A STUDY OF 2-DEMETHYLALLOCOLCHICINE AND ITS DERIVATIVES

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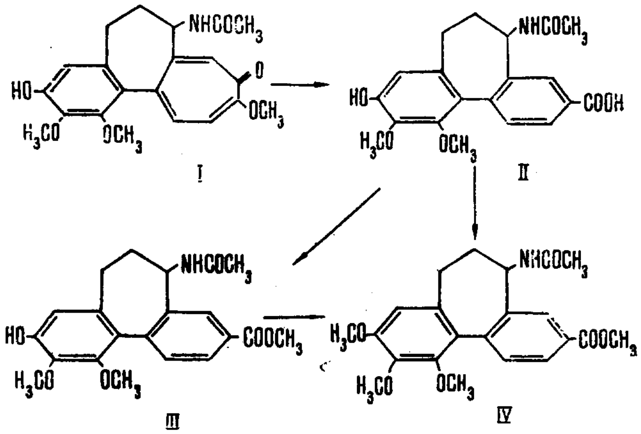
UDC 547.944.6

The structure of two new alkaloids isolated from Colchicum kesselringii Rgl. has been reported previously [1]. The structure of one of them – allocolchicine (alkaloid K-3) – was confirmed by its preparation from colchicine. The structure of the other – 2-demethylallocolchicine (alkaloid K-4) – was deduced on the basis of the identity of the carboxylic acids obtained from this compound and from 2-demethylcolchicine. Continuing a study of these compounds, we have performed a partial synthesis of 2-demethylallocolchicine. For this purpose, 2-demethylcolchicine (I) was converted by a known method [2] into 2-demethylallocolchiceine (II) and then by methanolysis into 2-demethylallocolchicine (III). On methylation with diazomethane, both (II) and (III) formed allocolchicine (IV):



Allocolchicine and its analogs were also isolated from plants and have been partially synthesized from tropolone alkaloids. At the same time, their spectral characteristics have remained little-studied. In the UV spectrum of allocolchiceine the absorption maximum is at 278 nm [2] and in its methyl ester – allocolchicine – it is shifted in the long-wave direction to 290 nm [1], which is also characteristic for the demethylated analogs of these compounds. In the IR spectrum of allocolchicine there are absorption bands characterizing an amide carbonyl (1660 cm^{-1}), an ester carbonyl (1735 cm^{-1}), an amide group (3300 cm^{-1}), methylene groups (1475 cm^{-1}), and aromatic rings (800-900 cm^{-1}).

We have also studied the NMR and mass spectra of the compounds isolated. It can be seen from Table 1 that the proton on the C_1 atom gives a signal in the stronger field than the other aromatic protons. The frequency of the signal of this proton is considerably affected by the acetyl group in the C_2 position. The signal of the C_1 proton is shifted downfield. In the carboxyl-containing compounds, conversely, the signals of the C_8 and C_{10} protons are shifted upfield. The signals of the O-methyl groups of the aromatic rings A and C in allocolchicine and its analogs are located in relation to the standard (HMDS) in the sequence C_4, C_2, C_3, as in the case of the tropolone alkaloids [3].

The mass-spectrometric decomposition of allocolchicine and its analogs takes place in the same way as in colchicine [4] with the initial ejection of an acetamide group (M−59). Subsequently, a methoxycarbonyl

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V. I. Lenin Tashkent State University. Translated from Khimiya Prirodnykh Soedinenii, No. 2, pp. 194-196, March-April, 1973. Original article submitted June 8, 1972.

TABLE 1

Compound	$C_1-H(s)$	$C_8-H(s)$	$C_{10}-H(d)$	$C_{11}-H(d)$	CH_3-CH_2	$NCO-CH_3$	$OCOCH_3$	$COOCH_3$	C_1-OCH_3	C_3-OCH_3	C_2-OCH_3
Allocolchicine	6,54	7,97	7,48	7,90	2,38	2,00	—	3,71	3,56	3,83	3,71
2-Demethylallocolchicine	6,52	7,97	7,47	7,90	2,32	2,00	—	3,72	3,54	3,82	—
Allocolchiceine	6,59	7,79	7,42	7,90	2,32	2,00	—	—	3,56	3,83	3,73
2-Demethylallocolchiceine	6,65	7,45	7,40	7,95	2,38	1,98	—	—	3,52	3,81	—
Acetyl-2-demethylallocolchicine	6,71	7,97	7,49	7,90	2,38	2,00	2,23	3,71	3,47	3,86	—
Acetyl-2-demethylallocolchiceine	6,74	7,46	7,40	7,95	2,36	2,00	2,30	3,72	3,53	3,84	—

Note. The one-proton signals were obtained in methanol and the three-proton signals in pyridine; s – singlets; d – doublets.

group is split off from allocolchicine and an O-acetyl group, as well, from the acetylated compounds. Compounds of the allocolchicine series demethylated in aromatic rings A and C undergo the same decomposition under the influence of electron impact, but the peaks of the ions in their mass spectra are shifted in the direction of lower masses by m/e 14.

EXPERIMENTAL

The UV spectra of the substances were taken on an SF-4A spectrometer, the IR spectra on a UR-10 double-beam spectrometer, the NMR spectra on a Hitachi H-60 spectrometer, and the mass spectra on an MKh-1303 mass spectrometer.

The individuality of the substances obtained and their identitites with authentic samples were confirmed by thin-layer chromatography on alumina [chloroform–methanol (24 : 1) system].

2-Demethylallocolchiceine. A solution of 0.4 g of 2-demethylcolchicine in 10 ml of methanol was treated with a solution of sodium methoxide (1.0 g of sodium in 15 ml of methanol). The solution was boiled for 1 h and the solvent was distilled off. The residue was dissolved in water and the solution was acidified and extracted with chloroform. This gave 0.3 g of 2-demethylallocolchiceine with mp 259-260°C (from ether–chloroform), $[\alpha]_D^{20}$ −152° (c 0.92; methanol).

2-Demethylallocolchicine. A solution of 0.2 g of 2-demethylallocolchiceine in 10 ml of 7% hydrogen chloride in methanol was boiled for 2 h. The solvent was distilled off and the residue was extracted with chloroform. This gave 2-demethylallocolchicine with mp 237-239°C (from ether–chloroform), $[\alpha]_D^{22}$ −150° (c 1.00; chloroform).

Allocolchicine. An ethereal solution of diazomethane was added to a methanolic solution of 0.2 g of 2-demethylallocolchiceine and 0.15 g of 2-demethylallocolchicine (separately). After the solvent had been distilled off, allocolchicine was obtained with mp 257-258°C (from methanol), $[\alpha]_D^{22}$ −150° (c 1.2; methanol).

Acetyl-2-demethylallocolchicine. A mixture of 0.1 g of 2-demethylallocolchicine, 0.2 g of freshly fused sodium acetate, and 3 ml of acetic anhydride was kept at 45-50°C for 24 h. The excess of acetic anhydride was evaporated off, methanol was added, and the dry residue was extracted with chloroform. The acetyl derivative of 2-demethylallocolchicine was obtained with mp 230-232°C (from ether and chloroform). $[\alpha]_D^{22}$ −150° (c 1.00; methanol). M^+ 427 (mass spectrometer).

Acetyl-2-demethylallocolchiceine. The substance was obtained by the acetylation of 2-demethylallocolchiceine by the method described above. Mp 223-224°C, $[\alpha]_D^{22}$ −140° (c 1.00; chloroform). M^+ 413 (mass spectrometer).

SUMMARY

The partial synthesis of 2-demethylallocolchicine (alkaloid K-4) has been effected from 2-demethylcolchicine.

The spectral characteristics of allocolchicine, 2-demethylallocolchicine, and some of their analogs have been studied.

LITERATURE CITED

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