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CYTOTOXIC AROMATIC TRITERPENES FROM *MAYTENUS ILICIFOLIA* AND *MAYTENUS CHUCHUHUASCA*

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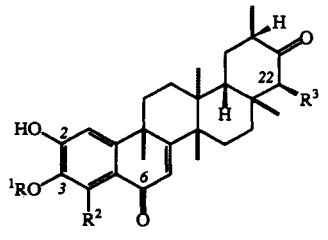
ABSTRACT.—The isolation and structure elucidation of four cytotoxic aromatic triterpenes [**1**–**4**] along with three known quinoid triterpenes [**5**–**7**] from the South American medicinal plants *Maytenus ilicifolia* and *M. chuchuhuasca* are described. The structures of these aromatic triterpenes contained aromatized A rings and C-6 oxygenated B rings, and were elucidated by ^{1}H- and ^{13}C-nmr spectroscopic studies and by X-ray crystallographic analysis of **3**.

We have recently been investigating the bioactive metabolites of the genus *Maytenus* in plants of the family Celastraceae (1–6), which are widely used as folk medicines in South America (7,8). From this genus and/or this family, many characteristic bioactive compounds, such as maytansinoids (9) with antitumor activity, quinoid triterpenes (2,10) and triterpene dimers (1,11,12) with cytotoxic activity, sesquiterpene pyridine alkaloids (3,4,6) with insect antifeedant (13) and immunosuppressive (14) activities, and sesquiterpene polyesters (5) with anti-tumor promoting activity (15), so far have been isolated.

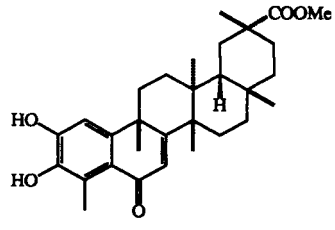
In our previous studies on the constituents of the Paraguayan medicinal plant "cangorosa" (*Maytenus ilicifolia*), we have reported the isolation and the structure determination of several characteristic compounds, such as oligo-nicotinated sesquiterpene polyesters (5), sesquiterpene pyridine alkaloids (6), triterpene dimers (1), and a cytotoxic quinoid triterpene along with aromatic triterpenes (2). Further investigation on the constituents of this material led us to isolate a novel aromatic triterpene [**1**].

In addition, the chemical study of the Brazilian medicinal plant "xuxuá" (*M. chuchuhuasca*) has led to the isolation of three novel aromatic triterpenes [**2**–**4**] together with three known quinoid triterpenes, pristimerin [**5**], tingenone [**6**], and 22β-hydroxytingenone [**7**].

The structures of the aromatic triterpenes **1** and **2**, derived from tingenone and pristimerin, and the further oxygenated triterpenes **3** and **4**, each containing an aromatized A ring and a 6-oxygenated B ring, were elucidated by a combination of spectral methods.



1 R^1,R^3=H; R^2=CH_3
3 R^1,R^2=CH_3; R^3=H
4 R^1=CH_3; R^2=CH_2OH; R^3=OH



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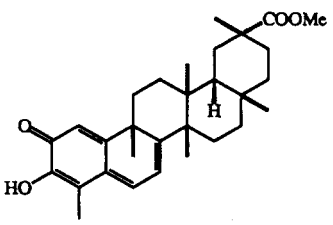

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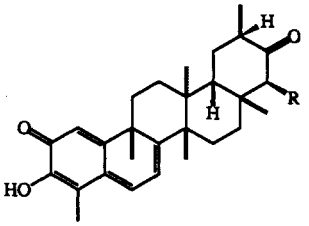

6 R=H
7 R=OH

RESULTS AND DISCUSSION

The $CHCl_3$-soluble portion of a MeOH extract of the root bark of *Maytenus ilicifolia* (1140 g) was subjected to Si gel cc. The fractions obtained were further separated by Si gel or ODS (octadecyl Si gel) mplc and hplc to give an aromatic triterpene [**1**] (0.0013%).

Also, a CH_2Cl_2-soluble portion of the MeOH extract of the stem bark of *M. chuchuhuasca* (5 kg) was subjected to Si gel cc, following ODS mplc and/or hplc to give three aromatic triterpenes: [**2**] (0.0025%), [**3**] (0.0016%), [**4**] (0.0012%), [**5**] (0.0015%), [**6**] (0.0020%), and [**7**] (0.0017%).

Compound **1** was obtained as white powder with a molecular formula, $C_{28}H_{36}O_4$, which was established by hrms. The ^1H- and ^{13}C-nmr spectra suggested **1** to be a triterpene, and it was found that a portion of the signals could be assignable to the D and E rings of tingenone [**6**] including a secondary methyl group (δ_H 0.83, 3H, d, J=6.5 Hz) and a saturated ketone [δ_C 215.08 (s)]. Furthermore, the ^{13}C-nmr spectrum showed that eight carbon signals [δ_C 108.19 (d), 121.17 (s), 125.53 (d), 125.87 (s), 141.42 (s), 148.87 (s), 150.99 (s), 171.02 (s)] could be assigned to four double bonds, and two proton signals [δ_H 6.08 (1H, s); 6.71 (1H, s)] assigned to olefinic protons. The uv and ir spectra suggested that **1** contained an aromatic ring system instead of an extensively conjugated system, as in tingenone. The remaining carbonyl carbon signal at δ_C 187.90 was assigned to the ketone at position 6 lying between the aromatic A ring and a double bond of the B ring. These spectroscopic analyses confirmed the structure of **1** as 6-oxotingenol.

Compound **2**, a colorless amorphous solid with a molecular formula of $C_{30}H_{40}O_5$, was also an aromatic triterpene. The nmr spectrum suggested that **2** had a substructure similar to the D and E rings of pristimerin [**5**] including a methyl ester group [δ_H 3.58 (3H, s); δ_C 50.81 (q), 187.91 (s)] at C-20. As in the case of **1**, compound **2** also had four double bonds, with one of them placed at the B ring and another at the A ring which was aromatic. Between these partial structures, the C-6 carbon was oxygenated as in **1**. Based on this spectroscopic evidence, the structure of **2** was determined to be 6-oxopristimerol.

Compound **3** was obtained as colorless plates, and its molecular formula was determined to be $C_{29}H_{38}O_4$ from hrms. In this aromatic triterpene, the partial structure of the D and E rings was identical with those in **1** and **6**, and that of the A, B, and C rings was similar to those of **1** and **2**, which contain an aromatized A ring and an α,β unsaturated ketone in the B ring. Compound **3** differs from **1** only in the additional methoxy methyl group [δ_H 3.76 (3H, s); δ_C 60.99 (q)] that must be located in the A ring. This methylated position was determined as C-3 by interpretation of 2D, HMBC, and NOESY nmr spectra as indicated below. The methoxy methyl group showed a nOe correlation with the C-23 methyl group [δ_H 2.67 (3H, s)], and a long-range H-C correlation with the C-3 carbon [δ_C 144.53 (s)] (Figure 1). This structure was also confirmed as 3-methyl-6-oxotingenol by X-ray crystallographic analysis (Figure 2).

Compound **4**, a white powder with a molecular formula of $C_{29}H_{38}O_6$, appeared to contain an aromatized A ring and an α,β unsaturated ketone in the B ring, as in

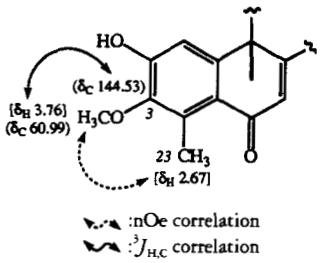

FIGURE 1. Partial structure of compound **3**.

compounds **1–3** by observations from its ^{1}H- and ^{13}C-nmr spectra. Its D and E rings were identical to those of 22β-hydroxytingenone [7], and one methoxy methyl group was present in the molecule. However, instead of a C-23 methyl group, three proton signals coupled to each other (δ_H 4.74, 1H, br dd, J=4.2 and 12.1 Hz; 4.92, 1H, dd, J=9.8 and 12.1 Hz; 5.10, 1H, br dd, J=5.0 and 9.8 Hz) and a methylene carbon signal [δ_C 56.97 (t)] were observed. These signals were ascribed to a C-23 hydroxy methyl group. The presence of an intermolecular hydrogen bond between the hydroxy proton at δ_H 5.10, which disappeared on addition of D_2O, and a C-6 carbonyl oxygen was also suggested. The position of the methoxy methyl group was assigned to C-3 by a nOe correlation between this methoxy methyl group and the C-23 methylene proton at δ_H 4.74 (Figure 3). The C-23 oxygenated methylene carbon signal which appeared at higher field could be reasonably explained by a steric compression effect due to the C-3 methoxy methyl group. Consequently, the structure of **4** was determined to be 3-methyl-22β,23-dihydroxy-6-oxotingenol.

These aromatic triterpenes showed moderate cytotoxic activities against a number of cultured tumor cell lines (Table 1).

EXPERIMENTAL

GENERAL EXPERIMENTAL DETAILS.—Mps were determined on a Yanagimoto micro-melting point apparatus and are uncorrected. Optical rotations were measured with a Jasco DIP-4 spectrometer and the [α]D values are given in 10^{-1} deg cm^2 g^{-1}. Ms, uv, and ir spectra were taken with a Hitachi M-80 spectrometer, a Hitachi 557 spectrophotometer, and a Perkin-Elmer 1710 spectrophotometer, respectively.

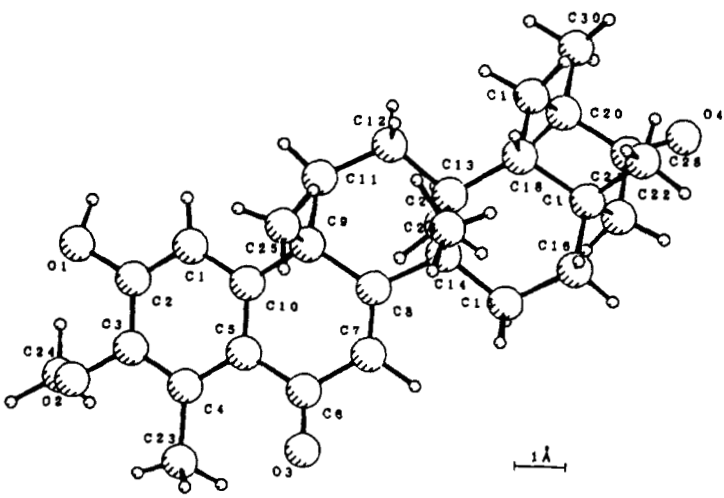

FIGURE 2. X-ray crystallographic structure of compound **3**.

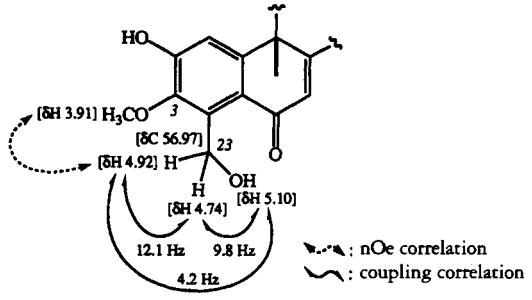

FIGURE 3. Partial structure of compound **4**.

Mplc was performed with a CIG column system (22 mm i.d.×300 mm, Kusano Scientific Co., Tokyo) packed with 10 μm Si gel or 20 μm ODS. Hplc was performed with an Inertsil PREP-ODS column (20 mm i.d.×250 mm, GL Science Inc., Tokyo) packed with 10 μm ODS. Tlc was conducted on precoated Kieselgel 60 F_{254} (Art. 5715; Merck) and the spots were detected by heating after spraying with 10% H_2SO_4. 1D and 2D ^1H- and ^{13}C-nmr spectra were recorded on Bruker spectrometers (AM400 and AM500) at 303° K and processed on a Bruker data station with an Aspect 3000 computer. NOESYPH experiments were made with a mixing time of 0.6 sec. The value of the delay to optimize one-bond correlations in the HMQC spectrum and suppress them in the HMBC spectrum was 3.2 msec and the evolution delay for long-range couplings in the HMBC spectrum was set to 50 msec. The nmr coupling constants (J) are given in Hz.

PLANT MATERIAL.—The reddish to orangish root bark of *Maytenus ilicifolia* Mart. ex Reiss. (1140 g), commonly known as "cangorosa" among the local people, was purchased at Asuncíon, Paraguay, in 1987. The botanical identification was made by Dr. Tanaka (Asuncíon University). A voucher specimen has been deposited in the herbarium of the Tokyo College of Pharmacy.

The dark reddish to brown stem bark of *Maytenus chuchuhuasca* Raymond-Hamet et Colas (5 kg), commonly known as "xuxuá," was purchased at São Paulo, Brazil, in 1992. The botanical identification was made by Dr. William Antonio Rodrigues (Instituto Nacional de Pesquisas da Amazonia). A voucher specimen has been deposited in the herbarium of the Tokyo College of Pharmacy.

EXTRACTION AND ISOLATION.—The root bark (1140 g) of *M. ilicifolia* was crushed and extracted with hot MeOH (12 liters) to give a MeOH extract (364 g), which was partitioned between $CHCl_3$ and H_2O. The $CHCl_3$-soluble fraction (62.3 g) was subjected to Si gel cc using an *n*-hexane-EtOAc gradient system (1:0–0:1) to give seventeen fractions. A cytotoxic fraction VI was further subjected to ODS mplc with a MeOH/H_2O solvent system to give **1** as an amorphous solid.

The bark (5 kg) of *M. chuchuhuasca* was crushed and extracted with hot MeOH (54 liters) to give a MeOH extract (1.5 kg), which was partitioned between CH_2Cl_2 and H_2O. The CH_2Cl_2-soluble fraction (155 g) was subjected to Si gel cc using an CH_2Cl_2-EtOAc gradient system (1:0–0:1) to give twelve fractions. Cytotoxic fractions V and VI were further subjected to ODS mplc with CH_3CN/H_2O, following elution with MeOH to give **2**–**4**. These compounds were further purified by ODS hplc with MeOH/H_2O or MeCN/H_2O solvent systems.

BIOASSAYS.—The extracts, fractions, and isolated compounds were routinely evaluated for cytotoxicity by the MTT assay method (16), with slight modification.

TABLE 1. Cytotoxic Activity Against Cultured Tumor Cell Lines.

	IC_{50} (μg/ml)		
	L-1210	P-388	KB
6-Oxotingenol [**1**]	6.0	2.6	30
6-Oxopristimerol [**2**]	2.8	1.5	2.8
3-Methyl-6-oxotingenol [**3**]	>100	>100	11
3-Methyl-22β,23-diol-6-oxotingenol [**4**]	—	4.3	—
Pristimerin [**5**]	0.36	0.12	0.55
Tingenone [**6**]	0.14	0.041	0.28
22β-Hydroxytingenone [**7**]	—	0.012	—

TABLE 2. Refined Fractional Atomic Coordinates of Compound **3**.

Atom	*x*	*y*	*z*
C-1	19832 (19)	36153 (18)	3028 (26)
C-2	10957 (20)	32395 (20)	4768 (27)
C-3	3422 (19)	37862 (21)	8177 (24)
C-4	4617 (19)	47102 (21)	9576 (23)
C-5	13759 (18)	50877 (18)	7734 (21)
C-6	15596 (20)	60643 (18)	9229 (23)
C-7	25510 (20)	63492 (17)	10454 (24)
C-8	32947 (18)	58458 (16)	7469 (20)
C-9	31288 (17)	49226 (16)	1764 (21)
C-10	21409 (17)	45370 (17)	4565 (21)
C-11	38933 (18)	42304 (16)	5526 (25)
C-12	48961 (17)	46094 (17)	6830 (23)
C-13	49319 (16)	54473 (16)	14608 (20)
C-14	43105 (18)	62061 (16)	8910 (22)
C-15	43542 (21)	70488 (17)	16783 (26)
C-16	53577 (23)	74172 (18)	17875 (27)
C-17	61453 (20)	67323 (17)	21131 (23)
C-18	59783 (17)	57773 (17)	15657 (21)
C-19	66693 (18)	50821 (18)	20814 (26)
C-20	67351 (20)	50470 (21)	34022 (27)
C-21	69123 (21)	59919 (22)	38334 (24)
C-22	62119 (22)	66851 (20)	34312 (25)
C-23	−3829 (23)	52664 (27)	13461 (35)
C-24	−6776 (29)	28254 (29)	19016 (31)
C-25	31478 (22)	50221 (22)	−11519 (23)
C-26	46689 (22)	64952 (20)	−3108 (25)
C-27	44911 (18)	51750 (17)	26207 (22)
C-28	71014 (23)	71171 (22)	16835 (30)
C-30	74855 (25)	43684 (25)	37955 (36)
O-1	9201 (15)	23412 (14)	3159 (23)
O-2	−5487 (14)	34094 (17)	9374 (18)
O-3	9333 (15)	66399 (15)	9756 (22)
O-4	75835 (16)	61798 (17)	44452 (21)
HC-1	2451 (20)	3214 (19)	26 (25)
HC-7	2653 (20)	7026 (19)	1404 (25)
HC-11	3712 (19)	3908 (18)	1390 (24)
H′C-11	3917 (20)	3706 (19)	73 (26)
HC-12	5201 (19)	4761 (18)	−75 (25)
H′C-12	5292 (19)	4089 (18)	1055 (23)
HC-15	3918 (24)	7536 (22)	1342 (30)
H′C-15	4126 (18)	6895 (17)	2485 (22)
HC-16	5353 (21)	7923 (21)	2370 (27)
H′C-16	5524 (23)	7703 (21)	991 (27)
HC-18	6187 (17)	5875 (16)	712 (21)
HC-19	6494 (17)	4434 (17)	1814 (21)
H′C-19	7349 (21)	5210 (19)	1806 (25)
HC-20	6043 (18)	4903 (17)	3707 (23)
HC-22	5555 (18)	6496 (17)	3828 (23)
H′C-22	6398 (20)	7261 (20)	3800 (25)
HC-23	−571 (25)	5785 (24)	860 (32)
H′C-23	−908 (24)	4879 (24)	1443 (33)
H′C-23	−269 (24)	5636 (24)	2108 (31)
HC-24	−697 (26)	3192 (26)	2486 (34)
H′C-24	−1422 (3)	2570 (28)	1890 (39)
H″C-24	−154 (27)	2337 (27)	1847 (34)
HC-25	2903 (24)	4487 (23)	−1448 (31)
H′C-25	2735 (22)	5563 (20)	−1388 (27)

TABLE 2. Continued.

Atom	x	y	z
H″C-25	3818 (23)	5095 (22)	−1385 (30)
HC-26	4117 (32)	6911 (31)	−691 (45)
H′C-26	5227 (21)	6787 (20)	−269 (27)
H″C-26	4890 (29)	5901 (29)	−862 (37)
HC-27	4560 (19)	5642 (18)	3206 (23)
H′C-27	3760 (18)	5076 (17)	2528 (22)
H″C-27	4800 (20)	4598 (19)	2911 (25)
HC-28	7621 (22)	6724 (22)	1946 (29)
H′C-28	7095 (24)	7173 (23)	875 (30)
H″C-28	7165 (24)	7755 (23)	2043 (30)
HC-30	8099 (25)	4581 (25)	3482 (33)
H′C-30	7486 (25)	4358 (23)	4570 (32)
H″C-30	7328 (29)	3721 (28)	3479 (38)
HO-1	1513 (27)	2026 (25)	416 (35)

6-Oxotingenol [**1**].—White powder; mp >300°; [α]D −151.8° (*c*=0.11, pyridine); ms *m/z* 436 (M^+, 16, calcd for $C_{28}H_{36}O_4$ 436.2614, found 436.2634), 419 (19), 258 (6), 217 (13), 105 (100); ir ν max (KBr) 3469, 1701, 1638, 1586, 1568 cm^{-1}; uv λ max (MeOH) (log ε) 209 (4.47), 251 (4.23), 304 (4.09) nm; ^1H nmr ($CDCl_3$-CD_3OD, 3:1, 400 MHz) δ 0.83 (3H, d, *J*=6.5 Hz), 0.86 (3H, s) (×2), 1.24 (3H, s), 1.43 (3H, s), 1.96 (1H, m), 2.06 (1H, dd, *J*=6.8 and 14.7 Hz), 2.16 (1H, br d, *J*=13.1 Hz), 2.37 (1H, br dq, *J*=6.5 and 13.0 Hz), 2.46 (3H, s), 2.79 (1H, d, *J*=14.4 Hz), 6.08 (1H, s), 6.71 (1H, br s); ^{13}C nmr ($CDCl_3$-CD_3OD, 3:1, 100 MHz) δ 13.23 (q), 14.55 (q), 19.30 (q), 20.40 (q), 28.14 (t) 29.93 (t), 31.81 (t), 32.12 (q), 33.99 (t), 35.23 (t), 38.09 (q), 38.18 (s), 39.75 (s), 40.07 (s), 41.74 (d), 43.23 (d), 44.02 (s), 52.35 (t), 108.19 (d), 121.71 (s), 125.53 (d), 125.87 (s), 141.42 (s), 148.87 (s), 150.99 (s), 171.02 (s), 187.90 (s), 215.08 (s).

6-Oxopristimerol [**2**].—Colorless amorphous solid; mp 173–178°; [α]D −80.4° (*c*=0.48, pyridine); ms *m/z* 480 (M^+, 100, calcd for $C_{30}H_{40}O_5$ 480.2876, found 480.2844), 465 (38), 421 (7), 285 (11), 255 (12), 218 (52), 203 (37); ir ν max (KBr) 3400, 1728, 1638, 1587 cm^{-1}; uv λ max (MeOH) (log ε) 207 (4.41), 250 (4.28), 255 (4.30), 305 (3.93) nm; ^1H nmr (C_5D_5N, 400 MHz) δ 0.63 (3H, s), 0.86 (1H, br d, *J*=13.8 Hz), 0.99 (3H, s), 1.15 (3H, s), 1.16 (3H, s), 1.53 (3H, s), 2.01 (1H, br ddd, *J*=5.2, 13.8, and 13.8 Hz), 2.07 (1H, br ddd, *J*=3.9, 14.0, and 14.0 Hz), 2.18 (1H, br d, *J*=11.8 Hz), 2.26 (1H, br d, *J*=14.1 Hz), 2.41 (1H, br d, *J*=15.7 Hz), 3.28 (3H, s), 3.58 (3H, s), 6.46 (1H, s), 7.25 (1H, s); ^{13}C nmr (C_5D_5N, 100 MHz) δ 14.82 (q), 18.51 (q), 20.87 (q), 28.86 (t), 30.11 (t), 30.21 (t), 30.64 (s), 31.08 (t), 31.55 (q), 32.73 (q), 34.59 (t), 35.13 (t), 36.62 (t), 37.76 (q), 39.30 (s), 40.14 (s), 40.58 (s), 44.38 (d), 44.61 (s), 51.47 (q), 109.99 (d), 122.67 (s), 126.80 (s), 126.88 (d), 144.04 (s), 150.67 (s), 151.38 (s), 170.17 (s), 178.66 (s), 187.32 (s).

3-Methyl-6-oxotingenol [**3**].—Colorless plates (EtOH); mp 273–276°; [α]D −93.4° (*c*=0.39, $CHCl_3$), ms *m/z* 450 (M^+, 68, calcd for $C_{29}H_{38}O_4$ 450.2770, found 450.2785), 437 (66), 383 (16), 299 (46), 243 (53), 201 (79), 133 (67), 105 (100); ir ν max ($CHCl_3$) 3516, 1704, 1646, 1602, 1578 cm^{-1}; uv λ max (MeOH) (log ε) 207 (4.29), 247 (4.13), 307 (4.03) nm; ^1H nmr ($CDCl_3$, 400 MHz) δ 0.91 (3H, d, *J*=6.4 Hz), 0.99 (3H, s) (×2), 1.37 (3H, s), 1.44 (1H, br d, *J*=14.0 Hz), 1.59 (3H, s), 2.13 (1H, dt, *J*=6.8 and 13.4 Hz), 2.16 (1H, dd, *J*=6.8 and 14.7 Hz), 2.30 (1H, br d, *J*=13.4 Hz), 2.48 (1H, br dq, *J*=6.5 and 13.5 Hz), 2.67 (3H, s), 2.89 (1H, d, *J*=14.5 Hz), 3.76 (3H, s), 6.26 (1H, s), 6.96 (1H, s); ^{13}C nmr ($CDCl_3$, 100 MHz) δ 14.61 (q), 15.09 (q), 19.69 (q), 20.84 (q), 28.45 (t), 30.21 (t), 31.99 (t), 32.59 (q), 34.22 (t), 35.56 (t), 38.18 (s), 38.49 (q), 40.13 (s), 40.20 (s), 41.89 (d), 43.56 (d), 44.34 (s), 52.59 (t), 60.99 (q), 109.31 (d), 123.03 (s), 126.09 (d), 133.21 (s), 144.53 (s), 152.34 (s), 154.94 (s), 170.21 (s), 186.98 (s), 213.54 (s).

3-Methyl-22β,23-dihydroxy-6-oxotingenol [**4**].—White powder, mp 240–245° (dec), [α]D −60.9° (*c*=0.88, $CHCl_3$); ms *m/z* 482 (M^+, 68, calcd for $C_{29}H_{38}O_6$ 482.2668, found 482.2675), 467 (100), 449 (7), 282 (5), 245 (12), 232 (14); ir ν max ($CHCl_3$) 3509, 1708, 1642, 1598, 1575 cm^{-1}; uv λ max (MeOH) (log ε) 206 (4.20), 249 (4.02), 313 (3.88) nm; ^1H nmr ($CDCl_3$, 400 MHz) δ 0.86 (3H, s), 1.00 (3H, s), 1.05 (3H, d, *J*=6.3 Hz), 1.40 (3H, s), 1.60 (1H, s), 2.13 (1H, br dt, *J*=9.8 and 13.7 Hz), 2.20 (1H, dd, *J*=6.9 and 14.5 Hz), 2.27 (1H, br dd, *J*=3.3 and 14.5 Hz), 2.36 (1H, br dt, *J*=3.2 and 13.8 Hz), 2.63 (1H, br dq, *J*=6.3 and 12.8 Hz), 3.67 (1H, br s), 3.91 (3H, s), 4.52 (1H, br s), 4.74 (1H, br dd, *J*=4.2 and 12.1 Hz), 4.92 (1H, dd, *J*=9.8 and 12.1 Hz), 5.10 (1H, br dd, *J*=5.0 and 9.8 Hz), 6.36 (1H, s), 7.07 (1H, s); ^{13}C nmr ($CDCl_3$, 100 MHz) δ 14.72 (q), 20.48 (q), 20.80 (q), 25.03 (q), 28.24 (t), 29.53 (t), 30.05 (t), 31.92 (t), 34.33 (t), 38.51 (q), 40.35 (s), 40.42 (s), 40.85 (d), 44.35 (s), 44.78 (s), 45.01 (d), 56.97 (t), 63.34 (q), 76.49 (d),

111.44 (d), 123.27 (s), 125.24 (d), 134.78 (s), 144.72 (s), 153.43 (s), 155.80 (s), 172.91 (s), 187.65 (s), 213.43 (s).

CRYSTALLOGRAPHIC ANALYSIS OF COMPOUND **3**.—Crystal data: molecular formula, $C_{29}H_{38}O_4$; formula weight, 450.6; crystal system, orthorhombic; space group, $P2_1P2_1P2_1$, Z=4, a=14.104 Å, b=14.758 Å, c=11.719 Å, V=2539.3 Å^3, Dx=1.227 g/cm^3. A colorless thick plate crystal was mounted on a Nonius CAD4 diffractometer with the graphite-monochromated CuKa radiation (μ=6.0 cm^{-1}) at 23°. A total of 2774 reflections was observed within the 2θ range from 3° through 150°. The structure was determined by the direct method using the SHELXS-86 program (17) and the refinement was carried out by the block-diagonal-matrix least-squared method using 2774 reflections. The final R value was 0.047. The numbers of atoms refined were 33 carbon and oxygen atoms with anisotropic thermal parameters and 38 hydrogen atoms with isotropic parameters which were found on the difference electron-density map and located at the calculated positions. The refined fractional atomic coordinates are shown in Table 2.[1] The molecular structure determined by this method is illustrated in Figure 2.

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[1]Refined fractional bond distances and bond angles for **3** have been deposited at the Cambridge Crystallographic Center and can be obtained on request from Dr. Olga Kennard, University Chemical Laboratory, 12 Union Road, Cambridge CB2 1EZ, UK.