THE STRUCTURE OF TALATISAMINE

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The alkaloid talatisamine was first isolated from Aconitum talassicum M. Pop. [1]. The composition $C_{24}H_{39}NO_5$ and a developed formula $C_{19}H_{23}(N—C_2H_5)(OH)_2(OCH_3)_3$ was established for it. In talatisamine one hydroxyl group is secondary and the other is tertiary [2, 3].

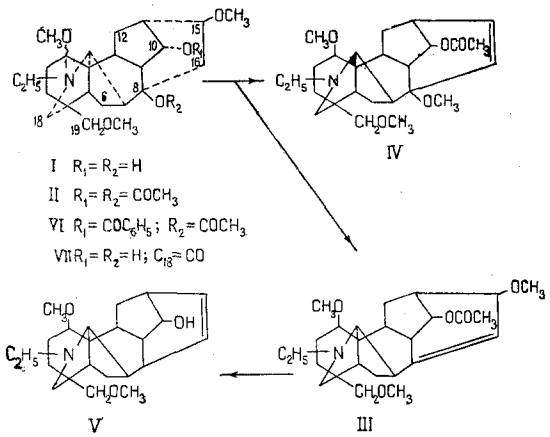
This paper gives the results which have permitted us to give talatisamine the structure I. The results of a study of the mass spectra of a series of compounds containing the lycoctonine skeleton [4] and a comparison of them with the mass spectrum of talatisamine has shown that the spectrum of the latter is characteristic for this group of alkaloids. To confirm this hypothesis, we performed the pyrolysis of diacetyltalatisamine (II). Two products were obtained which differed from the starting material by the elements of acetic acid. According to the NMR spectrum, the main reaction product still contained one acetyl and three methoxyl groups. In the region of olefinic protons an unresolved two-proton signal had appeared. In the other product again only one acetyl group and three methoxyl groups were shown, and in the region of olefinic protons there was a one-proton doublet. This behavior on pyrolysis is characteristic of alkaloids having the lycoctonine skeleton with a hydroxyl group in position 8 and a methoxyl group at C_{15} [5].

The production of two substances is connected with the appearance of a double bond between C_8 and C_{16} in pyroacetyltalatisamine (III) and a subsequent allyl rearrangement, leading to isopyroacetyltalatisamine (IV). The presence of one of the methoxyl groups at C_{15} in III is confirmed by its hydrogenolysis when the compound is treated with lithium aluminum hydride, leading to the formation of V.

An interesting feature is observed in the compounds of the pyro series, consisting in the appearance in their UV spectrum of an absorption maximum at 235–245 mμ [6]. The maximum disappears when the solution is acidified and reappears on neutralization. The isopyro derivatives do not absorb at all. The products of the pyrolysis of talatisamine have completely analogous properties. In the NMR spectrum of talatisamine at δ 4.03 there is a poorly-resolved triplet with an intensity of one proton unit and J = 5 Hz; this signal shifts in all the derivatives of talatisamine containing an acetyl group to δ 4.6–4.7 (J = 5 Hz), which shows the secondary nature of the hydroxyl group. The position of the signal and the spin-spin coupling constant are characteristic for a proton at C_{10} when the latter also bears a hydroxyl group [6].

The results of a study of models has shown that positions 6 and 12 are excluded for a hydroxyl group with this value of the splitting constant. The presence of a hydroxyl group at C_{10} is confirmed by the NMR spectrum of acetylbenzoyltalatisamine (VI) (benzoylation of the secondary hydroxyl group), in which the signals from the protons of the acetyl group appear in an unusually strong field (δ 1.27). This phenomenon takes place when a benzoyloxy group is present on C_{10} and an acetoxy group on C_8. In this case the methyl of the acetoxyl group falls under the influence of the anisotropic field of the benzene ring, which also causes the above-mentioned displacement of the signal in the strong-field direction [7].

The oxidation of talatisamine gave a ketone containing a carbonyl group in a five-membered ring [3], which agrees with the position of the hydroxyl at C_{10}. In the mass spectrum of the alkaloid, the maximum peak is M – 31, and in that of its oxo derivative (VII) it is M – 15. An investigation of the mass spectra of compounds with the lycoctonine skeleton has shown that the peak due to the detachment of the substituent from position 1 is the maximum peak in the spectra of these compounds, while in the oxo derivatives it becomes inconsiderable. Consequently, the second methoxyl group is located at C_1. In alkaloids of the lycoctonine type, the substituent at C_{19} is generally methoxyl, hydroxyl, or methyl. The presence of hydroxyl and methyl groups is excluded—the first because of the absence of the primary hydroxyl group from the alkaloid and the second because of the absence of the C-methyl group (apart from that in the $N—C_2H_5$ grouping).



The alkaloids of this group exist in only one conformation because of the rigidity of the lycoctonine skeleton. The configuration of the methoxyl at C_{10} follows from a consideration of the splitting constant (5 Hz) of the signal of the proton at C_{10}. This value is satisfied by a β-proton (dihedral angle between the vicinal protons and a β-H_{10} is approximately 40–45° while for an α-H_{10} it is 80–90°; in the first case J_{calc} = 5–6 Hz and in the second case it is 0–1 Hz). The olefinic proton in pyroacetyltalatisamine appears in the form of a doublet with a splitting constant of 6.2 Hz. Models show that the dihedral angle between the olefinic protons and the α-proton at C_{15} is 30–35° (J_{calc} = 6.5–7.0 Hz), while that between the olefinic and β_{15} protons is 85–90° (J_{calc} = 0). Thus, the NMR spectrum definitely shows that the methoxyl at C_{15} must be in the β-configuration.

EXPERIMENTAL

Chromatography was carried out with type ShSK silica gel. The NMR spectra were recorded on a JNM-4H-100/100 MHz instrument in deuterochloroform with HMDS as internal standard (the values are given in the δ scale), and the mass spectra on a MKh-1303 instrument fitted with a system for direct introduction into the ion source.

Diacetyltalatisamine (II). This was obtained by the usual method—by heating a mixture of talatisamine, acetic anhydride, and p-toluenesulfonic acid; mp 122–123° C (from methanol). NMR spectrum, ppm: 1.95, 1.87 (singlets, 2 $OCOCH_2$), 0.99 (triplet, NCH_2CH_3).

Benzoyltalatisamine. A mixture of 0.38 g of talatisamine, 0.25 ml of benzoyl chloride, and 3 ml of pyridine was left at room temperature for 1 hr. The reaction mixture was poured onto ice and made alkaline with potassium carbonate. The reaction product was extracted with chloroform. After the solvent had been distilled off, a dark oil remained which was dried in vacuum and was treated with hexane. The hexane was evaporated off to give 0.17 g of product in the form of a light yellow oil which was converted on drying in vacuum into a white powder. On chromatography in a thin layer of silica gel, the product exhibited a single spot. IR spectrum, cm^{-1}: 1720, 3400, 3590.

Acetylbenzoyltalatisamine (VI). A mixture of 0.17 g of benzoyltalatisamine, 4 ml of acetic anhydride, and 0.11 g of p-toluenesulfonic acid was heated in the steam bath for 2 hr. After cooling, the reaction mixture was poured onto ice, made alkaline with sodium carbonate, and shaken with ether. The ether was distilled off and the product isolated was chromatographed on alumina. It was eluted with chloroform, and the solvent was evaporated off. The residue, in the form of a white powder, was homogeneous on chromatography in a thin layer of silica gel. NMR spectrum, ppm: 1.27 (singlet, $OCOCH_3$).

Pyrolysis of diacetyltalatisamine. 0.24 g of diacetyltalatisamine was kept under vacuum at 185–190° C for 5 min. This gave 0.2 g of a product which was chromatographed on silica gel. Elution was carried out with chloroform and with chloroform–methanol (10 : 1). The chloroform eluate gave 0.035 g of pyroacetyltalatisamine (III). Mass spectrum: 445 (M^+); NMR spectrum, ppm: 1.92 (singlet, $OCOCH_3$), 3.24, 3.19, 3.15 (singlets, 3 OCH_3), 5.35 (doublet, 1 H); 4.58 (triplet, 1 H). The chloroform–methanol eluate contained 0.15 g of isopyroacetyltalatisamine (IV). Mass spectrum: 445 (M^+); NMR spectrum, ppm: 1.91 (singlet, $OCOCH_3$), 3.22, 3.18, 3.08 (singlets, 3 OCH_3), 5.60–6.06 (multiplets, 2 H), 4.59 (triplet, 1 H). The purity of both products was checked by chromatography in a thin layer of silica gel.

Desmethoxypyrotalatisamine (V). To 40 mg of pyroacetyltalatisamine in 30 ml of dry benzene was added 0.1 g of

lithium aluminum hydride in 20 ml of dry ether and the mixture was boiled for 15 hr. The excess of lithium aluminum hydride was decomposed with water, the ether-benzene layer was separated off, and the aqueous solution was washed several times with ether. The combined extracts were evaporated, and the residue was treated with hexane to give a pulverulent product. Mass spectrum: 373 (M^+).

Oxotalatisamine (VII). A solution of 0.25 g of talatisamine in 25 ml of acetone–water (4 : 1) was mixed with 0.25 g of potassium permanganate in 200 ml of acetone–water (1 : 1). The mixture was stirred for 15 min and then the excess of potassium permanganate was decomposed with sodium sulfite and the manganese dioxide was separated off. The filtrate was evaporated until the acetone had been driven off completely and the reaction product was extracted with chloroform. The chloroform was evaporated and the residue was treated with methanol. On standing for some days, a crystalline substance was obtained with mp 197–200° C (from methanol). IR spectrum, cm^{-1}: 1635; Mass spectrum: 435 (M^+); NMR spectrum, ppm: 1.10 (triplet, NCH_2CH_3).

CONCLUSIONS

The structure of talatisamine has been established by a study of the products of the pyrolysis of diacetyltalatisamine and of the NMR and mass spectra of talatisamine and its conversion products.

REFERENCES

1. R. A. Konovalova and A. P. Orekhov, ZhOKh, 10, 745, 1940.
2. S. Yu. Yunusov, E. V. Sichkova, and G. P. Potemkin, ZhOKh, 24, 2237, 1954.
3. M. A. Naimova, M. D. Palamareva, L. G. Grozdanova, N. M. Mollow, and P. P. Panov, AH, 20, 193, 1963.
4. M. S. Yunusov, Ya. V. Rashkes, V. A. Tel'nov, and S. Yu. Yunusov, KhPS [Chemistry of Natural Compounds], 5, 515, 1969.
5. O. Achmatowicz, V. Tsuda, Leo Marion, and T. Okamoto, Can. J. Chem., 43, 825, 1965.
6. S. W. Pelletier, L. H. Keith, and P. C. Parthasarathy, J. Am. Chem. Soc., 89, 4146, 1967.
7. Y. Tsuda and Leo Marion, Can. J. Chem., 41, 1634, 1963.

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