New Sesquiterpenes from *Crossopetalum tonduzii*†

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Received June 5, 1998

Five new sesquiterpenes (**1**−**5**) with a dihydro-*β*-agarofuran skeleton were isolated from *Crossopetalum tonduzii*. Their structures were elucidated by means of ^{1}H and ^{13}C NMR spectroscopic studies, including homonuclear and heteronuclear correlation experiments (COSY, ROESY, HMQC, and HMBC). The absolute configurations of **1** and **2** were determined by CD studies and chemical correlation. Compounds **1**−**3** were assayed against *Spodoptera littoralis* in an election test and showed low insect-antifeedant activity.

The flora of Panama is extraordinarily rich and diverse.[1] There are many plants that the native groups of Amerindians use for the treatment of different ailments. In addition, preliminary in vitro bioassays indicate that many of these plants are active.[2] The family Celastraceae is a rich source of dihydro-*β*-agarofuran sesquiterpene esters.[3] In recent years these compounds have been of increasing interest due to their cytotoxic,[4] antitumor-promoting,[5] immunosuppressive,[6] insecticidal,[7,8] and insect-antifeedant[8] activities and for reversing multidrug resistance[9] in cancer cells.

As a part of an intensive investigation into biologically active metabolites from the Celastraceae family, *Crossopetalum tonduzii* (Loes.) Lund.[10] is being studied. Previously the ethanol extract of the aerial part of this plant showed xanthine oxidase inhibitory activity.[11] In this communication we report the isolation and structure elucidation of five new sesquiterpene esters from the aerial part of *C. tonduzii*, a species that has not yet been subjected to thorough phytochemical analysis.

Results and Discussion

Repeated chromatography of the ethanol extract of the aerial part of *C. tonduzii* on Sephadex LH-20 and Si gel yielded five new metabolites (**1**−**5**). Compound **1** was assigned the structure and configuration (1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,-8*S*,9*S*,10*S*)-6,8-diacetoxy-1,9-dibenzoyloxy-15-(2)-methylbutyroyloxy-2,4-dihydroxy-dihydro-*β*-agarofuran as follows. Its molecular formula was determined as $C_{38}H_{46}O_{13}$ by HREIMS. The IR spectrum showed absorption bands for a hydroxyl group at 3450 cm^{-1} and an ester group at 1725 cm^{-1}. The MS contained fragmentation ions attributable to benzoate (*m*/*z* 105), 2-methylbutyrate (*m*/*z* 85), and acetate (*m*/*z* 43) groups. The ^{1}H NMR (C_6D_6) spectrum also indicated the presence of two acetates at *δ* 1.48 and 1.72 s (each 3H); one 2-methylbutyrate at 1.19 t (3H, *J* = 7.4 Hz), 1.58 d (3H, *J* = 7.0 Hz), 2.19 m (2H), and 3.12 m (1H), and two benzoyl groups at 6.70 m (2H), 6.92 m (1H), 6.99 m (2H), 7.06 m (1H), 7.83 m (2H), and 7.89 m (2H); which were confirmed by ^{13}C NMR. The ^{1}H NMR spectrum (Table 1) contained signals assignable to protons on the carbon atoms carrying four secondary ester groups at *δ* 6.92 s (1H, H-6), 6.55 d (1H, *J* = 9.8 Hz, H-9), 6.16 dd (1H, *J* = 3.2 Hz, 9.8 Hz, H-8), and 6.07 d (1H, *J* = 3.1 Hz, H-1); one primary ester group at *δ* 5.47 and 5.57 d_{AB} (2H, *J* = 13.6 Hz, H-15); and one secondary hydroxyl group at *δ* 4.0 m (1H, H-2); a tertiary methyl group at *δ* 1.81 s (3H, H-14) attached to a carbon at *δ* 69.9 bearing a hydroxyl group, two angular methyl groups at *δ* 1.37 and 1.70 s (each 3H, H-12 and H-13), which were confirmed by the ^{13}C NMR spectrum (Table 2); and four quaternary carbons at *δ* 69.9, 93.1, 52.4, and 83.8. The C═O signal of the 2-methylbutyrate group at *δ* 175.9 showed long-range correlation with the ^{1}H signals at *δ* 5.47 and 5.57 (H-15); the C═O signals of the acetate groups at *δ* 168.9 and 169.0 were correlated with the ^{1}H signals at *δ* 6.16 (H-8) and 6.92 (H-6), and finally, the C═O signals of the benzoate groups at *δ* 164.8 and 165.4 were correlated with the ^{1}H signals at *δ* 6.55 (H-9) and 6.07 (H-1) (Table 3).

The relative stereochemistry of **1** was determined on the basis of the coupling constants and from the results of ROESY (Figure 1). From COSY of **1**, we observed the *J* coupling of $H_1-H_2-H_3$, $H_7-H_8-H_9$. Furthermore, the coupling constants ($J_{1,2}$ = 3.1 Hz, $J_{8,9}$ = 9.8 Hz) indicated a cis-relationship between H-1 and H-2 and a trans-relationship between H-8 and H-9. In the ROESY of **1**, there were significant NOE effects between H-1 and H-9 and H-2; between H-15_{ab} and H-6, H-8, and Me-14; and finally between Me-12 and H-9. Therefore, the structure of **1** was established as 6*β*,8*β*-diacetoxy-1α,9α-dibenzoyloxy-15-(2)-methylbutyroyloxy-2α,4*β*-dihydroxy-dihydro-*β*-agarofuran.

To determine the absolute configuration of **1**, it was necessary to introduce another chromophore group. Benzoylation yielded the tribenzoate **6**, whose CD spectrum showed a split curve with a first positive Cotton effect at 233.4 nm (Δ*ε* = +19.1) and a second negative Cotton effect at 219.9 (Δ*ε* = −6.5), so that the absolute configuration of **6** was established as (1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*S*,10*S*)-6,8-acetoxy-1,2,9-tribenzoyloxy-15-(2)-methylbutyroyloxy-4-hydroxy-dihydro-*β*-agarofuran.

The structure of **2** was elucidated by spectral methods, ^{1}H and ^{13}C NMR studies (Tables 1 and 2), 2D ^{1}H−^{1}H and ^{1}H−^{13}C correlation (Table 3), and ROESY (Figure 1) experiments, while its absolute configuration was established by chemical correlation with **1**, inasmuch as acetylation of **1** and **2** yielded the same triacetate **7**.

Compound **3**, with the molecular formula $C_{34}H_{48}O_{12}$ (HREIMS), in a study of its IR, UV, ^{1}H and ^{13}C NMR data (Tables 1 and 2), and 2D experiments, was shown to be a dihydro-*β*-agarofuran sesquiterpene with one acetate, one benzoate, two 2-methylbutyrate, two secondary hydroxyl

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† This paper is warmly dedicated to Professor Antonio González on occasion of his 80th birthday.

10.1021/np980229g CCC: $15.00
Published on Web 10/31/1998

Table 1. ^{1}H NMR*,[a] of Compounds **1**−**10**

position	1	2	3	4	5	6	7	8	9	10
H-1	6.07 d (3.1)	5.74 d (3.0)	5.44 d (3.0)	5.45 d (2.9)	5.50 d (3.5)	5.79 d (3.2)	5.93 d (3.6)	5.49 d (2.8)	5.68[b]	5.49 d (3.1)
H-2	4.0 m	4.23 m	4.15 m	4.13 m	5.39 m	4.48 m	5.72 m	4.17 m	5.68[b]	5.37 m
H-6	6.92 s	5.28 d (4.9)	5.31 d (4.9)	6.54 s	5.23 d (5.1)	6.53 s	6.56 s	6.64 s	6.62 s	6.51 s
H-7	2.40 d (3.2)	2.59 d (3.2)	2.59 d (3.2)	2.52 d (3.3)	2.61 d (3.2)	2.54 d (3.3)	2.56 d (3.2)	2.72 d (3.2)	2.74 d (3.2)	2.50 d (3.3)
H-8	6.16 dd (3.2, 9.8)	5.57 dd (3.2, 9.9)	5.54 dd (3.2, 10.0)	5.69 dd (3.3, 9.8)	5.59 dd (3.2, 10.0)	5.77 dd (3.3, 9.7)	5.82 dd (3.2, 9.7)	5.83 dd (3.2, 9.8)	5.92 dd (3.2,9.8)	5.73 dd (3.3, 9.8)
H-9	6.55 d (9.8)	6.14 d (9.9)	6.09 d (10.0)	6.10 d (9.8)	6.09 d (10.0)	6.14 d (9.7)	6.20 d (9.7)	6.15 d (9.8)	6.20 d (9.8)	6.09 d (9.8)
Me-12	1.70 s	1.68 s	1.68 s	1.71 s	1.66 s	1.60 s	1.62 s	1.65 s	1.61 s	1.57 s
Me-13	1.37 s	1.58 s	1.59 s	1.63 s	1.61 s	1.53 s	1.57 s	1.57 s	1.56 s	1.50 s
Me-14	1.81 s	1.80 s	1.74 s	1.60 s	1.72 s	1.74 s	1.78 s	1.74 s	1.78 s	1.72 s
H-15	5.47, 5.57 d_{AB} (13.6)	4.92, 5.18 d_{AB} (13.4)	5.47, 5.03 d_{AB} (13.4)	4.82, 5.04 d_{AB} (13.4)	4.62, 4.94 d_{AB} (13.4)	4.84, 5.10 d_{AB} (13.2)	4.84, 5.10 d_{AB} (13.2)	4.36, 5.08 d_{AB} (13.5)	4.69, 5.30 d_{AB} (13.1)	4.65, 4.94 d_{AB} (13.5)

* δ, $CDCl_3$, J are given in Hz in parentheses. [a] C_6D_6. [b] Overlapping signals.

Table 2. ^{13}C NMR (δ, $CDCl_3$) Data of Compounds **1**−**5**[a]

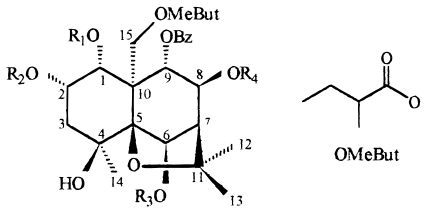
position	1[b]	2	3	4	5
C-1	78.2 d	78.1 d	78.0 d	78.2 d	75.0 d
C-2	67.5 d	67.3 d	75.3 d	67.3 d	67.3 d
C-3	44.4 t	43.1 t	43.0 t	43.7 t	41.5 t
C-4	69.9 s	72.5 s	67.0 s	69.8 s	72.1 s
C-5	93.1 s	92.0 s	92.0 s	92.6 s	91.5 s
C-6	76.0 d	77.3 d	76.9 d	75.8 d	76.8 d
C-7	52.4 d	53.5 d	53.5 d	52.2 d	53.5 d
C-8	74.1 d	74.4 d	72.4 d	73.8 d	73.7 d
C-9	76.0 d	75.4 d	74.1 d	75.5 d	75.0 d
C-10	52.4 s	51.1 s	50.8 s	51.6 s	50.5 s
C-11	83.8 s	84.3 s	84.2 s	84.0 s	84.5 s
C-12	25.5 q	26.3 q	26.3 q	25.8 q	26.2 q
C-13	29.3 q	30.1 q	30.1 q	29.8 q	30.0 q
C-14	25.2 q	24.3 q	24.3 q	25.1 q	24.0 q
C-15	62.5 t	62.1 t	62.0 t	62.0 t	61.6 t

[a] Data are based on DEPT and ^{1}H−^{13}C 2D experiments. [b] C_6D_6.

and one tertiary hydroxyl groups, positioned at 1α,2α,4β,-6β,8β,9α,15. An HMBC experiment established that the acetate was at C-1, the benzoate at C-9, the 2-methylbutyrates at C-8 and C-15, the secondary hydroxyls at C-2 and C-6, and the tertiary hydroxyl at C-4.

In an attempt to determine the absolute configuration, benzoylation of **3** gave **8** and **9**. Their CD spectra, however, did not exhibit splitting because the opposite 2,6 and 2,9 pairwise interactions canceled each other, and the 6,9 pairwise interaction was almost coplanar.[12]

Structures of **4** and **5** were elucidated by spectral methods (^{1}H and ^{13}C NMR bidimensional studies) and chemical correlation with **3**. Acetylation of **3**, **4**, and **5** gave the same compound (**10**). These new compounds all have the basic polyhydroxy skeleton of 8-*epi*-4β-hydroxyalatol.[13]



Compounds	R_1	R_2	R_3	R_4
1	Bz	H	Ac	Ac
2	Bz	H	H	Ac
3	Ac	H	H	MeBut
4	Ac	H	Ac	MeBut
5	Ac	Ac	H	MeBut
6	Bz	Bz	Ac	Ac
7	Bz	Ac	Ac	Ac
8	Ac	H	Bz	MeBut
9	Ac	Bz	Bz	MeBut
10	Ac	Ac	Ac	MeBut

Compounds **1**, **2**, and **3** were assayed against larvae of the Egyptian cottonleaf worm *Spodoptera littoralis* (Boisduval), using the leaf disk method,[8] showing low antifeedant activity at a concentration of 10 μg/cm^2. These results are in agreement with our previous work,[8] where the most active insect-antifeedant compounds were those with the isoalatol or 4β-hydroxyalatol skeleton.

Experimental Section

General Experimental Procedures. IR (film) spectra were obtained on a PE 681 spectrophotometer, and ^{1}H and ^{13}C NMR spectra, on a Bruker W-200SY at 200 and 50 MHz, respectively, with TMS as internal reference. The HMBC, HMQC, and ROESY spectra were recorded on a Bruker instrument at 400 MHz. Optical rotations were measured on a Perkin−Elmer 241 automatic polarimeter, and $[\alpha]^{25}_D$ are given in 10^{-1} deg cm^2 g^{-1}. UV spectra were collected on a Perkin−Elmer model 550-SE. EIMS were recorded on a VG Micromass ZAB-2F and a Hewlett−Packard 5995. HREIMS were recorded on a VG Autospec spectrometer. Derivatives **6** and **9** used for CD were purified by HPLC (semipreparative μ-porosil, 19 × 150 mm; *n*-hexane−EtOAc, 7:3; flow rate, 2.0 mL/min; UV detection at 250 nm; t_R 26 and 22 min, respectively).

Plant Material. *C. tonduzii* was collected at Boquete, Chiriquí, Panama, in August 1991. A voucher (FLORPAN 882) is deposited in the herbarium of the University of Panama. Air-dried, chopped aerial parts (1.5 kg) were extracted with EtOH in a Soxhlet apparatus, the solvent was evaporated under vacuum, and the residue (190 g) was chromatographed on Si gel and eluted with *n*-hexane−EtOAc mixtures of increasing polarity. The *n*-hexane−EtOAc (1:1) eluting fraction was then chromatographed on Sephadex LH-20 (*n*-hexane−$CHCl_3$−MeOH, 2:1:1) and Si gel (*n*-hexane-1,4-dioxan, 3:2) to yield compounds **1** (31 mg, R_f = 0.47), **2** (29 mg, R_f = 0.39), **3** (98 mg, R_f = 0.39), **4** (7 mg, R_f = 0.47), and **5** (13 mg, R_f = 0.47).

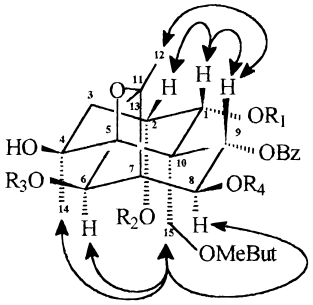
(1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*S*,10*S*)-6,8-diacetoxy-1,9-dibenzoyloxy-15-(2)-methylbutyroyloxy-2,4-dihydroxy-dihydro-β-agarofuran (1): colorless oil; $[\alpha]^{25}_D$ +11.4 ° (*c* 0.36, $CHCl_3$); UV (ETOH) λ_{max} 274.2, 262.8, 229.6, 213.2 nm; IR ν_{max} 3450, 2900, 1440, 700 cm^{-1}; ^{1}H NMR (C_6D_6) δ 1.19 t (3H, J = 7.4 Hz), 1.48 s (3H), 1.58 d (3H, J = 7.0), 1.79 s (3H), 1.56 m (2H), 2.19 m (2H), 2.75 s (1H), 3.12 m (1H), 6.70 m (2H), 6.92 m (1H), 6.99 m (2H), 7.06 m (1H), 7.83 m (2H), 7. 89 m (2H), for other signals, see Table 1; ^{13}C NMR (C_6D_6) δ OAc [19.8, 20.6 (2 × CH_3), 168.9, 169.0 (2 × $-CO_2-$)], OBz [127.5, 127.6, 127.7, 127.9, 129.5, 129.6, 132.2, 132.5 (8 × CH), 129.8, 130.1 (2C), 164.8, 165.4 (2 × $-CO_2-$)], OMe But 11.6, 16.6 (2 × CH_3), 26.8 (CH_2), 41.6 (CH), 175.9 ($-CO_2-$)], for other signals, see Table 2; EIMS *m*/*z* 710 ([M$^+$], 2), 695 (25), 473 (20), 632 (100), 588 (83), 546 (23), 530 (15), 510 (22), 486 (15), 202 (11), 105 (100), 77 (11), 43 (19); HREIMS *m*/*z* 710.2921 [M$^+$] (calcd for $C_{38}H_{46}O_{13}$, 710.2938).

Benzoylation of 1. Compound **1** (10 mg) was dissolved in dry pyridine (0.5 mL) and benzoyl chloride (6 drops), and some crystals of 4-(dimethylamino)-pyridine were added under argon

Table 3. Three-bond $^1H-C^{13}$ Coupling (HMBC) in Compounds **1**−**5**

position	1	2	3	4	5
H-1	C-5, C-10[a], C-15 $C_6H_9CO_2-$	C-9, C-10[a], C-15 $C_6H_5CO_2-$	C-9, C-10[a], C-15 CH_3CO_2-	C-9, C-10[a], C-15 CH_3CO_2-	C-9, C-10[a], C-15 CH_3CO_2-
H-6	C-5[a], C-7[a], C-8, C-11, CH_3CO_2-	C-5[a], C-8	C-5[a], C-8, C-10 CH_3CO_2-	C-5[a], C-7, C-8 C-11	C-5[a], C-8, C-11
H-7	C-5, C-8[a], C-9, C-11[a]	C-5, C-6[a], C-8[a], C-9	C-5, C-6, C-8[a], C-9 C-11[a]	C-5, C-8[a], C-9	C-5, C-8[a], C-9 C-11[a]
H-8	C-7[a], C-9[a], C-11 CH_3CO_2-	C-6, C-9[a], C-11 CH_3CO_2-	C-6, C-9[a], C-11 $C_4H_9CO_2-$	C-9[a], C-11	C-6, C-9[a], C-11 $C_4H_9CO_2-$
H-9	C-1, C-7, C-8[a], C-10, C-15, $C_4C_9CO_2-$	C-1, C-7, C-8[a], C-10 C-15, $C_4C_9CO_2-$	C-5, C-7, C-8[a], C-10 C-15, $C_4C_9CO_2-$	C-1, C-8[a], C-10 C-15, $C_4C_9CO_2-$	C-1, C-8[a], C-10 C-15, $C_4C_9CO_2-$
H-15	C-5, C-9, C10[a] $C_4C_9CO_2-$	C-1 C-5, C-9, C10[a] $C_4C_9CO_2$	C-1 C-5, C-9, C10[a] $C_4C_9CO_2$	C-1 C-5, C-9 C10[a], $C_4C_9CO_2$	C-1 C-5, C-9 C10[a], $C_4C_9CO_2$

[a] Two-bond coupling enhancement observed.



	R_1	R_2	R_3	R_4
1	Bz	H	Ac	Ac
2	Bz	H	H	Ac
3	Ac	H	H	MeBut
4	Ac	H	Ac	MeBut
5	Ac	Ac	H	MeBut

Figure 1. ROESY experiment of **1**−**5**

atmosphere. The mixture was heated at 60 °C for 15 h, poured over H_2O, extracted with EtOAc, and purified on Si gel with a mixture of *n*-hexane−EtOAc (7:3) to give compound **6** (9.3 mg).

(1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*S*,10*S*)-6,8-diacetoxy-1,2,9-tribenzoyloxy-15-(2)-methylbutyroyloxy-4-hydroxy-dihydro-*β*-agarofuran (6): colorless oil; $[\alpha]^{25}_D$ + 23.9 ° (*c* 0.4, $CHCl_3$); UV (ETOH) λ_{max} 272.6, 228.0, 210.8, 203.0 nm; IR ν_{max} 3556, 3421, 2925, 2840, 1731, 1452, 1376, 1281, 840, 709 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 t (3H, *J* = 7.4 Hz), 1.41 d (3H, *J* = 6.9 Hz), 1.83 s (3H), 1.99 m (2H), 2.15 s (3H), 2.86 m (1H), 6.86 m (2H), 7.09 m (4H), 7.32 m (3H), 7.50 m (4H), 8.06 m (2H); for other signals, see Table 1; EIMS *m*/*z* 814([M^+], 1), 799 (1), 754 (1), 692 (1), 632 (2), 572 (1), 336 (2), 202 (8), 105 (100), 85 (6), 77 (14), 57 (13); HREIMS *m*/*z* 814.3049 [M^+] (calcd for C_{41} H_{50} O_{17}, 814.3048); CD λ_{ext} (MeCN) nm: 233.4 ($\Delta\epsilon$ = +19.1), 224.1 ($\Delta\epsilon$ = 0), 219.9 ($\Delta\epsilon$ = −6.4)

Acetylation of 1. Ac_2O (4 drops) was added to compound **1** (5 mg) dissolved in pyridine (2 drops), and the mixture left at room temperature for 16 h. EtOH (3 × 2.0 mL) was added and carried almost to dryness in a rotavapor, and this process was repeated with $CHCl_3$ (3 × 2.0 mL), to give product **7** (5 mg).

(1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*S*,10*S*)-2,6,8-triacetoxy-1,9-dibenzoyloxy-15-(2)-methylbutyroyloxy-4-hydroxy-dihydro-*β*-agarofuran (7): colorless oil; $[\alpha]^{25}_D$ +13.3 ° (*c* 0.5, $CHCl_3$); UV (ETOH) λ_{max} 228.8, 212.8, 204.2 nm; IR ν_{max} 2959, 2928, 1734, 1451, 1236, 1108, 1039, 708 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.08 t (3H, *J* = 7.2 Hz), 1.40 d (3H, *J* = 6.9 Hz), 1.60 s (3H), 182 s (3H), 2.15 s (3H), 2.20 m (2H), 2.85 m (1H), 6.93 m (2H), 7.07 m (1H), 7.21 m (1H), 7.34 m (1H), 7.36 m (2H), 7.52 m (2H), for other signals, see Table 1; EIMS *m*/*z* 737([M^+ − 15], 1), 692 (1), 650 (1), 632 (4), 590 (1), 446 (1), 202 (17), 105 (100), 77 (11), 57 (20); HREIMS *m*/*z* 737.2784 [M^+ − 15] (calcd for C_{39} H_{45} O_{14}, 737.28 09).

(1*R*,2*S*,4*S*,5*S*,6*R*,7*R*,8*S*,9*S*,10*S*)-8-acetoxy-1,9-dibenzoyloxy-15-(2)-methylbutyroyloxy-2,4,6-trihydroxy-dihydro-*β*-agarofuran (2): colorless oil; $[\alpha]^{25}_D$ + 5.2 ° (*c* 1.49, $CHCl_3$); UV (ETOH) λ_{max} 274.4, 260.4, 229.6, 212 nm; IR ν_{max} 3450, 2950, 2900, 1710, 1725, 1590, 1440, 750, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.04 t (3H, *J* = 7.4 Hz), 1.32 d (3H, *J* = 8.0), 1.73 s (3H), 1.89 m (2H), 2.16 m (2H), 2.65 m (1H), 4.23 s (1H), 5.36 d (1H, *J* = 4.9 Hz), 7.12 m (2H), 7.22 m (2H), 7.38 m (2H), 7.64 m (2H), for other signals, see Table 1; ^{13}C NMR ($CDCl_3$) δ OAc [20.7 (CH_3) 169.9 ($-CO_2-$)], OBz [127.8, 128.7, 129.2 (2 × C), 129.2, 129.3 (each 2 × CH, 132.8, 132.9 (2 × CH) 165.0, 165.4 (each 2 × $-CO_2-$)], OMeBut [11.5 (CH_3), 16.9 (CH_3), 26.6 (CH_2), 41.7 (CH), 176.2 ($-CO_2-$)], for other signals, see Table 2; EIMS *m*/*z* 669 [M^+ + 1], 1), 653 (1), 608 (2), 546 (1), 528 (1), 468 (1), 202 (4), 105 (100), 85 (10), 43 (18); HREIMS *m*/*z* 669.2928 [M^+ + 1] calcd for C_{36} H_{45} O_{12}, 669.2911).

Acetylation of 2. Ac_2O (4 drops) was added to compound **2** (3 mg), dissolved in pyridine (2 drops), and the mixture left at room temperature for 16 h, EtOH (3 × 2.0 mL) was added and carried almost to dryness in a rotavapor, and this process was repeated with $CHCl_3$ (3 × 2.0 mL), to give product **7** (3 mg).

1α-acetoxy-9α-benzoyloxy-8*β*,15-di-(2)-methylbutyroyloxy-2α,4*β*,6*β*-trihydroxy-dihydro-*β*-agarofuran (3): colorless oil; $[\alpha]^{25}_D$ + 14.1°(*c* 3.4, $CHCl_3$); UV (EtOH) λ_{max} 279.6, 260.8, 231.0 nm; IR ν_{max} 3450, 2925, 2875, 1742, 1735, 1710, 1596, 1450, 1094, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 t (3H, *J* = 7.4 Hz), 0.87 d (3H, *J* = 7.0 Hz), 0.95 t (3H, *J* = 7.4 Hz), 1.28 d (3H, *J* = 6.8 Hz), 1.47 m (2H), 1.62 s (3H), 1.82 m (2H), 2.03 m (2H), 2.21 m (1H), 2.82 m (1H), 3.09 s (1H), 5.25 d (1 H, *J* = 4.9 Hz), 7.40 m (2H), 7.54 m (1H), 7.89 m (2H); for other signals, see Table 1; ^{13}C NMR ($CDCl_3$) δ OAc [20.9 (CH_3) 169.7 ($-CO_2-$)], OBz [128.6, 129.5 (each 2 × CH), 129.5 (C), 133.4 (CH), 165.8 ($-CO_2-$)], OMeBut [11.1, 11.7 (2 × CH_3), 16.1, 17.0 (2 × CH_3), 26.3, 26.6 (2 × CH_2), 41.2, 41.7 (2 × CH), 175.2, 176.2 (2 × $-CO_2-$)]; for other signals, see Table 2; EIMS *m*/*z* 648 ([M^+], 1), 633 (5), 546 (22), 528 (4), 364 (4), 322 (5), 262 (7), 202 (12), 106 (8), 105 (100), 85 (24), 43 (31); HREIMS *m*/*z* 648.3141 [M^+] (calcd for C_{34} H_{48} O_{12}, 648.3146)

Benzoylation of 3. Compound **3** (10 mg) was dissolved in dry pyridine (0.5 mL) and benzoyl chloride (6 drops), and some crystals of 4-(dimethylamino)-pyridine were added under argon atmosphere. The mixture was heated at 60 °C for 15 h, poured over H_2O, extracted with EtOAc, and purified on Si gel with a mixture of *n*-hexane−EtOAc (7:3), to give compounds **8** (3.5 mg, R_f = 0.47) and **9** (4.6 mg, R_f = 0.52).

1α-acetoxy-6*β*,9α-dibenzoyloxy-8*β*,15-di-(2)-methylbutyroyloxy-2α,4*β*-dihydroxy-dihydro-*β*-agarofuran (8): colorless oil; $[\alpha]^{25}_D$ + 31.7° (*c* 0.34, $CHCl_3$); UV (EtOH) λ_{max} 273.0, 260.0, 230.0 nm; IR ν_{max} 3500, 2926, 2840, 1728, 1603, 1453, 1376, 1027, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 t (3H, *J* = 7.6 Hz), 0.95 d (3H, *J* = 7.0 Hz), 1.02 t (3H, *J* = 7.5 Hz), 1.40 d (3H, *J* = 7.0 Hz), 1.59 s (3H), 1.74 m (2H), 1.92 m (2H), 2.10 m (2H), 2.22 m (1H), 2.82 m (1H), 7.42−7.63 m (4H), 7.95 m (2H), 8.1 m (2H), 8.22 m (2H), for other signals, see Table 1; EIMS *m*/*z* 737 ([M^+ − 15], 1), 692 (1), 612 (1), 572 (6), 468 (1), 366 (1), 346 (1), 336 (3), 289 (2), 248 (2), 244 (4), 207 (4), 164 (5), 105 (100), 85 (12); HREIMS *m*/*z* 737.3171 [M^+ − 15] (calcd for C_{40} H_{49} O_{13}, 737.3173).

1α-acetoxy-2α,6*β*,9α-tribenzoyloxy-8*β*,15-di-(2)-methylbutyroyloxy-4*β*-hydroxy-dihydro-*β*-agarofuran (9): colorless oil; $[\alpha]^{25}_D$ + 50.5° (*c* 0.4, $CHCl_3$); UV (EtOH) λ_{max} 279.5, 260.5, 231.0 nm; IR ν_{max} 3560, 2926, 2840, 1727, 1602, 1453, 1376, 1105, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 t (3H, *J* = 7.2 Hz), 0.97 d (3H, *J* = 6.7 Hz), 1.05 t (3H, *J* = 7.3 Hz), 1.43 (3H, *J* = 6.9 Hz), 1.61 s (3H), 1.73 m (2H), 1.98 m (2H), 2.22 m

(2H), 2.26 m (1H), 2.88 m (1H), 3.01 s (1H), 7.38−760 m (9H), 7.91 m (2H), 8.12 m (2H), 8.20 m (2H); for other signals, see Table 1; EIMS *m/z* 841 ([M^+ − 15], 5), 827 (3), 754 (14), 734 (11), 612 (25), 598 (18), 336 (35), 244 (9), 202 (11), 105 (100), 85 (12).

Acetylation of 3. Ac_2O (4 drops) was added to compound **3** (3 mg), dissolved in pyridine (2 drops), and the mixture left at room temperature for 16 h. EtOH (3 × 2.0 mL) was added and carried almost to dryness in a rotavapor, and this process was repeated with $CHCl_3$ (3 × 2.0 mL), to give product **10** (3 mg).

1α,2α,6β-triacetoxy-9α-benzoyloxy-8β,15-di-(2)-methylbutyroyloxy-4β-hydroxy-dihydro-β-agarofuran (10): colorless oil; $[\alpha]^{25}_D$ + 10.4° (*c* 0.24, $CHCl_3$); UV (EtOH) λ_{max} 279.5, 261.0, 230.0 nm; IR ν_{max} 3563, 2925, 1746, 1602, 1454, 1229, 1094, 712 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.57 t (3H, *J* = 7.6 Hz), 0.95 d (3H, *J* = 6.5 Hz), 1.03 t (3H, *J* = 7.2 Hz), 1.37 d (3H, *J* = 6.9 Hz), 1.54 s (3H), 1.86 m (2H), 1.93 m (4H), 2.11 s (3H), 2.14 s (3H), 2.18 m (1H), 2.80 m (1H), 7.40 m (2H), 7.53 m (1H), 7.90 m (2H), for other signals, see Table 1; EIMS *m/z* 717 ([M^+ − 15], 2), 672 (2), 630 (4), 612 (5), 588 (3), 471 (3), 336 (12), 318 (24), 237 (14), 213 (24), 202 (37), 186 (46), 105 (100), 85 (29); HREIMS *m/z* 717.3118 [M^+ − 15] (calcd for C_{37} H_{49} O_{14}, 717.3122).

1α,6β-diacetoxy-9α-benzoyloxy-8β,15-di-(2)-methylbutyroyloxy-2α,4β-dihydroxy-dihydro-β-agarofuran (4): colorless oil; $[\alpha]^{25}_D$ + 11.9° (*c* 0.41, $CHCl_3$); UV (EtOH) λ_{max} 274.2, 260.0, 230.6 nm; IR ν_{max} 3450, 2890, 1725, 1710, 1450, 1355, 1260, 1030, 705 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 t (3H, *J* = 7.5 Hz), 0.94 d (3H, *J* = 6.9 Hz), 0.99 t (3H, *J* = 7.2 Hz), 1.35 d (3H, *J* = 6.9 Hz), 1.43 m (2H), 1.56 s (3H), 1.83 m (2H), 2.13 s (3H), 2.17 m (2H), 2.21 m (1H), 2.77 m (1H), 7.40 m (2H), 7.56 m (1H), 7.93 m (2H); for other signals, see Table 1; ^{13}C NMR ($CDCl_3$) δ OAc [20.9, 21.4 (2 × CH_3) 169.4, 169.6 (2 × $-CO_2-$)], OBz [128.6, 129.6 (each 2 × CH), 129.5 (C), 133.4 (CH), 165.8 ($-CO_2-$)], OMeBut [11.1, 11.6 (2 × CH_3), 16.1, 16.5 (2 × CH_3), 26.2, 26.6 (2 × CH_2), 41.1, 41.4 (2 × CH), 175.1, 176.4 (2 × $-CO_2-$)], for other signals, see Table 2; EIMS *m/z* 690 ([M^+], 1), 675 (6), 630 (10), 612 (11), 510 (14), 336 (12), 202 (25), 105 (100), 85 (23), 57 (46); HREIMS *m/z* 690.3225 [M^+] (calcd for C_{36} H_{50} O_{13}, 690.3251).

Acetylation of 4. Compound **4** (3 mg) was treated under the same conditions as described above, to give **10** (3 mg).

1α,2-diacetoxy-9α-benzoyloxy-8β,15-di-(2)-methylbutyroyloxy-4β,6β-dihydroxy-dihydro-β-agarofuran (5): colorless oil; $[\alpha]^{25}_D$ + 40° (*c* 0.15, $CHCl_3$); UV (EtOH) λ_{max} 273.8, 260.2, 231.8 nm; IR ν_{max} 3405, 2968, 2934, 1736, 1452, 1368, 1275, 1031, 710 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.58 t (3H, *J* = 7.4 Hz), 0.94 d (3H, *J* = 7.0 Hz), 1.03 t (3H, *J* = 7.4 Hz), 1.33 d (3H, *J* = 7.0 Hz), 1.54 s (3H), 1.64 m (2H), 1.88 m (2H), 2.02 m (2H), 2.11 s (3H), 2.23 m (1H), 2.66 m (1H), 3.10 s (1H), 5.20 d (1H, *J* = 5.1 Hz), 7.40 m (2H), 7.56 m (1H), 7.88 m (2H), for other signals, see Table 1; ^{13}C NMR ($CDCl_3$) δ OAc [20.4, 21.1 (2 × CH_3), 169.4, 169.5 (2 × $-CO_2-$)], OBz [128.5, 129.4 (each 2 × CH), 129.4 (C), 133.3 (CH), 165.6 ($-CO_2-$)], OMeBut [11.1, 11.6 (2 × CH_3), 16.1, 16.8 (2 × CH_3), 26.2, 26.6 (2 × CH_2), 41.1, 41.2 (2 × CH), 175.2, 176.1 (2 × $-CO_2-$)], for other signals, see Table 2; EIMS *m/z* 675 ([M^+ − 15], 3), 612 (2), 588 (5), 528 (1), 471 (2), 451 (3), 202 (11), 105 (100), 85 (19), 57 (38); HREIMS *m/z* 675.2999 [M^+ − 15] (calcd for C_{35} H_{47} O_{13}, 675.3017).

Acetylation of 5. Compound **5** (6 mg) was treated under the same conditions as described above, to give **10** (5.5 mg).

Insect Bioassays. The study of the antifeedant activity of the sesquiterpenes against the Egyptian cotton leafworm *S. littoralis* was performed using the leaf disk method.[4]

Acknowledgment. One of us (R. M.) thanks Intercampus Program. This work has been supported by DGES (Project PB96-1039 and PB96-1033), M. E. C. (Spain), Gobierno Autónomo de Canarias (Project CAC 246/125/96), and Instituto Tecnológico de Canarias. We thank Prof. M. Gupta for plant collection and classification, Prof. J. T. Vázquez for carrying out the CD measurements, and Prof. J. Coll for insect bioassays.

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NP980229G