SPATIAL STRUCTURE OF DIACETYLDIHYDROUNGMINORINE

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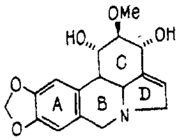
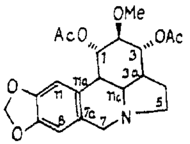
The structure of diacetyldihydroungminorine, $C_{21}H_{25}NO_7$ (I), has been determined by the x-ray structural method: diffractometer, CuK_α radiation, 1278 reflections, R = 0.089. An analysis has been made of the conformation of the (I) molecule in comparison with that observed for dihydrolycorine in solution and in the crystalline form. It was shown that the conformations of rings B, C, and D of the (I) molecule in the crystal and of dihydrolycorine in solution are identical. The lack of correspondence of the crystal—solution conformations in dihydrolycorine is connected with an inversion of the unshared electron pair of the nitrogen atom on the formation of a salt — the hydrobromide.

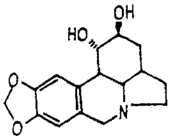
Ungminorine from <u>Ungernia</u> <u>minor</u> [1], which has the structure (Ia) [2, 3], belongs to a widely studied group of alkaloids of the indophenanthridine series [4]. Some time ago, on the basis of an analysis of PMR results, Kotera et al. [5] came to the conclusion that, in solution in deuterochloroform, ring C of dihdyrolycorine (II) is present in the twist conformation. However, a subsequent x-ray structural investigation of dihydrolycorine hydrobromide performed by Shiro et al. [6] showed that the hydroxy groups in it have the trans-diaxial orientation and ring C is present in a slightly distorted chair conformation. Consequently, from a comparison of PMR results on solutions and those of an x-ray structural study of the crystalline state it can be seen that the conformation of the cyclohexane ring C of dihydrolycorine changes from twist to slightly distorted chair.



Ia



I



II

An analysis of the PMR characteristics of ungminorine (Ia) and its diacetyldihydro derivative (I) using the double-resonance method [3] showed that in solutions of them in deuterochloroform ring C has the twist conformation. At the same time, by an x-ray structural investigation of the hydrobromide of narcissidine — an alkaloid having the same skeleton as ungminorine and the same substituents in ring C, Clardy et al. [2] established that in the crystalline state ring C of narcissidine hydrobromide, as in dihydrolycorine (II) has a slightly distorted chair conformation. Since the literature information given above shows a difference in the conformations of rings C and B of the ungminorine-related alkaloid dihydrolycorine in solution [5, 7, 8] and in the crystal [6], we have made an x-ray structural study of diacetyldihydroungminorine (I) and have correlated the results obtained with those of PMR in solution.

The spatial structure of the (I) molecule established by the x-ray method is shown in Fig. 1, from which it can be seen that the positions of the substituents in ring C of the (I) molecule correspond to those observed in the indophenanthridine group of alkaloids: The OAc group in the C1 position is oriented α-axially, the OMe group in the C2 position β-axially, and the OAc group in the C3 position α-equatorially.

The conformations of the rings are characterized by the intracyclic torsional angles given in the upper diagram in Fig. 1. The aromatic ring and the dioxolane ring (the C7a, C8–C11a, O6, C17, and O7 atoms) are coplanar to within 0.07 Å, while rings B, C, and D have half-chair, twist, and envelope conformations, respectively.

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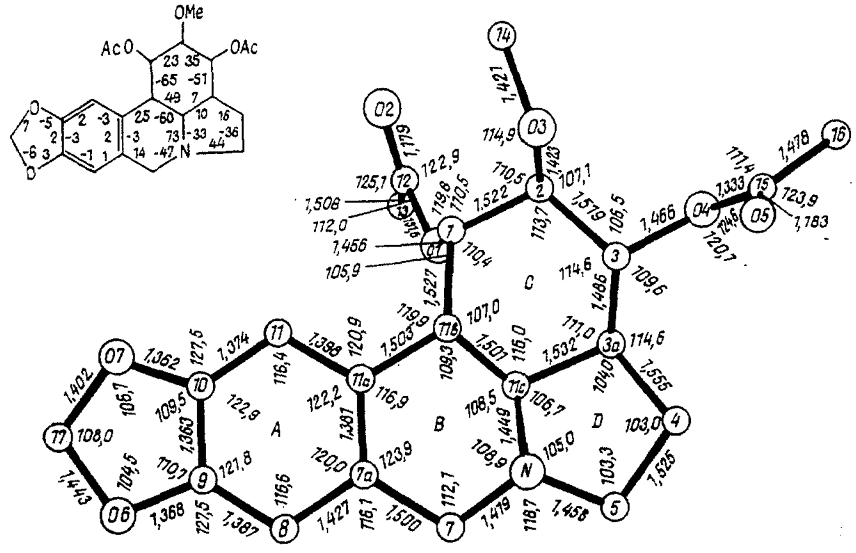

Fig. 1. Spatial structure of the (I) molecule; the values of the intracyclic torsional angles are given in the upper diagram.

TABLE 1. Coordinates ($\times 10^4$) of the Nonhydrogen Atoms of Structure (I)

Atom	x	y	z	Atom	x	y	z
C1	1815 (10)	0946 (6)	0923 (3)	C12	−0999 (10)	1468 (6)	0541 (4)
C2	2148 (10)	−0133 (6)	0629 (3)	C13	−2896 (10)	1521 (8)	0720 (4)
C3	2512 (8)	−0985 (6)	1125 (3)	C14	3228 (17)	0258 (8)	−0429 (4)
C3a	1528 (9)	−0874 (5)	1738 (3)	C15	3301 (12)	−2693 (5)	0683 (4)
C4	2169 (11)	−1601 (5)	2293 (4)	C16	2591 (14)	−3593 (7)	0316 (4)
C5	2143 (10)	−0875 (6)	2879 (4)	C17	3129 (11)	5572 (6)	2259 (5)
C7	2412 (10)	1057 (6)	2988 (3)	O1	−0039 (5)	1111 (4)	1019 (3)
C7a	2654 (9)	2041 (6)	2599 (3)	O2	−0417 (8)	1704 (5)	0035 (3)
C8	2763 (9)	2999 (6)	2956 (4)	O3	3303 (7)	−0098 (4)	0206 (2)
C9	2923 (9)	3918 (6)	2600 (4)	O4	2070 (7)	−1989 (4)	0818 (2)
C10	3005 (10)	3907 (6)	1943 (4)	O5	4763 (8)	−2630 (5)	0854 (3)
C11	2946 (10)	2996 (6)	1587 (3)	O6	3050 (79)	4924 (4)	2330 (3)
C11a	2724 (9)	2061 (5)	1933 (3)	O7	3234 (8)	4906 (4)	1721 (3)
C11b	2639 (8)	1019 (6)	1592 (3)	N6	2675 (8)	0137 (4)	2613 (3)
C11c	1719 (8)	0238 (5)	2014 (3)				

In dihydrolycorine (II), according to PMR in various solvents, the fairly stable half-chair and twist conformations of rings B and C are retained [8]. The (crystal–solution) difference in the conformations of rings B and C of dihydrolycorine reported previously is apparently not due to the crystal field, as suggested in [7] but to the transition to the salt involved – the hydrobromide. The conformations of rings B, C, and D in the (I) molecule and in other dihydro derivatives of this group of alkaloids are, in view of the identical orientations of the substituents in ring C, largely determined by the position of the free invertible electron pair on the nitrogen atom. Consequently, depending on the orientation of the unshared electron pair of the nitrogen atom (or the N–Me and N–H bonds in the corresponding salts) different linkages of rings B/D, and, consequently, different conformations of rings B, C, and D are observed. Thus, on the protonation of dihydrolycorine at the N atom an inversion of the electron pair takes place, with consequent transitions of the conformation of ring B from half-chair to twist and of ring D from 5α-envelope to 4β-envelope.

The observed conformation of the molecule of (I) confirms the hypothesis put forward above: The crystals of diacetyldihydroungminorine were investigated in the form of the base, and the conformations of three of the rings [B – half-chair (11cα, Nβ); C – twist; and D – envelope (5α)] were identical to those observed in solution both for diacetyldihydroungminorine itself [3] and for dihydrolycorine [5]. Thus, a comparative analysis of the results of PMR spectroscopy and of an x-ray structural investigation shows that in the molecules of (I) and (II) the conformations of rings B, C, and D are stable and do not change according to the substituents in the C1 and C3 positions, nor do they depend on the influence of the crystal field.

Analysis of interatomic distances revealed no anomalous deviations from the standard values [9] (see Fig. 1). The errors in the determination of bond lengths and valence angles did not exceed 0.007 Å and 0.6°, respectively. Increases in the C_{sp^2}C7C7aC11a angle (123.9°) and the C_{sp^3}C11aC11bC1 angle (119.9°), and also decreases in the C_{sp^2}C7C11aC11b angle (116.9°) and the C_{sp^3}C1C11bC11c angle (107.0°) may be considered the result of the steric repulsion of the O1Ac group and the C1 atom from the aromatic system. A similar tendency to a distortion of these angles relative to the normal values is observed in dihydrolycorine hydrobromide [6] and narcissidine methiodide [10].

EXPERIMENTAL

Crystals of compound (I) were first investigated by the photo method: The space group and parameters of the unit cell were established by rotation and Weissenberg x-ray diagrams. Then these parameters were refined on a Syntex $P2_1$ diffractometer using CuK_α radiation: a = 7.699(3), b = 12.711(9), c = 20.719(9) Å; d_{calc} = 1.322 g/cm³; space group $P2_12_12_1$; Z = 4. The intensities with $\theta \le 57.5°$ of ~1670 independent nonzero reflections were measured on the diffractometer mentioned ($\theta/2\theta$ scanning), 1278 structural factors exceeding 2σ were used in the calculations.

The structure was determined by the direct method, using the Rentgen-75 program in the automatic regime. For a more accurate localization of the atoms, several $\rho(x, y, z)$ syntheses were calculated. Then the structure was refined by the method of least squares in the isotropic–anisotropic approximation to R = 0.089. The hydrogen atoms (apart from those of the methyl groups) were found in an electron-density difference synthesis and their positions were refined isotropically. The coordinates of the nonhydrogen atoms are given in Table 1.

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