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A STUDY OF THE ALKALOIDS OF CODONOPSIS CLEMATIDEA

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In a study of the epigeal part of Codonopsis clematidea (family Campanulaceae) collected in the budding and incipient flowering phase in the Kashka-Dar'ya Oblast, it was found that it contains 0.04–0.08% of total alkaloids. By separating the mixture of bases with respect to their solubilities in chloroform, we isolated a base of the composition $C_{14}H_{21}O_4N$, which we have called codonopsine. The IR spectrum of the alkaloid exhibits absorption bands at 870 and 810 cm^{-1} (trisubstituted benzene ring) and 3380 cm^{-1} (active hydrogen). UV spectrum: $\lambda_{max}^{C_2H_5OH}$ 226, 278 mμ (log ε 4.1, 3.26).

Codonopsine contains NCH_3, two (OCH_3), $(>C-CH_3)$, and two (OH) groups. With acetic anhydride it forms an O, O'-diacetyl derivative. In the IR spectrum of the latter the band at 3380 cm^{-1} (active hydrogen) has disappeared and a strong band at 1750 cm^{-1} characteristic for a O-acetyl group has appeared. Saponification of the diacetyl derivative gave the initial base.

Thus, the developed formula of codonopsine can be shown as: $C_{10}H_7(>N-CH_3)\ (OCH_3)_2(OH)_2(>C-CH_3)$.

The oxidation of codonopsine yielded veratric acid. However, the oxidation of the alkaloid with periodic acid did not give a dialdehyde. Consequently, the two hydroxy groups of codonopsine are not located on adjacent carbon atoms.

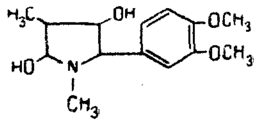
On being heated with an ammoniacal solution of silver oxide, codonopsine gives the silver mirror reaction, which is characteristic for piperidine and pyrrolidine derivatives. The qualitative reaction of codonopsine with a pine chip for pyrrole derivatives was positive.

The information given permits the assumption that the substance under study contains a pyrrolidine nucleus.

The alkaloid does not give the color reaction with isatin for the presence of a $-NH-CH_2-CH_2$ group [1], which shows the possible presence in it of substituents in the α, α', β, β'-positions of the pyrrolidine nucleus.

Two stages of the Hofmann degradation of codonopsine iodide gave a nitrogen-free substance. The reduction of the latter by Adams' method in ethanol and subsequent oxidation with potassium permanganate in acetone formed veratric acid; oxidation with chromic acid mixture gave acetic acid. Consequently, the neutral product retains the aromatic part of the base and a $C-CH_3$ group.

The above information makes it possible to propose for codonopsine the following most probable structure:



Experimental

Isolation of codonopsine. The usual chloroform extraction of the comminuted raw material gave the ethereal and chloroformic total alkaloids, by the treatment of which with chloroform was isolated a base with mp 150–151° C (acetone, methanol), $[\alpha]_D^{20}$ −16° (c 0.84; methanol), composition $C_{14}H_{21}O_4N$ in an amount of 25% of the total bases. Molecular weight 267 (mass spectrometry). R_f 0.52 [on paper in the 1-butanol–acetic acid–water (100 : 5 : 100) system]; R_f 0.25 [on a thin layer of silica gel with gypsum in the ethyl acetate–methanol (9 : 1) system].

On being heated with methyl iodide, codonopsine forms a methiodide with mp 207–208° C (from methanol).

When 0.02 g of the base was oxidized with 5 ml of chromic acid mixture, acetic acid, giving a spot identical with that of a reference sample, was detected chromatographically.

A mixture of 0.05 g of the base and an aqueous solution of the complex from 0.03 g of silver oxide and 0.1 ml of 25% ammonia solution in 1 ml of water gave the silver mirror reaction.

The oxidation of 0.05 g of the base with 0.04 g of periodic acid on heating in the water bath (55–60° C) for 2 hr did not lead to the formation of crystals. The reaction mixture gave no crystalline hydrazone with phenylhydrazine hydrochloride.

When 0.15 g of the base was heated with 8 ml of acetic anhydride (60–65° C) the diacetyl derivative of codonopsine was obtained in the form of an oily product.

Oxidation of codonopsine. With vigorous stirring, 0.2 g of the base in 5 ml of acetone was oxidized with potassium permanganate in acetone (0.8 g in 50 ml of acetone) for 6 hr. The usual working up yielded an acid with mp 180–181° C (from ether), identical from a mixed melting point and its UV and IR spectra with veratric acid.

Production of the nitrogen-free substance. After two stages of the Hofmann degradation, 0.2 g of codonopsine methiodide gave a neutral product and trimethylamine. When the product of the hydrogenation of the nitrogen-free substance was oxidized by the method described above, veratric and acetic acids were detected chromatographically.

Conclusions

From the epigeal part of Codonopsis clematidea, the new alkaloid codonopsine has been isolated; its most probable structure is 1,4-dihydroxy-1,3-dimethyl-5-veratrylpyrrolidine.

REFERENCE

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