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Longipinene Derivatives from *Santolina viscosa*

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The neutral fraction of the hexane extract of the aerial parts of *Santolina viscosa* afforded eight new longipinene derivatives (**1**−**8**), oblongifolidiol (**9**), and several other known compounds. The structures of **1**−**8** were established by spectroscopic methods and chemical transformations. The vulgarone A-type structure previously reported for oblongifolidiol has been reassigned as the longipinene derivative **9** using 2D NMR, chemical correlations, and X-ray diffraction.

As part of an ongoing study on medicinal and/or aromatic plants from southern Spain and northern Morocco, we are investigating the chemical composition of the genus *Santolina*.[1−4] This genus is constituted by a taxonomically complex group of species whose botanical classification has been periodically revised.[5−7] Several species in the genus have been reported to produce compounds with diverse biological and pharmacological properties,[8,9] and these are used widely in popular medicine. In a previous investigation on the chemical composition of the hexane extract of the aerial parts of *S. viscosa* Lag. (Asteraceae), we reported the presence of five new longipinanoic acid derivatives.[2] Longipinane was the only sesquiterpene skeleton found in the acid fraction. Herein, as the result of ongoing studies on the chemical composition of this plant, we describe the isolation and structure determination of eight new longipinane derivatives (**1**−**8**), together with five known compounds. The structure of one of the known compounds, oblongifolidiol (**9**), previously isolated from *S. oblongifolia*,[10] has been reassigned.

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Results and Discussion

The acid fraction from the hexane extract of *S. viscosa* has been reported to contain **10** as the major component.[2] Further investigation on the less polar fractions has allowed the detection of **1** as a minor stereoisomer inseparable from **10**. Allylic oxidation of the mixture of **1** and **10** (1:6 ratio) afforded, besides **11** and **12**, both oxidation products from **10**, a second allylic alcohol (**13**), also stemming from **1**, which could be purified by chromatographic means. The spectroscopic data of **13** were shown to be almost identical with those described for **12**,[2] with the only discernible difference being the multiplicity of H-11 and the chemical shift of the methyl group at C-6 in the ^{1}H NMR spectrum. Having determined in our previous work[2] that longipinene derivatives lacking functionalities in the seven-membered ring may exist in solution as a mixture of two interchangeable conformers, the NOEs observed for H-8 and H-7, after irradiating Me-15, could only be explained if **13** were an epimer of **12** at C-6 (Figure 1). The same NOEs were observed when Me-15 of **1** was irradiated in the mixture of **10** and **1**.

Analysis of the spectroscopic data obtained from **2** led

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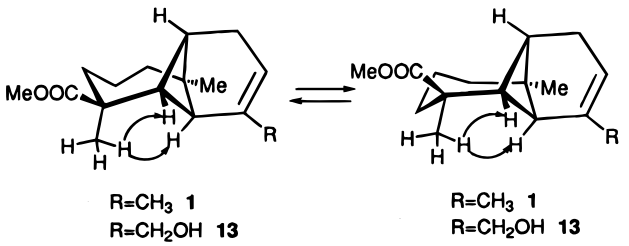


Figure 1. NOEs observed for **1** and **13**.

us to assign an α-longipinene structure for this compound. The molecular formula $C_{15}H_{24}O_2$ was deduced from its HRCIMS ($[M]^+$, *m/z* 236.1770). The most significant bands in the IR spectrum were due to hydroxyl group (3268 cm^{-1}) and double-bond (1662 cm^{-1}) absorptions. The presence of two protons on oxygenated carbons at δ 3.93 (d, J = 12.0 Hz) and 3.99 (d, J = 12.0 Hz) in the ^1H NMR spectrum, together with the chemical shift of the olefinic proton at δ 5.45, allowed the location of a hydroxyl group at C-12. An additional AB system due to two protons on oxygenated carbons at δ 3.30 and 3.42 (J = 10.8 Hz) was also observed. The chemical shifts of the carbons contiguous to C-2 in the ^{13}C NMR spectrum remained practically unaltered with respect to those of compounds showing an oxygenated function at C-6;[2] therefore, the second hydroxymethyl could be located at C-6.[2] The generation of **11** by treatment of **2** with pyridine dichromate in dimethylformamide (DMF), and then CH_2N_2, confirmed the placement of both hydroxyl groups at C-12 and C-15.

The mass spectrum of **3** showed a $[M]^+$ at *m/z* 278 which, together with the ^1H and ^{13}C NMR data, established the molecular formula $C_{17}H_{26}O_3$. Its NMR spectra were very similar to those of **2**, with the only difference being the presence of an acetyl group at C-2 (3H, s, δ 2.02; 1H, d, J = 10.7 Hz, δ 3.74; 1H, d, J = 10.7 Hz, δ 3.98). The production of **2** after treating **3** with KOH/MeOH confirmed the structure proposed for this compound.

Compound **9**, the major component of the hexane extract (>40%), was obtained as colorless crystals (mp 96−98 °C, $CHCl_3$). The molecular formula $C_{15}H_{24}O_2$ was deduced from its HRFABMS ($[M + Na]^+$, *m/z* 259.1676). The IR spectrum exhibited a hydroxyl group (3363 cm^{-1}) absorption band. The ^1H and ^{13}C NMR spectra revealed the presence of two hydroxymethyl groups on quaternary carbons (^1H: two AB systems at δ 3.40 and 3.47 ppm, J = 10.8 Hz, and at δ 3.49 and 3.57 ppm, J = 10.8 Hz; ^{13}C: δ 67.9 and 68.0 ppm). Following the same reasoning as used for **2**, the two hydroxyl groups were located at C-14 and C-15, leading to the assignment of the structure of longipin-9-ene-14,15-diol for **9**. Nevertheless, a diol isolated from *S. oblongifolia*, which showed the same spectroscopic data as **9**, was assigned with a vulgarone A-type structure.[10] The correlations observed in its COSY spectrum between H-11, H-10, and Me-12 rules against a vulgarone A-type structure for **9**. The X-ray diffraction analysis of **9** (Figure 2) confirmed the previous assignment by NMR techniques. The deviation of the atoms C-4 and C-5 from the least-squares C-2−C-3−C-6−C-7 plane permitted us to determine as type B[2] the conformation of the seven-membered ring in **9**. The same conformation has been described for the crystal structure of the *p*-bromobenzoate derivative of **14**, previously found in *S. viscosa* and three other longipinene derivatives,[11−13] whereas type-A conformation has been found only in one other case.[14] The crystal structure is stabilized by the formation of hydrogen bonds: d [O-1→O-2 (x, y+1, z), 2.791 Å] and d [O-2→O-1 (-x+1/2, y−1/2, −z+1), 2.719 Å]. Furthermore, **9** was obtained by $LiAlH_4$ reduction of the ester **14**.[2]

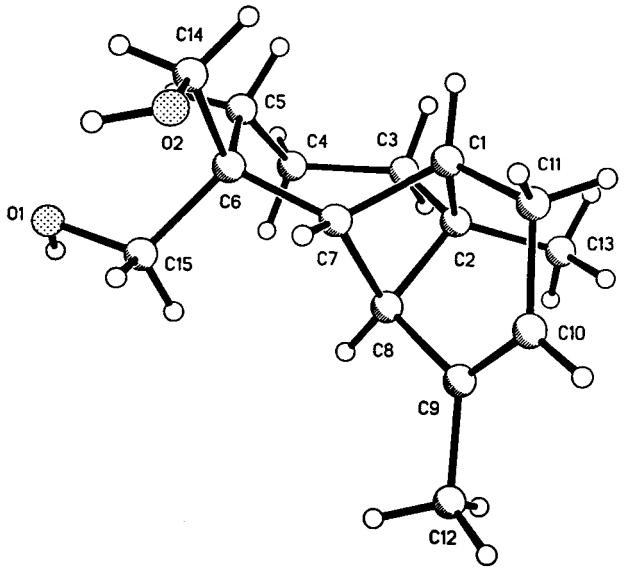
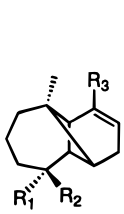
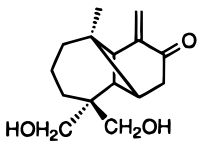


Figure 2. Deviations of C-4 (−0.495 Å) and C-5 (+0.398 Å) from the plane defined by C-2−C-3−C-6−C-7 permitting the characterization of the conformation of the seven-membered ring as type B in **9**. Positive values indicate deviations toward C-1. Negative values indicate deviations toward C-8.



	R_1	R_2	R_3
1	CH_3	COOMe	CH_3
2	CH_2OH	CH_3	CH_2OH
3	CH_2OAc	CH_3	CH_2OH
4	CH_2OAc	CH_2OH	CH_3
5	CH_2OH	CH_2OAc	CH_3
6	CH_2OH	CH_2OH	CH_2OH
9	CH_2OH	CH_2OH	CH_3
10	COOMe	CH_3	CH_3
11	COOMe	CH_3	CHO
12	COOMe	CH_3	CH_2OH
13	CH_3	COOMe	CH_2OH
14	COOMe	CH_2OH	CH_3



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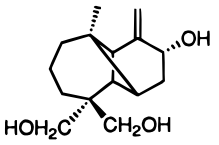

7

Compounds **4** and **5** were isolated as a mixture that could not be separated. Hydroxyl (3417 cm^{-1}) and acetate (1736 and 1240 cm^{-1}) group absorptions were observed in the IR spectrum. Duplication of signals detected in both the ^1H and ^{13}C NMR spectra of the mixture suggested the possible occurrence of C-6 epimers, as previously revealed for **1** and **10**. Comparison of their NMR data with those of **9** pointed to **4** and **5** as two possible monoacetylated derivatives of **9**. The production of **9** after treatment of the mixture with KOH/MeOH confirmed this structural proposal.

Compound **6** was isolated from the most polar fraction of the extract and assigned the molecular formula $C_{15}H_{24}O_3$ from its HRCIMS ($[M + 1]^+$, *m/z* 253.1806). The IR spectrum showed absorption bands due to one or more hydroxyl groups (3347 cm^{-1}). The ^1H and ^{13}C NMR data confirmed an α-longipinene skeleton for this compound. They also revealed the presence of three CH_2OH moieties, with two of these being hydroxymethylenes located on sp^3

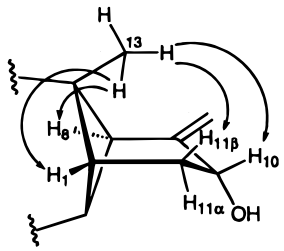

Figure 3. NOEs observed for **7**.

quaternary carbons, and the third in an allylic position (2H, br s, δ 3.87). On the basis of these data, the structure of longipin-9-ene-12,14,15-triol was assigned to **6**. This assignment was confirmed after obtaining **6** by allylic oxidation of **9** with SeO_2.

Less polar than **6**, a second triol (**7**) was isolated from the same polar fraction of the extract. The spectroscopic data pointed to **7** being an isomer of **6** (HRCIMS: $[M + 1]^+$ at *m*/*z* 253.1807) with an exocyclic disposition of the double bond. The NMR spectra of **7** confirmed the presence of both the terminal double bond (^{1}H: δ 4.73, s, 1H, δ 4.95, s, 1H; ^{13}C: δ 111.4) and the allylic oxygenated methine (^{1}H: δ 4.44, d, J = 8.1 Hz; ^{13}C: δ 67.3), with the rest of the signals being comparable to those of **9**. Accordingly, **7** was identified as longipin-9-ene-10,14,15-triol. The production of **7** by photooxidation and subsequent reduction of **9** confirmed this assignment. Finally, the stereochemistry at C-10 and the chair-type conformation of the six-membered ring were deduced from the analysis of NOE-difference experiments (Figure 3).

Compound **8** was assigned the molecular formula $C_{15}H_{22}O_3$ through the analysis of its HRCIMS ($[M + 1]^+$, *m*/*z* 251.1645). The IR spectrum showed hydroxyl-group (3398 cm^{-1}) and α,β-unsaturated-ketone (1700 and 1624 cm^{-1}) absorption bands. Comparison of the ^{1}H and ^{13}C NMR data of **7** and **8** led us to the characterization of **8** as the diol resulting from the oxidation of the allylic alcohol of **7**. The signals corresponding to the conjugated double bond appeared at δ 4.99 (1H, d, J = 1.2 Hz) and 5.93 (1H, d, J = 1.2 Hz) in its ^{1}H NMR spectrum, and at 116.4, 149.9, and 220.9 in the ^{13}C NMR spectrum.

Experimental Section

General Experimental Procedures. Melting points are uncorrected. Optical rotations were determined on a Perkin-Elmer model 141 polarimeter, using $CHCl_3$ as solvent. IR spectra were recorded on a Perkin-Elmer model 983 G spectrometer with samples between NaCl plates (film). NMR studies employed a Bruker AMX 300 (^{1}H 300 MHz/^{13}C 75 MHz), Bruker ARX 400 (^{1}H 400 MHz/^{13}C 100 MHz), and Bruker AMX 500 (^{1}H 500 MHz/^{13}C 125 MHz) spectrometers, including COSY, HMBC, HMQC, and NOESY, and chemical shifts are given in δ values relative to TMS as internal standard. Mass spectra were registered on a Hewlett-Packard 5972A mass spectrometer using an ionizing voltage of 70 eV (EIMS) coupled to gas chromatograph Hewlett-Packard 5890A. HREIMS were registered on an Autospec-Q VG-Analytical (FISONS) mass spectrometer.

Plant Material. *S. viscosa* Lag. (Compositae) was collected in Las Yeserías, Almería, Spain, in July 1996, and identified by Prof. J. Molero, Departamento de Biología Vegetal, Universidad de Granada. A voucher specimen is available for inspection at the herbarium of the Facultad de Farmacia, Universidad de Granada.

Extraction and Isolation. The air-dried material (7.9 kg) was extracted in a Soxhlet apparatus, resulting in 510 g of extract. A 60-g portion was defatted, dissolved in Et_2O, and extracted with 1 N NaOH solution to yield 35 g of a neutral fraction and 10.5 g of an acid fraction. A 10-g portion of the neutral fraction was subjected to column chromatography over Si gel using mixtures of hexane/Et_2O/EtOAc/MeOH of increasing polarity as eluents. Eleven main fractions were collected (F1−F11). The least polar fraction was mainly constituted by esters of fatty acids. However, 60 mg of a mixture of β-cholesterol, β-cholest-5-en-24-one, β-stigmasterol, and β-sitosterol were obtained by crystallization from CH_2Cl_2. F2 [hexane/Et_2O (3:2)] consisted of 87 mg of **4** and **5**. F3 [hexane/Et_2O (3:2)] yielded 339 mg of the mixture **3**−**5**. F4 [hexane/Et_2O (1:1)] represented 570 mg of **3**. F5 [hexane/Et_2O (1:4)] was constituted by 2.89 g of **9**. F6 (Et_2O) contained a mixture of 446 mg of **2** and **9**. F7 [Et_2O/EtOAc (1:1)] consisted of 730 mg of **2**. F8 (EtOAc) (90 mg) yielded a mixture of **2** and **8**. F9 [EtOAc/MeOH (1:1)] was constituted by 21 mg of **8**. F10 [EtOAc/MeOH (1:3)], a mixture of 133 mg of **6** and **7**, was rechromatographed [EtOAc/MeOH (1:1)] to obtain 42 mg of **7** and 71 mg of **6**. The most polar fraction of the extract, F11 (510 mg, MeOH), was constituted by **6**.

Methyl longipin-9-en-14-oate (1): obtained as an unseparable mixture with **10** in a 1:6 ratio, for $[\alpha]_D$ and IR of the mixture, see Barrero et al.,[2] ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.20 (1H, m, H-10), 3.62 (3H, s, COOC*H*$_3$), 2.25 (2H, m, H-11), 1.99−2.15 (3H, m, H-1, H-5a, H-7), 1.97 (1H, d, J = 6.0 Hz, H-8), 1.67 (3H, q, J = 2.0 Hz, H-12), 1.49−1.64 (4H, m, H-3, H-4), 1.33 (1H, m, H-5b), 1.16 (3H, s, H-15), 0.84 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 117.7 (d, C-10), 54.5 (d, C-7), 51.6 (q, COO*C*H$_3$), 46.6 (d, C-8), 40.8 (d, C-1), 40.6 (t, C-3), 34.8[a] (t, C-5), 33.7[a] (t, C-11), 25.0 (q, C-14), 24.7 (q, C-13), 23.3 (q, C-12), 22.3 (t, C-4) ([a]assignments with the same superscript letter may be interchanged); EIMS *m*/*z* 248 $[M]^+$ (5), 216 (4), 189 (13), 173 (8), 145 (13), 133 (18), 119 (100), 105 (31), 91 (26), 77 (14), 59 (9), 41 (15).

Oxidation of 1 and 10 with SeO_2. A solution of 110 mg of SeO_2 in 95% EtOH (8 mL) and 124 mg of a mixture of **1** + **10** was refluxed for 24 h. Workup as usual gave 48 mg of **11**, 12 mg of **12**, and 32 mg of **13**.

Compound 13: colorless syrup; $[\alpha]_D$ +14.4° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3437, 2925, 1727, 1455, 1373, 1256, 1113, 1021, 983, 913 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.50 (1H, m, H-10), 3.99 (2H, q, J = 1.7 Hz, H-12), 3.63 (3H, s, COOC*H*$_3$), 2.41 (1H, m, H-11a), 2.27 (1H, m, H-11b), 2.23 (2H, dd, J = 6.1, 1.0 Hz, H-8), 2.20 (1H, m, H-1), 2.10 (1H, m, H-5a), 2.04 (1H, s, H-7), 1.52−1.70 (4H, m, H-3, H-4), 1.40 (1H, m, H-5b), 1.15 (3H, s, H-15), 0.85 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 178.3 (s, C-14), 150.4 (s, C-9), 119.7 (d, C-10), 65.9 (t, C-12), 54.8 (d, C-7), 51.7 (q, COO*C*H$_3$), 46.2 (s, C-6), 42.8 (d, C-8), 41.1 (d, C-1), 40.3 (t, C-3), 40.0 (s, C-2), 34.8[a] (t, C-5), 33.7[a] (t, C-11), 24.9 (q, C-15), 23.8 (q, C-13), 22.2 (t, C-4) ([a]assignments with the same superscript letter may be interchanged); EIMS *m*/*z* 264 $[M]^+$ (1), 246 (10), 214 (8), 186 (30), 172 (61), 158 (37), 145 (40), 131 (61), 119 (40), 105 (68), 101 (56), 95 (47), 91 (100), 79 (69), 59 (51); HRCIMS *m*/*z* 265.1798 (calcd for $C_{16}H_{25}O_3$, 265.1803).

15-Acetoxylongipin-9-en-14-ol (4) and 14-acetoxylongipin-9-en-15-ol (5): obtained as a colorless syrup; $[\alpha]_D$ +16.1° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3417, 2925, 1736, 1456, 1378, 1240, 1038, 980, 908, 854, 757 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 5.20 (2H, m, H-10), 4.01 (2H, br s, H-14[a]), 4.00 (1H, d, J = 11.2 Hz, H-15[a]), 3.85 (1H, d, J = 11.2 Hz, H-15[a]), 3.41 (1H, d J = 11.6 Hz, H-14[b]), 3.32 (2H, d J = 10.8 Hz, H-14[b]), 3.26 (1H, d J = 11.6 Hz, H-14[b]), 2.03 (3H, OCOC*H*$_3$), 2.02 (3H, OCOC*H*$_3$), 1.96−2.36 (8H, m, H-1, H-8, H-11), 1.75 (1H, s, H-7), 1.72 (1H, s, H-7), 1.61 (6H, t, J = 1.9 Hz, H-12), 1.22−1.62 (12H, m, H-3, H-4, H-5), 0.81 (3H, s, H-13), 0.80 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.8 (s, O*C*OCH$_3$), 171.7 (s, O*C*OCH$_3$), 147.1 (s, C-9), 147.1. (s, C-9), 117.6 (d, C-10), 117.5 (d, C-10), 66.0 (t, C-15[a]), 65.9 (t, C-15[a]), 64.6 (t, C-14[b]), 64.5 (t, C-14[b]), 49.1 (d, C-7), 49.0 (d, C-7), 45.7 (d, C-8), 45.4 (d, C-8), 41.0 (s, C-6), 40.9 (s, C-6), 40.7 (t, C-3), 40.6 (t, C-3), 40.3 (s, C-2), 40.2 (s, C-2), 39.6 (d, C-1), 39.6 (d, C-1), 33.9 (t, C-11), 28.9 (t, C-5), 28.8 (t, C-5), 23.4 (q, C-13), 22.9 (q, C-12), 22.8 (q, C-12), 20.9 (q, OCO*C*H$_3$), 20.8 (t, C-4), 20.7 (t, C-4) ([a,b]assignments with the same superscript letter may be interchanged); EIMS *m*/*z* 278 $[M]^+$ (3), 267 (3), 251 (2), 221

(10), 187 (21), 186 (14), 173 (27), 159 (32), 158 (30), 145 (38), 131 (48), 119 (99), 105 (63), 91 (77), 43 (100).

15-Acetoxylongipin-9-en-12-ol (3): obtained as a colorless syrup; $[\alpha]_D$ +17.5° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3450, 2924, 2837, 1736, 1676, 1457, 1372, 1241, 1178, 1039, 984, 797 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.42 (1H, m, H-10), 3.98 (1H, d, J = 10.7 Hz, H-15a), 3.93 (2H, br s, H-12), 3.74 (1H, d, J = 10.7 Hz, H-15b), 2.25−2.32 (3H, m, H-8, H-11), 2.16 (1H, m, H-1), 2.03 (3H, OCOCH_3), 1.54 (1H, s, H-7), 1.22−1.67 (6H, m, H-3, H-4, H-5), 0.83 (3H, s, H-14[a]), 0.81 (3H, s, H-13[a]); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.5 (s, O*C*OCH$_3$), 150.8 (s, C-9), 119.1 (d, C-10), 71.4 (t, C-12[a]), 65.7 (t, C-15[a]), 54.4 (d, C-7), 42.8 (d, C-8), 40.6 (t, C-3), 40.1 (s, C-2), 39.4 (d, C-1), 36.6 (d, C-6), 34.2 (t, C-11[b]), 34.1 (t, C-5[b]), 23.7 (q, C-13), 21.9 (q, C-14), 21.1 (t, C-4), 21.0 (q, OCO*C*H$_3$) ([a,b]assignments with the same superscript letter may be interchanged); EIMS *m/z* 278 $[M]^+$ (1), 260 (3), 218 (4), 200 (26), 187 (27), 171 (25), 158 (29), 145 (35), 131 (55) 119 (40), 105 (52), 91 (58), 79 (36), 55 (29), 43 (100).

Longipin-9-ene-14,15-diol (9): obtained as colorless crystals ($CHCl_3$); mp 96−98 °C; $[\alpha]_D$ +16.1° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3363, 2919, 1709, 1440, 1373, 1262, 1035, 790 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.16 (1H, m, H-10), 3.57 (1H, d, J = 10.8 Hz, H-15a[a]), 3.49 (1H, d, J = 10.8 Hz, H-15b[a]), 3.47 (1H, d, J = 10.8 Hz, H-14a[a]), 3.40 (1H, d, J = 10.8 Hz, H-14b[a]), 2.20 (2H, m, H-11), 2.08 (1H, m, H-1), 1.96 (1H, da, J = 5.5 Hz, H-8), 1.69 (1H, s, H-7), 1.62 (3H, q, J = 1.9 Hz, H-12), 1.25−1.62 (6H, m, H-3, H-4, H-5), 0.81 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 147.3 (s, C-9), 117.5 (d, C-10), 68.0 (t, C-15[a]), 67.9 (t, C-14[a]), 49.4 (d, C-7), 45.7 (d, C-8), 40.9 (s, C-6[b]), 40.8 (t, C-3), 40.4 (s, C-2[b]), 39.5 (d, C-1), 34.0 (t, C-11), 28.6 (t, C-5), 23.4 (q, C-13), 22.9 (q, C-12), 21.0 (t, C-4) ([a,b]assignments with the same superscript letter may be interchanged); EIMS *m/z* 236 $[M]^+$ (1), 218 (1), 205 (4), 187 (11), 145 (11), 131 (37), 119 (97), 105 (79), 91 (100), 79 (58), 77 (57), 41 (27); HRFABMS *m/z* 259.1676 (calcd for $C_{15}H_{24}O_2Na$, 259.1674).

Generation of 9 by Reduction of 14 with $LiAlH_4$. To a solution of 100 mg of **14** (0.38 mmol) in 5 mL of THF, 30 mg (0.76 mmol) of $LiAlH_4$ were added. After being stirred for 2 h at room temperature and the usual work up, 80 mg of **9** were obtained.

X-ray Diffraction Analysis of Compound 9. Crystal data: $C_{15}H_{24}O_2$, mol wt 236.3, monoclinic, space group *C*2, a = 12.925(3) Å, b = 6.367(2) Å, c = 16.628(3) Å, β = 98.07(2)° (from 20 random-oriented reflections), V = 1354.8(6) Å^3, Z = 4, $F(000)$ = 520, D_c = 1.159 g/cm^3, Mo Kα radiation (λ = 0.71073), μ = 0.75 cm^{-1}. Crystal dimensions: 0.5 × 0.5 × 0.25 mm.

A total of 3575 reflections ($0 < h < 17$, $-8 < k < 8$, $-22 < l < 21$, $2\theta < 57°$) were recorded using a Siemens R3m/V (Mo Kα radiation, ω scan). Three standard reflections measured every 90 min showed no significant change during the data collection. Altogether 2811 reflections with ($|F| > 4\sigma(|F|)$ were retained for solving and refining the structure, and were corrected for Lorentz and polarization effects and empirically for absorption.

Non-hydrogen atoms were refined anisotropically by full-matrix least-squares calculations, minimizing $\sum w(F_o - F_c)^2$, with $w^{-1} = \sigma^2(F) + 0.0040F^2$. Hydrogen atoms were idealized, except for the hydroxyl groups, which were located in a ΔF map.

All calculations and drawings were performed with the SHELXTL PLUS program package[15] on a Micro VAX II computer. Final non-hydrogen atomic coordinates are included in Table 1.[16]

Longipin-9-ene-12,15-diol (2): obtained as colorless crystals ($CHCl_3$); mp 104−106 °C; $[\alpha]_D$ −18.2° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3268, 2920, 1662, 1451, 1371, 1283, 1114, 1044, 985, 855, 796 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.45 (1H, m, H-10), 3.99 (1H, d, J = 12.0 Hz, H-12a), 3.93 (1H, d, J = 12.0 Hz, H-12b), 3.42 (1H, d, J = 10.8 Hz, H-15a), 3.40 (1H, d, J = 10.8 Hz, H-15b), 2.16 (1H, m, H-1), 2.14−2.38 (3H, m, H-8, H-11), 1.66 (1H, s, H-7), 1.20−1.68 (6H, m, H-3, H-4, H-5), 0.83 (3H, s, H-14[a]), 0.81 (3H, s, H-13[a]); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 150.8 (s, C-9), 120.3 (d, C-10), 71.6 (t, C-12[a]), 66.2 (t, C-15[a]), 54.8 (d, C-7), 43.0 (d, C-8), 40.9 (t, C-3), 39.9 (s, C-2), 39.4 (d, C-1), 37.5 (s, C-6), 34.2 (t, C-5[b]), 34.1 (t, C-11[b]), 23.8 (q, C-13), 21.4 (q, C-14), 21.3 (t, C-4) ([a,b]assignments with the same superscript letter may be interchanged); EIMS *m/z* 236 $[M]^+$ (1), 218 (11), 215 (1), 187 (25), 159 (21), 145 (44), 131 (72), 119 (92), 105 (88), 91 (100), 79 (59), 77 (45), 55 (45), 41 (43); HRCIMS *m/z* 236.1770 (calcd for $C_{15}H_{24}O_2$, 236.1776).

Table 1. Atomic Coordinates ($\times 10^{-4}$) and Equivalent Isotropic Displacements Coefficients (Å $\times 10^3$) for **9**

atom	*x*	*y*	*z*	*U*(eq)[a]
C-1	889 (2)	851 (5)	7809 (1)	37 (1)
C-2	764 (2)	3070 (5)	8182 (1)	36 (1)
C-3	−69 (2)	4513 (6)	7690 (2)	49 (1)
C-4	137 (3)	5352 (7)	6866 (2)	59 (1)
C-5	288 (2)	3646 (6)	6275 (2)	54 (1)
C-6	1350 (2)	2524 (5)	6414 (1)	35 (1)
C-7	1703 (2)	1797 (5)	7297 (1)	32 (1)
C-8	1902 (2)	3443 (5)	7997 (1)	32 (1)
C-9	2655 (2)	2411 (6)	8671 (1)	42 (1)
C-10	2442 (2)	461 (6)	8857 (1)	47 (1)
C-11	1483 (3)	−623 (5)	8436 (2)	50 (1)
C-12	3578 (2)	3680 (8)	9056 (2)	66 (1)
C-13	560 (2)	3213 (6)	9070 (2)	48 (1)
C-14	1197 (2)	571 (6)	5859 (1)	46 (1)
C-15	2235 (2)	3888 (2)	6172 (2)	45 (1)
O1	1950 (2)	5000[b]	5424 (1)	58 (1)
O-2	2071 (2)	−785 (4)	5889 (1)	55 (1)

[a] Equivalent isotropic *U* defined as one-third of the trace of the orthogonalized U_{ij} tensor. [b] Atom used to fix the arbitrary origin in the *y* axis

Oxidation of 2 To Obtain 11. To a solution of 300 mg of **2** (1.48 mmol) in 8 mL of DMF, 2.8 g of PDC (7.4 mmol) were added under Ar. The mixture was kept at room temperature for 14 h. Then, 50 mL of H_2O were added and the mixture extracted with Et_2O. The organic layer was then dried with Na_2SO_4 and evaporated under a vacuum. The crude product was esterified with CH_2N_2 and column chromatographed. Elution with hexane/Et_2O yielded 85 mg of **11**.

4,15-Dihydroxylongipin-9(12)-en-10-one (8): colorless syrup; $[\alpha]_D$ +4.9° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3398, 2925, 1770, 1624, 1456, 1380, 1284, 1261, 1136, 1104, 1039, 980, 804, 755 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz) δ 5.93 (1H, d, J = 1.2 Hz, H-12a), 4.99 (1H, d, J = 1.2 Hz, H-12b), 3.52−3.66 (4H, m, H-14, H-15), 2.84 (1H, d, J = 6.6 Hz, H-8), 2.73 (1H, dd, J = 19.0, 2.7 Hz, H-11a), 2.57 (1H, dd, J = 19.0, 3.2 Hz, H-11b), 2.34 (1H, m, H-1), 1.83 (1H, s, H-7), 1.40−1.80 (6H, m, H-3, H-4, H-5), 0.80 (3H, s, H-13); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 200.9 (s, C-10), 149.9 (s, C-9), 116.4 (t, C-12), 67.7 (t, C-15[a]), 67.3 (t, C-14[a]), 49.4 (d, C-7), 46.3 (d, C-8), 44.5 (t, C-11), 43.0 (s, C-6), 41.5 (s, C-2), 40.8 (t, C-3), 36.6 (d, C-1), 29.4 (t, C-5), 23.1 (q, C-13), 20.7 (t, C-4) ([a]assignments with the same superscript letter may be interchanged); EIMS *m/z* 250 $[M]^+$ (1), 232 (10), 219 (27), 202 (78), 173 (34), 161 (48), 135 (92), 107 (68), 91 (100), 79 (86), 77 (79), 67 (47), 55 (50), 41 (56); HRCIMS *m/z* 251.1646 (calcd for $C_{15}H_{23}O_3$, 251.1647).

Longipin-9-ene-12,14,15-triol (6): colorless syrup; $[\alpha]_D$ −16.7° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3347, 2920, 1642, 1456, 1375, 1260, 1073, 1039, 851, 803, 757 cm^{-1}; ^1H NMR [$(CD_3)_2CO$, 400 MHz] δ 5.77 (1H, m, H-10), 3.87 (2H, br s, H-12), 3.33−3.52 (4H, m, H-14, H-15), 2.12−2.28 (4H, m, H-1, H-8, H-11), 1.83 (1H, s, H-7), 1.25−1.65 (6H, m, H-3, H-4, H-5), 0.81 (3H, s, H-13); ^{13}C NMR [$(CD_3)_2CO$, 100 MHz] δ 152.7. (s, C-9), 118.1 (d, C-10), 66.6 (t, C-15[a]), 66.5 (t, C-14[a]), 65.4 (t, C-12), 50.5 (d, C-7), 42.5 (d, C-8), 41.8 (s, C-6), 41.7 (t, C-3), 40.6 (s, C-2), 40.4 (d, C-1), 34.4 (t, C-11), 29.5 (t, C-5), 24.0 (q, C-13), 19.3 (t, C-4) ([a]assignments with the same superscript letter may be interchanged); EIMS *m/z* 252 $[M]^+$ (1), 234 (6), 221 (6), 203 (23), 185 (19), 173 (17), 157 (18), 145 (45), 131 (45), 119 (71), 105 (77), 91 (35), 79 (68), 67 (35), 55 (49), 41 (45); HRCIMS *m/z* 253.1806 (calcd for $C_{15}H_{25}O_3$, 253.1803).

Oxidation of 9 To Obtain 6. A solution of 212 mg of SeO_2 (2 mmol) and 236 mg (1 mmol) of **9** in 18 mL of 95% EtOH was refluxed for 2 h. Workup as usual gave 75 mg of starting material and 110 mg of **6**.

Longipin-9(12)-ene-10α,14,15-triol (7): colorless syrup; $[\alpha]_D$ −9.9° (*c* 1.0, $CHCl_3$); IR (film) ν_{max} 3351, 2925, 1645, 1570, 1457, 1376, 1259, 1144, 1031, 945, 896, 756 cm^{-1}; ^1H NMR [$(CD_3)_2CO$, 400 MHz] δ 4.95 (1H, s, H-12a), 4.73 (1H, s, H-12b), 4.44 (1H, d, J = 8.1 Hz, H-10), 3.39−3.57 (4H, m, H-14, H-15), 2.60 (1H, d, J = 6.7 Hz, H-8), 2.32 (1H, ddd, J = 14.2, 8.3, 2.7 Hz, H-11a), 2.14 (1H, s, H-7), 2.11 (1H, m, H-1), 1.84 (1H, dd, J = 14.2, 2.9 Hz, H-11b), 1.32−1.67 (6H, m, H-3, H-4, H-5), 0.59 (3H, s, H-13); ^{13}C NMR [$(CD_3)_2CO$, 100 MHz] δ 156.1 (s, C-9), 111.4 (t, C-12), 67.3 (d, C-10), 66.6 (t, C-15[a]), 66.4 (t, C-14[a]), 49.2 (d, C-7), 42.6 (d, C-8), 42.5 (s, C-6), 41.1 (s, C-2), 40.9 (t, C-3), 38.1 (d, C-1), 37.4 (t, C-11), 29.7 (t, C-5), 24.0 (q, C-13), 21.1 (t, C-4) ([a]assignments with the same superscript letter may be interchanged); EIMS *m*/*z* 251 $[M-1]^+$ (1), 234 (1), 216 (1), 204 (30), 189 (10), 173 (34), 157 (30), 145 (57), 131 (37), 119 (94), 105 (54), 91 (100), 79 (83), 67 (51), 55 (59), 41 (63); HRCIMS *m*/*z* 253.1807 (calcd for $C_{15}H_{25}O_3$, 253.1803).

Photooxidation of 9 To Obtain 7. A solution of **9** (1200 mg, 5.08 mmol) and 50 mg of bengale rose in 100 mL of *i*-PrOH was exposed to sunlight for 50 h. The solvent was then removed and the crude product dissolved in 100 mL of MeOH. To the resulting solution 1.2 g of $NaBH_4$ was added, and the reaction mixture was stirred at room temperature for 1 h. The crude extract obtained after usual workup was column chromatographed to yield 250 mg of starting material and 590 mg (EtOAc/MeOH 1:1) of **7**.

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(16) Crystallographic data for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre. Copies of the data can be obtained, free of charge, on application to the Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

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