Anti-androgenic Triterpenoids from the Brazilian Medicinal Plant, *Cordia multispicata*

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Compounds 1—6 were isolated from the AcOEt soluble fraction of leaves of the Brazilian medicinal plant, *Cordia multispicata*, and their structures were elucidated to be 3β,25-epoxy-21β-acetoxy-3α,22β-dihydroxyurs-12-en-28-al (1), 3β,25-epoxy-28-acetoxy-3α,21β,22β-trihydroxyurs-12-ene (2), 21β-acetoxy-22β-hydroxy-3-oxours-12-en-28-al (3), 28-acetoxy-6β,21β,22β-trihydroxy-3-oxours-12-ene (4), 21β,22β-dihydroxy-3-oxours-12-en-28-al (5) and 3β,21β,22β-trihydroxyurs-12-en-28-al (6), respectively, by means of spectral data, especially two dimensional NMR techniques. Triterpenes having the hemiketal structure at the A-ring, an acyloxy group at C-22 and/or ketone at C-3 showed potent anti-androgenic activity.

Key words *Cordia multispicata*; ursan-type triterpene; anti-androgenic activity; hemiketal

In the course of our program to find anti-androgenic constituents from plant sources, we have isolated anti-androgenic neoflavones and flavonoids from *Dalbergia conchinchinensis*[1] and prenyl flavones from *Sophora flavescens*.[2] In further screening of plant extracts, methanol extracts of *Cordia multispicata* (Boraginaceae) were shown to have potent activity. *C. multispicata* is a Brazilian medicinal plant that is used as an expectorant and as a drug for contusion, and is mainly distributed in the Amazon area. No chemical constituents have been reported from *C. multispicata*,[3] however, a few reports on the constituents from other *Cordia* sp. plants have appeared. The anti-androgenic constituents were isolated from leaves of *C. multispicata* by activity-guided fractionation, to give six new ursane type triterpenoids along with known oleanane and ursane triterpenes having relatively novel structures. This paper deals with the isolation and structural elucidation of the new triterpenes, **1**—**6** from *C. multispicata* and their inhibitory activity against testosterone 5α-reductase.

A methanol extract of leaves of *C. multispicata* showing anti-androgenic activity was partitioned between AcOEt and H_2O. The aqueous layer was further extracted with *n*-BuOH to give a *n*-BuOH soluble fraction and the aqueous layer. The AcOEt fraction showed the most potent anti-androgenic activity and was fractionated as described in the Experimental section to give new triterpenes, **1**—**6**, along with known triterpenes, lantanolic acid (**7**),[4] 3-epipomolic acid (**8**),[5] lantic acid (**9**),[4] icterogenin (**10**),[6] lantadene A (**11**),[7] lantadene B (**12**),[7] ursomic acid (**13**)[8] and pomonic acid (**14**),[9] and the flavonols pachypodol (**15**)[10] and retusin (**16**),[11] which were recently reported as anti-emetic principles of *Pogostemon cablin*.[12]

The high resolution (HR)-FAB-MS of **1** afforded a pseudo molecular ion $[MH]^+$ at *m/z* 529.3533, corresponding to the molecular formula $C_{32}H_{48}O_6$. The IR spectrum of **1** showed absorptions at 3434 (OH) and 1730 (carbonyl) cm^{-1}. The ^{1}H-NMR spectrum of **1** showed the presence of four singlet methyl groups (δ 0.70, 0.96, 1.03, 1.07), two doublet methyl groups [δ 0.92 (d, *J*=6.4 Hz), 0.97 (d, *J*=6.8 Hz)], characteristic methylene protons [δ 3.88 (d, *J*=10.2 Hz), 4.25 (dd, *J*=10.2, 2.4 Hz)] for the hemiketal group, which were the same as those of lantanolic acid (**7**), a formyl group [δ 9.54 (s)], an olefin proton [δ 5.49 (dd, *J*=4.8, 2.4 Hz)] and two secondary hydroxy groups [δ 3.89 (br s), 4.82 (dd, *J*=11.4, 2.4 Hz)]. The ^{13}C-NMR spectrum (Table 1) of **1** showed a characteristic hemiketal carbon (δ 97.9), a carbonyl group (δ 207.7), ester carbonyl group (δ 170.1), an oxymethylene carbon (δ 67.8), two oxymethine carbons (δ 73.5, 76.2) and a trisubstituted olefin group (δ 127.9, 136.4). These spectral

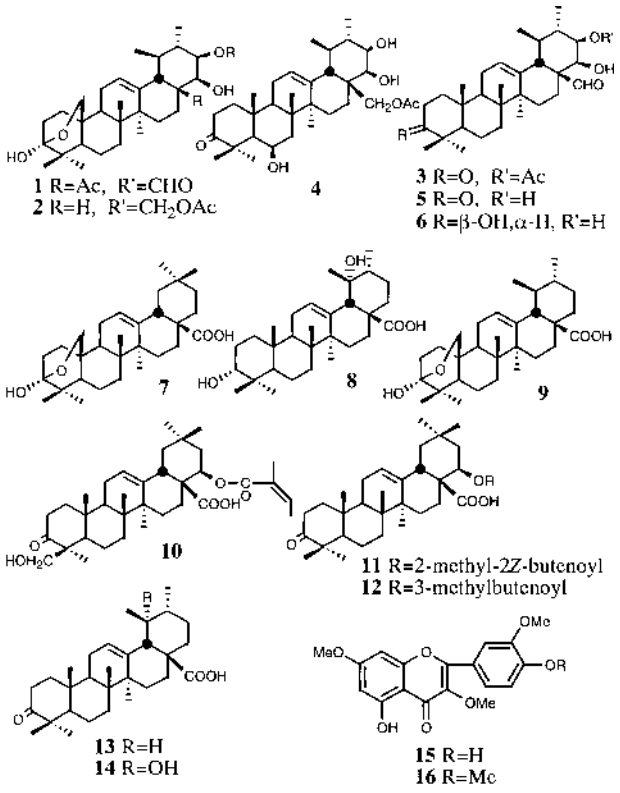

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Table 1. ^{13}C NMR Data of Compound **1**—**5**[a] and **6**[b] (125 MHz)

	1	2	3	4	5	6
C-1	35.2	35.2	39.4	41.8	39.4	38.1[c]
2	29.5	29.6	34.2	34.4	34.2	26.9
3	97.9	97.9	217.5	216.3	217.8	76.7
4	40.1	40.2	47.4	48.8	47.5	38.2[c]
5	50.4	50.4	55.3	56.6	55.3	54.6
6	19.4	19.5	19.1	69.2	19.6	19.8
7	31.3	30.9	32.6	40.5	32.5	32.5
8	38.8	39.0	40.0	39.5	40.0	39.8
9	41.8	41.8	46.8	47.3	46.8	46.9
10	34.8	34.8	36.3	36.3	37.8	36.4
11	23.9	23.8	23.4	23.9	23.4	22.9
12	127.9	126.4	127.9	126.6	127.8	126.0
13	136.4	137.8	136.6	137.1	136.7	137.0
14	42.8	42.5	43.2	43.2	43.2	42.3
15	26.6	25.6	26.6	25.8	26.7	26.2
16	23.2	21.7	23.4	21.9	23.5	22.3
17	53.5	42.8	53.5	42.8	53.6	53.1
18	47.9	49.5	47.6	49.1	47.8	47.1
19	38.0	37.9	38.1	37.9	36.3	37.3
20	36.1	39.1	36.7	39.3	39.0	38.3[c]
21	76.2	72.8	76.3	72.9	75.4	71.8
22	73.5	72.6	73.7	72.8	73.4	74.9
23	27.1	27.1	26.6	26.0	26.6	16.0
24	18.1	18.2	21.5	24.1	21.6	28.2
25	67.8	67.8	15.3	16.7	15.4	15.2
26	17.7	17.0	16.8	18.5	16.9	16.7
27	22.8	23.3	23.7	23.7	23.7	22.9
28	207.7	64.7	208.1	64.8	209.5	208.1
29	16.6	17.1	17.1	17.1	17.1	16.8
30	15.3	16.0	15.5	16.1	15.9	15.7
CO	170.1	172.6	170.2	172.6		
CH_3	20.9	20.9	21.1	21.0		

a) Spectra were taken in $CDCl_3$. *b*) Spectrum was taken in dimethyl sulfoxide (DMSO)-d_6. *c*) Assignment may be interchangeable. Assignments are based on HMQC and HMBC spectra.

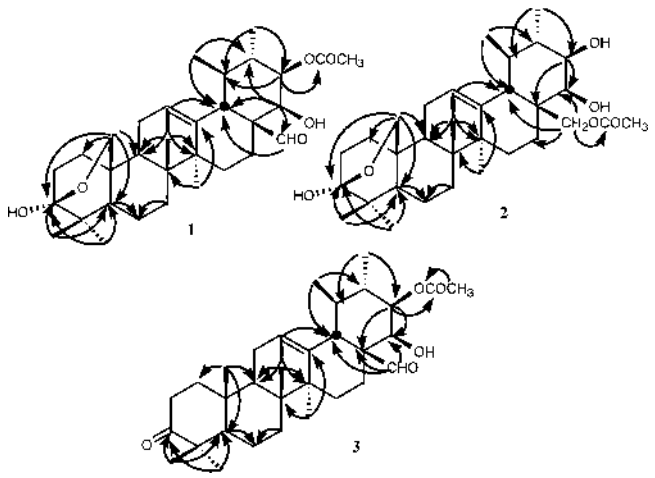

Fig. 1. Selected HMBC Correlations of **1**—**3**

data indicated that **1** was an ursane triterpenoid having hemiketal structure, formyl, acetoxy and hydroxy groups. The tentative structure of **1** and its ^{1}H- and ^{13}C-NMR (Table 1) assignments were confirmed by ^{1}H-detected multiple quantum coherence (HMQC) and heteronuclear multiple bond correlation (HMBC) experiments. In the HMBC experiment as shown in Fig. 1, Me-23 and Me-24 showed long range correlation with C-3, C-4 and C-5 carbons. H-25 showed correlation with C-1, C-3, C-5 and C-9. Me-26 showed correlation with C-7, C-8, C-9 and C-14. Me-27 showed correlation with C-8, C-13, C-14 and C-15. A formyl proton showed correlation with C-16 and C-18. H-21 showed correlation with C-19, ester carbonyl. H-12 showed correlation with C-9, C-14 and C-18. H-5 and H-7 showed correlation with C-6. H-22 showed correlation with the formyl, C-18 and C-20. Me-30 showed correlation with C-19 and C-21. The ^{13}C-NMR data of A, B, C and D-ring carbons of **1** showed almost the same chemical shifts with those of **7**. From these data the structure of **1** including an acetoxy group at C-21, a hydroxy group at C-22, a formyl group at C-28 and a hemiketal in the A-ring was determined. Stereochemistry at C-21 and 22 was determined to be a β-equatorial acetoxy group at C-21 and a β-axial hydroxy group at C-22 from the coupling constants of H-22 (br s). Thus, the structure of **1** was determined as 21β-acetoxy-3α,22β-dihydroxy-3β,25-epoxyurs-12-en-28-al, and named cordiaketal A.

The HR-FAB-MS of **2** afforded a pseudo molecular ion $[MH]^+$ at *m/z* 531.3689 corresponding to the molecular formula $C_{32}H_{50}O_6$. The IR spectrum of **2** showed absorption bands at 3383 (OH) and 1744 (ester) cm^{-1}. The ^{1}H-NMR spectrum of **2** showed the presence of four singlet methyl groups (δ 0.94, 0.98, 1.04, 1.09), two doublet methyl groups [δ 0.85 (d, J=6.0 Hz), 1.06 (d, J=6.6 Hz)], an acetyl methyl group [δ 2.09 (s)], the characteristic methylene group of the hemiketal on the A-ring [δ 3.89 (d, J=9.0 Hz), 4.28 (dd, J=9.0, 3.0 Hz)], an olefin proton [δ 5.22 (dd, J=3.6, 1.8 Hz)], acyloxymethyl group [δ 3.95 (d, J=11.4 Hz), 4.40 (d,

J=11.4 Hz)] and two secondary hydroxy groups [δ 3.36 (br d, J=9.6 Hz), 3.43 (br s)]. The ^{13}C-NMR spectrum of **2** showed the characteristic hemiketal carbon (δ 97.9), an ester carbonyl (δ 172.6), two oxymethylene carbons (δ 64.7, 67.9), two oxymethine carbons (δ 72.6, 72.8), an acetyl methyl group (δ 20.9) and trisubstituted olefin carbons (δ 126.4, 137.8). From this data, the structure of **2** was presumed to be an ursane-type triterpene having a hemiketal in the A-ring, hydroxy groups on the E-ring and a 28-acetoxy group. The structure and NMR assignments were confirmed by HSQC and HMBC experiments. The significant HMBC correlations are shown in Fig. 1. The stereochemistry at C-21 and 22 was determined from the coupling constants of the protons at C-21 and 22, and by difference nuclear Overhauser effect (NOE) experiments. H-21 showed a broad doublet signal, so the presence of an equatrial hydroxy group at C-21 and an axial hydroxy group at C-22 was resolved from NOE between H-22 and H-16. Thus, the structure of **2** was determined to be 28-acetoxy-3β,25-epoxy-3α,21β,22β-trihydroxyurs-12-ene, and named cordiaketal B.

The HR-FAB-MS of **3** afforded a pseudo molecular ion $[MH]^+$ at m/z 513.3568 corresponding to the molecular formula $C_{32}H_{48}O_5$. The IR spectrum of **3** showed absorption bands at 3447 (OH) and 1730 (carbonyl) cm^{-1}. The ^{1}H-NMR spectrum of **3** showed the presence of five singlet methyl groups (δ 0.83, 1.04, 1.06, 1.09, 1.10), two secondary methyl groups [δ 0.94 (d, J=6.4 Hz), 0.98 (d, J=6.4 Hz)], a formyl group [δ 9.58 (s)], an acetyl group [δ 2.10 (s)], two secondary hydroxy groups [δ 3.91 (dd, J=11.2, 2.8 Hz), 3.91 (d, J=2.8 Hz)], an olefin proton [δ 5.49 (t, J=3.6 Hz)] and unequivalent methylene protons at C-2 [δ 2.32 (ddd, J=15.6, 10.8, 7.6 Hz), 2.38 (ddd, J=15.6, 7.2, 4.0 Hz)]. The ^{13}C-NMR spectrum of **3** showed the presence of two carbonyl groups (δ 217.5, 208.1), an ester carbonyl group (δ 170.2), two secondary hydroxy groups (δ 73.7, 76.3) and a tri-substituted olefin group (δ 127.9, 136.6). From these facts, the structure of **3** was deduced to be an ursane derivative having 3-keto and 25-methyl groups instead of the hemiketal moiety, a 28-formyl group, a hydroxy and an acetoxy group on the E-ring. The structure and NMR assignments were carried out by HSQC and HMBC experiments. The C–H long range correlations from the HMBC experiment are shown in Fig. 1. Me-23 and M-24 showed correlation with C-3 (δ 217.5), C-5 and C-4. The formyl group showed correlation with C-17, C-18 and C-22. H-21 showed correlation with the ester carbonyl, C-17, C-19, C-22 and Me-30 carbons. The stereochemistries at C-21 and C-22 were presumed to be 21β-equatorial-acetoxy and 22-β-axial-hydroxy from the coupling constants of the carbinyl protons. Thus, the structure of **3** was determined to be 21β-acetoxy-22β-hydroxy-3-oxours-12-en-28-al, and named cordianal A.

The HR-FAB-MS of **4** afforded a pseudo molecular ion $[MH]^+$ at m/z 531.3674 corresponding to the molecular formula $C_{32}H_{50}O_6$. The IR spectrum of **4** showed absorption bands at 3471 (OH) and 1705 (carbonyl) cm^{-1}. The ^{1}H-NMR spectrum of **4** showed the presence of five singlet methyl groups (δ 1.07, 1.17, 1.38, 1.42, 1.52), two doublet methyl groups [δ 0.87 (d, J=6.4 Hz), 1.07 (d, J=6.0 Hz)], an acetyl methyl group [δ 2.10 (s)], a tertiary acyloxymethyl group [δ 4.04 (d, J=12.0 Hz), 4.43 (d, J=12.0 Hz)], three secondary alcohol groups [δ 3.37 (dd, J=12.0, 5.0 Hz), 3.43 (br s), 4.52 (br s) and an olefin proton [δ 5.27 (t, J=4.0 Hz)]. The ^{13}C-NMR spectrum of **4** showed the presence of a carbonyl carbon (δ 216.3), ester carbonyl carbon (δ 172.6), an oxymethylene carbon (δ 64.8), three oxymethine carbons (δ 69.2, 72.8, 72.9), an acetyl methyl carbon (δ 21.0) and a trisubsutituted olefin carbon (δ 126.6, 137.1). From this data, it was suggested that 3-keto and 25-methyl groups were presented instead of the ketal group in **2**. The positions of the functional groups were confirmed from the HMBC experiment. An oxymethine proton at C-6 showed correlation with C-8 and C-10. The stereochemistry of the three secondary hydroxy groups were deduced to be 6β-axial, 21β-axial and 22β-equatorial respectively from the coupling constants of the protons at C-6, 21 and 22. The stereochemistry of OH at C-6 was also confirmed from the down-field shift of methyl groups, Me-24 (δ 1.42), Me-25 (δ 1.52) and Me-26 (δ 1.38), having a 1,3-diaxial relationship with the OH group at C-6. Thus, the structure of **4** was determined to be 28-acetoxy-3-oxo-6β,21β,22β-trihydroxyurs-12-ene, and named cordianone.

The FAB-MS of **5** afforded a pseudomolecular ion $[MH]^+$ at m/z 471.3480 corresponding to the molecular formula $C_{30}H_{46}O_4$. The IR spectrum of **5** showed absorption bands at 3490 (OH) and 1711 (carbonyl) cm^{-1}. The ^{1}H- and ^{13}C-NMR spectra of **5** indicated almost the same signal patterns with those of **3** except for the presence of the acetoxy group. The signal patterns of the carbinyl protons at H-21 and H-22 of **5** were the same as those of **4**. Thus, the structure of **5** was determined to be 21β,22β-dihydroxy-3-oxours-12-en-28-al, and named cordianal B.

The HR-FAB-MS of **6** afforded a pseudo molecular ion $[MH]^+$ at m/z 473.3635 corresponding to the molecular formula $C_{30}H_{48}O_4$. The IR spectrum of **6** showed absorptions at 3540 (OH) and 1714 (carbonyl) cm^{-1}. The ^{1}H-NMR spectrum of **6** showed a similar signal pattern to **5**. The ^{13}C-NMR spectrum of **6** showed similar signals with those of **5**, but showed a hydroxy group at C-3 instead of the carbonyl of **5**. Stereochemistries at the secondary hydroxy groups were deduced from the coupling constants of the protons at C-3, 21 and 22. Thus, the structure of **6** was deduced to be 3β,21β,22β-trihydroxyurs-12-en-28-al, and named cordianal C.

The isolated triterpene and flavonol derivatives were examined for testosterone-5α-reductase inhibition and results

Table 2. Inhibitory Activity of the Constituents Isolated from *C. multispicata* against Testosterone 5α-Reductase

Sample	100 μg/ml	50 μg/ml	25 μg/ml
Glabridine[a)]	90.50%	48.20%	9.50%
1	92.68	70.57	50.00
2	94.87	70.75	36.49
3	67.57	36.87	15.41
5	18.87	12.31	8.04
7	96.59	95.83	73.77
8	6.09	−4.15	−4.50
9	93.57	86.16	60.76
10	91.72	78.55	43.35
11	78.56	75.08	67.94
12	85.77	72.49	49.12
14	41.71	35.60	23.97

a) Positive control.

are shown in Table 2. Of these compounds, compounds **1**, **2**, **7**, **9**—**12** showed potent anti-androgenic activity. These compounds all possess the hemiketal group in the A-ring of the oleanane and ursane skeletons or a 22-C_5-acyloxy group in the E-ring of 3-keto-oleanane, indicating that a hemiketal group in the A-ring or a C_5-acyloxy group at C-22 and/or C-3 carbonyl residue are essential for inhibitory activity toward testosterone 5α-reductase. Prenyl flavanone drivatives isolated from *Sophora flavescence* showed potent anti-androgenic activity,[2] but the flavonole derivatives **15** and **16** did not show anti-androgenic activity.

Experimental

Melting points were recorded on a Yanagimoto micro melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Spectrum GX-FT IR spectrometer (KBr). NMR spectra were recorded on a JEOL α-500 spectrometer (^{1}H-NMR at 500 MHz, ^{13}C-NMR at 125 MHz), and chemical shifts are given in parts per million (ppm) (δ), with tetramethylsilane (TMS) as an internal standard. FAB-MS were recorded on a JEOL JMS-SX102 mass spectrometer using *m*-nitrobenzyl alcohol as a matrix. HR-FAB-MS were recorded on a JEOL HX110 mass spectrometer. Optical rotations were recorded on a JASCO DIP-370 digital polarimeter (at 25 °C). Kieselgel 60 (Merck) was used for column chromatography. Analytical TLC was carried out on Kieselgel 60 F_{254} TLC plates (Merck). Analytical and preparative HPLC were carried out on YMC R-ODS7 packed columns.

Extraction and Isolation Air-dried leaves of *C. multispicata*, obtained from a market in Belem, Brazil, and identified by Dr. M. Satake, were extracted with MeOH under reflux to give a methanol extract, which showed potent antiandrogenic activities (60.1% inhibition against testosterone 5α-reductase and 88.1% inhibition against 5α-dihydrotestosterone (DHT)-receptor binding at 400 μg/ml). The MeOH extract was dissolved in H_2O and successively partitioned with EtOAc and *n*-BuOH to give an EtOAc-soluble fraction (115 g) and *n*-BuOH-soluble fraction (60 g), of which the EtOAc fraction showed the anti-androgenic activity (73.0% inhibition against testosterone 5α-reducase and 88.1% inhibition against DHT-receptor binding). Therefore, the EtOAc fraction was subjected to SiO_2 column chromatography using a gradient $CHCl_3$–MeOH solvent system (100 : 1 to 2 : 1). Based on TLC profiles, 7 fractions, F-1 (1.1 g), F-2 (5.1 g), F-3 (23.3 g), F-4 (22.2 g), F-5 (35.6 g), F-6 (10 g) and F-7 (15 g), were obtained. Of these F-3 and F-4 showed anti-androgenic activity (86.1% and 91.2% inhibition, respectively, against testosterone 5α-reductase at 400 μg/ml). F-3 (22 g) was successively separated by SiO_2 column chromatography and HPLC using an octadecyl silica (ODS) column and a CH_3CN–H_2O solvent system to give **5** (55 mg), **7** (22 mg), **10** (66 mg), **11** (17 mg), **12** (25 mg), **13** (12 mg), **15** (11 mg) and **16** (30 mg). F-4 (21 g) was successively separated by SiO_2 column chromatography and HPLC to give **1** (58 mg), **2** (18 mg), **3** (240 mg) , **4** (6 mg), **6** (2.2 g), **8** (112 mg), **9** (38 mg) and **14** (20 mg).

Cordiaketal A (1) Colorless needles (MeOH), mp 204—208 °C; IR (KBr) ν_{max} 3434, 2972, 1730, 1244 cm^{-1}; $[\alpha]_D$ +181.7° (*c*=0.5, MeOH); HR-FAB-MS *m/z* 529.3533 $[MH]^+$ (Calcd for $C_{32}H_{49}O_6$, 529.3529); ^{1}H-NMR ($CDCl_3$) δ 0.70 (3H, s, Me-26), 0.92 (3H, d, *J*=6.4 Hz, Me-30), 0.96 (3H, s, Me-24), 0.97 (3H, d, *J*=6.8 Hz, Me-29), 1.03 (3H, s, Me-23), 1.07 (3H, s, Me-27), 1.16 (1H, dt, *J*=13.8, 3.2 Hz, H-15α), 1.19 (1H, dd, *J*=10.3, 5.4 Hz, H-5), 1.34 (1H, dt, *J*=13.0, 3.5 Hz, H-7α), 1.38 (1H, dt, *J*=5.2, 13.0 Hz, H-7β), 1.55 (1H, dt, *J*=5.0, 13.8 Hz, H-15β), 1.78—1.81 (1H, overlap, H-16β), 1.80 (1H, overlap, H-11β), 1,84 (1H, dt, *J*=4.3, 12.7 Hz, H-16α), 2.05 (1H, dt, *J*=17.7, 4.7 Hz, H-11α), 2.10 (3H, s, $COCH_3$), 3.88 (1H, d, *J*=10.2 Hz, H-25), 3.89 (1H, br s, H-22), 4.25 (1H, dd, *J*=10.2, 2.4 Hz, H-25), 4.82 (1H, dd, *J*=11.4, 2.4 Hz, H-21), 5.49 (1H, dd, *J*=4.8, 2.4 Hz, H-12), 9.54 (1H, s, CHO). ^{13}C-NMR data is shown in Table 1.

Cordiaketal B (2) Amorphous powder; HR-FAB-MS *m/z* 531.3689 $[MH]^+$ (Calcd for $C_{32}H_{51}O_6$, 531.3686); IR (KBr) ν_{max} 3383, 2978, 1744, 1239 cm^{-1}; $[\alpha]_D$ +120.0° (*c*=0.8, MeOH); ^{1}H-NMR ($CDCl_3$) δ 0.85 (3H, d, *J*=6.0 Hz, Me-29), 0.94 (3H, s, Me-26), 0.98 (3H, s, Me-24), 1.04 (3H, s, Me-23), 1.06 (3H, d, *J*=6.6 Hz, Me-30), 1.09 (3H, s, Me-27), 1.11 (1H, dt, *J*=13.2, 3.0 Hz, H-15α), 1.16—1.26 (2H, overlap, H-1, H-5), 1.68 (1H, overlap, H-16β), 1.70 (1H, overlap, H-11β), 1.74 (1H, dt, *J*=1.8, 12.0 Hz, H-16α), 1.85 (1H, dt, *J*=4.8, 13.2 Hz, H-15β), 2.02 (1H, dt, *J*=18.0, 4.8 Hz, H-11α), 2.09 (3H, s, $COCH_3$), 3.36 (1H, br d, *J*=9.6 Hz, H-21) , 2.12—2.20 (2H, overlap, H-1, H-2), 3.43 (1H, br s, H-22), 3.89 (1H, d, *J*=9.0 Hz, H-25), 3.95 (1H, d, *J*=11.4 Hz, H-28), 4.28 (1H, dd, *J*=9.0, 3.0 Hz, H-25), 4.40 (1H, d, *J*=11.4 Hz, H-28), 5.22 (1H, dd, *J*=3.6, 1.8 Hz, H-12); ^{13}C-NMR data is shown in Table 1.

Cordianal A (3) Amorphous powder; HR-FAB-MS *m/z* 513.3568 $[MH]^+$ (Calcd for $C_{32}H_{49}O_5$, 513.3590); IR (KBr) ν_{max} 3447, 2973, 1730, 1241 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.83 (3H, s, Me-22), 0.94 (3H, d, *J*=6.4 Hz, Me-30), 0.98 (3H, d, *J*=6.4 Hz. Me-29), 1.04 (3H, s, Me-24), 1.06 (3H, s, Me-25), 1.09 (3H, s, Me-23), 1.10 (3H, s, Me-27), 2.10 (3H, s, $COCH_3$), 2.38 (1H, ddd, *J*=15.6, 7.2, 4.0 Hz, H-2α), 2.54 (1H, ddd, *J*=15.6, 10.8, 7.6 Hz, H-2β), 2.58 (1H, d, *J*=12.4 Hz, H-18), 3.91 (1H, d, *J*=2.8 Hz, H-22), 4.83 (1H, dd, *J*=11.2, 2.8 Hz, H-21), 5.49 (1H, t, *J*=3.6 Hz, H-12), 9.58 (1H, s, H-28); ^{13}C-NMR data is shown in Table 1.

Cordianone (4) Amorphous powder; HR-FAB-MS *m/z* 531.3674 $[MH]^+$ (Calcd for $C_{32}H_{51}O_6$, 531.3686); IR (KBr) ν_{max} 3471, 2930, 1705, 1245 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.87 (3H, d, *J*=6.4 Hz, Me-29), 1.07 (3H, d, *J*=6.0 Hz, Me-30), 1.07 (3H, s, Me-27), 1.17 (3H, s, Me-23), 1.23 (1H, br s, H-5), 1.38 (3H, s, Me-26), 1.42 (3H, s, Me-24), 1.52 (3H, s, Me-25), 2.10 (3H, s, COMe), 1.82 (1H, dd, *J*=14.4, 4.0 Hz, H-7β), 2.28 (1H, ddd, *J*=15.6, 4.8, 2.4 Hz, H-2α), 2.77 (1H, ddd, *J*=15.6, 13.6, 6.0 Hz, H-2β), 3.37 (1H, dd, *J*=12.0, 5.0 Hz, H-21), 3.43 (1H, br s, H-22), 4.04 (1H, d, *J*=12.0 Hz, H-28), 4.43 (1H, d, *J*=12.0 Hz, H-28), 4.52 (1H, br s, H-6), 5.27 (H, t, *J*=4.0 Hz, H-12); ^{13}C-NMR data is shown in Table 1.

Cordianal B (5) Colorless needles, mp 251—254 °C (MeOH); HR-FAB-MS *m/z* 471.3480 $[MH]^+$ (Calcd for $C_{30}H_{47}O_4$, 471.3474); $[\alpha]_D$ +73.0° (*c* 0.6, MeOH); IR (KBr) ν_{max} 3490, 2978, 1711, 1459, 1385 cm^{-1}; ^{1}H-NMR ($CDCl_3$) δ 0.83 (3H, s, Me-26), 0.95 (3H, d, *J*=6.0 Hz, Me-29), 1.04 (3H, s, Me-24), 1.06 (3H, s, Me-25), 1.08 (3H, d, *J*=6.6 Hz, Me-30), 1.09 (3H, s, Me-23), 1.10 (3H, s, Me-27), 2.38 (1H, ddd, *J*=15.6, 6.8, 3.6 Hz, H-2α), 2.52 (1H, d, *J*=11.2 Hz, H-18), 2.55 (1H, ddd, *J*=15.6, 11.3, 5.6 Hz, H-2β), 3.40 (1H, dd, *J*=10.6, 2.4 Hz, H-21), 3.83 (1H, d, *J*=2.4 Hz, H-22), 5.48 (1H, t, *J*=3.2 Hz, H-12), 9.63 (1H, s, formyl); ^{13}C-NMR data is shown in Table 1.

Cordianal C (6) Amorphous powder; HR-FAB-MS *m/z* 473.3635 $[MH]^+$ (Calcd for $C_{30}H_{49}O_4$, 473.3631); IR (KBr) ν_{max} 3540, 3418, 2969, 1714, 1460, 1385 cm^{-1}; ^{1}H-NMR (DMSO-d_6) δ 0.66 (6H, s, Me-23, 26), 0.84 (3H, d, *J*=6.3 Hz, Me-29), 0.85 (3H, s, Me-25), 0.88 (3H, s, Me-24), 0.96 (3H, d, *J*=6.3 Hz, Me-30), 1.08 (3H, s, Me-27), 1.53 (1H, dt, *J*=12.8, 3.5 Hz, H-1β), 1.59 (1H, dt, *J*=13.0, 2.5 Hz, H-16β), 1.84—1.89 (2H, overlap, H-11), 2.37 (1H, d, *J*=11, 5 Hz, H-18), 2.98 (1H, dt, *J*=10.0, 5.5 Hz, H-3), 3.19 (1H, ddd, *J*=10.5, 6.0, 3.2 Hz, H-21), 3.55 (1H, dd, *J*=4.0, 3.2 Hz, H-22), 4.26 (1H, d, *J*=5.0 Hz, OH at C-3), 4.36 (1H, br d, *J*=6.0 Hz, OH at C-21), 4.42 (1H, d, *J*=4.0 Hz, OH at C-22), 5.32 (1H, t, *J*=3.5 Hz, H-12), 9.38 (1H, s, CHO). ^{13}C-NMR data is shown in Table 1.

Anti-androgenic Activity Anti-androgenic activity tests were carried out by observation of inhibition against testosterone 5α-reductase as described previously.[1]

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