Chemistry of Natural Compounds, Vol. 34, No. 4, 1998

SPATIAL STRUCTURES OF PULCHELLIN C AND ALANTOLACTONE EPOXIDES

**N. S. Tleugabulov,[a] K. M. Turdybekov,[a] V. A. Raldugin,[b]
M. M. Shakirov,[b] A. T. Kulyyasov,[a] and S. M. Adekenov[a]**

UDC 547.314:548.737

The sesquiterpene lactone pulchellin C has been epoxidized with trifluoroperacetic acid. The spatial structures 4(15)-α-epoxypulchellin and 5α, 6α-epoxyalantolactone have been established by x-ray structural analysis.

The preparation of the products of the epoxidation of the linear eudesmanolides alantolactone (1) and isoalantolactone (2) has been reported previously [1]. In continuation of the search for bioactive substances based on natural compounds, the sesquiterpene lactone pulchellin C (3), isolated from *Inula caspica* Blume [2], has now been epoxidized. The synthesis was carried out by the method described in [1]. In the PMR spectrum of 4(15)-epoxypulchellin (4) (Table 1) we observed characteristic signals of the H-15 methylene protons of the epoxide ring. The signals were assigned by the double-resonance method. When the signal of the lactone proton, H-8, was suppressed, the multiplet at 2.81 ppm of the H-7 proton was converted into a doublet of doublets with the SSCCs 12 and 7 Hz, while the H-9a and H-9b protons appeared as doublets with a SSCC of 15.5 Hz. Suppression of the signal of the H-7 proton at 2.81 ppm led to changes in the multiplicities of the H-8, H-6a, and H-6b signals.

For the unambiguous determination of the orientations of the epoxide rings in epoxypulchellin and epoxyalantolactone (5), we made x-ray structural analyses of these compounds. General views of the (4) and (5) molecules are given in Figs. 1 and 2, respectively. The bond lengths and valence angles are close to the usual values [3], with the exception of the C7C8C9 angle of 117.5° and C8C9C10 angle of 116° in (4) and the C7C8C9 angle of 115.7°and C8C9C10 angle of 117.5° in (5), the distortions of which are obviously a consequence of the steric strains arising from the cis-linkage of rings B and C and the axial orientation of the lactone ring C [1]. In addition to those mentioned above, in the (5) molecule the valence angles at the C5 and C6 atoms differ from the ideal tetrahedral angle of 109.5° (C4C5C6 119.3°, C4C5C10 118.2°, C10C5C6 119.6°, C5C6C7 123.4°). The distortion of these angles is connected with the constriction of the C5-C6 bond (1.44Å) by the epoxide bridge.

In the (4) molecule the linkage of rings C1C2C3C4C5C10 (ring A) and C5C6C7C8C9C10 (ring B) is trans (the torsion angle C14C10C5H5 is 117.7°). The conformation of ring A is an almost ideal chair ($\Delta C_2^{2,3}$ = 0.5°). The values of the torsion angles (Table 2) are close to the ideal value of 56° in cyclohexane and range in absolute value from 54.4 to 60.0°. The linkage of rings B and C is cis (torsion angle H7C7C8H8 40.2°). The conformation of the six-membered ring B is a highly distorted chair: the absolute values of the torsion angles range from 36.0 to 62.8°. The ring is symmetrical in relation to the plane passing through the C5 and C8 atoms (ΔC_s^5 = 1.5°), while the asymmetry parameter $\Delta C_2^{6,7}$ = 26.3° is considerably greater.

The conformation of the lactone ring C is a 8α,7β-half-chair (ΔC_2^{12} = 4.8°). The C7 and C8 atoms depart from the plane of the other atoms of the ring by 0.2 and 0.3 Å in the β- and α-directions, respectively.

In the (5) molecule the linkage of rings A and B is trans (torsion angle C14C10C5O3 −155.0°). The conformation of the six-membered ring A is close to an ideal chair (ΔC_s^2 = 0.3°; the torsion angles are given in Table 2). The sum of the torsion angles $\Sigma\varphi$ = 317.9°. The conformation of ring B can be characterized as a highly distorted 9α,10β-half-chair. Of all the possible symmetry elements in it, only the second-order axis passing through the C9-C10 and C6-C7 bonds is actually realized ($\Delta C_2^{9,10}$ = 5.5°).

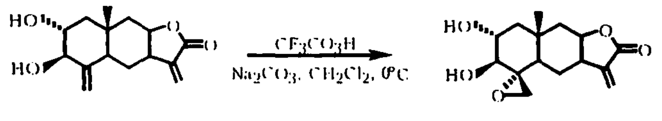
---

a) Institute of Phytochemistry, Academy of Sciences, Republic of Kazakhstan, Karaganda, fax (3212) 51 10 23; b) Novosibirsk Institute of Organic Chemistry, Siberian Division of the Russian Academy of Sciences, Novosibirsk, fax (3832) 35 47 52. Translated from Khimiya Prirodnykh Soedinenii, No. 4, pp. 499-504, July-August, 1998. Original article submitted March 18, 1998.

0009-3130/98/3404-0462$20.00

TABLE 1. Details of the PMR Spectra of Compound (4), 400 MHz, δ, Py-d_5, J, Hz

H-6, (H-6′)	H-7	H-8	H-9, H-9′	H-13, H-13′	H-14	H-15, (H-15′)
1.61 (1H, ddd) J_1=13.5 J_2=7.0 J_3=2.5	2.81 (1H, m)	4.38 (1H, ddd) J_1=4.5 J_2=4.5 J_3=1.5	1.98 (1H, dd) J_1=15.5 J_2=1.5	6.09 (1H, d) J=0.64	0.85 (3H, s)	3.32 (1H, d) J=5.0
0.93 (1H, ddd) J_1=13.5 J_2=13.0 J_3=12.0			1.35 (1H, dd) J_1=15.5 J_2=4.5	5.50 (1H, d) J=0.64		2.52 (1H, d) J=5.0



3 4

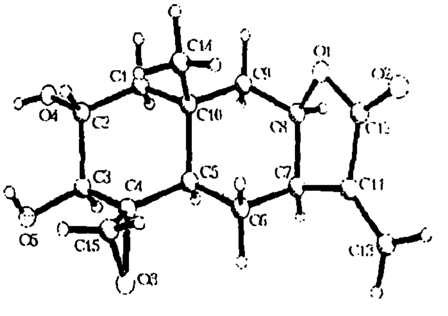


Fig. 1

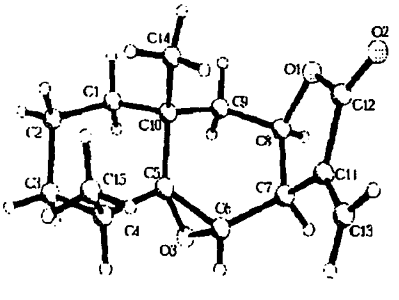


Fig. 2

Fig. 1. General view of the 4(15)-α-epoxypulchellin molecule.

Fig. 2. General view of the 5α,6α-epoxyalantolactone molecule.

The conformation of the lactone ring C is practically planar (Table 3). The atoms are coplanar to within 0.03 Å.

Thus, molecule (4) has the structure of 2α,3β-dihydroxy-4(15)-α-epoxy-5,8α,7α(H)-eudesm-11(13)-en-8,12-olide, and the molecule (5) that of 5α,6α-epoxy-4,8α,7α(H)-eudesm-11(13)-en-8,12-olide.

A comparison of the torsion angles in rings A of the molecules (3) and (4) shows that epoxidation of the C4═C15 double bond does not cause appreciable changes in the conformation of the ring (the change in the respective torsion angles does not exceed 4.2°). The differences in the torsion angles in rings B and C are also insignificant and do not affect the conformations of the rings. A distortion of ring B is observed both in the initial molecule (3) and in the epoxide (4) molecule, which is apparently connected with the axial orientation of the O1 atom and the consequent appearance of repulsions, in the first place between the Me-14 group at C10 and the O1 atom (the C14···O1 distance is 3.2 Å). An analogous distortion of ring B is also observed in other trans-, cis-linked linear eudesmanolides such as alantolactone and isoalantolactone [1].

On the epoxidation of the (1) molecule the epoxy group adds at the position of rupture of the double bond between the C5 and C6 atoms. At the same time a change is observed in the torsion angles in the position of linkage of rings A and B (the torsion angles C3C4C5C10 and C4C5C10C1 have increased by 9 and 10.6°, respectively). The changes in these angles are close in absolute value and symmetry and the conformation ring A has therefore remained as before (in the initial molecule — chair (ΔC = 1.5°)). The conformation of ring B in the (5) molecule, as compared with the initial conformation, has not undergone appreciable changes (the difference between the corresponding intracyclic torsion angles does not exceed 4°). The more pronounced distortion of ring B in the (1) and (5) molecules as compared with other linear eudesmanolides (pulchellin, isoalantolactone) can be explained by two factors. In addition to the above-described repulsion between C14 and O1, which is also characteristic of other molecules, there is a decrease in the distance between the C6 and C5 atoms because of the double bond in the (1) molecule (C6═C5 1.31 Å) and the addition of the epoxy group to the C5 and C6 atoms in (5)

TABLE 2. Torsion Angles φ (degrees) in the Rings

Angle	φ	
	molecule 4	molecule 5
Ring *A*		
C1C2C3C4	50.2	57.2
C2C3C4C5	-54.0	-51.4
C3C4C5C10	57.5	50.2
C4C5C10C1	-55.9	-50.0
C5C10C1C2	57.3	51.4
C10C1C2C3	-54.7	-57.7
Ring *B*		
C5C6C7C8	47.4	-18.2
C6C7C8C9	-36.0	-2.7
C7C8C9C10	38.0	39.7
C8C9C10C5	-48.8	-53.4
C9C10C5C6	61.9	32.0
C10C5C6C7	-62.8	2.2
Ring *C*		
O1C8C7C11	-30.7	-2.4
C8C7C11C12	23.8	-0.6
C7C11C12O1	-7.8	3.7
C11C12O1C8	-12.9	-5.5
C12O1C8C7	28.8	5.0

TABLE 3. Coordinates of the Atoms ($\times 10^4$; for H, $\times 10^3$) in the Structure of (**4**)

Atom	*x*	*y*	*z*
O1	1340(2)	0	9689(1)
O2	2571(2)	-123(5)	11461(2)
O3	4591(2)	4818(4)	6436(1)
O4	1338(2)	649(5)	3679(2)
O5	3936(2)	3228(4)	4156(2)
C1	1017(3)	548(5)	5679(2)
C2	2138(3)	833(6)	4808(2)
C3	2899(3)	2912(5)	4967(2)
C4	3572(2)	3129(5)	6220(2)
C5	2431(3)	2924(5)	7085(2)
C6	3037(3)	3335(5)	8341(2)
C7	1771(3)	3415(5)	9120(2)
C8	686(3)	1627(5)	8910(2)
C9	350(2)	859(5)	7681(2)
C10	1664(3)	817(5)	6949(2)
C11	2358(3)	3072(5)	10375(2)
C12	2143(3)	860(5)	10613(2)
C13	2963(3)	4372(6)	11166(2)
C14	2706(3)	-985(5)	7310(2)
C15	5144(3)	2734(5)	6542(2)
HO4	182(3)	68(6)	318(3)
HO5	437(3)	215(6)	411(2)
H1a	57(3)	-80(5)	559(2)
H1b	25(3)	153(5)	549(2)
H2	291(3)	-25(5)	493(2)
H3	216(3)	403(4)	485(2)
H5	166(3)	398(4)	686(2)
H6a	362(3)	219(5)	859(2)
H6b	351(3)	473(4)	841(2)
H7	125(3)	472(5)	898(2)
H8	-23(3)	195(5)	921(2)
H9a	-10(3)	-54(5)	767(2)
H9b	-38(3)	186(4)	732(2)
H13a	322(3)	382(6)	1197(3)
H13b	304(3)	584(5)	1095(2)
H14a	218(3)	-228(5)	714(2)
H14b	295(3)	-101(5)	810(3)
H14c	356(3)	-108(5)	684(2)
H15a	541(2)	228(4)	730(2)
H15b	578(3)	230(5)	594(2)

(C5–C6 1.44 Å). This leads to asymmetry of this ring and distortion of the torsion angles (the maximum asymmetry parameter $C_s^{12} = 36.1°$).

We may note that the lactone ring of the (**5**) molecule is somewhat flattened in comparison with the analogous ring in the (**1**) molecule.

TABLE 4. Coordinates of the Nonhydrogen Atoms ($\times 10^4$) of Structure (5)

Atom	x	y	z
O1	7418(4)	5000	4746(2)
O2	8498(5)	1715(10(10)	5042(3)
O3	5910(5)	7968(9)	1697(3)
C1	2486(6)	7872(11)	2471(4)
C2	1198(7)	7042(12)	1484(4)
C3	1971(6)	6882(12)	575(3)
C4	3583(7)	5464(11)	822(4)
C5	4832(6)	6187(10)	1854(3)
C6	6660(6)	5929(11)	2009(3)
C7	7963(3)	5853(11)	3085(4)
C8	7290(6)	6765(10)	3995(4)
C9	5490(6)	7673(11)	3671(4)
C10	4127(6)	6482(10)	2817(3)
C11	8496(6)	3622(11)	3436(4)
C12	8176(6)	3265(11)	4479(4)
C13	9103(8)	2083(12)	2965(4)
C14	3733(6)	4316(10)	3230(3)
C15	3176(8)	3078(13)	784(4)

Thus, the epoxidation of the linear eudesmanolides alantolactone, isoalantolactone, and pulchellin C forms α-epoxy derivatives of these lactones.

EXPERIMENTAL

Compound (5) was synthesized by the method of [1]. Melting points were determined on a Kofler stage. The PMR spectrum of compound (4) was recorded on a Bruker WP-400SY instrument, and its mass spectrum on a Finnegan MAT 8200 instrument.

4(15)-α-Epoxypulchellin C (4). Colorless cubic crystals with mp 204-206°C. $[\alpha]_{580}^{22}$ +52.4° (c 0.469; $CHCl_3$).

Mass spectrum EI, 70 eV, m/z(I_{rel}): 256.2[$M^+ - CH_3$](2.14), 249.1(39.76), 232.1(30.56), 217.1(14.39), 191.1(24.18), 165.1(100.00), 147.0(27.13), 145.1(18.84), 133.1(16.01), 131.1(20.17), 121.1(16.93), 119.1(22.60), 117.1(20.07), 109.1(15.00), 107.1(18.40), 105.1(20.26), 99.1(15.64), 95.1(44.88), 93.1(23.48), 91.1(40.59), 86.1(54.65), 79.1(30.30), 77.1(24.41), 68.1(25.35), 41.1(43.30).

X-Ray Structural Experiment. The cell parameters and the intensities of the reflection of a crystal of (4) were measured on a Siemens P3/PC four-circle diffractometer at 120°C (Mo$-K_\alpha$, graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 56°$). The crystals of (4) were monoclinic, a = 9.117(5), b = 6.536(4), c = 11.611(6) Å, β = 96.43(2), sp. gr. $P2_1$, μ = 0.101 cm^{-1}, Z = $2(C_{15}H_{20}O_5)$.

The cell parameters and the intensities of the reflections of a crystal of (5) were measured on a Syntex $P2_10$ four-circle diffractometer at 20°C (Mo-K_α, graphite monochromator, $\theta/2\theta$ scanning, $2\theta \leq 50°$). The crystals of (5) were monoclinic, a = 8.060(8), b = 6.273(7), c = 13.220(11)Å, β = 106.18°,. sp. gr. $P2_1$, μ = 0.09 cm^{-1}, Z = $2(C_{15}H_{20}O_3)$.

The structures were interpreted by the direct method. All the nonhydrogen atoms were refined anisotropically. In the (4) molecule the hydrogen atoms were found from a difference synthesis and were refined isotropically. In the (5) molecule all the hydrogen atoms were placed geometrically and were not refined. The final divergence factors were R = 0.032 and R_w = 0.033 for 1427 independent reflections in the structure of (4) and R = 0.052, R_w = 0.077 for 1154 independent reflections in the structure of (5). The coordinates of the atoms are given in Tables 3 (structure of (4)) and 4 [structure of (5)]. All the calculations were made on a Pentium PC by the SHELXTL (PC Version) program packet.

REFERENCES

1. A. T. Kulyyasov, T. S. Seitembetov, K. M. Turdybekov, and S. M. Adekenov, Khim. Prir. Soedin., 879 (1996).
2. S. M. Adekenov, M. A. Abdykalykov, K. M. Turdybekov, Yu. T. Struchkov, and A. N. Pushin, Khim. Prir. Soedin., 748 (1990).
3. F. H. Allen, O. Kennard, D. G. Watson, L. Brammer, A. G. Orpen, and R. Taylor, J. Chem. Soc., Perkin Trans., No. 47, 920 (1984).