STRUCTURE OF POLYMERIC COUMARINS.

I. DETERMINATION OF THE DOUBLE BONDS IN COPOLYMERS AND THE INITIAL COUMARINS BY OZONIZATION

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UDC 678.447.42–134.26:615.717

The paper gives the results obtained in a study of the structure of coumarin derivatives by the following metheds: ozonization of the double bonds in the monomeric and polymeric coumarins, and also in mixtures of polyvinylpyrrolidone with monomeric coumarins, and the treatment of the monomeric coumarins under the conditions of radical copolymerization but without the participation of N-vinylpyrrolidone.

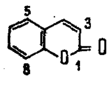
We have previously synthesized copolymers of N-vinylpyrrolidone (I) with coumarin **(II)** [1], and also with a whole series of its natural and synthetic derivatives substituted both in the benzene ring and in the α-pyrone ring [2-5].

It has been shown on the basis of UV, IR, and PMR spectra and the chemical properties of the copolymers that the copolymerization of coumarins takes place by a radical mechanism through the 3,4- double bond of the α-pyrrone ring, and the double bonds in the side chains and furan rings do not take part in the copolymerization reaction.

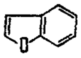
In recent years, reports have appeared [6, 7] on the capacity of bishydroxycoumarin for forming complexes with polyvinylpyrrolidone and proteins. In view of the high complex-forming capacity of polyvinylpyrrolidone and its copolymers, it might be expected that this type of complex can also be formed with other coumarins, especially those having –OH or –COOH groups.

We have studied this question further in relation to some coumarins studied previously and some new ones. In addition, we have obtained new monomeric and polymeric derivatives which have enabled us to compare their reactivities and structure with those partially described previously [2, 4, 5]. In the present investigation we have additionally used the method of analytical ozonization of double bonds that has become available thanks to the development of the Soviet instrument "Analizator dvoinykh svyazei-3" ["Double-Bond Analyzer 3"] ("ADS-3"), working automatically with a recorder and a pulse integrator. No such analysis has previously been carried out on monomeric and polymeric coumarins.

In the investigation we incorporated information on the ozonolysis of the double bonds of a series of monomeric coumarins: coumarin (II), coumarone (III), psoralen (IV), osthole (V), gosferol (VI), and isoimperatorin (VII), and their copolymers with N-vinylpyrrolidone.



II



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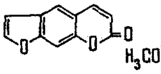

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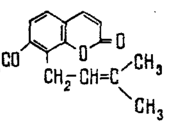

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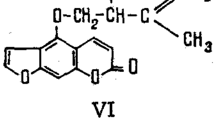
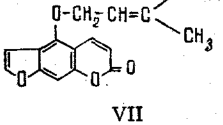


VI



VII

We studied a series of substances differing in molecular weights and in the distribution, nature, and number of the double bonds. The investigation showed that the time of ozon-

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Translated from Khimiya Prirodnykh Soedinenii, No. 5, pp. 637-642, September-October, 1979. Original article submitted May 11, 1979.

0009-3130/79/1505-0557$07.50

ization and the shape of the curves on the diagram provide a distinct possibility of determining the number and types of double bonds both in monomeric and in polymeric compounds. It must be particularly emphasized that conjugated double bonds in aromatic rings are not ozonized under the conditions adopted (and therefore they will be left out of account in the subsequent discussion).

Characteristic types of diagrams of the ozonization of double bonds are given in Fig. 1.

The curve of the ozonization of coumarin is flat with a very slow fall to the zero line (Fig. 1a). Ozonization takes place slowly — in 1.5-3 h (depending on the size of the sample) only about 80% of the double bonds are ozonized. Coumarins each contain a conjugated double bond in the 3,4- position of the α-pyrone ring which, because of the resonance stabilization of the ring has an "aromatic" nature [8, 9]. This possibly plays a part in the ozonolysis reaction, as well, which explains the form of the curve on the diagram and the course of ozonolysis, taking place slowly and incompletely.

A completely different picture is observed for the ozonization of an aliphatic double bond of a side chain and of a double bond in a furan ring. Figure 1b shows the ozonization curve of cinnamic acid (which was used as standard) and of benzofuran — coumarone (III). The form of the curve and the course of ozonization are the same in these cases. The curve on the diagram has the form of a high peak with a steep fall to the zero line. Ozonization takes place practically completely in 3-5 min (found: 0.98 of a double bond per molecule).

Figure 1c, shows a curve typical for the ozonization of coumarins and furocoumarins having, in addition to the 3,4-double bond in the α-pyrone ring, a double bond in the furan ring [psoralen (IV)] or a double bond in a side chain [osthole (V)], or both simultaneously [gosferol (VI) and isoimperatorin (VII)]. The ozonization curves of these compounds have a stepwise nature. Initially there is a sharp rise of the peak with a steep fall. After 3-5 min, the double bonds in the side chain and in the furan rings are ozonized (as in the ozonization of cinnamic acid and coumarone). Then there is a long (2-3 h) gentle course of the curve with a slow fall to the zero line. During this time the ozonization of the 3,4- double bond of the α-pyrone ring takes place. For psoralen and osthole, which each have two double bonds, 1.88 double bonds were found in the molecules; for gosferol and isoimperatorin, each having three double bonds, 2.89 and 2.98 double bonds were found in the respective molecules. It is indicative that the ozonization method permits us to see directly what type of double bonds and how many there are in monomeric and polymeric coumarin derivatives.

In the analysis of copolymers of N-vinylpyrrolidone with coumarin (IX)(with different compositions: from 10 to 47 mole % of coumarin in the copolymer) it was established that no ozonization took place. Consequently, there was no double bond in the 3,4- position of the α-pyrone ring. This once again confirms that (II) polymerizes precisely through the 3,4-double bond and is not bound in the monomeric form with polyvinylpyrrolidone (VIII) the formation of which is possible under the reaction conditions. We performed control experiments: mixtures made up from monomeric coumarins and (VIII) with different ratios of the components were ozonized. It was found that the course of ozonization and the formation of the curves on the diagrams coincided completely with the results of ozonization of the corresponding monomeric coumarins. Consequently, the presence of a high-molecular-weight substance [in this case, (VIII)] does not affect the course of ozonization.

The course of the ozonization of copolymers of N-vinylpyrrolidone with psoralen (X), osthole (XI), gosferol (XII), isoimperatorin (XIII), and oxypeucedanin hydrate (XIV) coincided completely with the course of the ozonization of compounds lacking the 3,4- double bond of the α-pyrrone ring but having double bonds in a side chain or in a furan ring (cinnamic acid and coumarone). Ozonization took 3-5 min and the peak was high with a steep fall to the zero line (Fig. 1b). The gently sloping line with a smooth fall that is characteristic for an α-pyrrone 3,4- double bond is absent in these cases.

Thus, the results of the ozonization of monomeric and polymeric coumarins completely confirms the conclusions that we drew previously [1-3] concerning the structure of copolymers of coumarins.

It was also important to investigate whether, under the conditions of radical polymerization, dimeric forms of the coumarins are produced (through the 3,4- double bond of the α-pyrone ring), these being similar spectrally to the polymeric forms of the coumarins. For this purpose, some of the monomeric coumarins (II, V-VII) were kept for a suitable time under

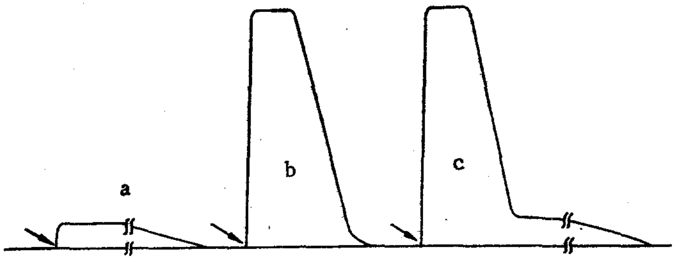

Fig. 1. Types of peaks on a diagram of the ozonization of the double bonds of monomeric coumarins and their copolymers with N-vinylpyrrolidone (the arrows indicate the beginning of ozonization).

the conditions in which the copolymerization process was usually performed (initiator, solvent, 70°C), but without the addition of N-vinylpyrrolidone (I). The compounds isolated from the reaction mixture corresponded completely to the initial coumarins in their physicochemical constants and their IR, UV, and PMR spectra.

The formation under certain conditions of complexes of (VIII) with bishydroxycoumarin in which the conjugated system of the coumarin is retained has been shown by Cho et al. [6]. We have established that under conditions of radical polymerization no complexes are formed between (II), (V-VII), 4-hydroxycoumarin, or esculetin and polyvinylpyrrolidone (VIII). It has been shown that broadening of the lines in the PMR spectra of the copolymers takes place through the inhibition of molecular motions because of the high molecular weights of the copolymers (40,000-80,000) and not because of the interaction of the monomeric coumarins with the (VIII). The results of a study of the PMR spectra of mixtures of (VIII) with a number of monomeric coumarins (II, V, VII) with a change in the concentrations of the coumarins from 10^{-1} to 10^{-3} M showed that there was no broadening of the lines of the spectra in a single case. This indicates that there is no interaction between (VIII) and the coumarins mentioned. Otherwise, a broadening of the lines would necessarily have been observed [10, 11].

EXPERIMENTAL

The molecular weights were determined by the sedimentation method on a Beckman model E analytical ultracentrifuge. Ozonization was carried out on a Soviet instrument "Analizator dvoinykh svyazei-3" (ADS-3) under the conditions recommended by the inventors of the instrument. During the work it was established that in our case the best solvent was not CCl_4 or $CHCl_3$ (at 0°C), but glacial acetic acid (at room temperature). For the ozonization of one material we took from three to five weighed samples (depending on the agreement of the results) of 5-10 mg each. It was shown by special experiments that the sensitivity of the instrument permits the double bonds of the compounds of the coumarin series to be detected reliably even with a sample weighing only 0.3 mg.

From the moment of the beginning of ozonization, the recorder of the instrument begins to draw a curve on the graph paper. The return of the curve to the zero line means the end of ozonization. Simultaneously, the number of pulses (consumption of ozone) is counted independently by an automatic counter. The number of double bonds is calculated from the final total of the pulses. For monomeric coumarins the number of double bonds is calculated to one molecule (since the substance is homogeneous and the molecular weight is accuractely known). For the coumarin copolymers, the number of double bonds is determined per gram of substance. Since in copolymers of N-vinylpyrrolidone with a series of coumarins the double bonds are retained only in the coumarin units (in the side chains and furan rings), on the basis of the number of double bonds determined it is possible to calculate the composition of the copolymer. We give two examples of the calculation of the compositions of copolymers starting from the number of double bonds (DBs) found.

1. Copolymer of N-Vinylpyrrolidone (VP) with Osthole (Ost). Ozonization was performed in glacial acetic acid at room temperature.

Each unit of the VP-Ost copolymer contains only one double bond (in the side chain). This was shown by the course of ozonization (which lasted 5 min) and the shape of the diagram, which was similar to that illustrated in Fig. 1b. The molecular weight of Ost is 244, and therefore 1 g of Ost contains 0.004098 mole and, consequently, the same fraction of a mole of the double bonds. A figure of 0.00073 mole of DBs/gram of copolymer was found. From this the composition of this polymer was calculated as: molecular composition: Ost = 17.8 mole %; VP = 82.2 mole %; weight composition: Ost = 32.3%; VP = 67.7%.

2. Copolymer of VP with Gosferol (Gf). The conditions of ozonization, its course, and the type of peak on the diagram were the same as for the copolymer of VP and Ost. The molecular weight of Gf is 286. Hence each gram of GF contains 0.006993 mole of DBs (since each unit of the polymeric Gf contains two double bonds — in the side chain and in the furan ring).

A figure of 0.00134 mole of DBs per gram of the given copolymer was found. From this its composition was calculated. Molar composition: Gf = 19.2 mole %; VP = 80.8 mole %. Weight composition: Gf = 37.9%; VP = 62.1%.

The compositions of the other copolymers of VP with coumarins having double bonds in side chains and in furan rings were calculated similarly. It was shown experimentally that aromatic double bonds are not ozonized. The consumption of ozone and, therefore, the area of the peak and the number of pulses depend on the size of the sample and the number of double bonds in the compound.

Stilbene and cinnamic acid were used as standards. The reactions of the monomeric coumarins with azobisisobutyronitrile, used as initiator in copolymerization, and also with polyvinylpyrrolidone were performed under the conditions usually adopted for the production of copolymers of N-vinylpyrrolidone with coumarins [1-4].

SUMMARY

The ozonization of the double bonds in polymeric coumarins has been performed for the first time. The results obtained have confirmed that the copolymerization of coumarin and its derivatives with N-vinylpyrrolidone takes place at the 3,4- double bond of the α-pyrone ring, and double bonds in furan rings and side chains do not take part in the polymerization reaction and are readily determined by ozonolysis. The time of ozonization, the shape of the curves on the diagram, and the number of pulses provide an easy possibility of determining the type of double bonds ozonized and their number.

It has been shown by PMR spectroscopy and by the ozonization of double bonds that under the conditions of radical copolymerization monomeric coumarins do not dimerize and do not form complexes with polyvinylpyrrolidone.

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