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MORPHOLINIZATION OF AMINOACYLOXY ACIDS AND HYDROXYACYLAMINO ACIDS AND THEIR ESTERS UNDER MASS SPECTROMETRY CONDITIONS

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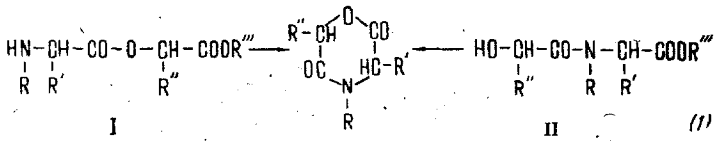
We have shown previously [1] that when the higher cyclodepsipeptides are subjected to mass spectrometry the formation of 3,6-dialkyl-2,5-dioxomorpholines takes place under the influence of the high temperature [2]. To effect this conversion the rupture of two bonds in the macrocycle with subsequent ring closure of an ester or an amide bond is required. Consequently, it appeared of interest to study the possibility of the formation of dioxomorpholines in the mass spectrometry of the aminoacyloxy acids and their esters (I) and also in that of the hydroxyacylamino acids and their esters (II), which are the simplest models of linear depsipeptides



I

II

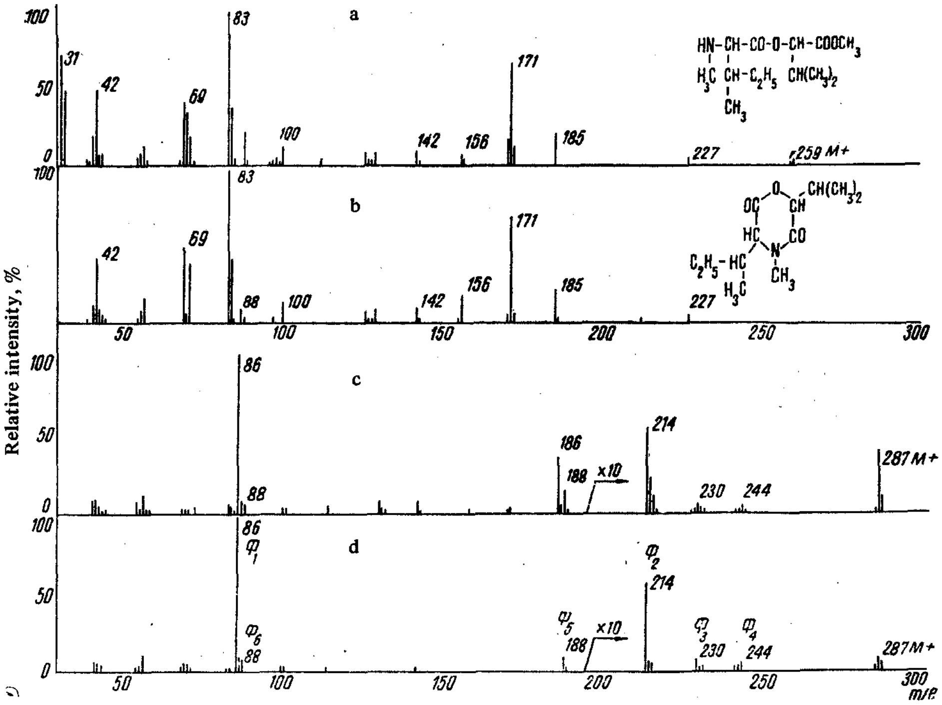
(1)

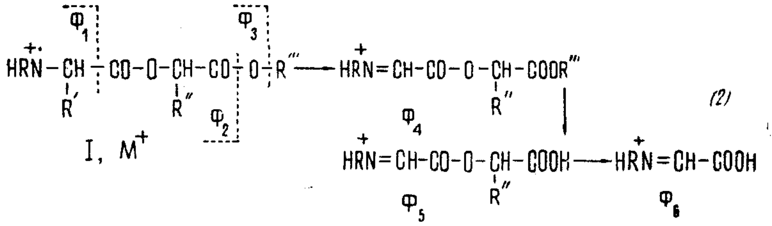
Compound	R	R′	R′′	R′′′
I a	H	$(CH_3)_2CH$	CH_3	H
I b	CH_3	$(CH_3)_2CH$	$(CH_3)_2CH$	CH_3
I c	CH_3	$(CH_3)_2CH$	$(CH_3)_2CH$	$(CH_3)_3C$
I d	CH_3	$(CH_3)_2CHCH_2$	$(CH_3)_2CH$	$(CH_3)_3C$
I e	H	$(CH_3)_2CH$	$(CH_3)_2CH$	$(CH_3)_3C$
I f	H	$(CH_3)_2CH$	CH_3	$(CH_3)_3C$
II a	H	$(CH_3)_2CH$	$(CH_3)_2CH$	H
II b	CH_3	$C_2H_5CH(CH_3)$	$(CH_3)_2CH$	CH_3
II c	CH_3	$(CH_3)_2CHCH_2$	$(CH_3)_2CH$	CH_3
II d	CH_3	$(CH_3)_2CH$	$(CH_3)_2CH$	$(CH_3)_3C$

All the compounds studied are divided into two groups differing markedly in their behaviour under mass spectrometry conditions. The first group includes the free acids Ia and IIa and also the methyl esters of the hydroxyacylamino acids IIb and IIc the mass spectra of which are similar to (and in the case of the free acids identical with) the spectra of the corresponding 3,6-dialkyl-2,5-dioxomorpholines [1, 3]. The absence of peaks of the molecular ions in the spectra of free acids is explained by the fact that compounds of this type readily cyclize even on vacuum sublimination (cf., for example, [4]). The mass spectra of the methyl esters IIb and IIc have peaks of the molecular ions, but their intensities depend on the temperature and decrease rapidly with time, which is a consequence of the thermal effect in mass spectrometry [2]. In addition to the morpholine fragments, the spectra of the methyl esters IIb and IIc show the presence of fragments with m/e 32 $(CH_3OH)^+$, 31 $(CH_3O)^+$, and 29 $(HCO)^+$, which are characteristic for methyl esters (figure, a).

Compound	m/e of the characteristic fragments						
	M^+	Φ_1	Φ_2	Φ_3	Φ_4	Φ_5	Φ_6
(Ib)	245	86	—	—	202	—	88
(Ic)	287	86	214	230	244	188	88
(Id)	301	100	228	244	214	188	88
(Ie)	273	72	200	216	230	174	74
(If)	245	72	172	188	202	146	74

The second group includes the tert-butyl esters Ic–If and IId and also the methyl ester of the aminoacyloxy acid Ib, in the spectra of which the morpholine peaks have a very low intensity and hardly increase with a rise in the temperature. Characteristic of the fragmentation of these compounds are processes generally observed in the mass spectrometry of esters of linear peptides and depsipeptides [5] (cleavage of amide and ester bonds, elimination of the radical R' from the amino acid residue, formation of a very high intensity amine fragment). The routes of the decomposition of the molecular ions of these compounds are given in schemes (2) and (3) and the m/e values of the fragments formed are given in the table and in scheme (3).

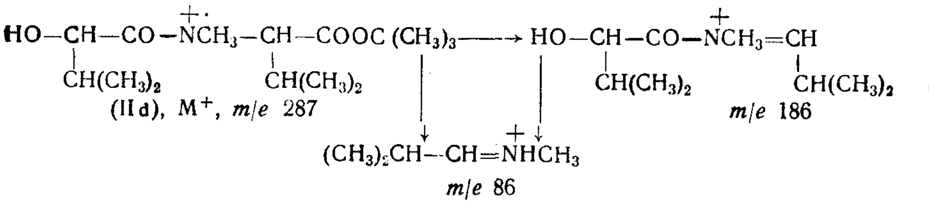




(2)

Mass spectra. a) IIb; b) 3-isopropyl-6-sec-butyl-2,5-dioxo-N-methylmorpholine; c) IId; d) Ic.

A characteristic difference of the mass spectrum of IId from that of Ic, which contains the same acid residues in the reverse sequence, is the presence of an intense peak of a fragment with m/e 186 arising as the result of the elimination of an alkoxycarbonyl group from the molecular ion (cf. scheme (3) and figure, c and d). In this case the amine fragment has the form of a rearranged ion. The other fragments in the in the spectrum of IId are formed by the same routes as the corresponding fragments Φ_2–Φ_6 in the mass spectra of the esters of the aminoacyloxy acids (cf. Scheme (2)].



$$\underset{\text{(IId), } M^+,\ m/e\ 287}{\mathrm{HO{-}\underset{CH(CH_3)_2}{CH}{-}CO{-}\overset{+\cdot}{N}CH_3{-}\underset{CH(CH_3)_2}{CH}{-}COOC(CH_3)_3}} \longrightarrow \underset{m/e\ 186}{\mathrm{HO{-}\underset{CH(CH_3)_2}{CH}{-}CO{-}\overset{+}{N}CH_3{=}\underset{CH(CH_3)_2}{CH}}} \quad (3)$$

$$\downarrow\qquad\downarrow$$

$$\underset{m/e\ 86}{\mathrm{(CH_3)_2CH{-}CH{=}\overset{+}{N}HCH_3}}$$

The mass spectra were taken on a standard MKh-1303 instrument with a glass inlet system at 120°–150° C and an energy of the ionizing electrons of 25–50 eV (the use of a system for the introduction of the sample directly into the ion source led to a fundamental change in the pattern of the mass spectrum).

Summary

1. Free hydroxyacylamino acids and their methyl esters, and also free aminoacyloxy acids, morpholinize under mass spectrometry conditions.

2. In the mass spectrometry of methyl esters of aminoacyloxy acids and tert-butyl esters of aminoacyloxy acids and hydroxyacylamino acids no morpholinization takes place. These compounds behave similarly to the esters of acylated peptides and depsipeptides.

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