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ACYLRESORCINOLS FROM *VIROLA SEBIFERA* AND *VIROLA ELONGATA**

MASSUO J. KATO, LUCIA M. X. LOPES,† HIPÓLITO F. PAULINO FO.,† MASSAYOSHI YOSHIDA and OTTO R. GOTTLIEB

Instituto de Química, Universidade de São Paulo, 05508 São Paulo SP, Brazil

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Key Word Index—*Virola sebifera*; *V. elongata*; Myristicaceae; fruits; arylacyl-2,6-dihydroxybenzenes; arylacyl-2,4,6-trihydroxybenzene; arylacylcyclohexan-2,6-dione.

Abstract—The fruits of *Virola sebifera* and *V. elongata* (Myristicaceae) contain three ω-phenylundecanoyl-substituted compounds, a 2,6-dihydroxybenzene, a 2,6-dihydroxy-4-methoxybenzene and a 3-hydroxycyclohexan-2,6-dione. Three additional 2,6-dihydroxybenzenes are substituted by hexadecanoyl, hexadec-4*Z*-enoyl and 8-hydroxyoctadec-4*Z*-enoyl groups.

INTRODUCTION

The fruits of *Virola sebifera* Aubl. (Myristicaceae) have been found to contain six lignans [2, 3] and 19 neolignans [2, 4, 5], in addition to the polyketide, **1a** [4]. This paper describes the isolation of further polyketides, **3a**, **4a** (in form of its acetate **4b**), **5**, **1b**, **2**, **3a** and **5**; the first three from the same plant material and the latter four from the fruits of *V. elongata* (Benth.) Warb.

RESULTS AND DISCUSSION

Spectral comparison (Table 1) of the known compound, **1a**, ($C_{23}H_{30}O_3$) [4], and the novel **1b** ($C_{24}H_{32}O_4$) revealed the replacement of one of the aromatic protons in the former by a methoxyl in the latter. Since this includes a symmetrical phloroglucinol unit (^{1}H NMR: δ5.95, 2 ArH, *s*) with two chelatable hydroxyl groups (δ10.6, 2 OH, *br s*), its structure is defined as **1b**.

A similar comparison of **1a** [4] with **2** ($C_{22}H_{36}O_3$) revealed the termination of the methylene chain by a methyl in the latter against a phenyl in the former. The chemical shift and multiplicity data of the methyl signal (^{1}H NMR: δ0.95, *t*, $J = 7$ Hz) are consistent with formula **2** for the compound.

Compound **3a** ($C_{22}H_{34}O_3$), upon catalytic hydrogenation, gave a dihydro derivative, $C_{22}H_{36}O_3$ identical with **2**. Compound **3a** is, thus, a dehydro hexadecanoyl resorcinol. The double bond should be separated by two CH_2 groups from the carbonyl since the ^{1}H NMR spectrum shows signals for two α-protons (δ3.15, *t*, $J = 7$ Hz) and for four allylic protons (δ2.1–1.6). A higher degree of equivalence would be expected for the latter two proton pairs had they been situated at a greater distance from the carbonyl. Besides, double resonance at the allylic methylene frequencies (δ1.82) collapses the triplets, due to both the α-protons and the olefinic protons, to singlets. The ^{13}C NMR spectra of **3a** and of the epoxide of its diacetate (**6**) (Table 2) not only confirm these deductions, but also indicate the *Z*-geometry of the double bond. The relevant fact concerns the chemical shift, δ27.6 ± 0.4, of the α-carbons to the double bond and the epoxide group in the model *Z*-compounds, **7** and **8**, against δ32.4 ± 0.2 for the analogous carbons in the model *E*-compounds, **9** and **10** [6]. In **3a** and **6** the signal assigned to C-6′ appears at δ27.5 ± 0.3, further evidence for the *Z*-geometry of the double bond. The signal due to the other allylic methylene would also be expected to occur at δ27.5 if more than two methylenes separated the double bond from the carbonyl. This signal, in fact, appears at δ23.1 ± 0.5 suggesting that C-3′ feels not only the γ-effect, which it also exerts reciprocally on C-6′, but also the γ-effect transmitted by the carbonyl.

Compound **4b** was isolated after acetylation (acetic anhydride–pyridine) of a benzene extract. The spectra of **3b** and **4b** were closely comparable with respect to the carbon and proton signals representative of the aromatic positions, as well as of the five initial (C-1′–C-5′) and three terminal positions of the aliphatic side chain (Table 2). In opposition to **3b**, which includes seven CH_2 groups between these two aliphatic moieties, **4b** includes eight CH_2 groups and one AcOCH group (^{1}H NMR: δ5–5.6; ^{13}C NMR: δ74.9, *d*). IR ($\nu_{\max}$ cm^{-1}: 1770, 1725) and mass spectra ($[M]^+$ 576) are consistent with this fact. Among the methylene carbon resonances which remain to be assigned, two appear at a relatively low field (δ34.6 and 31.2), two at a relatively high field (δ27.2 and 25.1) and five at the normal frequency (δ29 ± 0.3). This indicates the acetoxyl supporting methine to be flanked by two ethylenes, the vicinal methylenes sensing the deshielding β-effect of the oxy group and the non-vicinal methylenes sensing its shielding γ-effect. The occurrence of one of the latter CH_2 resonances at a relatively high field (δ25.1) testifies for an additional γ-effect and indicates the connection of the entire $(CH_2)_2CHOAc(CH_2)_2$ group directly to the *cis*-double bond, as shown in **4b**. Either **4a** or an *O*-acetyl derivative of **4a** may, thus, represent the natural compound.

The mass spectrum of compound **5** shows, in addition

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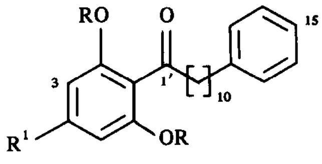
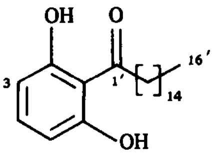
*Part XXIV in the series "The Chemistry of Brazilian Myristicaceae". For Part XXIII see ref. [1]. Taken from parts of the doctorate thesis of L.M.X.L. and the M.Sc. thesis of M.J.K. presented to the Universidade de São Paulo, 1983 and 1984, respectively.

†Present address: Instituto de Química, Universidade Estadual Paulista, 14800 Araraquara SP, Brazil.



1a R = R^1 = H
1b R = H, R^1 = OMe
1c R = Ac, R^1 = H



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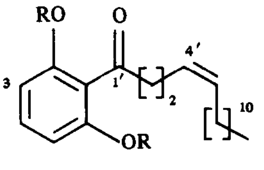

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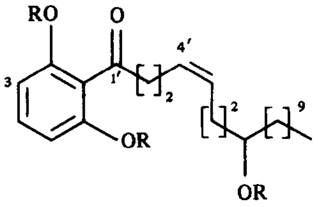
3b R = Ac



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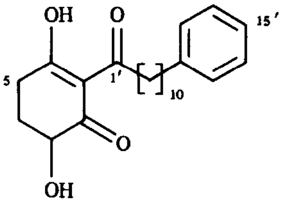

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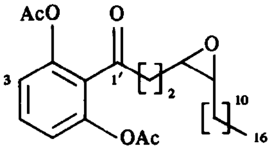

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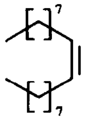

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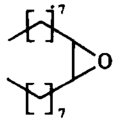

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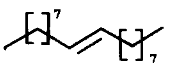

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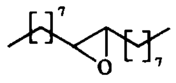

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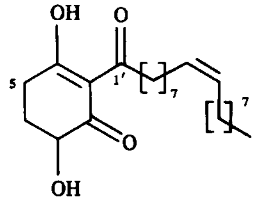

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to all the peaks of the analogous spectrum of **1a** ($C_{23}H_{30}O_3$) only a molecular ion peak at *m/z* 372 corresponding to $C_{23}H_{32}O_4$. The facile transformation of **5** into **1a** in the mass spectrometer can be reproduced on a preparative scale by trifluoroacetic acid catalysed dehydration. Attempted acetylation (acetic anhydride–pyridine) of **5** produces **1c**. ^{1}H and ^{13}C NMR spectra of **5** and **1a** are superimposable with respect to the signals corresponding to the 11-phenylundecanoyl moieties. The resorcinol group of **1a**, however, is replaced in **5** by the unit shown in the formula. The close proximity of all pertinent ^{13}C NMR signals of **5** and of the model compound **11** [7] (Table 1) excludes the only alternative possible. Analogy of data obtained for **5** and **11** extends to UV [λ_{max} nm: 230, 275 (**5**), 233, 274 (**11**) [7]], IR [ν_{max} cm^{-1}: 3450, 1650 (**5**), 3420, 1665 (**11**) [7]] and ^{1}H NMR [δ 14 (*s*, OH-6) (**5**), 18.3 (*s*, OH-6) (**11**) [7]; 3.8 (*s*, OH-3) (**5**), 4.03 (*s*, OH-3) (**11**) [7]; 4.2–4.6 (*m*, H-3) (**5**), 4.09 (*dd*, J = 13, 4 Hz, H-3) (**11**) [7]] spectra.

EXPERIMENTAL

Isolation of constituents from V. sebifera. Isolation of compounds **3a**, **4a** and **5** from plant material was described in full in a

Table 1. ^{13}C NMR chemical shifts (δ) of 1-acyl-2,6-dihydroxybenzenes (**1a**, **1b**) and 1-acyl-3-hydroxycyclohexan-2,6-diones (**5**, **11**) (20 MHz, $CDCl_3$)

Carbon No.	**1a**	**1b**	**5**	**11**
1	110.0	104.8	109.9	110.3
2	161.2	163.5	197.2	197.8
3	108.5	94.0	71.1	71.6
4	135.7	165.7	31.0	31.4
5	108.5	94.0	26.8	27.2
6	161.2	163.5	195.1	195.5
1′	208.2	207.0	205.3	206.0
2′	44.8	43.7	39.7	40.2
3′	24.5	24.7	24.1	24.6
4′	28.9–29.3	29.1–29.3	28.9–29.3	29.3
5′				
6′				
7′				
8′				27.2
9′				130.0
10′	31.5	31.1	31.0	
11′	36.0	35.7	35.5	27.2
12′	142.9	142.5	142.3	29.3
13′	128.3*	127.9*	127.7*	
14′	128.4*	128.7*	127.9*	
15′	125.6	125.2	125.1	
16′	128.4	128.7	127.9	32.0
17′	128.3	127.9	127.7	22.7
18′	—	—	—	14.0
OMe	—	55.0	—	—

*Assignments can be interchanged in each vertical column.

previous paper [5] in which the compounds are designated, respectively, by the asterisked numbers **8***–**10***.

Isolation of constituents from V. elongata. Fruits, collected from specimens near km 96 of the Santarém–Cuiabá road, Pará State, identified by Dr. W. A. Rodrigues, INPA, Manaus, Amazonas State, were separated into pericarps, arils, teguments and kernels. Air-dried, powdered teguments (55 g) were percolated with $CHCl_3$. The soln was evaporated and the residue (10 g) submitted to CC (100 g silica gel, C_6H_{14}–EtOAc, 4:1) and 15 150-ml fractions were collected. Fraction 4 was evaporated and the residue (0.4 g) was crystallized from C_6H_{14} to give **1b** (75 mg). The mother liquor was purified by prep. TLC (silica gel) into **2** (40 mg). Fractions 12–15 were evaporated and the residue (155 mg) separated by prep. TLC (silica gel, C_6H_6–EtOAc, 9:1) into four fractions. The most polar of these fractions, rechromatographed by the same system, gave **5** (7 mg).

11′-Phenylundecanoyl-2,6-dihydroxy-4-methoxybenzene (**1b**). Mp 79–80° (C_6H_{14}) ($C_{24}H_{32}O_4$ by ^1H and ^{13}C NMR counts and mass spectrometry). UV λ_{max}^{MeOH} nm: 230, 285, 320 (ε11 500, 12 900, 2200). IR ν_{max}^{KBr} cm^{-1}: 3400, 1639, 1590, 1520, 1430, 1380, 1210, 1170, 1080, 820. ^1H NMR (60 MHz, $CDCl_3$): δ7.20 (*br s*, C_6H_5), 5.95 (*s*, 2ArH), 3.85 (*s*, OMe), 3.10 (*t*, *J* = 7 Hz, 2H-2′), 2.60 (*t*, *J* = 7 Hz, 2H-11′), 1.25 (*br s*, $8CH_2$). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 384 (1), 367 (11), 219 (3), 205 (6), 195 (22), 182 (39), 168 (9), 167 (100), 153 (4), 105 (3), 91 (15).

1-Hexadecanoyl-2,6-dihydroxybenzene (**2**). Amorphous solid ($C_{22}H_{36}O_3$ by ^1H and ^{13}C NMR counts and mass spectrometry) IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3250, 1630, 1600, 1450, 1250, 1035, 965, 790, 715. ^1H NMR (60 MHz, $CDCl_3$): δ9 (*s*, 2OH), 7.22 (*t*, *J* = 8 Hz, H-4), 6.36 (*d*, *J* = 8 Hz, H-3, H-5), 3.13 (*t*, *J* = 7 Hz, 2H-2′), 1.33 (*br s*, $13CH_2$), 0.89 (*t*, Me). MS *m/z* (rel. int.): 348 $[M]^+$ (2), 330 (5), 190 (8), 189 (10), 165 (27), 152 (29), 137 (100), 123 (12).

(4′Z)-*1-Hexadec-4′-enoyl-2,6-dihydroxybenzene* (**3a**). Viscous

Table 2. ^{13}C NMR data of chemical shifts (δ) of 1-acyl-2,6-dihydroxybenzenes (**3a**, **3b**, **4b**, **6**) and of model compounds (**7**–**10** [6]) (20 MHz, $CDCl_3$)

Carbon No.	**3a**	**3b**	**6**	Carbon No.	**4b**	Carbon No.	**7**	**8**	**9**	**10**
1′	208.6 *s*	200.9 *s*	201.4 *s*	1′	201.0 *s*					
2′	44.8 *t*	43.8 *t*	43.9 *t*	2′	43.9 *t*					
3′	24.6 *t*	23.4 *t*	23.6 *t*	3′	23.6 *t*					
4′, 5′	128.4 *d* 129.9 *d*	128.2 *d* 129.6 *d*	57.2 *d*	4′, 5′	198.8 *d* 129.8 *d*	9	130.0	57.3	130.5	58.8
6′	27.3 *t*	27.0 *t*	27.8 *t*	6′	25.1 *t*	8	27.3	28.0	32.6	32.2
				7′	31.2 *t*					
				8′	74.9 *d*					
				9′	34.6 *t*					
7′	29.0–29.8	29.5–29.8	26.5 *t*	10′	27.2 *t*	7	29.4–29.5	26.7	29.4	26.2
8′–13′			29.3–29.6	11′–15′	28.8–29.7	4–6		29.6		29.6
14′	32.0 *t*	31.7 *t*	31.7 *t*	16′	31.1 *t*	3	32.0	32.2	32.0	32.2
15′	22.7 *t*	22.4 *t*	22.5 *t*	17′	22.4 *t*	2	22.7	22.8	22.7	22.8
16′	14.1 *q*	13.8 *q*	14.0 *q*	18′	14.0 *q*	1	14.1	14.1	14.0	14.1
1	110.3 *s*	125.3 *s*	125.5 *s*	1	124.6 *s*					
2, 6	61.5 *s*	147.5 *s*	147.7 *s*	2, 6	147.8 *s*					
3, 5	108.4 *d*	120.2 *d*	120.4 *d*	3, 5	120.4 *d*					
4	135.9 *d*	130.1 *d*	130.3 *d*	4	130.3 *d*					
2 Me		20.6 *q*	20.8 *q*		20.8 *q*					
2CO		168.3 *s*	168.4 *s*		168.4 *s*					
Me					21.2 *q*					
CO					170.2 *s*					

oil ($C_{22}H_{34}O_3$ by ^{1}H and ^{13}C NMR counts and mass spectrometry). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 222, 272, 345 (ε8350, 8300, 3950); $\lambda_{\max}^{\mathrm{MeOH+NaOH}}$ nm: 222, 240, 280, 380 (ε5350, 3850, 8550, 4900); $\lambda_{\max}^{\mathrm{MeOH+AlCl_3}}$ nm: 235, 295, 390 (ε6400, 13450, 4500). IR $\nu_{\max}^{\mathrm{film}}$ cm^{-1}: 3330, 1620, 1590, 1445, 1350, 1245, 1040, 795. ^{1}H NMR (60 MHz, $CDCl_3$): δ8.92 (*s*, 2OH), 7.23 (*t*, *J* = 8 Hz, H-4), 6.40 (*d*, *J* = 8 Hz, H-3, H-5), 5.36 (*t*, *J* = 4 Hz, H-4′, H-5′), 3.15 (*t*, *J* = 7 Hz, 2H-2′), 2.1–1.6 (*m*, 2H-3′, 2H-6′), 1.31 (*br s*, 9CH_2), 0.89 (*t*, Me). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 346 $[\mathrm{M}]^+$ (11), 190 (18), 189 (19), 176 (24), 166 (19), 165 (96), 163 (19), 153 (20), 152 (96), 149 (29), 138 (52), 137 (100), 123 (39).

Diacetate (**3b**). Oil, IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1765, 1700, 1610, 1520, 1460, 1375, 1200. ^{1}H NMR (60 MHz, $CDCl_3$): δ7.36 (*t*, H-4), 7.0 (*m*, H-3, H-5), 5.33 (*t*, *J* = 4 Hz, H-4′, H-5′), 2.71 (*t*, *J* = 7 Hz, 2H-2′), 2.23 (*s*, 2OAc), 1.82 (*m*, 2H-3′, 2H-6′), 1.31 (*br s*, 9CH_2), 0.86 (*t*, Me). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 430 $[\mathrm{M}]^+$ (6), 346 (13), 152 (94), 137 (89), 43 (100).

Epoxide of diacetate (**6**). Oil. IR $\nu_{\max}^{\mathrm{film}}$ cm^{-1}: 1765, 1700, 1610, 1460, 1365, 1180, 1030. ^{1}H NMR (60 MHz, $CDCl_3$): δ7.0–7.6 (*m*, 3ArH), 2.3–3.1 (*m*, 2H-2′, H-4′, H-5′), 2.3 (*s*, 2OAc), 1.1–1.7 (*m*, 11CH_2), 0.91 (*t*, Me). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 446 $[\mathrm{M}]^+$ (1), 362 (1), 235 (2), 180 (5), 179 (4), 168 (15), 165 (4), 156 (5), 149 (13), 139 (9), 137 (17), 127 (8), 126 (85), 108 (8).

Dihydro derivative of **3a**. Identified by direct comparison with **2**.

(4′Z)-1-(8′-*Acetoxyoctadec-4′-enoyl*)-2,6-*diacetoxybenzene* (**4b**). Oil [$C_{24}H_{35}O(OAc)_3$ by ^{1}H and ^{13}C NMR counts and mass spectrometry]. UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 280 (ε1400). IR $\nu_{\max}^{\mathrm{CHCl_3}}$ cm^{-1}: 1770, 1725, 1600, 1515, 1370, 1200, 1040, 750. ^{1}H NMR (60 MHz, $CDCl_3$): δ7.26 (*t*, *J* = 10 Hz, H-4), 6.92 (*m*, H-3, H-5), 5.0–5.6 (*m*, H-4′, H-5′, H-8′), 1.4–2.8 (*m*, 2H-3′, 2H-6′), 2.60 (*t*, *J* = 6 Hz, 2H-2′), 2.20 (*s*, 2OAc), 1.92 (*s*, OAc), 1.32 (*br s*, 10CH_2), 0.89 (*t*, Me). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 516 $[\mathrm{M}]^+$ (1), 474 (3), 456 (4), 432 (5), 429 (19), 390 (2), 386 (24), 371 (7), 369 (20), 368 (20), 362 (7), 343 (9), 217 (13), 206 (15), 192 (21), 191 (20), 190 (53), 179 (27), 165 (23), 163 (17), 153 (27), 152 (37), 151 (10), 149 (29), 137 (17), 135 (23), 123 (27), 109 (19).

1-(11-*Phenylundecanoyl*)-3-*hydroxycyclohexan*-2,6-*dione* (**5**). Oil ($C_{23}H_{32}O_4$ by ^{1}H and ^{13}C NMR counts and mass spectrometry). UV $\lambda_{\max}^{\mathrm{MeOH}}$ nm: 230, 275 (ε13 400, 12 300). IR $\nu_{\max}^{\mathrm{film}}$ cm^{-1}: 3450, 1655, 1550, 1445, 1245, 1075, 750, 695. ^{1}H NMR (60 MHz, $CDCl_3$): δ7.23 (*s*, C_6H_5), 4.2–4.6 (*m*, H-3), 2.0–3.2 (*m*, CH_2-4, CH_2-5, CH_2-2′, CH_2-11′), 1.31 (*br s*, 8CH_2), 14, 3.85 (2*s*, 2OH). ^{13}C NMR: Table 2. MS *m/z* (rel. int.): 372 $[\mathrm{M}]^+$ (3), 262 (30), 244 (42), 183 (6), 165 (7), 137 (10), 133 (15), 117 (16), 105 (40), 104 (21), 92 (80), 91 (100).

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