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THE STRUCTURE OF BADKHYSIN

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From the results of chemical studies and measurements of the UV and IR spectra and the partial interpretation of the NMR spectra (the NMR spectra were taken on a spectrometer with a working frequency of 40 MHz in chloroform) of badkhysin and some of its derivatives we have suggested that badkhysin has the carbon skeleton of geigerin and that its probable structure is (I) [1]. However, the proposed structure could not explain why during the hydrogenation of badkhysin no migration of the methylene double bond into the lactone ring is found, as is frequently the case with many lactones (aromatin [2], aromaticin [2], peruvin [3], hysterin [4], cumanin [5], badkhysinin [6], etc) having a methylene double bond on a lactone ring. It was also not clear what causes the strong maximum at 1678 cm^{-1} in the IR spectrum of badkhysin. This maximum is not found in the di- or tetrahydro derivatives of badkhysin and, consequently, is not connected with the tetrasubstituted double bond of a lactone ring.

A revision of the structure of badkhysin was carried out with an NMR spectrometer having a resolving power of 100 MHz. The NMR spectra of badkhysin and its di-, tetra-, and hexahydro derivatives and also the spectra of hydroxy keto lactones, a diketo lactone, a dienic keto lactone with mp 148-149° C, and a pyrazoline derivative of badkhysin were recorded.

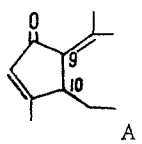
These substances, with the exception of the dienic keto lactone with mp 148-149° C, were obtained as described previously [1]. An analysis of the NMR spectra (figure, a-f) of badkhysin and its derivatives taken in deuterated chloroform permits the conclusion that the structure of badkhysin corresponds to formula (II) and not (I).

Thus, in the NMR spectrum of this substance (figure, a) the two usual doublets of the vinyl protons of a methylene group on a lactone ring are absent and, consequently, the signals in the region of vinyl protons are not connected with the protons of a methylene group but are due to protons of a different provenance. The NMR spectrum of badkhysin [1] has only one doublet with τ 8.62, J = 7 Hz (3H), which is characteristic for a secondary methyl group CH_3—CH; however, this may be expected in the NMR spectra of substances both with formula (I) and formula (II).

It is particularly important that, in addition to the vinyl methyl protons of an angeloyl group observed at τ 8.0 (6H), there is a singlet at τ 7.7 reflecting the presence of six protons in badkhysin, which shows the presence in it of two additional vinyl methyl groups. There is no doubt that these two vinyl methyl groups must be present at the CH_3 group of five- and seven-membered rings. In the region of vinyl protons, badkhysin has a signal at τ 3.82 (2H) which is based on a multiplet signal (area—one proton) of the vinyl proton of an angeloyl group upon which is superposed the singlet signal of the vinyl proton of a ring (area—one proton). In the NMR spectrum of dihydrobadkhysin, there is no singlet signal of a vinyl proton at τ 3.82, but there is a multiplet at the same τ value which is ascribed to the vinyl proton of an angeloyl group. In addition to this, the area of the vinyl methyl protons in the NMR spectrum of dihydrobadkhysin decreases to three (τ 7.78) and a second doublet of a secondary methyl group appears with a center at τ 8.72 (J = 6 Hz). This shows that one of the double bonds of hydrogenated badkhysin is secondary-tertiary.

Although such a double bond could occupy different positions in the molecule of badkhysin, its position at C_1—C_2 of the five-membered ring is most likely since in addition to the disappearance of this double bond the IR spectra of dihydrobadkhysin does not show the strong band at 1678 cm^{-1}, which obviously indicates the presence of strong conjugation in badkhysin. Correspondingly, the keto group of the five-membered ring must be present in position 3 and not 2 as suggested previously. The second double bond (tetrasubstituted at a CH_3 group) must be in position 4-9 in view of the fact that dihydro- and tetrahydrobadkhysins retain a conjugated keto group (UV and IR spectra).

Thus, it may be concluded that structural fragment A is present in the badkhysin molecule.



A

Lactones with a similar structural fragment are known. A comparison of the properties of badkhysin with the UV and IR spectra of these compounds shows that they are similar (table).

Previously, the presence of a methylenic double bond in badkhysin was shown on the basis of three facts: (1) the production of a pyrazoline derivative with mp 182-183° C, which suggested, as in many other cases, not only the

Substance	CO-group, cm^{-1}			Double bonds, cm^{-1}	UV spectrum, λ, mμ
	lactone	ester	ketone		
Lactucin [7]	1755	—	1662	1623 1610	255 (log ε 4.58)
Matricarin [8]	1793	1745	1693	1645 1623	255 (log ε 4.218)
Leukodin [9]	1788	—	1688	1640 1623	255 (log ε 4.12)
Austricin [10]	1777	—	1686	1640 1622	256 (log ε 4.14)
Jacquinelin [11]	1770	—	1680	1635 1610	255 (log ε 13.700)
Badkhysin	1768	1703	1678	1640 1610	334 (log ε 1.74) 254 (log ε 4.12)

presence of a CH_2 group in the substance but also its possible presence on a lactone ring; (2) the presence of a maximum at 892 cm^{-1} in the IR spectrum of badkhysin; and, (3) the ease of hydrogenation of the substance in the presence of deactivated Raney nickel.

A study of the pyrazoline derivative of badkhysin showed that this derivative has no bands of an unsaturated ester group in the IR spectrum (1703 cm^{-1}). Instead of this maximum, there is a band at 1730 cm^{-1} which is characteristic for a saturated ester group. At the same time, the pyrazoline derivative retains the maximum at 892 and 1678 cm^{-1} characteristic of badkhysin. In the NMR spectrum of the pyrazoline derivative of badkhysin (figure, f) there is no complex signal of a vinyl proton of an angeloyl group, and the total area of the vinyl protons at τ 3.82 has decreased to one proton, present in the form of a singlet. Furthermore, the NMR spectrum lacks the signal of the two vinyl methyl protons of the angeloyl group and a new singlet appears at τ 8.43 together with the doublet of a secondary methyl group with a center at τ 9.0 (J = 7 Hz). The singlet of the methyl vinyl protons with τ 7.73 (6H) is retained.

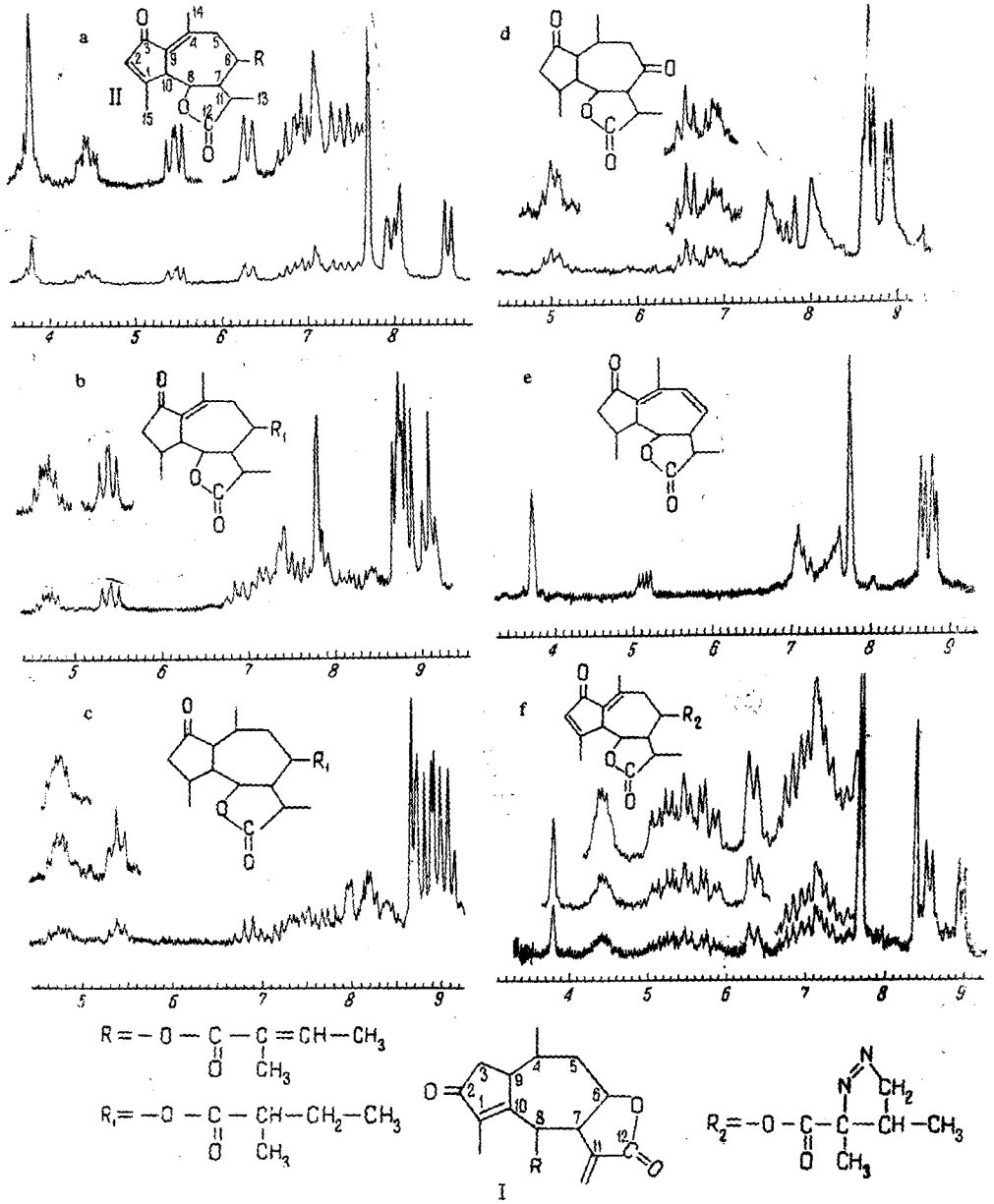
These results show that the pyrazoline derivative of badkhysin is nothing other than the product of the reaction of diazomethane with the double bond of the angeloyl group (VIII) and, consequently, the formation of this derivative cannot always confirm the presence of a methylene double bond. It has been shown that the maximum at 892 cm^{-1} in the IR spectrum of badkhysin may be an indication of the definite presence of a methylenic double bond, since this maximum, although not intense, is observed in some other badkhysin derivatives definitely not containing a CH_2 group. The capacity of the methylene double bonds for readily and selectively undergoing hydrogenation in the presence of deactivated Raney nickel is an important and frequently used reaction which, in many cases, is an excellent indication of the presence of methylenic double bonds, but it is not excluded that other types of double bonds, particularly in highly conjugated systems (as in badkhysin), may hydrogenate with the aid of this weakly active catalyst.

From the results of the NMR spectra of badkhysin and its derivatives, the lactone ring is extremely probable at $C_7 - C_8$.

Thus, the NMR spectrum of badkhysin has a signal in the form of a quartet with a center at τ 5.47 (one proton unit), which, in light of the analysis of the NMR spectra of the other derivatives, possibly represents a proton on a lactone ring (H_8). This signal retains its quartet form in the NMR spectra of di- and tetrahydrobadkhysins with a τ value of 5.4 (J_1 = 10 Hz; J_2 = 3 Hz) and only in the NMR spectrum of hexahydrobadkhysin (figure, c) does it acquire the triplet form with a center at τ 5.4 (J = 10 Hz).

The NMR spectrum of badkhysin also has three doublets (area one proton) with a center at τ 4.45.

The appearance of this signal can apparently be ascribed to a proton of an ester group, since it is retained in the di-, tetra-, (figure, b), and hexahydro (figure, c) derivatives of badkhysin but has a multiplet nature and is not observed in badkhysin derivatives not containing an ester group. Thus, in the NMR spectrum of the diketo lactone (figure, d) this signal is completely absent, and in the spectrum of the hydroxy keto lactones with mp 159–160° C and 186.5–187° C the multiplet signal is shifted in the direction of the strong field (τ 5.95 and 6.01, respectively). Taking into account the nature of the resolution of the signal, it may be assumed that the ester group occupies the C_6 position. Although this question requires further study, the dienic keto lactone (mp–148–149° C) arising by the saponification of di- and tetrahydrobadkhysins has permitted the above-mentioned position of the ester group to be demonstrated. The NMR spectrum of the dienic keto lactone (figure, e) has the signal of vinyl protons in the form of a singlet at τ 3.7 (area 2H), while the proton attached to the lactone oxygen gives a quartet with a center at τ 5.14 (J_1 = 10 Hz; J_2 = 4 Hz). The spectrum contains two doublets of secondary methyl groups at τ 8.67 (J = 6Hz) and 8.81 (J = 5 Hz) and also one singlet of a vinyl methyl group with a τ value of 7.76 (3 proton units).


a
b
c
d
e
f
II
I
R = —O—C(=O)—C(CH3)=CH—CH3
R1 = —O—C(=O)—CH(CH3)—CH2—CH3
R2 = —O—C(=O)—C(CH3)(CH2)—CH(CH3)—CH3

Thus, we concluded that badkhysin has the structure (II) and is 6-angeloyl-3-oxoguai-1(2),4(9)-dien-8,12-olide.

The NMR spectra were taken in the physical methods laboratory of the Institute of the Chemistry of Natural Compounds by V. I. Sheichenko.

Experimental

Tetrahydrobadkhysin (1 g) was dissolved in 50 ml of ethanol, an aqueous solution of caustic potash (2.3 g of KOH in 15 ml of water) was added, and the mixture was heated for 30 min. The solution was left to stand overnight and was then diluted with water and acidified. After 30 min, the reaction product was extracted with diethyl ether. The ethereal solution was filtered through alumina (activity grade III). The ether was evaportated and the residue was recrystallized from a mixture of diethyl ether and petroleum ether 1:1). Mp of the substance isolated 146–148° C; from ethanol 148–149° C.

Found, %: C 73.28; H 7.48. Calculated for $C_{15}H_{18}O_3$, %: C 73.17; H 7.31.

From its UV and IR spectra, the substance obtained is a dienic keto lactone, i.e., an isomer of the dienic keto lactone described previously with mp 128° C [1].

Conclusion

On the basis of a revision of the structure of bakhydsin, it has been established that it is 6-angeloyl-3-oxoguai-1(2),4(9)-dien-8,12-olide (II).

REFERENCES

1. N. P. Kir'yalov and S. V. Serkerov,, ZhOKh, 35, 70, 1965.
2. J. Romo and P. Joseph-Nathan, Diaz A. Chem. industry, 46, 1839, 1963.
3. P. Joseph-Nathan and J. Jomo, Tetrah., 22, 723, 1966.
4. Romo de Vivar, E. A. Brataeff, and T. Rios, J. Org. Chem., **31**, 673, 1966.
5. J. Romo, P. Joseph-Nathan, and G. Siade, Tetrah., **22**, (4), 1099, 1966.
6. N. P. Kir'yalov and S. V. Serkerov, KhPS [Chemistry of Natural Compounds], 2, 93, 1966.
7. D. H. K. Barton and C. R. Narayman, J. Chem. Soc., 963, 1958.
8. A. Čekan, Z. V. Prochazka, V. Herout, and F. Šorm, Coll., **24**, 1554, 1959.
9. M. Holub and V. Herout, Coll., 27, 2980, 1962; K. S. Rybalko and P. S. Massagetov, Med. prom., 11, 25, 1961.
10. W. Herz and K. Ueda, J. Am. Chem. Soc., **83**, 1139, 1961.
11. J. B. Barrera, J. Z. Breton Funes, and G. Gonzales, A J. Chem. Soc., 1298c, 1966.

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