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USE OF ALKENYLRESORCINOLS FROM *ONONIS SPECIOSA* AS SYNTHETIC PRECURSORS OF COMPOUNDS WITH POTENTIAL BIOLOGICAL ACTIVITY

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ABSTRACT.—Selective ozonization of the alkenylresorcinols isolated from *Ononis speciosa* was studied. The derivatives thus obtained were used as precursors in the synthesis of cannabinoids and macrocyclic lactones.

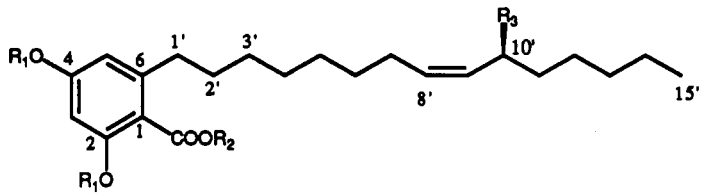
In previous studies of the chemical composition of species from *Ononis* that grow on the Iberian Peninsula (1–3) we reported the isolation and structural elucidation of components from the $CHCl_3$ and EtOH extracts of *Ononis speciosa* Lag. (Leguminosae) (1,2). In these extracts the major components are alkylresorcinols, glycosidated and free flavonoids, and other phenolic compounds. We report here studies carried out on the alkylresorcinols with the aim of establishing their reactivity and biological activity and their use in the synthesis of analogues of natural products of pharmacological interest.

RESULTS AND DISCUSSION

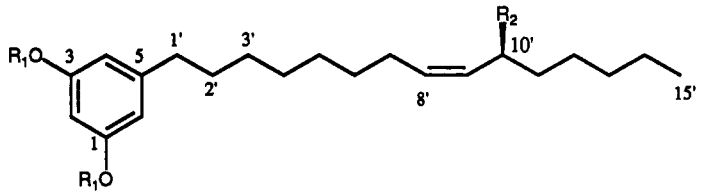
Optimization of the extraction, defatting, and fractionating processes, avoiding treatment with basic solutions, allowed us to isolate and characterize the components of the $CHCl_3$ extract without derivatization. In this way the carboxylic acids **1** (10% in weight of defatted extract) and **2** (12%) and the resorcinols **3** (9%) and **4** (8%) were isolated. Considering the structural similarity and the ease of the degradation of acids **1** and **2** into resorcinols **3** and **4** (under basic conditions), we assume that the latter are formed by decarboxylation of the former either in the plant or in the extraction process. Resorcinol **3** was identified earlier in extracts from plants of the genus *Anacardium* (4,5), *Grevillea* (6,7), *Hakea* (8,9), *Kneama* (10), and *Petrophila* (7).

The activity of **1**, **2**, **3**, and **4** towards several species of Gram-positive bacteria (*Bacillus megaterium, Bacillus subtilis* CECT 397, *Bacillus circulans, Bacillus licheniformis* CECT 20, *Enterococcus faecalis* S-86, *Micrococcus lysodeikticus,* and *Staphylococcus aureus* ATCC 8), Gram-negative bacteria (*Alcaligenes faecalis, Escherichia coli* U-9, *Pseudomonas reptilivora, Pseudomonas fluorescens* N5, *Proteus,* and *Salmonella*), yeasts (*Saccharomyces cerevisiae* S-1, K-2, and X-3) and filamentous fungi (*Aspergillus niger* ATCC 9142, *Botrytis cinerea* CECT 2100 and CECT 2850, *Gibberella fujikuroi* IMI 58289, and *Mucor mucedo*) have been studied (Table 1). None of the assayed products proved to be active towards the selected yeasts and fungi, nor to the Gram-negative bacteria. Nevertheless, all the assayed Gram-positive bacteria showed sensitivity towards acids **1** and **2**.

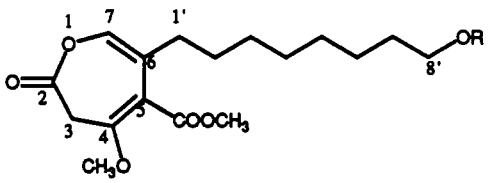
Although the location of the double bond in the aliphatic chains of **1–4** has already been determined (1) by analysis of the mass spectra of some of their derivatives, we tried to confirm the previous results through chemical degradation and identification of the obtained products. With this aim, we followed a procedure similar to that described (11) for the trimethyl derivative **1c**, which was identified in the seeds of *Ginkgo biloba* (11). Ozonization-$NaBH_4$ reduction of **1c** gave *n*-heptanol and a product **5** resulting from the aromatic ring degradation; structure **5** was elucidated with the spectral data of its acetate **5a**. The mass spectrum of **5a** shows a molecular ion at *m/z* 368, which, together with



1	$R_1=R_2=R_3=H$
1a	$R_1=R_3=H$, $R_2=Me$
1b	$R_1=Ac$, $R_2=Me$, $R_3=H$
1c	$R_1=R_2=Me$, $R_3=H$
2	$R_1=R_2=H$, $R_3=OAc$
2a	$R_1=H$, $R_2=Me$, $R_3=OAc$
2b	$R_1=Ac$, $R_2=Me$, $R_3=OAc$
2c	$R_1=R_2=Me$, $R_3=OAc$



3	$R_1=R_2=H$
3a	$R_1=Ac$, $R_2=H$
3b	$R_1=Me$, $R_2=H$
4	$R_1=H$, $R_2=OAc$
4a	$R_1=Ac$, $R_2=OAc$
4b	$R_1=Me$, $R_2=OAc$



5	R=H
5a	R=Ac

the analysis of its ^1H nmr and ^{13}C nmr, suggests the formula $C_{19}H_{28}O_7$. The ^1H-nmr spectrum has signals due to methoxycarbonyl (3.80 ppm), methoxyl on a conjugated system (3.71 ppm), a vinylic proton (7.11 ppm), and a broad singlet from two allylic and α to ester protons (4.01 ppm). Signals due to an aliphatic chain were seen at 1.32 ppm (12H, H-2′–H-7′), 4.05 (2H, t, H-8′ geminal to acetoxy group, 2.03 ppm, 3H, s), and 2.59 (two allylic protons on C-1′). The analysis of other spectroscopic features agrees with the structure of 6-(8-acetoxyoctyl)-4-methoxy-5-methoxycarbonyl-3*H*-oxepin-2-one. Scheme 1 illustrates a possible reaction mechanism.

In order to achieve higher selectivity in the ozonization process, the acetyl derivatives **1b** and **2b**, which possess a lower degree of activation of the aromatic ring towards electrophilic aromatic substitution, were used. Accordingly, when these compounds were treated in a manner similar to that described for **1c**, only double bond degradation

TABLE 1. Diameter of the Growth Inhibition Halo (mm).[a]

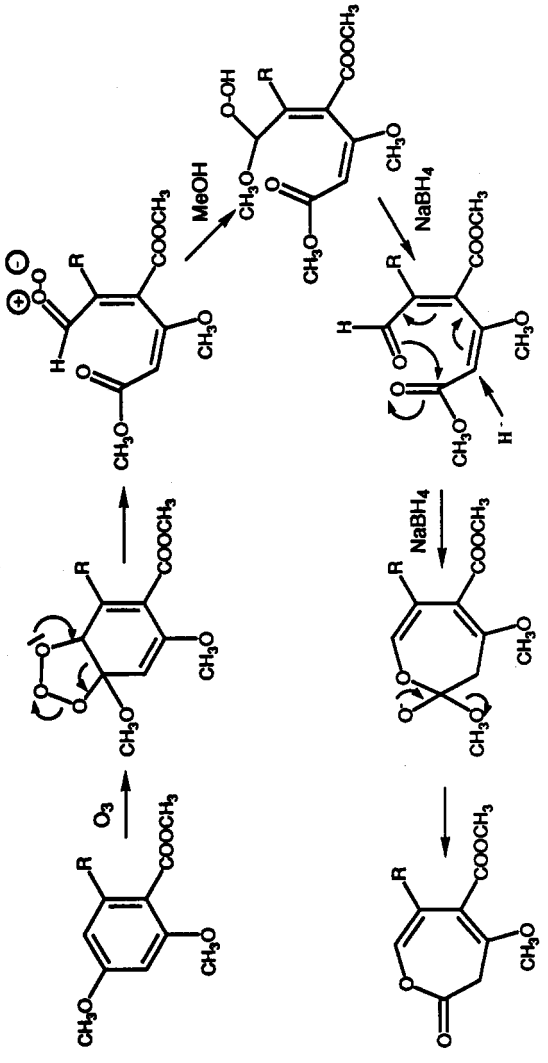
Gram-positive bacteria	Compound							
	1		**2**		**3**		**4**	
	c1	c2	c1	c2	c1	c2	c1	c2
Bacillus megaterium	[b]	[b]	7	7	[b]	[b]	[b]	[b]
Bacillus subtilis	[b]	[b]	8	7	[b]	[b]	[b]	[b]
Bacillus circulans	7	[b]	9	8	7	7	7	7
Bacillus licheniformis	15	15	22	18	8	10	9	7
Enterococcus faecalis	30	16	15	13	12	9	6	7
Micrococcus lysodeikticus	7	[c]	13	[c]	7.5	[c]	7	[c]
Staphylococcus aureus	7	[c]	7	[c]	7	[c]	[b]	[c]

[a] c1 = 200 μg/disk; c2 = 100 μg/disk.
[b] No inhibition detected.
[c] Not done.

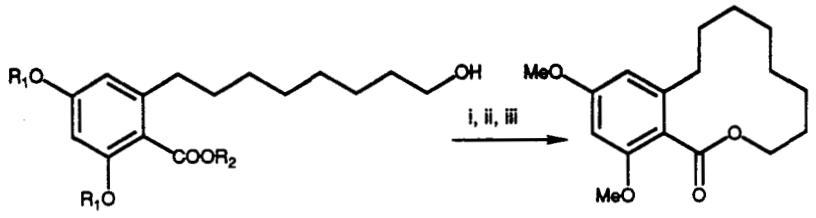
products were obtained. No aromatic ring ruptures could be detected; thus, when **1b** was subjected to ozonization, $NaBH_4$ reduction, and subsequent KOH/MeOH saponification, *n*-heptanol and methyl 2,4-dihydroxy-6-(8-hydroxyoctyl)benzoate [**6a**] were isolated. Under the same conditions, **2b** yielded the same hydroxyalkylbenzoate **6a** and (*S*)-1,2-heptanediol (12). Ozonization of **3a** and **4a** gave similar results. Identification of the diol allowed us to establish the absolute stereochemistry at C-10′ of the natural products **2** and **4**.

The degradation products thus obtained were used in the synthesis of macrocyclic lactones. First, the phenolic hydroxyls were protected by methylation [**6b**] and the carboxylic acid was freed by saponification [**6c**]. In this way, a hydroxy acid ready to be transformed into a 12-member lactone was available. The Corey lactonization procedure (13), in which the acid is transformed into a pyridylthioester, was then used. First, the acid **6c** was treated with 2,2′-dipyridyldisulfide in the presence of triphenylphosphine. When a xylene solution of this freshly prepared pyridylthioester was added dropwise to refluxing xylene, lactone **7** (9%) and unidentified products of intermolecular addition were obtained (Scheme 2). The mass spectrum of **7** shows a molecular ion at *m/z* 292, which is in agreement with the formula $C_{17}H_{24}O_4$. In its ir spectrum appears absorption of aromatic ester at 1720 cm^{-1} and in its ^1H nmr spectrum the oxygenated methylene appears as a triplet at 4.29 ppm.

The degradation products of alkylresorcinols have also been used in the synthesis of ω-carboxycannabinoids. With this aim, aldehyde **8a**, obtained by ozonization of **3a** followed by reduction with Me_2S, was oxidized with CrO_3/H^+ to yield acid **8b**. Afterwards, phenolic acetates were saponified (KOH/MeOH), and the acid **8c** was methylated with CH_2N_2. The ω-methoxycarbonylalkylresorcinol thus obtained, **8d**, was condensed with a mixture of (1*S*,4*R*)-(+)-*trans*- and (1*R*,4*R*)-(+)-*cis*-*p*-mentha-2,8-dien-1-ol [**9**] (14) in the presence of *p*-toluenesulfonic acid, under conditions that have been reported for the synthesis of cannabinoids (15). (3*R*,4*R*)-5″-methoxycarbonylethylcannabidiol [**10**] was obtained and characterized by comparison of its spectroscopic features with those reported for similar systems (16). When reaction conditions were altered by increasing the temperature, products with a cannabinol structure were obtained (Scheme 3). Thus, **11** was isolated, and its structure identified by comparison of its spectroscopic features with similar systems (15).



SCHEME 1. Proposed formation mechanism of **5**.



6a R_1=H, R_2=Me
6b R_1=R_2=Me
6c R_1=Me, R_2=H

7

SCHEME 2. i: Me_2SO_4/K_2CO_3, Me_2CO, Δ; ii: KOH/THF-H_2O; iii: 2,2′-dipyridyl disulfide/PPh_3, xylene, Δ.

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—Uv spectra were recorded on a UV-vis Bausch-Lomb model Spectronic 2000 spectrometer and ir spectra on a Perkin-Elmer Model 983 G spectrometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter. Low resolution ms was determined on a Hewlett-Packard 5988A mass spectrometer. ^{1}H and ^{13}C nmr were recorded on a Bruker AM 300 spectrometer (300 MHz for ^{1}H and 75 MHz for ^{13}C) and Bruker WP 80 SY (80 MHz for ^{1}H and 20 MHz for ^{13}C) using TMS as internal standard. Assignments of ^{13}C-nmr signals were made with the aid of additivity rules and DEPT experiments. Cc was carried out using Si gel Merck 60 (70–230 mesh) and eluting with mixtures of hexane/Et_2O/MeOH of increasing polarity. Analytical tlc was performed on layers of Si gel Merck 60 G of 0.25 mm thickness, using a 7% phosphomolybdic acid solution (EtOH) to visualize the spots.

PLANT MATERIAL.—Flowers of *O. speciosa* were collected at Izbor (Granada, Spain) in March of 1990. Plant material was identified by Professor F. Valle, Department of Botany, University of Granada. A voucher specimen is available for inspection at the Herbarium of the Faculty of Sciences of the University of Granada.

ISOLATION PROCEDURES.—Air-dried flowers (2.5 kg) of *O. speciosa* were extracted in a Soxhlet with $CHCl_3$, yielding an extract (264 g, 11% of dried plant) from which fatty acids (58 g, 22% of extract) were removed by precipitation in MeOH at low temperature. The defatted extract (206 g, 78%) was then column chromatographed on SiO_2, eluting hexane/Et_2O mixtures of increasing polarity. Unsaturated fatty acids (57.8 g, 28%), alkylbenzoic acids **1** (20.6 g, 10%) and **2** (24.7 g, 12%), the alkylresorcinols **3** (18.5 g, 9%) and **4** (16.5 g, 8%), and the flavonoids penduletin (39.1 g, 19%) and formononetin (28.8 g, 14%) were isolated.

PHYSICAL DATA.—*2,4-Dihydroxy-6-(8Z-pentadecenyl)benzoic acid* [**1**].—Oil: eims (70 eV) (rel. int.) *m/z* 362 (0.1), 344 (0.1), 318 (2), 137 (8), 124 (100), 123 (19); ir ν max (film) 3550–2300 (OH, COOH), 2925, 2854, 1690 (COOH), 1623 (Ar), 1605 (C=C), 1505, 1464, 1364, 1259, 1169, 1118, 1022, 920, 886, 850, 723 cm^{-1}; uv λ max (ε) (MeOH) 207 (5400), 253 (1300), 293 (700) nm; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 11.53 (1H, bs, COOH), 8.50–9.00 (2H, m,, OH×2), 6.28 (2H, s, H-3, H-5), 5.34 (2H, bt, J=5 Hz, H-8′, H-9′), 2.93 (2H, bt, J=7 Hz, H-1′), 2.03 (4H, m, $w_{1/2h}$=14 Hz, H-7′, H-10′), 1.28 (18H, m, $w_{1/2h}$=8 Hz, H-2′–H-6′, H-11′–H-14′), 0.88 (3H, m, $w_{1/2h}$=8 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 175.80 (C, COOH), 165.84 (C, C-4), 161.91 (C, C-2), 150.46 (C, C-6), 129.89 (CH, C-8′, C-9′), 111.50 (CH, C-5), 103.34 (C, C-1), 101.52 (CH, C-3), 34.02 (CH_2, C-1′), 31.85 (CH_2, C-2′), 31.74 (CH_2, C-13′), 29.65, 29.33, 29.24 (CH_2, C-3′–C-6′ and C-11′–C-12′), 27.14 (CH_2, C-7′, C-10′), 22.59 (CH_2, C-14′), 13.97 (Me, C-15′).

Methyl 2,4-dihydroxy-6-(8Z-pentadecenyl)benzoate [**1a**].—Oil: eims (70 eV) (rel. int.) *m/z* 376 (4), 344 (1), 316 (0.1), 191 (4), 182 (100), 177 (12), 163 (26), 151 (11), 150 (27), 149 (8), 138 (25), 123 (12); ir ν max (film) 3389 (OH), 1705 (COOMe), 1653 (Ar), 1616 (C=C) cm^{-1}; uv λ max (ε) (MeOH) 210 (4000), 260 (1700), 295 (800) nm; ^{1}H nmr (80 MHz $CDCl_3$) δ (ppm) 11.75 (1H, s, OH), 6.31 (2H, d, J=2 Hz, H-5), 6.25 (1H, d, J=2 Hz, H-3), 6.00 (1H, bs, OH), 5.37 (2H, bt, J=5 Hz, H-8′, H-9′), 3.94 (3H, s, $COOCH_3$), 2.85 (2H, bt, J= Hz, H-1′), 2.05 (4H, m, $w_{1/2h}$=14 Hz, H-7′, H-10′), 1.30 (18H, m, $w_{1/2h}$=16 Hz, H-2′–H-6′, H-11′–H-14′), 0.90 (3H, m, $w_{1/2h}$=8 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 171.66 (C *C*OOMe), 164.55 (C, C-4), 160.79 (C, C-2), 148.42 (C, C-6), 129.49, 129.37 (CH, C-8′, C-9′), 110.77 (CH, C-5), 104.08 (C, C-1), 100.99 (CH, C-3), 51.37 (CH_3, COO*Me*), 36.45 (CH_2, C-1′), 31.39 (CH_2, C-2′, C-13′), 29.35, 29.03, 28.59, 28.51 (CH_2, C-3′–C-6′, C-11′, C-12′), 26.82 (CH_2, C-7′, C-10′), 22.24 (CH_2, C-14′), 13.66 (Me, C-15′).

SCHEME 3. Synthesis of ω-carboxycannabinoids.

Methyl 2,4-diacetoxy-6-(8Z-pentadecenyl)benzoate [**1b**].—Oil: eims (70 eV) (rel. int.) *m/z* 460 (0.1), 428 (2), 385 (3), 376 (1), 336 (5), 294 (8), 224 (7), 191 (4), 182 (62), 177 (9), 163 (17), 151 (6), 150 (14), 149 (6); ir ν max (film) 1775, 1773 (ArOAc), 1611 (Ar) cm^{-1}; uv λ max (ε) (MeOH) 204 (3100), 225 sh (1200), 262 (500) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.90 (1H, d, J=2 Hz, H-5), 6.84 (1H, d, J=2 Hz, H-3), 5.36 (2H, bt, J=5 Hz, H-8′, H-9′), 3.88 (3H, s, COOMe), 2.70 (2H, bt, J=7 Hz, H-1′), 2.29 (3H, s, 4-OAc), 2.25 (3H, s, 2-OAc), 2.10 (4H, m, $w_{1/2h}$=8 Hz, H-7′, H-10′), 1.30 (18H, m, $w_{1/2h}$=6 Hz, H-2′–H-6′, H-11′–H-14′), 0.90 (3H, m, $w_{1/2h}$=8 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 167.99, 167.87 (C, Ar-*OCO*Me), 165.96 (C, *CO*OMe), 151.33 (CH, C-4), 148.53 (C, C-2), 143.64 (C, C-6), 129.42, 129.31 (CH, C-8′, C-9′), 123.07 (C, C-1), 119.64 (CH, C-5), 113.70 (CH, C-3), 51.60 (CH_3, COO*Me*), 33.34 (CH_2, C-1′), 31.33 (CH_2, C-13), 30.57 (CH_2, C-2′), 29.23, 28.93, 28.76, 28.66, 28.47, (CH_2, C-3′–C-6′, C-11′, C-12′), 26.72 (CH_2, C-7′, C-10′), 22.18 (CH_2, C-14′), 20.49, 20.14 (Me, Ar-OCO*Me*), 13.61 (Me, C-15′).

(8′Z,10′R)-2,4-dihydroxy-6-(10-acetoxy-8-pentadecenyl)benzoic acid [**2**].—Oil: $[\alpha]^{20}D$ −3.7° (*c*=2.01, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 376 (0.1), 360 (0.1), 316 (0.1), 137 (10), 124 (100), 123 (25); ir ν max (film) 3550–2300 (OH, COOH), 2925, 2854, 1703, (COOH), 1626 (Ar), 1605 (C=C), 1505, 1463, 1371, 1266, 1199, 1158, 1023, 999, 956, 891, 841, 724 cm^{-1}; uv λ max (ε) (MeOH) 204 (2800), 250 (500), 275 (400) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.28 (2H, d, J=2 Hz, H-5), 6.21 (1H, d, J=2 Hz, H-3), 5.88–5.13 (3H, m, H-8′, H-9′, H-10′), 2.88 (2H, m, $w_{1/2h}$=8 Hz, H-1′), 2.09 (3H, s, 10′-OAc), 2.05 (2H, m, H-7′), 1.25 (18H, m, $w_{1/2h}$=8 Hz, H-2′–H-6′, H-11′–H-14′), 0.88 (3H, m, $w_{1/2h}$=7 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 174.96 (C, COOH), 172.72 (C, 10′-*OCO*Me), 165.83 (C, C-5), 161.82 (C, C-2), 150.17 (C, C-6), 134.67 (CH, C-9′), 127.40 (CH, C-8′), 111.50 (CH, C-6), 103.44 (C, C-1), 101.23 (CH, C-3), 71.75 (CH, C-10′), 35.81 (CH_2, C-1′), 34.55 (CH_2, C-11′), 31.67 (CH_2, C-13′), 31.49 (CH_2, C-2′), 29.64, 29.30, 29.00 (CH_2, C-3′–C-6′), 27.83 (CH_2, C-7′), 24.58 (CH_2, C-12′), 22.55 (CH_2, C-14′), 21.30 (Me, 10′-OCO*Me*), 13.96 (Me, C-15′).

Methyl (8′Z,10′R)-6-(10-acetoxy-8-pentadecenyl)-2,4-dihydroxybenzoate [**2a**].—Oil: $[\alpha]^{20}D$ −3.9° (*c*=1.75, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 434 (0.7), 402 (0.2), 374 (8), 342 (8), 289 (2), 182 (63), 177 (10), 163 (23), 151 (8), 150 (22), 149 (9), 124 (38), 123 (19), 43 (100); ir ν max (film) 3381 (OH), 1734 (OAc), 1705 (COOMe), 1652 (Ar), 1618 (C=C) cm^{-1}; uv λ max (ε) (MeOH) 205 (3100), 260 (1200), 290 (500) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 11.63 (1H, s OH), 6.30 (1H, d, J=2 Hz, H-5), 6.25 (1H, d, J=2 Hz, H-3), 5.25–5.75 (3H, m, H-8′, H-9′, H-10′), 3.91 (3H, s, COOMe), 2.84 (2H, bt, J=7 Hz, H-1′), 2.15 (2H, m, $w_{1/2h}$=8 Hz, H-7′), 2.03 (3H, s, 10′-OAc), 1.29 (18H, m, $w_{1/2h}$=8 Hz, H-2′–H-6′, H-11′–H-14′), 0.89 (3H, m, $w_{1/2h}$=7 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 171.72, 171.26 (C, Ar*CO*OMe, Ar-*OCO*Me), 164.96 (C, C-4), 161.41 (C, C-2), 148.25 (C, C-6), 133.97 (CH, C-9′), 127.63 (CH, C-8′), 110.82 (CH, C-5), 103.92 (C, C-1), 101.10 (CH, C-3), 70.88 (CH, C-10′), 51.37 (Me, ArCOO*Me*), 36.49 (CH_2, C-1′), 34.42 (CH_2, C-11′), 31.41 (CH_2, C-13′), 31.28 (CH_2, C-2′), 29.43, 29.20, 28.96 (CH_2, C-3′–C-6′), 27.61 (CH_2, C-7′), 24.41 (CH_2, C-12′), 22.24 (CH_2, C-14′), 20.26 (Me, Ar-OCO*Me*), 13.62 (Me, C-15′).

Methyl (8′Z,10′R)-2,4-diacetoxy-6-(10-acetoxy-8-pentadecenyl)benzoate [**2b**].—Oil: $[\alpha]^{20}D$ −1.3° (*c*=2.00, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 518 (0.1), 476 (0.2), 458 (1), 444 (0.8), 443 (1), 416 (2), 401 (1), 384 (4), 374 (1), 342 (3), 182 (26), 177 (5), 163 (12), 151 (3), 150 (9), 149 (5), 43 (100); ir ν max (film) 1774 (Ar-OAc), 1730 (ArCOOMe), 1611 (Ar), 1583 (C=C) cm^{-1}; uv λ max (ε) (MeOH) 204 (3600), 225 sh (1300), 263 (400) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.89 (1H, d, J=2 Hz, H-5), 6.81 (1H, d, J=2 Hz, H-3), 5.75–5.20 (3H, m, H-8′, H-9′, H-10′), 3.88 (3H, s, COOMe), 2.68 (2H, bt, J=7 Hz, H-1′), 2.28 (3H, s, 4-OAc), 2.25 (3H, s, OAc), 2.23 (2H, m, H-7′), 2.03 (3H, s, 10′-OAc), 1.31 (18H, m, $w_{1/2h}$= 8 Hz, H-2′–H-6′, H-11′–H-14′), 0.88 (3H, m, $w_{1/2h}$=7 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 169.51 (C, 10′-*OCO*Me), 167.78 (C, 2-*OCO*Me, 4-*OCO*Me), 165.80 (C, *CO*OMe), 151.23 (C, C-4), 148.50 (C, C-2), 143.50 (C, C-6), 133.35 (CH, C-9′), 127.76 (CH, C-8′), 123.04 (C, C-1), 119.56 (CH, C-5), 113.66 (CH, C-3), 69.73 (CH, C-10′), 51.55 (Me, COOMe), 34.20 (CH_2, C-11), 33.21 (CH_2, C-1′), 31.05 (CH_2, C-13′), 30.47 (CH_2, C-2′), 28.89, 28.78, 28.57, (CH_2, C-3′–C-6′), 27.28 (CH_2, C-7′), 24.18 (CH_2, C-12′), 21.96 (CH_2, C-14′), 20.62 (Me, 10′-OCO*Me*), 20.34 (Me, 2-OCO*Me*), 20.03 (Me, 4-OCO*Me*), 13.40 (Me, C-15′).

(8′Z,10′R)-1,3-Di-O-acetyl-5-(10-acetoxy-8-pentadecenyl)resorcinol [**4a**].—Oil: $[\alpha]^{20}D$ −9.1° (*c*=1.82, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 460 (0.1), 418 (0.3), 400 (0.7), 358 (1), 316 (4), 124 (26), 123 (11), 43 (100); ir ν max (film) 1770 (Ar-OAc), 1734 (ArCOOMe), 1617 (Ar), 1591 (C=C) cm^{-1}; uv λ max (ε) (MeOH) 204 (3200), 225 sh (1200), 275 (300) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.75 (3H, m, $w_{1/2h}$=3 Hz, H-2, H-4, H-6), 5.63–5.13 (3H, m, H-8′, H-9′, H-10′), 2.58 (2H, bt, J=8 Hz, H-1′), 2.24 (6H, s, Ar-OAc×2), 2.03 (2H, m, H-7′), 1.98 (3H, s, 10′-OAc), 1.28 (18H, m, $w_{1/2h}$=8 Hz, H-2′–H-6′, H-11′–H-14′), 0.86 (3H, m, $w_{1/2h}$=7 Hz, H-15′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm): 170.03 (C, 10′-*OCO*Me), 168.70 (C, 1-*OCO*Me, 3-*OCO*Me), 150.75 (C, C-1, C-3), 145.06 (C, C-5), 133.80 (CH, C-9′), 128.05 (CH,

C-8′), 118.64 (CH, C-4, C-6), 112.42 (CH, C-2), 70.24 (CH, C-10′), 35.46 (CH_2, C-1′), 34.58 (CH_2, C-11′), 31.55 (CH_2, C-13′), 31.41 (CH_2, C-2′), 30.62, 29.46, 28.96 (CH_2, C-3′–C-6′), 27.66 (CH_2, C-7′), 21.04 (CH_2, C-14′), 20.83 (Me, 1-OCO*Me*, 3-OCO*Me*, 10′-OCO*Me*), 13.76 (Me, C-15′).

ANTIMICROBIAL SCREENING.—Products were assayed for antimicrobial activity by the disk diffusion method. Brain-heart agar (BHA) plates (Pronadisa, Hispanagar) were inoculated with 0.1 ml of 8-h-old cultures of the microbial strains, and the 3MM Whatman paper disks (6-mm diam.), previously impregnated with 100 and 200 μg of **1**, **2**, **3**, and **4**, were deposited onto the plates. The plates were kept at 4° for 1 h to allow diffusion and then incubated at the appropriate temperature. The results were read 18 h after incubation and measured as a function of the diameter of the growth inhibition halo that appeared around the disks (mm).

The Gram-positive bacteria, *Bac. megaterium, Bac. subtilis* CECT 397, *Bac. circulans, Bac. licheniformis* CECT 20, *Ent. faecalis* S-86, *Mic. lysodeikticus*, and *Staph. aureus* ATCC 8, were grown in BHA and incubated at 28°. Gram-negative bacteria, *Al. faecalis, Esch. coli* U-9, *Ps. reptilivora, Ps. fluorescens* N5, *Proteus*, and *Salmonella*, were grown in the same medium and incubated at 37°. Yeasts: Several *Sacc. cerevisiae* strains were assayed: S-1, K-2, and X-3, grown in YEPG and incubated at 28°. Filamentous fungi: *Asp. niger* ATCC 9142, *Bot. cinerea* CECT 2100 and CECT 2850, *Gib. fujikuroi* IMI 58289, and *Mu. mucedo*. All the species were grown in agar Sabouraud medium with chloramphenicol (BBL, Cockeysville, MD), except the species of *Botryitis*, which were inoculated on potato agar (BBL). The incubation temperature was 28°. All strains belong to the Collection of Microbiology Laboratory.

CHEMICAL TRANSFORMATIONS.—*Ozonolysis of methyl 2,4-dimethoxy-6-(8Z-pentadecenyl)benzoate* [**1c**].—A stream of dried ozone (13.54 mmol O_3/h obtained from a 20 liter/h O_2 flow) was passed through a solution of **1c** (455 mg, 1.13 mmol) in MeOH (50 ml) at −78°, until no starting material could be visualized in tlc. After reduction of the mixture with $NaBH_4$ (500 mg) and cc, *n*-heptanol (129 mg, 1.11 mmol, 98%) and 6-(8-hydroxyoctyl)-4-methoxy-5-methoxycarbonyl-3*H*-oxepin-2-one [**5**] (107 mg, 0.33 mmol, 29%) were isolated. Acetylation of **5** with Ac_2O and pyridine yielded 6-(8-acetoxyoctyl)-4-methoxy-5-methoxycarbonyl-3*H*-oxepin-2-one [**5a**]: oil; eims (70 eV) (rel. int.) *m/z* 368 (1), 337 (5), 336 (18), 212 (12), 181 (7), 180 (69), 165 (8), 43 (100); ir ν max (film) 1745, 1720 (COOMe, OAc), 1612, 1557 (C=C-C=C) cm^{-1}; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 7.11 (1H, t, *J*=1.5 Hz, H-7), 4.05 (2H, t, *J*=6 Hz, H-8′), 4.01 (2H, bs, H-3), 3.80 (3H, s, COOMe), 3.71 (3H, s, 4-OMe), 2.59 (2H, bt, *J*=7 Hz, H-1′), 2.03 (3H,s, OAc), 1.32 (12H, bs, H-2′–H-7′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 171.30 (C, Me*C*OO), 169.39 (C, C-2), 164.42 (C, 8′-O*C*OMe), 155.00 (C, C-4), 138.82 (CH, C-7), 126.50 (C, C-6), 114.82 (C, C-5), 64.66 (CH_2, C-8′), 52.39 (4-OMe), 51.27 (Me, 5-COO*Me*), 34.29 (CH_2, C-7′), 29.43, 29.33, 29.23, 29.20 (CH_2, C-2′–C-5′), 28.61 (CH_2, C-3), 25.91, 24.64 (CH_2, C-1′, C-6′), 21.07 (Me, 8′-OCO*Me*).

SYNTHESIS OF 3,4,5,6,7,8,9,10-OCTAHYDRO-12,14-DIMETHOXY-1H-2-BENZOXACYCLODODECIN-1-ONE [**7**].—*Methyl 2,4-dihydroxy-6-(8-hydroxyoctyl)benzoate* [**6a**].—A solution of **1b** (1.99 g, 4.33 mmol) in MeOH (150 ml), was ozonized at −75°. The ozonides mixture was reduced with $NaBH_4$ (4 g). The mixture was then acidified with 2 N HCl (pH=2), ,the MeOH distilled in vacuo, and the residue diluted with H_2O and extracted with Et_2O. Combined organic layers were washed with H_2O and dried with Na_2SO_4, and the solvent was removed in vacuo. In order to hydrolyze the phenolic acetates, the reaction crude was treated with 2 N KOH/MeOH (40 ml) for 30 min at room temperature. Then it was diluted with H_2O (150 ml), neutralized with 2 N HCl, and extracted with Et_2O. Combined organic layers were washed with H_2O and dried with Na_2SO_4, and the solvent was removed in vacuo. Cc afforded **6a** (1.220 g, 4.12 mmol, 95%): oil; eims (70 eV) (rel. int.) *m/z* 296 (17), 264 (9), 246 (7), 182 (100), 178 (10), 177 (16), 164 (26), 163 (67), 162 (15), 151 (20), 150 (82), 149 (18), 124 (23), 123 (25), 122 (25), 121 (35), 77 (19), 69 (51), 55 (40); ir ν max (film) 3422 (OH), 1738, 1715 (COOMe), 1621, 1578 (Ar) cm^{-1}; uv λ max (ε) (MeOH) 214 (5900), 260 (3100), 297 (1300) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.28 (1H, d, *J*=2 Hz, H-5), 6.20 (1H, d, *J*=2 Hz, H-3), 4.00–3.50 (2H, m, OH), 3.89 (3H, s, COOMe), 3.66 (2H, t, *J*=6 Hz, H-8′), 2.83 (2H, bt, *J*=7 Hz, H-1′), 1.31 (12H, bs, H-2′–H-7′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 172.06 (C, Ar*C*OOMe), 164.95 (C, C-4), 161.46 (C, C-2), 148.70 (C, C-6), 111.25 (CH, C-5), 104.37 (C, C-1), 101.33 (CH, C-3), 62.96 (CH_2, C-8′), 51.83 (Me, ArCOO*Me*), 36.67 (CH_2, C-1′), 32.33 (CH_2, C-7′), 31.61 (CH_2, C-2′), 29.57, 29.27, 29.27 (CH_2, C-3′, C-4′, C-5′), 25.61 (CH_2, C-6′).

Methyl 2-(8-hydroxyoctyl)-4,6-dimethoxybenzoate [**6b**].—Me_2CO_4 (1.25 ml) was added to a solution of **6a** (250 mg, 0.84 mmol) in Me_2CO (14.4 ml) in the presence of K_2SO_4 (6.5 g) and refluxed for 90 min. The mixture was then cooled, filtered, and the solvent removed in vacuo. Cc afforded **6b** (200 mg, 0.62 mmol, 73%): oil; eims (70 eV) (rel. int.) *m/z* 324 (6), 307 (2), 306 (1), 293 (8), 292 (4), 275 (2), 247 (1), 223 (6), 210 (100), 209 (23), 195 (5), 191 (46), 179 (14), 177 (11), 163 (9), 151 (31); ir ν max (film) 3429 (OH), 1725 (COOMe), 1604, 1591 (Ar) cm^{-1}; uv λ max (ε) (MeOH) 218 (36000), 245 (14000), 280 (8500) nm; ^1H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.31 (2H, bs, H-3, H-5), 3.86 (3H, s, COOMe), 3.79 (3H, s, 6-OMe),

3.77 (3H, s, 4-OMe), 3.65 (2H, t, J=6 Hz, H-8′), 2.55 (2H, bt, J=7 Hz, H-1′), 1.30 (12H, bs, H-2′–H-7′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 172.06 (C, Ar*C*OOMe), 164.95 (C, C-4), 161.46 (C, C-2), 148.70 (C, C-6), 111.25 (CH, C-5), 104.37 (C, C-1), 101.33 (CH, C-3), 62.96 (CH_2, C-8′), 51.83 (Me, ArCOO*Me*), 36.67 (CH_2, C-1′), 32.33 (CH_2, C-7′), 31.61 (CH_2, C-2′), 29.57, 29.27 (CH_2, C-3′, C-4′, C-5′), 25.61 (CH_2, C-6′).

2-(8-Hydroxyoctyl)-4,6-dimethoxybenzoic acid [**6c**].—A solution of **6b** (150 mg, 0.46 mmol) in THF (5 ml), H_2O (1 ml), and 8 N KOH/MeOH (5 ml) was refluxed for 5 h. Usual workup and cc yielded **6c** (100 mg, 0.32 mmol, 70%): oil; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.38 (2H, bs, H-3, H-5), 4.26 (2H, bs, OH), 3.88, 3.81 (3H, s each, 4-OMe, 6-OMe), 3.66 (2H, t, J=6 Hz, H-8′), 2.56 (2H, bt, J=7.5 Hz, H-1′), 1.75–1.25 (12H, m, H-2′–H-7′).

*3,4,5,6,7,8,9,10-Octahydro-12,14-dimethoxy-1*H*-2-benzoxacyclododecin-1-one* [**7**].—A solution of triphenylphosphine (105 mg, 0.40 mmol) in xylene (5 ml) and 2,2′-dipyridyldisulfide (88 mg, 0.40 mmol) were added to a solution of **6c** (73 mg, 0.24 mmol) in xylene (5 ml). The mixture was stirred for 12 h under Ar at room temperature. Then it was diluted with 10 ml of xylene and slowly added (9 h) to boiling xylene (50 ml). The mixture was refluxed for an additional period of 10 h. Cc of the product yielded **7** (6 mg, 0.02 mmol, 9%): oil; eims (70 eV) (rel. int.) *m/z* 292 (56), 275 (3), 247 (3), 220 (7), 208 (12), 207 (21), 206 (16), 205 (31), 196 (54), 195 (10), 192 (24), 191 (72), 179 (32), 178 (33), 177 (39), 165 (21), 164 (12), 163 (15), 152 (93), 151 (44), 150 (14), 149 (100), 135 (19); ir ν (film) 1720 (lactone), 1603, 1591 (Ar) cm^{-1}; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.31 (2H, bs, H-11, H-13), 4.29 (2H, t, J=5.5 Hz, H-3), 3.79 (6H, s, OMe×2), 2.58 (2H, bt, J=7.5 Hz, H-10), 2.00–1.25 (12H, m, H-4–H-9).

SYNTHESIS OF CANNABINOIDS.—*1,3-Di-*O*-acetyl-5-(7-formylheptyl)resorcinol* [**8a**].—A solution of **3a** (1.10 g, 2.74 mmol) in CH_2Cl_2 (110 ml), was ozonized during 2 h at −80°. The mixture of ozonides was reduced with Me_2S (11 ml). Cc afforded *n*-heptanol and **8a** (624 mg, 1.95 mmol, 71%): oil; eims (70 eV) (rel. int.) *m/z* 320 (0.7), 278 (13), 236 (26), 208 (21), 166 (8), 137 (12), 124 (100), 123 (26), 83 (13), 43 (51); ir ν (film) 1770 (ArOAc), 1741 (CHO), 1618, 1591, (Ar) cm^{-1}; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 9.75 (1H, t, J=2 Hz, H-8′), 6.79 (3H, m, $w_{1/2h}$=5 Hz, H-2, H-4, H-6), 2.70–2.30 (4H, m, H-1′, H-7′), 2.28 (6H, s, 2×OAc), 1.28 (10H, bs, $w_{1/2h}$=6 Hz, H-2′–H-6′); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 202.30 (C, C-8′), 169.19 (C Me*C*O), 150.91 (C, C-1, C-3), 145.29 (C, C-5), 118.95 (CH, C-4, C-6), 112.69 (CH, C-2), 43.88 (CH_2, C-7′), 35.64 (CH_2, C-1′), 30.78 (CH_2, C-2′), 29.16, 29.03, 28.96, (CH_2, C-3′, C-4′, C-5′), 22.05 (CH_2, C-6′), 21.15 (Me, *Me*COO).

8-(3,5-Diacetoxyphenyl)octanoic acid [**8b**].—Jones' reagent (1.2 ml) (2.67 g of CrO_3, 2.3 ml of H_2SO_4 and H_2O to reach 10 ml) was added to a solution of **8a** (1.49 g, 4.66 mmol) in Me_2CO (20 ml). The mixture was stirred during 10 min at 0°. The reaction was quenched by addition of H_2O (100 ml). Usual workup yielded **8b** (1.48 g, 4.39 mmol, 94%): oil; eims (70 eV) (rel. int.) *m/z* 336 (0.4), 318 (0.5), 294 (3), 276 (4), 252 (24), 234 (11), 208 (1), 207 (2), 166 (4), 165 (3), 124 (100), 123 (37), 43 (92); ir ν (film) 3600–2500 (COOH), 1770, 1741 (ArOAc), 1706 (COOH), 1618, 1590 (Ar) cm^{-1}; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 9.63 (1H, bs, COOH), 6.78 (3H, m, $w_{1/2h}$=4 Hz, H-2′, H-4′, H-6′), 2.60 (2H, bt, J=7.5 Hz, H-8), 2.34 (2H, bt, J=6 Hz, H-2), 2.26 (6H, s, 2×OAc), 1.75–1.25 (10H, m, H-3–H-7); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 179.31 (C, C-1), 169.27 (C, Me*C*O), 150.92 (C, C-3′, C-5′), 145.33 (C, C-1′), 116.98 (CH, C-2′, C-6′), 112.70 (CH, C-4′), 35.67 (CH_2, C-8), 33.97 (CH_2, C-2), 30.60 (CH_2, C-7), 29.05, 28.99, 28.95 (CH_2, C-4, C-5, C-6), 24.68 (CH_2, C-3), 21.18 (Me, *Me*COO).

8-(3,5-Dihydroxyphenyl)octanoic acid [**8c**].—Prepared by hydrolysis of **8b** with 2 N KOH/MeOH (30 ml) for 10 min at room temperature. Oil: eims (70 eV) (rel. int.) *m/z* 252 (11), 206 (1), 151 (3), 137 (16), 124 (100), 123 (27); ir ν (film) 3381 (OH, COOH), 1702 (COOH), 1601 (Ar) cm^{-1}; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 7.88 (2H, bs, OH), 6.12 (3H, s, H-2′, H-4′, H-6′), 2.43 (2H, bt, J=6 Hz, H-8), 2.24 (2H, bt, J=7 Hz, H-2), 1.75–1.25 (10H, m, H-3–H-7); ^{13}C nmr (20 MHz, $CDCl_3$) δ (ppm) 174.80 (C, C-1), 159.22 (C, C-3′, C-5′), 145.73 (C, C-1′), 107.62 (CH, C-2′, C-6′), 100.86 (CH, C-4′), 36.47 (CH_2, C-8), 34.15 (CH_2, C-2), 31.92 (CH_2, C-7), 29.84, 29.78, 29.72, (CH_2, C-4, C-5, C-6), 25.59 (CH_2, C-3).

Methyl 8-(3,5-dihydroxyphenyl)octanoate [**8d**].—Obtained by methylation of **8c** with a saturated solution of CH_2N_2 in Et_2O at 0°. Oil: ir ν (film) 3388 (OH), 1707 (COOMe), 1601 (Ar) cm^{-1}; ^{1}H nmr (80 MHz, $CDCl_3$) δ (ppm) 6.23 (3H, s, H-2′, H-4′, H-6′), 6.00–5.00 (2H, m, OH), 3.68 (3H, s, COOMe), 2.63–2.00 (4H, m, H-2, H-8), 1.70–1.25 (10H, m, H-3–H-7).

*(3*R*,4*R*)-5″-methoxycarbonylethylcannabidiol* [**10**].—A solution of **8d** (65 mg, 0.24 mmol) in CH_2Cl_2 (1 ml) was added to a solution of (4*R*)-*p*-mentha-2,8-dien-1-ol [**9**] (45 mg, 0.29 mmol) and *p*-toluensulfonic acid (20 mg, 0.12 mmol) in CH_2Cl_2 (20 ml) and stirred for 20 h at room temperature. The solvent was then removed in vacuo, and the residue was dissolved in Et_2O (50 ml), washed with H_2O, and dried with Na_2SO_4. Evaporation of the solvent in vacuo yielded a crude product (80 mg). Cc gave **10** (39 mg, 0.10 mmol, 41%):

oil; $[\alpha]^{20}D$ −36.4° (*c*=0.82, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 400 (60), 385 (7), 369 (10), 357 (11), 332 (9), 325 (12), 317 (84), 258 (73), 243 (16), 213 (27), 175 (17), 174 (23), 83 (100); ir ν (film) 3335 (OH), 1707 (COOMe), 1685 (Ar), 1606 (C=C) cm^{-1}; uv λ max (ε) (MeOH) 223 (11900), 270 (1700), 275 (1700) nm; ^1H nmr (300 MHz, $CDCl_3$) δ (ppm) 6.23–6.18 (2H, m, H-4′, H-6′), 5.57 (1H, bs, H-2), 4.63 (1H, dq, $J_1=J_2=1.73$ Hz, H-9a), 4.53 (1H, bd, $J=1.73$ Hz, H-9b), 3.85 (1H, bdd, $J_1=10.31$ Hz, $J_2=2.19$ Hz, H-3), 3.66 (3H, s, COOMe), 2.42 (2H, t, $J=7.63$ Hz, H-1″), 2.29 (2H, t, $J=7.51$, H-7″), 2.30–2.00 (3H, m, H-4, H-6), 1.78 (3H, bs, H-7), 1.64 (3H, s, H-10), 1.65–1.45 (2H, m, H-5), 1.28 (10H, bs, H-2″–H-6″); ^{13}C nmr (75 MHz, $CDCl_3$) δ (ppm) 174.56 (C, C-8″), 149.30 (C, C-8), 142.86 (C, C-5′), 140.04 (C, C-1), 124.26 (CH, C-2), 113.90 (C, C-2′), 110.92 (CH_2, C-9), 51.58 (Me, COO*Me*), 46.26 (CH, C-4), 37.20 (CH, C-3), 35.43 (CH_2, C-1″), 34.18 (CH_2, C-7″), 30.77 (CH_2, C-2″), 30.48 (CH_2, C-6), 29.04, 28.94 (CH_2, C-3″, C-4″, C-5″), 28.47 (CH_2, C-5), 24.95 (CH_2, C-6″), 23.75 (Me, C-7), 20.45 (Me, C-10).

(3R,4R)-5″-Methoxycarbonylethyl-Δ^6*-tetrahydrocannabinol* [**11**].—A solution of **9** (820 mg, 5.39 mmol) and **8d** (1.18 g, 4.43 mmol) in 10 ml of CH_2Cl_2 was added to a solution of *p*-toluenesulfonic acid (371 mg, 2.15 mmol) in CH_2Cl_2 (15 ml). The reaction mixture was stirred under Ar at room temperature for 6 h and refluxed for an additional period of 2 h. The solution was poured onto saturated Na_2CO_3 aqueous solution (100 ml) and ice (100 g), extracted with Et_2O, and dried with Na_2SO_4. Solvent evaporation in vacuo afforded 1.76 g of reaction crude. Cc yielded **11** (358 mg, 0.895, 20%): oil; $[\alpha]^{20}D$ −103.0° (*c*=1.26, $CHCl_3$); eims (70 eV) (rel. int.) *m/z* 400 (80), 385 (10), 369 (13), 357 (14), 332 (12), 325 (15), 317 (100), 258 (64), 257 (14), 243 (15), 175 (15), 174 (27), 43 (75); ir ν (film) 3331 (OH), 1700 (COOMe), 1648 (Ar), 1618 (C=C) cm^{-1}; ^1H nmr (300 MHz, $CDCl_3$) δ (ppm) 6.24 (1H, d, $J=1.57$ Hz, H-4′), 6.11 (1H, d, $J=1.57$ Hz, H-6′), 5.41 (1H, bd, $J=4.17$, H-6), 3.66 (3H, s, COOMe), 3.21 (1H, bdd, $J_1=16.28$, $J_2=4.53$ Hz, H-3), 2.69 (1H, td, $J_1=10.91$, $J_2=4.53$ Hz, H-4), 2.42 (2H, td, $J_1=8.35$, $J_2=2.02$ Hz, H-1″), 2.29 (2H, t, $J=7.51$, H-7″), 2.20–1.80 (4H, m, H-5, H-2), 1.68 (3H, bs, H-7), 1.36 (3H, s, H-10), 1.29 (10H, bs, H-2″–H-6″), 1.10 (3H, s, H-9); ^{13}C nmr (75 MHz, $CDCl_3$) δ (ppm) 174.65 (C, C-8″), 155.13 (C, C-3′), 154.60 (C, C-1′), 142.48 (C, C-5′), 134.87 (C, C-1), 119.35 (CH, C-6), 110.64 (C, C-2′), 109.95 (CH, C-4′), 107.69 (CH, C-6′), 76.68 (C, C-8), 51.61 (Me, COO*Me*), 44.97 (CH, C-4), 36.06 (CH_2, C-2), 35.38 (CH_2, C-1″), 34.17 (CH_2, C-7″), 31.66 (CH, C-3), 30.72 (CH_2, C-2″), 29.02 (CH_2, C-3″, C-4″, C-5″), 27.97 (CH_2, C-5), 27.64 (Me, C-10), 24.95 (CH_2, C-6″), 23.57 (Me, C-7), 18.56 (Me, C-9).

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