STRUCTURE OF PYRROLISIDINEDIONES – PRODUCTS OF THE INTRAMOLECULAR CYCLIZATION OF AMINOKETO-STABILIZED SULFONIUM YLIDES

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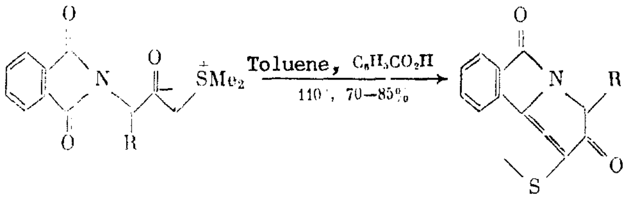
The structure of three pyrrolisidinediones was determined by x-ray crystallographic analysis. A pseudocentrosymmetrical structure of the dimer crystal with a molecule of water of crystallization close to the inversion center was detected in the oxidation product.

Pyrrolisidinedione alkaloids possess high physiological activity, which is the cause of the increased interest in the development of synthetic methods and a strategy for constructing five-membered nitrogen-containing heterocycles [1].

Pyrrolisidinediones, which are readily synthesized from cyclic N,N-diacyl amino acids [2], are similar to synthone in alkaloid synthesis. The key step in this synthesis is an intramolecular Wittig reaction of the corresponding phosphorus ylides.

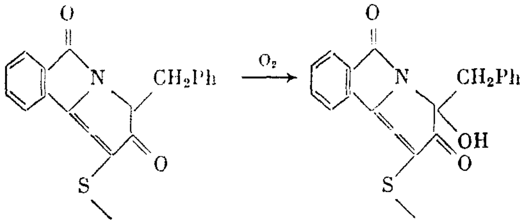
Tolstikov et al. [3] have synthesized substituted pyrrolisidinediones by intramolecular cyclization of amino-substituted keto-stabilized sulfonium ylides, produced from N-phthalyl-α-amino acids [4]



(Ia, b)

R = $CH(CH_3)_2$ (Ia), $CH_2C_6H_5$ (Ib).

In the case of longer boiling in acetonitrile, the pyrrolisidinediones formed are oxidized, yielding tertiary alcohols



(Ib) (II)

To establish the structure of (Ia), (Ib), and (II) and to study the stereochemistry of the condensed heterocycles, we conducted an x-ray crystallographic (XC) investigation of them.

EXPERIMENTAL

Crystals of (Ia), $C_{15}H_{15}O_2NS$, are monoclinic; at 23°C a = 10.301(9), b = 8.664(2), c = 15.762(9) Å, β = 99.20(8)°, Y = 1388.58 Å³, Z = 4, d_{calc} = 1.298 g/cm³, space group $P2_1/n$.

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TABLE 1. Coordinates of Atoms in the Structure (Ia)

Atom	X	Y	Z
S	0.68768(6)	0.06575(9)	0,05189(5)
O^1	1,2842(2)	0,1959(3)	0,1605(1)
O^2	0,8180(2)	0,0256(3)	0.2479(1)
N^1	1,0653(2)	0,1238(3)	0,1444(1)
C^1	0.8453(2)	0,0826(3)	0.1112(2)
C^2	0.9526(2)	0.1391(3)	0,0832(2)
C^3	0,9912(2)	0.2139(3)	0,0081(2)
C^4	0,9223(3)	0.2540(4)	−0,0708(2)
C^5	0.9886(3)	0.3279(4)	−0.1285(2)
C^6	1,1217(3)	0,3604(4)	−0,1078(2)
C^7	1,1917(3)	0,3203(4)	−0,0281(2)
C^8	1,1257(2)	0.2468(4)	0.0294(2)
C^9	1.1741(2)	0,1884(4)	0,1183(2)
C^{10}	1,0361(2)	0,0575(3)	0.2242(2)
C^{11}	0.8862(3)	0,0292(3)	0.2001(2)
C^{12}	0.5946(3)	0,1823(5)	0,1137(2)
C^{13}	1,0767(3)	0,1643(3)	0.3012(2)
C^{14}	1,0089(4)	0.3191(5)	0.2901(3)
C^{15}	1.0570(4)	0.0859(4)	0,3844(2)

Crystals of (Ib), $C_{19}H_{15}O_2NS$, are monoclinic; at 23°C a = 11.772(5), b = 8.558(6), c = 15.996(5) Å, β = 92.83(3)°, V = 1609.47 Å³, Z = 4, d_{calc} = 1.327 g/cm³, space group $P2_1/c$.

Crystals of (II), $C_{19}H_{15}O_3NS \cdot (1/2)H_2O$, are triclinic; at 23°C a = 8.489(5), b = 10.079(2), c = 10.01(2) Å, α = 87.9(1), β = 77.1(1), γ = 85.17(4)°, V = 831.39 Å³, Z = 2, d_{calc} = 1420 g/cm³, space group $P\bar{1}$.

The parameters of the cells and intensities of reflections 1436 and 1564 with $F^2 \geq 3\sigma$ for (Ia) and (Ib), respectively, and reflection 2528 with $F^2 \geq 4\sigma$ for (II) were measured on an Enraf–Nonius CAD-4 automatic four-cycle diffractometer (λMo Kα radiation, graphite monochromator, $\omega/2\theta$ scanning, $2\theta \leq 60°$).

The spectra were interpreted according to the MULTAN program and refined in an anisotropic approximation. All the H atoms, with the exception of the H_2O molecule in the structure of (II), were detected from differential synthesis and refined in an isotropic approximation. The crystal of (II) exists in crystal hydrate form with 1/2 H_2O, the O-atom of which is localized close to the center of inversion with coordinates X = 0.067, Y = 0.518, Z = −0.015, and refined with population 0.5. When the O atom was placed in the center of inversion, we obtained values of B_{iso}^{eq} without physical meaning. The H atoms of the water of crystallization could not be localized from differential synthesis. The final values of the discrepancy factors R = 0.036 and R_w = 0.048 for (Ia), R = 0.031 and R_w = 0.044 for (Ib), and R = 0.049 and R_w = 0.073 for the structure (II).

All the calculations were performed on a PDP-11/23 computer according to the SDP programs. General views of the molecules with bond lengths are shown in Figs. 1-3, respectively. The coordinates of the atoms are presented in Tables 1 and 2.

RESULTS AND DISCUSSION

It has been established that in all the investigated structures (Ia, b) and (II) the pyrrolisidine fragments are planar with a nodal planotrigonal N atom. The carbamide groups in position 9, as well as the S atoms, are coplanar with the plane of the tricycle. Resolution of the steric hindrances at the chiral C atom occurs on account of rotation of the isopropyl group in structure (Ia) and the benzyl fragment in structures (Ib) and (II) at the C–C bond relative to the pyrrolisidine tricycle and removal of the carbamide and hydroxyl groups from its plane: the dihedral angles between the planes of the benzyl and pyrrolisidine fragments in structures (Ib) and (II) are equal to 56.5 and 52°, respectively; the deviation of the O^2 atoms is 0.1 Å (Ib) and (II) and that of O^3 is 1 Å (II).

The mutual arrangement of the substituents at the chiral center is conveniently characterized with Newman projections along the bonds C^{10}–N^1 (1) and C^{10}–C^{11} (2)

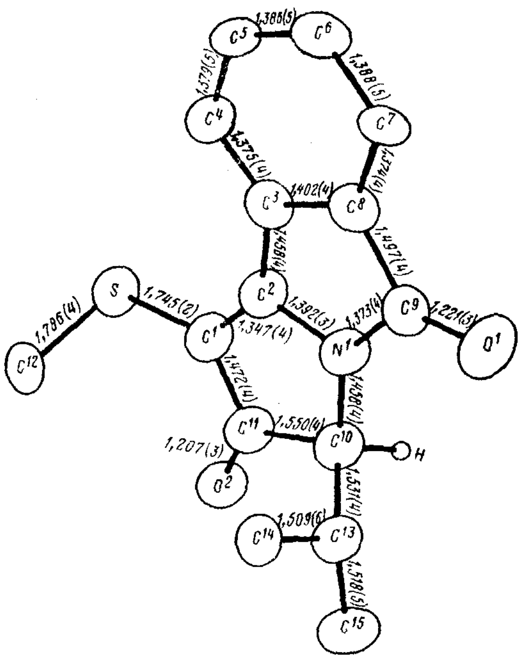


Fig. 1

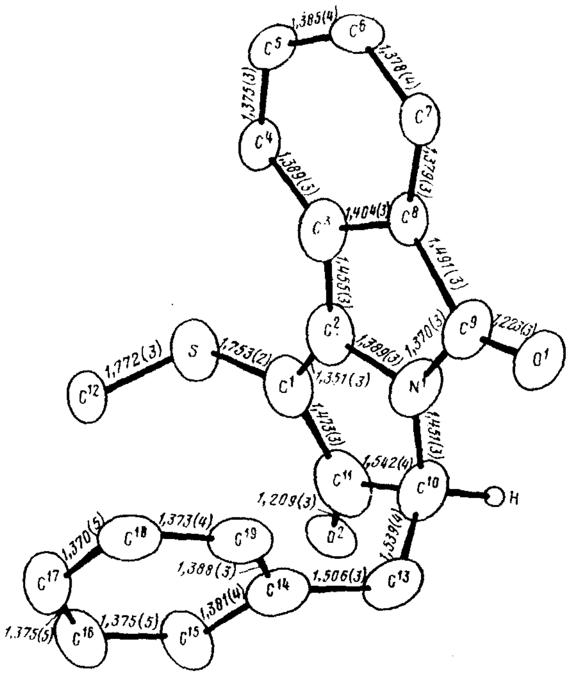


Fig. 2

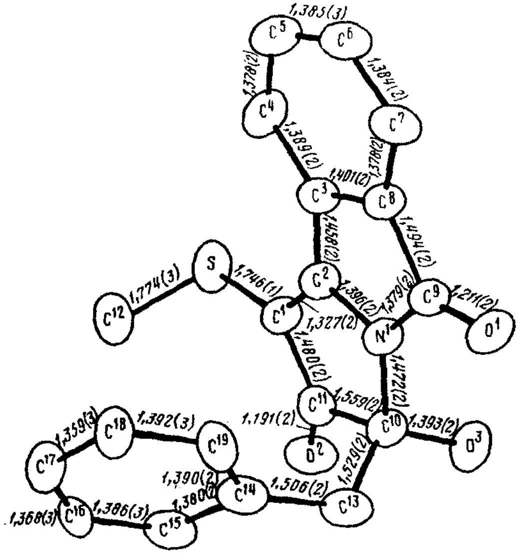


Fig. 3

Fig. 1. General view of the molecule (Ia); bond lengths and the H atom at the chiral center are shown.

Fig. 2. General view of the molecule (Ib); bond lengths are shown.

Fig. 3. General view of the molecule (II) with bond lengths.

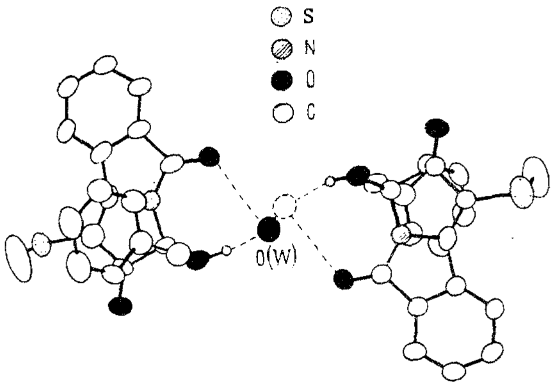
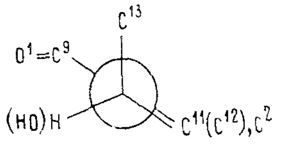


Fig. 4. Dimers formed by H-bonds with the bridge oxygen atom.

TABLE 2. Coordinates of Atoms in Structures (Ib) and (II)

Atom	(Ib)			(II)		
	x	y	z	x	y	z
S	0,27270(5)	0,02682(7)	0,58391(4)	0,6983(3)	0.1660(3)	0,3023(3)
O^1	−0,0291(1)	0,1523(2)	0,26055(8)	0,0883(8)	0,2288(7)	0,0516(8)
O^2	0,3466(1)	−0,1454(2)	0,4105(1)	0,5356(9)	0,4699(7)	0,2704(9)
O^3	–	–	–	0,3371(9)	0,4714(6)	0,0676(7)
N^1	0,1051(1)	0,0794(2)	0,36405(9)	0,3062(8)	0,2496(6)	0,1517(8)
C^1	0,2186(2)	0,0267(2)	0,4799(2)	0,526(1)	0,2327(9)	0,247(1)
C^2	0,1257(2)	0,1042(2)	0,4493(1)	0,426(1)	0,1667(8)	0,1955(9)
C^3	0,0355(2)	0,2051(2)	0,4773(1)	0,396(1)	0,0309(8)	0,1681(9)
C^4	0,0125(2)	0,2686(2)	0,5546(2)	0,475(1)	−0,0919(9)	0,190(1)
C^5	−0,0831(2)	0,3598(2)	0,5598(1)	0,413(1)	−0,2044(9)	0,154(1)
C^6	−0,1553(2)	0,3868(2)	0,4904(2)	0,279(1)	−0,1965(9)	0,096(1)
C^7	−0,1333(2)	0,3246(2)	0,4134(1)	0,201(1)	−0,0745(9)	0,073(1)
C^8	−0,0372(2)	0,2343(2)	0,4068(1)	0,260(1)	0,0384(8)	0,1093(9)
C^9	0,0088(2)	0,1533(2)	0,3331(1)	0,201(1)	0,1813(8)	0,0981(9)
C^{10}	0,1919(2)	−0,0191(2)	0,3299(1)	0,317(1)	0,3894(8)	1,184(1)
C^{11}	0,2652(2)	−0,0595(2)	0,4095(1)	0,475(1)	0,3763(9)	0,240(1)
C^{12}	0,3773(2)	0,1753(3)	0,5798(2)	0,630(2)	0,186(3)	0,482(2)
C^{13}	0,2618(2)	0,0654(3)	0,2648(1)	0,171(1)	0,4399(9)	0,294(1)
C^{14}	0,3236(2)	0,2075(2)	0,2918(1)	0,153(1)	0,3629(9)	0,428(1)
C^{15}	0,4326(2)	0,1989(3)	0,3344(2)	0,218(1)	0,403(1)	0,533(1)
C^{16}	0,4869(2)	0,3281(4)	0,3681(2)	0,203(1)	0,332(1)	0,656(1)
C^{17}	0,4332(3)	0,4706(3)	0,3640(2)	0,122(1)	0,218(1)	0,675(1)
C^{18}	0,3259(2)	0,4833(3)	0,3276(2)	0,058(1)	0,177(1)	0,573(1)
C^{19}	0,2785(2)	0,3531(3)	0,2953(1)	0,071(1)	0,248(1)	0,450(1)
O(W)	–	–	–	0,067(2)	0,518(2)	−0,015(2)



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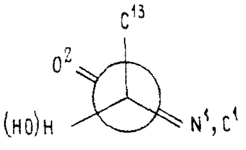

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which show a synclinal (SC) conformation.

A distortion of the tetrahedral structure of the chiral C atom is observed, in contrast to the close-to-ideal C_{sp^3} state of this atom in (II). Thus, in (Ia, b) the endocyclic angles $N^1C^{10}C^{11}$ are reduced to 101.3(2) and 100.7(2)°, respectively; the external bond angle $C^{11}N^{10}C^{13}$ is equal to 113.0(2)°, whereas in (II) the bond angles at the chiral C^{10} atom differ inconsequentially from the standard value 109.5°.

An interesting structural result is the distribution of bond lengths in the fragment $N^1–C^{10}–C^{11}–C^1–C^2$. In the structure (II) the bond lengths $N–C_{sp^3}$ and C=C are equal to 1.472(2) and 1.327(2) Å; the bonds corresponding to them take values 1.458(2) and 1.347(2) Å in (Ia) and 1.451(3) and 1.351(3) Å in (Ib). Comparing these values with one another and with the standard lengths of typical N–C single bonds and C=C double bonds (1.47 and 1.28 Å

[5]), we can assume substantial delocalization of the electron density in structures (Ia, b), in contrast to the more localized bonds in (II).

The cause of such a change in the bond lengths in (II) may be the interaction of the unshared electron pair of the O^3 atom with the antibonding σ* orbital of the C^{10}–N^1 bond, which is the basis of the anomeric effect. Such an interpretation is confirmed by the shortening of the C^{10}–O^3 bond to 1.393(2) Å in comparison with the usual C_{sp^3}–OH bond, equal to 1.413 Å [6].

The molecules in the crystal (II) are joined by strong hydrogen bonds, forming pseudo-centrosymmetrical dimers (Fig. 4). The molecule of water of crystallization, which lies close to the inversion center, plays the role of a "bridge" and acts as an acceptor in the H-bond O–H...O(W). The donor is the hydroxyl group. The parameters of the H-bond O^3...O(W) 2.610(3), H^3...O(W), 1.695(3) Å, <O^3–H^3...O(W) 168.8(1)°.

Moreover, the short distance O^1...O(W) 2.971(3) Å suggests that a second hydrogen bond is effected, in which the molecule of water of crystallization acts as a donor, and the carbonyl O^1 atom is the acceptor.

Only the usual van der Waals interactions occur between molecules in the crystals of (Ia) and (Ib).

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