Lignans from Chilean Propolis

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Three new (**1**, **3**, **4**) and two known lignans (**2** and **5**) were isolated from Chilean propolis. Compound **1** was identified as a trimeric coniferyl alcohol acetate and **3** as the diastereomer of the dimeric coniferyl alcohol acetate **2**. Compound **4** was identified as a dihydrobenzofuran lignan aldehyde, which was isolated together with the related known acetate **5**.

Propolis is a complex mixture of beeswax, small amounts of sugar, and plant exudates collected by honeybees (*Apis mellifera*).[1,2] Bees use it to seal their hives from penetration of water, to strengthen and join the cells, and to prevent the decomposition of creatures that have been killed by bees after an invasion of the hive.[2,3] Propolis is known for its antiseptic, antimycotic, antibacterial, antiviral, antiprotozoal, and antiinflammatory properties.[1,4] It has been employed since ancient times in folk medicine in many parts of the world and is still widely used in Europe as a component in pharmaceutical and cosmetic products, such as antiacne preparations, facial creams, ointments, and lotions.[1,5−7] The bud exudates of poplar trees (*Populus* spp., Salicaceae) and horse-chestnut trees (*Aesculus hippocastanum*, Hippocastanaceae) are mentioned as the main sources of European and North American propolis,[5,8] which is known to consist of volatile oils and phenolics, mostly flavones, flavanones, and flavonols.[9−12]

Chilean propolis, however, must have a different botanical origin than propolis of the Northern Hemisphere due to Chile's unique flora that had developed as a result of its geographical isolation between the Pacific Ocean to the west and the Andes Mountains to the east. Chile's flora consist of many endemic plant species that include neither poplar nor horse-chestnut trees.[13]

The Chilean propolis used in this study was collected in a small area called Quebrada Yaquil in the mediterranean semiarid region, near Pichilemu, Chile. This region's climate is characterized by hot, dry summers and cold, rainy winters. The natural vegetation in this area corresponds to the matorral, an evergreen shrub land, dominated by evergreen sclerophyllous and summer deciduous shrubs. The herbaceous stratum is seasonal, appearing only after the first rains of the year. The most dominant plant families in the forage fields where the beehives are located include the Asteraceae, Anacardiaceae, Rosaceae, Rhamnaceae, Monimiaceae, and Lauracea.

Because a different plant origin of Chilean propolis suggests a different chemistry as compared to the European and North American propolis, we investigated its chemical composition. Here, we report the isolation and structure elucidation of five lignans, three of which are new natural products. This is the first report on the chemical composition of Chilean propolis.

Results and Discussion

Compound **1** was obtained as a colorless oil. HR-FABMS established its molecular formula of $C_{36}H_{40}O_{12}$. The positive FABMS showed intense fragments at *m*/*z* 443 and *m*/*z* 221 corresponding to the cleavage of two $C_{12}H_{14}O_4$ moieties. The compound showed IR bands at 3445, 2945, 1736, 1598, and 1510 cm^{-1} and a UV maximum at 266 nm with a shoulder at 300 nm. The ^1H and ^{13}C NMR data of **1** indicated a trimeric phenyl propanol derivative. The ^1H NMR revealed the presence of three aromatic ABM-systems (H-2/5/6, H-2′/5′/6′, H-2″/5″/6″). The ^{13}C NMR shifts indicated two oxygen substituents on each of the aromatic rings. The singlets at δ_H 3.86, 3.78, and 3.75, which had HMQC correlations to the carbon signals at δ_C 55.8, 55.8, and 55.6, respectively, were assigned to the methyl groups of three phenyl methyl ethers. The meta-positions of the methoxy groups and the para-positions of the additional oxygen substituents at the three aromatic rings were established via HMBC correlation between the methoxy protons and aromatic carbons at δ_C 150.7 (C-3), 146.5 (C-3′), and 150.1 (C-3″), and HMBC correlations between the ortho-positioned aromatic protons (H-2/6, H-2′/6′, H-2″/6″) and oxygen-substituted carbons at δ_C 147.6 (C-4), 145.4 (C-4′), and 147.4 (C-4″), respectively (see Figure 1). The shift values of three additional methyl signals at δ_H 2.09, 2.08, and 1.97 were characteristic for acetoxy methyl groups, which were confirmed by HMBC correlation between the methyl protons and the carboxyl carbons (three signals overlapping at δ_C 170.8). The large coupling constants of two pairs of olefinic protons at δ_H 6.53 and 6.13 (br d, J = 16.2, H-7; dd, J = 15.9, 6.6, H-8, respectively), and at δ_H 6.54 and 6.14 (br d, J = 15.6, H-7″; dd, J = 15.9, 6.6, H-8″, respectively) indicated two (*E*)-configured double bonds. In the DQF−COSY, the double doublet signals of olefinic protons at δ_H 6.13 (H-8) and δ_H 6.14 (H-8″) showed cross peaks to acetoxy methylene protons (δ_H 4.70−4.66, m, 4H, H-9/9″). The olefinic doublets at δ_H 6.53 (H-7) and δ_H 6.54 (H-7″) showed HMBC correlations to aromatic carbons at δ_C 109.8 (C-2) and 119.6 (C-6) and to 109.7(C-2″) and 119.6 (C-6″), respectively.

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Table 1. ^{1}H-NMR Data for Compounds **1**−**3**

	1	**2**		**3**	
position	$CDCl_3$	C_6D_6	$CDCl_3$	C_6D_6	$CDCl_3$
2	6.87 (d, 1.8)	6.70 (d, 2.1)	6.94	6.69 (d, 1.8)	6.86
5	6.67 (d, 8.1)	6.96 (d, 8.1)	6.96	7.10 (d, 8.1)	7.08
6	6.77 (dd, 8.1, 1.8)	6.79 (dd, 8.1, 2.1)	6.92	6.78 (dd, 8.1, 1.8)	6.88
7	6.53 (br d, 16.2)	6.42 (d, 15.6)	6.58	6.41 (d, 15.9)	6.60
8	6.13 (dd, 15.9, 6.6)	6.09 (dt, 15.6, 6.6)	6.18	6.09 (dt, 15.9, 6.6)	6.21
9a+b	4.70−4.66 (m)	4.63 (dd, 6.3, 0.9)	4.70	4.62 (dd, 6.6, 0.9)	4.72
OCH_3	3.75 (s)	3.27 (s)	3.87[b]	3.29 (s)	3.92
OAc	2.09[a] (s)	1.73 (s)	2.08	1.73 (s)	2.11
2′	7.02 (d, 1.8)	7.10 (d, 1.8)	6.97	6.94 (d, 1.8)	6.97
5′	6.83 (d, 8.4)	6.98 (d, 7.8)	6.84	6.97 (d, 8.1)	6.88
6′	6.94 (dd, 8.1, 1.8)	6.77 (dd, 8.1, 1.8)	6.77	6.82 (dd, 8.1,1.8)	6.94
7′	5.35 (d, 6.6)	4.98 (d, 3.6)	4.85	4.95 (d, 7.2)	4.84
8′	4.72 (m)	4.62 (m)	4.41	4.30 (m)	4.20
9a′	4.64 (dd, 11.7, 5.7)	4.67 (dd, 11.1, 7.2)	4.37	4.10[c] (dd, 11.7, 5.1)	4.23
9b′	4.54 (dd, 11.7, 3.0)	4.39 (dd, 11.1, 2.7)	4.10	4.37[c] (dd, 11.4, 3.3)	4.03
OCH_3′	3.78 (s)	3.27 (s)	3.86[b]	3.19 (s)	3.87
OAc′	2.08[a] (s)	1.61 (s)	1.97	1.61 (s)	2.03
OH	5.81 (br s)	5.68 (br s)	5.61	5.72 (br s)	5.68
2″	6.92 (d, 2.1)				
5″	6.68 (d, 8.4)				
6″	6.73 (dd, 8.4, 2.1)				
7″	6.54 (br d, 15.6)				
8″	6.14 (dd, 15.9, 6.6)				
9”	4.70−4.66 (m)				
OCH_3″	3.86 (s)				
OAc″	1.97[a] (s)				

[a,b,c] Assignments are interchangeable.

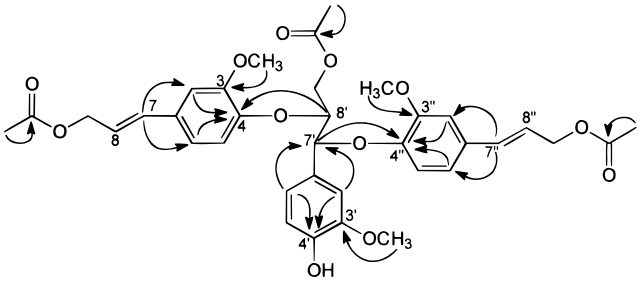


Figure 1. Selected HMBC correlations in **1**.

Based on these evidences, two monomer units of the trimer were elucidated as coniferyl alcohol acetates, which were linked through phenolic ether bonds to the third moiety.

The ortho-positioned protons (H-2′, H-6′) of the third and remaining ABM-system showed a HMBC correlation to a tertiary carbon signal at δ_C 80.1, whose one-bond correlated proton appeared at δ_H 5.35 (d, J = 6.6, H-7′). Both the ^{1}H and ^{13}C chemical shifts suggested the presence of an oxygen substitution. In the DQF−COSY, the proton at δ_H 5.35 (d, J = 6.6, H-7′) showed a vicinal coupling to a proton at δ_H 4.72 (m, H-8′), whose one-bond correlated carbon appeared at δ_C 81.8, again suggesting an oxygen substituent. The proton at δ_H 4.72 (m, H-8′) showed an additional ^3J connectivity to acetoxy methylene protons at δ_H 4.64 (dd, J = 11.7, 5.7, H-9a′) and δ_H 4.54 (dd, J = 11.7, 3.0, H-9b′). The HMBC correlation of the proton at δ_H 5.35 (H-7′) to the aromatic carbon at δ_C 147.4 (C-4″) and correlation of the proton at δ_H 4.72 (H-8′) to aromatic carbon at δ_C 147.6 (C-4) established the location of the ether connections between the three monomer units of the trimer. Based on these results, we elucidated **1** as 1-(4-hydroxy-3-methoxyphenyl)-1,2-bis{4-[(*E*)-3-acetoxypropen-1-yl]-2-methoxyphenoxy}propan-3-ol acetate. The stereochemistry of **1** was not determined.

The compounds **2** and **3** were also obtained as colorless oils. Both compounds were isolated from the same fraction (see Experimental Section), but **3** had a longer retention time ($t_{R\ 3} - t_{R\ 2}$ = 1.6 min) with HPLC on Si gel than did **2**. Their UV and IR spectra were similar to those of **1**. The ^{1}H and ^{13}C NMR of **2** and **3**, although similar to those of **1**, revealed fewer signals than in **1**, indicating two dimeric coniferyl alcohol derivatives. HRFABMS established a molecular formula of $C_{24}H_{28}O_9$ for both **2** and **3**. Intensive 1D- and 2D NMR of **2** and **3** showed that they had the same one- and multiple-bond C−H and H−H COSY correlations, and, although their NMR data were not identical, both **2** and **3** were identified as the dimeric coniferyl alcohol derivative 1-(4-hydroxy-3-methoxyphenyl)-2-{4-[(*E*)-3-acetoxypropen-1-yl]-2-methoxyphenoxy}propan-1,3-diol 3-acetate. The ^{1}H NMR data of **2** were identical with those of a known dimeric coniferyl alcohol acetate whose stereochemistry and optical rotation had not been reported.[14] Compounds **2** and **3** obviously differ only in their stereochemistry, which results in different optical rotations ($[\alpha]^{25}_D$ + 8.8° for **2**, $[\alpha]^{25}_D$ − 15.6° for **3**) and ^{1}H NMR data (Table 1). The signals for H-7′ and H-8′ appeared at δ_H 4.98 and δ_H 4.62, respectively, in **2** and at δ_H 4.95 and δ_H 4.30, respectively, in **3**. The differences in the chemical shifts of H-8′ in **2** and H-8′ in **3** are comparable to those reported for the erythro and threo isomers of a similar dimeric phenyl propane derivative,[15] indicating that **2** is the erythro isomer and that **3** is the threo isomer. The conformation of the two asymmetrical centers was assigned based on the coupling constants $J_{7',8'}$ = 3.6 Hz in **2** and $J_{7',8'}$ = 7.2 Hz in **3** and confirmed with NOE experiments. Irradiation of H-7′ caused signal enhancement of H-8′ in **2**. In **3**, no NOE effect was observed between H-7′ and H-8′, indicating syn-positions for H-7′ and H-8′ in **2** and anti-positions for H-7′ and H-8′ in **3**. Based on these observations, we assigned **2** as the erythro and **3** as the

2: erythro, syn **3**: threo, anti

Figure 2. Relative configuration and conformation of **2** and **3**.

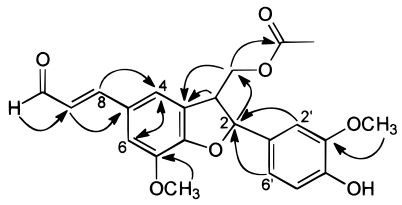
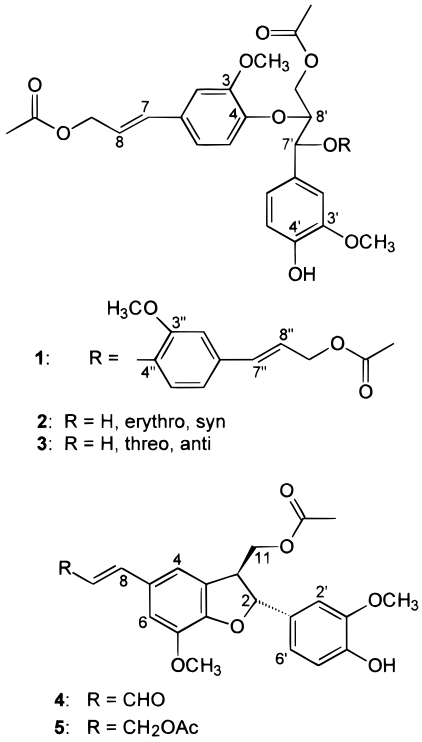


Figure 3. Selected HMBC correlations in **4**.

threo isomer of 1-(4-hydroxy-3-methoxyphenyl)-2-{4-[(*E*)-3-acetoxypropen-1-yl]-2-methoxyphenoxy}propan-1,3-diol 3-acetate with the conformations shown in Figure 2. Compound **3** was isolated for the first time as a natural product. The absolute configurations of **2** and **3** were not determined.

The spectral data of the oily compound **4** indicated a substituted diconiferyl aldehyde with a dihydrobenzofuran skeleton. The molecular formula of **4** was confirmed as $C_{22}H_{22}O_7$ by HRMS. The ^{1}H and ^{13}C NMR indicated two methoxy, one acetoxy, and one aldehyde function. In the DQF−COSY spectra, an aldehyde proton at δ_H 9.61 (d, J = 7.5, H-10) that correlated to the carbon signal at δ_C 192.3 showed a ^3J connectivity to a olefinic proton at δ_H 6.55 (dd, J = 15.9, 7.5, H-9) whose vicinal coupling to another olefinic proton at δ_H 6.83 (d, J = 15.9, H-8) indicated an *(E)*-double bond. In a HMBC-experiment, the olefinic protons H-8 and H-9 showed three-bond correlations to aromatic carbons of the dihydrobenzofuran (see Figure 3). The ^{1}H NMR also revealed the presence of an aromatic ABM-system (δ_H 6.75, br s, H-2′; δ_H 6.94, d, J = 8.1, H-5′; δ_H 6.73, br d, J = 8.1, H-6′). In the HMBC experiment, the two ortho-positioned protons H-2′ and H-6′ showed multiple-bond correlation to the dihydrofuran carbon C-2 (δ_C = 89.3) (see Figure 3), which showed HMQC cross peaks to a proton signal at δ_H 5.39 (d, J = 7.5, H-2). The DQF−COSY revealed vicinal coupling between H-2 and a proton at δ_H 3.57 (ddd, J = 7.5, 7.5, 5.1, H-3), which itself showed ^3J connectivities to acetoxy methylene protons (δ_H = 4.25/4.07, H-11). HMQC and HMBC experiments allowed us to establish **4** as 3-acetoxymethyl-5-[(*E*)-2-formylethen-1-yl]-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-2,3-dihydrobenzofuran. A coupling constant of 7.5 Hz for protons H-2/H-3 and the fact that no NOE effect was observed between these protons suggested a trans configuration of the substituents in position 2 and 3. The absolute configuration is not known.

Compound **5** was isolated as a colorless oil. Its IR and NMR data were similar to those of **4**. The most prominent differences in the ^{1}H and ^{13}C NMR spectra of **5**, when compared with those of **4**, are the lack of the aldehyde signal and the presence of the signals of an additional acetoxy methylene group. The multiplicity of the H-9 signal was increased from a double doublet in **4** to a doublet of a triplet in **5**, and the DQF−COSY revealed a ^3J connectivity between H-9 and the acetoxy methylene protons at δ_H 4.67. Compound **5** was identified as the known 3-acetoxymethyl-5-[(*E*)-3-acetoxypropen-1-yl)]-2-(4-hydroxy-3-methoxyphenyl)-7-methoxy-2,3-dihydrobenzofuran.[16−18]



Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO P-1020 polarimeter, UV spectra were acquired on a Beckman DU 640 spectrophotometer, and IR spectra were obtained with a Buck Scientific model 500 spectrophotometer using NaCl plates. ^{1}H and ^{13}C NMR were acquired on a Varian Unity-300 (300 MHz). All proton and carbon assignments are based on HMQC and HMBC experiments. FAB and HRFABMS were recorded on a JEOL HX 110. Negative ESIMS was recorded on a Finnigan MAT TSQ7000. Analytical TLC was carried out on Macherey−Nagel Si gel plates Polygram SIL G/UV$_{254}$. Compounds were visualized with a UV lamp and anisaldehyde sulfuric acid as the spray reagent.[19] Column chromatography was performed with Macherey−Nagel Si gel 60, 50−200 mm and Pharmacia Biotech Sephadex LH-20. Flash-chromatography was performed with Lagand Chemical Co. Si gel 60, 40−63 μm and Merck Si gel 60 RP-18, 40−63 μm. The HPLC system used was equipped with a Varian 9002 pump, a Varian Star 9040 RI detector, and an Alltech (Econosil silica 10 mm, 10 × 250 mm) HPLC column.

Biological Material. Propolis was collected in December 1995, and provided to us by Mr. Gustavo Adolfo Castillo Orozco at Rincon de Yaquil, Santa Cruz, Quebrada de Yaquil, VI Region, Chile, or at Orebro 485, Estación Central Santiago, Chile (Tel: 56-2-7414883. Fax: 56-2-2237319). The hives and forage fields are located in a small area called Quebrada Yaquil (34° 24′ LS; 71° 28′ LW; altitude 160 meters above sea level) in

the mediterranean semiarid region, near Pichilemu, Chile. Dominant species in the forage fields are the sclerophyllous shrubs *Lithrea caustica*, *Quillaja saponaria*, *Cryptocarya alba*, *Kageneckia oblonga*, *Colliguaja odorifera*, *Trevoa trinervia*, *Baccharis linearis*, and *Peumus boldus* and the herbaceous *Madia sativa*, *Helenium aromaticum*, and *Pasithea coerulea*.

Extraction and Isolation. Propolis (150 g) was cut into small pieces and extracted three times with MeOH (3 × 0.5 L) at room temperature for 24 h. After filtration through a paper filter, the filtrates were combined and the solvent evaporated in vacuo. The dried MeOH extract was dissolved in H_2O and extracted with CH_2Cl_2. The CH_2Cl_2 extract was applied in succession to column chromatography on Sephadex LH-20 with CH_2Cl_2−MeOH 1:1 and column chromatography on Si gel with a hexane−EtOAc gradient (0, 1, 2, 5, 10, 20, 50, 100% EtOAc) yielding seven fractions of increasing polarity. Fraction 2 was separated into six subfractions 2.1−2.6 by column chromatography on Si gel with hexane−EtOAc, 8:2. Fraction 2.6 was applied to column chromatography on Si gel with hexane-CH_2Cl_2−Me_2CO, 5:3:2, yielding crude **4** and crude **5**. HPLC with hexane-EtOAc 6:4 yielded 24 mg of **4**, and HPLC with hexane-CH_2Cl_2 −Me_2CO 60:35:5 yielded 200 mg of **5**. Fraction 3 was applied to column chromatography on Si gel with hexane-EtOAc 6:4 followed by flash chromatography on Si gel with a CH_2Cl_2−EtOAc gradient (10−20% EtOAc) yielding seven subfractions 3.1−3.7. Fraction 3.3 contained a mixture of **1** and **4**, which were separated by flash chromatography on Si gel RP-18 with CH_3CN−H_2O 1:1. Compound **1** (137 mg) was purified by HPLC with hexane−EtOAc 6:4. An additional 20 mg of **4** were purified by flash chromatography on Si gel RP-18 (MeOH−H_2O, 1:1) followed by HPLC with hexane−EtOAc 6:4. Fraction 3.7 was applied to flash chromatography on Si gel with CH_2Cl_2−EtOAc, 7:3, yielding a mixture of **2** and **3**, which were separated by HPLC with hexane−EtOAc 1:1 yielding 46 mg of **2** and 107 mg of **3**.

Compound 1: obtained as a colorless oil; $[\alpha]^{25}_D$ − 0.6° (*c* 1.5, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 266 (4.45), 300 (4.14) nm; IR (NaCl) ν_{max} 3445, 3010, 2945, 2845, 1736, 1598, 1510, 1460, 1416, 1362, 1240 br, 1134, 1030, 964, 920, 856, 730 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 170.8 (3 × s, OAc/OAc′/OAc″), 150.7 (s, C-3), 150.1 (s, C-3″), 147.6 (s, C-4), 147.4 (s, C-4″), 146.5 (s, C-3′), 145,4 (s, C-4′), 134.0 (d, C-7″), 133.9 (d, C-7), 131.1 (s, C-1″), 130.2 (s, C-1), 129.4 (s, C-1′), 121.8 (d, C-8), 121.4 (d, C-8″), 120.4 (d, C-6′), 119.6 (2 × d, C-6/6″), 118.4 (d, C-5), 116.2 (d, C-5″), 114.0 (d, C-5′), 109.8 (d, C-2), 109.7 (d, C-2″), 109.6 (d, C-2′), 81.8 (d, C-8′), 80.1 (d, C-7′), 65.1 (t, C-9), 65.0 (t, C-9″), 63.6 (t, C-9′), 55.8 (2 × q, OCH_3″/OCH_3′) 55.6 (q, OCH_3), 20.9 (2 × q, OAc), 20.7 (q, OAc); positive HRFABMS (thioglycerin) *m/z* 664.2543 (calcd for $C_{36}H_{40}O_{12}$, 664.2519).

Compound 2: obtained as a colorless oil; $[\alpha]^{25}_D$ + 8.8°(*c* 0.63, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 268 (4.49), 300 (4.20) nm; IR (NaCl) ν_{max} 3465, 3005, 2945, 1736, 1598, 1510, 1458, 1426, 1366, 1240 br, 1152, 1028, 964, 916 cm^{-1}; ^1H NMR (C_6D_6, $CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR (C_6D_6, 75 MHz) δ 170.4 (s, OAc′), 170.2 (s, OAc), 151.4 (s, C-3), 148.2 (s, C-4), 147.3 (s, C-3′), 146.1 (s, C-4′), 133.9 (d, C-7), 132.5 (s, C-1), 131.8 (s, C-1′), 122.8 (d, C-8), 120.2 (d, C-6), 119.5 (2 × d, C-6′/C-5), 114.3 (d, C-5′), 110.5 (d, C-2), 109.3 (d, C-2′), 83.7 (d, C-8′), 72.4 (d, C-7′), 64.8 (t, C-9), 62.7 (t, C-9′), 55.2 (2 × q, OCH_3/OCH_3′), 20.4 (q, OAc), 19.7 (q, OAc′); positive HRFABMS (thioglycerin) *m/z* 460.1727 (calcd for $C_{24}H_{28}O_9$, 460.1733).

Table 2. ^1H NMR and ^{13}C NMR Data for Compound **4** in C_6D_6

position	^{13}C	HMQC
2	89.3 (d)	5.39 (d, 7.5)
3	50.5 (d)	3.57 (ddd, 7.5, 7.5, 5.1)
3a	129.0 (s)	
4	118.2 (d)	6.71 (br s)
5	128.9 (s)	
6	113.0 (d)	6.66 (br s)
7	145.3 (s)	
7a	151.8 (s)	
8	151.8 (d)	6.83 (d, 15.9)
9	126.9 (d)	6.55 (dd, 15.9, 7.5)
10	192.3 (d)	9.61 (d, 7.5)
11	65.0 (t)	4.25 (dd, 11.4, 5.1)
		4.07 (dd, 11.7, 7.5)
1′	132.4 (s)	
2′	108.7 (d)	6.75 (br s)
3′	146.7 (s)	
4′	147.1 (s)	
5′	114.8 (d)	6.94 (d, 8.1)
6′	119.6 (d)	6.73 (br d, 8.1)
OH		5.44 (s)
OCH_3	55.7 (q)	3.37 (s)
OCH_3′	55.2 (q)	3.06 (s)
OAc	169.9 (s)	1.56 (s)
	20.2 (q)	

Compound 3: obtained as a colorless oil; $[\alpha]^{25}_D$ − 15.6°(*c* 0.85, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 268 (4.16), 300 (3.86) nm; IR (NaCl) ν_{max} 3460, 3005, 2935, 2845, 1736, 1600, 1510, 1460, 1428, 1364, 1240 br, 1160, 1030, 964, 920, 856, 730 cm^{-1}; ^1H NMR (C_6D_6, $CDCl_3$, 300 MHz), see Table 1; ^{13}C NMR (C_6D_6, 75 MHz) δ 170.2 (s, OAc), 170.0 (s, OAc′), 151.9 (s, C-3), 148.8 (s, C-4), 147.0 (s, C-3′), 146.3 (s, C-4′), 133.9 (d, C-7), 132.5 (s, C-1), 132.1 (s, C-1′), 122.9 (d, C-8), 120.8 (d, C-6′), 120.4 (d, C-6), 119.9 (d, C-5), 114.7 (d, C-5′), 110.6 (d, C-2), 109.9 (d, C-2′), 85.9 (d, C-8′), 74.5 (d, C-7′), 65.1 (t, C-9), 63.3 (t, C-9′), 55.3 (q, OCH_3′) 53.4 (q, OCH_3), 20.6 (q, OAc), 20.2 (q, OAc′); positive HRFABMS (thioglycerin) *m/z* 460.1740 (calcd for $C_{24}H_{28}O_9$, 460.1733).

Compound 4: obtained as a colorless oil; $[\alpha]^{25}_D$ + 13.1°(*c* 1.1, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 287 (3.75), 338 (4.07) nm; IR (NaCl) ν_{max} 3430, 2930, 2855, 1736, 1666, 1592, 1516, 1488, 1460, 1428, 1362, 1328, 1240 br, 1120, 1032, 968, 920, 822, 732 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz), see Table 2; ^{13}C NMR (C_6D_6, 75 MHz), see Table 2; positive HRFABMS (mNBA) *m/z* 398.1374 (calcd for $C_{22}H_{22}O_7$, 398.1365).

Compound 5: obtained as a colorless oil; $[\alpha]^{25}_D$ − 2.0°(*c* 1.2, CH_2Cl_2); UV (MeOH) λ_{max} (log ϵ) 279 (4.19), 304 (3.86), 347 (3.29) nm; IR (NaCl) ν_{max} 3460, 3020, 2955, 2855, 1740, 1732, 1604, 1516, 1500, 1464, 1432, 1380, 1364, 1332, 1250 br, 1146, 1034, 960, 928, 856, 734 cm^{-1}; ^1H NMR (C_6D_6, 300 MHz) δ 6.96 (1H, d, J = 7.8 Hz, H-5′), 6.85 (1H, d, J = 1.8 Hz, H-2′), 6.82 (1H, s, H-4), 6.80 (1H, s, H-6), 6.80 (1H, dd, J = 7.5, 1.8 Hz, H-6′), 6.50 (1H, d, J = 15.9 Hz, H-8), 6.12 (1H, dtr, J =

15.9, 6.9 Hz, H-9) 5.80 (1H, br s, OH), 5.43 (1H, d, J = 7.5 Hz, H-2), 4.67 (2 H, dd, J = 6.6, 0.9 Hz, H-10), 4.34 (1H, dd, J = 11.1, 5.1 Hz, H-11a), 4.15 (1H, dd, J = 11.1, 7.5 Hz, H-11b), 3.65 (1H, m, H-3), 3.49 (3H, s, OCH_3), 3.15 (3H, s, OCH_3'), 1.76 (3H, s, OAc), 1.60 (3H, s, OAc′); ^{13}C NMR (C_6D_6, 75 MHz) δ 170.1 (s, OAc′), 170.0 (s, OAc), 149.4 (s, C-7a), 147.1 (s, C-3′), 146.5 (s, C-4′), 145.1 (s, C-7), 134.7 (d, C-8), 133.0 (s, C-1′), 130.9 (s, C-5), 128.7 (s, C-3a), 121.5 (d, C-9), 119.7 (d, C-6′), 115.7 (d, C-4), 114.8 (d, C-5′), 111.9 (d, C-6), 108.8 (d, C-2′), 88.8 (d, C-2), 65.3 (t, C-11), 65.2, (t, C-10), 55.8 (q, OCH_3), 55.2 (q, OCH_3'), 50.9 (d, C-3), 20.6 (q, OAc′), 20.2 (q, OAc); negative ESIMS m/z 441 $[M - H]^-$.

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