STRUCTURE OF ISOBADKHYSIN. THE STEREOCHEMISTRY OF BADKHYSIN AND ISOBADKHYSIN

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By chromatography on alumina of the total lactones obtained by the sodium carbonate treatment of the resin from the roots of Ferula oopoda (Boiss. et Buhse) Boiss., we have isolated a substance with the composition $C_{20}H_{24}O_5$, mp 189–190° C, which we have called "isobadkhysin."

The IR spectrum of the substance (Fig. 1) has absorption bands at (cm^{-1}) 1760 (γ-lactone ring), 1702 (α,β-unsaturated ester group), 1658 (conjugated ketone group of a five-membered ring), 1618 and 1635 (double bonds). The UV spectrum has the maxima characteristic for a conjugated system (λ_{max} 340 and 252 mμ, log ε 1.82 and 4.45, respectively). These facts show that the isolated compound belongs to the sesquiterpene lactone group.

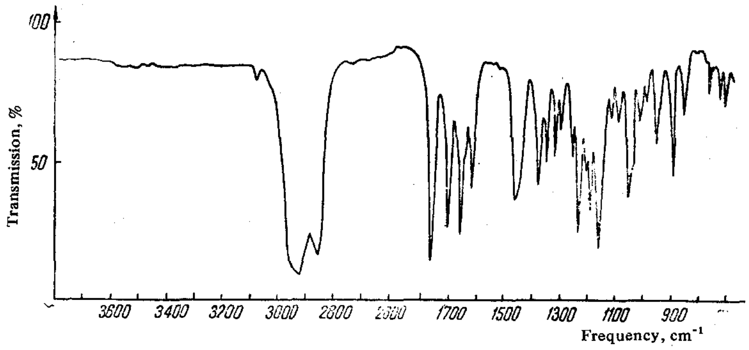


Fig. 1. IR spectrum of isobadkhysin.

By comparing the IR and UV spectra of isobadkhysin and badkhysin [1], ferulin [2, 3], jacquinelin [4], and other substances we may conclude that isobadkhysin is apparently a stereoisomer of badkhysin, or differs from the latter in the positions of the functional groups and the double bonds.

The NMR spectrum of the substance (Fig. 2a) shows the presence of a guaiane carbon skeleton as the basis of the lactone under investigation. A doublet with a center at τ 8.82 ppm (J = 7 Hz, 3H, CH_3—CH<) and two three-proton singlets at τ 7.85 ppm (CH_3—$\overset{|}{C}$=, 3H) and 7.52 ppm (CH_3—$\overset{|}{C}$=, 3H) determine the nature of the methyl groups in the isobadkhysin molecule. A weakly resolved signal with τ 8.10 ppm (J = 1.5 Hz, CH_3—$\overset{|}{C}$=, 3H) and a doublet at τ 7.98 ppm (J = 7 Hz, CH_3—CH=, 3H) belong to an ester group. The chemical shifts and the spin-spin coupling constants of the protons of the side chain in the isolated compound and in badkhysin and semopodin [5] are extremely similar to one another. This confirms the fact that the structures of the ester groups are identical. The saponification of isobadkhysin, like that of badkhysin [6], gave angelic acid with mp 44–45° C.

A broadened singlet in the NMR spectrum of isobadkhysin at τ 3.82 ppm (2H) with a diffuse base is the result of the superposition of the singlet signal of the olefinic proton at C_2 (1H) and the multiplet of —CH= (1H) of the angeloyl group. The signals of the protons adjacent to the lactone oxygen atom and in the ester group are also superposed on one another and are found in the 5.15-τ region (2H).

Direct comparison of the NMR spectra of badkhysin and isobadkhysin (Table) shows that they are stereoisomers.

When the resin, obtained by a known method [7], was chromatographed on a column of alumina, we were unable to isolate isobadkhysin. Thus, the latter is merely the product of the isomerization of badkhysin. In fact, brief treatment of badkhysin with sodium carbonate leads to the formation of a substance with mp 189–190° C which gives no

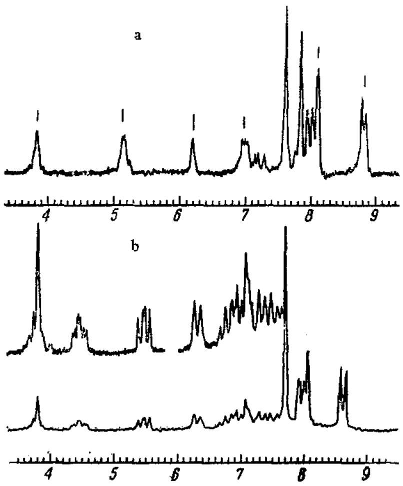


Fig. 2. NMR spectra of a) isobadkhysin and b) badkhysin.

depression of the melting point in admixture with isobadkhysin. The IR spectra of the substances compared were also identical while, as the NMR spectrum showed, there was no change in the positions of the substituents, functional groups, and double bonds.

Table

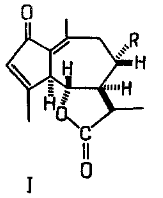
Substance	CH_3– at C_{11}	$CH_3-\overset{\vert}{C}=$	$\overset{CH_3}{-CH=}$	$CH_3-\overset{\vert}{C}=$ at C_1 and C_4	H at C_{19}	H at C_8	H at C_6	Olefinic proton at C_2 and ester group
		ester group						
Badkhysin	d 8,62 J=7 Hz	s 8,05 J=1.5Hz	d 7,95 J=7 Hz	s 7.7 (6H)	d 6,3 J=10 Hz	q 5.45 J_1=10 Hz J_2=7.5Hz	m 4.45 J_1=10 Hz J_2=10 Hz J_3= 4 Hz	3,82 (2H)
Isobadkhysin	d 8,82 J=7 Hz	s 8.10 J=1.5 Hz	d 7.98 J=7 Hz	s 7.85 (3H) s 7.62 (3H)	6.2 J<1 Hz		5.15 (2H)	3.82 (2H)

Note: s) singlet, d) doublet, q) quartet, and m) multiplet.

We used the spin-spin coupling constants to elucidate the stereochemical features of badkhysin and isobadkhysin.

On considering the NMR spectrum of badkhysin (Fig. 2b) the following conclusion can be drawn with respect to its stereochemistry. The coupling constants between the H_8 and H_{10} (10 Hz), H_8 and H_7 (7.5 Hz), and H_7 and H_6 (10 Hz) protons are comparatively large. This shows that the dihedral angles between these protons approximate to 180°. Consequently, the protons mentioned, taken in pairs, have the trans position with respect to one another. The coupling constant between the H_8 and H_{10} protons in isobadkhysin is less than 1 Hz. Furthermore, the sum of the coupling constants of the lactone proton and the hydrogen atom at C_6 is considerably diminished. In addition to the change in the coupling constants, there are considerable changes in the chemical shifts of the protons at C_6 (Δ 0.7 ppm) and of the methyl groups at C_1 (Δ 0.15 ppm) and C_{11} (Δ 0.2 ppm). The changes in the spectrum of isobadkhysin compared with the spectrum of badkhysin that have been pointed out show that isomerization of both the lactone ring at the C_8 center and the substituent at C_6 has taken place.

The results obtained permit badkhysin and isobadkhysin to be formulated as I and II.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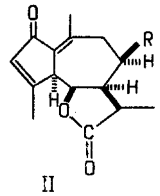
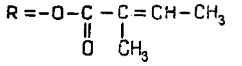

II


$$R = -O-\underset{\underset{O}{\Vert}}{C}-\underset{\underset{CH_3}{\vert}}{C}=CH-CH_3$$

EXPERIMENTAL

The IR spectra were taken on a UR-20 instrument (paraffin oil), the UV spectra on an SF-4a spectrophotometer (96% ethanol), and the NMR spectra on a JNM-4H-100 spectrophotometer (with deuterated chloroform as solvent). The internal standard was tetramethylsilane.

Isolation of isobadkhysin. A solution of 50 g of the resin (after the elimination of the bulk of the badkhysin) in 50 ml of ethanol was treated with 100 ml of 5% aqueous sodium carbonate solution and the mixture was heated in a water bath for 5 min, diluted with water, cooled, and extracted with ether (3 × 100 ml). The aqueous layer was acidified with dilute H_2SO_4 and extracted with ether (3 × 100 ml). The ethereal extract was washed with water, dried over Na_2SO_4, and filtered. The residue, after distillation of the ether, was chromatographed on a column of alumina (activity grade II, height 20 cm, diameter ~3 cm).

The substances were eluted from the column with a petroleum ether–ether mixture (2 : 1 and 1 : 1), with ether, and with an ether–chloroform mixture (2 : 1). The volume of each fraction was 200 ml. The fractions obtained by elution with the ether–chloroform mixture (2 : 1) yielded isobadkhysin with the composition $C_{20}H_{24}O_5$, mp 189–190° C (from aqueous ethanol).

Saponification of isobadkhysin. A solution of 0.1 g of isobadkhysin in 10 ml of ethanol was boiled in a water bath with 5 ml of 5% aqueous KOH for 30 min. Then it was diluted with water, the ethanol was evaporated off, and the residue was cooled and acidified with dilute H_2SO_4. The amorphous precipitate was filtered off and the filtrate was distilled with steam. The organic acid was extracted with ether, and the extract was dried over Na_2SO_4, filtered, and evaporated. The residue consisted of an oil which crystallized on standing with mp 44–45° C.

Isomerization of badkhysin. A solution of 0.2 g of badkhysin in 10 ml of ethanol was shaken with 10 ml of 5% sodium carbonate solution for 3 min. On treatment by the method described above, isobadkhysin with mp 189–190° C (from ethanol) was obtained.

CONCLUSIONS

1. By chromatography of the total lactones obtained from the sodium carbonate treatment of the resin of the roots of Ferula oopoda (Boiss. et Buhse) Boiss. we isolated a previously unstudied sesquiterpene lactone $C_{20}H_{24}O_5$, mp 189–190° C, which we called isobadkhysin.

2. It has been shown that isobadkhysin is a stereoisomer of badkhysin and is formed during the treatment of the resin with sodium carbonate.

3. The stereochemical characteristics of badkhysin and isobadkhysin have been established on the basis of their NMR spectra.

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