STUDY OF N-ALDONOYL AMINO ACIDS BY IR SPECTROSCOPY

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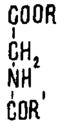
UDC 547.455

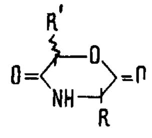
Derivatives of N-aldonoyl amino acids (I) and their lactones (II) are of interest as complexones of ions of polyvalent metals and as highly specific inhibitors of neuraminidases of various origins [1]. During the synthesis of these compounds, two interconverting forms are produced: acyclic – the N-aldonoyl amino acid (I) [2]; and cyclic – the δ lactone (dioxomorpholine) (II) [1]. To investigate the activity of compounds of types (I) and (II) it is necessary to develop a simple and reliable method of showing their cyclic or acyclic structure.

For this purpose we have studied the IR spectra in the 1800-600 cm^{-1} region of compounds (1-8) with the known structure (I) [2].



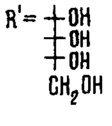
$COOR-CH_2-NH-COR'$

(I)

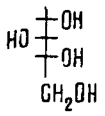


(II)

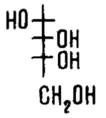
R=H, CH_3, t-Bu (8)



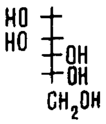
(1)



(2)



(3)



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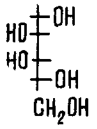

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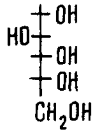
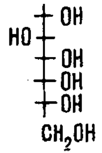


(6)



(7)

The determination of the cis or trans configuration of the ester grouping of the frequency of the vibrations of the C=O group is extremely difficult, since in the δ-lactone form (cis configuration) $\nu_{C=O} = 1740$ cm^{-1}, and in the linear esters (trans configuration) $\nu_{C=O} = 1720\text{-}1750$ cm^{-1} [3]. Consequently, we turned to a consideraion of the amide CONH group, which may also possess the cis or the trans configuration. The isomerism of the CONH group has been studied in amides [4, 5], short peptides [6], lactams [7], and cyclic peptides – dioxopiperazines [8] – in the solid state. It has been shown that for the cis and trans configurations there are considerable differences in the IR spectra in the region of the amide II vibrations (N–H plane deformation vibration): amide $II_{cis} = 1440\text{-}1460$ cm^{-1}, amide $II_{trans} = 1540\text{-}1570$ cm^{-1}; and in the amide V vibrations (N–H nonplanar deformation vibration): amide $V_{cis} = 760\text{-}850$ cm^{-1}, amide $V_{trans} = 690\text{-}720$ cm^{-1}.

M. M. Shemyakin Institute of the Chemistry of Natural Compounds of the Academy of Sciences of the USSR. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 381-384, May-June, 1974. Original article submitted February 19, 1973.

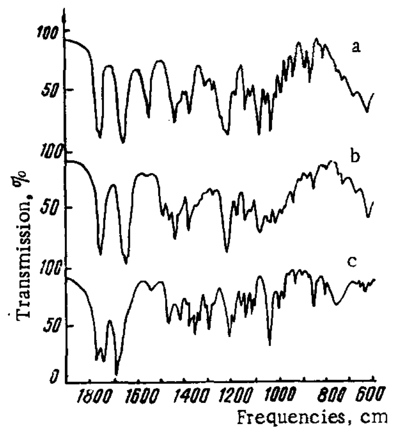


Fig. 1. IR spectra of N-arabonylglycine (3) (*a*), of O,N-deuterated N-arabonoylglycine (b), and of the diketomorpholine $\underline{\text{L-Val-L-HyIv}}$ (c).

In view of the fact that form (II) is a stereoanalog of the dioxopiperazines in which the CONH group is in the cis configuration [9] and drawing an analogy between form (I) and secondary amides or diamides of the type of $R_1COR_3NHC^{\alpha}$ $HCONHR_2$ (trans configuration), we assumed that when the acyclic form (I) was produced a strong band should appear in the IR spectrum in the 1540-1570 cm^{-1} region, corresponding to the amide II vibration, and a band in the 690-720 cm^{-1} region of the amide V vibration, while when form (II) was produced no bands of the amide II and V vibrations should appear in these regions. Figure 1 shows the IR spectrum of compound (3), which is typical for all the compounds (1-8). In actual fact, the spectrum of this compound shows a strong band at ~1550 cm^{-1}. We assign the bands at 1750, 1650, and 1550 cm^{-1} to the stretching vibrations of the C=O group in the $O{=}\overset{|}{C}{-}O$ grouping of the amide I and the amide II vibrations, respectively. The appearance of a shoulder at 1660 cm^{-1} should probably be assigned to the interaction of the vibrations of the C=O groups between neighboring molecules in the crystal. The assignment of the band at 1550 cm^{-1} to the amide II vibrations was checked from the IR spectrum of deuterated compound (3) (see Fig. 1b), in which the band in the 1550 cm^{-1} region has disappeared. In addition, the IR spectrum of the deuterated compound (3) also changed considerably in the 1000-1100 cm^{-1} and 710-690 cm^{-1} regions. In the first of them, apparently, are located the planar deformation vibrations of the C−OH groups, and in the second the amide V vibrations, overlaid by the band of the nonplanar deformation vibrations of the C−OH groups. It must be mentioned that for compounds (1-7) an increase in the length of the chain and a change in the configuration of the radical R have practically no influence on the form of the IR spectrum in the region studied, and the frequency of the vibrations of the carbonyl of the ester grouping changes within the range from 1740-1750 cm^{-1}, that of the amide I vibrations between 1650 and 1660 cm^{-1}, that of the amide II vibrations between 1540 and 1550 cm^{-1}, and that of the amide V vibrations between 690 and 700 cm^{-1}. Only when R is changed from CH_3 to tert-Bu in compound (8) does the amide I band shift from 1635 cm^{-1} and a band appear at 840 cm^{-1} corresponding to the vibrations of the $-C-(CH_3)_3$ grouping [10]. With the production of the cyclic form (II), however, the IR spectrum should be similar to the spectrum of dioxomorpholine (see Fig. 1c), in which there is no strong band at ~1550 cm^{-1} and the band of the amide V vibrations is found at 765 cm^{-1}. A low-intensity band at ~1530 cm^{-1} indicates the presence of a small amount of the acyclic form, which is produced in the synthesis of the dioxopiperazines. The appearance of a band at 1770 cm^{-1} must also probably be explained by the interaction of the molecules in the crystal.

EXPERIMENTAL

The IR spectra of compounds (1-8) were taken on a Perkin−Elmer 257 spectrophotometer with diffraction gratings (tablets with KBr and paraffin oil in the 2000-600 cm^{-1} region). The accuracy of the measurements was ± 2 cm^{-1}. The instrument was calibrated from the absorption band in the IR spectrum of polystyrene.

CONCLUSIONS

IR spectroscopy is suggested as a convenient method for determining the difference in the cyclic (dioxomorpholine) and acyclic forms of N-aldonoyl amino acid derivatives. It has been shown that in the acyclic forms, unlike the cyclic, there are strong absorption bands at 1570 cm^{-1} and 690-720 cm^{-1} corresponding to the amide II and V vibrations.

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