CONFORMATION OF THE CONFIGURATIONS OF BADRAKEMIN AND GUMMOSIN

A. I. Saidkhodzhaev and G. K. Nikonov

UDC 547.913.55:668.5+587.51

Gummosin has been isolated previously from Ferula gummosa, F. pseudoreoselinum Rgl. et Schmalh, and F. samarcandica Eug. Kor. [1] and badrakemin from F. badrakema [2]. Their structures have been established on the basis of chemical reactions and spectroscopic characteristics, and it has been shown that they are isomers with respect to the orientation of the substituent at C_9 ($-CH_2OAr$): in gummosin (I) the latter is present in the axial position and in badrakemin (II) in the equatorial position [3, 4]. The authors came to this conclusion after the passage from gummosin to farnesiferol A which they effected by the oxidation of gummosin to a ketone and its subsequent reduction with sodium tetrahydroborate. From its melting point and IR spectra, the reduction product was identified as farnesiferol A [1, 4].

The results of a comparative study of the NMR spectra of farnesiferol A, colladin, colladonin, isobadrakemin, badrakemin, and gummosin enabled us to identify isobadrakemin and colladonin with farnesiferol A and to propose configurations for gummosin and badrakemin. According to this, in gummosin the substituent at C_9 is in the equatorial position and in badrakemin it is in the axial position [5]. Our conclusions did not correspond to those drawn by Kir'yalov and Movchan [1] on the basis of chemical reactions, which caused us to doubt the correctness of the passage effected from gummosin to farnesiferol A [1, 4].

The configuration of farnesiferol A has been shown convincingly by chemical reactions: the substituent at C_9 is in the axial orientation [6]. Since in gummosin it is located in the equatorial orientation [5], it is impossible to pass from gummosin to farnesiferol A via the ketone with subsequent sodium tetrahydroborate reduction. This must form not farnesiferol A but the epimer of gummosin at C_3, since the asymmetric center at C_9 is not affected by this transition.

We have repeated this transition under the conditions described by Kir'yalov and Movchan [1] and have studied the products obtained by spectroscopy, comparing them with an authentic sample of farnesiferol A [the sample of the latter was given to us by A. P. Prokopenko and was characterized by us through its physicochemical constants (mp 155-156°C, $[\alpha]_D$ −60°) and its NMR spectrum (Fig. 1, curve a)].

The oxidation of gummosin with chromium trioxide gave a ketone with the composition $C_{24}H_{28}O_4$ (III), M^+ 380 (mass spectrum), mp 132-133°C, $[\alpha]_D^{21}$ −42° (c 1.1; chloroform) in the IR spectrum of which an absorption characteristic for a carbonyl group in a six-membered ring appeared at 1690 cm^{-1}. On subsequent reduction of the ketone with sodium tetrahydroborate, a substance was isolated with the composition $C_{24}H_{30}O_4$, M^+ 382 (mass spectrum), mp 157-158°C, $[\alpha]_D^{21}$ −60° (c 1.0; chloroform), the IR spectrum of which lacked the absorption band of a carbonyl group and had a maximum at 3400-3600 cm^{-1} due to a hydroxy group.

The NMR spectrum of this product (substance IV) has singlets at 0.90 ppm (3 H, angular $C_{10}-CH_3$ group), 0.72, and 0.95 ppm (3 H each, axial and equatorial methyl groups at C_4), 4.58 and 4.65 ppm (1 H each, exocyclic methylene group at C_8), two quartets with centers at 3.85 and 4.18 ppm, J_{gem} = 10.5 Hz, J_{vic} = 6 Hz (methylene protons in the $Ar-O-CH_2-$ grouping), and a broadened signal with its center at 3.14 ppm, $^1/_2\,\Sigma$ = 16 Hz (C_3-H proton gemimal to a hydroxy group). In the 6.05-7.49-ppm region there are the signals of five protons of a 7-hydroxy-substituted coumarin ring.

It has been shown previously that when the substituent $Ar-O-CH_2-$ is present in the axial orientation the methylene protons of this grouping appear in the NMR spectrum in the form of a doublet with a coupling

Order of the Red Banner of Labor Institute of the Chemistry of Plant Substances. Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 1, pp. 15-18, January-February, 1974. Original article submitted October 26, 1972.

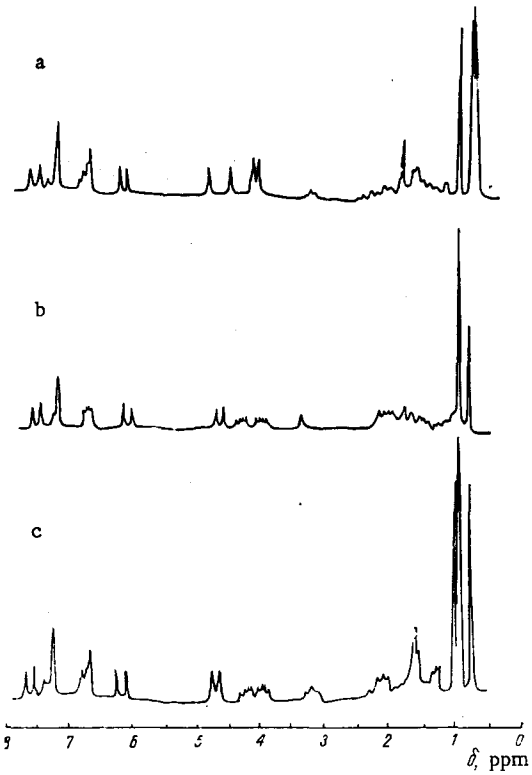
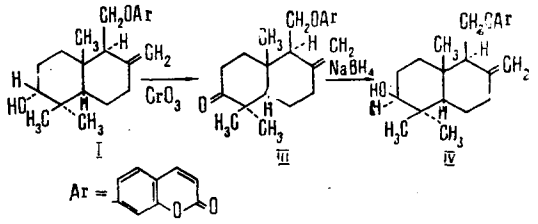


Fig. 1. NMR spectra of farnesiferol A (a), gummosin (b), and substance (IV) (c).

constant of 4-6 Hz or a doublet with insignificant splitting; in the case of the equatorial position they have the form of two quartets with J_{gem} = 10-12 Hz and J_{vic} = 4-6 Hz [5].

The results of a comparison of the NMR spectra of farnesiferol A, gummosin, and substance (IV) (see Fig. 1) show that in the last-mentioned compound the substituent at C_9 ($-CH_2-OAr$) is present in the equatorial orientation, i.e., in the same orientation as in gummosin. The multiplicities of the signals of the methylene protons in the $Ar-O-CH_2-$ groupings in the NMR spectra of substance (IV) and farnesiferol A differ sharply, as can be seen from Fig. 1. The signal of the methylene protons of the $Ar-O-CH_2-$ grouping in the NMR spectrum of farnesiferol A appears in the form of a doublet, and in the NMR spectrum of gummosin and in that of substance (IV), in the form of two quartets. Consequently, the substituent at C_9 has different orientations in farnesiferol A and in substance (IV). The position (3.14 ppm) and the half-width (16 Hz) of the signal of the C_3 methine proton in the iresane nucleus show that the hydroxy group is present in the energetically favorable equatorial position and the methine proton in the axial position.



The higher value of Rf for gummosin than of farnesiferol A and substance (IV) and the similar Rf values of farnesiferol A and substance (IV) on thin-layer chromatography are due to the fact that alcohols with an axial hydroxy group are adsorbed more feebly than those with an equatorial group [7].

The specific rotation changes on passing from gummosin (−54°) to substance (IV) (−60°). This is in harmony with the law found previously for the case of 5-α-steroids of the cholestane and androstane series on the basis of which substances with an equatorial group at C_3 have a higher levorotation than those with an axial equatorial group [7].

The facts given confirm that the product obtained by the reduction of the ketone from gummosin [substance IV)] is an epimer of gummosin at C_3 but is not farnesiferol A. Finally, a mixed melting point of an authentic sample of farnesiferol A (mp 155-156°C and of substance (IV) (mp 157-158°C) melted at 135-136°C, i.e., showed a depression of the melting point.

The results obtained permit the conclusion that the product of the reduction of the ketone of gummosin is not identical with farnesiferol A and the passage from gummosin to farnesiferol A performed previously does not correspond to the facts.

We have shown [5] that the fourth and last isomer of farnesiferol A with a diequatorial arrangement of the substituents at C_3 and C_9 has not yet been found in nature, and the product of the reduction of the ketone of gummosin [substance (IV)] in this isomer.

The experimental results confirm the corrections that we have proposed previously [5] to the configuration of gummosin and badrakemin and the above-mentioned identity of isobadrakemin, colladonin, and farnesiferol A.

EXPERIMENTAL

The conditions for taking the spectra have been described elsewhere [5]. Chromatography was performed in a thin layer of silica gel in the solvent system heptane–ethyl acetate (3:1) with Kutacek's reagent to reveal the spots.

Oxidation of Gummosin. A solution of 0.08 g of chromium trioxide in 6 ml of 80% acetic acid was added to a solution of 0.15 g of gummosin in 6 ml of glacial acetic acid. The reaction mixture was left overnight, and the ketone of gummosin was isolated in the usual way, giving colorless crystals with mp 132-133°C, R_f 0.27.

Reduction of the Ketone of Gummosin. A solution of 0.1 g of the ketone in 20 ml of 85% aqueous methanol was treated with 0.05 g of sodium tetrahydroborate. After an hour, the reaction mixture was diluted with water and acidified with 5% sulfuric acid, and the reaction product was extracted with ether. Acicular crystals were isolated with mp 157-158°C [heptane–ethyl acetate (3:1)], R_f 0.17; for farnesiferol A, R_f 0.17.

CONCLUSIONS

On the basis of the results of a spectral study of the products formed in the oxidation of gummosin and the reduction of the resulting ketone to an alcohol, it has been shown that the latter is not identical with farnesiferol A and has the substituent at C_9 in the equatorial orientation. It has been shown that the transition from gummosin to farnesiferol A performed previously does not correspond to the facts.

LITERATURE CITED

1. N. P. Kir'yalov and S. D. Movchan, Khim. Prirodn. Soedin., 383 (1966).
2. N. P. Kir'yalov, Khim, Prirodn. Soedin., 363 (1967).
3. V. Yu. Bagirov, N. P. Kir'yalov, V. I. Sheichenko, and V. V. Bochkarev, Khim. Prirodn. Soedin., 466 (1970).
4. N. P. Kir'yalov, Tr. BIN SSR, Ser. V, No. 15, 129 (1969).
5. A. I. Saidkhodzhaev and G. K. Nikonov, Khim. Prirodn. Soedin., 490 (1973).
6. L. Caglioti, H. Naef. D. Arigoni, and O. Jeger, Helv. Chim. Acta, 41, 2278 (1958).
7. L. Fieser and M. Fieser, Steroids, Reinhold (1959).