Dammarane-Type Triterpenes from the Brazilian Medicinal Plant *Cordia multispicata*

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From the Brazilian medicinal plant Carucaá (*Cordia multispicata*), oleanane- and ursane-type triterpenoids were previously reported as anti-androgenic constituents of the plant. In this study, purification of the polar elements of the EtOAc-soluble fraction of the plant revealed nine novel dammarane-type triterpenes, named cordianols A−I (**1**−**9**) along with the known compound cordialin A (**10**). The structures of these new compounds were elucidated by means of spectral methods including HRFABMS, ^{1}H NMR, ^{13}C NMR, and 2D NMR (HMQC, HMBC, NOESY). Absolute configuration at C-23 of compound **7** was determined by an excitone chirality method. Some of these new compounds revealed a hemiketal structure on the A ring and a hydroxylated or epoxidated 20(22)-(*E*)-ene side chain and showed weak anti-androgenic activity.

In the course of our program to study anti-androgenic constituents from plant resources, we have reported many kinds of anti-androgen active compounds, neoflavones and flavanones from *Dalbergia conchinchinensis*,[1] prenyl flavones from *Sophora flavescens*,[2] and gingerol and shogaol derivatives from *Zingiber offficinale*.[3] From the Brazilian medicinal plant Carucaá (*Cordia multispicata* Cham, Boraginaceae), several oleanane- and ulsane-type triterpenoids have been isolated as anti-androgenic constituents.[4] Some of these compounds exhibit potent anti-androgenic activity and also have a hemiketal structure on the A ring. In this investigation, we studied polar elements of fractions obtained from silica gel column chromatography of AcOEt-soluble fractions of the plant. The polar fractions were successively separated by means of silica gel column chromatography and HPLC using a reversed-phase (ODS) column as described in the Experimental Section to yield nine new compounds, cordianols A−I (**1**−**9**), along with the known compound cordialin A (**10**) (Chart 1).[5] Structures of these new compounds were determined by means of spectral data including HRFABMS, ^{1}H NMR, ^{13}C NMR, and 2D NMR analyses. Some of these compounds have 3,-19-hemiketal structures bridging over A rings, an 11α-hydroxy group, and 24,25-epoxy and 24,25-dihydroxy 20-(22)(*E*)-ene side chains. This report deals with the isolation and structural elucidation of these novel compounds and their anti-androgenic activity.

Results and Discusssion

Compound **10** was identified with cordialin A isolated from *Cordia verbenacea*. The structure including the absolute stereochemistry of **10** was determined by means of spectral data[5] and X-ray crystal analysis.[6]

Compound **1** revealed a molecular formula of $C_{30}H_{50}O_6$ from a pseudomolecular ion 529.3525 $[M + Na]^+$ by HRFABMS. The IR spectrum of **1** showed strong absorption bands at 3402 (OH) and 2961 (alkane) cm^{-1}. The ^{1}H NMR spectrum of **1** showed the presence of six singlet methyl groups (δ 0.91, 0.97, 1.00, 1.01, 1.21, 1.24), a vinyl methyl group [δ 1.66 (3H, d, J = 1.0 Hz)], an olefinic proton [δ 5.44 (1H, d, J = 9.0 Hz)], three secondary carbinol groups [δ 3.13 (1H, d, J = 3.0 Hz), 3.57 (1H, dt, J = 6.0, 12.5 Hz), 4.66 (1H, dd, J = 9.0, 3.0 Hz)], and a characteristic primary carbinol group [δ 4.15 (1H, dd, J = 8.5, 1.5 Hz), 4.33 (1H, dd, J = 8.5, 3.0 Hz)]. The ^{13}C NMR spectrum of **1** showed the presence of three secondary carbinol carbons (δ 68.4, 71.5, 80.2), a tertiary carbinol carbon (δ 74.1), a characteristic hemiketal group (δ 99.5, 68.7), and an olefin group (δ 140.3, 127.2). The ring part of **1** showed almost the same ^{1}H NMR and ^{13}C NMR signal patterns as those of **10**. These results indicate compound **1** to be a dammarane derivative having the same ring part and a different side chain than compound **10**. The planar structure of **1** was determined from HMBC analysis as shown in Figure 1. Me-28 and Me-29 protons correlated with C-3 (the hemiketal carbon), C-4, and C-5. The characteristic hemiketal methylene protons at C-19 showed a correlation with C-1, C-3, C-5, and C-9 carbons. Me-18 protons showed a correlation with C-7, C-9, and C-14 carbons. Me-30 protons showed a correlation with C-8, C-13, and C-15 carbons. Me-21 protons showed a correlation with C-17 and C-22 carbons. The H-22 olefinic proton showed a correlation with C-17 and C-24 carbons. The H-23 proton showed a correlation with C-20 and C-25 carbons. Me-26 and Me-27 protons showed a correlation with the C-24 carbon. The H-11 proton showed a correlation with the C-13 carbon. These NMR results indicate that the planar structure of **1** is 3,19-epoxy-3,11,23,24,25-pentahydroxydammara-20(22)-ene. Geometrical isomerism at the C-20(22) double bond was determined to be *E* from NOE (Figure 2). A difference NOE experiment of **1** showed that the Me-21 proton correlated with the H-23 proton and the H-22 proton correlated with the H-17 proton. The configurations of A, B, C, and D ring part of **1** were determined to be the same as those of cordialin A (**10**) by comparing ^{1}H NMR and ^{13}C NMR data. The configuration of the hydroxy group at C-11 was determined to be *R* from the coupling

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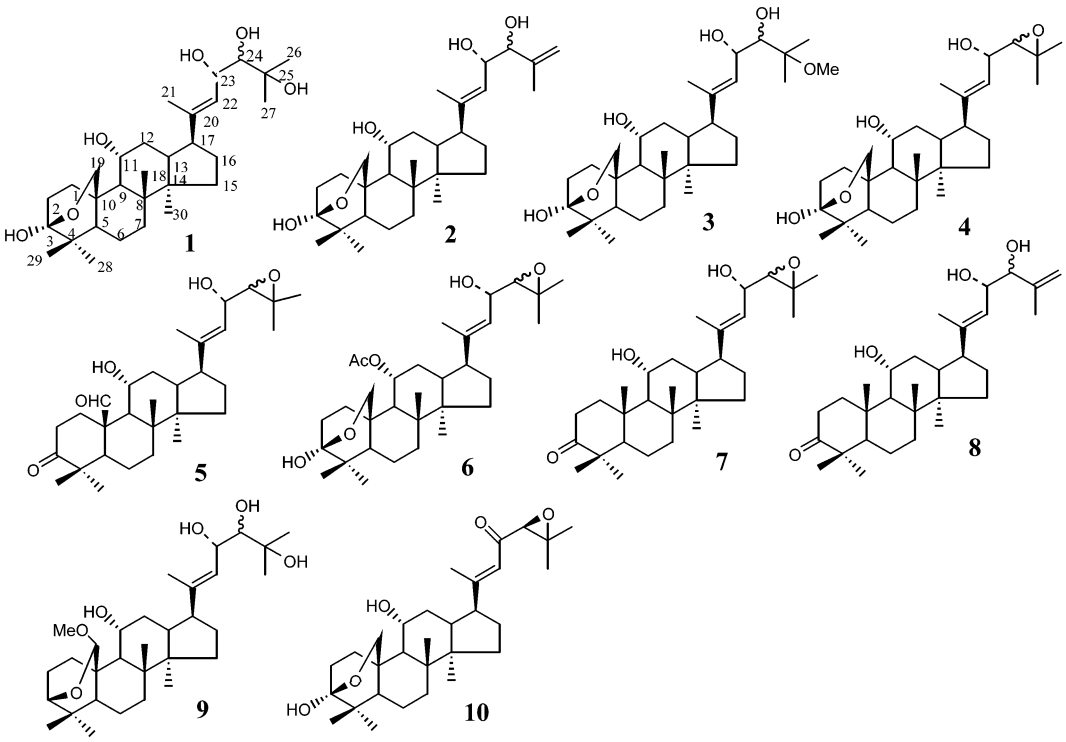
Chart 1



constant (J = 12.5 Hz) of the carbinol proton at C-11. The configurations of the hydroxy groups at C-23 and 24 have not been determined. From these data, the structure of compound **1** was determined to be (3*S*,11*R*)-3,19-epoxy-3,-11,23,24,25-pentahydroxydammar-20(22)(*E*)-ene and named cordianol A.

Compound **2** revealed a molecular formula of $C_{30}H_{48}O_5$ from a pseudomolecular ion 511.3390 $[M + Na]^+$ by HRFABMS. The IR spectrum of **2** showed strong absorption bands at 3395 (OH) and 2958 (alkane) cm^{-1}. The ^1H NMR spectrum of **2** demonstrated almost the same signal pattern as that for **1**, except for the disappearance of two singlet methyl groups and the appearance of a vinyl methyl group [δ1.69 (s)] and exomethylene groups [δ 4.93 (m), 4.83 (m)]. The ^{13}C NMR spectrum of **2** showed almost the same chemical shifts as those of **1**, as shown in Table 1, except for the disappearance of a tertiary carbinol carbon and appearance of an exomethylene group (δ 146.3, 113.7). These data suggest that the structure of **2** must be an exomethylene derivative converted from **1** by dehydration of the hydroxy group at C-25 and hydrogen at C-26. This was confirmed by HMBC, as in the case of compound **1**. The geometrical isomerism at the C-20(22) double bond was determined by differences in nuclear Overhauser effects (NOE). Thus, the structure of **2** was determined to be (3*S*,-11*R*)-3,19-epoxy-3,11,23,24-tetrahydroxydammar-20(22)-(*E*),25-diene and named cordianol B.

Compound **3** revealed a molecular formula of $C_{31}H_{52}O_6$ from a pseudomolecular ion 543.3683 $[M + Na]^+$ by HRFABMS. The IR spectrum of **3** showed strong absorption bands at 3413 (OH) and 2957 (alkane) cm^{-1}. The ^1H NMR spectrum of **3** showed almost the same signal pattern as that of **1**, except for the presence of a methoxy group [δ 3.23 (s)]. The ^{13}C NMR spectrum of **3** showed 31 carbon peaks and almost the same chemical shifts as compound **1**, except for a methoxy group (δ 49.6). These results suggest that **3** is a methoxylated derivative of **1**. The position of the methoxy group was confirmed by HMBC. The methoxy methyl group showed a correlation with the C-25 carbon (δ 79.1). The geometrical isomerism of **3** was determined by the difference NOE experiments as in the

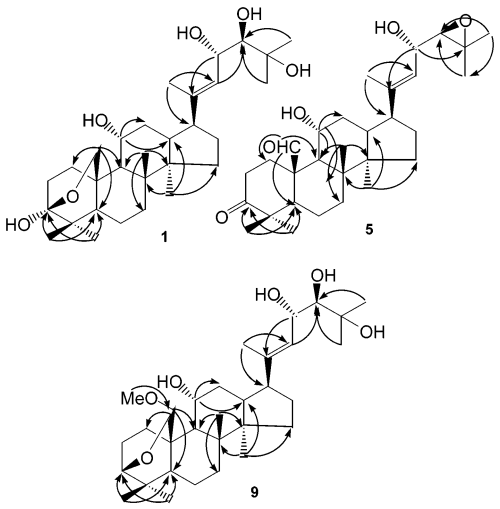


Figure 1. Selected HMBC of **1**, **5**, and **9**.

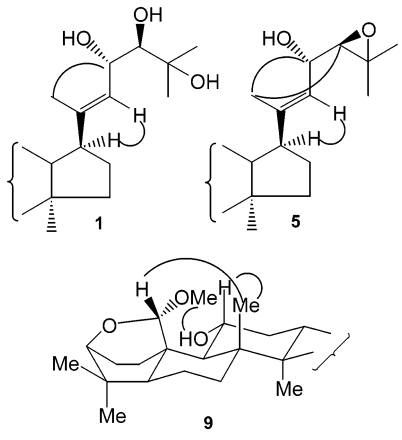


Figure 2. Selected NOEs of **1**, **5**, and **9**.

Table 1. ^{13}C NMR Data of Dammarane-Type Triterpenes from *C. multispicata* (125 MHz)[a]

C no.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
1	38.8	38.8	38.8	38.8	35.2	37.3	41.9	41.9	30.5	37.1
2	30.5	30.5	30.5	30.5	36.5	29.6	34.1	34.1	23.2	29.9
3	99.5	99.5	99.5	99.5	214.3	98.1	218.6	218.6	76.1	98.3
4	41.9	41.9	41.9	41.9	48.9	42.7	47.6	47.6	36.8	40.8
5	52.1	52.1	52.1	52.1	55.5	50.6	55.2	55.2	54.1	50.8
6	20.4	20.4	20.4	20.4	18.6	19.2	19.5	19.5	20.6	19.3
7	35.2	35.2	35.2	35.2	35.0	33.9	35.2	35.2	35.2	34.2
8	40.9	40.8	40.	40.9	40.7	40.0	40.7	40.7	40.3	39.8
9	51.2	51.2	51.2	51.2	57.9	47.5	54.8	54.8	49.8	51.2
10	37.1	37.1	37.1	37.1	54.5	35.8	38.2	38.3	40.5	36.0
11	71.5	71.4	71.4	71.4	70.6	73.0	71.1	71.7	71.8	70.8
12	37.6	37.6	37.5	37.5	35.9	32.2	37.1	37.1	34.1	37.7
13	44.5	45.0	44.5	44.6	42.8	42.7	43.0	43.1	43.7	44.5
14	49.5	49.6	49.5	49.6	48.8	48.3	49.0	49.0	49.0	48.9
15	32.1	32.1	32.1	32.1	31.3	31.0	31.0	31.0	31.1	31.5
16	28.4	28.9	28.6	28.6	27.6	27.6	27.5	27.7	27.4	27.7
17	50.6	50.5	50.6	50.7	49.0	50.6	49.3	49.2	49.1	50.0
18	16.9	16.9	16.9	16.9	18.4	16.5	16.3	16.3	16.8	17.1
19	68.7	68.7	68.7	68.7	206.7	67.7	16.7	16.8	101.4	66.2
20	140.3	142.6	140.1	143.0	142.1	141.9	142.4	144.2	141.9	164.2
21	14.1	14.9	14.1	14.3	14.5	14.1	14.1	14.4	14.2	16.7
22	127.2	125.1	127.4	127.2	122.5	123.1	122.6	123.3	124.5	120.2
23	68.4	71.1	68.1	69.0	67.6	67.7	67.6	69.9	68.2	195.6
24	80.2	80.7	79.7	68.9	67.3	67.3	67.3	79.0	77.9	67.8
25	74.1	146.3	79.1	59.9	59.8	59.6	59.8	142.8	73.4	60.9
26	26.4	113.7	22.5	25.0	24.8	24.8	24.8	113.4	26.1	24.8
27	26.9	18.5	21.3	19.7	19.5	19.5	19.5	18.6	27.0	18.7
28	26.7	26.7	26.7	26.7	24.3	26.2	27.4	27.5	29.2	26.2
29	19.3	19.2	19.2	19.2	21.6	18.6	20.6	20.6	24.2	18.6
30	15.6	15.6	15.7	15.6	15.8	15.2	15.6	15.6	15.7	15.3
CH_3						21.8				
CO						169.7				
MeO			49.6						54.7	

[a] **1**−**4** were measured in MeOH-d_4, and **5**−**10** were measured in $CDCl_3$.

case of compound **1**. Thus, the structure of **3** was determined to be (3*S*,11*R*)-3,19-epoxy-25-methoxy-3,11,23,24-tetrahydroxydammar-20(22)(*E*)-ene and named cordianol C.

Compound **4** revealed a molecular formula of $C_{30}H_{48}O_5$ from a pseudomolecular ion 511.3407 $[M + Na]^+$ by HRFABMS. The IR spectrum of **4** showed strong absorption bands at 3414 (OH) and 2959 (alkane) cm^{-1}. ^1H NMR and ^{13}C NMR spectra of **4** showed almost the same signal patterns as those of compound **1**. The molecular formula of **4** was produced by the reduction of H_2O from **1**. The ^1H NMR chemical shifts of H-22, H-23, and H-24 in **4** exhibited upper field shifts as described in the Experimental Section compared with those of **1**. The ^{13}C NMR chemical shifts of C-24 and C-25 shifted to upper fields (δ 68.9 and 59.9, respectively), as shown in Table 1. These data indicate that **4** must be a 24,26-epoxy derivative of **1**. The structure of **4** was confirmed by HMBC and difference NOE experiments. Thus, the structure of **4** was determined to be (3*S*,11*R*)-3,19;24,25-diepoxy-3,11,23-trihydroxydammar-20(22)(*E*)-ene and named cordianol D.

Compound **5** revealed a molecular formula of $C_{30}H_{46}O_5$ from pseudomolecular ions 509.3262 $[M + Na]^+$ and 487.3426 $[M + H]^+$ by HRFABMS. The IR spectrum of **5** showed strong absorption bands at 3444 (OH), 2962 (alkane), and 1708 (CO) cm^{-1}. The ^1H NMR and ^{13}C NMR spectra of **5** showed almost the same signal patterns as that of **4** except for the disappearance of the hemiketal group and appearance of a formyl group [δ 10.43 (1H, s) and 206.7]. The ^{13}C NMR spectrum of **5** showed the presence of the same side chain found in **4** (Table 1) and two carbonyl groups (δ 214.3 and 206.7). These data indicate that **5** has a carbonyl group and a formyl group instead of the hemiketal moiety of compound **4**. The locations of the carbonyl group and the formyl group were confirmed at C-3 and C-19, respectively, by HMBC experiments, as shown in Figure 1. The Me-28,29 protons showed a correlation with the carbonyl carbon. The formyl proton showed correlations with C-1, C-5, and C-9 carbons, which suggest the position of the carbonyl group is at C-3 and the formyl group at C-19. The geometrical isomerism at the C-20(22) double bond was determined to be *E* from NOE (Figure 2). A difference NOE experiment for **5** showed that Me-21 protons correlated with H-23,24 protons and the H-22 proton correlated with the H-17 proton. Thus, the structure of **5** was determined to be (11*R*)-11,23-dihydroxy-24,25-epoxy-19-formyl-3-oxo-dammr-20(22)(*E*)-ene and named cordianol E.

Compound **6** revealed a molecular formula of $C_{32}H_{50}O_6$ from a pseudomolecular ion 553.3506 $[M + Na]^+$ by HRFABMS. The IR spectrum of **6** showed strong absorption bands at 3372 (OH), 2961 (alkane), and 1734 (ester CO) cm^{-1}. ^1H NMR and ^{13}C NMR spectra of **6** showed almost the same signal patterns as those of **4** except for the presence an acetyl group [δ 2.04 (3H, s) by ^1H NMR and δ 21.8, 169.7 by ^{13}C NMR], as described in the Experimental Section and Table 1. The H-11 carbinol proton appeared at a lower field [δ 4.81 (dt, J = 4.8, 12.0 Hz)], indicating that **6** is an acetyl derivative at C-11 of compound **4**. The structure of **6** was confirmed by HMBC experiments, and its structure was determined to be (3*S*,11*R*)-11-acetoxy-3,19;24,25-diepoxy-3,23-dihydroxydammar-20(22)(*E*)-ene and named cordianol F.

Compound **7** revealed a molecular formula of $C_{30}H_{48}O_4$ from a pseudomolecular ion 473.3609 $[M + H]^+$ by HRFABMS. The IR spectrum of **7** revealed strong absorption bands at 3462 (OH), 2962 (alkane), and 1704 (CO) cm^{-1}. ^1H NMR and ^{13}C NMR spectra of **7** showed the same signal patterns as those of **4** and the presence of a carbonyl group (δ 218.6) and seven singlet methyl groups and the dis-

appearance of the hemiketal moiety. These facts suggest that **7** has a carbonyl group at C-3 and Me-19. The position of carbonyl was confirmed by HMBC, and the structure of **7** was determined to be (11*R*)-24,25-epoxy-11,23-dihydroxy-3-oxo-dammar-20(22)(*E*)-ene and named cordianol G.

Compound **8** revealed a molecular formula of $C_{30}H_{48}O_4$ from pseudomolecular ions 495.3475 $[M + Na]^+$ and 473.3656 $[M + H]^+$ by HRFABMS. The IR spectrum of **8** showed strong absorption bands at 3428 (OH), 2959 (alkane), and 1701 (CO) cm^{-1}. The ^1H NMR spectrum of **8** showed almost the same signal pattern as that of **7** except for the presence of an exomethylene group [δ 5.02 (1H, s), 5.21 (1H, s)] instead of a 24,25-epoxy group. The ^{13}C NMR spectrum of **8** also showed almost the same chemical shifts as those of **7** except for the presence of the exomethylene group (δ 142.8, 113.4). Thus, the structure of **8** was determined to be (11*R*)-3-oxo-11,23,24-trihydroxydammar-20(22)(*E*),25-diene and named cordianol H.

Compound **9** revealed a molecular formula of $C_{31}H_{52}O_6$ from pseudomolecular ions 543.3669 $[M + Na]^+$ and 521.3833 $[M + H]^+$ by HRFABMS. The IR spectrum of **9** showed strong absorption bands at 3421 (OH) and 2958 (alkane) cm^{-1}. ^1H NMR and ^{13}C NMR spectra of **9** showed the same signal patterns of the side chain as that of **1** and the presence of a methyl acetal moiety [δ_H 3.50 (3H, s), 5.18 (1H, s), 3.31 (1H, t, J = 2.4 Hz), and δ_C 54.7, 101.4, 76.1] instead of the hemiketal moiety. The location of the methyl acetal moiety was confirmed by HMBC analysis as shown in Figure 1. The methoxy proton showed the correlation with an acetal carbon (δ 101.4). The acetal proton showed correlations with C-1, C-5, and C-3 carbons. Me-28,29 protons showed correlations with the C-3 carbinyl carbon. These data suggest that the structure of **9** is a methylacetal derivative of the 3β-hydroxy-19-formyl derivative of **1**. The stereochemistry of the hydroxy group at C-11 was determined to be α from the coupling constant (J = 11.0 Hz) between H-11 and H-9 and NOE between H-11 and Me-18, as shown in Figure 2. The stereochemistry at the C-19 acetal carbon indicates it to be *S* from the NOESY experiment (Figure 2). The protons of the methyl acetal group correlated with the hydroxy proton at C-11. H-19 showed correlations with H-6 and Me-18. Thus, the structure of **9** was determined to be (3*S*,11*R*,19*S*)-3,19-epoxy-19-methoxy-11,23,24,25-tetrahydroxydammar-20-(22)(*E*)-ene and named cordianol I.

The stereochemistry at C-23 of **7** was determined from the exciton chirality[7] method using a CD spectrum. Cordianol **7** yielded mono-*p*-bromobenzoate (**7a**) and di-*p*-bromobenzoate (**7b**) by *p*-bromobenzoylation. The monobenzoate (**7a**) at C-23 of **7** showed a typical Cotton effect associated with a chiral allyl benzoate structure and showed a negative Cotton effect ($\Delta\epsilon$ = −11.4 at 243 nm (MeOH)). The chemical constant between H-22 and H-23 was shown as J = 10.0 Hz. This indicated that H-22 and H-23 possess an antiparallel conformation to each other, and the negative CD at 243 nm indicated that the configuration at C-23 should be *S*.[7]

Evidence that the C-23 configuration is *S* in compounds **4**−**7** is derived from analysis of both the ^{13}C and ^1H NMR spectra. The ^{13}C NMR chemical shifts of C-23 to C-25 in **4**−**7**, all of which have a 24,25-epoxide ring, are nearly identical, indicating that all of them possess the same configuration at C-23 and C-24. Similarly, the observation that the coupling constants between H-22 and H-23 (~9 Hz) in the ^1H NMR spectra of **1**−**9** are all very similar also suggests these compounds have the same 23*S*-configuration. Further experimental data will be required for a complete assignment of the stereochemistry of each compound.

In a previous paper,[4] oleanane- and ulsane-type triterpenes having the hemiketal moiety at the A ring were reported as potent anti-androgenic compounds. Dammarane-type triterpenes having the hemiketal moiety at the A ring were isolated from the more polar part of the AcOEt fraction, and compound **7** showed moderate anti-androgenic activity (43.1% at 100 μg/mL), but compounds **2**, **3**, and **4** showed weak activity (18,0%, 19.0%, and 15.1% at 100 μg/mL) and compound **1** showed no activity (−2.09% at 100 μg/mL). These results indicate that the presence of a hemiketal structure is not sufficient to produce this activity in dammarane-type triterpenes.

Experimental Section

General Experimental Procedures. IR spectral data were recorded on a Perkin-Elmer GX-FT-IR spectrometer. HRFABMS data were measured on JEOL HX110 mass spectrometer. ^1H NMR and ^{13}C NMR data were measured on JEOL α-500 (500 MHz for ^1H NMR and 125 MHz for ^{13}C NMR) with TMS as an internal standard. $[\alpha]_D$ were recorded on a JASCO P-1010 polarimeter at 20 °C. Analytical and preparative HPLC were carried out using a reversed-phase column (YMC R-ODS-5A packed column) using a CH_3CN-H_2O solvent systems.

Extraction and Isolation. More polar fractions, 5, 7, and 8, which were previously obtained from column chromatography of the AcOEt-soluble fraction of *C. multispicata*,[4] were further separated by silica gel column chromatography and HPLC using an ODS column. Fraction 5 (6.2 g) was chromatographed on a silica gel column using a hexane−AcOEt gradient solvent system (from hexane−AcOEt, 2:1) to give eight fractions, Fr-5-1−Fr-5-8. Fr-5-5 (1g) was purified by HPLC (60% CH_3CN) to give **5** (13 mg), **6** (13 mg), **7** (380 mg), and **10** (11 mg). Fr-5-7 (280 mg) was purified by HPLC (60% CH_3CN) to give **6** (14 mg). Fr-5-7 (320 mg) was purified by HPLC (60% CH_3CN) to give **8** (15 mg) and **9** (25 mg). Fraction 7 (1.2 g) was purified by HPLC (60% CH_3CN) to give **2** (30 mg), **3** (60 mg), and **4** (75 mg). Fraction 8 (800 mg) was purified by HPLC (60% CH_3CN) to give **1** (360 mg) and **2** (20 mg).

Cordianol A (1): colorless viscous oil; HRFABMS *m*/*z* 529.3525 $[M + Na]^+$ (calcd for $C_{30}H_{50}O_6Na$, 529.3505); $[\alpha]^{25}_D$ +219° (*c* 0.033, MeOH); IR ν cm^{-1} (KBr) 3402, 2961, 1378, 1065; ^1H NMR (MeOH-d_4) δ 0.91 (3H, s, Me-30), 0.97 (3H,s, Me-18), 1.00 (3H, s, Me-29), 1.01 (3H, s, Me-28), 1.17 (1H, overlap, H-15), 1.18 (1H, overlap, H-2), 1.20 (1H, overlap, H-12), 1.24 (3H, s, Me-26), 1.21 (3H, s, Me-27), 1.30 (1H, overlap, H-7), 1.45 (1H, overlap, H-6), 1.47 (2H, overlap, H-15, 16), 1.50 (1H, overlap, H-7), 1.60 (1H, d, J = 12.5, H-9), 1.65 (1H, 1H, dq, J = 3.2, 12.8, H-6), 1.66 (3H, d, J = 1.0 Hz, Me-21), 1.79 (1H, dt, J = 11.8, 4.6, H-12), 1.85 (1H, overlap, H-16), 2.26 (1H, dt, J = 6.2, 10.8 Hz, H-17), 3.13 (1H, d, J = 3.0 Hz, H-24), 3.15 (1H, dt, J = 6.0, 12.5 Hz, H-1), 3.57 (1H, dt, J = 6.0, 12.5 Hz, H-11), 4.15 (1H, dd, J = 8.5, 1.5 Hz, H-19), 4.33 (1H, dd, J = 8.5, 3.0 Hz, H-19), 4.66 (1H, dd, J = 9.0, 3.0 Hz, H-23), 5.44 (1H, d, J = 9.0 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol B (2): colorless viscous oil; HRFABMS *m*/*z* 511.3390 $[M + Na]^+$ (calcd for $C_{30}H_{48}O_5Na$, 511.3399); $[\alpha]^{25}_D$ +161° (*c* 0.013, MeOH); IR ν cm^{-1} (KBr) 3395, 2958, 1376, 1066; ^1H NMR (MeOH-d_4) δ 0.90 (3H, s, Me-30), 0.95 (1H, s, Me-18), 1.00 (3H, s, Me-29), 1.01 (3H, s, Me-28), 1.17 (1H, overlap, H-15), 1.18 (1H, overlap, H-1), 1.20 (1H, overlap, H-12), 1.33 (1H, overlap, H-7), 1.44 (1H, overlap, H-6), 1.45 (1H, overlap, H-16), 1.47 (1H, overlap, H-15), 1.52 (1H, overlap, H-7), 1.59 (1H, d, J = 11.3 Hz, H-9), 1.64 (3H, d, J = 1.0 Hz, Me-21), 1.65 (1H, dq, J = 3.2, 12.6 Hz, H-6), 1.69 (3H, s, Me-27), 1.77 (1H, dt, J = 11.9, 4.3 Hz, H-12), 1.85 (1H, overlap, H-16), 2.21 (1H, dt, J = 5.8, 10.7 Hz, H-17), 3.14 (1H, dt, J = 3.5, 12.5 Hz, H-1), 3.55 (1H, dt, J = 4.5, 11.0 Hz, H-11), 3.83 (1H, d, J = 8.0 Hz, H-24), 4.14 (1H, dd, 8.5, 1.5 Hz, H-19),

4.27 (1H, dd, J = 9.0, 8.0 Hz, H-23), 4.33 (1H, dd, J = 8.5, 2.5 Hz, H-19), 4.83 (1H, m, H-26), 4.93 (1H, m, H-26), 5.15 (1H, d, J = 9.0 Hz, H-22); ^{13}C NMR spectral data are shown in Table 1.

Cordianol C (3): colorless viscous oil; HRFABMS *m/z* 543.3683 $[M + Na]^+$ (calcd for $C_{31}H_{52}O_6Na$, 543.3662); $[\alpha]^{25}_D$ +149° (*c* 0.037, MeOH); IR ν cm^{-1} (KBr) 3413, 2957, 1379, 1067; ^{1}H NMR (MeOH-d_4) δ 0.91 (3H, s, Me-30), 0.96 (3H, s, Me-18), 1.00 (3H, s, Me-29), 1.01 (3H, s, Me-28), 1.20 (3H, Me-26), 1.22 (3H, s, Me-27), 1.20 (1H, overlap, H-12), 1.60 (1H, d, J = 11.3 Hz, H-9), 1.64 (1H, overlap, H-2), 1.65 (3H, d, J = 1.5 Hz, Me-21), 1.79 (1H, dt, J = 12.0, 4.6 Hz, H-12), 2.07 (1H, dt, J = 5.8, 11.9 Hz, H-2), 2.25 (1H, dt, J = 5.2, 10.1 Hz, H-17), 3.22 (1H, d, J = 3.0 Hz, H-24), 3.23 (3H, s, OMe), 3.57 (1H, 1H, dt, J = 4.5, 11.0 Hz, H-11), 4.15 (1H, dd, J = 8.5, 1.5 Hz, H-19), 4.33 (1H, dd, J = 8.5, 2.5 Hz, H-19), 4.58 (1H, dd, J = 9,0.0, 3.0 Hz, H-23), 5.40 (1H, d, J = 9.0 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol D (4): colorless viscous oil; HRFABMS *m/z* 511.3407 $[M + Na]^+$ (calcd for $C_{30}H_{48}O_5Na$, 511.3400); $[\alpha]^{25}_D$ +125° (*c* 0.027, MeOH); IR ν cm^{-1} (KBr) 3414, 2959, 1378, 1066; ^{1}H NMR (MeOH-d_4) δ 0.92 (3H, s, Me-30), 0.96 (3H, s, Me-18), 1.00 (3H, s, Me-29), 1.01 (3H, s, Me-28), 1.18 (1H, overlap, H-1), 1.22 (1H, overlap, H-12), 1.25 (3H, s, Me-26), 1.27 (3H, s, Me-27), 1.60 (1H, d, J = 11.0 Hz, H-9), 1.65 (1H, overlap, H-2), 1.66 (3H, d, J = 1.0 Hz, Me-21), 1.78 (1H, dt, J = 12.4, 5.0 Hz, H-12), 2.08 (1H, dt, J = 5.8, 12.6 Hz, H-2), 2.28 (1H, dt, J = 6.3, 11.1 Hz, H-17), 2.77 (1H, d, J = 8.0 Hz, H-24), 3.15 (1H, dt, J = 6.0, 13.2 Hz, H-1), 3.57 (1H, dt, J = 5.0, 11.0 Hz, H-11), 4.12 (1H, dd, J = 9.5, 8.0 Hz, H-23), 4.15 (1H, dd, J = 8.5, 1.0 Hz, H-19), 4.33 (1H, dd, J = 8.5, 2.5 Hz, H-19), 5.27 (1H, d, J = 9.5 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol E (5): colorless viscous oil; HRFABMS *m/z* 509.3262 $[M + Na]^+$ (calcd for $C_{30}H_{46}O_5Na$, 509.3243), *m/z* 487.3426 $[M + H]^+$ (calcd for $C_{30}H_{47}O_5$, 487.3424); $[\alpha]^{25}_D$ +96° (*c* 0.023, MeOH); IR ν cm^{-1} (KBr) 3444, 2962, 1708, 1382, 1013; ^{1}H NMR ($CDCl_3$) δ 0.94 (3H, s, Me-30), 0.96 (3H, s, Me-18), 1.08 (3H, s, Me-29), 1.17 (3H, s, Me-28), 1.17 (1H, overlap, H-15), 1.20 (1H, overlap, H-12), 1.21 (3H, s, Me-26), 1.30 (2H, overlap, H-5, H-7), 1.31 (3H, s, Me-27), 1.47 (2H, overlap, H-15, 16), 1.50 (1H, overlap, H-7), 1.64 (3H, d, J = 1.2 Hz, Me-21), 1.73 (1H, overlap, H-6), 1.79 (1H, dt, J = 11.8, 4.6 Hz, H-12), 1.85 (1H, d, J = 10.8 Hz, H-9), 1.85 (1H, overlap, H-16), 2.04 (1H, overlap, H-6), 2.22 (1H, dt, J = 15.0, 4.2 Hz, H-1), 2.26 (1H, dt, J = 6.2, 10.8 Hz, H-17), 2.42 (1H, dt, J = 6.0, 15.0 Hz, H-1), 2.81 (1H, d, J = 7.8 Hz, H-24), 3.80 (1H, dt, J = 4.8, 10.8 Hz, H-11), 4.21 (1H, t, J = 8.4 Hz, H-23), 5.28 (1H, d, J = 9.0 Hz, H-22), 10.43 (1H, s, H-19); ^{13}C NMR data are shown in Table 1.

Cordianol F (6): colorless viscous oil; HRFABMS *m/z* 553.3506 $[M + Na]^+$ (calcd for $C_{32}H_{50}O_6Na$, 553.3505); $[\alpha]^{25}_D$ +156° (*c* 0.023, MeOH); IR ν cm^{-1} (KBr) 3372, 2961, 1734, 1377, 1243, 1023; ^{1}H NMR ($CDCl_3$) δ 0.91 (3H, s, Me-30), 0.98 (3H, s, Me-18), 0.99 (3H, s, Me-29), 1.04 (3H, s, Me-28), 1.28 (1H, overlap, H-1), 1.30 (3H, s, Me-26), 1.33 (3H, s, Me-27), 1.63 (3H, s, Me-21), 1.65 (1H, overlap, H-2), 2.04 (3H, s, CH_3−CO), 2.14 (1H, dt, J = 6.0, 12.0 Hz, H-2), 2.66 (1H, dt, J = 6.0, 12.6 Hz, H-1), 2.80 (1H, d, J = 8.4 Hz, H-24), 3.68 (1H, d, J = 9.6 Hz, H-19), 4.20 (1H, t, J = 8.4 Hz, H-23), 4.28 (1H, d, J = 9.6 Hz, H-19), 4.81 (1H, dt, J = 4.8, 12.0 Hz, H-11), 5.29 (1H, d, J = 8.4 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol G (7): colorless viscous oil; HRFABMS *m/z* 473.3609 $[M + H]^+$ (calcd for $C_{30}H_{49}O_4$, 473.3631); $[\alpha]^{25}_D$ +160° (*c* 0.031, MeOH); IR ν cm^{-1} (KBr) 3462, 2962, 1704, 1380, 1009; ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, s, Me-30), 1.03 (3H, s, Me-18), 1.07 (3H, s, Me-19), 1.08 (3H, s, Me-29), 1.11 (3H, s, Me-28), 1.33 (3H, s, Me-26), 1.33 (3H, s, Me-27), 1.55 (1H, d, J = 10.8 Hz, H-9), 1.65 (3H, d, J = 1.0 Hz, Me-21), 1.70 (1H, overlap, H-1), 2.18 (1H, ddd, J = 14.0, 8.5, 5.5 Hz, H-1), 2.28 (1H, dt, J = 5.5, 10.5 Hz, H-17), 2.40 (1H, dt, J = 14.5, 7.5 Hz, H-2), 2.50 (1H, ddd, J = 15.0, 9.0, 5.5 Hz, H-2), 2.82 (1H, d, J = 7.5 Hz, H-24), 3.95 (1H, ddd, J = 15.5, 11.05, 5.0 Hz, H-11), 4.22 (1H, dd, J = 9.0, 7.5 Hz, H-23), 5.30 (1H, d, J = 9.0 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol H (8): colorless viscous oil; HRFABMS *m/z* 495.3475 $[M + Na]^+$ (calcd for $C_{30}H_{48}O_4Na$, 495.3450), *m/z* 473.3656 $[M + H]^+$ (calcd for $C_{30}H_{49}O_4$, 473.3631); $[\alpha]^{25}_D$ +223° (*c* 0.014, MeOH); IR ν cm^{-1} (KBr) 3428, 2959, 1701, 1459, 1383, 1013; ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, s, Me-30), 1.02 (3H, s, Me-18), 1.07 (6H, s, Me-19, 29), 1.11 (3H, s, Me-28), 1.54 (1H, d, J = 10.8 Hz, H-9), 1.65 (3H, d, J = 1.5 Hz, Me-21), 1.70 (1H, overlap, H-1), 1.74 (3H, s, Me-27), 2.40 (1H, dt, J = 15.0, 7.0 Hz, H-2), 2.50 (1H, ddd, J = 15.0, 8.8, 5.6 Hz, H-2), 2.67 (1H, ddd, J = 13.7, 4.9. 5.5 Hz, H-1), 3.91 (1H, d, J = 6.0 Hz, H-24), 3.93 (1H, dt, J = 4.5, 10.8 Hz, H-11), 4.34 (1H, dd, J = 9.0, 6.0 Hz, H-23), 5.02 (1H, s, H-26), 5.21 (1H, s, H-26), 5.22 (1H, d, J = 9.0 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordianol I (9): colorless viscous oil; HRFABMS *m/z* 543.3669 $[M + Na]^+$ (calcd for $C_{31}H_{52}O_6Na$, 543.3661), *m/z* 521.3833 $[M + H]^+$ (calcd for $C_{31}H_{53}O_6$, 521.3842); $[\alpha]^{25}_D$ +224° (*c* 0.010, MeOH); IR ν cm^{-1} (KBr) 3421, 2958, 1381, 1087; ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, s, Me-30), 0.99 (3H, s, Me-29), 1.01 (3H, s, Me-28), 1.02 (3H, s, Me-18), 1.26 (1H, s, Me-26), 1.31 (3H, s, Me-27), 1.52 (1H, d, J = 11.0 Hz, H-9), 1.68 (3H, d, J = 1.2 Hz, Me-21), 1.73 (1H, dt, J = 12.3, 4.2 Hz, H-12), 1.74 (1H, dt, J = 12.0, 6.3 Hz, H-12), 2.29 (1H, dt, J = 6.6, 11.4 Hz, H-17), 2.77 (1H, 1H, t, J = 11.4 Hz, H-1), 3.19 (1H, br s, H-24), 3.31 (1H, t, J = 2.4 Hz, H-3), 3.50 (3H, s, OMe), 3.85 (1H, tt, J = 11.0, 4.2 Hz, H-11), 4.21 (1H, d, J = 3.6 Hz, OH at C-11), 4.66 (1H, dd, J = 8.4, 2.4 Hz, H-23), 5.18 (1H, s, H-19), 5.51 (1H, d, J = 8.4 Hz, H-22); ^{13}C NMR data are shown in Table 1.

Cordialin A (10): colorless viscous oil; HRFABMS *m/z* 509.3213 $[M + Na]^+$ (calcd for $C_{30}H_{46}O_5Na$, 509.3243), *m/z* 487.3440 $[MH]^+$ (calcd for $C_{30}H_{47}O_5$, 487.3424); $[\alpha]^{25}_D$ +39° (*c* 0.017, MeOH); IR ν cm^{-1} (KBr) 3402, 2961, 1659, 1378, 1065; ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, s, Me-30), 0.96 (3H, s, Me-18), 1.01 (3H, s, Me-28), 1.04 (3H, s, Me-29), 1.27 (3H, s, Me-26), 1.42 (3H, s, Me-27), 2.13 (3H, s, Me-21), 3.66 (1H, br t, J = 10.0 Hz, H-11), 4.18 (1H, dd, J = 8.5, 2.5 Hz, H-19), 4.35 (1H, dd, J = 8.5, 2.5 Hz, H-19), 6.28 (1H, s, H-22); ^{13}C NMR data are shown in Table 1.

***p*-Bromobenzoate of 7.** To a solution of 11 mg of **7** in 1 mL of pyridine were added 50 mg of *p*-bromobenzoyl chloride and 50 mg of DMAP, and the mixture was left to stand for 24 h. To the reaction solution was added 50 mL of AcOEt, and the mixture was washed with diluted HCl, saturated $NaHCO_3$, and water, successively. The reaction product were purified by TLC to give two compounds, 23-monobenzoate (**7a**, 6 mg) and 11,23-dibenzoate (**7b**, 7 mg).

7a: FABMS *m/z* 658 $[M + H]^+$ $C_{37}H_{52}O_5{}^{82}Br$, *m/z* 656 $[M + H]^+$ $C_{37}H_{52}O_5{}^{80}Br$; ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, s, Me-30), 0.99 (3H, s, Me-18), 1.04 (3H, s, Me-19), 1.05 (3H, s, Me-29), 1,08 (3H, s, Me-28), 1.34 (3H, s, Me-26), 1.35 (3H, s, Me-27), 1.77 (3H, d, J = 1.0 Hz, Me-21), 3.05 (1H, d, J = 8,0 Hz, H-24), 3.89 (1H, dt, J = 5.0, 11.0 Hz, H-11), 5.27 (1H, br d, J = 10.0 Hz, H-22), 5.52 (1H, ddd, J = 10.0, 8.0 Hz, H-23); CD (MeOH) λ_{max} ($\Delta\epsilon$) 293 ($\Delta\epsilon$ +1.9), 243 ($\Delta\epsilon$ −11.4), 211 ($\Delta\epsilon$ −7.3).

7b: FABMS *m/z* 843 $[M + H]^+$ $C_{44}H_{55}O_6{}^{82}Br_2$, *m/z* 841 $[M + H]^+$ $C_{44}H_{55}O_6{}^{80}Br^{82}Br$, *m/z* 839 $[M + H]^+$ $C_{44}H_{55}O_6{}^{80}Br_2$; ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, s, Me-30), 0.98 (3H, s, Me-18), 1.02 (3H, s, Me-19), 1.08 (3H, s, Me-29), 1.09 (3H, s, Me-28), 1.31 (6H, s, Me-26, 27), 1.77 (3H, d, J = 1.0 Hz, Me-21), 3.04 (1H, d, J = 8.5 Hz, H-24), 5.24 (1H, br d, J = 9.5 Hz, H-22), 5.38 (1H, dt, J = 10.5, 4.5 Hz, H-11), 5.48 (1H, dd, J = 9.5, 8.5 Hz, H-23).

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References and Notes

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