times 10^{-3}$ mol/dm³

| Hetarene	n_{exp}, $\dfrac{mol\ O_3}{mol\ ArH}$	Concentration of peroxides, mol/dm³ × 10²		k_{eff}, dm³/(mol s)
		in 1 h	in 24 h	
Pyrrole	1.95	1.15	1.91	1.8×10^5
Furan	1.91	1.03	1.88	1.2×10^3
Thiophene	1.74	0.95	1.64	34.8
(I)	3.84	0.92	1.95	2.0×10^3
(II)	3.73	0.92	1.85	2.1×10^2
(III)	3.62	0.88	1.80	8.5
(IV)	5.61	1.95	1.82	76.0
(V)	5.63	1.92	1.78	0.9
(VI)	5.64	1.94	1.79	0.26

[11] with ozone in acetic acid, we detected linear hydroperoxyperoxides as the primary products. The experimentally found stoichiometric coefficient for ozone, n_{exp}, was 1.95−1.74 mol per mole of heteroaromatic substrate. The effective rate constant of ozonolysis of pyrrole, furan, and thiophene, k_{eff}, varies within $1.8 \times 10^5 - 34.8$ L/(mol s) depending on the nature of the heteroatom (table) [10].

On the basis of the experimental results and published data [7−9], the mechanism of ozone interaction with benzo derivatives **I−III** in acetic acid solution at 290 K was proposed, according to which the first step is the fast electrophilic attack of ozone across the double bond of heterocycle with absorption of 1 mol of O_3 per mole of substrate and formation of ozonides, which are subsequently transformed via the degradation of the heterocycle according to Scheme 1. In reactions with **I−III**, ozone acts as a typical electrophile and reacts by the (2−3) double bond of the heterocycle to give the products of decomposition of the aromatic system according to published data [7, 8] that showed ozone as a specific reagent for double bond to attack the bond with the lowest localization energy of the aromatic system.

Proceeding from the foregoing, it may be assumed that the interaction of ozone with compounds **I−III** can be described as given in Scheme 1 according to which the reaction follows the classical mechanism including the step of formation of the π-complex (**VII**) followed by the primary attack of ozone at the carbon atom predominantly in the β-position for hetarene **I** or **III** and in the α-position for **II**, giving rise to σ-complex (**VIII**) converting into ozonides (**IX**). The latter, depending on the structure of the reactant benzo derivative, are transformed by the ring opening of heterocycle into 2-aminobenzaldehyde (**X**), salicylaldehyde (**XI**), or thiosalicylaldehyde (**XII**).

Resulting benzaldehydes **X−XII**, in turn, are intermediate compounds; after ozone attack at the π-electron system of the aromatic ring, they are transformed into peroxide compounds. About 3 mol of O_3 per mole of substrate is additionally absorbed to give triozonide followed by the degradation of the aromatic cycle and the formation of peroxide compounds.
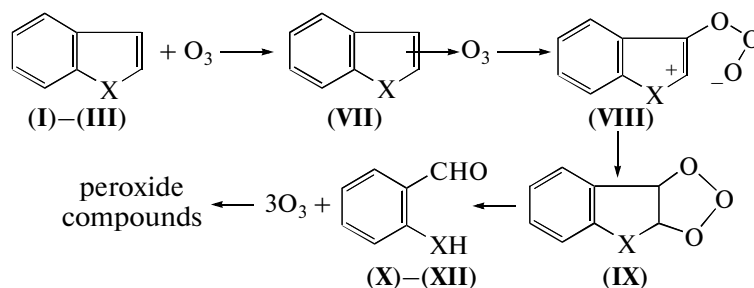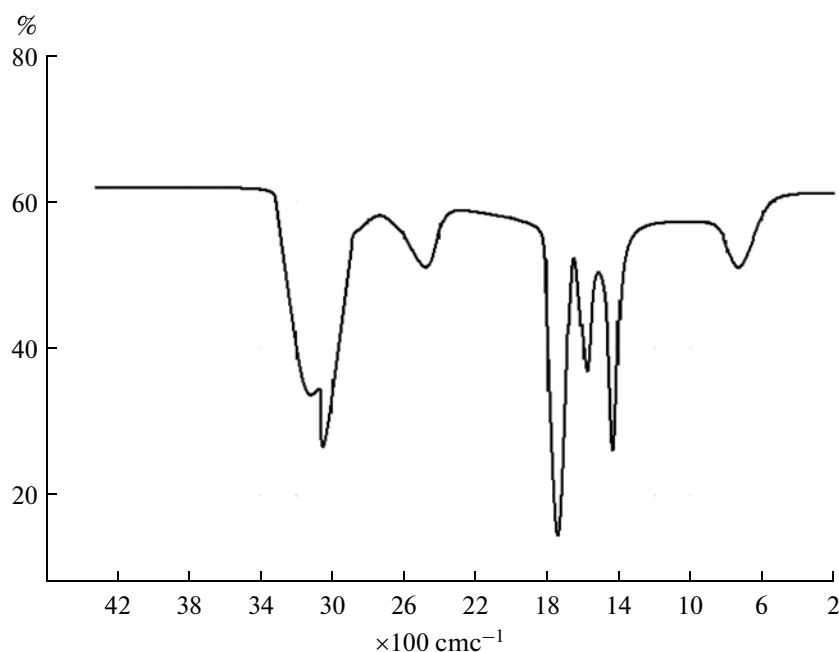

Scheme 1.

Fig. 1. IR absorption spectrum of 2,2'-dicarboxydiphenylsulfide (**XIII**) obtained through oxidation of thionaphthene (**III**) and dibenzothiophene (**VI**) with ozone in acetic acid at 290 K.

The peroxide compounds studied after completion of ozonation react with potassium iodide in two steps: molecular iodine is released in the amount equivalent to one final hydroperoxide group during the first, rapid step (duration 1 h) and the equivalent of another two groups is released during the second, slow (24 h) step (table). According to published data [10], hydroperoxide groups readily react with KI; whereas the peroxide groups of dialkylperoxides, are more difficult to reduce.

In the case of oxidation of thionaphthene **III**, 2,2'-dicarboxydisulfide (**XIII**) was detected as the final product; its yield 26.7%.of the oxidation products.
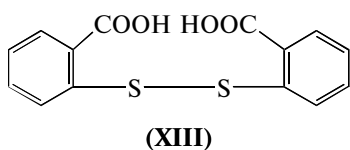
Thiosalicylaldehyde (**XII**) supposedly adds approximately 2 mol of O_3, and oxidative condensation yielding **XIII** occurs. The feasibility of this condensation has been demonstrated in [13].

To confirm the structure, the IR spectra of compound **XIII** were recorded. The resulting IR spectra depicted in Fig. 1 show absorption bands at 740 cm^{-1} due to C−S stretching vibrations, 1470 and 1590 cm^{-1} due to the benzene ring C−C vibrations, and 1720 cm^{-1} due to C=O carboxylic group vibrations. There are also moderately weak absorption bands at 2560 cm^{-1} due to sulfide group S−S vibrations and bands at 3020 cm^{-1} due to C−H vibrations in the aromatic ring.

Overall experimental stoichiometric coefficient n_{exp} found of ozone decreases in the order **I** > **II** > **III** from 3.84 to 3.56 mol per mole of hetarene (table). The reduced consumption of ozone for oxidation of **III** is associated with the fact that thiosalicylaldehyde **XII** can partially add 2, rather than 3 mol of O_3 involved in the oxidative condensation and formation of 2,2'-dicarboxydiphenylsulfide **XIII**.

During the ozonation of dibenzo derivatives **IV−VI** in a solution of acetic acid at 290 K, the first step is the electrophilic attack of ozone across the double bonds of one of the carbocycles with the absorption of 2 mol of O_3 per mole of the substrate and the formation of diozonide (**XIV**), which subsequently transforms via two routes according to Scheme 2.

By the first route according to Scheme 2, diozonide **XIV** adds another 2 mol of O_3 and transforms into tetraozonide (**XV**), which degrade to give peroxide compounds (their structures has not been studied in this work). The ozonation products, depending on the nature of the initial dibenzo derivative, were found to contain about 15−20% pyrroltetracarboxylic (**XVI**), furantetracarboxylic (**XVII**), and thiophenetetracarboxylic (**XVIII**) acids, which can be produced through the degradation of ozonide **IX**.

Scheme 2.
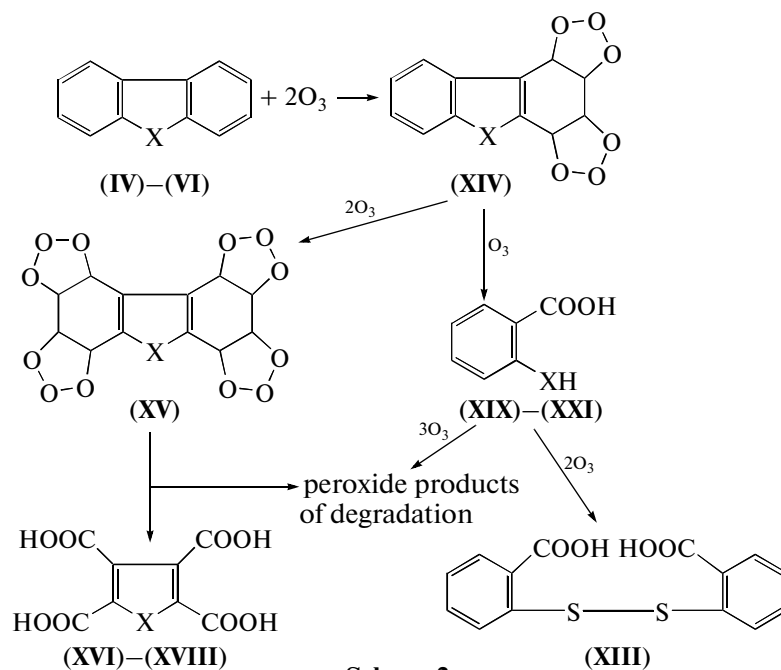
By the second route, the decomposition of carbocyclic ozonide **XIV** to give anthranilic (**XIX**), salicylic (**XX**), or thiosalicylic (**XXI**) acid depending on the structure of the initial hetarene is possible, which are intermediate products as in the case of ozonolysis of benzo derivatives **I–III**. Carboxylic acids **XIX–XXI** add about 3 mol of O_3 each to form peroxide products of degradation. As in the case of thionaphthene **III**, the products of ozonolysis of dibenzothiophene **VI** wee found to contain about 14% 2,2'-dicarboxydiphenylsulfide **XIII**, which can be formed through oxidative condensation of intermediate thiosalicylic acid **XXI**, as confirmed by the IR data (Fig. 1). According to the data in the table, the overall experimental stoichiometric coefficient of ozone n_{exp} is 5.61–5.64 mol per mole of hetarenes **IV–VI**.

To gain further insight into the mechanism of the reactions of interest, the kinetic features of the reactions of hetarenes **I–VI** with ozone in the medium of glacial acetic acid at 290 K were studied. The reaction kinetics was investigated by measuring the initial ozone consumption rates at the reactor outlet in the gas phase according to the procedure described in [14]. The current concentration of ozone in the liquid phase was determined with a Spektromom-202 spectrophotometer using a gradientless catalytic shaker reactor with respect to the gas phase.

It was found that the ozone uptake kinetics obeys the bimolecular rate law in the reactions with benzo derivatives **I–III** (Fig. 2) and dibenzo derivatives **IV–VI** (Fig. 3) to have the first order in each of the reactants:

$$-\frac{d[O_3]}{dt} = k_{eff}[ArCH_3]_o[O_3]_o, \qquad (1)$$

where k_{eff} is the effective rate constant of the reaction of ozone with **I–VI** that takes into account all types of interactions between the reactants, $dm^3/(mol\ s)$.

Ozone is likely consumed via a nonchain mechanism. Termination of ozone supply into the reaction mixture stops the oxidation. As can be seen from the data in the table, fusion of the benzene ring to a five-membered hetarene molecule leads to a reduction in the reactivity in the reaction with ozone to decrease in the reaction rate by a factor of 2 for **I** and a factor of 4 to 5 for **II** and **III**. The annelation of another benzene ting to the molecules of benzo derivatives **I–III** leads to a further reduction in the rate of the ozone react ion with **IV–VI**. The effective rate constant of the reaction of ozone regularly decreases in the order **I > II > III** for the benzo derivatives or **IV > V > VI** for the dibenzo derivatives, which is strongly determined by the nature of the heteroatom.

Thus, as a result of this study, it was shown that the oxidation of benzo derivatives **I–III** with ozone in an acetic acid solution involves as the fast electrophilic attack of ozone across the double bond of heterocycle with absorption of 1 mol of ozone per mol of substrate and formation of ozonides in the first step followed by the ozonide transformation via degradation of the heterocycle into intermediate benzaldehydes, which form peroxide compounds after the ozone attack at the π-electron system of the aromatic ring.
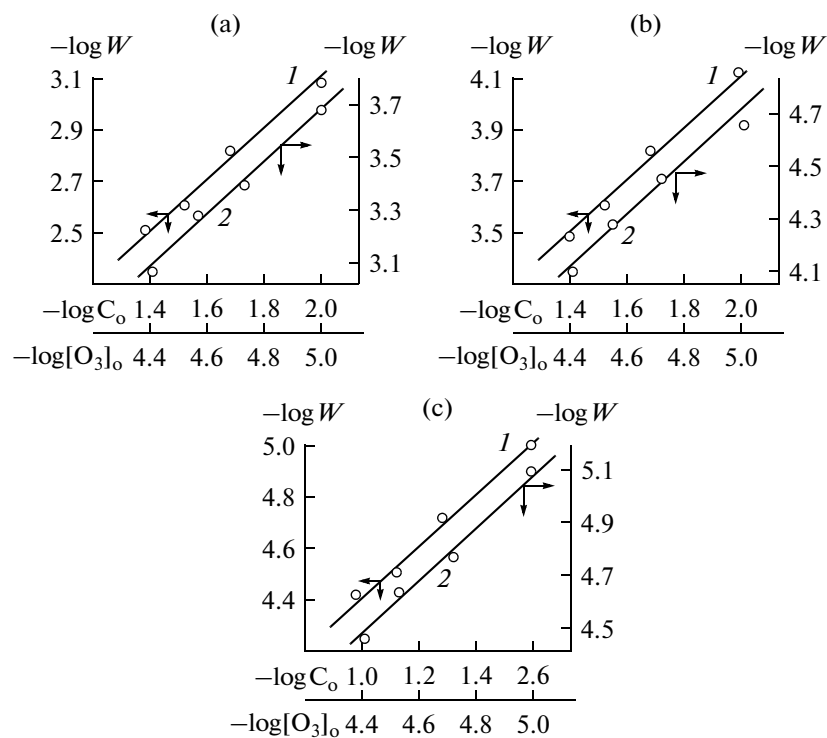
Fig. 2. Dependence of the oxidation rate (*w*) on the initial concentration of (*1*) benzo derivatives and (*2*) ozone: (a) **I**, (b) **II**, (c) **III** in logarithmic coordinates at 290 K. $V_{O_2} = 3.3 \times 10^{-3}$ dm^3/s, (*1*) $[O_3]_o = 4.0 \times 10^{-5}$ mol/dm^3, (*2*) $[ArH]_o = 1.0 \times 10^{-2}$ mol/dm^3.
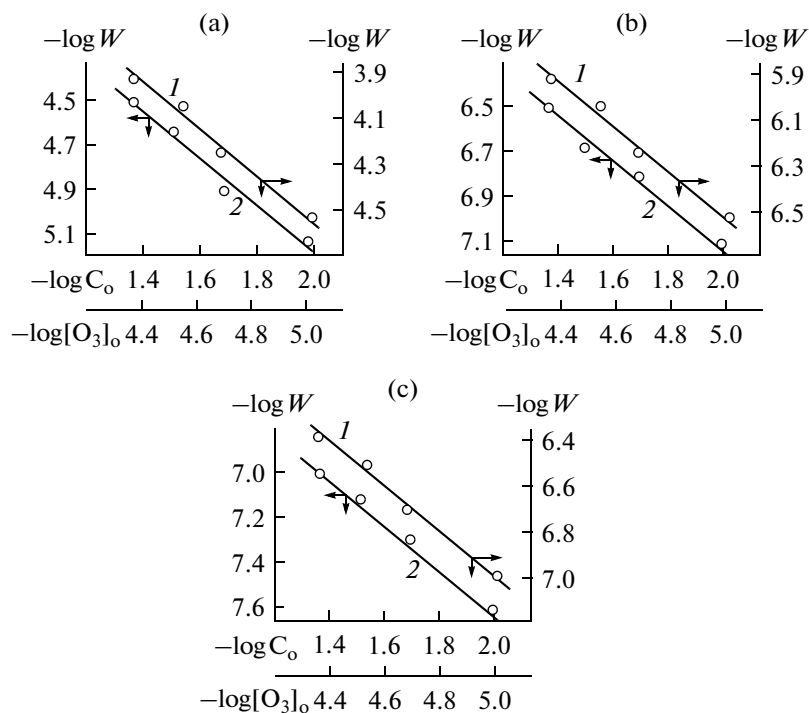

Fig. 3. Dependence of the oxidation rate (*w*) on the initial concentration of (*1*) dibenzo derivatives and (*2*) ozone: (a) **IV**, (b) **V**, (c) **VI** in logarithmic coordinates at 290 K. $V_{O_2} = 3.3 \times 10^{-3}$ dm^3/s, (*1*) ^{3}/c, $[O_3]_o = 4.0 \times 10^{-5}$ mol/dm^3, (*2*) $[ArH]_o = 1.0 \times 10^{-2}$ mol/dm^3.

It was also assumed that the ozonation of dibenzo derivatives **IV−VI** involves at the first stage the attack of ozone across the double bond of one of the carbocycles with absorption of 2 mol of ozone and formation of diozonide, which is further transformed via two routes resulting in peroxides and heterocyclic tetracarboxylic acids.

The kinetics of ozone consumption in the reactions with hetarenes **I−VI** follows the bimolecular rate law and has the first order in each of the reactants.

The fusion of the benzene ring to the five-membered hetarene molecules leads to a reduction in the rate of reaction with ozone. The annelation of another benzene ring into the molecule of benzo derivatives leads to a further reduction in the reaction rate. The effective rate constant of the reaction with ozone decrease in the orders for **I > II > III** and **IV > V > VI** for the benzo and dibenzo derivatives, respectively.

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