

alcohol and benzoic acid had the lowest P and D values as compared with the other compounds in the series. This was ascribed to intermolecular hydrogen bonding potential of benzyl alcohol and benzoic acid which produce dimers or trimers whose penetration into the polymer is not favorable.

In the case of 4-methylbenzaldehyde and 4-methylacetophenone, the D values obtained were similar to those of the parent compounds, benzaldehyde and acetophenone. The P and S values, however, were found to be larger. The difference in the P and S values was attributed to the effect of the methyl substituents which gave rise to higher solubility in the plastic.

Quantitative studies as reported here and similar studies with other compounds should be of value to those who may desire to package drugs, cosmetics, or other products in polyethylene.

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Crystal and Molecular Structure of 5-[1-(2'-Deoxy- α -D-ribofuranosyl)uracilyl] Disulfide

By ELI SHEFTER, MICHAEL P. KOTICK, and THOMAS J. BARDOS

The molecular structure of 5-[1-(2'-deoxy- α -D-ribofuranosyl)uracilyl] disulfide (I) has been determined by X-ray crystallographic analysis. The molecule crystallizes in the orthorhombic space group $P2_12_12_1$, with the following cell dimensions: $a = 9.492 \text{ \AA}$, $b = 14.061 \text{ \AA}$, $c = 16.328 \text{ \AA}$. The valence state about the S-S linkage appears to be markedly different from that observed in other disulfide structures. The torsional angle about this bond is 49° and the S-S bond length was found to be 2.108 \AA . The configurations of both the uracil and the deoxyribofuranosyl residues are different in the two nucleoside units of the molecule. The crystal is bound together by hydrogen bonds.

A STRUCTURAL ANALOG of thymidine, 5-mercapto-2'-deoxyuridine (MUDR), has been recently synthesized (1), and found to be a potent inhibitor in several bacterial systems. This compound and some of its congeners are of potential chemotherapeutic interest because of their ability to inhibit the biosynthesis of DNA (2, 3). Both the α and β anomers of MUDR exhibited rapid autoxidation in aqueous solutions to the corresponding disulfides (4). These disulfides have interesting biochemical and physicochemical properties. They are capable of being reduced nonenzymatically at a virtually instantaneous rate by stoichiometric amounts of thiols (2, 5), and their high

optical activities showed temperature dependence (6).

In an effort to gain further insight into the various properties that could be pertinent as to the mode of action on a molecular level of MUDR and its congeners, X-ray structural studies have been initiated on several of these compounds. This report concerns itself with the crystallographic structure of the first of these compounds to be completed, the disulfide of the α -anomer, 5-[1-(2'-deoxy- α -D-ribofuranosyl)uracilyl] disulfide (I). This compound has additional interest as it appears to be the first α -nucleoside whose crystal structure has been elucidated.

EXPERIMENTAL

The compound crystallizes from water as slightly yellow prisms belonging to space group $P2_12_12_1$, with the following crystallographic data:

$$\begin{aligned}
 a &= 9.492 \pm 0.003 \text{ \AA} \\
 b &= 14.061 \pm 0.002 \text{ \AA} \\
 c &= 16.328 \pm 0.003 \text{ \AA} \\
 \rho(\text{meas.}) &= 1.577 \text{ Gm./cm.}^3 \\
 \rho(\text{calcd.}) &= 1.579 \text{ Gm./cm.}^3 \\
 Z &= 4
 \end{aligned}$$

Received April 21, 1967 from the Departments of Pharmacuetics and Medicinal Chemistry, School of Pharmacy, State University of New York at Buffalo, Buffalo, NY 14214 Accepted for publication June 30, 1967.

Presented to the Medicinal Chemistry Section, A.Ph.A. Academy of Pharmaceutical Sciences, Las Vegas meeting, April 1967.

This research was supported by grants CA-10104-01 and CA-06695 from the National Cancer Institute, U. S. Public Health Service, Bethesda, Md.

The authors thank Professor David Harker, Center for Crystallographic Research, Roswell Park Memorial Institute, for permitting the use of his facilities, and the computing center of this university for a generous gift of computing time.

The density was measured by means of flotation in a mixture of chloroform and dibromoethane. The unit cell dimensions were obtained by least squares refinement of 30 general reflections measured on a General Electric XRD-6 diffractometer, using Cu $K\alpha$ radiation.

The intensity data were collected by the stationary counter-stationary crystal technique using balanced filters and Cu $K\alpha$ radiation. The crystal utilized for the data collection was mounted with a parallel to the ϕ axis of the goniostat and its dimensions were 0.66 mm. along a , 0.16 mm. along b , and 0.38 mm. along c . In the 2θ range between 0° and 142° , 2328 reflections of a total possible number of 2408, had intensities significantly greater than their background counts. The intensities of the various reflections were corrected for Lorentz and polarization factors in the usual manner. A correction for absorption as a function of the angle ϕ was measured for various h.o.o. reflections. The average transmission factor obtained was then used to correct the intensities for anisotropy of absorption.

Structure Determination—The positions of the two sulfurs were easily obtained from a Patterson synthesis. A Fourier synthesis calculated using the phases of the sulfur atoms uncovered all but 8 of the nonhydrogen atoms. From successive difference syntheses the positions of these eight atoms were found. The refinement was then continued by block diagonal least squares, using a modified version of the Trueblood, Sparks, and Gantzel program (ACA No. 317), which minimizes the function $\sum w||F_o| - |F_c||^2$. The initial isotropic refinement was carried out with the weight equal to $1/f_{(h)}$, where $f_{(h)}$ is the scattering curve for nitrogen. After anisotropic temperature factors were introduced, a difference Fourier showed positive electron density (ranged between 0.2 to 0.4 $e/\text{\AA}^3$) in the regions where the hydrogen atoms were expected to be found. In the final least squares refinement the hydrogen atoms were included with isotropic temperature factors, and the weighting scheme utilized was $1/\sigma(F^2)$, where the standard deviations of the structure factors were calculated in the manner described by Evans (7). The final R value (usual discrepancy index) was 0.054 for the observed reflections, and 0.062 for all the reflections, where the unobserved data were given an intensity equal to half the minimum observable value. Throughout the refinement the unobserved data were given zero weight.

The atomic form factors used in all the above computations were those given by Cromer and Waber (8), except for the hydrogens. McWeeny's (9) scattering curve for the hydrogen atom was utilized. The sulfur atoms were corrected for anomalous scattering using both the real and complex terms (10).

Results and Discussion—The final atomic positions and thermal parameters for the molecule together with their respective estimated standard deviations (ESD) are shown in Tables I, II, and III. The ESD's were calculated from the inverted matrix of the normal least squares equations. The intramolecular bond lengths and angles are shown in Figs. 1 and 2. The atomic names shown in these figures will be used throughout the text. The average standard deviation in bond length is 0.008 \AA . for the nonhydrogen atoms, with the exception

TABLE I—ATOMIC COORDINATES FOR NONHYDROGEN ATOMS AND (IN PARENTHESES) THEIR STANDARD DEVIATIONS $\times 10^4$

Name	x/a	y/b	z/c
S(1)	0.06212(2)	0.11176(1)	0.04133(1)
S(2)	0.22564(2)	0.21267(1)	0.05023(1)
1C5	0.13620(7)	0.01399(4)	0.09336(4)
1C4	0.12121(7)	-0.00103(5)	0.18075(4)
1O4	0.05717(5)	0.05052(3)	0.22987(3)
1N3	0.19054(6)	-0.08150(4)	0.20969(3)
1C6	0.21492(7)	-0.04713(4)	0.04872(4)
1C2	0.27194(7)	-0.14425(4)	0.16433(3)
1O2	0.32836(5)	-0.21203(3)	0.19594(3)
1N1	0.28048(5)	-0.12315(3)	0.08241(3)
1C1'	0.37220(7)	-0.18663(4)	0.03081(3)
1O1'	0.42662(4)	-0.13351(3)	-0.03338(2)
1C4'	0.36997(7)	-0.16612(4)	-0.11185(4)
1C3'	0.24462(7)	-0.23028(4)	-0.08848(4)
1C2'	0.29047(7)	-0.26992(4)	-0.00598(4)
1C5'	0.48862(7)	-0.21631(5)	-0.15740(4)
1O5'	0.44439(5)	-0.24139(3)	-0.23777(3)
1O3'	0.12131(5)	-0.17595(3)	-0.07703(3)
2C5	0.37218(7)	0.14789(4)	0.01707(4)
2C6	0.45885(7)	0.11237(4)	0.07660(4)
2N1	0.57756(6)	0.06194(4)	0.05893(3)
2C2	0.61891(7)	0.04136(5)	-0.02101(4)
2O2	0.72334(5)	-0.00253(3)	-0.03887(3)
2N3	0.52770(6)	0.07775(4)	-0.07989(3)
2C4	0.40222(7)	0.12551(4)	-0.06700(3)
2O4	0.32689(5)	0.14612(4)	-0.12560(3)
2C1'	0.65684(7)	0.01613(5)	0.12807(4)
2O1'	0.55915(5)	-0.04542(3)	0.16858(2)
2C2'	0.71567(7)	0.08665(5)	0.19145(4)
2C3'	0.62658(7)	0.06851(4)	0.26775(4)
2O3'	0.50564(5)	0.13261(3)	0.27191(3)
2C4'	0.56642(7)	-0.03245(4)	0.25573(4)
2C5'	0.65621(8)	-0.10901(5)	0.29494(4)
2O5'	0.80245(5)	-0.09730(3)	0.27145(3)

of the disulfide bond which is 0.003 \AA . The intramolecular angles between the various nonhydrogen bonds have an average error of 0.4° . The ESD's for the bonds and angles involving the hydrogens average around 0.1 \AA . and 3° , respectively. These angles are not shown in Fig. 2, and only those relevant to the discussion of the molecule will be given.

In discussing the crystal structure, the various portions of the molecule shall be considered individually and then the packing of the molecule will be discussed.

Disulfide Linkage—The various structural features of some of the more accurately determined disulfides are compared to the present structure in Table IV. There is a striking difference between the various values listed for I and the other compounds.

The torsional angle, ϕ_{SS} , defined as the projected angle of the two C—S bonds down the S—S bond (see Fig. 3), is much smaller in I than in any of the open chain disulfides. It is also much larger than the angle found in the cyclic disulfide structures. The angle in the open-linked disulfides is believed to be determined primarily by the repulsion of the electrons in the p orbitals of the sulfur atoms. This results in an energy minimum at 90° . Abrahams, in a review (18) of disulfide bonding, found that open disulfide structures have values distributed within the vicinity of 90° . This is seen to be true for the open-chain disulfides listed with the exception of I. The values for the constrained disulfides are

TABLE II—THERMAL PARAMETERS FOR NONHYDROGEN ATOMS AND (IN PARENTHESES) THEIR STANDARD DEVIATIONS^a

Atom	b_{11}	b_{22}	b_{33}	b_{12}	b_{13}	b_{23}
S(1)	624(19)	338(9)	213(6)	282(25)	-155(21)	37(14)
S(2)	754(20)	246(8)	177(6)	262(24)	-39(21)	-56(13)
1C5	653(82)	229(33)	105(23)	111(95)	-10(75)	-38(47)
1C4	581(79)	298(37)	131(23)	-161(100)	-80(77)	-78(50)
1O4	785(64)	412(29)	172(18)	233(78)	122(62)	-152(40)
1N3	694(71)	301(30)	91(18)	21(82)	65(63)	-6(41)
1C6	527(74)	241(31)	106(22)	21(87)	-62(77)	4(48)
1C2	505(73)	317(35)	101(22)	-237(98)	14(71)	-26(49)
1O2	889(65)	298(26)	180(18)	334(75)	95(60)	168(39)
1N1	568(61)	218(26)	76(17)	176(79)	59(59)	-40(38)
1C1'	523(75)	298(36)	100(22)	194(92)	34(71)	-50(48)
1O1'	552(52)	316(25)	103(16)	-334(65)	99(50)	-41(35)
1C4'	568(79)	259(34)	110(23)	43(91)	111(75)	-11(48)
1C3'	560(81)	292(36)	159(25)	-117(96)	-38(77)	-120(51)
1C2'	830(92)	192(35)	142(24)	-126(97)	148(84)	28(48)
1C5'	697(85)	311(36)	123(23)	149(105)	158(77)	-10(55)
1O5'	1214(78)	392(29)	154(18)	-112(88)	220(70)	-89(40)
1O3'	455(53)	455(30)	227(19)	-136(72)	42(57)	-135(42)
2C5	546(77)	281(35)	121(23)	34(94)	21(74)	47(49)
2C6	632(79)	263(34)	113(21)	87(97)	-37(74)	-34(50)
2N1	584(65)	317(30)	91(19)	272(78)	-34(61)	51(40)
2C2	691(86)	296(36)	128(23)	78(99)	261(79)	60(50)
2O2	811(67)	469(29)	236(21)	432(84)	394(68)	77(45)
2N3	794(75)	298(30)	73(17)	78(87)	35(64)	31(42)
2C4	700(81)	279(36)	100(22)	42(97)	1(72)	-3(49)
2O4	1080(71)	599(35)	119(17)	342(91)	-173(63)	-11(43)
2C1'	663(84)	308(37)	129(24)	152(102)	-209(79)	-10(52)
2O1'	1058(71)	296(25)	127(17)	-330(78)	-352(62)	64(36)
2C2'	478(76)	334(38)	164(25)	-91(102)	-74(79)	-75(54)
2C3'	558(78)	212(33)	188(26)	17(93)	-221(81)	-70(50)
2O3'	762(58)	295(26)	255(21)	119(73)	42(64)	-159(42)
2C4'	733(85)	284(37)	116(23)	-111(103)	-132(80)	2(50)
2C5'	1022(102)	278(38)	173(26)	-139(115)	-113(90)	85(56)
2O5'	887(68)	372(29)	259(79)	282(79)	-274(68)	2(44)

^a Values multiplied by 10^3 . The temperature factor is of the form: $\exp(-b_{11}h^2 - b_{22}k^2 - b_{33}l^2 - b_{12}hk - b_{13}hl - b_{23}kp)$.

TABLE III—POSITIONAL AND ISOTROPIC THERMAL PARAMETERS FOR THE HYDROGEN ATOMS^a

Name	x/a	y/b	z/c	B (\AA^2)
H1	0.181	-0.095	0.271	0.1
H2	0.239	-0.043	-0.013	-1.7
H3	0.449	-0.917	0.068	1.8
H4	0.337	-0.317	-0.016	-0.4
H5	0.203	-0.303	0.024	-0.4
H6	0.227	-0.274	-0.135	2.6
H7 ^b	0.145	-0.152	-0.050	0.9
H8	0.345	-0.113	-0.145	1.1
H9	0.516	-0.276	-0.132	-0.7
H10	0.584	-0.167	-0.145	1.9
H11	0.445	-0.214	-0.250	-0.1
H12	0.568	0.070	-0.133	0.7
H13	0.431	0.127	0.134	-0.5
H14	0.748	-0.026	0.093	0.5
H15	0.790	0.069	0.201	-2.5
H16	0.701	0.155	0.172	-0.5
H17	0.692	0.072	0.327	2.7
H18	0.534	0.169	0.275	1.3
H19	0.449	-0.040	0.275	1.3
H20	0.654	-0.101	0.357	0.0
H21	0.601	-0.165	0.273	2.7
H22	0.860	-0.132	0.256	4.3

^a Average standard deviations in the positional parameters for the hydrogens are 0.06 \AA . Standard deviations for B 's average 1.7 \AA^2 . ^b See text for discussion of this atom.

very much lower. Recently an analysis of these cyclic compounds has been presented by Hordvik

(19), and as it is felt to be nonrelevant to the bonding in I, these structures will not be discussed.

The electronic structure about the disulfide linkage of I also appears to be quite different from the other compounds listed in this table. A large degree of double bond character appears to exist in the C—S bond of I, as evidenced by the significantly shorter lengths for these bonds. This could increase the electron density in the d orbitals of the sulfurs and thereby cause an overlap of the

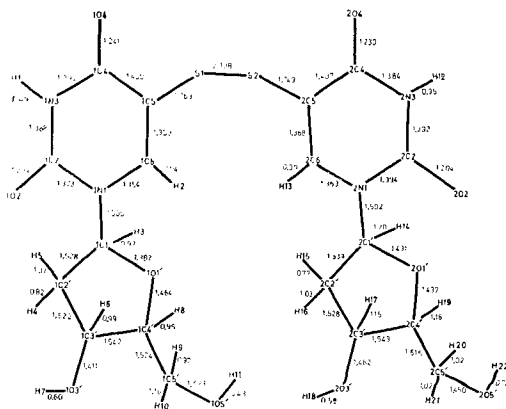


Fig. 1—Schematic drawing of I showing intramolecular bond distances. (Reduced to about $1/4$.)

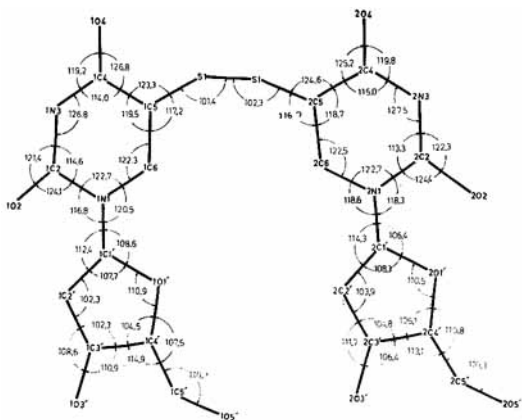


Fig. 2—Schematic drawing of I with intramolecular bond angles for nonhydrogen atoms. (Reduced to about $\frac{1}{4}$.)

TABLE IV—COMPARISON OF THE STRUCTURAL FEATURES OF SOME DISULFIDES WITH I

Compd.	ϕ_{SS} (deg.)	S-S (Å.)	C-S (Av.) Å.	C-S-S (Av.) (deg.)	Ref.
I	49.1	2.108 (0.003)	1.763 1.749 (0.007)	101.4 (0.2) 102.3 (0.2)	
L-Cystine	74	2.032	1.82	114.5	(11)
Dimethyldisulfide	84.7	2.038	1.81	102.8	(12)
Perfluorodimethyl- disulfide	90 ^a	2.05	1.83	105	(13)
N,N ¹ -Diglycyl-L- cystine di- hydrate	89	2.04	1.87	103	(14)
1,2-Dithiolane-4- carboxylic acid	27	2.096	1.84	95	(15)
Sporidesmin	9	2.08	1.90	98	(16)
Gliotoxin	12	2.076	1.875	98	(17)

^a ϕ_{SS} assumed to be 90°.

3 *d* electrons, which in turn may result in repulsion between the sulfurs, and subsequent lowering of the torsional angle. The greater S—S bond length in this structure, as compared to other disulfides, is in agreement with this postulation. The valence

state of the C—S bonds appears to be influenced by the uracil moieties. The C5—C6 bonds in the two pyrimidines are substantially longer than the average value observed for this bond in a number of pyrimidine nucleosides and nucleotides (average 1.33 ± 0.01 Å.).

Uracil Moieties—Within experimental error, the bond lengths and angles of the two rings are quite similar. The most striking difference between the two residues exists between the planarity of the pyrimidine rings. The least squares planes calculated through the six ring atoms of the two bases are shown in Table V. The atoms comprising ring 1 are coplanar within their standard deviations, whereas those comprising ring 2 are significantly nonplanar. Pyrimidine ring 2 is puckered substantially about N3-C4-C5, with N3 and C5 being displaced on the opposite side of the plane to C4. Puckering has been observed in a number of pyrimidine nucleosides (20), and is possibly the result of the valence state of the nitrogen involved being intermediate between sp^2 and sp^3 hybridization. The puckering in this ring may also reflect the close proximity of portions of the two pyrimidine rings to each other, as a result of the disulfide conformation. The distance between 2C5 and 1C5 is 3.2 Å., less than the sum of the van der Waals radii of the two atoms, 3.4 Å. In the puckered uracil residue, both 1C1' and 04 are displaced from the pyrimidine plane to a much greater extent than in ring 1.

The C4—O4 carbonyl groups have a significantly longer bond length than the C2—O2 groups. The greater degree of polarization in the 4 position of uracil derivatives has been discussed with respect to their hydrogen bonding (21). It can be pointed out that both O4 atoms are participating in hydrogen bonds, while only one O2 is involved in such a bond.

With the exception of the C4—C5 bonds of the two uracil moieties, the bond distances and angles are similar to those found in other pyrimidine containing nucleosides and nucleotides.

Deoxyribose Moieties—It is well established from structural data that the furanose ring in nucleosides

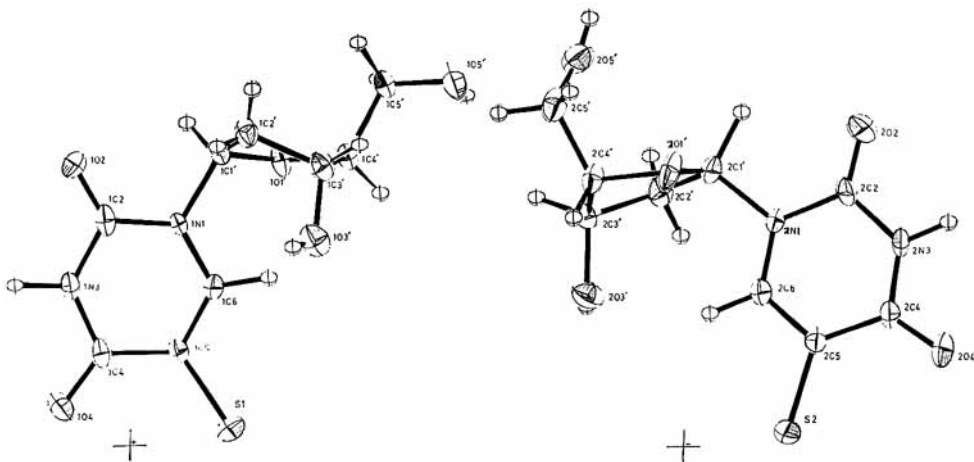


Fig. 3—The two nucleosidic portions of the molecule as viewed down the $S1 \rightarrow S2$ bond. In order to visualize the complete molecule the + sign should be overlayed on the - sign. The thermal ellipsoids of the nonhydrogen atoms are shown. (Reduced to about $\frac{1}{3}$.)

TABLE V—LEAST SQUARES PLANES CALCULATED IN THE MANNER OF SCHOMAKER *et al.*^a

Atoms Comprising the Plane	Displacements, Å.	Displacements of Other Atoms, Å.
Uracil 1		
1N1	0.003	10 ₄ 0.056
1C2	0.001	10 ₂ -0.006
1N3	-0.007	S(1) 0.045
1C4	0.008	1C ₁ ' 0.068
1C5	-0.004	H1 -0.015
1C6	-0.001	H2 0.045
Uracil 2		
2N1	0.010	2O ₄ 0.124
2C2	-0.001	2O ₂ -0.005
2N3	-0.023	2C ₁ 0.210
2C4	0.036	S(2) -0.056
2C5	-0.028	H ₁₂ -0.163
2C6	0.006	H ₁₃ 0.001

^aSchomaker, V., Waser, J., Marsh, R. E., and Bergman, G., *Acta Cryst.*, **12**, 600(1959).

is puckered and not planar. The common puckering found in β -nucleosides usually involves the C2' and C3' atoms (22). In sugar 1, one of the modes of puckering observed in β -nucleosides is found, with C2' and C3' displaced on opposite sides of the plane through C1', O1', and C4'. The puckering in sugar 2 is quite different from that found in other furanose structures (23). Its distortion involves the displacement of C3' and C4' from the plane of the other 3 atoms. This is evident from Figs. 3 and 4.

One of the best ways to describe the puckering of furanose structures is in terms of a twist angle about each ring bond (23, 24). This conformational angle for a given bond, *e.g.*, ϕ C2' \rightarrow C3', is the projected angle between the C1'—C2' bond and the

C3'—C4', in that order, measured clockwise. The twist angles for the sugars are given in Table VI. The smaller the absolute value of the twist angle, the greater is the displacement of the atom opposite the bond concerned.

The conformation about the exocyclic C4'—C5' is of interest, as it may be important in considering the hindered rotation about the disulfide bond. This can be seen in Fig. 4, which indicates that these exocyclic atoms may come in close contact upon rotation about the S—S bond. The conformation about this bond can be designated by the projected angles made by C5'—O5' with C4—O1' and C4'—C3' (25). These angles are listed in Table VI, as ϕ OO and ϕ OC, the former of these refers to the angle between C5'—O5' and C4—O1'. A value near 60° is considered to be *gauche* and a value near 180°, *trans*. Sugar 1 has *tg* conformation about this bond, while sugar 2 has the *gg* conformation (the first letter refers to ϕ OO and the second to ϕ OC). These conformations would possibly afford a minimum amount of contact between these exocyclic atoms if the nucleoside residues are rotated about the disulfide bond.

The C—C bonds average 1.530 Å. and 1.536 Å.

TABLE VI—CONFORMATION ANGLES

	Residue 1	Residue 2
ϕ C1' \rightarrow C2'	-27° 36'	-7° 58'
ϕ C2' \rightarrow C3'	-34° 19'	21° 0'
ϕ C3' \rightarrow C4'	30° 2'	-27° 39'
ϕ C4' \rightarrow O1'	-13° 39'	23° 32'
ϕ O1' \rightarrow C1'	-8° 44'	9° 51'
ϕ OC	70° 2'	49° 27'
ϕ OO	174° 9'	68° 16'
ϕ CN	-30°	-72°

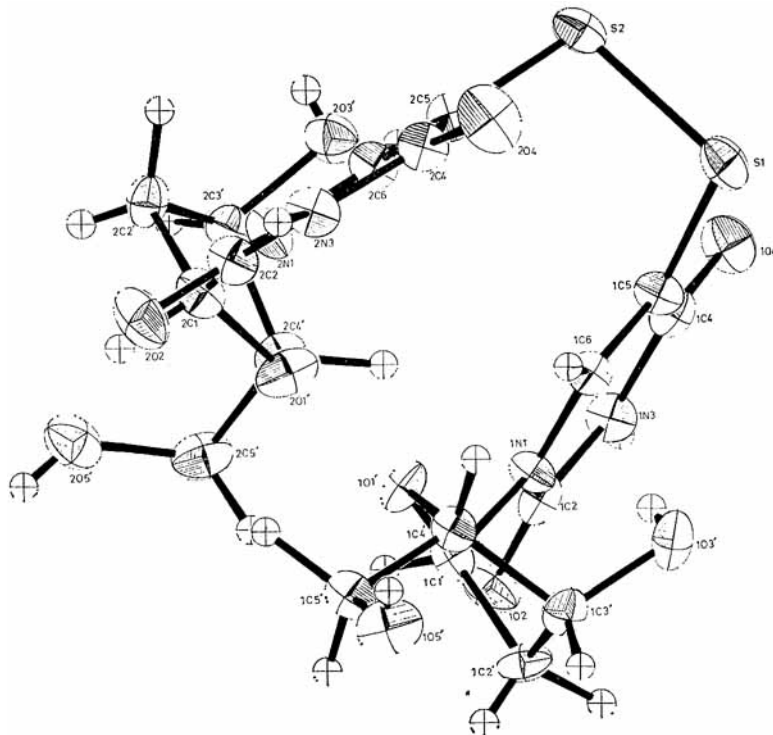


Fig. 4—The structure viewed along the c axis. (Reduced to about 1/2.)

TABLE VII—SHORT MOLECULAR CONTACTS

Hydrogen Bonds		Pertinent Distances and Angles	
Acceptor	Donor ^a		
104	H11-105' (1)	104 105'	2.736
		104 H11	2.32
		104 H11-105'	161°
102	H18-203' (3)	102 203'	2.745
		102 H18	2.17
		102 H18-203'	168°
105'	H22-205' (3)	105' 205'	2.695
		105' H22	1.97
		105' H22-205'	154°
204	H1-1N3 (4)	204 1N3	2.84
		204 H1	1.82
		204 H1-1N3	167°
205'	H12-2N3 (5)	205' 2N3	2.927
		205' H12	2.02
		205' H12-2N3	157°
203'	103' (1)	203' 103'	2.813
		203' 103'-1C3'	110.9°
Other Short Hydrogen Contacts			
203'	H13-2C6	203' 2C6	3.233
		203' H13	2.37
		203' H13-2C6	145°
103'	H2-1C6	103' 1C6	2.879
		103' H2	2.42
		103' H2-1C6	106°

^a The value in parentheses following the donor atom name denotes its equivalent position in fractional coordinates, as follows: (1) $0.5 - x, -y, 0.5 + z$, (2) $1 - x, y - 0.5, 0.5 - z$, (3) $x - 0.5, -(y + 0.5), -z$, (4) $0.5 - x, -y, z - 0.5$, (5) $1.5 - x, -y, 0.5 + z$.

for sugars 1 and 2, respectively. These values do not deviate significantly from the bond length between two tetrahedral carbon atoms, 1.533 ± 0.003 Å. (26). The exocyclic C4'—C5' in both sugars is substantially shorter than this distance, and as suggested by Sundaralingham and Jensen (27) for other nucleoside structures, that this effect may be due to the distortion of the C4' atom from a tetrahedral conformation (see angles in Fig. 2). In other nucleoside structures, it has been observed that the C—O bond lengths can deviate substantially from the commonly accepted value for a C—O single bond, 1.425 ± 0.007 Å. (28). There are a number of significantly longer and shorter C—O bonds in the two sugars. The C—O bonds in furanose ring 1 show a commonly occurring deviation that is found in a number of nucleosides (22), that is the C1'—O1' is significantly shorter than O1'—C4'. In sugar 2 this effect does not manifest itself to as great an extent, which may be a direct indication that this phenomenon is dependent on the conformation of the sugars.

Hydrogen Atoms and Bonding—The intramolecular bond lengths and angles (latter not shown) involving the hydrogen atoms agree fairly well with those found in other crystal structures. The O—H bond lengths are the only ones that deviate considerably from the commonly found values of 1.06 Å. for this bond. From various considerations (*i.e.*, C—O—H angles and hydrogen bond angles), it appears that only H7 has been positioned erroneously.

Table VII contains a list of all the hydrogen bonding contacts found in this structure. From a consideration of the distances and angles of various short intermolecular contacts, it appears that 103' is forming a hydrogen bond with a 203' atom. This would require that the 103' hydrogen (H7) be placed at the cross in Fig. 5, rather than the position given for this atom. Though difference syntheses did not show any electron density at the likely position, this may be a reflection of the difficulty in obtaining

accurate hydrogen positions in such a complex molecule. With H7 relocated, the hydrogen bonding scheme as shown in Fig. 5 is a very plausible one, *i.e.*, all angles and distances are reasonable. The molecules are held together in the lattice framework by these intermolecular hydrogen bonds.

Aside from the usual hydrogen bonding interactions, there also appears to be short C6—H . . . O3' intramolecular contacts. The H13 . . . 203' and H2 . . . 103' distances are 2.37 Å. and 2.42 Å., respectively. These are shorter than the normal van der Waals contacts between an oxygen and hydrogen. The sum of the van der Waals radii of hydrogen and oxygen is 2.60 Å. The existence of such interactions has been presented by Sutor (29), and the C6 hydrogen in other pyrimidine nucleosides has been found to form such interactions (25). These C—H . . . O close contacts may be a determining factor for the conformations about the glycosidic C1'—N1' bonds. The torsional angles (30), ϕ_{CN} , *i.e.*, the dihedral angle between the trace of the plane of the base with the C1'—O1' bond, are given in Table VII for each of these bonds. The short C—H . . . O contacts are represented in Fig. 5 by dotted lines.

Thermal Parameters—In Figs. 3 and 4 the magnitudes and directions of the thermal motion for the various atoms are shown. The thermal ellipsoids were drawn using a Cal. Comp. plotter with a program written by Johnson (31).

The isotropic temperature factors for the hydrogens are quite low. This behavior has been found in a large number of other organic structures, where the scattering factor curve used for hydrogen was that of the free atom (32).

CONCLUSION

In conclusion it is worthwhile to compare the

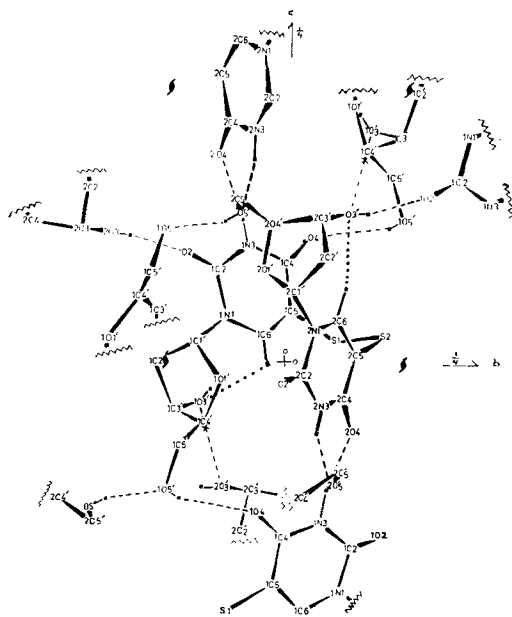


Fig. 5—Projection of molecule along the *a* axis. Key: — — —, postulated hydrogen bonding scheme;, short C—H . . . O intramolecular contacts. (Reduced to about 1/3.)

above structural observations with some of the properties found for this compound.

(a) The high optical rotation and its temperature dependence might find its explanation in that the electronic state about the disulfide linkage and the conformation of the sugar moieties may hinder free rotation of the two nucleoside residues about the S—S bond.

(b) The facile reducibility of the disulfide linkage for this compound appears to be attributable to the valence state of the disulfide bond.

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Essential Oils and Their Constituents XXXIV

Isolation of Khusenenic Acid and Isokhusenic Acid from Oil of Vetiver and Some Observations Concerning Their Structures

By ISHWAR C. NIGAM and HISASHI KOMAE

Khusenenic acid and isokhusenic acid, two new tricyclic sesquiterpene acids, were isolated from oil of vetiver (*Vetiveria zizanioides*, Linn). The physicochemical properties of the acids and their methyl esters were determined. Infrared, NMR, and mass spectral data as well as the results of dehydrogenation suggest that the two acids differ in the location of the double bond. Khusenenic acid and methyl khusenenate possess a terminal methylene group which rearranges in the presence of mineral acid to a tetrasubstituted double bond leading to the formation of isokhusenic acid and methyl isokhusenate, respectively. Dehydrogenation of the acids as well as their esters failed to yield any aromatic products, the main reaction being decarboxylation of the compounds to a C₁₄ hydrocarbon.

OIL OF VETIVER, an important essential oil used by the perfume and cosmetic industries, is obtained by steam distillation of the roots of *Vetiveria zizanioides* (Gramineae). Chemical examination of the oil has been carried

out by many investigators for almost a century. Most of this work concerned its ketone, alcohol, and hydrocarbon fractions. The acids present in the oil have so far received only limited attention (1-4). The present report describes the isolation and characterization of the major acidic constituent as well as of a closely related isomer.

It is suggested that the major acidic constituent be named khusenenic acid (3) rather than vetivenic acid (5) as the latter nomenclature may erroneously imply structural relationship with vetivane. The isomeric compound will accordingly be named isokhusenic acid.

Received May 2, 1967, from the Research Laboratories, Food and Drug Directorate, Department of National Health and Welfare, Ottawa, Ontario, Canada.

Accepted for publication July 5, 1967.

Previous paper: *Perfumery Essent. Oil Rec.*, **56**, 783(1965). The authors are grateful to Dr. Leo Levi for his interest in these investigations, to Dr. G. A. Neville and Dr. J. L. Holmes for the measurement of NMR spectra and mass spectra, respectively, and to Mrs. C. Radecka for her collaboration in some of the experiments. Special thanks are due to Dr. E. E. Langanau, Fritzsche Brothers, Inc., New York, N.Y., and Dr. Fausto Carreira, Ministerio da Economia, Lisbon, Portugal, who generously supplied samples of genuine reunion and angola vetiver oils, respectively, for this study.