THE CONFIGURATION OF BADRAKEMIN AND GUMMOSIN, AND THE IDENTITY OF ISOBADRAKEMIN, COLLADONIN, AND FARNESIFEROL A

A. I. Saidkhodzhaev and G. K. Nikonov

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Several stereoisomeric terpenoid coumarins of the iresane series with an exocyclic methylene group at C_8 have been described in the literature – farnesiferol A (I), gummosin (II), badrakemin (III), isobadrakemin (IV), and colladonin (V). The first four substances have been isolated from various species of Ferula [1-3], and colladonin from Colladonium triquestra [4].

Only the configuration of farnesiferol A has been established reliably [1]. The fact that the others belong to the iso series was established on the basis of some differences in their physicochemical constants and spectral characteristics.

In an investigation of terpenoid coumarins of the iresane group by NMR spectroscopy, we have also observed that these stereoisomers differ from one another. The values of the chemical shifts (CSs) and the spin–spin coupling constants of (IV) were given by Kir'yalov [3]. We obtained the same indices for substance (II) in a study of the coumarins that we had isolated from Ferula samarcandica. Substance (V) [4] has been isolated by one of us from Colladonium triquestra.

The molecules of substances (I-V) each have four asymmetric centers – at C_3, C_5, C_9, and C_{10}* – and, consequently, it is simply this that explains the difference between the stereoisomers named.

As is well known [5], gummosin and badrakemin differ in their configuration at C_9 [the substituent at C_3 (OH) in both substances has the axial orientation]. A most probable configuration has previously been proposed for these compounds [5]. In badrakemin, the angular methyl group and the substituent at C_9 ($-CH_2OAr$) are present in the cis position and in gummosin in the trans position to one another.

In the NMR spectrum of farnesiferol A (we obtained a sample of this substance from A. P. Prokopenko), in the strong-field region there are signals of the protons of an angular methyl group at 0.83 ppm (s, 3 H), of gem-dimethyl groups at 0.80 and 1.00 ppm (s, 3 H), a broadened signal with its center at 3.25 ppm relating to a proton geminal to a hydroxy group at C_3 (1 H, J = 16 Hz), a doublet at 4.12 ppm due to the protons in an $ArOCH_2-$ grouping (d, 2 H, J = 6 Hz), and singlets at 4.50 and 4.82 ppm from the protons of an exocyclic methylene group (1 H each). The signals of the protons of a 7-hydroxy-substituted coumarin nucleus appear in the 6.1-7.55 ppm region.

In the NMR spectrum of badrakemin [5] there are signals from an angular methyl group at 0.87 ppm, from gem-dimethyl groups at 0.87 and 1.02 ppm (s, 3 H), a signal with its center at 4.21 ppm (2 H, $ArOCH_2-$), and singlets from the protons of an exocyclic methylene group at 4.55 and 4.98 ppm. The spectrum of gummosin shows signals at 1.02 ppm (angular methyl group, s, 3 H) and at 1.02 and 0.87 ppm (gem-dimethyl group, s, 3 H each), two quartets with their centers at 4.43 ppm ($J_1 = 10$ Hz; $J_2 = 5$ Hz) and at 4.11 ppm ($J_1 = 10$ Hz, $J_2 = 7$ Hz), and singlets at 4.72 and 4.82 ppm (s, 1 H each). In farnesiferol A, the angular methyl group and the substituent at C_9 are in the trans position.

* For numbering used, see formula V – Translator.

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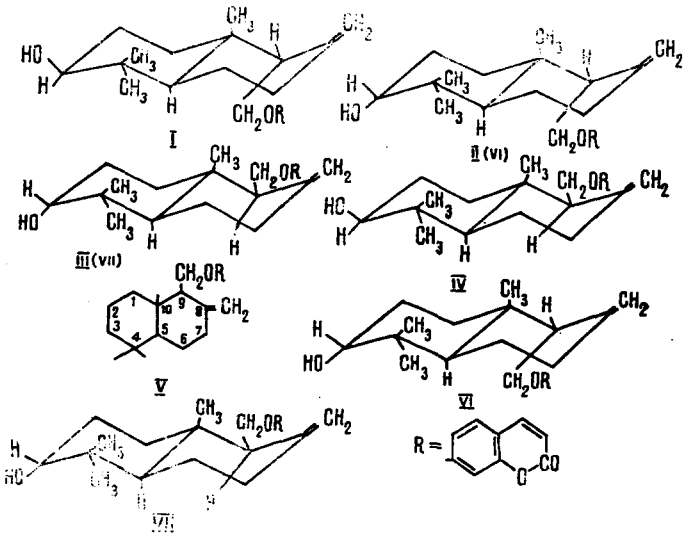
The results of a comparison of the CSs of the protons of farnesiferol A, badrakemin, and gummosin show that the protons in the $ArOCH_2-$ group in the first two compounds are equivalent and appear in the form of a doublet, while in gummosin they are nonequivalent, which causes the appearance of two quartets. When the substituent at C_9 ($ArOCH_2-$) is present in the axial position, i.e., trans with respect to the angular methyl group, the geminal interaction between the methylene protons is apparently absent, and only vicinal interaction is detected with the methine proton at C_9. Conversely, when the same substituent (CH_2OAr) is present in the equatorial position they appear in the form of two quartets, which shows the presence of both vicinal and geminal spin–spin coupling in the $ArOCH_2-CH$ grouping.

Thus, in a comparison of the NMR spectra of these substances it can be seen that in badrakemin the substituent at C_9 is in the axial position and in gummosin it is in the equatorial position: the configurations proposed previously for these substances do not correspond to their spectral characteristics. It is most likely that in badrakemin the angular methyl group and the substituent at C_9 ($ArOCH_2-$) are in the trans position and in gummosin they are in the cis position. On this basis, for badrakemin (III) and for gummosin (II) we propose the following configurations (VI and VII).



In a study of the NMR spectra and the physicochemical properties of colladonin it was established that colladonin is an isomer of farnesiferol A. In these circumstances, it must be isomeric with the latter at at least one of the asymmetric centers mentioned above. The results of a comparison of the NMR spectra of farnesiferol A and colladonin contradict this conclusion. cis Isomers at C_5 are so far unknown, since in all the iresanes isolated the A and B rings have the trans linkage. It is known that the signals of an angular methyl group in the NMR spectra of trans decalins are found in the strong field (at 0.78 ppm) and those of the cis isomers in a weaker field (0.92 ppm) [6].

The CSs of the angular methyl groups in the spectra of the two compounds are practically identical – 0.84 and 0.83 ppm – which corresponds to the trans linkage of the A and B rings of the decalin nucleus in both substances. The same values of the CSs of the proton at C_3 geminal to a hydroxy group (3.25 ppm) and its half-width (Σ 16 Hz) in the NMR spectra of farnesiferol A and colladonin (3.25 ppm, Σ 16 Hz) show that in the molecules of both these substances the hydroxy group has the equatorial orientation. This means that they do not differ in their configuration at C_3, either.

In farnesiferol A, the angular methyl group and the substituent at C_9 are in the trans position [1]; i.e., the $-CH_2OAr$ group has the axial orientation and the methine proton at C_9 the equatorial orientation. In the NMR spectra of farnesiferol and colladonin, the methylene protons in the $ArOCH_2-$ grouping appear in the form of doublets at 4.12 and 4.18 ppm, respectively, with a spin–spin coupling constant $J = 6$ Hz; consequently, the CH_2OAr substituent at C_9 is in the axial position in both substances.

Thus, farnesiferol A and colladonin do not differ in their configurations at C_3, C_5, C_9, and C_{10} and are therefore identical. This conclusion is confirmed by the identity of their IR spectra, the absence of a depression of the melting point of mixtures, and their practically identical optical activities. On the basis of what has been said, the name of colladonin should be eliminated from the literature.

Colladin – colladonin acetate – is the natural acetate of farnesiferol A. The same observations must be made in relation to isobadrakemin. The CS of the angular methyl group and also the CS and spin–spin splitting constants of the substituent at C_9 and the methine proton at C_3 of colladonin coincide completely with those of farnesiferol A.

The agreement of the physicochemical constants of colladonin and of isobadrakemin and the absence of a depression of the melting point of a mixture, to which Ban'kovskii et al. referred in a study of colladonin [4], unambiguously show that isobadrakemin, colladonin, and farnesiferol A are one and the same substance.

At the present time, only three of the four possible stereoisomers of farnesiferol A have been isolated. The fourth – with diequatorial substituents at C_3 and C_9 in this series – has not yet been discovered.

EXPERIMENTAL

The NMR spectra of the substances were taken on a JEOL 60 HL spectrometer. The solvent was $CDCl_3$ with HMDS as internal standard.

SUMMARY

The correlations between farnesiferol A, badrakemin, gummosin, and isobadrakemin have been investigated on the basis of their NMR spectra, which have enabled the configurations at C_3, C_5, and C_9 of the terpenoid coumarins of the iresane group to be determined from their chemical shifts and spin–spin coupling constants.

According to the chemical shifts and spin–spin coupling constants of the signals of the protons at C_3, C_9, and C_{10}, the configurations of gummosin and badrakemin do not correspond to those proposed previously. It has been established that in badrakemin the substituents at C_3 and C_9 have the axial orientation and in gummosin they are in the axial and equatorial orientations, respectively.

According to their spectra, physicochemical constants, and mixed melting points, colladonin and isobadrakemin are identical with farnesiferol A.

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