These data show that IV exists primarily in the A form in a dilute solution in chloroform, whereas an equilibrium between both forms with predominance of the A form is established in concentrated solution. The appearance of the band of an exocyclic azomethine group is associated with the existence of intermolecular hydrogen bonds. The same changes are also characteristic for a 20% solution of IV in $CHCl_3$. Only one peak for the $C=N$ bond at 1652 cm^{-1} is observed in the IR spectrum of a 20% solution of IV in dioxane. Thus the equilibrium is sensitive to the nature of the solvent.

In other words, an analysis of the spectra of the 2-aminobenzoxazole derivatives in the region of the frequencies of the $C=N$ vibrations provides evidence for the existence of two tautomeric forms and that the tautomerism of these types of compounds depends primarily on the medium and is independent of the form of the substituent attached to the nitrogen atoms.

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SPECTRA OF 3-BENZOXAZOLONYLPROPANONES

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The effect of substituents on the vibrational frequencies of oxazolonyl and acetonyl carbonyl groups was studied by means of the IR and PMR spectra of a series of substituted (in the benzene ring) 3-benzoxazolonylpropanones. The experimental data and the results of correlation analysis show that the carbonyl group of the acetonyl grouping is situated along the axis perpendicular to the plane of the benzene and heterocyclic rings and the substituent. The mechanism of transmission of the effect of substituents on the characteristic frequencies and the chemical shifts of the protons of the acetonyl group in the spectra are discussed.

Benzoxazolones have diversified pharmacological activity. 5-Chlorobenzoxazolone (Paraflex or Chloroxazone) and 6-chloro, 5-bromo-, and 6-bromobenzoxazolones [1, 2] are used in medicine as central myorelaxants. The activity of 5-chloro-3-benzoxazolonylpropanone and particularly its oxime surpasses the activity of the preparations Paraflex and Midocalm [3]. A number of N-substituted aryloxazolones have hypnotic, analgesic, anesthetic, anticonvulsive, and antimicrobial activity [4]. A study of the molecular and electronic structures of these compounds is therefore of definite interest, particularly in connection with the establishment of the relationship between the structure and activity. In the present research we investigated the effect of polar substituents on some characteristic vibrational frequencies and chemical shifts, as well as the conformation of substituted 3-benzoxazolonylpropanones. We first desired to thoroughly analyze the effect of substituents in the aromatic ring on the electronic structure of the oxazolone and acetonyl carbonyl groups of these substances, knowing that the IR spectra of such structures satisfactorily explain their reactivities [5, 6].

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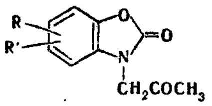
TABLE 1. Spectral Data and Substituent Constants for 3-Benzoxazolonylpropanones

Compound	IR spectrum, ν, cm^{-1}				F	M	Fs*	Ms*	σ^-	PMR spectrum δ, ppm			
	C=O (ring)	Δ	C=O acetonyl	Δ						CH_2	Δ	CH_3	Δ
Ia	1779	0	1743	0	0	0	0	0	0	4,847	0	2,295	0
Ib	1785	+6	1744	+1	0,65	−0,70	0,35	−0,10	0,227	4,882	0,035	2,307	0,012
Ic	1787	+8	1743	0	0,68	−0,77	0,36	−0,11	0,232	4,881	0,034	2,306	0,011
Id	1785	+6	1742	−1	0,61	−0,84	0,33	−0,12	0,180	4,873	0,026	2,305	0,010
Ie	1796	+17	1744	+1	1,23	1,14	0,66	0,16	1,270	5,024	0,177	2,347	0,052
If	1790	+11	1746	+3	0,80	1,19	0,43	0,17	0,820	4,956	0,109	2,331	0,036
Ig	1775	−4	1742	−1	0,20	−2,58	0,11	−0,37	−0,268	4,790	−0,057	2,276	−0,019
Ih	1792	+13	1743	0	—	—	0,71	−0,21	—	4,914	0,067	2,318	0,023

*The F^S and M^S constants are constant for specific system [they are identical for eqs. (1) and (3)].



I a-h

Ia-g $R'=H$; I a $R=H$, b $R=6\text{-}Cl$, c $R=6\text{-}Br$, d $R=6\text{-}I$, e $R=6\text{-}NO_2$,
f $R=6\text{-}SO_2NH_2$, g $R=6\text{-}OCH_3$; I h $R=5\text{-}Cl$, $R'=6\text{-}Br$

Two absorption bands of carbonyl groups are observed in the IR spectra of ketones I (see Table 1): The band at 1775-1796 cm^{-1} is associated with the stretching vibrations of the oxazolone carbonyl group, and the band at 1742-1746 cm^{-1} is due to the stretching vibrations of the carbonyl group of the acetonyl grouping. It has been shown [3] that substitution of the nitrogen atom in benzoxazolone does not substantially change the position of the band of the ring carbonyl group in the spectra. However, the frequency of this group varies appreciably (Δν 21 cm^{-1}) under the influence of substituents in the ring (R and R', see Table 1), while the second band remains virtually unshifted in the case of substitution in the benzene ring.

For the quantitative characterization of the effect of substituents on the carbonyl frequency of oxazolone we used the method of Dewar and Grisdale [7]. In view of the simultaneous presence of two transmission bridges (the oxygen and nitrogen atoms) for the transmission of the effect of the substituents correlation analysis with the use of σ substituent contants for these systems is not suitable. The F and M values used in this research and indicated in Table 1 were taken from [7] and consequently were reduced for the specific system: these values correspond to those for benzene with a correction for the constants of field effect F and were obtained by division of the Dewar values by 1.886. This value is the arithmetic mean between 2 and $\sqrt{3}$, which are the values recommended for p- and m-substituted benzenes, since in our case the carbonyl group is bonded with the aromatic ring through the oxygen and nitrogen atoms, which are in the meta and para positions relative to the substituent in the 6 position. According to [7], the overall effect of substituents can be divided into two components: an effect (inductive and mesomeric, which is characterized by M values) that is transmitted through the π-electron system, and a field effect that is transmitted directly through space to the reaction center and is characterized by F values. The σ-inductive effects can be disregarded when the substituent is sufficiently far away from the reaction center.

The relationship between the frequency of the carbonyl group of oxazolone and the F and M values of the substituents is shown by the correlation equation

$$\Delta\nu_{C=O} = 23.02F + 14.06M - 0.35 \tag{1}$$
$$(n = 8,\ R = 0.993,\ \text{frequency interval } 21\ cm^{-1})$$

The high correlation coefficient (R) shows that there is an excellent correlation relationship between the $\Delta\nu_{C=O}$ values and the calculated F and M factors. It is apparent from the ratio of the regression coefficients for the F and M values that the change in the frequency of the oxazolone carbonyl group is determined to a great extent by the field effect of the substituents, although the effect of transmission through the π-electron system also has definite weight.

Knowing the large role of the field effect of substituents in the first case, at first glance it is difficult to explain the absence of an appreciable change in the frequency of the acetonyl carbonyl group. In fact, this group is separated from the π-electron system by a methylene bridge, and it is obvious that electronic effects cannot have a substantial influence on it. However, on the other hand, the distances of the oxazolone and acetonyl carbonyl groups from the substituent in the 6 position are the same, and this should lead to extremely close frequencies due to the field effect of the substituents. We feel that the logical explanation for this disparity can be obtained if the experimental data on the change in the carbonyl frequency of the acetonyl group are regarded as an indication of the specific conformation of the acetonyl group, which is unfavorable for the transmission of the effect of the substituents in the aromatic ring, i.e., if it is assumed that the $C=O$ bond is situated along an axis that is approximately perpendicular to the plane of the benzene ring, the heterocyclic ring, and the substituent, all located in a single plane [8].

This conclusion has been satisfactorily confirmed by an examination of Dreiding models for the molecules of the investigated compounds: The most energetically favorable conformation is that in which the distance between the methylene hydrogen atoms and the hydrogen atoms attached to the C_4 atom, on the one hand, and between the oxygen atoms of the two carbonyl groups, on the other, is a maximum. In this case the acetonyl carbonyl group is situated along an axis that is approximately perpendicular to the plane of the benzoxazolone system.

The changes in the chemical shifts of the methyl and methylene protons of the acetonyl grouping in the PMR spectra of ketones I are given in Table 1. The change in the position of the signals of the methylene protons is greater by a factor of three than in the case of the methyl protons. In addition, there is a direct linear relationship between the chemical shifts of the methyl and methylene protons:

$$\Delta\delta_{CH_2} = 0.3066\,\Delta\delta_{CH_3} + 0.0006 \qquad (n=8,\ R=0.997) \tag{2}$$

This equation shows that the mechanism of transmission of the effect of substituents to the methyl and methylene protons is the same in each case. The relative role of the field effect and the mesomeric effect of the substituents was determined by the Dewar scheme. The following correlation relationship between the $\Delta\delta_{CH_2}$ values and the F and M factors was found:

$$\Delta\delta_{CH_2} = 0{,}176F + 0.244M + 0.001 \qquad (n=8,\ R=0.989,\ \text{interval } 0.234\ \text{ppm}) \tag{3}$$

From a comparison of the changes in the oxazolone carbonyl frequency in the IR spectra under the influence of substituents it is apparent that in this case the mesomeric effect predominates. This result is somewhat unexpected, since it is evident that the protons of the CH_2 group and particularly the CH_3 group are isolated from the π-electron system. Another confirmation of the dominating role of the mesomeric effect was obtained by calculation of the correlation dependence of the $\Delta\delta_{CH_2}$ value on the σ constants, which take into account the increased capacity for conjugation with electron-acceptor substituents:

$$\Delta\delta_{CH_2} = 6.839\sigma^- + 0.034 \qquad (n=7,\ R=0.995,\ \text{interval } 0.234\ \text{ppm}) \tag{4}$$

Equations (3) and (4) show that the changes in the chemical shifts are determined by the mesomeric effects. One should assume that the mesomeric effect is transmitted to the protons of the CH_2 and CH_3 groups through the nitrogen atom, the electron density of which depends markedly on the nature of the substituent. It is also extremely likely that the changes in the chemical shifts of the protons of the acetonyl grouping are to a certain extent due to the changes in the magnetic anisotropy of the benzoxazolone system as a consequence of the significant π-electron interactions of the ring with the substituents.

The results indicated above show that the field effect of substituents has a weak influence on relatively remote σ bonds such as the C—H bonds. On the other hand, when the spatial orientation is favorable, the bonds that contain labile π electrons are polarized even at a considerable distance.

EXPERIMENTAL

The IR spectra of the compounds at 700-2000 cm^{-1} were recorded with a UR-10 spectrometer with an NaCl prism. During calibration by means of the spectrum of water vapors the frequencies were read off with an accuracy of ±1 cm^{-1}. The PMR spectra of solutions of the compounds in d_6-acetone were recorded with a Tesla BS-487-C spectrometer (80 MHz) with tetramethylsilane as the internal standard; the chemical shifts were read off with an accuracy of ±0.004 ppm. Compounds Ia-c, f, h were obtained by previously described methods.

6-Iodo-3-benzoxazolonylpropanone (Id). A 2.6-g (0.01 mole) sample of 6-iodobenzoxazolone was added with stirring to a solution of 0.23 g (0.01 mole) of sodium in 10 ml of absolute ethanol, after which 1.4 g (0.01 mole) of freshly distilled bromoacetone was added dropwise, and the mixture was refluxed for 2 h. The precipitate was separated, washed with water, and recrystallized from 70% aqueous ethanol to give 2.5 g (80%) of a product with mp 154-155°C. Found: N 4.4%. $C_{10}H_8INO_3$. Calculated: N 4.2%.

6-Methoxy-3-benzoxazolonylpropanone (Ig). This compound, with mp 151-152°C, was similarly obtained in 75% yield, except that the reaction was carried out at room temperature, and the product was recrystallized from ethanol. Found: N 6.4%, $C_{11}H_{11}NO_4$. Calculated: N 6.3%.

6-Nitro-3-benzoxazolonylpropanone (Ie). A 2.06-g (0.01 mole) sample of 3-benzoxazolonylpropanone was dissolved with cooling in 4 ml of concentrated H_2SO_4, and a mixture of fuming nitric acid (sp. gr. 1.54) and 0.7 ml of concentrated H_2SO_4 was added dropwise with stirring. The mixture was stirred for another hour, after which it was poured over ice. The precipitate was removed by filtration, washed until the wash waters were neutral, and recrystallized from ethanol—ethyl acetate (1 : 1) to give a product with mp 175-176°C in 72% yield. Found: N 11.2%. $C_{10}H_8N_2O_5$. Calculated: N 11.4%.

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