X-RAY STRUCTURAL INVESTIGATION ON ALKALOIDS

V. CRYSTAL AND MOLECULAR STRUCTURE OF SIBIRICINE*

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Sibiricine (I) was first isolated from *Corydalis sibirica* (α. f.) Pers. [2]. The structure of (I) was established on the basis of spectral characteristics [3], and its synthesis was later effected [4]. The elucidation of the spiro-isomerism by NMR spectroscopy proved to be extremely difficult.

In order to establish more accurately the configuration of the spiro center, we have performed a complete x-ray structural investigation of the alkaloid sibiricine in the form of the base isolated from *Corydalis ledebouriana* Kar. et Kir. and shown to be identical with an authentic sample by Prof. D. B. MacLean.

The general form of the molecule, the lengths of the bonds, and the valence angles are shown in Fig. 1. The error in the bond lengths amounts to 0.005–0.006 Å and that in the valence angles to 0.3–0.4°. Figure 2 shows the symbols of the rings and the torsional angles which permit the conformations of the rings to be evaluated.

The benzene rings A and D are planar to within 0.007–0.008 (4) Å, but the substituents deviate appreciably from these planes. Departing to the greatest extent from the plane of ring D (Table 1) are the atoms C(8) [−0.025 (4) Å] and C(13) [0.131 (4) Å] forming part of the somewhat strained (because of condensation with the benzene ring D) five-membered ring C, while the O(3) and O(4) atoms of the oxygen-containing ring F deviate by only −0.013 (3)
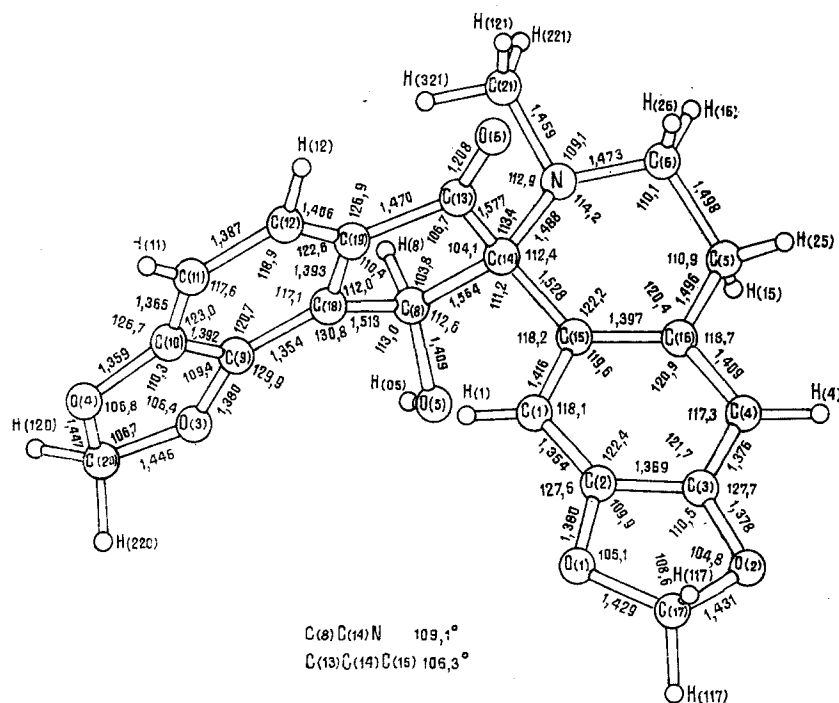

C(8)C(14)N   109,1°
C(13)C(14)C(15) 106,3°

Fig. 1. Structure and geometric parameters of the sibiricine
molecule.
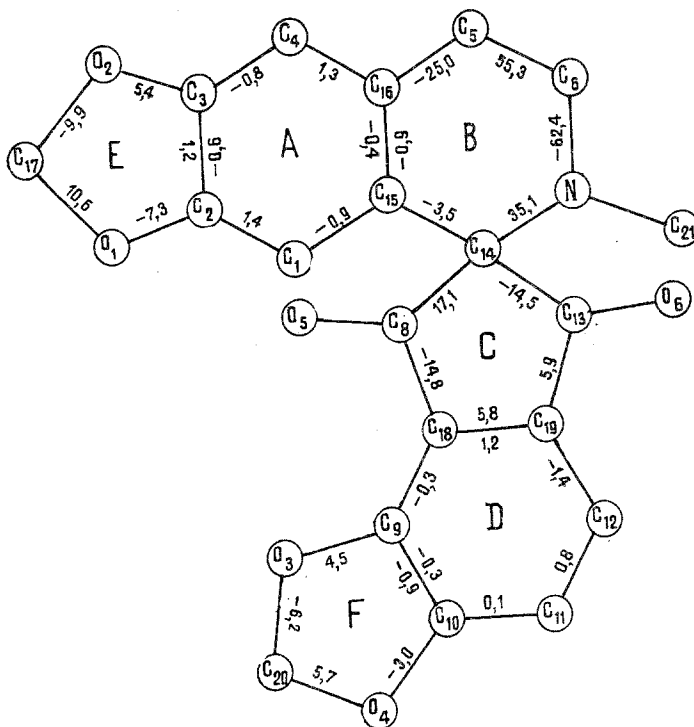
*For communication IV, see [1].

Fig. 2. Torsional angles and designation of the
rings in the sibiricine molecule.

and —0.016 (3) Å. The substituents of the second aromatic ring A depart from its plane to a
considerably smaller degree: O(2), 0.007(3); O(1) —0.026 (3); C(14) 0.026 (4); C(5) 0.057 (4)
Å. The dihedral angle between the planes of the benzene rings is 89.9° and coincides with
the analogous angle in the related alkaloids ochrobirine and ochotensine containing the same
spiro carbon atom as in sibiricine.

The five-membered rings F and E have flattened envelope conformations. In the system
of symbols given in the literature [7, 8], the conformations of these rings are $E_{C(20)}$ and
$E_{C(17)}$: the C(20) and C(17) atoms deviate from the planes of the other members of the rings
under consideration by 0.091 (5) and 0.153 (5) Å, respectively (in the ideal C_s envelope this
deviation is 0.75 Å) [7]. In contrast to rings E and F, the five-membered ring C has a flat-
tened half-chair conformation — $^{C(14)}T_{C(8)}$. The deviations of the C(14) and C(8) atoms from
the plane through the C(18), C(19), and C(13) are 0.156 (4) and —0.141 (4) Å; while in the
ideal C_s half-chair they would be ±0.39 Å [9].

The six-membered piperidine ring has the conformation of a distorted half-chair —
$^{C(6)}H_N$, the N and C(6) atoms departing from the plane passing through the C(14), C(15), C(16),
and C(5) atoms by —0.100 (3) and 0.340 (3) Å, respectively. The nitrogen atom has the py-
ramidal conformation of the bonds (sum of the valence angles 336.2°); its deviation from the
C(14)—C(6)—C(21) plane amounts to —0.424 (4) Å.

The conformation of all the rings of the molecule differs from the ideal conformation
that is generally characteristic for alkaloids and is explained by the general strain of poly-
cyclic condensed systems. This strain also appears in the difference in the lengths of cer-
tain bonds from the standard values. For example, the scatter of the bond lengths in the
benzene rings is 1.354–1.416 (5) Å, of the $C(sp^3)$—$C(sp^2)$ bonds 1.496–1.564 (5) Å, and of the
C—N bonds 1.459–1.488 (5) Å and exceeds 3σ. The greatest strain is concentrated on the C(14)
spiro atom; all the bonds in which this atom participates are appreciably lengthened. The
molecule contains one active hydrogen atom of an OH group which participates in the formation
of the O(5)—H···N' hydrogen bond. The molecules are joined into centrosymmetrical dimers
through two such bonds. The mutual positions of the molecules in the dimer are such that the
H(O5) atom of one molecule is located almost above the unshared electron pair of the N atom
of the other molecule: the H(O5)···N'—C(21'), H(O5)···N'—C(14'), and H(O5)···N'—C(15') angles
are, respectively, 95.5, 106.7, and 117.06°. The parameters of the hydrogen bond are as fol-
lows: O(5)···N' 2.819 (4) Å, O(5)—H 0.77 (4) Å, H(O5)···N' 2.12 (4) Å; the O(5)—H···N' angle
151 (4)°. The other intermolecular distances in the crystal, which are given in Table 2, cor-
respond to the van der Waals interactions.

TABLE 1. Equations Ax + By + Cz — D = 0 of the Planes of the Fragments of the Molecule and the Deviations of the Atoms from the Corresponding Planes

Plane	Atoms and their deviations, Å					A	B	C	D
I (ring A)	C(16) 0,006(4) C(4) −0,008(4)	C(15) 0,001(4) O(2)* 0,007(3)	C(1) −0,008(4) O(1)* −0,026(4)	C(2) 0,007(4) C(14)* 0,026(4)	C(3) 0,001(4) C(5)* 0,057(4)	−0,840	−0,494	−0,226	−1,790
II (ring B)	C(14) −0,002(4) C(6)* −0,605(5)	C(15) 0,004(4) C(21)* 0,340(5)	C(16) −0,004(4)	C(5) 0,002(4)	N* −0,100(3)	−0,844	−0,475	−0,250	−1,891
III (ring C)	C(18) 0	C(19) 0	C(13) 0	C(8)* −0,141(4)	C(14)* −0,156(4)	−0,398	0,843	−0,361	−4,481
IV (ring D)	C(9) −0,002(4) C(18) −0,003(4)	C(10) 0,003(4) O(3)* 0,013(3)	C(11) 0,001(4) O(4)* −0,016(8)	C(12) −0,006(4) C(8)* −0,025(4)	C(19) −0,007(4) C(13)* 0,131(4)	−0,432	0,857	−0,281	−4,587
V (ring E)	O(2) 0,004(3)	C(2) 0,006(4)	C(3) −0,006(3)	O(1) −0,004(3)	C(17)* 0,153(5)	−0,842	−0,484	−0,239	−1,805
VI (ring F)	O(3) 0,004(3)	C(9) 0,005(4)	C(10) −0,005(4)	O(4) 0,003(3)	C(20)* 0,091(5)	−0,430	0,861	−0,272	−4,598
VII	C(14) 0	C(6) 0	C(21) 0	N* −0,424(4)		−0,752	−0,454	−0,477	−2,340

*Atoms not included in the calculation of the equations of the planes.

TABLE 2. Short Intermolecular Distances d, Å*

Distance	d	Distance	d	Distance	d	Distance	d
N... O(5) V	2.819(4)	C(20)...C(2) II	3.295(6)	C(19)...C(6) VIII	3.451(5)	C(16)...H(26) III	3.15(3)
N... H(05) V	2.12(4)	C(20)...C(3) II	3.758(6)	C(19)...C(5) VIII	3.383(5)	C(1)...C(17) I	3.800(6)
O(1)... H(20) II	2.57(3)	C(12)...C(17) I	3.549(6)	C(5)...C(11) X	3.19(4)	H(11)...H(15) X	2.54(5)
O(2)... H(4)(VI)	2.84(4)	C(12)...C(5) X	3.747(6)	C(6)...H(05) V	3.08(3)	H(05)...H(8) V	2.35(5)
O(3)... H(15) V	2.75(3)	C(20)...H(221) VIII	3.14(4)	C(19)...C(3) I	3.749(5)	C(1)...H(220) II	2.76(4)
O(4)... C(21) VIII	3.367(6)	C(9)...C(10) IV	3.758(6)	C(19)...H(120) II	2.57(3)	C(2)...H(120) II	2.76(4)
O(4)... C(9) IV	3.250(6)	C(9)...C(11) IV	3.677(6)	C(19)...H(220) II	3.20(3)	C(2)...H(220) II	2.79(4)
O(4)... H(221) VIII	2.65(4)	C(9)...C(12) IV	3.794(6)	C(19)...H(16) VIII	2.81(4)	C(3)...H(120) II	3.03(3)
O(4)... H(321) IV	2.39(4)	C(10)...C(18) IV	3.645(6)	C(19)...H(117) I	2.91(3)	C(3)...H(26) III	3.05(4)
O(5)... C(8) V	3.275(4)	C(10)...C(21) VIII	3.583(6)	C(8)...C(8) V	3.716(5)	C(4)...H(11) X	3.00(3)
O(5)... C(21) V	3.124(5)	C(10)...C(221)VIII	2.74(4)	C(8)...H(05) V	2.80(4)	C(4)...H(25) III	2.73(4)
O(5)... H(05) V	3.00(4)	C(11)...C(18) IV	3.784(6)	C(13)...C(17) I	3.731(6)	C(4)...H(117) I	2.89(4)
O(5)... H(220) II	2.64(4)	C(11)...C(6) X	3.763(6)	C(13)...H(117) I	2.84(3)	C(17)...H(120) II	2.90(3)
O(6)... H(4) III	2.72(3)	C(11)...C(4) X	3.772(6)	C(14)...H(05) V	2.92(4)	C(17)...H(12) I	3.19(4)
O(6)... H(217) IX	2.63(4)	C(11)...H(15) X	2.96(4)	C(6)...C(4) III	3.16(6)	C(21)...H(05) V	2.68(4)
C(20)... C(19) II	3.307(5)	C(12)...H(15) VII	2.98(4)	C(5)...H(12) X	3.10(4)	H(12)...H(15) X	2.54(5)
C(20)... C(1) II	3.581(7)	C(12)...H(117) I	2.88(4)	C(16)...H(11) X	3.05(4)	H(12)...H(217) IX	2.45(4)

*The distances given are those between the atoms of the molecules bound by the following symmetry transformations: I) center at 0,0,0; II) center at 1/2,0,0; III) center at 0,0,1/2; IV) center at 1/2,−1/2,0; V) center at 1/2,0,1/2; VI) center at 0,1/2,1/2; VII) center at 0,−1/2,−1/2; VIII) by translation c; IX) by translation b; X) by translation b + c.

Crystals $C_{20}H_{16}NO_6$ triclinic: $a = 11.0186(2)$, $b = 9.604(1)$, $c = 8.824(2)$ Å, $\alpha = 115.98(1)$, $\beta = 95.39(2)$, $\gamma = 87.08(3)°$, $V = 835.61(4)$ Å³, $Z = 2$, space group P$\bar{1}$. The cell parameters and the intensities of the reflections were measured on a Hilger–Watts four-circle automatic diffractometer (λCu–K_α, graphite monochromator, $\theta/2\theta$ scanning, $\theta_{max} = 64°$). In the deciphering and refinement of the structure we used 2189 reflections with $F^2 > 2\sigma$.

The structure was deciphered by the direct method using the EXTL program on an Eclipse S/200 mini-computer. The E synthesis showing all the nonhydrogen atoms was calculated from the best variant of the signs. To refine the position parameters of the atoms an F synthesis was constructed from the signs calculated from the atomic coordinates found in the E synthesis. The refinement of the structure was performed by the method of least squares first in the full-matrix isotropic approximation (R = 0.128) and then in the anisotropic approximation (R = 0.090). All the hydrogen atoms appear in the "truncated" difference synthesis (sinθ/

TABLE 3. Coordinates of Nonhydrogen Atoms $\times 10^4$ and Their Anisotropic Temperature Parameters* $B_{ij} \times 10$

Atom	x	y	z	B_{11}	B_{22}	B_{33}	B_{12}	B_{13}	B_{23}
N	3039 (3)	—1090 (3)	5380 (4)	3,0 (2)	2,4 (1)	2,0 (1)	0,1 (1)	—0,1 (1)	1,0 (1)
O (1)	1089 (3)	1634 (3)	411 (3)	5,1 (2)	4,9 (2)	3,2 (1)	1,9 (1)	0,6 (1)	2,4 (1)
O (2)	204 (3)	3548 (3)	2721 (4)	5,4 (2)	4,1 (2)	4,4 (2)	2,2 (1)	0,7 (1)	2,1 (1)
O (3)	5860 (2)	—2372 (3)	—167 (3)	3,1 (1)	4,3 (1)	3,2 (1)	—0,7 (1)	0,7 (1)	0,8 (1)
O (4)	5291 (2)	—4363 (3)	—2795 (3)	4,0 (1)	3,8 (1)	3,0 (1)	—0,1 (1)	0,9 (1)	0,7 (1)
O (5)	4601 (2)	67 (3)	3120 (3)	2,6 (1)	2,5 (1)	3,3 (1)	—0,3 (1)	—0,4 (1)	0,8 (1)
O (6)	1303 (2)	—3234 (3)	2492 (3)	3,2 (1)	3,6 (1)	3,4 (1)	—1,2 (1)	0,4 (1)	0,7 (1)
C (1)	2013 (4)	176 (4)	1924 (5)	3,1 (2)	2,7 (2)	2,3 (2)	0,3 (1)	0,3 (2)	0,7 (2)
C (2)	1335 (3)	1348 (4)	1812 (5)	3,1 (2)	3,1 (2)	2,7 (2)	—0,1 (2)	0,1 (2)	1,3 (2)
C (3)	824 (3)	2489 (4)	3176 (5)	2,8 (2)	2,6 (2)	4,0 (2)	0,4 (1)	—0,1 (2)	1,7 (2)
C (4)	962 (4)	2503 (4)	4748 (5)	3,4 (2)	2,6 (2)	2,8 (2)	0,6 (2)	0,4 (2)	0,6 (2)
C (5)	1763 (4)	1223 (5)	6575 (5)	4,0 (2)	3,5 (2)	2,5 (2)	0,9 (2)	0,8 (2)	1,0 (2)
C (6)	1972 (4)	—406 (5)	6356 (5)	3,7 (2)	3,6 (2)	2,5 (2)	—0,2 (2)	0,5 (2)	1,3 (2)
C (8)	4194 (3)	—1355 (4)	2978 (5)	2,5 (2)	2,0 (2)	2,5 (2)	—0,1 (1)	—0,1 (1)	0,6 (1)
C (9)	4764 (3)	—2981 (4)	—124 (5)	2,4 (2)	2,5 (2)	3,2 (2)	—0,2 (1)	—0,2 (2)	1,1 (2)
C (10)	4440 (3)	—4182 (4)	—1702 (5)	3,0 (2)	2,7 (2)	2,7 (2)	0,4 (1)	0,5 (2)	1,1 (2)
C (11)	3403 (4)	—5020 (4)	—2045 (5)	4,0 (2)	2,3 (2)	2,5 (2)	0 (2)	—0,1 (2)	0,2 (2)
C (12)	2647 (4)	—4643 (4)	—745 (5)	3,3 (2)	2,0 (2)	3,4 (2)	—0,3 (2)	—0,1 (2)	0,6 (2)
C (13)	2242 (3)	—2749 (4)	2309 (5)	3,0 (2)	2,1 (2)	2,7 (2)	—0,1 (2)	—0,4 (1)	0,9 (2)
C (14)	2902 (3)	—1223 (4)	3628 (4)	2,5 (2)	1,9 (2)	2,0 (2)	—0,2 (1)	0,1 (1)	0,9 (2)
C (15)	2169 (3)	124 (4)	351 (4)	2,1 (2)	2,1 (2)	2,7 (2)	—0,2 (1)	—0,1 (1)	0,8 (2)
C (16)	1641 (3)	1281 (4)	4900 (5)	2,5 (2)	2,6 (2)	2,6 (2)	—0,3 (1)	0 (2)	0,8 (2)
C (17)	257 (5)	2919 (5)	928 (6)	5,3 (3)	4,2 (2)	4,4 (3)	0,9 (2)	—0,4 (2)	2,2 (2)
C (18)	4042 (3)	—2582 (4)	1167 (5)	2,3 (2)	2,2 (2)	2,6 (2)	—0,1 (1)	—0,1 (1)	0,7 (1)
C (19)	2973 (3)	—3415 (4)	838 (5)	2,7 (2)	2,1 (2)	2,5 (2)	0,1 (1)	0,1 (1)	0,7 (1)
C (20)	6182 (4)	—3161 (5)	—1897 (6)	4,0 (2)	4,6 (2)	3,9 (2)	—0,4 (2)	1,2 (2)	1,5 (2)
C (21)	3356 (4)	—2560 (5)	5439 (6)	4,7 (2)	3,2 (2)	3,5 (3)	0,2 (2)	—0,1 (2)	1,6 (2)

*The anisotropic temperature factor in the form $T = \exp[-(B_{11}h^2 + B_{22}k^2 + B_{33}l^2 + B_{12}hk + B_{13}hl + B_{23}kl)]$.

TABLE 4. Coordinates of the Hydrogen Atoms $\times 10^3$ and Distances d (Å) to the Atoms Connected with Them

Hydrogen atom	x	y	z	d	To the atom
H (05)	525 (3)	—4 (4)	352 (4)	0,77 (4)	O (5)
H (1)	240 (3)	—55 (4)	103 (4)	0,91 (4)	C (1)
H (4)	57 (3)	330 (4)	375 (4)	1,00 (4)	C (4)
H (15)	254 (3)	191 (4)	741 (4)	1,11 (3)	C (5)
H (25)	110 (3)	153 (4)	704 (5)	0,85 (4)	C (5)
H (16)	209 (3)	—42 (4)	741 (5)	0,94 (4)	C (6)
H (26)	121 (3)	—102 (4)	591 (4)	1,00 (4)	C (6)
H (8)	473 (3)	—183 (4)	362 (4)	1,01 (4)	C (8)
H (11)	318 (3)	—584 (4)	—310 (4)	0,94 (4)	C (11)
H (12)	186 (3)	—530 (4)	—90 (4)	1,06 (4)	C (12)
H (117)	—62 (3)	253 (4)	28 (4)	1,07 (4)	C (17)
H (217)	59 (3)	389 (4)	70 (4)	1,12 (4)	C (17)
H (117)	717 (3)	—358 (4)	—183 (4)	1,15 (3)	C (20)
H (217)	625 (3)	—232 (4)	—234 (4)	1,05 (4)	C (20)
H (121)	266 (3)	—331 (4)	497 (4)	1,01 (4)	C (21)
H (221)	366 (3)	—254 (4)	652 (4)	0,97 (4)	C (21)
H (321)	407 (3)	—309 (4)	466 (4)	1,05 (4)	C (21)

λ<0.45) calculated at this stage. Further refinement was carried out in the anisotropic approximation for the nonhydrogen atoms and in the isotropic approximation for the hydrogen atoms; the thermal parameters of the H atoms were not taken into account and were given as $B = 4$ Å^2. Finally ($R = 0.054$, $R = 0.038$).

The coordinates of the nonhydrogen atoms and their anisotropic temperature parameters B_{ij} are given in Table 3. Table 4 gives the coordinates of the hydrogen atoms and the distances to the atoms connected with them.

SUMMARY

A complete x-ray structural investigation of the spirobenzylisoquinoline alkaloid sibiricine in the form of the base has been carried out. The bond lengths and valence angles are the usual ones.

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ALKALOIDS OF *Haplophyllum latifolium*

THE STRUCTURE OF HAPLATINE

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Continuing a study of the alkaloids of *Haplophyllum latifolium* Kar. et Kir. [1], we have investigated the epigeal part and roots of plants growing in the Chimkent oblast in the "Syr-dar'ya" sovkhoz [communal farm] in the phase of vigorous flowering to the beginning of fruit bearing and the dying off of the epigeal part. The raw material was extracted with methanol. The evaporated extract was separated according to solubilities in organic solvents and then by the method described in a previous paper [1]. The amounts of alkaloids in the epigeal part and roots of *H. latifolium* were as follows (% of the weight of the dry raw material; the symbol + denotes alkaloids present in amounts of less than 0.005%):

Phase of development	Plant organ	Total alka-loids	Skimmi-anine	Evoxine	Haplo-pine	Glyco-perine	7-Isopen-tenyloxy-γ-faga-rine	Hapla-mine	Hapla-mide	Hapla-midine
Flowering—beginning of fruit-bearing	Epigeal part	0,74	0,21	0,03	+	÷	+	0,01		+
	Roots	0,17	0.02	0,01						
Withering of the epigeal part	Epigeal part	0,72	0,14	0,03	0.01	÷		0,01	0,01	÷
	Roots	0,06	+		+					