Phytochemistry, Vol 25, No 1, pp 279–280, 1986
Printed in Great Britain

0031-9422/86 $3.00 + 0.00

NEOLIGNANS FROM FRUITS OF *VIROLA ELONGATA**

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(*Received* 6 *March* 1985)

Key Word Index—*Virola elongata*; Myristicaceae; fruits; furofuran lignans; magnostellins.

Abstract—Fruits of *Virola elongata* contain, besides the furofuranoid lignans eudesmin, epieudesmin and fargesin, the aryl-benzyl-methyl tetrahydrofuran neolignans magnostellins A and C. The absolute configuration of the magnostellins was determined.

INTRODUCTION

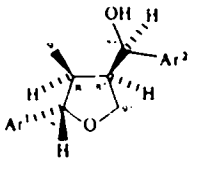
Bark resin of *Virola elongata* Warb. (Myristicaceae) is used as an hallucinogenic snuff and arrow poison by Amazonian Indians [2]. Chemical studies of the bark demonstrated the presence of several tryptamines [3] and two stilbene derivatives, as well as two neolignans, eusiderin and virolongin, four furofuranoid lignans, epi-sesartemin, sesartemin, epi-yangambin and yangambin, and two furanoid lignans, dihydrosesartemin and β-dihydroyangambin [4]. Fruits of the same species have also been examined and reported to contain acylphloroglucinols [5].

The present paper describes the presence in fruits of *V. elongata* of eudesmin (**1a**), epieudesmin (**1b**), fargesin (**1c**) and the magnostellins A (**2a**) and C (**2b**). The compounds of series **1** are again furofuranoid lignans and were identified by comparison of the complete sets of physical and spectral data with reported data [6–8]. The compounds of series **2** apparently require the coupling of propenylphenols and cinnamyl alcohols. Such crossed oxidative dimers are rare, **2a** having been isolated from *Magnolia stellata* Maxim. (Magnoliaceae) [9] with **2b** being a new compound.

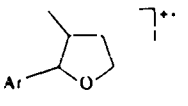
RESULTS AND DISCUSSION

The ^1H and ^{13}C NMR spectra of the two magnostellins differ solely with respect to signals due to two methoxyls (**2a**) versus one methylenedioxy group (**2b**). The relative position of the piperonyl (Pi) and veratryl (Ve) groups in **2b** must be as shown in view of the presence of a peak at *m/z* 162 corresponding to $[PiCH{=}CHMe]^+$ ions in the mass spectrum. As was consequently to be expected intense peaks, assignable to ions of type **3**, appear in the spectra of **2a** at *m/z* 222 (**3a**) and of **2b** at *m/z* 206 (**3b**).

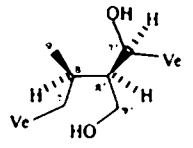
The *cis*-relation of the C(7)–H, C(8)–Me and C(8′)–C(7′) bonds in **2a** has been established by NOE experiments and the absolute configuration 7′*R* has been deduced by Horeau's method [9]. We confirmed the proposed *cis*-relation by Eu(fod)$_3$ induced ^1H NMR shifts and proceeded to establish the absolute configuration. This initially involved hydrogenolysis of **2a** into **4**. Acid catalysed cyclization of this diol gave, as sole reaction product, the aryltetralin **5**. Its ^1H NMR spectrum, in comparison with analogous spectra of aryltetralins [10], indicated the *trans*, *trans* arrangement of the methyl, hydroxymethyl and veratryl substituents. The ORD curves of such aryltetralins show two Cotton effects, one between 230 and 250 nm and another one between 275 and 290 nm. The latter is assigned to the diarylmethine chromophore and is negative for 7′*S*-neolignans of this type and positive for 7′*R*-neolignans [11]. The negative



2a $Ar^1 = Ar^2 = Ve$
2b $Ar^1 = Pi$, $Ar^2 = Ve$



3a $Ar = Ve$
3b $Ar = Pi$



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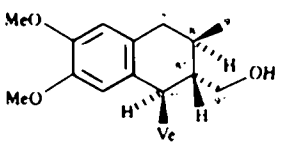

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*Part 29 in the series "The Chemistry of Brazilian Myristicaceae". For Part 28 see ref. [1]. Taken in part from the M.S. thesis submitted by M.J.K. to the Universidade de São Paulo (1984).

Cotton effect at 284 nm measured for **5** thus established the 7′*S*-configuration and hence, in view of the all-*trans* arrangement, the 8*R*,8′*S*-chiralities. The absolute configurations of the two magnostellins must be identical, since both show comparable specific optical rotations.

The relative configurations of **2a** being known, it again suffices to characterize the absolute configuration of one centre to deduce the complete stereochemistry. Let this centre be C-8 which must have passed unchanged through hydrogenation and acid treatment. Its 8*R*-configuration in **5** corresponds to 8*S* in **2a**. The 7*S*,8′*R*-chiralities of the other centres follow.

All neolignans and lignans isolated from the bark of *V. elongata* are oxidative dimers of 3,4,5-trioxyphenylpropanoids. In contradistinction, all neolignans and lignans of the fruits are oxidative dimers of 3,4-dioxyphenylpropanoids. The analyses, however, referred to materials collected from specimens at very considerable geographic distance. The bark used in the Canadian study [4] came from the village of Brillo Nuevo on the Rio Ampiyacu, a Peruvian tributary of the Amazon. The fruits used in the present study came from 96 km up the Santarém–Cuiabá road, Pará State, Brazil [5]. Clearly the analysis of bark and fruit collected from a single specimen should now be attempted.

EXPERIMENTAL

Isolation of constituents was performed as described in ref. [5]. Among the fifteen 150 ml fractions, fr. 1 gave fatty esters (2.8 g) and fr. 2 and 3 (4.3 g) gave triacylglycerols (4.3 g). Fr. 4 was treated as described in ref. [5]. Fr. 5–11 were evapd. The residue (2.8 g) was sepd by prep. TLC (silica gel) into **1e** (200 mg), **1b** (290 mg) and **1a** (60 mg). Fr. 12–15 were evapd and the residue (155 mg) separated by prep. TLC (silica gel, C_6H_6–EtOAc, 9:1) into four fractions. The least polar of these fractions gave triacylglycerols (15 mg), the following fraction gave a mixture of **1a** and **1b** (96 mg), the third fraction gave, after rechromatography in the same system, **2b** (6 mg). The most polar fraction gave, again after rechromatography in the same system, a compound described previously [5] and **2a** (15 mg).

(7*S*,8*S*,7′*R*,8′*R*)-7′-*Hydroxy*-3,4,3′,4′-*tetramethoxy*-7.O.9′,8.8′-*neolignan* (*magnostellin-A*, **2a**). $[\alpha]_D = +75°$ ($CHCl_3$, *c* 0.75); $[\alpha]_D = +68°$ ($CHCl_3$, *c* 0.75) [9]. For other physical data see ref. [9]. ^{1}H NMR (80 MHz, $CDCl_3$ + Eu(fod)$_3$): $\Delta\delta$ 2.42 (H-7′), 2.12 (H-8), 1.40 (3 H-9), 2.42 (H-7′), 2.42 (H-8′), 2.62 (H-9′β). *Acetate*. ^{13}C NMR (20 MHz, $CDCl_3$): δ 135.1, 131.6 (2*s*, C-1, C-1′), 108.7, 110.6 (2*d*, C-2, C-2′), 148.3 (*s*, C-3, C-3′), 149.9 (*s*, C-4, C-4′), 111.0 (*d*, C-5, C-5′), 117.6, 119.7 (2*d*, C-6, C-6′), 55.8 (*q*, 4 OMe). *Hydrogenolysis*. To a soln of **2a** (53 mg) in MeOH (10 ml) 10% Pd–C were added prior to hydrogenation (6 hr). The reaction product was purified by prep. TLC (silica gel, C_6H_6–EtOAc, 9:1) to yield **4** (10 mg). *Cyclization*. A soln of **4** (10 mg) in $CHCl_3$ containing a trace of HCl was left overnight and evapd. The residue was purified by prep. TLC (silica gel, C_6H_6–EtOAc, 7:3) to give **5** (4 mg).

(7*S*,8*S*,7′*R*,8′*R*)-7′-*Hydroxy*-3′, 4′-*dimethoxy*-3,4-*methylenedioxy*-7.O.9′,8.8′-*neolignan* (magnostellin-C, **2b**). Oil. $[\alpha]_D = +56.3°$ ($CHCl_3$, *c* 1.67). IR ν_{max}^{film} cm^{-1}: 3500, 1610, 1590, 1520, 1470, 1420, 1270, 1140, 1030. UV λ_{max}^{MeOH} nm: 230, 280 (ε11 100, 4600). ^{1}H NMR (60 MHz, $CDCl_3$): δ 7–6.8 (*m*, 6 ArH), 5.90 (*s*, O_2CH_2), 4.85 (*d*, *J* = 6.5 Hz, H-7′), 4.60 (*d*, *J* = 6.5 Hz, H-7), 4.1–4.3 (*m*, 2 H-9′), 3.85 (*s*, 2 OMe), 2.75 (*m*, H-8), 2.10 (*m*, H-8′), 1.10 (*d*, *J* = 7 Hz, 3 H-9). ^{13}C NMR (20 MHz, $CDCl_3$): δ 136.3, 136.8 (2*s*, C-1, C-1′), 106.0, 109.6 (2*d*, C-2, C-2′), 146.6, 148.4 (2*s*, C-3, C-3′), 147.4, 149.0 (2*s*, C-4, C-4′), 109.0, 111.2 (2*d*, C-5, C-5′), 118.9, 118.2 (2*d*, C-6, C-6′), 87.2, 72.8 (2*d*, C-7, C-7′), 44.0, 48.0 (2*d*, C-8, C-8′), 69.3, 12.7 (*q*, C-9, *t*, C-9′), 55.8 (*q*, 2 OMe), 100.7 (*t*, O_2CH_2). MS *m/z* (rel. int.): 372 [M]$^+$ (23), 234 (10), 206 (32), 167 (100), 162 (15), 151 (68), 150 (12), 149 (41), 139 (53).

(8*R*,7′*R*,8′*R*)-7′,9′-*Dihydroxy*-3,4,3′, 4′-*tetramethoxy*-8.8′-*neolignan* (**4**). Oil. IR ν_{max}^{film} cm^{-1}: 3450, 2950, 2850, 1600, 1520, 1460, 1250, 1150, 1040. ^{1}H NMR (60 MHz, $CDCl_3$): δ 6.80 (*br s*, 6 ArH), 4.60 (*d*, *J* = 6.5 Hz, H-7′), 4.20 (*m*, 2 H-9′), 3.90 (*s*, 2 OMe), 3.5 (*s*, 2 OMe), 2–2.8 (*m*, 2 H-7, H-8, H-8′), 1.80 (*br s*, 2 OH), 1.10 (*d*, *J* = 7 Hz, 3 H-9).

(8*R*,7′*S*,8′*S*)-9′-*Hydroxy*-3,4,3′, 4′-*tetramethoxy*-6.7′, 8.8′-*neolignan* (**5**). Mp 145–147° (hexane). [M]$^+$ found: *m/z* 372; $C_{22}H_{28}O_5$ requires: 372. IR ν_{max}^{film} cm^{-1}: 3500, 2930, 2840, 1610, 1510, 1470, 1250, 1150, 1030. ^{1}H NMR (80 MHz, $CDCl_3$): δ 6.8–6.55 (*m*, 4 ArH), 6.20 (*s*, H-5), 3.90, 3.85, 3.79, 3.59 (4*s*, 4 OMe), 3.50 (*d*, *J* = 10 Hz, H-7′), 2.80 (*m*, 3 H-9′), 2.00 (*m*, 2 H-7), 1.75–1.25 (*m*, H-8, H-8′), 1.45 (*br s*, HO-9), 1.10 (*d*, *J* = 7 Hz, 3 H-9). ^{13}C NMR (20 MHz, $CDCl_3$): δ 128.7, 132.1 (C-1, C-1′), 112.9, 110.6 (C-2, C-2′), 148.9, 147.4 (C-3, C-3′), 146.9, 147.4 (C-4, C-4′), 110.9, 112.0 (C-5, C-5′), 138.3, 121.6 (C-6, C-6′), 38.7, 50.6 (C-7, C-7′), 30.0, 47.1 (C-8, C-8′), 19.5, 60.9 (C-9, C-9′).

Acknowledgements—This work was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (research fellowship to M.Y., grant), Financiadora de Estudos e Projetos (grant) and Fundação de Amparo à Pesquisa do Estado de São Paulo (graduate fellowship to M.J.K., grant).

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