183. The Terpenoids of *Maytenus boaria* MOL. (Celastraceae)

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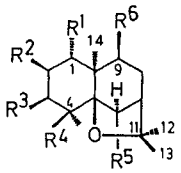
The known triterpenoids β-amyrin (= olean-12-en-3β-ol; **22**), lupeol (= lup-20(29)-en-3β-ol; **17**), betulin (= lup-20(29)-ene-3β,28-diol; **18**), lup-20(29)-ene-3β,30-diol (**20**), oleanolic acid (= 3β-hydroxyolean-12-en-28-oic acid; **21**), and betulonic acid (= 3-oxolup-20(29)-en-28-oic acid; **19**), together with epicatechol (= *cis*-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2*H*-1-benzopyran-3,5,7-triol; **23**), 5′-*O*-methylgallocatechol (= *trans*-2-(3,4-dihydroxy-5-methoxyphenyl)-3,4-dihydro-2*H*-1-benzopyran-3,5,7-triol; **24**), and 4-hydroxybenzaldehyde were isolated from the aerial parts of *Maytenus boaria* (MOL.). Additonally, the eight 4,C^4-dihydro-β-agarofuran sesquiterpenoids **1**–**8**, one of them a diol with a (4*R*)-configuration, and compound **9** were present in the extract. The structures of these compounds were established by spectroscopic and chemical means.

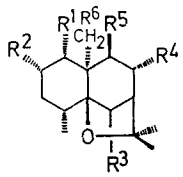
Introduction. – The sesquiterpene esters of the polyhydroxy-4,C^4-dihydro-β-agarofuran type (β-agarofuran = octahydro-2,2,5a-trimethyl-9-methylidene-2*H*-3,9a-methano-1-benzoxepin) are typical constituents of the Celastraceae family [1–3]. Some of these compounds exhibit insecticidal and/or antifeedant activity [4] [5], and several triterpenoids and triterpene quinones isolated from Celastraceae species show antitumor activity [6]. As part of a research program on the secondary metabolites from species of the Celastraceae used in Chilean folk medicine [7–10], we now report the results of a chemical study of the aerial parts of *Maytenus boaria* (MOL.) ('maitén'). This species is abundant in Chile and Argentina where it is used in the treatment of skin diseases and as an antifever agent [11] [12]. Although the use of *M. boaria* as a natural insecticide was not reported, we describe the results of preliminary bioassays done with the sesquiterpenes isolated in this study on *Spodoptera littoralis* larvae.

Previous studies on this species resulted in the isolation and chemical characterization of diterpenes, hydrocarbons [13] [14], sesquiterpenes [15], tannins and flavonoids [16]. The antiinflammatory and antipyretic effects of this plant were recently demonstrated [17].

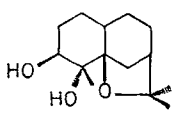
Results and Discussion. – The sesquiterpenes **1**–**8**, compound **9** as well as the triterpenoids **17**–**22** and the catechols **23** and **24** (see *Exper. Part*) were isolated from the aerial parts of *M. boaria* (MOL.). The sesquiterpenes **1**–**5** have the basic polyhydroxylated skeleton of magellanol (**10**), a new sesquiterpene skeleton recently described by us [18]. On the other hand, compounds **6** and **7** belong to the 9-epialatol and alatol-8-one, series, respectively [9] [19]. Of compounds **1**–**9**, all except boariol (**9**) showed in their mass



	R^1	R^2	R^3	R^4	R^5	R^6
1	OBz	OAc	OH	H	OAc	OBz
2	OBz	OAc	OH	OH	OAc	OBz
3	OBz	OH	OAc	OH	OAc	OBz
4	OBz	OAc	OH	OH	H	OBz
5	OBz	OAc	OAc	OH	OAc	OBz
10	OH	OH	OH	OH	OH	OH
11	OH	OH	OH	OH	OH	OBz
12	OH	OH	OH	OH	H	OBz
13	OBz	OH	OH	OH	H	OBz



	R^1	R^2	R^3	R^4	R^5	R^6
6	OAc	OAc	OAc	OAc	OBz	OH
7	OAc	OAc	OAc	=O	OBz	OH
8	OAc	OAc	OAc	OAc	OBz	OAc
14	OH	OH	OAc	OH	OBz	OH
15	OH	OAc	OH	OH	OBz	OH
16	OH	OH	OAc	OH	OH	OH



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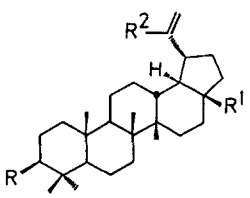
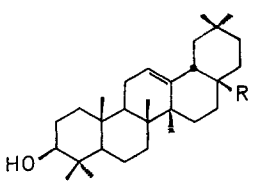
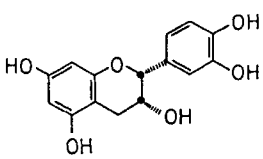


17 R = OH, R^1 = Me, R^2 = Me
18 R = OH, R^1 = CH_2OH, R^2 = Me
19 R = O, R^1 = COOH, R^2 = Me
20 R = OH, R^1 = Me, R^2 = OH



21 R = CO_2H
22 R = Me



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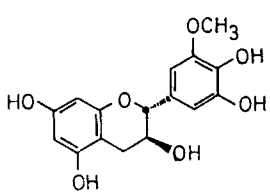

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spectra characteristic fragments at m/z 105, $[M-60]^+$, and $[M-42]^+$, suggesting the presence of benzoate and acetate esters in their structures. These groups were further confirmed by ^{13}C- and ^1H-NMR spectral data (see *Exper. Part*).

The structure of magellanol (**10**), with a dihydro-β-agarofuran (= 5,11-epoxy-5β,10α-eudesm-4(15)-ene) skeleton and 1α-, 2β-, 4β-, 6β-, and 9β-substituents, was extensively discussed and documented [18] and is based on ^1H,^{13}C heteronuclear correlation (HETCOR), long-range correlation spectra with inverse detection (HMBC), and NOE experiments. The structures of the sesquiterpenes **1**–**5** correspond to that of the parent model **10**, as shown by their spectra and chemical transformations.

Thus, **2** shows ^{1}H- and ^{13}C-NMR signals of 10 aromatic protons (δ 7.96–7.93), 2 AcO groups (δ 2.16 and 1.83 ppm), and 14 C-atoms of benzoate groups. The COSY spectrum confirmed that the substitution pattern was similar to that reported for **10**, H–C(1), H–C(2), and H–C(3) giving rise to an *ABX* system at 6.25 (*d*, J = 11.3 Hz), 5.32 ('*dd*', J = 11.3 and 2.5 Hz), and 3.77 ppm ('*d*', J = 2.5 Hz), respectively, only possible for a 1α,2β,3β-substitution in a dihydro-β-agarofuran skeleton.

When **2** was acetylated under the usual conditions, it afforded **5**, whose IR spectrum had bands arising from a tertiary OH group. In the ^{1}H-NMR spectrum of **5**, the signal of **2** at 3.77 ppm had moved to 5.88 ppm. Hydrolysis of **2** with 0.1M $NaHCO_3$ produced **11**, esterified at C(9). Analysis of its spectroscopic data (*Exper. Part*) identified it as a monobenzoate. Compound **2** is identical to a natural product previously isolated from *M. magellanica* [9].

Compound **3** had the same empirical formula as **2**, and its ^{1}H-NMR spectrum suggested it to be a positional isomer. Acetylation of **3** under the usual conditions afforded the same product **5** as previously obtained from **2**. This correlation established the structure and absolute configuration of **3** as (1*R*,2*S*,3*S*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-4,C^4-dihydro-2,4-dihydroxy-β-agarofuran-1,3,6,9-tetrayl 3,6-diacetate 1,9-dibenzoate.

The ^{1}H-NMR spectrum of compound **4** was almost superimposable with that of **2**, differing only in the signal assigned to H–C(6) and the absence of an Ac signal. Comparison of the mass spectra of **4** and **2** confirmed that **4** was the 6-deacetoxy derivative of **2**. When **4** was hydrolysed (0.1M $NaHCO_3$), it afforded **12** and **13**. This last product was identical to that previously obtained from *Salvia palaefolia*, whose absolute configuration is known. Therefore, **4** is (1*R*,2*S*,3*S*,4*S*,5*R*,7*R*,9*S*,10*R*)-4,C^4-dihydro-3,4-dihydroxy-β-agarofuran-1,2,9-triyl 2-acetate 1,9-dibenzoate.

A comparison of the ^{1}H-NMR spectral data led us to propose for **1** the structure of a 4-deoxy derivative of **2**. (Signal of secondary Me(15) at δ 1.19 (*d*, J = 7.6 Hz) and complex additional signal for H_α–C(3) at δ 4.0 (1 H, *t*), due to coupling with the equatorial H_β–C(4). The absolute configuration of **1** was previously established (for the tribenzoate derivative) as (1*R*,2*R*,3*R*,4*R*,5*S*,6*R*,7*R*,9*S*,10*R*)-4,C^4-dihydro-3-hydroxy-β-agarofuran-1,2,6,9-tetrayl 2,6-diacetate 1,9-dibenzoate [19].

Compounds **6** and **7** were previously obtained from *M. chubutensis* (SPEG) [7] [9] [19]. Hydrolysis of **6** in EtOH with 0.1M $NaHCO_3$ afforded **14**–**16** (see *Exper. Part*).

Boariol (**9**; $C_{15}H_{26}O_3$), finally, is a crystalline compound, and at present is the simplest sesquiterpenoid obtained from a Celastraceae species. The study of its ^{1}H- and ^{13}C-NMR spectra showed the presence of a secondary and a tertiary OH group, possibly at C(4). The ambiguity in the structure of **9** was clarified by X-ray analysis [20], and the absolute configuration was established by *Horeau*'s method [21]. The location of the OH groups (3β and 4α) and the lack of substituents at C(1) are the most relevant features of this new structure.

The results of the antifeeding assays performed with compounds **1**–**6**, **8**, and **9** are shown in the *Table*. All of them were active at a dose of 10 $\mu g/cm^2$, **6** and **8** being the most actives. It is difficult to compare these results with those reported in the literature for other compounds, where different bioassays were used [22]. However, triphenyltin acetate was tested under similar conditions, displaying a FR_{50} = 0.37 at a dose of 10 $\mu g/cm^2$ [23]. It is then possible to conclude that four of the compounds tested are more active than triphenyltin acetate, a product used as a standard in antifeeding studies.

Table. *Feeding Ratios of Test Compounds*[a])

	Dose [μg/cm²]	FR_{50} ± s.e.m.[b])		Dose [μg/cm²]	FR_{50} ± s.e.m.[b])
2	10	0.24 ± 0.19	**1**	10	0.63 ± 0.11
4	10	0.33 ± 0.13	**3**	10	0.56 ± 0.11
6	10	0.13 ± 0.05	**5**	10	0.65 ± 0.15
9	10	0.52 ± 0.10	**8**	10	0.13 ± 0.05

a) All assays were carried out five times under the same conditions.

b) $FR_{50} = A_{50}/B_{50}$; A_{50} = area of the test disk and B_{50} = area of the control disk, when the latter was eaten to 50%.

The data of the *Table* do not allow to establish conclusively that the sesquiterpenes isolated from *M. boaria* are feeding deterrents. Structurally related sesquiterpenes also showed moderate antifeeding properties against *S. littoralis* [23].

We thank Dr. *J. Coll*, and Dr. *X. Bellés*, *C.S.I.S.*, Barcelona, Spain, for the antifeeding bioassays.

Experimental Part

1. *General.* TLC: silica gel *60 F_{254}* Al sheets (*Merck*). Flash chromatography (FC): *Merck LiChroprep Si 60*, 25–40 μm. Optical rotations: *241-Perkin-Elmer* automatic polarimeter. M.p.: *Kofler* hot stage with polarizing filters; uncorrected. UV Spectra: *Perkin-Elmer-550-SE* spectrophotometer; $\lambda_{max}(\log\varepsilon)$ in nm. CD Spectra: *Jasco-J-600* spectropolarimeter; $\lambda_{ext}(\Delta\varepsilon)$ in nm. IR Spectra: KBr pellets, $CHCl_3$ films; *Perkin Elmer 700*; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra ($CDCl_3$): *Bruker-SY-200* spectrometer; chemical shifts δ in ppm rel. to Me_4Si, J in Hz. Mass spectra (MS): 70 eV; *VG-Micromass-LTD-ZAB-2F* spectrometer; in *m/z* (rel. %).

2. *Plant Material. Maytenus boaria* (MOL.) was collected in January 1987 at Parque Nacional V. Perez Rosales (IX Region), Chile, and a voucher specimen is kept at the Chemistry Department, Faculty of Science.

3. *Extraction and Separation.* Aerial parts (3.5 kg), dry and grounded, were treated with hexane and then EtOH, both at r.t., and processed as previously described [6] [8]. Repeated column chromatography on silica gel using hexane, $CHCl_3$/MeOH, and MeOH allowed the isolation of compounds **1**–**9** and **17**–**24**.

3.1. *(1R,2R,3R,4R,5S,6R,7R,9S,10R)-4,C⁴-Dihydro-3-hydroxy-β-agarofuran-1,2,6,9-tetrayl 2,6-Diacetate 1,9-Dibenzoate* (= *Octahydro-8-hydroxy-2,2,5a,9-tetramethyl-2H-3,9a-methano-1-benzoxepin-5,6,7,10-tetrayl 7,10-Diacetate 5,6-Dibenzoate*; **1**). White amorphous powder. M.p. 175–179° (AcOEt/cyclohexane). $[\alpha]_D^{20} = +71.0$ ($c = 0.12$, MeOH). UV (EtOH): 204, 234, 276. IR ($CHCl_3$): 3520, 3480, 3010, 2950, 2910, 1750, 1740, 1720, 1600, 1400, 1370, 1270, 1240, 1110, 1050. ^1H-NMR ($CDCl_3$): 1.19 (*d*, $J = 7.6$, 3 H); 1.46 (*s*, 3 H); 1.48 (*s*, 3 H); 1.57 (*s*, 3 H); 1.86 (*s*, 3 H); 2.15 (*s*, 3 H); 2.24 (*m*, 1 H); 2.42 (*m*, 1 H); 4.00 (*t*, 1 H); 5.01 (*d*, $J = 6.4$, 1 H); 5.36 (*dd*, $J = 2.6$, 11.0, 1 H); 5.44 (*s*, 1 H); 6.36 (*d*, $J = 11.0$, 1 H); 7.22–8.00 (*m*, 10 H). ^{13}C-NMR ($CDCl_3$): 69.02 (C(1)); 71.42 (C(2)); 73.70 (C(3)); 41.61 (C(4)); 91.45 (C(5)); 79.87 (C(6)); 48.11 (C(7)); 32.10 (C(8)); 73.33 (C(9)); 53.38 (C(10)); 85.59 (C(11)); 30.65 (C(12)); 26.34 (C(13)); 20.22 (C(14)); 16.22 (C(15)). MS: 579 (6, $[M - Me]^+$), 552 (19), 519 (3), 472 (2), 457 (3), 416 (10), 397 (2), 352 (2), 248 (5), 105 (100). HR-MS: 579.2236 ($[M - Me]^+$, calc. for $C_{32}H_{35}O_{10}$ 579.2243).

3.2. *(1R,2S,3S,4S,5S,6R,7R,9S,10R)-4,C⁴-Dihydro-3,4-dihydroxy-β-agarofuran-1,2,6,9-tetrayl 2,6-Diacetate 1,9-Dibenzoate* (= *Octahydro-8,9-dihydroxy-2,2,5a,9-tetramethyl-2H-3,9a-methano-1-benzoxepin-5,6,7,10-tetrayl 7,10-Diacetate 5,6-Dibenzoate* **2**). White powder. M.p. 114–116°. $[\alpha]_D^{20} = +180$ ($c = 0.11$, MeOH). UV (EtOH): 200, 230, 272. IR ($CHCl_3$): 3500, 3490, 3000, 2950, 1730, 1720, 1450, 1360, 1280, 1240, 1100. ^1H-NMR ($CDCl_3$): 1.49 (*s*, 6 H); 1.57 (*s*, 3 H); 1.61 (*s*, 3 H); 1.83 (*s*, 3 H); 2.16 (*s*, 3 H); 2.20 (*m*, 1 H); 2.45 (*m*, 1 H); 3.77 (*d*, $J = 2.5$, 1 H); 5.01 (*d*, $J = 6.4$, 1 H); 5.32 (*dd*, $J = 2.5$, 11.3, 1 H); 5.59 (*s*, 1 H); 6.25 (*d*, $J = 11.3$, 1 H); 7.23–7.96 (*m*, 10 H). ^{13}C-NMR ($CDCl_3$): 67.91 (C(1)); 70.51 (C(2)); 77.84 (C(3)); 71.33 (C(4)); 92.63 (C(5)); 80.21 (C(6)); 48.28 (C(7)); 31.66 (C(8)); 73.04 (C(9)); 51.85 (C(10)); 86.32 (C(11)); 29.57 (C(12)); 26.00 (C(13)); 20.87 (C(14)); 24.18 (C(15)). MS: 550 (1, $[M - AcOH]^+$), 490 (1), 446 (1), 428 (1), 410 (2), 386 (1), 368 (1), 325 (1), 306 (2), 105 (100). HR-MS: 610.2407 (calc. for $C_{33}H_{38}O_{11}$ 610.2401).

Acetylation of **2** (8 mg) under the usual conditions [7] afforded a product whose spectral data were identical to those of **5** (see below).

Hydrolysis of **2**: To a soln. of **2** (25 mg) in MeOH (5 ml), 0.11M $NaHCO_3$ (2 ml) was added and the mixture heated (60°, 3 h) with constant stirring. After extraction in the usual way, the product was purified by prep. TLC (silica gel, petroleum ether/AcOEt 1:3).

4,C⁴-Dihydro-1α,2β,3β,4β,6β-pentahydroxy-β-agarofuran-9β-yl Benzoate (= *Octahydro-6,7,8,9,10-pentahydroxy-2,2,5a-9-tetramethyl-2*H*-3,9a-methano-1-benzoxepin-5-yl Benzoate*; **11**). Oil. ^{1}H-NMR ($CDCl_3$ + D_2O): 1.28 (*s*, 3 H); 1.55 (*s*, 3 H); 1.58 (*s*, 3 H); 1.62 (*s*, 3 H); 2.19 (*m*, 1 H, partially overlapped with H at 2.20); 2.30 (*m*, overlapped signals, 1 H); 3.60 (overlapped signals, 2 H); 4.20 (*d*, *J* = 10.0, 1 H); 4.52 (*s*, 1 H); 5.10 (*d*, *J* = 6.5, 1 H); 7.51 (*m*, 3 H); 8.03 (*m*, 2 H). MS: 407 (42, $[M - Me]^+$), 389 (19), 371 (1), 317 (1), 300 (1), 285 (9), 267 (6), 249 (9), 105 (100).

3.3. *(1*R*,2*S*,3*S*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-4,C⁴-Dihydro-2,4-dihydroxy-β-agarofuran-1,3,6,9-tetrayl 3,6-Diacetate 1,9-Dibenzoate* (= *Octahydro-7,9-dihydroxy-2,2,5a,9-tetramethyl-2*H*-3,9a-methano-1-benzoxepin-5,6,8,10-tetrayl 8,10-Diacetate 5,6-Dibenzoate*; **3**). Pale yellow glass. $[\alpha]_D^{20}$ = +47.3 (*c* = 0.11, $CHCl_3$). UV (EtOH): 230, 278, 288. IR ($CHCl_3$): 3532, 3025, 2958, 2924, 2857, 1733, 1446, 1370, 1286, 1243, 1015. ^{1}H-NMR ($CDCl_3$ + D_2O): 1.47 (*s*, 6 H); 1.54 (*s*, 3 H); 1.56 (*s*, 3 H); 2.13 (*s*, 3 H); 2.29 (*m*, 1 H); 2.33 (*s*, 3 H); 2.48 (*m*, 1 H); 4.03 (*dd*, *J* = 3.2, 11.2, 1 H); 5.04 (*d*, *J* = 6.6, 1 H); 5.23 (*d*, *J* = 3.2, 1 H); 5.54 (*s*, 1 H); 6.00 (*d*, *J* = 11.2, 1 H); 7.21–7.77 (*m*, 1 OH). MS: 610 (1, M^+), 595 (2), 577 (3), 550 (5), 532 (2), 473 (2), 428 (5), 410 (2), 386 (2), 249 (2), 105 (100). HR-MS: 610.2390 (calc. for $C_{33}H_{38}O_{11}$ 610.2367).

Acetylation of **3** (2 mg) under usual conditions (r.t., 24 h) gave, after purification by prep. TLC, 1.5 mg of a product whose spectral and physical properties were identical to those of **5** (see below).

3.4. *(1*R*,2*S*,3*S*,4*S*,5*R*,7*R*,9*S*,10*R*)-4,C⁴-Dihydro-3,4-dihydroxy-β-agarofuran 1,2,9-triyl 2-Acetate 1,9-Dibenzoate* (= *Octahydro-8,9-dihydroxy-2,2,5a-9-tetramethyl-2*H*-3,9a methano-1-benzoxepin-5,6,7-triyl 7-Acetate 5,6-Dibenzoate*; **4**). Colourless oil. $[\alpha]_D^{20}$ = +71.81 (*c* = 0.19, $CHCl_3$). UV (EtOH): 197.224.277. IR ($CHCl_3$): 3500, 3450, 2980, 2910, 1740, 1710, 1590, 1450, 1370, 1368, 1310, 1270, 1120, 1110, 1020. ^{1}H-NMR ($CDCl_3$): 1.36 (*s*, 3 H); 1.44 (*s*, 3 H); 1.45 (*s*, 3 H); 1.51 (*s*, 3 H); 1.84 (*s*, 3 H); 3.42 (*s*, 1 H); 3.85 (*d*, *J* = 2.4, 1 H); 5.07 (*d*, *J* = 6.0, 1 H); 5.31 (*dd*, *J* = 2.4, 11.2, 1 H); 6.24 (*d*, *J* = 11.2, 1 H); 7.26–8.01 (*m*, 10 H). ^{13}C-NMR ($CDCl_3$): 68.20 (C(1)); 71.08 (C(2)); 77.79 (C(3)); 70.98 (C(4)); 92.14 (C(5)); 31.08 (C(6)); 42.46 (C(7)); 32.40 (C(8)); 73.67 (C(9)); 48.40 (C(10)); 85.64 (C(11)); 29.84 (C(12)); 24.53 (C(13)); 20.92 (C(14)); 23.95 (C(15)). MS: 552 (11, M^+), 537 (3), 492 (1), 477 (1), 430 (4), 388 (2), 370 (4), 355 (1), 266 (4), 248 (7), 105 (100). HR-MS: 552.2361 (calc. for $C_{31}H_{36}O_9$ 552.2363).

Hydrolysis of (**4**): A soln. of **4** (30 mg) in MeOH (5 ml) and 2 ml of 0.1M $NaHCO_3$ was heated (30°, 20 min) with constant stirring. After extraction in the usual way [19], prep. TLC (silica gel, petroleum ether/AcOEt 2:3) afforded **12** and **13**.

4,C⁴-Dihydro-1α,2β,3β,4β-tetrahydroxy-β-agarofuran-9β-yl Benzoate (= *Octahydro-6,7,8,9-tetrahydroxy-2,2,5a-9-tetramethyl-2*H*-3,9a-methano-1-benzoxepin-5-yl Benzoate*; **12**): Colourless oil. ^{1}H-NMR ($CDCl_3$): 1.21 (*s*, 3 H); 1.35 (*s*, 3 H); 1.49 (*s*, 3 H); 3.24 (*s*, 1 H); 3.64 (*m*, overlapped signals, 2 H); 5.17 (*d*, *J* = 4.8, 1 H); 7.52 (*m*, 3 H); 8.06 (*m*, 2 H). MS: 406 (3, M^+), 391 (55), 373 (15), 284 (4), 266 (14), 105 (100).

4,C⁴-Dihydro-2β,3β,4β-trihydroxy-β-agarofuran-1α,9β-diyl Dibenzoate (= *Octahydro-7,8,9-trihydroxy-2,2,5a,9-tetramethyl-2*H*-3,9a-methano-1-benzoxepin-5,6-diyl Dibenzoate*; **13**): Colourless oil. CD (MeCN): 236.5 (+21.1), 221.3 (−9.7). ^{1}H-NMR ($CDCl_3$): 1.25 (*s*, 3 H); 1.37 (*s*, 3 H); 1.45 (*s*, 3 H); 1.47 (*s*, 3 H); 3.33 (*s*, 1 H); 3.86 (*m*, overlapped signals, 2 H); 5.08 (*d*, *J* = 5.2, 1 H); 5.94 (*d*, *J* = 10.8, 1 H); 7.23–7.87 (*m*, 10 H). MS: 510 (3, M^+), 492 (5), 477 (12), 459 (1), 388 (7), 370 (3), 266 (4), 105 (100).

3.5. *(1*R*,2*S*,3*S*,4*S*,5*S*,6*R*,7*R*,9*S*,10*R*)-4,C⁴-Dihydro-4-hydroxy-β-agarofuran-1,2,3,6,9-pentayl 2,3,6-Triacetate 1,9-Dibenzoate* (= *Octahydro-9-hydroxy-2,2,5a,9-tetramethyl-2*H*-3,9a-methano-1-benzoxepin-5,6,7,8,10-pentayl 7,8,10-Triactate 5,6-Dibenzoate* **5**). Oil. $[\alpha]_D^{20}$ = +143.4 (*c* = 0.05, $CHCl_3$). UV (EtOH): 240, 474, 286. IR ($CHCl_3$): 3448, 3018, 2359, 2339, 2099, 1733, 1637, 1452, 1368, 1283, 1245, 1912, 1178. ^{1}H-NMR ($CDCl_3$): 1.49 (*s*, 3 H); 1.54 (*s*, 3 H); 1.55 (*s*, 3 H); 1.60 (*s*, 3 H); 1.74 (*s*, 3 H); 2.14 (*s*, 3 H); 2.31 (*s*, 3 H); 2.25 (*m*, 1 H); 2.45 (*m*, 1 H); 3.61 (*s*, 1 H); 5.03 (*d*, *J* = 6.1, 1 H); 5.18 (*d*, *J* = 2.8, 1 H); 5.28 (*dd*, *J* = 2.8, 11.2, 1 H); 5.57 (*s*, 1 H); 6.28 (*d*, *J* = 11.2, 1 H); 7.23–7.98 (*m*, 10 H). MS: 637 (1, $[M - Me]^+$), 592 (2), 550 (6), 515 (10), 470 (2), 455 (2), 428 (7), 410 (4), 368 (3), 105 (100). HR-MS: 637.2311 ($[M - Me]^+$, calc. for $C_{34}H_{37}O_{12}$ 637.2337).

3.6. *(1*R*,2*S*,4*R*,5*S*,6*R*,7*R*,8*R*,9*R*,10*S*)-4,C⁴-Dihydro-14-hydroxy-1,2,6,8,9-pentayl 1,2,6,8-Tetraacetate 9-Benzoate* (= *Octahydro-5a-(hydroxymethyl)-2,2,9-trimethyl-2*H*-3,9a-methano-1-benzoxepin-4,5,6,7,10-pentayl 4,6,7,10-Tetraacetate 5-Benzoate*; **6**). Oil. $[\alpha]_D^{20}$ = −20.6 (*c* = 1.79, $CHCl_3$). UV (EtOH): 234, 276, 285. ^{1}H-NMR ($CDCl_3$): 1.17 (*d*, *J* = 7.4, 3 H); 1.40 (*s*, 3 H); 1.51 (*s*, 3 H); 1.53 (*s*, 3 H); 1.82 (*dd*, *J* = 2.7, 15.0, 2 H); 2.07 (*s*, 3 H); 2.20 (*s*, 3 H); 2.52 (*d*, *J* = 2.9, 1 H); 3.98–4.74 (*AB*, *J* = 12.8, 2 H); 5.30 (*d*, *J* = 2.9, 1 H); 5.58 (*m*, 1 H); 5.73 (*d*, *J* = 3.7, 1 H); 5.89 (br. *s*, 2 H); 7.47 (*m*, 3 H); 8.00 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 73.76 (C(1)); 70.15 (C(2)); 31.20 (C(3)); 33.21 (C(4)); 89.78 (C(5)); 71.79 (C(6)); 53.70 (C(7)); 76.54 (C(8)); 75.25 (C(9)); 52.83 (C(10)); 81.95 (C(11)); 30.84 (C(12)); 25.95 (C(13)); 64.81 (C(14)); 17.69 (C(15)). MS: 590 (2, M^+), 584 (4), 530 (2), 515 (1), 488

(1), 470 (2), 468 (3), 426 (1), 423 (4), 348 (2), 288 (4), 237 (5), 105 (100). HR-MS: 590.2347 (calc. for $C_{30}H_{38}O_{12}$ 590.2332).

Acetylation of **6** (3 mg) in pyridine (4 drops) and Ac_2O (2 drops) at r.t. for 24 h gave **8** (see below), after the usual workup and prep. TLC (silica gel, petroleum ether/AcOEt 3:2).

Hydrolysis of **6**: A soln. of **6** (30 mg) in EtOH (3 ml) was heated with 0.1M $NaHCO_3$ (3 ml) at 50° for 45 min. The mixture was evaporated and extracted with AcOEt. The extract was then purified by prep. TLC (silica gel, C_6H_6/AcOEt 2:3) affording **14**–**16** separately and an additional mixture that could not be separated.

4,C⁴-Dihydro-1α,2α,8α,14-tetrahydro-β-agarofuran-6β,9β-diyl 6β-Acetate 9β-Benzoate (= *Octahydro-4,6,7-trihydroxy-5a-(hydroxymethyl)-2,2,9-trimethyl-2*H*-3,9a-methano-1-benzoxepin-5,10-diyl 10-Acetate 5-Benzoate*; **14**): Colourless oil. $[\alpha]_D^{20} = -20.5$ ($c = 0.83$, $CDCl_3$). ^{1}H-NMR ($CDCl_3$): 1.23 (*d*, $J = 7.4$, 3 H); 1.42 (*s*, 6 H); 1.90 (*dd*, $J = 2.7$, 15.0, 1 H); 2.09 (*s*, 3 H); 2.42 (*s*, 6 H); 1.90 (*dd*, $J = 2.7$, 15.0, 1 H); 2.09 (*s*, 3 H); 2.42 (*d*, $J = 2.9$, 1 H); 4.14–4.78 (*AB*, $J = 12.8$, 2 H); 4.22 (*m*, 1 H); 4.42 (*d*, $J = 2.9$, 1 H); 4.46 (*d*, $J = 3.7$, 1 H); 5.69 (*s*, 1 H); 5.90 (*s*, 1 H); 7.50 (*m*, 3 H); 8.00 (*m*, 2 H). MS: 446 (1, $[M - H_2O]^+$), 386 (3), 371 (1), 339 (3), 297 (5), 281 (3), 264 (7), 105 (100). HR-MS: 446.1921 ($[M - H_2O]^+$, calc. for $C_{24}H_{30}O_8$ 446.1902).

4,C⁴-Dihydro-1α,6β,8α,14-tetrahydroxy-β-agarofuran 12α-Acetate 9β-Benzoate (= *Octahydro-4,6,10-trihydroxy-5a-(hydroxymethyl)-2,2,9-trimethyl-2*H*,3,9a-methano-1-benzoxepin-5,7-diyl 7-Acetate 5-Benzoate*; **15**): Colourless oil. $[\alpha]_D^{20} = +1.8$ ($c = 1.0$, $CHCl_3$). ^{1}H-NMR ($CDCl_3$): 1.14 (*d*, $J = 7.4$, 3 H); 1.39 (*s*, 3 H); 1.56 (*s*, 3 H); 2.07 (*s*, 3 H); 2.37 (*d*, $J = 2.9$, 1 H); 4.10–4.80 (*AB*, $J = 12.8$, 2 H); 4.32 (*s*, 1 H); 4.52 (*d*, $J = 2.9$, 1 H); 4.69 (*d*, $J = 3.7$, 1 H); 5.65 (*m*, H); 5.80 (*s*, 1 H); 7.45 (*m*, 3 H); 8.08 (*m*, 2 H). MS: 446 (1, $[M - H_2O]^+$), 415 (3), 401 (1), 341 (1), 309 (2), 281 (7), 105 (100). HR-MS: 415.1749 ($[M - CH_2OH - H_2O]^+$, calc. for $C_{23}H_{37}O_7$ 415.1742).

4,C⁴-Dihydro-1α,2α,8α,9β,14-pentahydroxy-β-agarofuran-6β-yl Acetate (= *Octahydro-4,5,6,7-tetrahydroxy-5a-(hydroxymethyl)-2,2,9-trimethyl-2*H*-3,9a-methano-1-benzoxepin-10-yl 10-Acetate*; **16**). Colourless oil. ^{1}H-NMR ($CDCl_3$): 1.36 (*s*, 3 H); 1.51 (*s*, 3 H); 2.06 (*s*, 3 H); 2.25 (*d*, $J = 2.9$, 1 H); 4.00–4.64 (*AB*, $J = 11.5$, 2 H); 4.26 (overlapped signals, 2 H); 4.37 (*d*, $J = 2.9$, 1 H); 4.41 (*d*, $J = 3.7$, 1 H); 5.72 (*s*, 1 H). MS: 345 (5, $[M - 15]^+$), 318 (1), 313 (3), 311 (16), 300 (4), 285 (3), 283 (7), 255 (8). HR-MS: 345.1628 ($[M - 15]^+$, calc. for $C_{16}H_{25}O_8$ 345.1707).

3.7. *4,C⁴-Dihydro-4-hydroxy-8-oxo-β-agarofuran-1α,2α,6β,9α-tetrayl 1α,2α,6β-Triacetate 9α-Benzoate* (= *Octahydro-5a-(hydroxymethyl)-2,2,9-trimethyl-4-oxo-2*H*-3,9a-methano-1-benzoxepin-5,6,7,10-tetrayl 6,7,10-Triacetate 5-Benzoate*; **7**). Oil. $[\alpha]_D^{20} = +10.0$ ($c = 0.27$, $CHCl_3$). IR ($CHCl_3$): 2920, 1730, 1365, 1235, 1095, 710. ^{1}H-NMR ($CDCl_3$): 1.33 (*d*, $J = 7.5$, 3 H); 1.49 (*s*, 3 H); 1.51 (*s*, 3 H); 1.55 (*s*, 3 H); 2.06 (*s*, 3 H); 2.06 (*s*, 3 H); 2.14 (*s*, 3 H); 1.85 (*dd*, $J = 2.7$, 15.0, 1 H); 3.15 (*s*, 1 H); 4.50–4.28 (*AB*, $J = 12.3$, 2 H); 5.36 (*m*, 1 H). MS: 531 (1, $[M - 15]^+$), 504 (1), 458 (36), 444 (3), 416 (2), 413 (2), 383 (1), 338 (1), 279 (5), 105 (100). HR-MS: 546.2095 (calc. for $C_{28}H_{34}O_{11}$ 546.2089).

3.8. *4,C⁴-Dihydro-β-agarofuran-1α,2α,6β,8α,15,9β-hexayl 1α,2α,6β,8α,15-Pentaacetate 9β-Benzoate* (= *5a-(Acetoxymethyl)octahydro-2,2,9-trimethyl-2*H*-3,9a-methano-1-benzoxepin-4,5,6,7,10-pentayl 4,6,7,10-Tetraacetate 5-Benzoate*; **8**). Oil. M.p. 135–140° (AcOEt). $[\alpha]_D^{20} = +7.7$ ($c = 0.52$, $CHCl_3$). UV (EtOH): 234, 276, 287. IR ($CHCl_3$): 3000, 1730, 1365, 1275, 1240, 1095. ^{1}H-NMR: 1.16 (*d*, $J = 7.4$, 3 H); 1.43 (*s*, 3 H); 1.46 (*s*, 3 H); 1.56 (*s*, 3 H); 1.75 (*dd*, $J = 2.7$, 15.0, 2 H); 2.07 (*s*, 3 H); 2.10 (*s*, 3 H); 2.20 (*s*, 3 H); 2.26 (*s*, 3 H); 2.36 (*d*, $J = 2.9$, 1 H); 4.52–5.10 (*AB*, $J = 12.8$, 2 H); 5.27 (*d*, $J = 2.9$, 1 H); 5.51 (*s*, 1 H); 5.58 (*m*, 1 H); 5.70 (*d*, $J = 3.7$, 1 H); 6.38 (br. *s*, 1 H); 7.49 (*m*, 3 H); 8.00 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 74.11 (C(1)); 71.75 (C(2)); 31.18 (C(3)); 32.90 (C(4)); 89.91 (C(5)); 69.32 (C(6)); 53.27 (C(7)); 75.05 (C(8)); 77.16 (C(9)); 62.79 (C(10)); 81.63 (C(11)); 30.42 (C(12)); 25.92 (C(13)); 65.69 (C(14)); 17.05 (C(15)). MS: 632 (1, M^+), 617 (3), 590 (40), 572 (4), 548 (2), 530 (3), 512 (1), 497 (2), 488 (2), 470 (2), 437 (3), 408 (2), 348 (3), 306 (4), 288 (6), 105 (100). HR-MS: 632.2452 (calc. for $C_{32}H_{40}O_{13}$ 632.2436).

3.9. *Boariol* (= *Octahydro-2,2,9-trimethyl-2*H*-3,9a-methano-1-benzoxepin-8,9-diol*; **9**). Colourless crystals (25 mg). M.p. 146–147° (hexane/AcOEt). $[\alpha]_D^{25} = -39.3$ ($c = 0.6$, $CHCl_3$). IR (KBr): 3426, 3401, 2916, 2860, 1456, 1386, 1303, 1130, 1028, 874. ^{1}H-NMR ($CDCl_3$): 1.20 (*s*, 3 H); 1.28 (*s*, 3 H); 1.39 (*s*, 3 H); 1.40 (*s*, 3 H); 3.48 (*m*, 1 H); 3.87 (*d*, $J = 10.4$, 1 H, exchangeable with D_2O). ^{13}C-NMR ($CDCl_3$): 77.22 (C(3)); 75.00 (C(4)); 90.25 (C(5)); 44.16 (C(7)); 30.49 (C(10)); 84.64 (C(11)); 25.51 (C(1)); 25.83 (C(2)); 32.19 (C(6)); 33.22 (C(8)); 39.05 (C(9)); 23.49 (C(12)); 25.13 (C(13)); 30.65 (C(14)); 25.26 (C(15)). MS: 254 (3, M^+), 179 (100), 123 (70), 123 (70), 85 (50), 89 (60).

3.10. *Isolation of* **17**–**22**. *Lup-20(29)-en-3β-ol* (**17**; 0.12 g), *lup-20(29)-ene-3β,28-diol* (**18**; 0.288 g), *3-oxolup-20(29)-en-28-oic acid* (**19**; 0.045 g), *lup-20(29)-ene-3β,30-diol* (**20**; 0.021 g), *3β-hydroxyolean-12-en-28-oic acid* (**21**; 0.43 g), and *olean-12-en-3β-ol* (**22**; 0.40 g) were obtained by repeated column chromatography on silica gel in the fractions eluted with hexane and hexane/$CHCl_3$ mixtures. The identification of these products was achieved by transformation to the corresponding acetates and by comparison with authentic samples (IR, ^{1}H-NMR, MS) and with reported data [24] [26].

3.11. *Epicatechol* (= cis-*2-(3,4-Dihydroxyphenyl)-3,4-dihydro-2*H-*1-benzopyran-3,5,7-triol*; **23**) *and 5'-O-Methylgallocatechol* (= trans-*2-(3,4-dihydroxy-5-methoxyphenyl)-3,4-dihydro-2*H-*1-benzopyran-3,5,7-triol*; **24**) were isolated from the MeOH fraction of the column and were identified by comparison with authentic samples (IR, ^{1}H-NMR) [27].

4. *Antifeeding Bioassays.* The insects used for the assays were five-instar larvae of *Spodoptera littoralis* BOISDUVAL (Lepidoptera, Noctuidae) and the laboratory conditions of the colonies were 25 ± 2° with a rel. humidity between 60 and 70%, a photo period of 18 h, and a semiartificial diet [23].

The assays were carried out using a disc-election test with 1-cm^2 lettuce disks. The compounds tested were evenly distributed on the surface of the disks by application of 10 µl of a soln. of the compound in acetone. Control disks were also treated with acetone. In each test, 4 test and 4 control disks were placed alternately on a *Petri* dish (85 mm i.d.). Five larvae, weighing between 40 and 50 mg each, were placed in the *Petri* dish and left in darkness at 30 ± 0.5° and 70% humidity: Each experiment was repeated 5 times.

The consumed area A of test disks and that of the controls (B) were measured simultaneously at regular 30-min intervals for 4 to 5 h to calculate the feeding ratio ($FR\ A/B$) [23]. FR_{50}, the ratio when the control disk had been consumed to 50% was obtained by extrapolation of the closest empirical data.

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