THE STRUCTURE OF THE PRODUCTS OF THE INTERACTION OF BENZOXAZOLONE DERIVATIVES WITH α, β-DICHLOROPROPIONYL CHLORIDE IN THE PRESENCE OF TRIETHYLAMINE

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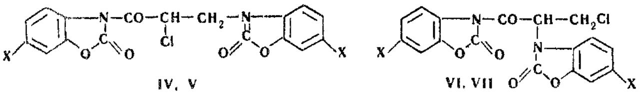
It has been shown that the products of the reaction of benzoxazolone (I) and 6-chlorobenzoxazolone (II) with α, β-dichloropropionyl chloride in the presence of triethylamine are, respectively, 3-[β-(N-benzoxazolonyl)-α-chloropropionyl] benzoxazolone and 3-[β-(N-6-chlorobenzoxazolonyl)-α-chloropropionyl]-6-chlorobenzoxazolone. A possible explanation of the fact that in the reaction of I and II in the presence of triethylamine only the chlorine atom in the β-position of derivatives of α, β-dichloropropionic acid takes part, is that the chlorine in the α-position is deactivated through enolization.

As a result of the reaction of benzoxazolone (I) and 6-chlorobenzoxazolone (II) with α, β-dichloropropionyl chloride (III) in the presence of triethylamine, we have obtained substances the structures of which might correspond to formulas IV and V or VI and VII [1].



IV, V VI, VII

IV, VI: X = H; V, VII: X = Cl

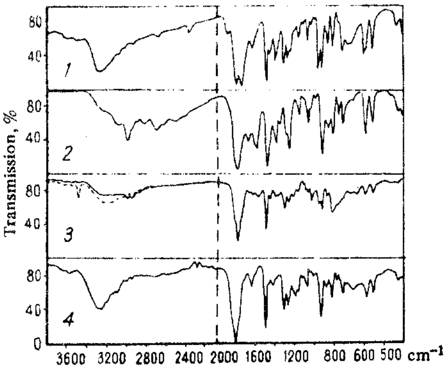


Fig. 1. IR spectra of N-(α-chloropropionyl)-6-chlorobenzoxazolone (XIV): 1) in a potassium bromide tablet; 2) ammonium salt of the enolic form of XIV in the pure state; 3) saturated solution in carbon tetrachloride (spectrum of a dilute solution in CCl_4 shown by a broken line); 4) in acetonitrile solution.

The fact that the reaction of I and III gives 3-[β-(N-benzoxazolonyl)-α-chloropropionyl]benzoxazolone (IV) was shown by reducing the latter with zinc dust [2] to 3-[β-(N-benzoxazolonyl)propionyl]benzoxazolone (VIII). The structure of (VIII) was confirmed by synthesis from the sodium derivative of benzoxazolone and β-chloropropionyl chloride in anhydrous dioxane.

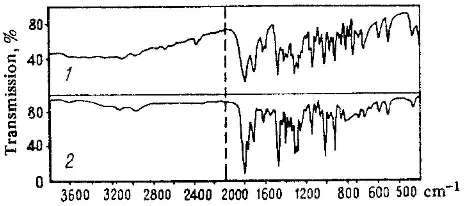


Fig. 2. IR spectra of N-(β-chloropropionyl(-6-chlorobenzoxazolone (XI): 1) in a potassium bromide tablet; 2) in carbon tetrachloride solution.

At first N-(β-chloropropionyl)benzoxazolone (X) was obtained, and then X was converted into VIII. The identity of the samples of VIII obtained by the reduction of IV and from X was shown by mixed melting points and their IR spectra. The structure of 3-[β-(N-6-chlorobenzoxazolonyl)-α-chloropropionyl]-6-chlorobenzoxazolone (V) was shown analogously, but the reduction of V was carried out with sodium borohydride [3], since treatment with zinc dust was accompanied by hydrolysis. The instability of the N-acyl derivatives of 6-chlorobenzoxazolone to hydrolysis is explained by the lower basicity of benzoxazolones containing electronegative groups in position 6.

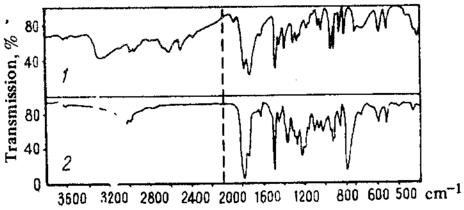


Fig. 3. IR spectra of ethyl β-(N-6-chlorobenzoxazolonyl)-α-chloropropionate (XV): 1) in a potassium bromide tablet; 2) in acetonitrile solution (cell thickness 0.06 mm).

When V was subjected to acid hydrolysis in aqueous ethanolic solution, esterification took place simultaneously with the formation of ethyl β-(6-chlorobenzoxazolonyl)-α-chloropropionate.

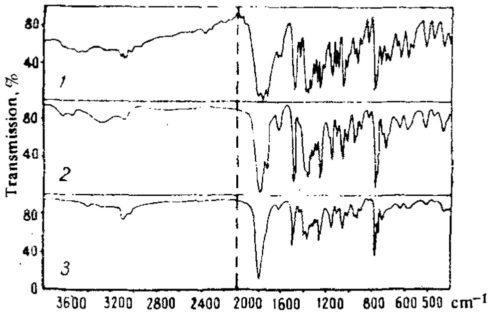
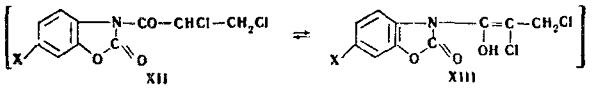


Fig. 4. IR spectra of 3-[β-(N-benzoxazolonyl)-α-chloropropionyl]benzoxazolone (IV): 1) in a potassium bromide tablet; 2) saturated solution in acetonitrile in a 0.06 mm cell with compensation of the absorption of the acetonitrile by means of a cell of variable thickness; 3) saturated solution in benzene under the same conditions.

We explain the formation of IV and V in the reaction of I and II with III in the presence of triethylamine by the fact that in **XII** and **XIII**, which are apparently intermediate reaction products, the chlorine the α-position is deactivated through enolization [4].



XII XIII

XII: X = H; XIII: X = Cl

To confirm the fact that enolization takes place, we synthesized N-(α-chloropropionyl)-6-chlorobenzoxazolone (**XIV**), the IR spectra of which were studied in detail in different states of aggregation. The spectrum of **XIV** compressed into a tablet of potassium bromide (curve 1) has strong bands in the region of the absorption of an OH group participating in the formation of hydrogen bonds. In the region of the absorption of carbonyl groups, there are two bands with frequencies of 1792 and 1742 cm^{-1}. The band at 1792 cm^{-1}, like that at 1633 cm^{-1}, is due to the vibrations of the benzoxazolone moiety. The first band represents the vibration of a carbonyl group in a five-membered ring and the second the fully symmetrical vibrations of a benzene ring. Both these bands are present in the spectrum of N-methylbenzoxazolone. The 1742 cm^{-1} band relates to the vibrations of a carbonyl group in an α-chloro amide grouping. The fairly high value of the frequency of its vibrations shows the considerable attraction of the electron pair of the nitrogen in the benzoxazolone system. The IR spectrum of **XIV** compressed into potassium bromide shows that in the crystalline state **XIV** is present as an equilibrium mixture of ketonic and enolic forms. The presence of the enolic form is confirmed by the absorption due to the vibrations of an OH group.

The absorption relating to the vibrations of the double bond of the enolic form in the 1600–1700 cm^{-1} region could not be detected, evidently because of the strength of the absorption in this region of the curve of the band with a frequency of 1742 cm^{-1}. However, a band relating to these vibrations can be seen clearly at 1680 cm^{-1} in the spectrum of the product of the interaction of XIV with triethylamine, which is the ammonium salt of the enolic form (Fig. 1, curve 2). In the spectrum of **XIV** in carbon tetrachloride (saturated solution, 0.4 mm cell), there is only one band in the region of the absorption of carbonyl groups, with a frequency of 1784 cm^{-1}, which relates to the vibrations of the carbonyl group of the benzoxazolone moiety (curve 3). The band at 1742 cm^{-1} has disappeared. In its place one can detect only a weak shoulder on the curve of the 1784 cm^{-1} band. In the region of the absorption of OH groups participating in hydrogen bonds, there are bands similar to the bands in the spectrum of **XIV** in the crystalline state. In the spectrum of a dilute solution (5 mm cell) in this region there is a narrow band with a frequency of 3480 cm^{-1} which must be ascribed to the vibrations of a free OH group. The appearance of this band on dilution shows that the molecule of the enolic form of **XIV** is associated by intermolecular hydrogen bonds in carbon tetrachloride. The absence of a band at 1742 cm^{-1} shows that in carbon tetrachloride solution **XIV** is present almost completely in the enolic form. This change in the equilibrium between the enolic and ketonic forms on passing from the crystalline state to a solution in carbon tetrachloride, the dielectric permeability of which is 2.23, gives grounds for assuming that the ketonic form possesses a higher dipole moment than the enolic form and that its concentration should rise on passing to a medium with a higher dielectric permeability [5]. The spectrum of **XIV** dissolved in acetonitrile, the dielectric permeability of which is 37.5, shows that in fact the shoulder at 1742 cm^{-1} has become more well-defined, but, nevertheless, no separate band like that in the spectrum of the crystalline sample has appeared.

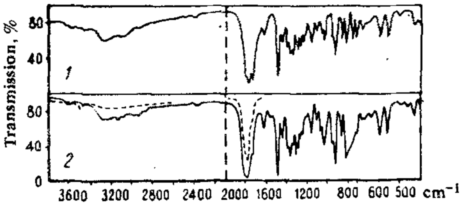


Fig. 5. IR spectra of 3-[β-(N-6-chlorobenzoxazolonyl)-α-chloropropionyl]-6-chlorobenzoxazolone (V): 1) in a potassium bromide tablet; 2) saturated solution in carbon tetrachloride (the spectrum of a dilute solution in a 5 mm cell is shown by the broken line).

Taking into account all that has been said, above, and also the fact that for **XII** and **XIII** the keto-enol equilibrium must be shifted in the direction of the enol more than for **XIV** because of the influence of an additional chlorine atom, and taking into consideration the dielectric permeability of benzene, which is 2.3, it can be stated that **XII** and **XIII** exist in benzene solution in the enolic form.

The presence of chlorine in the β-position to the carbonyl group is insufficient to cause the appearance of the enolic form in appreciable concentration, as can be seen from the **IR** spectra of N-(β-chloropropionyl)-6-chlorobenzoxazolone (Fig. 2), which show the absence of appreciable absorption in the region of the bands of OH group, while the pattern in the region of the carbonyl bands does not change on passing from the crystalline state to solution.

The presence of the enolic forms of **IV** and **V** is shown by their IR spectra (Figs. 4 and 5).

EXPERIMENTAL

3-[β-(N-Benzoxazolonyl)propionyl] benzoxazolone (VIII). a) With stirring, 6 g of zinc dust was added to a solution of 2 g (6.2 mM) of IV [1] in 20 ml of ethanol, and then 10 ml of concentrated hydrochloric acid was added in small portions over an hour and the mixture was left overnight. The reaction product was extracted with benzene, and the solvent was eliminated in vacuum. This gave **VIII**, yield 1.25 g (70%), mp 186° C (from a mixture of isooctane and benzene). Found, %: N 8.75; 8.95. Calculated for $C_{17}H_{12}N_2O_5$, %: N 8.64.

b) To the dry alkoxide obtained from 1.15 g (0.05 g-atom) of sodium in 20 ml of absolute ethanol were added 40 ml of dry dioxane and a solution of 6.75 g (0.05 mole) of benzoxazolone in 40 ml of dry dioxane. With stirring, 6.4 g (5 mM) of β-chloropropionyl chloride was added to the cooled reaction mixture at such a rate that the temperature did not rise above 10° C. Stirring was continued for another hour at room temperature and the mixture was left to the following day. The precipitate that had deposited was filtered off and the solvent was evaporated off in vacuum, after which the addition of petroleum ether precipitated N-(β-chloropropionyl)benzoxazolone (**X**), yield 47%, mp 88°-89° C (from a 3:1 mixture of petroleum ether and benzene). Found, %: Cl 15.02; 14.56. Calculated for $C_{10}H_8ClNO_3$, %: Cl 15.47.

With cooling and stirring, a mixture of 1.35 g (10 mM) of benzoxazolone and 1 g (10 mM) of triethylamine in 20 ml of benzene was added to a solution of 2.25 g (10 mM) of **X** in 20 ml of benzene. The mixture was stirred for an hour at room temperature and filtered. After partial elimination of the solvent, petroleum ether precipitated from the filtrate 3-[β-(N-benzoxazolonyl)propionyl] benzoxazolone (VIII), yield 60%, mp 184°-186° C (from a mixture of petroleum ether and benzene). It gave no depression of the melting point in admixture with the sample obtained by method (a).

3-[β-(N-6-Chlorobenzoxazolonyl)propionyl] -6-chlorobenzoxazolone (IX). a) A solution of 0.24 g (6.2 mM) of $NaBH_4$ in 25 ml of benzene was added in drops, with stirring, to a suspension of 2.6 g (6.2 mM) of V in 30 ml of benzene. The reaction mixture was boiled for an hour, cooled to 0° C, treated with 1 ml of water, and filtered, and the precipitate extracted with benzene. After the solvent had been distilled off, **IX** was obtained, yield 0.9 g (40%), mp 176°-178° C (from a small amount of ether). Found, %: Cl 18.43; N 7.24; 7.40. Calculated for $C_{17}H_{20}Cl_2N_2O_3$, %: Cl 18.06; N 7.12.

b) Under the conditions used for the synthesis of **X**, 6-chlorobenzoxazolone gave a 44% yield of N-(β-chloropropionyl)-6-chlorobenzoxazolone (**XI**), mp 106°-107° C (from a mixture of petroleum ether and benzene). Found, Cl 27.62; 27.63; N 5.53; 5.56%. Calculated for $C_{10}H_7Cl_2NO_3$, %: Cl 27.30; N 5.38. The action of 6-chlorobenzoxazolone and triethylamine on **XI** gave a 25.4% yield of **IX**, mp 178° C (from a mixture of petroleum ether and benzene). Found, %: Cl 18.14; 18.40; N 7.39; 7.39. Calculated for $C_{17}H_{10}Cl_2N_2O_5$, %: Cl 18.06; N 7.12.

Ethyl β-(N-6-chlorobenzoxazolonyl)-α-chloropropionate (XV). A solution of 1 g (0.23 mM) of V in 10 ml of ethanol was treated with 10 ml of 20% hydrochloric acid, and the mixture was boiled under reflux for 30 minutes and filtered. From the filtrate after partial evaporation in vacuum and the addition of water, XV was obtained with a yield of 44.3%, mp 93°-94° C (from a 4:1 mixture of petroleum ether and benzene). Found, %: C 47.58; 47.09; H 3.71; 4.20; Cl 23.38; 23.42. Calculated for $C_{12}H_{10}Cl_2NO_4$, %: C 47.52; H 3.30; Cl 23.10.

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