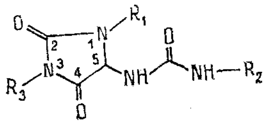
CRYSTAL AND MOLECULAR STRUCTURES OF 1,8-DIACETYL-3-METHYL-DL-ALLANTOIN

M. V. Reshetnyak, S. G. Il'in, N. K. Utkina,
A. I. Yanovskii, and Yu. T. Struchkov

UDC 548.737+593.4

DL-Allantoin (I) has been isolated from an alcoholic extract of a marine sponge Axinellidae gen. sp., and derivatives of it have been obtained: 1,8-diacetyl-DL-allantoin (II) and 1,8-diacetyl-3-methyl-DL-allantoin (III). The crystal and molecular structures of (III) have been established by X-ray structural analysis.

Allantoin is the final product of purine metabolism in the majority of mammals and also in some plants. So far as concerns marine invertebrates, allantoin has been detected in the sponges Tedania digitata [1] and Tethya aurantia [2], which contain purine nucleosides. We have now found allantoin in marine sponges Axinellidae gen. sp. from which a series of pyrrole derivatives characteristic for sponges of this family have previously been isolated [3]. The spectral characteristis of the DL-allantoin isolated agreed well with those given in the literature [1, 2]. But since the detection of allantoin in this sponge was unexpected and the melting point (230-231°C) differed somewhat from that given in the literature (233-234°C [2]). We obtained and characterized derivatives of it: 1,8-diacetyl-DL-allantoin (II) and 1,8-diacetyl-3-methyl-DL-allantoin (III).



	R_1	R_2	R_3
I	H	H	H
II	$COCH_3$	$COCH_3$	H
III	$COCH_3$	$COCH_3$	CH_3

In the present paper we give the results of an X-ray structural investigation of 1,8-diacetyl-3-methyl-DL-allantoin. The results obtained on the goemetry of the molecule have been compared with the geometric parameters of the crystal and molecular structures of DL-L-allantoin, which have been determined previously [4].

The structure of the molecule of (III) and the numbering of the atoms are given in Fig. 1. The five-membered ring in (III), as in (I), is a flat half-chair distorted on the N(3), C(4) side, the atoms being coplanar to within 0.031 Å. The greatest deviation from the mean plane passing through the N(6), C(7), and O(7) atoms of the side chain and the C(5) atom of the ring is 0.025 Å in (III), while in (I) it is 0.024 Å [4]. The angle between this mean plane and the mean plane of the ring in (III) is 80°, while in (I) it is 82°. The C(5) and N(8) atoms are in the trans relationship relative to the C(7)—N(6) bond, both in (III) and in (I) [4].

The bond lengths and valence angles in (III) are given in Table 1. With exception of some of them, which are discussed below, within the limits of the standard deviations their values agree with those obtained for DL-allantoin [4]. The length of the C(2)—N(1) bond in (III) at 1.395(1) Å is ~0.05 Å greater than the corresponding bond in (I), which is 1.341 Å [4]. This change in the C(2)—N(1) bond can be explained by the steric hindrance arising between the acetyl group at the N(1) atom and the oxgen atom of the keto group, O(2). The C(10)...O(2) distance of 2.852(2) Å is somewhat less than the sum of the Van der Waals radii of the C and O atoms (1.70 + 1.40 = 3.10 Å [5]) and the C(10)—C(9)—N(1)—C(2) and

---

Pacific Ocean Institute of Bioorganic Chemistry, Far Eastern Branch, USSR Academy of Sciences, Vladivostok. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 422—426, May-June, 1988. Original article submitted October 12, 1987.

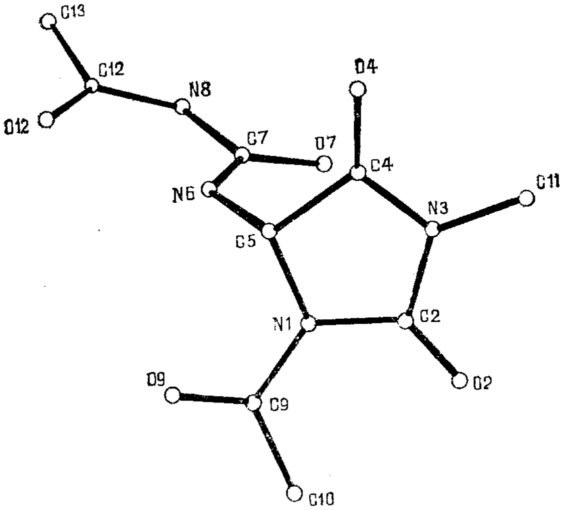


Fig. 1. Structure of the (III) molecule.

TABLE 1. Bond Lengths, d (Å), and Valence Angles ω (deg) in the (III) Molecule

Atom	*d*	Angle	ω
N (1) —C (2)	1,395 (1)	C (2) — N (1) — C (5)	111,13 (8)
N (1) — C (5)	1,463 (1)	C (2) — N (1) — C (9)	127,32 (7)
N (1) — C (9)	1,396 (1)	C (5) — N (1) — C (9)	120,27 (9)
C (2) — N (3)	1,386 (1)	N (1) — C (2) — N (3)	107,02 (7)
C (2) — O (2)	1,199 (1)	N (1) — C (2) — O (2)	128,01 (9)
N (3) — C (4)	1,363 (1)	N (3) — C (2) — O (2)	125,0 (1)
N (3) — C (11)	1,464 (1)	C (2) — N (3) — C (4)	112,7 (1)
C (4) — C (5)	1,531 (1)	C (2) — N (3) — C (11)	123,33 (8)
C (4) — O (4)	1,205 (1)	C (4) — N (3) — C (11)	123,39 (8)
C (5) — N (6)	1,432 (1)	N (3) — C (4) — C (5)	107,03 (6)
N (6) — C (7)	1,339 (1)	N (3) — C (4) — O (4)	127,0 (1)
C (7) — N (8)	1,391 (1)	C (5) — C (4) — O (4)	126,0 (1)
C (7) — O (7)	1,229 (1)	N (1) — C (5) — C (4)	101,84 (8)
N (8) — C (12)	1,376 (1)	N (1) — C (5) — N (6)	114,6 (1)
C (9) — C (10)	1,491 (1)	C (4) — C (5) — N (6)	112,4 (1)
C (9) — O (9)	1,207 (1)	C (5) — N (6) — C (7)	120,0 (1)
C (12) — C (13)	1,503 (1)	N (6) — C (7) — N (8)	117,8 (1)
C (12) — O (12)	1,206 (1)	N (6) — C (7) — O (7)	122,4 (1)
		N (8) — C (7) — O (7)	119,8 (1)
		C (7) — N (8) — C (12)	128,0 (1)
		N (1) — C (9) — C (10)	118,4 (1)
		N (1) — C (9) — O (9)	117,89 (7)
		C (10) — C (9) — O (9)	123,7 (1)
		N (8) — C (12) — C (13)	113,8 (1)
		N (8) — C (12) — O (12)	122,9 (1)
		C (13) — C (12) — O (12)	123,2 (1)

C(9)—N(1)—C(2)—O(2) torsional angles are 15.5(1) and 14.7(1)°. The length of the C(7)—N(8) bond in (I), 1.335 Å, [4] is less than the length of the corresponding bond in (III) (1.391(1) Å) by ~ 0.05 Å. The elongation of the C(7)—N(8) bond is probably connected with the presence of the acetyl group at the N(8) atom, the N(6)—C(7)—N(8)—C(12) torsional angle being 4.1(1)°.

Both "active" H atoms of the (III) molecule participate in H-bonds, that at the N(6) atom being involved in a bifurcated H-bond: in addition to the intramolecular bond N(6)—H...O(12), (N...O 2.694(2), H...O 2.00(2) Å, N—H...O angle 132(2)°), it also participates in an intermolecular H-bond, N(6)—H...O(4') (1/2 – X, 1/2 + y, 1'/2 – z) (2.943(1), 2.27(2) Å, 93(3)°). The H atom at N(8) forms only an intermolecular H-bond: N(8)—H...o(7') (1/2 – x, 1/2 – y, 1 – z) (2.861(2), 2.00(2) Å, 177(2)°).

EXPERIMENTAL

IR spectra were taken on a Specord 75 IR instrument, PMR spectra on a Bruker WM-250 instrument in DMSO-d_6 (δ scale, 0 — TMS), and mass spectra on an LKB 9000S with direct introduc-

TABLE 2. Coordinates of the Nonhydrogen Atoms and Their Equivalent Isotropic Temperature Factors B_{eq} (Å^2)

Atom	*x*	*y*	*z*	B_{eq}
N (1)	0,04909 (4)	0,3381 (1)	0,46070 (6)	2,65 (2)
C (2)	0,02737 (5)	0,1789 (2)	0,43667 (7)	3,02 (3)
N (3)	0,10186 (4)	0,0978 (1)	0,54231 (6)	3,11 (2)
C (4)	0,17325 (5)	0,1930 (2)	0,63083 (7)	2,80 (2)
C (5)	0,14142 (4)	0,3620 (1)	0,58406 (6)	2,46 (2)
N (6)	0,19205 (4)	0,4444 (1)	0,58807 (5)	2,57 (2)
C (7)	0,21249 (4)	0,3743 (1)	0,54866 (6)	2,37 (2)
N (8)	0,26899 (4)	0,4528 (1)	0,56559 (5)	2,75 (2)
C (9)	—0,00864 (5)	0,4655 (2)	0,39296 (8)	3,33 (3)
C (10)	—0,10170 (7)	0,4361 (2)	0,2665 (1)	4,61 (4)
C (11)	0,10654 (7)	—0,0738 (2)	0,5509 (1)	4,74 (4)
C (12)	0,31193 (5)	0,5929 (2)	0,62521 (8)	3,14 (3)
C (13)	0,37715 (6)	0,6335 (2)	0,64065 (9)	4,46 (4)
O (2)	—0,04190 (5)	0,1196 (1)	0,34396 (7)	4,68 (3)
O (4)	0,24765 (4)	0,1532 (1)	0,72777 (5)	3,85 (2)
O (7)	0,18335 (4)	0,2447 (1)	0,49904 (5)	3,22 (2)
O (9)	0,01980 (5)	0,5935 (1)	0,44053 (8)	5,26 (4)
O (12)	0,29681 (4)	0,6772 (1)	0,65900 (6)	4,66 (2)

TABLE 3. Coordinates of the Hydrogen Atoms

Atom	*x*	*y*	*z*
H (5)	0,1457 (5)	0,420 (2)	0,6328 (7)
H (6)	0,2161 (5)	0,539 (2)	0,6249 (7)
H (8)	0,2840 (5)	0,397 (2)	0,5462 (8)
H (10A)	—0,1026 (7)	0,390 (2)	0,220 (1)
H (10B)	—0,1324 (8)	0,358 (3)	0,265 (1)
H (10C)	—0,1342 (7)	0,528 (3)	0,221 (1)
H (11A)	0,1540 (8)	—0,121 (2)	0,570 (1)
H (11B)	0,0496 (7)	—0,117 (2)	0,475 (1)
H (11C)	0,1224 (9)	—0,121 (3)	0,613 (1)
H (13A)	0,421 (1)	0,690 (3)	0,713 (2)
H (13B)	0,3545 (9)	0,675 (3)	0,575 (1)
H (13C)	0,4000 (9)	0,535 (4)	0,643 (1)

tion of the sample into the ion source at an ionizing energy of 70 eV. Melting points were determined one Boetius stage. The analyses of all the compounds corresponded to the calculated figures.

Extraction and Chromatography. The sponges were collected during the 12th voyage of the Scientific Research Ship "Professor Bogorov" on the Mange reef in Tanzania. The animals were extracted with 70% ethanol, the solvent was driven off in vacuum, and the aqueous residue was lyophilized. From 225 g of the lyophilized fraction 32 g of a methanol-soluble fraction was obtained, and this was chromatographed on a column of silica gel L in $CHCl_3$–MeOH. Five compounds containing a pyrrole grouping in their structure [3] were isolated in system 1 ($CHCl_3$:MeOH = 4:1), and 190 mg of (I) and 80 mg of taurine in system 2 ($CHCl_3$:MeOH = 1:1).

1, 8-Diacetyl-DL-allantoin (II). With heating for 30 min, 32 mg of (I) was acetylated with a mixture of 0.5 ml of acetic anhydride and 0.5 ml of pyridine in 2 ml of o-xylene. The reaction mixture was evaporated to dryness and the residue was chromatographed on a column of Sephadex LH-20 in system 1, giving 40 mg of (II) with the composition $C_8H_{10}N_4O_5$, mp 225-229°C (MeOH). IR spectrum, cm^{-1}: λ_{max}^{KBr} 3348, 3179, 3067, 2761, 1807, 1756, 1721, 1706, 1608. PMR spectrum, ppm: 2.03 (s, $COCH_3$), 2.39 (s, $COCH_3$), 5.71 (d, J = 6.2 Hz, 1H), 9.10 (d, J = 6.2 Hz, 1H), 10.58 (s, 1H), 11.60 (exch., 1H) m/z 200 (M^+–42).

1, 8-Diacetyl-3-methyl-DL-allantoin (III). A solution of 25 mg of (II) in 2 ml of MeOH was methylated with an ethereal solution of diazomethane at room temperature for 3 h. The reaction mixture was evaporated to dryness and the residue was chromatographed on a column of Sephadex LH-20 in system 1, with the isolation of 26 mg of (III) having the composition $C_9H_{12}N_4O_5$, mp 229-231°C (ethanol). IR spectrum, cm^{-1}: λ_{max}^{KBr} 3410, 3304, 3138, 1803, 1738, 1711, 1684. PMR spectrum, ppm: 2.02 (s, $COCH_3$), 2.40 (s, $COCH_3$), 2.92 (s, CH_3), 5.83 (d, J = 7 Hz, 1H), 9.10 (d, J = 7 Hz, 1H), m/z 214 (M^+–42).

X-Ray Structural Analysis of Compound (III). Crystals of (III) obtained from solution in ehtanol belonged to the monoclinic system. Space group C2/c, Z = 8, a = 25.830(6), b = 8.514(2), c = 18.533(5) Å, β = 143.95(2)°, V = 2398 $Å^3$, D_{calc} = 1.42 g/cm^3. The intensities of 2185 reflections in the 2θ interval from 2 to 60° were measured on a CAD 4 automatic diffractometer (λMo K_α, graphite monochromator, ratio of the rates of scanning ω:θ = 1.2:1). In the recalculation of the reflection intensities to structure factors, corrections were introduced for the Lorentz factors and for polarization. The structure was solved by the direct method and was refined by the method of least squares in the full-matrix anisotropic approximation to R = 0.035 using 2065 reflections with $I \geq 5\sigma$. The positions of the hydrogen atoms were determined from difference syntheses and were refined in the isotropic approximation. All the calculations were performed on a PDP-11/23PLUS computer by the SDP—PLUS program [6]. The coordinates of the nonhydrogen atoms and their equivalent thermal parameters are given in Table 2, and the coordinates of the hydrogen atoms in Table 3.

SUMMARY

DL-Allantoin has been isolated from an unidentified species of marine sponge of the family Axinellidae.

The crystal and molecular strucutes of 1, 8-diacetyl-3-methyl-DL-allantoin have been established by X-ray structural analysis.

LITERATURE CITED

1. A. F. Cook, R. T. Bartlett, R. P. Gregson, and R. J. Quinn, J. Org. Chem., 45, 4020 (1980).
2. J. F. Weber, F. A. Fuhrman, G. J. Fuhrman, and H. S. Mosher, Comp. Biochem. Physiol., 70B, 799 (1981).
3. N. K. Utkina, S. A. Fedoreev, and O. B. Maksimov, Khim. Prir. Soedin., 578 (1985).
4. D. Mootz, Acta Crystallogr., 19, 726 (1965).
5. L. Pauling, The Nature of the Chemical Bond, 3rd edn, Cornell University Press, Ithaca, N. Y. (1960).
6. B. A. Frenz, Computing in Crystallography, Delft (1978), p. 64.