

Crystal and molecular structure of lactarorufin B 3,8-ether 14-p-bromobenzoate

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Abstract. The structure of lactarorufin B is verified by X-ray analysis. Crystals of the title compound, $C_{22}H_{23}O_5Br$, are monoclinic, $a = 16.55$, $b = 6.75$, $c = 20.07$ Å, $\beta = 111.7^\circ$, $Z = 4$, space group C2. The intensities were collected on a diffractometer using CuK_α radiation. A Patterson synthesis revealed the heavy-atom position. A block-diagonal and full-matrix least-squares refinement with anisotropic temperature factors for non-hydrogen atoms led to a final R of 6.9%. The results indicate that the lactone carbonyl oxygen occurs at C(5) and not at C(13) as was deduced earlier from chemical and spectroscopic evidences.

Introduction

An european mushroom species *Lactarius rufus* is very common in coniferous and mixed forests. Some 45 years ago the chemical constituents of *Lactarius rufus* were investigated and trehalose, lipides, dextrans, and lactic acid were isolated. Its milky juice was reported to possess certain antibiotic properties. It was, however, not until early 70's when attention was drawn to isolate chemical substances responsible for this activity. From ethanolic extract of fresh *Lactarius rufus* four new sesquiterpenes were isolated for which the name lactarorufins: A, B, C and D was proposed (Daniewski and Kocór, 1970). The structure of lactarorufin A was elucidated on the basis of chemical transformations, degradation, and spectral properties (Daniewski and Kocór, 1971). The structures of lactarorufin B

(Daniewski et al., 1973) and C (Daniewski and Thoren, 1975) were similarly established.

X-Ray crystal structure analysis of lactarorufin B, 3,8-ether 14-*p*-bromobenzoate given in this paper has verified the structure of lactarorufin B itself. The results proved the position of the lactone carbonyl oxygen at C(5) and not at C(13) as was announced earlier (Daniewski and Kocór, 1973). The remaining structural features were found to be in agreement with those of chemical and spectroscopic evidences.

Our findings also permit us to postulate that the same change in the position of the lactone carbonyl should be introduced in regard to closely related lactarorufin A, because chemical evidences for the structure of lactarorufin B were largely based on the correlation of its transformation products with the compounds obtained from lactarorufin A the structure of which was elucidated earlier.

Experimental and crystal data

Crystals of lactarorufin B 3,8-ether 14-*p*-bromobenzoate were grown from isobutanol-ethanol solution in the hexane atmosphere. The crystals were colourless prisms elongated along the *b*-axis suitable for X-ray work. The cell dimensions and space group were determined from the precession photographs of *h0l*, *0kl*, and *h1l* layers taken with CuK_α radiation. The diffraction symmetry and systematic extinctions indicated space groups *C2*, *Cm* or *C2/m*. However, the unit cell contains four asymmetric molecules and *C2* is the only possibility. The cell dimensions given are those obtained by least-squares fit of 14 high-angle reflexions measured on a diffractometer. The crystal density was measured by flotation in aqueous potassium iodide.

Crystal data: $\text{C}_{22}\text{H}_{23}\text{O}_5\text{Br}$, MW = 447, m.p. 162–165°, monoclinic, space group *C2*, $a = 16.55(2)$, $b = 6.75(1)$, $c = 20.07(2)$ Å, $\beta = 111.73(5)^\circ$, $V = 2081$ Å³, $D_m = 1.41$, $D_x = 1.42$ g · cm⁻³, $Z = 4$, $F(000) = 920$.

The crystal used to collect intensities on a Hilger-Watts four-circle full automatic diffractometer with graphite monochromatized CuK_α radiation was $0.3 \times 0.2 \times 0.2$ mm. The crystal was so oriented that the *b*-axis coincided with the φ -axis of the four-circle goniostat. 1728 reflexions with $\sin \theta/\lambda \leq 0.5$ were measured. Using the criterion $I > 3\sigma(I)$ 1584 intensities were considered observable, where $\sigma(I)$ is

given by $[N + k^2(N_{b1} + N_{b2})]^{1/2}$. In this expression N is the total number of counts accumulated during the scan, N_{b1} and N_{b2} are the background counts at either end of the scan range, k is the ratio (T_{scan}/T_{bkg}) of the total scan time. The integrated intensity measurement was made by scanning reflexions with $\theta : 2\theta$ scan technique at a rate of 1° per minute over 2θ range of 2° . The background was counted for 20 s at each of the scan limits. During data collection monitoring of a standard reflexion every 50 counts showed that the crystal was stable and properly aligned, the maximum intensity variation being 0.8% of its mean value. The intensities were corrected for the usual Lorentz and polarization factors. No absorption correction was applied. The reduction to structure amplitudes were performed after data collection using the Hilger and Watts Software System.

Structure determination and refinement

The bromine atom coordinates were found from the Harker section $P(u0w)$ of the Patterson function. Unrefined positional parameters of the heavy atom were $x = 0.62$, $y = 0.0$ (free choice), $z = 0.36$. The atomic scattering factors for C, H, N, O, Br were those of International Tables for X-Ray Crystallography, 1969. An initial residual $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ for unrefined bromine atom coordinates was 0.36. The phases yielded by the bromine atom were used to compute a three-dimensional Fourier map. There was a pseudo-plane of symmetry introduced into the first electron density distribution. Using the bond scan, structure factor and electron density calculations the whole structure was revealed, R value being 0.26. Minimizing the quantity $\Phi = \Sigma||F_o| - |F_c||^2$ a refinement of structural parameters was carried out by block-diagonal least-squares calculation. Three cycles of calculation with isotropic temperature factors for all atoms lead to $R \approx 0.22$. Three more cycles were applied, but R did not decrease. Molecular geometry calculations made at this stage had shown the molecule to possess a good chemical and stereochemical sense. A difference Fourier map did not supply evidence that any of the atoms was incorrectly placed and that there were any additional atoms in the unit cell. After consideration of all the chemical and spectral data on the structure of lactarorufin B, lactone carbonyl oxygen was removed and a new difference Fourier synthesis was

Table 1. Atomic coordinates and anisotropic thermal parameters ($\times 10^4$) with esd's in parentheses. The thermal parameters are of the form $\exp[-2\pi^2(U_{11}h^2a^{*2} + 2U_{12}hka^*b^* + \dots)]$

	<i>x</i>	<i>y</i>	<i>z</i>	U_{11}	U_{22}	U_{33}	U_{12}	U_{13}	U_{23}
C 1	4370(7)	4115(18)	2297(6)	530(13)	492(10)	574(12)	1(8)	99(12)	-40(12)
C 2	5042(6)	5549(17)	2210(5)	472(12)	517(15)	449(11)	41(8)	-39(10)	54(9)
C 3	5622(7)	4823(22)	1796(5)	458(13)	520(12)	560(12)	-53(9)	29(9)	131(11)
C 4	5232(8)	3101(20)	1267(6)	574(14)	495(12)	447(9)	6(9)	73(11)	60(11)
C 5	3821(9)	2728(23)	82(7)	726(13)	590(12)	583(11)	-61(10)	156(11)	-13(9)
C 6	4460(8)	3836(19)	657(7)	581(14)	475(11)	442(11)	-48(10)	168(10)	-49(12)
C 7	4263(8)	5726(22)	577(7)	562(15)	708(14)	428(7)	-7(7)	106(12)	106(13)
C 8	4758(8)	7276(18)	1084(6)	717(12)	355(12)	516(10)	71(9)	84(9)	120(10)
C 9	4542(8)	7327(18)	1771(5)	742(13)	474(10)	426(10)	21(8)	-14(10)	-18(9)
C10	3552(8)	6939(22)	1668(6)	604(10)	813(15)	588(12)	265(10)	30(8)	26(9)
C11	3579(7)	5470(23)	2264(6)	589(15)	866(15)	458(13)	15(10)	7(9)	-31(10)
C12	6592(6)	4373(21)	2313(6)	329(11)	905(12)	699(10)	3(9)	-165(10)	46(9)
C13	3454(9)	5977(24)	-116(7)	820(17)	753(15)	343(7)	183(10)	39(10)	51(12)
C14	3770(8)	6597(21)	2955(6)	746(11)	659(11)	475(11)	218(10)	137(11)	5(9)
C15	2701(8)	4317(26)	2057(7)	577(13)	1231(13)	817(11)	-29(9)	-54(10)	-251(11)
C16	3713(12)	5951(25)	4095(8)	1396(12)	696(12)	639(13)	-60(10)	198(11)	-180(11)
C17	3738(9)	4446(22)	4643(6)	912(12)	821(13)	393(10)	-8(12)	112(10)	-88(12)
C18	3602(13)	5075(30)	5235(7)	2063(13)	696(12)	745(10)	121(11)	596(12)	-123(12)
C19	3599(12)	3765(24)	5770(7)	1483(13)	730(11)	526(9)	35(9)	365(11)	-82(11)
C20	3755(10)	1835(24)	5684(7)	1093(12)	747(14)	525(12)	-60(11)	47(12)	-61(14)
C21	3877(16)	1227(26)	5101(9)	2311(12)	690(12)	949(11)	197(11)	561(13)	-147(12)
C22	3829(14)	2515(26)	4554(8)	1542(14)	599(12)	761(11)	280(12)	530(15)	-64(13)
O23	3606(17)	7651(21)	4124(8)	4733(14)	560(14)	1556(12)	-162(13)	2147(13)	-129(12)
O24	3809(5)	5234(19)	3517(4)	727(11)	802(10)	583(11)	183(9)	166(10)	7(9)
O25	5632(5)	6553(13)	1379(4)	513(10)	499(9)	623(11)	-61(9)	-18(12)	101(12)
O26	3234(6)	3971(16)	-376(4)	759(11)	762(10)	507(9)	-50(9)	-13(11)	-36(10)
O27	3757(7)	928(15)	-29(5)	1119(15)	624(13)	824(13)	-3(12)	-38(13)	-66(12)
Br28	3779(1)	0	6429(1)	1713(4)	850(3)	810(3)	-28(4)	218(5)	98(3)

Table 2. Fractional coordinates of hydrogen atoms ($\times 10^3$) (calculated geometrically)

	<i>x</i>	<i>y</i>	<i>z</i>		<i>x</i>	<i>y</i>	<i>z</i>
H(2)	547	581	275	H(41)	571	256	107
H(8)	463	866	80	H(42)	504	193	154
H(9)	470	878	200	H(101)	325	828	172
H(11)	463	336	280	H(102)	320	631	115
H(12)	417	305	187	H(131)	293	665	0
H(18)	349	663	529	H(132)	360	686	-50
H(19)	348	427	624	H(141)	423	775	320
H(21)	402	-32	505	H(142)	313	720	275
H(22)	386	196	406				

computed. It came out that at the carbon atoms C(5) and C(13) and at nearly the same distance to each of the atoms there were peaks of about the same height. Now the peak at C(5) was accepted. Three cycles of block-diagonal least-squares isotropic approximation were calculated giving $R = 0.17$. Next, three cycles of full-matrix least-squares anisotropic refinement were accomplished and R converged to 0.092 for 1538 reflexions. A third difference Fourier synthesis revealed 17 out of 23 hydrogen atoms. However, during the refinement procedure the hydrogen atoms behaved very poorly and we decided to publish the positional parameters of H-atoms computed geometrically with C-H distances of 1.07 Å. In the next refinement step two more cycles of full-matrix were applied, but the coordinates of the hydrogen atoms were not refined and isotropic temperature factors $B_{\text{iso}} = 4$ were affixed. The final R value was 0.069 for 1465 reflexions. All the calculations were done with the NRC crystallographic programmes system (Ahmed et al., 1966) on ICL-4/70 computer. Final atomic parameters are given in Tables 1 and 2.

Description and discussion of the structure

Interatomic distances and valency angles of non-hydrogen atoms are presented in Tables 3 and 4. Figure 1 illustrates the numbering of the atoms and the structural formula. The standard deviations range from 0.015 to 0.025 Å for the bond lengths and from 0.9 to 1.9° for bond angles. The molecular conformation is illustrated in Figure 2. The

Table 3. Bond distances (Å). Standard deviations in parentheses

C(1)–C(2)	1.532(17)	C(9)–C(10)	1.595(19)
C(1)–C(11)	1.577(19)	C(10)–C(11)	1.541(18)
C(2)–C(3)	1.562(16)	C(11)–C(14)	1.510(17)
C(2)–C(9)	1.536(16)	C(11)–C(15)	1.563(20)
C(3)–C(4)	1.545(18)	C(13)–O(26)	1.448(19)
C(3)–C(12)	1.584(16)	C(14)–O(24)	1.437(16)
C(3)–O(25)	1.440(16)	C(16)–C(17)	1.487(21)
C(4)–C(6)	1.490(18)	C(16)–O(23)	1.165(23)
C(5)–C(6)	1.450(20)	C(16)–O(24)	1.319(18)
C(5)–O(26)	1.354(18)	C(17)–C(18)	1.357(21)
C(5)–O(27)	1.232(18)	C(17)–C(22)	1.331(23)
C(6)–C(7)	1.311(20)	C(18)–C(19)	1.392(25)
C(7)–C(8)	1.477(18)	C(19)–C(20)	1.352(23)
C(7)–C(13)	1.541(19)	C(20)–C(21)	1.324(25)
C(8)–C(9)	1.547(17)	C(20)–Br(28)	1.930(15)
C(8)–O(25)	1.430(16)	C(21)–C(22)	1.378(25)

Table 4. Valency angles (°). Standard deviations in parentheses

C(2)–C(1)–C(11)	105(1)	C(8)–C(7)–C(13)	128(1)
C(1)–C(2)–C(3)	119(1)	C(7)–C(8)–C(9)	112(1)
C(1)–C(2)–C(9)	107(1)	C(7)–C(8)–O(25)	105(1)
C(1)–C(11)–C(10)	101(1)	C(7)–C(13)–O(26)	104(1)
C(1)–C(11)–C(14)	111(1)	C(9)–C(8)–O(25)	100(1)
C(1)–C(11)–C(15)	113(1)	C(8)–C(9)–C(10)	116(1)
C(3)–C(2)–C(9)	104(1)	C(9)–C(10)–C(11)	106(1)
C(2)–C(3)–C(4)	115(1)	C(10)–C(11)–C(14)	109(1)
C(2)–C(3)–C(12)	113(1)	C(10)–C(11)–C(15)	111(1)
C(2)–C(3)–O(25)	101(1)	C(14)–C(11)–C(15)	111(1)
C(2)–C(9)–C(8)	104(1)	C(11)–C(14)–O(24)	109(1)
C(2)–C(9)–C(10)	105(1)	C(14)–O(24)–C(16)	118(1)
C(4)–C(3)–C(12)	112(1)	C(17)–C(16)–O(23)	127(2)
C(4)–C(3)–O(25)	108(1)	C(17)–C(16)–O(24)	115(1)
C(3)–C(4)–C(6)	109(1)	C(16)–C(17)–C(18)	118(1)
C(12)–C(3)–O(25)	108(1)	C(16)–C(17)–C(22)	123(1)
C(3)–O(25)–C(8)	107(1)	O(23)–C(16)–O(24)	118(2)
C(4)–C(6)–C(5)	129(1)	C(18)–C(17)–C(22)	119(2)
C(4)–C(6)–C(7)	121(1)	C(17)–C(18)–C(19)	122(2)
C(6)–C(5)–O(26)	110(1)	C(17)–C(22)–C(21)	119(2)
C(5)–C(6)–C(7)	109(1)	C(18)–C(19)–C(20)	117(2)
C(6)–C(5)–O(27)	130(1)	C(19)–C(20)–C(21)	121(2)
C(5)–O(26)–C(13)	108(1)	C(19)–C(20)–Br(28)	118(1)
O(26)–C(5)–O(27)	120(1)	C(21)–C(20)–Br(28)	121(1)
C(6)–C(7)–C(8)	124(1)	C(20)–C(21)–C(22)	122(2)
C(6)–C(7)–C(13)	108(1)		

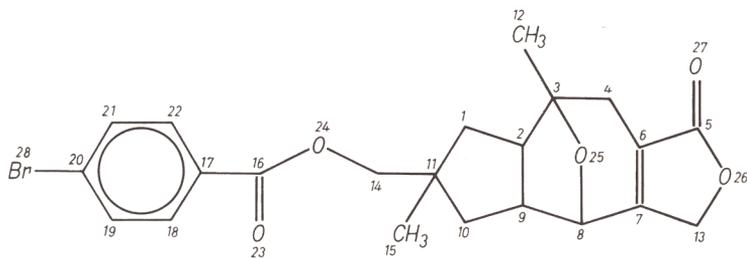


Fig. 1. Structural formula and numbering of atoms

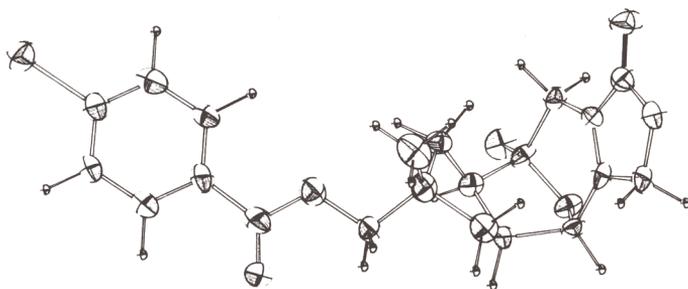


Fig. 2. The molecule of lactarorufin B

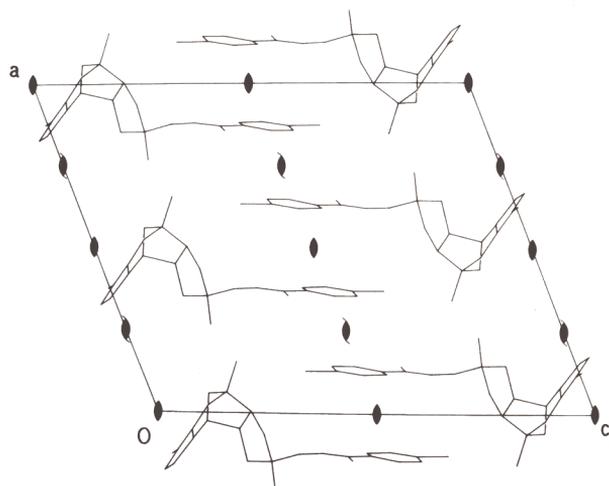


Fig. 3. The molecular packing in the crystal

Table 5. Selected dihedral angles (°)

Ring A		Ring C	
C(11)–C(1)–C(2)–C(9)	–28	O(25)–C(3)–C(4)–C(6)	–43
C(2)–C(1)–C(11)–C(10)	40	C(3)–C(4)–C(6)–C(7)	8
C(1)–C(2)–C(9)–C(10)	5	C(4)–C(6)–C(7)–C(8)	–2
C(2)–C(9)–C(10)–C(11)	21	C(6)–C(7)–C(8)–O(25)	30
C(9)–C(10)–C(11)–C(1)	–37	C(4)–C(3)–O(25)–C(8)	76
		C(7)–C(8)–O(25)–C(3)	–66
Ring B		Ring D	
C(9)–C(2)–C(3)–O(25)	20	O(26)–C(5)–C(6)–C(7)	2
C(3)–C(2)–C(9)–C(8)	9	C(5)–C(6)–C(7)–C(13)	–2
C(2)–C(3)–O(25)–C(8)	–44	C(6)–C(7)–C(13)–O(26)	2
O(25)–C(8)–C(9)–C(2)	–34	C(6)–C(5)–O(26)–C(13)	–1
C(9)–C(8)–O(25)–C(3)	50	C(7)–C(13)–O(26)–C(5)	–1

Table 6. Least-squares planes and atomic deviations (Å). All equations are expressed in orthogonal Ångstrom space. Atoms not included in planes calculation are denoted by (+)

Plane (1)	$0.212 X - 0.454 Y - 0.865 Z = -3.812$	
	C(1)	0.019
	C(2)	–0.029
	C(9)	0.028
	C(10)	–0.018
	C(3) ⁺	1.129
	C(8) ⁺	1.336
	C(11) ⁺	–0.614
	$\Sigma\delta^2$	= 0.0023
Plane (2)	$-0.602 X - 0.653 Y - 0.460 Z = -8.423$	
	C(2)	0.053
	C(3)	–0.035
	C(8)	0.036
	C(9)	–0.053
	O(25) ⁺	–0.636
	$\Sigma\delta^2$	= 0.0081

Table 6. (continued)

Plane (3)	$0.835 X + 0.111 Y - 0.539 Z = 5.381$	
	C(4)	0.022
	C(5)	-0.030
	C(6)	0.002
	C(7)	0.001
	C(8)	-0.023
	C(13)	0.028
	C(3) ⁺	-0.171
	O(25) ⁺	0.652
	$\Sigma\delta^2$	= 0.0026
Plane (4)	$0.838 X + 0.086 Y - 0.538 Z = 5.322$	
	C(5)	0.003
	C(6)	0.018
	C(7)	-0.018
	C(13)	0.002
	O(27)	-0.011
	C(4) ⁺	0.054
	C(8) ⁺	0.065
	$\Sigma\delta^2$	= 0.0008
Plane (5)	$-0.882 X - 0.133 Y - 0.452 Z = -6.700$	
	C(16)	-0.016
	C(17)	-0.021
	C(18)	0.012
	C(19)	0.034
	C(20)	-0.006
	C(21)	-0.021
	C(22)	0.036
	O(23)	-0.017
	O(24)	0.015
	Br(28)	-0.016
	C(14) ⁺	0.055
	$\Sigma\delta^2$	= 0.0045

Table 7. Angle between perpendiculars of planes (°)

Plane (1) and (2)	55.5	Plane (2) and (4)	108.2
(1) and (3)	53.6	(2) and (5)	34.4
(1) and (4)	52.8	(3) and (4)	1.5
(1) and (5)	74.7	(3) and (5)	120.5
(2) and (3)	109.1	(4) and (5)	120.5

results obtained allowed to verify the structure of lactarorufin B to indicate the lactone carbonyl group at C(5) and not at C(13) as deduced earlier from the chemical and spectroscopic evidences, (Daniewski and Kocór, 1973).

The conformation of the A, B, C, and D rings is described by the torsion angles, least-squares planes, and angles between perpendiculars of the planes listed in Tables 5, 6, and 7 respectively. The A ring has the ${}^{C(11)}E$ envelope conformation (Schwartz, 1973) with C(11) displaced by -0.614 \AA out of the plane defined by the remaining ring atoms. The five-membered B ring adopts ${}^{O(25)}E$ envelope conformation with O(25) displaced by -0.636 \AA out of the second plane. The six-membered C ring containing a double bond between C(6) and C(7) adopts a distorted half-chair ${}^{O(25)}H_{C(3)}$ conformation with O(25) and C(3) displaced by 0.652 and -0.171 \AA respectively out of the third plane. The D ring constrained by conjugation of double bonds C(6)–C(7), 1.311 \AA , and C(5)–O(27), 1.232 \AA , is planar. The ring junction between A and B is cis with both C(11) and O(25) exo. The B/C ring junction is also cis. The overall conformation of A, B, and C rings is cis-syn-cis.

The *p*-bromobenzoate moiety geometry is in agreement with the commonly accepted data.

The molecular packing in the crystal is shown in Figure 3. There are no intermolecular contacts that are significantly shorter than the sum of the corresponding van der Waals radii.

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