Tetrahedron Vol 37, No 16, pp 2769 to 2778, 1981
Printed in Great Britain

0040-4020/81/162769-10$02.00/0

STRUCTURE, CHEMISTRY AND STEREOCHEMISTRY OF RASTEVIONE, A SEQUITERPENOID FROM THE GENUS *STEVIA*

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(*Received in U.S.A. 9 February* 1981)

Abstract—The structure and relative stereochemistry of rastevione (**Ia**), the main constituent of the roots of *S. serrata* and *S. rhombifolia*, were deduced from chemical transformations combined with spectral data and by a single crystal X-ray diffraction study of rastevione acetate (**Ib**). Chemical correlation of a rastevione derivative with a molecule thought to have structure **IVb**, suggests the structures of several previously described longipinene and longipinane derivatives, should be revised. The behaviour of longipinane-7α,8β,9β-triol-1-one in the presence of periodic acid was studied, and the structure of the reaction product established from deuterium labeling experiments showed the 7α,8β diol split.

Both *S. serrata* Cav and *S. rhombifolia* HBK are widely distributed in México. Extensive study of their aereal parts, led to the isolation and structural elucidation of several sesquiterpene lactones,[1–4] but no studies of the roots have been published. In the present work, we describe the isolation, structure and relative stereochemistry of rastevione (**Ia**), the main constituent of the roots of these plants, together with some aspects of the chemistry of the natural product.

Direct crystallization of the hexane extracts of the roots of each *Stevia*, gave rastevione (**Ia**) $C_{25}H_{36}O_6$ as white plates m.p. 130–131°, $[\alpha]_D - 15°$. The IR spectrum showed hydroxyl absorption at 3600 cm^{-1} and an intense CO band at 1720 cm^{-1} while in the UV region an absorption was observed at 231 nm (log ϵ, 3.93).

The proton NMR spectrum (100 MHz) shows signals at 6.14 (2H) and in the 1.75–2.05 ppm region (12H) which is characteristic of angeloyl groups.[5] Two singlet absorptions (1H each) at 5.54 and 5.55 ppm are assigned to the ring carbons where the angeloyl esters are attached. A C$\underline{H}$–OH proton as a triplet (J = 1.2 Hz) at 3.82 ppm, an OH proton as a broad signal which disappears upon equilibration with D_2O is overlapped with other protons of the molecule in the 2.2–2.6 ppm region, a doublet (J = 6 Hz) at 3.09 ppm due to a proton *alpha* to a CO, three Me signals at 1.11, 1.05 and 0.93 ppm and a secondary Me (J = 7 Hz) at 1.09 ppm which is overlapped by two Me singlets.

The ^{13}C NMR spectrum allowed confirmation of the two angeloyl groups since two ester CO's at 166.1 and 165.8, two sp^2 singlets at 127.5 and 127.1, two sp^2 doublets at 139.8 and 139.0 and Me signals at 20.5 (2C), 15.8 and 15.7 ppm are present. In addition a ketone CO at 211.1, three O-bearing doublets at 75.0, 71.0 and 70.7 singlets at 46.0 and 35.3, doublets at 51.6, 46.4, 44.4 and 26.8, a triplet *alpha* to the CO at 41.9 and Me signals at 27.1, 20.3, 20.1 and 19.7 ppm are present.

The presence of the secondary OH group was confirmed by preparation of the monoacetate (**Ib**). The reaction required 10 hr on the steam bath to give a 27% yield, thus suggesting a strong steric hindrance. The proton NMR spectrum of **Ib** shows the acetyl singlet at 2.16, the shift of the H at the same carbon as the acetate from 3.82 in **Ia** to 5.33 and an upfield shift of one angeloyl Me group from 1.82 in **Ia** to 1.68 ppm, suggesting that the free OH group in **Ia** is *alpha* to one CH–O–angeloyl group.

Oxidation of **Ia** with chromium trioxide gave the dehydro derivative **IIa**, which shows an intense CO band in 1740–1710 cm^{-1} region and no OH absorption in the IR. The proton NMR spectrum of the diketo derivative (**IIa**) shows the protons attached to the same carbons as the angeloyl groups as an AB system (J = 12 Hz) at 5.87 and 5.31 ppm. Therefore the two angeloyl groups are located on vicinal carbons and in a *trans* arrangement. Since the secondary alcohol in **Ia** is *alpha* to one of the esters, the three O-bearing carbons in rastevione (**Ia**) are in a -CH(OH)-CH(O–angeloyl) arrangement. The small coupling constant of the CH–OH signal combined with the steric hindrance observed upon acetylation suggests that the OH and the neighboring angelate are *cis*.

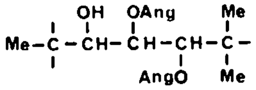
Attached to each side of the fragment containing the three O-bearing carbons, there are quaternary C atoms which were assigned from an analysis of the ^{13}C (Table 1) and proton NMR spectra. A singlet at 46.0 ppm in **Ia** is shifted to 55.0 ppm in **IIa** and is identified as the carbon adjacent to the secondary OH group. The clean AB system associated with the proton attached to the carbons containing the angeloyl moieties indicate an adjacent quaternary carbon.

Since rastevione (**Ia**) shows only two ^{13}C singlets but three Me singlets in the PMR, one of the quaternary carbons has a *gem*-dimethyl and the other carbon has an angular Me group. Therefore an eight carbon fragment of the natural product is represented either by substructure **A** or **A**'.

Further structural information about the constitution of rastevione (**Ia**) was obtained from the bisdesangeloyl derivative (**Ic**) which was prepared by catalytic hydrogenation of the double bond of the angeloyl groups to afford **Ie**, followed by alkaline hydrolysis. The sesquiterpenoid (**Ic**) showed strong OH absorption at 3530 cm^{-1} and a cyclohexanone CO band at 1715 cm^{-1} in the IR and no significative absorption in the UV. The proton NMR spectrum (270 MHz) showed the -CH(OH)-CH(OH)-CH(OH)-methine protons as a strongly coupled ABC system in the 3.6–3.9 region, Me singlets at 1.06, 1.04 and 0.95 and a Me doublet (J = 7 Hz) at 1.09 ppm. The remaining signals in the 1.7–3.2 region with the aid of spin decoupling experiments (Fig. 1) performed at 200 MHz, permitted the elucidation of a seven C atom fragment which is represented by substructure **B**.

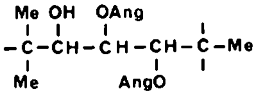
The lower trace of Fig. 1 shows the spectrum of bisdeangeloyl rastevione (**Ic**) with the exception of the Me signals. Upon equilibration with deuterium oxide, the spectrum is transformed to that shown in the next trace. The OH signals have disappeared and the coupling between the proton on the OH bearing carbon, 3.6–3.9 ppm region, and the labile proton have disappeared. The remaining traces correspond to homonuclear spin–spin decoupling experiments in which the decoupler frequency was set at 1.78, 2.04 and 2.90 ppm respectively. From these experiments one can make a complete there are now two methylene triplets at 26.9 and 23.6 ppm and no CO resonance.

In order to establish the structure of rastevione the



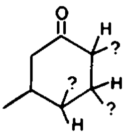
$\mathrm{Me-\overset{|}{\underset{|}{C}}-\overset{OH}{\overset{|}{C}H}-\overset{OAng}{\overset{|}{C}H}-\underset{AngO}{\underset{|}{C}H}-\overset{Me}{\overset{|}{\underset{Me}{\underset{|}{C}}}}-}$

A



$\mathrm{-\overset{Me}{\overset{|}{\underset{Me}{\underset{|}{C}}}}-\overset{OH}{\overset{|}{C}H}-\overset{OAng}{\overset{|}{C}H}-\underset{AngO}{\underset{|}{C}H}-\overset{|}{\underset{|}{C}}-Me}$

A'



B

Table 1. ^{13}C NMR data of rastevione **Ia** and derivatives*

atom	Ia	Ib	Ic	IIa	IIc	V	IX
C-1	211.1	210.4	213.8	208.7	23.6	214.4	211.7
C-2	41.9	41.4	42.0	42.3	26.9	40.9	40.8
C-3	26.8	26.5	26.8	28.1	34.1	27.1	26.8
C-4	44.4	44.2	43.9	45.7	44.0	43.8	44.8
C-5	46.4	45.8	46.1	47.0	49.0	44.3	47.5
C-6	35.3	34.8	35.3	36.7	35.0	37.3	38.5
C-7	75.0	74.4	76.2	75.7	77.4	110.7	111.7
C-8	71.0	70.5	71.4	72.6	72.2	96.2	170.9
C-9	70.7	68.3	70.6	202.2	71.2	86.1	78.7
C-10	46.0	45.0	45.7	55.0	44.3	45.9	46.8
C-11	51.6	52.2	51.5	54.8	30.8	55.4	55.2
Me	27.1	26.5	27.5	27.9	27.8	24.2	24.2
Me	20.3	20.6	20.7	21.1	21.1	21.1	20.9
Me	20.1	20.2	19.6	20.3	19.6	19.8	19.7
Me	19.7	19.4	18.6	16.8	18.8	18.9	18.3

* In ppm from internal TMS. Methyl signals are not ascribed specifically. Signals due to ester residues are given in the experimental.

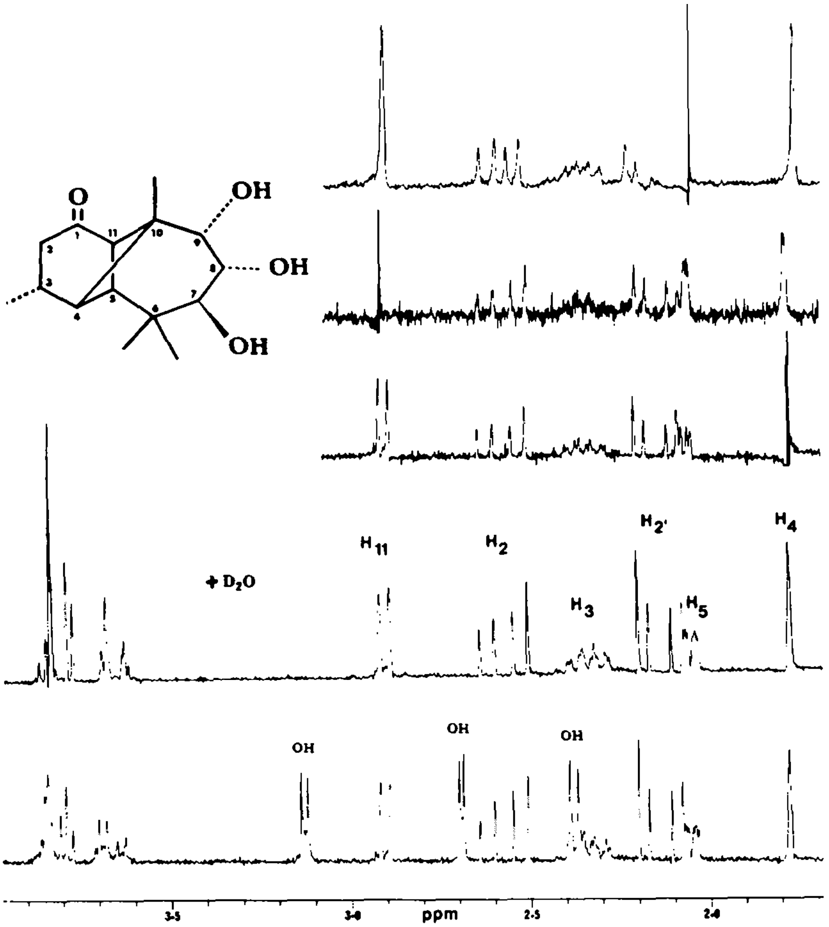


Fig. 1. Partial 200 MHz ^1H NMR spectra of Ic.

assignment of the signals in the 1.7–3.0 ppm region, if substructure **B** is considered. The protons of the methylene group *alpha* to the CO appear as the AB part ($\delta_2 = 2.57$ and $\delta_{2'} = 2.14$ ppm; $J_{2,2'} = 18.5$, $J_{2,3} = 8.5$ and $J_{2',3} = 5.8$ Hz) of an ABX system in which the X portion corresponds to H-3 and 2.33 ppm. The latter is a complex signal since it is further coupled to the secondary Me protons, to the broad singlet at 1.78 ppm which corresponds to H-4 and H-5 at 2.04 ppm with a long range coupling. In turn H-5 appears as a double doublet of doublets ($J_{5,11} = 5.5$, $J_{3,5} = 1.9$ and $J_{4,5} = 0.8$ Hz), the long range coupling being indicative of a "W type" arrangement[6] of H-3 and H-5. Finally, H-11 appears as a doublet ($J_{5,11} = 5.5$ Hz) at 2.91 ppm.

The sesquiterpenoid (**Ic**) was further characterized by preparation of the triacetate (**Id**) which showed the acetyl Me singlets at 2.13, 2.03 and 1.93 ppm in the proton NMR spectrum. Wolf-Kishner reduction of **Ia** gave the triol (**IIc**) since in the process the angelate esters are hydrolysed. The triol (**IIc**) showed no UV absorption and only OH absorption at 3540 cm^{-1} in the IR. The proton NMR spectrum (100 MHz) shows the hydrogens at the OH bearing carbons at 3.82 (1H) and 3.67 (2H), the Me doublet ($J = 7$ Hz) at 0.89 and the Me singlets at 1.02 (6H) and 0.84 (3H) ppm. The remaining signals appear in the 1.5–2.3 ppm region, in which no specific assignments can be made. In the ^{13}C NMR (Table 1) spectrum of **IIc**, substructure **B** must be properly linked to either substructure A or A′.

Since rastevione nor the described derivatives contain cyclopropyl rastevione is **Ia**.

A crystal of dimensions 0.30 × 0.30 × 0.60 mm was used to collect intensity data on a Syntex $P2_1$ diffractometer system by the $\theta:2\theta$ ($2\theta < 140°$) scanning technique using a variable scan speed and a graphite mono-chromator. Room temperature lattice parameters were refined by a least-squares procedure utilizing 15 reflections whose angles were measured by a centering routine associated with the Syntex diffractometer. Unit cell dimensions were found to be $a = 11.129(3)$, $b = 26.266(8)$, $c = 9.022(3)$ Å, $V = 2637(1)$ Å^3 with $Z = 4$ and $d_c = 1.195$ gcm^{-3}. Systematic absences were consistent with space group $P2_12_12_1$. A periodically monitored reflection showed no significant change in intensity. Of the 2679 independent reflections measured 284 had intensities less than $2\sigma(I)$ and were not used in the refinement. Four additional reflections showed significant secondary extinction and were dropped from the refinement. Lorentz and polarization corrections were applied, but no absorption corrections were made.

The direct methods program MULTAN was used[11] to calculated phases for the 300|E| values greater than 1.50. Routine application of the direct methods program did not yield a satisfactory starting set and manual selection of

Table 2. Positional parameters ($\times 10^4$, for H $\times 10^3$) for rastevione acetate **Ib**

Atom	x/a	y/b	z/c	Ueq/U$^+$
C (1)	6834(3)	4877(1)	4383(5)	5.7
O (1)	7824(2)	4766(1)	4848(5)	7.7
C (2)	6500(3)	5420(1)	4015(6)	6.1
C (3)	5127(3)	5519(1)	3923(5)	5.2
C (4)	4445(2)	5014(1)	3804(4)	4.3
C (5)	5147(3)	4668(1)	2714(4)	4.2
C (6)	4499(2)	4268(1)	1774(3)	4.2
C (7)	3916(2)	3846(1)	2695(3)	4.0
O (7)	3126(2)	3560(1)	1732(2)	4.5
C (8)	3138(2)	4051(1)	3950(3)	4.0
O (8)	2386(2)	3644(1)	4490(3)	4.9
C (9)	3853(3)	4217(1)	5294(4)	4.6
O (9)	4498(2)	3780(1)	5831(3)	5.1
C (10)	4782(3)	4650(1)	5105(3)	4.3
C (11)	5873(3)	4490(1)	4103(4)	4.6
C (12)	4837(4)	5863(1)	2606(5)	6.3
C (13)	5037(4)	4859(2)	6631(4)	5.9
C (14)	3579(3)	4543(1)	791(4)	5.3
C (15)	5451(3)	4016(2)	783(5)	5.6
C (16)	3260(3)	3050(1)	1654(5)	5.4
O (16)	4063(4)	2832(1)	2240(7)	10.6
C (17)	2291(3)	2825(1)	718(4)	5.6
C (18)	2251(4)	2332(2)	434(6)	7.2
C (19)	3069(7)	1917(2)	949(18)	11.0
C (20)	1345(4)	3180(2)	160(6)	7.6
C (21)	1199(3)	3663(1)	4182(4)	5.4
O (21)	769(2)	4008(1)	3508(5)	7.7
C (22)	577(3)	3208(2)	4805(5)	6.5
C (23)	-589(4)	3144(2)	4659(7)	8.0
C (24)	-1455(6)	3478(3)	3896(21)	11.1
C (25)	1360(5)	2818(2)	5615(7)	8.4
C (26)	4082(4)	3555(1)	7087(4)	5.6
O (26)	3294(3)	3723(1)	7833(3)	7.1
C (27)	4734(8)	3076(2)	7380(8)	8.6
H (2a)	666(6)	568(3)	471(8)	10.5
H (2b)	695(6)	552(3)	301(8)	10.2
H (3)	486(4)	565(2)	496(5)	5.4
H (4)	358(3)	509(1)	355(4)	4.8
H (5)	565(4)	485(2)	183(5)	6.7
H (7)	446(3)	362(1)	309(4)	4.1
H (8)	265(4)	432(2)	380(5)	5.5
H (9)	318(5)	435(2)	590(7)	9.0
H (11)	615(3)	407(1)	443(4)	4.5
H (12a)	491(5)	570(2)	158(7)	8.6
H (12b)	525(6)	621(2)	266(8)	10.8
H (12c)	395(5)	595(2)	263(6)	8.4
H (13a)	438(7)	497(3)	718(10)	12.6
H (13b)	534(5)	464(2)	720(7)	8.0
H (13c)	560(6)	519(3)	677(9)	11.7
H (14a)	322(4)	433(1)	-3(5)	5.5
H (14b)	400(5)	478(2)	30(6)	7.3
H (14c)	291(4)	469(2)	130(5)	7.0
H (15a)	578(5)	424(2)	24(7)	7.8
H (15b)	603(4)	381(2)	141(5)	6.2
H (15c)	506(5)	378(2)	9(7)	9.0
H (18)	152(5)	223(2)	-37(6)	7.2
H (19a)	354(8)	202(3)	175(10)	13.0
H (19b)	265(6)	161(3)	122(8)	11.5

Table 2 (*Contd*)

Atom	x/a	y/b	z/c	Ueq/U*
H (19c)	355(9)	191(3)	13(10)	13.3
H (20a)	60(4)	302(2)	-35(6)	7.2
H (20b)	85(6)	329(2)	99(8)	8.9
H (20c)	174(6)	351(3)	-23(9)	11.2
H (23)	-93(4)	283(2)	534(5)	6.1
H (24a)	-132(8)	362(4)	310(10)	12.6
H (24b)	-209(7)	331(3)	348(8)	11.1
H (24c)	-170(8)	375(4)	450(10)	14.3
H (25a)	186(7)	297(3)	644(10)	11.2
H (25b)	100(6)	256(3)	607(7)	9.5
H (25c)	208(7)	274(3)	502(10)	11.1
H (27a)	536(11)	309(4)	819(16)	17.4
H (27b)	422(7)	284(3)	762(9)	10.7
H (27c)	524(7)	302(6)	678(22)	22.9

*Ueq = (U1*U2*U3)exp(1/3)

origin and enantiomorph dependent 2-D reflections was required. Twelve different combinations were required before a satisfactory starting set was obtained. Alternate least-squares refinements and difference Fourier calculations led to the location of all atoms. Least-squares refinement was terminated at a final R of 0.056 where $R = \Sigma||F_0| - |F_c||\Sigma|F_0|$. The function minimized in the refinement was $\Sigma\omega(|F_0| - |F_c|)^2$ where $\omega = 1/\sigma(I)$ was determined from counting statistics. Hydrogen atom thermal parameters were refined isotropically.

A final difference map showed no peak larger than 0.22 e/Å^3. Atomic moieties, only alternatives **Ia** and **IV** are plausible. Complementary evidence for a longipinane[7] type structure for rastevione, was obtained by computer prediction of the ^{13}C spectra of **Ic** and **IIc** using the BASF CNMR Datenbanksystem program.[8] The theoretical resonances are in reasonable agreement with the experimental shifts; however, at present the program does not consider stereochemical differences.

A decision between structures **Ia** and **IV** was based upon X-ray work (*vide infra*), but can also be done using ^{13}C data. Analyses of the ^{13}C NMR spectra of rastevione and its chromium trioxide oxidation product revealed that upon oxidation only one Me signal is shifted from the 20 ppm region to 16.8 ppm, thus suggesting that the structure is **Ia**. However, in contrast to our conclusion, a literature search on the chemical constituents of the genus *Stevia* revealed that an oily mixture of longipinene derivatives (**III** mixed with the analog in which the ester at the central oxygen is saturated) was isolated from *S. serrata* collected in Guatemala.[9] The structures of the mixture were established primarily by comparing the proton NMR signals to those of an oily mixture of longipinanes isolated from *Polyptesis texana*.[10] This mixture also was not separated and contained **IVa** and the isovaleryl analog at the central O atom. Hydrolysis of that mixture gave a crude triolone which was immediately acetylated. The corresponding triacetate, to which structure **IVb** was ascribed, showed the same m.p. and spectral data as our derivative **Id**. Direct comparison of both samples, revealed that they are identical.

In order to obtain a definitive structural proof of rastevione (**Ia** or **IVa**) and stereochemical information, a single crystal X-ray diffracton study of rastevione acetate was undertaken. The structure and relative stereochemistry of the acetyl derivative were shown to be **Ib** and therefore positional parameters are given in Table 2 while interatomic distances, valence angles and torsion angles are presented in Tables 3–5. A perspective view of the molecular structure of rastevione acetate is shown in Fig. 2.

The 4-membered ring of rastevione acetate (**Ib**) exists in a normal puckered conformation with four equivalent torsion angles of ±23.9(1)°. The four C(sp^3)–C(sp^3) distances around the 4-membered ring average 1.562(5) Å while the remaining eleven C(sp^3)–C(sp^3) bonds average 1.530(9) Å. The four valence angles around the ring average (87.0(2). The 6-membered ring comprising C(1)...C(5)C(11) is highly distorted because of the bridging 4-membered ring. The conformation can be described as a sofa conformation which is distorted in such a way that two sets of torsion angles have the same sign (+ + − + − −). The 7-membered ring exists in a twist-chair conformation (+ − + − + − +). The bond distances and angles within the molecule are consistent with those expected from hybridization and ring strain considerations. The five C(sp^2)–C(sp^3) distances average 1.491(12) Å, while the two C(sp^2)=C(sp^2) distances average 1.319(3) Å. The three ester CO's average 1.189(2) Å, while the ketone distance is significantly longer at 1.215(4) Å. The three C(sp^2)–O(sp^3) distances average 1.353(4) Å. The two angelate groups C(7)...C(9) and C(8)...C(24) are planar as indicated by the torsion angles in Table 5.

Since the molecular constitution of rastevione has been established unambiguously as **Ia**, it would be adviseable to revise the structures of more than fifteen longipinene and longipinane, derivatives that have been isolated in recent years.[9, 10, 12, 13] These compounds were characterized mainly by proton NMR measurements and assignments were made only in mixtures.

The skeleton of rastevione (**Ia**) is quite interesting, since a 6-membered ring and a 7-membered ring, both in 1, 3 junctions are distributed around a central cyclobutane. The bisdeangeloyl derivative (**Ic**) has three OH groups on vicinal carbons, the central one being *trans* to

Table 3. Interatomic distances (Å) for rastevione acetate **Ib**

C(1)-C(2)	1.511(5)	C(9)-O(9)	1.439(4)
C(1)-C(11)	1.498(4)	C(10)-C(11)	1.571(4)
C(1)-O(1)	1.215(4)	C(10)-C(13)	1.510(5)
C(2)-C(3)	1.552(5)	O(7)-C(16)	1.350(3)
C(3)-C(4)	1.531(4)	C(16)-O(16)	1.186(6)
C(3)-C(12)	1.527(6)	C(16)-C(17)	1.492(5)
C(4)-C(5)	1.552(4)	C(17)-C(18)	1.322(5)
C(4)-C(10)	1.561(4)	C(18)-C(19)	1.494(9)
C(5)-C(6)	1.529(4)	C(17)-C(20)	1.493(6)
C(5)-C(11)	1.562(4)	O(8)-C(21)	1.351(4)
C(6)-C(7)	1.530(4)	C(21)-O(21)	1.190(5)
C(6)-C(14)	1.534(5)	C(21)-C(22)	1.492(5)
C(6)-C(15)	1.536(5)	C(22)-C(23)	1.316(6)
C(7)-C(8)	1.523(4)	C(23)-C(24)	1.475(12)
C(7)-O(7)	1.446(3)	C(22)-C(25)	1.531(7)
C(8)-C(9)	1.515(4)	O(9)-C(26)	1.359(4)
C(8)-O(8)	1.441(3)	C(26)-O(26)	1.190(5)
C(9)-C(10)	1.545(4)	C(26)-C(27)	1.475(7)

Table 4. Valence angles (degrees) for rastevione acetate **Ib**

O(1)C(1)C(2)	121.7(3)	C(8)C(9)C(10)	118.4(3)
O(1)C(1)C(11)	122.9(3)	O(9)C(9)C(10)	106.9(2)
C(2)C(1)C(11)	115.4(3)	C(9)O(9)C(26)	117.3(3)
C(1)C(2)C(3)	114.3(3)	C(4)C(10)C(9)	111.9(2)
C(2)C(3)C(4)	110.4(2)	C(4)C(10)C(11)	85.2(2)
C(2)C(3)C(12)	110.4(3)	C(4)C(10)C(13)	120.5(3)
C(4)C(3)C(12)	110.7(3)	C(9)C(10)C(11)	112.6(2)
C(3)C(4)C(5)	107.6(2)	C(1)C(11)C(5)	107.6(3)
C(3)C(4)C(10)	111.1(2)	C(1)C(11)C(10)	105.9(2)
C(5)C(4)C(10)	89.7(2)	C(5)C(11)C(10)	89.0(2)
C(4)C(5)C(6)	121.1(2)	O(7)C(16)O(16)	122.7(3)
C(4)C(5)C(11)	85.8(2)	O(7)C(16)C(17)	110.0(3)
C(6)C(5)C(11)	119.0(2)	O(16)C(16)C(17)	127.3(3)
C(5)C(6)C(7)	113.3(2)	C(16)C(17)C(18)	121.5(3)
C(5)C(6)C(14)	108.2(2)	C(16)C(17)C(20)	117.0(3)
C(5)C(6)C(15)	107.1(2)	C(18)C(17)C(20)	121.5(4)
C(7)C(6)C(14)	111.8(2)	C(17)C(18)C(19)	129.4(5)
C(7)C(6)C(15)	107.2(2)	O(8)C(21)O(21)	121.8(3)
C(14)C(6)C(15)	109.0(3)	O(8)C(21)C(22)	110.2(3)
C(6)C(7)O(7)	108.0(2)	O(21)C(21)C(22)	128.0(3)
C(6)C(7)C(8)	112.9(2)	C(21)C(22)C(23)	121.5(4)
O(7)C(7)C(8)	106.5(2)	C(21)C(22)C(25)	117.0(3)
C(7)O(7)C(16)	118.7(2)	C(23)C(22)C(25)	121.6(4)
C(7)C(8)O(8)	108.7(2)	C(22)C(23)C(24)	127.9(5)
C(7)C(8)C(9)	113.4(2)	O(9)C(26)O(26)	124.1(3)
O(8)C(8)C(9)	104.4(2)	O(9)C(26)C(27)	110.6(4)
C(8)O(8)C(21)	118.1(2)	O(26)C(26)C(27)	125.3(4)
C(8)C(9)O(9)	107.5(2)		

that at C-7 and *cis* to that at C-9. These facts made it attractive to study the behavior of **Ic** in the presence of periodic acid. It is well known[14] from mechanistic studies that *cis* glycols are more easily split than *trans* diols; however, steric factors must also be considered. Also it may be possible that during the oxidation, C-8 could be lost if the first reaction intermediate (a dialdehydealcohol) is further split in a process faster than the cyclization to a ketal.

Treatment of the triol (**Ic**) with periodic acid in

Table 5. Torsion angles (degrees) for rastevione acetate **Ib**

1-2-3-4	-15.7(5)	5-6-7-8	50.3(3)
2-3-4-5	-41.9(4)	6-7-8-9	-79.6(7)
3-4-5-11	88.1(3)	7-8-9-10	60.9(3)
4-5-11-1	-82.5(3)	8-9-10-11	-67.3(3)
5-11-1-2	33.9(4)	9-10-11-5	88.1(3)
11-1-2-3	19.7(5)	10-11-5-6	-99.6(3)
		11-5-6-7	39.1(3)
2-3-4-10	54.8(4)		
3-4-10-11	-84.9(3)	4-5-11-10	23.8(2)
4-10-11-1	84.3(3)	5-11-10-4	-23.7(2)
10-11-1-2	-60.1(4)	11-10-4-5	23.9(2)
		10-4-5-11	-24.0(2)
8-9-10-4	26.8(4)	7-O(7)-16-O(16)	- 6.8(6)
9-10-4-5	-88.6(2)	O(7)-16-17-18	177.7(4)
10-4-5-6	97.5(3)	O(16)-16-17-18	- 0.7(7)
4-5-6-7	-64.6(3)	O(7)-16-17-20	- 4.3(5)
		16-17-18-19	1.2(10)
8-O(8)-21-O(21)	- 1.3(5)	O(16)-16-17-20	177.3(5)
O(8)-21-22-25	- 0.9(5)		
O(8)-21-22-23	179.3(4)	9-O(9)-26-27	172.5(4)
O(21)-21-22-25	179.3(5)	9-O(9)-26-O(26)	- 7.0(5)
O(21)-21-22-23	- 0.4(7)		
21-22-23-24	0.7(11)		

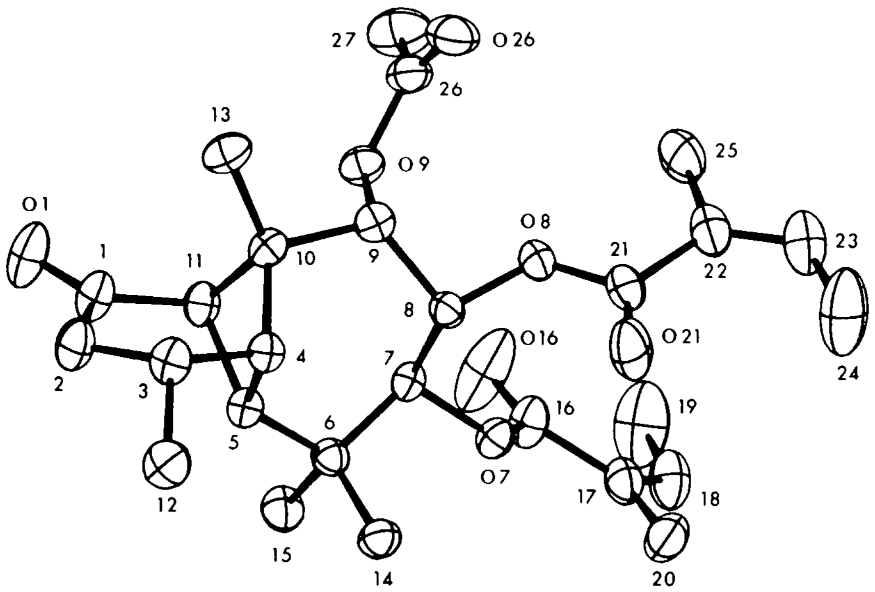
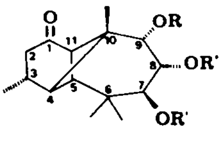
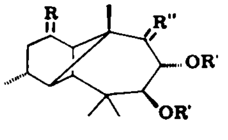


Fig. 2. Perspective view of the molecular structure of rastevione acetate **Ib**.

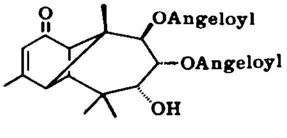
methanol gave in 84% yield a crystalline derivative $C_{15}H_{22}O_4$. All 15 C atoms of **Ic** are retained in the reaction product will no OMe singlet resonance observed, thus excluding the formation of a OMe containing ketal.[15] The 200 MHz NMR spectrum shows three Me singlets and a Me doublet in the high field region and the characteristic signals due to all the protons of the cyclohexanone ring in the 1.6–3.2 ppm region as in the case of **Ic**, except H-4 which now appears as a doublet (J = 2 Hz) with further unresolved small couplings. The remaining signals are a singlet at 3.91 due to a proton at a carbon having one oxygen and three doublets at 5.27 (J = 2 Hz), 5.23 (J = 9 Hz) and 2.80 ppm (J = 9 Hz). The latter disappears upon equilibration with D_2O, this causing also the signal at 5.23 ppm to collapse to a sharp singlet. The signals at 5.27 and 5.23 are due to protons at carbons having two O atoms and double irradiation experiments showed that H = 4 is coupled to the proton at 5.27 ppm. The ^{13}C NMR spectrum showed O-bearing carbons as doublets at 110.7, 96.2 and 86.1 ppm, the remaining signals showing similar chemical shifts as those of **Ic** (Table 1). These data are in agreement with either structure **V** or **VI** for the reaction product obtained after treatment of **Ic** with periodic acid.



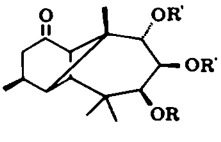
Ia: R: H ; R': Angeloyl
b: R: Ac; R': Angeloyl
c: R: H ; R': H
d: R: Ac; R': Ac
e: R: H ; R': COCH(Me)Et



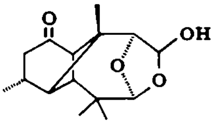
IIa: R: O ; R': Angeloyl ; R'': O
b: R: O ; R': COCH(Me)Et; R'': O
c: R: H$_2$; R': H ; R'': (→H)······OH



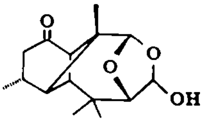
III



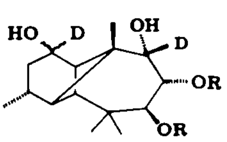
IVa: R = H ; R' = Angeloyl
b: R = Ac; R' = Ac



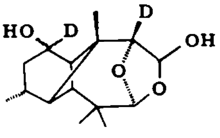
V



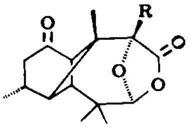
VI



VIIa: R = COCH(Me)Et
b: R = H



VIII



IXa: R: H
b: R: D

The choice between **V** or **VI** could be made by incorporating a D atom at C-9 followed by identification of the deuterated position in the product. If the rupture occurs at the C-7/C-8 bond of **Ic**, the product is **V** and D will be at a carbon bearing only one oxygen. If the C-8/C-9 bond breaks structure **VI** is obtained in which D is placed on a carbon attached to two oxygens.

In order to distinguish between **V** and **VI** the free OH group of the diester **Ie** was oxidized to the ketone **IIb**. Sodium borodeuteride treatment of **IIb** reduced the C-1 and C-9 carbonyls to a mixture of epimers (**VIIa**) at C-1. Hydrolysis of the ester groups at C-7 and C-8 gave a tetrol (**VIIb**) which was split with periodic acid to afford **VIII**. Oxidation of the latter with chromium trioxide, converted the C-1 mixture of epimeric alcohols to the ketone and the lactol to the lactone, which showed IR absorption at 1795 cm^{-1}. The product **IXb** was compared with **IXa** obtained by oxidation of **V**.

IXa and **IXb** were identical except for the isotopic composition at C-9. The reaction product obtained after treatment of **Ic** with periodic acid is clearly demonstrated to be **V**, on the proton NMR spectrum of **IXb** the 4.18 ppm singlet due to H-9 is absent and the C-9 signal at 28.2 ppm in the carbon NMR spectrum is not seen due to the repetition pulse time used to accumulate the free induction decay and the quadrupole moment of the D atom.[16] Thus in the treatment of **Ic** with periodic acid, the *trans* diol is more easily split than the *cis* diol and the intermediate alcohol–dialdehyde cyclizes faster than the attack of a second periodic acid molecule.

EXPERIMENTAL

M.ps are uncorrected. IR spectra in $CHCl_3$ were obtained on a Perkin–Elmer 421 and UV spectra in 95% EtOH on a Hitachi 200. ^1H NMR spectra in $CDCl_3$ with internal TMS were recorded on Varian Associates EM360, A60, XL-100A and XL-200 and on Bruker WH-270 spectrometers. ^{13}C NMR spectra in $CDCl_3$ with internal TMS on XL-100A-12-FT-16K using internal deuterium pulse lock. Rotations in $CHCl_3$ were obtained on a Perkin–Elmer 141M polarimeter. Chromatographic separations were made on Alcoa F-20 alumina or silica gel (Merck) and microanalyses were performed by the Alfred Bernhard Laboratories (West Germany).

Extraction of Stevia serrata *Cav*. The plant was collected near Tzindurio (State of Michoacán) in October 1978. The ground dried roots (927 g) were extracted twice with hexane (2.5 l) under reflux for 4 hr. The combined extracts were evaporated to dryness (20 g wt.). Crystallization from $CHCl_3$–hexane gave 4 g of **Ia**, m.p. 119–121°. The analytical sample was obtained by recrystallization from the same solvents and showed m.p. 130–131°; $[\alpha]_{589} - 15°$, $[\alpha]_{578} - 16°$, $[\alpha]_{546} - 18°$, $[\alpha]_{436} - 36°$ and $[\alpha]_{365} - 56°$ (c, 2); λ_{max} 231 nm, log ϵ, 3.93; ν_{max} 3600 (OH), 1720 (CO's) and 1645 cm^{-1} (C–C double bonds); ^1H NMR (100 MHz): 5.55 and 5.54 (2s, 1H each) H-7 and H-8; 3.82 (t, J = 1.2 Hz, 1H) H-9; 3.09 (d, J = 6 Hz, 1H) H-11; 1.09 (d, J = 7 Hz, 3H) Me at C-3; 1.11, 1.05 and 0.93 (3s, 3H each) *gem*-dimethyl and Me at C-10; 6.14 (qq, J_q = 7 Hz) and J_q = 1 Hz, 2H) angeloyl vinyls; 1.98 (dq, J_d = 7 Hz and J_q = 1 Hz, 6H) angeloyl Me's β to ester carbonyl; 1.82 (d_q, J_d = 1 Hz and J_q = 1 Hz, 6H) angeloyl Me's α to ester CO; the remaining 5 protons (H-2, H-2', H-3, H-4 and H-5) overlap in the 2.1 to 2.7 ppm region, where the OH proton, which disappears upon equilibration with D_2O, is also found; ^{13}C NMR;

angeloyl signals at 166.1 and 165.8 (2s, CO's), 127.5 and 127.1 (2s, C α to CO), 139.8 and 139.0 (2d, C β to CO) and 20.5 (2C), 15.8 and 15.7 ppm (4 q, methyls); the sesquiterpenoid signals are given in Table 1. (Found: C, 69.34; H, 8.22; O, 22.11; Calc. for $C_{25}H_{36}O_6$: C, 69.42; H, 8.39; O, 22.10%).

Extraction of Stevia rhombifolia *HBK*. The plant was collected 70 km east of Morelia, on the Morelia–Maravatio highway in November 1978. Extraction of 500 g of roots as in the case of *S. serrata*, gave **Ia**, m.p. 118–122°, which after recrystallization yielded the pure compound, identical in all respects with that from *S. serrata*.

Rastevione acetate **Ib**. A sample of 3 g of **Ia** in 6 ml pyridine was reacted with 6 ml Ac_2O on a steam bath for 10 hr. After work-up the residue was crystallized from EtOAc–hexane yielding 491 mg of **Ib** as white needls m.p. 165–169°. The mother liquors were chromatographed on alumina (30 g). The fractions eluted with hexane–benzene (1:1) yielded additional 399 mg of **Ib** and the more polar fractions gave 1.5 g of starting material (**Ia**). The analytical sample of **Ib** was obtained by recrystallization of EtOAc–hexane and showed m.p. 169–170°; $[\alpha]_{589} -24^\circ$, $[\alpha]_{578} -27^\circ$, $[\alpha]_{546} -32^\circ$, $[\alpha]_{436} -65^\circ$ and $[\alpha]_{365} -146^\circ$ (c, 2); λ_{max} 228 nm, log ϵ, 4.08; ν_{max} 1745 and 1720 cm^{-1} (carbonyls); ^1H NMR (100 MHz); 5.55 and 5.54 (2s, 1H each) H-7 and H-8; 5.33 (t, J = 1.1 Hz, 1H) H-9; 3.07 (d, J = 6.2 Hz, 1H) H-11; 1.12 (d, J = 7 Hz, 3H) Me at C-3; 1.11, 0.96 and 0.90 (3s, 3H each) *gem*-dimethyl and Me at C-10; 6.12 (qq, J_q = 7 Hz and J_q = 1 Hz, 2H) angeloyl vinyls; 1.97 (dq, J_d = 7 Hz and J_q = 1 Hz, 6H) angeloyl Me's β to ester CO; 1.73 and 1.68 (2dq, J_d = 1 Hz and J_q = 1 Hz, 3H each) angeloyl Me's α to ester carbonyl, 2.16 (s, 3H) acetyl Me; the remaining 5 protons (H-2, H-2', H-3, H-4 and H-5) overlap in the 2.1–2.7 ppm region; ^{13}C NMR: angeloyl signals at 165.8 and 165.4 (2s, CO's), 127.0 and 126.4 (2s, C α to CO), 140.3 and 138.8 (2d, C β to CO) and 19.7 (2C) and 15.5 (2C) ppm (4q, Me's), acetyl signals at 170.0 (s, CO) and 19.4 (q, Me), the sesquiterpenoid signals are given in Table 1. (Found: C, 68.33; H, 7.94; O, 23.42; Calc. for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07; O, 23.60%).

9-*Dehydrorastevione* **IIa**. A soln of 1 g of **Ia** in 15 ml AcOH was treated with 1 g CrO_3 in 1.5 ml H_2O and 10 ml AcOH. After 1 hr at room temp., it was diluted with ice water and extracted with Et_2O. The organic layer was washed with water, $NaHCO_3$ aq and water again, dried over Na_2SO_4, filtered and evaporated to dryness. The residue was chromatographed on silica gel (15 g) and the fractions eluted with benzene crystallized. They were combined and recrystallized to yield 520 mg of **IIa** as white plates m.p. 92–94°. The analytical sample was obtained by recrystallization from $CHCl_3$ hexane and showed m.p. 94–95°; $[\alpha]_{589} +47^\circ$, $[\alpha]_{578} +48^\circ$, $[\alpha]_{546} +46^\circ$, $[\alpha]_{436} +133^\circ$ and $[\alpha]_{365} +389^\circ$ (c, 2); λ_{max} 230 nm, log ϵ, 3.83; ν_{max} 1740–1710 (broad, CO's) and 1650 cm^{-1} (C–C double bonds); ^1H NMR (60 MHz): 5.87 and 5.31 (2d, J = 12 Hz, 1H each) H-7 and H-8; 1.17 (d, J = 7 Hz, 3H) Me at C-3; 1.25, 1.11 and 1.03 (3s, 3H each) *gem*-dimethyl and Me at C-10; 6.14 (qq, J_q = 7 Hz and J_q = 1 Hz, 2H) angeloyl vinyls; 2.1 to 1.8 (complex, 12H) angeloyl Me's; the remaining 6 protons (H-2, H-2', H-3, H-4, H-5 and H-11) overlap in the 2.0–2.8 ppm region: ^{13}C NMR: angeloyl signals at 167.2 and 166.9 (2s, CO's), 128.0 and 127.7 (2s, C α to CO), 141.0 and 140.6 (2d, C β to CO) and 21.5, 21.4, 16.8 and 16.4 (4q, Me's); the sesquiterpenoid signals are shown in Table 1. (Found: C, 69.82; H, 7.93; O, 22.18; Calc. for $C_{25}H_{34}O_6$: C, 69.74; H, 7.96; O, 22.30%).

Tetrahydrorastevione **Ie**. A soln of 3 g of **Ia** in 400 ml AcOEt was stirred in the presence of 200 mg prehydrogenated 10% Pd on activated charcoal catalyst under H_2 at room temp. and normal pressure until the uptake of H_2 ceased. The catalyst was removed by filtration and the solvent evaporated to dryness. The oily residue showed no significative UV absorption and contained a mixture of epimeric saturated esters, as could be deduced from ^{13}C NMR measurements.

Bisdeangeloyl rastevione **Ic**. The crude product **Ie** of the previous reaction was dissolved in MeOH, treated with 3 g $KHCO_3$ in 3 ml water and refluxed during 2 hr. The solvent was evaporated to a small volume, diluted with water and extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4 and evaporated to dryness. The residue was crystallized from $CHCl_3$–hexane yielding 1.5 g of the title compound m.p. 68–70°. The analytical sample obtained by recrystallization from the same solvents showed m.p. 76–78°; $[\alpha]_{589} +24^\circ$, $[\alpha]_{578} +24^\circ$, $[\alpha]_{546} +27^\circ$, $[\alpha]_{436} +32^\circ$ and $[\alpha]_{365} -5^\circ$ (c, 2); ν_{max} 3530 (OH's) and 1715 cm^{-1} (CO); ^1H NMR (200 MHz): 3.9 to 3.6 (complex, ABC system, 3H) H-7, H-8 and H-9; 2.91 (d, $J_{5,11}$ = 5.5 Hz, 1H) H-11; 2.57 (dd, $J_{2,2'}$ = 18.5 Hz and $J_{2,3}$ = 8.5 Hz, 1H) H-2; 2.33 (complex, 1H) H-3; 2.14 (dd, $J_{2,2'}$ = 18.5 Hz and $J_{2',3}$ = 5.8 Hz, 1H) H-2'; 2.04 (ddd, $J_{5,11}$ = 5.5 Hz, $J_{3,5}$ = 1.9 Hz and $J_{4,5}$ = 0.8 Hz, 1H) H-5; 1.78 (broad s, 1H) H-4; 3.02, 2.70 and 2.48 (3d, disappearing after equilibration with D_2O) 3 OH; 1.09 (d, J = 7 Hz, 3H) Me at C-3; 1.06, 1.04 and 0.95 ppm (3s, 3H each) *gem*-dimethyl and Me at C-10; ^{13}C NMR: see Table 1. (Found: C, 66.93; H, 8.90; O, 23.99; Calc. for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01; O, 23.85%).

Triacetate **Id**. Acetylation of 200 mg of **Ic** in 2 ml pyridine and 2 ml Ac_2O on the steam bath for 2 hr, followed by work and crystallization of the residue from $CHCl_3$–hexane gave 130 mg of the title compound. Recrystallization from the same solvents gave white needls m.p. 150–152°; $[\alpha]_{589} -2^\circ$, $[\alpha]_{578} -5^\circ$, $[\alpha]_{546} -6^\circ$, $[\alpha]_{436} -22^\circ$ and $[\alpha]_{365} -84^\circ$ (c, 2); ν_{max} 1745 and 1720 cm^{-1} (CO's); ^1H NMR (60 MHz) 5.25 (s, 2H) H-7 and H-8; 5.16 (t, J = 1.2 Hz, 1H) H-9; 3.01 (d, J = 6 Hz, 1H) H-11; 2.13, 2.03 and 1.93 (3s, 3H each) acetyl Me's; 1.00 (d, J = 7 Hz, 3H) Me at C-3; 1.05, 0.93 and 0.88 ppm (3s, 3H each) *gem*-dimethyl and Me at C-10; the remaining 5 protons (H-2, H-2', H-3, H-4 and H-5) overlap in the 2.1 to 2.7 ppm region. The sample (**Id**) is identical with a derivative from a natural products mixture, isolated from *Polypteris texana*.[10]

Triol **IIc**. A solution of 2 g of **Ia** in 15 ml 98% hydrazine, 15 ml ethylene glycol and 4 g powder KOH was refluxed for 7 hr. The residue obtained after work up, was chromatographed over 30 g silica gel. The fractions eluted with $CHCl_3$:AcOEt (3:1) crystallized. They were combined and recrystallized from $CHCl_3$–hexane to yield 300 mg of **IIc**, m.p. 129–131°; $[\alpha]_{589} +58^\circ$, $[\alpha]_{578} +67^\circ$, $[\alpha]_{546} +74^\circ$, $[\alpha]_{436} +122^\circ$ and $[\alpha]_{365} +174^\circ$ (c, 2); ν_{max} 3540 cm^{-1} (hydroxyls); ^1H NMR (100 MHz): 3.85 to 3.65 (complex, ABC system, 3H) H-7, H-8 and H-9; 3.12 (1H) and 2.50 (2H) which disappear with D_2O and are due to 3OH; 0.87 (d, J = 7 Hz, 3H) Me at C-3; 1.02 (s, 6H) and 0.84 (s, 3H) *gem*-dimethyl and Me at C-10; the remaining 8 protons (H-1, H-1', H-2, H-2', H-3, H-4, H-5 and H-11 overlap in the 1.5 to 2.3 ppm region; ^{13}C NMR: see Table 1. (Found: C, 70.93; H, 10.06; O, 18.89; calc. for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30; O, 18.87%).

Periodic acid oxidation of **Ic**. A soln of 630 mg of **Ic** in 10 ml MeOH was mixed with 630 mg HIO_4 in 1 ml water at room temp. After 2 hr, the mixture was diluted with water and extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4, filtered and evaporated. Crystallization of the residue from $CHCl_3$–hexane gave 530 mg of **V** as white needls m.p. 129–131°. The analytical sample, obtained by recrystallization from the same solvents showed m.p. 138–139°; $[\alpha]_{589} -83^\circ$, $[\alpha]_{578} -87^\circ$, $[\alpha]_{546} -98^\circ$, $[\alpha]_{436} -154^\circ$ and $[\alpha]_{365} -200^\circ$ (c, 2); ν_{max} 3580 (OH) and 1715 cm^{-1} (CO); ^1H NMR (200 MHz); 5.27 (d, $J_{4,7}$ = 2 Hz 1H) H-7; 5.23 (d, J = 9 Hz which collapses to a singlet upon addition of D_2O, 1H) H-8; 3.91 (s, 1H) H-9; 3.11 (d, $J_{5,11}$ = 6 Hz, 1H) H-11; 2.80 (d, J = 9 Hz which disappears upon addition of D_2O, 1H) OH; 2.52 (dd, $J_{2,2'}$ = 18.5 and $J_{2,3}$ = 8 Hz, 1H) H-2; 2.48 (d, $J_{5,11}$ = 6 Hz, 1H) H-5; 2.24 (complex, 1H) H-3; 2.04 (dd, $J_{2,2'}$ = 18.5 and $J_{2',3}$ = 5.5 Hz, 1H) H-2'; 1.61 (d, $J_{4,7}$ = 2 Hz, 1H) H-4; 1.06 (d, J = 7 Hz, 3H) Me at C-3 and 0.93 (s, 6H) and 1.00 ppm (s, 3H) *gem*-dimethyl and Me at C-10; ^{13}C NMR: see Table 1. (Found: C, 67.49; H, 8.14; O, 24.01; Calc. for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33; O, 24.03%).

Lactone **IXa**. A soln of 560 mg of **V** in 10 ml AcOH was treated with 560 mg of CrO_3 in 1 ml of water and 8 ml of AcOH. After 2 hr at room temp. the mixture was diluted with water and extracted with ether. The organic layer was washed with water, aq $NaHCO_3$ and water again, dried over anh Na_2SO_4, filtered and evaporated. The residue was crystallized from chloroform–hexane, yielding 344 mg of the title compound m.p. 126–128. The analytical sample, obtained after recrystallization from the same solvents showed m.p. 128–130°; $[\alpha]_{589} -90^\circ$, $[\alpha]_{578} -98^\circ$, $[\alpha]_{546} -106^\circ$, $[\alpha]_{436} -162^\circ$ and $[\alpha]_{365} -162^\circ$ (c, 2); ν_{max} 1795 (lactone) and

1710 cm^{-1} (ketone); ^{1}H NMR (100 MHz); 5.48 (d, $J_{4,7} = 2$ Hz, 1H) H-7; 4.18 (s, 1H) H-9; 3.20 (d, $J_{5,11} = 6$ Hz, 1H) H-11; 2.58 (dd, $J_{2,2'} = 18$ and $J_{2,3} = 8$ Hz, 1H) H-2; 2.38 (complex, 1H) H-3; 2.23 (d, $J_{5,11} = 6$ Hz, 1H) H-5; 2.08 (dd, $J_{2,2'} = 18$ and $J_{2',3} = 5$ Hz, 1H) H-2′; 1.76 (broad s, 1H) H-4; 1.06 (d, J = 7 Hz, 3H) Me at C-3; 1.09, 1.03 and 1.01 ppm (3s, 3H each) *gem*-dimethyl and Me at C-10; ^{13}C NMR see Table 1. (Found: C, 68.05; H, 7.56; O, 24.14; Calc. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63; O, 24.21%).

Lactone **IXb**. A solution of 1 g of **Ie** was oxidized with 1.0 g CrO_3 in AcOH as previously. After work up, an oily mixture of esters **IIb** was obtained. It showed ν_{max} 1740 and 1720 cm^{-1} (carbonyls) and ^{1}H NMR: 5.65 and 5.15 ppm (2d, $J_{7,8} = 12$ Hz, 1H each); the remaining signals overlap completely. The mixture **IIb** was dissolved in 15 ml of MeOH and treated with 500 mg of $NaBD_4$ at 0° for 30 min. The reaction mixture was diluted with water and extracted with AcOEt. The organic layer was washed with water, dried over anh Na_2SO_4, filtered and evaporated. This yielded an oily mixture of **VIIa**, which was immediately dissolved in 40 ml of MeOH and refluxed in the presence of 1 g of $KHCO_3$ in 2 ml water for 2 hr. The soln was concentrated, diluted with water and extracted with AcOEt. The organic layer was washed with water, dried over Na_2SO_4, filtered and evaporated. The colorless oily residue **VIIb** showed ν_{max} 3570 cm^{-1} (OH's); ^{1}H NMR C$\underline{H}$OH signals in the 4.66 to 3.53 ppm. This mixture of isomeric tetrols **VIIb** was treated with 500 mg of HIO_4 as previously. After work up, the residue containing C-1 epimers of **VIII** failed again to crystallize and it was immediately oxidized with CrO_3 in AcOH as previously. After work up, the residue was crystallized from $CHCl_3$–hexane. This yielded 90 mg of **IXb** as white needls m.p. 128–130°. It showed no depression in a mixed m.p. with **IXa**. The ^{1}H NMR and ^{13}C NMR were identical with those of **IXa** excepting the H-9 signal at 4.18 ppm and the C-9 signal at 78.7 ppm which were absent.

Supplementary material available. Crystallographic data including anisotropic thermal parameters and a listing of observed and calculated structure factors have been deposited. Ordering information is given on any current masthead page.

Acknowledgements—We are grateful to Dr. Jirzy Rzedowsky (Departamento Botánico, Escuela Nacional de Ciencias Biológicas, IPN, México) for the classification of the plant material, to Dr. J. N. Shoolery and the Varian Associates NMR Applications Laboratory (Palo Alto, U.S.A.) for granting the XL-200 instrument time, to Drs. W. Brügel and W. Bremser (BASF-AG, Ludwigshafen, West Germany) for the 270 MHz NMR spectrum and the BASF-Datenbanksystem calculations respectively and to Prof. F. Bohlmann (West Berlin) for establishing the identity of **Id**. The work in México was partially supported by CoNaCyT and SEP and that in U.S.A. by The Robert A. Welch Foundation (P-074).

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