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CRYSTAL AND MOLECULAR STRUCTURE OF THE DITERPENE ALKALOID TALATISINE

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As a result of x-ray studies, the spatial structure and conformation of the talatisine molecule have been determined. The mean bond lengths are C–C 1.539(6) Å, N–C 1.493(5) Å, HO–C(sp^3) 1.429(5) Å. The six-membered rings A and B have the chair conformation, and rings C and D have distorted boat conformations. The five-membered rings E, F, and G have the envelope conformation.

The alkaloid talatisine has been isolated from the roots of the plant *Aconitum talassicum* M. Pop. [1] collected in the mountains of the Talas Alatau. In order to determine the spatial structure of the diterpene alkaloid talatisine, we have performed an x-ray study.

The conformation of the talatisine molecule is shown in Fig. 1. It has a rigid three-dimensional skeleton consisting of seven rings. The conformations of the rings can be judged from the figures of Table 1. The cyclohexane ring A (the C(1), C(2), C(3), C(4), C(5), and C(10) atoms) is a $^{1,0}C_3$ chair close to the ideal form with the C(3) and C(10) atoms deviating in opposite directions from the main plane of the other four atoms by 0.60 and 0.61 Å. The six-membered ring B (the C(5), C(6), C(7), C(8), C(9), and C(10) atoms) is a distorted $^{6}C_9$ chair with the C(6) and C(9) atoms deviating in opposite directions by 0.65 and –0.86 Å. Ring C (the C(8), C(9), C(11), C(12), C(15), and C(16) atoms) is a distorted $^{8,12}B$ boat; the deviations of the C(8) and C(12) atoms are almost 0.65 and 0.69 Å, respectively, but the other members of the ring deviate from the mean plane by ±0.12 Å, and ring D (the C(8), C(9), C(11), C(12), C(13), and C(14) atoms) likewise has the $B_{8,12}$ boat conformation, the C(8), and C(12) atoms deviating in different directions by –0.62 and –0.75 Å. The five-membered rings E (the C(5), C(6), C(10), C(20), and N atoms) and F (the C(4) C(5), C(6), and C(19), and N atoms) have a ^{6}E envelope conformation differing somewhat from the ideal [2], the deviations of the C(6) atoms being, respectively, –0.886 Å and –0.87 Å, and ring G (the C(8), C(9), C(10), C(14), and C(20) atoms) is an almost ideal ^{8}E envelope, the deviation of the C(8) atom amounting to 0.78 Å.

The bond lengths and valence angles are given in Tables 2 and 3. The lengths of the ordinary C–C bonds in the rings vary from 1.496(5) to 1.596(6) Å, but the mean value of 1.539(6) Å coincides with the standard 1.541(3) [3], and also with the value for alkaloids [4, 5]. The mean length of the N–C bonds is 1.493(5) Å, i.e., it almost coincides with the value of 1.50 Å for a protonated quaternary nitrogen $H\text{–}\overset{+}{N}[C(sp^3)]_3$ [6], and in the diterpene alkaloids hypognavinol [4] and anhydrohypognavinol [5] this value is 1.53 Å. The mean length of the HO–C (sp^3) bonds is 1.429 (5) Å, fairly close to the usual values [3-5].

The sizes of the valence angles in the talatisine molecule vary: in the five-membered rings from 95 to 110°, and in the six-membered rings from 107 to 117°. In spite of the considerable variations in the valence angles, the values agree with those given for organic compounds [7]. The deviations of the rings from the ideal conformations, and also the variations in bond lengths and valence angles that have been mentioned are due to some overall strain of the talatisine molecule. The nature of the variation in the bond lengths for the hydrogen atoms is given in Table 4. The O(2)H and O(3)H hydroxy groups are located on the same side of the plane of ring C and form a O(2)•••O(3) intramolecular hydrogen bond with a length of 2.88 Å.

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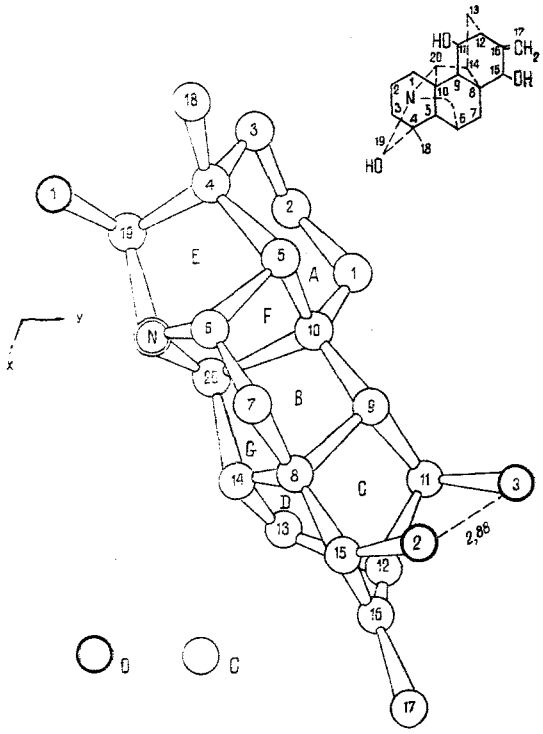

Fig. 1

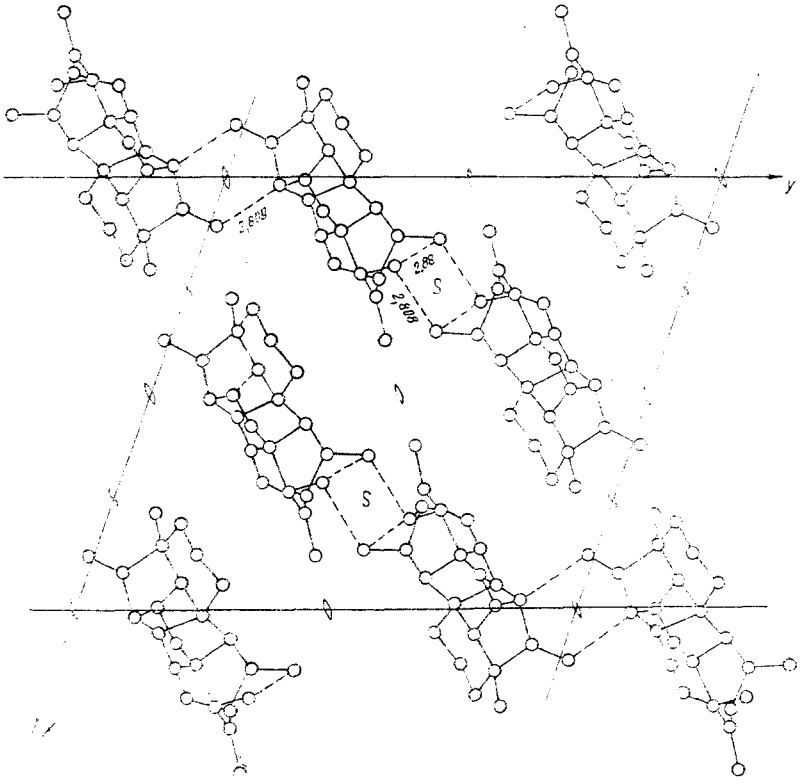

Fig. 2

TABLE 1. Equations of the Planes Ax + By + Cz + D = 0 and Deviations of the Atoms from these Planes, δ (Å)

Ring, atom	A	B	C	D	δ
	C(1)				−0.011
	C(2)				0.011
	C(4)	13.594	−11.853	1.428	3.779	−0.010
A	C(5)					0.010
	C(3)*					−0.600
	C(10)*					0.614
	C(5)					−0.070
	C(7)					0.071
	C(8)	6.553	−15.523	2.729	4.418	−0.077
B	C(10)					0.076
	C(6)*					0.646
	C(9)*					−0.857
	(15)					−0.117
	C(16)					0.120
C	C(11)	5.064	−14.301	3.786	5.418	−0.115
	C(9)					0.113
	C(8)*					0.648
	C(12)*					0.692
	C(11)					−0.063
	C(9)					0.068
D	C(14)	−9.507	−2.630	4.820	3.038	−0.068
	C(13)					0.063
	C(8)*					−0.876
	C(12)*					−0.717
	N					−0.003
	C(4)					−0.004
E	C(5)	1.487	5.384	6.494	1.301	0.003
	C(19)					0.004
	C(6)*					−0.866
	N					−0.006
	C(5)					0.006
F	C(10)	−8.422	−4.245	4.910	2.012	−0.008
	C(20)					0.008
	C(6)*					−0.876
	C(9)					0.031
G	C(10)					−0.046
	C(20)	−1.696	−5.698	−6.411	0.130	0.046
	C(14)					−0.031
	C(8)*					0.785

*Atoms not included in the calculation of the planes.

TABLE 2. Bond Lengths in the Talatisine Molecule (Å)

Bond	r	Bond	r
O(1)—C(19)	1.404(5)	C(1)—C(2)	1.496(5)
O(2)—C(9)	1.440(6)	C(1)—C(10)	1.521(6)
O(3)—C(11)	1.442(5)	C(2)—C(3)	1.545(7)
N —C(6)	1.501(5)	C(3)—C(4)	1.517(7)
N —C(20)	1.472(5)	C(4)—C(5)	1.546(5)
N —C(19)	1.505(5)	C(4)—C(19)	1.576(6)
C(5)—C(6)	1.541(6)	C(4)—C(18)	1.536(6)
C(5)—C(10)	1.559(5)	C(6)—C(7)	1.523(5)
C(7)—C(8)	1.523(5)	C(8)—C(15)	1.554(5)
C(8)—C(9)	1.522(6)	C(8)—C(14)	1.552(6)
C(15)—C(16)	1.500(5)	C(10)—C(11)	1.497(7)
C(16)—C(17)	1.338(5)	C(11)—C(12)	1.539(7)
C(12)—C(13)	1.576(6)	C(11)—C(9)	1.558(5)
C(9)—C(10)	1.540(4)	C(10)—C(20)	1.596(6)
C(20)—C(14)	1.531(5)	C(13)—C(14)	1.548(6)

TABLE 3. Valence Angles in the Talatisine Molecule

Angle	Size, deg	Angle	Size, deg
C(3) —C(1) —C(10)	113.3(4)	C(12)—C(11) C(9)	108.8(3)
C(1) —C(2) —C(3)	111.6(4)	C(12)—C(11) O(3)	105.6(4)
C(2) —C(3) —C(4)	114.3(4)	O(3) —C(11)—C(9)	110.7(4)
C(3) —C(4) —C(5)	112.1(3)	C(16)—C(12)—C(11)	109.7(4)
C(3) —C(4) —C(10)	113.9(4)	C(16)—C(12)—C(13)	107.8(3)
C(3) —C(4) —C(18)	107.9(4)	C(11)—C(12)—C(13)	107.3(5)
C(5) —C(4) —C(19)	99.4(3)	C(14) —C(13)—C(12)	108.6(3)
C(5) —C(4) —C(18)	110.9(4)	C(20)—C(14)—C(13)	111.1(4)
C(19)—C(4) —C(18)	112.5(4)	C(20)—C(14) C(8)	101.4(4)
C(4) —C(5) —C(6)	105.3(3)	C(8) —C(14)—C(13)	111.0(4)
C(4) —C(5) —C(10)	112.0(4)	C(8) —C(15)—C(16)	108.8(6)
C(6) —C(5) —C(10)	100.7(3)	C(8) —(15) O(2)	109.6(6)
C(5) —C(6) —C(7)	115.2(4)	O(2) —C(15)—C(16)	112.1(2)
C(5) —C(6) —N	95.0(5)	C(15)—C(16)—C(12)	112.2(5)
C(7) —C(6) —N	111.3(3)	C(15) C(16)—C(17)	122.6(4)
C(6) —C(7) C(8)	111.2(3)	C(12)—C(16)—C(17)	124.7(3)
C(7) C(8) C(15)	112.8(4)	C(4) —C(19)—O(1)	110.2(4)
C(7) C(8) C(9)	110.0(4)	O(1) —C(19)—N	109.7(3)
C(7) —C(8) C(14)	109.2(3)	C(4) —C(19)—N	105.9(3)
C(15)—C(8) —C(9)	111.8(3)	C(10)—C(20)—C(14)	103.3(4)
C(15)—C(8) —C(14)	113.4(4)	C(10)—C(20)—N	106.5(5)
C(9) —C(8) —C(14)	98.7(5)	C(14)—C(20)—N	110.3(3)
C(11)—C(9) —C(10)	117.2(4)	C(6) —N—C(20)	100.7(4)
C(11)—C(9) —C(8)	109.6(4)	C(6)—N—C(19)	101.3(4)
C(8) —C(9) —C(10)	102.7(4)	C(20)—N—C(19)	109.3(3)
C(9) —C(10)—C(20)	104.2(3)		
C(9) —C(10) C(1)	117.3(4)		
C(9) —C(10)—C(5)	107.1(3)		
C(1) —C(10)—C(5)	112.8(4)		
C(1) —C(10)—C(20)	115.1(4)		
C(5) —C(10) —C(20)	98.2(4)		

TABLE 4. Lengths of Bonds Including H Atoms, r (Å)

Bond	r	Bond	r
C(1) —H(1)	1.15	C(11)—H(13)	1.06
C(1) —H(2)	1.08	C (9)—H(14)	1.03
C(2) —H(3)	1.13	C(20)—H(15)	1.01
C(2) —H(4)	1.05	C(14)—H(16)	1.00
C(3) —H(5)	0.88	C(13)—H(17)	1.03
C(3) —H(6)	1.00	C(19)—H(18)	0.95
C(5) —H(7)	1.11	C(18) —H(19)	1.15
C(6) —H(8)	1.09	C(18)—H(20)	0.99
C(7) —H(9)	1.09	C(17)—H(21)	1.01
C(7) —H(10)	1.08	O(1)—H(22)	0.96
C(15)—H(11)	1.23	O(2)—H(23)	0.93
C(12)—H(12)	1.06	O(3)—H(24)	0.89

Packing of the Molecules. All three localized active hydrogen atoms participate in hydrogen bonds, which are shown by dashed lines in Fig. 2. This is shown by the interatomic distances of the atoms N•••O(1) and O(2)•••O(3) of 2.809 and 2.808 Å, respectively. Thus, these hydrogen bonds unite the talatisine molecules and form parallel planes lying along a twofold axis.

EXPERIMENTAL

Crystals of talatisine $C_{20}H_{27}NO_3$ grown from an ethanolic solution had the form of prisms with dimensions of 0.1 × 0.3 × 0.4 mm. The parameters of the monoclinic cell were determined from precession photographs and were refined on a Syntex-$P2_1$ automatic four-circle diffractometer (Institute of Crystallography of the Academy of Sciences of the USSR), using Cu K_α radiation: a = 15.401 (5) Å, b = 16.997 (4) Å, c = 7.032 (6) Å, γ = 109.76(9)°, V = 1732.32 Å^3 M = 329.22, ρ_{calc} = 1.26 g/cm^3, space group B2, z = 4.

A three-dimensional set of intensities was obtained on the same diffractometer. In the first treatment of the group, weak reflections with $I \leqslant 3\sigma$ were eliminated. The final group of structural amplitudes amounted to 1219 independent nonzero reflections.

TABLE 5. Coordinates of the Atoms and Their Anisotropic Thermal Parameters $\times 10^4$

Atom	x/a	y/b	z/c	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
O (1)	—1210	—101	3407	42	17	295	4	—51	—11
O (2)	2061	3994	5988	55	30	225	6	40	51
O (3)	1511	4690	2656	45	17	257	9	—30	—11
N	111	1114	2957	29	16	186	9	—4	—3
C (1)	—448	2661	183	46	26	194	20	20	—22
C (2)	—1174	1908	—617	39	39	204	15	80	16
C (3)	—1872	1436	922	44	35	255	27	42	21
C (4)	—1435	1226	2698	35	23	202	15	—2	20
C (5)	—664	1996	3501	34	17	183	15	—4	15
C (6)	—66	1590	4623	36	21	132	9	—16	—9
C (7)	830	2198	5417	36	21	155	0	31	—3
C (8)	1375	2794	3884	32	19	166	4	3	1
C (15)	2279	3445	4654	33	24	214	0	16	10
C (16)	2837	3912	3007	34	22	264	9	4	8
C (12)	2288	3794	1208	41	22	213	7	—47	—29
C (11)	1365	3930	1598	42	18	179	5	—15	—4
C (9)	764	3211	2903	31	18	143	4	—16	—4
C (10)	29	2471	1929	29	21	145	18	—15	—4
C (20)	533	1800	1611	30	21	148	13	—23	10
C (14)	1532	2278	2179	34	16	161	8	—18	—9
C (13)	2057	2859	553	47	23	189	15	—37	—7
C (19)	—857	633	2325	33	17	222	5	5	15
C (18)	—2202	867	4174	27	22	312	2	—53	10
C (17)	3726	4384	3169	37	37	361	—2	1	6

TABLE 6. Coordinates of the Hydrogen Atoms $\times 10^3$ in the Talatisine Molecule

Atom	x/a	y/b	z/c	Atom	x/a	y/b	z/c
H (1)	2	306	—98	H (12)	270	417	11
H (2)	—83	307	55	H (13)	101	393	31
H (3)	—88	145	—129	H (14)	48	347	395
H (4)	—145	203	—191	H (15)	59	164	24
H (5)	—217	176	133	H (16)	187	187	231
H (6)	234	93	36	H (17)	256	268	—10
H (7)	—95	239	44	H (18)	—75	56	102
H (8)	—47	117	572	H (19)	—246	138	477
H (9)	130	192	606	H (20)	—267	36	366
H (10)	69	254	661	H (21)	406	438	441
H (11)	267	308	567	H (22)	84	45	327
H (23)	184	433	523	H (24)	191	500	196

The structure was determined by the direct multivariant method using the tangent formula by means of the Rentgen-75 system of programs [8].

First, the structural amplitudes were normalized and the coefficient of reduction to the absolute scale $K_{tot} = 1.03$ and the total isotropic temperature factor $B_{tot} = 2$ Å^2 were determined. After the normalization of the structural amplitudes, to determine the phases of the program, 250 E-normalized amplitudes with $E_{min} \geqslant 1.2$ were selected. Attempts at deciphering in the automatic regime, i.e., by screening 1024 variants of the 15 E syntheses with the best S estimates was unsuccessful. In the manual regime for calculating the phases 200 normalized amplitudes with $E_{min} \geqslant 1.36$ were taken. After a number of selections of coordinates and of reference reflections the solution was found. The coordinate and reference groups consisted of the following reflections:

Index of the reflection	Coordinate reflections			Reference reflections		
h	2	13	1	1	2	2
k	1	2	2	0	4	9
l	0	1	1	1	2	4
E	1.62	2.29	1.81	2.26	2.55	2.09

In the E synthesis best with respect to the R factor (0.17) but not best with respect to the S evaluation 256 variants were calculated. All the nonhydrogen atoms of the talatisine molecule were revealed. After the atoms had been arranged according to types, several F syn-

theses were constructed. In this way, the structure was refined by the method of successive approximations the R factor then being 0.24.

The structure was refined by the method of least squares in the block-diagonal variant in the isotropic approximation to a R factor of 0.16 and then in the anisotropic approximation, whereupon the R factor amounted to 0.083. At this stage a Fourier difference series was constructed. The difference synthesis revealed 24 hydrogen atoms. The addition of the hydrogen atoms with a fixed temperature factor B_{iso} = 5 Å^2 lowered the R factor by 0.013. The final value of the R factor was 0.07.

The coordinates and anisotropic thermal factors for the nonhydrogen atoms are given in Table 5 and the coordinates of the hydrogen atoms in Table 6.

The experimental results on the Syntex diffractometer were obtained with the assistance of Yu. V. Nekrasov.

SUMMARY

The spatial structure and conformation of the diterpene alkaloid talatisine have been determined by an x-ray structural investigation.

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