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THE CONFORMATIONAL STUDY OF THE NEW ERGOT ALKALOIDS AGROCLAVINE-I AND EPOXYAGROCLAVINE-I BY PROTON MAGNETIC RESONANCE SPECTROSCOPY

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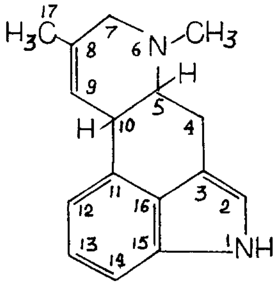
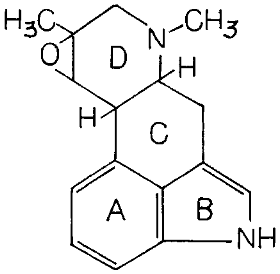
The 100 MHz p.m.r. data on the new ergot alkaloids agroclavine-I and epoxyagroclavine-I, metabolites of fungus *Penicillium kapuscinskii* strain UCM F-2156D, are reported. Their C and D rings are shown to exist in an "envelope" form. A *cis* orientation of the C/D ring junction is confirmed for both alkaloids.

In this paper we report the results of the study on the solution conformations of the new ergot alkaloids agroclavine-I (a) and epoxyagroclavine-I (b) by p.m.r. spectroscopy.



a.



b.

The samples of agroclavine-I and epoxyagroclavine-I were obtained as described earlier [1]. The p.m.r. spectra (in $CDCl_3$,O-TMS) were obtained on a Varian HA-100D spectrometer (USA). The chemical shifts and coupling constants of the two compounds are listed in Table I.

An "envelope" conformation for the ring C in agroclavine has been demonstrated earlier[2]. Consideration of the values of $^{4I}J_{2-H,4-Ha}$ and $^{4I}J_{2-H,4-He}$ of the both compounds (Table I) shows that the "envelope" conformation is also characteristic for C ring in agroclavine-I and epoxyagroclavine-I (Fig.1). The values of $^{4I}J_{12-H,10-H}$ for agroclavine-I and epoxyagroclavine-I (0.8 and 0.8 Hz, respectively) according to the Barfield angular dependences[3] correspond to a planar orientation of the 10-H proton with respect to the indole plane in both compounds.

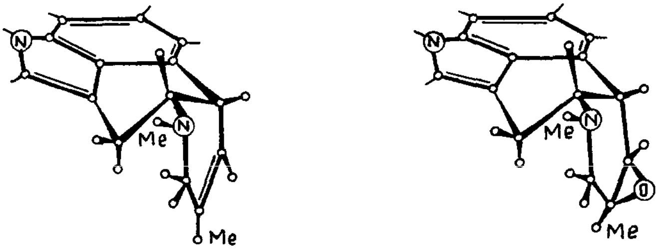
Table I

^{1}H Chemical shifts and spin-spin coupling constants of protons

Protons	Agroclavine-I		Epoxyagroclavine-I	
	δ(p.p.m.)	J(Hz)	δ(p.p.m.)	J(Hz)
1-H	8.05	1.4	8.05	1.7
2-H	6.81	1.4,1.4,0.8	6.76	1.7,1.6,0.9
4-Ha	2.85	9.9,1.4	3.08	9.2,9.2,1.6
4-He	2.90	5.2,0.8	2.89	9.2,5.9,0.9
5-H	3.35	9.9,5.2,5.0,0.8	3.11	9.2,5.9,4.3
7-Ha	3.07	3.2,1.9	2.86	13.6
7-He	3.07	3.2,1.9	3.11	13.6,0.6
9-H	5.51	1.9,1.9,1.6,0.8,0.6	3.39	2.3,0.6
10-H	3.93	5.0,3.2,3.2,2.2,0.8,0.6	3.62	4.3,2.3,0.8
12-H	6.90	4.6,3.3,0.8	6.96	5.1,3.0,0.8
13-H	7.10	4.6	7.13	5.1
14-H	7.10	3.3	7.12	3.0
17-H	1.62	2.2,1.6	1.55	singlet
N6-Me	2.61	singlet	2.44	singlet

Relatively higher values of $^{3I}J_{5-H,4-Ha}$ (9.9 and 9.2 Hz, respectively) and lower values $^{3I}J_{5-H,10-H}$ (5.0 and 4.3 Hz, respectively) were observed in agroclavine-I and epoxyagroclavine-I. Thus, in both compounds the 5-H proton is *trans*-oriented relative to 4-Ha and is in a *gauche* position relative to 10-Ha [4]. Such an arrangement of hydrogen atoms at positions C4, C5, C10, indicates a *cis* C/D ring junction for agroclavine-I and epoxyagroclavine-I, which thus can be designated as either 5R, 10S or the 5S, 10R isomers (Fig.1).

The double bond in the 8, 9 position suggests a ψ-chair or "envelope" conformations for the D-ring in agroclavine-I. The spectrum of agroclavine-I shows both allylic and homoallylic spin-spin interactions of the ring protons (Table I). Analysis of the $^{4I}J_{9-H,7-H}$ values for agroclavine-I points to a more expressed periplanar orientation of the 7-H protons according to Barfield angular dependences [3], relative to the plane formed by carbon atoms 10, 9, 8 and 7. This suggests that for the D-ring in agroclavine-I the "envelope" conformation is a more probable one (Fig.1). For epoxyagroclavine-I there are not enough experimental data to draw a definite conclusion about its D ring conformation. However, the increase of the $^{3I}J_{10-H,9-H}$ value (2.3 Hz) relative to agroclavine-I (0.6 Hz) indicates a change of the dihedral angle $\varphi_{9-H,10-H} = 90^{\circ}$ for the latter compound in the direction of a *gauche*-orientation of these protons in epoxyagroclavine-I. Thus, there is possibly a distortion of the "envelope" conformation to the side of an "arm-chair" conformation in epoxyagroclavine-I (Fig.1).



or enantiomer
I

or enantiomer
II

Fig.1. The three dimentional structures of I - agroclavine-I and II - epoxyagroclavine-I.

The formation of ring C is the stage of the biosynthesis at which the stereochemistry at carbon atoms (5 and 10) of the ergoline nucleus is determined [5]. The ability of *P. kapuscinskii** to produce agroclavine-I and epoxyagroclavine-I with a stereochemistry at C-5 or C-10 different from that of most known ergot alkaloids [6] may serve as evidence for a different mechanisms of C ring formation in this fungus than in such producers as, for example, fungi of the genus *Claviceps*.

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* The former name of the culture *Penicillium corylophilum* IBPhM F-152 was redetermined as *Penicillium kapuscinskii* UCM F-2156D in the cabinet of filamentous fungi of the All-Union Collection of Microorganisms (UCM).

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