dissolved in dioxane (40 mL) was hydrogenated over palladium-on-barium sulfate catalyst (0.02 g) in the presence of quinoline (0.2 g). When the hydrogen absorption ceased, the catalyst was filtered off and the solvent was removed in vacuo, leaving a residue (0.081 g), which was dehydrated in xylene–tetrahydrofuran (4:1 v/v) solution with boron trifluoride etherate (0.9 mL) in the presence of hydroquinone (0.02 g) by boiling in a reflux condenser during 3.5 h. After cooling, the reaction mixture was treated with 10% aqueous sodium hydroxide (4 mL), taken in ethyl ether (150 mL), washed with water, and dried over anhydrous magnesium sulfate. Upon removal of the solvent the residue was purified by chromatography which gave **4** oil (0.052 g, 56% yield): ^{1}H NMR δ 6.25, 5.20, 4.90 (3 × dd, 3 × 1 H, olefin, J_1 = 2.0, J_2 = 10.9, J_3 = 17.3 Hz), 1.51 (s, 3 H, C-6 CH_3), 0.98 (s, 3 H, C-4 CH_3), 0.88 and 0.85 (2 × s, 2 × 3 H, 2 × C-1 CH_3); IR (Nujol) 1640, 1600 cm^{-1} (C=C); UV (EtOH, *c* 1) λ_{max} 228 nm (ϵ 21 500); mass spectrum (70 eV), *m/e* 218, 136, 128. Anal. Calcd for $C_{16}H_{26}$: C, 88.10; H, 11.80. Found: C, 88.01; H, 11.98.

(±)-8ξ,13-Epoxy-13,13-dicarbethoxy-14,15,16-trisnorlabd-9(11)-ene (5). Compound **4** (0.05 g, 0.23 mmol), diethyl mesoxalate (0.044 g, 0.27 mmol), and dry methylene chloride (15 mL) were charged in special Teflon-brand vessel which was placed in very high-pressure apparatus. The pressure was set for 20 kbar. After stabilization of pressure, the temperature was set to 55 °C. The reaction mixture was kept under these conditions during 20 h. After decompression, the solvent was removed in vacuo and the residue was chromatographed by using hexane–ethyl acetate (95:5 v/v) solution. Pure **5**, oil (0.033 g, 35% yield), was obtained as a mixture of diastereoisomers, homogeneous by TLC analysis: ^{1}H NMR δ 5.65 (m, 1 H, C-11 H), 4.35 (m, 4 H, 2 × OCH_2CH$_3$), 2.45 (m, 2 H, C=CCH_2), 1.40–0.75 (m, 29 H, among them C-4 CH_3, C-8 CH_3, C-10 CH_3, OCH$_2$CH_3); IR (Nujol) 1740 (C=O), 1620 cm^{-1} (C=C); mass spectrum (70 eV), *m/e* 392, 350, 111, 109. Anal. Calcd for $C_{23}H_{36}O_5$: C, 70.40; H, 9.19. Found: C, 70.43; H, 9.35.

(±)-8ξ,13-Epoxy-13,13-dicarbethoxy-14,15,16-trisnorlabdan (6). Compound **5** (0.05 g, 0.12 mmol) was hydrogenated in methanol over 10% palladium-on-charcoal catalyst during 20 h. After removal of the catalyst and the solvent, the residue was separated into **6a** and **6b** by preparative HPLC (hexane–ethyl acetate, 95:5 v/v). The ratio of **6a**:**6b** was 65:35 (total yield 90%). Compound **6a**: ^{1}H NMR δ 4.30 (q, 4 H, 2 × OCH_2CH$_3$, *J* = 7.5 Hz), 1.35 (s, 3 H, C-8 CH_3), 1.30 (t, 6 H, 2 × OCH$_2$CH_3, *J* = 7.5 Hz), 1.20 (s, 3 H, C-10 CH_3), 0.85 (s, 6 H, 2 C-4 CH_3); IR (film) 1740 cm^{-1} (C=O); mass spectrum (70 eV), *m/e* 394, 350, 109. Anal. Calcd. for $C_{23}H_{38}O_5$: C, 70.06; H, 9.64. Found: C, 70.40; H, 9.70. Compound **6b**: ^{1}H NMR δ 4.35 (q, 4 H, 2 × OCH_2CH$_3$), 1.25 (t, 6 H, 2 × OCH$_2$CH_3), 1.25 (s, 3 H, C-8 CH_3), 0.95 (s, 3 H, C-10 CH_3), 0.80 (s, 6 H, 2 × C-4 CH_3); IR (film) 1740 cm^{-1} (C=O); mass spectrum (70 eV), *m/e* 394, 350, 126, 111. Anal. Calcd for $C_{23}H_{38}O_5$: C, 70.06; H, 9.64. Found: C, 70.25; H, 9.78.

(±)-8α,13-Epoxy-14,15,16-trisnorlabdan-13-one (7a, Ambreinolide). Compound **6a** (0.05 g, 0.12 mmol) was dissolved in 5% methanolic potassium methoxide solution (20 mL), and the reaction mixture was boiled on a reflux condenser during 4 h. After cooling, the mixture was neutralized with dilute hydrochloric acid, treated with water (50 mL), and extracted with ethyl ether. The ether extract was dried over anhydrous magnesium sulfate. Upon removal of the solvent the residue was dissolved in benzene (12 mL) and treated with oxalyl chloride (0.015 g, 0.12 mmol) and pyridine (0.009 g, 0.11 mmol). The reaction mixture was boiled on a reflux condenser during 1.5 h. Subsequently, the solvent and an excess of oxalyl chloride were removed in vacuo. The residue was dissolved in dry acetonitrile (8 mL), treated with sodium azide (0.014 g, 0.21 mmol), and stirred at room temperature for 2 h. Subsequently, acetonitrile was removed in vacuo and the residue was treated with cyclohexane (8 mL) and heated to boiling under nitrogen for 2 h. After removal of the solvent, the residue was treated with 5% tetrahydrofuran oxalic acid solution (15 mL) and the stirring was continued at room temperature for 1 h. The reaction mixture was taken in ethyl ether (60 mL), washed with diluted aqueous sodium hydroxide solution, water, and dried over anhydrous magnesium sulfate. Upon removal of the solvent the residue was chromatographed using hexane–ethyl acetate gradient system and gave **7a** (0.0047 g, 20% yield): solid, mp 139–141 °C; ^{1}H NMR δ 1.05 (s, 3 H, C-8 CH_3), 0.85 (s, 3 H, C-10 CH_3), 0.80 (s, 6 H, 2 × C-4 CH_3); IR ($CHCl_3$) 1720 cm^{-1} (C=O); mass spectrum (70 eV), *m/e* 264, 192, 109, 82.

(±)-8β,13-Epoxy-14,15,16-trisnorlabdan-13-one (7b,8-Epiambreinolide). Compound **7b** was prepared from **6b** in an analogous manner as **7a** from **6a**. Thus from **6b** (0.03 g, 0.076 mmol), **7b** (0.002 g, 18% yield) solid, mp 140–150 °C, was obtained: IR ($CHCl_3$) 1720 cm^{-1} (C=O); mass spectrum (70 eV), *m/e* 264, 221, 191, 126, 111.

Registry No. (±)-**1**, 65556-24-3; (±)-**2** (isomer 1), 98048-49-8; (±)-**2** (isomer 2), 98048-50-1; **3**, 97974-42-0; dihydro-**3**, 97974-46-4; (±)-**4**, 97974-43-1; (±)-**5** (isomer 1), 97974-44-2; (±)-**5** (isomer 2), 98048-51-2; (±)-**6a**, 97974-45-3; (±)-**6a** (diacid), 97974-47-5; (±)-**6a** (diacid chloride), 97974-48-6; (±)-**6a** (diazide), 97974-49-7; (±)-**6a** (diisocyanate), 97974-50-0; (±)-**6b**, 98048-52-3; (±)-**6b** (diacid), 98048-54-5; (±)-**6b** (diacid chloride), 98048-55-6; (±)-**6b** (diazide), 98048-56-7; (±)-**6b** (diisocyanate), 98048-57-8; (±)-**7a**, 7663-46-9; (±)-**7b**, 98048-53-4; CH≡CH, 74-86-2; diethyl mesoxalate, 609-09-6.

Structural and Stereochemical Studies of Naturally Occurring Longipinene Derivatives

Luisa U. Román,*[1a] Rosa E. del Río,[1b] Juan D. Hernández,[1a] Carlos M. Cerda,[1a] Daniel Cervantes,[1a] Raúl Castañeda,[1a] and Pedro Joseph-Nathan*[1b]

Instituto de Investigaciones Químico Biológicas, Universidad Michoacana de San Nicolás de Hidalgo, Morelia, Michoacán, 58240 Mexico, and Departamento de Química del Centro de Investigación y de Estudios Avanzados, Instituto Politécnico Nacional, A. P. 14-740 México, D. F., 07000 Mexico

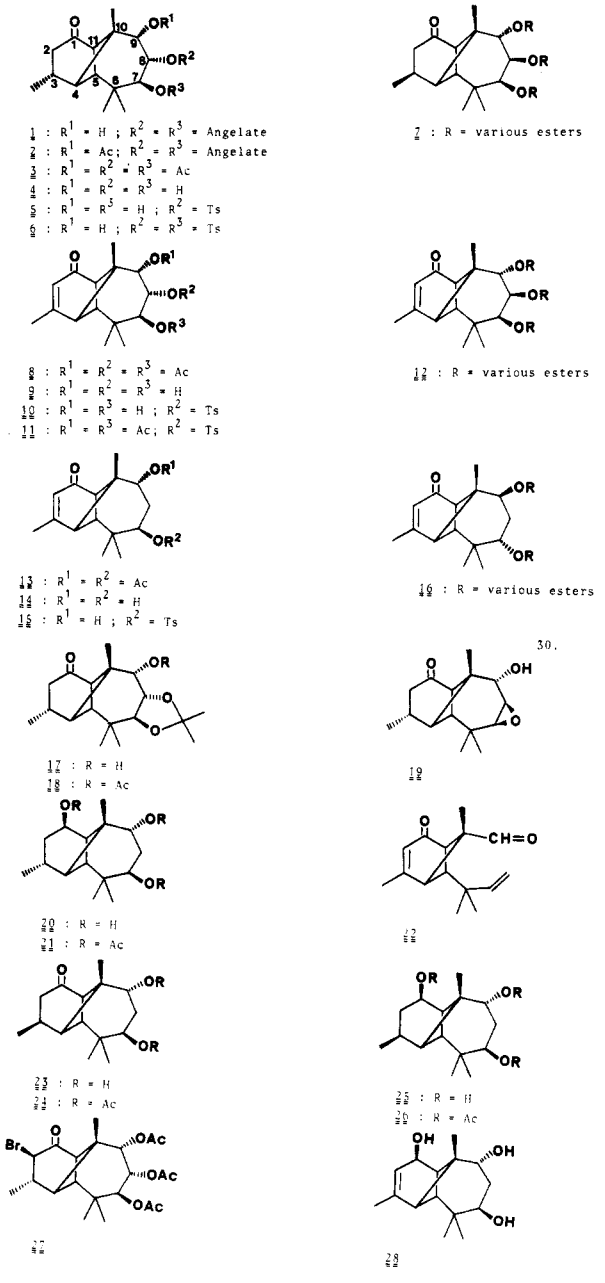
Received January 25, 1985

The introduction of a double bond into the six-membered ring of the rastevione (**1**) skeleton gave a compound (**8**) whose spectral data are in excellent agreement with those of a substance previously thought to be **12**. Further selective elimination of the oxygen atom from C-8 gave **14**, previously formulated as **16**. This allows us to reassign the structures of several longipinenetriolones and longipinenediolones found as constituents of *Stevia* and *Polypteris*. The selective derivatization of **14** followed by controlled cleavage of the seven-membered ring permitted us to assign the H-7 and H-9 NMR signals, which in turn allows us to ascertain the positions at which ester residues are placed by nature. Some NMR signals are reassigned in view of the results of a ^{13}C/^{1}H heteronuclear chemical shift correlation experiment.

Extensive studies of the genus *Stevia*, which is widely distributed through the American continent, have led to isolation and structural elucidation of a variety of sesquiterpene lactones,[2] diterpenes,[3] flavones,[4] and longipi-

0022-3263/85/1950-3965$01.50/0

Chart I



nane derivatives.[5-7] Most of the pertinent literature has been summarized recently.[2]

In previous work[8] we described isolation of rastevione (1) from the roots of the Mexican plants *Stevia rhombifolia* and *S. serrata*. The gross structure of the natural product 1 was ascertained from spectral studies combined with chemical transformations, but to establish the stereochemistry, we were force to resort to X-ray analysis of the derived acetate (2) (Chart I). In view of the identity of triacetate 3 with a sample to which stereochemistry 7 had been assigned previously,[6] we suggested that revision was necessary of the structures of several other longipinene derivatives to which stereochemistries 12 and 16 had been assigned.[5-7,9]

In the present paper we describe the chemical transformation of rastevione (1) to both 8 and 14. The results verified our assumption and require reassignment of naturally occurring longipinenes previously thought to be 12 and 16 as esters derived from 9 and 14, respectively.

Results and Discussion

The main chemical differences between rastevione (1) and longipin-2-ene-7β,9α-diol-1-one (14) are the degree of unsaturation at the six-membered ring and the oxygen atom at position 8. Thus, to correlate these two substances, chemical changes in both the six- and the seven-membered rings are required. In order to secure large amounts of triolone 4 as the substance for the correlation, rastevione (1) was hydrolyzed by means of potassium cyanide in ethanol–water mixtures. This procedure turned out to be simpler than catalytic hydrogenation of the unsaturated ester residues followed by alkaline hydrolysis.[8] Under these conditions initial Michael-type addition of HCN saturates the angelates and the basic medium thereby generated causes hydrolysis of the saturated esters.

It is known[8] that periodic acid treatment of 4 cleaves the trans diol at positions 7 and 8, rather than the cis diol at C-8 and C-9. To protect two of the oxygen atoms of 4 in order to operate on the third, it was converted to an acetonide whose structure could be deduced only after acetylation of the remaining free hydroxyl group. The ^{1}H NMR spectrum of the acetate 18 clearly showed that formation of the acetonide involves utilization of the 7β and 8α oxygen atoms since H-7 appears as a doublet ($J_{7,8}$ = 10 Hz) at 3.90 ppm, H-8 as a double doublet ($J_{7,8}$ = 10 Hz; $J_{8,9}$ = 3 Hz) at 4.10 ppm, and H-9 as a doublet ($J_{8,9}$ = 3 Hz) at 5.34 ppm. The remaining spectral data of this and other molecules are given in the Experimental Section, with the exception of the ^{13}C NMR data, which are summarized in Table I.

Consistent with this result, treatment of triolone 4 with *p*-toluenesulfonyl chloride gave a mixture of monotosylate 5 and ditosylate 6 in a 5:1 ratio as judged by ^{1}H NMR analysis. Chromatographic separation of this mixture turned out to be difficult. Consequently the mixture was allowed to react with potassium hydroxide in methanol–water. In this way the ditosylate 6 remained unchanged, while monotosylate 5 was converted to epoxide 19. Two clearly different types of crystals were separated mechanically from the mixture of 6 and 19 and recrystallized to afford the pure compounds.

Lithium aluminum hydride reduction of 19 afforded triol 20 by attack on C-8 from the α side and simultaneous reduction of the carbonyl group. That the C-1 hydroxyl was β was shown by the H-1 signal which appears as a td (J = 7.5, 3.5 Hz) at 4.35 ppm. The remaining two protons at C-7 and C-9 show the same multiplicities as those of longipin-2-ene-7,9-diol-1-one (14) that we obtained by hydrolysis of a mixture of natural esters isolated from the roots of *Stevia salicifolia*. One signal is a dd (J = 10, 3 Hz) at 3.96 ppm in the case of 20 and at 3.93 ppm in 14, while the other one is a t (J = 4 Hz) at 3.87 ppm in 14 and at 3.72 ppm in 20. Similarly, in triacetate 21 the H-1 signal

(1) (a) IIQB-UMSNH, Morelia. (b) CIEA-IPN, Mexico City.
(2) Oberti, J. C.; Sosa, V. E.; Herz, W.; Prasad, J. S.; Goedken, V. L. *J. Org. Chem.* **1983**, *48*, 4038.
(3) Kinghorn, A. D.; Soejarto, D. D.; Nanayakkara, N. P. D.; Compadre, C. M.; Makapugay, H. C.; Hovanec-Brown, J. M.; Medon, P. J.; Kamath, S. K. *J. Nat. Prod.* **1984**, *47*, 439.
(4) Rajbhandari, A.; Roberts, M. F. *J. Nat. Prod.* **1983**, *46*, 194; **1984**, *47*, 559.
(5) Bohlmann, F.; Zdero, C.; Schöneweiss, S. *Chem. Ber.* **1976**, *109*, 3366.
(6) Bohlmann, F.; Suwita, A.; Natu, A. A.; Czerson, H.; Suwita, A. *Chem. Ber.* **1977**, *110*, 3572.
(7) Bohlmann, F.; Dutta, L. N.; Dorner, W.; King, R. M.; Robinson, H. *Phytochemistry* **1979**, *18*, 673.
(8) Román, L. U.; de Río, R. E.; Hernández, J. D.; Joseph-Nathan, P.; Zabel, V.; Watson, W. H. *Tetrahedron* **1981**, *37*, 2769.
(9) Bohlmann, F.; Zdero, C. *Chem. Ber.* **1975**, *108*, 3543.

Table I. ^{13}C NMR Chemical Shifts for Longipinane Derivatives[a]

compd	C-1	C-2	C-3	C-4	C-5	ratio E/Z	C-7	C-8	C-9	C-10	C-11	C-12	quaternary methyls		
1	211.1	41.9	26.8	44.4	46.4	35.3	71.0	70.7	75.0	46.0	51.6	19.7	27.1	20.3	19.7
2	210.4	41.4	26.5	44.2	45.8	34.8	70.5	68.3	74.4	45.0	52.2	19.6	26.5	19.4	18.6
3	210.6	41.6	26.8	44.3	46.0	35.0	71.0	69.3	74.3	45.0	52.3	19.7	26.7	20.7	19.5
4	213.8	42.0	26.8	43.9	46.1	35.5	71.4	70.6	76.2	45.7	51.5	19.6	27.5	20.7	18.6
5	211.9	41.8	26.8	44.0	46.1	35.3	69.0	83.0	75.5	45.8	51.3	19.6	27.2	20.4	18.2
6	210.5	41.7	26.6	44.2	46.1	35.5	78.8	77.7	75.1	45.8	51.2	19.6	27.4	20.1	18.7
8	201.7	122.7	170.3	47.9	65.0	36.1	70.6	69.3	74.6	54.3	53.0	23.2	26.2	20.5	19.5
9	204.7	122.3	171.8	48.1	66.1	36.7	70.7	70.5	76.0	55.9	52.1	23.8	26.8	22.0	18.6
10	202.9	122.6	170.1	47.9	65.6	36.6	68.4	82.8	75.4	55.5	51.9	23.3	26.6	21.7	18.2
11	201.4	122.6	169.7	47.9	64.7	36.0	69.7	76.4	74.8	54.4	52.8	23.2	26.3	21.6	19.4
13	202.3	122.5	170.1	48.3	65.5	37.0	72.5	31.8	75.0	55.3	53.5	23.2	25.9	21.2	18.6
14	203.5	122.8	171.9	49.5	67.4	38.9	69.3	40.0	73.7	57.6	53.6	23.2	27.0	22.2	18.2
15	203.2	122.5	170.6	48.6	65.4	38.0	81.9	36.2	72.4	57.2	52.6	23.2	25.7	21.6	18.4
17	211.7	41.9	26.8	44.6	46.8	32.3	77.8	71.6	76.3	45.8	51.9	19.8	26.9	20.8	18.0
18	211.1	41.7	26.7	45.0	46.7	32.3	78.5	74.7	72.4	45.3	52.8	19.7	26.7	20.8	19.7
19	213.1	42.1	27.2	41.8	44.2	33.3	65.6	60.9	73.7	46.4	52.9	19.9	26.2	24.7	20.1
20	75.7	36.9	31.4	46.2	50.8	36.9	70.4	40.5	74.1	45.7	42.3	18.5	27.9	21.8	21.7
21	77.1	33.0	30.1	44.6	49.0	35.2	73.5	32.2	75.2	43.8	40.0	18.7	26.9	21.3	21.2
22	201.4	123.5	170.7	47.1	67.8	37.1	146.2	113.9	201.7	61.9	54.8	23.0	27.1	27.1	17.4
23	213.3	41.7	33.0	45.2	53.2	37.2	69.4	38.8	74.0	45.7	51.7	17.4[b]	26.9	22.8	20.9
24	210.8	41.5	32.8	45.1	52.8	36.1	72.8	32.0	75.7	44.5	52.8	18.4[b]	26.4	22.2	20.8
25	76.3	37.1	40.0	46.5	58.4	38.6	69.8	37.1	74.4	44.8	42.6	18.2[b]	27.5	23.0	22.2
26	77.5	33.1	37.2	45.1	56.4	35.5	73.1	32.1	75.6	42.9	40.5	18.5[b]	26.5	21.9	21.1
27	204.1	50.5	30.6	45.5	46.2	35.0	70.9	69.2	74.0	45.0	52.6	19.6	26.7	20.6	20.4
28	75.5	122.4	147.9	47.2	62.3	37.6	69.6	40.3	75.0	45.2	43.0	22.6	26.8	22.6	18.5

[a] In ppm from internal Me_4Si from $CDCl_3$ solutions, except **14**, **20**, **25**, and **28**, which were measured in $(CD_3)_2CO$. The shifts due to substituents at oxygen atoms are given in the Experimental Section. [b] Tentative assignment.

appears at 5.20 ppm with similar multiplicity than the signal in triol **20**, while the dd is found at 4.96 ppm and the t at 4.82 ppm. Specific assignment of the H-7 and H-9 signals in **14**, **20**, **21**, and related molecules is not directly possible. Careful inspection of Dreiding models reveals that depending on the conformation adopted by the seven-membered ring, either proton could originate the dd or the t.

The specific assignment of the H-7 and H-9 ^1H NMR signals was done after converting **14** into a monotosylate in which the proton geminal to the free hydroxyl group appears as a triplet (J = 3 Hz) at 3.84 ppm, and the proton geminal to the sulfonic ester appears as a dd (J = 11, 4 Hz) at 4.68 ppm. Alkaline treatment of the tosylate gave a substance to which structure **22** was assigned. The IR spectrum shows aldehyde absorption at 1710 cm^{-1} in addition to the α,β-unsaturated ketone at 1670 and 1610 cm^{-1}. The aldehyde group is further evident from the ^1H NMR singlet at 9.70 ppm and the ^{13}C NMR doublet at 201.7 ppm. The new sp^2 carbons which appear as a doublet at 146.2 ppm and a triplet at 113.9 ppm in the ^{13}C NMR spectrum and an ABC system (J_{AB} = 11, J_{AC} = 18, and J_{BC} = 2 Hz) at 5.66, 5.10, and 4.95 ppm in the ^1H NMR spectrum are due to a monosubstituted ethylene residue formed by elimination of the tosylate with concomitant cleavage of the seven-membered ring. That the aldehyde carbonyl is C-9 is readily deduced from the ^{13}C NMR chemical shifts of the two quaternary sp^3 carbon atoms. While C-6 remains essentially unshifted, C-10 is shifted to lower fields from 57.6 ppm in **14** to 61.9 ppm in **22**. Thus, from the ^1H NMR data of monotosylate **15**, it follows that H-9 corresponds to the triplet and H-7 corresponds to the double doublet. These results provide a method that might allow positional assignments of esters at the C-7/C-9 atoms in **14**. Such is the case for an angelate obtained by selective hydrolysis of an angelate acetate found in *S. lucida*.[10]

(10) Amaro, L. J. M.; Hung, M. *Mem. XIV Congr. Latinoam. Quim.* **1981**, *1*, 124.

The similarity of the H-7 and H-9 multiplicities in naturally occurring longipinenediolone esters to those displayed in compounds **20** and **21** suggests that all these molecules are derived from a 7β,9α-diol. However, only a direct correlation, provided later in the present paper, provides conclusive evidence for this deduction.

Catalytic hydrogenation of the α,β-unsaturated ketone in **14** and **13** gave **23** and **24**, respectively. Compound **23** was also obtained by hydrolysis of **24**. That the stereochemistry at C-3 is different from that in rastevione (**1**) is evident from the ^1H NMR chemical shift of the secondary methyl group, which appears in the 1.12–1.00 ppm region[8] when α (**1–4**), in contrast to its chemical shift of 1.20 and 1.21 ppm in **23** and **24**, respectively. Similarly, the ^{13}C NMR chemical shift of C-3 is near 27 ppm in compounds[8] with a 3α-methyl (**1–3**), whereas that of **23** and **24** is in the 33 ppm region. Furthermore, hydride reduction of the carbonyl in **24** gave triol **25**, which shows the same multiplicities for H-7 and H-9 as those of **20** but differs in the chemical shift of the secondary methyl group. A similar conclusion is reached when the NMR data of **26** are compared with those of **21**.

The above results suggested that the desired correlation might be achieved by introducing a double bond on the six-membered ring of a rastevione analogue and subsequent selective removal of the oxygen atom at C-8. Bromination of **3** gave **27**, the stereochemistry of the halogen atom being evident from the H-2 doublet (J = 8.5 Hz) at 4.60 ppm. The elements of hydrobromic acid were eliminated from **27** by action of lithium chloride in dimthylformamide. The physical data of the reaction product **8** are in excellent agreement with those reported[9] by Bohlmann and Zdero for a substance to which they assign structure **12** (when R = Ac). However, the esters derived from longipinenetriolone are now seen to be more properly represented by **8**.

Removal of the acetates from **8** provided **9**, which was treated with *p*-toluenesulfonyl chloride. This gave a mixture of monotosylates at C-7 and at C-8 in a 1:3 ratio as judged from ^1H NMR analysis. In this case column

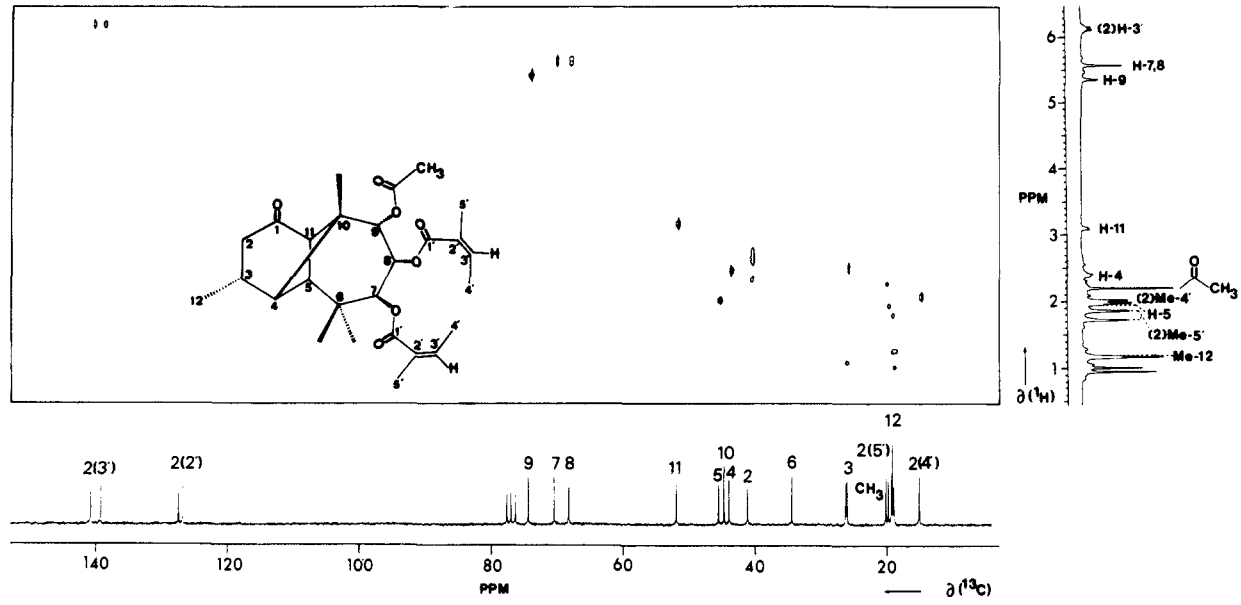


Figure 1. $^{1}H/^{13}C$ heteronuclear chemical shift correlation diagram of rastevione acetate (**2**).

chromatography allowed isolation of the desired 8-tosylate **10**. Removal of the sulfonic ester in compound **10** proceeded only in very poor yields. Therefore the diacetate **11** was reduced with lithium aluminum hydride. This afforded **28**, in whose ^{1}H NMR spectrum H-1 appears as a multiplet at 4.42, and the signals of the vinyl proton and methyl groups are shifted to 5.36 and 1.73 ppm, respectively.

A sample for direct chemical correlation was obtained by selective reoxidation of the C-1 allylic alcohol of **28**, on treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. The reaction product **14** and the sample obtained by hydrolysis of the naturally occurring longipinenediolone esters were identical in all respects. Acetylation of the samples of **14** from both origins gave diacetate **13**. The correlation provides conclusive evidence for reformulation of the structures of type **16** proposed by the German group[5-7,9] as derivatives of longipin-2-ene-7β,9α-diol-1-one (**14**).

Regarding the ^{13}C NMR data summarized in Table I, it has to be noted that some of our previous assignments[8] have been modified, in light of the evidence provided by a $^{13}C/^{1}H$ heteronuclear chemical shift correlation experiment of **2**, which is depicted in Figure 1. The dihedral angles between H-11 and H-5 and between H-4 and H-5 are close to 90°, while H-4 and H-11 show an M-type coupling of 7 Hz. Thus the signals owing to H-4, H-5, H-9, H-11, the secondary methyl, and the acetyl in the ^{1}H domain directly allow assignment of the correlated peaks in the ^{13}C domain. The vinyl methyl signals of the ester residues were assigned on the basis of our recent report[11] for tiglic and angelic acid. The distinction of C-7 and C-8 in those molecules having three oxygen atoms on the seven-membered ring is based on the magnitude of the residual coupling ($^{r}J_{CH}$) observed in spectra obained by setting the decoupler frequency on the ^{1}H Me_4Si signal. Since[12] $^{r}J_{CH} = \Delta fJ/(\gamma H_2/2\pi)$, for a ^{1}H $\Delta\delta$ of 0.23 ppm as is the case for H-7 and H-8 in **6**, at a given strength of the decoupling field ($\gamma H_2/2\pi$) and assuming similar J_{CH} for positions 7 and 8 in the undecoupled spectrum, this changes the corresponding $^{r}J_{CH}$ over 5%, which is indeed observed. The assignment of the secondary methyl group in compounds with the 3β configuration (**23–26**) is tentative. The vinyl methyl signal in compounds **8–11**, **13–15**, and **28** has been assigned in analogy with the data of **22**, where all methyls can be recognized. The quaternary methyl signals could in general not be assigned specifically.

(11) Joseph-Nathan, P.; Wesener, J. R.; Günther, H. *Org. Magn. Reson.* **1984**, *22*, 190.
(12) Joseph-Nathan, P.; González, Ma. P.; Johnson, L. F.; Shoolery, J. N. *Org. Magn. Reson.* **1971**, *3*, 23.

Experimental Section

Melting points are uncorrected. ^{1}H NMR spectra were measured at 90 and 200 MHz and ^{13}C NMR spectra at 25.2 MHz from solutions containing tetramethylsilane as the internal standard. Gravity column chromatography was done by using Merck silica gel 60 (70–230 mesh ASTM).

Longipinane-7β,8α,9α-triol-1-one (4). A solution of 250 mg (0.58 mmol) of rastevione (**1**) in 25 mL of ethanol was treated with 250 mg (3.85 mmol) of potassium cyanide in 1 mL of water. The reaction mixture was refluxed during 5 h and concentrated to a small volume. After addition of water (20 mL) the reaction mixture was extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was recrystallized from chloroform–hexane to afford 130 mg (0.49 mmol, 84%) of **4** as a white crystalline solid: mp 76–78 °C; identical by direct comparison with a sample obtained by hydrogenation of rastevione (**1**) followed by alkaline hydrolysis.[8]

Longipinane-7β,8α,9α-triol-1-one 7,8-Acetonide (17). A solution of 600 mg (2.23 mol) of longipinane-7β,8α,9α-triol-1-one (**4**) in 10 mL of acetone was treated with 60 mg (0.32 mmol) of *p*-toluenesulfonic acid. The reaction mixture was stored at room temperature during 2.5 h and evaporated to dryness under vacuum. The residue was extracted with ethyl acetate. The organic solution was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was recrystallized from chloroform–hexane to yield 520 mg (1.68 mmol, 75%) of **17** as white plates: mp 150–151 °C; IR ($CHCl_3$) 3590 (OH), 1712 cm^{-1} (C=O); $[\alpha]_{589}$ +2.6°, $[\alpha]_{578}$ +1.0°, $[\alpha]_{546}$ +5.2°, $[\alpha]_{436}$ 0°, $[\alpha]_{365}$ −38° (*c* 1.95, $CHCl_3$); ^{1}H NMR (90 MHz, $CDCl_3$) δ 4.0–3.8 (complex m, 3 H, H-7, H-8, H-9), 3.00 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.50 (br s, which disappears upon addition of D_2O, 1 H, OH), 1.73 (br s, 1 H, H-5), 1.47 (s, 6 H, acetonide *gem*-dimethyl), 1.06 (d, 3 H, J = 7 Hz, Me at C-3), 1.07, 1.03, and 0.97 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining four protons (H-2, H-2', H-3, and H-4) overlap in the δ 2.0–2.7 region]; ^{13}C NMR ($CDCl_3$) δ 108.9 (s), 27.4 (q), 27.2 (q, acetonide) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{18}H_{28}O_4$: C, 70.10; H, 9.15; O, 20.75. Found: C, 70.10; H, 8.95; O, 20.65.

Longipinane-7β,8α,9α-triol-1-one 7,8-Acetonide 9-Acetate (18). A solution of 300 mg (0.97 mmol) of longipinane-7β,8α,9α-triol-1-one 7,8-acetonide (17) in 3 mL of pyridine was treated with 3 mL of acetic anhydride. The reaction mixture was heated on a steam bath during 2 h, poured over ice–water, and extracted with ethyl acetate. The organic layer was washed with diluted hydrochloric acid, water, aqueous sodium bicarbonate, and water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was recrystallized from chloroform–hexane to provide 270 mg (0.77 mmol, 79%) of **18** as white needles: mp 142–144 °C; IR ($CHCl_3$) 1745 (Ac), 1710 cm^{-1} (C=O); $[\alpha]_{589}$ −3.4°, $[\alpha]_{578}$ −6.3°, $[\alpha]_{546}$ −4.6°, $[\alpha]_{436}$ −18.3°, $[\alpha]_{365}$ −84.0° (*c* 1.8, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.34 (d, 1 H, $J_{8,9}$ = 3 Hz, H-9), 4.10 (dd, 1 H, $J_{7,8}$ = 10 Hz, $J_{8,9}$ = 3 Hz, H-8), 3.90 (d, 1 H, $J_{7,8}$ = 10 Hz, H-7), 3.01 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.14 (s, 3 H, acetate), 1.77 (br s, 1 H, H-5), 1.41 and 1.38 (2 s, 3 H each, acetonide *gem*-dimethyl), 1.09 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.07, 1.00, and 0.93 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining four protons (H-2, H-2′, H-3, and H-4) overlap in the δ 2.1–2.7 region]; ^{13}C NMR ($CDCl_3$) δ 170.1 (s), 20.2 (q, acetate), 109.8 (s), 27.3 (q), 27.1 (q, acetonide) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{20}H_{30}O_5$: C, 68.55; H, 8.63; O, 22.83. Found: C, 68.52; H, 8.45; O, 22.73.

Reaction of Longipinane-7β,8α,9α-triol-1-one (4) with *p*-Toluenesulfonyl Chloride. (A) A solution of 1 g (3.73 mmol) of the title compound (**4**) in 6 mL of pyridine was treated with 1.5 g (7.88 mmol) of *p*-toluenesulfonyl chloride. The reaction mixture was stored at 4 °C during 24 h, poured over ice–water, and extracted with ethyl acetate. The organic layer was washed with diluted hydrochloric acid, water, aqueous sodium bicarbonate, and water, dried over anhydrous sodium sulfate, filtered, and evaporated under vacuum. The colorless oily residue (1.5 g) was shown by ^1H NMR analysis to be a mixture of longipinane-7β,8α,9α-triol-1-one 8-tosylate (**5**) and longipinane-7β,8α,9α-triol-1-one 7,8-ditosylate (**6**) in a ratio of 5:1 from the signals centered around 4.9–4.7 ppm. The mixture was chromatograhed on silica gel (30 g). The fractions eluted with benzene and benzene–chloroform (3:1) provided 150 mg (0.26 mmol, 7%) of **6** as while needles: mp 226–227 °C; IR ($CHCl_3$) 3595 and 3392 (OH), 1715 (C=O), 1599 2.64 (d, 1185 and 1175 cm^{-1} (S=O); UV (ethanol) λ_{max} 226 (log ε 4.60), 264 (3.36), 273 nm (3.36); $[\alpha]_{589}$ −10°, $[\alpha]_{578}$ −12°, $[\alpha]_{365}$ −32°, $[\alpha]_{334}$ −68° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 7.74, 7.71, 7.34 and 7.32 (4 d, 2 H each, *J* = 8.5 Hz, 2 tosylates), 4.93 (d, 1 H, $J_{7,8}$ = 11 Hz, H-7), 4.70 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{8,9}$ = 2 Hz, H-8), 4.06 (t, which collapses into a doublet upon additon of D_2O, 1 H, $J_{8,9}$ = 2 Hz, H-9), 2.92 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.64 (d, which disappears upon addition of D_2O, 1 H, OH), 2.50 (s, 6 H, 2 tosylate Me), 1.73 (s, 1 H, H-5), 1.07 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.06, 0.85, and 0.74 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining four protons (H-2, H-2′, H-3, and H-4 overlap in the δ 2.7–1.9 region]; ^{13}C NMR ($CDCl_3$) δ 145.0 (s), 144.5 (s), 133.9 (s), 132.4 (s), 129.4 (4 d), 128.3 (2 d), 128.0 (2 d), 21.6 (2 q, tosylate) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{29}H_{36}O_8S_2$: C, 60.42; H, 6.25; O, 22.22; S, 11.11. Found: C, 60.32; H, 6.34; O, 22.08; S, 11.23.

Those fractions eluted with chloroform–ethyl acetate (1:1) gave 50 mg (0.12 mmol, 3.2%) of **5** as a colorless oil: IR ($CHCl_3$) 3600 and 3400 (OH), 1710 (C=O), 1600 (aromatics), 1180 cm^{-1} (S=O); UV (ethanol λ_{max} 226 (log ε 3.97), 264 nm (2.97); ^1H NMR (90 MHz, $CDCl_3$) δ 7.87 and 7.38 (2 d, 2 H each, *J* = 8.5 Hz, tosylate), 4.76 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{8,9}$ = 3 H, H-8), 3.96 (d, 1 H, $J_{8,9}$ = 3 Hz, H-9), 3.83 (d, 1 H, $J_{7,8}$ = 11 Hz, H-7), 2.98 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.76 (s, which disappears upon addition of D_2O, 2 H, 2 OH), 2.45 (s, 3 H, tosylate Me), 1.73 (s, 1 H, H-5), 1.07 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.03, 1.00, and 0.80 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining protons (H-2, H-2′, H-3, and H-4) overlap in the δ 2.7–2.0 region]; ^{13}C NMR ($CDCl_3$) δ 145.0 (s), 133.2 (s), 129.7 (2 d), 127.8 (2 d), 21.6 (q, tosylate) [the sesquiterpenoid signals are given in Table I].

(B) In a second run the colorless residue (1.5 g) obtained after tosylation was dissolved in 20 mL of methanol and treated with 1.5 g (26.8 mmol) of potassium hydroxide in 1 mL of water. The reaction mixture was stored at room temperature during 20 min, concentrated to a small volume, diluted with water, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was crystallized from benzene, yielding a mixture of prisms and needles, which were separated mechanically. Recrystallization of the needles gave 250 mg (0.43 mmol, 11.6%) of **6**, identified by direct comparison with the sample obtained as described in A.

Recrystallization of the prisms from chloroform–hexane gave 400 mg (1.6 mmol, 43%) of **19**: mp 177–178 °C; IR ($CHCl_3$) 3610 and 3420 (OH), 1705 cm^{-1} (C=O); $[\alpha]_{589}$ −62°, $[\alpha]_{578}$ −62°, $[\alpha]_{546}$ −63°, $[\alpha]_{436}$ −102°, $[\alpha]_{365}$ −166°, $[\alpha]_{334}$ −256° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 4.14 (d, 1 H, $J_{8,9}$ = 2.2 Hz, H-9), 3.36 (dd, 1 H, $J_{7,8}$ = 4 Hz, $J_{8,9}$ = 2.2 Hz, H-8), 2.98 (dd, 1 H, $J_{7,8}$ = 4 Hz, $^4J_{5,7}$ = 2 Hz, verified by irradiating H-5, H-7), 2.88 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.80 (br s, which disappears upon addition of D_2O, 1 H, OH), 1.64 (br s, 1 H, H-5), 1.19, 1.10, and 1.03 (3 s, 3 H each, *gem*-dimethyl and Me at C-10), 1.07 (d, 3 H, *J* = 7 Hz, Me at C-3) [the remaining four protons (H-2, H-2′, H-3, and H-4) overlap in the δ 2.6–1.9 region]; ^{13}C NMR ($CDCl_3$), see Table I. Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86; O, 19.17. Found: C, 71.84; H, 8.73; O, 19.27.

Longipinane-1β,7β,9α-triol (20). A solution of 300 mg (1.2 mmol) of 7β,8β-epoxylongipinan-9α-ol-1-one (**19**) in 15 mL of tetrahydrofuran was treated portionwise and with vigorous stirring with 500 mg (13.2 mmol) of lithium aluminum hydride. The reaction mixture was stored at room temperature during 1 h and refluxed during 3 h. The mixture was treated portionwise with 100 mL of ethyl acetate and 50 mL of water and stirred at room temperature during 30 min. After filtration, the organic layer was separated, washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. This yielded 275 mg (1.08 mmol, 90%) of **20** as a white powder, mp 192–193 °C. Recrystallization from chloroform provided the pure compound: mp 196–197 °C; IR (KBr) 3450 cm^{-1} (OH); $[\alpha]_{589}$ +22.5°, $[\alpha]_{578}$ +22.9°, $[\alpha]_{546}$ +26.1°, $[\alpha]_{436}$ +45.0°, $[\alpha]_{365}$ +60.0°, $[\alpha]_{334}$ +77° (*c* 1.7, ethanol); ^1H NMR (90 MHz, Me_2CO-d_6 + 1 drop of D_2O) δ 4.35 (td, 1 H, $J_t \simeq 7.5$ Hz, $J_d \simeq 3.5$ Hz, H-1), 3.96 (dd, 1 H, $J_{7,8}$ = 10 Hz, $J_{7,8'}$ = 3 Hz, H-7), 3.72 (t, 1 H, $J_{8,9} = J_{8',9}$ = 4 Hz, H-9), 2.53 (t, 1 H, *J* = 5 Hz, H-11), 1.30 and 1.05 (2 s, 3 H each, 2 Me), 1.01 (d, 3 H, *J* = 7 Hz, Me at C-3), 0.90 (s, 3 H, Me) [the remaining seven protons (H-2, H-2′, H-3, H-4, H-5, H-8, and H-8′) overlap in the δ 2.2–1.6 region]; ^{13}C NMR (Me_2CO-d_6), see Table I. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30; O, 18.87. Found: C, 70.64; H, 10.25; O, 19.07.

Longipinane-1β,7β,9α-triol Triacetate (21). A solution of 70 mg (0.28 mmol) of longipinane-1β,7β,9α-triol (**20**) in 1 mL of pyridine was treated with 1 mL of acetic anhydride. The reaction mixture was heated on a steam bath during 3 h and worked up as in the case of **18**. Recrystallization of the residue from chloroform–hexane gave 50 mg (0.13 mmol, 47%) of **21** as white prisms: mp 114–116 °C; IR ($CHCl_3$) 1730 cm^{-1} (Ac); ^1H NMR (90 MHz, $CDCl_3$) δ 5.20 (td, 1 H, $J_t \simeq 7.5$ Hz, $J_d \simeq 3.5$ Hz, H-1), 4.96 (dd, 1 H, $J_{7,8}$ = 10 Hz, $J_{7,8'}$ = 3 Hz, H-7), 4.82 (t, 1 H, $J_{8,9} = J_{8',9}$ = 4 Hz, H-9), 2.62 (t, 1 H, *J* = 5 Hz, H-11), 2.14 (s, 3 H, Ac), 2.03 (s, 6 H, 2 Ac), 1.23 (br s, 1 H, H-5), 1.05 (s, 3 H, Me), 0.96 (d, 3 H, *J* = 7 Hz, Me at C-3), 0.93 (s, 6 H, 2 Me) [the remaining six protons (H-2, H-2′, H-3, H-4, H-8, and H-8′) overlap in the δ 2.5–1.7 region]; ^{13}C NMR ($CDCl_3$) δ 170.9 (s), 170.2 (s), 170.1 (s), 21.2 (q), 20.9 (q), 20.7 (q, acetates) [the sesquiterpenoid signals are given in Table I].

Longipin-2-ene-7β,9α-diol-1-one (14) from *Stevia salicifolia*. Air-dried roots of *S. salicifolia* Cav (1 kg), collected at km 35 of the Morelia-Tiripetío highway in the state of Michoacán, Mexico, during September 1981, and identified by Prof. J. Rzedowski, ENCB-IPN, Mexico City, were extracted with hexane under reflux during 4 h twice. Evaporation of the combined extracts furnished 20 g of a reddish viscous oil, which by ^1H NMR analysis showed to be a mixture of esters, probably angelates, acetates, seneciates, and tiglates, derived from the title compound. A solution of 4 g of this oily mixture in 25 mL of methanol was treated with 12 g of potassium hydroxide dissolved in 10 mL of water. The reaction mixture was refluxed during 7 min, concentrated to a small volume, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. This yielded 1.03 g of **14** as slightly yellow crystals, mp 180–183 °C. H-4), from chloroform gave the pure sample of **14** as white crystals: mp 183–184

°C (lit.[5] mp 183 °C); IR (KBr) 3532 (OH), 1680 and 1618 cm^{-1} (C=C—C=O); UV (ethanol) λ_{max} 250 nm (log ϵ 3.76); $[\alpha]_{589}$ +48°, $[\alpha]_{578}$ +51°, $[\alpha]_{546}$ +58°, $[\alpha]_{436}$ +110° (*c* 2.0, ethanol); ^1H NMR (90 MHz, $CDCl_3$) δ 5.78 (br s, 1 H, H-2), 3.93 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 2.5 Hz, H-7), 3.87 (t, 1 H, $J_{8,9'}$ = 4 Hz, H-9), 3.03 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.55 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.26 (br s, 1 H, H-5), 2.03 (d, 3 H, *J* = 1.5 Hz, vinyl Me), 1.87 (br s, which disappears upon addition of D_2O, 2 H, 2 OH), 1.09, 0.99, and 0.96 (3 s, 3 H each, *gem*-dimethyl and Me at C-10, the methylene protons at C-8 being obscured in the δ 1.9–2.5 region); ^{13}C NMR (Me_2CO-d_6), see Table I. The physical data are in excellent agreement to those reported[5] for a structure thought to be **16** (R = H).

Longipin-2-ene-7β,9α-diol-1-one Diacetate (13). A solution of 500 mg (2 mmol) of longipin-2-ene-7β,9α-diol-1-one (**14**) in 3 ml of pyridine was treated with 3 mL of acetic anhydride. The reaction mixture was heated on a steam bath during 3 h, followed by workup as in the the case of **18**, to yield 330 mg (1 mmol, 50%) of **13** as white prisms, mp 134–136 °C. Recrystallization from chloroform–hexane provided the pure compound: mp 137–139 °C; IR ($CHCl_3$) 1730 (Ac), 1670 and 1615 cm^{-1} (C=C—C=O); UV (ethanol) λ_{max} 249 nm (log ϵ 3.86); $[\alpha]_{589}$ +35°, $[\alpha]_{578}$ +35°, $[\alpha]_{546}$ +48°, $[\alpha]_{436}$ +109°, $[\alpha]_{365}$ +431° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.75 (br s, 1 H, H-2), 4.93 (apparent quintet due to overlap of a dd and a t, 2 H, H-7 and H-9), 3.15 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.59 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.27 (s, 1 H, H-5), 2.12 (s, 3 H, Ac), 2.04 (d, 3 H, *J* = 2 Hz, vinyl Me), 2.03 (s, 3 H, Ac), 1.01, 0.97, and 0.88 (3 s, 3 H each, *gem*-dimethyl and Me at C-10, the methylene protons at C-8 being obscure in the δ 2.4–1.9 region); ^{13}C NMR ($CDCl_3$) δ 170.0 (s), 169.8 (s), 21.0 (q), 20.9 (q, acetates) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{19}H_{26}O_5$: C, 68.24; H, 7.84; O, 23.92. Found: C, 68.18; H, 7.73; O, 24.04.

Longipin-2-ene-7β,9α-diol-1-one 7-Tosylate (15). A solution of 500 mg (2 mmol) of longipin-2-ene-7β,9α-diol-1-one (**14**) in 3 mL of pyridine was treated wth 750 mg (3.9 mmol) of *p*-toluenesulfonyl chloride at 0 °C. The reaction mixture was stored at 4 °C during 24 h, poured over ice–water, and extracted with ethyl acetate. The organic layer was washed with diluted hydrochloric acid, water, aqueous sodium bicarbonate, and water, dried anhydrous sodium sulfate, filtered, and evaporated under vacuum. The oily yellow residue was crystallized from chloroform–hexane to provide 450 mg (1.12 mmol, 56%) of **15** as white needles, mp 158–160 °C. The analytical sample obtained after recrystallization from methanol showed the following: mp 160–161 °C; IR ($CHCl_3$) 3620 (OH), 1675 and 1620 (C=C—C=O), 1605 (aromatics), 1143 cm^{-1} (S=O); UV (ethanol) λ_{max} 227 (log ϵ 4.34), 249 (4.03), 256 (4.06), 261 nm (3.98); $[\alpha]_{589}$ +21°, $[\alpha]_{546}$ +24°, $[\alpha]_{436}$ +42°, $[\alpha]_{365}$ +254° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 7.85 and 7.36 (2 d, 2 H each, *J* = 9 Hz, tosylate), 5.74 (br s, 1 H, H-2), 4.68 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 4 Hz, H-7), 3.84 (t, 1 H, $J_{8,9}$ = $J_{8',9}$ = 3 Hz, H-9), 2.95 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.51 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.46 (s, 3 H, tosylate Me), 2.17 (s, 1 H, H-5), 2.00 (d, 3 H, *J* = 2 Hz, vinyl Me), 1.10, 0.97, and 0.60 (3 s, 3 H each, *gem*-dimethyl and Me at C-10, the methylene protons at C-8 being obscured in the δ 2.4–2.0 region); ^{13}C NMR ($CDCl_3$) δ 144.6 (s), 133.4 (s), 129.6 (2 d), 128.0 (2 d), 21.6 (q, tosylate) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{22}H_{28}O_5S$: C, 65.33; H, 6.98; O, 19.78; S, 7.91. Found: C, 65.24; H, 6.86; O, 19.63; S, 7.88.

Aldehyde 22. A solution of 500 mg (1.24 mmol) of longipin-2-ene-7β,9α-diol-1-one 7-tosylate (**15**) in 20 mL of methanol were treated with 500 mg (8.9 mmol) of potassium hydroxide dissolved in 1 mL of water. The reaction mixture was refluxed during 1 h, concentrated to a small volume, diluted with ice–water, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The oily residue was chromatographed on silica gel (10 g). The fractions eluted with hexane–benzene (1:1) and with benzene gave 200 mg (0.86 mmol, 69%) of **22** as white plates. Recrystallization from chloroform–hexane afforded the pure compound: mp 78–80 °C; IR ($CHCl_3$) 1710 (aldehyde), 1670 (C=O), 1610 cm^{-1} (C=C); UV (ethanol) λ_{max} 254 nm (log ϵ 3.81); $[\alpha]_{589}$ +14.5°, $[\alpha]_{578}$ +14.5°, $[\alpha]_{546}$ +21.3°, $[\alpha]_{435}$ +51.1°, (*c* 2.4, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 9.70 (s, 1 H, CH=O), 5.85 (br s, 1 H, H-2), 5.66 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 18 Hz, H-7), 5.10 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{8,8'}$ = 2 Hz, H-8), 4.95 (dd, 1 H, $J_{7,8'}$ = 18 Hz, $J_{8,8'}$ = 2 Hz, H-8'), 3.30 (d, 1 H, $J_{4,11}$ = 7 Hz, H-11), 3.14 (d, 1 H, $J_{4,11}$ = 7 Hz, H-4), 2.35 (s, 1 H, H-5), 2.10 (d, 3 H, $J_{2,12}$ = 2 Hz, vinyl Me), 1.05, 0.99, and 0.97 (3 s, 3 H each, *gem*-dimelthyl and Me at C-10); ^{13}C NMR ($CDCl_3$), see Table I. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68; O, 13.77. Found: C, 77.49; H, 8.62; O, 13.83.

3-*epi*-Longipinane-7β,9α-diol-1-one Diacetate (24). A solution of 500 mg (1.5 mmol) of longipin-2-ene-7β,9α-diol-1-one diacetate (**13**) in 40 mL of ethyl acetate was stirred in the presence of 50 mg of prehydrogenated 10% palladium on activated charcoal catalyst under an hydrogen atmosphere at room temperature and normal pressure until the uptake of the gas ceased. The catalyst was removed by filtration and the solvent evaporated to dryness. The solid residue was recrystallized from chloroform–hexane to yield 450 mg (1.4 mmol, 89%) of **24** as white prisms: mp 166–168 °C; IR ($CHCl_3$) 1730 cm^{-1} (C=O and Ac); $[\alpha]_{589}$ −48°, $[\alpha]_{546}$ −57°, $[\alpha]_{436}$ −89°, $[\alpha]_{365}$ −183°, $[\alpha]_{334}$ −398° (*c* 2.0, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 4.92 (dd, 1 H, $J_{7,8}$ = 10 Hz, $J_{7,8'}$ = 3 Hz, H-7), 4.8 (t, 1 H, $J_{8,9}$ = $J_{8',9}$ = 4 Hz, H-9), 3.02 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.15 and 2.05 (2 s, 3 H each, acetates), 1.61 (br s, 1 H, H-5), 1.21 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.05, 1.04, and 0.90 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining six protons (H-2, H-2', H-3, H-4, H-8, and H-8') overlap in the δ 2.1–2.7 region]; ^{13}C NMR ($CDCl_3$) δ 170.6 (s), 170.0 (s), 21.0 (2 q, acetates) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{19}H_{28}O_5$: C, 67.83; H, 8.39; O, 23.78. Found: C, 67.97; H, 8.32; O, 23.68.

3-*epi*-Longipinane-7β,9α-diol-1-one (23). Method A. A solution of 500 mg (2 mmol) of longipin-2-ene-7β,9α-diol-1-one (**14**) was hydrogenated as in the case of **24**, yielding 470 mg (1.86 mmol, 93%) of **23** as a white powder, mp 180–183 °C. The analytical sample, obtained after recrystallization from acetone, showed the following: mp 185–186 °C; IR ($CHCl_3$) 3600 and 3400 (OH), 1700 cm^{-1} (C=O); $[\alpha]_{589}$ +10°, $[\alpha]_{578}$ +10°, $[\alpha]_{546}$ +22°, $[\alpha]_{436}$ +27°, $[\alpha]_{365}$ +8°, $[\alpha]_{334}$ −90° (*c* 1.9, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 3.87 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 3 Hz, H-7), 3.78 (t, 1 H, $J_{8,9}$ = $J_{8',9}$ = 4 Hz, H-9), 2.93 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.36 (s, which disappears upon addition of D_2O, 2 H, 2 OH), 1.60 (s, 1 H, H-5), 1.20 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.15, 1.00, and 0.96 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining six protons (H-2, H-2',- H-3, H-4, H-8, and H-8') overlap in the δ 2.5–1.8 region]; ^{13}C NMR ($CDCl_3$), see Table I. Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59; O, 19.02. Found: C, 71.29; H, 9.68; O, 18.88.

Method B. A solution of 500 mg (1.4 mmol) of 3-*epi*-longipinane-7β,9α-diol-1-one diacetate (**24**) in 20 mL of methanol was treated with 500 mg (8.9 mmol) of potassium hydroxide dissolved in 2 mL of water. The reaction mixture was refluxed during 1 h, concentrated to a small volume, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was recrystallized from chloroform, yielding 250 mg (1 mmol, 67%) of **23**, which was identical by direct comparison with the sample obtained in method A.

3-*epi*-Longipinane-1β,7β,9α-triol (25). A solution of 500 mg (1.5 mmol) of 3-*epi*-longipinane-7β,9α-diol-1-one diacetate (**24**) in 20 mL of tetrahydrofuran were treated with 700 mg (18.5 mmol) of lithium aluminum hydride as in the case of **19**. This afforded 350 mg (1.4 mmol, 93%) of **25** as a white powder, mp 195–199 °C. The analytical sample, obtained after recrystallization from acetone, showed the following mp 201–202 °C; IR (KBr) 3450 cm^{-1} (OH); $[\alpha]_{589}$ +34°, $[\alpha]_{578}$ +33°, $[\alpha]_{546}$ +43°, $[\alpha]_{436}$ +69°, $[\alpha]_{365}$ +103°, $[\alpha]_{334}$ +128° (*c* 1.4, ethanol); ^1H NMR (90 MHz, Me_2CO-d_6 + 1 drop of D_2O) δ 4.33 (ddd, 1 H, *J* = 3 Hz, *J'* = 7 Hz, *J''* = 11 Hz, H-1), 3.96 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 3 Hz, H-7), 3.72 (t, 1 H, $J_{8,9}$ = $J_{8',9}$ = 4 Hz, H-9), 1.43 (s, 3 H, Me), 1.19 (d, 3 H, *J* = 7 Hz, Me at C-3), 1.02 and 0.93 (2 s, 3 H each, 2 Me) [the remaining eight protons (H-2, H-2', H-3, H-4, H-5, H-8, H-8', and H-11) overlap in the δ 2.5–1.6 region]; ^{13}C NMR (Me_2CO-d_6), see Table I. Anal. Calcd for $C_{15}H_{26}O_3$: C, 70.83; H, 10.30; O, 18.87. Found: C, 70.70; H, 10.40; O, 19.09.

3-*epi*-Longipinane-1β,7β,9α-triol Triacetate (26). A solution of 100 mg (0.4 mmol) of 3-*epi*-longipinane-1β,7β,9α-triol (**25**) in 1 mL of pyridine was treated with 1 mL of acetic anhydride. The reaction mixture was heated on a steam bath during 3 h, followed

by workup as in the case of 18. Recrystallization of the solid residue from chloroform–hexane gave 100 mg (0.26 mmol, 66%) of **26** as white prisms: mp 119–121 °C; IR ($CHCl_3$) 1720 cm^{-1} (Ac): ^1H NMR (90 MHz, $CDCl_3$) δ 5.19 (ddd, 1 H, J = 3 Hz, J' = 7 Hz, J'' = 11 Hz, H-1), 4.92 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{7,8'}$ = 3 Hz, H-7), 4.84 (t, 1 H, $J_{8,9}$ = $J_{8',9}$ = 4 Hz, H-9), 2.17, 2.05, and 2.03 (3 s, 3 H each, 3 Ac), 1.19 (s, 3 H, Me), 1.12 (d, 3 H, J = 7 Hz, Me at C-3), 0.97 and 0.92 (2 s, 3 H each, 2 Me) [the remaining eight protons (H-2, H-2′, H-3, H-4, H-5, H-8, H-8′, and H-11) overlap in the δ 2.7–1.4 region]; ^{13}C NMR ($CDCl_3$) δ 170.8 (s), 170.2 (s), 170.0 (s), 21.5 (q), 21.3 (q), 21.1 (q acetates) [the sesquiterpenoid signals are given in Table I].

2β-Bromolongipinane-7β,8α,9α-triol-1-one Triacetate (27). A solution of 500 mg (1.26 mmol) of longipinane-7β,8α,9α-triol-1-one triacetate[8] (**3**) in 6 mL of acetic anhydride was treated portionwise with 3.74 g (23.4 mmol) of bromine. The reaction mixture was stored at room temperature during 4 days, poured over ice–water, and extracted with ethyl acetate. The organic layer was washed with water, aqueous sodium bisulfite, aqueous sodium bicarbonate, and water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was crystallized from chloroform–hexane to yield 508 mg (1.07 mmol, 85%) of **27** as white needles, mp 200–204 °C. Recrystallization from the same solvents gave the analytical sample: mp 216–218 °C; IR ($CHCl_3$) 1740 cm^{-1} (C=O and Ac); $[\alpha]_{589}$ +34.5°, $[\alpha]_{578}$ +29.8°, $[\alpha]_{546}$ +32.0°, $[\alpha]_{436}$ +44.9°, $[\alpha]_{365}$ −23.6° (*c* 1.8, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.30 (complex m, 3 H, H-7, H-8, and H-9), 4.60 (d, 1 H, $J_{2,3}$ = 8.5 Hz, H-2), 3.26 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.60 (quintet, 1 H, J = 7 Hz, H-3), 2.54 (br s, 1 H, H-5), 2.38 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.20, 2.09, and 1.97 (3 s, 3 H each, 3 Ac), 1.31 (d, 3 H, J = 7 Hz, Me at C-3), 1.07, 1.00, and 0.88 (3 s, 3 H each, *gem*-dimethyl and Me at C-10); ^{13}C NMR ($CDCl_3$) δ 170.4 (s), 169.5 (2 s), 20.6 (q), 20.5 (q), 20.4 (q, acetates) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{21}H_{29}O_7Br$: C, 53.28; H, 6.17. Found C, 53.00; H, 5.97.

Longipin-2-ene-7β,8α,9α-triol-1-one Triacetate (8). A solution of 200 mg (0.42 mmol) of 2β-bromolongipinane-7β,8α,9α-triol-1-one triacetate (**27**) in 5 mL of dimethylformamide was treated with 200 mg (4.72 mmol) of anhydrous lithium chloride. The reaction mixture was heated at 145 °C during 2.5 h, cooled to room temperature, poured over ice–water, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was purified by chromatography on silica gel (6 g). The fractions eluted with benzene gave 20 mg (0.04 mmol, 10%) of recovered **27**. Those fractions eluted with methylene chloride yielded 50 mg (0.12 mmol, 30%) of **8** as white needles, mp 163–165 °C. Recrystallization from chloroform–hexane gave the pure sample: mp 168–170 °C (lit.[9] mp 166–167 °C); IR ($CHCl_3$) 1750 (Ac), 1680 and 1615 cm^{-1} (C=C—C=O); UV (ethanol) λ_{max} (ethanol) 248 nm (log ϵ 3.73); $[\alpha]_{589}$ +57°, $[\alpha]_{578}$ +57°, $[\alpha]_{546}$ +79°, $[\alpha]_{436}$ +164°, $[\alpha]_{365}$ +487° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.83 (br s, 1 H, H-2), 5.33 (br s, 3 H, H-7, H-8, and H-9), 3.15 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.78 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.35 (br s, 1 H H-5), 2.18 (s, 3 H, Ac), 2.10 (s, 6 H, Ac and vinyl Me), 1.98 (s, 3 H, Ac), 1.10, 1.00, and 0.93 (3 s, 3 H each, *gem*-dimethyl and Me at C-10); ^{13}C NMR ($CDCl_3$) δ 169.5 (3 s), 20.9 (q), 20.6 (2 q, acetates) [the sesquiterpenoid signals are given in Table I]. The physical data are in excellent agreement to those reported[9] for a structure thought to be **12** (R = Ac).

Longipin-2-ene-7β,8α,9α-triol-1-one (9). A solution of 600 mg (1.53 mmol) of longipin-2-ene-7β,8α,9α-triol-1-one triacetate (**8**) in 30 mL of methanol was treated with 600 mg (10.7 mmol) of potassium hydroxyde in 1 mL of water. The reaction mixture was refluxed during 30 min, concentrated to a small volume, diluted with ice–water, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated to dryness. The residue was crystallized from chloroform–hexane to afford 300 mg (1.12 mmol, 74%) of **9** as white needles, mp 161–163 °C. The pure compound was obtained after recrystallization from the same solvents and shows the following: mp 166–167 °C; IR ($CHCl_3$) 3440 (OH), 1670 and 1618 cm^{-1} (C=C—C=O); UV (ethanol) λ_{max} 248 nm (log ϵ 3.70); $[\alpha]_{589}$ +48°, $[\alpha]_{578}$ +50°, $[\alpha]_{546}$ +61°, $[\alpha]_{436}$ +190°, $[\alpha]_{365}$ +475° (*c* 2.0, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 5.80 (br s, 1 H, H-2), 4.0–3.6 (complex m, 6 H, H-7, H-8, H-9, and 3 OH), 3.06 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.61 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.27 (s, 1 H, H-5), 2.05 (s, 3 H, vinyl Me), 1.16, 1.02, and 0.98 (3 s, 3 H each, *gem*-diemthyl and Me at C-10); ^{13}C NMR ($CDCl_3$), see Table I. Anal. Calcd for $C_{15}H_{22}O_4$: C, 67.65; H, 8.33; O, 24.03. Found: C, 67.57; H, 8.15; O, 23.92.

Longipin-2-ene-7β,8α,9α-triol-1-one 8-Tosylate (10). A solution of 300 mg (1.12 mmol) of longipin-2-ene-7β,8α,9α-triol-1-one (**9**) in 3 mL of pyridine was treated portionwise with 300 mg (1.57 mmol) of *p*-toluenesulfonyl chloride at 0 °C. The reaction mixture was stored at 4 °C during 15 h, poured over dried ice, and extracted with ethyl acetate. The organic layer was washed with water, 10% aqueous hydrochloric acid, water, 5% solution of sodium bicarbonate, and water, dried over anhydrous sodium sulfate, filtered, and evaporated. The pale yellow oily residue showed by ^1H NMR analysis to be a mixture of the monotosylates at C-7 and at C-8 in a ratio 1:3 from the signals in the 5.0–4.6 ppm region. The mixture was separated by chromatography on silica gel (20 g). The fractions eluted with hexane–ethyl acetate (8:2) yielded 320 mg (0.73 mmol, 68%) of **10** as white neeldes, mp 163–164 °C. Recrystallization from methylene chloride–hexane gave the pure compound: mp 168–169 °C; IR ($CHCl_3$) 3450 (OH), 1675 and 1620 (C=C—C=O), 1178 cm^{-1} (S=O); UV (ethanol) λ_{max} 225 (log ϵ 4.13)e, 250 nm (3.83); $[\alpha]_{589}$ +79.4°, $[\alpha]_{578}$ +82.2°, $[\alpha]_{546}$ +91.6°, $[\alpha]_{436}$ +177°, $[\alpha]_{365}$ +490° (*c* 1.8, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 7.90 and 7.38 (2 d, 2 H each, J = 8.5 Hz, tosylate), 5.80 (br s, 1 H, H-2), 4.77 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{8,9}$ = 3 Hz, H-8), 4.09 (d, 1 H, $J_{8,9}$ = 3 Hz, H-9), 3.87 (d, 1 H, $J_{7,8}$ = 11 Hz, H-7), 3.02 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.56 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.47 (s, 3 H, tosylate Me), 2.33 (s, which disappears upon addition of D_2O, 2 H, 2 OH), 2.26 (s, 1 H, H-5), 2.03 (d, 3 H, J = 1.5 Hz, vinyl Me, 1.13, 0.96, and 0.86 (3 s, 3 H each, *gem*-dimethyl and Me at C-10); ^{13}C NMR ($CDCl_3$) δ 145.0 (s), 133.2 (s), 129.7 (2 d), 128.0 (2 d), 21.7 (q, tosylate) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{22}H_{28}O_6S$: C, 62.85; H, 6.71; O, 22.83; S, 7.61. Found: C, 62.72; H, 6.62; O, 22.69; S, 7.74.

Further elution with hexane–ethyl acetate (1:1) gave 100 mg (0.24 mmol, 21%) of longipin-2-ene-7β,8α,9α-triol-1-one 7-tosylate as a pale yellow oil: ^1H NMR (90 MHz, $CDCl_3$) δ 7.88 and 7.33 (2 d, 2 H each, J = 8.5 Hz, tosylate), 5.78 (br s, 1 H, H-2), 4.88 (d, 1 H, $J_{7,8}$ = 11 Hz, H-7), 4.01 (dd, 1 H, $J_{7,8}$ = 11, $J_{8,9}$ = 3 Hz, H-8), 3.95 (d, 1 H, $J_{8,9}$ = 3 Hz, H-9), 3.51 (br s, which disappears upon addition of D_2O, 2 H, 2 OH), 3.03 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.56 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.45 (s, 3 H, tosylate Me), 2.23 (s, 1 H, H-5), 2.00 (d, 3 H, J = 1.5 Hz, vinyl Me), 1.15, 0.96, and 0.72 (3 s, 3 H each, *gem*-dimethyl and Me at C-10); ^{13}C NMR ($CDCl_3$) δ 203.2 (s, C-1), 170.7 (s, C-3), 144.6 (s, C-1′), 134.1 (s, C-4′), 129.6 (2 d, C-2′/C-6′), 127.6 (2 d, C-3′/C-5′), 122.3 (d, C-2), 84.2 (d, C-7), 76.2 (d, C-9), 68.6 (d, C-8), 61.5 (d, C-5), 55.7 (s, C-10), 52.0 (d, C-11), 47.7 (d, C-4), 36.7 (s, C-6), 26.9 (q, Me), 23.3 (q, Me), 21.6 (2 q, C-12 and C-5′), 19.4 (q, Me).

Longipin-2-ene-7β,8α,9α-triol-1-one 7,9-Diacetate 8-Tosylate (11). A solution of 150 mg (0.36 mmol) of longipin-2-ene-7β,8α,9α-triol-1-one 8-tosylate (**10**) in 3 mL of pyridine was treated with 3 mL of acetic anhydride. The reaction mixture was stored at room temperature during 130 h. Workup, as in the case described for **18**, gave 150 mg (0.3 mmol, 83%) of **11** as white needles, mp 225–227 °C. Recrystallization from chloroform–hexane provided the pure compound: mp 226–227 °C; IR ($CHCl_3$) 1750 (Ac), 1680 and 1622 (C=C—C=O), 1380 and 1180 cm^{-1} (S=O); UV (ethanol) λ_{max} 227 (log ϵ 4.25), 247 nm (3.98); $[\alpha]_{589}$ +66°, $[\alpha]_{578}$ +69°, $[\alpha]_{546}$ +70°, $[\alpha]_{436}$ +170°, $[\alpha]_{365}$ +526° (*c* 2.3, $CHCl_3$); ^1H NMR (90 MHz, $CDCl_3$) δ 7.80 and 7.40 (2 d, 2 H each, J = 8.5 Hz, tosylate), 5.81 (br s, 1 H, H-2), 5.37 (d, 1 H, $J_{8,9}$ = 3 Hz, H-9), 5.34 (d, 1 H, $J_{7,8}$ = 11 Hz, H-7), 5.02 (dd, 1 H, $J_{7,8}$ = 11 Hz, $J_{8,9}$ = 3 Hz, H-8), 3.08 (d, 1 H, $J_{4,11}$ = 6 Hz, H-11), 2.68 (d, 1 H, $J_{4,11}$ = 6 Hz, H-4), 2.45 (s, 3 H, tosylate Me), 2.34 (s, 1 H, H-5), 2.08 (d, 3 H, J = 1.5 Hz, vinyl Me), 2.05 and 2.02 (2 s, 3 H each, 2 Ac), 1.10, 0.97, and 0.90 (3 s, 3 H each, *gem*-dimethyl and Me at C-10); ^{13}C NMR ($CDCl_3$) δ 169.5 (2 s), 20.6 (q), 20.5 (q, acetates), 144.8 (s), 133.5 (s), 129.5 (2 d), 127.6 (2 d), 21.6 (q, tosylate) [the sesquiterpenoid signals are given in Table I]. Anal. Calcd for $C_{26}H_{32}O_8S$: C, 61.90; H, 6.39; O, 25.37; S, 6.34. Found: C, 61.79; H, 6.34; O, 25.24; S, 6.28.

Longipin-2-ene-1β,7β,9α-triol (28). A solution of 300 mg (0.6 mmol) of longipin-2-ene-7β,8α,9α-triol-1-one 7,9-diacetate 8-to-

sylate (11) in 15 mL of anhydrous ($LiAlH_4$) tetrahydrofuran was treated portionwise with 600 mg (15.8 mmol) of lithium aluminum hydride at 0 °C. The reaction mixture was refluxed during 2 h, cooled to 4 °C, acidified with diluted hydrochloric acid, concentrated at room temperature under vacuum, filtered, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was chromatographed on silica gel (5 g). The fractions eluted with chloroform–ethyl acetate (1:1) gave 20 mg (0.08 mmol, 13%) of **28** as white needles, mp 193–195 °C. Recrystallization from acetone provided the pure substance: mp 198–199 °C; IR (KBr) 3382 cm^{-1} (OH); $[\alpha]_{589}$ −2.8°, $[\alpha]_{578}$ −2.8°, $[\alpha]_{546}$ −3.9°, $[\alpha]_{436}$ −5.7°, $[\alpha]_{365}$ −19.9° (*c* 1.8, ethanol); ^1H NMR (90 MHz, Me_2CO-d_6) δ 5.36 (br s, 1 H, H-2), 4.42 (m, 1 H, H-1), 3.90 (d with further unresolved couplings, 1 H, *J* = 9 Hz, H-7), 3.76 (m, 1 H, H-9), 3.52 (d, 2 H, *J* = 4 Hz, 2 OH), 3.20 (d, 1 H, *J* = 4 Hz, OH), 2.63 (m, 1 H, H-11), 1.73 (t, 3 H, *J* = 1.5 Hz, vinyl Me), 1.51 (s, 1 H, H-5), 1.16, 0.91, and 0.88 (3 s, 3 H each, *gem*-dimethyl and Me at C-10) [the remaining three protons (H-4, H-8, and H-8′) overlap in the δ 2.3–1.8 region]; ^{13}C NMR ($(CD_3)_2CO$), see Table I. Anal. Calcd for $C_{15}H_{24}O_3$: C, 71.39; H, 9.59; O, 19.02. Found: C, 71.33; H, 9.44; O, 18.91.

Longipin-2-ene-7β,9α-diol-1-one (14). A solution of 70 mg (0.28 mmol) of longipin-2-ene-1β,7β,9α-triol (**28**) in 2 mL of dioxane was treated with 200 mg (0.88 mmol) of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone dissolved in 1 mL of dioxane. The reaction mixture was stored at room temperature during 65 h, diluted with water, and extracted with ethyl acetate. The organic layer was washed with water, dried over anhydrous sodium sulfate, filtered, and evaporated. The residue was chromatographed on silica gel (2 g). The fractions eluted with chloroform–ethyl acetate (1:1) were combined and recrystallized from chloroform to yield 7 mg (0.03 mmol, 11%) of **14** as white needles, mp 183–184 C, which was identical in all respects to the sample isolated from *Stevia salicifolia*.

Acknowledgment. We are grateful to Prof. *Jirzy* Rzedowsky (Departamento Botánico, Escuela Nacional de Ciencias Biológicas, IPN, Mexico) for the identification of the plant material, to Dr. J. N. Shoolery and the Varian Associates NMR Applications Laboratory (Palo Alto, CA) for granting the XL-200 instrument time, to A. Posada (CIEA-IPN) for optical rotations, and to CoNaCyT (México) for partial financial support.

Registry No. 1, 80388-43-8; **2**, 80388-57-4; **3**, 80433-25-6; **4**, 80388-60-9; **5**, 97279-98-6; **6**, 97279-99-7; **8**, 97335-20-1; **9**, 97280-00-7; **10**, 97280-01-8; **11**, 97280-02-9; **13**, 97280-03-0; **14**, 97335-21-2; **15**, 97280-04-1; **17**, 97280-05-2; **18**, 97280-06-3; **19**, 97280-07-4; **20**, 97280-08-5; **21**, 97280-09-6; **22**, 97280-10-9; **23**, 97280-11-0; **24**, 97280-12-1; **25**, 97335-22-3; **26**, 97335-23-4; **27**, 97280-13-2; **28**, 97280-14-3; 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, 84-58-2; longipin-2-ene-7β,8α,9α-triol-1-one 7-tosylate, 97280-15-4.

α-Amino Acids as Chiral Educts for Asymmetric Products. The Synthesis of α′-Amino-α,β-ynones

Thomas L. Cupps, Raymond H. Boutin, and Henry Rapoport*

Department of Chemistry, University of California, Berkeley, California 94720

Received March 15, 1985

α-Amino acid isoxazolidides have been developed as educts for the preparation of optically pure α′-amino-α,β-ynones. The α-amino acids were first N-protected as their ethoxycarbonyl, *tert*-butoxycarbonyl, or phenylsulfonyl derivatives. The isoxazolidides then were formed by the simple, high yield acylation of isoxazolidine by in situ generated α-amino acid isobutyl carbonic anhydrides. Individual isoxazolidides of L-α-N-substituted alanine, phenylalanine, and methionine, when treated with lithium acetylide, lithium (trimethylsilyl)acetylide, or 1-hexynyllithium, gave high yields of the corresponding optically pure α,β-acetylenic ketones.

Introduction

α,β-Acetylenic ketones are useful synthetic intermediates because of their potential conversion to such compounds as chiral acetylenic alcohols,[1] unsaturated ketones, allylic alcohols, and a variety of Michael addition compounds. Such ynones have thus proven crucial precursors for the total synthesis of some natural products and related analogues such as the marine sesquiterpene (±)-$\Delta^{9(12)}$-capnellene[2] and chiral insect pheromones[3] as well as for the synthesis of a number of heterocyclic compounds.[4]

Of the various methods[5] that have been developed for the synthesis of α,β-acetylenic ketones, besides the oxidation of propargylic alcohols, the acylation of an acetylene derivative by an activated carboxylic acid has been the most common. The choice of reaction conditions and substrates for this general type of acylation are crucial, since the acetylenic ketone product is often of comparable or greater reactivity than the activated carboxylic acid and could conceivably react further to yield side products such as tertiary carbinol and Michael adduct.

One such acylation route is the reaction of (trimethylsilyl)acetylenes with acyl halides and aluminum chloride.[6] Similarly, alkyl carbothioates[7] react with (trimethyl-

(1) Chiral α,β-acetylenic alcohols have been obtained in high enantiomeric excess via asymmetric reduction of the corresponding α,β-ynone. For example, see: (a) Noyori, R. *Pure Appl. Chem.* **1981**, *53*, 2315. (b) Cohen, N.; Lopresti, R. J.; Neukom, C.; Saucy, G. *J. Org. Chem.* **1980**, *45*, 582. (c) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.* **1980**, *102*, 867. (d) Vigneron, J.-P.; Bloy, V. *Tetrahedron Lett.* **1979**, 2683. (e) Brinkmeyer, R. S.; Kapoor, V. M. *J. Am. Chem. Soc.* **1977**, *99*, 8339.

(2) Huguet, J.; Karpf, M.; Dreiding, A. S. *Helv. Chim. Acta* **1982**, *65*, 2413.

(3) Sayo, N.; Azuma, K.; Mikami, K.; Nakai, T. *Tetrahedron Lett.* **1984**, *25*, 565.

(4) Utimoto, K.; Miwa, H.; Nozaki, H. *Tetrahedron Lett.* **1981**, *22*, 4277.

(5) Methods for α,β-ynone synthesis prior to 1969 have been reviewed: Katkevich, R. I.; Vereshchagin, L. I. *Russ. Chem. Rev.* **1969**, *38*, 900.

(6) (a) Birkofer, L.; Ritter, A.; Uhlenbrauck, H. *Chem. Ber.* **1963**, *96*, 3280. (b) Krapf, M.; Dreiding, A. S. *Helv. Chim Acta* **1979**, *62*, 852.

0022-3263/85/1950-3972$01.50/0