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FARNESYL-HOMOGENTISIC ACID DERIVATIVES FROM *OTOBA PARVIFOLIA**

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Key Word Index—*Otoba parvifolia*; Myristicaceae; xanthoxylol; phillygenol; farnesyl derivatives; oxocyclohexenyl-acetic acid; oxocyclopentanylpropionic acids; homogentisic acid pathway.

Abstract—The seeds of *Otoba parvifolia* contain six novel compounds, apparently derived from homogentisic acid, including 3-farnesyl-2,5-dihydroxybenzaldehyde, 2-(1′-farnesyl-2′-hydroxy-5′-oxocyclohex-3′-en-1′-yl)-acetic acid lactone, 3-(1′-farnesyl-2′-hydroxy-4′-oxocyclopentan-1′-yl)-3-methoxy (and ethoxy) propanoic acid lactones and methyl esters. New spectral evidence obtained for the known furofuran lignans xanthoxylol and phillygenol, isolated from the same source, was used as a basis for comments on the structure of horsfieldin.

INTRODUCTION

Seeds of *Otoba parvifolia* (Mkfg.) A. Gentry were collected in the Humaitá region of the Amazon valley by Dr. Hipólito F. Paulino Filho. Their kernels contain, besides sitosterol and the known furofuran lignans phillygenol (**1a**) and xanthoxylol (**1b**) [2], six new compounds **2**, **3**, **4a**, **4b**, **5a** and **5b**.

RESULTS

As easily verified by NMR comparison with models [3], compounds **1a** (xanthoxylol) and **1b** (phillygenol) belong to the *epi*-series of 2,6-diarylfurofuran lignans. Indeed, the NMR spectra of both compounds are similar with respect to the doublets representing equatorial (δ 4.8) and axial (δ 4.4) protons linked to the benzylic C-2 (δ 88) and C-6 (δ 82), respectively. The symmetrical structures in which both these hydrogens are equatorial or axial leads to single doublets for the oxybenzylic protons and carbons.

Xanthoxylol (for some unreported spectral data see Experimental) has been fully characterized in its laevorotatory form [3]. Both lignans isolated during the present work are dextrorotatory. The assignment of the relative positions of the guaiacyl and veratryl substituents in phillygenol is confirmed in the present report by a known method [4]. Addition of alkali to the compound in DMSO-d_6 solution produces a diamagnetic shift (δ 4.30→4.08) of the doublet at higher field which is thus due to the axial benzylic proton at C-6. In contrast the chemical shift of the doublet at lower field remains practically unchanged (δ 4.77→4.76) and represents the equatorial benzylic proton at C-2. Thus, as shown in **1b**, the guaiacyl, and not the veratryl, is linked to C-6 with the axial proton.

Comparison of the ^{13}C NMR data of **1b** with those of its phenolate furthermore confirm the 4-hydroxy-3-methoxyphenyl (guaiacyl) constitution of one of the aryl groups. Indeed, addition of alkali, as described above, produces a strong diamagnetic shift of the C-1″ signal (δ 132.36→120.49). C-1″ and the phenolate anion must thus keep a *para*-relationship [4]. Contrasting evidence was provided by a positive Gibbs test. This suggests the *para*-position with respect to the hydroxyl to be free of substitution, as in a 3-hydroxy-4-methoxyphenyl group. However, the Gibbs test is frequently misleading [5] and should not be considered definitive evidence, as in the case of horfieldin [6]. Hence, this additional 2,6-diarylfurofuran lignan of the *epi*-series may well again comprise a guaiacyl, and not a 3-hydroxy-4-methoxyphenyl unit, in spite of the positive Gibbs test.

Hydrogen and carbon counts by NMR spectroscopy combined with M_r weight determination by low resolution mass spectrometry led to the elementary formula $C_{22}H_{30}O_3$ for compound **2**. The three oxygens belong to one formyl (^{1}H NMR δ 9.7 *s*; ^{13}C NMR δ 196.22) and two hydroxyl groups (formation of a diacetate). The phenolic nature of the hydroxyl groups is indicated by UV shifts of maxima in the presence of base. Indeed, six of the carbons form an aromatic ring (as shown by ^{13}C NMR). The 15 additional carbons belong to a farnesyl unit, as evidenced by ^{1}H and ^{13}C NMR [7]. To complete the structural determination it suffices to localize two hydrogens, the two hydroxyls and the farnesyl on the benzaldehyde moiety. One of the hydroxyls forms a chelate with the formyl (strong UV shift in the presence of $AlCl_3$) and must hence occupy position C-2. The two aromatic protons are represented by doublets (J = 3.1 Hz) and can thus *a priori* occupy positions C-3, C-5 or C-4, C-6. Comparison of the ^{1}H NMR spectra of **2** and of its diacetate reveals the

*Part XXX in the series 'The Chemistry of Brazilian Myristicaceae'. For Part XXIX see ref. [1]. Based in part on the M.Sc. thesis presented by A.G.F. to Universidade de São Paulo (1985). Dedicated to the memory of Dr Hipólito F. Paulino Filho, a passionate observer of seed dispersal of Myristicaceae species by toucans in Amazonia.

second alternative to be correct. Indeed, acetylation produces comparable paramagnetic shifts of the proton doublets (δ +0.30 and +0.35) and a small diamagnetic shift of the benzylic methylene doublet (δ −0.13). In consequence the aromatic protons must occupy symmetrical positions with respect to the hydroxyls and the benzylic methylene of the farnesyl unit and a hydroxyl must be *ortho*-related.

The elementary formula of compound **3** ($C_{23}H_{32}O_3$) was determined as outlined for **2**. Although the peak at highest mass (*m/z* 356) in the electron impact mass spectrum of **3** was of very low intensity (<0.1%), it does represent the molecular ion. Indeed in the chemical ionization mass spectrum using NH_3 as reagent gas MH^+ is represented at *m/z* 357 by a peak of 59% relative intensity and the collisionally stabilized MNH_4^+ ion is represented by the base peak. The use of methane and *i*-butane leads to CI mass spectra with peaks at *m/z* 357 of 100% relative intensity (Table 1).

^1H (Table 2) and ^{13}C (Table 3) NMR spectra of **3** indicate the existence of a farnesyl group linked to a chiral quaternary carbon (two ^1H NMR *dd* at δ2.30 and 2.43). The presence of the additional moiety **6** and of two isolated methylenes was also verified by NMR spectra. Unit **6** takes care of two oxygens, one belonging to the α,β-unsaturated ketone evidenced by UV (λ_{max} 340 nm) and IR (ν_{max} 1683 cm^{-1}) maxima. The third oxygen must belong to the carbonyl of a δ-lactone (ν_{max} 1742 cm^{-1}) and must thus be linked to the oxy-group of **6**. Indeed only in this way can existence of two methylenes, none linked directly to oxygen, be conceived. The proton shifts of these methylenes agree well with the proposed adjacent functionalities. Inspection of models indicated that the HC_2, —C_3,H dihedral angles are *ca* 40° for a *cis*- and *ca* 100° for a *trans*-ring junction. Since the corresponding proton–proton coupling constant is 6 Hz, only the first alternative can be correct. Relatively large long range coupling constants connect several of the protons of the bicyclic system. Specially noteworthy is the one between H-2α and H-3′, representing a five-bond coupling through a zig-zag pathway.

Table 1. CI mass spectra of compound **3***

	m/z	NH_3	CH_4	*iso*-C_4H_{10}
		relative intensity		
MNH_4^+	374	100	—	—
$MNH_4^+ - H_2O$	355	17	—	—
$MC_3H_5^+$	397	—	weak	—
$MC_2H_5^+$	385	—	13	—
MH^+	357	59	100	100
$[M-H]^+$	355	18	91	32
$MH^+ - H_2O$	339	10	98	28
$MH^+ - CO_2$	313	0.6	7	—
$MH^+ - C_5H_8$	289	2	34	17
Fa^+	205	5	44	45
$[Fa-C_4H_8]^+$	149	0.3	26	12
$[Fa-C_5H_8]^+$	137	4	91	62
$[Fa-C_6H_{12}]^+$	121	—	10	3
$[M-Fa]^+$	151	—	4	2
$[M-Fa-O]^+$	135	0.6	45	14
$MH^+ - HFa - CO$	123	0.8	27	15
$MH^+ - HFa - C_2H_2O$	109	0.6	22	13
$MH^+ - HFa - CO_2$	107	—	7	1

*Fa farnesyl.

Some samples of **3** contained traces of other compounds, most probably one or more of the corresponding epoxides. Although their ^1H NMR and electron impact mass spectra were practically superimposable on the corresponding spectra of **3**, chemical ionization mass spectrometry showed additional peaks at 390 $[MNH_4]^+$, 371 $[M-1]^+$ and 355 $[MH-H_2O]^+$ in ammonia, 401 $[MC_2H_5]^+$, 373 $[MH]^+$, 371 and 355 in methane and 373, 371 and 355 in *i*-butane.

The elementary formulas for compounds **4a** ($C_{24}H_{36}O_4$) and **4b** ($C_{25}H_{38}O_4$) were determined as outlined for **2**. Comparisons of the ^1H and ^{13}C NMR spectra of the compounds indicated only one structural difference, the presence of a methoxyl in **4a** vs an ethoxyl in **4b**. All other structural features are shared by both substances. Evidence for the farnesyl stems again from ^1H (Table 2) and ^{13}C (Table 3) NMR data. Indeed, a hexahydro derivative is formed upon catalytic hydrogenation of **4a** (Table 3). The farnesyl is linked to a quaternary carbon as shown by ^1H NMR coupling data for its terminal methylene (δ 2.24, *d*, J = 8 Hz). The two additional moieties (**7**, **8**) and an isolated methylene were also formulated by consideration of ^1H NMR coupling constants (Table 2). Chemical shifts of the methine (δ 3.55) and methylene (δ 2.50 and 2.90) protons of **7** demonstrate the connection of the former group to an ether oxygen and of the latter to a carbonyl. Analogously, in the case of **8** the methine (δ 5–5.1) should be vicinal to the oxy-group of an ester and the methylene (δ 1.73 and 2.17) should again be linked to a carbonyl. Finally an isolated methylene (δ 2.48 and 2.59) must be vicinal to a carbonyl.

The connection of these partial structures as shown in **4a** and **4b** is perceived by analysis of the W-coupling (J = 2 Hz) between one of the methylene protons of each, C-3′ (see **8**) and C-5′ (the isolated methylene). This requires both these methylenes to be linked to the same carbonyl. All possible decoupling experiments were performed and are consistent with these structures.

IR carbonyl absorptions of **4a** (1730 and 1721 cm^{-1}), hexahydro-**4a** (1742 and 1712 cm^{-1}) and **4b** (1743 and 1722 cm^{-1}) confirm the existence of a cyclopentanone and a δ-lactone (1745 and 1735 cm^{-1}) rather than a γ-lactone and a cyclohexanone (1770 and 1715 cm^{-1}) [8].

The elementary formulas $C_{25}H_{40}O_5$ (**5a**) and $C_{26}H_{42}O_5$ (**5b**) differ from the formulas respectively of **4a** and **4b** by the additional presence of the elements of MeOH. In structural terms, this evidence leads to **5a** and **5b**. Again, the IR carbonyl maxima (1731 and 1713 cm^{-1} for **5a**; 1727 and 1704 cm^{-1} for **5b**) demonstrate the presence of a cyclopentanone unit and of an ester. In contradistinction to **4a** and **4b**, however, the IR spectra of **5a** and **5b** also indicate the presence of a hydroxyl (3650–3300 cm^{-1}) and the NMR spectra indicate the presence of an additional methoxyl (^1H δ 3.63, *s*; ^{13}C δ 51.34).

The relative configurations of the chiral centres indicated in the formulas **4a**, **4b**, **5a** and **5b** are based on the *W*-couplings, again confirmed by double resonance experiments, between H-3 and H-2′.

DISCUSSION

The biosynthesis of tocopherols and tocotrienols involves homogentisic acid **9** and geranylgeraniol [9]. The

Table 2. ^{1}H NMR spectral data (300 MHz, $CDCl_3$)

H	3	4a	4b	5a	5b
2α	2.20 *ddd*	2.90 *ddd*	2.86 *ddd*	2.82 *dd*	2.80 *dd*
2β	2.26 *ddd*	2.52 *dd*	2.54 *dd*	2.62 *dd*	2.61 *dd*
3	—	3.55 *ddd*	3.65 *m*	3.7 *m*	3.8 *m*
2′	5.0–5.1 *m*	5.0–5.1 *m*	4.9–5.1 *m*	4.2 *ddd*	4.2 *m*
3′	7.13 *ddd*	—	—	—	—
3′α	—	2.17 *dd*	2.16 *dd*	2.25 *dd*	2.23 *dd*
3′β	—	1.73 *dt*	1.73 *dt*	2.0 *m*	2.0 *m*
4′	6.13 *d*	—	—	—	—
5′α	—	2.59 *d*	2.59 *d*	2.59 *d*	2.65 *d*
5′β	—	2.48 *dd*	2.49 *dd*	2.56 *d*	2.57 *d*
6′α	2.67 *d*	—	—	—	—
6′β	2.57 *dd*	—	—	—	—
1″	2.30 *bdd*	2.24 *d*	2.23 *d*	2.36 *m*	2.36 *m*
1″	2.43 *bdd*				
4″, 5″ 8″, 9″	1.9–2.1 *m*	1.95–2.1 *m*	1.95–2.1 *m*	1.95–2.1 *m*	1.95–2.1 *m*
2″	5.0–5.1 *m*	5.0–5.1 *m*	4.9–5.1 *m*	4.96 *bt*	4.97 *bt*
6″, 10″				5.07 *m*	5.08 *m*
12″	1.68 *d*	1.68 *s*	1.68 *s*	1.68 *s*	1.68 *s*
13″	1.59 *s*	1.59 *s*	1.59 *s*	1.59 *s*	1.60 *s*
14″	1.60 *s*	1.60 *s*	1.60 *s*	1.60 *s*	1.60 *s*
15″	1.64 *s*	1.61 *s*	1.61 *s*	1.60 *s*	1.60 *s*
MeO-3	—	3.42 *s*	—	3.41 *s*	—
CHO-3	—	—	3.64 *dq*	—	3.70 *dq*
CHO-3	—	—	3.51 *dq*	—	3.48 *dq*
$\underline{Me}CH_2O$-3	—	—	1.23 *t*	—	1.20 *t*
COOMe	—	—	—	3.63	3.63

Coupling constants (J) in Hz; position of coupled proton indicated in brackets: **3** H-2α 14.5 (2β), 3 (2′), 1 (3′); H-2β 14.5 (2α), 2.5 (2′), 1.5 (6′β); H-3′ 10 (4′), 6 (2′), 1 (2α); H-4′ 10 (3′); H-6′α 19.5 (6′β); H-6′β 19.5 (6′α), 1.5 (2β); H-1″ 14.5 (1″), 9 (2″); H-1″ 14.5 (1″), 6.5 (2″); H-12″ 1 (10″); **4a** H-2α 16 (2β), 6 (3), 1 (2′); H-2β 16 (2α), 12 (3); H-3 12 (2β), 6 (2α), 2.5 (2′); H-3′α 14.5 (3′β), 4.5 (2′); H-3′β 14.5 (3′α), 2 (2′), 2 (5′β); H-5′α 19 (5′β); H-5′β 19 (5′α), 2 (3′β); H-1″ 8 (2″). **4b** H-2α 15.5 (2β), 6 (3), 1 (2′); H-2β 15.5 (2α), 12 (3); H-3′α 14.5 (3′β), 4.5 (2′); H-3′β 14.5 (3′α), 2 (2′), 2 (5′β); H-5′α 19 (5′β); H-5′β 19 (5′α), 2 (3′β); H-1″ 7.5 (2″); CHO-3 9, 7; CHO-3 9,7; $\underline{H}_3CCH_2O$-3 7. **5a** H-2α 15.5 (2), 5 (3); H-2β 15.5 (2), 3.5 (3); H-2′ 10 (3′α), 4.5 (3′β), 1.5 (3); H-3′α 14 (3′β), 10 (2′); H-5′α 16 (5′β); H-5′β 16 (5′α); H-2″ 7 (1″). **5b** H-2α 15.5 (2β), 5.5 (3); H-2β 15.5 (2α), 3.5 (3); H-3′α 14 (3′β), 9.5 (2′); H-5′α 16 (5′β); H-5′β 16 (5′α); H-2″ 7 (1″); CHO-3 14, 7; CHO-3 11,7; $\underline{H}_3CCH_2O$-3 7.

homogentisic acid is mostly decarboxylated to methyl-*p*-quinol, although in at least one case a homogentisic acid derived lactone, with retention of all eight carbons, has been isolated [7]. It is probable that the benzaldehyde **2** also stems from homogentisic acid, even if *via* oxidative decarboxylation and alkylation by farnesol.

The cyclohexenone **3** and the cyclopentanones **4a**, **4b**, **5a** and **5b** also each include a farnesyl moiety in addition to a unit of eight carbons. This fact justifies the hypothesis that homogentisic acid may also be responsible for the synthesis of these derivatives. Indeed alkylation by farnesol at an alternative active position could lead to **10**. Direct reduction of this common intermediate would give **3**, while addition of water (**10**→**11**), 1′,2′-rearrangement of CH_2CO_2H and ring contraction (**11**→**12**), again finalized by reduction, would give **4** and **5**, respectively.

A homogentisic acid ring-cleavage pathway has been observed [10] to lead to acetate in the plant family Droseraceae.

EXPERIMENTAL

Isolation of the constituents. Fruits of *Otoba parvifolia* were collected from a specimen identified by Dr William A. Rodrigues, INPA, Manaus. The seeds were separated, dried, reduced to powder (100 g) and extracted with $CHCl_3$ at room temp. The soln. was evapd and the residue (47 g) was crystallized from MeOH. Filtration gave fats (37 g) and a soln which was evapd. The residue (10 g) was submitted to CC (silica gel 240 g). Elution was performed with $CHCl_3$, 50 ml for each of frs 1–9, and 500 ml for each of fractions 10 onward. Evapn of frs 1–9 gave fatty material (682 mg). Analogously fr. 10 gave a residue A (447 mg), frs 11–13 gave B (287 mg), fr. 14 gave C (68 mg), frs 15 and 16 gave D (350 mg), frs 17 and 18 gave E (54 mg), frs 19–23 gave F (380 mg), frs 24–28 gave G (800 mg). Residue A was submitted to CC (30 g silica gel, elution with C_6H_6, 15 ml for each fraction). Fr. 9 was crystallized from EtOH giving sitosterol (15 mg). Residue B was purified by prep. TLC (silica gel, C_6H_6–Et_2O, 19:1) to yield **2** (45 mg). Residue C was purified by

Table 3. ^{13}C NMR spectral data (20 MHz, $CDCl_3$, δ)

C	3	4a	5a	Hexahydro-4a
1	168.96	168.71	171.94	168.34
2	33.63[a]	32.72	37.60	32.61
3	...	79.84	80.69	79.44
1′	45.99	46.63	49.93	45.67
2′	69.78	73.67	67.08	73.51
3′	144.46	38.58	39.34	39.09
4′	130.67	206.90	209.71	206.50
5′	200.31	41.08	39.60	40.79
6′	39.72	—	...	...
1″	33.53[a]	30.40	34.00	32.99[a]
2″	117.57	117.50	117.85	32.49[a]
3″	140.46	140.44	139.66	30.63[b]
4″	39.99	40.05	39.99	36.82[c]
5″	26.46	26.50	26.50	24.07[d]
6″	123.85	123.84	123.84	39.09[e]
7″	135.34	135.44	135.32	30.07[b]
8″	39.82	39.78	39.74	37.07[c]
9″	26.78	26.80	26.80	24.49[d]
10″	124.31	124.32	124.42	39.28[e]
11″	131.28	131.35	131.23	27.67
12″	25.69	25.68	25.64	22.42
13″	17.69	17.66	17.65	22.42
14″	16.05	16.06	16.02	19.23[f]
15″	16.41	16.36	16.35	19.39[f]
CHOMe	—	56.40	56.72	56.06
COOMe	—	—	51.34	—

[a–f]Chemical shifts marked by identical letters are interchangeable.

prep. TLC (silica gel, C_6H_6–Et_2O, 1:1) to yield **4b** (14 mg). Residue D, treated in the same way, gave **4a** (100 mg), **3** (84 mg) and **1a** (15 mg). Residue E was purified by prep. TLC (silica gel, C_6H_6–Me_2CO, 9:1) to give **5b** (13 mg). Residue F was purified by prep. TLC (silica gel, $CHCl_3$–AcOEt, 7:3) to yield **1b** (70 mg). Residue G gave, by successive crystallization from *n*-hexane, **5a** (12 mg).

rel-(1R,2R,5R,6S)-2-*Piperonyl*-6-*guaiacyl*-3,7-*dioxabicyclo*-[3.3.0]*octane* (*xanthoxylol*, **1a**). Mp 138–140° (MeOH), lit. [11] mp 140–142° IR ν_{max}^{KBr} cm^{-1}: 3472 (OH), 1601, 1485 (ArH). ^1H NMR (80 MHz, $CDCl_3$): δ 2.75–3.0 (*m*, H-1), 3.2–3.4 (*m*, H-5), 4.75 (*d*, $J = 5$ Hz, H-2), 4.35 (*d*, $J = 6.8$ Hz, H-6), 4.13 (*m*, 1H), 3.92 (*m*, 2H) and 3.27 (*m*, 1H) (2H-4, 2H-8), 3.85 (*s*, OMe), 5.85 (*s*, O_2CH_2), 6.7–6.8 (*m*, 6ArH). ^{13}C NMR (20 MHz, $CDCl_3$): δ 50.01 (C-1), 54.34 (C-5), 70.82 (C-4), 69.42 (C-8), 81.93 (C-2), 87.54 (C-6), 132.16 (C-1′), 132.89 (C-1″), 145.24 (C-3′), 146.62 (C-3″), 146.62 (C-4′), 147.48 (C-4″), 106.28 (C-2′), 107.96 (C-2″), 108.54 (C-5′), 114.16 (C-5′5″), 118.55 (C-6′), 119.04 (C-6″), 55.81 (OMe), 100.79 (O_2CH_2). MS *m/z* (rel. int.): 356 $[M]^+$ (5), 151 (18), 150 (22), 149 (100), 137 (24), 135 (34), 123 (16), 121 (30). $[\alpha]_D + 126°$ ($CHCl_3$; *c* 0.1, 25°); lit. [11] $-117°$ ($CHCl_3$; *c* 0.5, 16°).

rel-(1R,2R,5R,6S)-2-*Veratryl*-6-*guaiacyl*-3,7-*dioxabicyclo*-[3.3.0]*octane* (*phillygenol*, **1b**). Mp 134–135° (MeOH), lit. [12] mp 134.5°. IR ν_{max}^{KBr} cm^{-1}: 3480 (OH), 1601, 1516 (ArH). ^1H NMR (80 MHz, $CDCl_3$/DMSO-d_6/DMSO-d_6 + 0.5 N NaOD in D_2O): δ 2.75–3.05/2.7–3.0/2.88 (*m*, H-1), 3.2–3.45/3.0–3.3/3.1 (*m*, H-5), 4.84/4.77/4.76 (*d*, $J = 5$ Hz, H-2), 4.4/4.3/4.08 (*d*, $J = 7.5$ Hz, H-6), 3.2–4.1/3–4/3.1–3.9 (*m*, 2H-4, 2H-8), 3.78, 3.84, 3.87/3.37/3.6, 3.7 (*s*, 3 OMe), 5.87/8.33/– (*s*, OH), 6.8–6.9 (6H)/6.87 (4H), 6.7 (2H)/6.84 (3H), 6.4 (2H), 6.09 (1H) (6 ArH). ^{13}C NMR (20 MHz, $CDCl_3$/DMSO-d_6/DMSO-d_6 + 0.5 N NaOD in D_2O): δ 50.23/49.35/49.29 (*d*, C-1), 54.55/53.89/53.20 (*d*, C-5), 71.10/70.33/70.36 (*t*, C-4), 68.75/68.82/68.16 (*t*, C-8), 82.14/81.24/81.28 (*d*, C-2), 87.76/86.98/88.73 (*d*, C-6), 131.14/131.22/131.34 (*s*, C-1′), 133.17/132.36/120.49 (*s*, C-1″), 146.82/147.52/148.37 (*s*, C-3′), 145.44/146.00/150.71 (*s*, C-3″), 148.17/147.64/147.46 (*s*, C-4′), 149.04/148.50/161.57 (*s*, C-4″), 108.88/109.51/109.44 (*d*, C-2′), 109.25/110.34/108.50 (*d*, C-2″), 111.29, 111.57, 111.51 (*d*, C-5′), 114.35/115.16/116.39 (*d*, C-5″), 119.19/ 118.59/117.91 (*d*, C-6′), 117.85/117.56/117.49 (*d*, C-6″), 56.0/55.59, 55.47/54.55, 55.42 (*q*, 3 OMe). MS *m/z* (rel. int.): 372 $[M]^+$ (59), 219 (11), 205 (17), 177 (38), 166 (25), 165 (37), 163 (15), 152 (25), 151 (100), 137 (44). $[\alpha]_D^{21} + 128°$ ($CHCl_3$; *c* 0.8); lit. [12] $+121.7°$. Acetate: ^1H NMR (80 MHz, $CDCl_3$): δ 2.8–3.05 (*m*, H-1), 3.25–3.5 (*m*, H-5), 4.84 (*d*, $J = 5$ Hz, H-2), 4.48 (*d*, $J = 7.5$ Hz), 3.25–3.5, 3.6–3.8, 4.15 (*m*, 2H-4, 2H-8), 3.80, 3.87, 3.90 (*s*, 3 OMe), 6.9–7 (*m*, 4 ArH), 6.8 (*s*, 2 ArH), 2.3 (*s*, OAc).

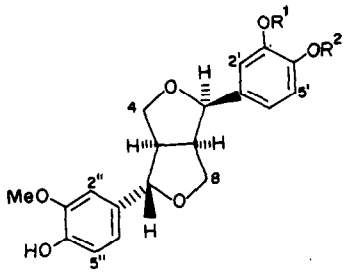
3-Farnesyl-2,5-dihydroxybenzaldehyde (**2**). Mp 86–90° (hexane). UV λ_{max}^{MeOH} nm: 240, 266 (ε 19 500, 11 950); $\lambda_{max}^{MeOH + AlCl_3}$ nm: 235, 266, 294 ($\varepsilon > 24\,000$, 9250, 4100); $\lambda_{max}^{MeOH + NaOH}$ nm: 230, 250, 277 ($\varepsilon > 24\,000$, 19 150, 10 950). IR ν_{max}^{KBr} cm^{-1}: 3291, 1630, 1581, 1479, 1457, 1378, 1302, 1298, 1150, 981. ^1H NMR (60 MHz, $CDCl_3$): δ 9.64 (*s*, CHO), 10.64 (*s*, OH), 6.7 and 6.85 (two *d*, $J = 3.1$ Hz, H-4, H-6), 3.28 (*d*, $J = 7.8$ Hz, 2H-1′), 4.9–5.3 (*m*, H-2′, H-6′, H-10′, OH), 1.9–2.2 (*m*, 2H-4′, 2H-5′, 2H-8′, 2H-9′), 1.66 (*s*, 3H-12′), 1.56 (*s*, 3H-13′, 3H-14′, 3H-15′). ^{13}C NMR (20 MHz, $CDCl_3$): δ 125.37 (C-1), 137.69 (C-2, C-5), 135.18 (C-3), 124.07 (C-4), 115.35 (C-6), 196.22 (CHO), 26.57 (C-1′), 120.90 (C-2′), 135.18 (C-3′), 39.78 (C-4′, C-8′), 26.79 (C-5′), 124.44 (C-6′, C-10′), 132.07 (C-7′), 27.10 (C-9′), 131.34 (C-11′), 25.67 (C-12′), 16.15 (C-13′), 16.06 (C-14′, C-15′). MS *m/z* (rel. int.): 342 $[M]^+$ (5), 205 (7), 191 (36), 177 (13), 151 (28), 137 (7), 135 (10), 107 (12), 69 (100), 41 (53). Diacetate: ^1H NMR (60 MHz, CCl_4): δ 9.7 (*s*, CHO), 7.0 and 7.2 (two *d*, $J = 3.1$ Hz, H-4, H-6), 2.15 and 2.25 (two *s*, 2AcO), 3.15 (*d*, $J = 7.8$, 2H-1′), 4.75–5.25 (*m*, H-2′, H-6′, H-10′), 1.85–2.05 (*m*, 2H-4′, 2H-5′, 2H-8′, 2H-9′), 1.6 (*s*, 3H-12′), 1.55 (*s*, 3H-13′, 3H-14′, 3H-15′).

rel-(1′R,2′R)-2-(1′-*Farnesyl*-2′-*hydroxy*-5′-*oxocyclohex*-3′-*en*-1′-*yl*)-*acetic acid lactone* (**3**). Oil, UV $\lambda_{max}^{CHCl_3}$ nm: 340 (ε 1300). IR ν_{max}^{film} cm^{-1}: 1742, 1683, 1440, 1377, 1313, 1206, 1162, 1093, 1069, 1063, 1040, 968. NMR ^1H (Table 2), ^{13}C (Table 3). EIMS *m/z* (rel. int.): 356 $[M]^+$ (0.1), 245 (0.8), 219 (16), 160 (14), 145 (12), 137 (20), 136 (48), 135 (41), 134 (16), 133 (10), 123 (13), 121 (22), 109 (18), 108 (10), 107 (44), 95 (23), 93 (30), 91 (12), 83 (10), 81 (57), 79 (11), 71 (12), 69 (100). CIMS (Table 1). $[\alpha]_D^{20} + 214°$ ($CHCl_3$; *c* 0.07).

rel-(3S,1′R,2′S)-3-(1′-*Farnesyl*-2′-*hydroxy*-4′-*oxocyclopentan*-1′-*yl*)-3-*methoxypropanoic acid lactone* (**4a**). Mp 67–69° (MeOH). IR ν_{max}^{film} cm^{-1}: 1730, 1721, 1439, 1377, 1093. ^1H NMR (Table 2), ^{13}C (Table 3). MS *m/z* (rel. int.): 388 $[M]^+$ (2), 286 (3), 277 (4), 251 (6), 233 (9), 205 (2), 184 (9), 137 (13), 136 (10), 135 (10), 121 (11), 107 (13), 93 (21), 69 (100), 55 (17). $[\alpha]_D^{20} + 28.1°$ ($CHCl_3$; *c* 0.037). *Hexahydro-derivative*. Oil, IR ν_{max}^{film} cm^{-1}: 1742, 1712, 1460, 1377, 1304, 1208, 1115, 1052, 983. ^{13}C NMR (Table 3). MS *m/z* (rel. int.): 394 $[M]^+$ (3), 350 (6), 155 (31), 85 (53), 81 (33), 71 (54), 57 (100), 43 (99).

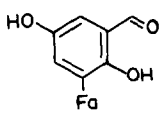
rel-(3S,1′R,2′S)-3-(1′-*Farnesyl*-2′-*hydroxy*-4′-*oxocyclopentan*-1′-*yl*)3-*ethoxypropanoic acid lactone* (**4b**). Mp 55° (MeOH). IR ν_{max}^{film} cm^{-1}: 1743, 1722, 1450, 1378, 1304, 1239, 1102. ^1H NMR (Table 2). MS *m/z* (rel. int): 402 $[M]^+$ (7), 346 (8), 265 (21), 247 (21), 180 (39), 137 (35), 136 (58), 81 (60), 69 (100), 41 (57). $[\alpha]_D^{20} + 37.7°$ ($CHCl_3$; *c* 0.018).

Methyl rel-(1′R,2′S)-3-(1′-*farnesyl*-2′-*hydroxy*-4′-*oxocyclopentan*-1′-*yl*)-3-*methoxy propanoate* (**5a**). Oil, IR ν_{max}^{film} cm^{-1}: 3650–3300, 1731, 1713, 1436, 1378, 1322, 1186, 1165, 1081, 1019,



1a $R^1 - R^2 = CH_2$

1b $R^1 = R^2 = Me$



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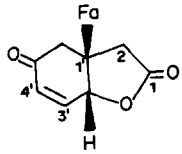

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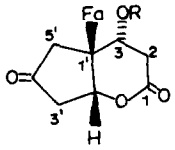
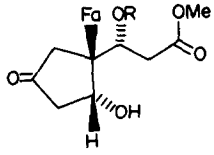


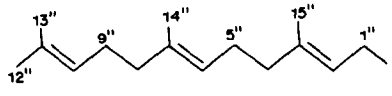
4a R = Me

4b R = Et

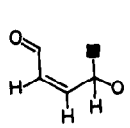


5a R = Me

5b R = Et



Fa = farnesyl



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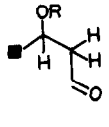

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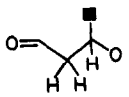

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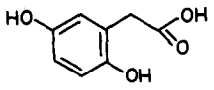

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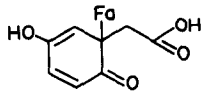

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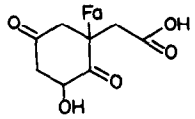

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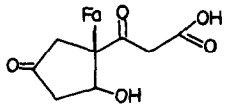

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989. NMR ^1H (Table 2), ^{13}C (Table 3). MS *m/z* (rel. int.): 420 $[M]^{+\cdot}$ (1), 388 (3), 332 (1), 319 (1), 286 (1), 277 (3), 251 (8), 233 (11), 184 (8), 166 (15), 137 (14), 136 (22), 135 (17), 121 (9), 107 (13), 93 (23), 81 (34), 69 (100), 41 (45). $[\alpha]_D^{20} -243°$ ($CHCl_3$; *c* 0.08).

Methyl rel-(1'R,2'S)-(1'-farnesyl-2'-hydroxy-4'-oxocyclopentan-1'-yl)-3-ethoxypropanoate (**5b**). Oil, IR ν_{max}^{film} cm^{-1}: 3650–3300, 1727, 1704, 1427, 1372, 1337, 1186,1158, 1081. ^1H NMR (Table 2). MS *m/z* (rel. int.): 434 $[M]^{+\cdot}$ (1), 402 (2), 346 (1), 291 (1), 287 (3), 286 (1), 265 (8), 247 (9), 180 (5), 137 (14), 136 (20), 135 (21), 121 (10), 107 (15), 93 (25), 69 (100), 55 (18), 41 (44). $[\alpha]_D^{20} -238°$ ($CHCl_3$; *c* 0.09).

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REFERENCES

1. Kato, M. J., Paulino Filho, H. F., Yoshida, M. and Gottlieb, O. R. (1986) *Phytochemistry* **25**, 279.
2. Pelter, A. and Ward, R. S. (1978) in *Chemistry of Lignans*, pp. 227–275 (Rao, C. B. S., ed.). Andhra University Press, Andhra Pradesh.
3. Pelter, A., Ward, R. S., Venkata Rao and Sastry, K. V. (1976) *Tetrahedron* **32**, 2783.
4. Highet, R. J. and Highet, P. F. (1965) *J. Org. Chem.* **30**, 902.
5. Mesquita, A. A. L., Corrêa, D. de B., Gottlieb, O. R. and Magalhães, M. T. (1968) *Anal. Chim. Acta* **42**, 311.
6. Gunatilaka, A. A. L., Silva, A. M. Y. J. de, Sotheeswaran, S. and Tillekeratne, L. M. V. (1982) *Phytochemistry* **21**, 2719.
7. Vieira, P. C., Gottlieb, O. R. and Gottlieb, H. E. (1983) *Phytochemistry* **22**, 2281.
8. Nakanishi, K. (1962) *Infrared Absorption Spectroscopy*. Holden-Day, San Francisco.
9. Haslam, E. (1974) *The Shikimate Pathway*. Wiley, New York.
10. Durand, R. and Zenk, M. H. (1974) *Phytochemistry* **13**, 1483.
11. Abe, F., Yahara, S., Kubo, K., Nonaka, G., Okabe, H. and Nishioka, I. (1974) *Chem. Pharm. Bull.* **22**, 2650.
12. Gripenberg, J. (1949) *Acta Chem. Scand.* **3**, 898.