IR SPECTRA OF DIASTEREOMERIC (WITH RESPECT TO PHOSPHORUS) 2', 3'-O-ALKYLPHOSPHONATES OF NUCLEOSIDES

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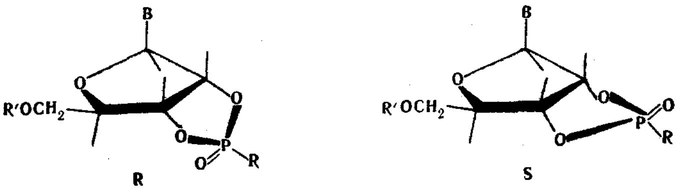
UDC 543.422.4:547.918:541.63

In a study of the IR absorption spectra of diastereomeric (with respect to phosphorus) 2',3'-O-alkylphosphonates of nucleosides it was shown that the IR spectra of the diastereomers differ at 820-860 (ν_{O-P-O}), 1040-1060 (ν_{P-O-C}), and 1250-1300 cm^{-1} ($\nu_{P=O}$). Higher $\nu_{P=O}$ and ν_{P-O-C} values and lower ν_{O-P-O} values are observed for the R isomers (as compared with the S isomers), and this provides a possibility for the determination of the orientation of the P=O group relative to the protons of the phospholane ring in alkylphosphonates of nucleosides by comparison of the spectra of the diastereomers.

Diastereomeric 2',3'-O-alkylphosphonates of nucleosides were obtained by the reaction of alkylphosphonic acid dichlorides with nucleosides. The configuration at the phosphorus atom was established by PMR spectroscopy. In analogy with the literature data, the configuration in which these protons and the P=O group are cis-oriented (the S configuration) was assigned to the isomers in the spectra which the signals of the protons of the phospholane ring are shifted to weaker field, whereas the R configuration was assigned to the isomers with more shielded protons of the phospholane ring [1-4].

In the present paper we present data from a study of these compounds by IR spectroscopy and from a study of the relationship between the IR spectra of the diastereomers and their configuration. We studied the R and S isomers of I-VII:



R

S

I–VII (R and S)

I B = 1-uracilyl, R = tert-butyl; II B = 1-uracilyl, R = triphenylmethyl; III B = 1-(5-fluorouracilyl), R = 1-adamantyl; IV B = 1-(5-bromouracilyl), R = 1-adamantyl; V B = 1-(5-bromouracilyl), R = 1-adamantyl; VI B = 9-adeninyl, R = 1-adamantyl; VII B = 9-(6-methylmercaptopurinyl), R = 1-adamantyl; R' = H for I, III, IV, and VII; R' = Ac for II, V, and VI

A number of examples of the study of five-membered and six-membered cyclophosphonates by IR spectrometry have been described [5-8]. Only the 1200-1300 cm^{-1} range was studied in all of these investigations, and it was shown that there are generally two bands of stretching vibrations related to P=O bonds in this range. Of these, the higher frequency corresponds to the isomer in which the P=O bond is equatorially oriented, and the low frequency is ascribed to the stretching vibrations of the P=O bond in an axial orientation. A doublet band of P=O stretching vibrations is also observed in the spectra of many noncyclic phosphonates; this is due to the existence of these molecules in different conformations. It is shown that the $\nu_{P=O}$ value is somewhat higher than for the conformers in which these parts of the mole-

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Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 181-184, February, 1979. Original article submitted July 18, 1978.

0009-3122/79/1502-0150$07.50

TABLE 1. Frequencies (ν) of I-VII (KBr Pellets)

Compound	ν, cm^{-1}					
	P=O		C–O(P)		P–O(C)	
	R	S	R	S	R	S
I	1268	1260	1060	1053	844	860
II	1271	1247	1056	1045	841	866
III	1261	1242	1059	1051	846	861
IV	1268	1250	1057	1048	844	861
V	1269	1250	1055	1048	845	859
VI	1255	1241	1060	1055	846	862
VII	1265	1246	1061	1055	840	860

TABLE 2. Frequencies (ν) of II, VI, and VII

Compound	ν, cm^{-1}					
	P=O		C–O(P)		P–O(C)	
	R	S	R	S	R	S
Solutions in benzene						
II	1270, 1286	1254	1066	1073	848	860–868
VII	1279	1277	1071	1091	835	846–857
Solutions in chloroform						
II	1285	1274	1071	1042	844	859
VI	1276	1274	1069	1061	846	863

cule are drawn together in the case of conformers in which the oxygen atom of the P=O bond is farther away from the hydrogen atoms of the alkyl groups [10].

We investigated the IR spectra of KBr pellets and solutions of I-VII in benzene and chloroform. Analysis of the data obtained showed that spectral differences are observed for each pair of stereoisomers only at 820-860, 1040-1060, and 1250-1300 cm^{-1}. The spectra turned out to be identical in the other regions. It is known [9-12] that bands of vibrations associated with the phosphorus atom are located in the indicated regions: bands of stretching vibrations of the O–P–O fragment are found at ∿ 850 cm^{-1}, the band at 1040-1060 cm^{-1} is characteristic for the vibrations of the C–O(P) bonds, and the band at 1250-1300 cm^{-1} corresponds to P=O stretching vibrations. In view of the fact that the investigated molecules are very complex, their spectra contain a large number of bands, and there are bands of vibrations of nucleosides that are identical for both diastereomers but are not related to the phosphorus atom in the examined regions, in addition to bands associated with the vibrations at the phosphorus atom. In a number of cases we were unable to achieve complete resolution of these bands, and the bands of the stereoisomers of interest to us appeared in the spectrum in the form of an additional maximum or shoulder on the interfering band. The 1250-1300 cm^{-1} region, which, in addition to the P=O vibrations, contains the vibrations of the uracil or purine rings, proved to be the most difficult to interpret. However, by comparison of the spectra obtained for the solid state with the spectra in different solvents and with the spectra of the starting nucleosides we were able to isolate the bands corresponding to each diastereoisomer.

We were able to achieve the best resolution for the solid state (Table 1). The results obtained for several pairs of stereoisomers in solution in benzene and chloroform are given in Table 2 as examples of the effect of solvents on the position of the bands under consideration. The remaining compounds were found to be too insoluble to obtain qualitative spectra.

It is apparent from Table 1 that $\nu_{P=O}$ is always lower for the isomers in which the P=O group is close to the hydrogen atoms in the 2' and 3' positions of the riboside ring (the S isomer) than for the isomer in which the P=O bond is remote from these hydrogen atoms (the R isomer); this is in agreement with the data in [5-8]. The maxima of the bands for the R isomers are found at 1260-1270 cm^{-1}, whereas the maxima of the bands for the S isomers are found at 1240-1260 cm^{-1}. The frequencies are increased somewhat in the case of solutions, but the frequency of the R isomer remains higher than that of the S isomer.

The bands at 850 and 1050 cm^{-1} in the spectra of the alkylphosphonates are usually assigned to the vibrations of the $C-O-P-O-C$ fragment [9-12]. The $P-O$ bonds make the greatest contribution to the vibrations with a frequency of 840-860 cm^{-1}, while the $C-O$ bonds make the greatest contribution to the 1040-1060 cm^{-1} band. It follows from Table 1 that the values of the frequencies in the 850 cm^{-1} region differ by 10-15 cm^{-1} for the isomers and that the dependence of the frequencies of the vibrations in this region on the orientation of the $P=O$ group is the opposite of the dependence observed for the $\nu_{P=O}$ bands. Thus the higher ν_{P-O} value (as compared with the value for the R isomers) always corresponds to the S isomers. The 840-860 cm^{-1} region is very convenient for the assignment of stereoisomers to the R or S series from the IR absorption spectra. It should be noted that weak bonds at 810-830 and 850-860 cm^{-1}, which do not change on passing from one isomer to the other but are partially overlapped by ν_{P-O} bands, are also present in this interval.

The 1040-1060 cm^{-1} region is of supplementary value in the assignment of the stereoisomers to the R or S series. Bands that differ for the R and S isomers are also observed in this region; however, the difference in the frequencies is only 5-10 cm^{-1}, and the results obtained are consequently less reliable than for the other regions examined above.

The investigated compounds are only slightly soluble in benzene and chloroform, and this made it possible to record sufficiently satisfactory spectra of solutions of any of the investigated compounds. However, an analysis of those cases for which we were able to obtain satisfactory data showed that the frequencies of the $P=O$ stretching vibrations increase somewhat on passing to solutions but that $\nu_{P=O}$ of the R isomer is always higher than the $\nu_{P=O}$ value of the S isomers (Table 2). Splitting of the $P=O$ band into two components was observed for the R isomer of II in solution in benzene. This is probably associated with the existence of a conformational equilibrium in solution. Similar effects on passing from solid samples to solutions in CCl_4 have been observed in the literature for six-membered cyclophosphonates [8]. The bands at 850 cm^{-1} are also shifted somewhat to the high-frequency region when the compounds are dissolved, but the difference between the spectra of the stereoisomers remains sufficiently large to distinguish them.

Identical regularities in the changes in the IR spectra in the regions of vibrations associated with the phosphorus atom are observed in the investigated pairs of diastereomeric cyclophosphonates of nucleosides of the pyrimidine and purine series on passing from the R to the S isomers: one observes high frequencies of the $P=O$ and $C-O(P)$ stretching vibrations and lower frequencies of the $P-O(C)$ vibrations for the R isomers as compared with the S isomers. A difference in the state of the conformational equilibrium of the ribose ring in purine and pyrimidine nucleosides is not displayed in this case. It has been previously assumed on the basis of an analysis of the dihedral $H-C-O-P$ angles calculated from ^{13}C NMR and PMR data that the preferred conformation in solutions is that in which the phosphorus atom deviates from the plane of the ring (exo for the R isomer and endo for the S isomer) and that $P=O$ in these isomers occupies a pseudoequatorial position. However, the data from the IR spectra make it possible to assume greater equatorial character of the $P=O$ bond in the R isomers as compared with the S isomers.

EXPERIMENTAL

The spectra of KBr pellets of the diastereomers of I-VII and of solutions of the diastereomers of VII and II in benzene and of VI and II in chloroform were recorded in sodium chloride cuvettes with a constant thickness of 1.04 mm for sample concentrations of $1 \cdot 10^{-2}$ mole/liter. The results are presented in Tables 1 and 2.

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EFFECT OF THE HETEROATOM ON THE ENERGIES OF THE BOUNDARY MOLECULAR ORBITALS OF DIBENZO DERIVATIVES OF FIVE-MEMBERED HETEROCYCLES

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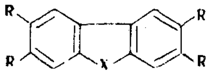
UDC 541.65

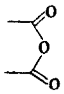
The effect of the heteroatom on the energy characteristics of their boundary molecular orbitals was studied by investigation of the charge-transfer complexes (CTC) of the dibenzo derivatives of five-membered heterocycles. Tetramethyl-substituted dibenzo derivatives of five-membered heterocycles were investigated as electron donors, and their corresponding dianhydrides were investigated as electron acceptors. Their ionization potentials and electron affinities, respectively, were determined. From the regularities in the change in these characteristics it was concluded that replacement of one heteroatom by another leads to approximately identical energy shifts of both boundary molecular orbitals.

The energy characteristics of the boundary molecular orbitals (BMO) for a number of similar compounds are directly related to their properties, such as, for example, their ability to undergo oxidation and reduction. The establishment of the regularities in the change in the BMO therefore makes it possible to predict certain properties of an unknown compound of a given series. In this connection, the problem of the effect of the heteroatom on the energy characteristics of the BMO of dibenzo derivatives of five-membered heterocycles (I) is extremely interesting since many practically important substances contain this fragment:



I–III

a X = SO_2, b O, c S, d $NCOCH_3$, e NH;

I R = H; II R = CH_3; III RR = 

The energies of the BMO can be characterized by the ionization potentials (IP) and the electron affinities (EA). The latter can be determined by a study of the charge-transfer complexes (CTC) of the investigated compounds both with electron-donor and electron-acceptor components. Since the principles of the effect of the heteroatom on the IP and EA of the I system should not change in the case of a certain modification of the system itself, stronger donors — tetramethyl-substituted dibenzo derivatives (II) — were investigated in the determination of the IP, and the corresponding dianhydrides (III) were investigated in the determination of the EA. For comparison, we investigated the properties of the corresponding sulfones IIa and IIIa.

Except for IIa, all electron donors II readily form CTC with such electron-acceptors as p-chloranil (HA) and tetracyanoethylene (TCNE). New long-wave bands associated with intermolecular charge transfer appear in the absorption spectra of mixed solutions of the compo-

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Riga Polytechnic Institute, Riga 226828. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 2, pp. 185-187, February, 1979. Original article submitted November 24, 1977.