Four Lignans from *Commiphora erlangeriana*

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Four new lignans, two of the polygamatin-type, named erlangerin A (**1**) and erlangerin B (**2**), and two related to podophyllotoxin, named erlangerin C (**3**) and erlangerin D (**4**), were isolated from the resin of *Commiphora erlangeriana*, a plant occurring in Ethiopia and Somalia. The structures of these compounds including their relative stereochemistry were elucidated on the basis of spectral evidence, chemical data, and X-ray crystallographic analysis.

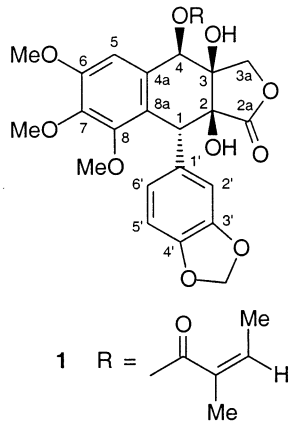
The culturally and commercially important resin product widely known as myrrh is derived from *Commiphora myrrha* (Nees) Engl. (Burseraceae), a plant found in abundance in the arid regions of Ethiopia and Somalia and to some extent in northern Kenya.[1] Furanosesquiterpenes are the main aromatic constituents of the resin of *C. myrrha*.[2,3] However, very little is known about the chemistry of resins derived from other *Commiphora* species, of which there are more than 50 in Ethiopia.[1]

This paper describes the isolation and structure elucidation of four new lignans from the resin of *C. erlangeriana* occurring in Ethiopia and Somalia and known as "Dhunkal". It is common knowledge among local people that "Dhunkal" resin is toxic to humans and animals. However, the fruits are edible and sold in markets during rainy seasons.

Results and Discussion

Extraction of the resin of *C. erlangeriana* with MeOH−EtOAc (1:1) gave a high yield (50%) of a colorless gummy material. TLC analysis ($CHCl_3$−MeOH, 95:5) on silica gel showed four major spots with R_f values of 0.67, 0.78, 0.79, and 0.43. Analysis of the crude extract by HPLC using a diode array detector also revealed one major (41%) and several minor components. Compounds **1** and **2** exhibited similar UV absorption maxima differing from that of **3** and **4**. The extract was then chromatographed repeatedly on silica gel using increasing polarities of *n*-hexane−$CHCl_3$−EtOAc mixtures to yield compounds **1**−**4**.

The most abundant compound (**1**) was obtained as white crystals, mp 76−78 °C. The molecular formula $C_{27}H_{28}O_{11}$ was deduced from HREIMS. Its UV spectrum (EtOH) exhibited absorption bands at 208, 223, and 284 nm. The IR absorption bands at 3441, 2941, 1772, 1714, and 1033 cm^{-1} indicated the presence of OH, C-H, lactone carbonyl, ester carbonyl, and C-O functional groups, respectively. Its ^1H NMR spectrum (Table 1) revealed the presence of a methylenedioxy group at δ 5.91, three aromatic protons with a typical 1,3,4-trisubstitution at δ 6.49 (br d, J = 8.2 Hz), 6.68 (d, J = 8.2 Hz), and 6.53 (br s), and an olefinic proton at δ 6.24 appearing as a quartet of quartets, which suggested the presence of an angelate moiety. The ^{13}C NMR (Table 2) and DEPT spectra indicated that compound **1** contains two methyls, two methylenes, six methines, three methoxy groups, one oxymethine, and 13 quaternary carbons.



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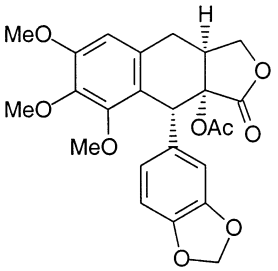

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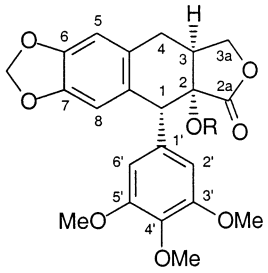
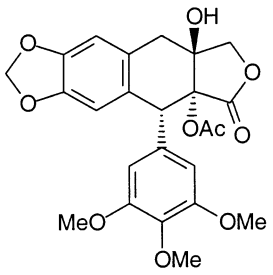


3 R = Ac
3a R = H



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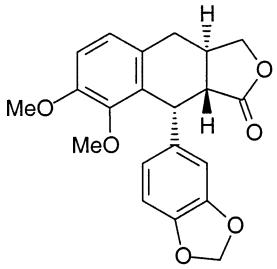

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In the HMBC spectrum of **1**, the aromatic proton signal at δ 6.98 (br s, H-5) showed cross-peaks with two *O*-linked carbons, C-6 (δ 153.2) and C-7 (δ 142.3), as well as with two other quaternary carbons, C-4a and C-8a. The methine proton at δ 4.95 (br s, H-1) correlated with C-2 and C-8a,

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Table 1. ^{1}H NMR Spectral Data of Compounds **1**−**4**[a]

proton	**1**	**2**	**3**	**4**
1	4.95 br s	5.12 br s	4.35 br s	4.59 br s
3		3.05 m	2.99 m	
3a	4.35 d (10.6)	3.79 dd (8.6, 3.4)	3.87 dd (8.7,3.8)	4.2 d (9.3)
	3.57 dd (10.6, 1.3)	4.76 t (8.6)	4.74 t (8.7)	4.3 d (9.3)
4	5.76 br s	2.45 dd (15.0, 1.7)	2.50 dd (4.2, 15.1)	2.89 d (16.3)
		3.33 dd (15.0, 5.6)	3.26 dd (6.0, 15.1)	3.40 d (16.3)
5	6.98 br s	6.55 s	6.72 s	6.62 s
8			6.61 s	6.40 s
2′	6.53 br s	6.81 m	6.49 s	5.98 s
5′	6.68 d (8.2)	6.70 d (8.3)		
6′	6.49 br d (8.2)	6.69 br d (8.3)	6.49 s	7.16 s
OCH_2O	5.91 s	5.91 s	5.90 d (1.3)	5.89 d (1.3)
			5.92 d (1.3)	
OMe-6	3.89 s	3.86 s		
OMe-7	3.86 s	3.82 s		
OMe-8	3.65 s	3.76 s		
OMe-3′			3.76 s	3.90 s
OMe-4′			3.82 s	3.82 s
OMe-5′			3.76 s	3.64 s
OAc		2.14 s	2.09 s	1.85 s
O-angeloyl				
	6.24 qq (6.2, 1.1)			
	2.06 br d (6.2)			
	2.04 d (1.1)			

[a] Spectra recorded at 600 MHz in $CDCl_3$. The values are ppm. Assignments were made by COSY, HMQC, and HMBC experiments. *J* values (Hz) in parentheses.

Table 2. ^{13}C NMR Spectral Data of Compounds **1**−**4**, **1a**, and **3a**[a]

carbon	**1**	**1a**	**2**	**3**	**3a**	**4**
1	45.8	45.8	43.6	50.8	50.0	46.1
2	77.3	77.4	81.5	81.9	75.8	77.5
2a	177.5	177.3	175.9	174.6	177.7	172.2
3	79.7	79.5	39.4	39.7	40.9	78.3
3a	78.5	78.1	72.9	72.5	71.4	74.6
4	69.9	68.8	34.1	33.2	30.0	34.0
4a	128.8	127.5	121.8	128.7	129.2	129.2
5	104.6	104.8	108.1	108.7	108.6	109.3
6	153.2	153.7	153.2	147.2	147.2	146.9
7	142.3	141.9	141.9	147.3	147.5	147.0
8	151.9	152.0	151.4	109.6	109.9	110.4
8a	120.9	119.5	130.4	128.3	127.2	124.8
1′	128.2	133.3	130.9	131.3	132.8	133.4
2′	108.8	108.9	110.8	108.1	108.0	107.4
3′	147.4	147.5	146.3	152.6	153.7	152.5
4′	148.2	148.4	147.3	137.4	[b]	137.6
5′	108.7	108.8	107.6	152.6	153.7	152.5
6′	121.9	122.1	123.1	108.1	108.0	111.7
OCH_2O	101.4	101.5	101.0	101.1	101.5	101.3
OMe-6	55.9	56.2	56.1			
OMe-7	60.9	61.1	60.9			
OMe-8	61.3	61.6	61.2			
OMe-3′				56.1	56.6	56.4[c]
OMe-4′				60.8	61.3	60.9
OMe-5′				56.1	56.6	56.2[c]
OAc			170.2	169.7		167.2
			20.9	20.8		20.9
O-angeloyl						
	167.4					
	126.8					
	140.6					
	16.0					
	20.6					

[a] Spectra recorded at 151 MHz in $CDCl_3$. The values are in ppm. Assignments were made by DEPT, COSY, HMQC, and HMBC experiments. [b] Signal not detected. [c] May be interchangeable.

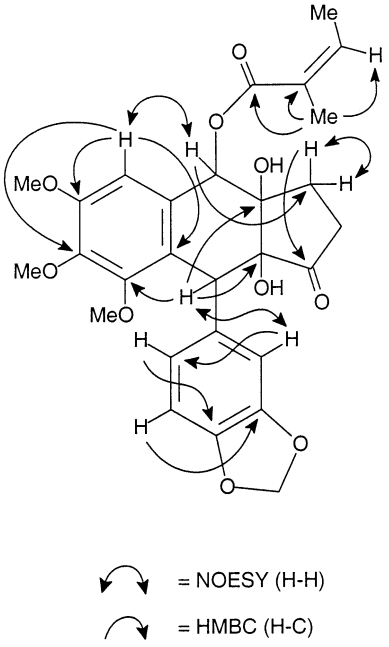


Figure 1. Selected HMBC and NOESY correlations of compound **1**.

whereas the methylene proton signals at C-3a correlated with C-2 (δ 77.3) and C-3 (δ 79.7), indicating a polygamatin[4] (**5**)-type skeleton, which in the case of **1** is oxygenated at the 2, 3, 4, and 6 positions. Further HMBC and NOESY correlations are shown in Figure 1. The angelate moiety was placed at C-4 because on hydrolysis the chemical shift of H-4 was shifted from δ 5.76 (br s) in **1** to δ 4.88 (s) in compound **1a**.

A HMBC correlation clearly demonstrated that the OMe group at δ 3.65 (s) should be placed at C-8 (δ 151.9) in **1**. However, it was not possible to deduce from the above-mentioned spectroscopic data whether the methylenedioxy group was attached to the C-3′, 4′ or to the C-6, 7 positions. This ambiguity was resolved by X-ray analysis of a crystal of **1**, which contained disordered chloroform and *n*-hexane. The X-ray analysis (Figure 2) confirmed structure **1** and clarified the relative stereochemistry at C-1, 2, 3, and 4. It also revealed the *Z*-configuration for the double bond of the angeloyl side chain. On the basis of the above results the novel compound **1** was characterized as 2β,3β-dihydroxy-

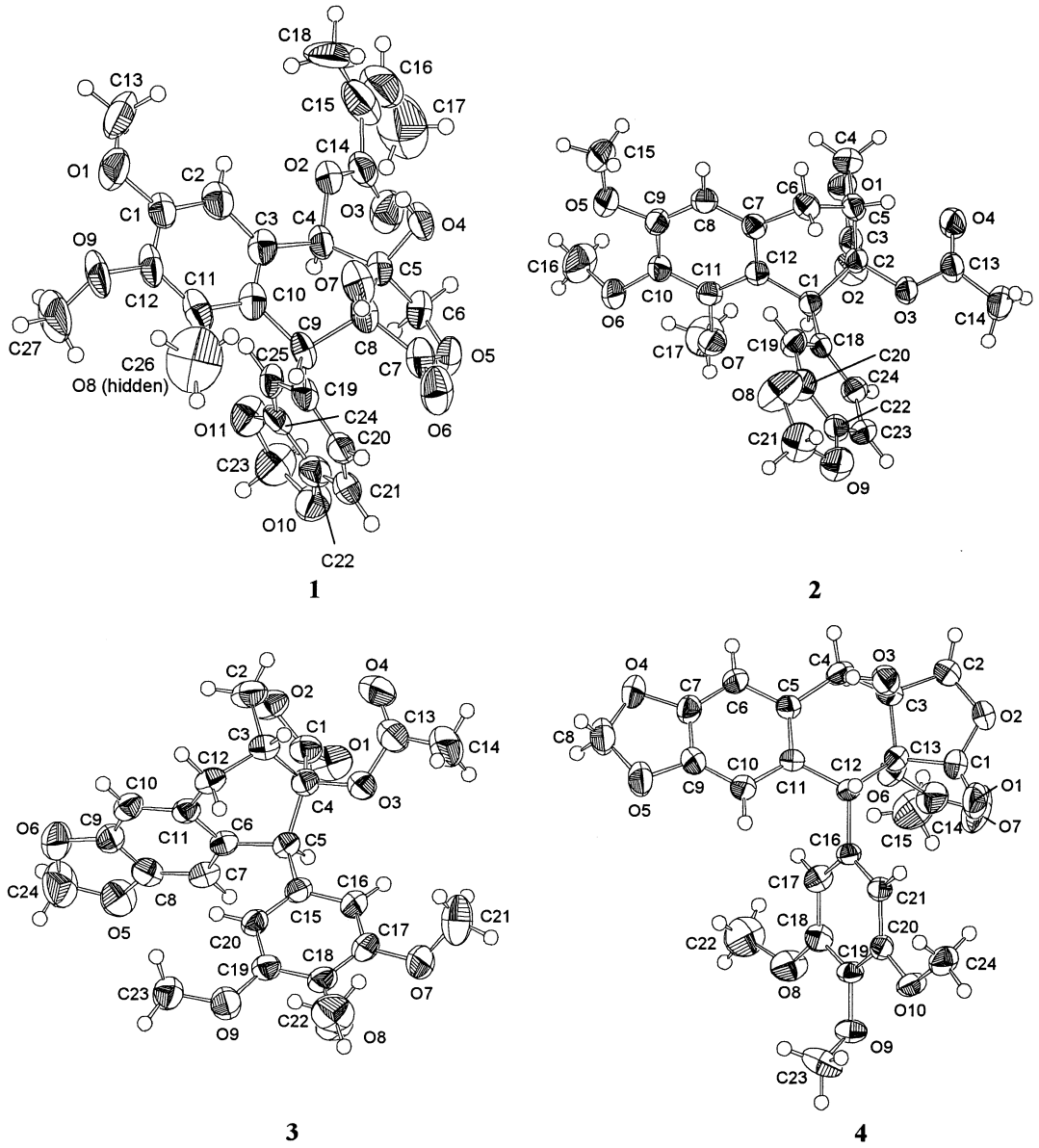


Figure 2. Computer-generated ZORTEP plots of compounds **1**−**4** showing the relative configuration. For reasons of X-ray processing, the atom labels differ from the common lignan numbering system[6] used throughout the text and the tables.

6-methoxy-4β-angeloyloxyisopicropolygamatin, to which the trivial name erlangerin A has been given.

Compound **2** was obtained as colorless crystals. Its UV spectrum measured in ethanol displayed absorption bands at 205 and 283 nm. The IR spectrum exhibited characteristic absorption bands of lactonic carbonyl (1773 cm^{-1}), ester carbonyl (1742 cm^{-1}), and C-O (1035 cm^{-1}). The molecular formula $C_{24}H_{24}O_9$ was derived from its HREIMS. The NMR experiments indicated that compound **2** has the same basic skeleton as **1** but with the absence of the angelate moiety at position 4 and the hydroxyl groups at positions 2 and 3. Furthermore, unlike **1**, the HMBC experiments of **2** showed correlations between the quaternary carbons at δ 147.5 (C-3′) and 148.4 (C-4′) with that of the methylenedioxy proton at δ 5.91 (s). As shown in Figure 3, cross-peaks between the respective methoxy protons and quaternary carbon signals were observed as follows: (OMe-6, δ 3.86 (s)/C-6, δ 153.2), (OMe-7, δ 3.82 (s)/C-7, δ 141.9), and (OMe-8, δ 3.76 (s)/C-8, δ 151.4), thus indicating placement of three methoxy groups on C-6, C-7, and C-8. Further important correlations were also observed between H-1 at δ 5.12 and seven quaternary carbons, namely, C-1′, C-2, C-2a, C-3, C-4a, C-8, and C-8a. The X-ray analysis summarized in Figure 2 confirmed the position of the acetate group and also the relative stereochemistry of structure **2**, thus enabling this compound to be assigned

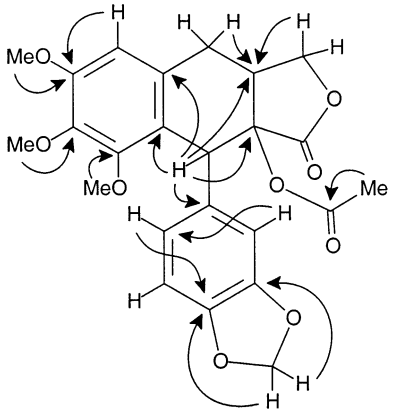


Figure 3. Selected HMBC correlations of compound **2**.

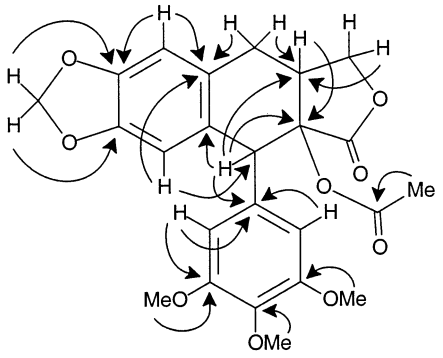


Figure 4. Selected HMBC correlations of compound **3**.

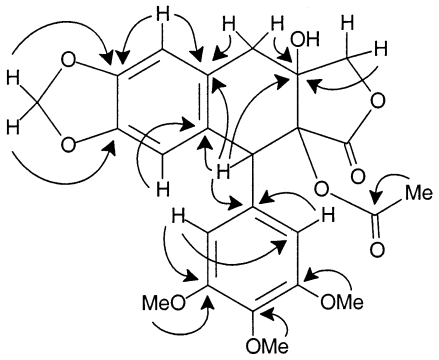


Figure 5. Selected HMBC correlations of compound **4**.

as 2α-acetoxy-6-methoxypicropolygamatin, to which the trivial name erlangerin B has been given.

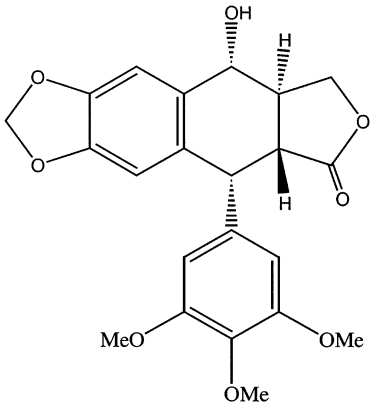
Compound **3** was isolated as colorless crystals, mp 224−226 °C. The UV spectrum (EtOH) slightly differed from **2** and showed absorption maxima at 205 and 292 nm. It exhibited the molecular formula $C_{24}H_{24}O_9$ (HREIMS), which was identical to that of **2**. The IR spectrum exhibited also characteristic absorption bands of lactonic carbonyl (1772 cm^{-1}), ester carbonyl (1745 cm^{-1}), and C−O (1030 cm^{-1}). Basic hydrolysis of **3** yielded the deacetylated compound **3a**.

The ^1H NMR spectrum of **3** (Table 1) differed from **2** particularly in the chemical shift of H-1 (δ 5.21, br s in **2** and δ 4.35, br s in **3**). Protons of two methoxy groups in **3** appeared as a singlet at δ 3.76, while the third methoxy group resonated at δ 3.82 (s). The three singlets at δ 6.72 (H-5), 6.61 (H-8), and 6.49 (H-2′ and H-6′) represented four aromatic protons. Likewise, in the ^{13}C NMR spectrum, signal overlap was observed between C-3′ and C-5′, 2′, and 6′, and OMe-3′ and OMe-5′, resulting in 21 signals for 24 carbons (Table 2). The HMBC correlations (Figure 4) between the methylenedioxy protons and the *O*-linked carbons at δ 147.2 (C-6) and 147.3 (C-7), between the methoxy protons at δ 3.76 (OMe-3′ and OMe-5′) and the overlapped carbon signals at δ 152.6 (C-3′ and C-5′), and between the methoxy protons at δ 3.82 (OMe-4′) and 137.4 (C-4′) revealed that the three OMe groups are located at positions C-3′, 4′, and 5′. The X-ray analysis (Figure 2) confirmed the new structure **3**, 2α-acetoxydeoxypicropodophyllin, or erlangerin C.

Compound **4** was obtained as colorless crystals. Its molecular formula of $C_{22}H_{24}O_{10}$ was determined by HREIMS. The UV spectrum showed absorption at 211 and 290 nm. Its IR spectrum showed absorption bands at 3445 (OH), 1778 (lactone carbonyl), 1714 (ester carbonyl), and 1035 (C-O) cm^{-1}. The ^1H NMR spectrum of **4** (Table 1) revealed three singlets for three methoxy protons (δ 3.90, 3.82, and 3.64) and four singlets for four aromatic protons (δ 5.98, 6.40, 6.62, and 7.16). In the ^{13}C NMR spectrum, 23 signals were observed due to the fact that C-3′ and C-5′ are in the same magnetic environment resonating at δ 152.5 (Table 2).

From the HMBC spectrum (Figure 5) it was possible to establish the basic structure of **4**. Thus, long-range $^1H-^{13}C$ correlations were observed between the methylenedioxy protons and the *O*-linked carbons (C-6 and C-7), between the protons of OMe-3′, OMe-4′, and OMe-5′ and the respective quaternary carbons C-3′, C-4′, and C-5′, and between the protons of H-1 (δ 4.59, br s) and six quaternary carbons. The placements of the acetate group at C-2 and the hydroxy group at C-3 and the relative stereochemistry of **4** were deduced from the X-ray analysis (Figure 2). Accordingly, structure **4** was determined to be 2α-acetoxy-3β-hydroxyisodeoxypodophyllotoxin, which has been named erlangerin D.

It is interesting to note that compounds **1** and **2** differ from **3** and **4** by their color reactions on TLC resulting from spraying with a concentrated HNO_3−HOAc (3:10) mixture.[5] Only the latter two compounds gave a red coloration, which is characteristic for substances possessing a podophyllotoxin (**6**)-type substitution pattern. The color development is believed to be caused by demethylation and oxidation to a quinone.[5]



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Nomenclature of the above aryltetralin lignans is based on the rule proposed by Dewick and Jackson.[6] Lignan-type compounds have been reported rarely from *Commiphora* species. Provan and Waterman[7] reported the lignans polygamain and picropolygamain as constituents of *C. incisa*, a plant which was later re-identified as *C. kua*.[8] Other members of the Burseraceae such as *Bursera fagaroides* are known to contain lignans.[9]

Podophyllotoxin (UV maxima 205, 292 nm) and other closely related aryltetrahydronaphthalene lignans isolated from *Podophyllum* species belonging to the family Berberidaceae are well-known for their powerful antimitotic activity. Based on structural modification of these compounds, numerous studies that focused on obtaining more potent and less toxic anticancer agents have resulted in the clinical introduction of etoposide, teniposide, and, more recently, etopophos.[10] Owing to the structural similarities of compounds **1**−**4** to podophyllotoxin, their potential anticancer and other biological activities are being investigated.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a Perkin-Elmer 241 polarimeter. IR spectra were obtained on a Perkin-Elmer 1600 infrared spectropho-

tometer with KBr pellets. ^{1}H, ^{13}C, and 2D NMR spectra were recorded on a Bruker AMX 600 spectrometer at 600 and 151 MHz using the solvent peak as reference (chloroform: δ_H 7.26, δ_C 77.10). EIMS and HREIMS were obtained on a Finnigan MAT 95Q spectrometer (70 eV).

TLC was performed on precoated plates (silica gel 60 F_{254}, Merck), solvent system: $CHCl_3$−MeOH (95:5). Spots were visualized with UV light at 254 or by spraying with HOAc−concentrated HNO_3 (10:3). The HPLC analysis was carried out using a Waters Liquid Chromatogram System fitted to a controller (Model 600), autosampler (717), PDA detctor (996), reversed-phase Waters ODS2 Symmetry C_{18} column (5 μm particle size, 24.6 × 255 mm), and guard column (5 μm particle size, 4.6 × 10 mm). The elution was isocratic (acetonitrile−H_2O, 60:40) and at a flow rate of 1 mL/min. Retention times (t_R) of 8.4, 6.8, 6.4, and 4.5 min were recorded for compounds **1**−**4**, respectively.

Plant Material. Botanical specimens and resins of *Commiphora erlangeriana* Engl., locally known as "Dhunkal" (Somali), were collected from Gode, Ogaden, Ethiopia, in October 1997 and were identified by Dr. Kaj Vollesen (Royal Botanical Gardens, Kew, Surrey, UK). A voucher specimen has been deposited in the National Herbarium of Addis Ababa University, Ethiopia, under the reference number 072799.

Extraction and Isolation. The powdered resin (55 g) was extracted with a mixture of MeOH−EtOAc (1:1) for 1 day. Removal of the solvent from the extract under reduced pressure gave 28 g of a gummy material. The extract (7 g) was then subjected to column chromatography over silica gel (230−400 mesh, 30 g), eluting with mixtures of *n*-hexane−$CHCl_3$−EtOAc of increasing polarity to yield eight fractions. Fractions 2, 3, 4, and 6 were further purified by silica gel column chromatography to yield **1** (2 g), **2** (0.1 g), **3** (0.5 g), and **4** (0.2 g), respectively. Compound **1** was then crystallized from *n*-hexane−$CHCl_3$ (1:1). Similarly, compounds **2**−**4** were also crystallized from MeOH−CH_2Cl_2 (9:1) and analyzed by X-ray crystallography.

2*β*,3*β*-Dihydroxy-6-methoxy-4*β*-angeloyloxyisopicropolygamatin (erlangerin A) (1): white crystals from *n*-hexane−$CHCl_3$ (1:1); R_f 0.67 ($CHCl_3$−MeOH, 95:5); mp 76−78 °C; $[\alpha]^{22}_D$ +55° (*c* 0.2, $CHCl_3$); UV λ_{max} (EtOH) (log ϵ) 208 (2.86), 223 (2.88), 284 (2.32) nm; IR ν_{max} (KBr) 3441, 2941, 1772, 1714, 1644, 1597, 1493, 1452, 1342, 1231, 1138, 1033, 928, 847, 754 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2, respectively; EIMS (70 eV) *m*/*z* 528 $[M]^+$ (3), 446 (1), 430 (31), 429 (15), 428 (63), 412 (31), 410 (20), 394 (24), 382 (20), 355 (39) 341 (18), 313 (48), 312 (38), 298 (18), 283 (34), 282 (40), 149 (20), 135 (24), 100 (89), 85 (25), 83 (28), 82 (22), 55 (100), 54 (29), 53 (23), 44 (70), 41 (20), 39 (37); HREIMS *m*/*z* 528.1628 (calcd for $C_{27}H_{28}O_{11}$, 528.1632).

Hydrolysis of 1. Compound **1** (0.5 g) was stirred with 5% methanolic KOH at room temperature for 12 h. The reaction mixture was acidified and extracted with $CHCl_3$, concentrated, and purified with column chromatography over silica gel to yield **1a** (0.45 g) as colorless needles (MeOH): mp 243−245 °C; $[\alpha]^{22}_D$ +16° (*c* 1.0, $CHCl_3$,); IR ν_{max} (KBr) 3411, 2919, 1766, 1603, 1487, 1410, 1333, 1232, 1116, 1034, 924 cm^{-1}; ^{1}H NMR (CD_3OD, 600 MHz) δ 4.81 (1H, s, H-1), 3.53 (1H, d, J = 10.0 Hz, H-3a), 4.28 (1H, d, J = 10.0 Hz, H-3a), 4.88 (1H, s, H-4), 7.21 (1H, s, H-5), 6.58 (1H, d, J = 2.0 Hz, H-2′), 6.72 (1H, d, J = 8.1 Hz, H-5′), 6.49 (1H, br d, J = 8.1 Hz, H-6′), 5.95 (2H, br s, OCH_2O), 3.96 (3H, s, OMe-6), 3.64 (3H, s, OMe-7), 3.85 (3H, s, OMe-8); ^{13}C NMR (Table 2); EIMS (70 eV) *m*/*z* 446 $[M]^+$ (100), 428 (15), 412 (9), 410 (22), 394 (11), 382 (12), 355 (21) 341 (9), 330 (35), 329 (43), 315 (11), 314 (12), 313 (48), 312 (36), 300 (13), 299 (27), 298 (15), 297 (17), 283 (18), 282 (23), 269 (10), 149 (17), 135 (29), 44 (28), 43 (13).

2α-Acetoxy-6-methoxypolygamatin (erlangerin B) (2): colorless crystals (MeOH−CH_2Cl_2, 9:1); R_f 0.78 ($CHCl_3$−MeOH, 95:5); mp 205−207 °C; $[\alpha]^{22}_D$ +131° (*c* 0.15, $CHCl_3$), UV λ_{max} (EtOH) nm (log ϵ) 205 (2.67), 283 (1.62); IR ν_{max} (KBr) 2929, 1773, 1742, 1583, 1499, 1477, 1420, 1367, 1320, 1235, 1119, 1035, 919, 861, 750 cm^{-1}; for ^{1}H NMR and ^{13}C NMR data, see Tables 1 and 2, respectively; EIMS (70 eV) *m*/*z* 456 $[M]^+$ (39), 396 (100), 365 (16), 313 (5), 283 (10), 135 (17), 43 (5); HREIMS *m*/*z* 456.1420 (calcd for $C_{24}H_{24}O_9$, 456.1420).

2α-Acetoxydeoxypicropodophyllin (erlangerin C) (3): colorless crystals (MeOH−CH_2Cl_2, 9:1); R_f 0.79 ($CHCl_3$−MeOH, 95:5); mp 224−226 °C; $[\alpha]^{22}_D$ +35° (*c* 0.34, $CHCl_3$); UV λ_{max} (EtOH) (log ϵ) 205 (2.71), 292 (1.68) nm; IR ν_{max} (KBr) 2982, 2926, 1772, 1745, 1582, 1503, 1480, 1415, 1369, 1318, 1234, 1119, 1030, 993, 928, 859, 757 cm^{-1}; for ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; EIMS *m*/*z* 456 $[M]^+$ (72), 413 (12), 396 (100), 381 (16), 365 (11), 313 (4), 283 (51), 181 (55), 135 (4), 43 (13); HREIMS *m*/*z* 456.1416 (calcd for $C_{24}H_{24}O_9$, 456.1420).

Hydrolysis of 3. Compound **3** (50 mg) and 5 mL of methanolic KOH were allowed to react at room temperature with stirring for 12 h to give a reaction mixture which was neutralized with 1% HCl in MeOH. The reaction product was extracted with $CHCl_3$, concentrated, and purified by preparative TLC to yield a white solid (**3a**) (30 mg); mp 74−76 °C; $[\alpha]^{22}_D$ +51° (*c* 0.075, $CHCl_3$); IR ν_{max} (KBr) 3439, 2914, 1766, 1583, 1484, 1324, 1236, 1119, 1037, 930, 754 cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 4.24 (1H, *s*, H-1), 2.93 (1H, m, H-3), 4.03 (1H, dd, J = 9.0, 6.4 Hz, H-3a), 4.58 (1H, dd, J = 9.0, 7.3 Hz, H-3a), 2.63 (1H, dd, J = 16.7, 4.0 Hz, H-4a), 3.28 dd (1H, dd, J = 16.7, 7.3 Hz, H-4b), 6.50 (1H, br s, H-5), 6.64 (1H, br s, H-8), 6.44 (1H, br s, H-2′), 6.44 (1H, br s, H-6′), 5.90 d (1H, d, J = 1.3 Hz, OCH_2O), 5.92 (1H, d, J = 1.3 Hz, OCH_2O), 3.80 (3H, s, OMe-3′), 3.85 (3H, s, OMe-4′), 3.80 (3H, s, OMe-5′); ^{13}C NMR (Table 2); EIMS (70 eV) *m*/*z* 414 $[M]^+$ (74), 396 (6), 356 (8), 314 (9), 313 (8), 284 (17), 283 (100), 252 (11), 239 (5).

2α-Acetoxy-3*β*-hydroxyisodeoxypodophyllotoxin (erlangerin D) (4): colorless crystals (MeOH−CH_2Cl_2, 9:1); R_f 0.43 ($CHCl_3$−MeOH, 95:5); mp 244−246 °C; $[\alpha]^{22}_D$ +70° (*c* 0.2, $CHCl_3$); UV λ_{max} (EtOH) (log ϵ) 211 (2.82), 290 (2.03) nm; IR ν_{max} (KBr) 3445, 2943, 1778, 1714, 1649, 1596, 1487, 1458, 1345, 1231, 1143, 1118, 1035, 926, 842, 754 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 1 and 2, respectively; EIMS *m*/*z* 472 $[M]^+$ (63), 412 (100), 394 (41), 379 (15), 368 (25), 351 (18) 339 (13), 283 (7), 200 (27), 172 (14), 168 (13), 153 (9), 60 (16), 45 (24), 44 (27), 43 (33); HREIMS *m*/*z* 472.1372 (calcd $C_{24}H_{24}O_{10}$, 472.1369).

X-ray Crystal Structure Analyses of Compounds 1−4. The data were collected on an Enraf-Nonius CAD4 diffractometer at 293(2) K using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). The structures were solved by direct methods using SHELXS-86[11] and refined by full-matrix least-squares on F^2 using SHELXL-93.[12] The structures were displayed using ZORTEP,[13] and displacement ellipsoids are shown at the 30% probability level.[14] Only relative configurations of **1**−**4** were determined.

Erlangerin A (1): colorless crystal (0.53 × 0.3 × 0.3 mm), $C_{27}H_{28}O_{11}$, M_r = 528.52, tetragonal system, space group $P4_1$, Z = 4, a = 15.203(2) Å, b = 15.203(2) Å, c = 14.035(2) Å, V = 3244.2(7) Å^3, D_{calc} = 1.447 g/cm^3, F(000) = 1462, μ = 0.344 mm^{-1}, 5794 collected reflections (2.68° ≤ θ ≤ 23.94°, −17 ≤ h ≤ 17, −17 ≤ k ≤ 17, −16 ≤ l ≤ 16), 5065 independent reflections (R_{int} = 0.0384), goodness-of-fit on F^2: S = 1.328, R1 = 0.1393, and wR2 = 0.3292 for all reflections, R1 = 0.1037 and wR2 = 0.3174 for 3446 observed reflections ($I > 2\sigma(I)$) due to strong loss of petroleum ether and chloroform during measurement, refining: 415 parameters and 1 restraint, no absorption correction, absolute structure parameter: 1.0(4), absolute structure not determined, final electron density between −0.471 and 0.479 e Å^{-3}.

Erlangerin B (2): colorless crystal (0.57 × 0.50 × 0.23 mm), $C_{24}H_{24}O_9$, M_r = 456.45, orthorhombic system, space group $P2_12_12_1$, Z = 4, a = 8.0139(6) Å, b = 8.3005(6) Å, c = 33.493(4) Å, V = 2227.9(4) Å^3, D_{calc} = 1.361 g/cm^3, F(000) = 960, μ = 0.105 mm^{-1}, 4090 collected reflections (2.43° ≤ θ ≤ 23.98°, −9 ≤ h ≤ 9, −9 ≤ k ≤ 9, −38 ≤ l ≤ 38), 3488 independent reflections (R_{int} = 0.0072), goodness-of-fit on F^2: S = 1.103, R1 = 0.0353 and wR2 = 0.0800 for all reflections, R1 = 0.0306 and wR2 = 0.0746 for 3213 observed reflections ($I > 2\sigma(I)$), refining: 302 parameters and no restraints, semiempirical absorption correction (T_{min} = 0.9582, T_{max} = 0.9973), absolute

structure parameter: 0.6(9), absolute structure not determined, final electron density between −0.151 and 0.139 e Å^{-3}.

Erlangerin C (3): colorless crystal (0.57 × 0.53 × 0.30 mm), $C_{24}H_{24}O_9$, M_r = 456.45, orthorhombic system, space group $P2_12_12_1$, Z = 4, a = 8.026(2) Å, b = 11.287(2) Å, c = 23.977(3) Å, V = 2171.9(7) Å^3, D_{calc} = 1.396 g/cm^3, $F(000)$ = 960, μ = 0.107 mm^{-1}, 3946 collected reflections (2.48° ≤ θ ≤ 24.00°, −9 ≤ h ≤ 9, −12 ≤ k ≤ 12, −27 ≤ l ≤ 27), 3404 independent reflections (R_{int} = 0.0105), goodness-of-fit on F^2: S = 1.164, R1 = 0.0496, and wR2 = 0.1022 for all reflections, R1 = 0.0397 and wR2 = 0.0952 for 2951 observed reflections ($I > 2\sigma(I)$), refining: 302 parameters and no restraints, semiempirical absorption correction from ψ-scans (T_{min} = 0.9474, T_{max} = 0.9944), absolute structure parameter: 1.0(14), absolute structure not determined, final electron density between −0.136 and 0.121 e Å^{-3}.

Erlangerin D (4): colorless crystal (0.53 × 0.47 × 0.27 mm), $C_{24}H_{24}O_{10}$, M_r = 472.45, monoclinic system, space group $P2_1$, Z = 4, a = 11.177(2) Å, b = 11.669(2) Å, c = 18.230(4) Å, β = 106.41(2)°, V = 2280.7(7) Å^3, D_{calc} = 1.376 g/cm^3, $F(000)$ = 992, μ = 0.108 mm^{-1}, 7526 collected reflections (2.91° ≤ θ ≤ 23.98°, −12 ≤ h ≤ 0, −3 ≤ k ≤ 13, −19 ≤ l ≤ 20), 7123 independent reflections (R_{int} = 0.0209), goodness-of-fit on F^2: S = 1.183, R1 = 0.0642, and wR2 = 0.1209 for all reflections, R1 = 0.0467 and wR2 = 0.1098 for 5776 observed reflections ($I > 2\sigma(I)$), refining: 623 parameters and 1 restraint, semiempirical absorption correction from ψ-scans (T_{min} = 0.9828, T_{max} = 0.9988), absolute structure parameter: −0.8(11), absolute structure not determined, final electron density between −0.190 and 0.170 e Å^{-3}.

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Supporting Information Available: X-ray data for **1**−**4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) All crystallographic data have been deposited at the Cambridge Crystallographic Data Centre (CCDC), UK. 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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