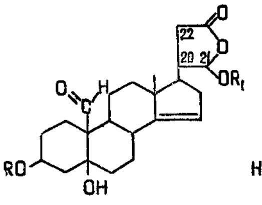
THE MASS SPECTROMETRY OF THE PRODUCTS OF THE ALKALINE ISOMERIZATION OF DIFFUGENIN

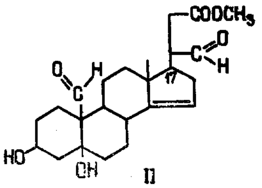
G. K. Makarichev* and Ya. V. Rashkes

UDC 543.51+547.926

It has been shown previously that under the action of alkalis the lactone ring of the cardiac aglycone diffugenin [1] forms a tautomeric pair – a hydroxy lactone and an aldehydo acid, the methyl derivatives of which can be isolated in the individual state [2]. The methoxy lactone (I) is more stable in an alkaline medium and the methyl ester of the aldehydo acid (II) in an acid medium.

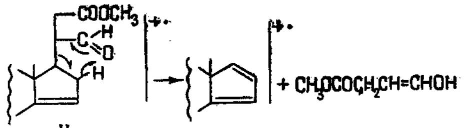


I. R=H; R_1=CH_3
III. R=R_1=H
IV. R=R_1=Ac



II

On comparing the mass spectra of the two substances, their fairly close similarity can be seen (Fig. 1). As in the spectra of the cardenolides of the strophanthidin series [3] the molecular ions do not appear. In the region of high masses, those peaks are strongest which characterize the successive alternate expulsion of CO, H_2O, a methoxy radical, and methanol from the ion with m/e 400 (M−H_2O) in each case. In spite of the differences in the structure of the substituents at C_{17}, the ejections of CH_3O and CH_3OH from the ions with m/e 400 take place with approximately equal intensities. At the same time, the elimination of CO and that of H_2O in the spectra of (I) and (II) differ quantitatively. One of the causes of this is the difference in the tendency of the substituent at C_{17} to split off. The contribution of this process to the total ion current is five times greater in (II) than in (I), which is apparently due to the possibility of the existence of a six-membered transition state.



II m/e 284

The ease of splitting out the substituent is confirmed by the presence in the spectrum of (II) of a peak with m/e 302 due to the splitting out of 116 amu directly from M^+.

The ion with m/e 284, by ejecting CO and H_2O, is converted into the ion with m/e 238. The satellites of this peak with m/e 239 and 237 are formed through different methods of splitting out of the substituent at C_{17} from the ion with m/e 354. In the spectra of (I) and (II) there is an inverse relationship between the

---

*Deceased.

Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances of the Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 301–304, May–June, 1971. Original article submitted March 26, 1971.

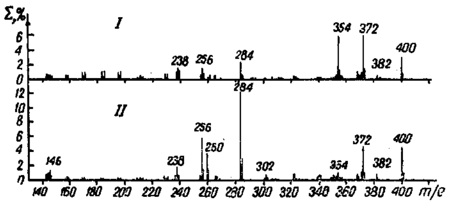
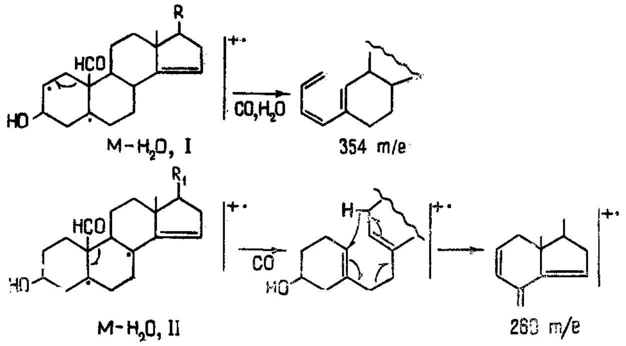


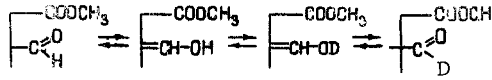
Fig. 1. Mass spectrum of the methoxy lactone (I) and of the methyl ester of the aldehydo acid (II).

intensities of the peaks with m/e 354 and (260 + 261), the coefficient of which ~5. This is explained by the dissimilar forms of stabilization of the ions, which takes place according to the following scheme:



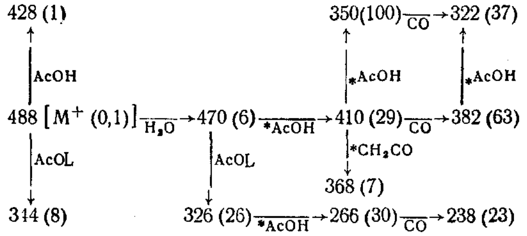
The hypothesis of the cleavage of the bond adjacent to the quaternary C_{10} atom is in good agreement with the fact that the substituent on this atom splits out in the form of CO and not as a formyl radical. A group of peaks with m/e 229-231 analogous to the ions with m/e 260 and 261 is present in the mass spectra of cardiac aglycones with a 5β-OH group that we have studied (strophanthidin, strophanthidol, periplogenin, diffugenin, and their derivatives). On the other hand, in the spectrum of pachygenin – an aglycone with a $\Delta^{5,6}$ bond – this group of peaks is absent. At the same time, in the latter case CHO splits off together with CO. The detachment of the substituent at C_{17} from the ions with m/e 260 and 261 forms a group of peaks with m/e 144-147.

We have performed the deuteration of (I) and (II) by briefly heating solutions of the substances with CD_3OD. The shifts of the peaks in the spectra of the D analogs confirmed the course of fragmentation described above. The peaks with m/e 400, 372, 284, and 256 in the spectra of (I) were shifted by one unit, and the peaks with m/e 354 and 238 did not change. Somewhat different results were obtained in the case of the methyl ester (II). The peaks with m/e 400 and 372 were shifted by two mass units, and the peaks with m/e 284, 260, and 256 by one mass unit. The group of peaks with m/e 237-238 did not undergo an isotopic shift. Thus, one excess atom of deuterium is fixed in the aldehydo acid side chain. It can hardly be assumed that the isotopic label is present in position 22, i.e., in the α position to the C=O bond, since the deuteration of (I) under analogous conditions does not lead to an additional shift. Most likely an equilibrium with the vinyl alcohol not completely shifted in the direction of the aldehyde form is observed, leading to the accumulation of deuterium by the following mechanism:



Substance (II) was also heated for a long time in CD_3OD solution (20 h, ~100°C). Under these conditions, the $M-H_2O$ peak shifted by five and partially even by six mass units. The fact that the peaks in the region of high masses shifted in corresponding fashion and the peak with m/e 284 shifted by only one mass unit permits the statement that all the deuterium atoms with the exception of one were present in the side chain at C_{17}. In addition to the introduction of deuterium at C_{20}, the transesterification of the methyl ester into the trideuteromethyl ester took place. Furthermore, a certain amount of the isotopic label penetrated into C_{22}. An analysis of the spectrum shows that the main form produced as a result of prolonged heating is the methoxy lactone form (I). In actual fact, the intensity of the peaks with m/e 284 and 260 decreased and that with m/e 354 increased.

In addition to the spectra of the methoxy derivatives (I) and (II), the spectra of the hydroxy lactone (III) and of the 3β,21-diacetoxy lactone (IV) were taken. The spectrum of (III) differed little from the spectra of cardenolide derivatives; here the splitting out of the hydroxy lactone substituent took place with a very low intensity. In the spectrum of the diacetate (IV), the main contribution was made by the successive splitting out of two molecules of acetic acid (see Scheme), but a fundamental role was also played by the splitting out of the substituent at C_{17} as a whole (the absence of the corresponding metastable peaks suggests that after the splitting out of the acetoxy group from C_{21} the splitting out of the lactone residue does not take place).



(The relative intensities, %, are given in brackets; AcOL – acetoxy lactone.)

Thus, on comparing the spectra of (I), (III), and (IV), it can be seen that the nature of the substituent at C_{21} has an influence mainly on the quantitative changes. The qualitative features include the ejection of ketene from the ion with m/e 410 (confirmed by a m* peak) in the spectrum of (IV). A similar property is possessed by the acetates of phenols or vinyl alcohols. Consequently, the electron density on the C_{21} atom is higher, which agrees well with the behavior of the hydroxy lactone grouping in the IR spectrum, where C=O absorbs about 1800 cm^{-1} [2], i.e., in the same range of frequencies as β,γ-unsaturated five-membered lactones [4].

Experimental conditions: MKh-1303 instrument fitted with a system for the direct introduction of the sample; temperature 120-140°C; ionizing voltage 40 eV.

SUMMARY

The features of the mass-spectrometric behavior of the products of the alkaline isomerization of diffugenin confirm the conclusions drawn previously concerning the structures and relative stabilities of these compounds.

LITERATURE CITED

1. G. K. Makarichev and N. K. Abubakirov, Zh. Obshch. Khim., 32, 2372 (1962).
2. G. K. Makarichev and N. K. Abubakirov, Khim. Prirodn. Soedin., 4, 92 (1968).
3. R. Brandt, H. Kaufmann, and T. Reichstein, Helv. Chim. Acta, 49, 1844 (1966).
4. W. West, Chemical Applications of Spectroscopy, Interscience, New York (1956).