15-*O*-Deacetylrhaposerin and rhaserin — new components of a lactone mixture from *Rhaponticum serratuloides*

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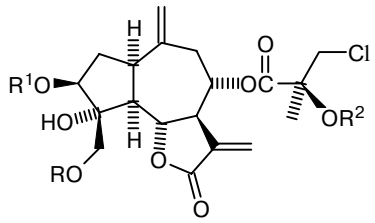
As part of our continuing studies of lactones from the aerial part of the plant *Rhaponticum serratuloides*, 15-*O*-deacetylrhaposerin and new guaianolide called rhaserin were isolated along with the well-known loliolide. The configuration of the C(17) asymmetric center in 15-*O*-deacetylrhaposerin was established by X-ray diffraction analysis. The molecular structure of rhaserin was determined based on the data from ^{1}H and ^{13}C NMR spectroscopy (including 2D NMR spectroscopy) of this lactone and its 4,15-*O*-isopropylidene derivative.

Key words: sesquiterpenoids, guaianolides, 15-*O*-deacetylrhaposerin, rhaserin, acetonides, 2D NMR spectroscopy, X-ray diffraction analysis, HPLC.

Previously,[1] we have isolated cynaropicrin and four related sesquiterpene lactones from the aerial part of the plant *Rhaponticum serratuloides* (Georgi.) Bobr. widespread in Kazakhstan and Russia. These four lactones are two known chlorine-containing guaianolides, *viz.*, centaurepensin and acroptilin, and two new lactones, *viz.*, rhaposerin (**1**) and rhaserolide. As part of our continuing studies on the compositions of the terpenoid components of this plant, three new crystalline compounds were isolated from an ethanolic extract of its aerial part. The new compounds belong to the same series of lactones.

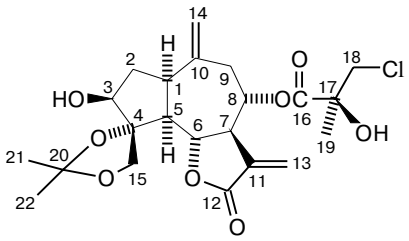
The structure of one of these lactones, *viz.*, of 15-*O*-deacetylrhaposerin (**2**), was established based on the ^{1}H and ^{13}C NMR spectral data. The assignment of the signals (Tables 1 and 2) was made using 2D NMR spectroscopy. The ^{13}C (Table 3) and ^{1}H NMR spectral data for 3,15-di-*O*- (**3**) and 3,15,17-tri-*O*-acetates (**4**) of lactone **2** and the chromatographic mobilities (TLC) of these compounds are identical to those of 3-*O*- and 3,17-di-*O*-acetates of rhaposerin, respectively.

Based on a comparison of the ^{1}H and ^{13}C NMR spectral data for this lactone and two C(17)-epimeric lactones, *viz.*, centaurepensin and 17-epicentaurepensin,[1] it was suggested that the asymmetric center at the C(17) atom of lactone **1** has the *S* configuration.[2] Consequently, lactone **2**, which is 15-de-*O*-acetyl-**1**, also should have the (17*S*) configuration. To confirm this conclusion, we prepared the isopropylidene derivative of this lactone, which was readily crystallized, and studied it by X-ray diffraction analysis. Based on the X-ray data, structure **5** was assigned to this derivative (Fig. 1). The



1—4

1: R = Ac; $R^1 = R^2 = H$ **2:** $R = R^1 = R^2 = H$
3: $R = R^1$ = Ac; $R^2 = H$ **4:** $R = R^1 = R^2$ = Ac



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crystal structure contains two independent molecules of compound **5**, their geometric parameters being identical within the experimental error. The cycloheptane fragment in both molecules adopts the *twist*-chair conforation, which is energetically most favorable.[3] The twofold axis C_2 passes through the C(8) atom and approximately through the midpoint of the C(1)—C(5) bond (in the second crystallographically independent molecule, the

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Table 1. ^{13}C NMR spectra of compounds **2** and **5**—**7** (Py-d_5, Me_4Si)

C atom	δ			
	2	**5**	**6**	**7**
1	47.07 d	46.88 d	52.46 d	53.39 d
2	39.84 t	38.73 t	78.36 d	79.74 d
3	77.07 d	75.52 d	84.46 d	82.05 d
4	85.77 s	93.20 s	80.97 s	90.09 s
5	57.74 d	57.06 d	54.79 d	54.46 d
6	77.89 d	77.17 d	77.70 d	77.15 d
7	47.00 d	47.49 d	47.84 d	48.47 d
8	75.57 d	75.49 d	74.45 d	74.61 d
9	36.22 t	35.74 t	39.59 t	39.86 t
10	144.61 s	143.82 s	141.41 s	141.75 s
11	138.91 s	138.83 s	138.22 s	138.37 s
12	169.36 s	169.19 s	169.27 s	169.42 s
13	121.09 t	121.22 t	121.01 t	121.58 t
14	116.65 t	117.66 t	116.81 t	117.75 t
15	63.92 t	66.13 t	63.63 t	65.54 t
16	173.45 s	174.44 s	166.01 s	166.38 s
17	75.38 s	75.37 s	136.32 s	136.67 s
18	52.17 t	52.15 t	126.04 t	126.43 t
19	24.31 q	24.29 q	17.90 q	18.25 q
20	—	108.48 s	—	108.94 s
21	—	28.00 q	—	27.78 q
22	—	24.45 q	—	26.62 q

twofold axis passes through the C(8A) atom and the midpoint of the C(1A)—C(5A) bond. All five-membered rings, except for the lactone rings, adopt a slightly distorted envelope conformation. The lactone rings have a *twist* conformation. The bond lengths in the molecules are close to standard values.[4] Structures containing such tetracyclic core are unavailable in the Cambridge Structural Database. Linichlorin B[5] is the closest analog of acetonide **5**. The geometric parameters and the conformations of the lactone and cycloheptane fragments of these two compounds are identical within the experimental error. The only difference is that the cyclopentane ring in linichlorin B adopts a *twist* conformation. The asymmetric center at the C(17) atoms has the *S* configuration, as in molecules of other lactones, which have been isolated previously from the plant under study.[1]

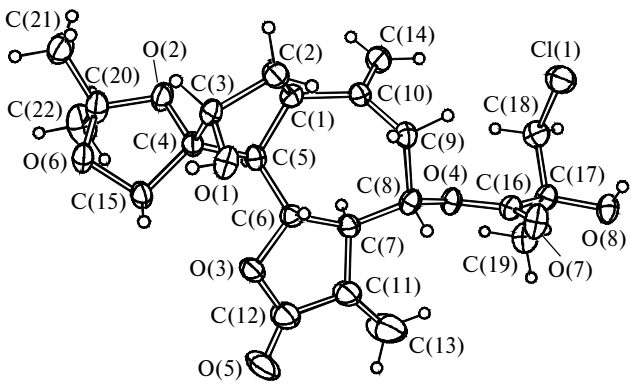


Fig. 1. Crystal structure of compound **5** established by X-ray diffraction analysis.

Only two compound containing, like acetonide **5**, the spiro-fused bicyclopentadioxolane fragment are available in the Cambridge Structural Database.[6,7] The bond lengths in these two compounds are identical to the corresponding values in acetonide **5**. The dioxolane ring in all three compounds adopts an envelope conformation. However, different atoms, *viz.*, the C(15) and C(15A) atoms in molecule **5** (the deviations are 0.55(1) and 0.60(1) Å, respectively) and the oxygen atoms in two other molecule, deviate from the planes of the remaining four atoms.

In the crystal, molecules of compound **5** are linked to each other through a network of OH...O hydrogen bonds (O(1)H(1B)...O(6A), 2.01 Å; O(8A)H(8AC)...O(1), 2.15 Å; O(8)H(8D)...O(1A), 2.29 Å; O(1A)—H(1AB)...O(6), 2.00 Å). In addition, two intramolecular OH...Cl interactions are observed (O(8)H(8D)...Cl(1), 2.72 Å; O(8A)H(8AC)...Cl(1A), 2.81 Å). Crystals of acetonide **5** prepared from a mixture of light petroleum and $CHCl_3$ are characterized by the presence of $CHCl_3$ molecules, as readily evidenced by the signal of $CHCl_3$ in the ^1H NMR spectrum of these crystals recorded in Py-d_5. The crystal stucture contains one $CHCl_3$ molecule per molecule of compound **5**.

It should be noted that structure **2** has been previously assigned to amorphous lactone cebelin J found in the plant *Centaurea bella* Trautv.[5,8] although the configurations of the substituents at the C(17) atom have not been established. The ^1H NMR spectra (in $CDCl_3$) of cebelin J [5] and lactone **2** isolated in the present study are virtually identical, which indicates that they are actually the same compound.

According to the ^{13}C NMR spectral data, new guaianolide rhaserin contains 19 carbon atoms. The mass spectrum of this compound, like the spectrum of lactone **2**, has the ion peak $[M - CH_2OH]^+$ corresponding to the formula $C_{18}H_{21}O_7$. The molecular structure of rhaserin (**6**) was established by ^1H and ^{13}C NMR spectroscopy. The assignment of the signals was made (Tables 1 and 2) using the data of 2D NMR spectroscopy. Thus, the spin-spin coupling constant $^3J_{2,3}$ between the H(2) and H(3) protons in molecule **6** is 6.5 Hz, which is indicative of their *trans* arrangement. For the known 2-hydroxyguaianolides, $^3J_{2,3}$ between the H(2) and H(3) protons is smaller than 2 Hz in the case of the *cis* arrangement and is 8.0 Hz in the case of the *trans* arrangement.[5]

The long-range spin-spin coupling between the H(1) and H(3) protons (W constant) is observed in the 2D ^1H-^1H NMR spectrum (COSY) of compound **6**, whereas there is no coupling between the H(2) and H(5) protons (the required geometry cannot occur), which is also consistent with the 2β orientation of the H(2) proton in rhaserin (**6**).

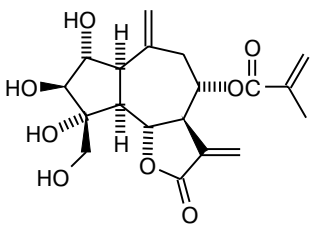
Dissolution of lactone **6** in dry Me_2CO in the presence of traces of TsOH afforded acetonide **7**, which was

Table 2. ^{1}H NMR spectra of compounds **2** and **5**—**7** (Py-d_5, Me_4Si)

Atom H	δ (*J*/Hz)			
	2	**6**	**5**	**7**
1	3.74 (ddd, $J_{1,2\alpha}$ = 10.5; $J_{1,5}$ = 11; $J_{1,2\beta}$ = 7.5)	3.44 (dd, $J_{1,5}$ = 11; $J_{1,2}$ = 8)	3.48 (ddd, $J_{1,2\beta}$ = 11; $J_{1,2\alpha}$ = $J_{1,5}$ = 8)	3.42 (dd, $J_{1,5}$ = 9.0; $J_{1,2}$ = 7.5)
2α	2.66 (ddd, $J_{2\alpha,2\beta}$ = 14.5; 10.5; $J_{2\alpha,3}$ = 6.0)	—	2.49 (m*, $J_{2\alpha,2\beta}$ = 14.5; 8; $J_{2\alpha,3}$ = 5.0)	—
2β	1.82 (ddd, *J* = 14.5; 7.5; $J_{2\alpha,3}$ = 2)	4.74 (dd, *J* = 8; $J_{2,3}$ = 6.5)	1.76 (ddd, *J* = 14.5; 11; $J_{2\beta,3}$ = 1.5)	4.80 (dd, *J* = 7.5, 5)
3	4.63 (br.dd, *J* = 6, 2)	4.69 (br.d, *J* = 6.5)	4.34 (br.d, *J* = 5)	4.52 (br.d, $J_{3,2}$ = 5.0)
5	2.57 (dd, $J_{5,6}$ = 10; 11)	2.95 (t, $J_{1,5}$ = $J_{5,6}$ = 11)	2.43 (ddd, *J* = 11; 8; 1)	2.79 (br.dd, $J_{5,6}$ = 11.5; *J* = 9.0)
6	5.23 (dd, *J* = 11; $J_{6,7}$ = 10)	5.05 (dd, *J* = 11; $J_{6,7}$ = 10)	5.15 (dd, *J* = 11; $J_{6,7}$ = 10)	4.80 (dd, *J* = 11.5; $J_{6,7}$ = 9.0)
7	3.12 (dddd, $J_{7,8}$ = $J_{6.7}$ = 10; $J_{7,13A}$ = $J_{7,13B}$ = 3.5)	3.18 (dddd, $J_{7,8}$ = $J_{6.7}$ = 10; $J_{7,13A}$ = 3, $J_{7,13B}$ = 3.5)	3.13 (dddd, $J_{7,8}$ = $J_{6.7}$ = 10; $J_{7,13A}$ = 3.5, $J_{7,13B}$ = 3)	3.22 (br.dddd, $J_{7,8}$ = $J_{6.7}$ = 10; $J_{7,13A}$ = $J_{7,13B}$ = 3)
8	5.29 (ddd, *J* = 10.0; $J_{8,9B}$ = 5; $J_{8,9A}$ = 2.5)	5.17 (ddd, *J* = 10; $J_{8,9A}$ = $J_{8,9B}$ = 5)	5.32 (ddd, *J* = 10; $J_{8,9B}$ = 5.0; $J_{8,9A}$ = 2.0)	5.23 (br.dt, *J* = 10.0; $J_{8,9A}$ ≈ 5)
9A	2.47 (dd, $J_{9A,9B}$ = 14.5; *J* = 2.5)	2.33 (dd, $J_{9A,9B}$ = 14; *J* = 5)	2.49 (m)*	2.33 (dd, $J_{9A,9B}$ = 14.0; *J* = 5.0)
9B	2.93 (dd, *J* = 14.5; 5.0)	2.93 (dd, *J* = 14; 5)	2.83 (dd, $J_{9A,9B}$ = 15; 5.0)	2.90 (dd, *J* = 14.0; $J_{8,9B}$ = 5)
13A	5.73 (d, *J* = 3.5)	5.33 (d, *J* = 3)	5.75 (d, *J* = 3.5)	5.59 (d, *J* = 3.0)
13B	6.11 (d, *J* = 3.5)	6.12 (d, *J* = 3.5)	6.16 (d, *J* = 3)	6.18 (m)*
14A	4.99 (br.d, *J* = 2)	5.00 (br.d, *J* = 2)	5.05 (d, *J* = 2.0)	5.02 (br.d, *J* = 1)
14B	5.06 (br.d, *J* = 2)	5.30 (br.dd, *J* = 2; 1)	5.08 (d, *J* = 2.0)	5.21 (br.s)
15A	4.39 (d, *J* = 11.5)	4.49 (d, *J* = 11)	4.53 (d, *J* = 11.0)	4.40 (d, *J* = 9.4)
15B	4.69 (d, *J* = 11.5)	4.54 (d, *J* = 11)	4.77 (d, *J* = 11.0)	4.76 (d, *J* = 9.4)
18A	3.93 (d, *J* = 11.5)	5.51 (t, *J* = 1.5)	3.97 (d, *J* = 11.0)	5.56 (quintet, *J* = 1.5)
18B	4.04 (d, *J* = 11.5)	6.14 (dd, *J* = 1.5; 1.0)	4.07 (d, *J* = 11.0)	6.18 (m)*
19	1.63 (br.s)	1.86 (br.s)	1.67 (br.s)	1.90 (br.s)
21			1.35 (s)	1.55 (s)
22			1.44 (s)	1.60 (s)

* The signals overlap.

readily crystallized from a mixture of light petroleum and $CHCl_3$. However, the crystals very rapidly and irreversibly decomposed in air, which did not allow us to study this derivative by X-ray diffraction analysis. Nevertheless, the ^{13}C and ^{1}H spectral data (Tables 1 and 2, respectively) indicate that the isopropylidenedioxy group is located at the C(4)—C(15) atoms in derivative **7** and its stereochemistry corresponds to that of acetonide **5**. Of special note is the fact that the chemical shifts of the signals for the C(4), C(6), and C(20) atoms in the spectrum of acetonide **7** are similar to those of derivative **5** (Table 1).



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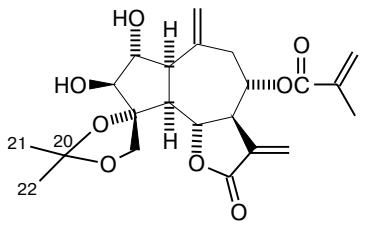

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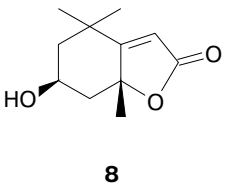
In addition to two guaianolides (**2** and **6**), crystalline lactone loliolide (calendin) (**8**) was isolated from the nonpolar fraction of the extract under investigation. Lactone **8** has been previously found in *Centaurea salmanica* L.,[9] *Calendula officinalis* L.,[10] and many other plants. This lactone, which is widespread in nature, is considered as a metabolite formed in the course of oxidative degradation of carotinoids, for example, of fucoxanthine.[11] Loliolide was identified based on the optical rotation and the ^{1}H and ^{13}C NMR spectral data.[9] Yet another known lactone, *viz.*, repdiolide (**9**), was isolated as diacetate **10** both upon chromatography of a mixture of acetates prepared by acetylation of the mother liquor and upon crystallization of raw rhaposerin.[1]

Table 3. ^{13}C NMR spectra of lactone **1** and acetates **3** and **4** (Py-d_5, Me_4Si)

C atom	δ		
	3 [a]	**4** [b]	**1** [s]
1	47.13 d	47.20 d	47.60 d
2	37.22 t	37.40 t	40.41 t
3	78.80 d	78.80 d	77.01 d
4	83.82 s	83.83 s	84.26 s
5	58.48 d	58.49 d	58.32 d
6	76.93 d	76.49 d	77.46 d
7	47.09 d	47.14 d	46.76 d
8	76.16 d	76.17 d	75.47 d
9	35.65 t	34.95 t	35.50 t
10	142.88 s	142.90 s	144.48 s
11	138.21 s	138.25 s	138.90 s
12	168.86 s	168.84 s	169.08 s
13	121.46 t	121.58 t	121.00 s
14	118.19 t	118.32 t	117.02 t
15	66.48 t	66.55 t	67.50 t
16	173.47 s	169.55 s	173.44 s
17	79.67 s	79.67 s	75.37 s
18	52.13 t	47.90 t	52.17 t
19	24.28 q	20.84 q	24.28 q

[a] The signals of two (OAc) groups: 169.79 (s), 170.67(s), 20.75 (q), 20.88 (q).
[b] The signals of three (OAc) groups: 170.68 (s), 170.32 (s), 169.77 (s), 20.71 (q), 20.75 (q), 20.83 (q); the signals for the C(1) and C(7) atoms were assigned based on the data of COSY ^{13}C-^1H NMR spectroscopy.
[c] Published data.[1]

Derivative **10** was identified based on the data of ^1H,[5,12] ^{13}C, and 2D ^1H-^1H NMR (COSY) spectroscopy.



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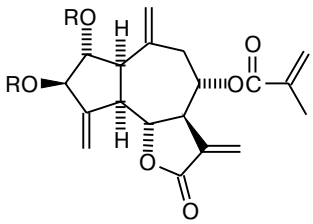

9: R = H
10: R = Ac

The chromatographic behavior of lactones **2** and **6** and derivative **5** on the reversed phase was studied by HPLC. The capacity coefficient (k') for lactone **2** is 2.3 (40% of MeOH in the eluent) and 6.8 (30% of MeOH in the eluent). Under the same conditions, the coefficient k' for lactone **6** is 2.7 and 7.9, respectively, and this coefficient for acetonide **5** (70, 60, and 50% of MeOH in the eluent) is 1.1, 2.7, and 9.6, respectively. The UV spectra of the compounds under study were recorded in the region of 190—300 nm in the stop-flow mode. The spectra of compounds **2** and **5** are similar (a maximum at 196 (for **2**) or 198 (for **5**) nm and a shoulder at 216 nm). The spectrum of lactone **6** has an absorption maximum as a plateau at 206—208 nm, which is attributable to the fact that compound **6** contains a new chromophore, *viz.*, the conjugated exomethylene group, in the side chain.[1]

Experimental

The melting points were determined on a Boetius instrument. The IR spectra were obtained on a Vector 22 instrument. The NMR spectra were recorded on a Bruker DRX-500 spectrometer (500.13 and 125.76 MHz for ^1H and ^{13}C NMR, respectively) using the standard Bruker software for recording 2D COSY (^1H-^1H and ^{13}C-^1H) and COLOC (^{13}C-^1H, 9 Hz) NMR spectra.

The high-resolution mass spectra (EI, 70 eV) were obtained on a Finnigan MAT 8200 instrument. The optical rotation was measured (at 580 nm) on a Polamat A polarimeter. Column chromatography was carried out on silica gel (KSK); the compound to sorbent ratio was ~1 : 20. Flash chromatography was carried out on silica gel Armsorbsil 100/160 μm. The TLC analysis was performed on Silufol plates; spots were visualized by spraying with a 1% vanilline solution in H_2SO_4.

We used rhaposerin (**1**) prepared previously.[1]

The aerial part of the plant *Rhaponticum serratuloides* (Georgi.) Bobr. was collected on June 1995 when the plant came in flower in the neighborhood of Karaganda, dried in air, and dispersed.

Acetone used for the preparation of acetonides was dried over molecular sieves and distilled.

The optical rotation and the concentrations of the solutions are expressed in (deg mL) $(g\ dm)^{-1}$ and g $(100\ mL)^{-1}$, respectively.

HPLC and UV spectroscopy of compounds **2**, **5**, and **6** were performed on a Milikhrom (Ob'-4) microcolumn liquid chromatograph[13] (64×2-mm column; LiChrosorb RP-18 (Merck) as the sorbent, 5 μm; the column temperature was 30 °C). The eluent was prepared by mixing MeOH with 0.05 *M* aqueous H_3PO_4. The compounds were detected at λ = 200 nm. The rate of elution was 100 μL min^{-1}. To record the UV spectra, the eluent flow was stopped at the maximum of the chromatographic peak. The concentrations of the samples were approximately 1.2 mg mL^{-1} in MeOH. The portion of the solution (1.4 μL) was transferred to the column.

Isolation of lactones. The extraction of a raw material (1.3 kg), the treatment of the initial ethanolic extract, and the

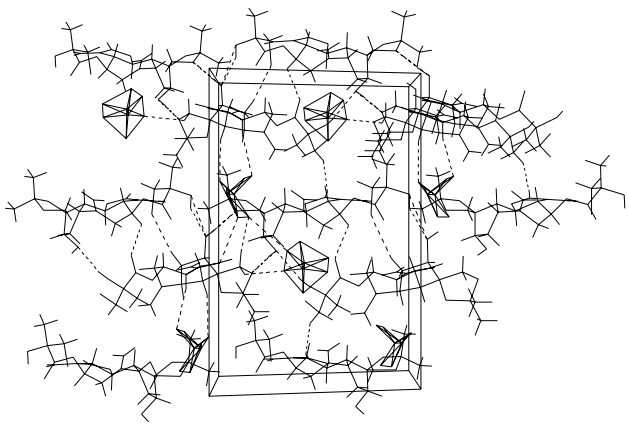

Fig. 2. Crystal packing of a solvate of compound **5** with $CHCl_3$ (projection along the axis *a*) according to the X-ray diffraction data.

isolation of the mixture of compounds soluble in PhH have been reported previously.[1] The starting mixture of compounds (10.0 g) was chromatographed on a column. Nonpolar compounds (40 mg) were eluted with mixtures of PhH and EtOAc (from 20 : 1 to 5 : 1). Flash chromatography of these compounds (light petroleum—EtOAc, from 20 : 1 to 10 : 1) afforded lactone **8** in a yield of 10 mg, m.p. 159—162 °C, $[\alpha]_{580}^{20}$ +90.0 (*c* 2.11; MeOH); *cf.* lit. data:[10] m.p. 149.5 °C, $[\alpha]_D$ +93.2 (MeOH). A fraction containing cynaropicrin and other lactones described previously[1] was eluted with mixtures of PhH and EtOAc (from 20 : 1 to 5 : 1). Subsequent elution with PhH—Me_2CO mixtures (from 3 : 1 to 1 : 1) gave rise to the fraction (900 mg) containing lactone **2**. A fraction containing component **6** (550 mg) was eluted with EtOAc—EtOH mixtures (from 20 : 1 to 15 : 1). Flash chromatography of the fraction containing lactone **2** (light petroleum—EtOAc; from 5 : 1 to 5 : 6) followed by crystallization of the raw material from a $CHCl_3$—Et_2O mixture afforded compound **2** in a yield of 195 mg (0.015% with respect to the initial air-dried raw material). Lactone **6** was prepared analogously by flash chromatography (EtOAc as the eluent) of the above-described fraction (550 mg) and recrystallization of the raw product from a mixture of EtOH and $CHCl_3$. The yield of lactone **6** was 26 mg (0.002%).

15-*O*-Deacetylrhaposerin (2), m.p. 153—155 °C; $[\alpha]_{580}^{19}$ +48.8 (*c* 0.66; Me_2CO). IR (KBr), ν/cm^{-1}: 1766 (γ-lactone), 1739 (C=O), 1668, 1643 (C=C), 1274, 1226, 1158, 1113, 1065 (C—O), 754 (C—Cl). MS, *m/z* (I_{rel} (%)): 387 $[M - CH_2OH]^+$ (^{37}Cl)] (18), 385 $[M - CH_2OH]^+$ (^{35}Cl)] (54), 265(59), 247(87), 229(71), 201(52), 175(91), 93(100). Found: *m/z* 385.10581 $[M]^+$. $C_{18}H_{22}ClO_7$. Calculated: M = 385.10539. The ^{13}C and ^1H NMR spectral data are given in Tables 1 and 2, respectively.

Rhaserin (6), m.p. 168—171 °C; $[\alpha]_{580}^{19}$ +110.9 (*c* 0.99; Me_2CO). IR ($CHCl_3$), ν/cm^{-1}: 1766 (γ-lactone), 1715 (C=O), 1632 (C=C), 1145, 1051, 910, 855. MS, *m/z* (I_{rel}(%)): 362 $[M - H_2O]^+$ (3), 349 $[M - CH_2OH]^+$ (5), 235 (10), 217(10), 175(7), 69(100). Found: *m/z* 349.12884 $[M]^+$. Calculated: M = $C_{19}H_{21}O_7$. The ^{13}C and ^1H NMR spectral data are given in Tables 1 and 2, respectively.

Acetylation of lactones 1 and 2. Pyridine (1.5 mL) and Ac_2O (2 mL) were added to a solution of lactone **1** (100 mg, 0.22 mmol) in $CHCl_3$ (1.5 mL). The reaction mixture was kept at 20 °C for 24 h, diluted with $CHCl_3$ (25 mL), and treated successively with a 5% aqueous solution of HCl (3×10 mL), a 5% aqueous solution of $NaHCO_3$ (3×10 mL), and water (2×10 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Acetates **4** and **3** were isolated by flash chromatography of the residue on a column (gradient elution with a light petroleum—EtOAc mixture; from 2.5 : 1 to 3 : 2) in yields of 24 mg (20%) and 34 mg (30%), respectively.

Acetates **4** and **3** were prepared analogously from lactone **2** (50 mg, 0.12 mmol) in yields of 10 and 19 mg, respectively. A mixture of the acetates was isolated in a yield of 110 mg from the mother liquor (120 mg) remained after crystallization of the chromatographic fraction containing lactone **1**.[1] Then diacetate **10** and a mixture of acetates **3** and **4** were successively isolated in yields of 10 and 90 mg, respectively, by flash chromatography.

Rhaposerin 3-*O*-acetate (3), a yellowish oil; $[\alpha]_{580}^{19}$ +90.1 (*c* 0.19; Me_2CO) (prepared from **1**); $[\alpha]_{580}^{19}$ +94.0 (*c* 0.23; Me_2CO) (prepared from **2**)). IR ($CHCl_3$), ν/cm^{-1}: 1770 (γ-lactone), 1740, 1640 (C=O), 1250, 1240, 1190, 1040, 1005, 955. R_f 0.24 (light petroleum—Me_2CO, 2 : 1). ^1H NMR (Py-d_5), δ: 1.62 (s, 3 H, C(17)Me); 1.69 (ddd, 1 H, H(2A), *J* = 15.0, 8.0, and 2.0 Hz); 1.81 and 1.89 (both s, 3 H each, 2×Ac); 2.49 (br.d, 1 H, H(9A), *J* = 15 Hz); 2.61—2.71 (m, 3 H, H(2B), H(5), H(9B)); 3.17 (tt, 1 H, H(7)), *J* = 9.0 and 3.0 Hz); 3.80 (ddd, 1 H, H(1), *J* = 10.5, 9.5, and 9.5 Hz); 3.92 (d, 1 H, H(18A), J_{AB} = 11.0 Hz); 4.02 (d, 1 H, H(18B), J_{AB} = 11.0 Hz); 4.69 (d, 1 H, H(15A), J_{AB} = 12.0 Hz); 4.88 (dd, 1 H, H(6), *J* = 11.5 and 9.0 Hz); 4.99 (d, 1 H, H(15B), J_{AB} = 12.0 Hz), 5.02 (br.d, 1 H, H(14A), J_{AB} = 2 Hz); 5.06 (br.d, 1 H, H(14B), J_{AB} = 2 Hz); 5.37 (ddd, 1 H, H(8), *J* = 9.0, 5.0, and 2.0 Hz); 5.55 (dm, 1 H, H(3), *J* = 7 Hz); 5.71 (d, 1 H, H(13A), $J_{7,13A}$ = 3.0 Hz); 6.08 (d, 1 H, H(13B), $J_{7,13B}$ = 3.5 Hz). The ^{13}C NMR spectral data are given in Table 3.

Rhaposerin 3,17-di-*O*-acetate (4), a yellowish oil. IR ($CHCl_3$), ν/cm^{-1}: 1770 (γ-lactone), 1740, 1640 (C=O), 1250, 1240, 1200, 1120, 1005, 955. IR (CCl_4), ν/cm^{-1}: 3590 (OH, intramolecular hydrogen bond). R_f 0.36 (light petroleum—Me_2CO, 2 : 1). ^1H NMR (Py-d_5), δ: 1.68 (s, 3 H, C(17)Me); 1.68 (ddd, 1 H, H(2A), *J* = 15.0, 8.0, and 2.0 Hz); 1.81 and 1.89 (both s, 3 H each, 2×Ac); 1.96 (s, 3 H, AcOC(17)); 2.56 (br.dd, 1 H, H(9A), *J* = 15 and 2 Hz); 2.62 (dd, 1 H, H(9B), *J* = 15.0 and 5.0 Hz); 2.65—2.72 (m, 2 H, H(2B), H(5)); 3.20 (tt, 1 H, H(7), *J* = 9.0 and 3.0 Hz); 3.82 (ddd, 1 H, H(1), *J* = 10.5, 9.5, and 9.5 Hz); 4.03 (d, 1 H, H(18A), J_{AB} = 12.0 Hz); 4.28 (d, 1 H, H(18B), J_{AB} = 12.0 Hz); 4.69 (d, 1 H, H(15A), J_{AB} = 12.0 Hz); 4.88 (dd, 1 H, H(6), *J* = 11.5 and 9.0 Hz); 4.99 (d, 1 H, H(15B), J_{AB} = 12.0 Hz); 5.02 (br.d, 1 H, H(14A), J_{AB} = 2 Hz); 5.07 (br.d, 1 H, H(14B), J_{AB} = 2 Hz); 5.37 (ddd, 1 H, H(8), *J* = 9.0, 5.0, and 2.0 Hz); 5.55 (dm, 1 H, H(3), *J* = 7 Hz); 5.76 (d, H(13A), $J_{7,13A}$ = 3.0 Hz); 6.17 (d, H(13B), $J_{7,13B}$ = 3.5 Hz). The ^{13}C NMR spectral data are given in Table 3.

Repdiolide diacetate (10), a yellowish oil. ^1H NMR (Py-d_6), δ: 1.92 (br.s, 6 H, Me(17), AcO); 1.97 (s, 3 H, AcO); 2.52 (dd, 1 H, H(9A), $J_{8,9A}$ = 2.2 Hz; J_{AB} = 15.0 Hz); 2.93 (dd, 1 H, H(9B), $J_{9B,8}$ = 5.5 Hz; J_{AB} = 15.0 Hz); 3.04 (br.t, 1 H, H(5), $J_{1,5} = J_{5,6}$ = 9 Hz); 3.08 (br.t, 1 H, H(1), $J_{1,2} = J_{1,5}$ = 9 Hz); 3.21 (tt, 1 H, H(7), $J_{6,7} = J_{7,8}$ = 9 Hz; $J_{7,13A} = J_{7,13B}$ = 3 Hz); 4.54 (br.t, 1 H, H(6), *J* = 9 Hz); 4.91 (br.d, 1 H, H(14A), J_{AB} = 2 Hz); 5.13 (br.d, 1 H, H(14B), J_{AB} = 2 Hz); 5.30 (ddd, 1 H, H(8), *J* = 2.2, 5.5, and 9.0 Hz); 5.35 (br.s, 1 H, H(15A)); 5.56 (br.d, 1 H, H(13A), $J_{7,13A}$ = 3.0 Hz); 5.57 (br.s, 1 H, H(18A)); 5.63 (br.s, 1 H, H(15B)); 5.67 (dd, 1 H, H(2), $J_{2,3}$ = 7.0 Hz, $J_{1,2}$ = 9.0 Hz); 5.92 (dt, 1 H, H(3), $J_{2,3}$ = 7.0 Hz, $J_{3,15A} = J_{3,15B}$ = 2 Hz); 6.18 (br.s, 1 H, H(18B)); 6.20 (d, 1 H, $J_{7,13B}$ = 3 Hz, H(13B)). ^{13}C NMR (Py-d_6), δ: singlets at 136.66 (C(17)), 138.57 (C(4)), 144.50 (C(10)), 166.43 (C(16)), 168.93 (C(12)), 170.27 and 170.52 (2×MeC=O); doublets at 46.89, 49.93, and 50.93 (C(1), C(5), and C(7)), 74.12 (C(8)), 77.27, 77.73, and 78.25 (C(2), C(3), and C(6)); triplets at 36.81 (C(9)), 116.05 (C(14)), 120.28 (C(13)), 121.70 (C(15)), 126.42 (C(18)); quartets at 18.22 (C(19)), 20.59, and 20.76 (2×MeC=O).

Acetonide 5. TsOH (1.5 mg) was added to a solution of compound **2** (100 mg, 0.25 mmol) in dry Me_2CO (2 mL). The reaction mixture was stirred at 20 °C for 30 min, diluted with EtOAc (30 mL), and washed with a 5% $NaHCO_3$ solution (2×10 mL). The organic phase was dried over Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the residue on SiO_2 (5 g, a 4 : 1 light petroleum—EtOAc mixture as the eluent) afforded acetonide **5** as crystals in a yield of 35 mg (32%), m.p. 160—162 °C (from a $CHCl_3$—light petroleum mixture); $[\alpha]_{580}^{19}$ +59.9 (*c* 2.37; Me_2CO). IR (KBr), ν/cm^{-1}: 1776 (γ-lactone), 1747(C=O), 1641(C=C), 1200, 1138, 1110, 1058, 1027, 1005, 965, 862. MS, *m/z* (I_{rel}(%)): 443 $[M^+(^{37}Cl) - Me]$ (36), 441 $[M^+(^{35}Cl) - Me]$ (100), 261(20), 244 (12), 243 (63), 225 (12), 215 (13), 197 (12), 95 (12), 93(24), 91(16), 59 (28), 43 (30). Found: *m/z* 441.12769 $[M]^+$. $C_{21}H_{26}ClO_8$. Calculated:

M = 441.13161. The ^{13}C and ^{1}H NMR spectral data are given in Tables 1 and 2, respectively.

Acetonide 7. TsOH (1 mg) was added to a solution of compound **6** (25 mg, 0.06 mmol) in dry Me_2CO (1.5 mL). The reaction mixture was kept at 20 °C for 30 min, diluted with EtOAc (15 mL), and washed with a 5% $NaHCO_3$ solution (2×5 mL) and water (2×5 mL). The organic layer was dried over Na_2SO_4 and concentrated *in vacuo*. Flash chromatography of the residue on SiO_2 (4 g, a 1 : 1 EtOAc—EtOH mixture as the eluent) afforded acetonide **7** as crystals in a yield of 23 mg (83%), m.p. 160—162 °C ($CHCl_3$—light petroleum); $[\alpha]_{580}^{19}$ +50.4 (*c* 1.39; Me_2CO); R_f 0.1 (light petroleum — Me_2CO (2 : 1)). IR ($CHCl_3$), ν/cm^{-1}: 1766 (γ-lactone), 1715 (C=O), 1664 (C=C), 1266, 1145, 1051, 855. MS, *m/z* (I_{rel} (%)): 405 $[M - Me]^+$ (61), 275 (4), 259 (5), 231 (7), 217 (6), 213 (17), 185 (11), 69 (100), 59 (19). Found: *m/z* 405.15422 $[M]^+$. $C_{21}H_{25}O_8$. Calculated: M = 405.15493. The ^{13}C and ^{1}H NMR spectral data are given in Tables 1 and 2, respectively.

X-ray diffraction study of acetonide **5** was performed on a Bruker P4 diffractometer (Mo-Kα radiation; graphite monochromator; 2θ/θ scanning technique; 2θ < 50°) using a crystal of dimensions 1.20×0.34×0.25 mm. The crystals are monoclinic: a = 10.545(1) Å, b = 20.100(2) Å, c = 13.688(1) Å, β = 104.01(1)°, V = 2814.9(4) Å^3, space group $P2_1$, Z = 4, $C_{23}H_{30}Cl_4O_8$, d_{calc} = 1.360 g·cm^{-3}, μ = 0.463 mm^{-1}. The intensities of 5110 independent reflections were measured. Absorption corrections were applied taking into account the crystal habitus (transmission was 0.61—0.89). The structure was solved by the direct method using the SHELXS-86 program package. The positions of the hydrogen atoms were calculated geometrically. The structural parameters were refined anisotropically by the full-matrix least-squares method using the SHELXL-97 program package. The parameters of the H atoms were not refined and their positions were calculated from the coordinates of the corresponding carbon atoms. The $CHCl_3$ molecules of solvation are disordered over two positions and form two "umbrellas" located in rather bulky cavities between the molecules of compound **5** (Fig. 2). The final refinement of the structure based on all F^2 converged to wR_2 = 0.1572, S = 1.03; 686 parameters were refined (R = 0.0535 for 4311 $F > 4\sigma$). The complete tables of the atomic coordinates and thermal parameters were deposited with the Cambridge Structural Database.

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